BIOLOGICAL HAZARD OF RADIOACTIVE STRONTIUM

R. A. Dudley, 6/17/54

I. Uptake and retention of Sr

In Table 2 is collected a set of data from Sr and Ca uptake and retention experiments reported in the literature. From these data it may be concluded that when Sr and Ca are administered under equivalent conditions, the Sr/Ca ratio retained falls between 0.25 and 1. These "equivalent conditions" include:

(1) Wide range of species (mice, rat, steer)

(2) Wide range of age

(3) Wide range of carrier Sr

(4) Conditions of normal or disturbed (rachitic, of P or Ca deficient variety) Ca metabolism.

(5) Oral or injected

With a few exceptions, these experiments extend over periods of only a few days. One may have confidence that similar experiments over prolonged periods would give closely similar results for these reasons:

(1) The two chronic feeding experiments on rats give a ratio of retained Sr/Ca = 0.4 and 0.25, respectively.

(2) Excretion of Sr and Ca is very slow after the first week. This is apparent in item 7 of Table 2. Extensive studies on Sr excretion in large animals have been carried out by Comar (13) (steers and sheep), and Kisieleski (14) (dogs). These data are summarized in Table 3, where daily excretion is expressed as a percentage of body burden and as the corresponding half life for retention. Since Ca is excreted less rapidly than Sr, the ratio Sr/Ca retained would be expected to drop with time, but perhaps less than 25% after 10 days.

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TABLE 3

Rate of Excretion of Sr^{90}

	Days after administration	% body burden in daily excretion	Associated half life
Yearling steers	10	0.6%	120 days
	20	0.1	700
	720	0.004	1.7×10^4
Mature sheep	10	2%	35 days
	20	1	70
	50	0.3	230
	100	0.15	460
	500	0.02	3500
Dogs	14	0.5%	140 days

From these metabolic experiments it appears that Ca and Sr behave nearly (though not exactly) like isotopes. Consequently, studies of Sr metabolism under unspecified conditions of Ca metabolism cannot be reliably interpreted. Parallel series of Sr and Ca experiments in similar animals, or better yet, double tracer experiments in the same animals, are to be strongly recommended.

II. Localization of Sr and its radiation in skeleton

A. Strontium atoms

The distribution of Sr in the skeleton has been extensively studied. Unfortunately, many experiments have been qualitative rather than quantitative in character. Within the accuracy of the experiments which have been performed, the localization of Sr is identical with that of Ca.

On the molecular scale, it is probable that Sr is located in "solid solution" within the bone crystals -- again essentially isotopic with Ca. MacDonald, et al[15], have carried out x-ray diffraction

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studies on rat bone ash which, by adjustment of the rat diet, contained a few percent Sr. The diffraction pattern indicated the presence of only a single phase in the crystal structure: hydroxyapatite, the same as control bone ash. Unit cell distances were distorted by the Sr, resulting in blurred diffraction lines. Support for the hypothesis that Sr is incorporated into the latice is given by the existence of a series of apatite-like minerals involving Ca, Sr, Ba, and Pb, all of which are capable of forming solid solutions, one with another.

On the microscopic scale, numerous autoradiographic studies have been performed showing the qualitative similarity in Ca and Sr localization. A good comparison of the two elements in growing large animals has been made by Comar, et al[16]. Weanling pigs (80 days) were injected with Ca, Sr, or P and sacrificed at intervals up to 60 days. The resultant pattern of activity is sufficiently familiar that a detailed description is unnecessary. Briefly, the initial deposition was very pronounced at the epiphyseal plate, under the periosteum and endosteum, and at spots throughout the trabecular and cortical structures. A lower concentration of activity was evident in diffuse distribution throughout the whole bone.

With time the epiphyseal growth left behind the initial epiphyseal deposit, which was then overtaken by the trabecular region and later resorbed altogether when replaced by the elongating marrow cavity. The sub-periosteal deposit was similarly overtaken by growth in the shaft diameter, and ultimately resorbed at the marrow cavity surface. Since little of the resorbed Sr is excreted, it must be redeposited. Very similar results were found in rabbit bones by Kidman, et al[17]. An additional mode of redistribution is the exchange process. Tomlin, et al[18], made quantitative autoradiographic measurements on Ca^{45} in rats; presumably Sr would have yielded the same results. It was found that in the period from

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4 to 6 weeks of age, 14% of the disphyseal Ca in femur and humerus were rev.ewed by exchange, and 24% by the 16th week. Exchange in adults was much lower.

A significant effect of this resorption and exchange must be a progressively more homogeneous distribution of activity, and therefore a more nearly uniform dose rate throughout the bone.

Arnold[19] has studied by quantitative autoradiography the localization of Ca^{45} in the cortical bones of rabbits. The hot spot activity concentration, relative to diffuse activity throughout the cortex, ranged up to about 15, with a mean of about 6.

On the scale of whole bones, differences in concentration of Sr per gram wet weight are found between different bones. Presumably, this is caused by differences in amount of Ca per gram wet weight or differences in rate of growth at time of injection. For example, in the bones of yearling steers Comar[20] found activity ratios of 2 or 3 between different bones.

The foregoing discussion assumed administration of the Sr in a single injection or feeding. However, if the Sr is incorporated into the skeleton under conditions of chronic feeding, the Sr would presumably be distributed in an essentially uniform mixture throughout the skeletal Ca.

B. Sr^{90} - Y^{90} radiation

The distribution of the parent Sr^{90} or Y^{90} atoms and the distribution of their radiation dose is not identical. If the bones or the regions of localization are comparable in size with the range of the radiation, dose distribution will be more nearly uniform than is the parent atom distribution. This effect may be especially significant when an attempt is made to extrapolate mouse toxicity data to larger animals. Despite corresponding localization of the atoms in epiphyses, etc., of mice and larger animals, dose distribution throughout the mouse bones would be much more uniform

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because the bone diameter (e.g. femur shaft diameter about 1.5 mm) is comparable with the Y^{90} range. Also, irradiation of surrounding soft tissue would be greater in the mouse than in larger animals. For toxicity studies the basic physical parameter is dose distribution, not parent atom distribution.

There are apparently no quantitative studies available on small scale distribution of Sr^{90} dose in animal bones. There are such studies, however, for Ca^{45} in dog bones, and presumably the Sr^{90} situation may be inferred by analogy. Maletskos will report in person on his measurements, which are still in progress. Dudley and Dobyns[21] examined the localized (0.005 mm^2) dose distribution from Ca^{45} in 2 dogs, 1 adult, 1 growing, and related these measurements to the blood activity, the average bone dose, and the effects of nominal decalcifying procedures. It was found that 5 weeks after administration the maximum local dose rates in rib, humerus, femur, tibia, and jaw were all substantially equal; they were from 5 to 10 times average bone dose in the young dog and 10 to 20 in the old. Successive rib resections following treatments with $CaCl_2$, NH_4Cl, and parathyroid hormone showed only small reductions in hot spot dose rates; these reductions were quite likely produced by normal exchange processes over the period of the experiment rather than by the treatment.

Presumably the much greater range of Sr^{90}-Y^{90} beta radiation would have given a somewhat more uniform dose distribution in the same dogs than did the Ca^{45} radiation. Quantitative autoradiographic studies of dose rate distribution from Sr^{90} in bone would add much information where little is now available.

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III. Localization of in Skeleton

Since the Y^{90} daughter of Sr^{90} has a half life of 64 hours, sufficient time is conceivably available for a significant redistribution of this element in the skeleton.

Studies of Y^{91} skeletal distribution following I. V. injection have shown differences between Y and Sr localization. For example, Comar [22] examined the distribution of Y^{91} in growing cattle at intervals up to 5 months, and Rayner et al[23] made similar measurements on rabbits (both young and adult) at intervals up to 3 months. The chief difference between Y and Sr is that Y is not laid down in such high concentration under the periosteum and endosteum. While Y is presumably associated with the protein bone matrix rather than with the mineral crystals like Sr, its chief initial concentration in growning animals is at the epiphysis. It is then held even more firmly than Sr as the bone grows, until finally being resorbed at the marrow cavity. A light diffuse distribution of Y throughout the bone cortex is also found, as in the case of Sr.

An outstanding characteristic of Y deposits, whether in bone or soft tissue, is the firmness with which they are retained. Comar found essentially constant activity in the steer bones and soft tissue between 13 days and 5 months and Rayner found retention higher than Sr. Although not yet experimentally established, it seems very unlikely that significant redistribution of Y^{90} takes place following its "birth" from Sr^{90}. The dose distribution from Sr^{90} Y^{90} would then be produced by parent atoms in the Sr and Ca distribution pattern.

IV. Comparison of Sr^{90} and Ra Dose Distribution

The distribution of Ra in the skeleton is covered in detain in Looney's talk. The localization is qualitatively, at least, identical with that of Ca and Sr. The "hot spot" dose rates in human bone have been examined by Looney and Woodruff[24] and by Hoecker and Roofe[25]. In all cases, Ra was administered when the individual was an adult. Between 2 and 15 % of the Haversian systems contained Ra, although in some cases only a fraction of the lamellae in any one system were active. Similar spotty localization were observed in the trabecular bone. From the data presented, it would appear that the ratio of hot spot to average dose rate throughout the bone is in the range of 10-100. This suggests a somewhat higher localization of Ra dose than the Ca^{45} dose observed by Dudley in adult dog bones (10-20) and the Ca^{45} concentration observed by Arnold in rabbit bones (5-10).

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It is quite possible that in animals of the same age and species the local concentrations of Ra, Sr, and Ca atoms would be the same, while dose concentration would be in the order Ra $> Ca^{45} > Sr^{90}$ in inverse relationship to the range of the radiation.

The difference between the ranges of Ra and Sr^{90} - Y^{90} radiation may have greater implications than the associated differences in hot spot dose concentration. First, for Ra Harrison systems are effectively isolated from radiation originating in adjacent systems, whereas for Sr^{90}-Y^{90} the immediately adjacent systems receive considerable radiation dose. Second, the high specific ionization of alpha rays may of course have a different biological effectivness from β radiation.

V. Toxicity of radioactive Sr

A set of experimental dataindicating Sr toxicity in various species is listed in Table 4. The data include essentially all the significant experiments I have been able to find, with the exception that some acute mouse and rat data are omitted. Skeletal dose rate is calculated under the arbitrary assumptions of skeletal weight equals 1/10 body weight, and retained dose equals 50% of administered dose (unless further data on retention obtained in experiment). While the list is fairly extensive, very few of the items are of much value in determining human tolerance for Sr^{90}. Most of the experiments used Sr^{89}, and were at the acute rather than long term hazard level. Several methods for estimating human tolerance are briefly discussed below.

A. Direct observations in humans

There is no supply of human Sr cases paralleling the Ra cases. The Sr^{89} patients in Table 4 are not numerous enough to be of much value.

B. Comparison of Sr and Ra toxicity

The comparison of Sr with Ra toxicity in animals would permit an estimate of human Sr toxicity from the known human Ra toxicity. This method is probably the most promising. However, few experiments have been designed to make this animal comparison at chronic levels of radiation. A small scale Ra mouse experiment, in parallel with Brues' large Sr^{89} mouse experiment, indicated[29, 38] a Sr^{89}:Ra toxicity ratio of 1:10 on

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a microcurie basis. If it is assumed that the Ra dose in humans, per microcurie, is twice as great as in mice on account of lower Rn exhalation, the Sr^{89}:Ra ratio for humans would be 1:20, and Sr^{90}:Ra ratio would be 1:10. The differences between bone size of mice and humans influence the respective dose distribution patterns, and may require a correction to this ratio for humans. From the human Ra "tolerance" of 0.1 microcurie/man, one would compute a value for Sr^{90} of 1.0 microcurie per man.

C. Comparison with x and gamma radiation of bone

The lowest value in Table 4 of bone dose required to produce a malignant tumor is about 5000 rads. There is no reason to suppose that this is a lower limit. The amount of Sr^{90} required to produce this cumulative skeletal dose in 50 years is about 35 microcuries per man.

The accepted whole body maximum permissible exposure is 0.3 rad/week, or 750 rads in 50 years. If Sr^{90} were distributed substantially uniformly throughout the bone, the dose character would be very similar to that from external x and gamma radiation, thereby justifying a comparison. A dose of 750 rads would be produced by 5 microcuries/man for Sr^{90}.

BIBLIOGRAPHY

1. Pecher, U. of Cal. Publications in Pharmacology 2 #11, 117 (1942)
2. Pecher and Pecher, Proc. Soc. Exp. Biol. 46 91 (1941)
3. Greenberg, J. Biol. Chem. 157 99 (1945)
4. Copp, et al, Am. J. Roent. and Ra Therapy 58 10 (1947)
5. Copp, et al, UCRL Quarterly Progress Report (April - June, 1948)
6. Norris and Kisieleski, Cold Spring Harbor Symposia on Quantitative Biology 13 164 (1948)
7. Copp, et al, UCRL 1464 (Sept 1951)
8. Comar, Personal communic tion
9. MacDonald, et al, J. Biol. Chem. 188 137 (1951)
10. Gross, et al, UCLA 274 (Jan, 1954)
11. MacDonald, et al, Arch. Biochem. and Biophysics 43 118 (1953)
12. Kidman, et al, J. Path. and Bact. 62 209 (1950)
13. Comar, ORO-110 (1954)
14. Kisieleski, ANL 5247, p.68 (1954)

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DOE ARCHIVES

15. MacDonald, et al, J. Biol. Chem. 189 387 (1951)

16. Comar, et al, Am. J. Anatomy 90 113 (1952)

17. Kidman, et al, J. Path. and Bact. 64 453 (1952)

18. Tomlin, et al, Brit. J. Nutrition 7 235 (1953)

19. Arnold, Personal communication

20. Comar, ORO-59, p. 8, (1951)

21. Dudley, Ph.D. thesis, Dept. of Physics, M.I.T. (1951)

22. Comar, ORO-98 (1953)

23. Rayner, et al, Brit. J. Exp. Path. 34 138 (1953)

24. Looney and Woodruff, Arch. Pathol. 56 1 (1953)

25. Hoecker and Roofe, Radiology 56 89 (1951)

26. Letter from J.G.Hamilton to Dunham dated Apr. 6, 1954

27. Swift and Prosser, MDDC 1388 (1947)

28. Finkel and Clark, ANL 5200 (1954)

29. Brues, Notes for Sr toxicity conference at Washington, Jan. 1954

30. Arnold, Personal communication

31. Comar, Personal communication

32. Edington, et al, Nature 172 122 (1953)

33. Swift, et al, AECU 108 (1946)

34. Colonel Rust, Personal communication

35. Anthony, et al, MDDC 1364 (1947)

36. Simmons and Jacobson, MDDC 1387 (1947)

37. Brues, et al, MDDC 145 (1946)

38. Brues, J. Clin. Investigation 28 1286 (1949)

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TABLE I -- Physical Properties of Significant Isotopes

	Sr^{89}	Sr^{90}	Y^{90}	Sr^{90} (+ Y^{90})	Y^{91}	Ra
Halflife	53 days	20 years	64 hours	------	60 days	1600 years
Av. energy/disintegration	0.6 Mev	0.2 Mev	0.9 Mev	1.1 Mev	0.6 Mev	14 Mev (man, 50% Rn exhaled) 8 Mev (rat, 85% Rn exhaled)
Maximum range						
Mass/unit area	0.7 gm/cm^2	0.2 gm/cm^2	1.2 gm/cm^2	------	0.7 gm/cm^2	----
Distance in tissue	7 mm	2mm	12 mm		7 mm	0.07 mm
Distance in bone	5 mm	1.3 mm	8 mm		5 mm	0.05 mm
Half thickness						
Mass/unit area	75 mg/cm^2	20 mg/cm^2	130 mg/cm^2	------	75 mg/cm^2	----
Distance in tissue	0.75 mm	0.2 mm	1.3 mm		0.75 mm	
Distance in bone	0.5 mm	0.13 mm	0.9 mm		0.5 mm	
Dose for 1 µc/gm						
Initial rate	33 rad/day	11 rad/day	50 rad/day	61 rad/day	33 rad/day	800 rad/day (50% Rn exhalation)
Total decay	2300 rad	1.1 x 10^5 rad	190 rad	6.1 ~~rad~~ x 10^5 rad	2900 rad	----
"Tolerance" (0.042 rad/day)	1.3 µc/kg	(4 µc/kg)	(0.8 µc/kg)	0.7 µc/kg	1.3 µc/kg	0.05 µc/kg (50% Rn exhalation)

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TABLE II
Sr and Ca Metabolism

Reference	Animal	Age At Admin.	Period of Retention	Method of Admin.	Sr Intake	Ca Intake	%Sr Retention	%Ca Retention	Sr/Ca Ratio Retained	Comments
1	Mice	-	24 hrs.	IV(lactate)	1.6mg		33%		-	IV uptake of Sr chloride, lactate gluconate essentially identical.
					0.017	0.8mg	45%	58%	0.8	
			48 hrs.	Oral(lactate)	-	1.6mg	11%	23%	0.5	Oral uptake of Sr chloride, lactate, gluconate essentially identical.
2	Mice	Adult	9-15 days	Injected	-	-	13-31%	53-65%	0.4	These mice were pregnant females which gave birth during period of retention.
3	Rats	Approx. 5 weeks	3 days	Oral(lactate)	0.5-2mg	1.5-4mg	10%	15%	0.7	Rats reared 15-20 days (shortly after weaning) on Ca deficient die then treated.
				Oral(lactate with vitamin D)	" "	" "	15%	31%	0.5	
				IP(lactate)	"	"	11%	28%	0.4	
				IP(lactate with Vitamin D)			26%	45%	0.6	

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Reference	Animal	Age at Admin.	Period of Retention	Method of Admin.	Sr Intake	Ca Intake	%Sr Retention	%Ca Retention	Sr/Ca Ratio Retained	Comments
4	Rats	Growing	4 days	Oral	Carrier free	(Low Ca) (diet)	73%	-	-	Effect of dietary Ca on Sr retention is apparent, though data not quantative.
					"	(High Ca)	17%	-	-	
		Adult	"		"	(Low Ca) (diet)	16%	-	-	
					"	(High Ca) diet)	2.8%	-	-	
		Growing and Adult	"	I.P.	"	Similar results, ranging from 70% Sr retention in young (low Ca) to 14% in old (high Ca).				
5	Rats	50days	4days	Intra-Muscular	-	-	70%	81%	0.9	Sr and Ca in different rats.
		50days	4days	"	Carrier free	-	65%	75%	0.9	Sr and Ca in same rats (double tracer.)
6	Rats	-	1day	IV	-	-	81%	86%	0.9	Ra studies carried out in same series; retention at succesive periods 73%, 58%, 55%, 53%, respectively.
			3day	"	-	-	81%	88%	0.9	
			10days	"	-	-	67%	87%	0.8	
			30days	"	-	-	55%	79%	0.7	

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Reference	Animal	Age At Admin.	Period of Retention	Method of Admin.	Sr Intake	Ca Intake	% Sr Retention	%Ca Retention	Sr/Ca Ratio Retained	Comments
7	Rats	8 weeks	8days	I.P.	Carrier free	-	72%	73%	1	
		6-12 mos.	8days	I.V. I.P.	Carrier free	-	29%	32%	0.9	
		8 weeks (low P rickets)	8days	I.P.	Carrier free	1.2mg 1.2mg	20%	13%	1.5	Rats in this group on low P diet, therefore rachitic.
8	Rats	Daily diet from birth	Months	Oral	Normal Sr/Ca ratio ($\sim 10^{-3}$)		-	-	0.35	Rats kept on standard diet of known Sr/Ca ratio throughout life.
9	Rats	Growing	Weeks	Oral	Sr/Ca intake $= 2.3 \times 10^{-3}$		Sr/Ca retained $= 5.5 \times 10^{-4}$		0.25	Rats kept on standard diet of known Sr/Ca ratio throughout period of growth.
10	Rats	Adult	4days	Oral	0.45 mg/day	-	4-5%	-	-	Dose fed for 7 consecutive days, animals sacrificed on 8th day.
					0.9	-	"	-	-	
					4.5	-	"	-	-	
					22.5	-	"	-	-	
					45	-	"	-	-	

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Reference	Animal	Age At Admin.	Period of Retention	Method of Admin.	Sr Intake	Ca Intake	%Sr Retention	%Ca Retention	Sr/Ca Ratio Retained	Comments
11	Rats	Adult	1 day	I.P.	0.1 -75mg	-	See Comment	-	-	Sr retention decreased by factor of only 5 over 750 fold range of Sr injection.
12	Rabbit	6weeks	9 days	I.V.	Carrier free to 0.02 g Sr per rabbit	0.02 gm Ca/day in diet	55%	-	-	Amount of Sr carrier had no influence on Sr retention within experimental error of 10%. Effect of dietary Ca on Sr retention is apparent, though data not quantitative since uptake of Ca from gut is unknown.
						0.2 gm Ca per day in diet.	46%			
						1.3 gm Ca per day in diet	31%			
		6 months	9 days	I.V.	"	0.04 gm Ca/ day in diet	57%	-	-	
						0.4 gm Ca/day in diet.	17%	-	-	
						2 gm Ca/ day in diet	12%	-	-	
		18 months	9 days	I.V.	"	0.4 gm Ca/ day in diet	8%	-	-	
13	Steer	1 year	7 days	Oral	Carrier free	-	30%	30%	1.	Retention computed by subtracting excretion from administration.

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Reference	Animal	No. of Animals	Isotope	μc/gm Administered	Estimated Rad/day in Skeleton	Biological Effects	Comments
	Rabbits		Sr^{89}	1.	160	Reduction in heterophils apparent	
37,29	Rats	19	"	0.7. 3	120	Tumors in 10 of 19 rats	
				0.03	5	50% with bone damage	
	Rabbits			2	330	Tumors within 1 yr.	
37,38	Mice	2100 altogether	"	5	820	Mean life duration about 1/3 control.	The most extensive experiment on chronic Sr toxicity. Tumor latent period appears to vary as inverse square root of dose. Dependence of incidence on dose suggests that each quantity of absorbed radiation confers on tissue absorbing it a probability of tumor formation which is without limit in time.
				2.5	410		
				1	160	Significant reduction in mean life duration	
				0.5	80	Negligible reduction in mean life expectancy	
				0.25	40		
				0.1	16		
				0.05	8	Significantly higher tumor incidence than controls at this and all higher dose levels.	

39 Humans: x and γ irradiation of bone produces malignant tumors. Incidence apparently low. 11 cases reviewed, mostly 200 KV x-ray treatment. In most cases, estimated bone dose about 8000-10,000 rads. One case about 5000 rad. Latent period 6-22 years.

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TABLE IV

Experimental Data on Radioactive Strontium Toxicity

Reference	Animal	No. of Animals	Isotope	μc/gm Administered	Estimated Rad/day in Skeleton	Biological Effects	Comments
26	Human	6	Sr^{89}	0.4-0.02	60-3	All died soon after treatment, presumably from disease for which treated (breast cancer, polycythemia vera, osteogenic and other sarcomas). Effects of radiation indistinguishable from disease.	Patients treated at U. C. Calif. hospital in early '40's. In many of the cases, the dose was administered in several subdivisions over a period of a few months. Other patients treated on which data at present unavailable. Dr. Dunham suggests surviving patients be followed, although with little expectation of significant findings.
	Human	1	Sr^{89}	0.06	10	Mycosis fungicides diagnosed. Effects indistinguishable from symptoms of disease. Survives without follow-up.	
	Human	1	Sr^{89}	0.1	16	Fibromyxosarcoma diagnosed. Effects indistinguishable from symptoms of disease. Survives apparently without ill effects.	
	Dogs (beagles)	24	Sr^{89} plus small Sr^{90} contamination	0.1 - 3.1	16-500	30 day LD50 about 1 μc/gm retained. Biological response was acute radiation symdrome.	Dogs included adults, young adults, pups. Somewhat better correlation of effect with injected dose than with retained dose.

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Reference	Animal	No. of Animals	Isotope	μc/gm Administered	Estimated Rad/day in Skeleton	Biological Effects	Comments
28, 29	Dogs (adult)	9	Sr^{89} plus small Sr^{90} contamination	0.25 - 1.0	40-160	4 died within 135 days, all suffered early hemorrhages, survivors had numerous bone fractures. 1 with maximum dose died at 8 yrs. with skeletal changes, no tumor. 1 with 0.5 μc/gm has bone tumor at 8 yrs.	Some survive at 8½ yrs.
	Dogs (adult)	4	Sr^{89} plus small Sr^{90} contamination	0.1	16	1 suffered bone fracture at 3 yrs., slight localized changes in mandibles.	" " " " "
	Dog (puppy)	2 or more	"	0.5	80	Fractures, loss of teeth, underdevelopment of mandibles. Tumor in 1 dog.	Alive at 8 years
	Dog (adult)	1	Sr^{90}	0.25	70	Died 18 days	
		1	"	0.15	50	Acute radiation symdrome, survived more than 3 months	Retention not measured
		3	"	0.01	3	1 suffered fracture, 2 no lesions at 6 years	" " "
30	Dogs (beagles)		"	.025	7.5		Experiment started spring 1954

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Reference	Animal	No. of Animals	Isotope	μc/gm Administered	Estimated Rad/day in Skeleton	Biological Effects	Comments
31	Lambs	4	Sr^{90}	(0.25 retained)	75		Experiment started spring 1954
		4		0.05 "	15		
		4		0.005 "	1.5		
		4		10^{-4} "	0.03		
32	Monkeys	2	Sr^{90}	2.0	1000	Died at 13-56 days, acute radiation syndrome	Chronic toxicity experiments promised. According to Loutit (Feb. '54), little progress.
		4		1.0			
		2		0.5			
33	Goats	14	Sr^{89}	(1-1.5)	150-250	30 day LD50 about 1-1.5 μc/gm injected, 50% retained	
34	Steer	1	Sr^{90}	2×10^{-3}	0.5	Suggestion of hemorrhagic condition under epiphyseal plate several months after active region left behind plate as bone grows.	
35	Mice		Sr^{89}	(3.5 retained)	1200	30 day LD50	
				(2 ")	660	150 " "	
	Rats			(2 ")	"	30 day LD50	
				(1 ")	330	150 " "	
	Rabbits			(0.9 ")	300	30 day LD50	
				(0.85 ")	280	150 " "	
	Mice		"	0.07	12	Reduction in heterophils apparent	
	Rats			0.25	40	" " " "	

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May 25, 1954

Col. R. G. Butler
Ordnance Corps Assistant
Office of the Chief of Ordnance
Department of the Army
Washington 25, D. C.

Reference 00/4C-5470

Dear Col. Butler:

In your letter of March 17 you requested us to review comments of the Army Chemical Corps, Chemical and Radiological Laboratories, on the health and safety aspects of "Benny".

We have prepared some comments, copy attached, according to the topics specified in your letter, and hope they may be of value to you, especially in the light of our earlier discussion with Messrs. J. W. Moseman and J. I. Kistle of your office.

Sincerely yours,

Walter D. Claus, Chief
Biophysics Branch
Division of Biology and Medicine

Enclosure
(cys 1&2A)

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