NOTICE

**CERTAIN DATA
CONTAINED IN THIS
DOCUMENT MAY BE
DIFFICULT TO READ
IN MICROFICHE
PRODUCTS.**

DECLASSIFIED

UNCLASSIFIED

HW--29615

DE92 007558

BIOLOGY SECTION
RADIOLOGICAL SCIENCES DEPARTMENT

HAZARDS OF EXPOSURE TO TRITIUM AND TRITIUM OXIDE

January 1, 1954

UNCLASSIFIED

AEC RESEARCH AND DEVELOPMENT REPORT

GENERAL ELECTRIC

HANFORD ATOMIC PRODUCTS OPERATION
RICHLAND, WASHINGTON

DISTRIBUTION RESTRICTED TO U.S. ONLY

DECLASSIFIED

UNCLASSIFIED

DECLASSIFIED
UNCLASSIFIED

~~CONFIDENTIAL~~
~~RESTRICTED~~

HW-29615

Health and Safety

This document consists
of 47 pages.

HAZARDS OF EXPOSURE TO TRITIUM AND TRITIUM OXIDE

by

Roy C. Thompson and H. A. Kornberg

Biology Section
Radiological Sciences Department

January 1, 1954

HANFORD ATOMIC PRODUCTS OPERATION
RICHLAND, WASHINGTON

Operated for the Atomic Energy Commission by the
General Electric Company under Contract #W-31-109-Eng-52

~~CONFIDENTIAL~~

~~CONFIDENTIAL~~
~~RESTRICTED~~

Route To:	Payroll No.	Location	Signature	Date

Classification Cancelled

Or Changed To

By Authority Of

By

UNCLASSIFIED

DOC

Date 11-2-77

MASTER

UNCLASSIFIED

DECLASSIFIED

DISTRIBUTION RESTRICTED TO U.S. ONLY

1 8855

DECLASSIFIED

5

HW-29615

ABSTRACT

Experimental data pertinent to the evaluation of hazards involved in the exposure of personnel to tritium and tritium oxide are reviewed. Conclusions are drawn and recommendations made with regard to the control of these hazards.

DECLASSIFIED

DECLASSIFIED

6

HW-29615

TABLE OF CONTENTS

	<u>Page</u>
INTRODUCTION	8
TYPES OF TRITIUM CONTAMINATION	10
MODES OF BODY ENTRY	12
Pulmonary absorption of tritium oxide vapor	12
Pulmonary absorption of tritium gas	12
Absorption of tritium oxide from the gastro-intestinal tract	14
Percutaneous absorption of tritium oxide vapor	14
Percutaneous absorption of tritium gas	16
Summary - Modes of body entry	17
BODY DISTRIBUTION AND RETENTION	18
Distribution and retention of tritium administered as the element	18
Distribution and retention of tritium oxide	20
Distribution and retention of tissue-bound tritium	21
Isotope effects in the biological incorporation of tritium	26
Summary - Body distribution and retention	28
RBE OF THE TRITIUM BETA PARTICLE	29
SUGGESTED MPL FOR EXPOSURE TO TRITIUM	31
Maximum permissible body burden	31
Maximum permissible concentration of tritium oxide in air	34
Maximum permissible concentration of tritium oxide in water	35
Maximum permissible concentration of tritium gas in air	36

DECLASSIFIED

DECLASSIFIED

7

HW-29615

TABLE OF CONTENTS (contd.)

	<u>Page</u>
Summary - Suggested maximum permissible limits for exposure to tritium	38
APPLICATION TO PRACTICAL HAZARD CONTROL	
PROCEDURES	39
BIBLIOGRAPHY	42

DECLASSIFIED

DECLASSIFIED

8

HW-29615

HAZARDS OF EXPOSURE TO TRITIUM AND TRITIUM OXIDE

INTRODUCTION

Tritium, the mass 3 isotope of hydrogen, was first produced in 1939 by cyclotron bombardment of deuterium with deuterons⁽¹⁾. The reaction currently employed for production of macro amounts of tritium, the bombardment of lithium with neutrons, was described a year later⁽²⁾.

The most reliable measurements of the half-life of tritium indicate a value of about 12.4 years^(3, 4, 5). The isotope decays by emission of a very weak beta particle, the maximum energy corresponding to approximately 17 Kev⁽⁶⁾. The complete energy spectrum has been studied⁽⁶⁾ and the average energy has been determined by calorimetric methods to be 5.69 Kev per disintegration⁽⁴⁾. No gamma ray accompanies the beta emission.

Because of the low energy of the beta particle and the absence of gamma radiation, the biological hazard involved in the handling of tritium is due only to that tritium which by some means gains entry into the body. Such entry might occur most probably as a result of atmospheric contamination with tritium, tritium oxide, or other tritium containing compounds; or less probably as a result of the contamination of water or food supplies. Considering the small quantities required for most chemical and biological tracer studies, the hazard of exposure to tritium in the course of such studies, assuming the employment of normal precautions, should not constitute any unusual problems as compared with the handling of other radioisotopes. Chief concern attaches to those operations in which relatively large quantities of the pure substance are involved, as, for example, in the large scale production of tritium.

DECLASSIFIED

DECLASSIFIED

9

HW-29615

Production of tritium in macro quantities was first conducted at the Argonne National Laboratory. Later, the entire process was transferred to the Hanford Works. A review of hazard control procedures in effect at the Argonne National Laboratory during their period of production, together with preliminary recommendations for such procedures at the Hanford Works, is contained in Document HW-11305⁽⁷⁾. At the time of appearance of this document virtually no experimental studies had been made with the specific view toward evaluation and control of tritium hazards.

With the startup of tritium production at the Hanford Works, a "Tritium Hazards Control Committee" was established⁽⁸⁾ with representatives from the various sections concerned with tritium hazard control and tritium production. This committee met over a period of 17 months to formulate plans for research and development directed toward improvement of hazard control in tritium production, and to recommend and apply policies governing hazard control. A summary report of the accomplishments of this committee appears in HW-21231⁽⁹⁾. While many of the research and development programs initiated by this committee were not completed in time to be of value in the control of hazards during the initial period of Hanford tritium production, practical problems were met as they arose and contamination of personnel decreased as experience was gained.

Coincident with the broad study of tritium hazard control which was instituted at the Hanford Works, studies of a somewhat similar nature were undertaken at the Los Alamos Scientific Laboratories. Studies from Hanford and Los Alamos, plus some work done at the Argonne National Laboratory and a few published reports of English workers, constitute our current total knowledge of tritium hazards. The present report is designed to collect and summarize these findings.

DECLASSIFIED

DECLASSIFIED

10

HW-29615

TYPES OF TRITIUM CONTAMINATION

Tritium contamination may be conveniently classified as due to: (a) elemental tritium (or HT), (b) tritium oxide (presumably HTO), or (c) other tritium containing compounds. Biological hazards as they arise from elemental tritium and tritium oxide have been separately studied and are considered separately in this report. Other tritium compounds might constitute hazardous contaminants in specialized operations, but they are not considered in this report except as they may arise within the animal organism as a consequence of exposure to the element or the oxide.

Whether elemental tritium or tritium oxide is the most likely contaminant in the varied operations involved in the production, purification, and manipulation of macro quantities of tritium has not been shown. In production operations high levels of atmospheric contamination usually occurred suddenly, without prior warning, and, due to rapid air flows in the operating galleries, disappeared as quickly. Although the concentration of tritium in the air was usually automatically recorded, there was available no technique unequivocally successful in differentiating between the elemental and oxidized states of tritium. In many cases of contamination it was possible to deduce, from the circumstances of the incident, the probable nature of the contaminant. A break in a glass line known to contain elemental tritium would result in elemental tritium contamination; however, the presence of a nearby flame or active catalyst might rapidly convert the element to the oxide. Contamination resulting from diffusion of tritium through the extraction furnace would most probably be present as the oxide.

Evaluation of the relative probability of elemental tritium or tritium oxide contamination in a given situation would be greatly aided by additional knowledge of the factors influencing the oxidation of tritium. As judged from studies with deuterium, elemental hydrogen does not exchange at an appreciable

DECLASSIFIED

DECLASSIFIED

11

HW-29615

rate with the hydrogen of water, at room temperature, in the absence of a catalyst⁽¹¹⁾. The exclusion of catalysts in the deuterium studies proved to be a matter of some difficulty, and it seems reasonable to assume that under practical conditions of atmospheric contamination, catalysts for this reaction would be present. It is also possible that this reaction is catalyzed by the radiation from the tritium disintegrations. Observations on this point are contradictory, Pinson and Anderson reporting that exchange did not occur in two weeks at room temperature between HT and H₂O sealed in a glass bulb⁽¹²⁾; while the opposite conclusion was reached in a similar experiment performed by DeHollander⁽¹³⁾. Smith and Hollis have studied this exchange in a closed glass system, heated in one portion and cooled in another portion to effect circulation of tritium gas and water vapor over a liquid water phase⁽¹⁴⁾. Exchange was shown to occur principally in the vapor phase. With the hot portion of the system at 150°C, the cold portion at 20°C, and the liquid water at 24°C, the exchange proceeded at a constant rate over a period of 1,340 hours. At the end of this time 19 per cent of the tritium, originally present at a concentration of 180 µc/ml, had been converted to the oxide. This represents a conversion of approximately 0.014 per cent per hour.

In view of the above uncertainties and because of the greater biological hazard associated with exposure to tritium oxide, maximum permissible levels for contamination of air have been established on the assumption that measured contamination is present as the oxide⁽¹⁰⁾.

DECLASSIFIED

DECLASSIFIED

12

HW-29615

MODES OF BODY ENTRY

The obvious portals of entry for either tritium or its oxide are the lungs, the skin, and the gastro-intestinal tract. For each of these portals one is interested in the rate at which tritium and tritium oxide are absorbed and enter the tissues. In the case of the lungs and gastro-intestinal tract a direct radiation hazard exists, the significance of which will be considered in a later section.

Pulmonary Absorption of Tritium Oxide Vapor

Essentially all tritium oxide inhaled is retained and rapidly mixed with body fluids. This has been shown to be true for rats⁽¹²⁾, mice⁽¹⁵⁾, and humans⁽¹⁶⁾. In the human studies, reported by Pinson, et al, tritium oxide vapor atmospheres were inhaled for a five minute period. Tritium exhaled during this period amounted to less than two per cent of the quantity inhaled. Following exposure the tritium oxide content of expired water vapor decreased rapidly and reached equilibrium with the body water in about 30 minutes. During exposure the tritium oxide content of venous blood rose rapidly and continued to increase slightly for a few minutes following exposure; it then decreased to an equilibrium level which was attained in about 80 minutes⁽¹⁶⁾.

Pulmonary Absorption of Tritium Gas

The situation with respect to absorption of elemental tritium from the lung is more complex due to the limited solubility of the gas in body fluids, and complications arising from the conversion of the element to the oxide. Studies have been of two types: those which measure tritium retained (probably as the oxide) following chronic exposure to tritium gas, and studies of the tritium content of the blood during and following short period of exposure. Experiments of the first type have indicated that only a very small fraction of inhaled tritium is retained in the body for any

DECLASSIFIED

DECLASSIFIED

13

HW-29615

[REDACTED]

appreciable period following exposure. Smith, et al, exposed rats to tritium gas for one or two hour periods and noted retention (as the oxide) of from 0.025 - 0.05 per cent of the inspired tritium⁽¹⁷⁾. Pinson has reported a retention of about 0.1 per cent in rats exposed for periods of from 100 to 145 hours, and a retention of about 0.004 per cent in experiments on two humans⁽¹²⁾.

The concentration of tritium gas dissolved in body fluids and tissues during chronic exposure will be determined by the solubility characteristics of tritium gas. Considerable time may be required, however, for uniform distribution of such dissolved tritium following initiation of exposure. When rats were exposed to a tritium gas atmosphere and the blood from the tail sampled at intervals during the exposure, an initial lag period in blood tritium concentration of three to four minutes was followed by an approximately five minute period during which the concentration increased rapidly⁽¹⁸⁾. Following this period the blood tritium concentration increased at a reduced rate and had not reached equilibrium at the end of 30 minutes. The slow approach to equilibrium may be due in large part to the sluggish circulation in the tail of the rat. After 30 minutes exposure of a rat to an atmosphere containing 300 μc of elemental tritium per ml of air, the blood concentration reached 4 $\mu\text{c}/\text{ml}$. Assuming that the absorption coefficient for normal hydrogen in water at 37° (0.016)⁽¹⁹⁾ applies to tritium in body fluids, this blood sample was about 80 per cent saturated.

Upon cessation of exposure to tritium gas, the blood tritium concentration of the rat decreased rapidly, reaching within approximately 10 minutes a value of 5 - 10 per cent of that attained during exposure. This rapidly lost tritium must have been present as dissolved gas. The small residual blood tritium concentration is not appreciably decreased over a period of hours following exposure and may be attributed to tritium oxide or to tritium converted by the animal to the organically bound state.

[REDACTED]

DECLASSIFIED

DECLASSIFIED

14

HW-29615

Absorption of Tritium Oxide from the Gastro-intestinal Tract

Ingested tritium oxide is completely absorbed from the gastro-intestinal tract and uniformly distributed in body fluids. Pinson, et al, have reported studies on three human subjects who were administered tritium oxide in 100 to 1000 ml of water⁽²⁰⁾. Tritium appeared in venous blood within two to nine minutes following ingestion and increased linearly, reaching a maximum concentration in about 40 to 45 minutes. This increase was usually followed by a slight decline until an equilibrium value was reached at about 2 1/2 hours post ingestion. The rate of appearance of tritium in the blood was not influenced by the volume of water ingested with the tritium oxide.

Percutaneous Absorption of Tritium Oxide Vapor

The absorption of both tritium oxide and elemental tritium through the skin has been rather thoroughly studied, since the skin represents the portal of entry which is most difficultly controlled by use of protective equipment. Passage of water inward through the skin has long been a subject of controversy among physiologists. That such inward passage does occur was first demonstrated unequivocally by Szczesniak, et al, using deuterium as a tracer, in experiments performed on rats⁽²¹⁾. This experiment involved immersion of the rat in liquid water. From the standpoint of biological hazards of tritium oxide contamination, primary interest attaches to the percutaneous absorption of water in the vapor state.

DeLong reported studies on the percutaneous absorption of water vapor by rats using tritium oxide as a tracer⁽²²⁾, and these studies have since been refined and extended to include data on mice and man. In the animal experiments a prescribed skin area on the abdomen was exposed to a saturated water vapor atmosphere containing tritium oxide⁽²³⁾. Tritium oxide absorption was measured by analyzing total body water following a one-hour exposure period. Absorption rate constants ($\mu\text{c absorbed/cm}^2/\text{min}/\mu\text{c/cc atmosphere}$) obtained were 0.188 ± 0.018 for the rat, and 0.67 ± 0.16 for

DECLASSIFIED

DECLASSIFIED

15

HW-29615

the mouse (temperature, 30°C). These values were obtained on animals which had been shaved a day prior to exposure. Unshaved animals exhibited absorption rates lower by a factor of two to three. Heavy cloth covering the skin during a one hour exposure had no detectable effect on water vapor absorption.

Exposures similar to those described above were performed on the volar surface of the forearm of 12 human subjects^(24, 25). Absorption was determined by measuring the peak urine activity following exposure and assuming a body water content of 62 per cent of body weight⁽²⁶⁾. The absorption rate constant obtained from these studies was $0.28 \pm 0.05 \mu\text{c}/\text{cm}^2/\text{min}/\mu\text{c}/\text{cc}$ (temperature, 30°C). A single total body exposure of a human subject to tritium oxide vapor led to an absorption rate constant of 0.84 (temperature, 30°C, relative humidity, 70 per cent, 53 minute exposure)^(25, 27). The rather large difference between forearm and total body absorption rates is felt to be not unreasonable in view of previously reported differences in the rate of insensible perspiration from different skin areas⁽²⁸⁾.

In further studies on rats, it was shown that the rate of percutaneous water vapor absorption, as measured with tritium oxide as a tracer, is directly proportional to total water vapor pressure^(25, 27). Stated in terms more applicable to hazard considerations, this means that the absorption of tritium oxide is independent of total water vapor pressure and, consequently, that isotopic dilution with water of tritium oxide-containing atmospheres does not decrease the hazard.

Pinson has studied the percutaneous absorption of tritium oxide vapor in humans by exposing the entire forearm to a saturated, tritium oxide labeled water vapor atmosphere at 24°C^(29, 30). Results of repeated studies on two subjects showed an average absorption of $0.019 \text{ mg water}/\text{cm}^2/\text{min}$. Correcting for the difference in water vapor pressure at 24°C and 30°C and converting to other units, this figure becomes $0.80 \mu\text{c}/\text{cm}^2/\text{min}/\mu\text{c}/\text{cc}$ at

DECLASSIFIED

DECLASSIFIED

16

HW-29615

30°C, in excellent agreement with the value of 0.84 obtained from total body exposure (see above). Pinson studied in some detail the effect of short exposures to tritium oxide vapor, and found the absorption rate to be a factor of two to four times lower when the exposure was limited to periods of ten minutes or less. This phenomena he attributed to a holdup of the absorbed water vapor in the horny outer layer of the skin from which it might be easily lost following exposure. This interpretation was reinforced by the observation that insensible perspiration from the exposed skin area, collected following exposure, contains a much higher concentration of tritium oxide, for several hours following exposure, than the concentration attained in total body fluids as measured in the urine. Attempts to accelerate this loss of water from the skin by prolonged rinsing with water or immersion in 100 per cent alcohol were unsuccessful. The half-time for appearance of tritium oxide in the blood varied from 20 minutes to an hour, depending on the blood circulation rate in the skin, as influenced by temperature.

The general magnitude of the hazard associated with percutaneous absorption of tritium oxide is indicated by the fact that, based on the absorption rate constant of $0.84 \mu\text{c}/\text{cm}^2/\text{min}/\mu\text{c}/\text{cc}$, the absorption rate through the total skin area is approximately equal to that through the lung^(25, 30).

Percutaneous Absorption of Tritium Gas

Percutaneous absorption of tritium gas has been less exhaustively studied, but appears to be a relatively insignificant hazard compared with absorption through the lung. Smith, et al, have exposed rats to tritium gas, with uncontaminated air supplied to the lungs via tracheal cannula⁽¹⁸⁾. Parallel exposures were made in which the tritium gas was supplied via tracheal cannula. Following exposures, tritium retained as the oxide was measured. For the lung exposed animals, retention averaged $5 \times 10^{-3} \mu\text{c}/\text{g}$ tissue/hr exposure/ μc tritium/cc atmosphere. The corresponding average figure for skin exposure was 7.5×10^{-5} . While these experiments did not

DECLASSIFIED

DECLASSIFIED

17

HW-29615

measure absorption rates, they indicate the relative effects of the two types of exposure, the skin exposure resulting in only about 1/70 as great a retention as the lung exposure. In similar experiments rats were exposed via the skin and the tritium expired via tracheal cannula was collected and analyzed. From this data an effective skin absorption rate constant of approximately $6.5 \times 10^{-4} \mu\text{c}/\text{cm}^2/\text{min}/\mu\text{c}/\text{cc}$ was calculated⁽¹⁸⁾.

In another approach to this problem, DeLong, et al, made measurements of the rate of passage of tritium gas through excised pieces of mouse, rat and human skin⁽²⁷⁾. While these results might be expected to differ considerably from those obtained on intact animals they do provide an inter-species comparison which would be difficult to obtain in any other manner. The values obtained (μc passed/ $\text{cm}^2/\text{min}/\mu\text{c}/\text{cc}$) were $(2.54 \pm .44) \times 10^{-4}$ for mouse skin (15 exposures), $(2.07 \pm 0.26) \times 10^{-4}$ for rat skin (20 exposures), and $(0.72 \pm 0.16) \times 10^{-4}$ for human skin (6 exposures). The value for rat skin is a factor of three lower than that obtained from studies on the intact animal. The value for human skin is a factor of three lower than that for rat skin.

Summary - Modes of Body Entry

Ingested tritium oxide is completely absorbed, inhaled tritium oxide is completely absorbed, and from an atmosphere of given tritium oxide content, absorption through the skin will approximately equal absorption through the lung. The absorption of tritium gas through the skin is relatively insignificant compared to that which enters through the lung. Tritium gas concentration attained in the body during exposure is determined by its solubility in body fluids. The gas is rapidly lost upon termination of exposure and the tritium which remains is that which has been converted to tritium oxide or organically bound tritium. This residual tritium amounts to a small fraction of one per cent of the total tritium inhaled.

DECLASSIFIED

DECLASSIFIED

18

HW-29615

BODY DISTRIBUTION AND RETENTION

Having gained entry to the body, the radiation delivered by tritium to a given tissue will depend upon the concentration of tritium in the tissue and the length of time it remains. In considering this phase of the total problem we will again give separate consideration to elemental tritium, tritium oxide, and other tritium containing compounds. A consideration of the possible effects of isotopic differentiation between tritium and protium will also be pertinent to this discussion.

Distribution and Retention of Tritium Administered as the Element

As pointed out previously, the distribution of elemental tritium in the animal organism is largely dependent on its solubility in body fluids. Actually, the presence in body fluids of dissolved tritium gas, per se, is of little hazard consequence, since the concentration of such dissolved tritium must always be greatly exceeded by the concentration of gaseous tritium in the lung required to maintain this much lower concentration in body fluids. Removal of the organism from the tritium atmosphere will result in rapid loss of dissolved tritium from the body fluids. Direct radiation to the lung would therefore be the critical consideration in uncomplicated exposure to tritium gas. An inherent complication exists, however, in the fact that elemental tritium will be converted in the animal to tritium oxide and other tritium compounds which will not be lost upon removal of the subject from the contaminating atmosphere. In addition to direct exposure to the lung, then, an important consideration in tritium gas exposures is the extent to which compounds of tritium will be formed in the body during exposure.

Two processes may account for the conversion of elemental tritium in the animal body: exchange of tritium with the hydrogen of body water (perhaps catalyzed by radiation or normal constituents of the body) and metabolic incorporation of tritium into water or other tissue compounds.

DECLASSIFIED

DECLASSIFIED

19

HW-29615

Exchange of tritium with the hydrogen of water under atmospheric conditions has been previously discussed. In the body one might expect this exchange to occur more rapidly due to the presence of many substances which might serve as catalysts for the process. However, experimental data indicate that this exchange process is of relatively little significance compared with processes of metabolic incorporation.

Hydrogen is not a normal metabolic substrate for mammalian tissues, and the ability of such tissues to metabolize hydrogen has not been unequivocally demonstrated. Many bacteria, however, possess the enzyme hydrogenase which will effect the oxidation of hydrogen. The oxidation of tritium by such microorganisms, including some not previously shown to possess hydrogenase activity, has been demonstrated by Smith and Marshall^(31, 32). Some of these microorganisms are normal inhabitants of the gastro-intestinal tract of man and animals. By a variety of means it has been shown that most of the oxidation of tritium which occurs within the rat is due to the action of these bacteria.

Feeding dihydrostreptomycin and sodium sulfathiazole for three days prior to exposure to tritium caused retention following exposure to be reduced by over one-third⁽¹⁷⁾. By surgical removal of the entire gastro-intestinal tract prior to exposure, retention following exposure was reduced by 99 per cent⁽¹⁷⁾. The marked ability of the intestinal microorganisms to convert tritium was demonstrated by an experiment in which tritium gas was injected into a tied-off segment of the ileum. Over 50 per cent of this tritium was recovered from the sacrificed animal, four hours later, in the form of tritium oxide or organically bound tritium⁽¹⁸⁾. In this and other experiments in which animals were exposed to tritium gas, about 95 per cent of the tritium retained following exposure was present as tritium oxide; the remaining five per cent was organically bound. This ratio of essentially 1:20 between organically bound tritium and tritium oxide is considerably higher than the corresponding

DECLASSIFIED

DECLASSIFIED

20

HW-29615

ratio established following direct administration of tritium oxide (see below). The distribution of bound tritium following gas exposure also seems to be somewhat different from that following administration of tritium oxide⁽¹⁸⁾. For these reasons it would be interesting to follow the time course of retention of bound tritium following exposure to tritium gas, and such studies are in progress in this laboratory at the present time. Although, as previously mentioned, only 0.05 to 0.1 per cent of inhaled tritium gas is converted by the rat to tritium compounds, and the fraction seems to be even smaller in man, this very small fraction might still be significant in chronic exposures, if the compounds so formed were retained for long periods of time following exposure.

Distribution and Retention of Tritium Oxide

Tritium oxide, by whatever means it may gain entry to the body, is rapidly and uniformly distributed throughout body fluids. The kinetics of this distribution following ingestion, inhalation, or percutaneous absorption have been previously discussed.

There is no evidence of a significant isotope effect in the distribution of tritium oxide in mammalian body fluids. Tritium oxide concentration in tissue water did not vary among 13 different organs and tissues removed from rats previously injected with tritium oxide⁽³³⁾. In experiments on man the tritium oxide concentration in water from sweat, insensible perspiration, expired water vapor, sputum, urine, blood gastric juice, and seminal fluid was found to be identical within limits of experimental measurement^(12, 34). Simultaneous administration of tritium oxide and deuterium oxide to rats resulted in an equal dilution of both isotopes in the body water⁽³⁵⁾, and the ratio of these isotopes to each other remained essentially constant over a period of 60 days^(36, 37). Glascock has reported data indicating fractionation of deuterium oxide and tritium oxide in the blood water of a rat. However, the observation was made on a single animal, and the other animal in the same experiment showed no such effect⁽³⁸⁾.

DECLASSIFIED

DECLASSIFIED

21

HW-29615

Loss of tritium oxide from body fluids will occur almost entirely via excretion with small amounts being lost through exchange of tritium ions with labile hydrogens of organic compounds and through metabolism of the tritium oxide, which will also result in the formation of tritium-containing organic compounds. Excretion is best considered in terms of the biological half-life of body water, which includes loss of water through all avenues of excretion or secretion.

The International Commission on Radiological Protection has assumed for the "standard man" a water turnover rate of five per cent per day⁽¹⁰⁾. This corresponds to a biological half-life of approximately 14 days. The most reliable of recent studies of body water turnover indicate a more rapid average turnover rate. Schloerb, et al, using deuterium oxide as a tracer, made studies on 21 human subjects, both male and female, and obtained an average value of 9.3 days for the body water half-life⁽²⁶⁾. The standard deviation of the mean was 1.5 days and the extreme values were 7.3 and 13.0 days. Pinson and Anderson, using tritium oxide as a tracer, obtained body water half-lives ranging from 9.3 to 14 days in 9 human subjects⁽¹²⁾. The half-life of body water is, of course, dependent upon fluid intake and may be markedly shortened by forcing fluids. Half-lives as short as 2.4 days have been obtained by such procedures⁽¹²⁾.

The half-lives for body water in several experimental animals have been determined using tritium oxide as a tracer. Values of 1.1 days⁽³⁹⁾ and 1.5 - 2.0 days⁽¹²⁾ have been reported for the mouse; 3.3 days⁽³³⁾, and 3 - 5 days⁽¹²⁾, for the rat; and 5.2 days⁽⁴⁰⁾ for the sheep.

Distribution and Retention of Tissue-Bound Tritium

Tritium which becomes incorporated into tissue compounds by replacement of labile hydrogens* with tritium ions from body water does not constitute an increased radiation hazard. Tritium in the resulting compound is itself presumed to be labile - freely exchangeable with hydrogen ions in the body

* These are, in general, hydrogens which are not directly linked to carbon.

DECLASSIFIED

DECLASSIFIED

22

HW-29615

water. Retention of tritium which, through metabolic processes, becomes incorporated in non-labile positions in tissue compounds, will bear no relation to body water turnover, but rather, will be determined by the metabolic stability of the molecule in which the tritium is incorporated. Such tritium will be lost only as a result of metabolic processes which alter the structure of the molecule in such a manner as to eliminate the tritium or place it in a labile position in the molecule. The extent of tritium incorporation in tissue compounds and the rate at which this bound tritium is lost, have been studied in several experimental animals and analyses have been performed on biopsy samples from a single human.

In two experiments employing 37 mice, Thompson obtained data on the gross retention of tissue-bound tritium for periods up to 160 days following initial exposure^(39, 41, 42). The mice were injected daily, intraperitoneally, over a two-week period with tritium oxide. At the conclusion of the injection period, from 7 to 10 per cent of the tritium present in the animals was in the tissue-bound state. This corresponded to from 0.5 to 1.0 per cent of the total tritium oxide injected over the previous two weeks. The tissue-bound tritium was lost from the animals at a much slower rate than the body water tritium. Tissue-bound tritium remaining in the mice 160 days following tritium oxide injection amounted to 0.01 per cent of the total tritium administered and was being lost from the animals with a half-life of about 90 days.

In experiments reported by Pinson, et al,⁽⁴³⁾ three mice were administered tritium oxide in drinking water over a five month period. The tritium oxide concentration in body water over this period was maintained at approximately 3 $\mu\text{c}/\text{ml}$. Thirty-two days after cessation of administration the animals were sacrificed. At this time body water tritium oxide was reduced to a level of 0.004 $\mu\text{c}/\text{ml}$ and was being lost with an apparent half-life of about 11 days. Various tissues from these mice were dried and combusted and the tritium content of the combustion water determined. The

DECLASSIFIED

DECLASSIFIED

23

HW-29615

most active combustion water was obtained from brain, skin and muscle, with tritium concentrations of 0.26, 0.18, and 0.14 $\mu\text{c}/\text{ml}$, respectively. The lowest activity, 0.027 $\mu\text{c}/\text{ml}$, was found in combustion water from the liver.

The retention of tritium in the rat was studied by Thompson in an experiment extending over a period of 280 days, involving 40 animals which were sacrificed at intervals following the administration of a single intraperitoneal injection of tritium oxide⁽³³⁾. Twenty-four hours after tritium oxide administration, the highest concentrations of tissue-bound tritium were found in those tissues generally considered to be the most active metabolically, e.g., liver, small intestine, and blood. The concentration of bound tritium in the pelt was also among the highest noted. Those tissues which one would consider least active metabolically, e.g., muscle, bone and depot fat, showed the lowest bound tritium concentration at 24 hours; however, their tritium concentration was greatly increased by the sixth day post-injection. At this time, 1.3 per cent of the originally administered tritium was present in the tissue-bound state and this amounted to about 6 per cent of the tritium remaining in the animal at that time. After 280 days, 0.05 per cent of the originally administered tritium was still retained in the tissue-bound state and this amounted to about 98 per cent of the total tritium remaining in the animal. The highest tritium concentrations 280 days after administration were found in pelt, bone, brain, and depot fat.

Study of the retention of bound tritium in various tissues as a function of time indicated the presence of several groups of components in each tissue, turning over at different rates. While most of the tritium was present in relatively short-lived components, all tissues studied (except blood) gave evidence of the presence of tritium-binding components with biological half-lives of from 80 to 350 days. It was estimated that these relatively inert components probably constitute a major fraction of most tissues⁽³³⁾.

DECLASSIFIED

DECLASSIFIED

24

HW-29615

[REDACTED]

In additional studies of these metabolically sluggish components, compound fractions were isolated from rats sacrificed four months and eight months after administration of 0.1 c HTO/rat (given in 5 weekly injections)⁽⁴⁰⁾. Based on the decrease in tritium content between sacrificings, biological half-lives were estimated for various protein and fat fractions. Collagen fractions isolated from muscle showed no decrease in tritium content over the four month period. Saturated fatty acids isolated from abdominal depot fat, from pelt, and from total carcass exhibited biological half-lives of 65, 130, and 200 days respectively. Unsaturated fatty acids from the same sources exhibited half-lives of 70, 250, and 300 days. It is apparent that the turnover rates are a function not only of the type of compound, but also of the functional involvement of the compound in the organism. These long biological half-lives, of course, are not representative of the total fatty acids, but apply only to those fractions still retaining tritium during the interval from four to eight months following tritium oxide administration.

Preliminary results from chronic feeding studies indicate that after four months on a tritium oxide-labeled drinking water regimen, the organic hydrogen of mature female rats had acquired an average of 20 per cent of the tritium concentration of the body water hydrogen. Values for individual tissues varied from a high of 28 per cent for liver to a low of 8 per cent for heart⁽⁴⁴⁾.

Young rats, born to the chronically tritiated animals mentioned above, were raised to maturity on the same tritium oxide-labeled drinking water regimen. Their organic hydrogen, at maturity, had approximately 20 per cent of the tritium concentration of their body water hydrogen. Individual tissues showed concentrations as high as 37 per cent (brain). This result can be interpreted to indicate that 20 per cent of the organic hydrogen in the animal was derived from water, the remaining 80 per cent being

[REDACTED]

DECLASSIFIED

DECLASSIFIED

25

HW-29615

incorporated in the form of preformed organic molecules obtained from food. It can be calculated that the average total body radiation dose being received by these animals was increased 9 per cent, as a consequence of tritium incorporation into tissue compounds, over the dose which would have been received from body water tritium alone⁽⁴⁴⁾.

Data were obtained by Thompson and Ballou on long-term retention of tritium in a single sheep⁽⁴⁰⁾. The animal received approximately 3 c tritium as the oxide in a single intraperitoneal injection. It was sacrificed 235 days later and bound tritium determined in a variety of tissues. The proportion of administered tritium which was retained by the sheep was, in all tissues, greater than the proportion retained by the rat in similar tissues over the same time period. The highest concentration of bound tritium found in the sheep was 0.42 $\mu\text{c/g}$ wet weight in the mesenteric fat, which represents a proportional retention 20 times greater than that observed in the rat.

Tritium retention was studied time-wise in blood fractions from this sheep. Maximum tritium incorporation of approximately 2.7 $\mu\text{c/g}$ and 2.2 $\mu\text{c/g}$ (dry weight) were observed in serum globulin and serum albumin, respectively. The biological half-lives measured for globulin and albumin were, respectively, 20 days and 27 days, with some indication of a longer-lived component in the globulin fraction. Maximum tritium incorporation in total red cell protein was attained in about 30 days with a concentration of approximately 1.1 $\mu\text{c/g}$ (dry weight). This concentration was maintained essentially constant over a period of 100 days. The average life of the red cell of the sheep was estimated from these data as 140 days.

Direct experimental information on the incorporation of tritium into the tissue components of man is limited to the analysis of biopsy samples of skin and fat obtained from the abdomen of a person exposed over a period

DECLASSIFIED

DECLASSIFIED

26

HW-29615

of 8 months to concentrations of tritium oxide in body fluids averaging $0.023 \mu\text{c}/\text{ml}$ ⁽⁴⁵⁾. The samples were taken after the tritium concentration in body fluids had decreased to $2 \times 10^{-4} \mu\text{c}/\text{ml}$. The skin contained tritium equivalent to $4 \times 10^{-4} \mu\text{c}/\text{g}$ of dry tissue, and the fat, $3 \times 10^{-4} \mu\text{c}/\text{g}$ of dry tissue. The radiation dose rate from this bound tritium was estimated at 1 to 2 per cent of the average radiation dose rate from tritium in body water over the 8-month exposure period.

A rather detailed analysis of all data available on the influence of tissue binding of tritium on the radiation hazard of exposure to tritium oxide has appeared as Document HW-30340⁽⁴⁶⁾. It was concluded that bound tritium would not appreciably affect dose rates immediately following exposure, but might increase the total absorbed dose by an average of 10 per cent for the total body, and perhaps by as much as 100 per cent for certain specific locations within the organism.

Isotope Effects in the Biological Incorporation of Tritium

Pertinent to any consideration of tritium incorporation and retention is the question of the existence of a significant isotope effect. In comparisons of deuterium and protium, rather large isotope effects have been reported for a number of specific reactions^(47, 48). For the complex system of equilibria involved in higher organisms, however, it has usually been assumed that no significant isotope effects were to be anticipated⁽⁴⁹⁾. This conclusion is supported by the many studies of the deuterium-protium ratio in living and non-living materials of all sorts which have in nearly all cases indicated the absence of significant enrichment or depletion of deuterium in materials of biological origin^(47, 50). The application of tritium as a tracer in biological systems has stimulated new interest in this question, and the results of several recent investigations raise serious questions as to the applicability of, not only tritium, but also deuterium, as a tracer for protium in many biological systems.

DECLASSIFIED

DECLASSIFIED

27

HW-29615

Several studies have recently been reported comparing the metabolic behavior of tritium and deuterium in living systems. Glascock⁽³⁸⁾ and Glascock and Duncombe⁽⁵¹⁾ observed a 20 per cent decrease in the tritium-deuterium ratio between the fed solution and the combustion water from mammary fat of lactating rats. In experiments using tritium- and deuterium-labeled methanols, Verly, et al, observed a greater retention of the carbon-tritium bond in the utilization of the methyl group of methanol in the biosynthesis of the labile methyl group⁽⁵²⁾. Eidinoff, et al, have reported results on four rats administered tritium and deuterium oxides over periods of 1 to 4 days which indicate preferential incorporation of deuterium by approximately 8 and 18 per cent in liver glycogen and liver fatty acids, respectively⁽⁵³⁾.

Thompson and Ballou reported the absence of any extensive isotope effect in the incorporation of deuterium and tritium (administered as oxides) into pelt, muscle, liver, fat, or brain of rats⁽³⁵⁾. The probability of small isotope effects in certain of these tissues was noted, however, and in more extensive studies, recently completed, statistically significant preferential incorporation of deuterium was observed in fat, muscle, and brain⁽³⁷⁾. Thirty-two rats were administered tritium oxide-labeled deuterium oxide, over a period of five weeks following which animals were sacrificed at intervals over a period of sixty days. The significant preferential incorporation of deuterium amounted to a difference of 7 per cent in depot fat, and 6 per cent in muscle and brain. There was no evidence for an isotope effect in the retention of incorporated tritium and deuterium over the sixty-day period. The smaller effects observed in this study as compared with the results of Eidinoff, et al,⁽⁵³⁾ and Glascock and Duncombe⁽⁵¹⁾, may be due to the longer period of isotope administration which would have allowed greater opportunity for metabolic equilibration of the isotope.

DECLASSIFIED

DECLASSIFIED

28

HW-29615

It would appear that, while small isotope effects may be expected in man, these effects will probably not be significant from the hazard standpoint. Further work is required, however, to settle this point. Even though tritium and deuterium may behave very similarly in a given system, this is only presumptive evidence that these isotopes will not differ greatly from protium. Recent studies on the comparative metabolism of tritium, deuterium, and protium oxides in algae have shown that while tritium is incorporated to about 90 per cent of the extent of deuterium, the extent of deuterium incorporation is only about 50 per cent of that measured for protium⁽⁵⁴⁾.

Summary - Body Distribution and Retention

For the case of exposure to tritium gas, the hazard during exposure is primarily due to direct irradiation of the lung. Significant retention following exposure is limited to compound forms of tritium (principally the oxide) formed largely through the action of bacteria in the intestinal tract. The oxide is uniformly distributed throughout body fluids and is lost at a rate which is well known and which can be influenced quite markedly by variation of water intake. The small fraction of tritium, from tritium oxide, which will be incorporated into tissue compounds may contribute significantly to the total hazard during a period of chronic exposure. Certain of these tritium-labeled compounds will be retained for very long periods following exposure.

DECLASSIFIED

DECLASSIFIED

29

HW-29615

RELATIVE BIOLOGICAL EFFECTIVENESS OF THE TRITIUM BETA PARTICLE

There was some early concern expressed that the tritium beta particle might have an unusually high relative biological effectiveness (RBE) because of its very low energy and consequent high specific ionization⁽⁷⁾. It now appears, based on results from a number of different approaches to the problem, that the RBE is somewhat greater than that for more energetic radiations, but probably not by more than a factor of two.

Acute toxicity studies in mice and chronic toxicity studies in rats, while leading to no precise value for the RBE, have indicated that no unusual factor of biological effectiveness exists. A 20-day LD₅₀ of about 1 mc/g body weight was estimated by Brues, et al, from acute toxicity studies in mice⁽⁵⁵⁾. Jennings and Brues reported a median lethal radiation dosage from tritium oxide administered chronically to rats over a two-month period, of between 57 and 77 rep per day on the basis of dosage rate in body water. The mean accumulated dosages to death were between 3000 and 3700 rep⁽⁵⁶⁾.

Getzendaner, et al, have compared the effectiveness of tritium, phosphorus-32, and sulfur-35 in inhibiting the growth of Lactobacillus casei. From these studies, an RBE of 1.7 was reported for tritium relative to P³²⁽⁵⁷⁾. More recent application of the method has led to an average value of 2.1⁽⁵⁸⁾.

Powers and Shefner compared the effects of tritium, Sr⁸⁹⁻⁹⁰, Y⁹⁰, and X-rays, on death after autogamy of Paramecium aurelia⁽⁵⁹⁾. The effects measured were presumed to be genetic in nature. Tritium appeared to be slightly less effective than the more energetic beta emitters at similar dose levels.

DECLASSIFIED

DECLASSIFIED

30

HW-29615

[REDACTED]

A comparison was made by Hall and Stroud of the effects of irradiation with tritium and X-rays, in vitro, on the growth and survival of mouse tumor implants⁽⁶⁰⁾. Tumor fragments were aseptically irradiated prior to implantation in Urbana-Swiss mice. Effects of equivalent dosages of the two types of radiation were similar.

Stroud and Brues have studied the effect of tritium on chick embryo muscle fibroblasts cultivated in vitro^(61, 62). Observations were consistent with what was expected from similar studies with other types of irradiation. With increasing dose and intensity there was a decrease in mitotic activity and an increase in the per cent of abnormal mitoses and the number of degenerate cells.

Comparing tritium with an external gamma emitter, cobalt-60, for their effect in depressing iron-59 uptake in rats, Furchner, et al, obtained an RBE for tritium of 1.6⁽⁶³⁾.

Worman, et al, in a study involving 300 CF-1 female mice, used spleen and thymus weight loss as an index of radiation effect in comparing tritium oxide and external radium gamma irradiation. Exposure was for 120 hours and results indicate an RBE for tritium beta radiation of approximately 1.4⁽⁶⁴⁾.

From these results obtained in a variety of biological systems it would seem most reasonable to assume an RBE for tritium of 2.0.

[REDACTED]

DECLASSIFIED

DECLASSIFIED

31

HW-29615

SUGGESTED MAXIMUM PERMISSIBLE LIMITS FOR EXPOSURE TO TRITIUM

From the biological data summarized in this report it should be possible to calculate with relatively little uncertainty, quantities of tritium in the human, in water to be ingested by humans, and in air to which humans are exposed, which will result in radiation of the human subject at the maximum permissible level of 0.3 rad/week. Many calculations of this sort have been reported, most of them having been made before the accumulation of much of the data summarized in this report. In Table 1 are summarized the recommendations of three national or international committees on radiation protection. These include the Chalk River Conference on Permissible Internal Dose held at Chalk River, Canada in September of 1949, the International Commission on Radiological Protection which met in London in July of 1950, and the report of the Sub-Committee on Permissible Internal Dose of the National Committee on Radiation Protection, published in March, 1953. In addition to these recommendations several other values have been proposed at one time or another^(7, 67, 12), none of which differed greatly from the values presented in Table 1. All values in Table 1 are based on the assumption that tritium is present in the form of tritium oxide. Pinson and Anderson have suggested a maximum permissible level of 0.6 $\mu\text{c}/\text{ml}$ for tritium gas in air⁽¹²⁾.

Maximum Permissible Body Burden

In evaluating the maximum permissible body burden one must take cognizance of the chemical form of the tritium in the body. Elemental tritium may be eliminated from consideration, since its retention in the body will be of negligible duration compared with other forms. Tritium incorporated in organic compounds should not be ignored in any over-all consideration of tritium hazards. For the present purpose of establishing a practical guide to exposure control, it seems expedient, however, to neglect the effect of organically bound tritium. Such bound tritium will

DECLASSIFIED

DECLASSIFIED

32

HW-29615

TABLE 1

Permissible Limits for Tritium

	μc in Total Body	$\mu\text{c}/\text{ml}$ Water	$\mu\text{c}/\text{ml}$ Air	Ref.
Chalk River, 1949	10^3	0.01	10^{-6}	(65)
London, 1950	10^4	0.1	5×10^{-5}	(10)
National Committee, 1953	10^4	0.2	2×10^{-5}	(66)

contribute significantly to the permissible total body burden only following long period of exposure at near maximum permissible levels. To properly treat the problem of chronic high-level exposure, more information would be required than is presently available. Such a situation pertains in the case of nearly all potentially hazardous radioisotopes, and calculations of maximum permissible limits should be considered, in practice, as limits to be approached as infrequently as possible⁽⁶⁶⁾. Should a situation arise where chronic exposure to tritium was required, present evidence would seem to dictate a reduction by a factor of two in the permissible body burden calculated without regard to organically bound tritium. This problem is considered in more detail in Document HW-30340⁽⁴⁶⁾.

In previous considerations of the maximum permissible body burden for tritium the choice of critical organ has been either total body or body water. The assumption of the total body as the critical organ implies a uniform distribution of tritium oxide throughout the organism. This is not strictly true, since some tissues contain a greater proportion of water than others⁽⁴⁶⁾. Assuming equal radiosensitivity the most critical tissue would be that with the highest water content. Since quite dilute solutions may be encountered in the micro-environment of cells, it would seem most

DECLASSIFIED

DECLASSIFIED

33

HW-29615

reasonable to assume the body water as the critical organ. While this assumption would be approached in reality only in the case of infinitely dilute solutions, it errs but slightly, and in a conservative direction.

The maximum permissible level of tritium in body water can be calculated from the formula:

$$\text{Dose (rads)} = \frac{51 E Q T}{W}$$

where: E = average energy of beta particles in Mev

Q = quantity of radioisotope in μc

t = time of exposure in days

W = weight of tissue in grams containing the $Q\mu\text{c}$.

The number 51 is the product of the number of disintegrations/ $\mu\text{c}/\text{day}$, times ergs/Mev, times rads/erg⁽⁶⁸⁾.

If we substitute in this equation the permissible dose in rads/week (0.3), the time (7 days), the average energy of the beta particle (0.0057 Mev), and solve for Q/W, a value of 0.15 $\mu\text{c}/\text{g}$ is obtained. Correcting this for an RBE of two for the tritium beta particle (see p.30, this report) the value becomes .075 $\mu\text{c}/\text{g}$. To convert to total body burden one must multiply this figure by the weight of body water in grams. The "standard man" has been assumed to contain 50 liters of water in a total weight of 70 kg⁽¹⁰⁾. This is a higher percentage of water than has been found in the most careful recent work⁽²⁶⁾, and a value of 43 liters is used in the present calculation, yielding a maximum permissible body burden of approximately $3 \times 10^3 \mu\text{c}$. This limit is a factor of 3 lower than that proposed by the Sub-Committee on Permissible Internal Dose⁽⁶⁶⁾. The difference is due to the introduction into the calculations of an RBE of 2 for the tritium beta, a factor which was not considered by the Sub-Committee, and the choice of body water as the critical organ, rather than total body.

DECLASSIFIED

DECLASSIFIED

34

HW-29615

Maximum Permissible Concentration of Tritium Oxide in Air

The maximum permissible concentration of tritium oxide in air is that concentration which will maintain the tritium oxide content of a human subject exposed to the air, at the maximum permissible body burden. The rate of uptake of tritium oxide from the air must therefore be βQ , or $0.693 Q/T$, where β is the effective decay constant for tritium in the body, Q is the maximum permissible body burden and T is the effective half-life of tritium in the body. If we neglect tissue-bound tritium, for reasons discussed previously, the half-life of tritium in the body will be the half-life of body water. Ten days would seem to be the best average value for body water half-life in the human (see p. 21, this report). The required rate of uptake of tritium oxide from the air will therefore be $0.693 \times 3 \times 10^3 / 10$, or $210 \mu\text{c/day}$.

Uptake of tritium oxide from the air will occur via two routes, the lung and the skin. Since inhaled tritium oxide is completely retained, uptake via the lung will equal the volume of air respired times the concentration of tritium in the air. A breathing rate of $2 \times 10^7 \text{ ml/day}$ is assumed for the "standard man"⁽¹⁰⁾. Uptake of tritium oxide via the lung will therefore equal $2 \times 10^7 C_a$ per day, where C_a is the concentration of tritium in air in $\mu\text{c/ml}$.

The best value for the rate of uptake of tritium oxide through the skin is $0.84 \mu\text{c/cm}^2/\text{min}/\mu\text{c/ml}$ atmosphere (see p. 15, this report). The surface area of the "standard man" is estimated at $1.8 \times 10^4 \text{ cm}^2$ ⁽⁶⁹⁾. The total percutaneous uptake rate per man, per day, will therefore equal $0.84 \mu\text{c} \times 1.8 \times 10^4 \text{ cm}^2 \times 1440 \text{ min} \times C_a$, or $2.2 \times 10^7 C_a$.

The sum of lung and skin uptake, $4.2 \times 10^7 C_a$ must equal $210 \mu\text{c}$ per day. Therefore C_a equals $210 / 4.2 \times 10^7$, or $5 \times 10^{-6} \mu\text{c/ml}$. This value, for continuous exposure, is a factor of 4 lower than that proposed by the Subcommittee on Permissible Internal Dose⁽⁶⁶⁾. The difference is due to the lower value employed for maximum permissible body burden, and the

DECLASSIFIED

DECLASSIFIED

35

HW-29615

recognition of the skin as a significant route of entry, the effects of which are partially cancelled by the use of a shorter half-life for body water than that assumed by the Sub-Committee.

The above calculations assume continuous exposure to the contaminated atmosphere. Of more practical utility is an MPC based upon occupational exposure. The volume of air respired during an 8-hour working day is conventionally taken as half the total day's volume, or 10^7 ml⁽¹⁰⁾. Absorption of tritium oxide through the skin for an 8-hour period should be 1/3 that absorbed in 24 hours, or approximately $0.7 \times 10^7 C_a$. Since exposure will occur only 5 or 6 days during the week, the permissible daily uptake will be increased over the 210 μ c by factors of 7/5 or 7/6. On the basis of these assumptions the maximum permissible concentration of tritium oxide in air becomes 1.7×10^{-5} μ c/ml for a 5-day, 40-hour work week, and 1.4×10^{-5} μ c/ml for a 6-day, 48-hour work week.

Maximum Permissible Concentration of Tritium Oxide in Water

This limit can be calculated by a method similar to that employed above for air, the only additional information required being the amount of water ingested daily, exclusive of that present in foods. To be consistent with previous assumptions employed in these calculations, a body water content of 43 liters and a body water half-life of 10 days requires a daily water turnover of approximately 3000 ml. If we assume a daily intake from non-fluid sources of 1000 ml⁽¹⁰⁾, 2000 ml must be consumed as drinking water. This estimate is 500 ml higher than that postulated for the "standard man"⁽¹⁰⁾, and 200 ml lower than that employed by the Sub-Committee on Permissible Internal Dose⁽⁶⁶⁾.

If the 210 μ c of tritium required per day to maintain the maximum permissible body burden are contained in 2000 ml (or 2200 ml) of water, the maximum permissible concentration of tritium oxide in water is approximately 0.1 μ c/ml. This value is lower by a factor of two than that

DECLASSIFIED

DECLASSIFIED

36

HW-29615

recommended by the Sub-Committee on Permissible Internal Dose⁽⁶⁶⁾, the effect of using a threefold lower value for the maximum permissible body burden being partially counterbalanced by the use of a shorter half-life for body water than that assumed by the Sub-Committee.

On the assumption of 1000 ml of water consumed during an 8-hour work day, the MPC for occupational exposure becomes approximately 0.29 $\mu\text{c}/\text{ml}$ for a 5-day, 40-hour week; and 0.24 $\mu\text{c}/\text{ml}$ for a 6-day, 48-hour week.

Maximum Permissible Concentration of Tritium Gas in Air

All of the previous calculations were for exposure to tritium oxide. The case of tritium gas has relevance only in terms of an MPC for air, since it will not be retained in significant amounts, as the gas, in the body or in water. In calculating an MPC for tritium gas in air, one is faced with a choice of critical organ. Radiation from the gas itself will occur primarily to the lung, but a small fraction of the gas will be converted to the oxide in the body, and radiation from this oxide, distributed throughout body water, may be the critical factor. Percutaneous absorption of tritium gas may be ignored as negligible compared with pulmonary absorption.

Assuming body water to be the critical organ, an MPC may be calculated in the same manner as previously described for tritium oxide. The critical datum required is the fraction of inhaled tritium gas which is converted to the oxide and retained as such in the organism. The only information on this point is the value of 0.004 per cent retention obtained by Pinson, et al.,⁽¹²⁾ from exposures of two humans. Using this value, the MPC will be approximately $2/0.00004$ times that for tritium oxide, the two in the numerator arising from the fact that there is no absorption of tritium gas through the skin, comparable to that which occurs in the case of tritium oxide. The value so calculated for the MPC is 0.25 $\mu\text{c}/\text{ml}$.

DECLASSIFIED

DECLASSIFIED

37

HW-29615

On the other assumption, that the lung is the critical organ, we may calculate an MPC from the previously derived concentration of tritium which will deliver 0.3 rem/week to body water: 0.075 $\mu\text{c/g}$.

This body water figure of 0.075 $\mu\text{c/ml}$ should be doubled to yield the MPC for tritium gas in the lung, due to the fact that the tritium is actually on the surface of the tissue and, because of the very short range of the tritium beta, only half of the beta particles will penetrate lung tissue. The MPC for tritium gas in air, on this basis, then becomes 0.14 $\mu\text{c/ml}$.

From the two previous calculations it would appear that the two effects, direct radiation of the lung, and total body radiation due to conversion of the gas to the oxide, are of comparable magnitude. It would be unwise, however, to accept these calculations at face value. The value of 0.004 per cent for conversion of inhaled tritium gas to tritium oxide in man is based on single experiments on only two human subjects, and the value is lower by a factor of about 20 than results obtained from more extensive experiments on rats. Acceptance of the rat value would reduce the MPC of tritium gas in air to approximately 10^{-2} $\mu\text{c/ml}$.

A further word of caution must be added in regard to MPC's for tritium gas. Although the gas is less hazardous than the oxide by a factor of at least 10^3 , the practical utilization of a tritium gas MPC would require instrumentation capable of distinguishing small amounts of tritium oxide in the presence of large amounts of tritium gas. For example, if 0.1 per cent of the radioactivity in a supposed tritium gas atmosphere were actually due to tritium oxide, this would at least double the hazard over that which would be predicted on the assumption that no tritium oxide were present.

DECLASSIFIED

DECLASSIFIED

38

HW-29615

Summary - Suggested Maximum Permissible Limits for Exposure to Tritium

The maximum permissible limits for tritium oxide calculated in this report are summarized in Table 2. As pointed out in the previous discussion, the physiological parameters employed in the calculation of these limits differed in several instances from those of the "standard man." If calculated using the assumptions for the "standard man" these limits would be changed only slightly. For continuous exposure the permissible body burden would be increased to $3.5 \times 10^3 \mu\text{c}$; the MPC for water would be increased to $0.12 \mu\text{c/ml}$; and the MPC for air would be decreased to $4 \times 10^{-6} \mu\text{c/ml}$.

TABLE 2

Suggested Maximum Permissible Limits for Tritium
Assumed to be Present as Tritium Oxide

	μc in Total Body	$\mu\text{c/ml}$ Water	$\mu\text{c/ml}$ Air
For continuous exposure	3×10^3	0.1	5×10^{-6}
For occupational exposure		0.29	1.7×10^{-5}
5-day work week		0.24	1.4×10^{-5}
6 day work week			

DECLASSIFIED

DECLASSIFIED

39

HW-29615

APPLICATION TO PRACTICAL HAZARD CONTROL PROCEDURES

It is not the intent in this section to provide detailed recommendations of tritium hazard control procedures, but rather to point out the major considerations which derive from the nature of the materials involved and their behavior in the human organism.

The spread of tritium contamination, whether as the gas or the oxide, is apt to be largely via the atmosphere. The first line of defense should therefore be confinement of the contamination at the source. This would involve operation in gas tight apparatus, or failing in this, in well-ventilated hoods. Despite these precautions there will occasionally occur incidents of general contamination of laboratory air which will necessitate constant monitoring and the availability of personnel protective devices.

Air monitoring devices must, of course, be capable of detecting tritium at levels well below the MPC and ideally should be capable of distinguishing between tritium oxide and tritium gas. Whether advantage can be taken of the much higher MPC for tritium gas as compared to tritium oxide is highly doubtful with present instrumentation, because of the great difference in hazard between the two substances and the consequent necessity of detecting very small concentrations of tritium oxide in the presence of large concentrations of tritium gas. Because atmospheric contamination is apt to occur intermittently in "bursts" rather than at a constant level it is important that the monitoring instruments respond rapidly to changes in the activity level.

In tritium gas-contaminated atmospheres, an efficient air-supplied respirator offers noteworthy protection, since absorption of the gas through the skin is probably less than 1 per cent of that absorbed through the lung. This situation does not hold, however, in the case of a tritium oxide-contaminated atmosphere, where skin absorption is of comparable magnitude to lung absorption. Even in this case, however, the air-supplied respirator

DECLASSIFIED

DECLASSIFIED

40

HW-29615

would be of value in the most probable situations of intermittent bursts of contamination. There appears to be an inherent time lag in percutaneous absorption of the oxide, and this lag would probably be somewhat lengthened by the presence of normal laboratory clothing which would retard circulation of the contaminated air over the skin.

For the case of continuous exposure to tritium oxide-contaminated atmospheres respiratory protection alone can be expected to reduce exposure only by a factor of two. For complete protection, the total body would need to be covered with material impervious to the contaminated atmosphere.

An early suggestion that human absorption of tritium oxide might be reduced by humidification of the atmosphere, i. e., dilution of the tritium oxide with ordinary water, would appear to have no merit. Exchange of water vapor in the lung is essentially complete, regardless of total water vapor pressure, and the percutaneous absorption of tritium oxide has been shown to be independent of total water vapor pressure.

Because of the obvious difficulties in controlling and monitoring atmospheric tritium contamination, a routine bioassay program for all personnel subject to exposure is of the utmost importance. Urine samples are the most conveniently obtainable sample of body water, and rapid and accurate methods are available for determination of tritium at concentrations well below that corresponding to the maximum permissible concentration of tritium oxide in body water. Bioassay results are of importance not only from the standpoint of protecting the individual worker from continued over-exposure, but in many cases they may offer the only evidence as to the hazard involved in a particular operation. In other words, the worker at a given operation may constitute the "only practical monitoring instrument for that operation. While such conclusions drawn from bioassay results are "after the fact" data, they may be invaluable in the design and planning of future operations.

DECLASSIFIED

DECLASSIFIED

41

HW-29615

In the event of a significant over-exposure, an effective and simple therapeutic measure is the forcing of fluids to increase the rate of body water turnover and thus speed the elimination of tritium oxide. If immediately instituted, such measures should reduce the ultimate exposure by a factor of 3 or 4 without great discomfort to the individual.

DECLASSIFIED

DECLASSIFIED

42

HW-29615

BIBLIOGRAPHY

1. Alvarez, L. W., and R. Cornog, "Helium and hydrogen of mass 3", Phys. Rev., 56, 613 (1939).
2. O'Neal, R. D., and M. Goldhaber, "The decay constant of H^3 ", Phys. Rev. 58, 574 (1940).
3. Jones, W. M., "Half-life of tritium by absolute counting", Phys. Rev. 83, 537 (1951).
4. Jenks, G. H., J. A. Ghormley, and F. H. Sweeton, "Measurement of the half-life and average energy of tritium decay", Phys. Rev. 75, 701 (1949).
5. Novick, A., "Half-life of tritium", Phys. Rev. 72, 972 (1947).
6. Curran, S. C., J. Angus, and A. L. Cockcroft, "Beta spectrum of tritium", Nature, 162, 302 (1948).
7. Adley, F. E., and J. M. Smith, Jr., "Tritium extraction process - H. I. considerations", Document HW-11305 (1948) (SECRET).
8. Parker, H. M., "P-10 Hazards", Document HW-15634 (1950) (SECRET).
9. Kornberg, H. A., "Terminal report - P-10 Hazards Control Committee", Document HW-21231 (1951) (SECRET).
10. International Commission on Radiological Protection, "Supplement on maximum permissible amounts of radioactive isotopes", Amer. J. Roentgenol. Rad. Therapy, 65, 610 (1951).
11. Gould, A. J., and W. Bleakney, "Possibility of interchange between deuterium and hydrogen in compounds", J. Am. Chem. Soc. 56, 247 (1934).
12. Pinson, E. A., and E. C. Anderson, "The body absorption, distribution and excretion of tritium in man and animals", Document LA-1218 (1951) (OFFICIAL USE ONLY).
13. DeHollander, W. R., private communication.
14. Smith, G. N., and O. L. Hollis, unpublished data.

DECLASSIFIED

DECLASSIFIED

43

HW-29615

15. Campbell, S. G., D. F. White, and P. R. Payne, "The uptake of tritium-labelled water vapour by the mammalian lung", Brit. J. Radiol. 24, 682 (1951).
16. Pinson, E. A., E. C. Anderson, and Virginia Lotz, "Lung absorption of HTO by man upon inspiration of HTO water vapour", Document LA-1465 (1952) (OFFICIAL USE ONLY).
17. Smith, G. N., R. J. Emerson, L. A. Temple, and T. W. Galbraith, "The oxidation of tritium by the rat", in Biology Research - Annual Report 1951, Document HW-25021, p. 73 (1952) (RESTRICTED).
18. Smith, G. N., L. A. Temple, R. J. Emerson, and T. W. Galbraith, "The metabolism of tritium gas in the rat", in Biology Research - Annual Report 1952, Document HW-28636, p. 43 (1953) (UNCLASSIFIED).
19. Lange, N. A., "Handbook of Chemistry", 7th Ed., Handbook Publishers, Sandusky, Ohio (1949).
20. Pinson, E. A., E. C. Anderson, and Virginia Lotz, "The absorption of ingested tritium water and the water dilution volume of man", Document LA-1464 (1952) (OFFICIAL USE ONLY).
21. Szczesniak, A. S., H. Sherman, and R. S. Harris, "The percutaneous absorption of water", Science 113, 293 (1951).
22. DeLong, C. W., "The percutaneous absorption of water vapor", Science 114, 397 (1951).
23. DeLong, C. W., "Percutaneous absorption of tritium and tritium oxide", in Biology Research - Annual Report 1951, Document HW-25021, p. 53 (1952) (RESTRICTED).
24. DeLong, C. W., "Percutaneous absorption of tritium oxide", Document HW-21778, (1951) (SECRET).
25. DeLong, C. W., R. C. Thompson, and H. A. Kornberg, "Percutaneous absorption of tritium oxide", J. Roentgenol. Rad. Therapy and Nuclear Medicine, 71, 1038 (1954).
26. Schloerb, P. R., B. J. Fries-Hansen, I. S. Edelman, A. K. Solomon, and F. D. Moore, "Measurement of total body water in the human subject by deuterium oxide dilution, with consideration of the dynamics of deuterium distribution", J. Clin. Invest., 29, 1296 (1950).

DECLASSIFIED

DECLASSIFIED

27. DeLong, C. W., R. C. Thompson, and H. A. Kornberg, "Percutaneous absorption of tritium and tritium oxide", in Biology Research - Annual Report 1952, Document HW-28636, p. 52 (1953) (UNCLASSIFIED).
28. Peiss, C. N., A. B. Hertzman, W. C. Randall, and H. E. Ederstrom, "Regional rates of cutaneous insensible perspiration", Fed. Proc. 10, 103 (1951).
29. Pinson, E. A., "Water exchanges and barriers as studied by the use of hydrogen isotopes", Physiol. Rev., 32, 123 (1952).
30. Pinson, E. A., E. C. Anderson, and Virginia Lotz, "Absorption of liquid HTO and HTO vapor through the skin of man", Document LA-1466 (1952) (OFFICIAL USE ONLY).
31. Smith, G. N., R. O. Marshall, "Fixation of molecular tritium by bacterial suspensions", Arch. Biochem. and Biophys., 39, 395 (1952).
32. Smith, G. N., and R. O. Marshall, "The oxidation of tritium by bacteria", in Biology Research - Annual Report 1951, Document HW-25021, p. 83 (1952) (RESTRICTED).
33. Thompson, R. C., "Studies of metabolic turnover with tritium as a tracer. II. Gross studies on the rat", J. Biol. Chem., 200, 731 (1953).
34. Myers, L. S., Jr., J. Jackson, and J. Schubert, "The distribution of tritium in body fluids", in Division of Biological and Medical Research Quarterly Report, August, September, October, 1950, Document ANL-4531, p. 157 (1950) (UNCLASSIFIED).
35. Thompson, R. C., and J. E. Ballou, "On the metabolic equivalence of deuterium and tritium in animal experimentation", Arch. Biochem. and Biophys., 42, 219 (1953).
36. Thompson, R. C., and J. E. Ballou, "Comparative metabolism of deuterium and tritium in the rat", in Biology Research - Annual Report 1952, Document HW-28636, p. 67, (1953) (UNCLASSIFIED).
37. Thompson, R. C., and J. E. Ballou, "Studies of metabolic turnover with tritium as a tracer. III. Comparative studies with tritium and deuterium", Document HW-28595 (1953) (UNCLASSIFIED); J. Biol. Chem., 206 101 (1954).
38. Glascock, R. F., "Estimation of tritium and some preliminary experiments on its use as a label for water", Nucleonics 9, No. 5, 28 (1951).

DECLASSIFIED

DECLASSIFIED

UNCLASSIFIED

45

HW-29615

39. Thompson, R. C., "Studies of metabolic turnover with tritium as a tracer. I. Gross studies on the mouse", J. Biol. Chem., 197, 81 (1952).
40. Thompson, R. C., and J. E. Ballou, "Long-term retention of tritium in the rat and sheep", in Biology Research - Annual Report 1952, Document HW-28636, p. 59, (1953) (UNCLASSIFIED).
41. Thompson, R. C., "The gross retention and metabolism of tritium oxide in the mouse", Document HW-20092 (1951) (UNCLASSIFIED).
42. Thompson, R. C., "Retention by mice of tritium administered as the oxide", Document HW-21494 (1951) (UNCLASSIFIED).
43. Pinson, E. A., E. C. Anderson, and Virginia Lotz, "Incorporation of tritium into the organic components of various tissues of the mouse", Document LA-1467 (1952) (UNCLASSIFIED).
44. Thompson, R. C., and J. E. Ballou, unpublished data.
45. Pinson, E. A., E. C. Anderson and Virginia Lotz, "The specific activity of tritium in the organic components of the skin and fat of man following eight months' chronic exposure to HTO in body fluids", Document LA-1468 (1952) (OFFICIAL USE ONLY).
46. Thompson, R. C. "Effect of body distribution and retention of tritium on the hazard of exposure to tritium oxide", Document HW-30340 (1954) (UNCLASSIFIED).
47. Thompson, R. C., "Bibliography of tracer applications of deuterium to biochemical studies", Document HW-20283 (1951) (UNCLASSIFIED).
48. Thorne, M. B., "Studies on the enzymatic oxidation of succinic acid containing deuterium in the methylene groups", Biochem. J., 49, 602 (1951).
49. Schoenheimer, R. and D. Rittenberg, "The study of intermediary metabolism of animals with the aid of isotopes", Physiol. Rev., 20, 218 (1940).
50. Dole, M., "The concentration of deuterium in organic compounds. II. A general discussion with particular reference to benzene", J. Am. Chem. Soc. 58 580 (1936).

DECLASSIFIED

DECLASSIFIED

UNCLASSIFIED

46

HW-29615

51. Glascock, R. F., and W. G. Duncombe, "Biological fractionation of hydrogen isotope in mammary gland and other tissues", Biochem. J., 51, xl (1952).
52. Verly, W. G., J. R. Rachele, V. duVigneaud, M. L. Eidinoff, and J. E. Knoll, "A Test of tritium as a labeling device in a biological study", J. Am. Chem. Soc., 74, 5941 (1952).
53. Eidinoff, M. L., G. C. Perri, J. E. Knoll, B. J. Marano, and J. Arnheim, "The fractionation of hydrogen isotopes in biological systems", J. Am. Chem. Soc., 75, 248 (1952).
54. Weinberger, D., "Metabolism of hydrogen isotopes by algae" in Biology Research - Annual Report, 1952, Document HW-28636, p. 72 (1953) (UNCLASSIFIED).
55. Brues, A. M., A. N. Stroud, and L. Reitz, "Toxicity of tritium oxide to mice", in Biological and Medical Divisions' Quarterly Report, May, June, July 1949, Document ANL-4333, p. 136 (1949) (UNCLASSIFIED).
56. Jennings, F. L., and A. M. Brues, "Toxicity of tritium oxide on continued administration in rats", in Division of Biological and Medical Research Quarterly Report, February, March, April 1951, Document ANL-4625, p. 142 (1951) (UNCLASSIFIED).
57. Getzendaner M. E., M. P. Fujihara, and H. A. Kornberg, "Determination RBE's by microbiological methods", in Biology Research - Annual Report, 1952, Document HW-28636 (1953) (UNCLASSIFIED).
58. Kornberg, H. A., H. J. Dishburger, and M. P. Fujihara, unpublished data.
59. Powers, E. L., and D. Shefner, "Tritium induced effects in Paramecium aurelia", Document AECU-1485 (1951) (UNCLASSIFIED).
60. Hall, B. V., and A. Stroud, "Progress report: Comparison of the effects of irradiation in vitro with tritium and x-rays on the growth and survival of mouse tumor implants", in Biological and Medical Divisions Quarterly Report, February, March, April 1950, Document ANL-4451, p. 66 (1950) (UNCLASSIFIED).

UNCLASSIFIED

DECLASSIFIED

DECLASSIFIED UNCLASSIFIED

47

HW-29615

61. Stroud, A. N., "Progress report: Tissue culture", in Biological and Medical Divisions Quarterly Report, August, September, October 1949, Document ANL-4360, p. 81 (1949) (UNCLASSIFIED).
62. Stroud, A. N., and A. M. Brues, "The effect of tritium (H^3) on cells cultivated in vitro", in Biological and Medical Divisions Quarterly Report, February, March, April, 1950, Document ANL-4451, p. 111 (1950) (UNCLASSIFIED).
63. Furchner, J., J. Storer and Virginia Lotz, "The relative biological effectiveness of tritium in depressing iron uptake in rats", Document LA-1544 (1953) (UNCLASSIFIED).
64. Worman, F. C. V., Donna F. Turney, and Virginia Lotz, "The relative biological effectiveness of tritium beta rays in producing splenic and thymic weight loss in mice", Document LA-1641, (1954) (UNCLASSIFIED).
65. "Minutes of the permissible doses conference", R. M-10 Chalk River, Canada (1949).
66. Subcommittee on Permissible Internal Dose of the National Committee on Radiation Protection, "Maximum permissible amounts of radiosotopes in the human body and maximum permissible concentrations in air and water, "Handbook 52, U. S. Department of Commerce, Natl. Bur. of Standards, Washington, D. C. (1953).
67. Parker, H. M., "Basic health standards P-10 - Elaboration of stack discharge criteria", Document HW-18879 (1950 (SECRET).
68. Recommendations of the International Commission on Radiological Units, Brit. J. Radiol., 27, 243 (1954).
69. Best, C. H., and Taylor, N. B., The Physiological Basis of Medical Practice 4th Ed., Williams and Wilkins Co., Baltimore, (1945), pp. 534-35.

DECLASSIFIED UNCLASSIFIED

END

**DATE
FILMED**

4/9/92

2