FACT SHEETS '82
Betty P.

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INTRA-LABORATORY MEMO

702524

November 23, 1982

TO: All CHR Staff

FROM: J. Rundo

I attach a set of 12 Fact Sheets that were prepared for the Review Committee. The first six were distributed to all Committee members, while the second group were only given to Drs. Matanoski and Sagan. You may find these of interest in seeing how your own work relates to that of others in CHR.

I would like to take this opportunity to thank those who prepared these Fact Sheets, and also those who prepared and set up the material for the poster sessions with the Committee members.

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COLLECTION RECORD RELATING TO INDUSTRIAL/MEDICAL EXPOSURES TO RADIUM
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CENTER FOR HUMAN RADIOBIOLOGY

Fact Sheet on

Fibrosarcoma in a Radium Worker 60 Years After Exposure

As of December 31, 1980, the last reported case of bone sarcoma had been diagnosed in 1977; the average skeletal absorbed dose recorded for that dial painter was 6589 rads. Up to December 19, 1980, the lowest absorbed dose in a case of bone sarcoma was 888.

A new case of fibrosarcoma of the femur has now been reported. The patient was a dial painter in Orange, New Jersey, for three months in 1918 and six months in 1919. During the 1960's she was followed by the New Jersey Health Department where she had skeletal x-rays and measurement of her radium body burden. Her major health complaint at that time was rheumatoid arthritis which affected her hands and feet; she had had radiation treatment for arthritis of the ankle and wrists in 1954.

Her original x-ray survey of the skeleton in 1962 reported coarsening of the trabecular pattern of the radius, ulna, tibia and fibula. In addition multiple radiolucent areas were noted in the skull, mandible, both femoral condyles, both tibias and both fibulas. Her body burden of ^{226}Ra as of 1962 was reported to be 0.177 μCi. By 1971 areas of "dense bone necrosis" were being reported in the distal femurs and proximal tibias and fibulas.

On August 7, 1981, she was found to have a pathologic fracture of the right distal femur. The femur was described as "moth-eaten", with no remaining cortical bone in the area of the tumor. Sclerotic changes in the proximal tibia were reported. Amputation was done April 28, 1982 and the pathologic diagnosis was fibrosarcoma. The pathologist commented on "bone infarcts" in the medullary cavity of the tibia as well as in areas of the tumor.

Since this patient's ^{226}Ra input was calculated to be 25 μCi and her average skeletal absorbed dose 390 rads, she is the lowest dose radium worker to date to develop a bone tumor. It seemed desirable to compare her earlier bone findings with workers who had similar doses. Using criteria of birth date before 1910, employment before 1925, ^{226}Ra intake dose of 25-35 μCi and ^{228}Ra <5 μCi, the charts and x-rays of twelve patients were reviewed.

No x-ray reports were available for one patient in this group. Of the remaining eleven, four showed areas of lucency and/or coarse trabeculation in the radius, ulna, tibia, and fibula. No radium-related findings were recorded for the femurs except in one case (05-025) which showed isolated sclerosis in the femurs and tibias, but no radiolucencies; these findings were ascribed by our reader to non radium-related causes (? pancreatitis).

Prepared by Evelyn E. Adams, M.D. Argonne National Laboratory

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Review of the bone tumor case with the next lowest radium burden (888 rads) revealed striking similarities to the present case. The patient had drunk radium water in 1922 for rheumatoid arthritis and had developed fibrosarcoma of the distal right femur when in her 70's. X-ray findings included radiolucencies and dense sclerosis of the distal femur and proximal tibia. She also had lucencies in the skull, radius, ulna, and fibula.

Thus our present case has x-ray findings which resemble much more closely those of another patient calculated to have more than twice as much radium than they resemble x-rays of cases with a calculated dose similar to hers. It is also interesting that the two similar cases both had rheumatoid arthritis (this diagnosis preceded radium exposure in the second case). It would be desirable to confirm the radium dose in our present case. In addition, one must raise the question of what association, if any, there is between tumor development in radium cases and rheumatoid arthritis.

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Fact Sheet on

The Distribution and Retention in Bone of ^{226}Ra and Comparison with the ICRP 20 Model

(Total effort 1.0 p-y)

Over 650 bone samples were analyzed from 66 female and 26 male subjects who had acquired significant amounts of radium as dial painters, as radium chemists, or in the course of medical treatment, and had died from less than one to 60 years after first exposure to radium. The extent to which the data provided support for the ICRP model of alkaline earth metabolism in man[1] was examined and evidence was sought for an effect of radiation on the metabolism of radium in man.

To analyze these results the ratios of ^{226}Ra to calcium were normalized to the terminal ^{226}Ra skeletal content. The $^{226}Ra/Ca$ ratios for vertebra were essentially identical to those for other cancellous bone for a given subject.

Comparison of the data with predictions of the ICRP model showed that for compact bone (femoral and tibial shaft) from females the normalized $^{226}Ra/Ca$ ratios tended to be less than predicted, while those for males were fitted better by the model, as shown in Figures 1 and 2, respectively (overleaf). A version of this model with modified parameters[2] gave a somewhat better fit for the data from females, but was essentially identical for males (dashed lines). Straight line linear least squares fits to the data appeared to fit the data as well as, or better than, the models as shown by the dotted lines on the figures. For cancellous bone the ratios tended to be greater than predicted by the model.

A radiation effect was suggested in that the normalized $^{226}Ra/Ca$ ratio for vertebrae relative to the ratio expected increased with skeletal absorbed dose for vertebrae. However, no such effect was apparent for compact bone or for the cancellous bone as a whole.

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Prepared by R. B. Holtzman

Argonne National Laboratory

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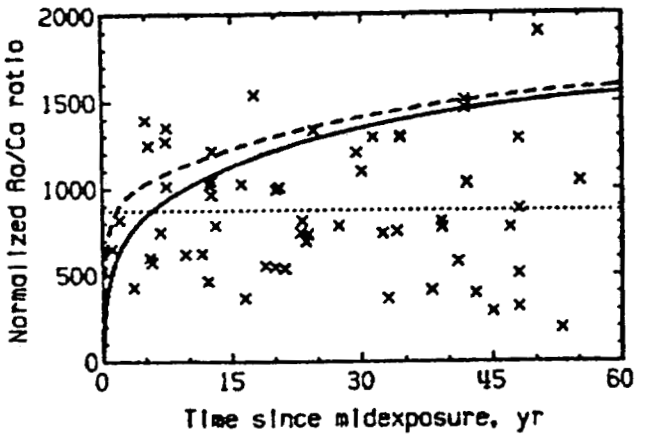

Fig. 1. Ra/Ca ratios for compact bone from females.

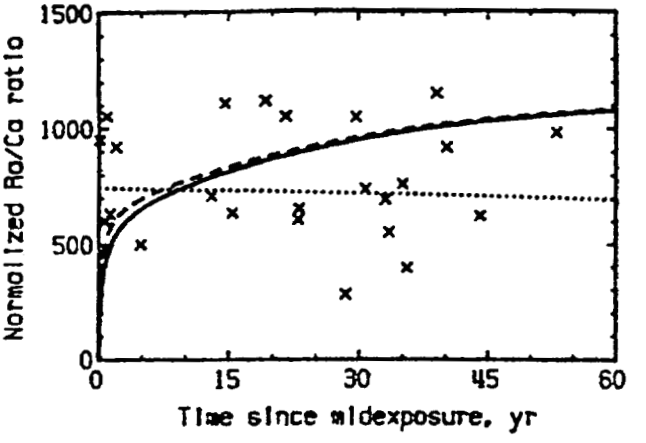

Fig. 2. Ra/Ca ratio for compact bone from males.

——— ICRP 20 model
- - - Modified model
..... Straight line least squares fit

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Fact Sheet on

Status of Cell Culture Studies
(Total effort 1.0 p-y)

History

Cell culture studies were begun in the mid-1970's by Dr. E. Lloyd. The purpose was to investigate the mechanisms of tumor induction with emphasis on those aspects which would improve our understanding of bone and mastoid tumor risk in radium patients. The work culminated with survival and transformation studies of C3H 10T1/2 cells, a line of fibroblast-like cells derived from the embryo of the C3H mouse.

The survival studies shattered the long-held belief that the passage of a single alpha particle through a cell would kill the cell. Dr. Lloyd found that cells could easily survive many alpha particle hits. The transformation studies demonstrated for the first time that alpha particles could induce malignancy. Prior to this, it was only supposed from in vivo evidence that alpha particles themselves could be carcinogenic in the absence of any other known or potential carcinogen.

Dr. Lloyd was hospitalized in the spring of 1981 and died early this year. Her group dissolved about a year ago when it became clear that Dr. Lloyd's recovery would be slower than expected. DOE funding continued at a level sufficient to support one person. Funding reductions in other programs precluded the replacement of Dr. Lloyd. We have sought to continue her work with staff members who had no prior cell culture experience.

Current Efforts and Plans

Through reading, trial and error, occasional advice from others and the recent aid of a consulting cell culture technician from the University of Chicago, we are accumulating the necessary experience with aseptic and sterile technique to begin serious experimentation. The development of technical skills is a process which will continue. During 1983, it will include formal training for two staff members (R. A. Schlenker and E. G. Thompson) at short courses given by cell culture experts at the W. Alton Jones Cell Science Center and the Cold Spring Harbor Laboratory.

Work has continued on an alpha particle irradiation facility designed by Dr. Lloyd but left unfinished. Weak alpha particle sources have been used to determine the variables which most significantly affect dose and to estimate the dose rates which will be obtained when the intense alpha particle source is installed. It appears that irradiation times of a few seconds to a few minutes will provide the range of doses required for cell transformation studies. This will be discussed further during the poster presentations.

Prepared by R. A. Schlenker Argonne National Laboratory

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We expect to commission the irradiation facility at year's end, to be able to conduct cell survival studies by the end of winter and to be ready for cell transformation studies by the end of summer. Our first goal is to repeat Dr. Lloyd's work with cells of lower passage number, thus removing a major criticism of her work. Following that, we plan to determine transformation frequency as a function of alpha particle beam angle, an experiment suggested by theoretical studies of Dr. J. Marshall, which predict a dependence of frequency on angle. If verified, this would indicate that the shapes of the dose response curve for bone cancer are different for surface seekers, e.g., ^{239}Pu than for volume seekers, e.g., ^{226}Ra. Such a difference has already been observed in dogs and would be important for the prediction of cancer risk in humans.

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Fact Sheet on

Non-Stochastic Effects of ^{226}Ra and ^{228}Ra in the Human Skeleton

(Total effort 0.6 p-y)

A comparative study has been carried out of graded responses determined by evaluation of skeletal radiographs in two groups of former radium dial workers exposed at an average age of 20 yr.[1] All were female. One group was employed in Illinois in 1921-1937 and was exposed predominantly to ^{226}Ra. The other was employed in Connecticut in 1917-1935 and was exposed predominantly to ^{228}Ra before 1926. The higher systemic intakes of radium occurred prior to 1926 in both locations. Consequently, at the levels of dosage associated with clinically-significant radiographic lesions, the study virtually constituted a comparison of the separate effects of the two radium isotopes.

The skeleton was divided into 20 radiographic areas, each of which was rated numerically for changes attributable to radium:[2,3] 0 for no effects; 0.5 for barely detectable changes such as minimal trabecular alteration; 1, 2, or 3 according to the extent of radiolucent and dense bone necrosis, occurring most frequently in long bones and skull; and 4 for large areas of aseptic necrosis, occurring generally in areas of greatest mechanical stress and particularly in the heads of the femurs. The ratings for the twenty skeletal areas were added to obtain the "reduced score" for the skeleton, as opposed to the "classical score", which would have included ratings of 4 for pathological fracture and 5 for malignancy of bone or of paranasal sinuses or mastoids.[3] Means and standard errors of the reduced scores in ten classes of systemic intake or dosage D and six classes of time t post exposure were determined for the two groups of dial workers. The data at t 40 yr (mean = 50 yr) and a function of dosage and time fitted to all the Illinois data only, but which seems to describe the Connecticut-worker (^{228}Ra) data also, are shown in Fig. 1.

The degree of change in an individual skeleton falls into one of five categories corresponding to the reduced score: negative (0), minimal (0.5 to 8); mild (8.5 to 16), moderate (16.5 to 25); and advanced (> 25). A rating of 4 or 5 in any area places the case in the advanced category irrespective of the reduced score. The vast majority of workers at intakes < 10 μCi showed a negative response. The low frequency of scores in the minimal category at intakes < 10 μCi varied unsystematically among the dosage and time classes and showed an average frequency similar to that observed in unexposed subjects.

The relationship was investigated between the dosage D and the percentage of exposed workers in the two groups combined whose skeletal radiographs at t > 30 yr (mean = 42 yr) were rated in a category of change above minimal (score > 8). This relationship was described both by a lognormal cumulative frequency distribution and by a function that was virtually linear at dosages < 10 μCi. The value of χ^2 for the fit of the former was 3.99 ($n = 2$, $P > 0.1$) and for the latter it was 6.35 ($n = 3$, $P > 0.05$). The dose-response data and fitted functions are shown in Fig. 2. The reduced-score data suggested a "practical threshold" for clinically-significant radiographic lesions of the order of 1 μCi systemic intake of either radium isotope. Pathological fractures were not observed at dosages below 280 and 180 μCi in the Illinois and Connecticut groups, respectively. Both dosages corresponded to an absorbed dose of about 2600 rad to the skeleton. Above these dosages, 43% of the workers in each group had one or more pathological fractures.

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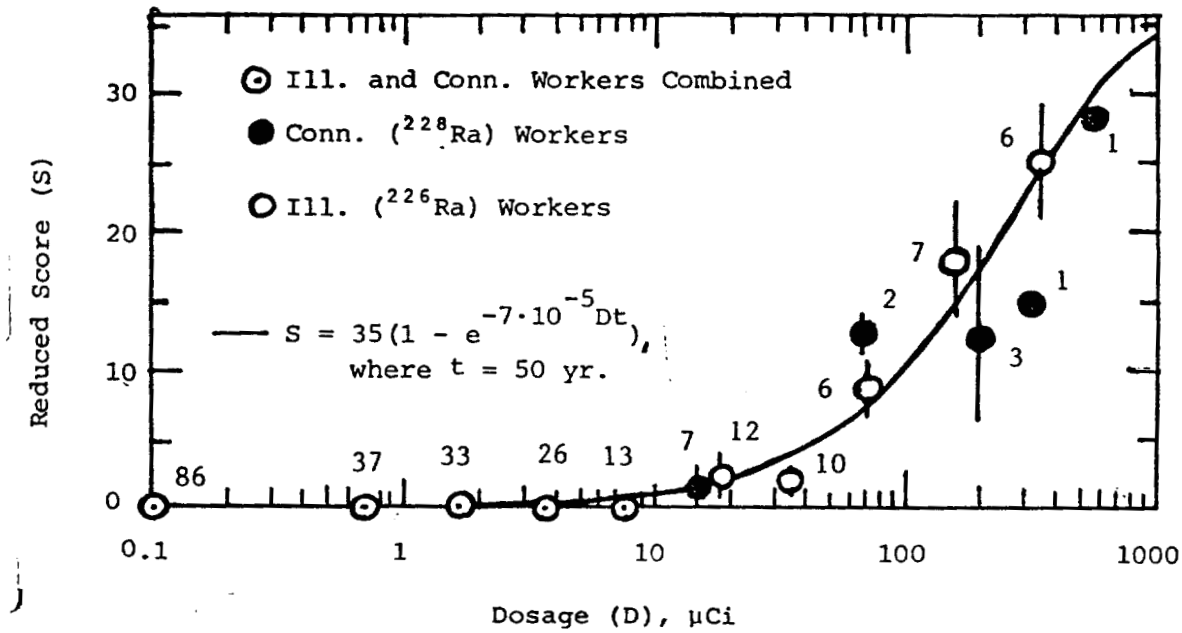

FIG. 1. Reduced Score at 50 yr post exposure vs. dosage. Number of workers whose data were averaged to obtain each data point is indicated. Vertical lines are ± 1 standard error.

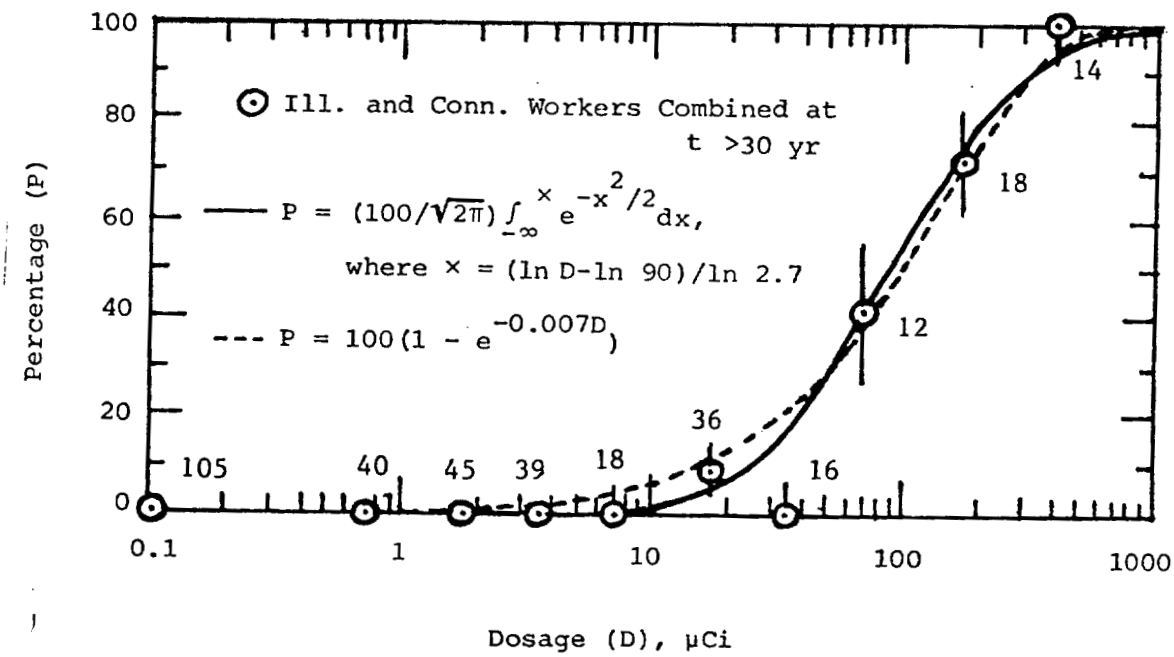

FIG. 2. Percentage of exposed workers showing greater than minimal change (reduced score > 8) vs. dosage. Vertical lines are ± 1 binomial standard error. The solid curve is the lognormal cumulative frequency distribution with a geometric mean of 90 μCi and a geometric standard deviation of 2.7.

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CENTER FOR HUMAN RADIOBIOLOGY

Fact Sheet on

Radium Exposure Registry
(Total effort 5.0 p-y)

Industrial and medical usage of radium began in the U.S. about 1913. Workers were heavily exposed in the radium dial and other industries until 1925, when the toxic effects of radium became known and safety measures were adopted. Therapeutic exposures occurred through 1930, along with lesser occupational exposures. The radium dial industry revived during World War II, creating a large cohort with lower exposures. The early radium cohort is the only large group of humans exposed (non-therapeutically) to internally deposited alpha-emitting radionuclides at levels causing unequivocal health effects. This permits dose-response estimates. The later cohorts both validate the lower end of the dose-response curves and are invaluable as low-dose controls in the analysis of other cancers. Knowledge of the effects of alpha-emitters is vital in predicting health effects in the nuclear power industry, especially with respect to fuel reprocessing, and in the nuclear defense industry. Exposure standards for plutonium and other alpha-emitters have been set on the basis of human experiences with radium. Radium is currently of major concern as a trace substance in water supplies.

Current findings. The principal effects of radium are osteosarcomas, carcinomas of the paranasal sinuses and mastoids, and skeletal changes such as bone necrosis and coarsening of trabeculation. Over 80 cases of bone sarcoma and over 30 cases of sinus or mastoid tumor have been identified. A recent finding is that time-to-tumor relationships for osteosarcoma have been incorrectly stated: age at appearance rather than induction period relates to dose. This is important in the definition of "practical thresholds" based on lifespan.

The excess multiple myeloma among early dial workers has been shown to be more closely associated with gamma than radium exposures.[1] Erythrocytic leukemia has been identified as an outcome of chronic internal or external irradiaton, but only in males. A previously reported association of breast cancer to radium has been shown not to exist.[1] Among females, it is clear that there has been no excess of leukemia.[2] Study of the relationship between radium body burdens and fertility[3] is now a separate project.

Status of fieldwork and follow-up. From records of earlier radium research projects and efforts of the Center since 1969, over 6000 persons exposed to radium have been identified. Most were in the radium dial industry. The following table summarizes the current follow-up status of radium cases:

Prepared by J. H. Stebbings

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	Alive		Deceased		Lost and	
	Measured	Unmeasured	Measured	Unmeasured	Unlocated	Total
Dial workers						
before 1930	513	157	482	530	355	2037
after 1930	944	478	95	286	475	2278
Non-dial radium	56	32	120	168	67	443

Not included above are approximately 1000 exposed and 600 non-exposed workers from U.S. Radium Co. in Bloomsburg, Pennsylvania, on whom intensive follow-up began in late August, 1982. A random sample of these are being brought in for measurement. In addition, all living subjects in the data base are followed by mail and phone every 18 months.

Future plans. We will continue to register all authenticated cases of radium exposure, so that potential for future investigations is maintained. Some research interest has reverted to osteosarcoma and head carcinomas, since the dose correlations with time-to-tumor imply practical thresholds and the correlations clearly have not been carefully investigated. Further documentation of the negative breast cancer findings is of priority. A mortality analysis of cancer in the male radium cases is also planned.

Two projects have been separately identified: the studies of reproductive effects in the dial painters, and a lung cancer study which particularly involves an effort to estimate radon daughter exposures in the workplace.

Two long-term investigations still need to be furthered: statistical reconstruction of underlying populations to resolve the "objective-nonobjective" ascertainment question, and epidemiological investigations into factors associated with radium retention beyond duration of employment. Analyses suggest that current radium levels show associations with factors other than duration and external radiation.

References

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CENTER FOR HUMAN RADIOBIOLOGY

Fact Sheet on

γ-Ray Spectrometric Analysis of Thorium Daughters in Vivo by Least Squares

(Total effort 0.2 p-y)

Introduction

At least five of the decay products of ^{232}Th have half-lives which are long enough (e.g. >1 hour) for them to translocate in vivo before they decay. In order to determine the radiation dose received by a patient containing ^{232}Th, it is therefore necessary to have some information on the degree of equilibrium present among the daughters in vivo. The daughters are not expected to be in equilibrium in vivo because of their different chemical natures and therefore metabolic behavior, and also because of exhalation of ^{220}Rn. Fortunately, such information can be obtained by careful analysis of γ-ray spectra observed in vivo.

Method

In the entire ^{232}Th decay chain, appreciable γ-ray emission occurs at only two points: ^{228}Ac, and ^{212}Pb and its daughters. Note that ^{228}Ac and ^{212}Pb precede and follow ^{220}Rn, respectively. The amount of ^{212}Pb present in vivo is necessarily equal to the fraction of its precursor, ^{220}Rn, which was not exhaled but retained. By adding the amount of ^{220}Rn retained to the amount exhaled (measured by collecting and analyzing a breath sample), the total amount of ^{220}Rn is obtained. Because of its 55-sec half-life, the amount of ^{220}Rn is equal to the amount of its parent, ^{224}Ra present in vivo. The amount of ^{224}Ra present can then be compared with the amount of its precursor, ^{228}Ac present in vivo, as determined from the γ-ray spectrum.

If the ratio of ^{224}Ra to ^{228}Ac is equal to 1.0, no ^{224}Ra is being lost by excretion. If no ^{224}Ra is being lost, it is presumed that no ^{228}Ra is being lost, and consequently that it is in equilibrium with its parent ^{232}Th. The finding that the daughters are in equilibrium in vivo is also evidence that the material inhaled was monazite, rather than separated thorium.

The amounts of ^{228}Ac and ^{212}Pb present are determined by least squares analysis of the γ-ray spectrum. Briefly, the observed spectrum is assumed to be a linear combination of standard spectra of various nuclides which are stored in the computer's memory. The amounts of the standard spectra which must be added to give the best fit, channel-by-channel, to the observed spectrum are then found. An example is shown in the figure (overleaf).

Results

This technique has been applied to γ-ray spectra from 23 thorium cases. The weighted mean ratio of ^{224}Ra to ^{228}Ac was 0.97 ± 0.02, with a range of

Prepared by R. E. Toohey

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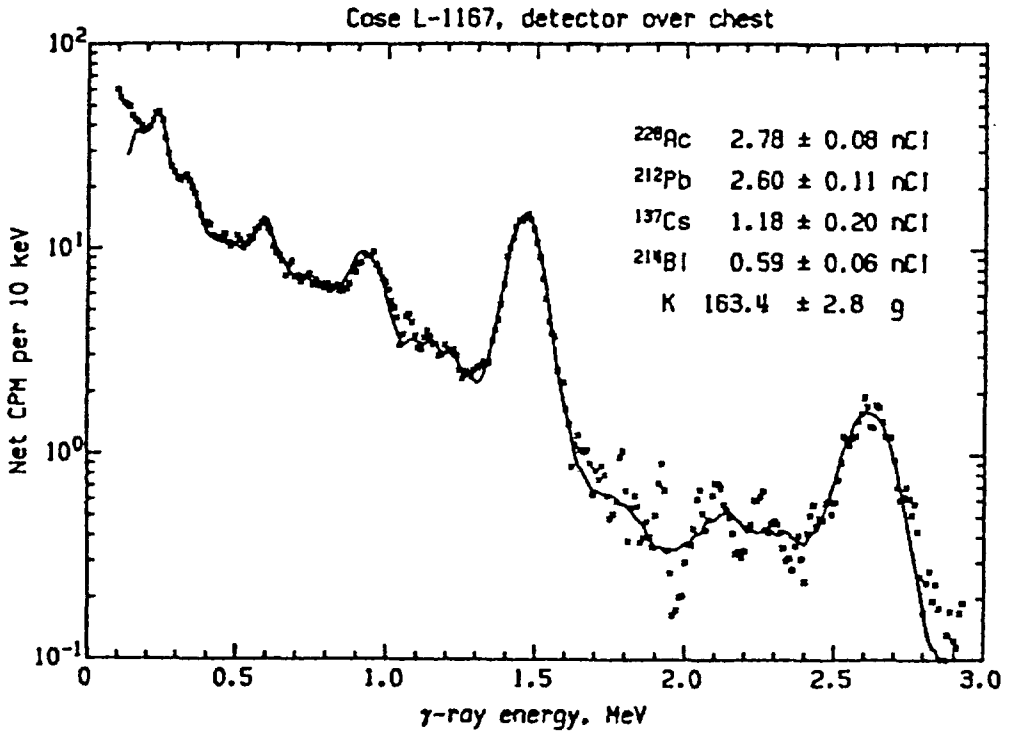
0.71 ± 0.15 to 1.48 ± 0.42, and a variance ratio of 0.91. Thus it appears that on the average, little or no ^{224}Ra is being excreted by these subjects. Consequently we may assume that there is little excretion of ^{228}Ra, and that the daughters of ^{232}Th are in equilibrium with each other and their parent. It therefore seems likely that these cases inhaled monazite, rather than separated thorium. However, confirmation of these results by radiochemical analysis of tissues obtained at autopsy of former thorium workers is required.



The least-squares fitting technique applied to the γ-ray spectrum of case number L-1167. The primary component of the spectrum is the 1.46-MeV γ-ray from ^{40}K. The ^{228}Ac γ-rays occur mostly around 0.9 MeV, while the ^{212}Pb content is largely based on the 2.62-MeV γ-ray arising from the decay of ^{208}Tl. Radon (^{222}Rn) daughters and ^{137}Cs (fallout) were also included as standards.

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Fact Sheet on

Detection Efficiencies for Low-Energy Photon Emitters - Comparison of the Livermore Phantom and Results In Vivo

(Total effort 0.3 p-y)

Introduction

The calibration of detector systems for the assessment of internal deposition of transuranic elements is a formidable problem. Because many of these nuclides are α emitters, their maximum permissible organ burdens are small, and their photon emissions are characterized by low abundance and low energy. In the case of ^{239}Pu for example, uranium L x rays with a mean energy of 17 keV are emitted following only 4.6% of the α decays; at this energy, the half-value thickness of soft tissue is about 7 mm. Therefore the emission is very sensitive to variation in chest wall thickness. It can be shown that for an average-sized individual, only one or two x-ray photons per minute will escape the anterior chest surface from a maximum permissible lung burden of 16 nCi of ^{239}Pu. Consequently, the detector system must be calibrated as accurately as possible. An interlaboratory calibration exercise in 1972 showed that most calibration methods in use at that time were woefully inadequate.[1]

The Livermore Phantom

In response to the above findings, a realistic thorax phantom was designed and constructed at Lawrence Livermore National Laboratory. Design criteria for the phantom included that it be the size of the average U.S. male plutonium worker, have lungs, livers and tracheobronchial lymph nodes which could be loaded with known amounts of activity, have a chest wall adjustable both for total thickness and fractional adipose tissue content, and be constructed entirely of materials which are tissue-equivalent in their photon attenuation properties at 17 keV.[2] A prototype phantom was constructed and circulated among participating laboratories beginning in 1978. Production phantoms are now available from a commercial supplier and are being used at most, if not all, U.S. laboratories which have responsibility for monitoring plutonium workers for internal contamination. The only difference between the prototype phantom and the production models is that the former contained a human rib cage obtained from a cadaver, while the latter contain rib cages made of bone-equivalent plastic.

Phantom Use and Validation

Detectors are calibrated for a given individual by first obtaining a calibration curve from the phantom covered with muscle-equivalent chest plates. Adipose-equivalent chest plates are used to determine the appropriate attenuation coefficient for adipose tissue. The individual's chest wall thickness is determined either from published correlations with height and weight,[3] or ultrasonically. The percent adipose composition of the chest wall is similarly determined from correlations with various body dimensions,[4] or ultrasonically. The calibration factor for the muscle thickness of the chest

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Prepared by R. E. Toohey Argonne National Laboratory

wall is interpolated from the muscle-equivalent calibration curve, and this value (cpm/μCi) is then decreased by attenuation through the appropriate adipose-equivalent thickness.

The validity of this procedure and of the phantom in general is being investigated by comparing calibration factors predicted by the phantom with those obtained in vivo. Volunteers have inhaled an aerosol labelled with ^{92m}Nb, and then visited various laboratories where the photon emission from the chest was measured. ^{92m}Nb emits 16-keV zirconium K x-rays, and also a 934-keV γ-ray, which enables the chest content to be determined by standard whole-body counting techniques. At the Center for Human Radiobiology, the x-ray emission from each subject's chest was measured with a 180-mm diameter phoswich detector. Predicted counting efficiencies (counts recorded per x-ray emitted in the lungs) were obtained from the phantom containing lungs loaded with a known amount of ^{92m}Nb. The results are shown in the table:

Subject	Chest wall thickness, mm Muscle	Adipose	Efficiency x 10^4 Predicted	Observed
DN	15.2	4.8	6.54	5.30
WMH	13.1	7.9	7.60	5.91
JNP	15.1	7.9	5.07	5.50
GWC	17.7	10.3	2.43	2.16
MNF	18.6	11.4	1.84	2.21
RET	15.2	17.8	2.07	2.17
ALA	17.8	19.2	2.15	2.30

The mean ratio of predicted to observed values for the seven subjects is 1.0 ± 0.2, indicating that on the average, the phantom predicts counting efficiencies quite well; however there are still considerable variations in its applicability from individual to individual. Nevertheless, it is a significant improvement over earlier calibration methods, which were in error by factors of three or more.[1]

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CENTER FOR HUMAN RADIOBIOLOGY October 1982

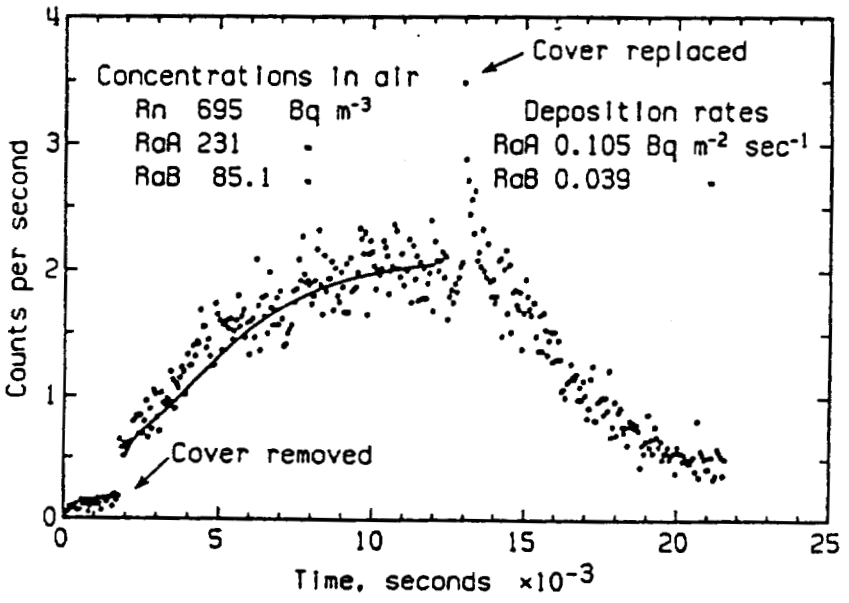
Fact Sheet on

Measurements of the Deposition Rates of Radon Daughters on Indoor Surfaces

(Total effort 0.5 p-y)

Introduction

We have measured the deposition rates of radon daughters on indoor surfaces by exposing the window of a proportional counter to the air of a house with high concentrations of radon and its daughters. A series of consecutive counts, each one minute in duration, was made and the data are shown in the figure. The results of a least-squares fit of the deposition rates of RaA (^{218}Po) and RaB (^{214}Pb) and the best-fitting curve obtained thereby are also shown.



Analysis

The removal of radon daughter products from the air by deposition on surfaces can be characterized by a rate constant, λ_d (sec^{-1}); it can be shown that this parameter is equal to the surface-to-volume ratio (m^{-1}) of the location in question multiplied by a parameter known as the deposition velocity, v_g ($m\ sec^{-1}$), where v_g equals the area deposition rate ($atoms \cdot m^{-2} \cdot sec^{-1}$) divided by the air concentration ($atoms \cdot m^{-3}$).[1] We can

Prepared by R. E. Toohey Argonne National Laboratory

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obtain values of v_g from our deposition rate values found above and the concentrations of RaA and RaB which were measured during the deposition experiments.

However, it is first necessary to determine what fraction of the daughters is free, or unattached, and what fraction is attached to the atmospheric aerosol, since the deposition velocities, v_g^u and v_g^a, of the two species differ by about two orders of magnitude.[1] For RaA, a value for the unattached fraction of about 0.1 is reasonable,[1] and this yields a value for v_g^u of 4.5×10^{-3} m sec^{-1}. This value is in excellent agreement with values reported by other workers.[1] Note, however, that it assumes that all the deposited activity is due to the unattached fraction. This assumption is justified based on other workers' measurements of v_g^a, the deposition velocity for aerosol particles. The maximum value reported is 1×10^{-4} m sec^{-1},[1] and so the maximum deposition we could have obtained due to attached RaA would have been 0.021 Bq m^{-2} sec^{-1}, less than 20% of the observed rate.

In the case of RaB, the unattached fraction is expected to be negligible.[1] However, our data suggest a different conclusion. For a value of v_g^a of 1×10^{-4} m sec^{-1}, the maximum deposition of attached RaB we could observe is 0.0085 Bq m^{-2} sec^{-1}, vs the actual value of 0.039 Bq m^{-2} sec^{-1}. If we assume that unattached RaB deposits with the same deposition velocity as unattached RaA, we find that some 10% of the RaB in the air must be unattached. This surprising finding may be due to an extremely low aerosol concentration in the house, leading to a longer mean lifetime for unattached species, and also to the detachment of RaB from aerosol particles because of recoil following its production by the α-decay of attached RaA.

Reference

1. W. Jacobs, Activity and potential α-energy of ^{222}Radon- and ^{220}Radon-daughters in different air atmospheres, Health Phys. 22, 441 (1972).

0019832

CENTER FOR HUMAN RADIOBIOLOGY October 1982

Fact Sheet on

Atmospheric Concentrations of Rare Earth Elements at the Lindsay Chemical Company

(Total effort 1.0 p-y)

The Center for Human Radiobiology is currently engaged in an assessment of possible health effects of employment in the thorium refining industry. An important part of this study is the determination of thorium and rare earth exposure conditions at a thorium refinery located in West Chicago, Illinois, and the resultant uptake in the workers.

The West Chicago plant was operated by the Lindsay Light Company and its corporate successors, Lindsay Chemical Company and Kerr-McGee Chemical Corporation, from 1932 until 1973. It is presently an empty shell being stripped and decontaminated for eventual demolition. Fortunately, we have obtained approximately 10,000 air filter samples which were collected by Lindsay from 1962-1973. We have also obtained records on the sampling date, location in the plant, and alpha counting data corresponding to each filter. Properly interpreted, these records provide a survey of the time and location distribution of airborne thorium and in some cases thoron as well. Since the plant also produced rare earth chemicals (in fact, almost exclusively in its last years), health effects in workers may be due to these chemicals instead of, or as well as, thorium. Analysis of the filters for these elements can provide information on their airborne concentrations.

We have determined by energy dispersive x-ray fluorescence spectrometry the amounts of La, Ce, Pr and Nd directly on a group of 14 filters collected between 1967 and 1970, and by atomic absorption spectrophotometry with electrothermal atomization in a graphite furnace, the rare earth elements, La, Nd, Sm, Eu, Gd, Dy, Ho, Tm and Yb and the rare-earth-like elements, Sc and Y, in an additional 20 air filter samples. The median concentrations and the ranges are shown in the table. That the median values are near the lower ends of the ranges is due to the presence of only a few extreme values at the upper ends of the ranges. These medians are 3 to 4 orders of magnitude greater than those found in urban aerosols, which are usually in the range of 0.001 to 10 pCi/L.[2,3] Recent calculations indicate that when the data are grouped by time and location, the rare earth contents of the filters are correlated with the radioactivity measurements.

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0019833

Concentrations of rare earths, scandium and yttrium in 34 air filter samples.

Element	Concentration, ng/L Median	Range
Sc	0.14	0 - 3.8
Y	5.3	0.4 - 2040
La[a]	147	0 - 4140
Ce[b]	12.3	0 - 108
Pr[b]	6.1	0 - 11.6
Nd[a]	14.1	0 - 8950
Sm	4.6	0 - 1590
Eu	0.25	0.01 - 22
Gd	17.5	1.5 - 1280
Dy	1.3	0.08 - 260
Ho	1.7	0.1 - 70
Tm	0.081	0.0006- 16
Yb	0.022	0.002 - 4.5

[a]These elements were determined in 14 samples by x-ray fluorescence spectrometry and 20 by atomic absorption spectrophotometry.

[b]These elements were determined in 14 samples by x-ray fluorescence spectrometry only.

References

1. U. S. Nuclear Regulatory Commission, Rules and Regulations, Title-10-Chapter 1, Code of Federal Regulations, Part 20, Standards for protection against radiation, U.S. Government Printing Office, Washington, D.C. (codified and reissued September 1978).

2. J. A. Cooper, Battelle Northwest Laboratories Report BNWL-SA-4690.

3. H. J. M. Bowen, Environmental Chemistry of the Elements (Academic Press, London, 1979), Chapter 13.

CENTER FOR HUMAN RADIOBIOLOGY October 1982

Fact Sheet on

Dosimetry of ^{224}Ra in Bone
(Total effort 0.4 p-y)

Introduction

Since the early 1940's, intravenous injections of ^{224}Ra have been made in Europe to relieve pain from ankylosing spondylitis and bone tuberculosis. Several thousand patients have been treated and some have contracted bone cancer. Complete retention of ^{224}Ra daughters is assumed when calculating dose. The assumption is suspect, however, because most of the carcinogenic dose is delivered from thin radium deposits on bone surfaces from which highly mobile daughters, such as the noble gas ^{220}Rn, may readily escape. This possibility casts doubt on the dosimetry and on the accuracy of the dose-response data. It also raises questions about the dosimetry of ^{228}Ra in our subjects because much of the bone cell dose is due to ^{224}Ra ingested with dial paint or produced on bone surfaces following ^{228}Ra decay.

To improve the dosimetry, we are studying the retention on bone surfaces of two daughter products, ^{220}Rn and ^{212}Pb, following ^{224}Ra injection into dogs. These daughters were selected because they determine, to a large extent, the retentions of all other daughters. Three young adults from the University of Utah beagle colony were injected with about 100 μCi ^{224}Ra nearly in equilibrium with its daughters. Two other dogs were injected with similar amounts of ^{212}Pb or ^{226}Ra. The dogs were sacrificed 24 hours after injection and retention was studied, in vacuum or air, by alpha spectrometry of the endosteal bone surfaces.

^{220}Rn

Because of its 56-second half-life, ^{220}Rn retained in vivo disappears soon after death, and only the retention in vitro can be determined. The latter increases with the duration of measurement, the rate of increase being much higher in vacuum than in air. The increase is associated with water loss from bone and is consistent with other observations, e.g., ^{222}Rn retention is greater in dry bone samples than in wet ones and is greater in vitro, when tissues may be dessicated, than in vivo. In the dog injected with ^{226}Ra, 3% of the ^{222}Rn produced at bone surfaces was retained in vivo but after 13 days in vacuum about 30% was retained.

In air or vacuum, all of our samples were much drier than in life and it seems certain that the observed retention exceeded the retention in vivo. Average values for several bone samples are presented below as fractional retention, $(^{220}Rn/^{224}Ra)_{vitro}$. The letters A and V designate air and vacuum measurements respectively.

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Dog (Method)	$(^{220}Rn/^{224}Ra)_{vitro}$
T28Q5 (V)	0.58
T29Q5 (V)	0.76
T30Q5 (V)	0.58
T30Q5 (A)	0.30

In dog T30Q5, retention was higher in vacuum than in air and the water content of the samples was lower. Based on the association between retention and water content, we believe the following to be correct: retention in vivo < retention in vitro measured in air < retention in vitro measured in vacuum.

The assumption of complete retention implies $(^{220}Rn/^{224}Ra)_{death} = 1$, a value which is not supported by our observations.

^{212}Pb

a. Retention

Much of the ^{212}Pb present at death survives to the time of measurement. By application of the radioactive decay equations, the fractional retention at death $(^{212}Pb/^{224}Ra)_{death}$ can be determined from the data. Average values are listed below, based on the assumption that 30% of the ^{220}Rn produced between sacrifice and death is retained.

Dog (Method)	$(^{212}Pb/^{224}Ra)_{death}$
T28Q5 (V)	0.7
T29Q5 (V)	0.3
T30Q5 (V)	0.3
T30Q5 (A)	0.4

If retention were complete $(^{212}Pb/^{224}Ra)_{death}$ would exceed 1. This is clearly not the case here.

b. Role of injected lead.

Radium-224 injection solutions often contain much ^{212}Pb. To determine if this is a significant factor in the dosimetry, lead uptake on bone surfaces was determined following injection of ^{224}Ra and of ^{212}Pb. The values listed below are proportional to the average surface concentration at death normalized to the amount of ^{212}Pb injected. Dog T28Q5 received nearly equal amounts of ^{224}Ra and ^{212}Pb and dog T21L5 received almost pure ^{212}Pb.

Dog (Method)	Uptake
T28Q5 (V)	1.0
T21L5 (V)	0.1

Clearly, the total amount of lead for T28Q5 greatly exceeds that attributable to injected lead, and we conclude that ^{212}Pb in the injection solution is of little importance for dosimetry.

October 1982

CENTER FOR HUMAN RADIOBIOLOGY

Fact Sheet on

Theory of the Induction of Bone Cancer by Ionizing Radiation
(Total effort 1.5 p-y)

In our attempt to find a model of bone cancer induction which is consistent with the data on bone cancer, we have extended the Marshall-Groer[1] model of 1977 (two initiating events in one cell) to the level of the DNA molecule in order to test for consistency with fundamental mechanisms and data on ionization as they could be relevant for deletion of information from the DNA strand.

Extension to the level of DNA suggests that we calculate the probability of generating in or near the molecule clusters of ionizations that are sufficiently dense to disrupt it. While such questions have been addressed in the literature before, we soon found that the input data used from physics were very inadequate. The cross sections and LET values used would only poorly represent even the physics data. We found that we had to begin almost from scratch in constructing reliable ionization distribution functions. As Ra, Sr and Pu are alpha and beta emitters with known spectra, we began by constructing accurate ionization cross sections for all the required energies for alpha and beta particles. For this, we used experimental data in the first place. Theory was used in those places where data were inadequate or for interpolation purposes.

For the beta rays, this has led to a very accurate distribution function for the single ionization distribution on the main track and on all subsidiary delta-ray tracks down to fourth order. This distribution function has been subjected to a large number of tests and satisfies all the known physical boundary conditions such that now it can be used to make reliable biological calculations. Specifically, over the past year this distribution was constructed to satisfy the criteria stemming from theory, including the Bethe theory for electron-atom collisions, with full account of relativistic kinematics. It fits all the accurate experimental data on differential cross sections, integrated cross sections, stopping power and energy per ion pair.

For the problem of cancer initiation, this is being used in the following way: Assuming a Poisson distribution for the incidence of successive ionizations (an assumption to be tested), we have combined our results for the alpha and the beta particles and have computed (in a preliminary way) the frequency and cross section for the incidence of two successive ionizations on the main track, on any delta ray track or on the main track and on the first delta ray track, within a given distance. If one makes the probably simplified, working hypothesis that such double ionizations have anything to do with cell killing, we obtain an RBE versus LET curve which, interestingly enough, is quite comparable to the ascending branch proposed by Barendsen[2] on the basis of biological investigations and to those published in ICRU Report

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16 (p. 15).

It should also be mentioned that this summer our analytical calculations were compared with the much more extensive (and expensive) Monte Carlo calculations carried out by H. Paretzke and his group at Neuherberg, Germany. The comparison showed some advantages of the Monte Carlo method but also convincingly showed the much greater flexibility and comprehensive value of the analytical method.

References

1. J. H. Marshall and P. G. Groer, A Theory of the Induction of Bone Cancer by Alpha Radiation, Radiat. Res. 71, 149-192 (1977).

2. G. W. Barendsen, RBE-LET Relations for the Induction of Reproductive Death and Chromosome Aberrations in Mammalian Cells, Proc. Sixth Symp. on Microdosimetry, Brussels, Belgium, May 22-26, 1978, p. 55.

0019838

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CENTER FOR HUMAN RADIOBIOLOGY

Fact Sheet on

CHRIS: The Center for Human Radiobiology Information System
(Total effort 1.0 p-y)

CHRIS is an unnormalized relational database system which was designed in 1970 by a programmer in what is now known as the Computing Services Division at ANL. This design was selected because it provided features not available at that time in any commercial system. The data manipulation language is imbedded in a versatile high-level language (PL/1), and the source code was available for adding future enhancements and modifications. The current implementation includes the following features:

1. Read/Write password protection of a scrambled data file so that privacy of sensitive medical data is assured.

2. A variable number of records per KEY (a unique identifier of each person under study) so that longitudinal studies are possible.

3. A sophisticated query language capable of one-to-many and many-to-many relationships.

4. A powerful report generator that handles multi-line column headings as well as varying length character and numeric data types.

5. An efficient multi-file update facility that incorporates data logging, selective backup and restoration. In addition, a data validation feature ensures that all changes are being made to the proper KEY. This feature is required for a high degree of data integrity.

6. On-line display of the data for any KEY in any file.

7. Automatic re-utilization of all disk storage space.

8. Data types which include varying length character, floating point, fixed decimal and "missing values".

9. Upward compatibility of computer programs is achieved through a structured program design which isolates the data access method. This ensures separation of the data base from changes in either the hardware or software of the operating environment.

CHRIS is an unusually versatile and powerful database system which has successfully responded to all requests since its inception. It has continued

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to grow and become even more powerful as new features and enhancements are added. CHRIS is very easy to use and does not require any training or expertise in the use of computers. Extensive error checking is provided at the time of the initiation of the query so that approximately 95% of all requests for data are answered without error.

An interface has been developed between CHRIS and the statistical programs available in the Statistical Analysis System (SAS). This interface is used to prepare the data needed for lifetable, morbidity, or mortality analyses using programs such as those of Monson or of Marsh.

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