STUDIES ON THE METABOLISM OF INHALED AEROSOLS OF STRONTIUM AND LANTHANUM

Research and Development Technical Report USNRDL-TR-175
NM 006-015
FCDA

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U.S. NAVAL RADIOLOGICAL DEFENSE LABORATORY

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Biology and Medicine

Technical Objective
AW-6

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ABSTRACT

The problem of determining the relative importance of the G.I. tract and the respiratory system as portals of entry of aerosols into the systemic circulation following inhalation exposure was studied by obtaining data on the kinetics of uptake and retention of various inhaled and ingested fission product aerosols.

Exposure of mice to a $Sr^{85}Cl_2$-dry particle aerosol indicated that the ratio of G.I. tract/respiratory system activity was 100 immediately after exposure. Administration of aqueous suspensions of the same material by stomach tube indicated that the amount of Sr^{85} deposited in the skeleton was a considerable fraction of that found in the skeleton following an inhalation exposure, thus emphasizing the importance of the G.I. tract as a portal of entry.

The high concentration of activity in the G.I. tract resulted in an initial dose rate to the small intestine many-fold that received by the respiratory system. The integrated dose received by the large intestine over the 28-day period was twice that received by the respiratory system, stomach or small intestine. The total dose received by the skeleton during the experimental period was 10-fold that received by any other organ.

The importance of the aerosol carrier material was emphasized by the finding that absorption of Sr into the body was 2 to 3 times greater following the liquid aerosol than following the dry particle aerosol.

The finding, that the G.I. tract can serve as an important portal of entry for soluble fission product aerosols following an inhalation exposure, implies that an evaluation of the internal hazard associated with exposure to radioactive fallout must take into account those parameters which influence the transport of particles across the G.I. membrane as well as the more commonly considered factors which determine transport across the alveolar tissue.

SUMMARY

The Problem

The assessment of the radiation hazard resulting from the inhalation of fallout from nuclear detonation requires knowledge of the metabolism of various types of fission-product aerosols. The kinetics of the uptake, distribution and retention in mice of two fission-product aerosols, strontium (highly soluble) and lanthanum (insoluble), were studied. Aerosols of $Sr^{85}Cl_2$ and $La^{140}Cl_3$ were generated both as liquid droplets and adsorbed on kaolin particles. In addition, aqueous suspensions of these aerosols were administered to mice by stomach tube.

Findings

It was found that the gastrointestinal tract can serve as an important portal of entry into the body for soluble fission-product aerosols following an inhalation exposure. This finding implies that an evaluation of the internal hazard associated with an inhalation exposure to radioactive fallout must take into account those factors which influence transport across the gastrointestinal membrane as well as the more commonly considered factors which determine transport across the alveolar tissue.

ADMINISTRATIVE INFORMATION

This work was done as a part of Bureau of Medicine and Surgery Project Number NM 006-015.04, Phase 1, Technical Objective AW-6, as described in the U.S. Naval Radiological Defense Laboratory Research Progress Report to the Bureau of Medicine and Surgery, NAVMED 1343, of 31 December 1956.

This study was also a Federal Civil Defense Administration project, described in part A of this laboratory's "Progress Report to Federal Civil Defense Administration — Biomedical Research" for the period 1 January to 30 June 1957, USNRDL-P-3, dated August 1957.

INTRODUCTION

The general problem of determining the degree of internal hazard to a biological organism resulting from inhalation of radioactive fallout is so complex that it can be treated only by breaking the problem down into simpler and more easily analyzed aspects. The complexity of the problem derives from the large number of factors which influence the uptake, retention and elimination of radioactive particles by a biological system.[1-4]

Determination of the radiotoxicity of inhaled materials can readily be separated into two aspects: the nature of the aerosol itself, and the reaction of the biological organism to the particular aerosol. In the production of fallout, the radioactive particles become attached to a carrier material. The physical and chemical characterization of the aerosol, therefore, includes not only determination of the chemical form of the fission product itself but also the physical and chemical nature of the carrier with which it is associated. The nature of the carrier material and its physical association with the radioactive isotope influences the metabolism of the inhaled aerosol.

The reaction of the organism to the radioactive aerosol can be considered in terms of (1) the routes of entry into the body (respiratory system and/or G.I. tract); (2) the uptake and distribution of the particles in the body; (3) their retention and eventual clearance. It is obvious that the biological reaction is greatly dependent on the characteristics of the particular aerosol to which the organism is exposed. Further, the reaction of the organism is not a simple fixed process but varies considerably with the physiological state of the organism.

The radiotoxicity of inhaled radioactive fallout has been studied in terms of the metabolism of specially prepared simulants of fallout.[5,6] The rate of uptake, the distribution in the body tissues, and the ultimate fate of particles which gained entry into the body were measured. During the course of these experiments it was observed that following an inhalation

exposure, a large amount of material appeared in the G.I. tract. As the phenomenon would not be predicted from the conditions of the experiment and, further, has interesting implications concerning the route of entry of radioactive material into the body, it was felt that this aspect of the problem merited further attention.

The present study attempts to obtain data on the relative importance of the G.I. tract and the respiratory system as portals of entry into the systemic circulation for particulate material following an inhalation exposure.

EXPERIMENTAL

Two prototype fission products were selected for this experiment, representing two extremes of solubility and thus indicating the probable range of response to this important characteristic of an aerosol. The fission products selected were the highly soluble $SrCl_2$ and the very insoluble $LaCl_3$. In addition to the use of the two fission products, two different types of carrier material were selected: a biologically inert kaolin clay particle, and sea water administered in the form of a liquid aerosol.

Each of three groups of 48 mice were exposed for 3 hours to one of three radioactive aerosols. The aerosols were (1) a dry particle aerosol consisting of kaolin particles with $Sr^{85}Cl_2$ adsorbed on the surface; (2) a dry particle aerosol consisting of clay particles with $La^{140}Cl_3$ adsorbed on the surface; and (3) a liquid aerosol of $Sr^{85}Cl_2$ in sea water. In addition, the two dry particle aerosols of $Sr^{85}Cl_2$ and $La^{140}Cl_3$ were suspended in H_2O and administered to two groups of 24 mice by stomach tube. An ionic solution of $Sr^{85}Cl_2$ was also given to 24 mice by stomach tube.

The animals were sacrificed in groups of six, at intervals up to 28 days starting at 0.5 hours after exposure. The distribution of gamma activity of the Sr^{85} and La^{140} was determined for the respiratory tract (starting at the larynx) and lungs, and for the liver, tibia, head and G.I tract and contents (from the top of the oesophagus to the anus). The skin was first removed from the animals, and the autopsies were carried out

with care in order to avoid cross contamination. The tissue gamma activity was measured in a sodium-iodide crystal scintillation counter.

A diagram of the flow system for the experimental apparatus for exposing the animals to the various aerosols is shown in Fig. 1. The equipment consisted of: (1) an aerosol generator, (2) the animal exposure chamber, (3) millipore filter sample collectors (for determining size and concentration of the particle), and (4) supporting equipment (flow meters, pressure controls, pump, filters, etc.). The animal exposure chamber and the method of exposing mice to the radioactive aerosol is illustrated in Fig. 2. The mice are positioned in such a manner as to maximize inhalation and to minimize the possibility of ingestion of the aerosol by the mice.

Aerosol Preparation

The dry particle aerosols were prepared by adding Sr or La chlorides to suspensions of previously prepared particles. These particles were of kaolin of less than 5 μ in diameter. The particles and fission products were evaporated to dryness in a ball mill. The particles were ground to fineness and placed in the elutriator, as described below. The aerosol to which the animals were exposed consisted of particles having a maximum diameter of 10 μ. About 60 percent of the particles had a diameter in the range of 1 to 3 μ. The Sr and La were adsorbed on the surface of the particles.

The ionic $SrCl_2$ aerosol was prepared by dissolving $Sr^{85}Cl_2$ in sea water and aspirating it as a liquid aerosol. The mean particle diameter was 1.8 μ. This method of generating the liquid aerosol and measuring its size was previously described.[5,7]

Aerosol Generation

The animal inhalation apparatus consisted of a Roller particle-size analyzer coupled to the mouse exposure chamber. The Roller apparatus analyzes a powder sample by successively removing and collecting larger particle-size fractions of the powder by air elutriation.[8] A study of the operating characteristics of the Roller particle-size analyzer has shown that for small particle sizes the rate of separation of material during the first three hours of operation remains relatively constant.[9,10,11] Thus, the Roller separator is a suitable instrument for use as an aerosol generator in animal inhalation studies.

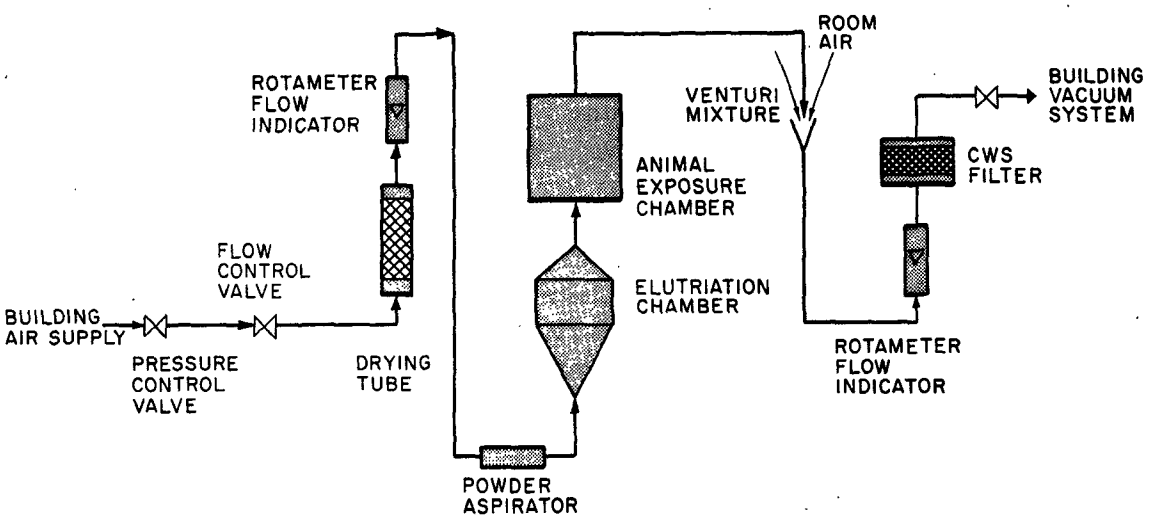

Fig. 1 Flow System for Animal Inhalation Apparatus.

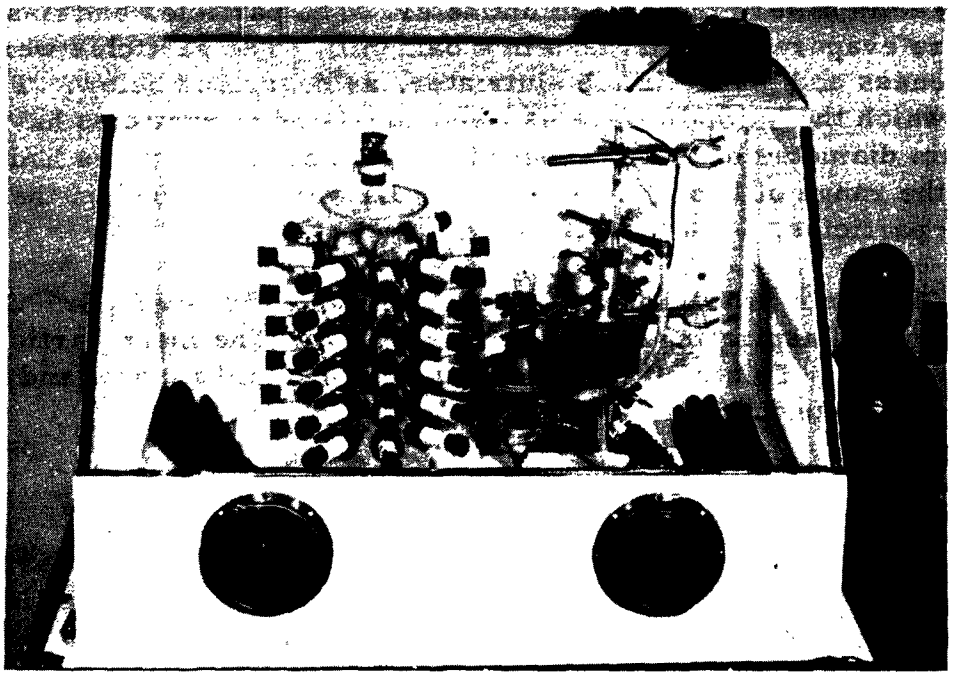

Fig. 2 Mouse Inhalation Chamber, Showing Method of Exposing Mice to Radioactive Aerosol.

Building service compressed air was dried and the pressure and flow suitably controlled. This air was then introduced into the Roller separator. The powder sample was placed in a U-shaped glass tube and the powder was suspended in the air stream by agitation of the tube with a mechanical tapper. The particle-laden air stream then entered the separating chamber. This chamber is designed in such a way that only those particles with a given maximum terminal velocity are carried over into the animal exposure chamber. This terminal velocity is determined by the linear velocity of the air through the settling chamber. Those particles having lower terminal velocities are returned to the inlet tube, and a mechanical tapper minimizes the tendency of the small particles to cling to the wall of the separating chamber. The animal exposure chamber is mounted directly over the separating chamber outlet. The generator provided a stream of airborne dry particles at a constant size and concentration level (0.21 μc/l). The animal chamber is exhausted through a venturi mixer through which outside room air is also drawn, and then through a CWS filter to remove the radioactive particles. The laboratory vacuum system serves as the exhaust for the filtered air stream. The entire system is mounted inside enclosures which are maintained at a pressure slightly below room pressure during operation. The safety precautions described are necessary to reduce to a minimum possible hazard to laboratory personnel.

RESULTS AND DISCUSSIONS

Analysis of the distribution of Sr^{85} in mice exposed to the dry particle $Sr^{85}Cl_2$ aerosol for 3 hours revealed that at 0.5 hours after exposure the activity of the G.I. tract and its contents was over 80 percent of the total activity in the mice. The distribution of Sr^{85} in the animal tissues (expressed as a percentage of the initial activity of the G.I. tract and its contents), is shown in Fig. 3A. The activity in the G.I. tract was almost 100 times that found in the lungs at this time. The large amount of Sr in the G.I. tract presumably resulted from the rapid clearance of the aerosol from the tracheo-bronchial tree and the naso-pharyngeal region of the animal, and its subsequent ingestion.

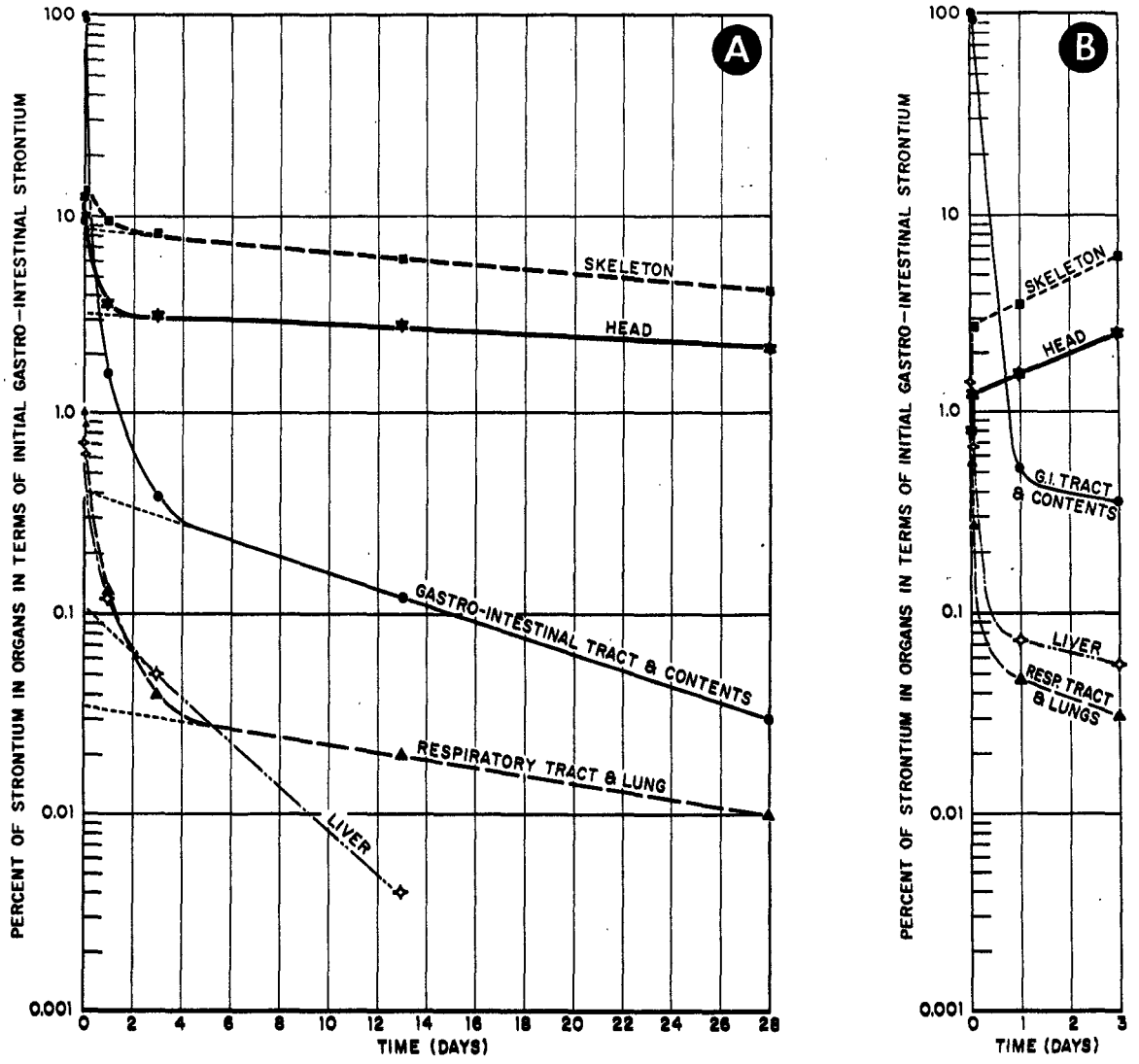

Fig. 3 Uptake and Retention of Strontium in Mice Following:
A Exposure to Dry Particle Aerosol
B Administration of Suspension of Dry Particle Aerosol by Gavage.

The activity in the head was 13 percent of that in the G.I. tract at 0.5 hours after exposure. About 80 percent of the Sr in the head appears to be associated with aerosol particles trapped in the naso-pharyngeal region. (This apparatus appears to have a high filtering efficiency in the mouse.) The remainder (20 percent) of the Sr in the head is fixed in the bones of the skull.

Similar $Sr^{85}Cl_2$ dry particles were suspended in water and administered by stomach tube. The amount present in the G.I. tract at 0.5 hour was used as the basis of comparison (Fig. 3B). The Sr in the respiratory tract was 0.6 percent of that found in the G.I. tract at this time. It is interesting to note (in terms of the G.I. tract activity at 0.5 hour) that about half the amount of activity in the respiratory tract found after inhalation was present after gavage. This indicates that approximately half the material in the lung is derived from alveolar exchange with the circulation. The rate of clearance of material from the G.I. tract, liver, and respiratory system was similar following inhalation exposure and gavage (Fig. 3). Following gavage, however, the activity in the head and skeleton continued to increase for the first few days, and by the third day this activity had reached 80 percent of the value observed following the inhalation exposure. The activity in the liver after 2 hours was approximately the same following gavage or inhalation exposure. These findings suggest that under the conditions of this experiment, a considerable fraction of the activity deposited in the skeletal tissue and liver after inhalation may have been transported across the membranes of the G.I. tract.

As a means of investigating further the role of G.I. absorption following an inhalation exposure, the oesophagi of a group of mice were ligated and severed, and these mice along with a group of controls were subjected to an inhalation exposure in the manner previously described. Half of the control animals underwent a sham operation prior to exposure to indicate the effects of the surgical operation itself on the animals. At 20 hours following exposure, the amount of internally deposited Sr in the skeleton and liver of the experimental animals was approximately 35 percent of that found in the controls (normal and sham-operated, Table 1). The activity in the stomach and the small and large intestines in the oesophagus-ligated animals gives an indication of the endogenous excretion of absorbed activity. While the effect of closing off one portal of entry appears to be that of lowering the internal deposition to approximately one-third, it must be borne in mind that the results here are

TABLE 1

Effect of Ligating the Oesophagus on the Tissue Distribution of an Inhaled $Sr^{85}Cl_2$ Aerosol

Tissue	Gamma Activity (c/m) at 20 Hours Following Exposure		
	Controls (6 mice)	Sham-operated Controls (6 mice)	Ligated Oesophagus (8 mice)
Skeleton	18,800	21,300	8,150
Liver	838	879	261
Head	9,246	10,722	5,272
Trachea	63	65	44
Alveolar Tissue	339	867	715
Oesophagus (above ligation)	20	17	149
Stomach and Contents	591	1,589	517
Small Intest. and Contents	1,861	2,148	616
Large Intest. and Contents	12,474	5,169	1,663
Total G.I. Tract Contents	14,926	8,906	2,796

only indicative. The respiratory rate of the animals, which influences the metabolism and therefore the uptake of the radioactive material, was probably altered by the operation, but since it was not measured in the experiment, an evaluation of the effect of this factor on the internal deposition is not possible.

The influence of a soluble carrier (sea water) on $SrCl_2$ generated as a liquid aerosol as compared with a biologically inert carrier administered as a dry particle was also studied. The ratio of activity in the G.I. tract as compared to that in the lung was approximately 50:1 for the liquid aerosol as compared to 100:1 for the dry particle aerosol at 0.5 hour after exposure (Table 2). Thus, it appears that the higher solubility of the carrier, the manner of association of $SrCl_2$ with the carrier, or the administration of the aerosol in liquid form enabled more material to be absorbed and transported to the circulation and ultimately to be deposited in the bone. About three times as much Sr appears in the skeleton during the 28-day experimental period after exposure to the liquid aerosol as was observed following inhalation of the dry particle aerosol (Table 2).

The ionic solution of $Sr^{85}Cl_2$ and the suspension of $Sr^{85}Cl_2$ dry particles were also administered by gavage as well as by inhalation. The tissue distribution of Sr when administered by the two methods is shown in Table 3. Again it was found that the ionic solution of $SrCl_2$ was absorbed and retained by the tissue to a greater extent than the dry particle $SrCl_2$. About twice as much Sr administered in ionic solution was found in the skeleton as after the exposure to the dry particle suspension. The liver content was not significantly different after 2 hours following administration.

Finally, a study was made of the uptake and distribution of the very insoluble La absorbed on the surface of an insoluble dry clay particle to determine the extent to which such a particle can penetrate to the internal tissues. The $La^{140}Cl_3$ was administered both by inhalation and gavage. The ratio of activity in the G.I. tract and its contents to that of the lungs and respiratory tract was about 75 at 1 hour after inhalation exposure (Table 4). At this time the liver had about 0.1 percent of the activity in the G.I. tract, and the skeleton, about 0.6 percent. The head retains 5.8 percent of the G.I. activity at this time, consisting almost entirely of activity from material trapped in the naso-pharyngeal region.

TABLE 2
Tissue Distribution of Sr^{85} Following Exposure to
Dry Particle and Liquid Aerosols

Tissue	Time After Inhalation Exposure									
	0.5 hr		24 hr		3d		13d		28d	
	DP(a)	L(a)	DP	L	DP	L	DP	L	DP	L
Resp. Tract and Lungs	1.0(b)	1.0(b)	0.13	0.078	0.04	0.050	0.02	0.032	0.01	0.032
G.I. Tract and Contents	100	56	1.6	-	0.38	0.29	0.12	-	0.03	-
Skeleton	9.2	27	9.5	23	8.1	21	6.1	-	4.3	12
Head	12.2	14	3.7	8.3	3.1	7.2	2.8	-	2.1	4.2
Liver	0.70	0.95	0.12	0.046	0.05	0.026	0.004	-	0	0

(a) DP - Dry Particle Aerosol with $SrCl_2$ adsorbed.
L - Liquid aerosol containing $SrCl_2$ in sea water.

(b) Activity of the respiratory tract and lungs is expressed as 1. All other values are expressed in terms of this value.

TABLE 3

Distribution of Sr^{85} in Tissues Following Gavage of $Sr^{85}Cl_2$ in Solution and Adsorbed on Dry Particles

Tissue	Time after Gavage							
	0.5 hr		2 hr		24 hr		3 d	
	L(a)	DP(a)	L	DP	L	DP	L	DP
G.I. Tract and contents	100(b)	100(b)	95	94	1.3	0.51	-	0.35
Head	1.9	0.76	2.0	1.2	2.5	1.5	-	2.5
Skeleton	1.1	0.74	4.4	2.7	7.8	3.5	-	6.2
Respiratory Tract and Lungs	0.24	0.57	0.12	0.27	0.025	0.045	-	0.031
Liver	3.0	1.4	0.53	0.66	0.068	0.074	-	0.057

(a) L = $Sr^{85}Cl_2$ solution.

DP = $Sr^{85}Cl_2$ adsorbed on dry particles.

(b) Activity of G.I. tract and contents is expressed as 100. All other values are expressed in percent of this value.

TABLE 4

Distribution of La^{140} in the Tissues of Mice Following Inhalation and Gavage of a Dry Particle Aerosol Containing $La^{140}Cl_3$

Tissue	Time After Inhalation Exposure or Gavage						
	1 hr		3 hr	24 hr		3 d	
	I[a]	G[a]	I	I	G	I	G
G.I. Tract and Contents	100[b]	100[b]	87	58	0.28	3.8	0.02
Head	5.8	-	1.8	0.89	-	0.34	-
Skeleton	0.65	0.011	0.30	-	-	-	-
Resp. Tract and Lungs	1.34	0.00001	0.71	0.58	-	0.44	-
Liver	0.13	0.004	-	0.10	0.003	0.12	0.004

(a) I = Inhalation of $La^{140}Cl_3$ adsorbed on dry particles.
G = Gavage administration of above particles.

(b) Activity of gastro-intestinal tract and contents is expressed as 100. All other values are expressed in percent of this activity.

Following ingestion, barely detectable levels of activity were present in the liver and skeleton (0.004 and 0.011 percent) of the activity in the G.I. tract. The La on the dry particle appears to enter the body almost completely through the alveolar membranes. It is probable that because of its insoluble nature the $LaCl_3$ cannot be absorbed through the G.I. membrane. The larger amounts which are able to penetrate the alveolar tissue are probably transported as particles by macrophages and subsequently leached from the particles into body fluids.

Thus it appears that only with soluble fission products is the G.I. route of entry of importance.

Analysis of Biological Decay Curves

Studies made of the activity of the various tissues of the animals after inhalation exposure or administration of radioactive material by gavage were carried out over a period of 28 days in order to provide data on the effect of the route of entry on the rates of clearance from the individual tissues and on the doses received by these tissues. Following exposure to the dry-particle aerosol, the gamma activity of each tissue was determined at fixed intervals and was corrected for radioactive decay. Thus, the curve of the biological decay of Sr in each tissue was determined.

The curves were analyzed mathematically, and it was found that in most cases a simple sum of two exponentials was sufficient to characterize the decay curve over the 28-day period studied. The equations took the form

$$A_t = K_1 e^{-\lambda_1 t} + K_2 e^{-\lambda_2 t}.$$

The constants determined for the various curves previously illustrated in Fig. 3A are summarized in Table 5.

The activity of the G.I. tract and its contents decreased the most rapidly, as would be expected from the system with the natural excretory function (Table 5). The initial component of biological loss of Sr from the stomach (λ_1 = 6.06/day) and small intestine (λ_1 = 9.09/day) probably corresponds to the rapid loss of material by excretion. The second component (λ_2 = 0.128/day and 0.133/day) probably reflects the appearance of lung "fixed" activity and the excretion of material deposited in internal tissues.

TABLE 5

Biological Decay Constants for Sr^{85} in Organs of Mice Following Exposure to the Dry Particle Aerosol

Organ	K_1 c/m x 10^{-4}	K_2 c/m x 10^{-3}	λ_1 $days^{-1}$	λ_2 $days^{-1}$
Stomach	2.3	0.26	6.06	0.133
Small Intestine	27.0	0.44	9.09	0.128
Large Intestine	94.0	1.2	3.24	0.119
Liver	0.23	0.31	2.77	0.162
Respiratory Tract & Lung	0.34	0.15	2.31	0.040
Head	4.4	11.4	3.47	0.015
Skeleton	2.6	25.5	1.54	0.019

Note: General form of equation for biological decay over 28 day period:

$$A_t = K_1 e^{-\lambda_1 t} + K_2 e^{-\lambda_2 t}$$

The very rapid clearance of radioactivity from the G.I. tract contrasts with the slower biological decay observed in the respiratory system. Two rate constants are also sufficient to describe the loss from the respiratory system. The initial rapid loss of material (λ_1 = 2.31/day) probably reflects the rapid upward movement of material in the respiratory tract, while the second component (λ_2 = 0.040/day) may be associated with the slower loss of particles which had been "fixed" in the alveolar tissue or leaching of Sr from the deposits in the lung.

The slowest rate of clearance of Sr by any tissue is, of course, that from the skeletal system. The two components of this curve describe an initial fairly rapid loss (λ_1 = 1.54/day) and a secondary slower turnover (λ_2 = 0.019/day) of the bone-fixed Sr.

Radiotoxicity of Inhaled Strontium Aerosol--Relative Dose to Organs

The dose delivered to tissues by beta particles emitted from radioactive isotopes can usually be estimated by relatively simple methods when the tissue concentration of the isotope is known. In this experiment the gamma emitter Sr^{85} (carrier free) was used as a tracer for estimating the tissue concentration of the beta-emitting Sr^{90}. Since the range of beta particles in tissue is usually a few millimeters, the dose from deposited isotopes is confined largely to the organ containing the material, particularly for an organ with dimensions large with respect to beta particle range[12]. Calculations of tissue dose from beta particles are essentially estimates of the energy made available by the decay of a quantity of the isotope per gram of tissue. The isotope concentration divided by an appropriate constant permits direct conversion to a unit of dose[12]. Thus, dose as used here refers to the concentration of the beta-emitting Sr^{90} per gram of tissue since there is a direct relationship between the concentration of the beta emitter and the radiation dose received by the tissue. The "relative dose" refers to the ratio of doses received by two organs. In this paper relative doses received by organs are expressed in terms of the dose received by the skeleton.

Calculation of the relative dose is based on several assumptions. First, the Sr^{85} gamma activity per gram of tissue is assumed to reflect accurately the Sr^{90} concentration. Secondly, it is assumed that the radioactivity is evenly distributed in the organs. Calculation of dose is also based on the assumption that the energy emitted in an organ

is completely absorbed in that organ. The dimensions of the organs of mice are such that a considerable fraction of the more energetic beta particles may not be stopped in the organ and thus may expend their energy in other tissues. The organs in man, on the other hand, have dimensions sufficiently large as compared to the range of the beta particles to make valid the assumption of the equivalence of energy emission and absorption. Thus by extrapolating the values of concentration and distribution as observed in the mouse (based on the assumptions of similar organ distribution and similar ratio of organ sizes in mice and men), calculation of dose may be made in man.

With these assumptions the relative dose that might be received by the various organs of man following an exposure to a dry-particle $Sr^{90}Cl_2$ aerosol were calculated. The Sr concentration in organs as determined from measurements of the Sr^{85} tracer (gamma activity per gram of tissue) are listed in Fig. 4.

Values for the initial relative dose rate (at 0.5 hour) and the total relative dose* (28-day period) are presented in Table 6, based on 100 percent for the skeleton. At early times following inhalation, the stomach and the G.I. tract receive the highest dose rates, due to the heavy concentrations of activity. Measurement of the stomach and intestine was done on the whole specimen, including its contents. The intrinsic geometric and self-absorption factors involved in the determination of the beta dose to the mucosa of the stomach and intestine, which have been neglected in this simplified calculation, would markedly reduce the dose as listed in Table 6. The rapid excretion of activity is reflected, however, in the dose calculations, which indicate that by far the highest total dose is delivered to the skeletal system, which "fixes" Sr and releases it only very slowly (rate constant $\lambda_2 = 0.019$/day, equivalent to $t_{1/2} = 36$ days (see Table 5)).

The dose to the head is the next largest, about one-fourth that received by the total skeletal system. The components of the G.I. tract are next in order, with the large intestine receiving more than twice the dose to the stomach and small intestine and twice that delivered to the respiratory tract and lungs.

*The doses were calculated mathematically, with the use of the constants obtained for the biological decay curves (Table 5) and were checked by mechanical integration of the curves performed with a planimeter.

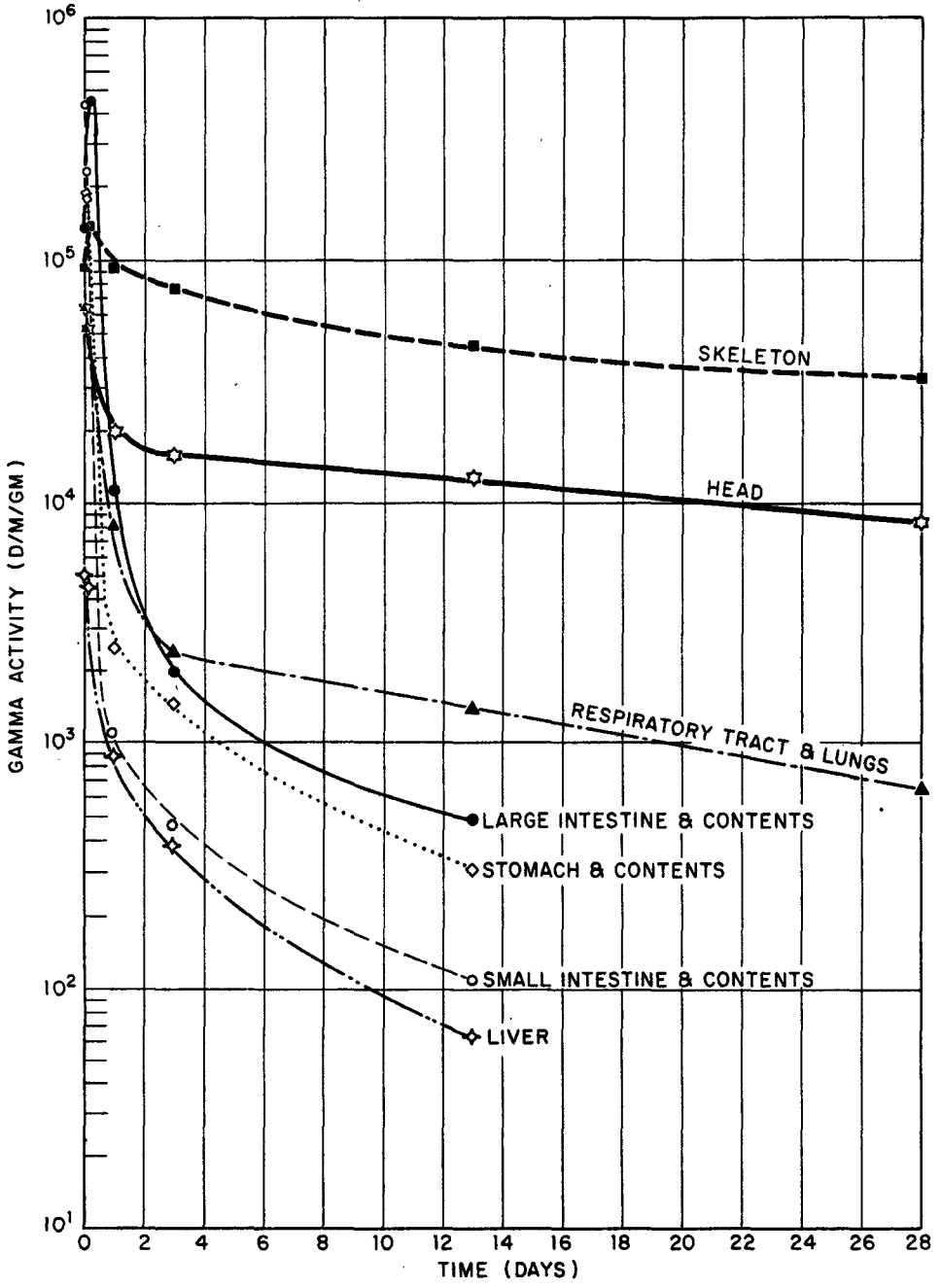

Fig. 4 Strontium per Unit Weight of Organ Following Exposure to a Dry Particle Aerosol.

TABLE 6

Initial Dose Rate (0.5 hr) and Relative Dose (28 Days) From an Inhaled Strontium Dry-particle Aerosol

Tissue	Dose Rate (at 0.5 hr after exposure)	Total Dose (0 to 28 Days)
Skeleton	100[a]	100[a]
Head	71	26.4
Stomach and Contents	203[b]	3.15[b]
Small Intestine and Contents	489[b]	2.26[b]
Large Intestine and Contents	149[b]	8.85[b]
Respiratory Tract and Lungs	68	4.36
Liver	5.5	0.39

(a) The dose rate and dose received by the skeleton are expressed as 100. All other doses are expressed in terms of this value.

(b) The intrinsic geometric and self-absorption factors involved in the determination of the beta dose to the mucosa of the stomach and intestine, which have been neglected in this simplified calculation, would markedly reduce the dose as listed above.

SUMMARY AND CONCLUSIONS

Exposure of mice to a dry particle aerosol ($Sr^{85}Cl_2$ adsorbed on kaolin particles) resulted in a G.I. tract/respiratory system activity ratio of 100,0.5 hr after exposure. Following administration of aqueous suspensions of the same material by stomach tube, the amount of Sr^{85} deposited in the skeleton was 80 percent of that found in the skeleton following an inhalation exposure (in terms of initial gastrointestinal Sr activity). The findings of the high activity in the G.I. tract and the fixation of large amounts of Sr by the skeletal system following administration by gavage suggest that a considerable fraction of the internally deposited activity after inhalation may have gained entry via the G.I. tract.

After the mice were exposed to a liquid aerosol of $SrCl_2$ in sea water, the ratio of activity in the G.I. tract/respiratory system at 0.5 hr after exposure was found to be 50. Three times as much Sr was found in the skeleton following exposure to the liquid aerosol as resulted from exposure to the dry particle aerosol. A two-fold increase in skeletal activity was also observed following administration by stomach tube of the ionic liquid $SrCl_2$ aerosol over that found following the dry-particle suspension similarly administered. Thus, absorption of Sr into the body was greater with the liquid aerosol than with the dry particle (2 to 3 times), due to either the greater solubility of the carrier or the nature of the association of the Sr with the carrier.

Similar inhalation and gavage experiments performed with La adsorbed on an insoluble dry clay particle indicated that only a very small amount of this highly insoluble combination was able to penetrate to the internal tissues. The small amount gaining entry appeared to do so via the alveolar tissue, possibly being transported as particles by macrophages.

Calculation was made of biological decay constants and the relative dose to various organs that might be received by a man exposed to a dry-particle aerosol of $Sr^{90}Cl_2$. Most of the biological decay curves could be adequately described by the sum of two exponential functions, a rapid component and a much slower one. The first component reflects rapid clearance of activity from each organ, while the slower component corresponds to the biological loss of activity "fixed" in the organ.

Calculation of the relative dose to the various organs indicated that the skeletal system received by far the highest dose over the 28-day period studied, as would be expected following exposure to a highly soluble bone-seeking metal. The high concentration of activity in the G.I. tract resulted in an initial dose rate to the small intestines many-fold

higher than that received by the respiratory system. The integrated dose received by the large intestine over the 28-day experimental period was twice that received by the respiratory system, stomach or small intestine.

The finding that the G.I. tract can serve as a portal of entry for soluble fission-product aerosols following an inhalation exposure implies that an evaluation of the internal hazard associated with an inhalation exposure must take into account those parameters which influence transport across the G.I. membrane as well as the more commonly considered factors which determine transport across the alveolar membrane.

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