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The derivation of tritium transfer parameters for farm animals on the basis of a metabolic understanding

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Abstract. In contrast to many radionuclides (which often have no biological function) ^{3}H has a stable analogue which is an elemental component of major nutrients, animal tissues and drinking water. Therefore concepts used to predict the transfer of other radionuclides are not valid for ^{3}H.In this paper we present an approach for the derivation of tritium transfer parameters which is based on the metabolism of hydrogen in animals. The derived transfer parameters separately account for transfer, to and from, free (i.e. water) and organically bound tritium. A novel aspect of the approach is that tritium transfer can be predicted to any animal product for which the required metabolic input parameters are available.

Predicted equilibrium transfer coefficients are compared to available independent data. Agreement is good (R^2=0.97) with the exception of the transfer from tritiated water to organically bound ^{3}H in ruminants. This may be attributable to characteristics of ruminant digestion.

Tritium transfer coefficients will vary in response to the metabolic status of an animal and the use of a single transfer coefficient from diet to animal product is inappropriate. However, we demonstrate that concentration ratios are less subject to metabolic variation and are a more useful parameter than transfer coefficients.

1. INTRODUCTION

Tritium can be released to the environment by facilities such as heavy water reactors, fuel reprocessing plants, tritiated radio-pharmaceutical factories and weapons installations. Because ^{3}H is an isotope of hydrogen it directly enters the hydrological cycle, and ^{3}H transfer in the biosphere cannot be readily modelled using approaches developed for other radionuclides, which are largely trace contaminants. Tritium can enter the diet of farm animals and man as either tritiated water (HTO) or organically bound ^{3}H (OBT). Animal products constitute up to 50 % of the OBT intake by humans. An ability to predict ^{3}H transfer to animals is therefore important. However, previous approaches generally make simplistic assumptions; single transfer coefficient values having been recommended [e.g. 1].

On its own the existing radioecological literature is inadequate to derive models of ^{3}H transfer to farm animals. However, HTO behaves like water within the body, whilst OBT is bound, with carbon, in compounds such as carbohydrates. The wealth of knowledge concerning carbon and hydrogen metabolism can be utilised used with the available radioecological data to derive more applicable models. Here, we derive a steady state model for predicting ^{3}H transfer to animal products from an understanding of animal nutritional needs and body composition.

2. Derivation of Equilibrium Transfer Parameters

There are four pathways of ^{3}H transfer that need to be considered: (i) dietary HTO to tissue HTO, (ii) dietary HTO to tissue OBT, (iii) dietary OBT to tissue HTO and (iv) dietary OBT to tissue OBT. Each can be represented in terms of a transfer coefficient, F (d kg^{-1}):

$$F = \frac{\text{tissue or other food product equilibrium activity concentration (Bq kg}^{-1}\text{ fresh weight)}}{\text{daily intake rate (Bq d}^{-1}\text{)}} \tag{1}$$

The equilibrium concentrations of HTO and OBT in a tissue (or a pool such as milk) ($[HTO_t]$ and $[OBT_t]$ respectively) are given by:

$$[HTO_t] = F_{HH} I_{HTO} + F_{OH} I_{OBT} \qquad [OBT_t] = F_{HO} I_{HTO} + F_{OO} I_{OBT} \qquad (2,3)$$

Where: F_{HH} is the transfer coefficient from dietary HTO to tissue or milk HTO; F_{HO} is the transfer coefficient from dietary HTO to tissue or milk OBT; F_{OH} is the transfer coefficient from dietary OBT to tissue or milk HTO; F_{OO} is the transfer coefficient from dietary OBT to tissue or milk OBT.

2.2 Dietary HTO and OBT to Tissue or Milk HTO, F_{HH} and F_{OH}

If we make the following assumptions: (i) dietary water absorption is complete; absorption of organically bound hydrogen (OBH) is described by the diet digestibility (F_D); all OBH is lost via oxidation to HHO (direct excretion of body OBT is negligible being only a few percent of the total loss [2]); the loss of water from the body is described by a first order rate coefficient, λ_w=0.693/T_w where T_w is the body water turnover half-life. We can then write the rate of change of body hydrogen in the form of water (HHO kg H) and organically bound hydrogen (OBH kg H) as:

$$\frac{dHHO}{dt} = I_{HHO} + f(OBH) - g(HHO) - \lambda_w HHO \qquad (4)$$

$$\frac{dOBH}{dt} = I_{OBH} F_D - f(OBH) + g(HHO) \qquad (5)$$

Where: I_{HHO} is the daily dietary hydrogen intake as water (kg H d^{-1}); OBH is the whole body organically bound hydrogen (kg H); f(OBH) is a function describing the rate of transfer of organically bound hydrogen to hydrogen as water (kg H d^{-1}); g(HHO) is a function describing the rate of transfer of water hydrogen to organically bound hydrogen (kg H d^{-1}); λ_w is the rate coefficient for the loss of water from the body (d^{-1}). At equilibrium we can set equation (5) equal to zero and rearrange to obtain:

$$g(HHO) = f(OBH) - I_{OBH} F_D \qquad (6)$$

We can also set equation (4) equal to zero and substitute equation (6) for g(HHO):

$$HHO^{eqm} = \frac{I_{HHO} + I_{OBH} F_D}{\lambda_w} \qquad (7)$$

The equilibrium concentration of hydrogen in the form of water in the body, [HHO^{eqm}], (kg H kg^{-1} live-weight) is therefore:

$$[HHO^{eqm}] = \frac{I_{HHO} + I_{OBH} F_D}{\lambda_w M_B} \qquad (8)$$

Where M_B is the live-weight (kg). Specific pools may have water contents which differs from the mean for the whole animal. We can rewrite equation (8) for a given pool, *t*, assuming complete mixing of the various water pools, as:

$$[HHO_t^{eqm}] = \frac{v_{tw}}{v_{Bw}} \frac{I_{HHO} + I_{OBH} F_D}{\lambda_w M_B} \qquad (9)$$

Where: v_{tw} is the fraction of tissue or pool, *t*, composed of water; v_{Bw} is the fraction of the whole body composed of water. Equation (8) has a component due to the intake of dietary water and a component due to the intake of organically bound hydrogen. Transfer coefficients are therefore described by:

$$F_{HH} = \frac{v_{tw}}{v_{Bw} \lambda_w M_B} \qquad F_{OH} = \frac{v_{tw} F_D}{v_{Bw} \lambda_w M_B} = F_{HH} F_D \qquad (10,11)$$

2.3 Dietary HTO to Tissue or Milk OBT, F_{HO}

Experimentally following HTO intake, equilibrium specific activities of OBT in tissues (SA_{OBT}^{tissue}) in the range 0.2-0.3 of those of HTO in body water (SA_{HTO}^{body}) [3] have been determined. Assuming that the specific activity of HTO in whole body water is equal to the specific activity of HTO in tissue water (i.e. that these pools are in rapid equilibrium):

$$SA_{OBT}^{tissue} = \frac{I_{HTO} F_{HO}}{m_{ot}} \qquad SA_{HTO}^{body} = \frac{I_{HTO} F_{HH}}{0.111 v_{tw}} \qquad (12,13)$$

Where: m_{ot} is the mass of organically bound hydrogen in 1 kg of tissue (kg kg^{-1}) and 0.111 is the mass of hydrogen in water (kg kg^{-1}). Assuming the observed relationship ratio between SA_{OBT}^{tissue} and SA_{HTO}^{body}:

$$\begin{aligned} SA_{OBT}^{tissue} &\approx 0.25 SA_{HTO}^{body} \\ \frac{I_{HTO} F_{HO}}{m_{ot}} &\approx 0.25 \frac{I_{HTO} F_{HH}}{0.111 v_{tw}} \\ F_{HO} &\approx \frac{0.25 F_{HH} m_{ot}}{0.111 v_{tw}} \qquad (14) \end{aligned}$$

Substituting F_{HH} from equation (10) we obtain:

$$F_{HO} \approx \frac{0.25 m_{ot}}{0.111 v_{Bw} M_B \lambda_w} \qquad (15)$$

Note, here we define specific activity as activity of free or bound ^{3}H per unit mass of free or bound hydrogen in a given pool, and not per unit mass of tissue.

2.4 Dietary OBT to Tissue or Milk OBT, F_{OO}

F_{OO} can be estimated from the concentration of OBH in tissues, making a correction for the component of OBH which is transferred from dietary water, which can be calculated from F_{HO} (equation 15):

$$F_{OO} = \frac{m_{ot} - F_{HO} I_{HHO}}{I_{OBH}} \qquad (16)$$

2.5 Concentration ratios

From the above we can derive expressions to estimate concentration ratios from dietary OBT (CR_{OBT}) or HTO (CR_{HTO}) to tissue ^{3}H:

$$CR_{OBT} = (F_{OO} + F_{OH}) \times \text{Daily Dry Matter Intake (kg d}^{-1}) \qquad (17)$$

$$CR_{HTO} = (F_{HH} + F_{HO}) \times \text{Daily Water Intake (kg d}^{-1}) \qquad (18)$$

3. DATA REQUIREMENTS

To apply the derived transfer parameter equations, data are required for the animals: (i) body mass; (ii) body, tissues and milk water fractions; (iii) water turnover half-time; (iv) bound hydrogen concentration in tissues and milk; (v) the intake of water and OBH; (vi) feed digestibility; (vii) production level. These data are widely available for food producing animals as recommended values or relationships to live-weight and production level [e.g. 4]. To calculate the results presented below dry matter (DM) intake was estimated using relationships of recommended intakes depending upon live-weight, production level, physiological status, activity level and age [e.g. 4]. Water turnover time was estimated assuming that the animal's water balance was at equilibrium and that the total input of water (i.e. drinking water, water from feed, metabolic water) was equal to the loss. We have neglected the effects of inhalation and skin absorption which amount to only a few percent of the overall water balance. Oral water intake (drinking + feed) was estimated using reported ratios of water to dry matter intake [4]. Where the dry matter or water intakes of animals is known actual values could be substituted for the relationships we have used.

4. RESULTS AND EVALUATION

Estimated transfer parameters for a number of animals and products are presented in Table 1; as will be demonstrated later transfer coefficient values are only applicable to the metabolic scenario given.

Table 1: Predicted transfer coefficients and concentration ratios (CR) for a number of animal products.

Animal Product	Live-weight (kg)	Production* (kg d^{-1})	DM intake (kg d^{-1})	Water Intake (kg d^{-1})	F_{HH} (d kg^{-1})	F_{OH} (d kg^{-1})	F_{HO} (d kg^{-1})	F_{OO} (d kg^{-1})	CR_{HTO}	CR_{OBT}
Veal	160	0.80	4.84	23.23	2.80E-02	1.90E-02	2.00E-03	5.30E-02	7.00E-01	3.50E-01
Beef	400	0.80	8.58	41.19	1.50E-02	1.00E-02	1.00E-03	3.90E-02	6.60E-01	4.20E-01
Lamb	20	0.20	1.02	3.45	1.84E-01	1.20E-01	1.30E-02	2.64E-01	6.80E-01	3.90E-01
Mutton	50	0.08	1.22	5.36	1.16E-01	7.60E-02	1.00E-02	2.56E-01	6.70E-01	4.00E-01
Goat	50	0.05	1.15	3.46	1.81E-01	1.19E-01	1.40E-02	2.66E-01	6.80E-01	4.40E-01
Pig	100	1.01	2.66	9.59	5.50E-02	4.90E-02	6.00E-03	1.50E-01	5.90E-01	5.30E-01
Broiler	1.7	0.04	0.11	0.21	2.68E+00	2.33E+00	2.06E-01	3.50E+00	6.00E-01	6.40E-01
Egg	2.5	0.05	0.15	0.32	1.93E+00	1.68E+00	1.29E-01	2.67E+00	6.70E-01	6.70E-01
Cow milk	550	15.00	13.96	62.80	1.30E-02	9.00E-03	3.30E-04	9.00E-03	8.20E-01	2.50E-01
Sheep milk	50	1.30	1.84	6.99	1.07E-01	7.30E-02	5.00E-03	1.07E-01	7.80E-01	3.30E-01
Goat milk	50	2.50	1.15	6.77	1.14E-01	7.50E-02	3.00E-03	5.20E-02	7.90E-01	1.50E-01

*Production refers to the daily live-weight gain or milk production, as appropriate.

4.1 Comparisons to Experimental Results

Predicted transfer coefficients have been compared to available observed values [5-11]. In some cases the required metabolic parameters are defined in the literature, but in others we have had to estimate them using recommended values and relationships [see 12]. The comparisons are presented in Figure 1; the slope and intercept are close to one and zero respectively. In the case of F_{HH}, F_{OH} and F_{OO} there is good agreement between the observed and predicted transfer coefficient values. The mean Predicted/Observed ratios are 0.96, 1.07 and 1.16 respectively and these values are not significantly different to 1.0 (t-test, $P>0.5$ (F_{HH} F_{OH}); $P>0.05$ (F_{OO})). In the case of F_{HO} there is an under-prediction; the mean Predicted/Observed ratio is 0.75. We have estimated F_{HO} using an observed specific activity ratio (0.25) derived from small mammal experiments however, all the observed data are for ruminants. Ruminants have a greater capability to synthesise OBH in the foregut than monogastric animals and consequently it is possible that the specific activity ratio used is not applicable to ruminants (a ratio of *c.* 0.46 predicts the reported value of F_{HO} in both dairy cows studies). However, this disagreement is of little importance as the pathway from HTO to OBT contributes little to a tissue's overall ^{3}H content.

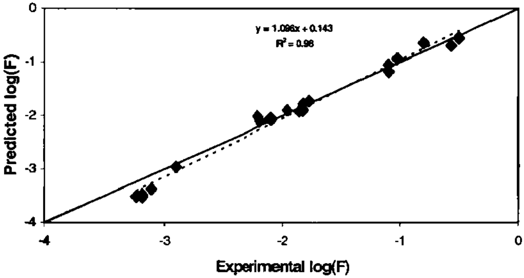

Figure 1: Comparison between predicted log(F) with experimentally observed log(F); solid line is the 1:1 relationship, dotted line is the best fitting line through the data.

4.2 Parameter Effects

The estimation of the transfer values relies on a number of input parameters the selection of which will influence the resultant transfer value. In some instances, this will lead to uncertainty in the transfer value estimate (due to input parameter uncertainty) whilst in others the ability to investigate the effect of varying parameters within known ranges is useful. Table 2 presents examples of transfer parameter estimates for cow milk; in each case one input parameter is varied over a realistic range. The other input parameters remain constant with the exception of water and DM intakes which are determined by a number of other input parameters.

Table 2: Transfer parameter values for cow milk for a number of varying input parameter. In each case a range ratio has been calculated, this is the ratio of transfer calculated for the maximum value of the input parameter to that calculated for the minimum value of the input parameter.

Parameter value	Water Intake (kg d^{-1})	DM intake (kg d^{-1})	F_{HH}	F_{OH}	F_{HO}	F_{OO}	CR_{HTO}	CR_{OBT}
Milk yield (kg d^{-1})								
5	39.4	8.8	2.04E-02	1.41E-02	5.18E-04	1.39E-02	8.24E-01	2.45E-01
15	62.8	14.0	1.28E-02	8.86E-03	3.25E-04	8.72E-03	8.24E-01	2.45E-01
40	121	27.0	6.62E-03	4.59E-03	1.68E-04	4.51E-03	8.24E-01	2.45E-01
Range			0.32	0.32	0.32	0.32	1.00	1.00
Live- weight (kg)								
350	54.8	12.2	1.46E-02	1.02E-02	3.73E-04	9.98E-03	8.24E-01	2.45E-01
550	62.8	14.0	1.28E-02	8.86E-03	3.25E-04	8.72E-03	8.24E-01	2.45E-01
750	70.1	15.6	1.15E-02	7.95E-03	2.92E-04	7.81E-03	8.24E-01	2.45E-01
Range			0.78	0.78	0.78	0.78	1.00	1.00
Water : DM intake								
4	55.8	14.0	1.43E-02	9.88E-03	3.62E-04	8.74E-03	8.16E-01	2.60E-01
4.5	62.8	14.0	1.28E-02	8.86E-03	3.25E-04	8.72E-03	8.24E-01	2.45E-01
7	97.7	14.0	8.45E-03	5.86E-03	2.15E-04	8.64E-03	8.47E-01	2.02E-01
Range			0.59	0.59	0.59	0.99	1.04	0.78
Diet digestibility								
0.5	62.8	14.0	1.30E-02	6.52E-03	3.32E-04	6.29E-03	8.22E-01	1.75E-01
0.72	62.8	14.0	1.30E-02	9.40E-03	3.32E-04	9.06E-03	8.22E-01	2.52E-01
1	62.8	14.0	1.30E-02	1.30E-02	3.32E-04	1.26E-02	8.22E-01	3.50E-01
Range			1.00	2.00	1.00	2.00	1.00	2.00
Milk Fat								
3	58.2	12.9	1.38E-02	9.56E-03	3.51E-04	9.17E-03	8.24E-01	2.45E-01
4	62.8	14.0	1.28E-02	8.86E-03	3.25E-04	8.50E-03	8.24E-01	2.45E-01
5	67.4	15.0	1.19E-02	8.26E-03	3.03E-04	7.92E-03	8.24E-01	2.45E-01
Range			1.16	1.16	1.16	1.16	1.00	1.00
$SA_{OBT}^{tissue} : SA_{HTO}^{body}$								
0.2	62.8	14.0	1.28E-02	8.86E-03	2.60E-04	8.50E-03	8.20E-01	2.53E-01
0.25	62.8	14.0	1.28E-02	8.86E-03	3.25E-04	8.50E-03	8.24E-01	2.45E-01
0.3	62.8	14.0	1.28E-02	8.86E-03	3.90E-04	8.50E-03	8.28E-01	2.38E-01
Range			1.00	1.00	0.67	1.00	0.99	1.06

The relative effect on individual transfer value was the same for both meat and milk. Variation in most input parameters resulted in the same relative changes in all transfer coefficients. Changes in either the ratio of water intake to DM intake or diet digestibility resulted in different relative effects for different transfer coefficients. For dairy cows the parameter which resulted in the greatest variation in estimated transfer coefficients was milk yield. The range in estimated transfer coefficients demonstrates the potential errors associated with assuming single values of transfer coefficient for ^3H.

However, in most cases the estimated concentration ratios remain constant over a wide range of input parameters (e.g. milk yield and live-weight). Variation in diet digestibility and the ratio of the intake of water to dry matter do result in changes in concentration ratios. The example of varying diet digestibility between the extremes of 0.5 and 1.0 probably represents the maximum expected variation in CR_{OBT}.

5. DISCUSION

A number of organisations [e.g. 1] have recommended transfer coefficients for animal products. We have shown that ^3H transfer coefficients cannot be regarded as constants but depend on an animals metabolic status. However, concentration ratios are more robust, remaining constant over a wide range of metabolic states. While they will vary in response to changes in the digestibility and water content of an animals diet, and the composition of its tissues, the potential variability in these parameters is relatively small.

Dose coefficients to humans after ingestion of OBT are about 2.4 times higher than after ingestion of HTO [13]. Therefore, the ability of our approach to model HTO and OBT separately is an important advantage. We can also model HTO in drinking water separately to that in feed water.

We have considered only a limited number of metabolic factors, and have ignored the influence of the animals ambient environment. In particular temperature and humidity are expected to affect an animals water balance, and thereby its ^3H transfer. Some authors have suggested methods to account for these variables [14] which could be used to extend our approach. Although we have concentrated on food producing animals the approach described here could be extended to consider humans or other animals.

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