SERUM ENZYME LEVELS AND ELECTROCARDIOGRAPHIC

CHANGES IN DOGS WITH SURGICALLY-INDUCED

CARDIAC ALTERATIONS

by

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A Thesis Submitted to the

Graduate Faculty in Partial Fulfillment of

the Requirements for the Degree of

MASTER OF SCIENCE

Major Subject: Veterinary Physiology

Iowa State University
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Ames, Iowa

1962

1494000

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I. INTRODUCTION

Today, small animal pets are receiving increasingly
better care. This leads to greater longevity. The treatment
of geriatric problems by the small animal clinician has be-
come an important phase of practice, and this phase will con-
tinue to grow. Many of these problems are centered around
cardiac and liver pathologies, and the means now available
for diagnosing these abnormalities in dogs often fail to give
unequivocal information. Therefore, treatment is often
based on intuition and past experience with no guarantee that
the treatment is specific for the condition presented.

As our knowledge of diseasescontinues to increase,
methods to diagnose them must improve. Some of the problems
that faced the veterinarian in recent years have been re-
solved; however, very little progress has been made in the
area of diagnosis of cardiac problems. The electrocardio-
graph has been used as a diagnostic aid in veterinary medicine
yet most of the information, which can be derived from it,
is empirical since much of the interpretation of the canine
electrocardiogram has been based on studies from the human
electrocardiogram.

In the past few years great advances have been made in
enzyme chemistry. Many serum enzymes have been investigated
and a few of them have been shown to be of value as diagnos-
tic aids in human medicine. It appears that the

concentrations of some of these same enzymes in blood serum
may be used by the veterinary profession as diagnostic aids.
The ones which have proved to be most useful in human medi-
cine in diagnosing certain abnormalities of the myocardium
and which have given some indication of responding in the same
manner in dogs have been serum glutamic oxalacetic trans-
aminase (SGOT), serum glutamic pyruvic (SGPT), and serum
lactic dehydrogenase (SLDH).

The primary objectives of this investigation were to
1) establish a normal set of values for serum enzyme levels
of glutamic oxalacetic transaminase, glutamic pyruvic trans-
aminase, and lactic dehydrogenase in dogs; 2) to establish the
accuracy of a clinical assay test commonly used by research
workers; 3) to examine the usefulness of these serum enzymes
as diagnostic indexes of myocardial necrosis, valvular insuf-
ficiency and epicarditis; 4) to determine what constitutes a
normal canine electrocardiogram; and 5) to define any electro-
cardiographic changes which may be of importance in diagnosing
these pathologic conditions and correlating them with the
changes observed in serum enzymes levels.

II. REVIEW OF LITERATURE

A. Enzymes

In the past ten years there has been an explosive increase in interest in the enzymes of blood and other tissues. Many laboratories have become concerned with this intriguing field with considerable volumes of data being accumulated. Following the demonstration of the normal range of activity of certain enzymes in the serum of animals and man, a sizable experience has accrued attesting to the experimental as well as the clinical implications of alterations in the serum activity in pathological conditions of certain tissues and organ systems. The major part of this work was done in human medicine and several reviews are available which describe the clinical significance of these enzymes as well as some of the work done experimentally with dogs (15, 46, 57, 60, 101, 143, 161). Even though much of the early work was done with dogs, the emphasis was soon placed on the importance of these enzymes in human medicine and animal data were either forgotten or disregarded. Very little work has actually been done by the veterinarian in the study of these enzymes and their possible clinical significance in diagnosis. Early studies were merely pilot studies and results were used mainly for comparison with those found in human serum levels. The early work in veterinary medicine has been done largely by Cornelius et al. (31, 32, 33) of California.

Many methods have been devised for measuring these serum enzyme levels. The first methods were based on chromatography (78, 133), later spectrophotometry and colorimetry (17, 22, 64, 65, 76, 77, 107, 128, 134, 149, 150, 154, 163) then fluorimetry (87, 88). Both macro and micro determinations are possible. There are available for the clinician today simple, inexpensive, clinical methods (14, 34, 145).

Clinicians, impressed by the ease of frequent, adequate sampling of blood and the elegance of spectrophotometric enzyme assay, have done a great deal of the work on the investigation of enzyme alterations. In only a few cases, chiefly with cellular enzymes, have any clinical studies been directed toward an understanding of the mechanisms of enzyme alterations in disease conditions. Only in the past two or three years have factors such as the movement of enzymes across cell membranes, the origin and excretion of enzymes of serum, the relationship to stress, the influence of diet, and the characteristics of these enzymes come under investigation. With such studies came progress in the study of basic physiologic and pathologic processes as well as in the clinical areas.

Enzymes are organic catalysts produced as a result of cellular activity but independent of the presence of living cells in their operation. The name "enzyme" (from the Greek, "in leaven"; "in yeast") is associated with the process of

fermentation. Enzymes act on bio-chemically important sub-
stances. One essential difference must be stressed between
inorganic catalysts such as platinum, which catalyzes many
chemical reactions, and organic enzymes such as SGOT, SGPT,
and SLDH which are extremely specific. It is well known that
most chemical reactions do not proceed entirely in one direc-
tion. Several reactions of the substrate are possible, de-
pending upon the nature of the enzyme. Because of its spe-
cificity, the enzyme catalyzes only one of these reactions.

A chemical reaction which is reversible will attain a
state of equilibrium when the velocity of the forward reaction
is equal to the velocity of the reverse reaction. The factors
which influence the equilibrium state are temperature, pres-
sure, concentration of the reacting substances and the pres-
ence of a catalyst. The catalyst speeds up both the forward
and backward reaction and thus allows the system to attain a
state of equilibrium in a shorter time. A catalyst will not
make a reaction proceed unless that reaction can proceed of
its own accord, no matter how slowly.

The chemical properties of enzymes, as well as their
stability and solubility characteristics, are closely related
to those of proteins. As more and more enzymes have been
isolated in a crystalline form and have proved to be single
components, it has become more certain that enzymes are
indeed proteins. Recently, it has been found that certain

enzymes are composed of component enzymes termed isozymes.

So far, no enzyme has been isolated which is not a protein. It is also true, however, that in many instances for an enzyme to be active some co-factor of a non-protein nature is required. These inorganic ions may be attached to the enzyme protein. Such ions include Ca^{++}, Mg^{++}, Mn^{++}, or Zn^{++}.

The broad category of enzymes can be broken down into a classification on the basis of several criteria. In this research interest has been placed on a particular group of enzymes, termed transferases, and more specifically on a group of enzymes designated as transaminases.

The role of the transaminase reaction in metabolic transformations is twofold (62). First, it provides a machanism for the interconversion of amino acids via keto acids. Thus one can visualize the synthesis of an important amino acid like glutamic acid from alpha-ketoglutaric acid, which arises as the result of the oxidation of carbohydrates. In this way, an interrelationship between glutamic acid, aspartic acid, alanine and the tricarboxylic acid cycle intermediates is established. Secondly, transamination provides a mechanism for the oxidation of many L-amino acids, according to the following reactions:

L-Amino acid + α-ketoglutaric acid > α-keto acid

+ L-glutamic acid

L-Glutamic acid + $1/2$ O_2 α-ketoglutaric acid + NH_3
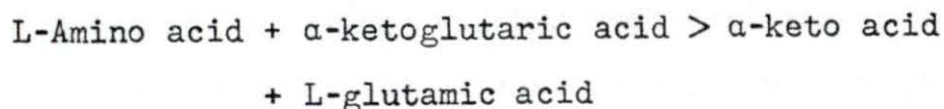
Glutamic acid dehydrogenase, the enzyme involved in the last reaction is capable of linking the metabolism of amino acids and carbohydrates without the need for oxidative deamination, which, in the mammal, is not quantitatively important, and can be forgotten as far as this discussion is concerned (62). In addition, transamination is important in the biosynthesis of many amino acids.

There is evidence that separate transaminases exist for the separate reactions (23). These purified enzymes are stimulated by the addition of pyridoxal phosphate (vitamin B_6), for when an animal is placed on a diet deficient in this vitamin, the transaminase content of tissues decreases (62). In addition, the amine form of vitamin B_6, pyridoxamine phosphate, is also a stimulant for these enzymes. This has led to the hypothesis that the enzymatic activity involves the interconversion between the two co-enzyme factors. Meister (103) has suggested the following formulation of the reaction:

Pyridoximine phosphate and enzyme $\longrightarrow$ enzyme-pyridoxamine
phosphate

or (pyridoxal phosphate)   (enzyme-pyridoxal
phosphate)
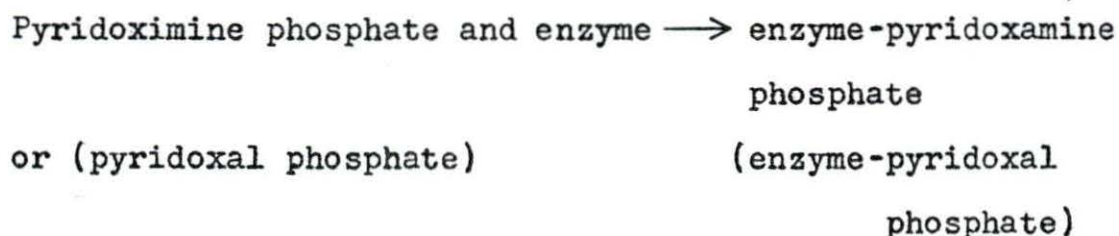
Enzyme-pyridoxamine phosphate and keto acid = enzyme-pyridoxal phosphate and amino acid. Jenkins (74) reports that there is no doubt that the over-all reaction is as follows:

Glutamate   ) (Pyridoxal Enzyme   ) (Aspartate
Ketoglutarate   Pyridoxamine Enzyme   Oxalacetate
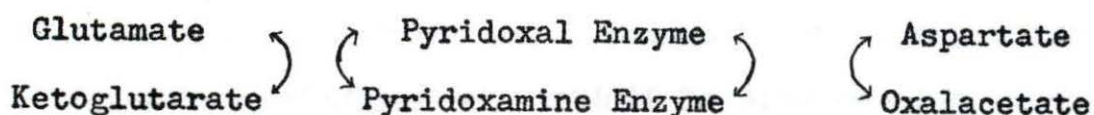
Indications for the existence of a coenzyme activator for the apo-transaminases were supported by the evidence from experimental studies of vitamin B_6 deficiency. Deficiency of vitamin B_6 was associated with lowered levels of transaminase activity, and the addition of pyridoxal phosphate to the tissue or cell preparation resulted in at least partial restoration of enzyme activity (8, 12, 91, 140). Recent studies have confirmed earlier work on the activation of transaminase by pryidoxal phosphate, and have shown as well that many of the newly discovered transaminases also require this coenzyme (103).

In 1955 Marsh et al. (100) reported that in both man and monkeys, increasing the intake of pyridoxal resulted in a significant increase in the blood level of the transaminase and of vitamin B_6. Reductions in the pyridoxal intake were followed by a lowering of the blood concentration of both factors. The changes in the level of transaminase were often more gradual, however, than were those of vitamin B_6. The time required to reduce the levels to a minimum after withdrawal of all pyridoxine or to the initial levels after the supplemental dosage was discontinued seemed to be dependent to some extent upon the duration of the period of the increased intake.

In 1959 Jenkins and co-workers (75) showed that glutamic aspartic transaminase contains two residues of tightly bound

pyridoxal phosphate per molecule. Their data support the theory that the "pyridoxal" form is more stable than the "pyridoxamine" form of this enzyme.

Ranke et al. (126) reported on the relationship of vitamin B_6 and transaminases in 1960. They found that there is a mild state of vitamin B_6 deficiency among healthy, old adults. It was also found that these older individuals had a lower SGOT than young individuals, regardless of which groups of old and young subjects were compared. Daily oral adminis- tration of 15 mg. of vitamin B_6 to the elderly individuals elevated the SGOT content. The addition of pyridoxal phos- phate to the sera in vitro elevated the SGOT content of the sera of old individuals.

It is unlikely that the observed differences in SGOT can be explained solely by differences in dietary vitamin B_6 in- take, since this study was done on three groups of young sub- jects and three groups of old subjects on a variety of diets. It does not seem that differences in the SGOT content with age are primarily due to a progressive decrease of dietary content of vitamin B_6. On the other hand, the SGOT levels can be raised if the intake is sufficiently large. The in vitro ex- periment showed that the decrease in SGOT activity in the aged is due primarily to the decrease in the coenzyme, pyridoxal phosphate, and not to the protein moiety or the apoenzyme of the SGOT molecule. The possibility of regression of leukocyte

pyridoxal phosphate content with age has been suggested by others and this could possibly be the factor involved.

In 1950 Cammarata and Cohen (24) showed that at least 25 amino acids participate in the transamination reaction. The reaction was catalyzed by aqueous extracts of pig heart, liver, and kidney (later many more tissues have been used). Each transamination reaction appeared to be due to a different transaminase. They found that the reaction was accelerated by pyridoxal phosphate and slightly inhibited by ammonia.

The variety of amino and keto acids capable of participating in transamination makes it necessary to distinguish the different effects. Accordingly, it has become customary to distinguish the enzymes responsible for transamination reactions in one of several ways. The enzymes which catalyze reversible transamination reactions are designated by a term referring to both amino acids concerned, e.g., glutamate-aspartate transaminase. Another method of designating the enzymes is to name them by a term describing the favored products of the equilibrium reaction, e.g., glutamic oxalacetic transaminase (GOT) and glutamic pyruvic transaminase (GPT). The latter method of designation has been used in the clinical literature.

Although it now appears that at least several distinct transaminases exist in each of the tissues that have thus far been studied, final characterization of the individual catalytic systems is yet to be achieved. However, the chemical

separation and purification of the GPT and GOT of heart
muscle have been reported by several groups (23, 55, 75).
Both of these enzymes have also been separated from each other
electrophoretically, using as an enzyme source, serum obtained
from patients with hepatitis (161). It would thus appear that
at least GPT and GOT are separable, distinct, and individual
catalytic systems.

Transamination was first suggested as a possibility by
Nadham in 1927 and later demonstrated in pigeon breast muscle
in 1937 by Braunstein and Kritzmann (19). They found that
when L-glutamic acid and pyruvic acid were incubated with
chopped liver or muscle α-ketoglutaric acid and alanine were
produced, the amino group of the glutamic acid being trans-
ferred to pyruvic acid. Transamination, thus, involves the
transferral of an amino group (NH_2). As was mentioned earlier
many amino acids can take part in this reaction, glutamic
acid is especially active in this respect, and it is with
this amino acid that this review is especially concerned. The
two transaminases which have been found to have clinical use-
fulness are GOT and GPT, both of which have glutamic acid as
part of the substrate upon which they exert their action. L-
aspartic acid may replace glutamic acid, but the reaction is
much slower.

The actual reactions are as follows:

1. L-Glutamic acid + oxalacetic acid

$$\downarrow \uparrow$$

  α ketoglutamic acid + L-aspartic acid

2. L-Glutamic acid + pyruvic acid

$$\downarrow \uparrow$$

  α ketoglutamic acid + L-alanine
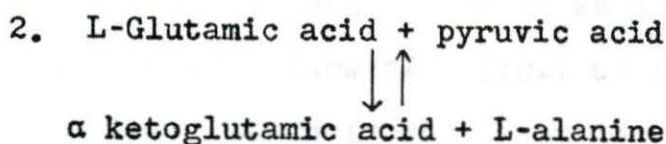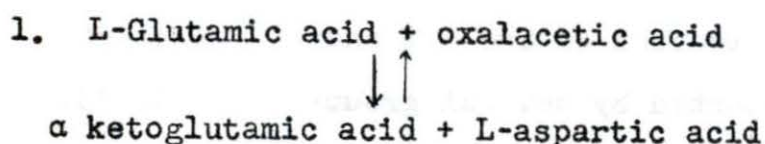
According to Cohen and co-workers (30), reaction 1 pro-ceeds to the right at the fastest rate in all tissues studied. The reaction to the left proceeds only 1/2 to 1/3 as rapidly. Reaction 2 is very slow when compared with reaction 1.

These two systems are widespread in higher plants, many microorganisms, and in the blood and tissues of animals and appear to be a function of tissues in general; the following descending order of concentration has been reported in man: heart muscle, skeletal muscle, brain, liver, kidney, testes, lung, and spleen (60).

Table 1. Average distribution of enzymes in human tissues (units/gm. wet tissue)

	GOT	GPT	LDH
Heart	155,000	7,130	240,000
Liver	142,400	43,800	390,000
Skeletal Muscle	99,300	4,750	600,000
Kidney	90,900	19,300	640,000
Pancreas	28,300	1,950	150,000
Spleen	13,600	1,210	140,000
Lung	10,000	668	25,000
Serum	20	15	400
	(141)	(141)	(162)

In 1959 Cornelius et al. (32) reported on various tissue activities of GOT and GPT in normal horses, cattle, calves, pigs, dogs, and fowls. They found considerable GOT activity in almost all tissue analyzed in each species, but high GPT activity was found only in the canine liver. After the administration of carbon tetrachloride and during subsequent hepatic necrosis, significant elevations in serum GOT activity were found in the horse, cow, pig and dog, but marked elevations of serum GPT activity were confined to the dog. Normal ranges of SGOT activity have been reported as 5 to 40 units, of SGPT as 5 to 40 units, and of SLDH as 100 to 600 units (132).

In the reaction shown above, pyruvic acid and oxalacetic acids, products of carbohydrate metabolism, are transferred into amino acids, thus showing how the body is able to synthesize some of its amino acids. The reverse reaction indicates how the more complex glutamic acid might be produced from alanine or aspartic acid and another intermediate in carbohydrate metabolism, alpha-ketoglutaric acid.

Since transamination is a rapid process and concerned chiefly with those compounds which play key roles in intermediary metabolism, Cohen (29) suggests that it represents a "shuttle" mechanism in tissue respiration "Whereby certain key protein and carbohydrate intermediates are rapidly interconverted". The demonstration of transamination affords further

evidence for the highly dynamic character of protein-metabolism. Amino groups are being continually exchanged between nitrogenous and non-nitrogenous compounds, and amino acids thereby synthesized. Transamination may be important from another standpoint. The non-nitrogenous compounds formed in these two-way reactions - pyruvic acid, alpha-ketoglutaric acid and oxalacetic acid - are concerned in oxidation-reduction systems.

Under normal conditions the abundant transaminases are confined, almost exclusively, within tissue cells and only very small amounts are found in the circulation. It is this relatively small "baseline" serum level which first suggested and has permitted ready detection of increased serum values resulting from the destruction of tissue and the assumed release of enzyme from the large tissue stores. However, whether or not all the serum increase comes from the particular tissue involved or if some other mechanism is involved is not known. It is relatively certain that most of it comes from the damaged tissue as much work has been done showing the great decrease of enzyme content in the pathologic tissue compared with the normal (4, 82, 89, 104, 116, 131, 132). Hamolsky and Kaplan (60) reported that the clinical findings of LaDue, Wroblewski and Karmen (85) have been strongly supported by experimental studies of myocardial damage by several workers using various techniques, revealing excellent correlations of

increased serum levels of enzyme activity with tissue damage.
Significant elevations of SGOT, although short-lived, have
been found with experimentally induced infarcts of less than
1 gm. of myocardium. There was a suggestive correlation be-
tween the size of the infarct and the height and duration of
increased serum enzyme activity. Enzyme levels decrease
rapidly in infarcted muscle as compared with normal muscle.
In almost every instance, serum enzyme levels were not in-
creased in the presence of significant myocardial ischemia
without histologic necrosis. They further report that SGPT
is frequently normal in the face of elevated SGOT in the less
extensive infarctions, but may rise in the presence of large
infarcts. Although it has been stated and generally believed
that SGPT is not elevated until SGOT values of 150-200 units
are reached, Rowell and Smith (130) found 14 episodes of ele-
vation in human subjects of SGPT with SGOT values below 150
units.

There appears to be a highly effective mechanism for the
rapid elimination or degradation of the enzyme from the
serum. Dunn (40) reported on this in 1958. He found that
following intravenous injection three-fourths of the injected
enzyme disappeared from the blood within six hours. The re-
maining portion was cleared within 20 to 72 hours depending
upon the amount injected. The rapid disappearance phase was
due to a diffusion of the enzyme into the interstitial fluid.
Equilibrium of serum and lymph GOT was reached within six to

eight hours and marked the end of the rapid disappearance phase. A diffusion of GOT from blood to interstitial fluid was also found following myocardial infarction and hepato-cellular necrosis. In no case was any GOT found in the spinal-fluid or urine. He felt that no inactivation occurred in the kidney. The exact mechanism of destruction and elimination still remains obscure.

Recently it has been suggested by Van Rymenant and co-workers (155) that there is evidence that the elevated transaminase levels, found in patients with cancer, may decrease to normal following the administration of large quantities of protein. This opens the door for a vast amount of research upon protein levels and qualities and their effect upon serum transaminases.

Recently, a study was made of the effect of physical exercise on the serum GOT and GPT in humans (139). It was demonstrated that physical exercise of a moderately strenuous nature (running slowly, chin ups, swimming, and rowing) regularly raises the level of SGOT (in most instances to levels above the upper limit of normal). The SGPT, although showing a slight rise, tended to remain within normal limits. In other work involving rats, it was reported that there was a 2- to 6-fold increase in the serum GOT, GPT and LDH levels after exercise (7). This was much greater than that reported in man, but may be due to the longer period of exercise. In this study in rats, pathologic studies revealed transient

fatty changes in skeletal muscle fibers, heart, liver, kidney, and adrenal cortex; some rats also showed a few foci of inflammation and necrosis in the muscles. Highman and associates have published several papers relating to the stress of hypoxia and the effect of autonomic drugs upon serum enzyme activities (67, 68, 69). Gollnick and Hearn (54) reported that LDH activity was increased in the heart ventriclar muscle but remained unchanged in skeletal muscle following excercise in rats.

LDH refers to a group of enzymes which catalyze the reversible oxidation-reduction reaction between lactate and pyruvate, involving the conversion of the reduced and oxidized forms of the pyridine nucleotide (DPNH and DPN).

$$\text{Lactate} + \text{DPN}^+ \underset{\longleftarrow}{\overset{\text{LDH}}{\longrightarrow}} \text{Pyruvate} + \text{DPNH} + \text{H}^+$$
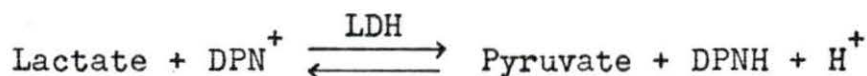
This reaction is a critically important step in the carbohydrate metabolic cycle and accordingly, the enzyme, a zinc-containing compound, is widespread, having been found in virtually every vertebrate and invertebrate species tested, in almost every mammalian tissue studied, and in many microorganisms (60). It is also present in body fluids such as urine, serum, serous effusion, and cerebrospinal-fluid (162).

In the presence of the enzyme, lactate is oxidized to pyruvate while DPN is reduced to DPNH; conversely, the enzyme will also catalyze the reverse reaction in which pyruvate is

reduced to lactate while the reduced DPNH is oxidized to DPN.
Thus, measurement of enzyme activity can be carried out in
either direction depending on the initial substrates employed
and other factors, and different clinics have adopted one or
the other method.

Meister (102) emphasizes the fact that LDH catalyzes the
reduction of several different alpha-keto and alpha-gamma-
diketo acids. The kinetics of LDH-catalyzed reactions have
been explored in several reports (58, 113, 142, 151, 159).

Under normal conditions these enzymes are confined al-
most entirely within the tissue cells although a small amount
is normally found in the blood and an even smaller amount in
the cerebrospinal-fluid. Wroblewski (162) reported on the
activity of human tissues in the following order from most to
least: kidney, skeletal muscle, liver, heart, pancreas,
spleen, brain, and lung (see Table 1). Unfortunately no cor-
responding figures are available for the various species of
domestic animals.

LDH activity varies in body fluids in response to path-
ological processes in tissues bathed by these fluids.(162).
Necrosis of tissue results in the release of intracellular
LDH, which finds access into the extracellular fluid compart-
ment, resulting in an increase in SLDH. In experimentally
produced myocardial infarction in dogs, Wroblewski (162) re-
ports that SLDH increases in proportion to the amount of
necrotic myocardial tissue.

The determination of SLDH requires certain precautions in the handling of blood specimens. Erythrocytes are rich in LDH, and the slightest hemolysis can significantly elevate serum levels in a specimen. The erythrocytes also contain transaminases, but in lesser amounts, however, hemolysis is to be avoided (46). Hsieh and Blumenthol (72) reported that serum taken from clotted blood after one hour at room temperature showed a 25 percent increase in LDH as a result of leakage from the erythrocytes. They state that it is imperative to separate serum within thirty minutes after blood is drawn, unless refrigerated promptly. Blood can be stored for 24 hours with no increase in SLDH if kept at $4^{\circ}C$. Plasma from oxalated or citrated blood should not be used for serum enzyme determinations. (81, 114).

LDH is a relatively stable enzyme. Erickson and Morales (46) found that serum could be stored for at least a week at $4^{\circ}C$. and could be frozen for periods up to a month with negligible loss of LDH. King (81) found no change in serums stored for three weeks at 0 to $4^{\circ}C$., and Wroblewski and LaDue (167) reported no loss of activity in serum stored at room temperature for 96 hours. Sigma Chemical Company (145) recommends that undiluted serum be used within three days when stored at $4^{\circ}C$. or within 10 days when frozen when using their clinical reagents.

The transaminases are probably more stable than SLDH.
Wroblewski (161) reports that storing serum at room temperature for 24 hours or at 4°C. for five days does not significantly alter transaminase activity. It has been reported that frozen samples remain stable for long periods of up to at least four months.[1]

Hess (66) discussed some of the possible mechanisms involved in maintenance of normal serum levels as well as the pathological serum levels of "DPN-dependent" enzymes. He states that the physiological disintegration of erythrocytes and other blood cells that lead to their normal end state might play a role in the maintenance of normal enzyme concentration, as may also that of the intestinal mucosa, whose high cellular turnover is indicated by its high mitotic rate. He thinks that there is insufficient evidence to support either of these possibilities; however, the former seems more likely. The cellular turnover rate of muscle and nervous tissue is minimal and may be neglected; in addition he has as yet been unable to determine any arteriovenous differences in enzyme activity either in normal persons or in tumor patients, which indicates the participation of either of these tissues, the possible physiological internal secretion of enzymes is a

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[1]Buck, W. Animal Disease Eradication Division, National Animal Disease Laboritories, Ames, Iowa. Serum enzyme stability. Personal Communication. 1960.

highly interesting aspect of the matter, but evidence for this is lacking at present.

Since these enzymes are also found in the cerebrospinal-fluid and since there have been several reports on the possible diagnostic significance of these enzymes in pathological conditions of the central nervous system it is of interest to discuss briefly the controversy over the existence of a "blood-brain" barrier. Its presence with respect to GOT and LDH has been mentioned in a few reports, usually when an elevation of the enzymes in the serum was not reflected in the spinal fluids. Wroblewski et al. (164) reported that with LDH there was no relationship between serum and spinal-fluid activity and that each varied independently of the other, presumably because of a blood-brain barrier. Wakim and Fleisher (156) gave more definite evidence of a barrier in dogs with experimental cerebral infarction, in which marked elevations of spinal-fluid transaminase was associated with only minimal change of serum levels. Conversely, high serum levels resulting from acute hepatic necrosis were not reflected in spinal-fluid. In 1957 Lieberman and co-workers (93) however, reported serum transaminase elevations in 43 percent of patients who had suffered recent cerebrovascular accidents, and in whom myocardial infarction was ruled out by serial ECG's and absence of other clinical signs. Shortly thereafter, Fleisher, Wakim and Goldstein (50) reported moderate elevations of transaminase activity in both serum and spinal-

fluid in a study of cerebrovascular disease in human beings.
This differed from the results of their previous work with
dogs. Green et al. (55), on the other hand, observed no
elevations of transaminase in the serum after cerebral in-
farction, but did find moderate increased activity in the
spinal-fluid in 7 of 11 patients. Later in 1957 Lieberman
and his group did more work on this problem (92). They re-
ported cases of striking dissociation between levels of en-
zyme activity in simultaneously drawn specimens of blood and
spinal-fluid which lend support to the hypothesis that a
"blood-cerebrospinal-fluid barrier" is operative so far as
GOT is concerned. In the cases in which elevation occured in
both serum and spinal-fluid, the serum level was always
greater than that of the spinal-fluid. There may be species
differences which are yet to be discovered, but it is probably
safe to assume that there is a blood-brain barrier in all
animals for these three enzymes. However, work to support
this hypothesis is in order.

Recently, it has been found that certain enzymes are
composed of component enzymes termed isozymes. In 1959
Markert and Moller (97) proposed the term isozymes for the
different molecular forms in which protein can exist with the
same enzymatic behavior. Beef heart LDH was first separated
into two such isozymes or catalytic active components by
electrophoresis (112). Since that time five LDH isozymes have

been identified in rabbit and human tissues; typical patterns were observed for each tissue (165). Markert and Moller (97) also found characteristic isozyme patterns for each tissue and species, and observed that the pattern for a single tissue changed during embryological differentiation. Other properties of these LDH isozymes have been studied by various workers.

Fleisher et al. (48) reported the separation of GOT from crude extracts of heart and liver into two fractions by electrophoresis. They could not show the presence of more than one component with GPT. In 1961, Augustinsson and Erne (11) reported the existence of isozymes in serum GOT and GPT from man, cows, horses, and pigs. For all species of animals studied, both GPT and GOT activities were found in the alpha and beta globulin fractions of the serum.

The existence of these fractions of enzyme activity in mammalian sera may be of importance in clinical studies. If the heterogenity of these enzymes is actually due to different molecular forms, these may differ in relative concentration from one disease to another; e.g., in myocardial disease and hepatic disorders. In addition, it may well be that the various forms have different cellular origins. It follows then that such isozyme determinations would be much more specific as to the tissue and organ involved.

The three enzymes are expressed as units per ml. of serum per minute. Karmen (77) defined SGOT activity as: 1

unit equals a decrease in optical density (O. D.) of 0.001
under standardized conditions. The SGPT has been defined
similarly. There has been more controversy regarding SLDH;
however, enzyme activity is usually expressed in terms of
units. A unit of LDH is defined as an increase in O. D. of
0.001 per minute per ml. of serum (60).

The spectrophotometric method of measuring SGOT was
devised in which the GOT reaction is coupled to the oxidation
of reduced diphosphopyridine nucleotide (DPNH) by oxaloacetate
in the presence of an excess of purified water dehydrogenase.
The oxidation of DPNH, and thereby the transamination re-
action, is followed by measuring the decrease in light ab-
sorption at 340 mμ. at which wavelength the reduced pyridine
nucleotides have an absorption peak. The spectrophotometric
measurement of SGPT is accomplished by utilizing a technique
analogous to that described for SGOT. The GPT reaction is
coupled to the reduction of pyruvate to lactate by DPNH in
the presence of an added excess of purified LDH. The colori-
metric methods are generally based upon measuring the amount
of hydrazone present, which is highly colored.

The determination of LDH is facilitated by the spectral
properties of the coenzyme as discussed by Erickson and
Morales (46). DPNH has a maximum light absorption at a wave
length of 340 mμ., whereas DPN absorption at this wave
length is negligible. LDH can be determined spectrophoto-
metrically by measurement of the rate at which DPNH is

oxidized or reduced, depending on whether the reaction is studied from the pyruvate or the lactate side. With the reagents, pyruvate and DPNH or lactate and DPN, in excess, the measured rate of reaction is proportional to the concentration of LDH in the sample assayed. In the colorimetric method of Sigma (145) pyruvic acid reacts with 2,4-dinitrophenylhydrazine to form an intensely colored hydrazone which has a high O. D. over the broad wavelength range of 400 to 500 mμ. Lactic acid, beta-DPN and beta-DPNH do not contribute a significant O. D. at this wavelength. Therefore, by formation of the same hydrazone O. D., one can measure the varying O. D.'s resulting from the conversion of part of the pyruvic acid to lactic acid due to LDH activity.

Determination of SGOT, SGPT, and SLDH activities have been used extensively in human medicine to aid in the diagnosis of myocardial infarctions and hepatic disease (9, 26, 55, 63, 79, 82, 83, 85, 105, 108, 109, 124, 155, 166, 168). Although SGOT and SGPT activities are elevated in both of these conditions, SGOT elevations more sensitively reflect myocardial infarctions and chronic liver disease, whereas elevations in SGPT activity are more constant in acute liver disease (20, 26, 63, 161, 167). This is also apparently true in laboratory animals and dogs (20, 31, 35, 49, 60, 101, 161). There is very little information relating SLDH changes to pathology in dogs, however, there are a few reports

relating to laboratory animals (16, 51, 70, 73, 96). It is
reported that SLDH is a highly valuable indicator of myo-
cardial necrosis in humans, failure to observe elevations on
serial testing is an important negative finding, and it af-
fords the added advantage over SGOT of a more persistent
abnormality (up to 10 to 14 days after infarction)(60). The
results on dogs from the small amount of work done indicates
that SLDH is increased following myocardial infarction but
not to as relatively as high level as SGOT (116, 127, 132).

Several groups of workers produced various types of
cardiac, liver and pulmonary pathology experimentally in
dogs (2, 3, 4, 18, 62, 53, 83, 84, 89, 116, 127, 131, 132,
144, 150). Their work indicated that myocardial infarction
and liver necrosis resulted in elevation of all three enzymes.
However, serum levels remained near normal in pericarditis,
myocardial ischemia, valvular insufficiency and pulmonary
infarction. One clinical report from California indicates
that serum transaminase determinations can be of considerable
aid in diagnosing liver pathology (170). Cornelius reports
(31) that SGPT levels are used as the test of choice in liver
function in hepatocellular necrosis in the dog and cat.

Detweiler in his early work on canine cardiology re-
ported that the incidence of cardiovascular disease among
dogs is considerably higher than is generally realized (37).

He further states that there is little understanding of the
degree and character of cardiovascular involvement and that
myocarditis and myocardial degeneration generally go unrecog-
nized, except at necropsey.

Since then it has been reported by workers at Pennsylvania
(38, 39) that the incidence of heart disease in dogs of all
ages selected at random is about 15 percent, it appears that
more work should be carried out on the value of these serum
enzymes in the diagnosis of various pathological conditions
occurring in this species.

B. Electrocardiography

Volumes of descriptive literature are available on the
configuration, timing, and lead systems relevant to electro-
cardiograms of man and animals. Although many workers have
made significant contributions to the study of the electro-
cardiogram, two are especially noteworthy both for the merit
of this work and for their influence on the approach taken by
others in this field as it relates to the human subject. As
described by Abildskov (1), the early history of electro-
cardiography is dominated by the work of Sir Thomas Lewis.
In a very short time, use was made of his observations to form
an important part of the clinical evaluations of patients.
Wilson played a similar role in the history of electrocardio-
graphy in later years (1). His contributions may be summar-
ized as the application of mathematics and basic principles

of physics to this study, and resulted in bringing order to
a field which would otherwise consist of a bewildering col-
lection of empiric data.

During the past few years the techniques employed in
human clinical electrocardiography have undergone relatively
little change, although a new type of recording, the spatial
vectorcardiogram, has been developed recently. The 1943
recommendations of the American Heart Association's committee
on standardization of electrocardiographic nomenclature and
precordial leads have been widely adopted, and both the range
of usefulness and the limitations of the electrocardiogram as
currently used have been well defined. The technique of
spatial vectorcardiography is still in its infancy and new
discoveries about it are still occurring and hence it is not
so clearly defined.

The boundaries and guidelines which are so well provided
for the human electrocardiogram have not been so clearly de-
fined for the canine electrocardiogram. Although volumes of
literature are available, on canine electrocardiography, most
of the information is empirical with much of the nomenclature
and guidelines being borrowed from those set down for the human
electrocardiogram. Much of this literature is worthless in
the light of newer information, especially since the major
differences between the human and canine anatomy have been
recognized. However, the basic electrical phenomena occurring

within the dog's heart and the human heart are very similar
and this does furnish some basis for the exchange of infor-
mation between the two species physiologically speaking.
Work cited in the following review is on dogs unless other-
wise stated.

The structure of clinical electrocardiography has been
built on limited knowledge of the sequence in which electrical
events involve various portions of the heart. The general
path of activation in the atria was relatively easily defined
because these structures are thin and for most purposes the
spread of electrical events through them may be considered
as surface phenomenon (1). Ashworth and Nahum (10) describe
an auricular electrocardiogram showing a QRS wave, an ST seg-
ment, and a T wave. It is a well known concept that the
impulse starts at the S-A (sino-atrial) node located in the
right atrium. The innervation to and of the dog's heart was
described and discussed by Tcheng (152). Puech et al. (125)
described the septal auricular activation as occurring from
above downward, and from back forward. They reported, con-
trary to the classical concept, that the posterior-inferior
region of the left auricle, near the entrance of the pul-
monary veins, was found to be the last zone of activation.
They found the conduction rate of the right atrial body and its
appendage range from 487 to 1,000 mm/sec. In reference to
the P wave, in most cases, sinus activity takes place from

.005 to .015 seconds before inscription of the P-wave. The
end of the right auricular activity never goes beyond the
apex of the P-wave. The left auricular activity encompasses
most of the ascending segment of P, to the middle or lower
third of the descending portion of the wave.

The impulse travels from the auricles to the ventricles
through the A-V node also terms the bundle of His. Alanis
and Guillermo (6) reported on the propagation of impulses
through this structure and the connection to the Purkinje
cells of the ventricles. There is much controversey about
the sequences of electrical events within the ventricles.
The events of activation on the surface, unlike those of the
auricles, cannot be presumed to indicate the same as that in
the underlying muscle, because of the thickness of the muscle
mass and the finding of various types of nervous tissue there.

The classical study by Lewis and Rothschild (90) indi-
cated that activation began high on the septal wall. Later
Sodi-Pallares et al. (148) and Burchell and associates (21)
found evidence indicating that the apex of the septum was
excited before the base. Harris' (61) findings generally con-
firmed those of Lewis, whereas the results reported earlier
by Nahum and co-workers (110) were similar to that of the
groups of Sodi-Pallares and Burchell.

More recently Scher et al. (135, 136, 137, 138) and
Durrer et al. (42, 43, 44, 45) have investigated this

phenomenon independently using similar techniques. Both
groups confirmed earlier studies indicating that the general
sequence of activation of the left ventricular wall proceeds
from apical toward basal regions. Scher's et al. studies,
which included study of the intraventricular septum, also
confirmed the finding that the left side of the septum was the
earliest portion of the ventricular muscle to be activated.
His results indicated that activation begins in the mid por-
tion of the left septal endocardium. Results of the two
groups differed with regard to the manner of excitation in
the subendocardial regions. Both found a very rapid acti-
vation of the endocardial surface of the ventricular wall as
did Harris (61). Studies by Scher's group, however, indi-
cated a spread of activation through the remainder of the
ventricular wall in an endocardial to epicardial fashion.
Harris also reported this and that the spread through the wall
was much slower than the activation of the entire endocardium.
The results of the work by Durrer and associates seem to indi-
cate myocardial extensions of the Purkinje system so that
activation in the inner layers may be progressing toward the
endocardium as well as the epicardial surfaces. In this
respect the findings of Durrer are similar to those of
Prinzmetal and associates (122).

In 1961 Durrer et al. (41) reported that the question of
intramural extension and the degree of this extension of the

Purkinje network is still not solved. They have looked for evidence of such a network in the left ventricular wall for years, but never found it. Previous reports gave only indirect evidence for its presence. However, they did find such an intramural extension in goats as has been reported by other workers (106). It again must be pointed out that there is danger in over extrapolation from one species to another.

In the outer layers of the ventricular wall the excitatory process progresses with nearly constant velocity, approximately 50 cm. per second, toward the epicardial surface (41). The ventricular septum is activated from both sides (137). No functional boundary between the portion supplied by the right and left bundle can be demonstrated. (137). The basal regions of the septum are activated latest in the cardiac cycle; therefore, the excitation wave in the ventricular septum progresses in an apico-basal direction (41).

Pruitt, Essex and Burchell (123) related the speed of activation to direction of the muscle fibers. They stated that endocardial activation is rapid, not because of the Purkinje fibers, but because the subendocardial bonds of the myocardial muscle form a network through which excitation can move rapidly along the axis of the fibers. Spread across the septum in bundle branch block and across the free wall of the left ventricle in the normally activated heart is slow because excitation is moving through fibers in which the long axis is perpendicular to the advancing wave of excitation.

Hamlin and Smith (59) have summarized the data and ex-
plained the series of events as follows: After the excita-
tory impulse traverses the atrioventricular nodal conduction
system, it is quickly carried by the Purkinje fibers to all
areas of the endocardium and subendocardium at a velocity of
2.5 meters per second. The Purkinje system affords a method
whereby almost all areas of the ventricles are stimulated and
therefore contract simultaneously. Activity represented
electrocardiographically occurs only when the wave of exci-
tation traverses muscle by conduction from fiber to fiber.
The electrocardiograph is silent during the time when the
Purkinje system alone is carrying the impulse. The first area
activated is the interventricular septum. After this septal
activation, the impulse spreads by fiber-to-fiber conduction
through the ventricular myocardium from subendocardial termi-
nations of the Purkinje system to the epicardial surfaces.
This activation occurs simultaneously through both ventricles.
However, the peripheral electrocardiogram, which represents
the resultant of the simultaneous activities of both ventri-
cles, is recorded as if the front were moving only from the
left ventricular endocardium to the left ventricular epi-
cardium because the left ventricle is 4 to 6 times as thick
as the right. Finally, the ventricular activation process is
terminated when the base of the heart is activated in an
apicobasilar direction.

Despite the conflicts of these reports it is apparent
that much of the electrical impulse phenomenon of the heart
is fairly well understood and that it is from these facts that
clinical interpretations can be made. However, it is obvious
that when a detailed order of activation is defined, the
electrocardiogram will give a much more realistic picture of
the location of the lesion involved in cardiac pathology.

The repolarization pathway has presented even more dif-
ficulties in its study. It cannot be investigated with the
methods applied to the analysis of depolarization because
opening the thorax changes the T wave. The literature is
notably lacking in explanations for this phenomenon. Al-
though there are several papers in the available English
literature, only one seems worthy of mention at this time.
Studies by Reynolds and VanderArk (129) show that in general
the order in which local ventricular muscle units recover
excitability is correlated with the epicardial T-waves as
recorded in direct unipolar leads. The effective refractory
period was determined at the surface and in the deeper layers
of the dog heart and was correlated with the surface T-waves.
A small delay in recovery of cardiac excitability appeared
at the surface when T-waves were negative and in the deeper
layers when T-waves were positive. They further showed that
both surface and deeper layers in a limited area normally com-
plete recovery within a short space of time, thus suggesting

that a majority of cardiac fibers recover during the same period of time. Since only slight changes in the rate of recovery at the surface or in the deeper layers are apparently necessary to alter the polarity of the T-wave, this partly explains the lability of the T-wave. However, it is apparent that this is not a complete explanation of the origin and direction of the T-wave. This phenomenon awaits further study and clarification.

Abildskov (1) has gone into a brief discussion of the origin of bioelectric potentials. It is beyond the scope of this paper to delve into the vast amount of research in this area of biochemistry and biophysics. However, as he so aptly points out, considerable clinical usefulness of the electrocardiogram has been achieved in spite of only meager knowledge of the processes which give rise to the electric phenomenon of the heart. Hamlin and Smith (59) state that the heart is an electric generator within the thorax and that an electrocardiogram is a tracing of variations in body potential which has been generated by the heart and transmitted through the body volume to a surface point.

In this same paper they point out the variation in the anatomy of the dog and man and the danger of over-extrapolation from species to species.

Eyster, Meek, and Goldberg (47) reported on the relationship between the electrical and mechanical events of the dog heart. They concluded that different local regions of the

dog's heart start contracting at different time instants and
that the occurrence of mechanical activity is coincident with
or separated by a brief interval from the occurrence of maxi-
mum flow of electric current and maximum time rate of change
of current, resulting from a potential gradient established
between neighboring regions in which the potential is respec-
tively above and below the potential of the resting muscle.

At the present time the author knows of no textbook which
is primarily concerned with canine electrocardiography. How-
ever, for a basic understanding of the principles underlying
this science the reader is referred to texts by Wolff (160)
and Marriott (99).

While position during recording and methods of place-
ment of electrodes are well established for human electro-
cardiography there is much controversy in canine electro-
cardiography. The general concensus seems to be that dogs
should be placed in lateral recumbency on their right side
(10, 38, 86, 94, 95, 146, 153, 157). However, there is evi-
dence that the supine position is best (71, 115, 121). In
preliminary studies by the author, the sternal position was
found to give good reproduceability. Wallace in his treatise
on technique of canine electrocardiography states that having
dogs on their right sides is the technique of choice (157).
Katz and co-workers (80) reported on positioning in 1934,
stating that there were variations in the electrocardiographic

tracings with dogs placed on their right sides, but they felt
this was due to normal variations in the position of the
heart. They found changes in amplitude and even direction of
all complexes, especially the T-wave. They found these same
changes when animals were recorded in the normal standing
position. Lannek in his classical work also preferred the
right side (86). Lumbard and Witham (95) varied positions on
50 dogs and found variations in all positions from dog to dog.
The effect of changing of position varied in a random way.
Peterson et al. (121) used the supine position because of the
variabilities previously reported from the right lateral
position. They reported that variations were much less in
the supine positions than those reported in the lateral posi-
tion. Horwitz, Spanier, and Wiggers (71) using the supine
position reported that variations on the same dog taken at
different times were as great as among different dogs.
Newton, Ellis, and Zaremski (115) recently described a
technique in which they reported that virtually no contour
changes in serial electrocardiograms occurred on anesthetized
dogs in the supine position, and it is therefore suitable for
chronic experiments. Because of the random changes in the
recording Lumbard and Witham (95) stressed the fact that it
is important to have the dog in the same position in chronic
experiments to insure correct interpretation of serial re-
cordings. Tsagan (153) recently reported that changes in
ECG following myocardial infarction were most marked when the

dog was on its right side with the right front leg forward and the left back. He reported that the position of the front limbs altered the Q and T-waves, and had a considerable effect on the ST interval. It is therefore of importance to maintain the front legs in a fixed position when recording the electrocardiogram.

Litvak, Siderides, and Vineberg (94) summarized extreme variation of the electrocardiogram of the dog as compared with the human as being due mainly to positional change. The heart of the dog lies more centrally in the thorax and assumes a more vertical position than does the human heart. The absence of the mediastinum as compared with the human being, makes the heart easily susceptible to positional changes. Consequently, pneumothorax, paralysis of the diaphragm, abdominal distention, and even variations in heart rate tend to displace and rotate the heart producing electrocardiographic changes.

The clinical approach to position seems to favor having dogs positioned on their right sides[1] (38, 86, 157).

The use of needle electrodes, wires, plate electrodes, and clambs of various types has been described in the literature (38, 80, 86, 94, 115, 121). Clipping of hair or leaving it in place does not effect the recording (120, 121).

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[1]Baker, D. L. Professor Medicine and Surgery. Iowa State University, Ames, Iowa. Positioning dogs for clinical ECG recordings. Private communication. 1962.

The use of anesthetics and tranquilizers has been described as having little effect upon the electrocardiogram (153, 157). The use of morphine is to be avoided because it increases vagal tone (157). Cannard et al. (25) discussed the electrocardiogram during anesthesia in the human.

The placement of electrodes upon the animal body has been quite clearly defined in regard to limb leads (146, 157). However, there is some discrepancy among various workers as to where precordial lead electrodes should be placed or even if they should be used at all (38, 86, 95, 115, 146, 157).

Several papers have reported on the configuration of the electrocardiogram of normal dogs. The results have varied from one group of workers to another, partly because of different techniques, but probably more important because of the normal variation in the canine electrocardiogram. In 1949, Lannek (86) published a detailed statistical analysis of the normal canine electrocardiogram, together with observations on a series of animals showing electrocardiographic abnormalities. This work served as a cornerstone of clinical canine electrocardiography in the following years. Petersen et al. (121) reported on the electrocardiographic tracings in normal beagle dogs in 1951. Following this there were papers by Grollman and co-workers in 1952 (56), Horwitz, Spanier and Wiggers in 1953 (71), Soave in 1954 (146) and Lombard and Witham in 1955 (95). The following tables summarize findings:

Table 2.   Heart rate of normal dogs

No. of dogs	Breed	Position	Range	Ave.	Author
32	Beagle	Supine	90-180	138	(121)
50	Indeterminate	Right side	62-158	100	(95)
30	Mongrel	Supine	72-162	121	(71)
50	Indeterminate	Right side	80-160		(146)

Lannek (86) reported that sex differences are not
probable in electrocardiographic tracings. He also found that
breed differences are improbable except for the amplitude of
the T-wave on certain breeds (collie, dachbrache, dachshound,
greyhound, harrier, rottweiler and setter) being greater. He
did find significant differences in certain parts of the com-
plex based upon age difference. He also reported a signifi-
cant difference in heart rate among dogs less than six months
and those over but no additional differences with increased
age.

The time duration of the various segments and the ampli-
tude of the various waves as reported by other workers are
shown in Table 3 and 4. In preliminary investigation the
author found considerable differences in amplitudes from day
to day and from position to position and it is thought that
the relative rather than the absolute amplitude is of more
significance. Lannek states that the R amplitudes are in
themselves of no great diagnostic value, they become

important on low voltage and on calculating the negative T-wave as a percentage of the R amplitude. He also states that the variations in amplitudes of the tracings, measured at four-five hour intervals during one day are considerable.

Table 3. Time duration (seconds) of various segments of ECG complex as reported by others

	P	P-R	QRS	QT	Ref.
Average		.106	1046	.19	(121)
Range		.08-.12	.04-.06	.14-.24	
Average		.10	.05	.26	(95)
Range		.08-.15	.04-.06	.20-.38	
Average	.07	.12	.06	.21	(71)
Range	.04-.12	.10-.15	.04-.08	.16-.28	
Average	.06	.106	.045[b]	.187	(86)[a]
Range	.02-.10	.06-.17	.03-.06	.14-.25	
Range	.04-.08	.08-.10	.03-.06	.16-.21	(146)
Range		.06-.18	.03-.08		(56)

[a]Longest interval in standard leads I, II, III, and aVF.
[b]Medium weight breeds.

Lannek (86) reports the P wave is often isoelectric in lead I and the amplitudes are never high. In leads II and III, P is in nearly every case positive on inspiration but may become negative in lead III on expiration. A P-wave which remains negative throughout should be regarded as an abnormality in all leads with the exception of lead I.

There has been much discussion of the presence and significance of Q-waves in the canine electrocardiogram. So much

Table 4.   Amplitudes of the various components of the dog ECG as reported by others (1 cm. = 1 mv.)[a]

Q	R	S	T	Ref.
Lead I				
0 (0-.2)	.35 (.15-.70)	0 (0)	0 (-.1-.1)	(121)
.10 (.00-.60)	.3 (.00-1.00)		-.03 (-.30-.15)	(95)
.16 (0-1.15)	1.05 (.20-2.22)	.09 (0-.80)	.05 (-.36-.63)	(71)
.03 (0-.6)	.12 (0-.35)	.01 (0-.2)	-.005 (-.1-.7)	(56)
.77	1.11	.45		(86)[b]
.14	.7	.06	.05	(146)[c]
Lead II				
0 (0-.20)	1.8 (1.0-2.7)	.25 (0-1.0)	.3(.05-.8)	(121)
.24 (0-.90)	1.14 (.25-2.30)	.10 (0-1.50)	-.07 (-.45-1.00)	(95)
.17 (0-.89)	1.77 (.30-3.09)	.09 (.0-.79)	.18 (-.27-.74)	(71)
.04 (0-.10)	1.08 (.10-2.3)	.14 (0-.40)	.15 (-.10-.60)	(56)
1.02 (	2.52	.55		(86)[b]
.21	1.7	.09	.14	(146)[c]
Lead III				
.1 (.1-.2)	1.5 (.9-2.5)	.4 (0-1.4)	.3 (.1-1.0)	(121)
.12 (0-.45)	.76 (.05-1.35)	.14 (0-2.5)	-.03 (-.25-.70)	(95)
.13 (0-.44)	1.11 (.14-2.43)	.23 (0-1.48)	.13 (-.26-.81)	(71)
.02 (0-.35)	.92 (.1-1.95)	.16 (0-.6)	.16 (-1.0-.6)	(56)
.62	2.09	.71		(86)[b]
.12	1.00	.18	.15	(146)[c]
Lead aVF				
0	.67 (.5-1.3)	.05 (0-.25)	.11 (-.1-.4)	(56)
.17 (0-.7)	1.35 (.1-2.52)	.17 (0-.67)	.13 (-.25-.74)	(71)

[a]Average and range.

[b]Upper limits of normal amplitude.

[c]Average only.

importance has been attached to this complex presumably be-
cause of its diagnostic importance in human electrocardio-
graphy in myocardial infarction. Lombard and Witham (95) re-
ported that Q-waves appeared in all three limb leads in 60
percent of the records, in 32 percent in leads II and III and
in the other 8 percent they occurred in one or more leads or
were not present at all. They found the Q/R ratios in lead I
never exceeded 2.5:1. However, they found by changing posi-
tion of the dog from its right side to its back, belly or left
side they could cause a reduction in size or a disappearance
of the Q-wave. They further reported significant day-to-day
variations in leads I and II, but not in lead III. Horwitz
et al. (71) found a Q-wave in approximately 1/3 of their
tracings in lead I and in 82 percent this was followed by an
inverted T-wave. They reported that Lalick had found this
occurring in 78 percent of his records. However, Lombard and
Witham (95) could not confirm these results.

Probably one of the most baffling aspects of canine
electrocardiography is the extreme variability of the T-wave.
This is reported and discussed in almost all the papers deal-
ing with the normal canine electrocardiogram. Without going
into a detailed discussion it will suffice to say that this
variability is apparently normal and until the underlying
phenomenon which causes this particular complex is better
understood this will, in all probability, stand. Horwitz

et al. (71) did find that in 84 percent of the cases in which an S-wave was recorded in lead III of 1 mm. or more, an upright T-wave followed. They reported Lalick had recorded this same occurrence in 75 percent of his tracings. Petersen's group (121) found on serial recordings that in no instance did a positive T-wave in leads II, III, and aVF become negative. As mentioned earlier Lannek (86) found a deeper negative T-wave in leads II and III of certain breeds. He noted that this might be attributed to the temperament of the breeds involved.

Bellet, Gazes, and Steiger (13) reported typical T-wave patterns observed in acute infarction and in those dogs with small infarcts involving chiefly the endocardial portion of the left ventricle. In the former, observed in transmural in-farcts, the T-waves were characterized by inversion and an increase in amplitude. The latter showed inversion and a diminuation in amplitude which remained small. It should be remembered that they had control electrocardiograms to compare with before pathology occurred.

Another important segment deviation occurrence which has been studied extensively is the ST segment. This also has been important in human electrocardiography. In preliminary studies the author found it to be the most reliable of any change in the recording for detecting cardiac pathology. Petersen (121) found that there was sometimes depression or elevation of the ST segment up to 1 mm. in dogs in the

supine position, chiefly in leads II, III, and aVF. Groll-
man et al. (56) found no deviation in lead I but up to 2 mm.
up or down in leads II, III, and aVF in 18 normal dogs in the
supine position. Litvak, Siderides, and Vineberg (94) found
only a slight ST elevation in lead I in one of 12 normal dogs.
Lombard and Witham (95) make the comment that the merging of
the terminal part of the QRS complex with the ST-T segment is
so characteristic a picture of the dog electrocardiogram when
taken under anesthesia at a paper speed of 50 mm/second that
it must be considered normal. They found it occurring to some
degree in all leads. They further found that in the limb
leads, 22 percent of the records showed no S-T deviation. 30
percent up to .09 mv. and 48 percent between .10 and .20 mv.
Other authors reporting S-T deviations of this order of mag-
nitude have attributed the phenomenon to a variety of experi-
mental causes or as a "normal" occurrence. They found that
on day-to-day recordings that the shift was most noticeable
in lead II. Nahum, Hoff, and Kisch (111) reported from their
experimental work that elevations of the R-T in any lead
denotes damage to the surface of the left ventricle, while
depression of the S-T indicates damage to the right ven-
tricle, however, this appears to be an over simplification
of the situation. Lannek (86) states that the shifting of
the ST segment towards the negative side, is clinically, by
far the most important factor. He states that the ST segment
may be described as a straight line or, seen from above, a

concave or convex curve. The straight and the concave forms
are the most common, whereas the convex type is seen less
often in normal cases but is relatively common in myocardial
lesions. He further states that most of the deviations from
the normal picture are to be found in the ST segment and the
T-wave, in the form of depression of the ST, decrease of the
T amplitude and shifting of the T/R relation (negative T ex-
pressed as a percentage of the amplitude of R in the same
complex) towards higher values. The depressions of the ST
segment are usually small although in many instances signifi-
cant. The cause is probably currents of injury.

Durrer et al. (41) found that all epicardial complexes
show S-T elevations from an ischemic area when recording
directly through an open thorax. Detweiler, Hubben, and
Patterson (38) found early myocardial degeneration and
arterial thickenings upon necropsy of three hearts of dogs
showing an RS-T segment deviation of .2 mv. or greater in
several leads. Tsagan (153) describes in great detail the
changes occurring in the ST segment following experimental
myocardial infarction. Zao, Yen, and Herrmann (169) studied
the effects of oxygen gradient upon the ST segment. The ECG
revealed a positive correlation between the ST segment ele-
vation and the oxygen gradient, i.e., the ST segment increased
in height with an increasing oxygen gradient, and decreased in
height with a decreasing oxygen gradient. They discussed the
possibilities involved.

The question of arrhythmias is often brought up in the dog. Because of the normal sinus arrhythmia of the dog's heart it is often difficult to detect the abnormal arrhythmias without the use of the electrocardiograph. Almost any type of arrhythmia, other than the normally occurring sinus arrhythmia can be detected by the electrocardiograph and can be considered as indicating cardiac pathology (86).

Ventricular extrasystoles (ectopic beats) are rare in dogs and available evidence (36, 37) indicates that myocardial lesions are usually present when this arrhythmia is encountered under clinical conditions in dogs which have received no drugs or toxins known to cause ventricular premature beats. Lannek (86) also states that ventricular extrasystoles and block are regarded as significantly abnormal features, not appearing in the normal animal. Patterson and co-workers (120) concur with this opinion.

The knowledge in this basic field of electrocardiography is advancing rapidly and as more information is obtained the increased understanding of the physiology involved will aid in the clinical application of this knowledge. Thus, treatment will be based increasingly on facts instead of empiricism.

III. METHODS AND MATERIALS

A. Procurement and Care of Normal Dogs

A total of 50 normal, mongrel dogs of all ages and both
sexes were used in this study. As dogs were obtained by the
Department of Physiology and Pharmacology, they were given a
complete physical examination as described by Detweiler (38)
which included observation of the condition of the animal,
palpation, and auscultation of lungs and heart. Dogs which
appeared to have some abnormal characteristics were discarded
at this point. Those dogs which appeared normal then had a
complete hematological examination including hematocrit and
hemoglobin determination, total erythrocyte count, total
leukocyte count, and a differential leukocyte count. Dogs
having hematologic values within normal ranges were kept for
surgery, provided the presurgical electrocardiogram appeared
to be normal. Table 5 shows the results of the blood studies
of the normal dogs. A vaccination program[1] over a five-week
period prepared the animals for further experimental use.
The animals were vaccinated with 1 cc. of an antigen[2] intra-
dermally at 7-day intervals for five weeks. A serum sample

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[1]Booth, R. R. 3920 E. Jackson Blvd., Elkhart, Indiana.
Distemper-hepatitis Immunization. Personal Communication.
1960.

[2]Virogen D-H: Pitman-Moore Co., Indianapolis, Indiana.

was collected from all dogs at this point and again prior to any surgical procedure for enzyme determination (see Table 6).

The cages in which the dogs were housed were made of galvanized iron. They were cleaned twice daily. Water and dry commercial dog food[1] containing 24 percent protein and 6 percent fat were fed _ad libitum_ to the experimental dogs.

Dogs were divided into three groups as to age for pre-surgical ECG recordings. Dogs in group I were 4 to 12 months of age; group II, one year to five years; and group III, over five years. Estimation of age was based entirely upon appearance and characteristics of teeth.

B. Blood Serum Enzymes

SGOT was measured by the method of Hergt and Langin (64)(see appendix) which is a slight modification of Karmen's original procedure (77). SGOT, SGPT, and SLDH were measured by the clinical Sigma methods (14, 45). The Sigma method of SGOT determination was compared with the research method of Hergt and Langin (see Table 7). All determinations were made using the Beckman Model B spectrophotometer.[2] All blood samples collected for serum were allowed to clot, immediately centrifuged, the serum removed with pipettes, placed in 15 ml.

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[1]General Mills, Minneapolis, Minnesota.

[2]Beckman Instrument Co., Instruments Division, 2500 Fullerton Road., Fullerton, California.

test tubes, and sealed with waxed corks. These samples were frozen immediately and sixteen samples were run at a time at various time intervals later. In preliminary trials it was found that very little loss in activity from freezing occurred; however, it has been reported that repeated freezing and thawing will decrease enzyme activity.[1] SLDH samples were not stored in the freezer for longer than ten days.

C. Electrocardiography

Electrocardiograms were taken with the Sanborn Viso-cardiette Model 51 electrocardiograph.[2] Needle electrodes were placed subcutaneously as the dog was placed on its sternum and belly, front limbs extended straight forward with head resting between them, and hind legs directed to the rear. The standard limb leads I, II, III were recorded plus augmented unipolar limb lead aVF. The needles were placed in a position adjacent to the lateral epicondyle of the femur and radius. (Shown in Figure 10, Appendix). A small area of hair was kept clipped at these points so as to insure placing the electrodes in the same position each time a recording was made. A recording was taken prior to surgery and if the ECG appeared to be normal, surgery was performed as described later. Several recordings were made at various intervals

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[1]Buck, W. Animal Disease and Eradication Division, National Animal Disease Laboratories, Storage of Serum-Enzymes, Personal Communications, Ames, Iowa. 1960.

[2]Sanborn Co., Medical Division, Waltham, Mass.

following surgery to monitor any changes in the electrical phenomenon of the heart. All recordings were made while the dogs were anesthetized with sodium pentobarbital (prior to and immediately following surgery) or while they were tran-quilized with promazine hydrochloride[1] (later serial studies).

Methods of measuring the electrocardiogram were quite similar to those used by Lannek (86). The isoelectric line was established as being that segment of the cycle extending from the end of the T-wave to beginning of the P-wave. Segments for measuring, if possible, were selected where the base line runs parallel to the paper and where the lower contour of the preceding and succeeding T-P segment and the engraved line have formed a straight line.

Errors due to measuring have been minimized through multiple determinations. Lannek (86) found that the error of measuring varies with the technical quality of the tracings. He found that 99.7 percent of the error of measurement for amplitudes may be considered to lie within the limits $\pm$ 0.48 mm., and that for durations within $\pm$ 0.012 seconds.

All amplitudes and durations were measured with dividers and then calculated from a known set of reference points. In those cases of an odd time interval it was rounded off to the

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[1]Promazine Hydrochloride - Fort Dodge Laboratories, Inc., Fort Dodge, Iowa.

nearest even interval, i.e., the duration has been measured with an exactitude of 0.01 seconds. The amplitude for upward deflections has, as is customary, been measured to the upper contour of the base line, for downward deflections to the lower contour of the base line. The durations of deflections have been measured from the point where the convex or concave curvature leaves the contour of the isoelectric line to the point where this curve rejoins said contour.

Measurement of the S-T junction displacement and voltages of the QRS deflections are referred to the level at which the first QRS deflection takes off from the P-R segment. Ratios are given as they occurred unless one of the amplitudes was 0.5 mm. or less in which case the ratio was calculated so that all ratios could be compared to 1. P-R interval was measured from the beginning of the P-wave to the earliest component of the QRS complex in the lead in which it was longest. The QRS interval was measured from the point where the first deflection of the QRS group departs from the base line to the point at which the last deflection comes to rest at the S-T junction. This was measured on several groups and an everage taken for each recording. The Q-T interval was measured from the beginning of the QRS complex to the end of the T-wave in that lead in which the end points were most clearly defined, and in which the largest value was found.

A 3-channel physiograph[1] was used to record the phono-
cardiogram and to monitor any changes in the heart sounds of
those dogs used in the valvular insufficiency part of this
project. Phonocardiograms of dogs were recorded once or twice
presurgically and at various intervals following surgery. In
addition all dogs were examined periodically by ausultation
and palpation to determine the course of their condition.

D. Surgery

1. General considerations

Three types of cardiac pathology were produced by
surgical methods. In each case other dogs were sham-operated
performing the same procedures except for production of the
actual pathological process. A total of fifty animals had
surgery performed; however, nine of these died during surgery
or shortly after before all phases of the project could be
completed.

All materials which were used in the surgical procedures
were sterilized by one of two methods. Steam sterilization
under pressure was used for surgical instruments, gloves,
linens, vetafil[2] and silicone rubber tubing[3]. Chemical

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[1]E and M Instrument Co., 5815 Sidney St., Houston, Texas.

[2]Fort Dodge Laboratories, Synthetic nonabsorbable sutur-
ing. Fort Dodge, Iowa.

[3]Silatube - Ronthor Reiss Corp., Ronsil Products Division,
Little Falls, New Jersey.

disinfection by immersion in aqueous 0.02 percent chlor-hexidine[1] provided the means for disinfecting materials with low heat tolerance and instruments with sharp cutting edges which become dulled by repeated autoclaving.

Anesthetization of the dogs used in surgical procedures was accomplished by the intravenous administration of sodium pentobarbital solution given to effect. The dose was approximately 30 milligrams per kilogram body weight. Solid food was withheld for at least 12 hours prior to surgery. Hair over and adjacent to the surgical field was removed by using an electric clipper with a No. 40 blade. The skin was then prepared for surgery by repeated scrubbings with a 25 percent aqueous germicidal detergent which contained 0.6 percent benzethonium chloride[2]. The lather was removed with cotton after each scrubbing. An endotracheal catheter with cuff was inserted into the trachea and the cuff was inflated.

The tube was then taped to the upper jaw to prevent accidental dislodgment. The catheter was attached to an artificial respirator apparatus[3] if thoracic surgery was to be performed and the oxygen pressure was set for 11 to 14 centimeters of water.

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[1]Nolvasan - Fort Dodge Laboratories, Fort Dodge, Iowa.
[2]Germicidal Detergent. Parke, Davis and Co., Detroit, Michigan.
[3]PR-3 Prothoracic Respirator with breathing bag. Professional Veterinary Service, 819 SW 12th Ave., Miami, Florida.

The hands and arms of the surgeon were repeatedly scrubbed with the 25 percent aqueous germicidal detergent and then rinsed with tap water. After completing the scrubbing, the surgeon dried his hands and arms with a sterile towel and donned a sterile, full-length operating gown. He then put on dry, sterile surgical gloves.

The animal was then draped with sterile cloths leaving the surgical field exposed. Adjacent areas of hair and skin were securely covered.

There are four principles of good surgical techniques which, if observed, enhance the chance for successful results. These principles are devoted to minimizing undesirable sequalae to tissue injury (27).

These principles are first, aseptic technique, or preventing the introduction of infectious organisms into the field of surgery. This is accomplished by using sterile equipment and avoiding contamination. The second is atraumatic technique, or minimizing unnecessary devitalization of tissue. The third requirement is hemostasis or the control of hemorrhage to prevent shock. Finally, the last requirement is careful closure of exposed tissues. This is achieved by accurate apposition of divided parts and by meticulous suturing technique.

2. Myocardial infarction

The production of experimental myocardial infarction was accomplished in two stages. Preliminary trials by the author and Cholvin[1] indicated that the procedure described below is very satisfactory.

The procedure was made on 14 dogs and consisted of two stages. The first stage involved thoracic surgery. The thorax was entered from the left side at the fourth or fifth intercostal space depending on whether the anterior or posterior left descending coronary artery was to be ligated. An incision was made through the skin from 2 to 3 cm. above the point of the scapula, depending on the size of the dog, extending ventrally to within 2 to 3 cm. of the ventral midline. The incision was continued through the subcutaneous tissue and the muscular tissue: latissimus dorsi, superficial pectoral, serratus ventralis, and intercostal muscles. The parietal pleura was carefully penetrated with scissors and cut the full length of the incision. The ribs were spread by self-retaining rib retractors and the lungs were packed off with sterile-saline-soaked or blood-soaked-swabs. This procedure was followed in all thoracic surgery. The pericardial sac was incised parallel to and approximately 1 cm. ventral to

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[1]Cholvin, N. R. N. I. H. Research Fellow - Department of Physiology and Pharmacology, College of Veterinary Medicine, Iowa State University, Ames, Iowa. Now Department of Medicine and Surgery, College of Veterinary Medicine, Michigan State University, East Lansing, Michigan.

the phrenic nerve and fixed to the body wall by means of two or three strategically located stay sutures. A piece of vetafil ligature was then placed around either the anterior or posterior left descending coronary artery or some large branch of the anterior artery at various levels. One throw was placed in the ligature thus enclosing the artery in a loose knot. The ends of the ligature were then threaded through two, 3-5 inch pieces of silicone rubber tubing. This material was used because of the report that it caused very little tissue reaction (27). The pericardial sac was sutured with vetafil incorporating the tips of the silicone tubing within the sacs. These were fixed in place by a purse-string suture around the tubes and through the sac. The pleura and ribs were brought together and sutured with interrupted vetafil ligatures. The silicone tubes with the vetafil ligature within were incorporated within the body wall, one arising near the top of the rib and the other near the bottom of the ribs. The tubes were sutured in place at the junction of the ribs with a purse-string suture. The ends of the vetafil ligatures were brought through the extending end of the silicone rubber tube with a straight needle and tied leaving a loop of excess vetafil. The pleura and muscle layers were brought into apposition and sutured with continuous catgut. The tubes were laid down upon the muscles lying subcutaneously and one stay suture affixed. The subcutaneous tissues

were sutured with interrupted catgut and the skin closed with simple interrupted vetafil sutures. The same suturing techniques were used throughout each surgical procedure with respect to closing the pericardium, thorax, muscles, subcutaneous tissues, and skin.

In preliminary work the vetafil ligatures were brought out together to lie subcutaneously. This often resulted in the vetafil becoming adhered to tissues so that the ligature could not be tightened down and the angle for tightening the ligature was very poor and occasionally resulted in rupturing the artery.

The animal was allowed to recover for six to eight days at which time it was again anesthetized and prepared for surgery. A small incision was made over each of the silicone tubes and they were brought to the surface. The vetafil ligatures were isolated, pulled taut to ligate the vessel and the ends tied together tightly. The subcutaneous tissues were sutured as were the incisions in the skin. In some cases the silicone tubes were removed; in others, they were left in place. The vetafil was cut as close to the skin as possible at top and bottom 20 to 30 minutes later.

The first post surgical ECG was taken at one hour and the second at two hours. Further recordings were made at various intervals. Serum samples were collected every 6 to 10 hours for three to four days starting at 10 to 15 hours post-

surgery and then at various intervals until the dog was
sacrified. Hematological studies were made at various inter-
vals commencing at 4 days to one week post surgery.

Eight sham-operated animals were handled in exactly the
same manner except the vetafil ligature was merely passed
under the artery with no knot and the amount of tension
placed on the ligature was not as great as that put on the
dogs in which an infarction was later produced.

3. Epicarditis

The production of epicarditis was also accomplished in
two stages in six dogs. In this case the thorax was entered
at the right fourth intercostal space in the region of the
cardiac notch. The first step involved the placing of a sili-
cone rubber tube into the pericardial sac through a very small
incision in the sac. The tube was sutured in place within
the sac with a purse-string vetafil suture. The tube was then
brought to lie subcutaneously in the same manner as that des-
cribed for the infarction dogs.

Six to ten days later the tube was isolated while the
dog was under anesthesia and 10 ml. of a sterile talc sus-
pension were deposited within the pericardial sac. The end
of the tube was closed with a piece of rubber tubing and a
vetafil ligature. The tube was fixed in place subcutan-
eously and the tissues sutured. ECG recordings were taken at

various intervals following surgery as were serum and blood samples. Three dogs were sham-operated in precisely the same manner except for the deposition of sterile talc.

4. Valvular insufficiency

In preliminary trials an attempt at producing valvular insufficiency via venous catherization was made. However, without the aid of a fluoroscope and because of the inconsistency of the damage produced, this technique was abandoned. A second method as described by Markowitz et al. (98) by sectioning the chordae tendinae was used, but after problems with fibrillation and failure to produce clinically obvious pathology, this method was also abandoned.

A technique described for the removal of heart worms (Dirofilaria immitis) (157) was modified by the author and Cholvin[1] and used to produce valvular insufficiency in five dogs. An incision was made over either the right or left fourth intercostal space depending on whether a left or a right A-V valvular insufficiency was being produced. Dogs were atropinized at the rate of .02 grain for average-sized dogs. Once inside the thoracic cavity a 15-inch piece of 1/8 inch wide umbilical tape was passed around the anterior vena cava. This was much easier from the right side approach than from the left. The free ends were passed through a

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[1]Ibid. page 56.

3-inch section of 3/16 inch rubber tubing. The posterior
vena cava was similarly exposed and prepared for occlusion.
The pericardium was then incised approximately 1 cm. ventral
to the phrenic nerve and parallel with it and extending from
the anterior to the posterior extremities of the sac. The
sac was retracted dorsally and ventrally lifting the heart up
and held in place with stay sutures. The placement of stay
sutures varied depending upon which method presented the sur-
face of the atrium best for the surgical procedure. Two,
12-inch pieces of vetafil suture were passed through the
atrium 3 to 4 cm. apart with an atraumatic needle. These
were used to apply tension to the atrium to attach the non-
crushing clamp.[1] The clamp was then applied to the atrium
while lifting it up with the vetafil sutures as far away from
the auricle as possible. A 2 to 3 cm. incision was made in
the atrium in the clamped tissue. The venous flow through
the posterior vena cava was interrupted by applying tension
to the ends of the umbilical tape and forcing the rubber
tubing against the vessel. This tension was maintained by
applying hemostatic forceps on the umbilical tape at the
distal end of the rubber tubing. The anterior vena cava was
similarly occluded. The blood supply from the brain was
never occluded for more than 2 1/2 minutes. The clamp was

[1]Satinsky Vena Cava Clamp. J. Sklar Mfg. Co. 38-04
Woodside Ave., Long Island City 4, New York.

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removed by an assistant who at the same time applied mild
tension to the vetafil suture in the atrium. The surgeon then
used a spay hook to pick up the chordae tendinae and the
amount of damage desired is made with a scalpel on the cusps
of the valve. A hook with an inside cutting edge may also be
used but it is more difficult to control the amount of damage.

The valve was then released and the clamp was applied
under the tension sutures while the assistant applied tension
to them. The hemostats on the umbilical tape were released
thus restoring the patency of the vessels. The amount of
regurgitation can be fairly well ascertained at this time.
If more damage is desired, the process can be repeated after
several minutes.

The incision was sutured with 5-0 black braided cardio-
vascular silk with a swaged atraumatic needle.[1] One row of
simple continuous was made. The assistant applied tension to
the stay sutures and the clamps were released to allow a
slight amount of hemorrhage. Then a second row of simple
continuous suture was continued back over the first, making
sure to place the needle between sutures already present.
The clamps were then removed and the area checked for signs
of hemorrhage. If no hemorrhage occurred the stay sutures
were removed and the pericardial sac and thorax were closed

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[1]K-870 A Cardiovascular silk - Ethicon, Inc., Somerville,
New Jersey.

as described previously. If some hemorrhage occurred which
did not cease shortly, several interrupted matress sutures
were applied. This procedure allowed a very minimal amount
of blood loss and provided a method where the amount of in-
sufficiency produced could be well controlled and failure to
produce damage was almost impossible.

One left A-V valvular insufficiency and four right A-V
valvular insufficiencies were produced in this manner. Five
dogs were sham-operated. All procedures were the same except
for production of valvular damage. Two of these were ap-
proached from the left and the other three from the right.

E. Postsurgical Care

Care of dogs following surgery was intentionally kept
to a minimum except for routine examinations. Immediately
following surgery the air was aspirated from the pleural
cavity so that the lungs would assume their normal functioning
rapidly and lack of oxygen would not be an additional stress
factor. Antibiotics were not used routinely following surgery
and bandaging was found not to be necessary. Each animal was
examined daily for the first 7 to 10 days and then at 2 to 4
day intervals. Only two animals developed an infection in the
surgical incision, both of them were cured shortly with anti-
biotic therapy. No cardiac drugs were given to any of the
dogs. They were not exercised, but remained in a cage at all

times except for bleeding and taking ECG and phonocardiogram recordings.

One dog in the valvular insufficiency group was administered a diuretic and was treated for anasarca by surgical drainage several times. Other treatments were merely routine.

F. Necropsy and Histopathology

Dogs were sacrificed and necropsied at various times following the production of pathology. Necropsy procedure as outlined by Coffin was followed (28). Following gross post-mortem examination, a descriptive protocol was written and, where appropriate, photographs of the lesion were taken. Representative portions of tissues from lesions were selected and fixed in 10 percent buffered formalin (4 percent formaldehyde solution) for histological examination. Tissue samples were taken routinely from the heart, liver, kidney and spleen. Other tissues were taken if a part appeared abnormal grossly, including tumorous-like growths.

Tissues were processed in the usual manner and the sections stained with hematoxyin and eosin. In a few cases a connective tissue (Mallory Triple Stain) stain was used to show a greater contrast between normal and abnormal tissues.

Samples for microbiological examination were not taken routinely. However, in three cases of epicarditis which were cultured there was no growth seen on blood agar.

IV. RESULTS AND DISCUSSION

A. Hematological Studies

Dogs were given a routine hematological examination as they were obtained for experimentation. Table 5 is a summary of the presurgical hematological data of 50 normal dogs used in this research project.

Table 5. Pretreatment hematologic data from 50 normal dogs

	Average	Range
Hemoglobin	16.5	(12.3-19.4) gm/100 ml.
Hematocrit	45.5	(36-55) percent
RBC 10^6	7.1	(4.5-8.7) cu. mm.
WBC 10^3	12.0	(6.1-22.2) cu. mm.
Differential WBC (%)		
Mature Neutrophils	70.0	(51-90)
Immature Neutrophils	3.0	(0-10)
Eosinophils	3.5	(0-13)
Basophils	.5	(0-4)
Lymphocytes	19.0	(7-34)
Monocytes	4.0	(0-15)

Hematological studies are of utmost importance in any physiological study as well as in any clinical study. Therefore, blood samples from each dog were studied at intervals to follow any possible changes occurring in the blood picture. Since dogs were sacrificed at various intervals throughout the research, some dogs were studied only once postsurgically while others were studied several times over periods of up

to 45 weeks. Generally, speaking, infarction dogs were sacrificed from 1 to 4 weeks following surgery whereas the epicarditis and valcular insufficiency dogs were kept for much longer periods.

Serial hematological data are shown in the appendix for all dogs arranged in groups as to type of operation performed. Very little can be said as to any constant changes which occurred in the hematology of the dogs undergoing surgery. All dogs stayed within normal limits in hemoglobin, hematocrit, and total erythrocyte count. Most dogs remained within normal ranges in total leukocyte and differential leukocyte counts; however, epicarditis dogs generally had elevated leukocyte counts early in the syndrome (not seen in shams) which returned to lower regions after several weeks. The only other general trend noted was in the valvular insufficiency dogs where a higher eosinophil count was present following surgery. It was thought that this might be due to a reaction to the silk foreign body in the atrium; however, this could not be confirmed on histological study of the area involved.

It can be said generally that hematological studies are of little aid in determining the presence or extent of lesions of the heart in the three conditions produced when strict asepsis was practiced as done in this research.

B. Normal Serum Enzyme Activity Assay Methods
    and Factors Involved

As dogs were selected for surgery, serum samples were
collected for GOT, GPT, and LDH determinations. These pre-
surgical values are within the normal range and compare very
well with those previously reported (31, 32, 116, 144).
Table 6 is a summary of the presurgical serum enzyme activity.
At least one other presurgical determination was made on
each dog and occasionally as many as three different pre-
surgical samples were analyzed. These varied as much as 10
units on SGOT and SGPT and up to 200 units on SLDH. However,
all determinations were within the normal ranges set by
original samples.

Table 6. Pretreatment serum enzyme values (Karmen Units)

	Transaminase (50 dogs)			SLDH (22 dogs)
	SGOT		SGPT	
	Method		Method	Method
	Hergt	Sigma	Sigma	Sigma
Average	24.6	24.2	21.2	220.7
Range	18-37	12-53	12-36	45-455

The Sigma method (145), which is a commonly used
clinical method for SGOT, was compared for accuracy with the
method of Hergt and Langin (64). It was found that there

was no significant difference between the two methods when SGOT was within normal range. In addition, the reproducibility of the two methods was studied. Both methods showed no significant difference in reproducibility; however, the Hergt method was more variable and approached the 5 percent significance level in variability. Tables 7 and 9 present the details of this study.

Table 7. Comparison of Hergt and Sigma methods on duplicate SGOT determinations

	Method	
	Hergt	Sigma
Average difference	1.0	1.0
Range of difference	-8.0 to 5.0	-6.0 to 4.0

No significant differences in either method on repeatability.

Hergt method is approaching 5 percent significance level on variability.

Since it had been reported that repeated freezing and thawing decrease serum enzyme activity, samples were frozen, thawed, assayed and refrozen, thawed and assayed again a few days to a few weeks later. Table 8 shows the results of this study. It was found that there was a significant loss of activity at the 1 percent level with the Sigma method and at the 5 percent level, approaching the 1 percent level, with the Hergt method.

Table 8. Comparison of samples analyzed after a second
freezing and thawing on duplicate SGOT deter-
minations

	Method	
	Hergt	Sigma
Average difference	2.4	2.3
Range of differences	0 to -8***	0 to -6***

**Significant at 5 percent level approaching the 1
percent level.
***Significant at 1 percent level that there is a
loss of activity.

Table 9. Comparison of Hergt vs Sigma method at various
SGOT concentrations

	SGOT Concentration (units)					
	15 - 39		41 - 69*		70 - 410*	
	Hergt	Sigma	Hergt	Sigma	Hergt	Sigma
Average	25.6	24.6	48.8	51.8	159.1	202.4
Range	18-38	17-38	40-62	41-69	70-320	75-410

*Significant at the .1 percent level.

In comparing the Hergt method with the Sigma method at
increased serum enzyme concentrations, it was found that
there was a significant difference between the two methods
at the 0.1 percent level (See Table 9, and Figures 1 and 2).
However, since neither method could be compared with a known
concentration of enzyme, it is impossible to say which method

Figure 1. Graphic representation of SGOT levels of
           selected dogs following myocardial infarction
           (Sigma method).

UNITS
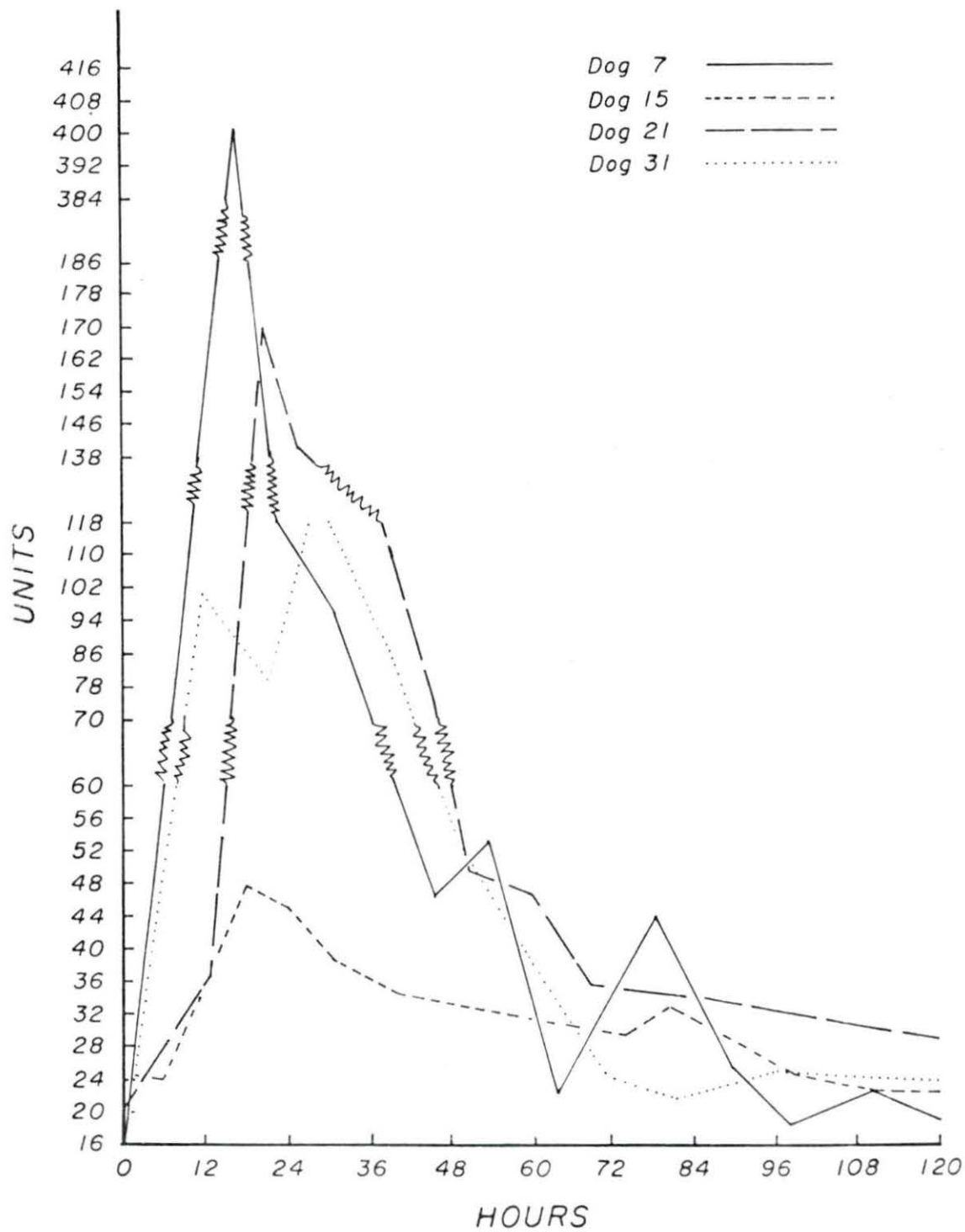
Figure 2.   Graphic representation of SGOT levels of
            selected dogs following myocardial infarction
            (Hergt method).

UNITS
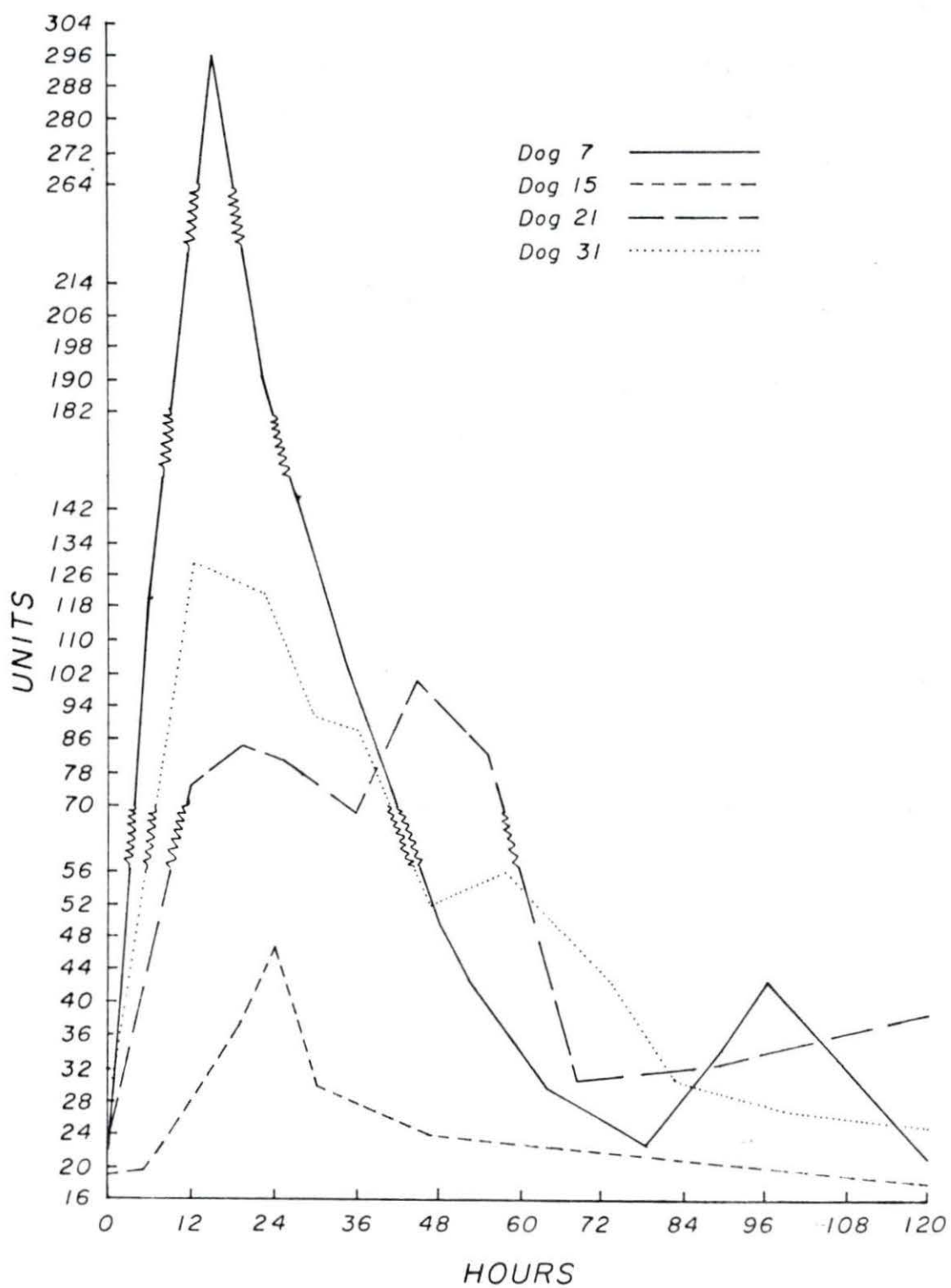
is the most accurate at these increased concentrations. It is thought that the Sigma method is the more advantageous because it spreads out the range of activities, thus separating abnormally high activities from the normal low activities.

Since it was reported by Ranke et al. (126) that there may be a difference in serum enzyme concentration in human subjects with age, dogs which were divided into three age groups for ECG purposes were analyzed as to serum enzyme concentration from presurgical data. Table 10 is a compilation of the results. It was found there was no significant difference in serum enzyme activity due to age differences, and age was not considered as a factor in further studies.

Table 10. Normal serum enzyme levels arranged as to age[a] (Sigma method)

Age	No. dogs	SGOT[b]	SGPT[b]	No. dogs	SLDH[b]
1	11	22.1 (12-28)	21.4 (13-30)	8	160.6 (70-325)
2	28	25.8 (13-53)	21.2 (12-35)	12	260.4 (140-455)
3	11	21.6 (14-30)	21.1 (16-36)	4	136.2 (45-200)

[a]Age differences are not significant statistically.

[b]Average and range.

C. Surgery and Associated Factors

As described previously, three types of cardiac pathology were produced by surgical methods. Each surgical procedure was followed by serial enzyme and ECG studies. All dogs were necropsied and gross and histopathological studies were made of organs and tissues. Each of these studies will be discussed under separate headings. Table 11 is a summary of surgery performed.

Table 11. Summary of experimental surgery

Procedure	No. Operated	No. Lived	No. Necropsied
Infarction	17	14	17
Sham	8	8	8
Vulvular insufficiency	11	5	11
Sham	5	5	5
Epicarditis	6	6	6
Sham	3	3	3
TOTALS	50	41	50

D. Serial Enzyme Studies Following Surgery

1. Myocardial infarction studies

Seventeen dogs underwent surgery to produce myocardial infarction. Two of these dogs did not survive surgery and one

died 10 hours after production of myocardial infarction.
Fourteen dogs had various degrees of myocardial infarction
produced. Table 12 is a summary of enzyme activity presur-
gically and peaks reached.

Eight dogs were sham-operated. All dogs lived and serial
enzyme activity determinations were made for three to four
weeks. Table 13 is a summary of enzyme activity presurgi-
cally and peaks reached.

One dog, No. 25, had two infarctions produced. While
attempting to put a ligature around the anterior left des-
cending coronary artery, it was accidentally punctured. The
artery had to be ligated to stop the hemorrhage. Several
weeks later the dog underwent surgery again and a second in-
farct was produced by ligating the left posterior descending
coronary artery (See Figure 14, Appendix B). Upon necropsy
one dog, No. 38, was found to have an accompanying epi-
carditis.

The serial serum enzyme studies indicate that activity
starts to increase at 8 to 15 hours following infarction.
Peaks are reached at 18 to 24 hours with SGOT and SGPT at
25 to 30 hours with SLDH. It has been reported (60, 85,
132), as described previously, that SGPT does not rise to
any significant level in myocardial infarction of humans.
However, it was reported (132) that SGPT may rise following
myocardial infarction in the dogs. Cornelius (31) feels

Table 12. Enzyme levels of infarction dogs (Karmen units)

	Method			
	Hergt	Sigma		
	SGOT(14)[a]	SGOT(14)	SGPT(14)	LDH(9)
Presurgery I				
average	23.5	23.4	22.8	242
range	19-32	14-37	17-36	130-450
Presurgery II				
average	25.2	22.4	21.0	283 (5)
range	20-38	13-32	18-25	170-500
Range of peaks[b]	40-320	49-410	21-240	280-1225

[a]Number of dogs in parenthesis.

[b]Began to elevate from 8-18 hours post surgery. Transaminase reach peak in 12-31 hours and LDH, 5-10 hours later usually. Transaminase remain elevated for 25-60 hours, LDH, 10-20 hours longer.

Table 13. Enzyme levels of sham infarction dogs (Karmen units)

	Method			
	Hergt	Sigma		
	SGOT(8)[a]	SGOT(8)	SGPT(8)	LDH(3)
Presurgery I				
average	22.9	22.2	19.5	257
range	18-27	18-27	12-26	205-325
Presurgery II				
average	22.9	26.1	22.1	-
range	20-26	21-30	15-40	-
Range of peaks[b]	26-41	25-43	18-39	130-280

[a]Number of dogs in parenthesis.

[b]Time to reach peaks varied from 14 to 61 hours -- all returned to normal shortly after peak was reached and continued within normal ranges.

that elevated SGPT in dogs is indicative of liver necrosis alone. The results from this research indicate that SGPT may rise to high levels but not as high a level as SGOT (Figures 1, 2 and 3). This fact must be kept in mind when suspecting liver damage because of the high SGPT values, the heart could be involved instead of the liver. From the reports of other workers it would seem that the time-concentration curve would be more prolonged in cases of liver pathology than in those involving the myocardium. In addition, the increased SGPT activity will be nearly as high as, or higher than SGOT in necrosis of the liver.

This work indicates that SLDH is not as reliable as SGOT as an index of myocardial necrosis (Table 12 and Figure 4). Results are erratic (See Table 27, Appendix A) and because of the wide range of normal values, it was frequently impossible to confirm a diagnosis of myocardial infarction with this enzyme assay, i.e., although the serum activity might be increased several times the normal value for the particular dog involved, it often falls within what must be considered the normal range. This presents a real problem in clinical work where the clinician seldom has a "normal" for the dog presented.

SGOT and SGPT levels remained elevated for 40 to 80 hours depending somewhat on the amount of necrosis present, i.e.,

Figure 3. Graphic representation of SGPT levels of selected dogs following myocardial infarction.

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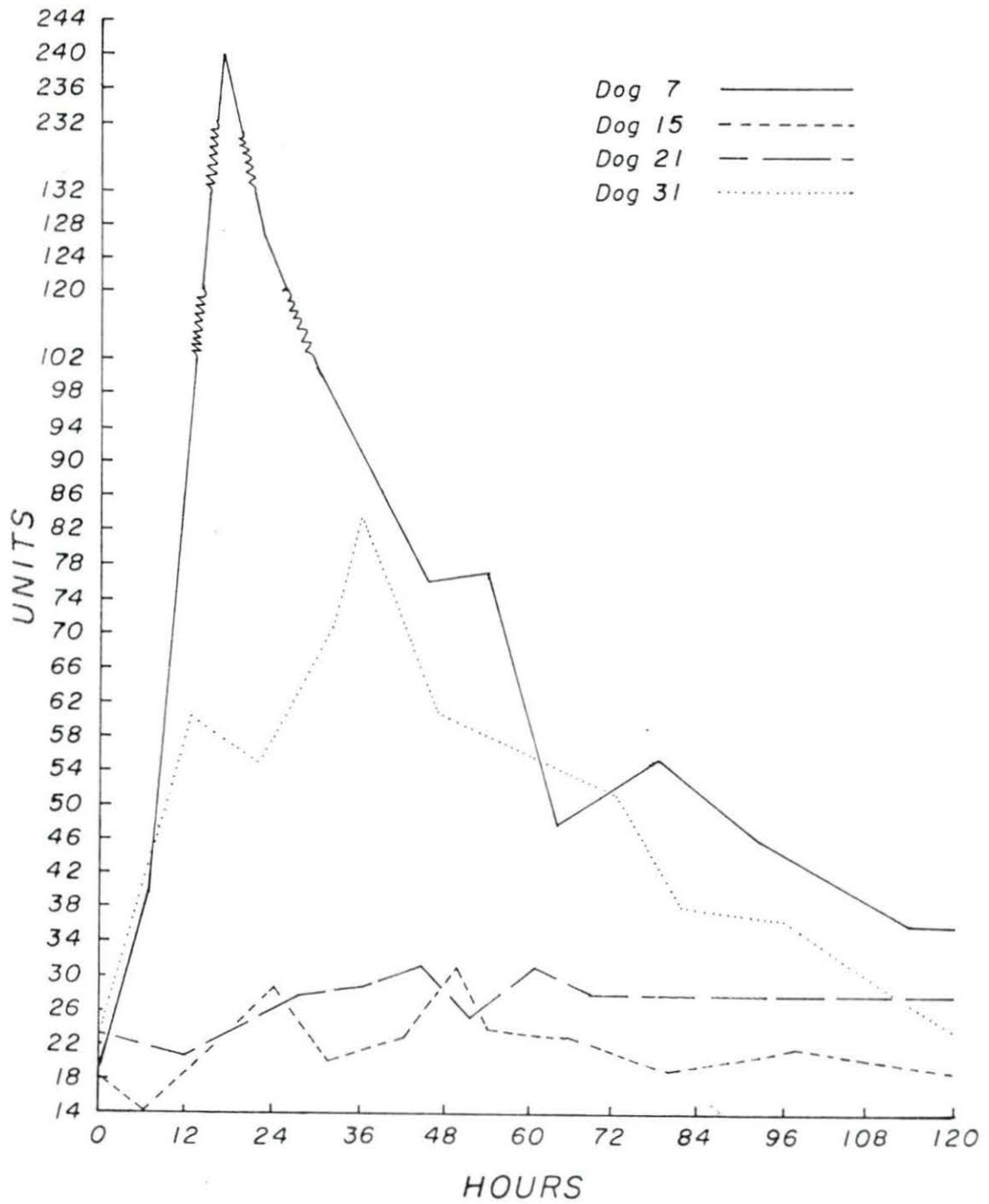
Figure 4.   Graphic representation of SLDH levels of
            selected dogs following myocardial infarction.
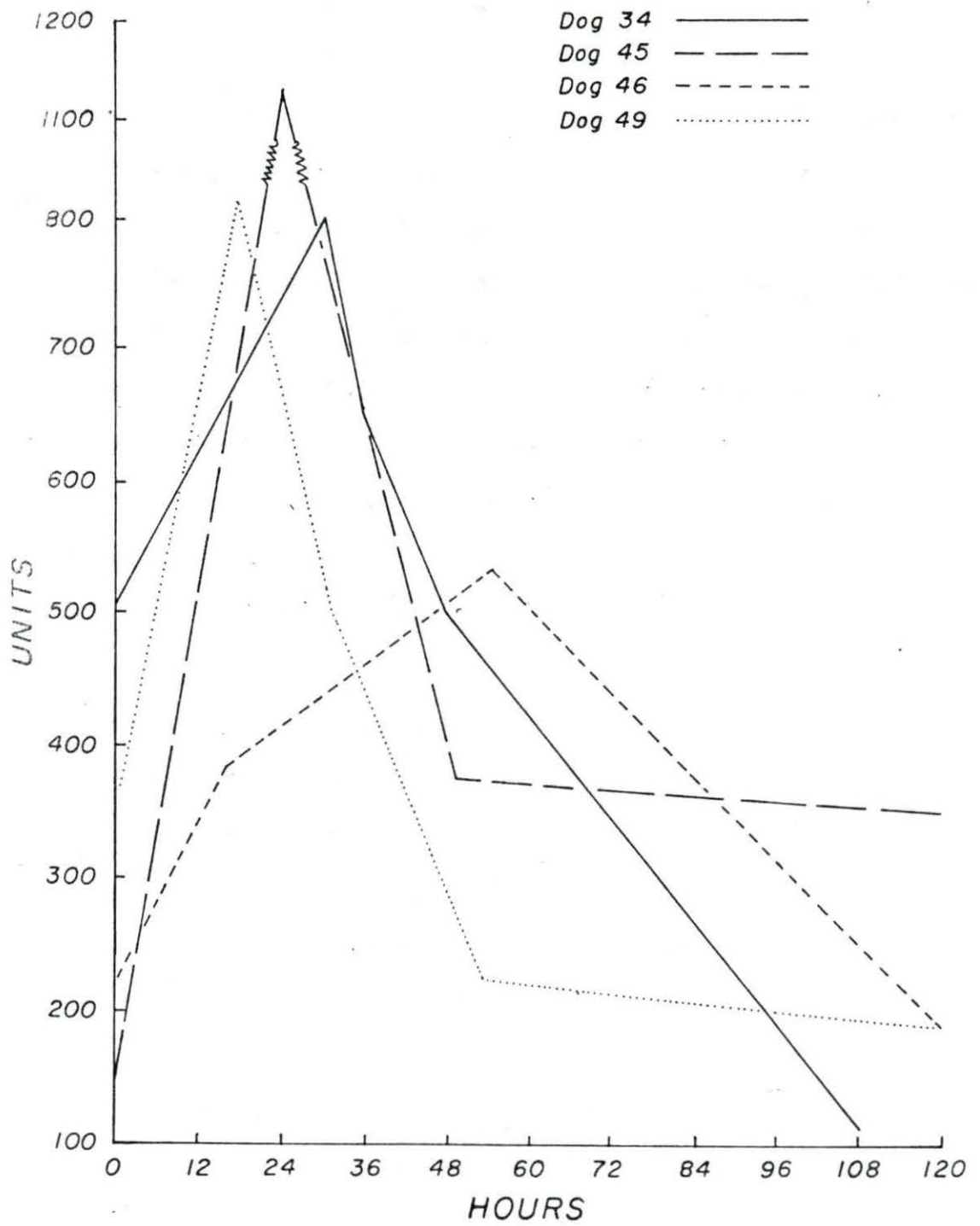
as the amount of infarcted tissue is increased the peak
concentrations are higher, and the length of time the enzyme
remains elevated is prolonged (See Table 14). However, this
is still a relatively short period since frequently the
patient may not be presented to the clinic until three to
four days after the onset of symptoms. It is reported (46,
72, 161) that SLDH levels remain elevated for longer periods
(six days) in humans. It was found in this work that SLDH
activity remained at abnormally high levels in dogs with myo-
cardial infarction for 10 to 20 hours longer than the
transaminases. Figures 1, 2, 3, and 4 depict the changes
in enzyme concentrations in dogs suffering from various
amounts of infarction. (See Tables 25 through 27, Appendix
A for serial enzyme changes of each dog with myocardial in-
farction.)

Once the enzyme returns to the normal range there was
seldom any marked elevation of the serum levels again in
these studies. However, one dog, No. 11, did show a rise
several weeks after production of an infarct. Upon necropsy,
two small infarcted areas were found, one where the ligature
had been placed and one more posteriorly on the endocardial
surface of the left ventricle. It is thought that the
second rise was due to this infarct; however, the dog did
not show any outstanding symptoms at this time. This will
be discussed in more detail later.

Infarcts were measured at the time of necropsy and these were correlated with the SGOT elevations. Table 14 gives the results. The results compare very favorably with the reports of other workers where tissue enzyme analyses were compared from necrotic areas and correlated with serum concentration. As a matter of interest SGPT was also correlated with amount of necrosis found at necropsy (Table 15). From this table it appears that only the more severe infarcts result in a great increase in SGPT and this may partially explain the controversy appearing in the literature regarding the elevation of SGPT in myocardial infarction. One can be misled by measuring only the diameter of the lesion since the depth of the infarcted area is not considered. In general the total amount of infarcted tissue correlated very well with the rise in SGOT. Individual dog serial SGOT and SGPT relating to amount of infarction are presented in Tables 25 and 26 (Appendix A).

As can be seen from Table 13 most of the sham-operated dogs remained well within normal serum enzyme ranges following surgery. However, a few animals did approach very high normal values or low abnormal values (40 units or over). Individual serial levels for the first 90 hours following surgery are shown in Table 28 (Appendix A) for sham-operated dogs. Serum levels continued within normal ranges until

Table 14. Comparison of presurgical and postsurgical SGOT levels of dogs with myocardial infarction (Sigma)

No. dogs	Dia. inf.	Pre-surg.	Hours postsurgery					
			17 - 22	23 - 27	28 - 34	35 - 41	42 - 50	51 - 72
4	< 1 cm.	20.5 (18-22)	63.5 (48-75)	59.0 (45-64)	45.5 (39-57)	39.2 (35-51)	34.0 (30-42)	32.0 (30-35)
3	1-2 cm.	27.7 (18-37)	150.3 (121-170)	108.3 (88-140)	105.7 (82-130)	78.3 (50-118)	51.0 (30-75)	39.3 (29-50)
7	> 2 cm.	23.1 (14-32)	277.1 (80-400)	236.6 (118-410)	139.7 (72-280)	69.9 (45-150)	64.7 (40-130)	38.6 (25-65)

Table 15. Comparison of presurgical and postsurgical SGPT levels of dogs with myocardial infarction

No. dogs	Dia. inf.	Pre-surg.	Hours postsurgery					
			17 - 22	23 - 27	28 - 34	35 - 43	44 - 50	51 - 72
4	< 1 cm.	24.5 (17-36)	38.5 (24-48)	39.2 (29-48)	34.2 (20-42)	36.2 (23-41)	36.2 (31-46)	29.5 (20-40)
3	1-2 cm.	26.0 (20-30)	34.3 (25-44)	33.7 (27-42)	33.3 (28-39)	34.7 (29-38)	30.7 (25-36)	23.3 (20-28)
7	> 2 cm.	20.4 (17-24)	125.9 (60-240)	118.9 (55-220)	110.4 (65-220)	105.1 (69-171)	83.1 (55-139)	46.7 (29-64)

85

sacrifice. Figure 5 depicts the levels of each of the enzymes at various times following surgery.

The exact reason for the small elevation occurring has not been determined. It may be just coincident with a normal physiological elevation, but more likely it is from damage to skeletal muscles which occurred on two or three occasions in attempting to isolate ligatures. However, this does not seem quite logical since transaminase activities following thoracic surgery were seldom over 100 units GOT and then much more skeletal muscle was damaged. A third possibility could be some liver damage following the repeated use of sodium pentobarbital, however, here again, it seems the liver could tolerate the anesthetic dose without causing any harm. Perhaps it is a combination of these and other factors. Since much of the physiology involved is not understood at this time, the answer will have to remain speculative for the present.

Serum GOT and GPT concentrations can be a definite aid to the diagnosis of myocardial infarction in dogs. More work needs to be done with SLDH before it is valuable in the diagnosis of myocardial infarctions in dogs.

2. Epicarditis studies

Nine dogs have been included in this group. Of these, three were sham-operated. Table 16 presents presurgical data as well as postsurgical averages on dogs with pathology

Figure 5. Graphic representation of enzyme levels of
selected sham-operated myocardial infarction
dogs (Sigma).
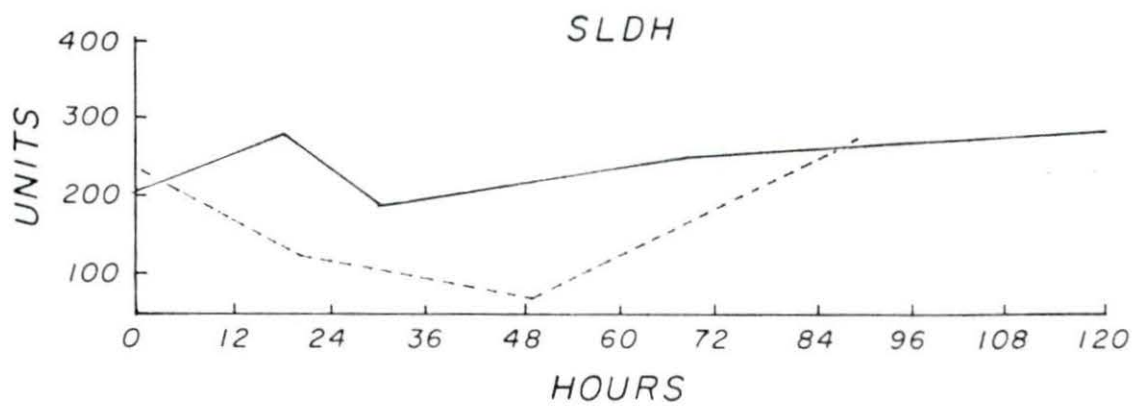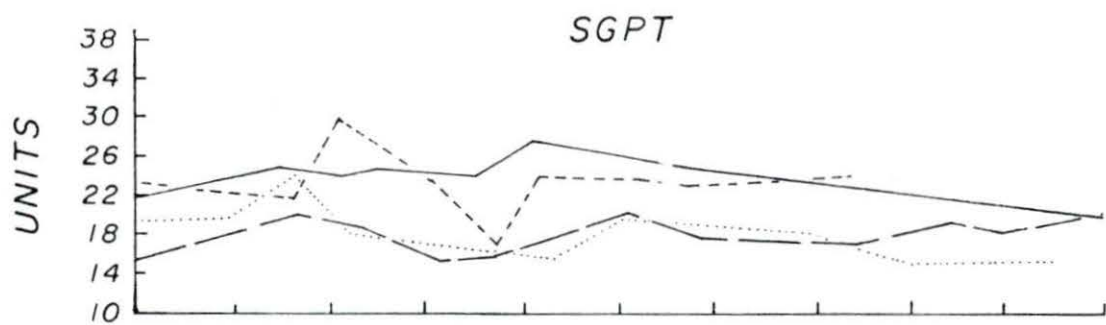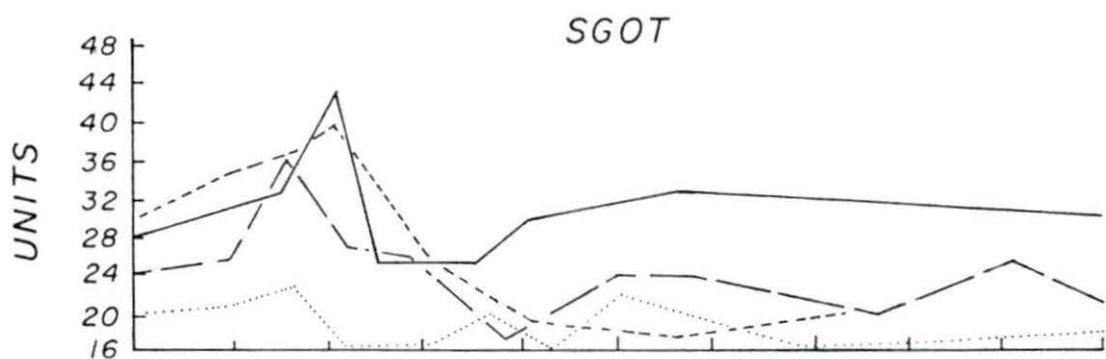
produced. All but one dog remained well within normal range. This dog, No. 10, presented an increase in both SGOT and SGPT of 48 and 37 units, respectively, four months after surgery. This was apparently a transient rise which had disappeared when another serum sample was taken two weeks later. No pathology which could account for this rise was found upon necropsy four weeks later. Dog 43 showed a progressive rise in SLDH from a presurgical value of 200 units up to 555 units at 5 weeks. This level then declined gradually back to 255 units at 4 months. The reason for this rise is not known, but is believed to be a result of the natural variation of the normal levels and of the test. Individual serial enzyme data are shown in Table 29 (Appendix A).

Table 16. Enzyme levels of dogs with epicarditis (Karmen units)

	Method			
	Hergt.	Sigma		
	SGOT(6)[a]	SGOT(6)	SGPT(6)	SLDH(2)
Presurgery I				
average	22.7	24.7	18.8	-
range	18-29	14-33	13-23	120-200
Presurgery II				
average	28.0	25.0	20.5	-
range	22-31	16-30	16-27	125-130
Postsurgery[b]				
average	26.6	26.0	22.9	246 (4)
range	18-44	13-48	12-37	100-555

[a]Number of dogs in parenthesis.

[b]Average for samples taken at intervals for three months or more.

Data from sham-operated dogs appeared to be well within normal ranges for the three enzymes upon serial study. Table 17 shows presurgical and postsurgical averages and ranges. Individual serial enzyme data are shown in Table 30 (Appendix A).

From this study it can be concluded, concurring with the reports of other workers, that serum enzyme levels are of little value in diagnosing an epicarditis and peri-carditis. However, they might be an important negative finding when considered in conjunction with clinical symptoms and ECG recordings. Figures 6 and 7 depict serial enzyme levels in epicarditis dogs and shams.

Table 17. Enzyme levels of sham-operated dogs for epicarditis (Karmen units)

| | Hergt | Sigma | | |
	SGOT(3)[a]	SGOT(3)	SGPT(3)	LDH(2)
Presurgery I				
average	23.0	19.3	19.7	-
range	20-27	18-21	16-23	75-150
Presurgery II				
average	20.7	18.3	19.0	-
range	16-26	16-20	18-20	75-130
Postsurgery[b]				
average	25.1	23.8	19.9	124
range	14-36	14-36	14-30	75-225

[a]Number of dogs in parenthesis.

[b]Average for samples taken at intervals for three months or longer.

Figure 6. Graphic representation of serial enzyme levels of selected epicarditis dogs (Sigma).

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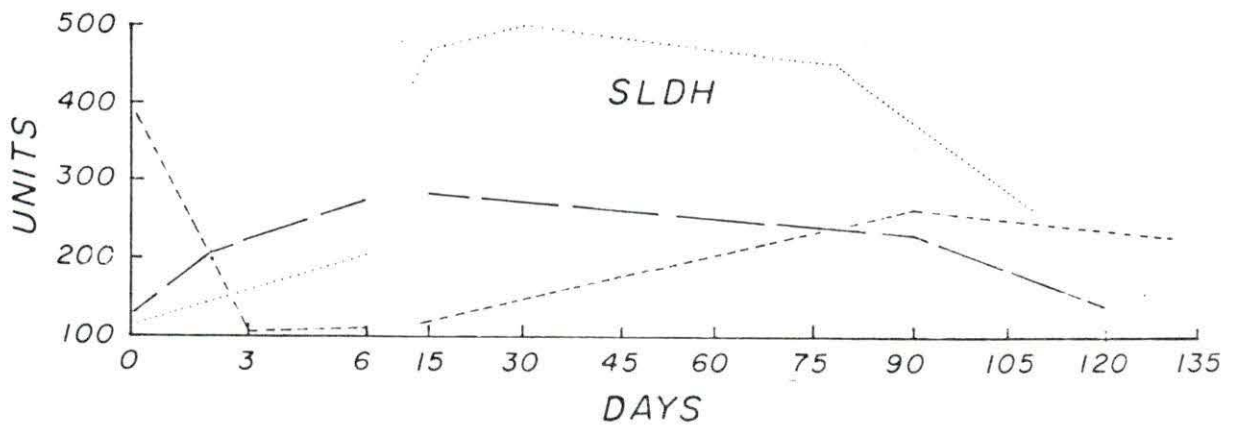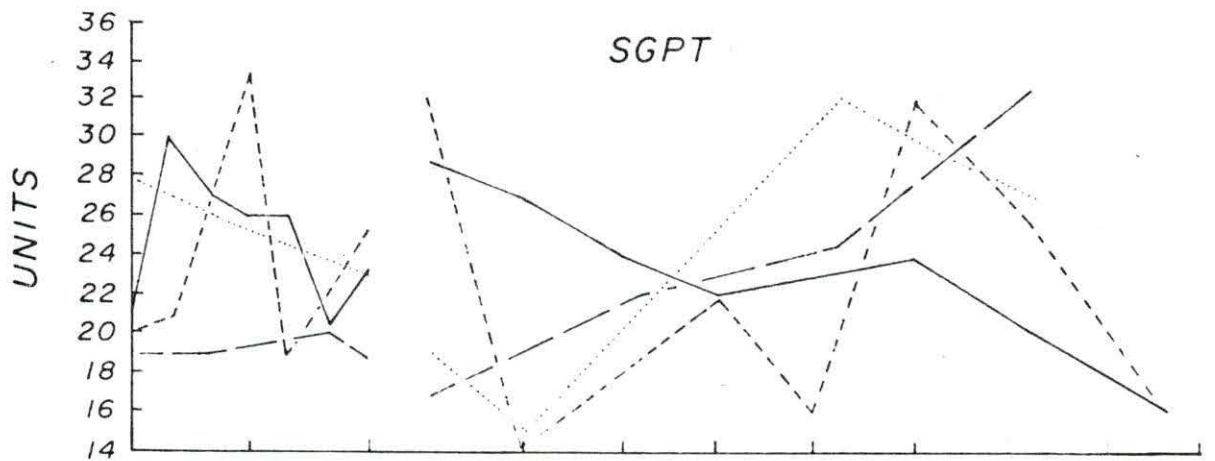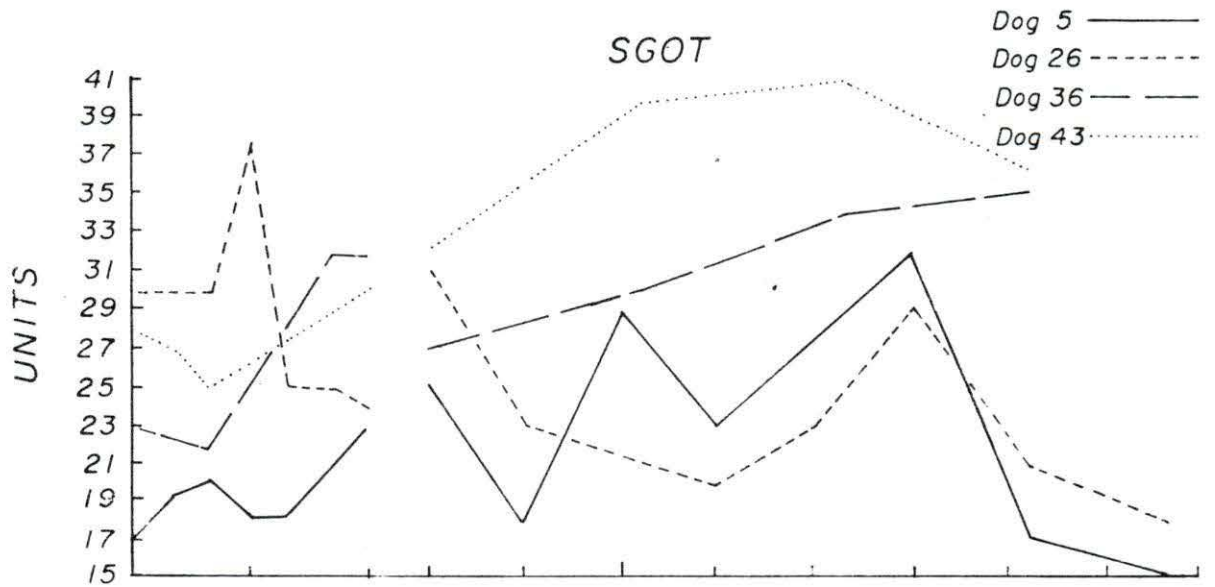
Figure 7. Graphic representation of serial enzyme levels
of selected sham-operated epicarditis dogs
(Sigma).
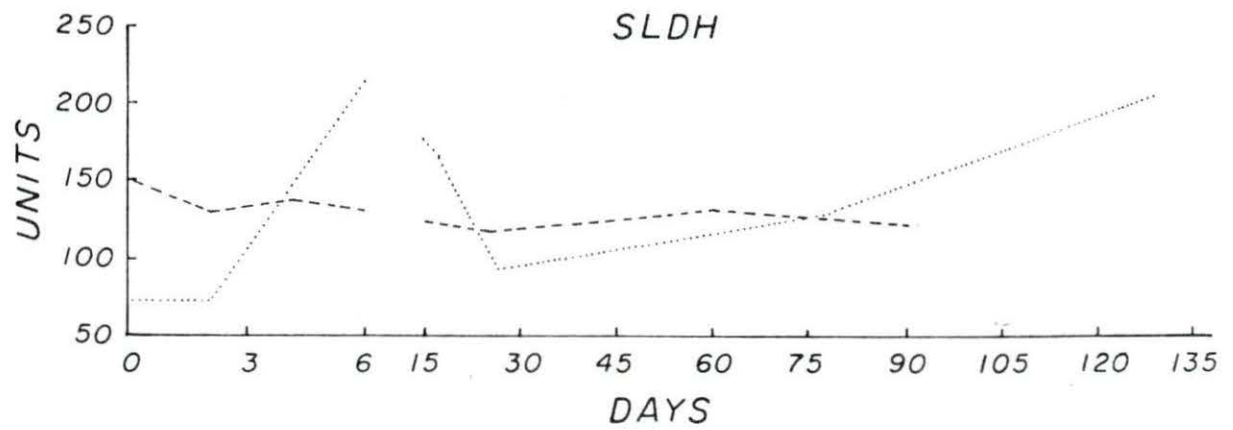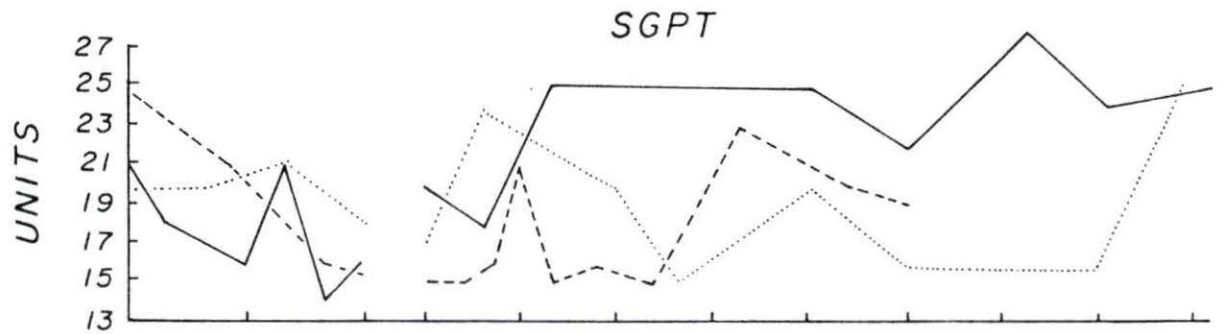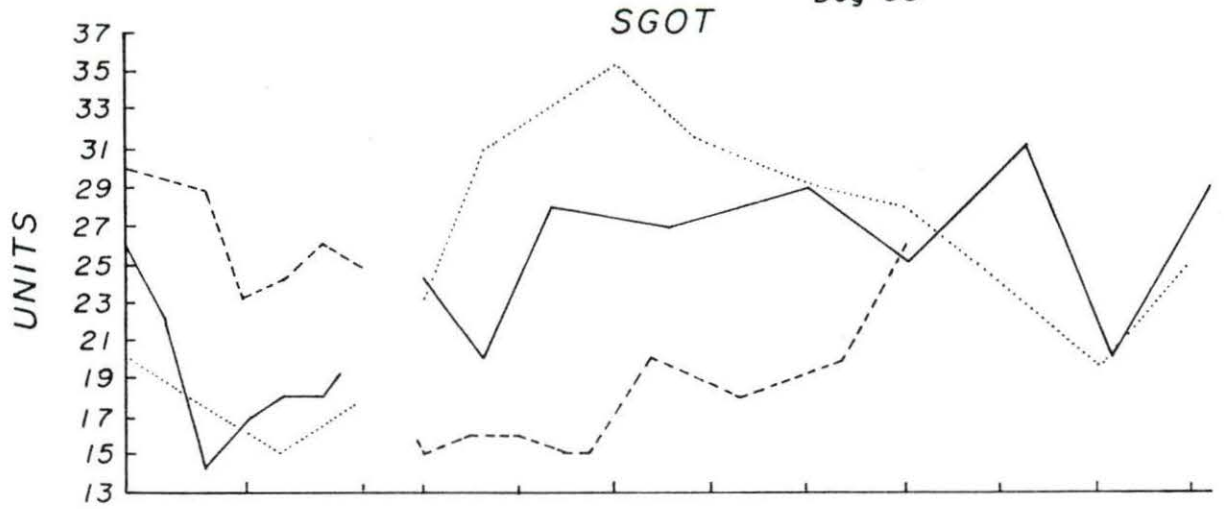
3. Valvular insufficiency studies

Sixteen dogs had surgery. Five of them were sham-
operated. Four dogs had a right A-V valvular insufficiency
produced and one a left A-V valvular insufficiency. The
rest died during surgery or shortly after from a variety of
causes. All dogs were necropsied and varying grades of
pathology observed in the dogs with lesions produced. These
lesions will be described in more detail later. Dog 42
showed the greatest amount of damage. This dog had shown
severe symptoms from the pathology and succumbed 72 days
following surgery from excessive fluids in the pleural
cavity. Table 18 summarizes the results of the serial enzyme
study. Figure 8 depicts the serial studies after the fourth
day when enzyme levels returned to near normal following the
surgical procedure. Table 31 (Appendix A) shows serial
studies of individual dogs through 12 weeks.

All dogs returned to normal following surgery and re-
mained at normal levels for several weeks. There was then a
trend to a slight increase in enzyme levels; however, for the
most part these stayed within normal ranges. Dogs 41 and 42
showed a rise in SGOT and SGPT over a period of about two
weeks which were definitely elevated beyond normal levels.
In both cases SGPT rose to higher levels than SGOT. The
sampling at this time was at two-week intervals so no time-
concentration curve was made. Still, it seems reasonable to

expect that some liver damage was occurring from the passive hyperemia. This theory was confirmed upon necropsy when histological and gross studies indicated necrosis of the liver. However, this damage apparently was not severe enough to cause clinical symptoms over and above those of the cardiac pathology.

Table 18. Enzyme levels of valvular insufficiency dogs (Karmen units)

	METHOD			
	Hergt	Sigma		
	SGOT(5)[a]	SGOT(5)	SGPT(5)	LDH(4)
Presurgery				
average	29.2	25.0	21.8	231.2
range	24-34	18-34	15-31	45-455
Peak				
average	120.8	139.8	56.6	421.8
range	75-215	80-230	23-115	177-590
Time to peak				
hours	17-21	17-25	17-21	25-50
Time to normal[b]				
hours	55-100	55-100	50-90	60-100

[a]Number of dogs in parenthesis.

[b]Dogs returning to normal remained within normal range except dogs 41 and 42.

Table 19 is a summary of the sham-operated dogs. Results were very similar to those seen in the dogs with lesions produced. However, once dogs returned to normal serum levels they continued within normal ranges. The serum levels of all three enzymes remained quite stable throughout

the research. Dog 4 remained in the doubtful zone of 40 to
60 SGOT units throughout the rest of his life; however, this
dog had a high presurgical level of 53 units. This points
out the fact that certain animals may have normal levels in
what could be considered indicative of pathology in the
majority of cases. Hence, the clinician must consider the
overall clinical picture very carefully in those dogs showing
serum levels between 40 to 60 units. It is fairly safe to
assume that anything below 35 is normal. Figure 9 indicates
serial enzyme changes in representative sham-operated dogs.
Individual serial serum enzyme activity up to eight weeks is
given in Table 32 (Appendix A).

Table 19. Enzyme levels of dogs sham-operated for valvular
insufficiency (Karmen units)

	Method			
	Hergt	Sigma		
	SGOT(5)[a]	SGOT(5)	SGPT(5)	LDH(2)
Presurgery				
average	24.6	31.2	22.4	185
range	18-30	20-53	17-32	160-210
Peak[b]				
average	119.0	119.6	43.6	260
range	56-178	42-232	18-70	230-550

[a]Number of dogs in parenthesis.

[b]Peak at 17-27 hours. Peaks are usually a few hours
later in GPT and 10-25 hours later in LDH. Shams return
to normal in 50-100 hours and continue within normal range.

40
38
36
34
32
30
2
2
2
2
2
1
1
1

UNITS

Figure 8. Graphic representation of serial enzyme levels
of valvular insufficiency dogs (Sigma).

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4
3
3

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SGOT

Dog 20 ....
Dog 27 ———
Dog 30 —··—··—
Dog 41 ————
Dog 42 - - - - -

SGPT

SLDH

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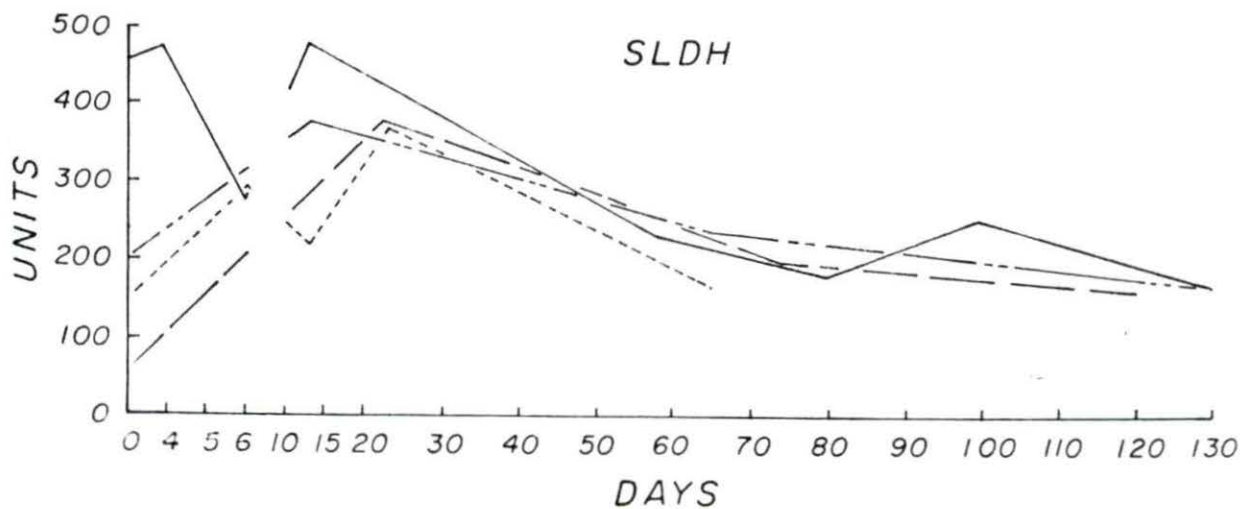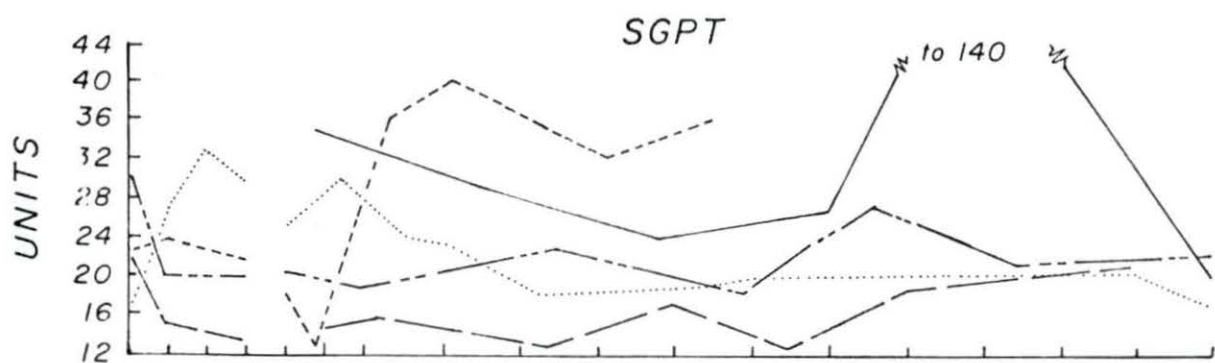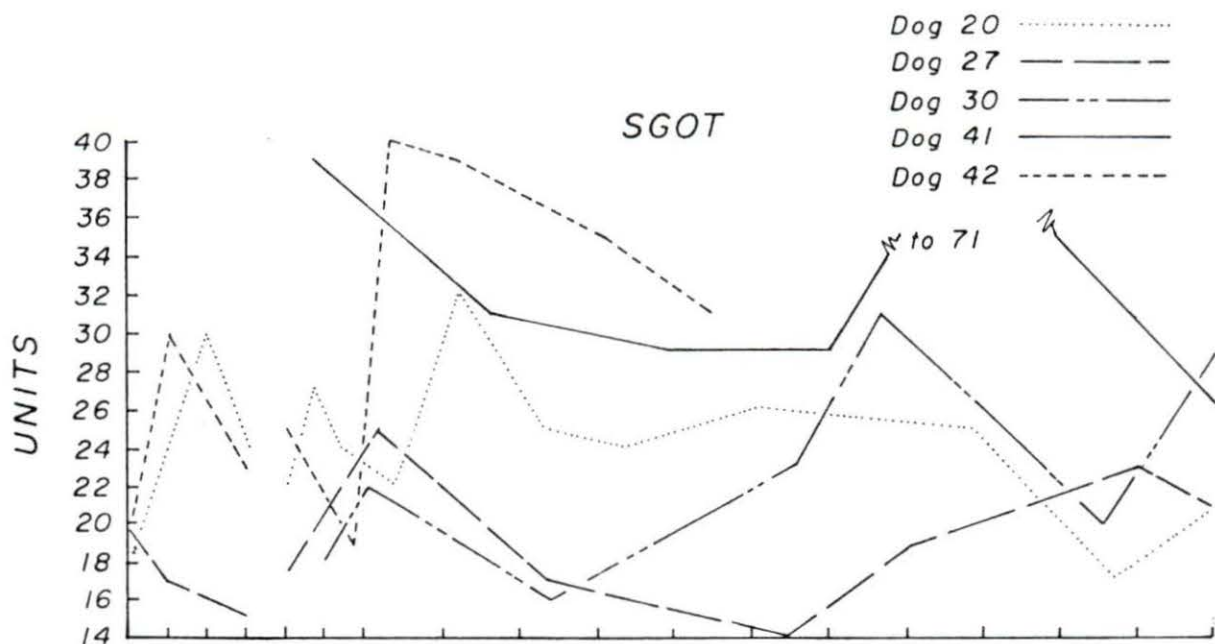
Figure 9. Graphic representation of serial enzyme levels
of sham-operated valvular insufficiency dogs
(Sigma).

UNITS

UNITS

UNITS

SGOT

SGPT

SLDH

DAYS
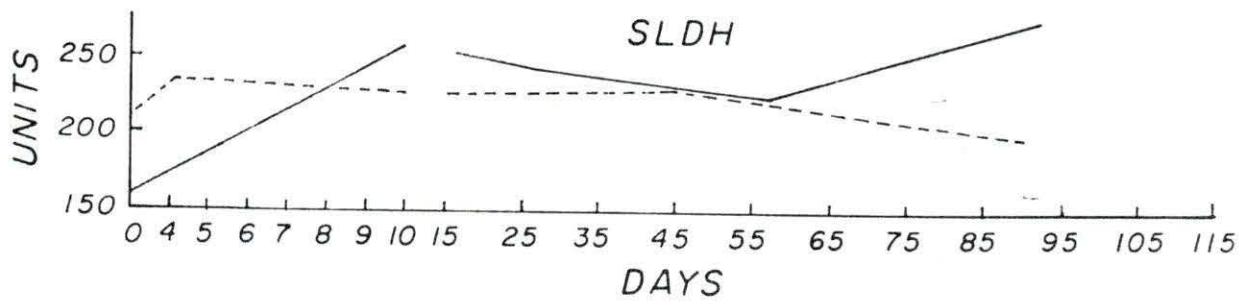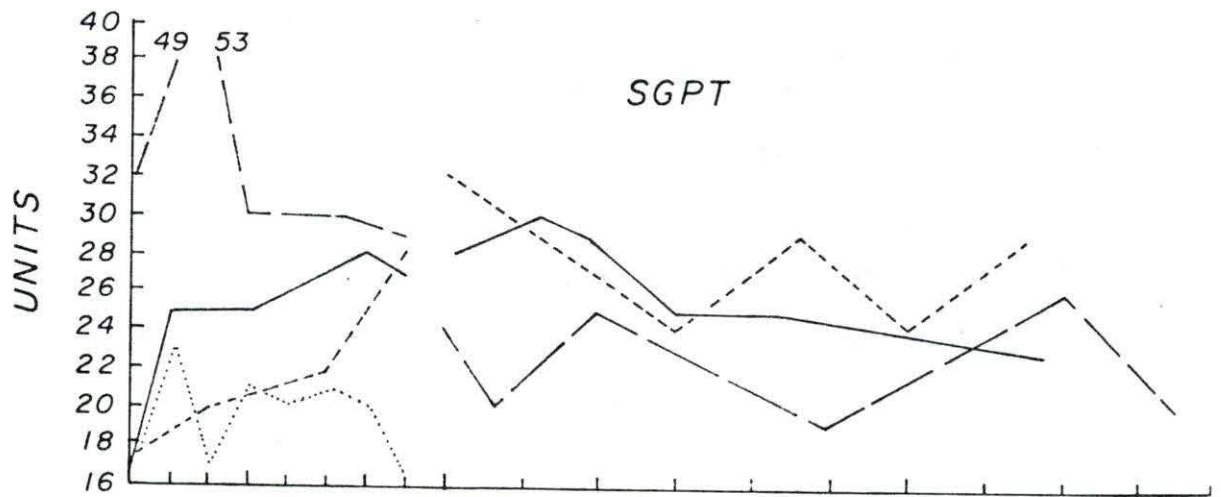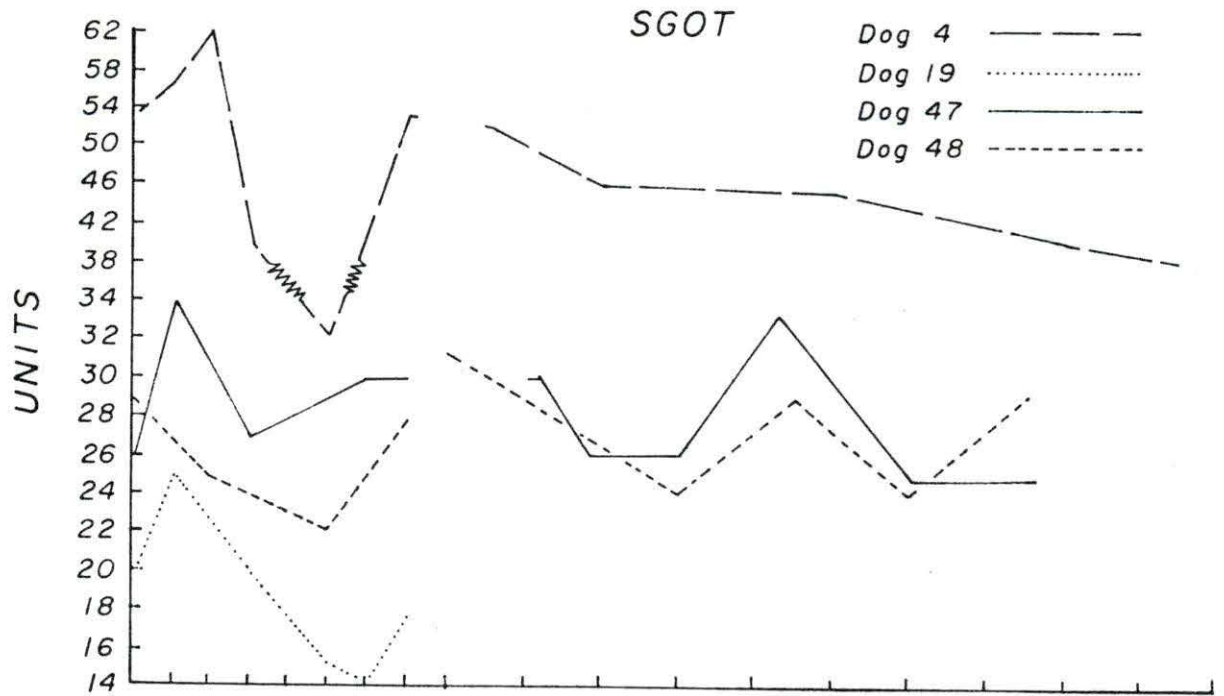
From this study it can be concluded that serum enzyme levels are of no aid in diagnosing valvular insufficiency. However, it must be pointed out that liver damage may occur secondarily to valvular insufficiency and increased SGOT and SGPT may follow. Therefore, the clinician must not lose sight of the cause and effect relation which occurs in many conditions.

E. Presurgical ECG Data and Factors Involved

It was found that ECG data could not be analyzed statistically with any degree of confidence because of the wide variability within any one recording with respect to voltage and time. However, measurements were made carefully and averages obtained from records of all individual leads and these means were used in further generalizations for comparison purposes and for discussion. Presurgical ECG's were taken on 46 dogs which were normal, healthy animals and in which the ECG appeared to be normal. Since the normal ECG in the dog has such a wide variability, certain parameters were examined as described previously in the hope of finding that factor or combination of factors which could be accepted as being normal in the greatest majority of recordings.

Because of the discrepancies reported in the literature on electrodardiographic values and the wide variability

103

found on preliminary studies on amplitudes of the various
complexes from day to day, a ratio was made and this is re-
ported instead of absolute measurements. This ratio in each
case is compared to R with other values, Q, S, or T, taken as
1 mm. (0.1 mv.). In cases where Q, S, or T is 0, the value
was omitted in calculating averages. However, these values
are shown in Tables 33 through 38 (Appendix A). In cases
where Q, R, or S was less than 1 mm., necessary computations
were made to compare R to 1 mm. In these cases the relative
error is quite large due to measuring difficulties and the
fact that increasing such ratios magnifies error. Tables 20,
21, and 22 are a compilation of the normal values obtained
from 46 mongrel dogs of both sexes and all ages. Since age
had been suggested as being a factor affecting ECG values,
these data were analyzed statistically for age differences.
The only significant change was in heart rate which decreased
with age.

Table 20. Age effect of dogs on heart rate

Age[a]	Heart rate	
Group 1	151	(100-175)
Group 2	141	(100-185)
Group 3	120	(65-175)

[a]Group 1: 4 to 12 months; Group 2: 1 to 5 years;
Group 3: over 5 years.

Presurgical electrocardiographic values are presented
as standards which is the usual way of reporting such data,
since it is unwise to break with tradition all together.

Table 21. Electrocardiographic standards of normal dogs
(1 mm. = .1 mv.)

	Lead			
	I	II	III	aVF
Q average	4.15	2.51	1.68	1.46
range	0.5-12.0	0.5-7.75	0.5-5.25	0.5-5.0
R average	6.95	19.20	15.78	18.42
range	1.5-15.0	3.0-33.0	5.0-31.0	8.0-33.0
S average	1.84	4.42	4.91	5.10
range	0.25-12.0	0.5-17.0	0.5-16.0	0.5-20.0
ST± average	.80	1.08	1.14	.91
range	0.5-1.0	-1.25-2.0	-1.5-2.0	-1.0-1.5

Durations (seconds)

	PR	QRS	QT
Average	.105	.052	.230
Range	.06--.18	.03-.08	.18-.28

Other workers (71, 86) have reported high incidences
of Q_I followed by an inverted T-wave and of S_{III} followed by
an upright T. The results of this study agree with such
reports. It was found that 49 percent of the recordings had
a Q_I, 88 percent had an S_{III} and 60 percent showed a negative

T in lead I. A negative T followed a Q-wave in lead I 95 percent of the recordings and an upright T-wave followed an S-wave in lead III in 89 percent of the records. (See Table 23). S_{II} and S_{aVF} occurred together in approximately 90 percent of the records. Upward T-waves occurred in 80 to 90 percent of the records in leads II, III and aVF. Q-waves and S-waves occurred most often in lead II and because of this it was used for all further R/Q, R/S, and R/T ratios. ST deviation occurred in only 20 percent of all recordings but in 46 percent of the dogs in one or more leads. However, as can be seen from Table 21, this deviation was quite small, being $\pm$ 1 mm. or less in 90 percent of the recordings showing deviation and never over 2.0 mm. (in two leads). ST deviation was always up in lead I and was seen in only 25 percent of the recordings showing deviation, or less than 11 percent of all dogs, and was always less than 1 mm.

Records taken on separate days presurgically followed similar patterns; however, there was a lot of difference in absolute amplitudes and some difference in duration of complexes. Ratios, although varying considerably, did not vary as much as the absolute amplitudes in R/Q and R/S. However, R/T varied about as much as absolute T amplitudes and T also varied back and forth from positive to negative in all leads; however, there was a trend to continue as positive in most instances in lead II, III and aVF. This same pattern was seen in sham-operated dogs.

Table 22. ECG data from normal dogs

	Lead[a]			
	I	II	III	aVF
R/Q average	3.4	11.2	14.9	16.8
range	0.5-22.0	3.0-42.0	2.5-44.0	4.5-46.0
R/S average	6.0	8.12	8.8	6.8
range	1.0-20.0	1.5-56.0	1.0-62.0	1.0-27.0
R/+T average	6.0	9.2	8.5	8.5
range	1.75-12.0	2.25-40.0	1.5-50.0	1.75-34.0
R/-T average	7.4	21.0	13.8	16.4
range	2.5-20.0	1.25-42.0	5.25-28.0	10.0-30.0
ST± deviation[b]	11	22	24	24

[a]Ratios expressed on basis of R:1 and 0 values omitted.

[b]Percent of total dogs showing deviation in lead.

Notching and slurring are very rare in occurrence in the presurgical records with the exception of the T-wave which takes on many odd forms. The only other notching which occurred was in the R-wave in lead I in one dog and in lead III in another.

P-waves were always upright in leads II, III, and aVF with one exception of an isoelectric P-wave in one lead III. P-waves are usually upright in lead I, but may occasionally be inverted or diphasic.

Sinus arrhythmia is a normal occurrence; other types of arrhythmias were not seen.

F. Postsurgical ECG Data

Since no absolute ECG pattern could be found consistently in recordings taken on dogs following production of the various pathological conditions, only those values which showed a trend to be different from the presurgical controls will be discussed.

Table 23 presents as percentages some of the complexes which were thought to possibly have some importance in diagnosis of cardiac pathology as compared with normal presurgical percentages.

Table 23. Incidence of ECG values expressed in percent during presurgical and postsurgical periods

Treatment	Q_I	Q_I-T	S_{III}	S_{III}+T	-T_I
Presurgery	49	95	88	89	60
Infarct[a]	75	14	100	71	11
Shams[a]	44	75	55	100	56
Infarct[b]	68	54	95	81	32
Shams[b]	13	100	75	100	12
Epicarditis	33	38	75	94	17
Shams	62	75	92	100	54
Valvular Insuff.	62	63	77	95	58
Shams	94	88	83	80	88

[a]Two to twelve days postsurgery.

[b]Two to seven weeks postsurgery.

Q-waves occur in approximately 50 percent of the cases
in each lead and any two leads having a Q-wave from the same
dog at any one time is a very random type phenomenon. Al-
though S_{II} and S_{aVF} occurred at the same time in 90 percent
of the presurgical records, the same pattern was found post-
surgically. S_{III} occurred in the greatest percentage of
records in each of the six groups, and it is followed by an
upright T in 90 percent or more of the records except in the
infarcted and valvular insufficiency dogs. It is thought
that the failure of the S in lead III to be followed by an
upright T is an important indication of myocardial damage.
In addition to the dogs with infarction and epicarditis, three
records in which it appeared in the valvular insufficiency
shams came from one dog in which the left ventricle had been
punctured rather then using the atrial approach, and conse-
quently had a small amount of myocardial damage. Another
factor which appears to be important is the presence of a
Q-wave in lead I being followed by an upright or absent T-
wave. In all cases the incidence of this phenomenon was
higher in dogs with lesions. This is especially true in the
recently infarcted dogs and in the epicarditis dogs. Twenty-
four of 30 recordings taken on 14 dogs, 2 to 12 days, fol-
lowing infarction showed: a) 16 with Q-waves with absent
or upright T-waves in lead I, b) 6 with S-waves with inverted
T-waves in lead III, and c) 2 showing both a and b. In

addition, 3 showed a Q-S complex in lead I and one showed it in lead III. Six showed ectopic beats at 2 to 3 days following surgery and 4 showed inverted P-waves in one or more leads.

In the six remaining records four had inverted P-waves in lead I and three of these had ST deviation in 2 or more leads. However, two looked normal. Figures 39 through 48 (Appendix B) show the appearance of the various complexes discussed.

It was thought that the decreased percentage of negative T-waves in lead I might be of some importance. However, its occurrence in only about 50 percent of normal records and infarct shams having a decreased percentage prevent this observation from being of any consequence. ST deviation did not turn out to be as good an index of cardiac pathology as had been anticipated from preliminary studies. ST deviation did occur following the production of pathology, however, a large percentage of normal ECG's showed ST deviation also. But, as was pointed out earlier, the deviation in presurgical normals were quite small. This same pattern was seen in sham-operated dogs (See Table 24) where a good share of the dogs showed ST deviation in 2 or more leads. Here again the values were usually 1 mm. or less. ST deviation did occur more often in dogs with pathology than in shams except the early infarction dogs. This in itself cannot be considered

to be especially important in the light of the normals. Here
is one phase where absolute measurements are probably war-
rented for in the infarcted dogs 64 percent of the records in
which deviation occurred were 2 mm. or more in the early
stages and 82 percent in the later stages. The R/ST ratios
did not show this difference as well as expected. Deviation
up or down seemed to be a random occurrence.

R/Q ratios varied considerably. Q-waves were not present
in many cases and when they were present they were often so
small that measuring and calculation of ratios were subject
to a large error. No particular pattern was noticed. In-
dividual dog data on a serial basis are presented in Tables
33 through 38 (Appendix A) with respect to certain complexes
and values (R/S, R/T, Q_I, S_{III}, T-waves, QT and PR).

An observation which was noted, but which is not evi-
dent from Table 24, was that the R/S and R/T ratios decreased
in the recordings following production of lesions. Actually,
the R did not decrease in size so much, in fact it may have
even increased, but both S and T amplitudes were increased.
The reason the table does not show this well is that some
large ratios increased the over-all average. The figures
for negative T are not very reliable because only a very few
records showed negative T_{II} (12.5 percent and 59 percent of
these were in infarcted dogs). Since negative T occurs in
lead II in a relatively high percentage of the records after

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infarction it might be considered as having some importance. However, if one examines individual serial records (Table 33, Appendix A) one sees the pattern is very random.

Time durations of the various complexes varied so much that they are relatively unimportant as diagnostic aids for the three conditions present.

Notching of R did not occur as often as had been anticipated. Only 25 percent of infarction records from 2 to 12 days showed notching and less than 10 percent of the records after 12 days. The incidence of notching in recordings from the other groups was less than 3 percent.

Other than infarction dogs, ectopic beats were seen in only two recordings of a valvular insufficiency subject (dog 41).

In summary it may be said it is quite understandable as to why canine electrocardiography remains an empiric science. With the tremendous variations in the normal recording it is difficult to set up definite standards and deviations from these standards which can be considered definitely abnormal. From the above data the following points indicate pathology:

1. Presence of ventricular extrasystole (ectopic beats).
2. Presence and persistence of inverted P-waves.
3. ST deviation of 2.0 mm. or more.
4. Q-waves in lead I followed by positive T-waves.

Table 24. Comparison of complexes of dogs with lesions to shams

	Lead II[a]							
	I	IS	I	IS	E	ES	VI	VIS
	2 - 12 days		2 - 7 weeks					
R/S mean	6.0	7.6	6.1	6.8	12.6	17.5	13.8	15.2
range	0.3-28.0	1.0-21.0	1.25-22.0	1.0-16.0	3.0-29.0	1.5-44.0	1.25-66.0	1.75-64.0
R/+T mean	6.7	3.5	8.0	9.2	6.2	10.8	7.6	10.6
range	1.0-20.0	1.45-6.0	1.0-32.0	2.5-16.5	3.0-25.0	3.25-36.0	1.25-24.0	2.0-21.25
R/-T mean	7.1	17.0	20.9	0	7.5	20.0	32.0	3.75
range	1.0-28.0	-	6.75-39.0	-	-	-	-	3.0-4.5
ST± %[b]	33	45	73	28	62	31	42	14
% record[c]	50	75	55	33	62	56	66	25
PR mean	.114	.118	.108	.115	.123	.108	.121	.125
range	.08-.14	.10-.14	.08-.16	.10-.12	.10-.16	.10-.16	.08-.18	.08-.14
QT mean	.221	.229	.212	.234	.208	.228	.215	.208
range	.16-.28	.20-.26	.16-.26	.20-.26	.16-.26	.20-.28	.18-.24	.16-.24

[a]Amplitudes expressed as ratio of R to complex durations expressed in seconds.

[b]Percent of dogs showing deviation.

[c]Percent of records having deviation of dogs with deviation.

5. S-waves in lead III followed by inverted T-waves.

6. Decreased R/S and/or R/T ratios.

No correlation could be found between ECG recordings and the severity of cardiac lesions found upon necropsy or with the rise in serum enzymes. There are apparently no consistent changes in the ECG with respect to amount of pathology i.e., a small lesion will cause as much change as a large lesion if a change occurs.

G. Necropsy Findings

1. Infarction dogs

Fourteen dogs in which infarction was produced were sacrificed at various intervals from 10 days to 20 weeks following production of pathology. Three others were necropsied immediately after death. One of these dogs died of massive myocardial infarction 10 hours after surgery. The other two died from hemorrhage when the coronary artery was punctured or burst.

The 14 dogs sacrificed showed various amounts of infarcted tissue in the left ventricle ranging from less than 1 cm. in diameter and involving only the endocardium to those involving nearly one-half the left ventricular musculature and varying in depth from involving only the endocardial portion of the myocardium to being transmural in nature. (See Figures 14 through 20, Appendix B.)

Generally speaking most dogs had a very slight amount
of adhesions of the lung to the pleural wall and to the peri-
cardial sac in the area of surgery. There were adhesions of
the sac to the epicardium in every case. It seemed that the
larger the infarcted area was the more adhesions of the sac
to the epicardial surface occurred. Usually little other
gross pathology was noted. Those cases in which other ab-
normalities occurred will be found in the individual dog ne-
cropsy synopsis in the appendix (Appendix C).

Sham-operated dogs showed very little evidence of any
abnormalities. There was generally a small amount of ad-
hesions of lungs to pleural wall and/or pericardial sac in
the surgical area. Adhesions of the sac to the epicardium
were minimal and often completely absent. The kidneys of dog
14 were very jaundiced in appearance but were of normal size
and no signs of pathology could be seen. Dog 32 showed two
small infarcted areas in the left kidney, one old depressed
scar tissue area and one raised and red. The liver of dog
33 seemed to be enlarged and quite congested; however, no
other signs of pathology were noticed. A small circumscribed
tumor was found in the area of the bifurcation of the
uterine horns in dog 40.

Other dogs appeared to be completely normal. It is be-
lieved that pathology found in the four dogs discussed above
did not contribute large enough amounts of enzymes to the

serum to be of any great significance. The adhesions which occurred could possibly affect the ECG because of the effect of position. The exact effect, if any, would be very difficult to access.

Figures 12 and 13 (Appendix B) show examples of hearts of sham-operated dogs.

2. Epicarditis dogs

Six dogs were necropsied in which an epicarditis and pericarditis were produced. (See Figures 21, 22, and 23, Appendix B). The amount of pathology did not vary much among individuals. In most cases about three-fourths of the surface of the heart was involved. In one case the entire pericardial sac was adhered to the epicardium and was very difficult to remove (Figure 21). This dog died from pathology produced. The surface of the heart was generally granulated in appearance with some areas of small hemorrhage and hyperemia. A purulent exudate was never seen. There was no odor from any of the specimens. However, one had a small amount of dark viscous fluid in the pericardial sac. This dog had been dead several hours before it was necropsied and there was a slight odor which was attributed to post-mortem changes.

As in the infarction dogs there were a few adhesions of lungs to the pleural wall in the area of the incision and

also to the pericardial sac. In all cases the amount of adhesions of the sac to the epicardium was extensive.

Three of the six specimens were cultured aerobically and anaerobically on blood agar. No growth was seen. It was thought that all cases were sterile.

The three sham-operated epicarditis dogs were very near to normal. There were no adhesions of the pericardial sac to the epicardium. There was no indication of any type of lesion in any of the hearts. Dog 18 had a fairly severe pleuritis on the right side. This was cultured and found to be negative for bacterial growth. This same dog had a slight right A-V valvular proliferative endocarditis. In dog 35 there was a slight amount of irritation (about 5 mm. in diameter) on the left ventricle apparently from the silicone rubber tube.

All other organs and tissues appeared to be normal.

3. Valvular insufficiency dogs

Eleven dogs were operated on to produce a valvular insufficiency. Four of these were done using the Markowitz (98) technique. Two died of cardiac rupture and one died from too great of insufficiency. Seven were done by the method described previously. The first two of these died during surgery, one from ventricular fibrillation and one from rupture of the anterior vena cava. The other five survived surgery and upon necropsy showed various degrees of insufficiency. Dog 41 had a left A-V insufficiency which was quite severe. There was also a negatative endocarditis

found on the right A-V valves, apparently a result of the
left A-V insufficiency. The liver was swollen and appeared
to be mildly cirrhotic. Dog 42 had the greatest amount of
insufficiency of the 5 dogs in this group. This dog showed
necrosis and cirrhosis of the liver grossly, plus a passive
congestion throughout. The other three dogs had milder A-V
insufficiencies, and showed nothing spectacular other than
some right ventricular dilation. See Appendix C for more
details. (See Figures 24 through 27 and 36 through 38,
Appendix B.)

Five dogs were sham-operated, one by the Markowitz
Method (No. 3) and four by open heart surgery. Dog 3 showed
a small area of scar tissue in the left ventricle where it
had been punctured. The other four hearts appeared to be
normal except for the area of silk in the atria where the
incision was made. There was a slight amount of adhesion
of lungs to the pleural wall and pericardial sac. There were
also adhesions of the sac to the heart in the region of the
sutures. These adhesions were easily broken down. There
were no other gross indications of pathology.

H. Histopathological Findings

1. Infarction dogs

The type of histopathology found in the infarcted area
of the ventricle of each dog was very similar in appearance.

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(See Figures 27 through 30, Appendix B.) These lesions were
characterized by predominant replacement fibrosis with scar
tissue formation, myocardial necrosis and infiltration of mono-
cytes and some calcification of the necrotic myocardium. In
some cases it appeared the area was enlarging as the cells
adjacent to the fibrotic area showed swollen granular myo-
cardial fibers with light, round, swollen or pyknotic nuclei.
Congestion and hemorrhage were often seen in and adjacent to
necrotic areas. In addition, adjacent areas of myocardium
which were pale and grey, yet not frankly necrotic, showed
considerable cloudy swelling with granular cytoplasm micro-
scopically. Nuclear changes were not prominant in these
cells.

Sections taken from the myocardium of sham-operated ani-
mals appeared to be normal.

In those dogs sacrificed earliest following myocardial
infarction there was some cloudy swelling of the liver with
some fatty infiltration. There was no evidence of actual
necrosis, however. In a few cases there were small foci of
swelling and some cells appeared granular, otherwise livers
appeared normal. In the dogs sacrificed later the livers
appeared to be normal.

Other organs, which were sectioned and studied micro-
scopically, generally appeared normal. In one case an
infarct was seen in a kidney. This was very small and the

rest of the section was normal. Sham-operated dogs were normal throughout.

The tumor found in dog 40 was a fibroma.

2. Epicarditis dogs

Pathology was confined almost entirely to the epicardial surface of the heart. In only one case was there any indication of the myocardium being involved. This dog showed some necrotic changes, pyknotic nuclei and some hyaline degeneration of the muscle fibers. In the other dogs the myocardium appeared to be entirely normal except for a hyperemia of the outer layers of muscle. The main changes seen were confined to a fibrosis with many spindle shaped nuclei of the connective tissue cells appearing. Polynuclear cells were minimal as was the appearance of other circulatory cells. In some areas there was hemorrhage on the epicardial surface. A few giant cells were noted throughout the area involved. There was also an increase in capillaries throughout the involved area. Figures 31 through 34 (Appendix B) are examples of histopathologic findings.

Studies of other organs and of the sham-operated dogs indicated no significant changes.

3. Valvular insufficiency dogs

Grossly cardiac dilatation in dogs was based upon the finding of enlarged cavernous ventricular chambers, thin

ventricular walls, and flattened papillary muscles. Micro-
scopic changes were also present. These changes were thin and
sometimes wrinkled or curled myocardial fibers.

In most cases thickening of the cusps of the A-V valve
involved occurred. In dog 41, where left A-V valve was im-
paired, the opposite A-V valve also showed this pathology.
The edge of the cusps consisted of proliferative fibroblasts
and collagen fibers. Figure 35, Appendix B, shows an example
of the valvular change.

No other changes were noted in the cardiac muscles. At
the sight of entry in the atrium there was a thin line of
scar tissue and some monocyte infiltration. However, cellular
changes were minimal and there was a noticable lack of
eosinophils which had been expected to appear in this area
because of the increase in the peripheral circulation.

In dogs 41 and 42 there was distinct evidence of early
cardiac cirrhosis of the liver. Central veins were very
enlarged and cells surrounding these veins were in various
stages of degeneration (Figures 37 and 38, Appendix B).
Other tissues showed excess interstitial fluids and most
organs showed cells with cloudy swelling. Both dogs were
suffering from a passive congestion. The other three dogs
in this group showed no significant changes upon histolog-
ical examination of any organs other than the heart.

Histological examination of the five sham-operated dogs
revealed only an area of fibrosis in the left ventricular

musculature of dog 3, and a thin line of scar formation in the atrium of the other four dogs. All other organs appeared to be normal.

I. Symptoms

Dogs in which myocardial infarction was produced showed symptoms of severe depression for three to seven days following surgery. Heart rate was usually increased as was respiration. In the first few days there were indications of pain. The dogs then showed rapid improvement and appeared to be normal in two to four weeks. It must be pointed out that dogs were maintained under cage rest and were not permitted to exercise or were not bothered for any reason other than routine care, taking blood samples, and ECG recordings.

Epicarditis dogs showed severe depression for approximately one week following surgery. Upon auscultation of the heart, fluids could be heard for a few days. This sound disappeared and no abnormalties could be auscultated on most dogs. One dog did seem to have a sound which sounded gritty for one day on the fourth day following surgery. The dogs generally showed improvement and appeared normal for several weeks. This was followed by a mild depression which became very severe in dog 37. This dog died three months after production of the epicarditis. Several dogs had a fremitus or thrill upon palpation of the femoral arteries and a decreased

pulse. This continued throughout the remainder of the experimental period once it had appeared. Dog 5 showed no symptoms after the first week and got along very nicely. In all cases appetite seemed to be normal.

Dogs with valvular insufficiency generally showed increased respiration and heart rate. They were more depressed than the epicarditis dogs but not as much as the infarction dogs early in the experiment. Dogs 41 and 42 suffered from periods of anorexia. They both developed a cough and some dyspnea. In addition dog 41 definitely suffered from an anasarca. This dog was treated with a diuretic and had a peritoneal puncture several times to remove the ascites fluid.

All dogs indicated a valvular insufficiency upon auscultation by various degrees of systolic murmur. The pulse of dog 41 was barely palpable. Other dogs had periods of intermittent fremitus in the femoral artery, but pulses remained fairly strong except dog 42 which had a fairly strong pulse at first but which gradually became weaker and was impalpable shortly before death.

V. SUMMARY

Various types of cardiac pathology (myocardial, in-
farction, epicarditis, and A-V valvular insufficiency) were
produced in 50 dogs by surgical methods. These dogs were
classified prior to surgery as normal based on physical ex-
amination, hematological studies, and electrocardiograms.

The upper ranges for normal serum enzyme levels were
40 units for glutamic oxalacetic transaminase (SGOT), 35
units for glutamic pyruvic transaminase (SGPT), and 500 units
for lactic dehydrogenase (SLDH). The clinical Sigma method,
which has been used in research also, for the assay of SGOT,
was compared with an established research method of Hergt
and Langin. It compared very favorably with the latter
method and in some respects was more advantageous.

It was found that repeated freezing and thawing of
serum significantly reduced the amount of enzyme activity.

It was further found that age is not a factor in
normal serum enzyme levels.

Based upon serial enzyme studies following the produc-
tion of myocardial infarctions it was found that SGOT was
the most reliable, of the three enzymes studied, as a diag-
nostic aid. In addition the relative amount of infarction
could be fairly well ascertained by the rise in SGOT activity.
It was found that SGOT began to elevate 8 to 15 hours

following infarction, reached peak levels (up to 15 times normal values) from 18 to 24 hours and returned to normal ranges within 40 to 90 hours. Also, SGPT may rise considerably, up to 10 times normal values, following the more severe infarctions. Its pattern was similar to SGOT although SGPT never reached the elevations of SGOT following infarction. SLDH was much more erratic, both for normal serum levels and for those following infarction. This enzyme reached peak values at 25 to 30 hours post-infarction and did not return to normal until 80 to 100 hours in most cases. However, because of its wide range of normal activity among dogs and because of its radical behavior following infarction, it cannot be recommended as a diagnostic aid for myocardial infarction in dogs at this time. Both SGOT and SGPT should be assayed because of the high levels of SGPT and SGOT seen in liver necrosis as reported by other workers.

Serum enzyme assays are of little aid in diagnosing epicarditis or valvular insufficiency in dogs; however, they may be an important negative finding when coupled with symptoms and ECG findings.

Routine hematological studies are of little aid in diagnosing any of the conditions presented.

Electrocardiograms from normal dogs were studied and it was revealed 1) when a Q-wave occurred in lead I, it was followed by an inverted T-wave 95 percent of the cases;

2) when an S-wave occurred in lead III, it was followed by
an upright T-wave in 89 percent of the records; 3) although
an ST deviation occurred in one or more leads fairly frequent-
ly (20 percent of all recordings in one or more leads I, II,
III, and aVF), it was never more than 2.0 mm. and in 95 per-
cent was not over 1.5 mm.; 4) inverted P-waves in lead II,
III and aVF and ventricular extrasystoles (ectopic beats) in
any lead never occurred; and 5) that there is considerable
variability from dog to dog and from day to day in voltages
and time intervals of the ECG.

Following the production of certain pathological con-
ditions of the heart it was found that certain changes in
the ECG may be indicative of pathology. These changes in-
cluded: the presence of ventricular extarsystoles; the
presence and persistence of inverted P-waves in leads II,
III, or aVF; the presence of ST deviation ± 2.0 mm. or more
in one or more leads; the presence of Q-waves in lead I
followed by an upright T-wave; the presence of S-waves in
lead III followed by inverted T-waves; and the presence of
decreased R/S and/or R/T ratios. No correlation could be
made with changes in the ECG following surgery with the amount
of pathology or with the rise of serum enzymes.

This research has presented many questions which need to
be investigated. It has been only a beginning into a vast
area of study in the realm of enzymatic chemistry in

veterinary medicine. Investigations should continue on all
species of domestic animals as there are known species
variabilities and there is always much danger in extrapolating
results from one species to another. In addition, because of
the many tissues containing relatively high concentrations of
the various enzymes, it is imperative that all pathological
processes which may contribute to the serum activity be in-
vestigated so there is less chance of error in diagnosis.
Finally, more basic biochemistry and physiology involved in
these processes must be studied further to understand the
significance of observed changes.

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VII. ACKNOWLEDGMENTS

encouragement and patience and for assuming the major share
of family responsibilities during the completion of this work.

VIII. APPENDIX A: TABLES

Table 25. Serial SGOT levels of dogs with myocardial infarction (Sigma method)

Lesion size	Dog. no.	Pre-surgery	Hours post surgery					
			17-22	23-27	28-34	35-43	44-50	54-72
< 1 cm.	15	18	48	45	39	35	31	31
	11	22	75	64	41	35	33	30
	38	20	68	64	45	36	30	35
	46	22	63	63	57	51	42	32
1-2 cm.	21	18	170	140	130	118	75	50
	25	37	160	97	105	50	30	29
	51	28	121	88	82	67	48	39
> 2 cm.	7	14	400	118	95	46	53	30
	24	18	140	193	72	45	49	25
	31	23	80	130	105	62	58	40
	34	27	320	260	110	66	76	47
	45	21	370	410	280	150	130	65
	49	32	400	305	235	70	47	33
	50	27	230	240	81	50	40	30

Table 26. Serial SGPT levels of dogs with myocardial infarction

Lesion size	Dog no.	Pre-surg-ery	Hours post surgery						
			17-22	23-27	28-34	35-43	44-50	51-72	73-90
< 1 cm.	15	25	24	29	20	23	31	24	20
	11	17	48	46	42	41	46	32	30
	38	20	46	48	40	38	32	31	28
	46	36	36	34	35	34	36	33	40
1-2 cm.	21	20	25	27	28	29	31	25	28
	25	28	44	42	39	37	25	24	22
	51	30	34	32	33	38	36	35	20
> 2 cm.	7	19	240	125	101	87	76	77	56
	24	20	88	93	89	80	55	62	29
	31	17	60	55	65	83	61	56	38
	34	24	100	100	92	86	64	53	44
	45	18	160	220	220	171	139	100	49
	49	24	150	140	130	160	125	78	64
	50	21	83	99	76	69	62	50	47

Table 27. Serial SLDH levels of dogs with myocardial infarction

Dog no.	Pre-surg-ery	Post surgery						
		Hours			Days			
		18-30	31-48	49-70	4-8	9-13	14-18	< 19
46	130	385	495	535	180	-	-	140
25	165	1225	1075	1150	360	-	175	
51	100	580	265	240	-	550		
31	170	280	230	-	100			
34	450	800	650	500	110	-	-	280
45	140	1125	375	370	350	-	190	
49	350	820	500	225	190	210		
50	365	375	290	180		225		

Table 28.   Serial enzyme levels of dogs sham-operated for myocardial infarction (Sigma)

Dog no.	Pre-surgery	Hours post surgery						
		17-22	23-27	28-34	35-43	44-50	51-72	73-90

SGOT

Dog no.	Pre-surgery	17-22	23-27	28-34	35-43	44-50	51-72	73-90
1	23	25	23	23	25	23	21	16
13	25	35	32	24	32	33	27	30
14	24	36	26	25	22	17	24	20
22	20	23	16	16	18	20	20	16
32	20	41	41	39	29	25	27	25
33	18	37	40	25	25	19	18	20
39	27	27	20	25	19	24	28	24
40	21	37	43	25	25	30	33	32

SGPT

Dog no.	Pre-surgery	17-22	23-27	28-34	35-43	44-50	51-72	73-90
1	12	15	14	12	15	15	19	18
13	23	38	39	38	36	35	32	38
14	18	20	19	17	15	16	20	17
22	20	24	18	17	17	16	20	18
32	15	32	29	29	34	20	20	20
33	18	22	30	26	24	24	24	24
39	26	26	21	20	29	18	28	25
40	24	25	24	25	24	28	25	22

SLDH

Dog no.	Pre-surgery	17-22	23-27	28-34	35-43	44-50	51-72	73-90
33	240	130	110	70	120			
39	325	85	165	-	-	-	150	
40	205	280	190	175	-	160		

Table 29. Serial enzyme levels of epicarditis dogs (Sigma)

Dog no.	Pre-surgery	Post surgery Days				Post surgery Weeks			
		2	5	8	12	3	4	5	6
					SGOT				
5	17	20	21	24	13	22	18	-	29
10	27	16	22	17	14	23	25	22	22
26	29	-	25	37	31	25	23	22	21
36	14	22	32	20	27	-	28	29	30
37	28	28	30	23	-	27	19	26	27
43	33	25	32	30	-	23	-	21	-
					SGPT				
5	18	27	20	23	27	18	24	-	27
10	17	13	21	12	14	15	25	19	15
26	22	21	36	37	25	25	16	20	22
36	13	19	30	19	17	-	22	25	23
37	23	28	25	24	-	21	26	23	21
43	20	26	-	23	-	19	-	15	-
					SLDH				
26	400	-	100	-	-	-	110	-	190
36	120	205	-	-	-	290	-	-	260
37	70	-	-	205	-	-	-	-	265
43	200	-	200	-	300	470	-	555	-

Table 30. Serial serum enzyme levels of sham-operated
           epicarditis dogs (Sigma)

Dog no.	Pre-surgery	Post surgery							
		Days				Weeks			
		2	5	8	12	3	4	5	6
					SGOT				
18	18	14	18	17	24	20	28	27	27
29	19	29	26	25	15	16	16	15	15
35	21	17	17	19	23	31	33	35	34
					SGPT				
18	16	17	14	18	20	18	21	25	25
29	23	22	16	19	15	15	21	15	16
35	20	20	20	18	17	24	22	21	20
					SLDH				
29	150	130	175	-	-	-	140	-	150
35	75	75	-	225	-	-	90	-	120

Table 31. Serial enzyme levels of valvular insufficiency dogs (Sigma)

Dog no.	Pre-surgery	Post surgery							
		Days				Weeks			
		4	6	9	12	3	5	8	12
					SGOT				
20	18	24	24	23	27	22	32	24	25
27	20	17	15	16	19	25	20	15	19
30	34	26	18	26	18	22	19	18	28
41	29	34	29	-	39	36	31	29	71
42	24	30	23	25	24	19	39	35	-
					SGPT				
20	16	27	33	25	26	30	23	18	20
27	23	15	13	14	15	16	14	17	18
30	31	20	20	20	20	19	22	21	24
41	24	38	24	-	35	32	29	24	140
42	15	24	22	21	16	36	40	32	-
					SLDH				
27	45	-	175	-	-	380	-	250	180
30	200	-	-	-	380	-	325	250	200
41	455	475	280	-	480	-	355	230	250
42	225	-	290	-	225	375	300	170	-

Table 32. Serial enzyme levels of sham-operated valvular insufficiency dogs (Sigma)

Dog no.	Pre-surgery	Post surgery							
		Days				Weeks			
		4	6	9	12	3	4	6	8
					SGOT				
3	26	24	23	15	22				
4	53	56	40	41	51	50	46	46	45
19	20	25	20	14	22				
47	28	35	27	30	30	30	26	26	33
48	29	27	24	25	28	29	26	24	29
					SGPT				
3	20	22	21	15	21				
4	32	49	30	29	31	30	28	24	29
19	17	23	21	20	18				
47	26	25	25	28	26	30	29	25	25
48	17	19	21	25	28	30	28	24	29
					SLDH				
47	160	-	-	255	-	240	-	230	225
48	210	230	-	230	225	-	-	230	-

Table 33. ECG data from myocardial infarction dogs -
           arranged by age and as to severity of lesion
           found at necropsy

| | | | Post surgery | | | | |
| | | | Days | | Weeks | | |
Age	PS I	PS II	2-5	6-12	2-4	5-7	9-17
					R/S ratios		
1	5.5	5.5	7.25	8.0			
1	3.0	2.5	3	3.5	3.0	2.0	
1	9.5	8.0	13.25	7.0	10.5	9.75	
2	5.0	56.0[a]	28.0	25.0	6.75	-	8.0
2[b]	15.0	50.0[a]	18.0	-	21/0		
2	10.0	20.0	-	20.0	-	2.25	
2	2.5	3.5	3.0	16/0	3.5		
2	14.0	17.0	10.0	-	22.0		
2	11.5	24.0	8.0	16/0	12.0		
2	4.0	6.0	1.5	-	5.75		
2	2.0	-	0.3	0.5	1.75	1.25	2.5
3	3.0	2.5	2.75	1.75	2.0	3.0	
3	20.0	19/0	5.0				
3	1.5	2.0	1.0	1.25	1.0		2.75
					R/T ratios		
1	11.0	10.0	6.0	8.0			
1	6.0	3.75	3.0	3.5	2.5	1.0	
1	-9.5	1.25	11.25	-28.0	32.0	-39.0	6.0
2	6.75	14.0	7.0	17.0	-6.75	-	6.0
2[b]	-30.0[a]	-10.0	-6.0	-	21.0		
2	6.25	-6.0	-	20.0	-	2.25	
2	-40.0[a]	8.5	3.0	-4.0	-17.0		
2	5.5	5.5	4.0	-	7.25		
2	6.5	8.0	3.0	4.0	12.5		
2	13.25	12.5	-1.0	-	3.25		
2	4.75	-	-2.0	1.0	3.5	2.0	6.0
3	7.5	3.25	8.5	5.5	3.5	5.5	
3	10.0	9.5	7.5				
3	2.75	4.0	-1.5	1.5	1.0	-	-4.25

[a] < 1 mm.

[b] Second infarction.

Table 33. (Continued)

| Age | PS I | PSII | Post surgery | | | | |
| | | | Days | | Weeks | | |
			2-5	6-12	2-4	5-7	9-17
				P-R interval (sec.)			
1	.08	.08	.10	.08			
1	.10	.14	.10	.12	.10	.10	
1	.12	.12	.12	.10	.12	.10	
2	.12	.12	.14	.12	.16	-	.14
2[b]	.12	.10	.10	-	.10		
2	.12	.12	-	.14	-	.12	
2	.12	.08	.08	.12	.10		
2	.10	.10	.10	-	.08		
2	.10	.12	.14	.12	.12		
2	.08	.10	.12	-	.10		
2	.10	-	.10	.10	.08	.10	.08
3	.12	.12	.12	.12	.12	.12	.12
3	.10	.10	.10				
3	.10	.14	.14	.14	.12	-	.10
				Q-T interval (sec.)			
1	.24	.24	.22	.20			
1	.22	.22	.24	.24	.22	.24	
1	.20	.20	.20	.20	.22	.18	
2	.24	.26	.24	.24	.26	-	.26
2[b]	.20	.18	.16	-	.22		
2	.24	.20	-	.24	-	.24	
2	.22	.22	.20	.20	.18		
2	.20	.18	.20	-	.20		
2	.24	.22	.22	.22	.20		
2	.20	.20	.20	-	.16		
2	.20	-	.24	.22	.20	.20	.22
3	.26	.26	.28	.24	.20	.26	
3	.24	.24	.24				
3	.22	.20	.24	.20	.20	-	.22

Table 33. (Continued)

Age	PS I		PS II		Post surgery Days 2-5		6-12		Weeks 2-4		5-7		9-17	
	Q_1	-T	Q_1	-T	Q_1	-T	Q_1	-T	Q_1	-T	Q_1	-T	Q_1	-T
1	-		+	+	+	+	-							
1	+	+	+	+	+	-	-		+	-	-			
1	-		-		-		-		-		+	-		
2	-		+	-	+	+	+		-	+	+		-	
2b	-		+	+	+	+			+	+				
2	-		+	+			+	-	-					
2	-		+	+	+	-	+		-	+	+			
2	-		-		-				+	+				
2	-		+	-	+	-	+		-	+	+			
2	-		+	-	+	-			+	+				
2	+	+			-		+		-	+	-	+	+	-
3	+	+	+	-	+	-	-		-					
3	+	-	+	-	+	-								
3	+	+	+	+	+	+	+		-				+	+

Age	S_3	+T	S_3	+T	S_3	+T	S_3	+T	S_3	+T	S_3	+T	S_3	+T
1	+	+	+	+	+	+	+	+						
1	+	+	+	+	+	+	+		+	+	+	+		
1	+	-	+	+	+	-	+		-	-	+	-		
2	+	+	+	+	+	+	+		+	-			+	+
2b	+	-	+	-	+	-			+	+				
2	+	+	+	+			+		+		+	+		
2	+	-	+	+	+	-	+		+	-				
2	+	+	+	+	+	-			+	+				
2	+	+	+	+	+	+	+		+	+				
2	+	+	+	+	+	-			+	+				
2	+	+		+	+	-	+		+	+	+	+	+	+
3	+	+	+	+	+	+	-		+	+	+	+		
3	+	+	+	-	+	-								
3	+	+	+	+	+	-	+		+				+	-

Table 34. ECG data from sham-operated myocardial infarction dogs

Age	PS I	PS II	Post surgery Days 2-5	Days 6-14	Weeks 3-7	Weeks 14-16
			R/S ratios			
1	1.5	1.75	2.75			
1	4.25	5	6.75	-	7.0	
2	10.5	4.25	-	5.0		
2	1.5	1.5	-	2.0	1.0	
2	7.25	9.0	-	21.0	5.5	
2	13.0	12.0	8.5	13.0	-	16.0
2	2.25	2.5	4.5	4.5	2.5	2.25
3	12.5	13.5	25/0	-	12.5	8.0
			R/T ratios			
1	3.0	2.75	1.5			
1	-17.0	4.5	3.25	-	8.75	
2	8.0	5.25	-	6.0		
2	3.5	2.75	-	4.0	2.75	
2	11.0	-44.0[a]	-	4.25	11.0	
2	2.25	5.0	-17.0	2.25	-	8.0
2	4.75	4.0	4.5	1.75	2.5	2.5
3	50.0[a]	9.0	4.0	-	16.5	4.0
			PR interval			
1	.10	.08	.12			
1	.14	.12	.12	-	.12	
2	.12	.12	-	.12		
2	.08	.12	-	.10	.12	
2	.08	.08		.12	.10	
2	.12	.12	.10	-	-	.12
2	.12	.12	.10	.14	.12	.12
3	.12	.12	.14	-	.10	.12

[a] T was on 0.5 mm.

Table 34.   (Continued)

| | | | Post surgery | | | |
| | | | Days | | Weeks | |
Age	PS I	PS II	2-5	6-14	3-7	14-16
				QT interval		
1	.20	.20	.24			
1	.24	.22	.24	-	.24	
2	.22	.20	-	.22		
2	.24	.24	-	.24	.24	
2	.24	.24	-	.26	.26	
2	.20	.24	.20			
2	.24	.26	.22	.20	.20	.24
3	.24	.24	.24	-	.20	.26

	Q_I -T		Q_I -T		Q_I -T		Q_I -T		Q_I -T		Q_I -T	
1	+	+	-		-							
1	+	+	-		-				-			
2	+	+	+	-			+	+				
2	-		-				-		-			
2	-		+	+			-		-			
2	-		+	-	+	+	-					
2	+	+	+	+	+	+	+	-			+	+
3	-		+	-	+	-			+	+		

	S_{III}+T		S_{III}+T		S_{III} +T		S_{III}+T		Q_{III}+T		Q_{III}+T	
1	+	+	+	+	+	+	+	+	+	+	+	+
1	+	+	+	+	+	+			+	+		
2	-		-				+	+				
2	+	+	+	+			+	+	+	+		
2	+	+	+	-			+	+	+	+		
2	-		-		-		-					
2	+	+	+	+	+	+	+	+	+	+	+	+
3	+	+	+	+	-				-		+	+

Table 35. ECG data from epicarditis dogs

Age	PS I	PS II	1-3	4-6	Weeks 7-12	15-17	18-24
					R/S ratios		
1	23.0	7.25	-	15.0	12.5	11.0	
1	12.0	7.5	8.0	6.5	4.0		
2	11.0	6.0	12.0	10.0	16.5	13.5	29.0
2	3.25	5.1	5.5	4.0	4.5	3.0	3.5
2	5.5	9.25	10.0	11.25	16.0	9.0	12.5
3	4.75	-	5.75	-	-	23.0	6.25
					R/T ratios		
1	5.75	2.0	-	8.0	4.0	7.25	
1	8.0	10.0	2.25	4.25	3.0		
2	16.0	8.0	3.0	4.0	3.75	6.75	10.0
2	8.0	12.0	4.5	3.0	7.0	4.0	3.0
2	14.0	14.0	1.5	7.0	5.0	6.25	25.0
3	4.75	-	1.75	-	-	-7.5	17.0
					PR interval		
1	.12	.12	-	.14	.14	.12	
1	.10	.10	.12	.10	.12		
2	.06	.08	.10	.12	.12	.14	.10
2	.10	.10	.16	.14	.16	.12	.14
2	.10	.10	.12	.12	.12	.10	.10
3	.12	-	.14	-	-	.10	.12
					QT interval		
1	.22	.24	-	.20	.20	.20	
1	.22	.20	.20	.20	.26		
2	.24	.18	.20	.18	.20	.20	.20
2	.22	.24	.24	.22	.24	.24	.22
2	.20	.20	.18	.20	.22	.20	.16
3	.24	-	.24	-	-	.18	.22

Table 35. (Continued)

Age	PS I Q_I -T		PS II Q_I -T		Weeks 1-3 Q_I -T		4-6 Q_I -T		7-12 Q_I -T		15-17 Q_I -T		18-24 Q_I -T	
1	-		-				+	+	+	-	+	+		
1	+	+	+	+	-		-		-					
2	-		+	+	-		-		-		-		-	
2	-		+	+	+	-	-		-		-		+	-
2	-		+	+	-		+	-	-		+	-	-	
3	-				-						+	+	-	

Age	S_{III} +T		Q_{III} +T		S_{III} +T		S_{III} +T		S_{III} +T		S_{III} +T		S_{III} +T	
1	+	+	+	+			+	+	+	+	+	+		
1	+	+	+	+	+	+	+	+	+	+				
2	+	+	+	+	-		-		-		+	+	-	
2	+	+	+	+	+	+	+	+	+	+	+	+	+	+
2	+	+	+	+	+	+	+	+	+	+	+	+	+	+
3	+	+			-						+	-	+	+

Table 36. ECG data from sham-operated epicarditis dogs

Age	PS I	PS II	Weeks					
			1	6-8	10-14	20-23	28	30
					R/S ratio			
1	7.5	14.0	25.0	20.0	9.5	20.0		
2	21/0	22.0	44.0[a]	1.5	18/0	42.0[a]	10.5	10.0
2	3.5	2.75	-	6.0	4.5			
					R/T ratio			
1	7.5	-14.0	3.25	6.75	12.5	10.0		
2	-42.0	11.0	5.5	9.0	36.0	21.0	6.5	-20.0[a]
2	-24.0	8.25	-	4.0	4.0			
					PR interval			
1	.08	.08	.10	.10	.10	.10		
2	.10	.12	.14	.16	.12	.16	.12	.10
2	.10	.10	-	.12	.10			
					QT interval			
1	.20	.20	.24	.22	.20	.20		
2	.22	.28	.28	.26	.24	.20	.22	.22
2	.22	.20	-	.22	.24			

	Q_I	-T	Q_I	-T	Q_I	-T	Q_I	-T	Q_I	-T	Q_I	-T	Q_I	-T	Q_I	-T
1	+	+	+	+	+	+	+	+	+	+	+	+				
2	+	+	+	+	-		+	+	+	-	+	+	+	+	-	
2	+	+	+	+			•		-							

	S_{III}+T		S_{III}+T		S_{III}+T		S_{III}+T		S_{III}+T		S_{III}+T		S_{III}+T		S_{III}+T	
1	+	+	+	+	+	+	+	+	+	+	+	+				
2	-		+	+	-		+	+			+	+	+	+	+	+
2	+	-	+	+			+	+	+	+						

[a] < 1 mm.

Table 37. ECG data from valvular insufficiency dogs

Age	Pre-surgery	Weeks						
		2	4-7	10-12	13-20	22-27	31-32	36-38
				R/S ratio				
2	3.0	7.5	6.0	6.5	8.5	12.0	14.0	15.25
2	5.75	1.75	3.0	3.0	32.0	3.0		
2	5.0	3.0	-	1.25	10.0[a]			
3	11.5	-	7.25	5.75	4.5	12.0		
3	29/0	-	-	29/0	30/0	62.0[a]	62.0[a]	35/0
				R/T ratio				
2	5.0	8.5	7.5	6.5	2.5	8.75	4.5	7.5
2	4.25	1.75	2.0	1.75	9.0	3.5		
2	6.25	1.25	-	2.0	10.0[a]			
3	23/0	-	7.25	7.5	4.5	24.0		
3	10.0	-	-	8.25	15.0	-32.0	13.0	17.5
				PR interval				
2	.10	.12	.12	.12	.16	.14	.16	.10
2	.10	.10	.12	.12	.10	.12		
2	.12	.12	-	.08	.18			
3	.08	-	.10	.12	.10	.10		
3	.12	-	-	.14	.10	.10	.16	.12
				QT interval				
2	.24	.26	.24	.24	.24	.24	.22	.22
2	.24	.20	.24	.22	.24	.20		
2	.22	.20	-	.22	.18			
3	.20	-	.18	.20	.18	.24		
3	.24	-	-	.22	.20	.18	.20	.20

[a] < 1 mm.

Table 37. (Continued)

Age	Pre-surgery		Weeks 2		4-7		10-12		13-20		22-27		31-32		36-38	
	Q_I	-T	Q_I	-T	Q_I	-T	Q_I	-T	Q_I	-T	Q_I	-T	Q_I	-T	Q_I	-T
2	+	+	+	+	+	+	-		-		+	-	+	-	+	+
2	+	+	+	-	+	-	-		-		+	+				
2	-		-				+	+	-							
3	+	+			+	-	+	+	+	-	+	+				
3	+	+					-		-		-		+	+	+	+
	S_{III}	+T	S_{III}	+T	S_{III}	+T	S_{III}	+T	S_{III}	+T	S_{III}	+T	S_{III}	+T	S_{III}	+T
2	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
2	+	+	+	+	+	+	+	+	+	+	+	+				
2	+	+	+	+			+	+	+	+						
3	+	+			+	+	+	+	+	+	+	+				
3	-						-		-		-		-		-	

Table 38. ECG data from sham-operated valvular insufficiency dogs

Age	Pre-surgery	Days 2	Days 10-12	Weeks 4	Weeks 6	Weeks 10	Weeks 13
			R/S ratio				
1	4.0	6.0	22/0				
2	3.0	19.0					
2	56.0[a]		30/0		64.0[a]	37.0	8.5
2	1.5		9.0	4.5	6.0		2.75
3	38/0	30/0	20/0				
			R/T ratio				
1	- 8.0	-4.5	7.25				
2	- 1.25	-3.0					
2	28.0		15.0		21.25	18.5	17.25
2	3.0		6.0	3.0	2.5		2.0
3	-19.0	15.0	9.25				
			PR interval (sec.)				
1	.08	.14	.12				
2	.12	.08					
2	.10		.12		.12	.12	.12
2	.10		.14	.14	.14		.14
3	.14	.12	.12				
			QT interval (sec.)				
1	.20	.24	.16				
2	.28	.20					
2	.18		.20		.18	.20	.20
2	.22		.20	.22	.24		.22
3	.24	.20	.24				

Age	Q_I	-T	Q_I	-T	Q_I	-T	Q_I	-T	Q_I	-T	Q_I	-T	Q_I	-T
1	+	+	+	+	+	-								
2	+	+	+	+										
2	+	+			+	+			+	+	+	+	-	+
2	-				+	+	+	+	+	+			+	+
3	+	+	+	+	+	+								

Age	S_{III}	+T	S_{III}	+T	S_{III}	+T	S_{III}	+T	S_{III}	+T	S_{III}	+T	S_{III}	+T
1	+	-	+	-	+	+								
2	+	-	+	-										
2	+	+			+	+			+	+	+	+	+	+
2	+	+			+	+	+	+	+	+			+	+
3	-		-		-									

[a] < 1 mm.

Table 39. Hematological studies of dogs during course of experimentation

No.	Date	HT	Hb	WBC	RBC	Baso	Eos	Lymph	Stab	Ses	Mono
					Infarction						
14	Pre-surgery	45.0 (37-53)	16.4 (12.9-19.4)	13.04 (6.25-22.2)	6.91 (5.22-7.9)	.71 (0-4)	2.0 (0-7)	19.0 (7-28)	3.3 (0-7)	70.6 (61-73)	4.14 (1-15)
9	1 wk.	44.4 (40-50)	16.2 (13.9-17.8)	16.18 (6.04-25.2)	7.09 (5.93-7.74)	.67 (0-1)	2.67 (1-4)	16.67 (12-22)	5.1 (2-9)	72.8 (67-76)	3.1 (1-5)
3	2 wk.	41 (37-43)	4.1 (12.7-15.6)	15.67 (12.9-18.52)	6.14 (5.26-6.85)	.33 (0-1)	3 (1-5)	25.6 (18-35)	4 (1-6)	63 (60-66)	4 (3-6)
6	3 wk.	45.5 (42-49)	16.6 (14.3-18.8)	14.09 (7.65-23.5)	6.9 (5.74-8.5)	.75 (0-5)	6.2 (1-20)	14.2 (9-18)	4.2 (1-10)	69.3 (53-74)	4.7 (2-8)
1	4 wk.	48	16.0	10.85	7.35	0	2	33	3	59	3
1	15 wk.	46	18.2	8.76	7.66	1	2	18	3	74	2
					Infarct Sham						
8	Pre-surgery	46.4 (43-51)	17.0 (16.0-19.1)	12.28 (6.72-19.4)	6.51 (6.69-8.68)	.625 (0-1)	2.63 (1-9)	20.0 (11-29)	2.12 (0-4)	70.0 (61-80)	4.1 (2-7)
4	1 wk.	46 (43-49)	16.5 (16-17)	10.77 (8.5-12.6)	7.23 (6.87-8.07)	.75 (0-1)	4 (2-7)	18.5 (15-24)	3 (2-5)	68.8 (65-72)	5 (4-7)
2	2 wk.	44.5 (44-45)	17.3 (16.7-18.0)	14.13 (12.36-15.9)	7.08 (6.76-7.4)	0 (0)	5.5 (2-9)	21.5 (13-30)	4 (3-5)	66 (63-69)	3 (2-4)
2	4 wk.	46 (45-47)	16.2 (16.2)	9.8 (8.99-10.6)	7.19 (7.1-7.28)	.5 (0-1)	2 (1-3)	21 (16-26)	1.5 (0-3)	71.5 (71-72)	4 (2-6)

Table 39.   (Continued)

	HT	HB	WBC	RBC	Baso	Eos	Lymph	Stab	Seg	Mono
					Infarct sham (cont.)					
1 6 wk.	47	18.8	13.72	7.39	0	5	14	3	74	4
2 12 wk.	50 (50)	18.5 (18-19)	10.93 (10.24-11.62)	8.12 (7.32-8.92)	0 (0)	4 (2-6)	19.5 (19-20)	5.5 (4-7)	64 (61-67)	7 (7)

<p style="text-align:center">Epicarditis</p>

	HT	HB	WBC	RBC	Baso	Eos	Lymph	Stab	Seg	Mono
6 Pre-surgery	48.5 (45-55)	19.95 (16.4-19.0)	9.298 (6.12-12.94)	7.107 (5.38-8.59)	.5 (0-2)	2.5 (1-7)	17.0 (9-23)	5.5 (1-10)	70.5 (66-74)	4.0 (2-6)
5 1 wk.	43.2 (37-51)	16.2 (14.2-17.8)	13.576 (8.86-18.4)	7.12 (4.84-9.24)	.8 (0-3)	3.6 (2-4)	14.2 (10-19)	3.8 (0-7)	73.8 (70-79)	3.8 (2-5)
2 2 wk.	45 (44-46)	17.5 (17.4-17.6)	15.56 (12.5-18.6)	7.12 (6.52-7.72)	1 (1)	5 (4-6)	10 (8-12)	6 (6)	76.5 (74-79)	2 (1-3)
4 4 wk.	47 (43-50)	17.5 (16.0-18.8)	14.75 (7.6-25.4)	7.568 (6.78-8.5)	0 (0)	3.25 (0-12)	11.25 (10-13)	4.5 (3-7)	76.5 (67-84)	4.5 (8-0)
4 7 wk.	46.25 (38-50)	16.85 (15.1-18.0)	14.91 (10.0-24.3)	7.717 (6.0-8.48)	.8 (0-2)	3.5 (2-8)	14.75 (13-16)	4 (1-9)	72.25 (69-75)	4.5 (3-6)
6 11 wk.	47.67 (43-55)	16.86 (14.0-18.8)	12.02 (7.55-19.35)	7.672 (6.65-8.55)	1.5 (0-4)	7 (3-13)	17 (13-21)	2.33 (0-7)	66.8 (59-72)	5.33 (2-8)

Table 39. (Continued)

No. Date	HT	Hb	WBC	RBC	Baso	Eos	Lymph	Stab	Seg	Mono

Epicarditis (cont.)

No. Date	HT	Hb	WBC	RBC	Baso	Eos	Lymph	Stab	Seg	Mono
3 15 wk.	47.67 (56-51)	17.8 (17.5-18.5)	15.26 (10.4-22.5)	7.672 (7.33-8.26)	.33 (0-1)	6.67 (1-12)	19 (1-8)	4.6 (1-8)	67 (63-72)	4.3 (2-7)
5 19 wk.	46.2 (43-51)	17.3 (15.0-18.8)	10.8 (5.56-15.88)	7.31 (5.73-8.32)	.6 (0-2)	7.4 (3-11)	18.8 (13-23)	3.4 (0-7)	65.4 (57-72)	4.4 (2-10)
3 23 wk.	49 (45-56)	17.6 (12.5-18.8)	12.29 (10.96-13,22)	7.83 (7.15-9.39)	.6 (0-2)	4.67 (4-6)	20 (14-25)	1.67 (0-3)	68.3 (64-74)	4.6 (4-5)
1 27 wk.	40	18.8	11.22	5.83						
1 29 wk.	43	17.0	14.78	7.29	0	3	18	4	68	7

Epicarditis sham

No. Date	HT	Hb	WBC	RBC	Baso	Eos	Lymph	Stab	Seg	Mono
3 Pre-sur-gery	44 (40-46)	16.6 (15.2-18.4)	14.293 (13.44-14.82)	6.92 (6.23-7.27)	.33 (0-1)	2 (0-3)	18.67 (9-25)	3 (0-7)	71.3 (56-91)	4.67 (0-11)
3 1 wk.	42.67 (41-44)	16.67 (15.2-17.8)	14.95 (13.7-16.64)	6.76 (6.4-7.1)	.33 (0-1)	1.67 (1-2)	18.3 (13-21)	6 (4-9)	69.3 (63-77)	4.33 (0-8)
3 4 wk.	42 (39-43)	16 (15.1-16.8)	14.62 (13.3-16.3)	6.79 (6.46-7.43)	0 (0)	1.67 (1-3)	18 (12-22)	2.87 (2-3)	73.67 (71-78)	4.67 (4-6)

Table 39. (Continued)

No. Date	HT	Hb	WBC	RBC	Baso	Eos	Lymph	Stab	Seg	Mono
				Epicarditis sham (Cont.)						
2 7 wk.	49.5	17.5	15.32	8.28	(0)	8	15.5	9.5	62	5
	(47-52)	(17-18)	(13.9-16.74)	(8.18-8.38)	((0)	(2-14)	(10-21)	(3-16)	(54-70)	(4-6)
2 12 wk.	45.5	15.2	8.81	7.11	.5	2.5	28	2	56.5	10.5
	(45-46)	(15-15.23)	(6.65-10.96)	(5.94-8.28)	(0-1)	(2-3)	(22-34)	(0-4)	(44-69)	(1-20)
2 16 wk.	44.5	16.3	11.37	6.86	0	10	19.5	1	64	5.5
	(44-45)	(15.6-17)	(10.2-12.54)	(7.39-6.32)	(0)	(5-15)	(11-28)	(0-2)	(51-77)	(5-6)
1 20 wk.	46	17.4	5.40	6.20	0	2	21	6	62	10
1 24 wk.	45	18.0	9.74	6.72	0	6	24	4	59	7
1 27 wk.	46	18.4	12.96	8.28	0	2	25	3	67	3
1 30 wk.	38	18.6	10.60	6.33	0	3	20	2	63	12
1 36 wk.	45	16.0	8.24	7.50	0	6	21	4	63	6
				Valvular Insufficiency						
5 Pre-surgery	44.6	16.1	12.86	7.28	.6	6.8	13.8	1.8	57.6	4.6
	(36-50)	(14-17.2)	(10.2-15.75)	(6.18-8.71)	(0-1)	(1-13)	(2-19)	(0-4)	(8-77)	(0-9)
5 1 wk.	44.0	16.2	14.57	6.95	.8	4.6	1.68	2	69.6	6
	(34-48)	(13.3-18.2)	(9.57-21.74)	(5.23-7.64)	(0-2)	(1-13)	(14-21)	(0-4)	(64-77)	(3-11)

Table 39.   (Continued)

No.	Date	HT	Hb	WBC	RBC	Baso	Eso	Lymph	Stab	Seg	Mono

VI (cont.)

No.	Date	HT	Hb	WBC	RBC	Baso	Eso	Lymph	Stab	Seg	Mono
4	3 wk.	46.0 (45-47)	16.4 (15-17.5)	12.08 (6.35-18.62)	7.11 (6.04-8.14)	.75 (0-2)	6 (1-15)	18 (14-22)	2 (1-3)	66.5 (59-78)	6.75 (3-10)
5	7 wk.	44.6 (30-52)	16.08 (13-19)	12.17 (7.25-16.74)	7.18 (4.8-8.4)	.2 (0-1)	6.6 (1-14)	15.2 (13-19)	5.6 (0-16)	67.2 (54-78)	5.2 (3-9)
4	12 wk.	50 (48-54)	16.13 (15.2-16.8)	13.5 (11.3-19.96)	8.38 (8.15-8.77)	.5 (0-1)	6.5 (2-11)	18 (16-19)	2.5 (1-5)	68.5 (64-73)	4 (3-5)
3	16 wk.	52 (48-58)	16.67 (16-17)	8.29 (7.98-8.65)	8.34 (8.12-8.65)	0 (0)	3.33 (2-4)	22 (14-34)	2.67 (1-4)	64.67 (56-70)	7.33 (2-11)
3	20 wk.	49.3 (43-54)	16.6 (15.8-17.2)	9.93 (8.9-10.58)	7.89 (6.56-8.58)	2 (0-5)	8.3 (5-14)	22 (13-29)	4.3 (1-8)	60.3 (50-74)	4 (3-5)
2	24 wk.	50 (49-51)	17.4 (16.8-18)	(13.11) (9.65-16.56)	8.09 (7.95-8.22)	.5 (0-1)	1.5 (1-2)	17 (15-19)	4 (2-6)	70.5 (69-72)	6 (4-8)
2	28 wk.	52 (51-53)	17.1 (16.2-18)	11.44 (7.76-15.12)	7.11 (66.8-7.53)	1.5 (1-2)	10 (6-14)	14.5 (10-19)	3 (2-4)	64.5 (63-66)	6.5 (6-7)
2	32 wk.	505 (48-53)	17.2 (16.8-17.5)	8.54 (8.18-8.9)	7.76 (7.13-8.35)	1 (1)	11 (9-11)	21 (14-29)	4.5 (4-5)	60.5 (51-70)	2 (2)
1	37 wk.	50	17.3	7.91	7.91	0	15	16	1	64	4
1	42 wk.	50	16.9	10.5	8.46	6	3	23	3	65	6
1	45 wk.	46	16.0	10.52	5.64	4	9	11	5	68	3

Table 39.   (Continued)

No. Date	HT	Hb	WBC	RBC	Baso	Eos	Lymph	Stab	Seg	Mono
				Valvular Insufficiency Sham						
5 Pre-surgery	45.8 (38-52)	15.96 (12.3-19.4)	11.23 (7.04-14.75)	7.04 (6.0-8.34)	.8 (0-4)	3.4 (1-9)	26.2 (21-34)	3 (0-6)	62.2 (51-70)	4.4 (1-10)
4 1 wk.	46.0 (44-49)	16.5 (1.49-18.6)	10.99 (8.7-12.9)	7.21 (6.8-7.96)	.5 (0-2)	4 (2-8)	24.5 (21-27)	3.5 (0-5)	63 (57-68)	4.5 (2-8)
2 4 wk.	42 (38-46)	13.3 (12.6-14)	13.0 (10.35-15.65)	6.67 (5.57-7.77)	5.5 (3-8)	5 (4-6)	12 (12)	6.5 (3-10)	60.5 (56-65)	10 (5-15)
2 8 wk.	42 (42)	15.05 (15-15.1)	14.3 (13.8-14.8)	6.43 (5.9-6.95)	1 (0-2)	10.5 (10-11)	29.5 (26-33)	6 (5-7)	48.5 (45-52)	4.5 (2-7)
2 13 wk.	46 (45-47)	16 (15.3-16.8)	16.6 (16.14-17.06)	7.77 (7.69-7.86)	0 (0)	9.5 (3-16)	25.5 (15-46)	8 (2-14)	505 (49-52)	6.5 (3-10)
1 16 wk.	50	17.0	14.04	7.47	1	6	26	8	53	6
1 25 wk.	49	18.8	11.2	7.44	1	4	20	7	62	6

Figure 10. Positioning of dog and placement of electrodes for serial ECG studies.

Figure 11. Placement of electrodes for serial ECG study.
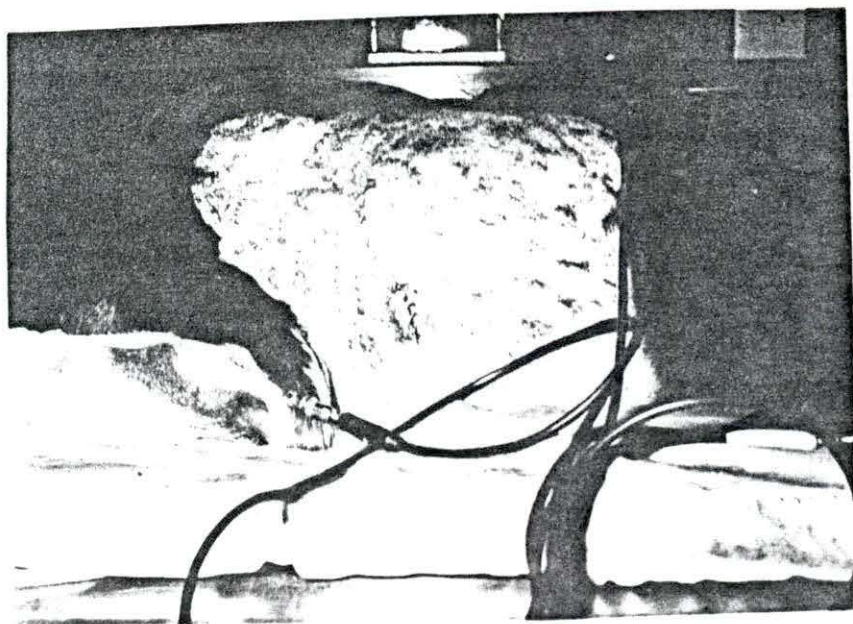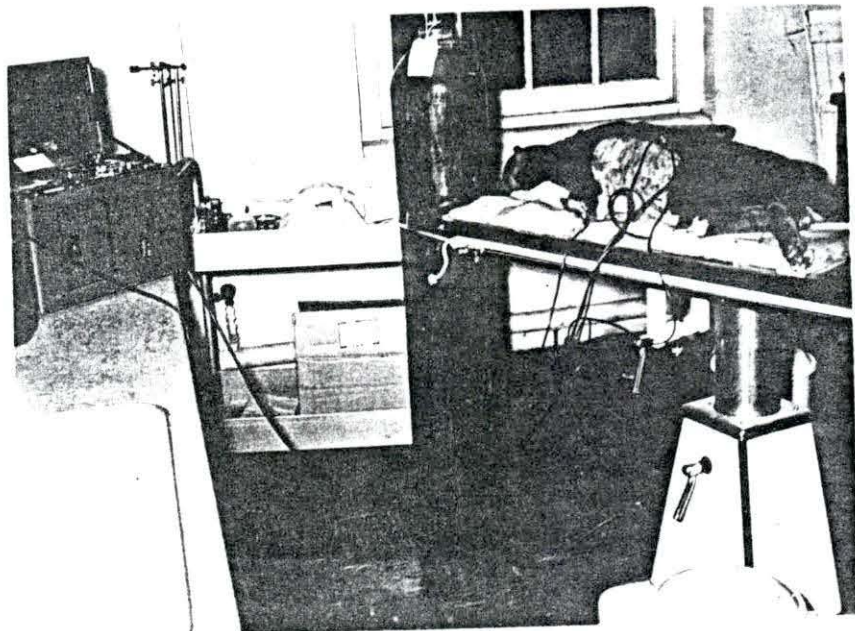
Figure 12. Heart from a dog sham-operated for myocardial infarction.

Figure 13. Closeup of a heart from a dog sham-operated for myocardial infarction.

Figure 14. Heart from dog 45 showing area of infarction at apex and a second smaller linear infarct between the papillary muscles.

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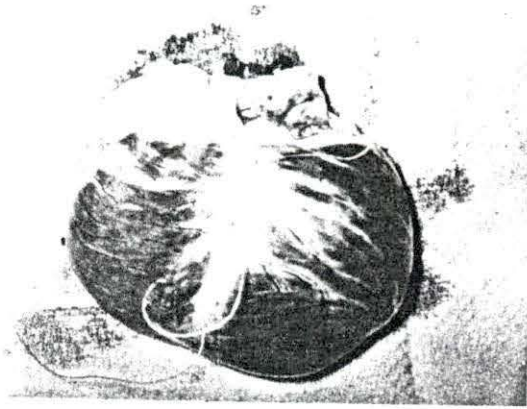
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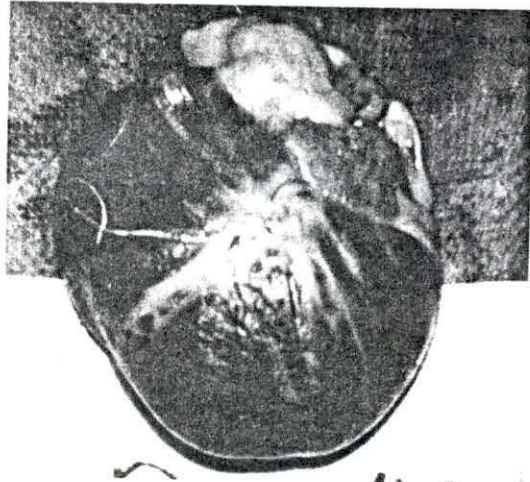
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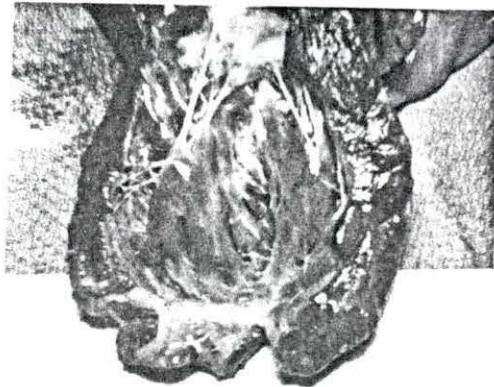
Figure 15.   Heart from dog 46 showing small infarct on tip
            of papillary muscle.

Figure 16.   Heart from dog 49 showing large area of fibrosis
            involving nearly one-half of the left ventricle
            musculature.

Figure 17.   Heart from dog 31 showing classical staircase
            infarction in posterior laterial wall of the
            left ventricle.
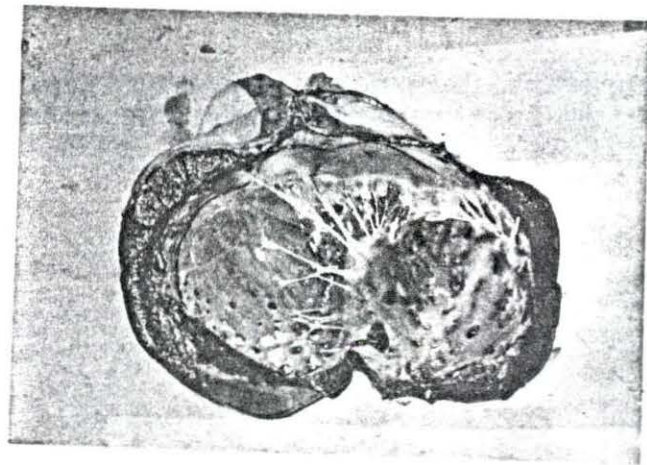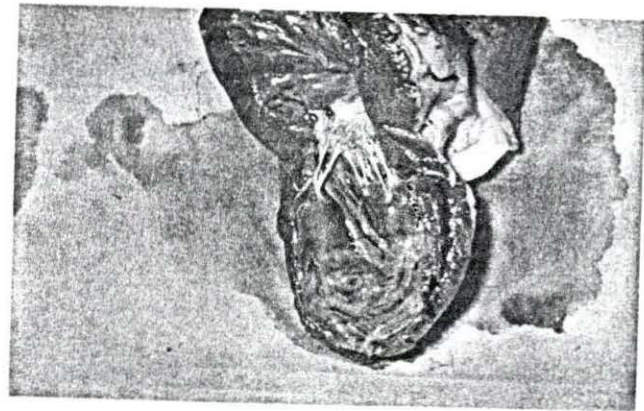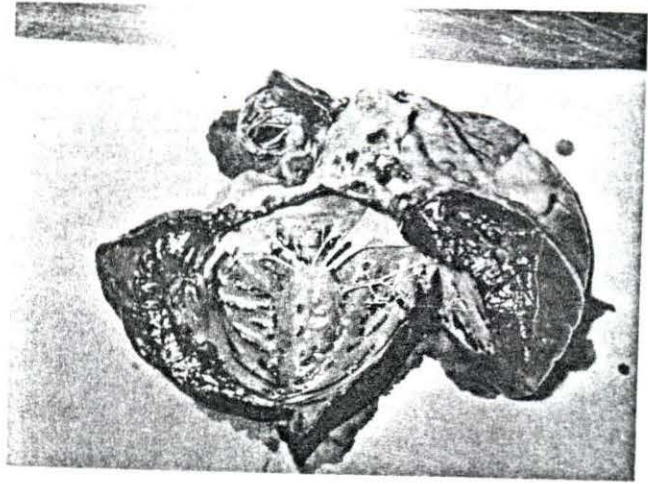
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Figure 18. Heart from dog 50 showing fibrosis and the
severe decrease in thickness of the left
ventricle musculature.

Figure 19. Heart from dog 34 showing large infarction
involving nearly all of the papillary muscle.

Figure 20. Heart from dog 7 showing infarction near apex
of left ventricle and the decrease in the
thickness of the muscle mass.

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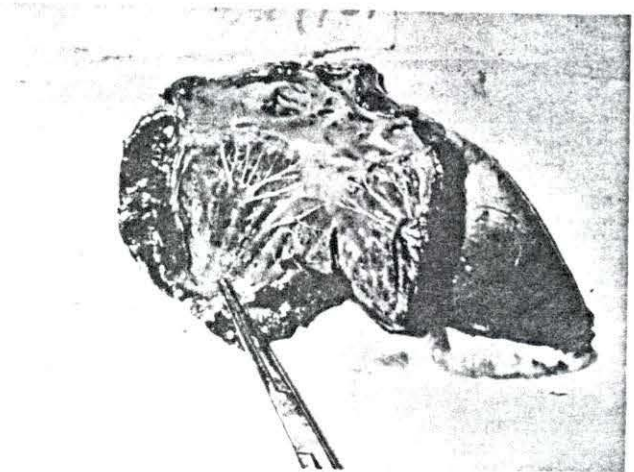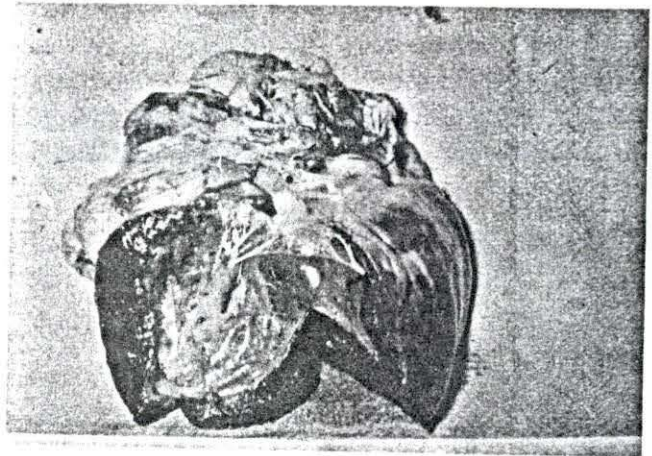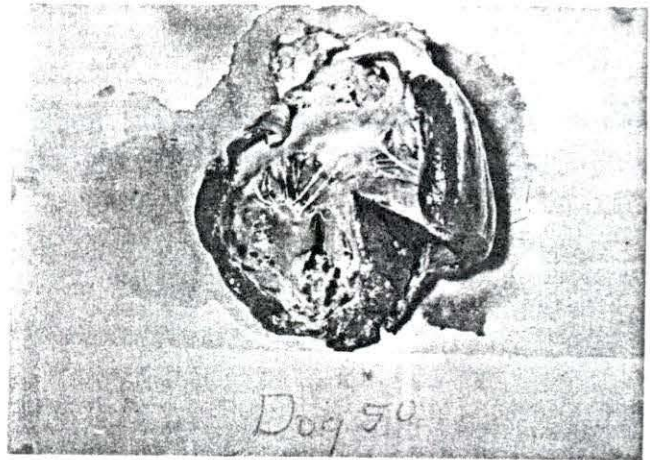
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Figure 21. Heart and pericardium from dog 37. (The
pericardium could not be removed from the
heart.)

Figure 22. Heart and pericardium from dog 26 showing
adhesions and epicarditis.

Figure 23. An epicarditis-pericarditis heart from
dog 36.
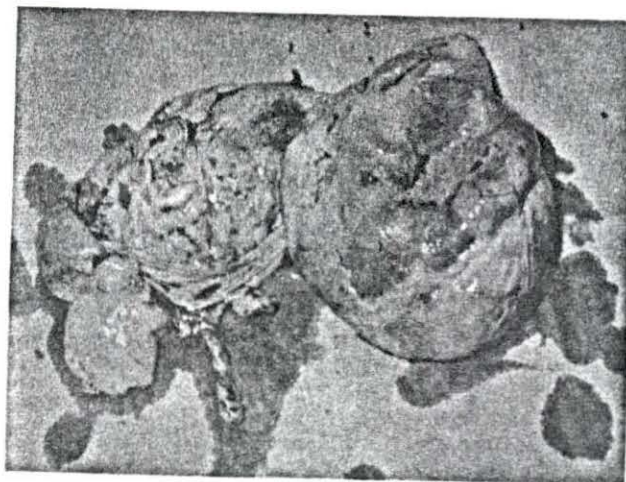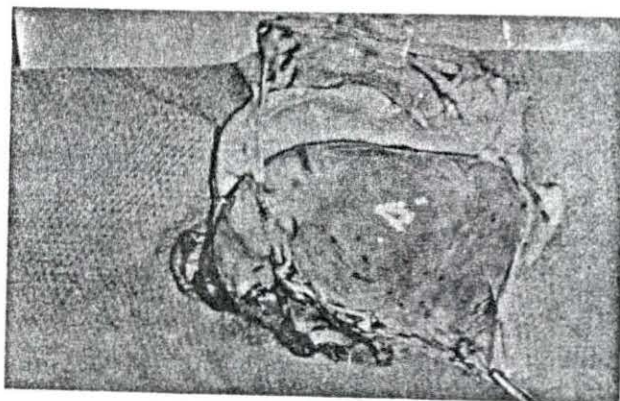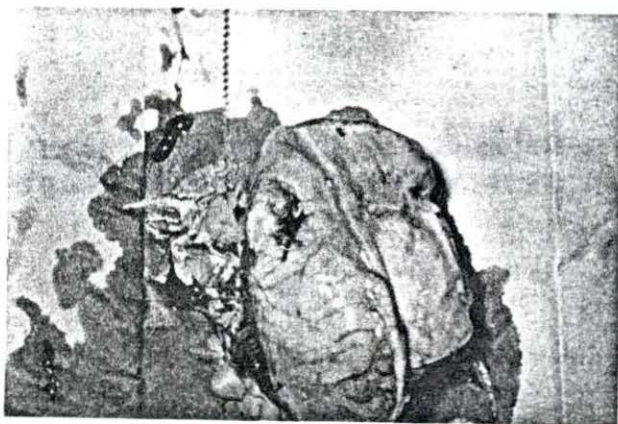
Figure 24.   Heart from dog 42 (notice dilatation of right
             ventricle and "pumpkin-shape" of the heart).

Figure 25.   Example of valvular insufficiency (Dog 27).

Figure 26.   Example of valvular insufficiency (Dog 20).

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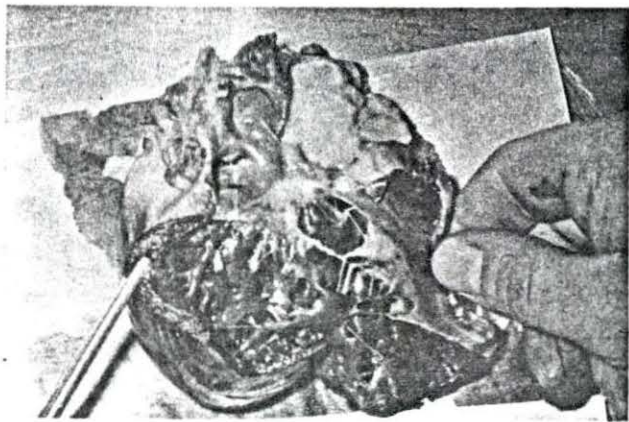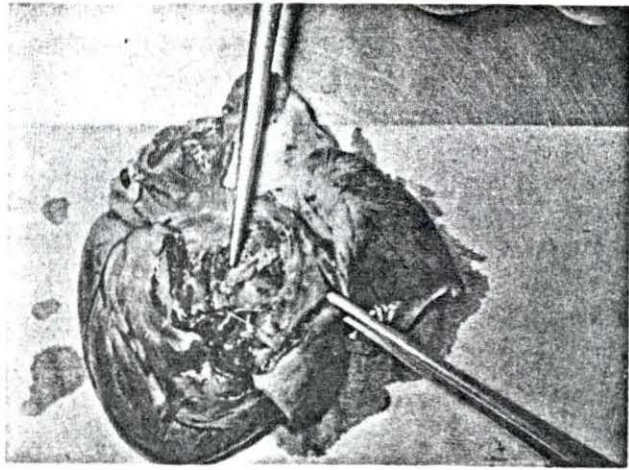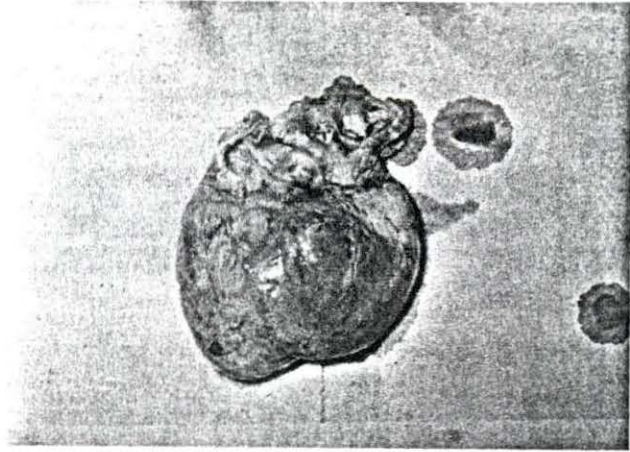
Figure 27.   Section of fibrosis of an infarcted area.
(Shows junction with normal cardiac muscle
tissue fixed in buffered, neutral formalin
and stained with the Mallory triple stain.
36X).

Figure 28.   Section of fibrotic area of an infarction.
(Shows junction with normal cardiac muscle.
Fixed in buffered, neutral formalin and
stained with hematoxylin and eosin.   36X.)

Figure 29.   Increased magnification of Figure 28 (160X).

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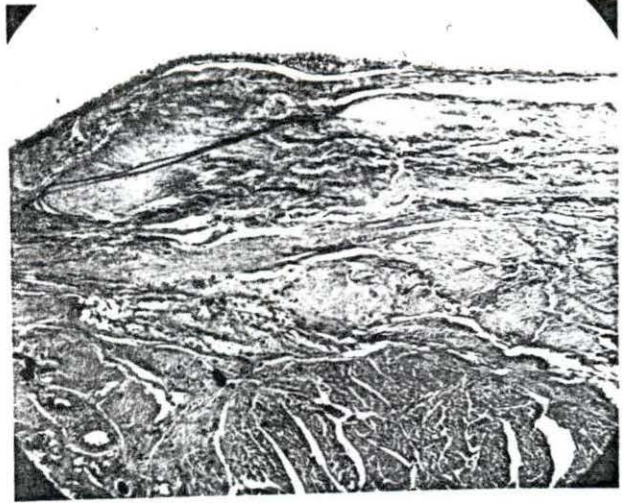
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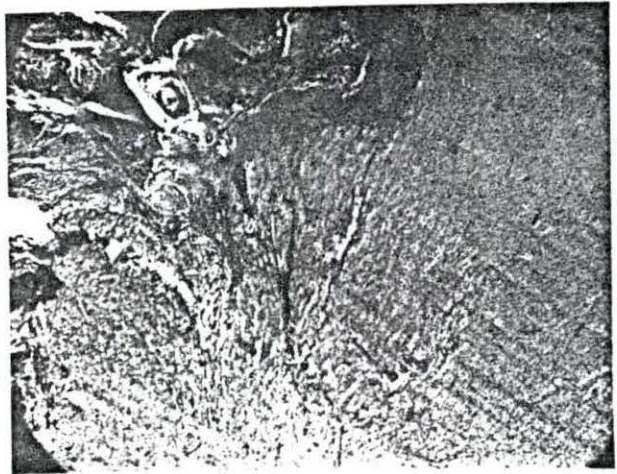
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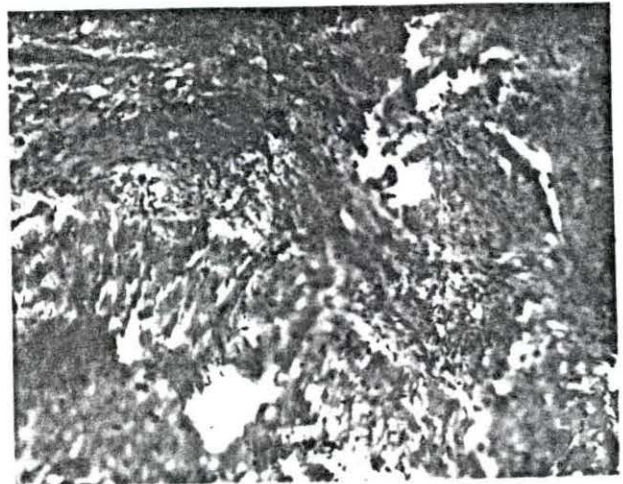
Figure 30. Section of fibrosis of an infarcted area.
(Tissue fixed in buffered, neutral formalin
and stained with the Mallory triple stain.
240X.)

Figure 31. Section of heart at junction of area of
epicarditis with normal myocardium in dog 5.
(Tissue fixed in buffered, neutral formalin
and stained with the Mallory triple stain.
36X.)

Figure 32. Increased magnification of Figure 31.
(Notice presence of giant cells (240X).)

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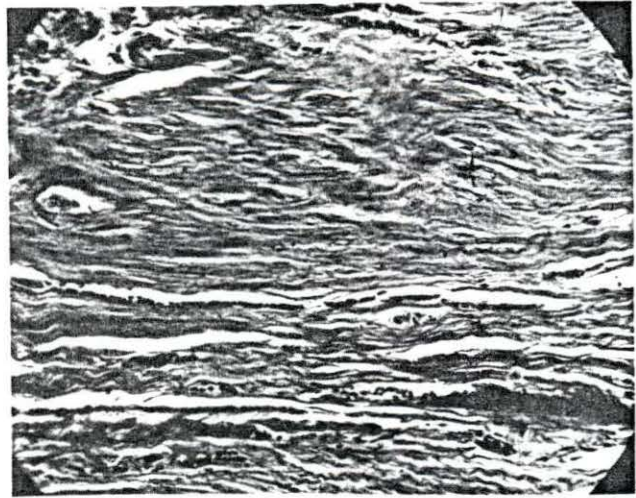
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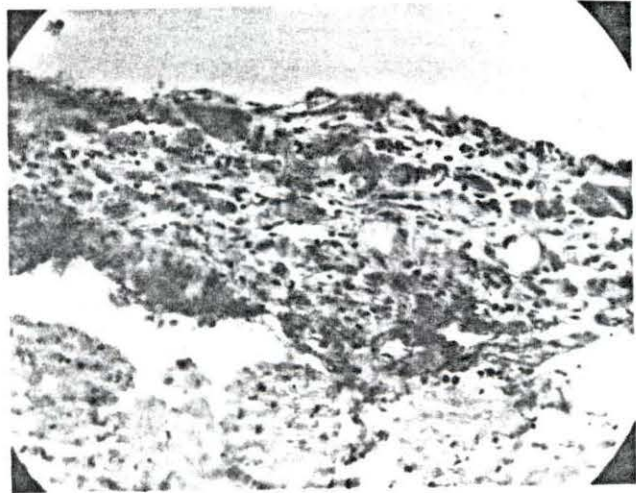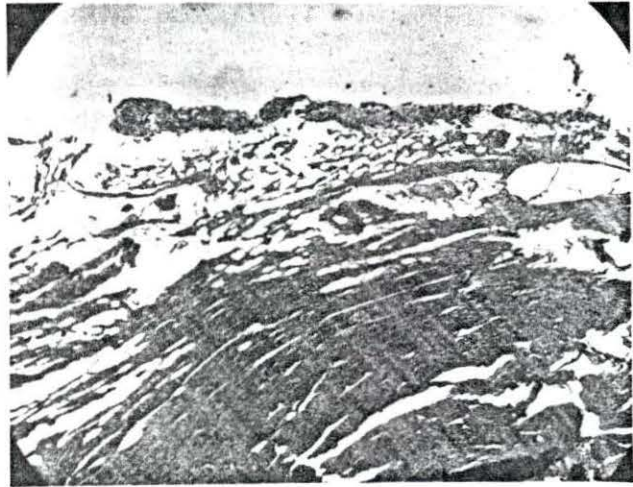
Figure 33. Section of heart at junction of area of epicarditis with normal myocardium in dog 37. (Notice involvement of the myocardium. Fixed in buffered, neutral formalin and stained with hematoxylin and eosin 36X.)

Figure 34. Increased magnification of Figure 33 (240X).

Figure 35. Section of a cusp from the right A-V valve showing increased thickness. (Tissue fixed in buffered, neutral formalin and stained with hematoxylin and eosin 36X.)
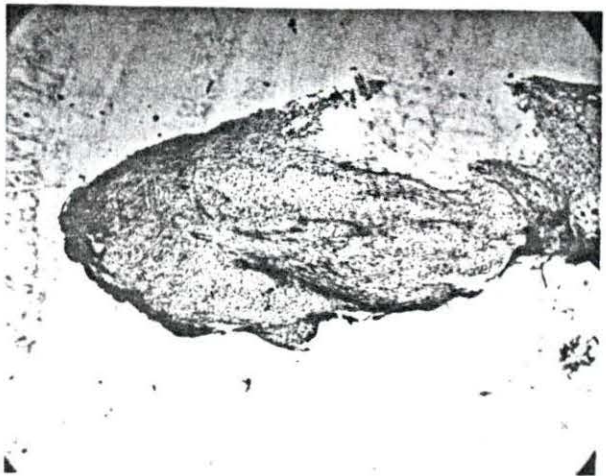
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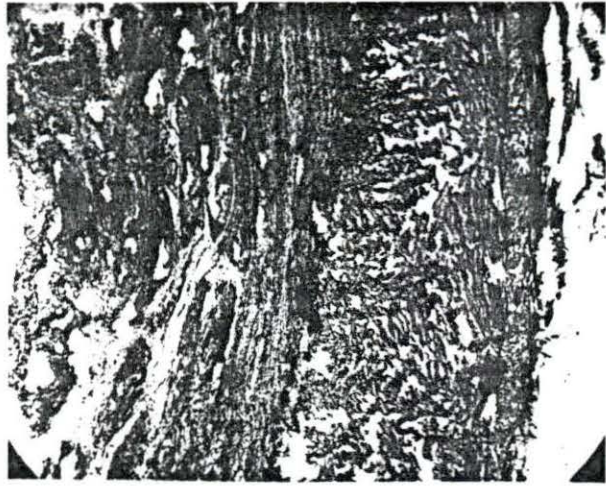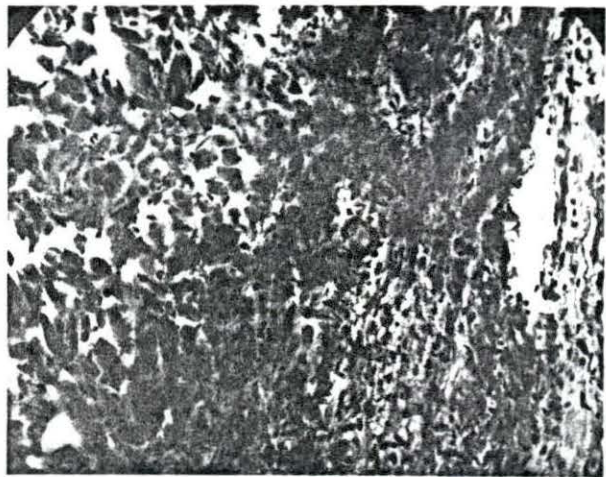
Figure 36. Liver from dog 42 showing early cardiac
            cirrhosis.

Figure 37. Section of liver from dog 42. (Notice
            greatly enlarged central veins. Fixed
            in buffered, neutral formalin and stained
            with hematoxylin and eosin. 36X.)

Figure 38. Increased magnification of Figure 37.
            (Notice cells around central vein in
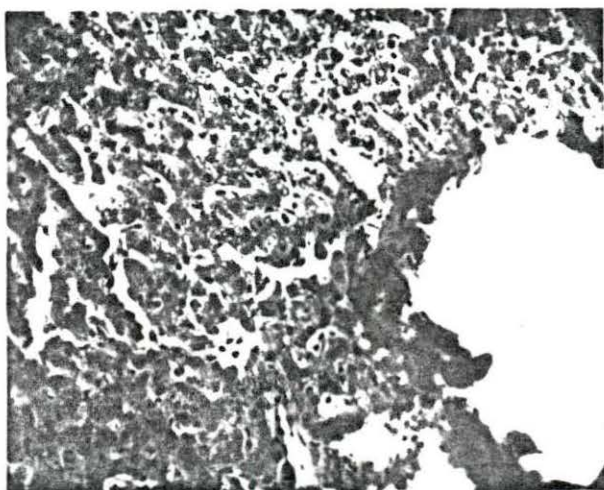   various stages of degeneration. 240X.)

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Figure 39.   ECG recording of a normal lead I with no Q-
            wave and an upright T-wave.

Figure 40.   ECG recording of a normal lead I with no Q-
            wave and an isoelectric T-wave.

190

6 SEC.

6 SEC.

Figure 41.   ECG recording of a normal lead I with a Q-
wave followed by an inverted T-wave.

Figure 42.   ECG recording of an abnormal lead I with a
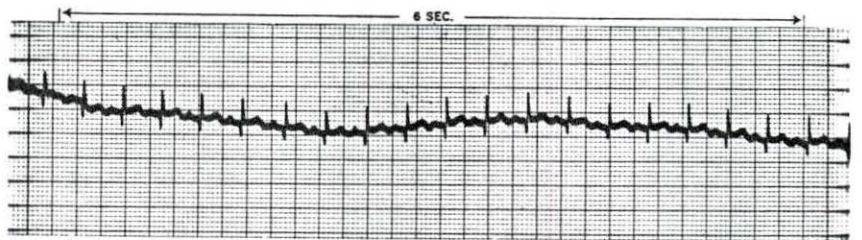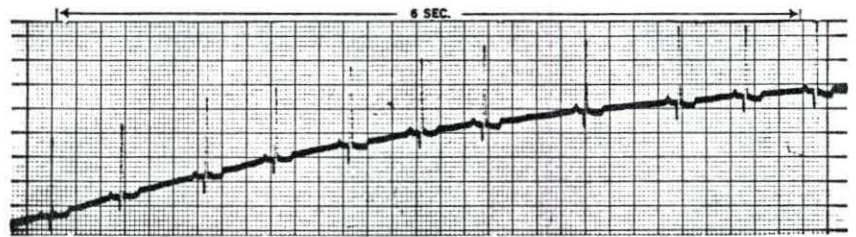Q-wave followed by an upright T-wave.

Figure 43.   ECG lead II recording from a dog taken 9 days
following myocardial infarction showing a
small S/T ratio and elevated ST segment.

Figure 44.   ECG lead III recording from a dog following
infarction showing an inverted P-wave.

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Figure 45. ECG recording of a normal lead III with S-
wave followed by an upright T-wave.

Figure 46. ECG of an abnormal lead III with an S-wave
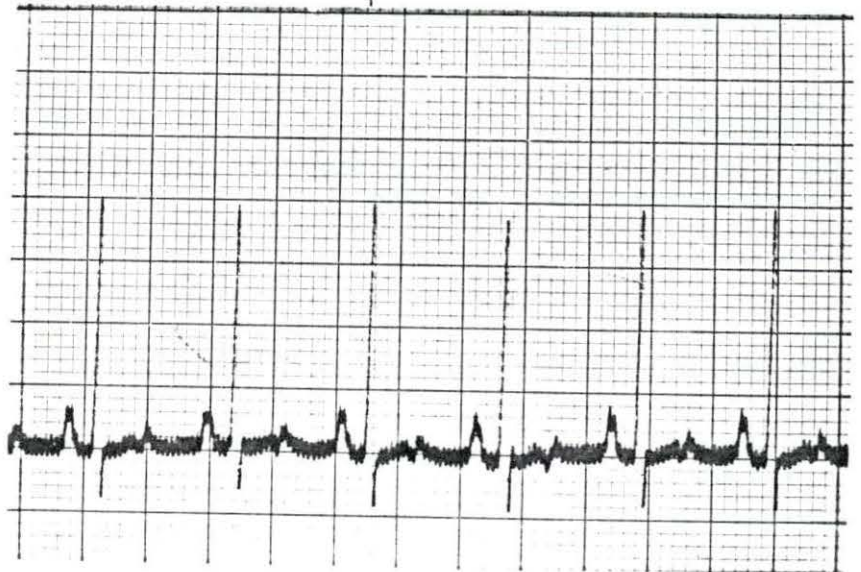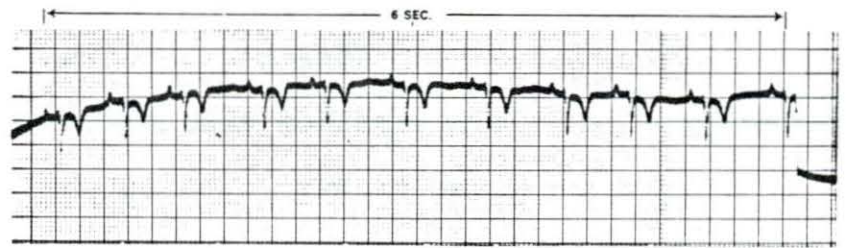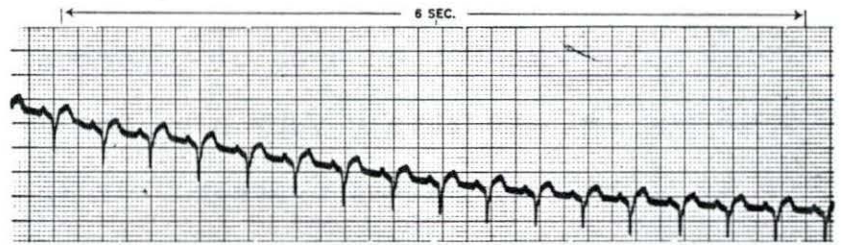followed by an inverted T-wave.

Figure 47. Abnormal ECG recording showing a Q-S
complex in lead I.

Figure 48. Abnormal ECG recording showing a Q-S
complex in lead III.

X. APPENDIX C: DATA

A. Pathological Findings of Dogs with Cardiac Pathology

1. Myocardial infarction

Dog 7   There was an area of infarction at the right border of the left ventricle very near the apex. From the outside it showed as a small depressed area. Upon opening the heart there was an area of scar tissue about 2 cm. square and the thickness of the ventricular mass was about 1 cm. There were very few adhesions of lungs to thoracic wall and pericardial sac. Other organs and tissues appeared to be normal.

Dog 11   A very small infarct was found on the endo-cardial surface just ventral to the left anterior papillary muscle. This area was about 5 mm. in diameter. A second slightly larger infarction was seen more posteriorly on the endocardial surface of the left ventricle. There were no adhesions and other organs appeared to be normal.

Dog 15   A small, shallow area of infarction slightly less than 1 cm. in diameter was found in the left ventricle about midway between the apex and base of the heart. There was a small area of adhesions of lung to the pericardium. The kidneys were yellow and appeared to be friable from fatty infiltration. Other organs and tissues appeared normal.

Dog <u>21</u>   An area of infarction approximately 1.5 cm. in diameter was seen on the anterior portion of the left endocardial surface about midway down the ventricular mass. Other organs and tissues were normal.

Dog <u>24</u>   The heart of this dog showed a transmural infarction. It was slightly over 1 cm. in diameter on the epicardial surface; however, it spread in three fingers down to the apex on the endocardial surface. The involved area commenced over the interventricular septum about one-half of the way down the left ventricle. There were some adhesions of the pericardial sac to the epicardium. There were no adhesions of the lungs. The liver appeared to be swollen grossly and upon microscopic examination there was evidence of fatty infiltration. Other tissues seemed to be normal.

Dog <u>25</u>   On the epicardial surface there was very little indication of pathology. Upon palpation a very thin area was found in the apex of the left ventricle. A hard mass was found near the region of the atrial-ventricular junction in the posterior portion of the left ventricle. Upon opening the heart a large fibrotic area was seen in the apex of the left ventricle about 3 cm. in diameter. There was a fibrotic streak 5 mm. wide and about 2.25 cm. in length between the two papillary muscles extending from the A-V junction to the base of the anterior papillary muscle.

There were some adhesions of the pericardial sac to the epicardium and to the lungs. The left diaphragmatic lobe showed areas of grey hepatization. There were no significant changes in the other tissues.

Dog 31   There was no indication of pathology from the external appearance of the heart except for a small area of adhesions of the pericardial sac to the epicardium in the area of pericardial suturing. Upon opening the left ventricle an abnormal area could be seen extending diagnally across the heart wall. It extended from below the papillary muscle almost to the attachment of the A-V valves on the posterior lateral wall. Its total length was nearly 7 cm. and it was 2 cm. wide at its greatest width very near the papillary muscle. Its width generally was between 1 and 1.5 cm. There were two fresh infarcts in the spleen. There was an old infarct on the left kidney. These were all small infarctions. The liver was hyperemic, but appeared normal otherwise. Other tissues were normal.

Dog 34   There were a few adhesions of the pericardial sac to the lungs and epicardium. There was a fibrotic area on the surface of the left ventricle. Upon opening the heart an extensive fibrotic area was evident. It extended for a distance of 7 cm. from the base of the papillary muscle to the apex of the heart in the area of the ventricular septum; however, the septum did not appear to be

involved. This area was approximately 3.5 cm. at its widest point and was more or less wedge-shaped with its point at the apex of the heart. The area around it was hyperemic and there were several rays of necrotic tissue extending from the mass of fibrosis. Liver appeared to be swollen and there was some cloudy swelling upon microscopic examination. Other tissues seemed to be normal.

Dog 38   This dog showed a fairly extensive area of epicarditis. The pericardial sac was adhered to approximately two-thirds of the epicardial surface. A small area of infarction was present on the endocardial surface in the base of the papillary muscle. This did not extend very deeply into the myocardium; however, there appeared to be 3 small projections of necrotic tissue extending towards the apex of the heart from the area of fibrosis. There seemed to be no significant changes in any of the other tissues.

Dog 45   This dog was allowed to exercise several weeks after production of the infarct. He did real well. However, he became tired in a relatively short time and would refuse to play or run for several minutes. After this short rest he would again resume normal activity. There were no other indications of any stress. Upon necropsy all tissues and organs were normal with the exception of the heart. An area of infarction about 3 cm. long and 2 cm. wide was seen in the left ventricular wall. This was not transmural, but

the entire muscle-fibrotic mass was reduced to a width of about 1 cm. In addition a slight valvular endocarditis was present on the left A-V valve.

Dog 46   There were no adhesions of the pericardial sac to the lungs or of the lungs to the pleura. There was a very small area of adhesions of the sac to the epicardium which was easily broken down. Heart appeared normal from the epicardial surface. On opening the heart an area of fibrotic tissue about 1 cm. in diameter was found on the papillary muscle where the chordae tendinae attach. Other tissues were normal.

Dog 49   This dog had the greatest amount of in-farcted tissue. Upon palpation the left ventricle was nearly as thin as the atria and had much the same consis-tency. The fibrotic area covered the entire extent of the endocardial surface from the apex to about one-third of the way up the papillary muscles. The interventricular septum was also involved somewhat near the apex. The epicardial surface appeared to be normal.

The left lobe of the lung had some exudate in the bronchi and a few small areas of pneumonia were present. The left kidney was swollen and hyperemic; the other kidney was normal. Other organs seemed to be normal.

Dog 50   This dog showed a transmural infarct of the anterior left apex. It was about 3 cm. in diameter

encroaching on the lower part of the anterior papillary
muscle. There was also some involvement of the septum near
the apex. The center area was very thin, approximately 5
mm. in thickness. Other organs showed no significant
changes.

Dog 51   There were a few adhesions of lungs to the
pleura and pericardial sac and of the sac to the epicardium.
There was no evidence of pathology from external appearance
of the heart. Upon opening the heart, the involved area was
not nearly so well defined as seen previously in other dogs.
There was necrosis, but not nearly as much fibrosis had oc-
curred. The infarct covered an area from the middle of the
anterior papillary muscle to near the apex of the heart in a
wedge-shape with its apex in the papillary muscle. This area
was about 1.5 cm. wide at its widest point and nearly 3 cm.
long. It appeared to be only about 1 cm. deep.

2. Epicarditis

Dog 5   There were no adhesions of the lungs. The
pericardial sac of this animal was nearly normal. There was
a diffuse epicarditis with the right side being more in-
volved than the left. There was a slight valvular endo-
carditis of one cusp of the tricuspid valve. There was a
slight right heart dilatation. The spleen was large and
appeared nodular. Other organs looked normal.

Dog 10   This dog showed a severe pericarditis and much of the epicardium was involved. Some areas of pete-chiation and a lot of hyperemia were present. Fluids were minimal. The liver was slightly swollen and congested. The spleen was large and congested. The kidneys were very dark, nearly black, in color but of normal size and consistency. Other organs appeared to be normal.

Dog 26   The pericardium of this dog was severely involved. It was nearly 5 mm. thick. There was a mild epicarditis throughout with a minimum of hyperemia and almost no hemorrhage. There were two small cysts which appeared to be encased talcum powder. There were no adhesions of the lungs to the pericardium or the pleura. Other organs indicated no pathology.

Dog 36   The pericardial sac was adhered to the lungs and the pleural wall, and part of the cardiac lobe of the right lung was atelectatic. There was an extensive epi-carditis on the right side which extended to the left. There was a large amount of petechial hemorrhage and hyperemia. Other tissues and organs were normal.

Dog 37   This dog died during the night about three months after pathology had been induced and had severe post-mortem changes when necropsied. The thoracic cavity was full of fluids and there was little functional lung remaining. There were many large vessels extending into the pericardium.

The pericardial sac was entirely adhered to the epicardium and was impossible to remove. There was a small amount of dark, viscous fluid in the sac. It did have an odor. The heart muscle was hypertrophied and the chambers were smaller than normal. The auricles were almost entirely fibrotic. Other organs were badly decomposed and could not be studied effectively.

Dog 43   There were some adhesions of the right lung to the pleura and pericardium. Mediastinum was thickened with many large vessels in it. The pericardial sac was completely adhered to the epicardium. Epicarditis involved the entire surface of the heart. There was little or no exudate. The right ventricle was considerably dilated and the tissue had a very soft, flabby consistency. Other organs showed no significant changes.

3. Valvular insufficiency

Dog 20   This dog showed a minimal amount of right valvular insufficiency with one cusp having a cut about one-half of the way through, yet the right atrium was very dilated. The heart looked normal other than this. Other organs and tissues appeared to be normal.

Dog 27   The right ventricle was hypertrophied and the atrium was dilated. One cusp of the right A-V valve was completely destroyed. Liver was swollen slightly and somewhat congested, but there was no indication of necrosis upon

microscopic examination. The spleen was large and knobby. Other organs and tissues showed no significant changes.

Dog 30 The heart showed very little evidence of pathology from external appearance. The medial cusp of the right A-V valve was cut and the edges were granulated. Two tendinae were also cut, but the valve probably remained partially functional. There was a small lesion on the right kidney which may have been a cyst. Other tissues and organs looked normal.

Dog 41 This dog had a very dilated heart. The left A-V valve had one cusp which was adhered to the endocardium. The right A-V valve had a mild vegetative endocarditis on all cusps. The liver was swollen and very hyperemic. There was evidence of necrosis around the central veins upon microscopic examination. Other organs were hyperemic but showed no other pathology.

Dog 42 This dog had the most severe valvular insufficiency of the five dogs in this group. One cusp of the right A-V valve was completely destroyed and a small cut was present in the second cusp. There was also a piece of granulation tissue extending from the area of the cut into the atrium.

The pleural and peritonal cavities were partially filled with fluids. The left lung was collapsed and very little of

the right was still functional. Other organs and tissues were very edematous.

The liver was partially cirrhotic and swollen. A severe passive hyperemia was present throughout the body. Upon histological examination there was necrosis around the central veins; other liver cells were in various stages of degeneration.

Hergt and Langin Method (64) for SGOT Determination

(All materials listed below, except the buffer, are commercially obtainable from the California Foundation of Biochemical Research, 3408 Fowler Street, Los Angeles 63, California.)

Phosphate Buffer, 0.1 M., pH 7.5: 84 parts 0.1 M. dibasic sodium phosphate (Na_2HPO_4) are combined with 16 parts 0.1 M. monobasic potassium phosphate (KH_2PO_4). The solutions are stored separately in the refrigerator and discarded if growth of mold appears.

Reduced diphosphopridine nucleotide (DPNH): DPNH in solution is very unstable, but it can be stored dry indefinitely with no loss of activity.

Five mg. of powdered DPNH are weighed on a sheet of parafilm and divided into 12 parts of about equal size with a scalpel blade and each portion is placed into a small (12 x 75 mm.) test tube. The tubes are placed in a desicator

over night in the dark, then sealed with paraffinized corks, and stored in the refrigerator. Each tube contains enough DPNH for two determinations. The contents are dissolved in 1.4 ml. of buffer for use.

Aspartic Acid, 0.05 M: 333.0 mg. aspartic acid are dissolved in 50.0 ml. of buffer, and the pH adjusted to approximately 7.5 with 1 or 2 drops of saturated sodium hydroxide (NaOH). The solution is then stored in the refrigerator and prepared anew if growth of mold appears.

Alpha - ketoglutaric acid, 0.1 M: Because of the instability of this material in solution, a similar technique as in the preparation of DPNH is employed.

Seventy-six mg. of alpha -ketoglutaric acid are weighed on a sheet of parafilm and divided into 12 equal portions. The material is then distributed into 12 small test tubes, placed in a desicator over night, then stoppered with parafinized corks, and stored at room temperature. For use, the contents of a tube are dissolved in 0.5 ml. of buffer. Each tube contains enough material for two determinations.

Malic Dehydrogenase, stabilized: This is used as it is supplied; the enzyme concentration varies with each lot. It is indicated on the label and must be checked carefully before use. A total of 200 units is required for each determination and the quantity is transferred directly from the vial into the cells by means of a micropipette at the time

of actual determination. The material is stored in the refrigerator.

Procedure:

1. Set up the Beckman Model B spectrophotometer in the usual manner using a blue-sensitive phototube with a 500 megohm resistor and a blue filter. The wave length setting is 340 mμ. 10 mm. cells are used (pyrex quality).

2. Use nonhemolyzed serum fresh or after freezing or refrigeration.

3. Remove all test constituents from the refrigerator and allow to come to room temperature. Mix the phosphate solution proportionately as indicated above.

4. Add 0.5 ml. and 1.4 ml. of the buffer to the tubes containing alpha - ketoglutaric acid and DPNH, respectively.

5. Using two cells, pipette as follows:

	Blank	Unknown
Buffer	2.9 ml.	___
DPNH	___	0.7 ml.
Aspartic Acid	___	2.0 ml.
Malic Dehydrogenase	___	200 units
Serum	0.1 ml.	0.1 ml.

Mix well, let stand for 10 minutes at room temperature.

6. Add 0.2 ml. of alpha - ketoglutaric acid to the
    unknown. Mix well.

7. Set the instrument to 0 O.D. with the blank and
    then read O.D. of the unknown immediately. Repeat
readings after timed intervals, usually 5 minutes.
Two equally timed intervals are sufficient if the re-
sults agree within 10 percent of each other.

Calculations:

The change (decrease) in O.D. during timed intervals is
averaged and divided by the average time per interval
to obtain the average change in O.D. in one minute.
Since one unit of GOT activity is defined as a decrease
in O.D. of 0.001 per minute, using 1.0 ml. serum, the
above quotient is multiplied by 10,000 to obtain
"units of transaminase activity per ml." of the unknown
material.

Example of Statistical Analysis

(Hergt vs. Sigma Methods for Measuring SGOT Concentrations)

Sample No.	Unit SGOT Hergt	Sigma	X= Diff.
1	113	133	20
2	82	140	58
3	85	170	85
4	100	75	-25
5	188	193	5
6	106	140	36
7	87	105	18
8	70	80	10
9	128	139	11
10	280	320	40
11	241	260	19
12	122	102	-20
13	320	410	90
14	295	370	75
15	110	150	40
16	185	305	120
17	260	400	140
18	155	235	80
19	160	240	80
20	95	82	-13
Total	3182	4049	909

$$S^2 = \frac{\sum(X-\bar{x})^2}{N-1} = \sum X^2 - \frac{(\sum X)^2}{N}$$

$$\sum X^2 = 78135 \quad (\sum X)^2 = 826281$$

$$\sum X^2 - \frac{(\sum X)^2}{N} = 78135 - \frac{826281}{20}$$

$$= 78,135 - 41,314.05$$

$$S^2 = \frac{36,820.95}{19}$$

$$S^2 = 1,937.94$$

$$S_{\bar{x}}^2 = \frac{S^2}{20} = 96.90$$

$$S_{\bar{x}} = \sqrt{\frac{S^2}{20}} = \sqrt{96.90} = 9.83$$

$$t = \frac{45.45}{9.83} = 4.62*$$

*Student t-test significant at the 0.1 percent level that there is a difference in the two tests.

$$\bar{x} = 45.45$$