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APPLICATIONS OF RADIOISOTOPE TECHNIQUES
TO CLINICAL VETERINARY MEDICINE

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Introduction

The Department of Physical Biology of the New York State Veterinary College has maintained an effort in the clinical applications of radioisotopes in veterinary medicine over the last several years. This program, supported by the Atomic Energy Commission, has resulted in the elaboration and widespread utilization of a number of radioisotope techniques in routine veterinary practice. The New York State Veterinary College is one of the very few veterinary colleges in the United States with the availability of the facilities and personnel necessary for the development of a nuclear medical effort in veterinary practice. Thus, the nuclear medical effort of the New York State Veterinary Medical College has contributed significantly to the growth of information and utilization of radioisotope applications in veterinary medicine.

It also should be pointed out that during the last two years, the amount of funding of the previous AEC-Phase I contract funds for the nuclear medicine effort has been relatively small amounting to only approximately 10,000 dollars per year. This has effectively restricted the amount of effort that could be mounted in the area of nuclear veterinary medicine and it is hoped that with additional funding under a new contract arrangement, the amount of effort may be expanded along the lines set forth in the proposal accompanying this report.

Probably the most significant effort made by this Department in the Nuclear medicine area over the past two years has been related to the diagnosis of thyroid gland function in numerous domestic animal species. Before the elaboration of nuclear medical techniques for diagnosing thyroid function, such diagnosis in veterinary medicine was extremely difficult, if not impossible due to the high levels of

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circulating inorganic iodine in most animal species and the consequent errors involved in the determination of protein bound iodine by the chemical method, as well as by the impossibility of performing basal metabolic rate studies in domestic animals. Thus the development of the resin sponge uptake of labeled triiodothyronine and the determination of total serum thyroxine by competitive protein binding for use in veterinary medicine, initiated in this Department, has resulted in a revolution in the diagnostic capabilities for thyroid gland evaluation in veterinary medicine.

In addition to the effort put forth in the area of thyroid gland function, other studies have been undertaken and reported in many other areas including the estimation of renal function using labeled compounds for evaluation of glomerular filtration rate and total renal blood flow, the use of labeled fatty acids in differential diagnosis of various malabsorptive states in domestic animals, the use of radioactive labels for studies of hematopoietic function in domestic animals, which studies showed the inadvisability of giving blood transfusions to cattle, the evaluation of protein loss to the gut by the use of labeled serum albumin, and others. The recognition of the contribution of this Department in the area of veterinary nuclear medicine is probably best exemplified by the invitation from the editors of Advances in Veterinary Science and Comparative Medicine to this Department to provide a chapter on "Nuclear Veterinary Medicine" for the 1974 edition. The purpose of this yearly periodical is to bring the profession up-to-date on the latest advances in the profession. A copy of this manuscript, which is still in press, accompanies this report.

With the recent donation to the veterinary college of a rectilinear scanner by the Upstate Medical Center in Syracuse, N.Y., nuclear imaging techniques have now for the first time become available as an addition to the list of procedures available from the nuclear medicine unit. The clinicians in both the Small and Large Animal Clinics have made significant use of these procedures during the past year, particularly for the diagnosis of brain and bone lesions which, without the availability of isotope techniques, would be impossible.

The remainder of this report is divided into sections corresponding to the areas of endeavor during the past year, each of the sections is compiled in manuscript form for possible future publication. The sections include: Studies of Albumin Metabolism in Dogs Using ^{51}Cr -Chromium and ^{125}I -iodine labeled albumin; Semen characteristics in thyroidectomized stallions; chromium EDTA as a gastrointestinal reference marker in the neonatal bovine calf, and evaluation of thyroid function using irradiation-immunoassay for total serum triiodothyronine.

✓
Radioimmunoassay ~~for~~
~~and 511 and 125I tracer studies~~
~~discovery~~

FOR
COMPARISON OF SERUM TOTAL THYROXINE AND SERUM TRIIOTHYRONINE LEVELS
evaluation
IN THE ~~DIAGNOSIS~~ OF THYROID FUNCTION IN GLAND FUNCTION IN THE DOG

by

Francis A. Kallfelz and Robert J. Wallace

Introduction

The existence of L-triiodothyronine - (T_3) in circulating blood serum was discovered in 1952 by Gross and Pitt-Rivers (1). During recent years, evidence has accumulated indicating that the contribution of L-triiodothyronine to overall thyroid function in many is indeed significant. Since methods for precise quantitation of this hormone have become available (11) it has become apparent that in some human patients thyroxine concentration alone is inadequate for assessing the overall level of thyroid function. Nevertheless, the importance of serum T_3 assays in the routine assessment of patients suspected with abnormalities in thyroid function has yet to be established clearly. The role of the triiodothyronine radio immunoassay in the evaluation of thyroid function will be more clearly defined in the human when additional large scale studies have been completed.

In the dog, very little effort has been expended in the role of serum triiodothyronine levels in normal thyroid hormone physiology. Previous experience that the therapy of hypothyroidism with L-triiodothyronine is ineffective in the dog might indicate that this hormone is of little significance in this species. However, recent unpublished observations (12) have indicated that the determination of total serum triiodothyronine may be a more sensitive indicator of thyroid status in the dog than the more usual determination of total serum thyroxine. Thus, it appeared warranted to investigate the normal levels of serum triiodothyronine levels in the dog and compare responses to thyrotrophin (TSH) in both total serum thyroxine and total serum triiodothyronine concentrations.

Materials and Methods

Total serum thyroxine was determined by competitive protein binding and total serum triiodothyronine by radioimmunoassay. Initial blood samples were taken from a group of normal dogs and from another group of thyroidectomized dogs. Thereafter, a dose of 10-USP units of TSH was given intramuscularly to each animal and subsequent blood samples were taken at 2 hour intervals from two to twelve hours thereafter with a final sample taken at 24 hours after administration of the TSH.

Results

Table 1 shows the levels of total serum thyroxine and total serum triiodothyronine in both intact and thyroidectomized animals before and at various time periods after the administration of thyrotrophin. It can be seen that in intact animals, serum thyroxine levels increased from a level of approximately three micrograms percent before TSH to a maximum of 7.5 micrograms percent at 10 hrs after administration of the hormone. This pattern of increased serum thyroxine levels is consistent with increases seen previously in similar studies. At the same time, serum triiodothyronine level increased from a pre-TSH level of approximately 50 millimicrograms percent to a maximum of approximately 100 millimicrograms percent at 6 hrs after administration. The increase in the serum triiodothyronine level was, therefore, similar to that of thyroxine with the exception that serum T_3 level appeared to peak slightly earlier than that of T_4 . In thyroidectomized animals, the pre-TSH serum thyroxine level was approximately 0.8 μ g percent and there was no significant increase in this level throughout the period of study after TSH. Again, this has been seen previously. In regard to serum triiodothyronine levels in thyroidectomized animals, the pre-TSH level was approximately 6 millimicrograms percent. Again, there was no significant increase in

serum triiodothyronine levels after TSH administration.

The results of this study indicate that the percentage increase in hormone levels after TSH is slightly greater with serum thyroxine than it is with serum triiodothyronine. This information might indicate that the serum thyroxine level is a more sensitive indicator of thyroid status than is the total serum triiodothyronine level. However, if one compares the levels of thyroxine to triiodothyronine in thyroidectomized animals, as compared to intact controls, it can be seen that there is approximately a 10-fold difference between the serum T_3 levels in thyroidectomized animals as compared to control animals, while there is only a 3-fold difference in the thyroxine levels in the two situations. The reason for the relatively high apparent level of circulating thyroxine in thyroidectomized animals is unknown. It may be due to either normal variation in the test system used or might possibly be due to some non-thyroxine compounds which are reacting in the system. The serum triiodothyronine level on the other hand appears to reach very close to zero levels in thyroidectomized animals.

These results, of course, are in experimental animals and whether or not similar findings will occur in clinical situations is unknown at the present time. Therefore, we have proposed in the accompanying proposal that the serum triiodothyronine determination be used in conjunction with the determination of total serum thyroxine for a period of time in clinical evaluations to determine if, indeed, the serum triiodothyronine level is more sensitive an indicator of thyroid function than is the serum thyroxine level in the dog.

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Table 1. Total serum thyroxine (T_4) and serum triiodothyronine (T_3) in a group of intact and thyroidectomized dogs as a function of time after administration of 10 USP cc of thyrotrophin.

	<u>Intact</u>		<u>Thyroidectomized</u>	
	T_4 ($\mu\text{g } \%$)	T_3 ($\text{m}\mu\text{g } \%$)	T_4 ($\mu\text{g } \%$)	T_3 ($\text{m}\mu\text{g } \%$)
0	2.87 ± 0.59	51.50 ± 9.52	0.83 ± 0.44	5.75 ± 7.23
2	3.55 ± 1.03	75.33 ± 4.93	0.68 ± 0.32	6.00 ± 1.41
4	5.14 ± 2.90	82.00 ± 1.41	0.56 ± 0.49	8.50 ± 3.54
6	6.89 ± 0.34	101.00 ± 1.41	0.52 ± 0.45	5.00 ± 7.07
8	6.45 ± 1.27	82.00 ± 17.07	0.85 ± 0.07	1.00 ± 1.41
10	7.37 ± 1.09	86.67 ± 2.89	0.66 ± 0.12	13.50 ± 3.54
12	6.13 ± 0.90	96.67 ± 38.28	1.05 ± 0.42	10.50 ± 2.12
24	4.57 ± 0.88	65.33 ± 8.39	0.86 ± 0.14	9.00 ± 1.41

✓ Studies of Albumin Metabolism in
Dogs Using ^{51}Cr and ^{125}I Labeled Albumin

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Excessive loss of proteins into the gastrointestinal tract has been shown to be a major pathophysiologic disorder associated with gastrointestinal disease in both man and animals. Various techniques have been developed over the years which allow quantitation of this loss. Perhaps the most widely used technique, at the present time, is the determination of plasma protein turnover rate and gastrointestinal protein loss using ^{125}I and ^{51}Cr -labeled serum albumin. Using this approach, Waldman et al. (1) have studied 180 human patients with suspected gastroenteric protein loss and have shown that this technique is an effective means of diagnosing protein losing enteropathy.

However, there is considerable disagreement in the literature regarding the role of the intestinal tract in normal plasma protein metabolism. For example, Glennert et al. (2) found in dogs that the intestinal tract accounted for approximately 40% of the normal turnover of plasma proteins while Waldman in studies of normal humans indicated that only 2 to 15% of the total daily plasma turnover was cleared to the gut.

The following studies were performed in an attempt to determine more accurately the role of the gastro-intestinal tract in the physiological turnover of plasma proteins in the dog.

Materials and Methods

Experiment 1. In the first experiment, six Labrador Retriever dogs were placed in metabolism cages and fed a commercial dry dog chow and water ad libidum. After two days accommodation each dog was given an intravenous injection of 20 μCi of ^{51}Cr -labeled human serum albumin which had been obtained from a commercial radiopharmaceutical supply house. Heparinized

blood samples were taken at $\frac{1}{2}$, 1 and 4 hours and then daily for 12 days following injection of the isotope. In addition urine and feces were quantitatively collected on a daily basis over the twelve days period.

Blood samples were centrifuged, and 3-4 ml aliquots of plasma were counted in a well type scintillation counter along with an aliquot of the dosing solution. Daily urine and fecal samples were placed in quart jars, brought to constant volume with water, and counter for total ^{51}Cr content in a large sample counter. Aliquots of the dosing solution were also counted in this manner.

The data for each plasma disappearance curve of ^{51}Cr was entered in a digital computer and a least squares estimate of the curve was made. In all cases a two exponential curve gave the best fit to the data. It was assumed that the first exponential represented removal of ionic ^{51}Cr , while the second represented removal of ^{51}Cr -serum albumin. By using the second exponential of the plasma disappearance curve, and the data from four to twelve days for urinary and fecal elimination of ^{51}Cr , the clearance of ^{51}Cr into urine and gut was determined according to the equation shown in Figure 1.

The metabolic clearance of albumin from the body was determined from the product of the removal constant of the second exponential and the plasma volume as determined from the zero time y intercept of the removal curve as shown in Figure 2.

The validity of the first experiment could be challenged due to the fact that human rather than canine albumin was used. Also it had been previously shown that the plasma ^{51}Cr curve could not be used for calculation of the metabolic clearance since the label was eluted from the protein, in vivo and thus the curve was not representative of actual protein degradation.

Experiment 2. A second experiment was thus performed in which canine serum was employed and in which both ^{51}Cr and ^{125}I were used as labels. The albumin fraction was isolated from pooled dog sera by Sephadex chromatography and preparative disc electrophoresis as shown in Figure 3. This slide demonstrates electrophoretograms of dog serum, the albumin fraction after passage through Sephadex G-100, and purified albumin after preparative disc electrophoresis. Iodination of the albumin was accomplished by the method of Reif, and chromation by the method of Waldman. Handling of the animals and data were similar to the first experiment with the exception that only 5 animals were used and the the albumin degradation rate was calculated from the ^{125}I removal curve.

Experiment 3. Since it had been reported that injection of $^{51}\text{CrCl}_3$ gives results similar to those obtained when labeled albumin is used, a third experiment was performed and analyzed as were the first two with the exception that $^{51}\text{CrCl}_3$ rather than labeled albumin was administered.

Experiment 4. Finally, to check the validity of the assumption that ^{51}Cr secreted in the intestinal tract is not reabsorbed, a group of dogs was given an oral dose of $^{51}\text{CrCl}_3$ and urine and feces were collected and counted for the next four days.

Results

Figure 4 demonstrates the plasma disappearance curve of ^{51}Cr after administration of human labeled albumin. The double exponential nature of the curve is apparent and, as mentioned previously, the second exponential was assumed to represent plasma protein catabolism.

Table 1 shows the clearance rate of ^{51}Cr from the plasma to urine and feces based on the second exponential. Fecal radioactivity is assumed to represent loss of labeled protein to the gut while urinary radioactivity probably represents inorganic ^{51}Cr lost in the urine after elution or breakdown of plasma protein elsewhere in the body.

Table 2 summarizes parameters of plasma protein metabolism as determined in this experiment. Metabolic clearance of protein was approximately 10 ml/hr and loss in the gut was about 4.5 ml/hr. Approximately 16% of the plasma albumin pool was turned over per day and fecal catabolism represented about 47% of the total. The reason for the discrepancy between metabolic clearance as determined from the plasma disappearance curve and the sum of urinary and fecal loss of label is unknown but may be due to experimental error.

The results of this study tend to support the Danish workers in that a large fraction of the plasma protein catabolism appeared to occur via the intestinal route. However, the use of canine albumin and of ^{125}I labeled protein for the measurement of albumin degradation was deemed necessary and thus the second experiment was performed.

Figure 5 shows the disappearance curves for ^{125}I and ^{51}Cr after intravenous injection of labeled serum albumin. As previously shown by Waldman in man, the chromium label is removed at a faster rate than that of ^{125}I . Presumably, the ^{125}I curve represents actual plasma albumin turnover rate while the ^{51}Cr label is removed more rapidly due to elution of ^{51}Cr from the circulating protein. The ^{125}I curve was thus used to determine the rate of degradation of albumin while the ^{51}Cr plasma curve as well as the urine and fecal ^{51}Cr data were used to determine elimination

rates in urine and feces.

Table 3 demonstrates the urinary and fecal clearance rates of ^{51}Cr for the five dogs used in this experiment. Assuming that this represents plasma protein catabolism, approximately 1.9 ml of plasma was cleared to the gut each hour while 5 ml was cleared by other mechanisms with ^{51}Cr elimination in the urine. Kinetic parameters from this experiment are shown in Table 4. The metabolic clearance was about 4.3 ml per hour and the fecal clearance about 44% of the total. Albumin degradation was 8% per day.

The results of this experiment differ from the first experiment in that the metabolic and fecal clearance, as well as the albumin degradation rate were about half of what had been determined previously using labeled human albumin. This might be due to a more rapid removal rate for human albumin, a foreign protein in the dog, while canine albumin data may represent a more physiological situation. The results of this experiment do, however, agree with the first, and with the Danish workers, in that somewhat over 40% of the plasma albumin turnover appears to be due to loss in the gut.

Table 5 shows total elimination of ^{51}Cr in urine and feces for the 12 days of the experiment. About 54% of the dose was recovered with 48% appearing in the urine and about 6% appearing in the feces.

In a further experiment, $^{51}\text{CeCl}_3$ rather than labeled albumin was given by i.v. injection and plasma, urine and feces samples as before. Figure 6 compares the plasma disappearance curves of ^{51}Cr labeled albumin

and $^{51}\text{CrCl}_3$. It can be seen that while there is an initial rapid fall off of activity with inorganic chromium, after the 4th day the slopes of the removal curves are similar. This result is probably due to in vivo labeling of protein with ^{51}Cr but that the extent of labeling is not as great as with the in vitro labeling procedure. Table 6 demonstrates that with inorganic ^{51}Cr , the elimination of label is also greater, about 60% more of the dose being eliminated during the study than with the labeled albumin. This corresponds nicely with the difference in plasma disappearance curves seen in the previous slide.

Finally, a group of dogs was given an oral dose of $^{51}\text{CrCl}_3$ and urine and feces collected for the next four days. Results are shown in Table 7. About 93% of the dose was recovered in the four day period. Ninety percent of this was found in the feces and only 3% in the urine. This experiment shows that very little of the ^{51}Cr secreted into the intestinal tract would be expected to be reabsorbed.

In summary, the experiments reported here appear to support the previous evidence that gastro-enteric protein loss accounts for almost half of the normal plasma albumin turnover in the dog as opposed to reports in man which indicate that only 2-15% of plasma protein loss is by way of the gut. The techniques used in the study are also of value in estimating enteric protein loss in pathological conditions, where increased loss is suspected. We have found up to 25% of the dose lost in the feces in an initial four day period in some cases as opposed to normal loss of only about 1-4% of the dose during the same time period. The results reported here also show that $^{51}\text{CrCl}_3$ can be used as a label rather than labeled albumin as long as a large enough dose is administered to provide sufficient protein labeling in the in vivo situation.

$$C_{LF \text{ OR } U} = \frac{{}^{51}\text{Cr}_{F \text{ OR } U}}{\int_{T_1}^{T_2} {}^{51}\text{Cr}_{PL} \, dt}$$

WHERE:

$C_{LF \text{ OR } U}$ = ML OF PLASMA CLEARED OF CR BY FECAL OR URINARY ELIMINATION

${}^{51}\text{Cr}_{F \text{ OR } U}$ = % DOSE OF ${}^{51}\text{Cr}$ ELIMINATED IN FECES OR URINE FROM T_1 TO T_2

$\int_{T_1}^{T_2} \text{Cr}_{PL}$ = INTEGRATED PLASMA DISAPPEARANCE CURVE FROM T_1 TO T_2 BASED ON THE SECOND EXPONENTIAL

Figure 1. Equation to determine urinary and fecal clearance of ${}^{51}\text{Cr}$ -albumin.

$$C_{LF \text{ OR } U} = \frac{{}^{51}\text{CR}_{F \text{ OR } U}}{\int_{T_1}^{T_2} {}^{51}\text{CR}_{PL} \, DT}$$

WHERE:

$C_{LF \text{ OR } U}$ = ML OF PLASMA CLEARED OF CR BY FECAL OR URINARY ELIMINATION

${}^{51}\text{CR}_{F \text{ OR } U}$ = % DOSE OF ${}^{51}\text{Cr}$ ELIMINATED IN FECES OR URINE FROM T_1 TO T_2

$\int_{T_1}^{T_2} \text{CR}_{PL}$ = INTEGRATED PLASMA DISAPPEARANCE CURVE FROM T_1 TO T_2 BASED ON THE SECOND EXPONENTIAL

Figure 1. Equation to determine urinary and fecal clearance of ${}^{51}\text{Cr}$ -albumin.

$$C_{\text{MET}} = V_P \cdot \lambda_2$$

WHERE:

V_P = PLASMA VOLUME

λ_2 = REMOVAL CONSTANT OF SECOND EXPONENTIAL OR THE PLASMA
PROTEIN DEGRADATION RATE

C_{MET} = TOTAL REMOVAL OF LABELED ALBUMIN IN ML PER UNIT TIME

Figure 2. Equation to determine metabolic clearance of ^{51}Cr or ^{125}I labeled serum albumin.

Figure 3. Acrylamide disc electrophoretograms of normal dog serum (right), albumin fraction after Sephadex chromatography (middle), and albumin fraction after preparative disc electrophoresis (left).

Figure 4. Plasma disappearance curve of ^{51}Cr labeled human serum albumin in dogs.

Figure 5. Serum disappearance curves of ^{51}Cr and ^{125}I labeled canine serum albumin.

Figure 6. Plasma disappearance curves of ^{51}Cr -labeled canine serum albumin and $^{51}\text{CrCl}_3$.

Table 1

Clearance of ^{51}Cr Labeled Human
Serum Albumin in Dog Feces and Urine

Dog #	Cl_F (ml/hr)	Cl_U (ml/hr)
1	4.68	8.86
2	3.04	6.12
3	3.64	8.90
4	3.91	9.27
5	5.38	9.81
6	<u>6.19</u>	<u>10.80</u>
$\bar{X} \pm \text{S.E.}$	4.47 ± 0.48	8.96 ± 0.64

Table 2

Parameters of Albumin Metabolism

After i. v. Administration of ^{51}Cr Labeled

Human Serum Albumin to Dogs

Cl_{met}	(ml/hr)	9.60 ± 0.59
Cl_{U}	(ml/hr)	8.96 ± 0.64
Cl_{F}	(ml/hr)	4.47 ± 0.48
Alb. deg. (%/day)		15.65 ± 0.84
fecal alb. (% of total)		46.74 ± 4.00

Table 3

CLEARANCE OF ^{51}Cr LABELED CANINE
SERUM ALBUMIN IN DOG FECES AND URINE

Dog #	C_F (ML/HR)	C_U (ML/HR)
1	1.80	5.48
2	1.87	5.23
3	1.47	5.56
4	2.63	6.08
5	1.56	3.47
$\bar{x} \pm \text{S.D.}$	1.87 ± 0.46	5.16 ± 1.00

Table 4

PARAMETERS OF ALBUMIN METABOLISM
AFTER I.V. ADMINISTRATION OF ^{51}Cr LABELED
SERUM ALBUMIN TO DOGS

CL_{NET} (ML/HR)	4.29 ± 0.66
CL_{U} (ML/HR)	5.16 ± 1.00
CL_{F} (ML/HR)	1.87 ± 0.66
ALB. DEG. (%/DAY)	8.33 ± 0.66
FECAL ALBUMIN (% OF TOTAL)	43.51 ± 7.23

Table 5

12 DAY URINARY AND FECAL ELIMINATION
OF ^{51}Cr AFTER I.V. ADMINISTRATION OF
 ^{51}Cr LABELED CANINE SERUM ALBUMIN TO DOGS

Dog #	U (% DOSE)	F (% DOSE)
1	51.59	5.67
2	47.17	7.38
3	47.79	4.47
4	46.47	6.20
5	45.74	5.58
$\bar{x} \pm \text{S.D.}$	47.75 ± 2.28	5.86 ± 1.06

Table 6

11 DAY URINARY AND FECAL ELIMINATION
OF ^{51}Cr AFTER I.V. ADMINISTRATION OF
 $^{51}\text{CrCl}_3$ TO DOGS

Dog #	U (% DOSE)	F (% DOSE)
1	82.3	8.8
2	73.6	7.5
3	73.0	7.7
4	73.6	5.9
5	71.9	8.3
$\bar{x} \pm \text{S.D.}$	74.9 ± 4.2	7.6 ± 1.1

Table 7

URINARY AND FECAL ELIMINATION
OF ^{51}Cr AFTER ORAL ADMINISTRATION OF $^{51}\text{CrCl}_3$

DAY	U (% DOSE)	U (CUM.) (% DOSE)	F (% DOSE)	F (CUM.) (% DOSE)
1	1.50 ± 0.67	---	55.61 ± 38.69	---
2	0.54 ± 0.28	2.03 ± 0.54	27.46 ± 32.40	83.07 ± 7.51
3	0.26 ± 0.13	2.29 ± 0.65	3.33 ± 4.05	86.40 ± 3.52
4	0.30 ± 0.19	2.59 ± 0.82	3.22 ± 2.50	89.62 ± 2.90

✓ ⁵¹CrEDTA As A Gastrointestinal

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Reference Marker in the Neonatal
Bovine Calf¹

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Inert reference markers facilitate measurements of digesta passage, rates of absorption and volumes when used in digestive function studies. Useful markers must be non-digestible, non-absorbable, easily and accurately assayed, not adherent to mucus or cells, physiologically similar to the digesta material under study, and not likely to modify normal gastrointestinal motility or digestion by their presence in the bowel. The chelate of chromium ethylenediamine tetraacetic acid (CrEDTA), using either radiolabeled or stable Cr is a satisfactory soluble fluid reference marker for many digestive function studies (1,2,3). Several authors have stressed that marker recovery studies using supposedly non-absorbable markers must be carried out under conditions which closely simulate the experimental conditions (4,5). Additionally, studies should be conducted to ascertain that the reference marker behaves in a manner which answers the questions under study.

This report describes the unsuitability of trace doses of CrEDTA as a volume marker but its acceptability as a fluid transit marker in the g.i. tract of the neonatal bovine calf.

Materials and Methods

Six bull calves were obtained from a single source when twelve hrs of age. These calves remained with their dams from birth to 12 hrs of age and consumed an unknown amount of colostrum. Additional amounts (0.1 to 0.5 liter) of bovine colostrum were consumed from a nipple bottle by these calves between 12 and 24 hours of age. At 24 hrs of age 0.5 ml of

⁵¹CrEDTA was mixed with 0.5 liter of colostrum (A and C), or saline (B)

or cows milk (D) and each calf was allowed to consume this fluid from a nipple bottle. Calves were held in individual metabolism cages and given water ad libitum. One to three liters of colostrum or cows whole milk was fed at twelve hr intervals by nipple bottle.

Feces were collected in polyethylene bags secured to the perineal region by rubber cement and supported by elastic straps secured to the collar. Urine was collected through a floor grating of the metabolism cage. The calves were loosely restrained with a neck collar and chain and adjusted well to the metabolism cage.

Three calves (A, B, and D) given $^{51}\text{CrEDTA}$ at 24 hrs of age, were given a second $^{51}\text{CrEDTA}$ trace dose at 151 hrs of age. Calf A was given 0.5 ml $^{51}\text{CrEDTA}$ in colostrum, calves B and E were given 0.5 ml $^{51}\text{CrEDTA}$ in cow's milk. Feces and urine were collected separately as described above. The excretion of ^{51}Cr in feces and urine from the first dosing period was less than 0.5% of the dose at the time of the second study.

Urine and feces were transferred to quart bottles, weighed, mixed with tap water and brought to a constant volume. Each quart jar was counted for one min in a solid scintillation total body counter.

Two calves (E and F) were injected with 5.0 ml of $^{51}\text{CrEDTA}$ at 24 hr (E) and 32 hr (F) of age. Calf F remained healthy with normal bowel movements over 198 hours. Calf F was orally dosed with 10^{12} organisms of an enterotoxic strain of Escherichia coli (09:K30) at 14 hrs of age. Large volume fluid diarrhea occurred at 30 hr of age. This calf continued to drink 1.150 liters of milk every 12 hrs and was supplemented with 8 liters

of lactated ringers solution plus 1% dextrose iv beginning after 30 hrs of continuous diarrhea. Feces and urine were collected as before, except in calf F where separate collection of urine and feces was only accomplished through the first 30 hr of diarrhea.

^{51}Cr activity was counted as described above. Calf E was sacrificed at 198 hr and calf F at 102 hr of age. The g.i. tract was removed from each carcass and divided into three segments consisting of rumen plus abomasum, small intestine, and large intestine. The carcass and three segments were counted separately for 5 min in an inverted liquid scintillation whole body counter.

^{51}Cr EDTA chelate was prepared by the method of Downes and McDonald (1), utilizing 500 μCi of $^{51}\text{CrCl}_3$ supplied by ICN, Isotope and Nuclear Division, Cleveland, Ohio 44128 and reagent grade disodium EDTA supplied by Fisher Scientific Company, Fairlawn, New Jersey 07410.

Results

Figure 1 displays the cumulative recovery of ^{51}Cr in the urine of calves given ^{51}Cr EDTA orally at 24 hrs and at 151 hrs of age. Calves given ^{51}Cr EDTA at 24 hrs of age absorbed significantly more ^{51}Cr EDTA from the g.i. tract and excreted it into the urine ($P < 0.05$).

Oral dosing of ^{51}Cr EDTA in bovine colostrum or 0.85% saline had no consistent effect on the cumulative urinary excretion of ^{51}Cr . Calf A given marker with colostrum, had the highest cumulative ^{51}Cr excretion but calf B, given the marker in 0.85% saline and calf C, given the marker in colostrum, had similar cumulative ^{51}Cr excretion rates. Calf D, given marker in milk, had a cumulative marker excretion intermediate between Calf A and Calves E and F.

Calf A, given the tracer ^{51}Cr EDTA dose in colostrum at both 24 and 151 hrs of age, excreted less ^{51}Cr in the urine when inoculated at the older age.

Table I indicates the magnitude of fecal and urinary loss and the ^{51}Cr recovery during the first 30 hrs following onset of diarrhea. Calf E passed only one stool in this period while Calf F passed eleven. The urinary recovery from Calf E represents six voided volumes while Calf F voided no urine until after 8 liters of fluids were administered iv.

Discussion.

The magnitude of $^{51}\text{CrEDTA}$ absorption from the g.i. tract obviates its use as a fluid volume marker in bovine calves less than 6 days of age. In adult ruminants using CrEDTA administered orally or intraruminally usually less than 5% of this marker is recovered in the urine (1, 2, 6). Goodall and co-workers reported up to 12% Cr recovery in the urine in a group of sheep (no age stated) given CrEDTA by esophageal tube (2). Pickard and Stevens found trace amounts of ^{51}Cr in the urine of mature rabbits within 48 hrs of administration via fistulae into various parts of the g.i. tract (3). Total recovery in feces of greater than 95% of trace doses of $^{51}\text{CrEDTA}$ given via esophageal tube to mature dogs, pigs and ducks has been found by Dr. C. E. Stevens and associates (personal communication).

Low rates of CrEDTA absorption from the g.i. tract may not significantly alter volume measurements when large net fluid volumes occur. However, marker absorption leads to underestimation of fluid volumes and will contribute to significant errors when small net fluid volumes are involved.

$^{51}\text{CrEDTA}$ serves as an adequate g.i. fluid transit marker in the neonatal bovine calf in that less than 2% of the systemic ^{51}Cr activity appears in luminal contents, even in large volume diarrhea. In addition, since no ^{51}Cr activity was detected in the three g.i. tract segments, ^{51}Cr is not preferentially deposited in any one intestinal compartment.

Therefore, of the approximately 27% of ^{51}Cr absorbed by 24 hr old calves at 30 hrs (Figure 1), the 1.75% which appears in the lumen must enter uniformly along the bowel and only represents 0.5% of the total dose administered.

The mechanism of absorption of this small molecular weight molecule (430.25) is not elucidated from these studies. Oral administration with either colostrum or saline does not influence the amount absorbed. At 151 hr of age, when intestinal closure to protein macromolecules is expected to be complete (7), greater than 15% of the oral dose is accumulated in the urine in 48 hours. Therefore, a mechanism of absorption other than that for macromolecular proteins (pinocytosis) accounts for the absorption of this small molecular weight molecule in the young calf.

Summary.

Using orally administered trace amounts of ^{51}Cr EDTA chelate as a fluid transit marker in 24 and 151 hr old bovine calves, 32% and 16% respectively, was absorbed and excreted in the urine in 48 hrs. Administering the trace dose orally mixed in saline or bovine colostrum had no effect on the amount absorbed and excreted. Of the ^{51}Cr EDTA absorbed, less than 0.5% of an oral dose was calculated to re-enter the g.i. tract and this amount shows no preferential site of entry into the lumen.

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Figure 1

Figure 1. Cumulative ^{51}Cr recovery from the urine of four calves fed 0.5 ml of $^{51}\text{CrEDTA}$ mixed with milk, colostrum or saline at 24 hrs of age. (.____.) and three calves at 151 hrs of age (x____x) (Mean $\pm$ SEM).

TABLE I. ^{51}Cr Recovery, Fecal and Urine Weight in Two Calves

During First 30 hrs Following iv $^{51}\text{CrEDTA}$.

<u>Calf</u>	<u>Stool</u>	<u>Fecal $^{51}\text{Cr}(\%)$</u>	<u>Fecal Wt. (kg)</u>	<u>Urinary Cr%</u>	<u>Urine Wt. (kg)</u>
E	Normal	0.12	0.2	88.29	1.8
F	Diarrhea	1.75	4.8	0	0

Semen Characteristics in Thyroidectomized Stallions

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Introduction

The effects of thyroidectomy on metabolism and growth in mares and stallions was reported by us in The Cornell Veterinarian (1974). The abstract from that paper follows:

"Surgical thyroidectomies (Thx) were performed in 6 yearling grade colts, (3 males, 3 females). Five control colts (3 males, 2 females) were included and comparative studies were carried out for 67 weeks. The comparative measurements included rectal temperature, heart rate, feed consumption, packed cell volume, serum cholesterol, serum calcium, serum phosphorus, serum T₄, height, heart girth, body weight, epiphyseal plate closure and tooth eruption times. A thyroprotein supplement was fed to the Thx males during weeks 46 to 53.

The Thx animals failed to grow in height, were sensitive to cold, shed their winter hair coats late and had dull coarse hair coats. The Thx animals were generally docile and lethargic with a sleepy appearing expression. Edema of the rear limbs and a coarse thickened appearance of the face was evident. Rectal temperatures were significantly depressed and cholesterol levels were significantly elevated. Feed consumption and body weight gains were decreased compared to controls. This was particularly pronounced in females; Thx females consumed 46% less feed and gained 47% less weight than the controls. Serum calcium was unaffected; however, serum phosphorus was depressed, particularly in the females. Epiphyseal plate closure time was delayed as was eruption of incisor teeth.

Thyroprotein supplementation resulted in a rapid and dramatic reversal of the signs of hypothyroidism. Discontinuance of thyroprotein supplementation resulted in a return of hypothyroidism but not to the degree seen prior to supplementation, except the T_4 values fell again to non-detectable levels."³

The stallions were used concurrently for the semen study.

We still have the three Thx mares from the trial. The mares are 6¹/₂ months old and in two of the three the epiphysis of the distal radius and tuber calcis has not yet fused.

We are convinced by these results that total thyroidectomy through surgery is possible and yields a satisfactory experimental model to study equine hypothyroidism.

Materials and Methods

Three grade quarter horse male colts were thyroidectomized at 18 months of age. Semen was collected at weekly intervals from the three Thx and three control stallions starting at 26 months of age and concluding at 39 months of age except for months 34 and 35. One control stallion, # 3, showed delayed descent of both testicles. No sperm were seen in his ejaculates until Summer II so he was eliminated in the semen evaluation. He was not, however, eliminated from the minutes to ejaculation observations. For comparative purposes 5 seasonal collection periods have been designated being Summer I (6/1/71-8/30/71); Fall (9/6/71-11/19/71); Winter (12/3/71-1/13/72); Spring (4/6/72-5/25/72) and Summer II (6/1/72-7/27/72).

As stated in the abstract printed above, a thyroprotein supplement* was fed to the Thx stallions for 6 weeks starting 3 weeks prior to the winter semen collection period.

Semen was collected with a Japanese style artificial vagina containing water at approximately 45°C. A teaser mare showing behavioral estrus was used at first, but as the stallions became accustomed to the artificial vagina, they would mount the hobbled teaser mare and enter the A.V. with little regard to whether the teaser was showing behavioral estrus.

The time from introduction to the mare until ejaculation

* Protomone, Agri-Tech, Kansas City, Missouri U.S.A.

was recorded (except for Summer I). If the stallion failed to mount and/or ejaculate in 30 minutes, further teasing was discontinued. Only 1 teaser mare was used for each weekly collection period.

Semen characteristics compiled for each ejaculate were total volume, sperm concentration, total sperm, percent progressive motility, percent unstained sperm and percent normal sperm.

Mares were bred to two of the three thyroidectomized stallions and one control stallion.

A week following the final semen collection, the stallions were castrated. The testes were weighed and sections for histological study were taken from the anterior, medial and posterior areas of each. Stains used were PAS hematoxylin and feulgen fast green. The general morphology was noted and the number of tubules in stage 8 was counted.

Data was analyzed using the Satterthwaite procedure for approximating F. This means that each horse was given equal weight regardless of the number of ejaculates actually collected.

The graphs of mean and standard error were drawn giving each ejaculate equal weight.

Results: Figure 1 shows time from introduction of the mare until ejaculation by the stallion. The Thx stallions were significantly slower in Fall ($P < .01$) and Summer II ($P < .01$).

Figure 2 shows total semen volume for each collection period. No significant differences between Thx and controls

were found.

Figure 3 shows semen concentration $\times 10^6$. The Thx stallions showed significantly less semen concentration during Summer I ($P < 0.01$) Fall ($P < 0.05$) and Winter ($P < 0.05$). Significant differences in concentration were not evident in Spring and Summer II.

Figure 4 shows total sperm $\times 10^6$. Significant differences were not evident.

Figure 5 shows percent motility of the sperm. Significant differences were not evident.

Figure 6 shows percent unstained sperm in the semen. Significant differences were not evident.

Figure 7 shows percent normal sperm in the semen. Significant differences were not evident.

One Thx stallion was mated successfully to a control mare and a Thx mare. A second Thx stallion was mated successfully to a control mare. A control stallion was also mated successfully to a Thx mare.

The weights of the testes are listed in table 2. Significant histologic abnormalities were not apparent in either Thx or control tissues.

The percentage of stage 8 tubules counted in the histologic sections was 13.1 ± 0.9 for Thx stallions and 15.2 ± 0.5 for control stallions. The difference was not statistically significant. The testes from control colt # 3 whose testes had remained retained until Summer II and the retained right

testicle from Thx colt # 5 were not included in the counts.

Discussion

A decrease in sexual desire accompanied by a generalized lethargy was apparent in the Thx stallions prior to the short period of thyroprotein supplementation. This behavior is characteristic of the hypothyroid state in other species including men (4,6). In sheep, however, Brooks et al did not observe decreased libido in Thx rams. We have been unable to find other reports of confirmed hypothyroidism in stallions. The reversal of hypothyroid signs including elevation of body temperature, weight loss, appetite improvement, and increased animation also seems apparent in the minutes to ejaculation time decreasing from a mean of 14.7 ± 2.4 in the Fall to 7.3 ± 0.8 during thyroprotein supplementation. The Thx stallions began to diverge again during Summer II becoming slower in their responses compared to controls.

Pickett showed a reaction time mean for 170 ejaculates for all seasons of slightly under 7 minutes (range 819 seconds in January to 206 seconds in August)⁷. One half minute also has to be added for what Pickett has designated Copulation Time (time from penis entering vagina until dismounting following ejaculation) in order to compare with what we have designated Minutes to Ejaculation. Thx stallion # 4 lacked libido to the point of seldom mounting prior to the thyroprotein supplementation. Following thyroprotein supplementation, we were able to collect him satisfactorily.

Total semen volume was higher for Thx stallions but not significantly higher compared to controls. Gel was not separated since it was only seen in 1 ejaculate. Total semen volume from our experiment compares favorably with Gel-Free Semen Volume as reported by Pickett.⁷

The upward trend in total volume for Thx and control stallions from Winter to Summer II appears to be a result of maturing and seasonal influence in these three year old animals.

The significant difference in semen concentration was offset by the increase in volume of the Thx stallions. Semen concentration in the control stallions compares favorably with that reported by Pickett of $300-450 \times 10^6$ /ml in first ejaculates.⁷ Others have reported lower concentrations.^{5,8} We have no explanation for the lower concentration and higher volume in the Thx compared to control stallions.

Significant differences were not noted in total sperm. The range of $9-12 \times 10^9$ total sperm for Thx and control stallions in Spring and Summer II compares satisfactorily with that reported by Cornwell, et al² in mature Quarter Horse stallions. They reported a mean of 11.3×10^9 with a range of 6.3×10^9 in December to 16.1×10^9 in April.

Percent of sperm showing progressive motility in the raw semen, percent unstained sperm and percent normal sperm were quite similar in Thx and control stallions for all periods. Percent motility was similar to that reported by Pickett. Pickett showed a mean of 48% motility for 1st

ejaculates with a low of 37% in October and a high of 58% in December. Cornwell et al reported a mean of 67% normal sperm from Quarter Horse stallions which is lower than our results.²

No attempt was made to study the degree of fertility of each Thx stallion. We did, however, wish to know if the semen was capable of fertilization in Thx and control mares. Two of the three Thx stallions were used and each was fertile. Each produced normal foals. Male sheep, goats, cattle and laboratory animals have also been shown to be fertile in spite of being hypothyroid.

The histology of Thx testes and the controls was normal. Based on the semen characteristics and fertility observed, this is not unexpected. The percentage of stage 8 tubules for Thx and control stallions was similar to that reported by Swiestera et al for normal stallions.⁹

Summary and Conclusions

Three Quarter Horse type stallions were surgically thyroidectomized (Thx) at 18 months of age. Weekly semen collection was started in the three Thx and three control stallions at 25 months of age and concluded at 39 months. Although the number of stallions used was not great enough to make emphatic conclusions, there is substantial evidence for the following:

- 1) The induced state of hypothyroidism in young stallions has a depressing effect on libido and general animation.

2) The depression of libido and general animation is correctible by thyroprotein supplementation.

3) Semen characteristics show little or no alteration in the hypothyroid stallion.

4) Hypothyroid stallions are fertile but we do not know whether they are less fertile than normal stallions.

5) Light microscope histological differences are not evident in testicular tissue sections from hypothyroid compared to control stallions.

Acknowledgements

We thank Mrs. S. Hallett, Mr. C. Marquis and Mr. P. Daniluk for technical assistance.

We extend special thanks to Mr. R. Hintz for performing the statistical analysis.

Table I. Semen Characteristics of Control and Thx Stallions, Mean $\pm$ S.E.

Season	<u>Observations</u> (N)		<u>Semen Volume(ml)</u>		<u>Semen Concentration</u> ($\times 10^6$ /ml)		<u># Sperm/ejaculate</u> ($\times 10^6$)	
	<u>Control</u>	<u>Thx</u>	<u>Control</u>	<u>Thx</u>	<u>Control</u>	<u>Thx</u>	<u>Control</u>	<u>Thx</u>
Summer I	28	37	17.5 $\pm$ 3.2	19.9 $\pm$ 1.7	333 $\pm$ 31	137 $\pm$ 12**	3870 $\pm$ 229	2441 $\pm$ 211
Fall	22	12	12.3 $\pm$ 1.0	39.2 $\pm$ 4.8	377 $\pm$ 31	86 $\pm$ 15*	4402 $\pm$ 420	2957 $\pm$ 366
Winter	14	16	19.4 $\pm$ 2.4	26.1 $\pm$ 4.3	356 $\pm$ 32	188 $\pm$ 25*	6307 $\pm$ 725	3938 $\pm$ 675
Spring	16	23	25.4 $\pm$ 3.0	37.6 $\pm$ 5.9	432 $\pm$ 43	394 $\pm$ 66	9946 $\pm$ 1122	9354 $\pm$ 765
Summer II	18	27	38.1 $\pm$ 3.7	52.6 $\pm$ 5.0	359 $\pm$ 33	264 $\pm$ 32	11824 $\pm$ 524	10326 $\pm$ 492

Season	<u>% Motile Sperm</u>		<u>% Unstained Sperm</u>		<u>% Normal Sperm</u>		<u>Minutes to Ejaculation</u>	
	<u>Control</u>	<u>Thx</u>	<u>Control</u>	<u>Thx</u>	<u>Control</u>	<u>Thx</u>	<u>Control</u>	<u>Thx</u>
Summer I	39.1 $\pm$ 3.2	40.5 $\pm$ 1.9	77.8 $\pm$ 2.3	77.6 $\pm$ 1.7	89.1 $\pm$ 1.5	87.3 $\pm$ 1.7	-	-
Fall	38.6 $\pm$ 4.3	30.8 $\pm$ 4.4	68.5 $\pm$ 2.6	63.1 $\pm$ 5.4	83.4 $\pm$ 2.0	70.9 $\pm$ 4.8	4.4 $\pm$ 0.6	14.7 $\pm$ 2.4*
Winter	49.3 $\pm$ 5.5	43.8 $\pm$ 3.9	66.1 $\pm$ 4.6	70.3 $\pm$ 3.1	85.1 $\pm$ 2.5	82.4 $\pm$ 1.5	5.9 $\pm$ 1.4	7.3 $\pm$ 0.8
Spring	45.6 $\pm$ 6.6	53.5 $\pm$ 2.5	75.5 $\pm$ 4.5	82.1 $\pm$ 2.9	82.0 $\pm$ 3.6	85.2 $\pm$ 2.1	4.6 $\pm$ 0.4	5.1 $\pm$ 0.5
Summer II	50.4 $\pm$ 6.5	56.3 $\pm$ 3.5	76.4 $\pm$ 4.3	83.4 $\pm$ 1.6	84.3 $\pm$ 2.6	85.4 $\pm$ 1.5	3.0 $\pm$ 0.3	6.0 $\pm$ 0.6*

Treatment groups within season different P < .05

* Treatment groups within season different P < .01

Table II. Weight of Testes in Control and Thx Stallions

<u>Stallion</u> <u>#</u>	<u>Treatment</u>	<u>Weight in Grams</u>	
		<u>Left Teste</u>	<u>Right Teste</u>
1	Control	120.5	109.0
2	Control	162.0	146.5
3	Control	117.5	104.5
4	Thx	155.0	153.0
5	Thx	205.5	36.5*
6	Thx	185.0	192.0

* Testicle retained just outside inguinal canal.

Fig. 1 Minutes from introduction of mare to stallion until ejaculation for control and Thx stallions. Each point represents mean $\pm$ S.E.; For N see table 1.

Fig. 2 Total semen volume per ejaculate (ml) for control and Thx stallions. Each point represents mean $\pm$ S.E.; For N see table 1.

Fig. 3 Semen concentration per ml $\times 10^6$ for control and Thx stallions. Each point represents mean $\pm$ S.E.; For N see table 1.

Fig. 4 Total sperm $\times 10^6$ per ejaculate for control and Thx stallions. Each point represents mean $\pm$ S.E.; For N see table 1.

Fig. 5 Percent motility of sperm per ejaculate in undiluted semen for control and Thx stallions. Each point represents mean $\pm$ S.E.; For N see table 1.

Fig. 6 Percent unstained sperm per ejaculate for control and Thx stallions. Each point represents mean $\pm$ S.E.; For N see table 1.

Fig. 7 Percent normal sperm per ejaculate for control and Thx stallions. Each point represents mean $\pm$ S.E.; For N see table 1.

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VETERINARY NUCLEAR MEDICINE

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✓ VETERINARY NUCLEAR MEDICINE

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I. Introduction

Veterinary nuclear medicine is that branch of veterinary medical science which deals with the use of radioactive materials in all aspects of animal disease, including research, diagnosis, and treatment. This review is intended to convey the scope of present and possible applications of veterinary nuclear medicine, with the emphasis on diagnosis, and to provide leads to existing reference material in both the veterinary and human literature. Lately there have been widespread advances in human nuclear medicine as evidenced by the recent institution of a nuclear medicine speciality board. Except for the widespread use of animals in human research, however, there has been little direct veterinary application. Therefore, it is useful to examine developments in human medicine for guidelines and to determine those techniques which have been used and also those which may be applicable in the veterinary field.

II. Human and Veterinary Nuclear Medicine

There are many excellent textbooks and reviews of human nuclear medicine.^{9,12,63,97} To conserve space, references to the literature on the human aspects will be made basically to these textbooks and reviews and not to the vast number of individual papers. Most references to veterinary applications will be to individual scientific papers. During the year 1957 the number of human diagnostic examinations made with the use of radioactive materials was estimated to be between 150,000 and 200,000; by the mid 1960s there was a five-fold increase in the number of techniques performed and a seven-fold increase has been projected for the mid 1970s.³ Thus, it can be seen that nuclear medicine is a vital part of the armamentarium of the

modern physician. American Hospital Association regulations now state that all accredited hospitals must have nuclear medical facilities available.

Factors that tend to restrict the application of nuclear medical procedures in the veterinary field include: (a) the value of the animal relative to the cost of diagnosis and treatment (although this is much less of a factor in small animal medicine); (b) the necessity of heavy sedation or general anesthesia for virtually all imaging procedures in animals that may often be poor anesthetic risks; (c) the prohibitive costs of equipment necessary for private clinics, thus, restricting such procedures mainly to veterinary medical colleges and publicly funded or privately endowed major veterinary hospitals; (d) lack of adequately trained personnel; (e) increased danger of contamination of the environment; and (f) restrictions on the introduction of radioactivity to food products. Factors that tend to promote veterinary nuclear medicine include: (a) research and instrument development from human nuclear medicine is available, (b) newer procedures may be evaluated in animals before being applied to human patients and (c) herd or flock screening procedures similar to the recently developed biochemical profiling concept may be inexpensive on a per capita basis.

In regard to herd or flock screening procedures, the recent upsurge in the development of competitive protein binding and radioimmunoassay techniques for estimating hormone and enzyme contents of the body should provide added impetus in this direction.⁸⁹ These in vitro procedures, require no administration of radioactive materials to the patient and can be done rather easily on a herd or flock-wide basis.

III. Radioactive Materials

A. Radionuclides

A radionuclide is an unstable form of a nuclear species, and refers to any unstable nuclear conformation capable of existence. A radioisotope is defined as an unstable form of a given element. The two terms are often used interchangeably. A very large number of radionuclides are available and a list of some of those most commonly used in medical practice is given in Table I. Most radioisotopes are produced in large quantity in nuclear reactors or in particle accelerators. Another method of providing adequate quantities of short-lived radionuclides is by the use of the radioisotope generator, or "cow", from which a radionuclide can be eluted periodically as required. Such generators have been developed to provide technetium $99m$ from the decay of molybdenum 99, which is located in an ion exchange column within the generator system; a similar generator produces indium $113m$ from tin 113. Generally, only those short-lived isotopes which decay from a longer half-lived parent can be prepared in generator form.

Most of the radioisotopes used as such in nuclear medicine are purified, sterilized, and supplied in single or multiple dose vials by radiopharmaceutical manufacturing concerns.

B. Radiopharmaceuticals

Broadly speaking, radiopharmaceuticals are defined as any radioactive element or compound that is used in nuclear medicine. More precisely, however, the pharmaceutical might be defined as a drug or compound that contains a radionuclide. This distinguishes it from a single radionuclide, such as strontium $87m$, calcium 47, iodine 125, or iodine 131, which would be used alone. Radiopharmaceuticals differ from other drugs because they are not generally used to produce a pharmacologic effect; rather, the

radionuclides they contain are used for localization or measurement in diagnostic procedures and possibly for radiation effects in therapy.

A list of a number of diagnostic radiopharmaceuticals which have been or are being used in human or veterinary nuclear medicine is given in Table II. This list should not be taken as absolute since newer radiopharmaceuticals are constantly being developed which can be used for new techniques or to replace previously used radiopharmaceuticals. Table II also lists a number of radiopharmaceuticals which are only used in in vitro procedures, such as radioimmunoassay and competitive protein binding techniques. Since these compounds are not actually administered to the living organism the use of the term radiopharmaceutical in referring to them may be a misnomer.

IV. Instrumentation

One of the most important aspects of developing a nuclear medical facility is the obtainment of instrumentation necessary for performing the techniques desired. The cost of equipment necessary for such a facility varies according to the sophistication of the procedures to be performed; however, most radiation detection equipment is relatively costly. Broadly speaking, the instrumentation can be divided into categories of radiation safety equipment, and instrumentation used for the performance of nuclear medical procedures. 37,54,88,100

A. Radiation Safety Instruments

The general purpose of radiation safety equipment is to measure the integrated dose received by personnel working in a nuclear medical facility, to measure the radioactivity content of doses received by patients, and to detect areas of contamination or insufficient shielding of sources. Personnel monitoring equipment includes film badges, condensor ionization chambers,

and thermal luminiscent dosimeters. Instruments giving area surveillance or dose content information include portable Geiger-Mueller detectors, ionization chamber detectors, neutron survey meters, and portable gamma detectors.

B. Nuclear Medicine Instruments

Geiger-Mueller counters are useful in counting tracer levels of beta emitting nuclides. The counting of low level beta emitters, such as ^{14}C and ^3H is difficult, if not impossible, with a Geiger-Mueller counter; however, higher energy beta particles from such isotopes as ^{45}Ca , and ^{131}I may be counted on a G.M. system. For these isotopes sample preparation may be difficult. Samples to be counted on a G.M. system are usually in the form of a liquid solution or partially digested suspension (higher energy beta), or as a thin film on the bottom of a small metal cup.

Gamma ray counting systems may be used whenever gamma emitting radionuclides are employed. The use of gamma emitting radionuclides in clinical procedures is popular due to the ease of sample preparation. Since there is a minimum of interference due to the sample state, liquids and even solid materials may need no preparation before counting. With appropriate instrumentation it is also rather easy to assay for two or more gamma emitting radionuclides in the same sample.

The most common gamma counting system consists of a crystal of Tl activated NaI employed as the detector of gamma rays. A "well" type of crystal is often used for in vitro studies as it enables the sample to be placed in the center of the crystal, thus making it possible for the detector to capture a high percentage of the gamma rays emitted. Most systems for counting gamma rays include an analyzer which allows one to distinguish between emissions of one radionuclide and another. When the

activity of a series of samples is to be measured, a scaler is employed to furnish the necessary numeric data. If one is interested in observing the change of activity with time a rate meter would be the appropriate output device. A chart recorder can be used to plot the changes that occur. Common applications of such systems include the counting of ^{131}I and ^{125}I in thyroid uptake tests, fat absorption, renal function, blood volume, and other tests.

A liquid scintillation counter is essential for detecting low energy beta emissions which are very difficult to assay in any other way. While most useful for low energy beta emitters, such as ^3H and ^{14}C , liquid scintillation counters may be used to detect any beta or low energy gamma emission. Samples to be counted are usually dissolved in a solvent. A scintillator is also dissolved with the sample. An interaction between the beta particles, solvent, and scintillator produces minute flashes of light which are detected, analyzed, and recorded by the liquid scintillation counter.

A multichannel analyzer is used primarily with gamma ray counting equipment. This instrument sorts incoming signals from such counting equipment into one hundred to several thousand channels. The purpose of such analysis of signals is to identify a specific radionuclide present in an animal or patient or to quantitatively count samples containing several gamma emitters. The multi-channel analyzer has found wide use in analyzing signals from a whole-body counter when assessing the quantity of contamination of patients or after neutron activation analysis of cadavers, research animals, or patients.

A whole-body counter is a device which is used to determine the total radioactivity in an animal or person. Thus, it is possible to determine

the retention by a patient of an element or labeled compound, or to determine the level and type of contamination after an accident. Whole-body counting has the advantage of less effort and often greater accuracy than collection of excretions to determine retention of radioactivity. Turnover rates of labeled materials are also measured by whole body counting.

A whole-body counter usually consists of a detector enclosed in a large steel room. The detector may consist of one or more large crystals or a large cylindrical tank containing liquid scintillation solutions. Another type of counter consists of a small shielded area containing the detectors; the patient is carried through an opening in the shielding on a moving belt such that a scan of activity in the whole body is obtained.

The assaying of amounts of a radionuclide located at a specific site in a patient may be accomplished with an external counter. The most common system employs a Tl activated NaI crystal detector which is collimated so that only radiation from the site of interest is measured. The detector is usually mounted on a movable stand so that alignment with the patient is simplified. A scaler or rate meter and a radiation analyzer are needed to complete such a counter.

A rectilinear radioisotope scanner is an important piece of diagnostic equipment in the nuclear medicine laboratory. Such an instrument allows a visualization of the location of radionuclides in specific sites or organs of the body. Determination of hot or cold areas of the thyroid, localization of brain tumors, detection of metastases to the liver, determination of the size and position of organs such as the lungs, kidneys, heart, placenta, etc. are among the common uses of the scanner.

The typical scanner consists of a finely collimated detector which is moved back and forth across the subject and, at the end of each path,

it is also moved slightly at right angles, in a horizontal plane, with the main scan direction, so that a rectangular area is viewed. The output of such a system consists of a two dimensional graphic representation of the concentrations of radioactivity of the site being scanned. Such "pictures" may be placed on paper, sometimes with a color gradient, or on photographic film, with the density of development of the film proportional to the amount of radioactivity present at that point.

The Anger camera or gamma scintillation camera performs the same function as the radioisotope scanner i.e. imaging the distribution of radioisotopes in vivo. However, the gamma camera has important advantages over the rectilinear scanner. The gamma camera consists of a single large sodium iodide crystal, approximately 10 inches in diameter, backed by a matrix of 19 photo multiplier tubes with electronic circuitry allowing the delineation of the location of each impulse at the face of the crystal. The detector head of the camera does not move but is collimated in such a way that it presents a view of the entire organ or field of study at one time. Thus, a given image can be obtained very rapidly dependent only on the number of impulses needed to produce the image. With acceptable levels of radioactivity administered to the patient an image of an organ can be obtained in a matter of a few seconds. In addition, there is great flexibility in positioning the patient and the camera so that several views of the site of interest can be made in a reasonably short time period. One of the most important advantages is that pictures can be taken in rapid sequence at time intervals of a second or less so that dynamic function studies of organs can be obtained.

Table III is a summary of the pertinent features, uses, and approximate costs of the various instruments mentioned in the preceding paragraphs. It

should be cautioned that the expense of some of the instruments will increase, while that of others will decrease depending on changes in the economy and the development of instruments with new and simpler features.

V. Therapy

The use of radioactive materials for therapy has received much attention during the past few decades.¹² Such procedures generally fall into three main categories: (1) teletherapy or use of high energy gamma ray emitting sources for external irradiation of sites within the body; (2) brachytherapy or use of implanted encapsulated radioactive sources, such as radon seeds or cesium needles, which are inserted in the lesion in a geometric pattern; (3) administration of radiopharmaceuticals which become concentrated in particular organs or spaces and provide sufficient radiation for a therapeutic effect.

Teletherapy is considered to be similar in most cases to super voltage x-ray therapy and is not included in the domain of nuclear medicine.

While many therapeutic isotopic procedures have been investigated, few of them have been found to have sufficient value to warrant their continued use. Perhaps the technique that has found the widest application is the use of ¹³¹I for the treatment of thyroid carcinoma, hyperthyroidism, and cardiac disease in euthyroid patients.^{9,12} In humans doses of anywhere from 40 microcuries to 200 millicuries have been used depending on the specific dosage needed by the patient. Hyperthyroidism in the dog has been successfully treated with radioiodine.^{82,83} Another frequently used therapeutic nuclear medical technique involves the use of ³²P in the treatment of polycythemia vera.^{9,12} Doses of up to five millicuries have been found to be useful in depressing hematocrit values in man. We have used

equivalent doses in treating dogs with this disease but do not have sufficient follow-up information to indicate the efficacy of this agent in the dog.

Brachytherapy has been useful in human medicine in treating carcinoma of the cervix and in the handling of other tumors which are considered to be inoperable.^{9,12} Several reports from the field of veterinary medicine, indicated the value of brachytherapy in treating lesions in both small and large animals.^{23,26}

VI. Diagnostic Applications

By far the most significant contribution of nuclear medicine is to the area of diagnosis. A vast number of reports have been published concerning the use of radioisotopes, both in vivo and in vitro, for the diagnosis of disease. While far fewer reports have appeared in the veterinary literature than in the human literature, some contributions have been made in the former field, and many human medical techniques have potential for adaptation to veterinary medicine.

A comprehensive review of diagnostic nuclear medicine would require a tome. A general review of many of the techniques available is given in Table IV. Column two of Table IV defines the major body system involved, column three defines the primary objective of the procedure, and column four indicates the radionuclide or radiopharmaceutical required. Column five lists the equipment needed for the procedure, by number, as enumerated in footnote one of the table. Column six similarly indicates, by number, the duration of observation of the patient, as given in footnote two of the table. Column seven indicates the species on which the technique has been used, while the last column gives the references for the technique. In many cases, references to techniques used on man are from standard texts

of nuclear medicine and the reader is referred to these volumes for specific original references. References to veterinary applications are primarily to the original work.

Of the techniques already widely used in veterinary medicine many of the hormone assays (Table IV, 28-36), as well as the in vitro thyroid function tests (Table IV, 56-60), are particularly important. These techniques have potential for wide application since no radioactivity is administered to the patient and only a serum sample is needed for performance of the test. The serum sample can be sent to any diagnostic laboratory and, as long as the practitioner is aware of the range of normal values in animal patients, he will be able to interpret the results obtained. With increased use of metabolic profiling in domestic animals these in vitro nuclear medical techniques should become even more valuable.

Perhaps the most widely used in vivo veterinary nuclear medical technique is the radioiodine thyroid uptake test (Table IV, 57) which has been used for at least 20 years. Hematological studies (Table IV, 19-26) have been increasingly used over the past few years and tests of gastrointestinal function (Table IV, 15-16) are also frequently employed.

Bone kinetic analyses and other tissue kinetic techniques (Table IV, 49-50) have been frequently used for research and should be of clinical medical value as well. Imaging procedures which have found vast application in human medicine have been employed infrequently by veterinary medical colleges and clinics chiefly because of the cost of the equipment required (Table III) and the lack of trained personnel. Hopefully, as the value of nuclear medical techniques becomes more widely recognized, veterinary colleges and major veterinary clinics will obtain such equipment.

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VII. Summary

The purpose of this presentation has been to provide a brief review of the expanding horizons of nuclear medicine, to list the equipment necessary for a nuclear medicine laboratory, and to indicate the value of this relatively new field to the veterinary clinician. While clinical applications to veterinary medicine have not kept pace with those of human medicine, many advances have been made, particularly in the use of in vitro techniques. Areas for expanded applications should include competitive protein binding and other in vitro procedures, particularly in connection with metabolic profile studies. Indicated also is more intensive application by the veterinarian of imaging procedures which have been found to be of such great value to the physician.

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Table I. Some Radionuclides Used in Medicine and Research

<u>Element</u>	<u>Radio-nuclide</u>	<u>Half-life</u>	<u>Element</u>	<u>Radio-nuclide</u>	<u>Half-life</u>
Antimony	^{122}Sb	67 hr.	Fluorine	^{18}F	112 min.
	^{124}Sb	60 da.	Gallium	^{72}Ga	14.3 hr.
Argon	^{37}Ar	35 da.		^{67}Ga	78 hr.
Arsenic	^{74}As	17.5 da.	Gold	^{198}Au	2.69 da.
	^{76}As	26.8 hr.		^{199}Au	3.15 da.
Beryllium	^7Be	53 da.	Hydrogen	^3H	12.26 yr.
Bismuth	^{210}Bi	5 da.	Iodine	^{125}I	60 da.
Bromine	^{82}Br	35.7 hr.		^{130}I	12.6 hr.
Cadmium	^{109}Cd	1.3 yr.		^{131}I	8.1 da.
Calcium	^{45}Ca	164 da.		^{132}I	2.33 hr.
(with			Iron	^{55}Fe	294 hr.
scandium 47)	^{47}Ca	4.7 da.		^{59}Fe	45 da.
Carbon	^{11}C	20.4 min.	Indium	$^{113\text{m}}\text{In}$	1.7 hr.
	^{14}C	5570 yr.	Krypton	^{85}Kr	10.3 yr.
Cerium	^{141}Ce	33 da.	Lanthanum	^{140}La	40 hr.
Cesium	^{134}Cs	2.3 yr.	Magnesium		
(with			(with		
barium $^{137\text{m}}$)	^{137}Cs	30 yr.	aluminum 28)	^{28}Mg	21.2 hr.
Chlorine	^{38}Cl	37.3 min.	Manganese	^{52}Mn	5.8 da.
Chromium	^{51}Cr	27.8 da.		^{54}Mn	320 da.
Cobalt	^{57}Co	270 da.	Mercury	^{197}Hg	2.7 da.
	^{58}Co	72 da.		^{203}Hg	47.9 da.
	^{60}Co	5.2 yr.	Molybdenum	^{99}Mo	66 hr.
Copper	^{64}Cu	12.8 hr.	Nickel	^{56}Ni	6.4 da.
				^{63}Ni	125 yr.

Table I. (continued)

<u>Element</u>	<u>Radio-nuclide</u>	<u>Half-life</u>	<u>Element</u>	<u>Radio-nuclide</u>	<u>Half-life</u>
Niobium	^{95}Nb	35 da.	Tellurium	^{121}Te	17 da.
Phosphorus	^{32}P	14.3 da.	Thallium	^{204}Tl	4.1 yr.
Potassium	^{42}K	12.5 hr.	Thulium	^{170}Tm	125 da.
Praesodymium	^{142}Pr	19.3 hr.	Tin		
	^{143}Pr	13.7 da.	(with indium -		
Promethium	^{147}Pm	2.5 yr.	^{113}m)	^{113}Sn	115 da.
Radium			Tungsten	^{185}W	74 da.
(in equilibrium			Vanadium	^{48}V	16 da.
with Rn, Ra. B,			Xenon	^{133}Xe	5.27 da.
and C)	^{226}Ra	1620 hr.	Yttrium	^{90}Y	64.6 hr.
Rubidium	^{86}Rb	18.6 da.		^{91}Y	58 da.
Scandium	^{46}Sc	85 da.	Zinc	^{65}Zn	245 da.
	^{47}Sc	3.4 da.	Zirconium		
Selenium	^{75}Se	127 da.	(with niobium -		
Silver	^{111}Ag	7.5 da.	95)	^{95}Zr	65 da.
Sodium	^{22}Na	2.6 yr.			
	^{24}Na	15 hr.			
Strontium	^{85}Sr	65 da.			
	$^{87\text{m}}\text{Sr}$	2.8 hr.			
	^{89}Sr	54 da.			
(with yttrium 90)	^{90}Sr	28 hr.			
Sulfur	^{35}S	87 da.			
Technetium	$^{99\text{m}}\text{Tc}$	6 hr.			

Table II. Some Commonly Used Diagnostic Radiopharmaceuticals*

<u>Radiopharmaceutical</u>	<u>Diagnostic Use</u>
Potassium bromide Br 82	Measurement of extracellular water
Cyanocobalamin Co 57	Pernicious anemia and malabsorption syndromes
Chromated Cr 51 serum albumin	Intestinal protein loss
Diatrizoate I 131	G.F.R.
Sodium chromate Cr 51	Red cell mass
	Red cell survival
	Spleen scanning
Sodium fluoride F 18	Bone scanning
Gallium 67 Ga	Tumor localization
Gold Au 198	Liver scanning
Indium 113m DTPA	Brain scanning
Indium 113m iron hydroxide	Liver scanning
	Lung scanning
	Spleen scanning
Indium 113m	Cardiac scanning
	Placental scanning
Iodinated I 131 serum albumin	Blood volume
	Cardiac output
	Cardiac blood pool scanning
	Placental localization
Iodinated I 131 macro-aggregated serum albumin	Lung scanning
Oleic acid I 125 or I 131	Fat absorption
Sodium iodide I 131	Thyroid uptake studies
	Thyroid gland scanning

Table II. (continued)

<u>Radiopharmaceutical</u>	<u>Diagnostic Use</u>
Sodium iodohippurate I 125 or I 131	Kidney function R.B.F.
Sodium rose bengal I 131	Liver function Liver scanning
Triolein I 125 or I 131	Fat absorption
Ferrous citrate Fe 59	Iron metabolism
Chlormerodrin Hg 203 or Hg 197	Kidney scanning Brain scanning
Potassium chloride K 42	Distribution and metabolism of potassium
Selenomethionine Se 75	Pancreas scanning, parathyroid scanning
Sodium chloride Na 22	Distribution and metabolism of sodium
Strontium chloride or nitrate Sr 85, Sr 87m	Bone scanning
Serum albumin Tc 99m	Cardiac blood pool scanning Blood volume Placental scanning
Serum albumin Tc 99m aggregated	Lung scanning, cardiac scanning
Sodium pertechnetate Tc 99m	Brain scanning
Technetium iron ascorbate Tc 99m	Renal flow and imaging
Technetium sulfur colloid Tc 99m	Liver, spleen, and bone marrow scanning
Tritiated water	Measurement body water
Xenon Xe 133	Pulmonary function study

Table II. (continued)

<u>Radiopharmaceutical</u>	<u>Diagnostic Use</u>
Polyphosphate - Sn - Tc 99m	Skeletal imaging
Diphosphonate - Sn - Tc 99m	Skeletal imaging
Inulin - Tc 99m	C.S.F. studies

* In addition, many labeled enzymes and hormones (e.g. ^{125}I -thyroxine, ^3H -parathormone) are used in competitive binding assay and radio-immunoassay procedures. Since these labeled compounds are not administered to the patient they are probably not, theoretically, considered to be radiopharmaceuticals.

Table III. Instrumentation for the Nuclear Medicine Laboratory

<u>Instrument</u>	<u>Cost</u>	<u>Features</u>	<u>Use</u>	<u>Range</u>
Film badges	\$.50-\$2.00 (service)	Small badge worn continuously in laboratory. Usually processed at 1 week to 1 month intervals. Processing service available.	Recording total beta, gamma, and X-ray dosage wearer receives.	.03-10R up to 1000 R
Condenser ionization chamber	\$45 each, direct read \$55 charger	Reusable cylindrical chambers worn by worker. Must be charged before use. Reading is rapid, either in a reader or directly in some models.	Beta, gamma and X-ray recording. Usually used when rapid reading is important, and when time of dose measurements is not more than a few days, usually hours.	0-200 mR
Thermoluminescent dosimeters	Dosimeters less than \$1 Reader \$4000-\$5000	Small wearable containers of thermoluminescent material.	Economical in large installations or where size of dosimeter is important, as in implantation (beta, gamma, X-ray)	10 mr- 1000 R

Table III. (continued)

<u>Instrument</u>	<u>Cost</u>	<u>Features</u>	<u>Use</u>	<u>Range</u>
Geiger-Müller counters		GM detector with cable connection to rate meter. Visual or audible.	Most common monitor equipment for beta, gamma, and X-ray.	0-50 mR/hr
Bench monitor	\$400-\$600	Semi-portable, A.C. Meter, loudspeaker output optional.	In laboratory use; checking hands, work areas, equipment, etc.; rough assay of radioactive materials present.	"
Survey meter	\$120-\$700	Portable, battery operated meter; earphone output.	See bench monitor; useful also wherever portability is needed.	"
Personnel monitor	\$50-\$80	Small, carried in pocket. Audible or light output.	Warns wearer if he should enter area of high radiation intensity.	"

Table III. (continued)

<u>Instrument</u>	<u>Cost</u>	<u>Features</u>	<u>Use</u>	<u>Range</u>
Ionization chamber instruments	\$1200-\$5000	Accurate dose rate or activity calibrations possible. Can measure higher dose rates than G.M. counter.	Beta, gamma and X-ray monitoring. Besides "cutie pie" other ionization chamber instruments are used for area monitors (fixed location), calibration of source, radiation flux, etc.	0.5-10 ⁶ mR/hr
"Cutie Pie"	\$300-\$700	Portable survey instrument.	Monitor sources or areas where levels of activity are moderately high.	"
Neutron survey meter	\$650	Specially constructed proportional counting tube with neutron moderator. Portable, battery operated.	Monitor thermal and fast neutron sources.	0-45 mrem/hr.

Table III. (continued)

<u>Instrument</u>	<u>Cost</u>	<u>Features</u>	<u>Use</u>	<u>Range</u>
G-M counting systems manual	\$2000	GM detector and sample holder connected to scaler timer.	Counting high energy Beta samples.	Tracer level counting
Automatic sample changing systems	\$13,000	As above but automatic sample changing.	As above.	As above.
Gamma counting systems, manual	\$6-10,000	Crystal detector with analyzer, H.V. supply, scaler or rate- meter, and recorder.	Counting small samples containing gamma emitting isotopes.	Tracer levels
Automatic sample	\$8-30,000	As above but with automatic sample changing capability.	As above.	As above.
Liquid scintillation counters				
Manual	\$6-8,000	Light tight chamber, P.M. tubes, scaler and associated electronics, quench correction capability.	Counting small samples of low energy beta emitting nuclides e.g. ^{14}C or ^3H .	Tracer levels

Table III. (continued)

<u>Instrument</u>	<u>Cost</u>	<u>Features</u>	<u>Use</u>	<u>Range</u>
Automatic systems	\$8-30,000	As above but with automatic sample changing capability.	As above.	As above.
Multi-channel Analyzer	\$7-15,000	Electronic sorting of signals into 10^2 - 10^3 channels, detector, H.V. supply, cathode ray display, output device (printer).	Identify specific gamma emitting nuclides in a sample or count several nuclides simultaneously; useful in analyzing samples after activation analysis.	Tracer levels
Whole body counter	\$30-100,000	Steel, or steel and lead shielded large detector capable of counting human or larger sized samples, H.V. supply, scaler etc.	Determine radioactivity levels present in large samples the size of a man or even larger.	Tracer levels

Table III. (continued)

<u>Instrument</u>	<u>Cost</u>	<u>Features</u>	<u>Use</u>	<u>Range</u>
External counter	\$4-6,000	Collimated detector, moveable stand, H.V. supply, scaler or ratemeter, analyzer.	Determine levels of radio-activity in an organ or body space <u>in vivo</u> with a detector located outside of the body.	Tracer levels
Rectilinear scanner	\$8-20,000	Collimated detector, driving mechanism, H.V. supply, analyzer, visual output device.	Visual representation of distribution of radio-actively in organ or space, gamma ray emitters only.	Tracer levels
Anger camera	\$40-60,000	Large (8" diameter) detector with collimators, positioning stand, instrument console, photographic readout.	As above but much more rapid, dynamic function studies possible.	Tracer

Table IV. Diagnostic Nuclear Medical Applications

Tech. No.	Major System	Objective of Procedure	Nuclide or Preparation Used	Equipment Required ¹	Duration of Observations on Patient ²	Species	References
1	Body composition	body chloride	^{82}Br , ^{36}Cl , ^{38}Cl	2, 3	2	man	12
2	Body composition	body magnesium	^{28}Mg	3	3	man	12
3	Body composition	body potassium	^{42}K , ^{86}Rb	3	3	man	12
4	Body composition	body sodium	^{22}Na , ^{24}Na - NaCl	3	3	man	12
5	Body composition	extracellular water	^{82}Br - NaBr	3	3	man	12
6	Body composition	lean body mass	^{40}K , ^{42}K	4, 9	2	man animals	12,17,60
7	Body composition	total body water	^3H - H_2O (tritiated water)	2	2	man	12
8	Brain	cerebral blood flow dynamics	$^{99\text{m}}\text{Tc}$ sodium pertechnetate	6	2	man	12,40,63
9	Brain	cerebral spinal fluid flow	^{131}I - serum albumin $^{99\text{m}}\text{Tc}$ - serum albumin $^{99\text{m}}\text{Tc}$ - inulin	6, 7	3	man	11,12,63

Table IV. (continued)

<u>Tech. No.</u>	<u>Major System</u>	<u>Objective of Procedure</u>	<u>Nuclide or Preparation Used</u>	<u>Equipment Required¹</u>	<u>Duration of Observations on Patient²</u>	<u>Species</u>	<u>References</u>
10	Brain	lesion & hematoma detection	^{197}Hg - chlormerodrin ^{131}I - serum albumin $^{99\text{m}}\text{Tc}$ - sodium pertechnetate	6, 7	2	man	12,40,63
11	Circulation	cardiac output	^{131}I - serum albumin $^{99\text{m}}\text{Tc}$ - serum albumin	5	2	man	12,97
12	Circulation	myocardial scanning	^{131}I - macroaggregated serum albumin $^{99\text{m}}\text{Tc}$ - macroaggregated serum albumin ^{131}Cs	6, 7	2	man animals	12,63 79, 101
13	Circulation studies	cardiac blood pool	^{131}I - serum albumin $^{99\text{m}}\text{Tc}$ - serum albumin $^{99\text{m}}\text{Tc}$ - sodium pertechnetate	6, 7	2	man	12,63,96
14	Fetus	placental localization	^{131}I - serum albumin $^{99\text{m}}\text{Tc}$ - sodium pertechnetate $^{99\text{m}}\text{Tc}$ - serum albumin, ^{51}Cr	5,6,7	2	man	12,40,63

Table IV. (continued)

<u>Tech. No.</u>	<u>Major System</u>	<u>Objective of Procedure</u>	<u>Nuclide or Preparation Used</u>	<u>Equipment Required¹</u>	<u>Duration of Observations on Patient²</u>	<u>Species</u>	<u>References</u>
15	Gastrointestinal function	gastrointestinal bleeding	⁵¹ Cr - labeled RBC	3	3	man	12,40,63
16	Gastrointestinal function	vitamin B ₁₂ absorption	⁵⁷ Co - cyanocobalamin	3	3	man	12,63
17	Gastrointestinal tract	fat absorption	¹³¹ I - glyceryl trioleate ¹³¹ I - oleic acid	3	3	man animals	12,47 50,63,94
18	Gastrointestinal tract	plasma protein loss	¹³¹ I or ⁵¹ Cr - serum albumin ¹³¹ I - PVP	3	4	man animals	12,32,40 44,63,99
19	Hematological studies	ferrokinetics plasma iron utilization	⁵⁹ Fe - ferrous citrate	3	2	man animals	30,40,49,63
20	Hematological studies	ferrokinetics, red cell incorp- oration of labeled iron	⁵⁹ Fe - ferrous citrate	3	4,5	man animals	12,30 40,49
21	Hematological studies	plasma volume	¹²⁵ I - serum albumin ⁵⁹ Fe ^{99m} Tc - serum albumin	3	2	man animals	12,30 40,55 57,63

Table IV. (continued)

Tech. No.	Major System	Objective of Procedure	Nuclide or Preparation Used	Equipment Required ¹	Duration of Observations on Patient ²	Species	References
22	Hematological studies	red blood cell volume	⁵¹ Cr labeled red cells ^{DF} ³² P labeled red cells ⁵⁹ Fe labeled red cells	1,2,3	2	man animals	12,30,40 55,63
23	Hematological studies	red cell survival	⁵¹ Cr, ^{DF} ³² P, ⁵⁹ Fe	1,2,3	5	man animals	12,28,40 63,65,86
24	Hematological studies	splenic seques- tration	⁵¹ Cr, ⁵⁹ Fe	5	5	man	12,40,63
25	Hematological studies	unsaturated iron binding capacity	⁵⁹ Fe	3	1	man animals	15,49,97
26	Hematological studies	vitamin B ₁₂ metabolism	⁵⁷ Co-cyanocobalamin	3, 9	3	man	12,40,63
27	Hormone assays	FSH-RIA	³ H-follicle stimulating hormone	2	1	man	75
28	Hormone assays	insulin RIA	³ H or ¹⁴ C-insulin	2	1	man animals	14,104
29	Hormone assays	LH - RIA	³ H - lutenizing hormone	2	1	man	74,76
30	Hormone assays	parathormone RIA	¹³¹ I - parathormone	3	1	animals man animals	6,61

Table IV. (continued)

<u>Tech. No.</u>	<u>Major System</u>	<u>Objective of Procedure</u>	<u>Nuclide or Preparation Used</u>	<u>Equipment Required¹</u>	<u>Duration of Observations on Patient</u>	<u>Species</u>	<u>References</u>
31	Hormone assays	serum cortico-steroid concentration	³ H - cortisol ³ H-11-desoxycortisol ³ H-corticosterone ³ H-cortisone ³ H-aldosterone	2	1	man animals	7,62,71
32	Hormone assays	serum estrogen concentration	³ H or ¹⁴ C estrogen	2	1	man animals	1,2,41
33	Hormone assays	serum progesterone concentration	³ H or ¹⁴ C progesterone	2	1	man animals	8,67,91
34	Hormone assays	somatotrophin-RIA	³ H-somatotrophin	2	1	man animals	58,85,95
35	Hormone assays	testosterone-RIA	³ H-testosterone	2	1	man	21,29
36	Hormone assays	vitamin B ₁₂ analysis	⁵⁷ Co cyanocobalamin	3	1	man animals	33,97

Table IV. (continued)

<u>Tech. No.</u>	<u>Major System</u>	<u>Objective of Procedure</u>	<u>Nuclide or Preparation Used</u>	<u>Equipment Required</u>	<u>Duration of Observations on Patient</u>	<u>Species</u>	<u>References</u>
37	Kidney	blood flow & function	^{99m}Tc - iron ascorbic acid complex	6	2	man	10,63
38	Kidney	function	^{131}I - sodium iodohippurate	5-8	2	man	12,40,44
			^{131}I - sodium didiatrycate			animals	63,70
			^{197}Hg - chlormerodrin				
			^{99m}Tc - DTPA				
39	Kidney	size, shape, function	^{131}I - sodium iodohippurate	6, 7	2	man	12,63
			^{197}Hg - chlormerodrin				
			^{99m}Tc - iron ascorbic acid complex				
40	Liver	function	^{131}I - rose bengal	3,5,8	2	man	12,22,
						animals	39, 40
41	Liver	scanning	^{131}I - rose bengal	6, 7	2	man	12,40,63
			^{99m}Tc - sodium pertechnetate				64, 98
			^{198}Au				
			^{99m}Tc - sulfur colloid				
42	Lung	pulmonary embolism	^{131}I - macroaggregated albumin	6,7	2	man	12,40,63
			^{99m}Tc - macroaggregated albumin				

Table IV. (continued)

<u>Tech. No.</u>	<u>Major System</u>	<u>Objective of Procedure</u>	<u>Nuclide or Preparation Used</u>	<u>Equipment Required</u>	<u>Duration of Observations on Patient</u>	<u>Species</u>	<u>References</u>
43	Lung	regional ventila- tion and pulmonary blood flow	^{133}Xe xenon ^{13}N ^{15}O	6, 7	2	man	12,63
44	Lymph nodes	evaluation	$^{99\text{m}}\text{Tc}$ - sulfur colloid ^{198}Au - colloid	6, 7	3	man	12,63
45	Pancreas	function	^{131}I - glyceryl trioleate ^{131}I - oleic acid	3	3	man animals	12,40 47,63
46	Pancreas	morphology- scanning	^{75}Se - selenomethionine	6, 7	2	man	12,40,63
47	Parathyroid glands	visualization	^{75}Se - selenomethionine ^{57}Co - cyanocobalamine ^{131}I - toluidine blue	6, 7	4	man	12,40,63
48	Salivary glands	pathology	$^{99\text{m}}\text{Tc}$ - pertechnetate	6, 7	2	man	40,63
49	Skeletal system	bone kinetic analysis	^{47}Ca , ^{85}Sr	3,5,9	4	man animals	48,52,59,87, 103
50	Skeletal system	densitometric techniques	^{125}I , ^{241}Am	5	2	man animals	19,53,66 90,102

Table IV. (continued)

<u>Tech. No.</u>	<u>Major System</u>	<u>Objective of Procedure</u>	<u>Nuclide or Preparation Used</u>	<u>Equipment Required</u>	<u>Duration of Observations on Patient</u>	<u>Species</u>	<u>References</u>
51	Skeletal system	focal lesion	^{85}Sr , ^{18}F , $^{87\text{m}}\text{Sr}$	6, 7	2,4	man	12,13,20
		detection	$^{99\text{m}}\text{Tc}$ -Sr-polyphosphate			animals	24,25,40
			$^{99\text{m}}\text{Tc}$ -Sr-diphosphanate				63,84,92
52	Skeletal system	total body	^{48}Ca (activation analysis)	9	2	man	5,73,78
		calcium					
		determination					
53	Spleen	configuration	^{51}Cr - RBC	6, 7	2	man	12,40,63
			$^{99\text{m}}\text{Tc}$ - sulfur colloid				
			$^{113\text{m}}\text{In}$ - colloid				
			^{198}Au - gold colloid				
54	Spleen	function	$^{99\text{m}}\text{Tc}$ - sodium pertechnetate	5,6,7	2	man	40, 4
55	Thyroid	conversion to PBI	^{131}I , ^{125}I	3	3	man	12,40, 42
56	Thyroid	function (T-3	^{125}I or ^{131}I -tri-	3	1	animals	12,27,40,42
		resin uptake)	iodothyronine			animals	

Table IV. (continued)

<u>Tech. No.</u>	<u>Major System</u>	<u>Objective of Procedure</u>	<u>Nuclide or Preparation Used</u>	<u>Equipment Required</u>	<u>Duration of Observation on Patient</u>	<u>Species</u>	<u>References</u>
57	Thyroid	uptake, suppression, stimulation, washout, etc.	^{131}I , ^{125}I $^{99\text{m}}\text{Tc}$ - sodium pertechnetate	5, 6, 7	3	man animals	12, 18, 40, 51, 56 63, 80, 93
58	Thyroid	visualization, scanning	^{131}I , ^{125}I $^{99\text{m}}\text{Na}$ -pertechnetate	6, 7	2	man	12, 36, 40 63, 81
59	Thyroid	serum TSH-RIA	^3H - thyrotropin	2	1	man	77
60	Thyroid	T_4 test - circulating thyroxine level	^{125}I - thyroxine	3	1	man animals	4, 12, 40 43, 71, 72
61	Thyroid hormone assay	T_3 - RIA	^{125}I - triiodothyronine	3	1	man	16, 38, 69, 31
62	Tumor	tumor detection	^{67}Ga	6, 7	2	man	34

Footnotes to Table IV

1. Equipment enumerated in column 5 include:

1. G-M counter
2. Liquid scintillation counter
3. Gamma counter (single channel)
4. Multi-channel analyzer
5. External counter
6. Anger (scintillation) camera
7. Rectilinear scanner
8. Gamma counter plus chart recorder
9. Whole body counter

2. Duration of Patient Observations

1. In vitro samples only
2. Less than one day
3. One to three days
4. Three to ten days
5. Longer than ten days