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Retention of Radioisotopes by Hair, Bone and Vascular Tissue[1,2,3]

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INTRODUCTION

Recent studies have shown that significant amounts of administered iodine-131 (1), selenium-75 (2), strontium-90 (3, 4), and zinc-65 (5-8) accumulate in the hair. Since this appendage contains many inorganic elements, it is desirable to know how well hair reflects concentrations of radioisotopic and stable elements in the body. In the present work retention of vanadium-48 and zinc-65 are contrasted because of the importance of their stable forms to vascular tissue, dissimilarity of body burden, and differences in metabolism. Vanadium, present in the body in microgram quantities (9), is an inhibitor of cholesterol biosynthesis (10-15) and is excreted largely in the urine (16, 17). Zinc, found in the body in amounts nearly equal to iron (9), protects testicular blood vessels from damage by cadmium (18) and is eliminated principally by the pancreas (19). Accordingly, comparative studies have been made of vanadium-48 and zinc-65 retention in hair, bone, aorta, and other tissues using young and old rats of both sexes.

METHODS

Sprague-Dawley rats, maintained on Purina Laboratory Chow with free access to food and water, were used. The radioisotopes were carrier free HCl solutions of $V^{48}OCl_3$ (T/2 = 16 days) and $Zn^{65}Cl_2$ (T/2 = 245 days)[7]. The experiments were conducted over a twenty day period with groups consisting of young and old male and female rats. The young males and females were three to four months old with the former weighing 300-450 gms and the latter 210-300

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[7]The $V^{48}OCl_3$ was obtained from Nuclear Science and Engineering Corporation, Pittsburgh, Pennsylvania, and the $Zn^{65}Cl_2$ from Oak Ridge National Laboratory, Oak Ridge, Tennessee.

gms. The old rats were discarded breeders over one year of age with the males weighing 400-540 gms and the females 280-390 gms. All rats were injected without anesthesia via tail vein with 1 ml of normal saline containing approximately 5 μc of the isotope under study. Four rats from each group were sacrificed on the first, second, fourth, sixth, tenth, and twentieth days post-injection. Tissue and organ samples were weighed fresh and analyzed for vanadium-48 or zinc-65 content in a well-type gamma scintillation counter. All counts were corrected for decay by simultaneously counting aliquots of the injection solutions.

RESULTS

The radioisotope retention data for blood, liver, femur, aorta, and hair are expressed in percent of injection dose per gram. The values for vanadium-48 are given in Table I and in Figure 1 whereas those for zinc-65 are given in Table II and Figure 2.

Blood. The blood data show that vanadium-48 retention declines more rapidly than zinc-65. Radiovanadium uptake is 0.34 per cent per gram of tissue at one day and drops to less than 0.03 per cent by six days, whereas radiozinc retention is 0.24 per cent at one day and reaches 0.05 per cent by twenty days.

Liver. In both studies, liver retention is generally representative of the other visceral organs with zinc-65 retention greater than vanadium-48 in all comparable groups. Radiovanadium uptake is similar in all four groups. Young females are

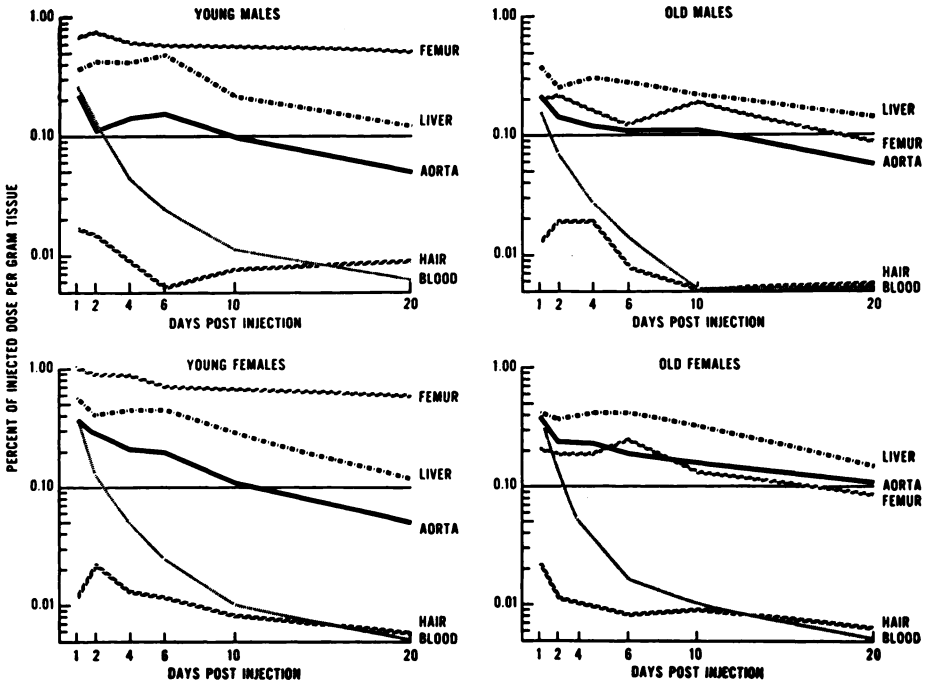

Fig. 1. Vanadium-48 retention values for five tissues in young and old, male and female rats. Hair retention correlates with aorta, bone, and liver, but not with blood. Bone retention is much higher in young than in old rats.

TABLE I

VANADIUM-48 RETENTION IN PERCENT OF INJECTED DOSE PER GRAM TISSUE

	YOUNG FEMALES		*OLD FEMALES*		*YOUNG MALES*		*OLD MALES*	
Organs	*Range*	*Average*	*Range*	*Average*	*Range*	*Average*	*Range*	*Average*
				A. DAY 1				
Blood	0.31—0.36	0.34	0.27—0.34	0.31	0.19—0.31	0.25	0.10—0.21	0.17
Liver	0.53—0.61	0.57	0.22—0.50	0.42	0.27—0.44	0.37	0.34—0.45	0.38
Femur	0.77—1.24	1.04	0.17—0.27	0.21	0.62—0.79	0.68	0.12—0.36	0.20
Aorta	0.24—0.46	0.37	0.29—0.53	0.39	0.12—0.32	0.22	0.17—0.30	0.21
Hair	0.009–0.015	0.012	0.010–0.046	0.022	0.004–0.032	0.017	0.007–0.026	0.013
				B. DAY 2				
Blood	0.12—0.15	0.13	0.11—0.17	0.13	0.088–0.18	0.12	0.059–0.079	0.070
Liver	0.36—0.48	0.41	0.30—0.41	0.37	0.35—0.49	0.43	0.22—0.30	0.25
Femur	0.86—1.00	0.92	0.16—0.21	0.19	0.74—0.80	0.77	0.15—0.25	0.22
Aorta	0.32—0.40	0.35	0.20—0.28	0.24	0.10—0.12	0.11	0.11—0.19	0.14
Hair	0.008–0.031	0.022	0.009–0.012	0.011	0.015–0.017	0.015	0.008–0.028	0.015
				C. DAY 4				
Blood	0.043–0.051	0.048	0.043–0.059	0.053	0.037–0.050	0.046	0.024–0.031	0.027
Liver	0.38—0.51	0.46	0.34—0.48	0.42	0.34—0.47	0.41	0.26—0.32	0.30
Femur	0.86—0.97	0.90	0.15—0.24	0.19	0.53—0.81	0.71	0.12—0.20	0.16
Aorta	0.13—0.27	0.21	0.13—0.37	0.23	0.11—0.20	0.14	0.10—0.14	0.12
Hair	0.005–0.022	0.013	0.009–0.011	0.010	0.003–0.014	0.009	0.014–0.023	0.019

TABLE I *(con't)*

Organs	*YOUNG FEMALES*		*OLD FEMALES*		*YOUNG MALES*		*OLD MALES*	
	Range	*Average*	*Range*	*Average*	*Range*	*Average*	*Range*	*Average*
				D. DAY 6				
Blood	0.020–0.028	0.025	0.012–0.024	0.017	0.018–0.031	0.025	0.008–0.018	0.013
Liver	0.31—0.59	0.46	0.38—0.45	0.42	0.29—0.61	0.48	0.21—0.36	0.28
Femur	0.55—0.88	0.72	0.19—0.30	0.25	0.43—0.69	0.58	0.10—0.13	0.12
Aorta	0.13—0.24	0.20	0.12—0.26	0.19	0.10—0.23	0.15	0.07—0.14	0.11
Hair	0.006–0.017	0.012	0.005–0.011	0.008	0.003–0.007	0.005	0.003–0.011	0.008
				E. DAY 10				
Blood	0.010–0.011	0.010	0.006–0.014	0.010	0.011–0.012	0.012	0.003–0.007	0.005
Liver	0.26—0.31	0.28	0.27—0.40	0.32	0.16—0.26	0.21	0.16—0.26	0.22
Femur	0.65—0.78	0.69	0.11—0.14	0.13	0.40—0.64	0.56	0.07—0.47	0.19
Aorta	0.10—0.13	0.11	0.12—0.18	0.16	0.07—0.13	0.10	0.07—0.18	0.11
Hair	0.004–0.016	0.008	0.005–0.013	0.009	0.007–0.009	0.009	0.003–0.006	0.005
				F. DAY 20				
Blood	0.002–0.006	0.004	0.003–0.005	0.004	0.005–0.007	0.006	0.000–0.003	0.002
Liver	0.09—0.14	0.12	0.12—0.19	0.15	0.10—0.13	0.12	0.11—0.17	0.14
Femur	0.51—0.72	0.58	0.05—0.15	0.09	0.43—0.58	0.51	0.08—0.09	0.08
Aorta	0.03—0.06	0.05	0.09—0.12	0.11	0.03—0.06	0.05	0.03—0.07	0.06
Hair	0.004–0.008	0.006	0.002–0.011	0.006	0.004–0.017	0.009	0.004–0.009	0.006

higher initially with retention gradually decreasing from an initial median value of 0.57 to 0.12 per cent by day twenty. Radiozinc retention by liver falls from a one day high of 2.5-3.5 per cent to a twenty day level of 0.1-0.4 per cent.

Femur. The effects of age and sex are particularly prominent in femur retention values. Vanadium-48 accumulation patterns for young males and females are almost identical, varying between 1.0 and 0.6 per cent retention during the study period. Old males and females are also similar to each other but have much less retention than the young rats. Femur uptake in young rats is significantly higher than any other organ examined except the kidney, the major route of vanadium excretion. In all groups other than old females, peak femur radiozinc uptake occurs within the first two days, and thereafter declines.

Aorta. Since previous radioisotopic retention studies have not included examination of vascular tissue, it is noteworthy that the aorta accumulates significant amounts of both vanadium-48 and zinc-65. Aortic tissue shows an initial rapid fall of radiovanadium content within two days post-injection, and then a more gradual decline paralleling the liver curve. Female rats have a higher initial vanadium-48 uptake by the aorta than males, and old females retain much more in the aorta than any of the other three groups. Aortic retention of zinc-65 is similar in all four groups and shows greater radioactivity at twenty days than the visceral organs, liver and pancreas. Age has a definite influence on radiozinc retention by the aorta since young rats show a maximum buildup at two days, and old rats at four days.

Hair. Hair retention patterns for both elements are strikingly different. Although the initial zinc-65 uptake is lower than vanadium-48, by twenty days the radiozinc activity is 20-100 times greater than the radiovanadium in the hair. Thus, while the radiovanadium content of hair shows a gradual decline similar to the visceral organs, radiozinc continues to accumulate in the hair with time. The most noticeable difference in vanadium-48 retention is the prolonged four day uptake phase in old males versus the shorter one to two day peaks in the other groups. The maximum radiozinc uptake occurs earlier in the old females than in the other rats, and females show higher retention than males of the same age. After ten days, young rats develop a plateau of radiozinc retention, whereas old rats show a continued buildup.

DISCUSSION

The results of studies on vanadium-48 retention indicate that hair radioactivity correlates with that of aorta, femur, and liver, but not with blood. This correlation and the accessibility of hair suggest the use of this appendage as an indicator of the stable vanadium content of these tissues. Because vanadium inhibits cholesterol biosynthesis, a way of estimating aortic vanadium levels, even though indirect, is important experimentally and clinically. Retention variations associated with age and sex cannot be completely interpreted until stable vanadium concentrations are known. This is extremely difficult because of the very low levels of vanadium in body tissues, but spectrographic analyses show that rat hair contains 30-50 parts per billion of the element.[1]

[1]The spectrographic analyses were performed by National Spectrographic Laboratories, Inc., 6300 Euclid Ave., Cleveland 3, Ohio.

There is good qualitative agreement among the data of the present study and of previous investigations of radiovanadium retention in experimental animals. Scott *et al.* (20) found that pentavalent radiovanadium was retained principally by the skeleton, testes, kidney, liver and muscle of rats, decreasing in the order given. Söremark and associates (21, 22) after injecting $V_2{}^{48}O_5$ in mice found by autoradiographic and retention studies that bone and dentine retain the largest content of the radioisotope.

Recent work has shown that increasing the dietary vanadium intake of experimental animals reduces cholesterol aortic deposition (23), lowers the blood cholesterol level (24), and reduces the predeposited cholesterol content (25). Lewis (26, 27), investigating industrial workers exposed to vanadium, concluded that their blood cholesterol values were significantly lower than suitable controls. Metabolic studies by Curran *et al.* (28) with normocholesterolemic medical students given 125-150 mg daily of diammonium tartarovanadate, similarly showed blood cholesterol reduction without development of toxic effects. Variant clinical results have been obtained by Sommerville and Davies (29) and by Dimond *et al.* (30) with reputedly the same preparation. Strain (31) pointed out in 1961 that the drinking water in New Mexico, the State with the lowest death rate

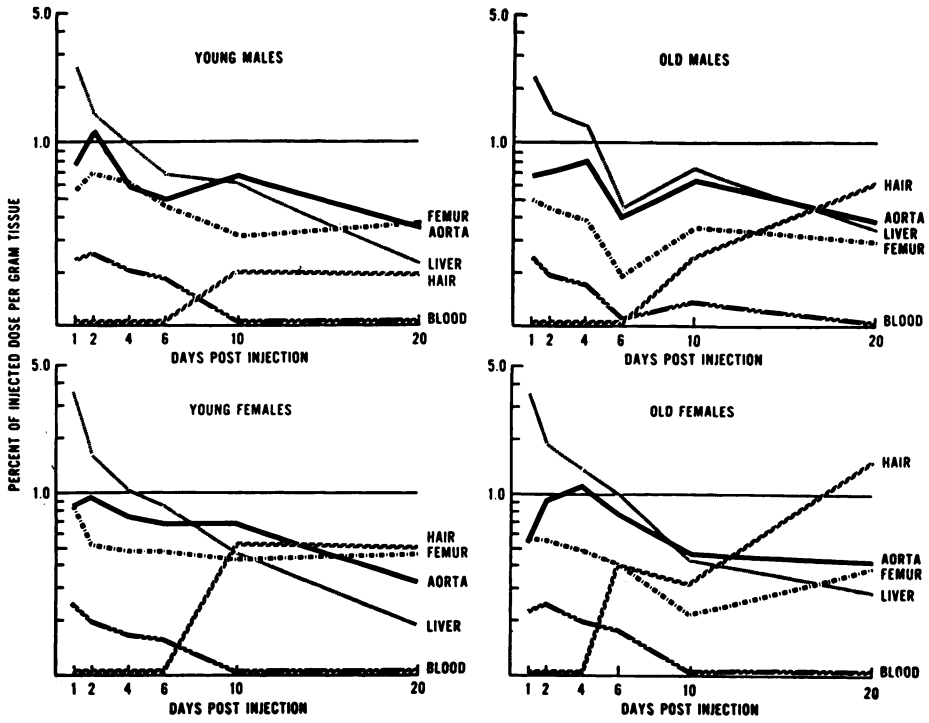

Fig. 2. Zinc-65 retention values for five tissues in young and old, male and female rats. The aortic retention exceeds that of all tissues, except in old males, at ten days and is greater than the liver in all groups at twenty days. Hair retention increases with time and correlates only with bone retention.

TABLE II

ZINC-65 RETENTION IN PERCENT OF INJECTED DOSE PER GRAM TISSUE

	YOUNG FEMALES		*OLD FEMALES*		*YOUNG MALES*		*OLD MALES*	
Organs	*Range*	*Average*	*Range*	*Average*	*Range*	*Average*	*Range*	*Average*
				A. DAY 1				
Blood	0.24–0.27	0.25	0.20–0.25	0.23	0.22–0.23	0.23	0.22–0.25	0.24
Liver	3.15–3.94	3.60	2.72–4.45	3.59	2.34–2.87	2.56	2.16–2.49	2.31
Femur	0.53–0.74	0.65	0.43–0.67	0.54	0.45–0.55	0.51	0.42–0.47	0.44
Aorta	0.62–1.10	0.84	0.41–0.70	0.56	0.66–0.89	0.76	0.44–0.86	0.67
Hair	0.01–0.01	0.01	0.00–0.02	0.01	0.00–0.01	0.01	0.00–0.01	0.01
				B. DAY 2				
Blood	0.19–0.21	0.20	0.23–0.28	0.25	0.17–0.19	0.18	0.19–0.20	0.19
Liver	1.54–1.75	1.63	1.73–2.12	1.90	1.24–1.55	1.42	1.44–1.49	1.46
Femur	0.41–0.54	0.48	0.42–0.55	0.48	0.57–0.66	0.62	0.32–0.40	0.38
Aorta	0.90–1.01	0.96	0.76–1.14	0.94	0.89–1.31	1.14	0.52–0.80	0.70
Hair	0.01–0.02	0.02	0.01–0.09	0.04	0.00–0.01	0.01	0.00–0.01	0.01
				C. DAY 4				
Blood	0.15–0.18	0.17	0.18–0.21	0.20	0.13–0.15	0.14	0.16–0.17	0.17
Liver	0.85–1.17	1.01	1.31–1.52	1.39	0.94–1.01	0.97	1.11–1.37	1.23
Femur	0.28–0.42	0.35	0.37–0.43	0.40	0.44–0.59	0.52	0.23–0.39	0.32
Aorta	0.65–0.93	0.76	0.85–1.32	1.11	0.45–0.71	0.57	0.71–0.93	0.80
Hair	0.01	0.05	0.01–0.02	0.02	0.01–0.07	0.03	0.03–0.06	0.04

TABLE II *(con't)*

Organs	YOUNG FEMALES		OLD FEMALES		YOUNG MALES		OLD MALES	
	Range	*Average*	*Range*	*Average*	*Range*	*Average*	*Range*	*Average*
				D. DAY 6				
Blood	0.15–0.16	0.16	0.15–0.19	0.18	0.11–0.17	0.14	0.10–0.11	0.11
Liver	0.86–0.91	0.88	0.77–1.21	1.01	0.52–0.99	0.66	0.37–0.51	0.44
Femur	0.33–0.62	0.41	0.26–0.41	0.33	0.32–0.48	0.41	0.13–0.19	0.16
Aorta	0.59–0.85	0.69	0.61–0.90	0.79	0.41–0.63	0.49	0.34–0.45	0.40
Hair	0.01–0.11	0.06	0.04–0.76	0.41	0.00–0.10	0.05	0.03–0.05	0.04
				E. DAY 10				
Blood	0.10–0.10	0.10	0.07–0.09	0.08	0.08–0.11	0.10	0.11–0.16	0.14
Liver	0.44–0.50	0.48	0.41–0.48	0.44	0.33–0.77	0.61	0.62–0.88	0.75
Femur	0.28–0.37	0.33	0.10–0.18	0.15	0.09–0.36	0.26	0.24–0.38	0.30
Aorta	0.54–0.81	0.69	0.40–0.55	0.48	0.36–0.81	0.66	0.57–0.71	0.63
Hair	0.43–0.63	0.56	0.10–0.74	0.32	0.08–0.35	0.20	0.07–0.35	0.24
				F. DAY 20				
Blood	0.04–0.08	0.06	0.07–0.08	0.08	0.05–0.07	0.06	0.08–0.08	0.08
Liver	0.15–0.23	0.19	0.27–0.31	0.29	0.18–0.34	0.22	0.27–0.37	0.34
Femur	0.22–0.72	0.50	0.19–0.41	0.32	0.18–0.45	0.32	0.16–0.29	0.21
Aorta	0.21–0.49	0.33	0.31–0.56	0.43	0.17–0.53	0.35	0.29–0.44	0.03
Hair	0.50–0.50	0.50	0.21–2.84	1.41	0.07–0.37	0.19	0.03–1.49	0.61

from cardiovascular disease in the United States (32), contains up to 70 parts per billion (ppb) of vanadium. He suggested this may contribute to the low death rate. Other reports (33, 34) supporting the presence of vanadium in New Mexican drinking water show a range of 20 to 150 ppb in the water.

Zinc-65 retention studies indicate that hair radioactivity correlates to some degree with that of femur but not with aorta, blood and liver. The work of Gilbert and Taylor (5) and of Ballou and Thompson (6) in similar experiments with rats, using a single injection of zinc-65, showed that only femur and hair continued to retain significant radioactivity for more than 250 and 300 days, respectively. In chronic zinc-65 feeding experiments (6) the buildup of activity occurred principally in hair and femur. At 407 days, the hair activity was roughly twice that of the femur, 27 versus 12 percent of the daily dose. This unique 2:1 relationship for hair:bone zinc content is also seen in stable zinc tissue analyses of pigs grown on different levels of supplemental zinc (35). Since it appears that both stable and radioisotopic zinc levels of hair reflect bone zinc concentrations, and soft tissue content of zinc-65 correlates well with blood levels, both hair and blood analyses might serve as indicators of the various zinc metabolic pools.

In recent years there has been a very active interest in zinc metabolism with special attention to calcium/zinc and cadmium/zinc antagonisms. In food animals, an important determinant of growth and feed efficiency is the dietary level and availability of zinc. Calcium is antagonistic to zinc and the proper calcium/zinc ratio is needed for maximum growth (35, 36). Parizek (18) and others (37, 38) have shown that cadmium administration produces permanent sterility in rats and other species with external testes. Coincident zinc administration protects the testes from cadmium damage which includes tubular epithelial degeneration, lowered sperm count, gross testicular atrophy, small vessel thrombosis, and hemorrhage. Thus, animal studies indicate that zinc is an important factor for growth, testicular viability, and vascular tissue integrity. Prasad *et al.* (39-41) have recently described a zinc deficiency syndrome in man presenting with dwarfism, hypogonadism, and lack of secondary sex characteristics. This condition is apparently completely alleviated by the administration of zinc.

The biological mechanisms by which various radionuclides are incorporated in hair evidently differ. Ryder (42) has shown that rats and mice injected with copper-64 did not localize the isotope in the follicle. It is known from the work of Leblond (43) that iodine is present in the hair as inorganic iodine, and presumably radioiodine is inorganic also. Selenium-75 is present largely in the cystine fraction, but there is no information on the form of strontium-90 and zinc-65 in hair. There is no doubt other isotopes accumulate in this appendage, and the uptake may be determined by a variety of factors.

SUMMARY

Comparative studies have been made on the retention of intravenously administered vanadium-48 and zinc-65 by blood, liver, femur, hair, and aorta in young and old rats of both sexes over a period of twenty days. Although it is extremely low, the vanadium-48 hair retention pattern generally reflects the ac-

cumulation of the radioisotope by the other tissues examined, except blood. Zinc-65 retention in hair continues to build up with the passage of time and appears to correlate only with the femur radioactivity. Age and sex are shown to be important variables in the retention of the two isotopes.

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