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MASTER

Animal Metabolic Studies of Strontium and Calcium with Specific
Reference to Fallout Radionuclides

Sixth Progress Report

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TABLE OF CONTENTS

	<u>Page</u>
1. SUMMARY: SCOPE OF INVESTIGATION AND SIGNIFICANT RESULTS OBTAINED	1
a. Kinetic Studies of Calcium Metabolism in Goats:	1
Effects of Dietary Intake of Ca and P	2
Effects of Ovariectomy and Alloxan-Induced Diabetes	4
b. Kinetic Study of Phosphorus Metabolism in Goats:	4
Effects of Dietary Intake of Ca and P	4
c. Kinetic Study of Calcium Metabolism in Cows:	5
Effect of Age	5
d. Retention of Strontium in Swine	7
Effects of Age, Dietary Ca and P Intake and Breed	7
Effects of Separation of Piglets From the Sow	7
e. Hydroxyproline Excretion in Swine as a Function of Age ..	9
f. Hypophysectomy of Swine with Yttrium-90	9
g. Effect of Thyroparathyroidectomy on Strontium Retention in Beagles	10
h. Transcapillary Movement of Ca, Sr and Na into Muscle of Dogs	11
2. TECHNICAL REPORTS PREPARED FOR PUBLICATION	16
3. REPRINTS OF PUBLICATIONS	18
4. OTHER ACTIVITIES	20

1. SUMMARY: SCOPE OF INVESTIGATION AND SIGNIFICANT RESULTS OBTAINED

The two major areas of investigation during the current contract year have been studies of calcium metabolism in goats and strontium-85 retention in swine. Considerably minor effort has been expended in preliminary studies of calcium and strontium metabolism in dogs. These studies with dogs will be discontinued under this contract at the conclusion of the contract period.

a. Kinetic Studies of Calcium Metabolism in Goats

(J. J. B. Anderson, Y. H. Kuo, W. C. Crackel, and A. R. Twardock)

Female goats have been used as a model for dairy cows in studies designed to investigate the physiological basis of parturient paresis or milk fever. A basic premise in these studies has been that older multiparous high-producing dairy cows undergo a breakdown in calcium homeostasis and become hypocalcemic because of an inadequate supply of calcium (Ca) from a rapidly available or readily exchangeable calcium pool (RECaP), distributed throughout the body and, particularly, on bone surfaces. Thus, measurement of the three parameters, size (E), biological half-life ($T_{1/2}$), and transfer rate (TR), of the RECaP using Ca-47 kinetics has been considered essential in goats under different physiological conditions and different dietary intakes of Ca and Phosphorous (P) in order to better understand Ca homeostatic mechanism.

A statement of the method used for the kinetic measurements is largely repeated from previous reports: Approximately 12 μ Ci of Ca-47 is injected into the jugular vein of each goat and the same quantity is placed in a 15-gallon water-filled barrel which serves

as a machine standard. Heparinated blood samples are withdrawn shortly after injection (about 1 hour), at 4 to 6 hours, and six more times between 20 and 64 hours post-injection. Plasma Ca-47 radioactivity and stable Ca (Ca-40) are determined and used in calculating the percent of the injected dose per gram of Ca (specific activity) in the plasma. This calculated value is plotted on the logarithmic coordinate as a function of time on the linear abscissa. From the linear portion of such a plot extrapolated to y-axis (intercept at 0 time), E of the RECaP is obtained by dividing the intercept specific activity into the total dose which is 100% at zero time, if distribution had been instantaneous. The biological $T_{1/2}$ of this pool is then determined from the slope (k) of the extrapolated line. The TR of Ca into and out of the pool is calculated by multiplying E by k. The values of the three parameters vary according to the animal's physiologic status.

An overview of this method with some data from our goat studies is included in a publication, entitled "Measurement of Calcium Kinetics in Dairy Goats" (See publication C00-1339-27).

Effects of Dietary Intake of Ca and P

Since the last Progress Report (C00-1339-22), the data obtained from the dietary intake studies have been analyzed in two papers, one of which is in press, "Effects of High and Low Dietary Calcium on the Size and Half-Life of the Readily Exchangeable Calcium Pool in Female Goats Under Two Different Feeding Conditions" (See publication C00-1339-28), and one of which is in manuscript, "Long Term Effects of High and Low Calcium Diets on Calcium Kinetics in Dairy Goats" (See publication C00-1339-30).

The major findings reported in the first paper which compared the effects of a loose hay-loose grain diet (pre-dietary trial) versus a pelleted hay-loose grain ration (dietary trial) on calcium-47 kinetics in goats were: (1) a significantly reduced calcium TR to and from the RECaP in goats on a control ration (1.3 Ca:1 P) as well as those on a high (4 Ca:1 P) or low (1 Ca:3 P) Ca intake from the pre-dietary to the dietary trial; and (2) a greater reduction in blood Ca concentration in goats fed the high or low Ca ration compared to goats fed the control ration during the dietary trial.

A more thorough statistical analysis (see manuscript) of 14 Ca-47 kinetics experiments in non-pregnant non-lactating goats over a nine-month period showed that the mean E and the TR into and out of the RECaP significantly decreased in goats on either the high (2.90% Ca:0.72% P) or low (0.24% Ca:0.72% P) intakes compared to goats on a control ration (0.49% Ca:0.39% P). The blood Ca concentration was lower and the P concentration higher in goats fed either of the two experimental rations compared to the controls. The data suggest that the RECaP is modified in response to the perturbing experimental dietary intakes, possibly by a calcium homeostatic mechanism involving parathyroid hormone.

Based on whole-body measurements and blood specific activity determinations, values of bone accretion rates (A) and size (E) of the exchangeable Ca pool have been calculated according to a modification of the method of Bauer, Carlson and Lindquist. These data are not included in the report as they are still being processed.

Effects of Ovariectomy and Alloxan-Induced Diabetes

These studies were undertaken by Dr. Kuo in partial fulfillment of the requirements for the degree of Doctor of Philosophy at the University of Illinois (See publication C00-1339-39). The major finding was that goats with alloxan-induced diabetes, hence hypoinsulinemia and high blood glucose concentration had no change in their blood calcium concentration over periods of a month or longer post-treatment. It can be tentatively extrapolated from the results of goats that blood calcium concentration is not affected in cows that become diabetic in the course of their pregnancy. On the other hand, Littledike and co-workers (Proc. Soc. Exp. Biol. Med., 129:135 1968) have shown the converse, namely that hypocalcemia can induce hypoinsulinemia in pregnant dairy cows. Diabetic symptoms in parturient paretic cows would, thus, appear to be an effect of hypocalcemia rather than a cause of it.

A few goats were ovariectomized at the beginning of this study, but analysis of the calcium data indicated that this line of investigation was not very fruitful in goats.

b. Kinetic Study of Phosphorus Metabolism in Goats: Effects of Dietary Intake of Ca and P (R. A. McMullen, A. R. Twardock, W. C. Crackel and J. J. B. Anderson)

This kinetic study was undertaken to determine the significance of the dietary intake of Ca and P on the parameters of the readily exchangeable phosphorus pool (REPP) with the use of P-32 as the tracing radionuclide. The kinetic methods employed in the Ca-47 studies were also used for P-32 except that the Cerenkov radiation

produced by the interactions of the highly energetic beta particles emitted by P-32 present in diluted plasma (solution) was measured in a liquid scintillation counter. The same goats were used concurrently in this experiment as well as in the Ca-47 dietary study.

Figures 1 and 2 are plots of the parameters, E and $T_{1/2}$, which were calculated from the blood plasma P-32 specific activity decay curve. Tables 1 and 2 summarize the data on E, $T_{1/2}$ and TR of the REPP and RECaP.

From this study it is concluded that both E, $T_{1/2}$ and TR are much greater for the P pool than for the Ca pool and that variations in E and TR of the REPP were much greater than for E and TR of the RECaP. The level of dietary Ca intake appeared to have little influence on the REPP. Further investigation of the REPP in the future is desirable.

c. Kinetic Study of Calcium Metabolism in Cows: Effect of Age

(J. J. B. Anderson, W. C. Crackel, and A. R. Twardock)

The cows of this study include two calves purchased for the project as well as cows belonging to other investigators in the Departments of Veterinary Clinics and Dairy Science. Three other cows have been purchased since this study began, but since they are pregnant, the preliminary experimental data from them has not been included in this report.

The purpose of this work is to obtain baseline information on the RECaP parameters of non-lactating, non-pregnant cows, which can be used in future studies designed to examine the effects of pregnancy, parturition and lactation and of dietary Ca and P intake on the

RECaP. The method of analysis used is almost the same as used in the goat studies, except that plasma specific activity is determined for periods up to 120 hours post-injection.

The results of this study are presented in the manuscript "Ca-47 Kinetics in Cattle" (COO-1339-35). The major findings were that younger animals have larger values of E, shorter values of $T_{1/2}$ and larger values of TR than older animals. In fact, calves about 6 months old have pool sizes about three times as large as mature cows 7 years of age. Part of this work was presented at the annual meeting of the Federation of American Societies for Experimental Biology (COO-1339-26).

In addition a preliminary study using rats was undertaken to determine the effect of estrogen, or lack of it, on the retention of Sr-85 in normal and castrated female rats. This experiment was done to determine the feasibility of related studies which are planned to test the hypothesis of an inhibitory role of estrogen on bone turnover in peripartum cows and goats (See Proposed Technical Program, 1969-1972). The rat study showed that daily administration of estrogen at a replacement dose level reduced bone mineral turnover in ovariectomized adults compared to non-treated ovariectomized rats (See publications COO-1339-41 and 42). In agreement with other studies in the literature, estrogen does indeed have an effect on calcium homeostasis. It will be important to know what effect dose level (physiologic vs. pharmacologic) has on bone turnover as a function of time of gestation, during which period plasma estrogen concentration increases to a maximum just prior to parturition.

Housing for all goats and cows has been moved from facilities previously provided by the Animal Science Department at the whole body counter (ILLASCO) to satisfactory housing at the Veterinary Research Farm.

d. Retention of Strontium in Swine (J. J. B. Anderson and W. C. Crackel)

Effects of Age, Dietary Ca and P Intake and Breed

Several more standard-sized swine litters have been examined since the last Progress Report. The number of animals on experimentation at any one time has been limited by the availability of only one holding pen at the whole body counter (ILLASCO) provided by the Animal Science Department. This pen with an attached outside run has been split down the middle into two holding areas, one for swine on the higher Ca and P intake (1.2 Ca to 0.8% P) and the other one for those on the lower Ca and P ration (0.8 to 0.6%). No miniature swine were used in the study the past year because of insufficient housing at the whole body counter.

Part of this work was reported at the Annual Meeting of the Radiation Research Society this past Spring in Cincinnati (See publication C00-1339-31) and a more complete analysis of the retention findings for standard-size swine is to be found in manuscript (C00-1339-37).

Significant results of this study are as follows:

1. mean fractional Sr-85 retention as measured 200 days post-injection (P.I.) was practically the same (range: 0.27 to 0.31) for standard pigs injected from at any time

between birth and 6 months of age, except for those injected at 2 months, and fed the higher Ca and P rations;

2. mean fractional retention 200 days P.I. of standard swine fed the low Ca and P ration had a much broader range, from 0.09 when injected at 2 months of age to 0.14 at 1 month to 0.26 at 6 months to 0.28 at birth, and retention in these swine was less than in pigs on the higher Ca and P intake, except for those pigs injected at birth when the mean retentions were nearly identical;
3. mean rate of gain in weight of the standard pigs was highly similar in each age group whether the pigs were ingesting a high or low Ca diet;
4. mean fractional retention 200 days P.I. in a small sample (one litter) of miniature swine injected at 1 or 2 months of age was much higher than for standard swine (0.49 and 0.41), but retention was the same in both sizes of pigs injected at 4 and 6 months;
5. mean fractional retention was slightly higher in each age group of miniature swine fed the higher Ca and P ration, except those injected at 1 month of age; and
6. mean rate of gain in weight of the miniature group was similar in each age group whether the pigs were on high or low Ca intake.

In addition, the experimentally determined retention curves were fit mathematically by a two-exponential function, a power function and a modified power function. In most cases the two-exponential fit of the data was better than the fit of either power function.

Effect of Separation of Piglets from the Sow

This study was undertaken to determine if the retention of Sr-85 in swine injected at birth was affected by feeding an artificially prepared diet as compared to the intake of piglets normally getting sow milk. Little or no difference in retention was observed between piglets raised on or off the sow as long as the post-weaning ration was the same with respect to Ca and P intake. This work was reported at the Ninth Annual Hanford Biology Symposium, entitled "Radiation Biology of the Fetal and Juvenile Mammal" this past spring (See Publication COO-1339-29).

- e. Hydroxyproline Excretion in Swine as a Function of Age (J. J. B. Anderson and W. C. Crackel)

Urinary hydroxyproline has been measured at periodic intervals in several litters of swine from birth to one year of age in order to use the excretion of this imino acid as an index of organic bone turnover, particularly collagen, and to compare its excretion to Sr-85 retention or, conversely, Sr-85 removal. A good correlation of these two parameters in growing swine might indicate that a similar correlation could be expected in humans from infancy through adolescence. This information is presented in manuscript (See Publication COO-1339-38).

- f. Hypophysectomy of Swine with Yttrium-90 (L. E. St. Clair and J. J. B. Anderson)

Because our University Nuclear Reactor was not in operation during the past 12 months or longer, no experiments utilizing neutron-activated Y-90 could be undertaken. The reactor became operable during the latter half of this July and the few experiments necessary to complete this

part of the project will be undertaken prior to the conclusion of the current contract year. As would be expected, costs of using our own reactor are very low compared to outside jobbers and this has been the only reason for delaying the completion of this study.

When a number of 1 to 3 month-old standard swine are satisfactorily hypophysectomized (90% destruction or more), they will be injected with Sr-85 in order to determine their fractional retention up to 200 days post-injection. Daily hormonal supplementation (growth hormone and thyroid-stimulating hormone) does not appear feasible at present because of the large outlay of money required. A preliminary study of hypophysectomized and control, nearly mature rats (140-150 grams) demonstrated that growth hormone administered at a maintenance level had little or no effect on the retention of Sr-85 as measured up to 45 days P.I. (See Publications C00-1339-25 and C00-1339-33).

g. Effect of Thyroparathyroidectomy on Strontium Retention in Beagles

(J. J. B. Anderson and W. C. Crackel)

The retention of Sr-85 was measured in 17 mature male and female beagles, about half of which had been thyroparathyroidectomized for over a year. The measurements were made with our new small animal whole-body counting equipment which includes two 2" x 2" solid sodium iodide crystals. The purpose of this first experiment was to determine what effect twice daily injections of porcine calcitonin (Armour Pharmaceutical Co., Kankakee) over a 30-day period had on bone turnover as measured by Sr-85 retention and on blood Ca and P concentrations as measured by

standard chemical procedures. Retention data are not fully analyzed and are thus not included here. Although retention varied according to the age of the dog, control dogs paired by age with operated dogs had similar retentions whether treated with calcitonin or not. The lack of effect of calcitonin is apparently due to the low bone turnover rate of fully mature dogs, irregardless of sex or parathyroid status. Blood calcium measurements did not reveal any difference between treated and untreated animals either (See Publication C00-1339-34). Radiographic examination of selected bones by Dr. R. Slusher revealed no changes in any dogs whether treated or not with calcitonin.

Experimental studies with beagles under this contract will be phased out at the conclusion of this contract year.

h. Transcapillary Movement of Ca, Sr and Na into Muscle of Dogs*

(H. F. Downey and J. J. B. Anderson)

In 20 experiments in 5 animals, small depots (0.1-0.04 ml) of radioactive calcium, sodium, and strontium were injected into myocardium to determine the relative permeability of capillaries to these elements. The rate of clearance of isotopes from the intramuscular depot should be directly related to their ability to diffuse into the capillary blood flow. The clearance of sodium consistently exceeded that of calcium and strontium by a factor of about 1.3. While the clearances of calcium and strontium are more similar, in some experiments, the clearance of strontium slightly exceeded that of calcium (Fig. 3).

*Partially supported by General Research Support Grant FR-05460 from the General Research Support Branch, Division of Research Facilities and Resources, National Institute of Health to the College of Veterinary Medicine, University of Illinois.

Although these elements are predominantly extracellular in myocardium, it is possible that differences in their clearances might be due to differences in their ability to be mobilized from the tissue depot. This problem will be studied in the next series of experiments where the isotopes will be injected intra-arterially and their relative extractions determined in venous blood. Then, for example, if sodium extractions exceed those of calcium or strontium, a difference in capillary permeability is indicated. To be sure that vascular protein binding does not influence the extractions, a dextran-Ringers perfusate will be used in some experiments.

These studies with dogs under this contract will be phased out at the conclusion of this contract year.

JJBA:mrn;csc

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Legends

Fig. 1 Plot of poolsize (E), biological half life ($BT\ 1/2$) and transfer rate (TR) of the readily exchangeable phosphorus pool (REPP) in 3 groups of 3 goats each which were fed rations containing different levels of Ca and Pi.

Fig. 2 Plot of the same parameters as in Fig. 1 for the readily exchangeable calcium pool (RECaP) of the same 9 goats split into 3 groups according to dietary Ca and Pi intake.

Fig. 3 Relative ratios of radioactivities in coronary venous blood following simultaneous intramyocardial injection of ^{47}Ca , ^{24}Na , and ^{85}Sr . Initial ratios near one reflect an intravascular component of the injection due to damaged capillaries. Later ratios indicate differences in the clearances of these elements from the interstitial fluid by the circulation.

Fig. 1

Fig. 2

Injection #1 4-2-69

Fig. 3

Ratio

Ratios of Radioactivities

Ca/Sr .

Na/Sr x

Na/Ca +

Sample Number

Table 1
Phosphorus REPP

High Ca:P Diet					<u>Significance between animals</u>	
Goat	<u>1</u>	<u>14</u>	<u>16</u>	<u>Group</u>		
$\bar{x}$	.2228	.3502	.3850	.3194	1 vs 14	1%**
s^2	.0181376	.0259578	.0221384	.02337390	1 vs 16	1%**
s	.1347	.1611	.1488	.1529	14 vs 16	n.s.

Low Ca:P Diet						
	<u>4</u>	<u>6</u>	<u>7</u>	<u>Group</u>		
$\bar{x}$	.2920	.3793	.2834	.3182	4 vs 6	n.s.
s^2	.0157654	.0269098	.0026685	.01441241	4 vs 7	n.s.
s	.1256	.1640	.0517	.1201	6 vs 7	n.s.

Control Diet						
	<u>35</u>	<u>38</u>	<u>312</u>	<u>Group</u>		
$\bar{x}$	.2476	.2937	.2104	.2506	35 vs 38	n.s.
s^2	.0018869	.0085128	.0184598	.00913865	35 vs 312	n.s.
s	.0434	.0923	.1359	.0956	38 vs 312	n.s.

Significance

High Ca:P Diet vs Low Ca:P Diet	n.s.
High Ca:P Diet vs Control Diet	1% **
Low Ca:P Diet vs Control Diet	0.1% ***

**Significantly different ($p < .01$)

***Significantly different ($p < .001$)

Table 2

Calcium RECaP

High Ca:P Diet					Significance between animals	
<u>Goat</u>	<u>1</u>	<u>14</u>	<u>16</u>	<u>Group</u>		
$\bar{x}$	.0896	.1774	.2095	.1588	1 vs 14	1%**
s^2	.0001546	.0007349	.0013054	.00340231	1 vs 16	1%**
s	.0124	.0271	.0361	.0583	14 vs 16	n.s.
Low Ca:P Diet					Significance between animals	
	<u>4</u>	<u>6</u>	<u>7</u>	<u>Group</u>		
$\bar{x}$	.1180	.1223	.1327	.1244	4 vs 6	n.s.
s^2	.0000194	.0004060	.0002266	.00021915	4 vs 7	n.s.
s	.0044	.0201	.0151	.0148	6 vs 7	n.s.
Control Diet					Significance between animals	
	<u>35</u>	<u>38</u>	<u>312</u>	<u>Group</u>		
$\bar{x}$	.3916	.3334	.1776	.3009	35 vs 38	20%
s^2	.0034411	.0014044	.00082834	.01045021	35 vs 312	1%**
s	.0587	.0375	.1022	.1022	38 vs 312	1%**

Significance

High Ca:P Diet vs Low Ca:P Diet

n.s.

High Ca:P Diet vs Control Diet

1%**

Low Ca:P Diet vs Control Diet

1%**

**Significantly different ($p < .01$)

2. Technical Reports Prepared for Publication

- COO-1339-30 Long Term Effects of High and Low Calcium Diets on Calcium Kinetics in Dairy Goats. J. J. B. Anderson, W. C. Crackel, Y. H. Kuo, A. R. Twardock, and H. W. Norton
- COO-1339-32 Effect of Time on Distribution of Injected Radiostrontium in the Skeleton of Six-Month Old Swine and Its Relation to Calcium Accretion and Bone Growth. J. J. B. Anderson, J. W. Greenfield, J. R. Posada, M. Cupp, and W. C. Crackel
- COO-1339-33 Effects of Growth Hormone on Bone Mineral Turnover in Hypophysectomized and Normal Rats. J. J. B. Anderson
- COO-1339-34 Long Term Effects of Calcitonin on Plasma Calcium and Phosphorus Concentrations in Thyroparathyroidectomized and Normal Mature Beagles. J. J. B. Anderson, M. W. Balk, W. C. Crackel, M. K. Austin, and E. C. Bollmeier
- COO-1339-35 Calcium-47 Kinetics in Cattle. J. J. B. Anderson, W. C. Crackel and A. R. Twardock
- COO-1339-36 Calcium-47 Kinetics in Goats During Pregnancy and Lactation. J. J. B. Anderson, Y. H. Kuo, W. C. Crackel and A. R. Twardock
- COO-1339-37 Strontium-85 Retention in Swine as a Function of Age and Dietary Calcium and Phosphorus Intake. J. J. B. Anderson and W. C. Crackel

- COO-1339-38 The Effect of Age on Urinary Hydroxyproline
Excretion in Swine and Its Relation to Strontium-85
Removal. J. J. B. Anderson and W. C. Crackel
- COO-1339-39 Effects of Alloxan Diabetes on the Clinical
Chemistry and Calcium Metabolism of Dairy Goats.
Y. H. Kuo, Ph.D. Thesis, University of Illinois
- COO-1339-40 Calibration of Liquid-Scintillation Counter for
Measuring Human Whole-Body Potassium. T. G. Lohman,
P. R. Ribisl, J. J. B. Anderson, A. R. Twardock,
and H. W. Norton
- COO-1339-42 Estrogen Inhibitory Action on Bone Mineral Turnover
in Female Rats. J. J. B. Anderson, J. W. Greenfield
and W. C. Crackel

3. Reprints of Publications

- COO-1339-14 Cesium-137 Retention by Cattle, Sheep and Swine.
A. R. Twardock, and W. C. Crackel. Health Physics
16:315-323, 1969.
- COO-1339-17 Effect of Time on Distribution of Injected Radio-
strontium in the Skeleton of Young Pigs. J. J. B.
Anderson. Health Physics 15:237-241, 1969.
- COO-1339-21 Whole-body Retention of Strontium-85 in Swine Given
Sodium Alginate or Barium and Sodium Sulfates. L.
Milin and J. J. B. Anderson. Journal of Nutrition
97:181-184, 1969.
- COO-1339-25 Effect of Growth Hormone on Bone Mineral Turnover in
Hypophysectomized and Normal Rats (Abstract). J. J.
B. Anderson and J. D. McKean. Federation Proceedings
28(2):373, 1969.
- COO-1339-26 Calcium-47 Kinetics in Cattle (Abstract). W. C. Crackel,
J. J. B. Anderson and A. R. Twardock. Federation
Proceedings 28(2):760, 1969.
- COO-1339-27 Measurement of Calcium Kinetics in Dairy Goats. A. R.
Twardock, Y. H. Kuo, W. Crackel and J. J. B. Anderson.
In: Parturient Hypocalcemia, J. J. B. Anderson, ed.
New York: Academic Press, 1969 (In Press).
- COO-1339-28 Effects of High and Low Dietary Calcium on the Size and
Half-Life of the Readily Exchangeable Calcium Pool in
Female Goats under Two Different Feeding Conditions.
J. J. B. Anderson, Y. H. Kuo, W. Crackel and A. R. Twardock.
In: Parturient Hypocalcemia, J. J. B. Anderson, ed.
New York: Academic Press, 1969 (In press).

- COO-1339-29 Strontium-85 Retention in Neonatal Swine: Effect of Rearing on the Sow Versus Separation from the Sow. J. J. B. Anderson and W. C. Crackel. In: Radiation Biology of the Fetal and Juvenile Animal, M. R. Sikov, ed. Oak Ridge, Tenn.: Division of Technical Information, U.S.A.E.C., 1969 (In press).
- COO-1339-31 Effect of Two Different Dietary Calcium and Phosphorus Levels on ⁸⁵Sr Retention in Swine (Abstract). J. J. B. Anderson and W. C. Crackel. Radiation Research Society, 17th Annual Meeting, May 18, 1969.
- COO-1339-41 Effect and Lack of Estrogen on Bone Retention of Sr-85 in Normal and Castrate Female Rats (Abstract). J. J. B. Anderson, J. Greenfield, J. R. Posada and W. C. Crackel. Proceedings of International Union of Physiological Sciences. VII: 12, 1968 (24th International Congress).

4. Other Activities

- a. "Conference on Parturient Paresis in Dairy Animals", November 17 to 19, 1968. 25 papers were presented by participants from throughout the world. Conference was organized by committee consisting of J. J. B. Anderson, Chairman, A. R. Twardock and K. A. Kendall. Proceedings are to be published under the title, Parturient Hypocalcemia, by Academic Press, New York, 1969.
- b. Book review by J. J. B. Anderson on Animal Function: Principles and Adaptations by G. S. Malcolm, G. A. Bartholomew, A. D. Grinnel, G. B. Jorgensen and F. N. White. MacMillan, New York, 1968. Review appeared in Journal of American Veterinary Medical Association, 153:1340, 1968.
- c. Direction by J. J. B. Anderson of Ph.D. Thesis Research of Gaylord E. Shaw, entitled "A Comparative Study of Calcium and Strontium Metabolism in the Pack Rat (Neotoma albigula) and White Rat (Rattus albinus).". Work to be completed in the Fall of 1969 and degree should be awarded in February, 1970.
- d. Direction by A. R. Twardock and J. J. B. Anderson of Ph.D. Thesis Research of Y. H. Kuo, entitled "Effects of Alloxan Diabetes on the Clinical Chemistry and Calcium Metabolism of Dairy Goats".

- e. Seminars based on work done under AEC contract were presented by J. J. B. Anderson at:
1. Department of Pharmacology, University of Vermont College of Medicine
 2. Dept. of Medicine, Harvard Medical School
 3. Dept. of Animal Veterinary Science, College of Agriculture, University of Massachusetts
 4. Dept. of Physiology and Biophysics, College of Arts and Sciences, University of Illinois.
 5. Dept. of Physiology and Pharmacology, College of Veterinary Medicine, University of Illinois.
- f. Development of new graduate course entitled "Mineral Metabolism" by J. J. B. Anderson

Special Research Support Agreement

University of Illinois

Contract No. AT (11-1)-1339

for the Period December 1, 1968 through November 30, 1969

1. Estimated Total Shared Costs at the End of the Contract Period	\$66,071
2. Total Amount Chargeable to AEC	\$37,000
3. Approved AEC Support Ceiling	\$37,000
4. Minus Item 2, "Total Amount Chargeable to AEC"	\$37,000
5. Estimated Free AEC Support Funds	0

Equipment Report

University of Illinois

Contract No. AT (11-1)-1339

for the Period December 1, 1968 through November 30, 1969

Equipment Items

None