THE ELECTROCARDIOGRAM IN THE EUCALCEMIC, HYPERCALCEMIC AND HYPOCALCEMIC ANIMAL

by

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INTRODUCTION AND PURPOSE OF STUDY

It has been known for some time that calcium is present in all cells of the body and has a vital role in their normal function. Further, it is known that calcium is essential to the irritability of muscle and nervous tissue. A combination of these factors makes apparent the paramount role that calcium plays in maintaining the proper environment for forceful and rhythmic contractions of the heart.

Considerable studies have been made upon the relationship of serum calcium levels and the function of the heart. This relationship has been shown by means of changes in the electrocardiogram (EKG). Extensive studies have been made on man, dog, domestic and laboratory animals, but few investigations have been made on the dairy cow other than that within the normal blood calcium range.

During their lifetime, dairy cattle undergo physiological changes resulting in periods of eucalcemia, hypocalcemia and induced hypercalcemia.

In the frequently encountered syndrome of so called "Milk Fever" of parturient dairy cattle, hypocalcemia has been shown to be a constant finding. A better name for this syndrome might be parturient hypocalcemia. As a result of this hypocalcemia the function of the heart is altered and is involved in the cause of death in untreated cases. Since milk fever is often difficult to distinguish from other disease entities encountered at the time of parturition the EKG could prove useful in arriving at an accurate diagnosis.

The treatment of choice for milk fever today is the administration of calcium intravenously. As the serum calcium rises it will eventually reach a point of hypercalcemia. This also has an effect upon the function of the heart and this condition may lead to various grades of heart block and terminal tachycardia and/or ventricular fibrillation.

Electrolyte variations in the blood induce changes in the EKG of ruminants. In calves on low potassium diets, the QRS complex is prolonged and its contour and voltage is altered. Milk fever in dairy cattle is marked by a hypocalcemia. Little is known about the EKG deviations associated with this condition.

Because of the economic importance of milk fever in dairy cattle the following experiments were designed to evaluate the EKG in the eucalcemic, hypocalcemic, and hypercalcemic subject and whether the EKG could serve as a diagnostic aid in milk fever.

Electrocardiograms of adult dairy cattle were made on cattle confined in the laboratory and on cattle under field conditions. EKG's and serum calcium determinations were made on dairy cattle under the following conditions:

a. Apparently normal dry cow

b. Apparently normal lactating cow

c. "Milk Fever" cow before, during and after intravenous calcium treatment

d. Apparently normal dry cow at the time of injection of excess calcium

REVIEW OF LITERATURE

Effects of Calcium on the Heart

Historically man has been interested in the action of calcium upon the various organisms and their organs. Calcium therapy was recommended for Phthisis by

Fourcroy in 1783 (34). About the same time, 1793, there first appeared in the literature a description of the malady of milk cows that we now know as "Milk Fever" or parturient paresis (19). In this review an attempt will be made to show a correlation between the effects of calcium upon a specific organ, the heart, and the metabolic disorder milk fever. This correlation will be based upon serum calcium levels and the electrocardiogram.

The calcium ion is present in all tissues and cells and is essential for the maintenance of life. To review all the functions of calcium in the body would be a sizable task and is not the intent of this review. It will suffice to only list these functions of calcium as follows (23): 1. Calcium is essential for the ossification of bones; 2. Calcium serves as a constituent of the intercellular cement; 3. Calcium is essential for selective cellular permeability; 4. Calcium is essential for the clotting of blood; 5. Calcium is necessary for the control of the excitability of nerve centers; 6. Calcium is essential for the contraction of skeletal and smooth muscle; 7. Calcium is necessary for the maintenance of the rhythm, tonicity, and contractility of the heart. This study is concerned with the role of calcium in the function of the heart.

As early as 1882 Sidney Ringer studied the influence of different constituents of the blood on the contraction of the heart (29, 30). Using excised frog hearts he found that calcium ions had a stimulatory effect upon the heart. He observed that the addition of excess calcium ions to the bathing fluid greatly prolonged diastolic dilation. If he added excess calcium ions to the bathing solution, prolonged contractions and occurrence of partial fusion of beats occurred, sometimes resulting in persistent spasms with stoppage of the heart in extreme systole. Ringer also observed the antagonism of the effect of the calcium ion by the potassium ion.

From the beginnings of Sidney Ringer the effects of calcium ions on the heart have been studied by many workers throughout the years. That the calcium ion was necessary for normal rhythm and contractility of the heart, and that excess calcium brought about increased contractility while decreased calcium concentration brought about a decrease in the contractility of the heart to a point of stand-still in the absence of calcium, was conclusively shown. The challenge then to the workers in this field was to determine the mode and site of action of the calcium ion in the heart. The underlying physical or chemical changes through which calcium influences the heart beat is not definitely known. It has been proposed (18) that the increased strength and duration of contraction of the heart musculature in response to calcium probably results, partly or entirely, from a direct stimulatory effect of calcium ions on the contraction of actomyosin in the cardiac muscle fibers.

Niedergerke (26) studied the staircase phenomenon and action of calcium on the heart. Using isolated heart muscle he showed that repeated stimuli produced increased facilitation (staircase phenomenon). Similar facilitation (i.e., a large increase in the contraction without a corresponding increase of the action potential) can be produced without repeated stimuli by certain changes in ionic environment, notably by an increase of the calcium concentration. This points out that even if the electrical impulse to cardiac muscle remains constant an increase in calcium ion concentration in the muscle will bring about increased contractility. Niedergerke (26) stated that his results were consistent with the hypothesis of earlier investigators that the strength of contraction is controlled by the concentration of calcium in a superficially located region of the heart cell.

To exclude the interaction of the calcium ion with other ions, such as potassium and sodium, at the cellular level is impossible. Luttgau and Niedergerke (25) demonstrated the interrelationship between calcium and sodium on the frogs heart. In their work they found that a reduction in membrane potential would lead to the inward movement of the calcium complex. This calcium complex was postulated and not experimentally demonstrated. The relationship of calcium and sodium at the cellular level has been described as an antagonism, but actually it would seem to be more of a cause and effect relationship. Removal of sodium ions causes the concentration of combined calcium in a certain region of the cell to rise so that the calcium concentration becomes sufficient, at the existing level of membrane potential, to activate contraction (25). To further study the movement of calcium in the cell and the role of calcium in the activation of contraction radioactive calcium was utilized (27). By measuring the uptake of ^{45}Ca by the heart ventricles at rest and during contracture, an inward movement of calcium in the cell was noted in the latter. It was postulated that the inward movement of calcium activated the contraction of the heart.

Throughout the body there exists the phenomenon of a nerve impulse bringing about or stimulating a certain action by a specific cell or group of cells. Thus, there must be some means by which the electrical activity of the nerve impulse can be transformed into mechanical activity, as in the heart muscle fiber. Weidman postulated that the calcium ion mediates between electrical and mechanical activity throughout the period of membrane depolarization (39). He experimentally showed that by increasing calcium concentration at the beginning of systole (i. e., after onset of membrane depolarization) increased contractility was obtained.

The effect of calcium upon nerve transmission cannot be overlooked as a possible factor in the relationship of the calcium ion upon heart function. It has been shown (8) using frog skeletal muscle that the amount of acetylcholine released by a single maximal motor volley is a direct function of the concentration of calcium ions. This then would play a vital role in the mechanism by which the autonomic nervous system functions in adjusting the heart to its environment.

The Bovine Electrocardiogram

The work in the field of bovine electrocardiography is not as extensive as that in the field of human electrocardiography. Consequently, the normals are not as well known and the interpretation of the abnormal is practically without reference in the literature. Many workers (1, 28, 24, 35) studied the bovine EKG using principles and leads described for human electrocardiography. The standard EKG leads and nomenclature of the components of the electrocardiogram used in this review are as stated by Burch (7). Sellers, et al. (32) made a study using unipolar and bipolar EKG leads for cattle which could be most advantageously applied to the detection of conduction changes, rhythm changes, and myocardial changes. Standard bipolar limb leads show great variation from animal to animal and in the same animal from time to time (1). Using a series of 28 unipolar leads Sellers, et al. (32) demonstrated a bipolar lead (IV) which appeared to have promise for general use. The bipolar chest lead (IV) with electrodes at (a) a point about a hands bredth below the point of the withers on the right side, and (b) a point just medial to the left olecranon, in the normal standing position, showed less variability from animal to animal than the other three standard bipolar leads used.

Alfredson and Sykes (1) studied the EKG in 97 normal dairy animals. Using the standard EKG limb leads I, II, and III they recorded the following data: the PR interval ranged from 0.1 to 0.3 second with an average during of 0.19 second; the QTS interval ranged from 0.06 to 0.12 second with an average value of 0.09 second; and the QT interval ranged from 0.29 to 0.47 second with an average duration of 0.39 second. Consistent throughout their data was considerable variation between leads, between cows, and in the same cow from time to time. The duration of QT and, to a lesser extent, of PR was inversely proportional to the heart rate.

Platner, et al. (28) recorded electrocardiograms of the various species of farm animals. Using a smaller number of cattle their data for the various intervals of the EKG agreed with the data as published by Alfredson and Sykes.

Lank and Kingery (24) made a series of three electrocardiograms recorded over a 15 day period on each of 45 normal lactating dairy cows. They also utilized standard EKG limb leads. Their interval data was as follows: PR 0.17 to 0.28 second with an average of 0.216 second; QRS 0.08 to 0.12 second with an average of 0.092 second; and QT 0.32 to 0.52 second with an average of 0.409 second. They described the heart rates of the cows as ranging from a minimum of 48 cycles per minute to a maximum of 84 cycles per minute with an average of 64.5 cycles per minute.

Striking dissimilarities exist between electrocardiographic records reported above (1, 28, 24, 32, 35) and those for man (7, 5, 18). Sellers, et al. (32) listed these dissimilarities. For example, (a) there is discord in general reference to the QRS and T waves. In most leads in cattle, these waves are "discordant" (i.e., the direction of the T wave is opposite to the main deflection of the QRS complex). In man, the QRS and T waves tend to be "concordant" (i.e., the direction of the T wave tends to follow the direction of the major deflection of the QRS complex). (b) The QRS potentials, in general, tend to have opposite polarity in cattle to analagous locations in man and the dog.

According to Robb (31), in his study of the QT intervals in various species, the QT interval varies according to metabolic rate within one species and also varies with the metabolic rate from one species to another.

Effects of Calcium on the Electrocardiogram

If the serum calcium ion concentration is altered in either direction from the normal it will have a profound effect upon the electrocardiogram. Animals may be rendered hypocalcemic by artificial means. Using rabbits, Kleenfeld and Gross (22) brought about a state of hypocalcemia by using injections of Ethylenediaminetetra-acetic acid (EDTA). The EDTA induced hypocalcemia manifested its influence upon the heart as measured by the EKG. Alterations found in the EKG were as follows: (a) prolongation of the QT interval; (b) inversion of the T wave; and (c) bizarre ventricular complexes. The mechanism of action of EDTA in producing the T wave alternans was questioned by Kleenfeld and Gross. They postulated that it might be other than its chelation of the calcium ion and consequently hypocalcemia.

In studies on hypocalcemic human patients Yu (40) reported a prolonged ST segment and QT interval. No mention was made of abnormal T waves in the human patient. German workers (35) reported prolongation of the QT interval in hypocalcemic cows.

To study the effect of excess calcium upon the electrocardiogram Garb (16) used the papillary muscle of the cat ventricle. Garb used the papillary muscle technique described by Cattell and Gold (1938) in which the papillary muscle is mounted in a chamber and the electrogram is taken directly from the muscle. He found that by increasing the calcium concentration in the environment the force of contraction increased markedly and in proportion to the increase in calcium concentration. The T deflection became lower and finally inverted. If the calcium concentration was returned to normal, the electrogram and myogram returned to approximately the control configuration. Garb also found that reducing the calcium concentration in the environment would bring about a marked drop in the force of contraction of the muscle. He also noted complete disappearance of measurable systolic force upon further lowering of calcium concentration. The RT interval was decreased. Upon restoration of the calcium concentration he found a return to normal configuration.

Using unanesthetized rabbits, (20) Hoff and Nahum found that intravenous administration of calcium chloride produced the following: (a) widening of the QRS interval; (b) increase in the amplitude of S; (c) disappearance of the ST interval; (d) displacement of the ST take off, and (e) characteristic changes in the contour of the T wave. Hoff and Nahum also noted, under influence of excess calcium ions, abundant ventricular extrasystoles, periodic cardiac arrest, and alternated ectopic ventricular beats. They also found that the injection of Sodium Amytal would protect the rabbits from the calcium induced irregularities noted above, although the heart speeded up. Hoff, et al. (21) also studied the effect of hypercalcemia in dogs pre-treated with morphine. They found a preliminary period of cardiac inhibition and partial A-V block. Succeeding the phase of inhibition or partially superimposed upon it, they described a phase of enhanced activity (i.e., extrasystoles and tachycardia). This period of enhanced activity often terminated in ventricular fibrillation. In those dogs that survived this second phase the heart then entered a third phase of slowing and arrest. In the deaths attributed to excess calcium concentration in the heart, approximately one-half were due to cardiac arrests and one-half due to ventricular fibrillation. They summarized the action of excess calcium upon the heart as follows: (a) an initial period of marked bradycardia; (b) a period of tachycardia and ventricular fibrillation; and (c) a period of slowing and cardiac arrest. This is in agreement with the work of Clarke (9) who studied the action of calcium on the human EKG. Hoff (21) found that atropine suppressed the early bradycardia produced by increased calcium levels and that the period of acceleration was enhanced. He attributed the initial bradycardia to a stimulatory action of calcium upon the vagus.

Bannister and Miller (2) studied the relationship of calcium and vagal inhibition of the anuran heart. They observed that stimulation of the vagus nerve altered the EKG by producing changes in the T wave, lengthening of PQ interval, and shortening of the QT interval. When calcium was omitted from the perfusing environment, stimulation of the vagus failed to modify the EKG.

Waife observed in human patients suffering from hyperparathyroidism that the resulting hypercalcemia had a marked effect upon the heart. He found that the QT interval was shortened and the PR interval was prolonged (38). He also observed that incomplete heart block may be found in the presence of hypercalcemia. It may not completely disappear when the serum calcium level returns to normal or subnormal. This condition as described by Waife differs from the heart block associated with calcium as reported by Hoff, et al. (21).

The classical experiments of intravenous calcium infusion were adapted to dairy calves by Bergman and Sellers (3, 4). Calcium gluconate was administered intravenously into dairy calves until death or severe symptoms resulted. They observed an initial marked bradycardia, presumed to be due to vagal stimulation. As the injections were continued, various grades of heart block and isolated or small groups of extrasystoles became apparent. Tachycardia and ventricular fibrillation followed. Using precordial leads (lead IV) the changes observed in the electrocardiogram were shortened QT interval, prolonged PR interval, and increased amplitude of the QRS complex. The blood pressure per beat seemed to be roughly proportional to the amplitude of the QRS complex.

Similar observations on the effect of increased calcium concentration in the body in producing initial bradycardia, tachycardia, and terminal heart failure were made by Craige (10) and Detweiler (12).

Calcium Levels in the Normal and Parturient Paretic Cow

According to Hibbs (19) in his review of milk fever (paturient paresis) in dairy cows it is stated that there are some 30 theories concerning the cause and effects of milk fever in the dairy cow. The theory accepted by most workers at the present time is one of hypocalcemia. Many workers (37, 15, 6, 17, 36, 33) have investigated serum calcium levels of parturient paretic cows in relation to the serum calcium levels of normal and paturient dairy cows. Fish (15) observed the average milk fever blood plasma values for calcium to be 3.31 mg. per 100 ml. In experiments involving 82 cases of milk fever Greigg (17) recorded a minimum serum calcium level of 3.00 mg. per 100 ml., maximum serum calcium level of 7.76 mg. per 100 ml., and an average serum calcium level of 5.13 mg. per 100 ml. Sjollema and Seekles (33) compared the levels of the calcium ion and total calcium in blood serum of milk fever and normal dairy cows. They found in the milk fever cattle a calcium ion concentration of 0.44 mg./100 ml. and total calcium concentration of 4.35 mg./100 ml. In the normal cattle they found the calcium ion concentration to be 1.65 mg./100 ml. and total calcium to be 9.35 mg./100 ml. Ward, et al. (36) found an average blood serum calcium, pre-treatment, for parturient paretic cows to be 5.0 mg./100 ml. Four to six days post treatment the serum calcium level had risen to 9.7 mg./100 ml. and at the end of 32 days serum calcium level was 10.2 mg./100 ml. Blosser and Albright (6) found normal preparturient calcium levels of 10.4 mg./100 ml., calcium levels of 8.7 mg./100 ml. on the day of parturition, and that the post parturition calcium levels gradually increased to the normal level. Ward (37) in his experiments observed that milk fever cows had a severe negative calcium balance for about 15 days prior to parturition. Other groups of normal parturient cows maintained their calcium reserves. Dukes, in his textbook of "Physiology of Domestic Animals", (13) states that in parturient paresis the serum calcium level may fall as much as 70 per cent.

Diagnosis of Parturient Paresis

The Sulkowitch test as a guide in the diagnosis and therapy of bovine hypocalcemia was evaluated by Detweiler and Martin (11). They correlated the results of 63 tests on urine samples with the determined serum calcium levels. They found a negative Sulkowitch test at serum calcium levels of 8.2 mg. per 100 ml. and below. They found positive Sulkowitch tests at serum calcium levels of 8.3 mg. per 100 ml. and above. They observed that milk fever cows elicited negative Sulkowitch tests. The confusing results of their work was that some apparently normal cows also elicited a negative Sulkowitch test.

Together with history and symptomatic observations, the most reliable test for parturient paresis is to determine serum calcium levels. A spectrophotometric method for the determination of serum calcium was described by Ferro and Ham (14). Their experimental data was consistent with Beers law in a range from 4 to 40 mg. per 100 ml. with great accuracy and excellent reproducibility.

MATERIALS AND METHODS

Six mature dairy cows were selected on the basis of their adaptability for the study with no emphasis placed upon age, breed, lactation record, or pedigree. They were of the common dairy breeds such as, Jersey, Guernsey, and Ayrshire. Four animals were housed and studied in the laboratory. They were fed a ration of alfalfa hay and grain. Two animals belonged to dairymen in the surrounding area and were studied at the respective farms.

The recordings of the electrocardiograms (EKG's) were made on a Physiograph, a pen writing, three channel recorder manufactured by E. and M. Instrument Company, Houston, Texas. This instrument utilizes a low level pre-amplifier coupled to a D. C. amplifier for the recording of the EKG's. The console model was used in the laboratory. A portable wooden carrying case was devised in order to take the unit to the field. The limiting factor in using this unit under field conditions was the availability of 110 volt alternating current.

EKG's were obtained using standard EKG leads I, II, and III. Another EKG was simultaneously recorded using the precordial lead (apex of heart to top of right scapula) as described by Sellers, et al. (32). The positive electrode was located at a point just medial to the left olecranon in a normal standing position. The negative electrode was located at a point about a hands bredth below the point of the withers on the right side. Subcutaneous needle electrodes were utilized using 18 gauge, 1 inch hypodermic needles. The amplifiers for the recording of the standard leads were calibrated so that a 1 millivolt signal would give 2 centimeters of pen deflection. The amplifiers for the recording of the precordial lead were calibrated so that a 1 millivolt signal would give 1 centimeter of pen deflection. Standard electrocardio-graphic paper and an operating speed of 25 millimeters per second was used for depicting the EKG.

Blood samples from the jugular vein were taken prior to the EKG recordings on the eucalcemic cows. Other blood samples were taken before, during, and at the end of the recordings on the hypocalcemic (milk fever) and hypercalcemic cows. Serum calcium levels were determined by the spectrophotometric method of Ferro and Ham (14).

Injections of calcium were made intravenously into the jugular vein. Calcium borogluconate, 20 per cent solution, was utilized in the laboratory for rendering cows hypercalcemic. For the treatment of the milk fever cows a commercial preparation containing calcium equal to 25.5 per cent calcium gluconate was used.

RESULTS

The EKG of Eucalcemic Dairy Cows

This study includes a series of EKG's obtained on four pre-parturient dairy cows. Nine recordings were made on cow # 1 at weekly intervals; three recordings were made on cow # 4 at weekly intervals; two recordings were made on cow # 5, five days apart; and two recordings on cow # 6, seventy-three days apart. Plate I illustrates representative precordial lead recordings of the four cows. The heart rates of the four cows ranged from 72 to 120 with a mean heart rate of 85. The PR interval range was from 4.5 mm. to 5.5 mm. with a mean PR interval of 4.6 mm. The QT interval range was from 8.5 mm. to 10.5 mm. with a mean QT interval of 9.8 mm. Data from each of the individual recordings appear in Table 1. The EKG configuration of all four cows recorded was consistent. Amplitude differences were noted in component waves (QRS and T) between cows.

EXPLANATION OF PLATE I

Electrocardiograms of Dairy Cattle with Serum Calcium Levels Within Normal Ranges.

(a) Cow # 5 Serum Calcium - 7.3 mg./100 ml.

(b) Cow # 1 Serum Calcium - 9.0 mg./100 ml.

(c) Cow # 4 Serum Calcium - 9.5 mg./100 ml.

(d) Cow # 6 Serum Calcium - 10.3 mg./100 ml.

(e) Time marker - 25 mm./second

PLATE I

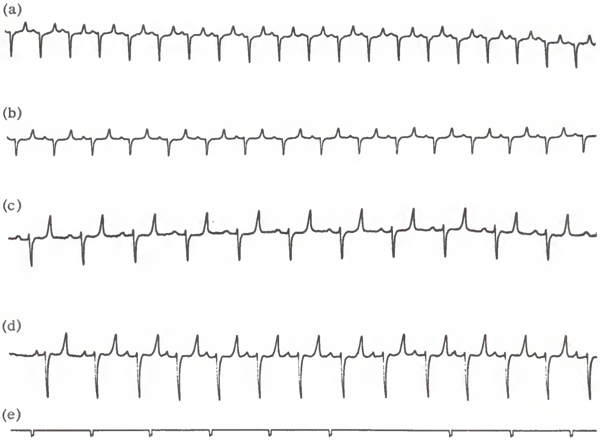


Table 1. Heart rates and duration of intervals of the EKG of dairy cows with serum calcium levels within normal range.

Animal	Serum Ca levels	Heart rate	PR interval	QT interval
# 1[1]	9.4	72	5 mm.	10.5 mm.
# 1	12.1	81	5 mm.	10 mm.
# 1	11.6	78	5 mm.	10 mm.
# 1	9.2	78	5 mm.	10.5 mm.
# 1	11.0	81	4.5 mm.	10 mm.
# 1	9.4	84	4 mm.	10 mm.
# 1	11.0	84	4 mm.	9.5 mm.
# 1	9.4	96	4 mm.	9.5 mm.
# 1[4]	8.9	90	4.5 mm.	10 mm.
# 4[1]	9.5	72	5 mm.	9.5 mm.
# 4	8.5	78	5 mm.	9.5 mm.
# 4[4]	9.0	78	5.5 mm.	10 mm.
# 5[2]	9.1	114	4 mm.	9 mm.
# 5[4]	7.3	120	4 mm.	8.5 mm.
# 6[3]	10.3	70	5 mm.	10.5 mm.

[1]Recordings were 1 week apart.

[2]Recordings were 5 days apart.

[3]Recordings were 73 days apart.

[4]Recordings were post parturient.

The serum calcium levels ranged from 7.3 mg./100 ml. to 12.1 mg./100 ml. All of these values fell within the normal physiological range. Standard EKG leads I, II, and III were run simultaneously with the precordial lead. Because of noted inconsistencies, greater variation, and susceptibility to outside interference; data from these leads were not evaluated.

The EKG of Hypocalcemic Dairy Cows

Two EKG recordings were made in the field on clinical cases of parturient paresis. Data from the recording on cow # 3 were not presented because of post-mortem diagnosis of complications of metritis, mastitis, and enteritis. Cow # 2 was a typical clinical case of milk fever. When the recording was initiated the cow was comatose and had a temperature of 96^{o} F. Serum calcium level was 5.2 mg./100 ml. at time of initial recording.

Plate II (a) and Plate III (b) illustrate the EKG of the hypocalcemic cow # 2. The hypocalcemia markedly altered the configuration of the EKG. The QT interval was greatly prolonged. The amplitude of the T wave was reduced and the T wave was intermittently inverted. The QRS complex was alternately diphasic and negatively monophasic. In sudden sporadic bursts the T wave amplitude would jump from 3 mm. to 15 mm. and the QRS complex amplitude would jump from 15 mm. to 30 mm. The data from the recording of the hypocalcemic cow are shown in Table 2. Bizarre configuration of the EKG were consistent in the recordings on the hypocalcemic animals.

The EKG of a Hypercalcemic Dairy Cow

The serum calcium level of cow # 6 was gradually increased from normal to a state of hypercalcemia by means of the slow intravenous drip of a 20 per cent solution of calcium boro-gluconate. Data for this experiment appears in Table 3. The EKG's of the hypercalcemic cow are illustrated in Plate II (c) and Plate III (d). The QT interval was shortened from 10 mm. at the onset of the experiment to 7 mm.

EXPLANATION OF PLATE II

Electrocardiogram of Eucalcemic Hypocalcemic and Hypercalcemic Dairy Cattle.

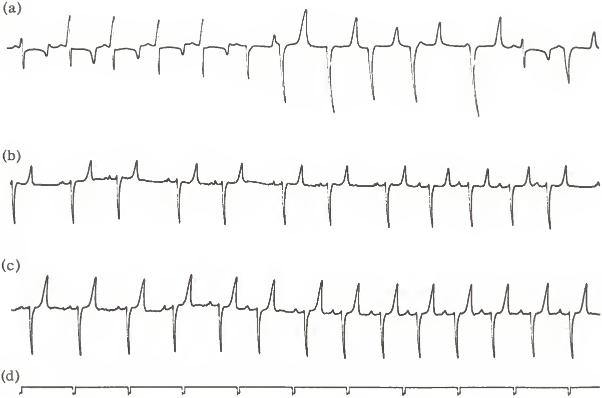
(a) Cow # 2 Serum Calcium - 5.2 mg./100 ml.

(b) Cow # 6 Serum Calcium - 10.3 mg./100 ml.

(c) Cow # 6 Serum Calcium - 40.6 mg./100 ml.

(d) Time marker - 25 mm./second

PLATE II

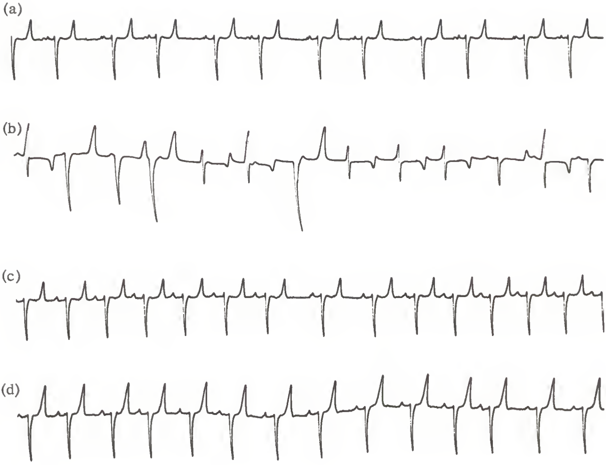


EXPLANATION OF PLATE III

Electrocardiogram of Eucalcemic, Hypocalcemic and Hypercalcemic Dairy Cattle.

(a) Cow # 6	Serum Calcium -	10. 3 mg. /100 ml.
(b) Cow # 2	Serum Calcium -	5. 2 mg. /100 ml.
(c) Cow # 6	Serum Calcium -	10. 3 mg. /100 ml.
(d) Cow # 6	Serum Calcium -	40. 6 mg. /100 ml.

PLATE III



at the state of hypercalcemia. A marked change in the T amplitude was noted. The T wave amplitude increased from 8 mm. at the normal serum calcium level to 14 mm. at the state of hypercalcemia. The amplitude of the QRS complex was relatively unchanged. Throughout the course of the intravenous calcium infusion the heart rate was very irregular. There were frequently noted pauses followed by two or three regular beats, then another pause, then two or three regular beats with this cycle repeating itself over and over periodically. The trend of the heart rate showed an initial slowing followed by a period of acceleration. Due to the appearance of occasional bizarre EKG configurations, the extreme distressed condition of the cow, and the symptoms of impending cardiac embarrassment, the experiment was terminated at this time.

Table 2. Heart rates, and EKG interval and amplitude changes on a parturient paretic cow.

Heart rate	PR interval	QT interval	T amplitude	QRS amplitude
78	4.0 mm.	15.0 mm.	3.0 mm.	15.0 mm.
72	5.0 mm.	15.0 mm.	2.5 mm.	15.0 mm.
72[1]	5.0 mm.	14.0 mm.	3.0 mm.	15.0 mm.
84	5.0 mm.	12.0 mm.	7.0 mm.	20.0 mm.
78	5.0 mm.	11.0 mm.	12.0 mm.	16.0 mm.
78	P absent	11.0 mm.	14.0 mm.	16.0 mm.
84	6.0 mm.	9.5 mm.	11.0 mm.	15.0 mm.
90[2]	6.0 mm.	9.0 mm.	11.0 mm.	15.0 mm.

[1] Calcium therapy initiated.

[2] Five minutes before cow got up.

Table 3. Heart rates, and EKG interval and amplitude changes on an induced hypercalcemic cow.

Heart rate	PR interval	QT interval	T amplitude	QRS amplitude
70	5.0 mm.	10.0 mm.	8.0 mm.	19.0 mm.
66[1]	5.0 mm.	10.0 mm.	9.0 mm.	20.0 mm.
70	4.5 mm.	9.0 mm.	8.0 mm.	19.0 mm.
66	5.0 mm.	9.0 mm.	8.0 mm.	20.0 mm.
72	5.0 mm.	9.0 mm.	9.0 mm.	20.0 mm.
54	4.5 mm.	9.0 mm.	9.0 mm.	19.0 mm.
60	5.0 mm.	8.5 mm.	9.0 mm.	19.0 mm.
54	5.0 mm.	8.0 mm.	10.0 mm.	19.0 mm.
50	4.0 mm.	8.0 mm.	13.0 mm.	21.0 mm.
66	4.0 mm.	8.0 mm.	12.0 mm.	20.0 mm.
72	4.5 mm.	7.5 mm.	12.0 mm.	19.0 mm.
80	5.0 mm.	7.5 mm.	13.0 mm.	19.0 mm.
72	4.5 mm.	7.5 mm.	14.0 mm.	21.0 mm.
78	5.0 mm.	7.0 mm.	14.0 mm.	20.0 mm.

[1]Calcium infusion started.

The EKG of a Milk Fever Cow During Calcium Therapy

Data from the EKG of cow # 2 during calcium therapy are recorded in Table 2. The EKG's of this experiment are illustrated in Plate IV. The heart rate was very irregular during the course of the calcium therapy. The trend of the heart rate was one of acceleration. The heart rate changed from 72 beats per minute to 90 beats per minute. The PR interval showed a slight prolongation from 4 mm. to 6 mm. The P wave was extremely variable and was periodically absent as illustrated in Plate IV (b) and (c). In these instances the P wave is covered up by the superimposed T wave. The QT interval is markedly decreased from 15 mm. in the hypocalcemic

EXPLANATION OF PLATE IV

Electrocardiographic Sequence Monitoring a Milk Fever Cow from Beginning through Successful Calcium Therapy.

(a) Before Calcium therapy; Cow down; Serum Calcium -5.2 mg./100 ml.

(b) Before Calcium therapy; Cow down; Serum Calcium -5.2 mg./100 ml.

(c) 5 minutes after Calcium therapy began.

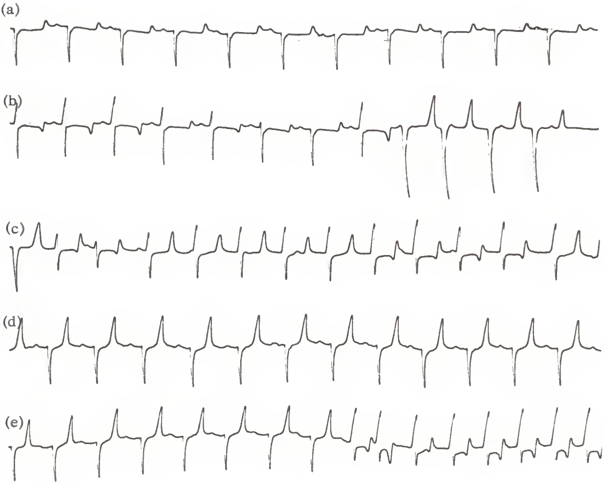
(d) 15 minutes after Calcium therapy began.

(e) 10 minutes after Calcium therapy completed.

5 minutes before cow got up.

Serum Calcium 17.6 mg./100 ml.

PLATE IV



cow to 9 mm. at the conclusion of the calcium therapy. The T amplitude was increased from 3 mm. in the hypocalcemic cow to 11 mm. at the conclusion of therapy. Early in the experiment, with the cow in a state of hypocalcemia, the T waves were periodically inverted. The QRS complex was relatively consistent in amplitude throughout the experiment with occasional bursts to an amplitude of 26 mm. Throughout the course of the calcium therapy the QRS complex was periodically diphasic and in the later stages of therapy the complex was extremely bizarre (Plate IV (e)).

Comparison of Standard and Precordial EKG Leads

The standard EKG leads (I, II, and III) were compared to the precordial lead (IV) in order to evaluate the faithfulness of the precordial lead in monitoring metabolic changes in the heart. This comparison is illustrated in Plate V. It was noted throughout this study that the precordial lead faithfully and accurately monitored the metabolic changes of the heart as recorded in the EKG. It was noted that any change in configuration or amplitude of the components of the EKG as recorded by the standard leads also appeared in the precordial lead.

DISCUSSION

The calcium ion is present in all normal tissues of the body. The calcium ion is necessary for the proper function of many organs and organ systems. The organ that is probably most vulnerable to any alteration in calcium ion concentration is the heart. The action of the calcium ion upon the heart can be described, but the

EXPLANATION OF PLATE V

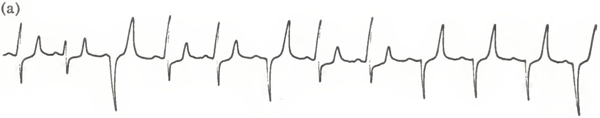
Comparison of Simultaneous Recording of Precordial Lead (IV) and Standard Lead II

(a) Precordial lead (IV); 1 mv. = 1 cm. deflection.

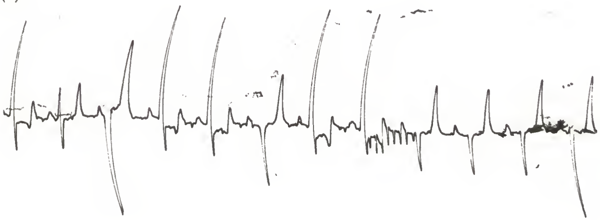
(b) Standard lead II; 1 mv. = 2 cm. deflection.

PLATE V

(a)



(b)



mechanism of its action is not clear. That the metabolism of the heart musculature is altered by changes in calcium ion concentration, is very evident. If the serum calcium level falls below the normal, the contractile force of the heart also falls. If the calcium level falls drastically low, the contractile force of the heart disappears and the heart, as a pump, is non-functional. Many cows that have died of milk fever (hypocalcemia) exhibit post-mortem lesions of marked circulatory failure.

To gain further knowledge of the action of calcium upon the heart, the EKG may be used. The EKG is one of the means of monitoring the metabolism of the heart musculature at a given time. This study provided data to aid in the interpretation of the correlation of the calcium ion concentration in the blood and alterations in the EKG of dairy cows. When subjected to analysis, the data obtained from the normal EKG's in this experiment were found to be in agreement with the findings of other workers (1, 3, 4, 24, 32). The electrocardiograms of the parturient paretic cows depicted altered configurations. The QT interval was prolonged. The QT interval of the EKG represents the time required for depolarization and repolarization of ventricular muscle. The increased duration of the QT segment is brought about by a decreased efficiency of metabolism in the heart musculature. The exact cause of the decreased efficiency in ventricular musculature is not known. One possible explanation might be the lack of available calcium ion, since the calcium ion is necessary to activate the enzyme adenosinetriphosphatase, which causes the breakdown of adenosinetriphosphate (ATP) to ADP and yields energy. Due to the deficiency of the calcium ion, in the paturient paretic cow, the contraction of the heart musculature is impaired because of the lack of available energy. Another possible explanation of the impaired function of the ventricular muscle might be found at the locus of altered impulse transmission. The amount of acetylcholine released by nervous tissue is proportional to the calcium ion concentration. Since acetylcholine is the chemical mediator of nerve impulses, it would follow that a deficiency of the calcium ion would impair impulse transmission to the heart and/or within the heart musculature. It has been established that the serum calcium levels in parturient paretic cows are lowered. It is questionable whether the altered physiology of the milk fever cow is due entirely to the drop in serum calcium level. It has been suggested that the milk fever cow is in a state of alkalosis. In a state of alkalosis there is a decrease in the amount of ionized calcium due to the fact that more of the serum calcium is in a bound form. Thus, it is probably the combination of a decrease in the serum calcium level and the decrease in ionized calcium that leads to the altered physiology of the heart.

It was demonstrated in this experiment that the amplitude of the T wave increased markedly in the parturient paretic cow as the serum calcium levels rose. The T wave represents the electrical activity as the ventricular musculature repolarizes. It is evident that the calcium ion plays a vital role in the metabolism involved in this phenomena.

The PR interval remained very constant throughout all of the experiments. The PR interval represents the time required to depolarize the musculature of the auricles. Since the contraction of the auricles is not vital to the dynamics of the circulatory system and since the mass of this muscle is much less than that of the ventricle and since the work produced and energy required by the auricles is much less, it is understandable that changes in calcium ion concentration would not exert as evident an alteration in the PR interval as compared to the alteration in the QT interval.

When excess calcium ions are added to the environment of the heart, the changes produced in the metabolism of the heart musculature, as monitored by the EKG, are basically the opposite to the changes found in hypocalcemia. In this study the QT interval was decreased as serum calcium levels increased. The amplitude of the T wave increased as the serum calcium levels increased. Both of these findings suggest an increase in the metabolism of the heart musculature. As calcium was infused, the heart rate was at first slowed and then accelerated. The initial bradycardia was probably due to stimulation of the vagus. The period of acceleration, or tachycardia, was probably the result of stimulation of the sympathetic nervous system. Intravenous calcium will stimulate the sympathetic nervous system bringing about a subsequent release of epinephrine. If the infusion of calcium salts are continued in an animal, the over-stimulation of the sympathetic nervous system and its release of epinephrine, coupled with the increased metabolic activity of the heart musculature, will bring about failure of the heart. The heart will stop in systole, or will fail in ventricular fibrillation.

The analysis of the recordings from the several EKG leads used in this experiment showed a superiority of the precordial lead (IV) as a means of monitoring the bovine heart in the laboratory and in the field. The recordings from the precordial lead were much clearer, were not as susceptible to outside electrical interference, were not as susceptible to alterations due to movement of the animal, exhibited less variation from animal to animal and in the same animal, and were much easier to analyze.

As the Sulkowitch test has been shown not to be too reliable as a means of diagnosing milk fever in the parturient paretic cow, additional diagnostic aids would be of benefit. It was shown in this study that the EKG is a reliable method of monitoring the serum calcium levels (within certain ranges) in the dairy cow. Because of the marked alteration in the EKG of the hypocalcemic cow, it was postulated that the EKG would be a possible aid in the differential diagnosis in the parturient paretic cow.

SUMMARY

EKG's of adult dairy cattle were recorded on cattle confined in the laboratory and on cattle under field conditions. EKG's and serum calcium determinations were made on dairy cattle under the following conditions: (a) apparently normal dry cows, (b) apparently normal lactating cows, (c) milk fever cows before, during, and after intravenous calcium treatment, and (d) apparently normal dry cow at the time of injection of excess calcium.

This study furnished data from the EKG's of eucalcemic, hypocalcemic, and hypercalcemic dairy cows to aid in the interpretation of the relationship of the levels of serum calcium to the metabolism of the bovine heart. It was shown that the QT interval was markedly prolonged in the hypocalcemic (milk fever) cows. The

increased duration of the QT segment was brought about by a decrease in the efficiency of the metabolism of the ventricular musculature. Inversion of the T wave was also demonstrated in the hypocalcemic cow. The QRS complex was alternately diphasic and negatively monophasic. Bizarre configurations of the EKG were a frequent finding in the hypocalcemic cow.

As serum calcium levels were increased by intravenous infusion of calcium gluconate, the configuration of the EKG was altered. The QT interval was shortened. The amplitude of the T wave increased as the calcium ion concentration was increased. Again, bizarre configurations of the EKG were noted in the hyper-calcemic animals. The heart rate became irregular as calcium was administered. Initially there was a pattern of bradycardia followed by a period of tachycardia.

It was noted in this study that the precordial lead (IV) faithfully and accurately monitored metabolic changes in the heart and proved superior to the standard EKG leads (I, II, and III) for this purpose in the bovine.

It was postulated that the EKG would be a possible aid in the differential diagnosis in the parturient paretic cow. The limiting factor in the use of the EKG as a diagnostic aid would be the availability of a source of 110 volt alternating current.

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THE ELECTROCARDIOGRAM IN THE EUCALCEMIC, HYPERCALCEMIC AND HYPOCALCEMIC ANIMAL

by

DAN WILLIAM UPSON

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During their lifetime, dairy cattle undergo physiological changes resulting in periods of eucalcemia, hypocalcemia, and induced hypercalcemia. In the frequently encountered syndrome of so called milk fever of parturient dairy cattle, hypocalcemia is a constant finding. As a result of this hypocalcemia, the function of the heart is altered and is involved in the cause of death in untreated cases. The treatment of choice for milk fever today is the administration of intravenous calcium. As the serum calcium level rises, during therapy, it will eventually reach a point of hypercalcemia. This also has an effect upon the function of the heart and this condition may lead to various grades of heart block and terminal tachycardia and/or ventricular fibrillation. Because of the economic importance of milk fever in dairy cattle, this study was designed to aid in the correlation of serum calcium levels and its effect on the metabolism of the heart in the bovine.

The experiments were performed using six mature dairy cows of Jersey, Guernsey, and Ayrshire breeding. Four animals were housed and studied in the laboratory, while two of the cows were studied in the field. The recordings of the electrocardiograms (EKG'S) were made on a Physiograph, a pen writing, three channel recorder. EKG'S were obtained using standard EKG leads I, II, and III and a simulataneous recording using a precordial lead (apex of heart to top of right scapula). Blood samples, from the jugular vein, were taken prior to the EKG recordings on the eucalcemic cows. Other blood samples were taken before, during, and at the end of the recordings on the hypocalcemic (milk fever) and hypercalcemic cows. Serum calcium levels were determined by the spectrophotometric method of Ferro and Ham. Injections of calcium were made intravenously into the jugular vein.

A series of sixteen EKG's were obtained on pre and post parturient, eucalcemic, dairy cows. Two EKG's were made in the field on clinical cases of milk fever. The serum calcium level of one of the cows was gradually increased, by the intravenous infusion of calcium boro-gluconate, to a state of hypercalcemia; and its effect on the heart monitored by an EKG.

The effects of a state of hypocalcemia on the EKG of the bovine, as found in this study, may be summarized as follows: (a) the QT interval was greatly prolonged; (b) the amplitude of the T wave was reduced; (c) the T wave was intermittently inverted; (d) the QRS complex was both diphasic and negatively monophasic, showing bizarre configurations; and (e) sporadic bursts in amplitude of T wave and QRS complex.

The effects of a state of hypercalcemia on the EKG of the bovine, as found in this study, may be summarized as follows: (a) the QT interval was shortened; (b) the amplitude of the T wave was increased; (c) bizarre configurations of all components; and (d) an initial period of bradycardia followed by a period of tachycardia.

The effects of calcium therapy on the EKG of a milk fever cow, as found in this study, may be summarized as follows: (a) accelerated heart rate; (b) slight prolongation of PR interval; (c) P wave periodically absent; (d) QT interval markedly decreased; (e) the amplitude of the T wave was increased; and (f) diphasic QRS complex and bizarre configurations.

The precordial lead was found to be preferable for monitoring the heart in the bovine. It was postulated that the EKG would be a possible aid in the differential diagnosis in the parturient paretic cow.