(E)

OOK AT THE OLD DATA

ibution of americium-241
tional Laboratory, Radio-
-7489, 19-23 (1968).

ation of retention patterns
injections 33 years earlier:
roup Annual Report ANL-

is: Dynamics of ^{241}Am in
nship between behavior of
us: in *Delayed Effects of*
et al., editors), University

F. DOUGHERTY: Speculat-
Phys. *19*:601-610 (1970).

od. Über die Ursache des
27:1-245 (1927).

osis. Selected Methods for
Year to Maturity: Univ.

Entwicklung des Muskel-
I. Das Skelett: Nova Acta
Forsch. *46*: No. 3, 437-471

AFUMA: An experimental
^{238}Pu, ^{239}Pu, ^{241}Am, and
ogical Implications of the
ngton, Sept. 26-29, 1971.

OSE: Plutonium deposition
Biological Implications of
ington, Sept. 26-29, 1971.

William D. Norwood *

703931

U.S. TRANSURANIUM REGISTRY: PROGRESS AND EXPECTATIONS

INTRODUCTION

Since the transuranium elements are both very hazardous and extremely useful, it is vital that we know as much as possible about the disposition and effects of these elements when they accidentally gain entry to the human body. It is anticipated that there will be a rapid increase in the use of the already-discovered elements, and that in addition to present transuranium elements with atomic numbers from 93 to 103, many new elements will be discovered with atomic numbers far above 103.[1, 2] In anticipating the increasing benefits from these elements, we must be ever aware of their potential hazards and continue a most vigorous program of evaluating and minimizing the hazard to employees and to the environment in general. To assist in the evaluation of these hazards, the National Plutonium Registry was authorized by the U. S. Atomic Energy Commission in August 1968. It is operated by the Hanford Environmental Health Foundation with the cooperation of Battelle Northwest. The name of the Registry was recently changed to U. S. Transuranium Registry to indicate that all transuranic elements are included, since the original title appeared to exclude transuranic elements other than plutonium. Since other nations have indicated an intention to establish similar registries, use of the term United States better delineates the area covered than does National. This paper discusses the purpose, progress and expectations of the Registry.

* Hanford Environmental Health Foundation, Richland, Wash. 99352
Supported by the U. S. Atomic Energy Commission.

NEED FOR REGISTRY

Animal vs Human Experiments

Maximum information must first be obtained by subjecting a variety of laboratory animals to the effects of the various compounds of transuranium elements, administered via all possible routes of entry. Our present permissible limits for plutonium are based on the results of such experiments, still in progress, plus information on the toxicity of radium in animals and in man. The metabolism of plutonium in the body differs greatly from that of radium, especially under the usual methods of entry: by inhalation and via wounds. Extrapolation from animals to man leaves much to be desired. For example, Evans observed that the concentration of radium to produce bone sarcomas in rats was 400 times as great as that required in man.[3] Hence, it is highly desirable to determine actual toxicity of the transuranium elements in man.

Experiments Using Humans

Many years ago, Langham and associates administered small quantities of plutonium citrate intravenously to men who were suffering from incurable diseases, and determined the daily output of plutonium in urine and feces over a comparatively long period of time.[4] The decay curves relating input with daily output are reasonably accurate for cases in which plutonium citrate is injected in the veins. However, while many accidental depositions have occurred, I do not know of one in which plutonium citrate was injected into a vein. Deposition is usually by inhalation or via flesh wounds, and the plutonium is usually in the form of the metal, the oxide, the nitrate or the fluoride. Most of these compounds are poorly soluble in the body fluids and are metabolized in the body quite differently than is the intravenously-administered soluble citrate.

Animal Experiments

In animals receiving variable sized doses of plutonium by inhalation and through wounds, malignant disease has been produced in lung, bone, liver, nasal sinus, lymph node, skin and subcutaneous tissue.[5, 6, 7, 8, 9, 10]

HEALTH RECORD

To our knowledge no serious injury which might be attributable to plutonium deposition at work has occurred to date to man. However, a lesion described as probably precancerous resulted from a relatively

small subcutaneous depo
these things, it seems hig
plutonium to normal hun
metabolism of this eleme
of the extremely long ha
and the long residence ti
the volunteer. Pu-237 ha
239 in human tests becau
ever, it is difficult to pre
is so great that amount
would be too minute to

ESTIMATE OF INT

While many inter
radiation measurable out
and many of the other
ing, cannot escape from
organ content. Estimates
fecal excretion may be
culates. Relationship of
work exposure may be
Carefully conducted stu
epidemiological studies,
the degree of probability
tion of a transuranium
reasonably conclude that

FUNCTION OF RE

The function of the
exposure to the transurar
worker's subsequent mo
complishes this by coll
material on the health a
posed employees during
bioassay and mortality fir

NEW HORIZONS I

The Registry repres

ned by subjecting a vari-
rious compounds of tran-
routes of entry. Our pre-
d on the results of such
on the toxicity of radium
onium in the body differs
e usual methods of entry:
om animals to man leaves
ed that the concentration
as 400 times as great as
able to determine actual

dministered small quanti-
who were suffering from
put of plutonium in urine
time.[4] The decay curves
ly accurate for cases in
s. However, while many
t know of one in which
m is usually in the form
ride. Most of these com-
d are metabolized in the
sly-administered soluble

plutonium by inhalation
produced in lung, bone,
neous tissue.[5, 6, 7, 8, 9, 10]

might be attributable to
date to man. However,
esulted from a relatively

small subcutaneous deposition of plutonium in a wound.[11] Considering these things, it seems highly desirable to administer minute quantities of plutonium to normal humans by inhalation to determine whether human metabolism of this element simulates that of animals. However, because of the extremely long half life (24,400 years) of plutonium-239 (^{239}Pu) and the long residence time in the body, it could result in undue risk to the volunteer. Pu-237 has been considered as a possible substitute for Pu-239 in human tests because of its short physical half life (45 days). However, it is difficult to prepare in pure form and its specific radioactivity is so great that amounts considered absolutely safe for administration would be too minute to allow comparative human studies to be made.

ESTIMATE OF INTERNAL DEPOSIT

While many internally-deposited radionuclides emit penetrating radiation measurable outside the body, the alpha emission from plutonium and many of the other transuranic elements, while locally very damaging, cannot escape from the body for measuring as an aid in determining organ content. Estimates of internal deposit based upon urinary and/or fecal excretion may be very inaccurate, especially for insoluble particulates. Relationship of delayed illness, such as malignancy, to chronic work exposure may be difficult to determine without long-term studies. Carefully conducted studies in depth of individuals at risk, as well as epidemiological studies, are required to improve our ability to determine the degree of probability that a malignancy has resulted from a deposition of a transuranium element. From the above discussion one may reasonably conclude that there is a real need for a Registry.

FUNCTION OF REGISTRY

The function of the Registry is to ensure that the details of workers' exposure to the transuranic elements of interest can be correlated with the worker's subsequent morbidity, postmortem and mortality record. It accomplishes this by collecting, coding, analyzing and data processing material on the health and health physics aspects of present and past exposed employees during life, and comparing these data with pathological, bioassay and mortality findings after death.

NEW HORIZONS IN PREVENTIVE MEDICINE

The Registry represents one of the most advanced programs in the

field of preventive occupational medicine. Through periodic medical examinations, autopsy studies, morbidity, mortality and nation-wide epidemiological studies, in addition to animal pharmacological studies, every presently known method is being used to determine the metabolism of transuranic elements in man, and what changes may result, at a time when no serious effects have been observed. The U. S. Transuranium Registry differs in this respect from the Radium and Beryllium Registries, which were started only after it was observed that many individuals were seriously ill apparently due to work exposures to these elements. The Registry will try to determine the minimum deposition of the transuranic elements which will cause serious deleterious effects during the lifetime of the worker.

OPERATING METHODS

The Registry endeavors to protect the interests of workers, employers, and the public by serving as a national focal point for the acquisition and dissemination of the latest and most precise information about the effects of transuranic elements on man. This is done by data processing methods of storage and retrieval. Permission forms for release of medical information and to perform autopsies have been developed, in accordance with standard medical practice, and approved by counsel.

The study was started at the U. S. Atomic Energy Commission Hanford Project to evaluate methods of data collection and for securing permission for medical information and autopsy. Such permission is requested by physicians at the time of periodic medical examination. Support for the program has been most gratifying. After 12 months of operation, 770 transuranium workers have been identified and cooperation requested. 747 (97%) have signed medical releases and 205 (27%) have authorized autopsies. In requesting autopsies, major stress is placed on the fact that knowledge gained may help prevent illness in other employees.

Past, present and future transuranium workers constitute the population at risk and these are being compared with employees not at risk, with respect to health, longevity and cause of death. A transuranium worker is defined as one whose occupational activities offer reasonable opportunity to acquire internal deposition from unsealed sources of any of the transuranium elements; quantities greater than those present as a result of non-occupational exposures. Generally at contractor and certain

licensee plants these
assay of urine or fe
ternal whole body o
ing from certain inte
has made provision
time of the day or ni

A library for
and health physics
blished. The inform
trieval.

AUTOPSY TEC

Recent finding
that by far the higl
bronchial lymph no
are inhaled. Concer
and hepatic lymph
and mediastinal no
results may be obta
contents, with the
with 10% formald
lungs and then imm
is then cut in 3 to 5
x-ray film viewer. T
for bioassay.

LABOR RELAT IMPLICATION

Coding and da
of employees. Wher
obtained, all employ
the apprehension w
estimated deposition
burden were includ
positions may be g
techniques and equi
more than a year in
Hanford, there have

licensee plants these are the employees who are placed upon routine bioassay of urine or feces for suspected transuranium elements, or have external whole body or organ counts to detect penetrating radiation emanating from certain internally-deposited transuranium elements. The Registry has made provision for the receipt of information by telephone at any time of the day or night.

A library for accumulating the latest information on the medical and health physics aspects of the transuranic elements has been established. The information on record is being computerized for easy retrieval.

AUTOPSY TECHNIQUES

Recent findings in both laboratory animals and man have shown that by far the highest organ concentration of plutonium is in tracheobronchial lymph nodes, when relatively insoluble plutonium compounds are inhaled. Concentration may be high in other bronchial, mediastinal and hepatic lymph nodes.[12] In usual autopsy procedures, the thoracic and mediastinal nodes are located with difficulty. When feasible, best results may be obtained by securing a complete lung and mediastinal contents, with the exception of the heart. The bronchial tube is filled with 10% formaldehyde to maintain the anatomical structure of the lungs and then immersed in 10% formaldehyde for two days. The lung is then cut in 3 to 5 mm sections with a meat slicer and viewed with an x-ray film viewer. The lymph nodes are thus identified and made available for bioassay.

LABOR RELATIONS AND MEDICO-LEGAL IMPLICATIONS

Coding and data processing methods are used to cloak the identity of employees. Where the full cooperation of contractors and licensees is obtained, all employees at risk are included in the study. This minimizes the apprehension which might be engendered if only employees whose estimated depositions exceed some arbitrary percentage of the permissible burden were included. Under many conditions, estimates of organ depositions may be grossly inaccurate, even though the most acceptable techniques and equipment are used in making the estimate. During the more than a year in which the program has been very actively pursued at Hanford, there have been no labor relations or medico-legal problems that

have come to our attention. The program has the wholehearted support of the Atomic Energy Commission, which is asking for voluntary participation of contractors and licensees. Following the excellent results to date at Hanford, many of the contractors and licensees have entered the program and others will become a part of the program as soon as funds and personnel are available to handle the expansion.

CONCLUSION

Since the transuranium elements are both very useful and extremely toxic, it becomes necessary to study their metabolism and measure their toxicity in man. While human testing would be helpful, it appears to be too hazardous. A registry collects, codes, analyzes and data processes material on the health and health physics aspects of present and past exposed employees during life and compares these data with pathological, bioassay and mortality findings after death. This appears to be the most satisfactory method to determine whether the toxicity findings in animals are applicable to man and to improve our ability to determine internal deposition of the transuranium elements. The Registry's progress to date has been highly satisfactory.

REFERENCES

1. G. T. SEABORG: Mass production and practical applications of actinide elements: Isotopes and Radiation Technology *6*:1, Supt. of Documents, U.S. Government Printing Office (1968).
2. G. T. SEABORG: Prospects for further considerable extension of the periodic table: Isotopes and Radiation Technology *7*:3 (1970).
3. R. D. EVANS: The effect of skeletally deposited alpha-ray emitters in man: Brit. J. of Radiol. *39*:468, 881-895 (1966).
4. W. H. LANGHAM, et al.: Distribution and Excretion of Plutonium Administered Intravenously to Man: Los Alamos Scientific Laboratory Report, LA-1151 (1950).
5. J. F. PARK, W. J. CLARKE AND W. J. BAIR: Chronic effects of inhaled plutonium in dogs: Health Phys. *10*:1211-1217 (1964).
6. C. W. MAYS: Bone-Seeking Radionuclides: Resume of Papers at Symposium on Delayed Effects of Bone-Seeking Radionuclides, Science 161:816 (1968).
7. R. C. THOMPSON: Biological Factors: in *Plutonium Handbook* (O. J. Wick, editor), Gordon & Breach, New York, Vol. II, 787-829 (1967).
8. W. D. NORWOOD AND
tion of plutonium (
Accidents, Proceedir
Eenergy Agency, Vie
9. B. J. MCCLANAHAN,
Late effects of intrac
Northwest Laborato
10. H. LISCO, M. P. FINK
properties of radioa
49:361 (1947).
11. C. C. LUSHBAUGH A
planted plutonium: .
12. J. F. PARK, W. J. BAI
of inhaled. $^{239}PuO^2$
for 1969 . . .
Medicine, Vol. I, Lif
(January 1970).

as the wholehearted support
asking for voluntary parti-
ving the excellent results to
id licensees have entered the
ie program as soon as funds
insion.

th very useful and extremely
etabolism and measure their
l be helpful, it appears to be
analyzes and data processes
aspects of present and past
these data with pathological,
This appears to be the most
e toxicity findings in animals
ability to determine internal
ie Registry's progress to date

...l applications of actinide
nology 6:1, Supt. of Docu-
1968).

considerable extension of the
Technology 7:3 (1970).

deposited alpha-ray emitters
5 (1966).

and Excretion of Plutonium
s Alamos Scientific Laboratory

IR: Chronic effects of inhaled
-1217 (1964).

es: Resume of Papers at Sym-
eeking Radionuclides, Science

Plutonium Handbook (O. J.
York, Vol. II, 787-829 (1967).

8. W. D. NORWOOD AND P. A. FUQUA: Medical care for accidental deposition of plutonium (^{239}Pu) within the body: in *Handling of Radiation Accidents,* Proceedings of a Symposium, Vienna, International Atomic Eenergy Agency, Vienna, Austria, 147-161 (1969).

9. B. J. MCCLANAHAN, E. B. HOWARD, H. A. ROGAN, AND J. L. BEAMER: Late effects of intradermally administered plutonium in swine: Battelle Northwest Laboratory Report 714, Biology Annual Report for 1967.

10. H. LISCO, M. P. FINKEL, A. M. BRUES: Plutonium project: carcinogenic properties of radioactive fission products and plutonium: Radiology *49*:361 (1947).

11. C. C. LUSHBAUGH AND W. H. LANGHAM: A dermal desion from implanted plutonium: Arch. Dermatology *86*:461 (1962).

12. J. F. PARK, W. J. BAIR, E. R. HOWARD AND W. J. CLARKE: Chronic effects of inhaled $^{239}PuO^2$ in beagles: in *Pacific Northwest Annual Report for 1968 to U. S. Atomic Energy Commission,* Division of Biology and Medicine, Vol. I, Life Sciences, Part I. Biology Series, No. BNWL-1050, (January 1970).