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REDUCTION OF RADIATION HAZARD IN TRITIUM METHOD OF MEASURING TOTAL BODY WATER

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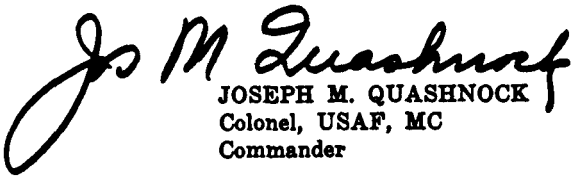
FOREWORD

This report was prepared in the Internal Medicine Branch under task No. 775502. The work was accomplished between July and September 1969, and the report was submitted for publication on 15 September 1969.

This report has been reviewed and is approved.



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ABSTRACT

The current procedure for measurement of total body water in vivo using a 250-μc. dose of tritiated water produces 18.98 mrads of total body radiation. It was found that the amount of radiation activity (number of counts) necessary for usable test results could be achieved as effectively by extending the counting time or increasing the amount of serum sampled. These changes in procedure allowed for a reduction in the total amount of tritiated water administered to 25 μc. Increasing the counting time reduced the exposure dose by a factor of 5; doubling the serum sampled decreased the exposure dose by a factor of 2; combining these two procedures decreased the total body exposure by a factor of 10. If a lower degree of test accuracy can be accepted, the amount of activity measured can be reduced and the dose of tritiated water correspondingly decreased.

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I. INTRODUCTION

In studies of body composition, total body water is routinely measured by tritium dilution. Since tritium emits relatively weak beta radiation (0.18 mev), the total dose must be higher than the dose used with other radioisotopes. Therefore, the exposure dose from this procedure is a potentially hazardous one, and reduction of this exposure is an important goal. The procedure currently in use requires a 250-μc. dose of tritiated water which produces 18.98 mrads of total body radiation. In this study methods are presented for extending the counting time and increasing the serum sample, thereby reducing the total exposure dose from tritium by a factor of 10.

II. MATERIALS

Tritiated water is received from the manufacturer as a sterile solution of distilled tritiated water, containing 26.8 mc./ml. In our laboratory this solution is further diluted with sterile distilled water to 25 μc./ml. Ten milliliters of this dilution (250 μc.) are then used to measure the total body water.

The activity of tritium samples is measured by use of a liquid scintillation spectrometer. Samples of serum or water must first be completely mixed with scintillant fluid, and then added to a special scintillator vial for measurement. The scintillator vial, plus contents, is then placed inside a freezer, an attachment to the liquid scintillation counter. The actual counting chamber is built inside the freezer attachment and connected by wiring to the main components of the spectrometer. The vial is kept in the freezer, in the dark, for about 1 hour before the activity is measured, thereby reducing background noise produced by heat and light acting upon the scintillant fluid. Without this period of cooling darkness the sample would be measured as having much more activity than was actually present in the vial.

The scintillant fluid is a mixture of 2,5-diphenyloxazole (PPO) and 1,4-bis[2-(5-phenyloxazolyl)]-benzene (POPOP) in a dioxane solvent. The exact amounts of each ingredient and the method of preparation have been described earlier (3).

The exposure doses for varying amounts of tritium were calculated using the following formula:

$$D_\beta = 73.8 \times \overline{E}_\beta \times T\tfrac{1}{2} \times \frac{\mu c.}{gm.}$$

where

D_β = beta dose

$\overline{E}_\beta$ = mean beta-ray energy

$T\tfrac{1}{2}$ = effective half-life.

The factor values for tritium are: $\overline{E}_\beta = 0.006$; $T\tfrac{1}{2} = 12$ days; and weight in grams = 70,000 (the gram-weight of the average man). The exposure dose was calculated for amounts of tritium ranging from 25 μc. to 500 μc. by substituting the microcurie value in the formula. The calculated exposure doses for increasing amounts of tritium are shown in table I.

TABLE I

Change in millirads of exposure dose with change in microcuries of tritium

Tritium (μc.)	Exposure dose (mrads)
25	1.89
50	3.78
75	4.74
100	6.63
125	9.49
150	11.38
175	13.27
200	15.16
225	17.05
250	18.98
275	20.87
300	22.76
325	24.65
350	26.58
375	28.47
400	30.36
425	32.25
450	34.14
475	36.03
500	37.96

III. METHOD

The procedure for measuring total body water (TBW) is that of Vaughan and Boling, and Prentice et al., as modified by our laboratory (1-3). The patient (or subject) reports to the laboratory after an 8-hour fast (nothing by mouth). If a previous TBW determination has been made within the last three months, a 5-ml. sample of blood is drawn in order to measure the tritium still remaining in the circulation. This residual level of tritium then becomes the background activity for the next TBW measurement. If no previous tritium dose has been administered, or the period is over three months, the next step in the procedure is followed.

The patient is given 10 ml. (250 μc.) of tritiated water orally, followed by 10 ml. of distilled water as a rinse. The patient is then instructed to return to the laboratory in 3 hours. The 3-hour period is necessary to allow complete equilibration of the tritiated water with the total body water.

After 3 hours, a 5-ml. sample of blood is drawn. The sample is allowed to clot and the serum separated. One milliliter of serum is used for the measurement of total body water: 0.5 ml. of serum is added to a centrifuge tube plus 0.5 ml. of distilled water; the second 0.5 ml. of serum is added to a centrifuge tube plus 0.5 ml. of a tritiated water standard. The standard is prepared by diluting 10 ml. of the tritiated water solution (250 μc./10 ml.) to 50,000 ml. with distilled water. After addition of serum, plus water or standard, to the two centrifuge tubes, 10 ml. of scintillant fluid are added.

The tubes are now centrifuged to remove the precipitated protein. The supernatant fluid is decanted into labeled scintillator vials marked "sample" and "standard" and is ready for activity measurement. If a background sample was drawn, the serum from this sample is treated in exactly the same way as the sample drawn from the patient: 0.5 ml. of serum is mixed with 0.5 ml. of distilled water, plus 10 ml. of scintillant fluid. After centrifugation, the supernatant fluid is decanted into a scintillator vial marked "background."

The tritium activity is measured as counts per minute (c.p.m.). The natural background is found by counting a scintillator vial containing 10 ml. of scintillant fluid alone. The first step in the calculation of the total body water is the subtraction of the background value from the sample value. (The background value can be either the natural background or the patient's own background.) The net standard value is then multiplied by the dilution factor (50,000) and the net sample value is multiplied by 1.06. The first product divided by the second product equals the total body water in liters. The formula for this calculation is as follows:

$$\text{TBW} = \frac{\text{net standard c.p.m.} \times 50{,}000}{\text{net sample c.p.m.} \times 1.06}$$

The factor of 1.06 (the reciprocal of 94) is used because the serum is 94% water.

IV. RESULTS

There are two basic methods by which the exposure dose can be reduced: (1) by increasing the counting time, or (2) by increasing the volume of sample measured. In both methods, the radioisotope dose is reduced but the sample counting rate is kept constant. We have applied both methods to reduce the exposure dose from tritiated water.

From experience, we know that the sample counting rate with 250 μc. of tritium is about 450 counts per minute (c.p.m.). The accuracy of the sample counting rate depends on the total counts accumulated—increasing the total count decreases the counting error. In table II we have presented the change in error with increased counting time (4). The error is expressed as a plus or minus percentage error around the mean value of 450 c.p.m. We have also shown this error in terms of plus or minus counts per minute. If this error in counts per minute is added to or subtracted from the sample value (450 c.p.m.), and these new values used to calculate a TBW value, the error can be expressed in terms of plus or minus liters of total body water. These values are also shown in table II.

Examination of table II shows that a 20-minute counting time reduces the error to $\pm$ 1%, or a $\pm$ 1 liter variance in the total body water. Since a normal body water is about 50 liters, a $\pm$ 1 liter variance actually represents a $\pm$ 2% error in the total body water value.

Depending on the amount of statistical counting error that is considered acceptable, the amount of tritium can be reduced and the counting time increased. For example, if a $\pm$ 1% error is acceptable, the amount of tritium can be reduced to 50 μc., with a counting time required of 100 minutes. The total count in this case would be 9,000 counts, which from table II would represent a $\pm$ 1% error.

A previous study of reproducibility of repeated TBW measurements over a restricted period of time showed that a 2:1 sample-to-background counting ratio is a minimum for reproducibility for this procedure (3). The counting rate of 90 c.p.m., with a natural background of 35 c.p.m., is close to this minimum. Therefore, the reduction of the tritium dose to 50 μc. from 250 μc. is close to the maximum reduction obtainable by simply increasing the counting time. This reduction represents a 5-fold drop in the total body exposure dose.

If the counting error must be less than $\pm$ 1%, then a higher total count is necessary. This limits attempts to reduce the amount of tritium, since the total counting time to reach lower error becomes greatly extended as the amount of tritium is reduced below 250 μc. For example, if the error must be no more than $\pm$ 0.38%, the total count must be 36,000. Therefore, if the amount of tritium is reduced to 50 μc., which gives a counting rate of 90 c.p.m., the time needed to reach 36,000 counts is 400 minutes.

The second method for reducing the exposure dose is to increase the amount of sample.

TABLE II

Effect of counting time on the error of counting

Counting time (min.)	Total counts	Percentage error	Error in c.p.m.	Error in liters
10	4,500	$\pm$ 1.4	$\pm$ 6	$\pm$ 1.5
20	9,000	$\pm$ 1.0	$\pm$ 4	$\pm$ 1.0
40	18,000	$\pm$ 0.76	$\pm$ 3	$\pm$ 0.75
80	36,000	$\pm$ 0.38	$\pm$ 1.5	$\pm$ 0.25

The scintillant fluid is designed to count 1 ml. of water per 10 ml. of scintillant fluid. Increasing the water above 1 ml. will cause the water to form a separate layer, and the tritium in this layer will not be measured. Therefore, the 1 ml. of water per 10 ml. of scintillant fluid is an upper limit. Another limitation is the scintillator vial, which will hold no more than 23 ml. of fluid. The present method uses 10 ml. of scintillator fluid plus 1 ml. of water. This amount of water can easily be doubled to 2 ml. and mixed with 20 ml. of scintillant fluid, without exceeding the vial capacity. This doubling of the amount of serum sampled will double the sample counting rate. Increasing the serum volume by a factor of 2 will also allow a reduction in the amount of tritium used by the same factor.

By carrying this reasoning a step further, if a total of 9,000 counts (error = ± 1%) is permissible, then the tritium dose can be reduced to 25 μc. if a 1 ml. serum sample is used. Twenty-five microcuries will give 90 c.p.m. per 1 ml. of serum, and counting for 100 minutes will give a total count of 9,000 (± 1% error). Reducing the tritium dose to 25 μc. lowers the exposure dose by a factor of 10—from 18.98 to 1.9 mrads.

V. DISCUSSION

Analysis of the total body water procedure indicates that the 250-μc. dose of tritiated water is a reasonable dose for convenient and reliable measurement of total body water. This amount of activity will produce a sample count rate of 450 c.p.m., with a counting error of ± 0.25 liter, if the counting time is extended to 80 minutes.

The dose can be easily decreased by a factor of 2 if the serum sampled is increased from 0.5 ml. to 1 ml. The counts per minute per sample remain the same (450 c.p.m.); therefore, the counting error, with a counting time of 80 minutes, will remain the same.

Further decreases in the total body exposure dose can be accomplished by the acceptance of a higher degree of counting error, or by using very long counting times. If an error of ± 1% is allowable, the amount of tritium can be reduced by another factor of 5. One-milliliter serum samples would give a total of 9,000 counts in 100 minutes, or a counting error of ± 1%. The final dose reduction from increasing the sample size and increasing the allowable error would be 2 times 5, or a 10-fold reduction.

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