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ABSORPTION OF LIQUID HTO AND HTO VAPOR THROUGH THE SKIN OF MAN

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EXPERIMENTAL BIOLOGY AND MEDICINE

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ABSTRACT

When the arm of a man was exposed at 24°C for 15 min or longer to an atmosphere saturated with HTO vapor, it was found that an average of 0.019 mg/cm^2/min of the HTO was transferred across the skin into the body. This rate of absorption was comparable to the rate of water loss at 24°C through the skin as insensible perspiration, i.e., the water loss through the skin when sweat glands are inactive. Both processes are concluded to be due to the diffusion of water vapor back and forth through the skin barrier and are dependent on vapor pressure.

The HTO vapor took 2 to 5 min to diffuse across what appears to be an inert barrier in the skin before coming in contact with diluting volumes from where it was picked up by the blood stream. The half-time of appearance in the blood ranged from 20 min to 1 hr, depending on the circulation rate in the skin. The diluting volume between the outer inert layer of the skin and the circulating fluids appeared to be equivalent to a water layer only about 0.064 mm deep.

When the arm was immersed in liquid HTO at 34°C for periods of 5 min or less, the rate of HTO water transfer across the skin ranged from 0.040 to 0.065 mg/cm^2/min. This rate of transfer was higher than could be accounted for by diffusion during the time of exposure due to vapor pressure alone. It was concluded therefore that there is a "blotter effect" in the outer skin layer that retained some of the HTO water per se in the skin after removal from the exposure solution. No significant reduction was made in the amount of HTO subsequently showing up in the general body fluids when the exposed area was rinsed and dried after exposure, or washed for 30 min, or rinsed, dried, and immersed in 100 per cent alcohol for 30 min.

The absorption rate of HTO through the skin when the arm is immersed in liquid HTO for 10 min or longer was less than that observed during shorter exposure periods and appeared to decrease with increasing lengths of exposure until the rate of transfer inward through the skin per unit of vapor pressure was comparable to that found during long exposures to HTO in the saturated vapor state.

The rates of transfer of HTO through the skin was compared with the absorption through the lung which has been reported (LA-1465). The comparison indicated that the tritium taken into the body through the total skin surface from an environment containing HTO or T_2O would approximately equal that absorbed via the respiratory tract when the possible but undetermined protective effect of clothing is ignored.

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1. INTRODUCTION

Evaluation of the radiation hazard that may be produced when man is exposed to an atmosphere containing HTO or T_2O requires consideration of the possibility of absorption through the skin. The skin is not impermeable to water vapor as indicated by the normal loss of water outward through the skin surface by the process known as insensible perspiration. Therefore the experiments reported in this paper were undertaken to determine the rate at which HTO passes through the skin into the body of man when he is exposed to an atmosphere containing HTO and when he is exposed to liquid HTO applied to the exterior surface of the skin. From such information it is possible to determine the radiation exposure hazard presented by skin absorption of tritium water and to relate it to the hazard resulting from other routes of entry, such as through the lungs.

In the process of collecting data on the rate of absorption of HTO through the skin, it was possible to gain some information on the basic physiological factors which are involved in water transfer across the skin surface. HTO is a unique and useful tool for such studies.

2. METHODS

The lower arm of a subject, from the elbow to the finger tips, was exposed for variable lengths of time to various activities of HTO as water vapor in the atmosphere. In other experiments this arm area was immersed in HTO water containing known tritium activities.

Exposures to HTO as water vapor were accomplished by using a cylindrical chamber 16 in. long and 4 in. I.D. This chamber was covered on the inside surface with blotting paper saturated with liquid HTO of known tritium activity. Wire screen covered the blotting paper to prevent the arm, when placed in the chamber, from coming in contact with the liquid HTO in the blotting paper. Oxygen saturated with HTO vapor at room temperature from a liquid of the same activity as that in the blotting paper was passed through the exposure chamber at a rate of about 6 liters/min during the exposure. Exposure was made by inserting the arm up to the elbow in this chamber. Closure at the end of the chamber and around the arm at the elbow was made by means of a rubber cuff. The area exposed was measured and found to be about 1100 cm^2.

Exposures to liquid HTO were made in the following way: The chamber described above was closed at one end, filled to the required level with liquid HTO (at about 34°C) of

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appropriate activity, and the arm inserted until the liquid HTO covered the arm up to the elbow.

To measure the HTO absorbed, urine samples were collected prior to exposure and at intervals after exposure until the urine activity had reached apparent equilibrium. The tritium activity (A') absorbed during the exposure is given by the expression

$$A' = (A - B)V$$

where A is the activity in the urine at equilibrium, B is the activity in the urine prior to exposure, and V is the dilution volume for HTO in the body. This figure, when divided by the specific activity of the HTO to which the arm was exposed, gives the weight of the water absorbed. The weight of water absorbed was then divided by the area exposed and the length of the exposure to obtain the water absorbed per unit area per unit time. Exposure times ranged from 1 min to 1 hr in different experiments. The dilution volume for HTO in the body of these subjects was measured by ingestion of a known quantity of HTO and observation of the dilution of activity which occurred when the water was absorbed and equilibrated with the body fluids. This work has been previously reported.[1]

In addition to urine samples, insensible perspiration was sometimes collected from the exposed area at intervals for several hours after exposure. To collect insensible perspiration the exposed arm was placed in an empty cylinder similar to that used for the exposure, and dry oxygen was passed into the cylinder at a rate of about 6 liters/min. The water vapor of insensible perspiration was condensed from the oxygen in a dry ice trap placed in the exit tube of the system. The presence or absence of sweat as a contaminant in the water condensed was determined by sensitive methods[2] previously described.

The HTO activity in all fluids collected or used in these experiments was analyzed by methods previously described.[3]

3. RESULTS

3.1 Absorption of HTO Through the Skin as a Result of Exposure to HTO Vapor in the Atmosphere

When the arm was exposed at a room temperature (24 ± 2°C) for a period of 15 min to 1 hr to an atmosphere saturated with HTO vapor, it was found that the amount of HTO appearing in the body indicated a water absorption rate through the exposed skin area ranging from 0.010 to 0.018 mg/cm^2/min (Table I). All the values except one fell within the above range. The one value of 0.048 mg/cm^2/min which appears to be unduly high may have been due to the subject's arm touching the side of the exposure chamber during the experiment,

vapor. In one of these experiments the subject was at normal room temperature with normal skin temperature prevailing and the half-time of decline was about 20 min. In the other the subject was cooled so that blood flow to the skin was reduced. In this experiment the half-time of decline was about 55 min. Further substantiation of this concept was evidenced by the length of time required for the activity absorbed during the exposure to appear in the body fluids following exposure. When the subject was comfortably warm, the activity in the urine reached essential equilibrium in about 2 hr, whereas when the subject was cooled, the activity in the urine was still rising 4 hr after the exposure (Figs. 2 and 3). These results will be discussed in more detail subsequently in this paper.

By extrapolating the slower component of the decay of HTO activity in the insensible perspiration back to zero time and subtracting this extrapolated curve from the measured activity at short times after exposure, one may obtain the exponential decay of the faster component alone. The faster component appears to have a half-time of less than 10 min in the two experiments discussed above. It may be noted that the faster component is not greatly altered by blood flow as was the slower component. The faster component is presumed to represent the half-time for diffusion of HTO vapor across the inert barrier in the surface of the skin, and the result agrees well with the time deduced for diffusion across this barrier from the data given in Table I.

Knowing the rate of entry of HTO through the skin and the half-time for its removal from the skin by the circulating blood, it was possible to calculate the HTO remaining in the extravascular skin area at any time during exposure. The calculation may be made by using the formula:

$$C(t) = \frac{k_1}{k_2} \left(1 - e^{-k_2 t}\right)$$

where C(t) is the weight in mg/cm^2 of HTO remaining in the skin at time t during exposure, k_1 is the rate of entry of HTO in mg/cm^2/min, k_2 is the rate constant for passage of HTO from the extravascular area into the circulating blood ($\frac{\ln 2}{T_{1/2}}$), and t is the exposure time. C(t) calculated for experiment 7-22-52 graphed in Fig. 1 at the end of the 20 min exposure was:

$$C(t) = \frac{0.012 \times 55}{0.693} \left(1 - e^{-\frac{0.693 \times 20}{55}}\right) = 0.212 \text{ mg/cm}^2$$

This value corresponds to 88.5 per cent of the 0.240 mg/cm^2 absorbed during the 20 min period and is the amount of HTO in the extravascular skin at the end of the exposure. Extrapolation of curve II in Fig. 1 to zero gives the activity in μc/mg prevailing in this

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water is 39.5 mm Hg. When correction was made for this difference in vapor pressure, the data for exposures in Tables I and II agreed fairly well.

3.3 Changes in the HTO Activity in Urine with Time Following Exposure of the Skin to HTO in the Liquid and Vapor State

Activity changes in the urine with time following exposure of the skin to HTO, either in the liquid or vapor state, are dependent to a large extent on the circulation in the area of the skin exposed. Most of these experiments were conducted with the subject clothed and at normal room temperatures. When this was the case, the urine activity increased with time for about 2-1/2 hr after exposure, reaching essential equilibrium at that time (Fig. 2). The rate of appearance of HTO in the urine could be considerably retarded by cooling the subject after exposure, as indicated in Fig. 3. In this experiment the subject was chilled by being placed in an environment at about 60°F for 3 hr and 40 min following exposure. In 3 hr and 40 min only about 70 per cent of the HTO absorbed into the skin had been distributed in the general body fluids as indicated by activity in the urine. When the subject was placed in a hot bath subsequent to chilling, the activity remaining in the skin was quickly absorbed into the general body fluids and the urine activity rapidly increased (Fig. 3). If the exposed arm was warmed immediately after exposure by immersion in warm water, there was a rapid increase in HTO activity in the urine which went above the final equilibrium value and subsequently declined to equilibrium in about 2-1/2 hr (Fig. 4, top graph). In this situation the HTO was obviously transferred quite rapidly into the circulating fluids from the exposed area. It had previously been shown that with exposure to HTO by inhalation or ingestion it took about 2-1/2 hr for 99 per cent of ultimate equilibrium to be attained in the urine. The relative rates of appearance of HTO in the urine following skin exposure when the arm was warmed, when the subject was at normal room temperature, and when the subject was chilled are shown in Fig. 4. There was a marked difference in the rate of appearance of HTO in the urine, which probably reflects largely the difference in uptake of HTO by the blood from the skin area exposed.

4. RELATIVE RADIATION HAZARD OF THE ABSORPTION OF HTO THROUGH THE SKIN AND THROUGH THE LUNG

It was observed (Table I) that on exposures of 15 min or longer to an atmosphere saturated with water vapor at normal room temperatures, man absorbed through the skin an average of 0.019 mg/cm^2/min of the water vapor. Assuming a total skin area of 2 square meters for the average man and exposure of this total area to a saturated environment at normal room temperatures, it is possible for him to absorb 380 mg of water vapor per

minute through the skin into the body.

Work already reported[4] showed that 98 to 99 per cent of all HTO vapor inspired by man was absorbed into the body through the lungs. Assuming a minute respiratory volume of 20 liters, it is calculated that 425 mg/min of water would be absorbed from an atmosphere saturated with HTO vapor at 24°C (21.5 mg/liter of water in a saturated atmosphere at 24°C x 20 liters/min x 0.99 = 425 mg/min). In an atmosphere less than 100 per cent saturated with HTO vapor the quantity absorbed would be proportionally reduced for both the skin and lungs. Thus the quantity of HTO entering the body through the total skin, when exposed to an atmosphere containing a given activity per unit volume of HTO, would be about equal to that entering through the lungs. These two routes of entry are of approximately equal importance in considering the protection of personnel against high activities of HTO in the environmental atmosphere if any protective effect of clothing is ignored.

5. SUMMARY

When the arm of a man was exposed to an atmosphere saturated with HTO vapor at 24°C for periods of 15 min or longer, it was found that an average of 0.019 mg/cm^2/min of the HTO vapor was transferred across the skin into the body. This absorption rate was comparable to the rate of insensible perspiration or passage of water vapor out through this skin area at this temperature when sweat glands are inactive. Both processes are concluded to be due to diffusion of water vapor back and forth through the skin barrier and are dependent on vapor pressure. For exposure periods of 10 min or less the rate of transfer of HTO into the body was smaller per unit time of exposure.

It appeared that the HTO vapor took 2 to 5 min to diffuse across an inert barrier in the outer skin before it came in contact with diluting volumes from where it was picked up by the blood stream. The half-time of appearance in the blood ranged from 20 min to 1 hr, depending on the circulation rate in the skin. The diluting volume between the outer inert layer of the skin and the circulating fluids appeared to be equivalent to a water layer about 0.064 mm deep.

When the arm of man was immersed in liquid HTO at 34°C for periods of 5 min or less, the rate of HTO water transfer across the skin ranged from 0.040 to 0.065 mg/cm^2/min. This rate of transfer was higher than could be accounted for by diffusion due to vapor pressure alone during the exposure period, and it was concluded that there was a "blotter effect" in the outer skin layer which resulted in some of the HTO water being retained per se in the skin after removal from the exposure solution. It appeared to make no significant

reduction in the amount of HTO subsequently showing up in the general body fluids when the exposed area was rinsed and dried after exposure, or washed for 30 min, or rinsed, dried, and immersed in 100 per cent alcohol for 30 min.

The HTO absorption rate per unit time resulting from immersions of the skin in liquid HTO for 10 min or longer was less than that observed for shorter exposures and appeared to decrease with increasing lengths of exposure until the rate of transfer inward through the skin per unit of vapor pressure was comparable with those found for long exposures to HTO in the saturated vapor state.

When the rates of transfer of HTO through the skin of man are compared with absorption through the lungs, the amount of HTO entering the body by absorption through the total skin area from HTO vapor in the atmosphere is approximately equal to that entering through the lungs.

After exposure of a skin area to HTO either in the liquid or vapor state, the rate of appearance of the HTO in general body fluids as indicated by activity in the urine was dependent to a large extent on the circulation in the exposed area. If the exposed area was warmed after exposure, activity in the urine increased rapidly for about 20 min and then declined to essential equilibrium in about 2-1/2 hr. If the subject was kept at normal room temperature after exposure, the urine activity rose slowly for about 2 to 2-1/2 hr, leveling off at essential equilibrium. If the subject was placed in a 60°F environment after exposure, the urine activity rose at a very slow rate such that it was estimated it would take 6 to 8 hr to reach maximum activity and essential equilibrium.

6. REFERENCES

1. E. A. Pinson, LA-1464 (1952).
2. E. A. Pinson, Am. J. Physiol. 137: 492 (1942).
3. E. A. Pinson, LA-1218 (1951).
4. E. A. Pinson, LA-1465 (1952).

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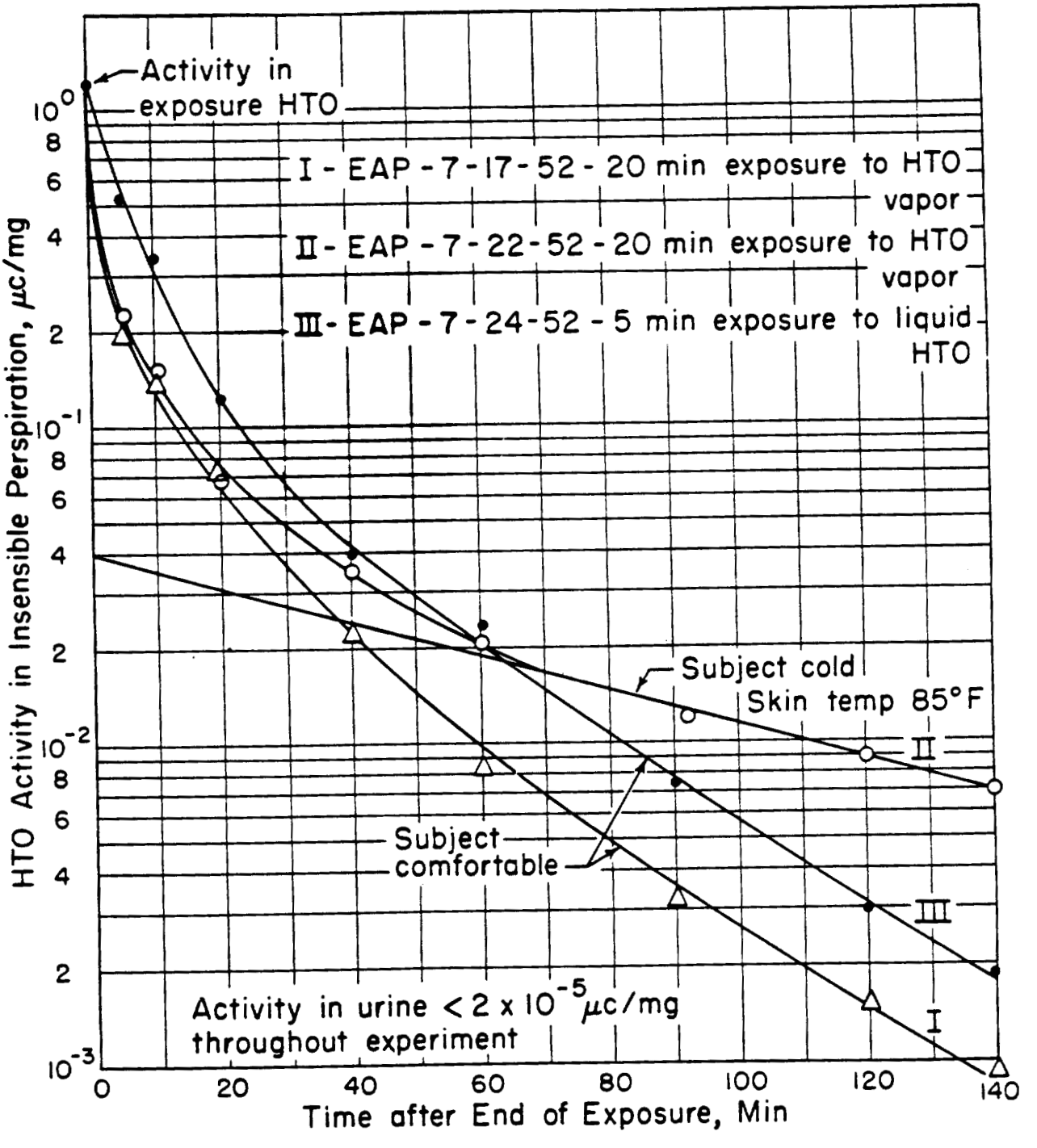

Fig. 1. Changes in the HTO activity of insensible perspiration from a skin area following its exposure to HTO.

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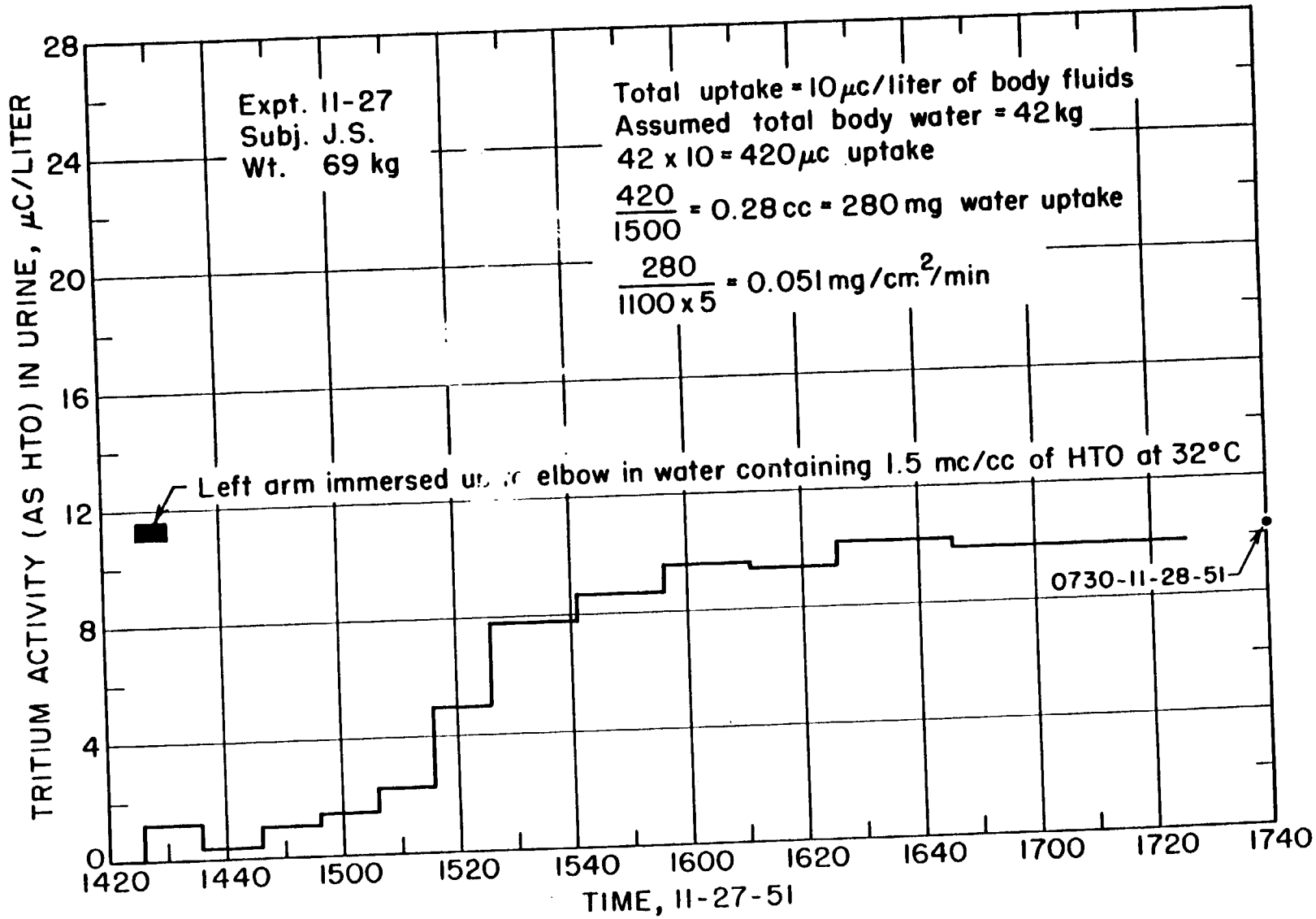

Fig. 2. Appearance of HTO in the urine of man following exposure of the skin of the arm to liquid HTO at 32°C.

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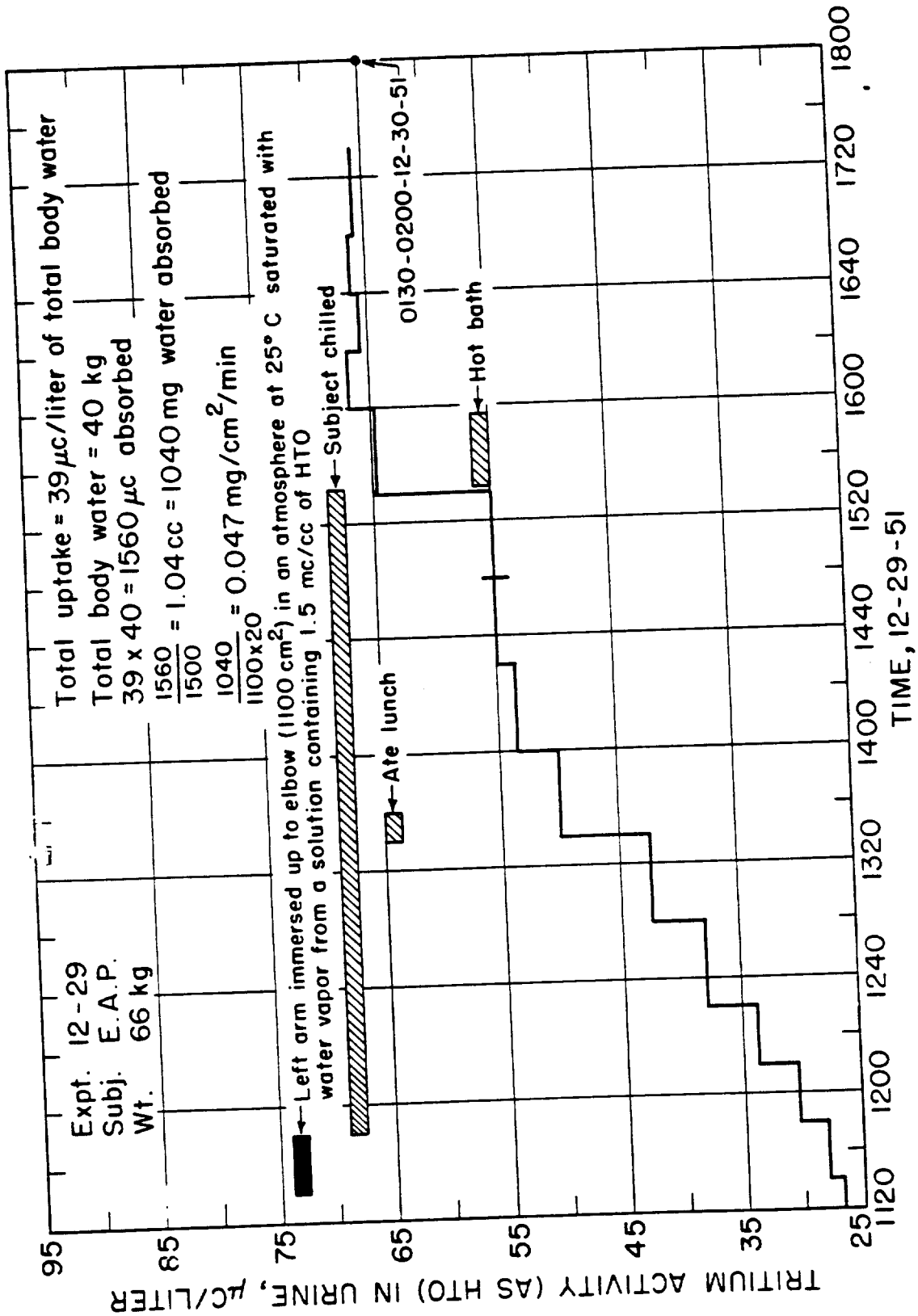

Fig. 3. Appearance of HTO in the urine of man following exposure of the skin of the arm to an atmosphere saturated with HTO vapor at 25°C.

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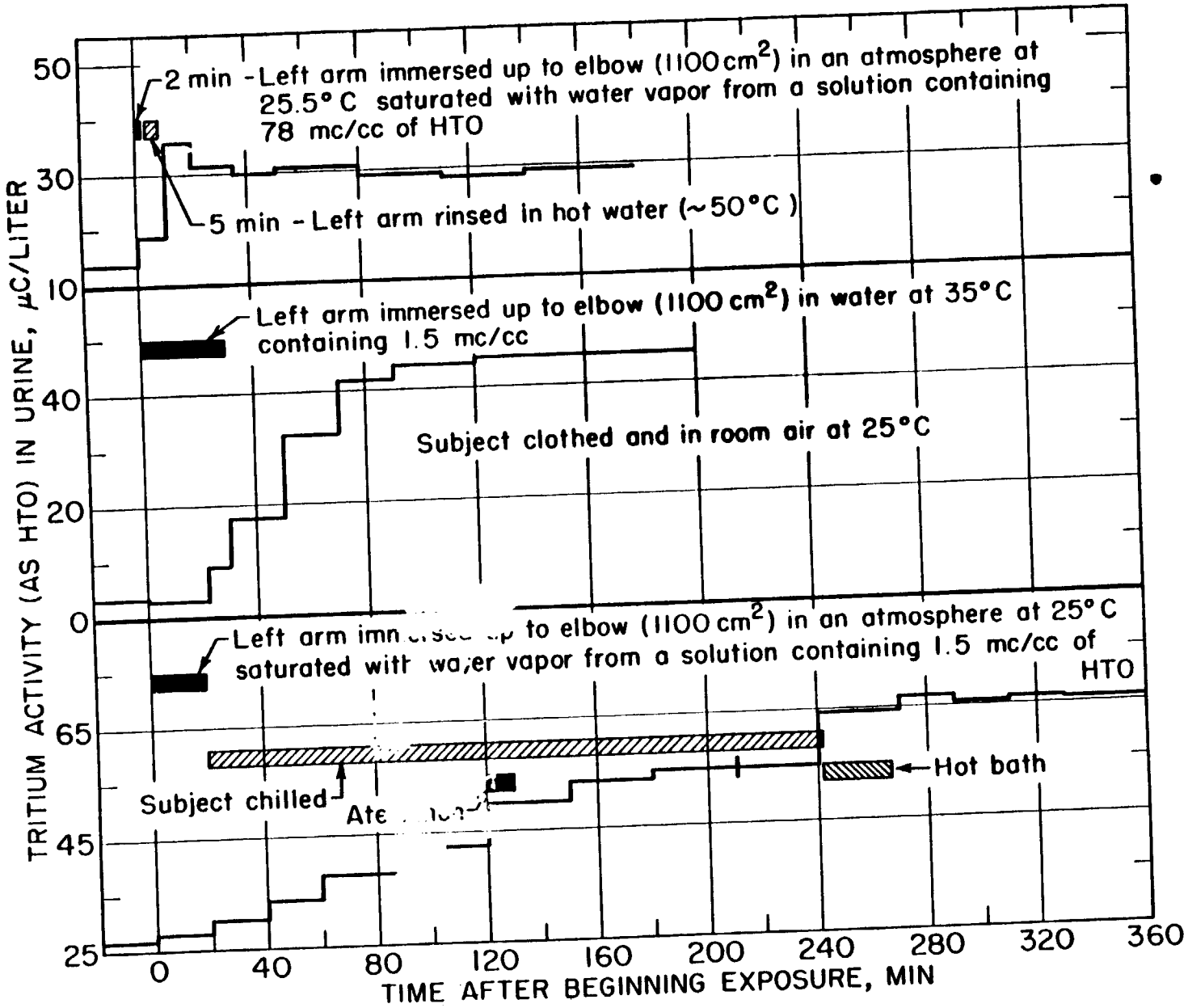

Fig. 4. Effect of temperature on the rate of appearance of tritium activity in the urine following exposure of the skin of the arm to HTO.

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Table I

RATES OF ABSORPTION OF HTO THROUGH THE SKIN OF MAN WHEN THE LOWER ARM WAS EXPOSED FOR VARIABLE LENGTHS OF TIME TO AN ATMOSPHERE SATURATED WITH HTO VAPOR AT 24 ± 2°C

Date	Subject	Length exposure, min	HTO activity in exposure water, μc/mg	HTO activity absorbed into body, μc	Water absorption rate,[a] mg/cm²/min
12-22-51	JS	1	78	378	0.0044
12-22-51	EAP	2	78	604	0.0035
12-15-51	EAP	5	7.8	180	0.0042
12-17-51	JS	5	7.8	218	0.0051
12-19-51	JS	10	7.8	450	0.0053
4-4-52	EAP	15	1.2	213	0.011
7-17-52	EAP	20	1.2	479	0.018
12-29-51	EAP	20	1.5	1560	0.047
7-22-52	EAP	20	1.2	305	0.012
4-26-52	JS	25	1.2	476	0.014
2-1-52	JS	45	1.4	790	0.010
2-7-52	JS	45	1.4	883	0.013
12-1-51	EAP	61	1.5	1680	0.017

[a]Calculated from the increase in HTO in body fluids at equilibrium, the HTO dilution volume in the body, the area of skin exposed, and the length of exposure.

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Table II

EFFECT OF LENGTH OF EXPOSURE AND OF VARIOUS PROCEDURES AFTER EXPOSURE ON THE WATER ABSORPTION RATE THROUGH THE SKIN (SKIN OF LOWER ARM EXPOSED TO LIQUID HTO AT 34 ± 1°C)

Subject	Length of exposure, min	Water absorption rate,[a] mg/cm^2/min: Short H_2O rinse, then dried		Long H_2O wash	Short H_2O rinse, dried, and immersed in 100% EtOH
EAP	2	0.040			0.065
JS	2	0.048		0.049	
EAP	5	0.063	0.059	0.058	
JS	5	0.051	0.046		0.042
EAP	10	0.038			
JS	30	0.036			
EAP	45	0.029			

[a]Calculated from the increase of HTO in body fluids at equilibrium, the area of skin exposed, and the length of exposure.

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