

12-3-48
Doses Observed to
Organs of Man by C¹⁴ in Methyl-labeled glycine.

To: Dr. John H. Lawrence

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The following report is a brief evaluation of the evidence for believing that tracer quantities of C¹⁴ can be administered to man ^{out} with exceeding the tolerance dose or producing prolonged exposure (excessive total dose) to radiation sensitive tissue^S. The estimates of dose to various organs are based on the investigations of Dr. Nardi on C¹⁴ distribution and uptake in organs of mice. It is assumed that the uptake per gm. of tissue in man will not differ from that for mice by more than a factor of five.

The metabolic fate of C¹⁴ from methyl-labeled glycine was investigated in mice which were given a single intravenous injection of glycine with a specific activity of ~~3.0~~ ^{3.0} ~~mc~~ ^{mg} per ~~g~~ (report of Dr. Nardi.) No attempt was made to determine the ~~rate~~ ^{intermediate metabolism} of the labeled glycine but the C¹⁴ content of 11 organs and the excreta was measured periodically during the interval 6 h. to 43 d. The maximum concentration in the various tissues was found to occur at about 1 day, after which steady elimination reduced ^{in all organs} the concentration by a factor of ~~10~~ ⁵ to 40 by the 43rd day, as shown below:

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The rates of elimination from all 11 tissues were in the same order of magnitude and there appeared no evidence to believe that an appreciable portion of the administered C¹⁴ remained fixed in these tissues. Blood activity, however, was not measured ⁺ ~~by~~ ⁱⁿ from the work of Shemin and Rittenberg, *

* Shemin, D. and Rittenberg, D., J. Bio. Chem. 166, (27) (1946).

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Estimated dose (max.) in r.e.p./day delivered to various organs of man (70 Kg) due to 1 mc of C^{14} administered as methyl labeled glycine.

	% wt. 25 gm mouse	% wt. 70 Kg. man	man / mouse	max. % C^{14} mouse	max. % C^{14} man	Daily dose C^{14} organ in man in r.e.p./day
Bone (marrow)		4.3	~1	13.	13	1.3 .13 .01
Brain	1.4	2	1.4	.5	.7	.015 .00
Heart	.4	.43	1	.5	.5	.05 .00
Kidney	1.1	.43	.4	~3	1.2	.12 .000
Liver	5.	2.1	.4	17	7	.14 .001
Spleen	.6	.22	.37	9	3.3	.65 .007
Panc.	.45	.12	.27	5	1.4	.5 .02
Lung.	.5	1.7	3.4	1.4	4.8	.12 .002
Al. tract (whole gut)	10	3.2	.32	21	6.7	.09 .004
estimated) red cells		3.6			< 1	< .012
total body (assuming uniform distribution)						< .043

Note: To obtain dose by any other quantity of C^{14} , multiply figures in last column by the amount in mc.

it can be assumed, at least for humans, that a fraction of the C 14
(about 120 days).
will be retained for the period of life of the red cell. Judging from
the amounts taken up in other tissue and the amount eliminated within
one week, it appears likely that C 14 in red cells could not be more than
several percent at the most.

Elimination of C 14 in urine and as C¹⁴O₂, as measured by Dr. Nardi,
accounted for as much as 90% in 5 days. C¹⁴O₂ elimination was responsible
for 40 to 80 percent in this period, and urine about 10-15%. Data for
feces are not yet computed.

N₂
C-14
In view of previous uncertainties regarding C 14 metabolism, one
of the important results of this investigation reveals that the turnover
rates in bone, marrow and liver are about the same. If this can be assumed
to be essentially true for humans there would appear to be little danger
of excessive or prolonged dose delivered to bone marrow in tracer studies
of red cell life.

It is realized that uptake and elimination in organs of mice and humans
will doubtless show considerable differences but correcting for the relative
weights of the various organs in mice and man and assuming that the cor-
responding maximum concentrations per gm. in these organs is about the
same, the probable doses delivered by 1.0 mc. of C¹⁴ in methyl labeled
glycine to various organs are given below:

It is seen from the table that for 1 mc. of administered C 14 the
maximum daily dose delivered to certain organs appears to be greater than
the acceptable daily dose. However, since C¹⁴ is rapidly eliminated
from these tissues, it is likely that the actual dose will be somewhat less