TRITIUM SKIN-CONTACT DOSIMETRY

DOSIMETRY OF SKIN-CONTACT EXPOSURE TO TRITIUM GAS CONTAMINATED SURFACES

By

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A Project report

Submitted to the School of Graduate Studies

in Partial Fulfilment of the requirements

for the Degree

Master of Science

McMASTER UNIVERSITY

MASTER OF SCIENCE (1991) McMaster University
(Health & Radiation Physics) Hamilton, Ontario

TITLE: Dosimetry of Skin-Contact Exposure to Tritium Gas Contaminated Surfaces

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NUMBER OF PAGES: ix, 87

ABSTRACT

The radiological hazards from tritium are usually associated with exposure to tritium oxide either by inhalation, ingestion or permeation through skin. However, exposure from skin-contact with tritium gas contaminated surfaces represents a different radiological hazard in tritium removal facilities and future fusion power plants.

Previous experiments on humans by Eakins et al. (8), and more recent experiments on hairless rats at Chalk River Laboratories have shown that when a tritium gas-contaminated surface is brought into contact with intact skin, high concentrations of organically-bound tritium in urine and skin are observed which were not seen from single tritiated water (liquid or vapour form) contamination.

The results of the rat experiments, which involved measurements of tritium activity in urine and skin, after contact with contaminated stainless steel, are described. These results are also compared to previous data from human experiments. The effect of various exposure conditions and different contaminated surfaces such as

brass, aluminum and glass are analysed and related to the results from contaminated stainless steel exposure.

Dosimetric models are being developed in order to improve the basis for dose assessment for this mode of tritium uptake. The presently studied model is explained along with the assumptions and methods involved in its derivation. The features of 'STELLA', the software program used to implement the model, are discussed. The methods used to estimate skin and whole body dose from a model are demonstrated. Finally, some experiments for improving the accuracy of the model are proposed. Briefly, this study compares the results from animal and human experiments as well as different exposure conditions, and determine the range of whole body and skin dose that may be involved from skin-contact intake. This information is essential for regulatory purposes particularly in the derivation of doses for skin-contact contamination.

ACKNOWLEDGMENTS

The author wishes to express her gratitude to Frank Horvath for his invaluable advice and sense of humour. Special thanks to Dr Akhilesh Trivedi, from Chalk River, for his support, cooperation, and many useful discussions with respect to this project. Also sincere thanks to the Dosimetric Branch team (Marian DeAbreu, Emilie Lamothe, Jim Leon, Bob McElroy, Ric Surette) at Chalk River for their friendliness and patience in answering my numerous questions. I am also very grateful to Dr Colin Webber of McMaster University for his guidance and for reviewing my work so efficiently.

Acknowledgments are also directed to the Atomic Energy Control Board for giving me the opportunity of participating in this project and supporting my efforts, and to Canadian Fusion Fuel Technology Project (CFFTP).

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1. INTRODUCTION

Because of the low energy of the beta particles emitted by tritium (E_{max}=18.6 keV), the radiological hazards from this radionuclide arise mostly from internal contamination. The extent of this hazard depends upon the routes of entry into the body and the chemical form of the nuclide. These routes are inhalation, ingestion and percutaneous absorption, and the forms mostly encountered are tritium gas or tritium oxide (8). The commonly encountered ways of contamination with tritium are usually through inhalation or permeation through skin of tritium oxide (HTO)[1]. In tritium removal facilities or in the experimental fusion centres the hazards may be different (26). In these facilities, high concentrations of tritiated hydrogen gas (HT or T_2) become adsorbed onto metal surfaces (e.g. stainless steel) and skin contamination may occur from contact with the contaminated metals.

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1 Tritium oxide (HTO): Tritium atom bound to another hydrogen isotope and oxygen to form a tritiated water molecule.

1.1 HISTORICAL REVIEW

Before describing the more recent experiments, an outline of the previous papers on the subject will be given.

In the 1950's, De Long et al. (4), and Pinson & Langham (23), showed that HTO in liquid or vapour phase can be absorbed through the skin of mice, rats or man, and also that HT was converted to HTO in the body. As early as 1961, Vaughan & Davis (27) realized that other mechanisms of tritium intake seemed to exist and found that tritium adsorbed on glass could be transferred to the skin by contact.

Hutchin & Vaughan (10), in 1964, decided to extend the studies of tritium uptake through skin to other contaminated metals exposed to HT. In their experiment, they used brass planchets exposed to HT and massaged the skin of the rats against each planchet for 20 seconds, in a delimited area behind the neck. The rats hair had been clipped prior to exposure. Urine samples (24 hrs collections) were taken on various days post-exposure. Skin samples were excised and immediately combusted and counted for total tritium with a liquid scintillation counter. They found that HTO excretion displayed a single exponential behavior. They also illustrated, from the multi-

exponential behaviour of OBT[2] retention in skin, that there was undoubtedly several different processes involved in the translocation of tritium through skin.

Eakins, Hutchinson & Lally (8) were the first ones, in 1975, to study the hazards on humans from percutaneous absorption and ingestion following skin contamination. Four subjects volunteered for the experiment. An area of 38 cm^2 on the inside forearm was brought into contact with a metal strip (brass), contaminated with tritium gas and with a metal cylinder for exposure of the palm. From skin exposure, all subjects showed a maximum tritiated water concentration in urine about 24 hrs after exposure with a biological half-life of about 15 days compared to the half-life for simple tritiated water contamination of 10 days. Eakins and his co-workers (8) also found evidence for organic tritium (OBT) in urine from the decrease in the half-life of the tritiated water in the excretion curve after the first week indicating that some of the organic tritium initially in the body was being converted to tritiated water. When the OBT compounds in urine were examined by infra-red

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2 Organically bound tritium (OBT): Tritium bound to bio-organic molecules that is not readily exchangeable with hydrogen in body fluids.

spectroscopy, a broad spectrum was obtained giving some indications that the OBT belongs to the carboxylic acids group. Similar results were obtained when the same experiments were carried out with steel and aluminum surfaces, with different exposure times and using the palm of the hand as the exposed area. When looking at the effect of decontamination of the skin, it was found that washing the skin 30 minutes after exposure reduced the total amount of tritium absorbed by about 76 per cent, leading to an important dose reduction. The study also included the ingestion of tritium following the transfer to the hands from food to a contaminated surface. In the excretion curves, it was found that the ratio of organic tritium to tritiated water was about 60:1. This ratio was much higher than that found following application of HT contaminated surfaces to skin and results in an increased tissue dose because of the longer retention of OBT.

Because of the planned tritium extraction facilities and the significant quantities of tritium gas to be processed, Johnson and Dunford (14) decided to try to quantify the dose to skin and to body tissues by constructing two dosimetric models based on Eakins et al (8) excretion curves. The studies by Johnson et al (15), Johnson &

Peterman (16), Trivedi et al (26), were all done on animals (rats). These studies concentrated on metabolism and dosimetry from exposure with contaminated surfaces using different dosimetric models and calculating the dose to different tissues. The modelling showed that the dose to skin may be the limiting factor in radiation protection purposes.

1.2 OBJECTIVES OF PRESENT STUDY

The objective of this project is to analyse the results of experiments recently performed at Chalk River on hairless rats. This includes the determination of short and long term components of HTO and OBT in urine and skin, excretion patterns of HTO and OBT in urine, and retention pattern of HTO and OBT in exposed and non-exposed skin. Since the purpose of this work is to estimate the dose to humans from this mode of tritium intake (particularly the inference of skin dose from bioassay measurements), results from experiments with rats will be compared with results from human experiments. The study also includes the validation of a model proposed by the Chalk River group to improve the basis for dosimetry for skin-contact exposures to tritium gas contaminated surfaces and to evaluate the importance of the dose to the skin.

2. EXPERIMENTAL PROCEDURES

2.1 EXPOSURE OF METAL PLANCHETS

Circular stainless steel planchets of 11 cm^2, 0.5 mm thick, were used for skin exposure. The planchets had been washed with acetone and then exposed to 370 torr of HT gas for 30 minutes in the Chalk River tritium handling facility. The planchets were put in an open container for 24 hours to allow loosely adsorbed volatile HT labelled compounds to escape. This limited the possible exposure of experimenters to a high concentration of tritium gas and other volatile compounds. However, this may explain the presence of tritium oxide on the surface of the planchet, arising from the oxidation of the tritium gas with the oxygen in the atmosphere. To measure most of the tritium sorbed onto and into the planchets (25), they were placed in a desorption furnace with its temperature raised to about 400 degrees celsius. The evolved HTO was collected in a first set of bubblers and the evolved HT collected in the second set of bubblers, after having been oxidized by a heated copper oxide bed. The total tritium evolution was recorded on a chart recorder connected directly to an ion chamber. The collected activity was in

the form of HTO and HT, the largest fraction being HTO. The observations suggest that there was a large HTO component of the activity as soon as the exposure chamber was opened to the atmosphere after the exposure process. The exact quantity could not be measured accurately. It is not known if any non-volatile organic compounds of tritium were present on the planchet and which would not have been accounted for in the total planchet tritium inventory. The residual activity which could be easily removed from the surface was determined from multiple swipe measurements. The total average activity sorbed on the planchet was measured to be about 1 mCi. The activity detected on the planchet was attributed to non-exchangeable tritium (NET)[3]. It was found that 10% of the surface activity was removed in a single swipe, and that the fraction of removable activity was dependent on the surface history. For example, when a surface is left undisturbed for a period of time, the surface activity may regrow from the bulk of the metal and migrate to the surface. On the other hand, if the surface is left for a longer period of time, some of the activity in the planchet will be

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3 Non-exchangeable tritium (NET): tritium bound to either inorganic or organic molecules that is not exchangeable with hydrogen in water.

lost to the atmosphere, as HT or HTO, which is formed by the oxidation of some tritium gas on the metal surface.

2.2 ANIMAL EXPOSURE

The animals used were 10 female hairless rats (Sprague-Dawley) of approximately 500 g and 17 to 29 months old. Hairless rats are chosen to both limit the stress to the animal and to eliminate abrasions of the skin due to the shaving procedure required with normal rats. Prior to exposure, all rats were placed in a metabolic cage and their urine collected for 24 hours to assay background levels of HTO and OBT. In a fume hood, the contaminated planchets were pressed against the skin of the left flank of the rats for 60 seconds with a constant pressure of 0.5 kg/cm^2. All rats were placed in metabolic cages for urine collection. The urine was collected every 12 hours up to day 4 and for 24 hours on days 4, 6, 13, and 20 after exposure to the contaminated planchet. For the measurements of activity in skin with time, 3 groups of 3 rats (male hairless, female hairless, normal male) were used. Before exposure, 1 rat of each group was euthanized and a small area of skin was excised for control purposes i.e. background measurement. The animals were serially sacrificed at times up to 28 days, and approximately 20 cm^2 of exposed and unexposed skin was collected.

In an other study which is not part of this report, organs and blood of these rats were also collected.

2.3 MEASUREMENT OF TRITIUM ACTIVITY IN URINE AND SKIN

The total tritium in urine was measured by liquid scintillation counting (0.5 ml of urine with 4 ml of scintillation cocktail). To differentiate between HTO and OBT, a low temperature distillation method (LTD) was used. This method was previously used by Eakins et al (8) in his experiments with humans. Briefly, the total tritium concentration of the initial urine sample is measured by aliquoting the urine (0.5 ml) in a scintillation vial and then measuring the activity by liquid scintillation counting (LSC) technique. Approximately 15 ml of the urine is placed in a small (20 ml) Petri dish, and covered with a lid. The Petri dish is placed on a pre-heated hot plate (40°C), and a small beaker of crushed ice is put on the Petri dish to cool its surfaces and so gather the condensate on the underside of the lid. The condensate (~1 ml) is collected for measurement of the tritium activity. The condensate represents the volatile (HTO) component of the urine sample. The difference in total activity of tritium and HTO in urine is attributed to the activity of OBT in urine. This assumption is reasonable since the

likely organic compounds of tritium will be less volatile than HTO. The LTD method is not a closed system and as such a fraction of the water vapour (including HTO) escapes during the distillation process. However, the HTO concentration measured in the water of the condensate will be the same as that of the HTO in the sample, and therefore the loss of HTO during the LTD procedure has little effect on the accuracy of the method. The recovery of HTO and OBT activity from a standard tritiated sample is 90 ± 7%. However, since the OBT activity arises from the subtraction of two potentially equal values, the error on their difference may be large.

In excised skin, the HTO is measured by soaking the tissue sample in distilled water. The distilled water and free tissue water, tagged with tritium, is collected under vacuum in a dry ice cold trap during the drying process and counted by liquid scintillation counting. The procedure is repeated until the activity in collected water is no longer detectable at the background level (where background is taken as the activity in a rat which was not exposed to the contaminated planchet, with an error range of ± 20%). To estimate the amount of OBT in skin, the remaining dried skin was then placed in an oxygen combustion bomb and combusted at 30

times atmospheric pressure. The combustion of the sample occurs almost instantaneously. The water formed during the combustion was trapped by a cold trap and counted in a liquid scintillation counter. From the combustion of known amounts of tritiated thymidine, it was previously found that the percentage of recovery of the OBT was 89 ± 7 % (16).

2.4 STATISTICS

The time variation in activity concentrations of tritium (HTO and OBT) in urine and skin was measured in 10 rats. The error on individual concentrations was found to be about 10 % for the first days data with high activity samples and about 20 % for the lower activity samples i.e. after 5 days. These errors are mainly based on counting statistics, since the errors on volume measurements were negligible compare to the counting errors. Semi-log plots of the data for each animal were drawn, and when these plots were found to be non-linear, the half-life were calculated for the short and long-lived components. This was done by regression analysis for each component until a satisfactory fit was obtained, when the normalized square of the residuals was greater than 0.9 (where a perfect correlation would have a normalized residual value of 1). Here the main difficulty was to determine which data points belonged to the short or long term component when performing the regressions. A statistical method (17) using the F-distribution test, for determining the breakpoint of two lines was tested with a few curves. This method did not yield good results especially when more

than three components appeared to be present. In this case, it would still assume the presence of only two components and consequently find an inappropriate breakpoint. Therefore, the method was not further utilized in the regression analysis. Instead, the components were stripped in the following way:

1) Data points near the breakpoint of the curve (determined by eye) were included or excluded in the regression;

2) the contribution from the long-lived component was subtracted;

3) the best fit chosen was the one giving the highest residual coefficient (closest to one) while including all data points within the error bars.

To calculate the average half-life for each component, the statistical software package "STATVIEW" was used. The standard error, variance, and the 95% confidence interval for the slope of each component were computed using the *t* distribution.

3. RESULTS

3.1 PATTERN OF TRITIUM EXCRETION IN URINE

To examine the daily variation of tritium concentration in urine, measurements were made in 10 female hairless rats during a period of 21 days. Urine samples were collected at intervals ranging from 0.25 to 7 days after exposure. Each was analyzed for total tritium[4], tritium oxide, and organically-bound tritium using the methods described in section 2.3. Organically-bound tritium represents about 80% of the total tritium activity in skin, and tritiated water the remaining 20%. Although the excretion patterns were similar for each rat, the excretion rates for individual rats varied over a broad range. For this reason, and since there were only a few animals per experiment, every data point was normalized to the largest total tritium activity in urine, occurring at about 24 hours post-exposure. In other words, the activity measured at different times for each component was divided by the maximum activity (HTO + OBT) observed at 24 hours for each rat (the point on

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[4] Total tritium is the sum of organically-bound tritium and tritium oxide.

the x-axis where the time derivative is zero). Individual plots were obtained for each animal (for HTO, OBT and total tritium), and the excretion rates of the different components calculated. Figures 1, 2, 3, show the semi-log plots of the excretion patterns normalized to the maximum total tritium among the 10 rats for HTO, OBT, and total tritium, respectively. The normalization was accomplished in the following manner:

1) the maximum activity concentrations were extracted for each rat;

2) each data point was divided by the highest activity concentration to obtain the normalized values.

Figure 4 shows the semi-log plot of the average of the normalized excretion curves which shows the relative contribution of HTO and OBT to total tritium. This normalization was performed in the following way:

1) every data point for each rat (for HTO, OBT and total tritium) was divided by the highest value of total tritium (OBT + HTO) for that rat,

2) the average for each component for each time where the measurement was calculated.

From these curves (figure 1 and 4), one can see that the HTO excretion curve after 1 day can be represented by a single exponential which can be fit to a straight line which has a half-life of 3.3 ± .5 days. The retention curve of OBT can best be represented by two exponentials; a fast and a short term component. The half-life of the fast component is about 0.71 ± 0.18 day while that of the slow component is about 1.4 ± 0.5 days. In all cases, the concentration excreted was observed to increase rapidly at early times, possibly reflecting a high diffusion rate of tritium through the skin. For this reason, only a few data points are present in the first few hours of the concentration curve and no regression analysis was performed on the positive part of the curve. At the peak excretion time, which occurs around 1 day, the ratio of OBT to HTO is 11 ± 2. However, about 6 days after exposure, the amount of OBT excreted per day is very small and HTO then constitutes most of the total tritium excreted in urine.

Table 1 shows the half-lives for the excretion of HTO, OBT, and total tritium, and for comparison, the half-lives obtained by Johnson and Peterman in a previous experiment (16).

Figure 1: Activity of HTO in urine, 10 rats

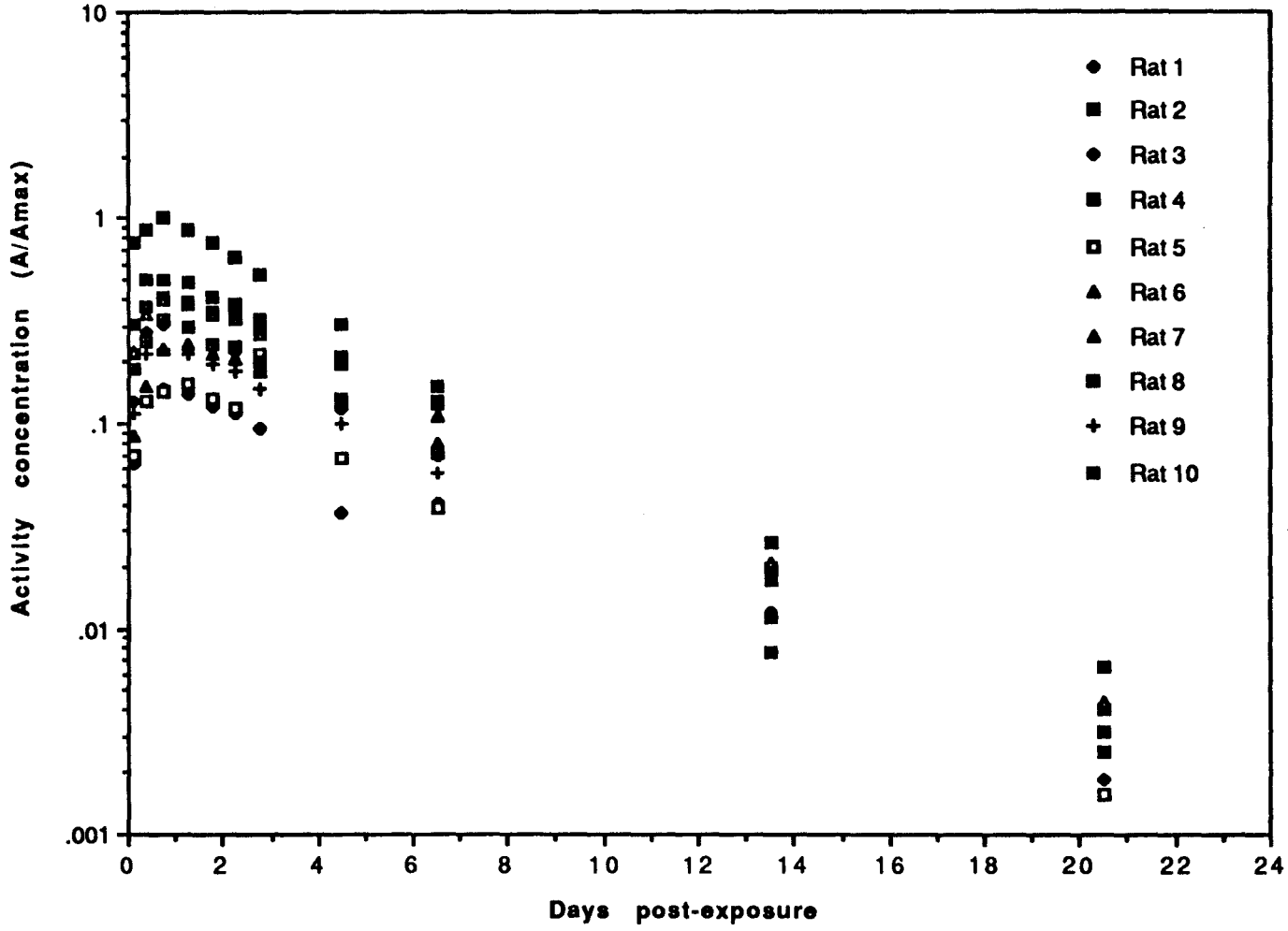


Figure 2: Activity of OBT in urine, 10 rats

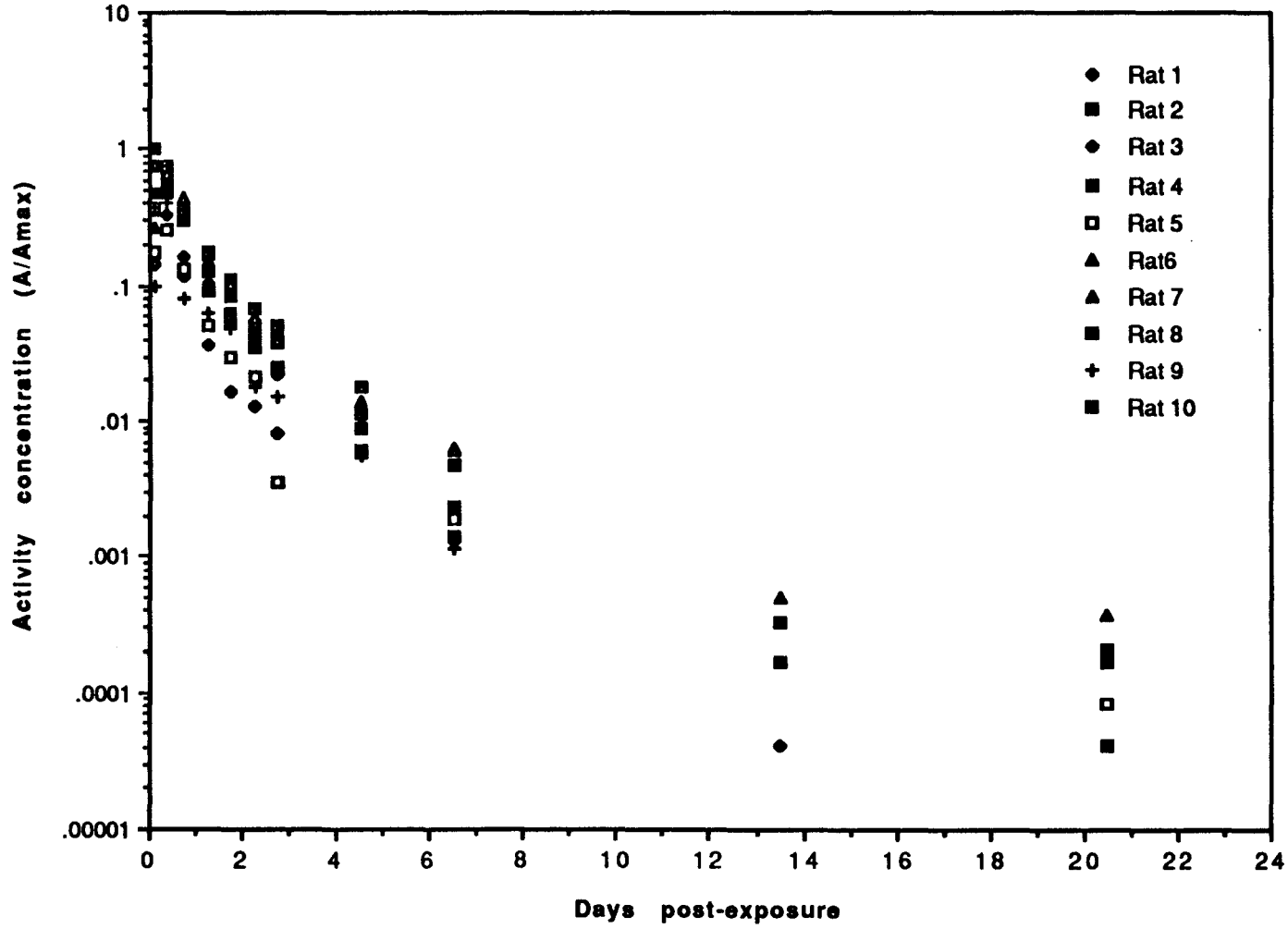


Figure 3: Activity of total tritium in urine, 10 rats

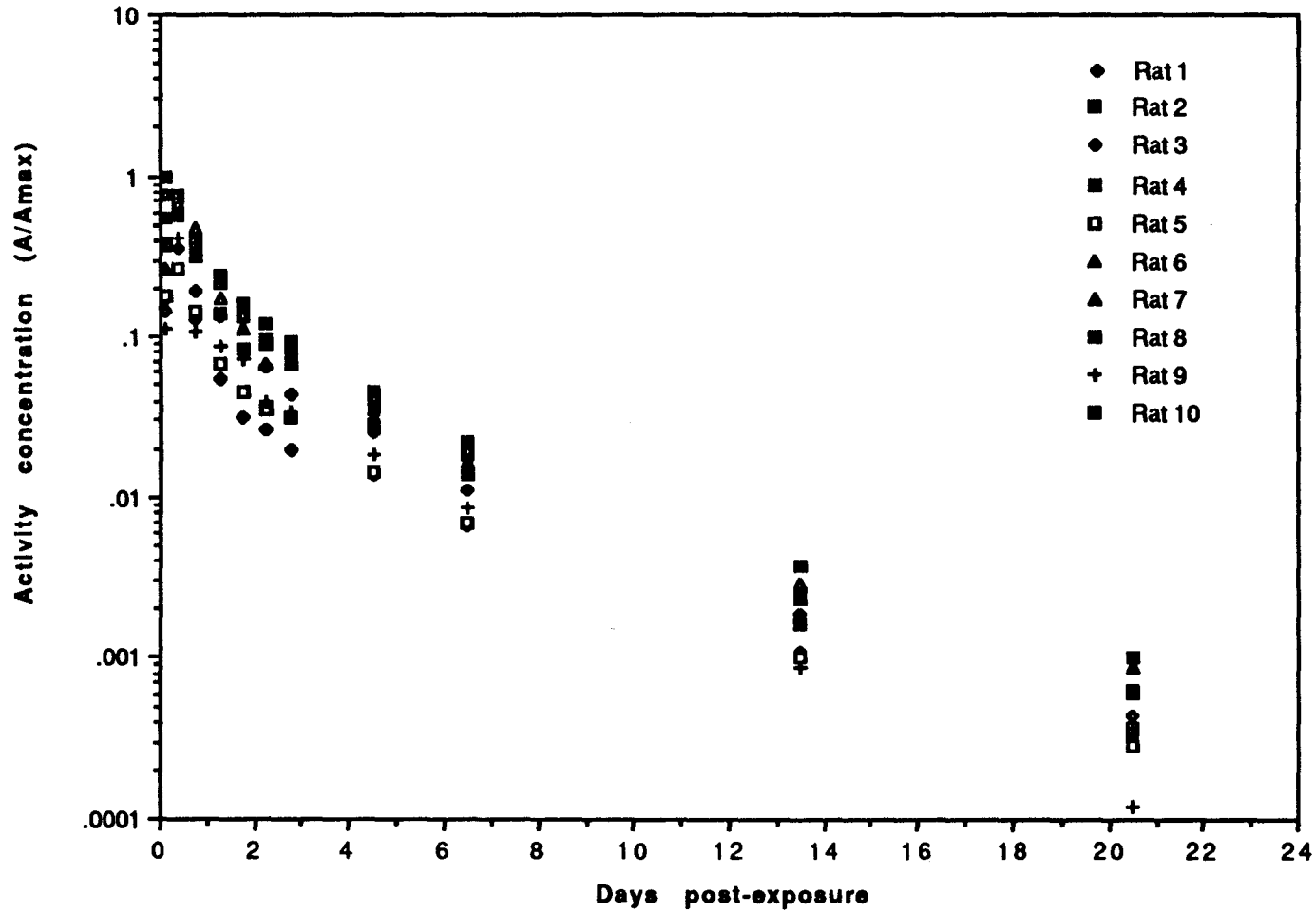


Figure 4
Normalized average of HTO, OBT and total tritium excretion

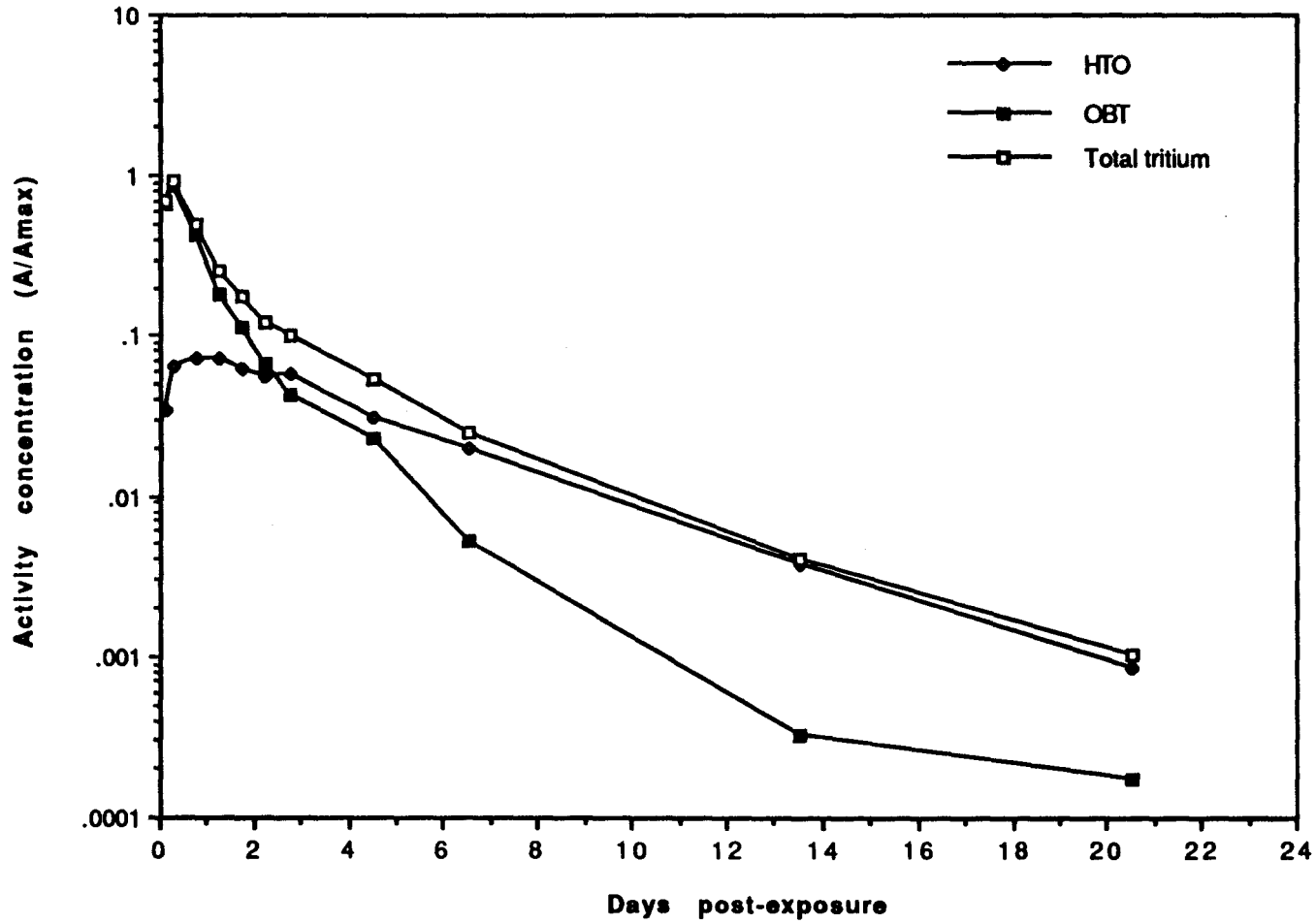


TABLE 1

HALF-LIVES FOR EXCRETION OF OBT AND HTO

Animal	OBT (days) Component 1	OBT (days) Component 2	HTO (days) Component 1
1	0.93	1.78	3.30
2	0.77	0.94	3.01
3	0.58	1.26	4.08
4	0.85	1.60	4.08
5	0.75	xxx	3.15
6	0.83	1.78	3.65
7	0.94	1.41	3.46
8	0.46	1.70	2.67
9	0.53	xxx	2.77
10	0.49	1.50	3.15
Averaged normalized curve	0.48	1.50	2.97
Mean:	0.71	1.35	3.33
Standard deviation:	0.18	0.47	0.49
Variance:	0.06	0.17	0.24
Johnson-Peterman mean:	0.46	1.45	3.22
Peak ratio OBT/HTO	11		

3.2 VARIATION OF EXPOSURE PARAMETERS

The experimental conditions were varied in order to demonstrate the dependence of intake on the following factors: type of surfaces, area of exposure, duration of exposure, pressure of the contaminated surface on the skin, and the mode of decontamination.

To look at the effects of skin-contact with different contaminated surfaces, four surfaces were exposed to tritium gas, under the same conditions. The surfaces compared were: stainless steel, brass, aluminum, and glass. All rats were exposed to the different surfaces, with identical surface areas, for 60 seconds, under the same application conditions. The excretion curves for brass, aluminum, and glass are shown in figure 5, 6, and 7 respectively, and the results summarized in table 2 (including stainless steel). The tritium excretion curves for all surfaces displayed similar excretion rates but with HTO being excreted more slowly and OBT slightly more rapidly in the case of stainless steel. The main difference, however, was observed in the OBT to HTO ratio at the concentration peaks. The ratios varied from 4 for brass, to 52 for glass. This will be of importance when calculating the skin and

whole body dose from the activity in urine. If this factor is not taken into account when contamination occurred with a different material, the dose could be underestimated by a factor of about 10, if the contaminated material is assumed to behave like brass. Further experiments with more rats are therefore needed to verify these values in order to elucidate the possible differences for these ratios. The difference may in fact be due to possible contamination of the surfaces with oil or to the amount of OT radicals available on the different surfaces.

To study the possible effects of varying the area of exposure, one rat (rat 2) was exposed with a 2.5 cm diameter planchet (5.1 cm^2) while the other, chosen as the standard, was exposed with a 3.8 cm diameter planchet (11.3 cm^2); all other parameters were unchanged. No difference in the half-lives of the excretion rates was observed for either HTO or OBT, within the standard deviation (see Table 1). Table 3 shows a comparison of other parameters such as: peak HTO, peak OBT, OBT/HTO ratio, and percentage of total activity with respect to standard rat, rat 1. The peak in OBT occurs at a later time and with a smaller OBT/HTO ratio than for the control rat. The main difference is that only 48 % of the

total activity is excreted compared to the rat exposed to a 11.3 cm^2 area planchet. From this result, it appears that a 45 % reduction in planchet area leads to a proportional reduction in activity transferred to the skin. A linear relationship appears to be present between the planchet area and the total activity concentration in urine, although a larger number of planchets of various size is required in order to confirm this observation.

The third parameter varied was the pressure of the contaminated surface on the skin. The pressure of the planchet on one rat (rat 3) was 0.1 kg/cm^2, 0.3 kg/cm^2 on rat 4, and 0.5 kg/cm^2 on rat 1. According to table 3, the peak in OBT occurred at a later time for rat 3 but at an earlier time for HTO for rat 4. Within the error range, there were no differences in the observed half-lives (table 1). The total activity excreted in urine was reduced by 70 % for the rat where the applied pressure was reduced by a factor of five (rat 3). However, nothing can be concluded for rat 4 since the 18 % difference may be due to the individual rat differences.

To investigate the effect of exposure durations of less than one minute, one rat (rat 5) was exposed with a 3.8 cm planchet for a period of 15 seconds and the second one (rat 6) for 30 seconds. The

Figure 5: BRASS
Normalized activity of tritium in urine
semi-log plot

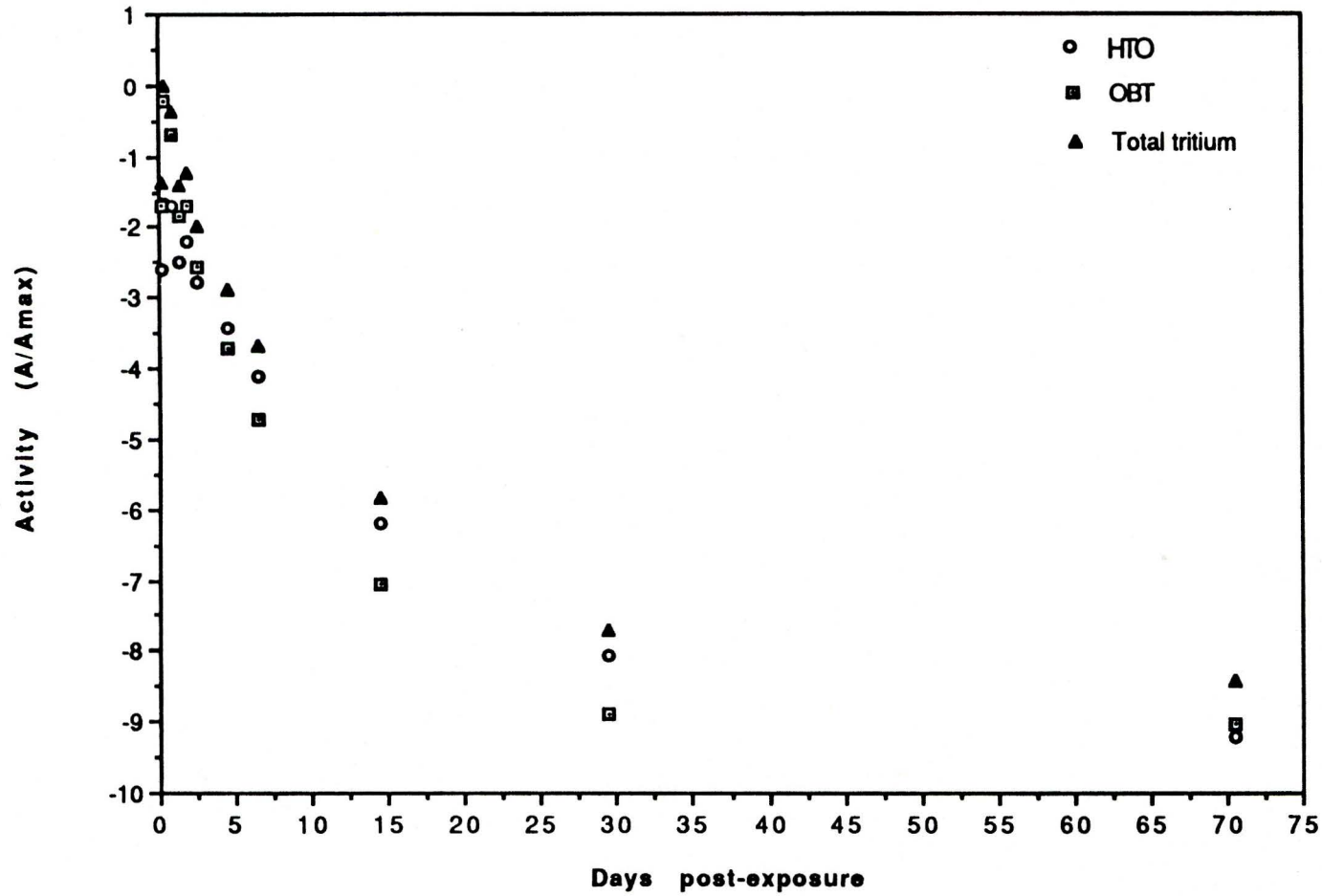


Figure 6: ALUMINUM
Normalized activity of tritium in urine
semi-log plot

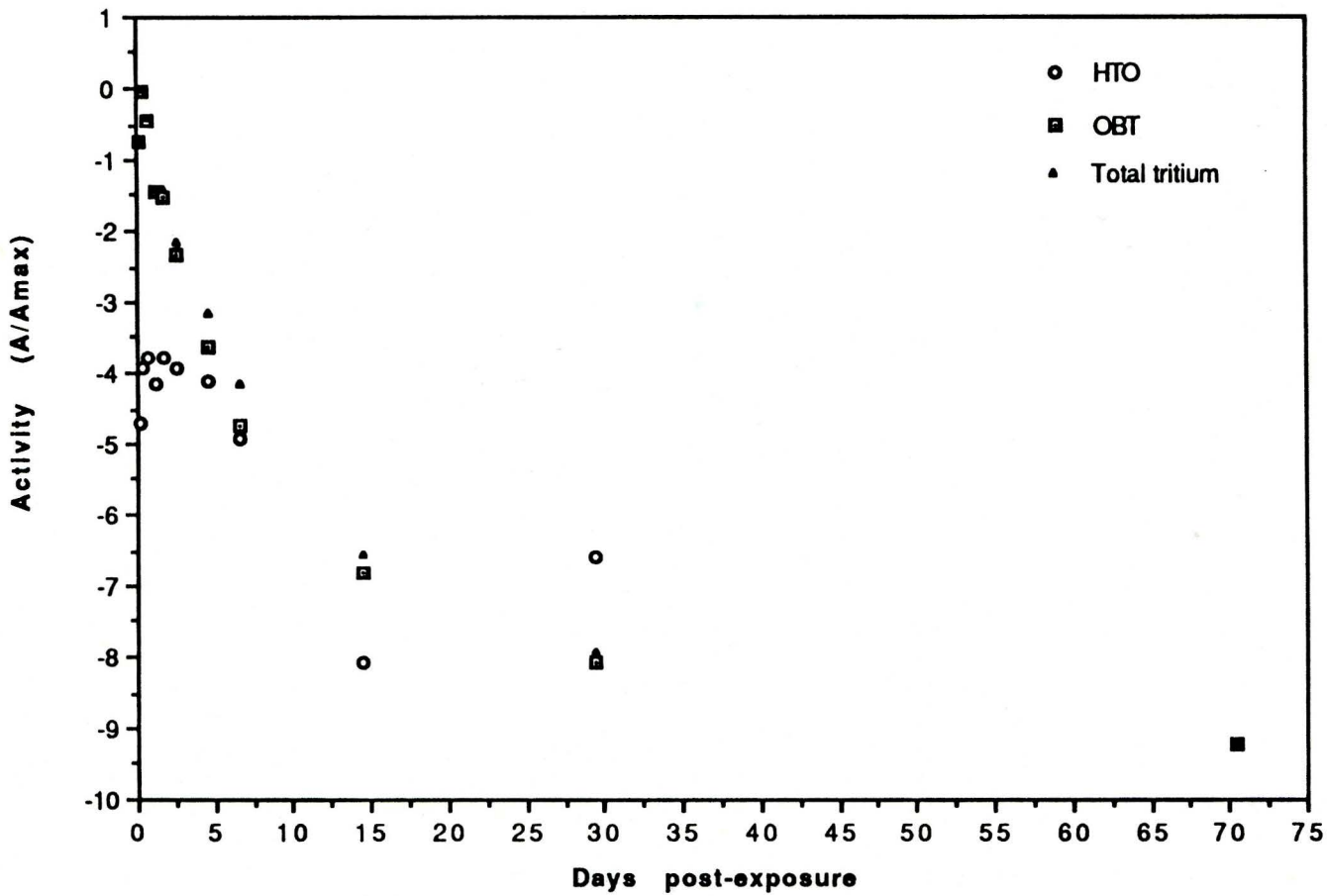


Figure 7: GLASS
Normalized activity of tritium in urine
semi-log plot

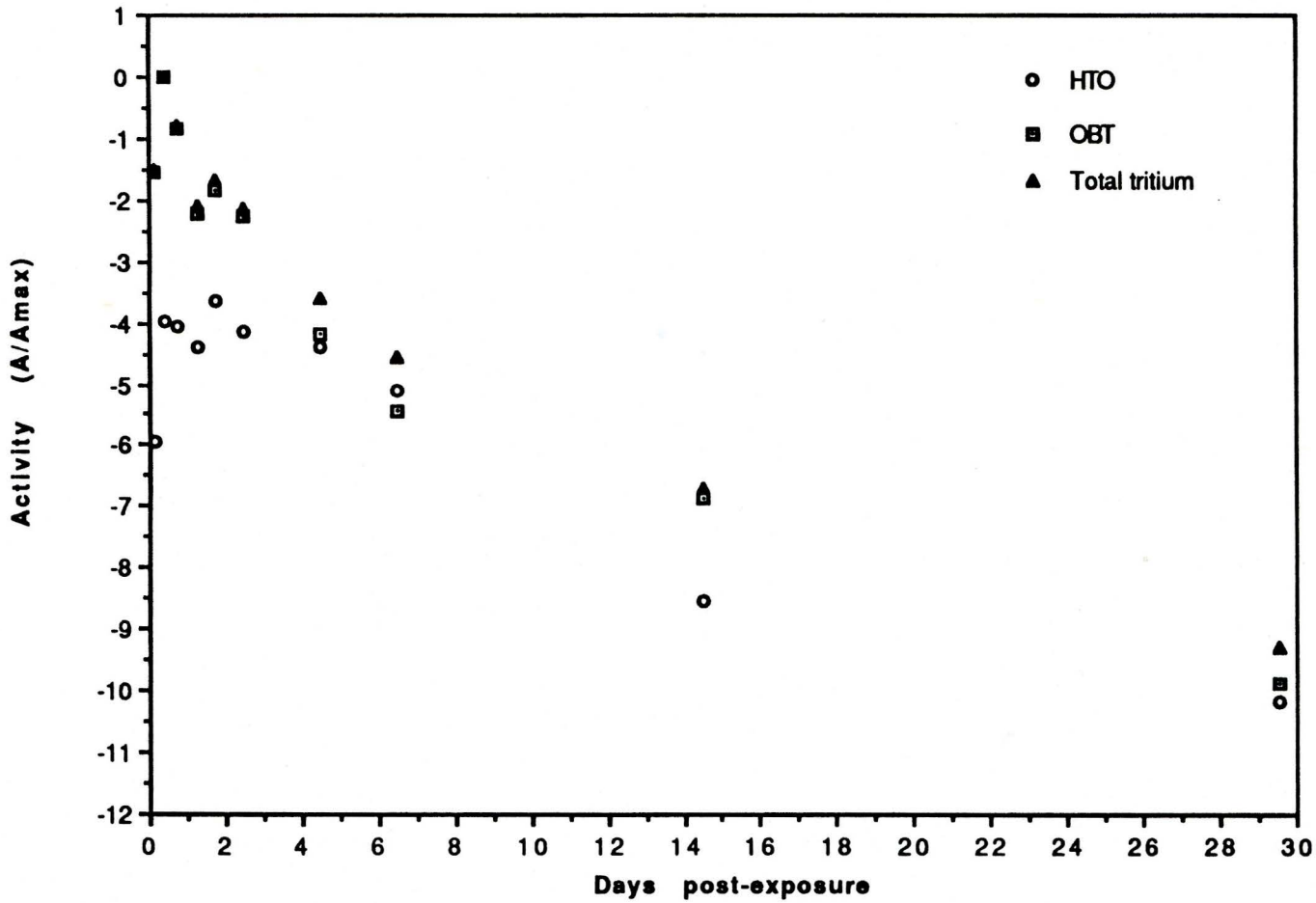


TABLE 2

EXCRETION CURVES PARAMETERS FOLLOWING CONTAMINATION WITH DIFFERENT SURFACES

PARAMETERS	STAINLESS STEEL	BRASS	ALUMINUM	GLASS
Peak HTO:	.5 to 1 day	.5 to 1 day	.5 to 1 day	.5 to 1 day
Peak OBT:	8 hrs	8 hrs	8 hrs	8 hrs
Peak H3:	8 hrs	8 hrs	8 hrs	8 hrs
HTO half-life:	3.3 days	2.2 days	1.8 day	1.7 day
OBT half-life 1	.71 day	.65 day	1.1 day	1.1 day
OBT half-life 2	1.4 day	4.0 days	18 days	3.6 days
OBT/HTO:	11	4	42	52

TABLE 3

Effects of varying the exposure conditions

Rat	Parameter varied	Planchet size diameter cm	Pressure (kg/cm2)	Duration of exposure (sec)	Peak HTO (hours)	Peak OBT (hours)	OBT/HTO ratio at peak	Total activity in urine (Bq/L)	% of total activity (standard)
1	Standard	3.8	0.5	60	24 +- 6	6 +- 3	13 +- 2	2.10 E 7	100%
2	Planchet size	2.54	0.5	60	24 +- 6	12 +- 3	8 +- 3	1.00 E 7	48%
3	Pressure	3.8	0.1	60	24 +- 6	12 +- 3	13 +- 3	6.41 E 6	30%
4	Pressure	3.8	0.3	60	18 +- 6	6 +- 3	14 +- 4	2.49 E 7	118%
5	Duration	3.8	0.5	15	30 +- 6	12 +- 3	12 +- 3	7.32 E 6	35%
6	Duration	3.8	0.5	30	30 +- 6	12 +- 3	18 +- 4	1.54 E 7	73%

control rat was exposed for 60 seconds. The half-lives were the same within error (table 1), but the peaks in activity concentrations for HTO and OBT occurred at later times after exposure than for the control rat. The percentage of total activity recovered also increased with the exposure duration (table 3).

Decontamination of the skin shortly after exposure means that the skin was washed with a solution immediately after the contaminated planchet was removed from the skin. To perform this experiment, 4 cotton swabs were soaked in water, ethanol, acetone, and Radiacwash, respectively, and then used to wash the exposed skin for a duration of 1 minute, beginning 10 seconds after exposure. The excretion patterns were similar to the control rat (rat 1), but the total removed activity concentrations varied from one rat to the other. According to the percentage of total tritium recovered in urine after 21 days (compared to non-decontaminated skin), the acetone solution was found to be the most effective in removing the applied activity from the skin, with a value of tritium activity excreted reduced to 33% of that without washing. The next most efficient solution was Radiacwash (74%), then water (76%), and finally ethanol with 80% of the initial activity collected in urine.

However, if expressed as a percentage of the activity removed from the skin by the cotton swab (compared to the initial activity transferred to skin), ethanol is the most efficient, with 49% of the activity removed by the swipe, followed by radiacwash (29%) and water (20%), and finally acetone (13%). These results are presented in table 4.

The percentages of activity removed by the swipe do not all agree with the percentages recovered in urine. It is not understood at the moment why the order is not the same when the comparison is done differently. Since both acetone and ethanol are organic solvents of weak polarity, as opposed to the highly polarized molecules of water, they should be the most efficient in removing surface activity. The differences may come from variations among the rats and the experiments, particularly from the activity transferred to the skin from the planchet. A repeated experiment with a larger number of rats would help in clarifying this question. A dry swipe should also have been taken to see if the reduction in activity excreted arises truly from the washing solution and not only from the effect of rubbing the skin with a dry swipe. Therefore, no firm conclusions from the effect of different

decontamination solution, or the effect of washing alone, may be drawn from this experiment. The removal efficiency from washing is also expected to decrease rapidly as the time between decontamination an exposure increases. However, this assumption needs to be verified experimentally before conclusions may be drawn.

As compared to the non-decontaminated surfaces, the OBT to HTO ratio is 2.5, about 4 times less than before. The maximum concentration of HTO in urine occurs after about 6 to 12 hours as opposed to 24 hours for non-washed skin. The cross-over point between HTO and OBT appears at 2 days rather than 6 days post-exposure and there is no equilibrium period for HTO. Figure 8 shows the normalized activity from HTO, OBT and total tritium present in urine with time after decontamination.

Figure 8:
Activity concentration in urine after washing (normalized to maximum total tritium)

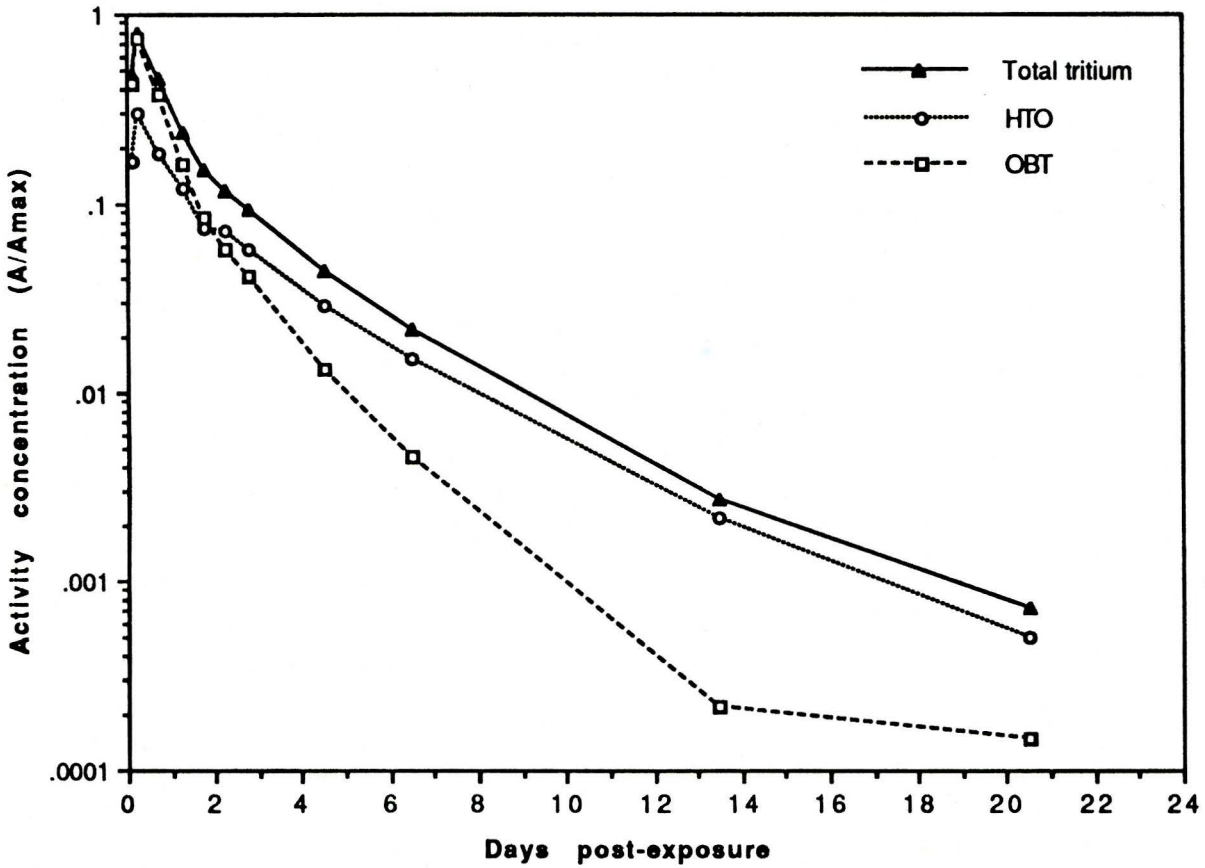


TABLE 4

COMPARISON OF DECONTAMINATION SOLUTIONS

SOLUTIONS	% Activity in urine	% Activity removed by swipe
ACETONE	33	13
RADIACWASH	74	29
WATER	76	20
ETHANOL	80	49

3.3 RETENTION PATTERN OF TRITIUM IN EXPOSED AND UNEXPOSED SKIN

Thirty rats were used to study the retention pattern of tritium in skin. Three rats were sacrificed prior to exposure and excised skin used for control purposes. The remaining rats were exposed with 3.8 cm stainless steel planchets, on the left flank with a pressure of 0.5 kg/cm^2 for 60 sec. Groups of three animals were euthanized simultaneously at sequential intervals and their skin excised. The HTO and OBT activity in the skin was determined as described in section 3. From a previous paper (25), it was found that 10% of the total activity sorbed into and onto the planchet was removed by a single swipe of the planchet surface, when using a piece of dry filter paper. The total evolved activity on the planchet after desorption was measured to be about 1 mCi. Assuming that the same amount of activity is removed from contact with the rat skin as with contact with the filter paper, approximately 0.1 mCi would have been transferred to the skin. The importance of the above assumption that the activity removed by the skin is the same as the activity removed by the filter paper should be emphasized. Although

10 % is found to be removed from a planchet by a single swipe with a filter paper, a much smaller or larger fraction may indeed be removed by the rat skin. In order to determine the exact amount removed by a single contact with the skin, an experiment could be performed in which the activity in the skin would be counted immediately after exposure and then the residual activity in the planchet counted by desorption, as described above. The fraction of the removable activity recovered in urine (total activity in urine/removable activity) where the removable activity is taken as 0.1 mCi, yields a value of 4%. A possible explanation for the small recovered fraction of the activity is that most of the tritium gas being transferred to the skin surface on contact can be oxidized and lost to the atmosphere, or maybe a much smaller fraction than 10% of the total activity on the planchet is removed by the rat skin. Although the initial activity in the skin cannot be estimated with any degree of certainty, the small recovered fraction of tritium inventory may indicate that an important quantity is retained in the body organs or tissues contributing to the whole body dose. The measurement of activity in the organs will give us indication of where, if any, longer term retention occurs. Figure 9 shows the

semi-log plot of the tritium retention pattern and of the activity concentration vs time for the exposed skin i.e. the skin directly in contact with the planchet. Regression analysis was performed on this curve to determine the half-life of the different components. The same analysis was carried out for the unexposed skin which was taken on the flank of the rat opposite to the planchet contact area (figure 10). This was done to investigate the phenomena of diffusion and retention of tritium in the skin. A high concentration of OBT was found in the unexposed skin.

The retention curves for HTO (exposed and unexposed) are both best represented by two exponentials. For the exposed area the first component has a half-life of 1.9 ± 0.2 days and the second 12.1 ± 2.9 days. For the non-exposed skin, the half-lives are 4.0 ± 2.0 and 7.1 ± 1.8 days respectively. OBT behaves similarly in both exposed or unexposed skin. Regressions were performed and the respective half-lives found to be 1.8 ± 0.4 and 22.5 ± 1.1 days for exposed skin and 1.7 ± 0.1 and 12 ± 6 days for unexposed skin. The contribution to the initial activity is as follow: OBT fast component (61%), OBT slow component (2%), HTO component (37%). These observations suggest that there may be a conversion process from OBT to HTO

within the skin. However, it is important to note that only a few data points were available to evaluate the second components since there was no measurements performed between days 28 and 91 post-exposure. The uncertainty in the second component is thus very large (50%). We also note that the OBT seems to have spread to the other flank and to be retained with the same half-life as in the exposed skin, in contrast to HTO where a difference in the half-lives was perceived. This appears similar to the whole body retention where the OBT/HTO ratio is greater than one in urine, and where the OBT half-life in the body fluids is also faster than HTO. Also the OBT behaviour, in the case of non-exposed skin, suggests that a transfer function is present between OBT in exposed and unexposed skin. Table 5 displays the half-lives for the different forms of tritium, along with their standard deviation. The averaged normalized curve was obtained from averaging every data points at a given time and express as a fraction of the maximum total tritium value. The half-lives were subsequently obtained from this curve. This is different than the mean half-live which are the average of the half-lives obtained from each individual curves. Also shown in this table is the peak OBT/HTO ratio in the skin of 110. This shows

that OBT is preferentially retained in the skin as compared to body fluids.

Figure 9
Normalized activity in exposed skin (HTO, OBT, total tritium)

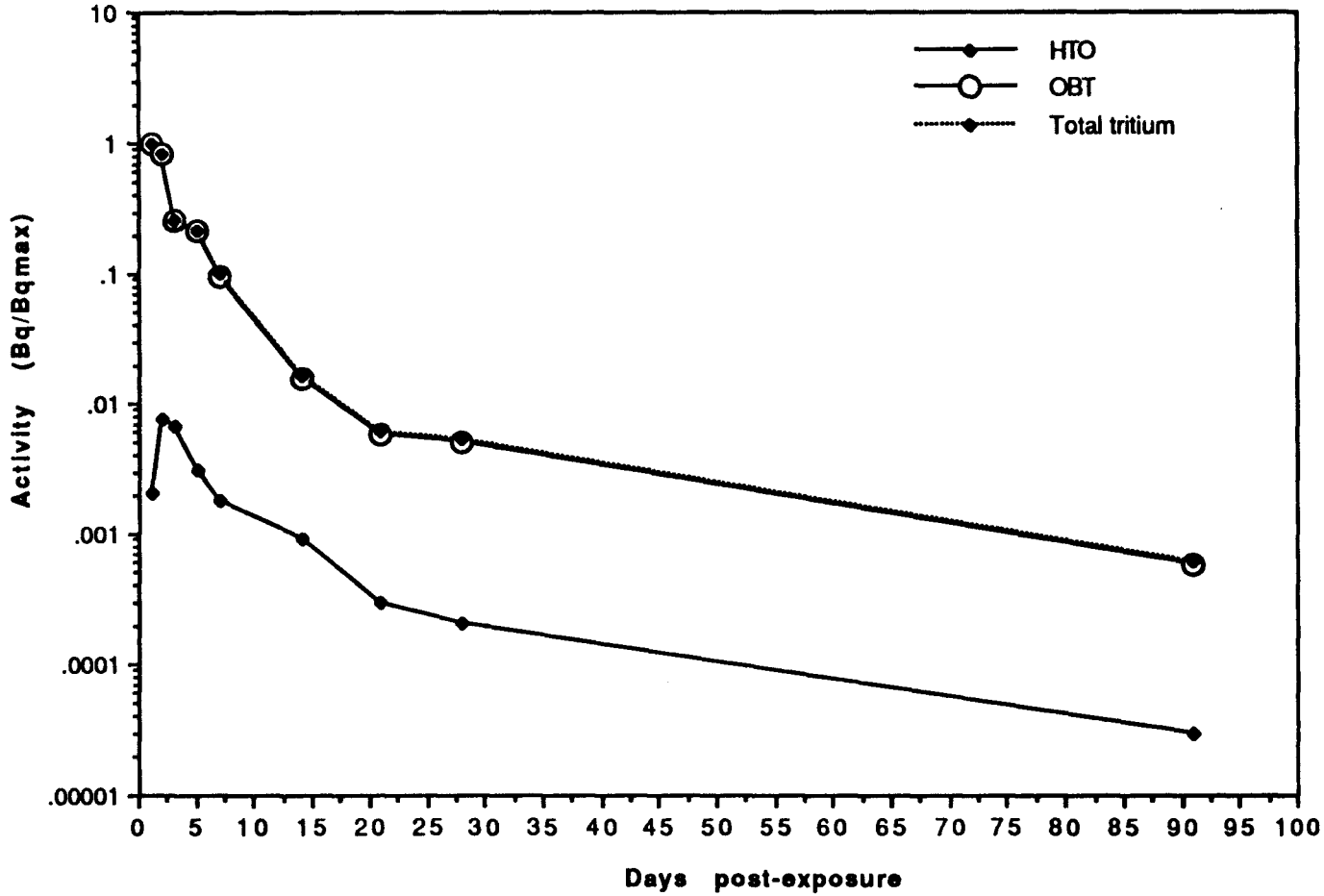


Figure 10
Normalized activity for unexposed skin (HTO, OBT, total tritium)

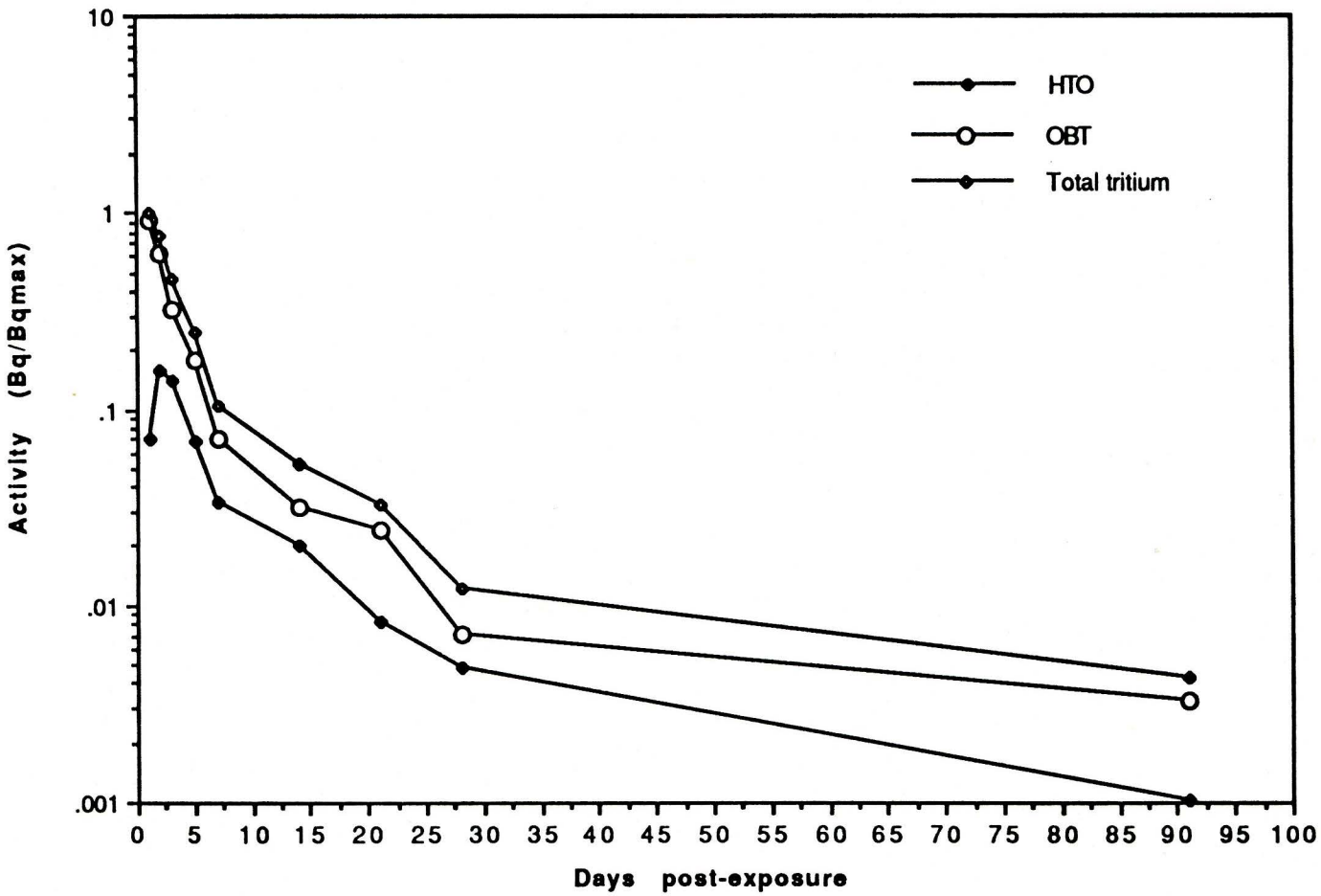


TABLE 5

HALF-LIVES FOR RETENTION OF OBT, AND HTO IN THE SKIN

STAINLESS STEEL

	EXPOSED SKIN				UNEXPOSED SKIN			
	OBT (days)		HTO (days)		OBT (days)		HTO (days)	
Animal	Component 1	Component 2	Component 1	Component 2	Component 1	Component 2	Component 1	Component 2
1	1.9	xxx	1.8	8.8	1.6	xxx	5.1	6.3
2	2.1	21.7	1.7	13.3	1.6	xxx	5.2	9.2
3	1.3	23.3	2.1	14.1	1.9	11.9	1.7	5.8
Mean:	1.8	22.5	1.9	12.1	1.7	11.9	4.0	7.1
Standard deviation:	0.4	1.1	0.2	2.9	0.1	xxx	2.0	1.8
Variance:	0.2	1.3	0.04	8.2	0.1	xxx	1.1	3.4
Peak ratio OBT/HTC in skin:	110.				5.3			

4. MODELLING

4.1 ASSUMPTIONS

The purpose of modelling is to mathematically and graphically describe the experimental results in order to derive further information that cannot always be obtained from laboratory experiments. The ultimate goal here is to use the animal data to develop a model that could be extended to humans. If the model can be validated using some previous experiments on human volunteers, then it can be used with confidence to estimate the dose to different organs or tissues of the human body. In particular, since the dose to the skin will never be measured directly on humans, one can only infer the skin dose from bioassay results and skin dose conversion factor provided from the model.

In developing the model, however, assumptions based on experimental observations are required. These assumptions are described below.

From the data on reference man (11), we know that about 47% of tritiated water entering the body is excreted in urine, the remainder exiting the body through exhalation, perspiration, and

feces. In the model derived from the rat experiments, it is also assumed that the same fraction of HTO entering the rat body is excreted in urine. This fraction is included in the model between the compartment for HTO in body fluids and HTO in urine. But in contrast, all the organically-bound tritium formed is assumed to be excreted in urine which could lead to an underestimated dose if other excretion routes such as sweat and feces are significant. Also, OBT in some chemical forms may be excreted very slowly or even not be excreted at all and remain in a particular organ. In such a case, the dose from this OBT would not be accounted for since it would not be observed in urine. Moreover, it has been shown (section 3.3) that only a fraction of the activity removed from the surface of the planchet was subsequently recovered in urine. Again, there might be a fraction staying in the body which is not observed in urine, excreted by some other pathway such as feces or perspiration, or released to the atmosphere from contaminated areas of the skin. It is also assumed that no important fractions of HT in the urine were inhaled by the rats or ingested through grooming.

With respect to the skin, two compartments are assumed for OBT: one to represent the fast OBT component in skin, the other

for the slow component. The latter appears to be responsible for the slower decrease of HTO concentration in the urine and is supported by the long skin retention of OBT.

Finally, this particular model assumes that no recycling takes place between the OBT in body fluids and the OBT in tissues. In order to determine whether or not recycling occurs, measurements of the concentrations of OBT in blood would be required.

4.2 DOSIMETRIC MODEL

Any model is designed to simulate and quantify the steps of a physical process. In the situation where tritium gas comes into contact with the skin through a stainless steel planchet, the physical processes to be characterized are the retention and excretion patterns of tritium in the form of either tritiated water or organically-bound tritium. The model needs then to describe the metabolic processes followed by the OBT or HTO. The proposed dosimetric model is shown in figure 11 (26).

At the time of contact between the metal and the skin, a fraction of the HT gas present on the planchet will be transferred to the skin. However, some tritium will have been oxidized to HTO or reactive radicals which are also transferred to the skin. In figure 11, compartment (A) will account for the HT and HTO in the skin. The tritiated water in the skin is then dispersed to the body fluids represented by compartment (E). The presence of OBT in skin may be explained by the transfer of OBT contamination from metal surfaces to, and subsequent diffusion into, skin, or by the metabolism of bio-organic molecules following the intake of tritium gas from metal

surfaces. Further work is needed to clarify the origin of the organically-bound tritium. Once the OBT is incorporated into skin it can be transferred to the body fluids, or a fraction may stay bound in the skin. The retention pattern of OBT in skin shows a two-component clearance; an initial rapid transfer followed by a slower one. Two compartments are therefore required to simulate both the slow and fast clearance of OBT in skin: compartments (C) and (D), respectively.

As opposed to HTO, not all the OBT is directly transferred from the body fluids to the urine but some is probably stored in other tissues then excreted or catabolized into HTO. This explanation is supported by the slower than normal decrease in HTO concentration in urine, in comparison with pure HTO exposures. The OBT in body fluids is described as compartment (F), the storage and conversion compartment is (B), and the excreted OBT is symbolized by compartment G_2, while the excreted HTO is represented by compartment G_1.

To solve the differential equations of the model, the software 'STELLA' was used, on a MacIntosh computer. This provides a pictorial view of the model and its execution, either in a diagram,

graphic or a table mode. With 'STELLA', the model is first constructed on the screen using the appropriate icon symbols and the relevant equations describing the kinetics of the model. The relationship between differential equations and the STELLA diagram is as follows. In calculus terms, flows in STELLA represent time derivatives; stocks are the integrals (or accumulations) of flows over time; converters contain logic (or equations) of flows. Chalk River's model (26) constructed on STELLA is illustrated in figure 12 followed by the utilized equations (figure 12 a,b).

STELLA solves the differential equations numerically and allows the user to choose the integration technique, the step size, and execution time. The integration techniques available to perform the simulation are: Euler's method, and second and fourth order Runge-Kutta. These methods typically are used to solve ordinary differential equations given a set of initial conditions, in this case, the initial activities in the skin compartments.

There are, however, sources of errors in these techniques. One is from the assumptions employed in the integration method. The second, of lesser importance, is the round-off error from the finite precision of the computer. In Euler's method, the area under the

curve is approximated by a small rectangle of chosen step size. The smaller the rectangle, the more accurate the integration will be since this method assumes a constant rate of change over each area. Consequently, as the step size decreases, so will the error in the Euler's approximation but the number of calculations required will increase and so will the computer time to execute the program. Therefore, the primary concern here is choosing the numerical method that will represent the best trade-off of computational speed for accuracy of the numerical method. The Runge-Kutta methods will provide more accurate estimates for a given step size but require more calculations in each single step. In contrast to the Euler's method, the Runge-Kutta methods do not assume a constant transfer rate over each interval but attempt to estimate the direction of the flow over a given interval. This is accomplished by estimating the flow at a number of points within the interval. If the error introduced with the different methods are compared, one should find that the errors are significantly less with the Runge-Kutta techniques, even while choosing step sizes two times (second order) or four times (fourth order) larger than Euler's.

Regarding the choice of a step size, a good initial rule of

thumb is to choose the step size equal to one third the fastest time constant. The next step was to test the simulation using this value. If the value did not represent the normal situation, then a smaller step size was used until satisfactory results were obtained i.e. artifacts introduced from the step size were eliminated.

In order to further validate the results and check for consistency between the numerical and analytical solution, the first order differential equations were also solved exactly. The two methods agreed perfectly. This exercise proved that STELLA can be used with confidence and will be particularly useful when dealing with higher order or partial differential equations, in cases where feedback is present.

Figure 11 **Dosimetric Model**

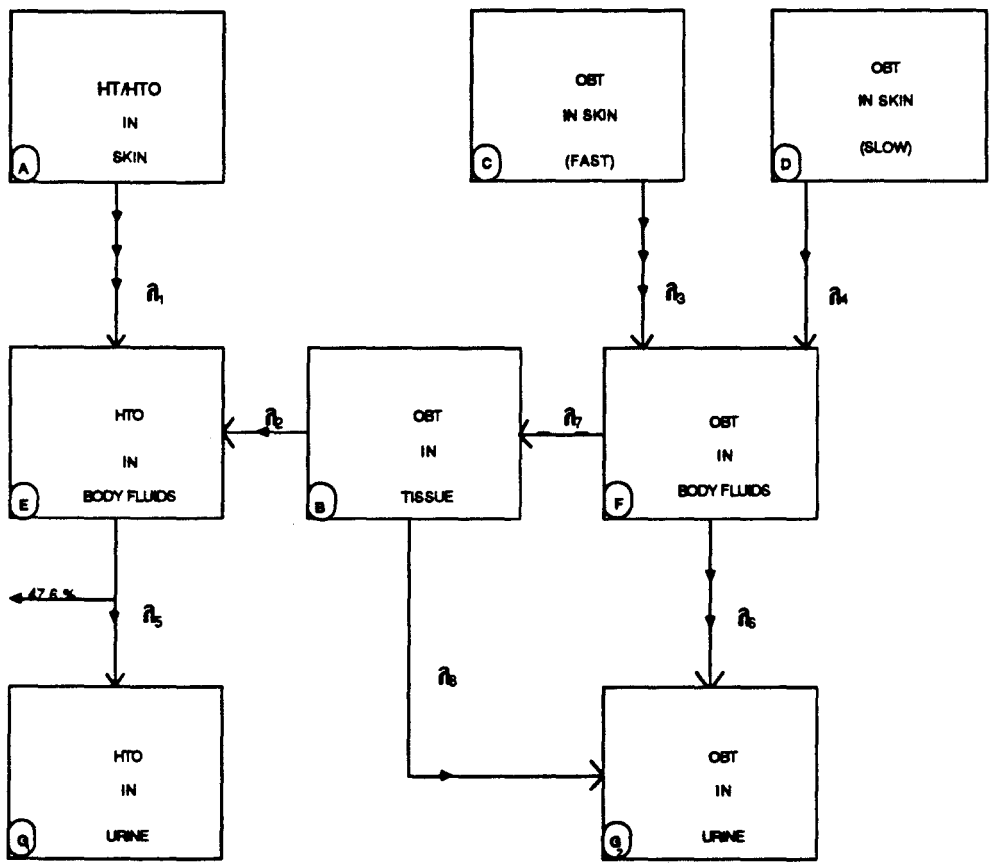


FIGURE 12: "STELLA" MODEL

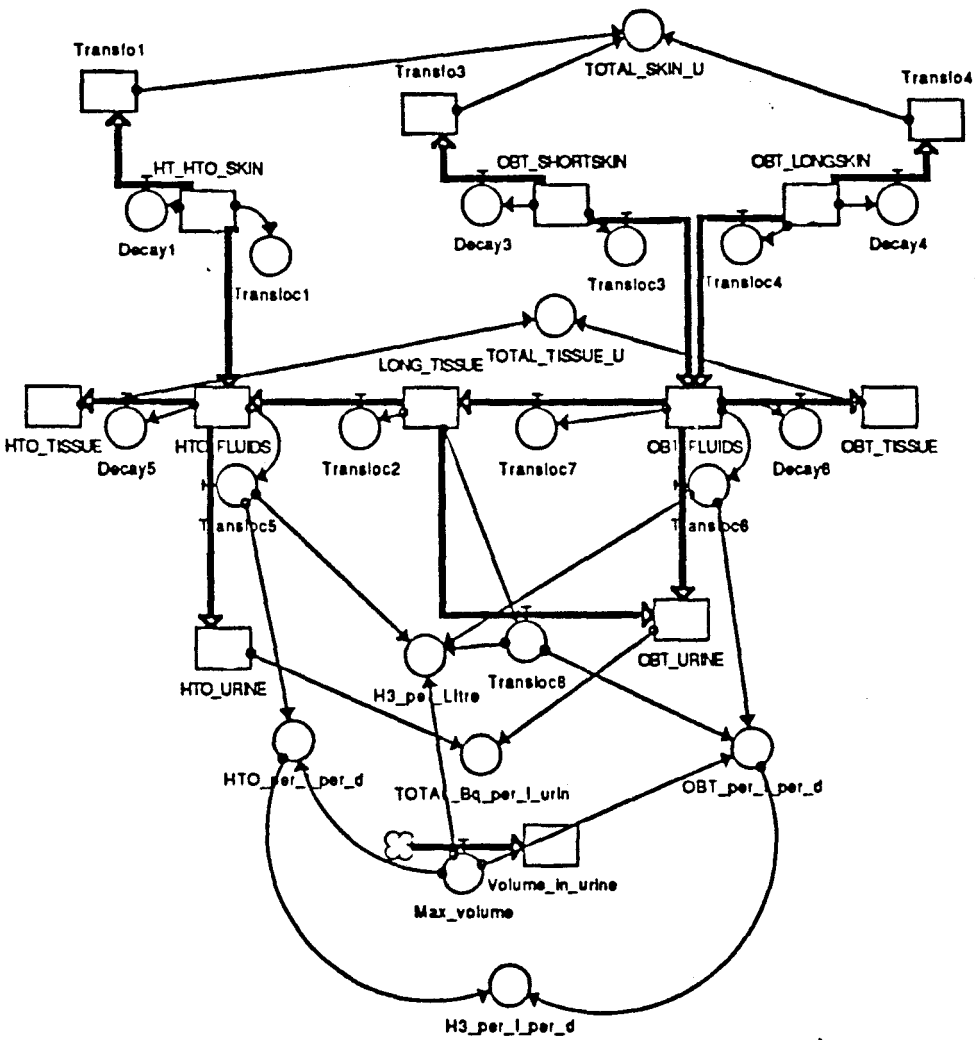


FIGURE 12 A: EQUATIONS

- HTO_FLUIDS = HTO_FLUIDS + dt * (Transloc1 + Transloc2 - Transloc5 - Decay5)
  INIT(HTO_FLUIDS) = 0 {Initially no HTO in body fluids}
- HTO_TISSUE = HTO_TISSUE + dt * (Decay5)
  INIT(HTO_TISSUE) = 0 {Initially no HTO in body: represents the total activity from HTO in body fluids}
- HTO_URINE = HTO_URINE + dt * (Transloc5)
  INIT(HTO_URINE) = 0 {Initially no HTO accumulated in urine, represents total activity from HTO in urine}
- HT_HTO_SKIN = HT_HTO_SKIN + dt * (-Transloc1 - Decay1)
  INIT(HT_HTO_SKIN) = .29{Initial activity in skin due to HT/HTO per Bq uptake}
- LONG_TISSUE = LONG_TISSUE + dt * (Transloc7 - Transloc2 - Transloc9)
  INIT(LONG_TISSUE) = 0 {Initially no OBT stored in tissue}
- OBT_FLUIDS = OBT_FLUIDS + dt * (Transloc3 + Transloc4 - Transloc7 - Transloc6 - Decay6)
  INIT(OBT_FLUIDS) = 0 {Initially no OBT in body fluids}
- OBT_LONGSKIN = OBT_LONGSKIN + dt * (-Transloc4 - Decay4)
  INIT(OBT_LONGSKIN) = .01{Initial activity due to slow OBT transfer in skin per Bq uptake}
- OBT_SHORTSKIN = OBT_SHORTSKIN + dt * (-Transloc3 - Decay3)
  INIT(OBT_SHORTSKIN) = .7{Initial activity due to fast OBT transfer in skin per Bq uptake}
- OBT_TISSUE = OBT_TISSUE + dt * (Decay6)
  INIT(OBT_TISSUE) = 0 {Initially no OBT in body: represents the total activity from OBT in tissue}
- OBT_URINE = OBT_URINE + dt * (Transloc8 + Transloc6)
  INIT(OBT_URINE) = 0 {Initially no OBT accumulated in urine, represents total activity from OBT in urine}
- Transfo1 = Transfo1 + dt * (Decay1)
  INIT(Transfo1) = 0 {Initially no transfo in skin at t=0 due to HT/HTO}
- Transfo3 = Transfo3 + dt * (Decay3)
  INIT(Transfo3) = 0 {Initially no transformation in skin due to fast OBT in skin}
- Transfo4 = Transfo4 + dt * (Decay4)
  INIT(Transfo4) = 0 {Initially no transformation due to slow OBT in skin}
- Volume_In_urine = Volume_In_urine + dt * (Max_volume)
  INIT(Volume_In_urine) = 0 {Initial volume of urine is zero}
- Decay1 =HT_HTO_SKIN*.693/(12*365){HT_HTO_SKIN*0.693/(12*365) # transfo at any time in skin due to HT/HTO, units are transfo/day}
- Decay3 = OBT_SHORTSKIN*.693/(12*365){OBT_SHORTSKIN *0.693/(12*365) # transfo at any time in skin due to fast OBT in skin}
- Decay4 =OBT_LONGSKIN*.693/(12*365){ OBT_LONGSKIN *0.693/(12*365)# transfo at any time in skin due to slow OBT in skin}
- Decay5 = HTO_FLUIDS*.693/(12*365){HTO_FLUIDS *0.693/(12*365) # transfo at any time in tissue due to HTO in body fluids}
- Decay6 =OBT_FLUIDS*.693/(12*365){OBT_FLUIDS *0.693/(12*365) # transfo at any time in tissue due to OBT in body fluids}
- H3_per_Litre = IF Max_volume > 0 THEN (Transloc5*.467+Transloc6 +Transloc8)/Max_volume ELSE 0 {Total activity concentration of tritium in urine}
- H3_per_l_per_d = HTO_per_l_per_d+OBT_per_l_per_d {total tritium per litre per day excreted in urine}
- HTO_per_l_per_d = IF Max_volume > 0 THEN (Transloc5 *.467/Max_volume)/34.16 ELSE 0 { Fraction of HTO in Bq per litre eliminated through urine}
- Max_volume = .025 {Maximum volume of urine to be eliminated per day by reference rat is .025 litre}

FIGURE 12 B: EQUATIONS

- OBT_per_l_per_d = IF Max_volume >0 THEN((Transloc6+Transloc8)/Max_volume)/34.16 ELSE 0 {Amount of OBT in Bq per litre eliminated per day}
- TOTAL_Bq_per_l_urin = (HTO_URINE*.467 + OBT_URINE)/.025 {Total activity per litre of urine from HTO and OBT. The factor .467 is the fraction of HTO exiting the body through urine}
- TOTAL_SKIN_U = (Transfo1 + Transfo3 + Transfo4)*(3600*24) {Total number of transformations in skin}
- TOTAL_TISSUE_U = (HTO_TISSUE + OBT_TISSUE)*(3600*24) {Total number of transformations in tissue}
- Transloc1 = 5*HT_HTO_SKIN {Exponential translocation of HT/HTO activity from skin to body fluids}
- Transloc2 = .02*LONG_TISSUE {Exponential translocation of activity in long term tissue storage to HTO in body fluids: OBT was combusted to become HTO in storage compartment}
- Transloc3 =4*OBT_SHORTSKIN {Exponential translocation of OBT from skin to body fluids}
- Transloc4 = .05*OBT_LONGSKIN {Exponential translocation of OBT from skin to body fluids}
- Transloc5 = .2 * HTO_FLUIDS {Exponential translocation of HTO from body fluids to urine}
- Transloc6 = 1.5 * OBT_FLUIDS {Exponential translocation of OBT from body fluids to urine}
- Transloc7 = 1.5*OBT_FLUIDS {Exponential translocation of OBT in body fluids to long term tissue storage compartment}
- Transloc8 = .003*LONG_TISSUE {Exponential translocation of OBT from storage compartment to urine}

4.2.1 PARAMETERS

Parameters involved in the model fitting are basically the initial activities and the clearance rates from each compartment (lambda). The clearance rates (or half-live) were measured from semi-log plots of the experimental retention or excretion patterns. These measured values were then used in their corresponding compartments. The initial amount in the skin compartments were estimated by finding the intercept of the retention curve with the y-axis i.e. the activity. The values obtained were 0.37 for compartment (A), 0.61 for compartment (C), and 0.02 for compartment (D). The values utilized in the model were 0.33, 0.66, 0.01, respectively. The lambda parameters were kept fixed and the initial amount varied slightly until a generally good agreement was reached. The value of lambda could be varied a lot without large fluctuations in retention, or dose, as long as lambda was large. This meant that the transfer of HTO from the skin to the body fluids was essentially instantaneous. Variations of other parameters, such as the ratio of OBT to HTO at the peak and the day at which the peak occurs, were also found to be useful in fitting the model to the data,

particularly for the short term component.

The parameters used in the model, which fitted the results of a preliminary experiment on rats, are tabulated in table 6. The model agreed quite well with the experimental excretion curves for HTO, OBT, and total tritium from a previous CRNL experiment (15). To test the validity of this model, the excretion curves from the simulation will be compared to the new results discussed in this report. If the comparison is not satisfactory, then the parameter values will be adjusted to see if an improved agreement can be reached with the new data.

Table 6

PARAMETERS FOR DOSIMETRIC MODEL

CLEARANCE RATES (Day-1)	INITIAL ACTIVITIES (Bq)
λ_1 = 5	
λ_2 = .02	A(0) = .33
λ_3 = 4	
λ_4 = .05	C(0) = .66
λ_5 = .2	D(0) = .01
λ_6 = 1.5	
λ_7 = 1.5	
λ_8 = .003	

4.2.2 VALIDATION

In validating a model, one needs to look at the goodness of the fit between the excretion curves obtained from the dosimetric model and the ones from the experimental data. The first way to compare is to look at the two graphs together. Since the two sets of curves were normalized in the same manner, a visual comparison is possible. Specific characteristics of the excretion curves were examined to obtain a more quantitative comparison:

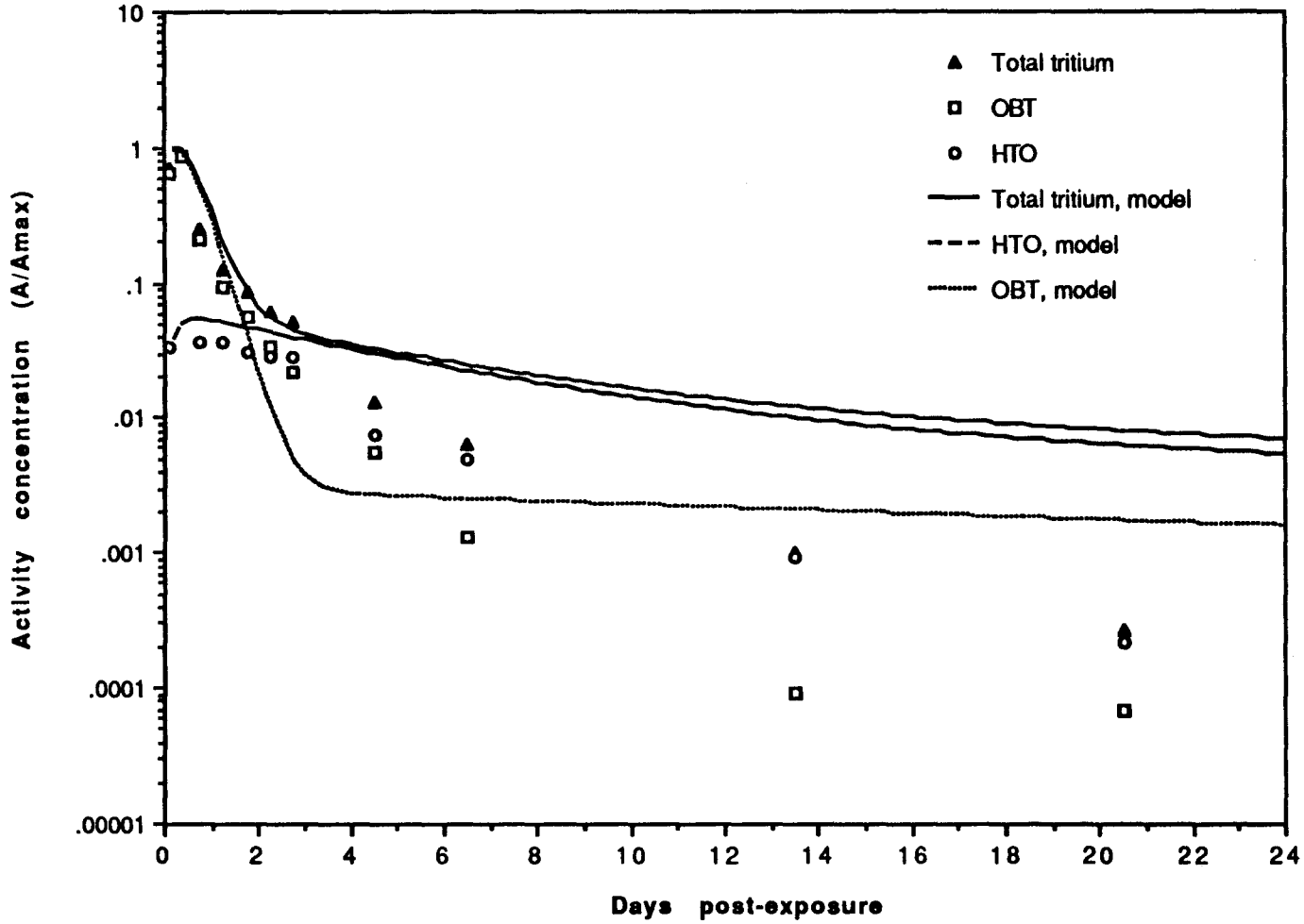
- the time of occurrence of the maxima for activity concentration in urine for total tritium, OBT and HTO;
- the ratio of OBT to HTO maxima;
- the cross-over point between HTO and OBT;
- the clearance rate (half-life) of the short and long term components for HTO, OBT, and total tritium.

The next step in validation is to compare the rat and human data. If the patterns are similar, we can then verify if the model also holds once the parameters are adjusted according to the different clearance rates of HTO of humans.

4.2.2.1 COMPARISON WITH RAT DATA

When the model output using the initial set of parameters is compared to the data, we notice that the model fits the data fairly well within the first 36 hours post-exposure, but deviates quite drastically after that time. The peaks in activity occur at roughly the same time, although the ratio of OBT to HTO is slightly larger in the case of the model. Furthermore, the clearance of all forms of tritium is faster in the early days and much slower for the second component, in comparison to the rat data. The cross-over point between HTO and OBT also appears about a day earlier in the model. See Figure 13. It must be emphasized that the purpose of this comparison was to validate the model, developed in a previous experiment, using this set of data. The parameters were therefore not adjusted since the model would not fit the earlier data if they were modified. These observations, however, suggest that changes to the existing models are required.

Figure 13
Comparison of experimental curves with CRL model



4.2.2.2 COMPARISON WITH HUMAN DATA

If the results from the rat experiments are similar to the results obtained for humans (8) then there is good indication that the findings for the rats can be extrapolated to humans and that a better estimate of the dose to skin and body fluids can be found. A parallel comparison of the excretion patterns will help to determine similarities between rat and human results, table 7. The HTO and OBT peaks in activity concentrations in urine occur at 24 and 8 hrs after exposure, respectively, for both humans and rats. There is a short equilibrium period of about 1 day in the HTO curves and the OBT curve crosses the HTO curve at about 3 days in both cases. Another similarity is the total curve which follows closely the HTO curve starting at about day 6. The comparison can be extended to the ratio of OBT to HTO at the concentration peak. For the rat, the ratio is about 11 ± 2 while for the human, it is about 13. The differences in excretion patterns for humans and rats mainly occur in the clearance rates of HTO from body fluids to urine due to different metabolism rates, being much faster in the rat than in the human. The excretion half-life for HTO in humans is 15 days compared to 3

days for the rat. The OBT excretion curve is best represented by two exponentials with half-live of 0.48 and 1.5 days for rats and, 0.1 to 0.2 and 1 to 2 days for humans. The slow component for OBT is similar for rats and humans but the HTO component is 5 times faster in rats while the first OBT component is about 5 times slower.

The chemical form of OBT in urine is an important factor in deciding to what extent the animal data can be compared to human. If the form is drastically different in rats, then one has to be more careful in the extrapolation of the results from animal to man when attempting to evaluate the dose to skin and body fluids.

The effects from washing the skin after exposure were also investigated on the rat. In both humans and rats, the OBT to HTO ratio in urine is decreased by a factor of about 4 when the skin is washed. The time of maximum concentration of HTO in urine decreases from 24 to 12 hours in humans and from 24 to 6-12 hours in rats. This may possibly be explained by the physical abrasion taking place during the washing process, since the removal occurs before the transfer process from skin surface to body fluids is complete. Again the early HTO maximum and smaller OBT/HTO ratio in urine after decontamination are observed in the human as well as

the rat. This shows that, indeed, washing the skin early after exposure may be an effective decontamination technique. Since the substances used in the decontamination process appear to have different levels of efficiency, the dose reduction factor from washing will depend on the solution utilized.

Besides looking at the comparison of the tritium excretion curves, parameters and metabolism, the physiological and anatomical differences in the skin of the two species may be important. With respect to the skin type, there are two different categories of animal: the loose-skin animals like rats, cats, dogs, monkeys..., and the fixed-skin animals which includes only pigs, whales, and humans. The main distinction between these two types is in the vascular supply system. Since in the man the muscle, fat, and skin are all attached, there is only one vascular system to irrigate the skin, muscles and fat. But in the rat, for example, there are two vascular supplies, one for the deeper layer (muscles and fat), and one for the skin. However in the last category, even pig skin is slightly different from human skin since it does not have any functional sweat glands. Despite these dissimilarities, the retention in the skin may still be the same, especially for those

transfer mechanisms which rely only on diffusion and exchange mechanisms. More confidence will be gained concerning such differences once the experiments are repeated on pigs.

TABLE 7

COMPARISON BETWEEN CHARACTERISTICS IN TRITIUM EXCRETION CURVES OF HUMAN AND RAT

CHARACTERISTICS	RAT	HUMAN
HTO PEAK:	24 +- 6 hours	24 +- 5 hours
OBT PEAK:	8 +- 4 hours	8 +- 4 hours
TOTAL TRITIUM PEAK:	8 +- 4 hours	8 +- 4 hours
RATIO OBT/HTO AT THE PEAK:	11 +- 2	13 +- 3
CROSS-OVER POINT, HTO & OBT:	3 +- .5 days	3 +- .5 days
TOTAL TRITIUM BECOMES MOSTLY HTO:	6 +- .5 days	6 +- .5 days
APPROXIMATE PLATEAU DURATION:	1 day	1 day
REDUCTION FACTOR IN OBT/HTO RATIO AFTER WASHING:	4.4 +- .8	3.2 +- .8
HTO EXCRETION HALF-LIFE: (HT CONTAMINATION)	*3 +- .5 days*	*15 +- 2 days*
OBT EXCRETION HALF-LIFE: (SHORT TERM COMPONENT)	0.48 +- .1 days	0.1 to 0.2 days
OBT EXCRETION HALF-LIFE: (LONG TERM COMPONENT)	1.5 +- .4 days	1 to 2 days
HTO EXCRETION HALF-LIFE: (HTO CONTAMINATION)	*≈2 +- .5 days*	*10 +- 2 days*

4.3 DOSE ESTIMATION

Some assumptions are also necessary in order to estimate the dose to the body fluids and the skin. Since the dose is defined as the mean energy absorbed per unit mass, an estimate of the mass of skin that was exposed is needed. The known quantities are the area of the surface exposed and the skin density. Now, if it is assumed that the skin is about 0.1 cm thick, the mass can be calculated. It is also assumed that the distribution of tritium in the skin is uniform. In calculating the dose to the body fluids from the OBT in urine, it is also supposed that all OBT is uniformly distributed in the body and not confined to a particular organ. The implications of these assumptions on the estimated dose will be discussed in section 5.1. The absorbed dose in any compartment of the model can be calculated using the following equation:

$$\text{Dose (Gy)} = C * 1.38 \times 10^{-8} * E/M$$

where: C is the cumulated activity concentration in the compartment,

E is the average energy of the beta particle of tritium (5.7 kev),

M is the mass of the tissue exposed.

In the case of the skin, the mass is found through the formula:

$$M = p * t * a$$

where: p is the density of the skin,

t is the thickness of the skin,

a is the area of the skin exposed.

Two dosimetric models were developed by Johnson (14) to describe the observations on tritium excretion by humans. The first model was constructed to give the maximum retention in skin consistent with observed results (8), while the second one gave the minimum retention in skin. These two models lead to effective dose equivalents to the body fluids of 8.7×10^{-12} Sv and 9.7×10^{-12} Sv per Bq intake, respectively. Assuming that the area of contaminated skin was 40 cm^2 and that the total tritium was in a layer 0.1 cm thick in the dermis with a tissue density of 1 g/cm^3, the mass of the exposed skin is .004 kg. The skin dose equivalent per Bq intake for the two models are, respectively, 4.5×10^{-8} and 4.9×10^{-9} Sv. For example, a 37 MBq (1 mCi) uptake would lead to a skin dose between 180 and 1700 mSv, exceeding the skin dose limit of 500 mSv for worker. Then, the ratio of skin dose equivalent to effective

dose equivalent per Bq intake is 5.2 x 10^3 and 5.1 x 10^2, for models 1 and 2 respectively. However, a qualitative comparison between the output curve from these models and the experimental excretion curves was performed by looking at specific excretion characteristics listed in section 4.2.2. It was found that Johnson's models are not completely adequate in describing the results of human experiments. Neither the 24 hour maximum nor the equilibrium period observed in the human experiments were present. Moreover, neither of the two components of total tritium excretion were reproduced in the first model, and the cross over point between HTO and OBT occurs at about 1 day in the model as opposed to 3 days for the experimental curves.

The model developed at Chalk River (described in section 4.2) will help in confirming and narrowing the range of dose values given by Johnson's model (14). Moreover, since the model is derived from animal data, the dose to the rat can be calculated (skin and whole body), but the values must be extrapolated to human. Basically, it is assumed that the maximum area of skin exposed for human is the same as for rat (27). Also, since a reference man weighs at least 200 times more that the average rat, the whole body

dose should be 200 times less than that of the rat. So by dividing the rat whole body dose by 200 we can obtain the skin to whole body dose ratio for human. Since this ratio is quite large, the main concern in radiation protection will be the dose to skin. Futhermore, according to the International Commission on Radiological Protection (12), the annual skin dose limit for a worker is 500 mSv, and therefore the whole body dose will be of the order of a few μSv. Whole body doses of this magnitude are considered marginal in operating facilities and again the dose to skin is the one of concern.

5. DISCUSSION AND CONCLUSIONS

5.1 DISTRIBUTION OF TRITIUM IN SKIN

The investigation of tritium distribution in skin will be part of a future experiment. Some preliminary experiments, however, have been done at Chalk River (16) and the findings will briefly be described here. It was initially assumed that the activity was distributed uniformly in the skin. If the distribution is not uniform, the dose to skin may be smaller or greater than expected. The microdistribution of the activity in the skin will help to determine the importance of the dose to the skin. For example, if the activity is mainly confined to the dead layer of the epidermis, the concerns of a dose to the skin are minimal. On the other hand, if the activity is present in the dividing cells of the basal layer, then the radiological hazards would be greater and will have to be accounted for in the calculation of the effective dose.

To examine the distribution of tritium with depth in the rat skin, slices about 25 μm thick were cut parallel to the skin surface using a microtome, and counted for HTO and OBT. The highest activity concentration was found between 50 μm and 100 μm. This

represented about 70 to 90 % of the surface activity. In humans, the epidermis constitutes the first 20 to 500 μm of the skin and includes the dead layer as well as the most sensitive one, the basal layer, located at about 70 to 100 μm below the surface. The dermis is situated between 400 μm and 4000 μm. The subcutaneous layer includes lipids, sebaceous glands, hair follicles and muscles. Figure 14 shows a diagram of the skin and figure 15 shows an enlarged version of the epidermis.

Autoradiography of skin sections showed highest OBT concentration in the basal layer (16). However, because of the very short range in tissue of the tritium beta particles (6 μm), they may not reach the cell nuclei and the hazard to skin becomes almost negligible. It has been shown that the activity was concentrated in the region of cells in the basal layer but it is not known if the tritium is actually in or around the dividing cells, or in the DNA. Some work has been done on the estimation of dose in cell nuclei due to DNA-Bound tritium (24). In a worst case situation where all the tritium is located in the cell nuclei, then the fraction of the total tritium in these cells needs to be measured to provide a correction factor for the dose calculated on the basis of a uniform distribution.

In the equation for the effective dose (H=DQN), the 'N' factor could take into account these distributional effects.

FIGURE 14

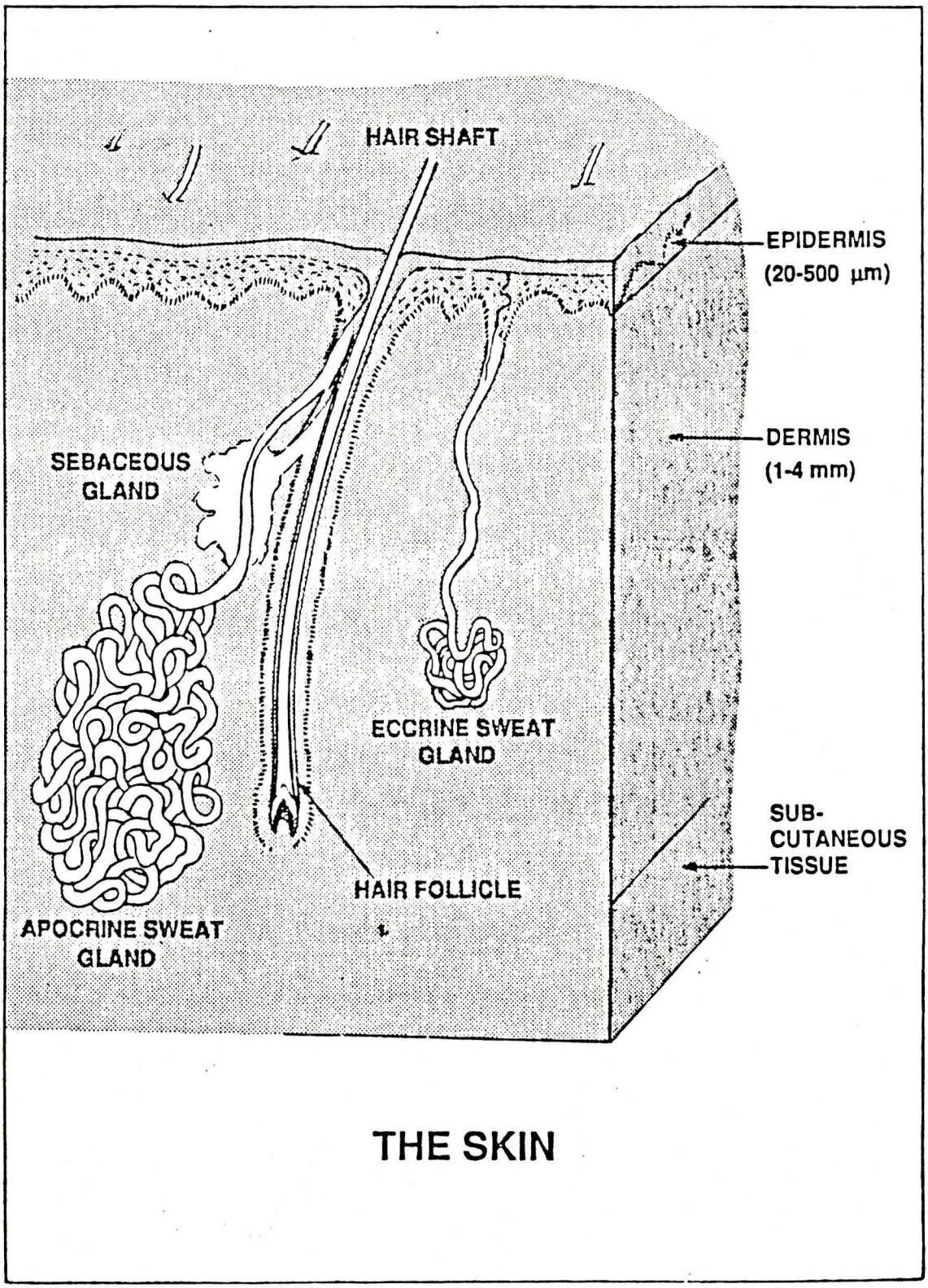
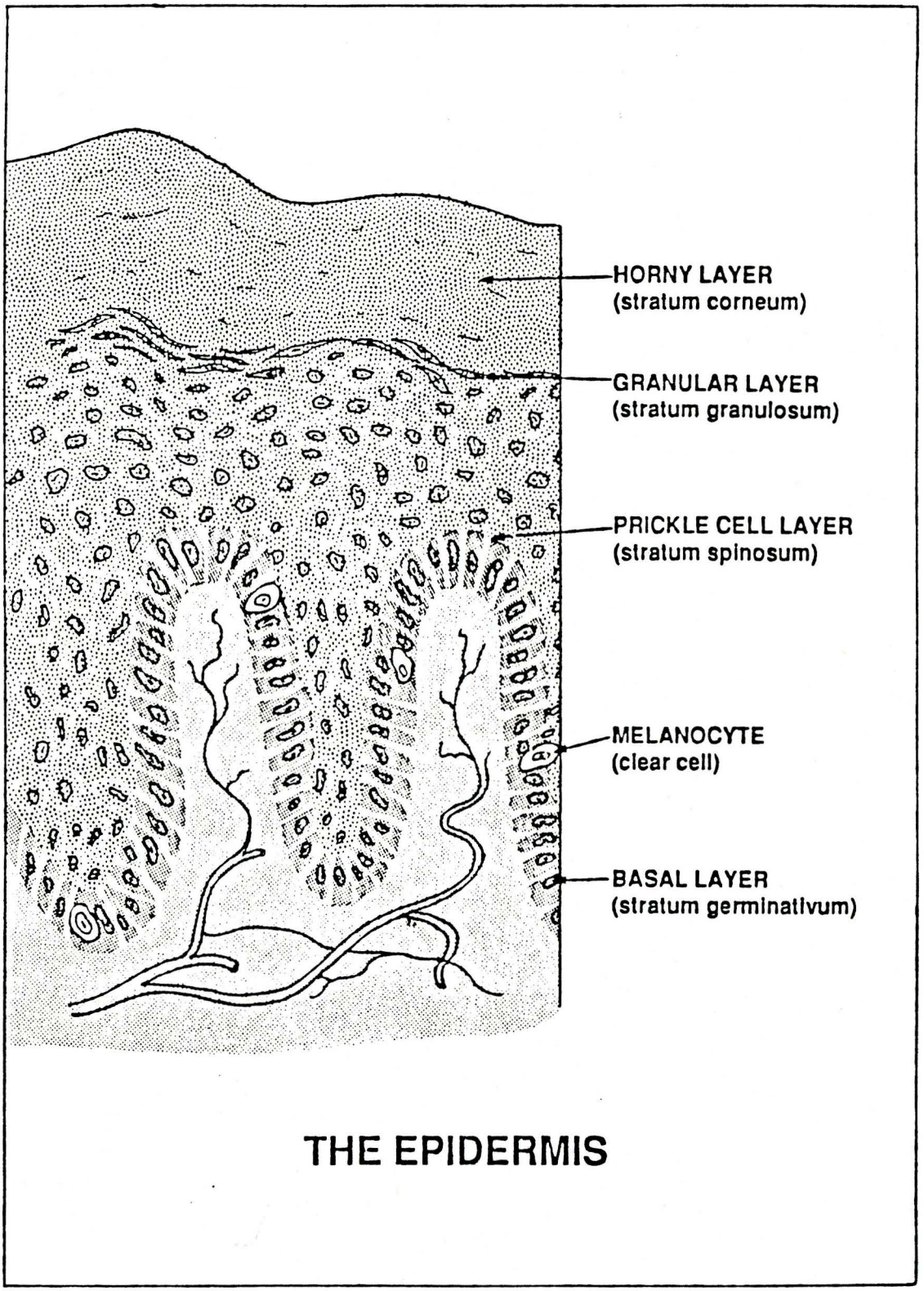

HAIR SHAFT
EPIDERMIS
(20-500 µm)
DERMIS
(1-4 mm)
SEBACEOUS
GLAND
ECCRINE SWEAT
GLAND
SUB-
CUTANEOUS
TISSUE
HAIR FOLLICLE
APOCRINE SWEAT
GLAND
THE SKIN

FIGURE 15


HORNY LAYER
(stratum corneum)
GRANULAR LAYER
(stratum granulosum)
PRICKLE CELL LAYER
(stratum spinosum)
MELANOCYTE
(clear cell)
BASAL LAYER
(stratum germinativum)
THE EPIDERMIS

5.2 IMPROVEMENT OF MODEL

For radiation protection purposes, the present model needs to be improved and validated before it can be used in a radiation protection program. To make the model as close to reality as possible, compartments need to be added that can adequately mimic effects of variation of exposure parameters. As noted earlier (section 3.2), decontamination of the skin after exposure resulted in reduced activity in the urine and skin. To account for this effect, one or two compartments (HTO and OBT) are needed, above the actual skin compartments, to represent what happens before the tritium is already in the skin or body fluids. These would regulate the transmission of tritium in the skin by stopping the process (or imposing a fractional tritium intake) when the decontamination is initiated. These would also account for other loss of tritium from the skin that may occur from shedding of the skin (dead layer of the epidermis). A link from the fast OBT compartment should be established to account for a fraction of the OBT that is readily converted to HTO in the skin.

When more details become available from the effects of the

other exposure parameters, for example, pressure, material type, time of exposure, the model should be adjusted to take into play these other changes. Moreover, further knowledge of the metabolism may show where recycling occurs between the compartments. A good example is the OBT in the body fluids going to the tissues, part of which returns to the body fluids.

5.3 FURTHER STUDIES AND RECOMMENDATIONS

This work has shown that doses to the body fluids and skin may not by trivial and must not be overlooked in radiation protection practices since simple measurement of tritium in urine may lead to an underestimation of the dose. The whole body effective dose could range from 0.32 to 0.36 mSv for an intake of 37 MBq. Since the skin to whole body dose ratio ranges from 5.1 x 10^2 to 5.2 x 10^3 (16), the skin dose could range from about 180 to 1700 mSv and be the limiting factor for radiation protection purposes. Therefore, to improve our understanding of the problem, more studies should be done in the areas described below.

As it was shown that the distribution of tritium in skin could have serious impact on the dose calculation, it is important to determine more precisely the microdistribution of activity in the skin by performing further autoradiography studies of skin sections (16). As stated before, if the activity is concentrated in the sensitive area of the cell, then the risk of damage is much higher and the dose is underestimated when a uniform distribution is assumed. Another point of concern is in the determination of the

surface area of the exposed skin. Since the area appears in the denominator of the dose formula, the choice of a larger area than the actual exposed area would also result in the underestimation of the dose to the skin. For real life situations, a technique will have to be found that will allow a good determination of the size of the area of skin exposed to the contaminated surface.

With respect to the contaminated surface, the analysis of the sorbed tritium on the surface could help in determining the origin of the non-exchangeable or organically-bound tritium. The identification of the metallurgical characteristics of the surface and its influence on the molecular species of sorbed tritium may help to clarify the situation.

The current technique of OBT measurement by low temperature distillation is somewhat time consuming and could not be efficiently applied to a large number of samples. This three step method needs to be mechanized and simplified before it can be used on a large scale basis, as would be needed in a nuclear power plant bioassay program.

Another issue that requires further investigation regarding OBT is the characterization of the compounds present in the urine.

The identification of the chemical form(s) of OBT both in the urine of rats and humans will help us to determine the similarity in the metabolism of the two species. If indeed the same compounds are observed, this will increase our level of confidence in the extrapolation from rat to human. Furthermore, the knowledge of the specific compounds present may give us an indication where in the body the OBT may concentrate. It may also help to select a solution, or chemical that would eliminate the accumulation or accelerate the excretion of the OBT.

The next step in this study will be to use pig as an experimental system. As mentioned earlier, the pig belongs to the same skin structure category as humans. These experiments would then confirm results from the rat studies and bring a deeper knowledge of the mechanisms involved.

A new technique under development is the use of isolated perfused human skin flaps (21). These flaps are being used to study the metabolism of pharmaceutical products through skin by such processes as: evaporation and degradation, adsorption, permanent binding, transcutaneous metabolism. The skin is kept alive by continuous blood flow and tested for vasoactivity and vasostability.

It is planned to study the clearance rates and concentrations of HTO and OBT in this skin preparation after contact with a tritium gas contaminated surface, following the same procedures as with the rat experiments.

Finally, the last step, once we are confident that the modeling and dosimetry will not seriously underestimate actual doses, would be a human validation study where all of the previous results (except for the skin data) can be tested against the ones of concern, directly from humans.

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