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Strontium-90 in Man III

The annual increase of this isotope and its pattern of world-wide distribution in man are defined.

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The investigation of the mechanism of the distribution of strontium-90 from nuclear detonations and its uptake in man has continued. This article (*1*) presents new data on strontium-90 concentration in human bone, largely from samples obtained in 1957–58. The measurements extend the earlier work (*2, 3*) in time and location and add details which give greater understanding of the principles of the movement of strontium-90 in the biosphere. The results of the past year also clearly define the annual increment in strontium-90 in the skeleton for the years 1953 to 1957 in a single location (New York City).

The ultimate goal of this study is to predict the future distribution of strontium-90 for the entire world population. Enough data have been obtained on the strontium-90 levels in human bone, in food, in soil, and in rainfall as a function of geographical location so that a first approximation to the world distribution curve can be made. The curve for the present distribution of strontium-90 in adults has been calculated and this is used to predict the distribution for young children in 1966, when the maximum level of strontium-90 in the diet from tests made to date will have been reached.

Experimental Procedures

Samples of human bone are received at regular intervals from about 35 stations in a world-wide network. During 1957–58 an attempt was made to divide the samples somewhat equally according to whether the individuals had been older or younger than 20 years at death. Since it appeared from earlier work (*3*) and from data given in Table 1 that age is not an important determinant of the amount of strontium-90 deposited in adults, equal portions of adult bone from a given locality were integrated to reduce the number of analyses required. Exceptions to this practice were made where new stations were involved, in order that data on local variation might be obtained. Individual samples containing less than 3.0 grams of calcium in the case of an adult or 1.0 gram of calcium in the case of a child were not analyzed during 1957–58, since larger statistical counting errors result from the inclusion of such samples, as a result of the small quantity of strontium-90 that is present.

Most of the bone analyses were made by two commercial laboratories (*4*). Some analyses and intercalibration tests were performed at this laboratory, by methods described elsewhere (*5*).

The samples were all single bones (some were integrated samples) with the exception of 160 whole skeletons obtained from cadavers in New York City. Measurements have shown that the distribution of natural strontium is uniform in the adult skeleton to within at least 10 percent (*6*). Detailed studies in adults in which strontium-85 and calcium-45 tracers were used (*7*), and studies of fallout strontium-90 in both children and adults (*8*) show that the strontium-90 from the diet is nearly uniform in the bones of the skeletons of young children, while in the bones of adults it occurs in different concentrations that are systematic and reproducible. Schulert *et al.* (*8*) have determined these relations and have shown that the average concentration of strontium-90 in a particular adult skeleton can be estimated from the analysis of a single bone of that skeleton. The results reported below are all given in micromicrocuries of strontium-90 per gram of calcium. In the case of children, the level of strontium-90 in a single bone is taken as the skeletal average. The concentration of strontium-90 in the whole skeleton of an adult (of age 20 or more) is computed, by Schulert *et al.* (*8*), from the analysis of a single bone by using the actual strontium-90 distribution found in skeletons of people who died in 1957:

Vertebrae/whole skeleton = 1.8
Rib/whole skeleton = 1.0
Femur/whole skeleton = 0.5

The standard errors for these ratios are 12, 14, and 25 percent, respectively.

The uncertainty that results from computing the concentration of strontium-90 in the whole skeleton from the analysis of a single bone is generally less than the counting error attributable to the low activity levels of the single-bone samples. This is particularly true for the femur and for small samples of any adult bone (*8*).

Regional Averages and Time Effect

The concentrations of strontium-90 that were found in human bone from various localities in 1957–58 are compared in Table 2. All adult samples were combined for this purpose, since, as was noted above, no effect attributable to the age of the individual has been observed. Note that the samples for the United States have about the same concentration as the average for other parts of the world in the same latitude band. Note also that rice-diet areas (for example, Thailand, Japan, and the Philippines) have a concentration somewhat

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Table 1. Levels of strontium-90 in adult skeletons in relation to age. Samples were from the area of Western culture, 20° to 60° north latitude. Number of samples is given in parentheses.

Period	Level of Sr^{90} ($\mu\mu c$/g of Ca)				
	Age (yr)				
	20–29	30–39	40–49	50–59	Over 60
1955–1956	0.12 (93)	0.13 (80)	0.09 (22)	0.16 (4)	0.12 (9)
1956–1957	0.13 (56)	0.15 (36)	0.12 (42)	0.15 (48)	0.12 (62)
1957–1958	0.15 (3)	0.36 (12)	0.22 (14)	0.17 (9)	0.17 (77)

higher than the average. A world average of 0.19 μμc of strontium-90 per gram of calcium is obtained by weighting each latitude band according to its adult population but treating the Western and rice-diet areas separately. The standard deviation is given for localities contributing more than 20 samples, to give some idea of the spread encountered in samples from a given station. Larger variations generally indicate that the number of samples was small, and the mean values therefore fluctuate considerably from year to year for a given station (*3*). Also included in Table 2 is the latest estimate of the cumulative fallout per unit of rainfall for each latitude band to January 1958, based on all available determinations of strontium-90

Table 2. Regional averages for strontium-90 in adult skeletons in 1957–1958.

No. of samples	Location	Sr^{90} ($\mu\mu c$/g of Ca)	Standard deviation	Cumulative fall-out [mc of Sr^{90}/mi^2/unit of rainfall (Jan. 1958)]
	40° to 60°N			
13	Vancouver	0.30		
73	Boston	0.18	0.10	20
1	Denmark	0.17		
6	England	0.25		
18	Germany	0.14		
	20° to 40°N			
12	Houston	0.18		17
2	Taiwan	0.18		
22	Israel	0.18	0.13	
4	Japan	0.33		
4	Hawaii	0.15		
	0° to 20°N			
25	Puerto Rico	0.12	0.08	3
4	Colombia	0.07		
46	Guatemala	0.10	0.07	
4	Philippines	0.27		
21	Thailand	0.36	0.29	
	0° to 20°S			
13	Belgian Congo	0.21		4
	Ecuador	0.13		
	20° to 40°S			
16	Argentina	0.14		6
29	Chile	0.07	0.05	
4	Union of South Africa	0.18		
5	Cape Town	0.07		
36	Australia	0.20	0.11	

in soil and rainfall. There is less apparent difference in the levels in bone than in the recorded fallout, between the Northern and Southern hemispheres (Tables 2 and 3). This fact may be due in part to the widespread flow of wheat and powdered milk from the Northern to the Southern Hemisphere. Other equalizing factors may be the higher rainfall of the local food-producing areas of the tropical regions and the higher ratio of vegetable calcium to milk calcium in the diet in the Southern Hemisphere.

The gradual build-up of strontium-90 in human bone that has occurred over the past four years is shown in a general way by the regional averages (Table 4). The anomalies reflect changes in the number and location of sampling stations during the three-year period. The best indication of the time effect is given by the whole-body samples from New York (Fig. 1); a large number of samples were available from this station, and the size of the samples made it possible to make more accurate analyses than could be made with smaller samples. It may be noted that the concentrations of strontium-90 in the skeletons of these cadavers was about 30 percent lower, on the average, than concentrations in other skeletons from the same area; this probably reflects the poorer nutritional state of these persons.

Strontium-90 in Children and Variation with Age

A general summary of the 1957–58 findings for samples of human bone of individuals who died at less than 20 years of age is given in Table 3. This is the largest number of samples for a single year yet obtained, and most of them were of sufficient size to give reasonably accurate analyses. Note the near-equality of the concentrations in North America and Europe in each category where an appreciable number of samples exists. The average difference in concentration for samples from the Northern and Southern hemispheres is in agreement with that obtained for adults.

The concentration of strontium-90 varies with age for young people at the present time, since there has not been sufficient time for their skeletons to equilibrate with strontium-90 in the diet. Strontium-90 is deposited directly in the formation of new bone and through exchange and other turnover processes in preexisting bone. It is instructive to compute the concentration of strontium-90 as a function of age for a population with a given strontium-90 content in the diet and to compare this theoretical curve with the experimental data. Since the United States, Canada, and Europe appear to have strontium-90 levels in soil, food, and human skeletons that are closely similar (*9, 10*), bone samples from these areas can be grouped for this purpose, thus providing a larger number of samples to test the theory.

The calculation requires knowledge of: (i) the strontium-90 concentration in the average diet for the past five years; (ii) the discrimination factor for strontium relative to calcium from diet to bone; (iii) the number of grams of bone deposited per year at each age as a result of skeletal growth; and (iv) the magnitude of the average bone turnover per year.

The strontium-90 concentration in the average diet of individuals in these areas has been estimated from the data of the Atomic Energy Commission's Health and Safety Laboratory (*11*), the Lamont Geochemical Laboratory (*9, 12*) and the British group (*10, 13*). The re-

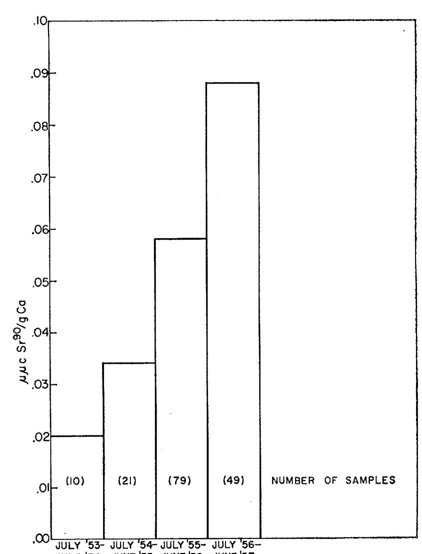

Fig. 1. Concentration of strontium-90 in whole skeletons of New York City adults.

Table 3. Level of strontium-90 in children's bones, 1957–1958. Number of samples is given in parentheses.

Age	Level of Sr^{90} ($\mu\mu c$/g of Ca)				
	North America	Europe*	South America	Asia	Africa, Australia
Fetus	0.64 (9)	0.60 (27)		1.3 (15)	0.25 (2)
0– 6 mo	1.18 (8)	1.15 (28)		0.21 (4)	0.45 (1)
7–12 mo	1.84 (1)	1.47 (5)	0.58 (38)	1.15 (4)	
1– 2 yr	1.53 (7)	1.39 (9)	0.54 (5)	0.11 (1)	0.27 (1)
2– 3 yr	1.49 (9)	1.71 (4)	1.28 (1)		0.60 (1)
3– 4 yr	1.23 (7)	0.87 (3)			0.43 (5)
4– 5 yr	0.74 (5)	0.73 (3)			0.48 (3)
5– 6 yr	0.70 (12)	0.66 (6)	0.28 (10)		0.55 (2)
6– 8 yr	0.60 (12)	0.61 (5)	0.39 (4)	0.28 (2)	0.53 (5)
8–10 yr	0.88 (11)	0.39 (4)	0.28 (8)	0.09 (1)	1.50 (2)
11–15 yr	0.51 (21)	0.55 (5)	0.22 (5)	0.50 (3)	0.49 (8)
16–19 yr	0.39 (11)	0.24 (3)	0.20 (15)	0.45 (2)	0.22 (4)

* Data from Bryant *et al.* (*28*) on European children for 1957–1958 were included to give a better comparison for Europe and North America.

sultant averages in micromicrocuries of strontium-90 per gram of calcium for North America and western Europe for 1 July of each year from 1953 through 1957 are 0.4, 1.6, 3.6, 5.1, and 6.5, respectively.

The data for the average amount of bone deposited per year are taken from Mitchell *et al.* (*14*) for males in the United States.

Schulert *et al.* (*7*) obtained a discrimination factor of 4 for calcium against strontium from diet to bone, on the basis of double-tracer (calcium-45, strontium-85) intravenous single doses in human patients and of previous work by Spencer *et al.* (*15*) on discrimination across the gastrointestinal wall in man. In an experimental study involving the stable strontium-to-calcium ratios in the normal diet and the skeletons of people in communities of Wales and northwest England, Bryant *et al.* (*10*) obtained a discrimination factor of 4 for calcium against strontium. Comar *et al.* (*16*) have obtained discrimination factors of about 2 and 4, respectively, for calcium against strontium from diet to bone for rats fed a milk and a nonmilk diet, and a discrimination factor of about 2 for several human patients on a milk diet. This suggests that the actual discrimination factor for human beings may depend somewhat on the diet. Nevertheless, the experiment of Bryant *et al.* (*10*) shows that the average discrimination factor for calcium against strontium in the average man in areas of Western culture must be close to 4. A placental discrimination factor of 2 was found by Comar in animals (*17*). The data in Fig. 2 for North America and Europe indicate that this factor is about the same in human beings.

If a discrimination factor of 4 for calcium against strontium from diet to bone is assumed, the average turnover rate for the normal adult can be calculated from the known concentration of strontium-90 in the diet over the past five years and the present average concentration of strontium-90 in adult bone. The result is 3.8 percent per year. If the behavior of strontium is assumed to be similar to that of calcium, a maximum of 1 percent may be accounted for by intracrystalline exchange, whereas perhaps another 1 percent is due to remodeling. The rest is accounted for by passage to the more spongy bone, where the rate of turnover is much higher. Once this latter reservoir becomes saturated, the apparent average turnover rate will drop to the intracrystalline exchange and remodeling rate. From the experimental data the gross average turnover for adults is calculated to be 3.8 percent per year during this period. It is assumed for purposes of calculation that this same rate applies to children, although their rate of turnover is probably higher. Since the proportion of calcium deposited in the process of growth relative to that deposited through turnover is large in the case of young children, no great uncertainty is introduced through basing the calculation for children on this rate.

Table 4. Levels of strontium-90 in adult bone from 1955 through 1958. Number of samples is given in parentheses.

Location	Sr^{90}($\mu\mu c$/g of Ca)		
	1955–1956	1956–1957	1957–1958
40°–60°N	0.12 (177)	0.12 (176)	0.19 (111)
20°–40°N	0.14 (88)	0.13 (114)	0.19 (44)
0°–20°N	0.11 (130)	0.20 (63)	0.16 (101)
0°–20°S	0.07 (41)	0.08 (22)	0.25 (16)
20°–40°S	0.11 (88)	0.12 (78)	0.14 (90)

The theoretical curve computed in this way is given in Fig. 2 and is compared with the experimenal data for children's bones in North America and in western Europe obtained in this study and by Booker *et al.* (*13*). The standard deviation in the analyses for any given age group is about 30 percent of the mean for those sets in which there are at least eight samples. This variation is probably due primarily to individual differences in diet. It is seen that the points for the various age groups follow the curve reasonably well, the greatest divergence being found in early adolescence. The ratio of the maximum, which occurs at about age 1 year, to the adult average is about 8; this ratio will be reduced if the concentration of strontium-90 in the diet becomes more constant with time.

On the basis of the values given above for the bones of individuals in North America between the ages of 0 and 20, it is now possible to weight the level of strontium-90 in bone by the fraction of the population in each age group and thus to compute the present world average concentration of strontium-90 in human bone. This calculated world average as of 1 January 1958 is 0.52 $\mu\mu c$ of strontium-90 per gram of calcium.

Future Human Burden of Strontium-90

The accumulation of new data relative to the concentration of strontium-90 in human bone and diet and to the deposition of strontium-90 on the earth's surface makes it possible to predict future levels in the human population with greater accuracy. This calculation is based upon atmospheric contamination from nuclear tests to the end of 1958 and on the assumption that the diet level is proportional to total fallout. The calculation tacitly implies that strontium-90 will be distributed in the future approximately as it has been in the past, although the Soviet tests of October 1958 may alter the distribution to a minor extent in the direction of increasing the amount deposited in the North Temperate Zone in the future. The quantities of greatest interest are the anticipated concentrations of strontium-90 in the diet and the related anticipated levels of strontium-90 in newly formed bone.

The concentration of strontium-90 in the average Western diet was 6.5 $\mu\mu c$

per gram of calcium on 1 July 1957, when the level in milk was 6.1 μμc per gram of calcium. A comprehensive survey of U.S. milk in the United States in July of 1958 gave an average of 8.2 μμc of strontium-90 per gram of calcium (*18*), which is equivalent to a level in the diet of 8.7 μμc of strontium-90 per gram of calcium. To extrapolate to 1 January 1959, it follows that the Western diet included 9.7 μμc of strontium-90 per gram of calcium on that date. Also, on 1 January 1959 the cumulative deposition of strontium-90 on the surface of the earth was about 2.2 megacuries (*19*). In the light of data on the isotopic composition of stratospheric debris that have been derived from new rain and from balloon sample analyses (*20*), it seems likely that the mean residence time of strontium-90 in the stratospheric reservoir is three years rather than the five (*21*) or ten (*22*) that have been estimated previously. From this figure and from the deposition rate it is possible to estimate that the stratospheric reservoir contained about 1.8 megacuries on 1 January 1959, exclusive of debris from the Soviet tests of October 1958. If the latter contributed as much as a major test series—for example, the United States' Redwing series of 1956 (*22*)—the total stratospheric reservoir would be about 2.6 megacuries. On the basis of these three assumptions—2.6 megacuries to be deposited, a mean residence time of about three years, and a discrimination factor of 4—when due allowance has been made for radioactive decay, the strontium-90 concentration in the diet, and hence in newly depositing bone, can be readily computed. The result (Fig. 3) shows that a peak in the level of strontium-90 in new bone will occur about 1966. The average concentration in the skeletons of young children on a Western diet in the Northern Hemisphere at that time will approach but not reach this peak level.

This estimate of the future levels that will be reached if there is no further introduction of fission debris into the atmosphere is probably maximal. One of the fundamental assumptions in the calculation is that the strontium-90 levels in the diet will be proportional to the *cumulative* fallout (*23*), and others have emphasized that the level in the diet may be related also to the *rate* of fallout, and that in some cases the rate factor may predominate. At present the data are not adequate for quantitative assessment of the relative importance of the rate factor. If it should be determined, for example, that as much as half of the uptake of strontium-90 by plants is due to the rate of fallout, the predicted curve might have to be lowered by as much as a factor of 2. The rate of fallout, however, did not change appreciably from 1954 to 1957, whereas the skeletal concentration of strontium-90 in an urban population increased markedly (Fig. 1). It is concluded, therefore, that cumulative fallout is the dominant factor for the average diet in areas of Western culture, but the data cannot rule out the possibility of a contribution from the rate factor which would reduce the predicted levels (Fig. 3). Other factors that would also reduce the levels in diets in the future would include loss of strontium-90 by vertical migration in the soil, or chemical fixation. Neither of these factors is considered significant (*19*). The plowing of pasture land, however, will probably cause some reduction in the levels of strontium-90 in food over those that have been predicted.

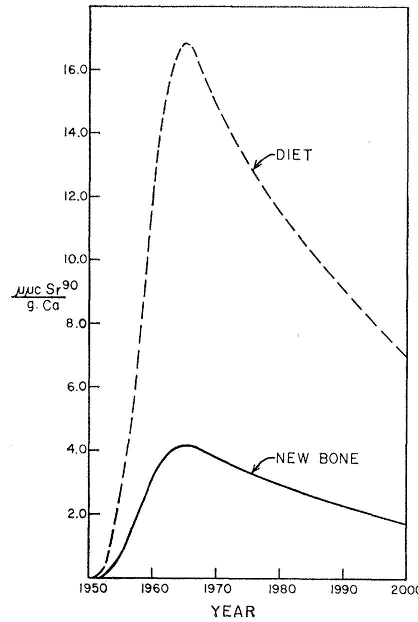

Fig. 3. Uptake of strontium-90 in food and new bone in the area of Western culture, 20° to 60°N.

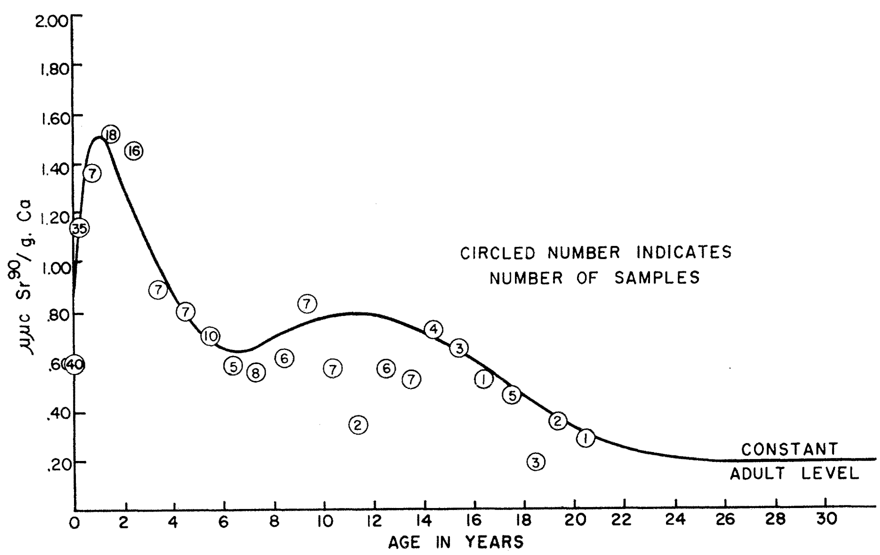

Fig. 2. Concentration of strontium-90 in the skeleton, in January 1958, in North America and western Europe.

World-wide Distribution

The other question of importance is that of the ultimate distribution of concentrations of strontium-90 in the world population. This is complicated to such an extent by the fact that there is great variation with age in children—a result of the rapidly changing levels of strontium-90 in the diet (Figs. 2 and 3)—that a histogram of all bone samples would not be significant. The fact that the strontium-90 concentration in adult bone is independent of age and that the average values over large geographical areas are rather similar provides a suitable characteristic for a frequency plot. As the rate of change of levels of strontium-90 in the diet decreases, it is to be expected that the shape of the distribution curve for the whole population will approach that obtained from adult samples at the present time. The ultimate variation for the world population occasioned by the differences in the concentration of strontium-90 in individual diets is already reflected in the skeletons of adults.

Four histograms are presented in Fig. 4. These cover all the more recent (1957–58) samples. They represent, from top to bottom, (A) values for whole-body adult samples (80 skeletons) from New York City; (B) computed skeletal values from the measurement of individual adult bone samples from the northeastern United States (100 samples); (C) computed skeletal values from individual adult bone samples from rice-diet areas (Thailand, Taiwan, the Philippines, and Japan) (126 samples); and (D) computed skeletal values from individual adult bone samples from the whole world (838 samples).

Although the number of samples represented in histogram A (whole-body adult samples from New York City) was limited, the radiochemical analyses of the whole-body ash are more accurate than the skeletal values computed from analyses of single bones.

The histogram (B) of the skeletal burden computed from 100 analyses of individual bones from Boston and New York shows a larger spread than (A). This range is more apparent than real since the analyses of the single bones show an average counting error of about 30 percent, whereas the counting error on the whole-body ash averages about 10 percent for 1957–58 samples. Furthermore, the biological variation within a single bone and variation in the particular-bone–whole-skeleton ratio extend the range of the data. These factors may readily account for the difference in the values shown in histograms A and B; hence it may be concluded that the whole-body samples from New York City give the more accurate representation of the distribution of concentrations of strontium-90 in the population of the northeast United States and probably in most of the population living on a Western diet in the latitude band of 20° to 60°N.

Histograms B (northeastern United States) and C (rice-diet areas) may be compared directly, since they are both derived from single-bone analyses. It is clear that in the rice-diet areas the variation in strontium-90 concentration in the population is larger by a factor of about 2 than in the northeastern United States. This is probably a result of the more restricted flow of food in the Orient, the higher average contribution of vegetable calcium to the diet, and the greater variability of the vegetable-calcium–milk-calcium ratio in the diet in rice-diet areas. Also, the concentration of strontium-90 tends to vary to a much greater extent in vegetables than in milk (*12*).

Histogram D represents analyses of individual adult bones for the entire world for the period 1 July 1956 to 30 June 1958. Although the sampling is not proportional to the total population in each area, this curve provides the best empirical basis available on which to base an estimate of the world distribution of strontium-90 in man. The true distribution is no doubt narrower, as may be deduced from the comparison of histograms A and B above. Nevertheless, the curve given in histogram D is adopted in the discussion that follows, though it is acknowledged to be somewhat too broad. This distribution is clearly not normal, nor does it correspond closely to a lognormal pattern. A large fraction of the world's population gets most of its calcium from milk products, while the rest (largely Oriental) gets calcium from a variety of foods, cereals being the most important. That this distribution curve adequately represents the world adult population can be tested in a number of ways. It is useful to examine the range of strontium-90 concentration in milk in areas of Western culture, where milk products are the dominant source of calcium. Milk from a large variety of sources has now been analyzed (*11, 24*). These samples include a set of about fifty collected by this laboratory from untilled farms or from poor land in many parts of the United States. The highest concentration found in these samples was only about five times the mean for the United States. In the high-acidity–low-calcium areas in Kentucky, the highest concentrations in the milk samples were only twice the average for the United States

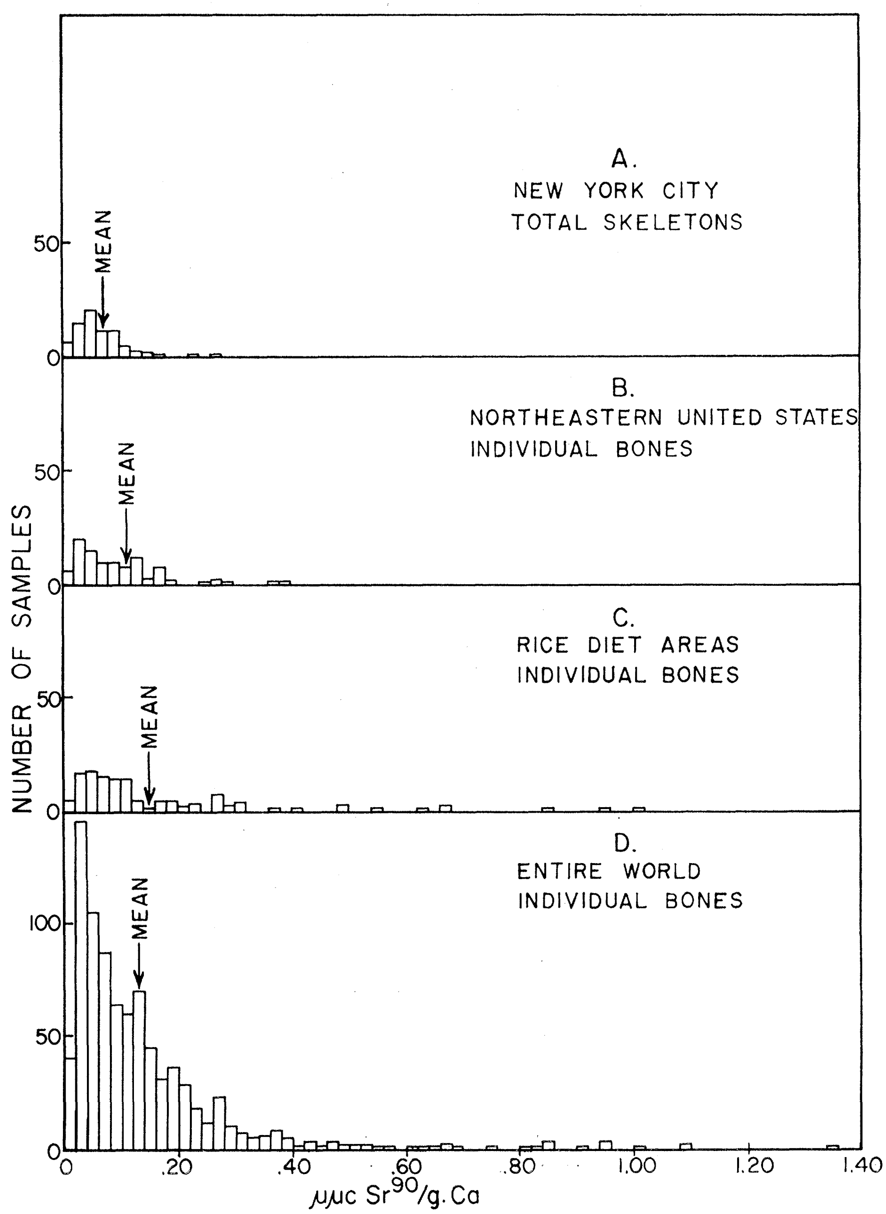

Fig. 4. Histograms showing comparative distributions of strontium-90 in bone.

and represented isolated farms. A restricted area in western North Dakota produces a milk that averages three to five times the mean for the United States. The people affected would be those who actually live on the farms that produce this milk, for if the milk is sold into the urban markets and combined with milk from other areas, the level of strontium-90 is quickly reduced. The population that might conceivably be affected is less than 0.1 percent of the population of the United States. Histogram D suggests that concentrations in foodstuffs at twice the mean level do not contribute greatly to the distribution curve.

Numerous food samples have been obtained from various parts of the world and analyzed for strontium-90. Levels in the foods which contribute significantly to the calcium in the diet do not vary by more than a factor of 2 or 3 from the mean in almost all cases. Again, the mixing of foodstuffs prevents individuals from maintaining a diet which is consistently high in strontium-90.

A special field study (*9*) was undertaken to sample the foods of the truly isolated Indian tribes of the uppermost part of the Amazon basin. Here the tropical conditions cause intensive leaching of the calcium from the soil. These people eat only what they can grow within a half mile or so of their village, and they have a very restricted diet. Most of their calcium comes from the yuca, which they prepare in various ways. Studies of a considerable number of sites showed the yuca to contain four to five times more strontium-90 per gram of calcium than components of the average world diet, despite the fact that the actual fallout in this area is considerably less than in latitudes 20° to 60°N. The number of people involved in this primitive situation, where there is virtually no inflow of food and where the mean annual temperature and rainfall are high, does not appear to exceed a few tens of thousands and constitutes less than 0.001 percent of the world population. In the world histogram (D) it is seen that the contribution to the distribution curve from these special groups whose diets contain concentrations of strontium-90 of five times the world average is quite small. It is concluded, therefore, that the empirical distribution curve (D) is reasonably representative of the entire adult world population in 1958 and probably of the whole world population at some future time if the concentration of strontium-90 in the diet becomes fairly constant with time.

A further critical problem is that of the proper method of extrapolating the distribution curve to the higher values. The curve cannot proceed indefinitely to the right for several reasons. Since the fallout is somewhat proportional to integrated rainfall for a given latitude band, and since the highest local rainfall does not exceed the world average by much more than a factor of 5, there is a limit set on the initial variation. Actually, the major agricultural areas have rainfall ranging only from about 20 to 60 inches per year, except in irrigated areas. With time, local variations become averaged out. The available calcium content of the soil can vary widely but, again, the variation is not large over most agricultural areas. The mixing of food completely obscures any local highs from the two factors discussed above so that, except for a few primitive areas, the high and low concentrations of strontium-90 in plants will not produce an equivalent range in man. Even the most primitive people tend to get their calcium from more than one type of food, and, further, they vary the source of their foods during their lifetime. Again, all these factors tend to equalize the diet. From all of the data at hand, it appears doubtful that any person in the world will have a sustained diet which exceeds the world average for strontium-90 concentration by as much as a factor of 20. This, then, sets the upper limit to the distribution curve.

Finally, it is of interest to consider what the distribution of strontium-90 among young children will be in 1966 when, it is estimated on the basis of tests to date, the maximum intake of strontium-90 in the diet will occur. The average concentration of strontium-90 in the skeletons of young children will then be about 4 μμc of strontium-90 per gram of calcium. The curve for the present distribution of strontium-90 in adults (Fig. 4, D) probably also represents the distribution for children of a specific age, since it comprehends the variation in world diet. On this basis it is predicted that at the time of maximum intake in the diet (1966), 10 percent of the young children will be found to have a skeletal concentration of strontium-90 of twice the mean, and 1 percent, of about five times the mean, and that none will have a concentration exceeding 80 μμc of strontium-90 per gram of calcium.

What hazards these levels present to the human race are still not certain. If suggestions, by Brues (*25*) and Finkel (*26*), that there is a threshold for the induction of leukemia or bone tumor are correct, no person will be injured by the strontium-90 that will be deposited by world-wide fallout from nuclear detonations that occurred up to the end of 1958. If the incidence of bone cancer and leukemia is linear down to zero radiation, as Lewis (*27*) and others have suggested, the number of cases can be readily computed for any future year (Figs. 3 and 4; Table 2).

Conclusions

1) In January of 1958 the average burden of strontium-90 in the skeletons of adults throughout the world was 0.19 μμc of strontium-90 per gram of calcium. This burden is independent of age above the age of 20. The concentrations of strontium-90 in bone differ less than the total fallout, as between the Northern and Southern hemispheres. This is attributable largely to the movement of food, particularly of powdered milk and wheat from the Northern Hemisphere into the Southern Hemisphere.

2) A theoretical curve for concentration of strontium-90 versus age has been constructed on the basis of findings on levels of strontium-90 in the diet for the past five years, data on bone growth reported by Mitchell *et al.*, and a discrimination factor of 4 for calcium against strontium from diet to bone. This curve corresponds closely to that for actual data from bone samples from the zone of Western culture of 20° to 60° N.

3) The average concentration of strontium-90 in the skeleton for all people in the world as of January 1958 was about 0.52 μμc of strontium-90 per gram of calcium.

4) On the basis of data on the strontium-90 in diet and bone, the world deposition, and the level of strontium-90 in the stratosphere at the end of 1958, curves have been drawn to show the anticipated concentrations of strontium-90 in the diet of individuals in the area of Western culture of 20° to 60°N and in newly deposited bone to the year A.D. 2000. It is estimated on the basis of these data that the maximum concentration in young children will occur about 1966.

5) A histogram representing 838 samples indicates the present distribution of strontium-90 in the adult population of the world. It is assumed that this reflects the actual spread of all age groups as a result of dietary variations throughout the world. The indicated distribution

may be somewhat wider than the actual distribution, due to analytical errors and biological variation in the ratio of single bone to whole skeleton. It is predicted that in 1966 the average young child in the world will have a skeletal concentration of strontium-90 of about 4 μμc of strontium-90 per gram of calcium; that 10 percent may have a concentration of 8 μμc; that 1 percent may have a level of 20 μμc; and that none will have a level exceeding 80 μμc of strontium-90 per gram of calcium.

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Isosterism and Competitive Phenomena in Drugs

A study of structure-activity relationships in agents acting upon autonomic effector cells

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Making use of the considerable means offered by organic synthesis, many investigators have directed their efforts to the field of therapeutics and have sought to lay the groundwork for a pharmaceutical chemistry or, better, for a chemical pharmacology. If such an ambitious program has not yet been fully realized, nevertheless, during the last five decades, one can notice the emergence of a few basic concepts whose usefulness continues to be confirmed. This is particularly true of the concepts of isosterism and of competition.

Numerous drugs were first derived from products of biological origin, particularly the alkaloids. The elucidation of their structure helped chemists to embark on syntheses of analogous compounds. In this respect cocaine, atropine, and morphine are good illustrative examples. The molecules synthesized according to their models exhibited clinically useful anesthetic properties, spasmolytic activity, or pronounced analgesic effects. In each case, chemical similarity produces in-some-way-related physiological properties.

Analogous observations have subsequently been gathered in many other fields, but it has also become evident that sometimes very different, even antagonistic, pharmacological properties may be found in chemically similar molecules.

Despite the fact that the concept of "antimetabolite" is based on rather old experiments, it was defined essentially in the field of "antivitamins"; the work of Woods (1940) and Fildes (1940) on the antisulfonamide component of yeast and its identification as *p*-aminobenzoic acid found a large acceptance. The idea that a compound structurally similar to one normally present in the organism is able to interfere with the function of this metabolite could be applied in many ways. Its success, especially in enzymology [where, for the first time, it was clearly formulated by Quastel (1925–1928)], in chemotherapy, in vitaminology, and in endocrinology, obviates a detailed discussion of the underlying physicochemical and biological principles. Instead, I would like to draw your attention to the importance of studies of competitive phenomena in pharmacodynamics, especially in the pharmacology of drugs of the autonomic nervous system. I would like to show how a very large part of therapeutical chemistry depends on the relations between many alkaloids or synthetic compounds and a few hormones, chemical transmitters, and products of tissue metabolism of rather simple chemical structure: epinephrine and norepinephrine, acetylcholine and propionylcholine, histamine, and 5-hydroxytryptamine (Table 1).

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