Effect of Food Intake on the Tissue Distribution of Gallium-67: Concise Communication

Raymond L. Hayes, Janusz J. Szymendera*, and Billy L. Byrd

Oak Ridge Associated Universities, Oak Ridge, Tennessee

Fasting affects the body retention and tissue distribution of Ga-67 in experimental animals. In Ga-67 experiments, therefore, a difference in food intake between treated and control animals might result in confusing side effects. We have observed this in irradiation studies. It is suggested that a fasting regimen should be imposed in any Ga-67 animal study where an alteration in food intake might be experienced in the treated group.

J Nucl Med 20: 938–940, 1979

The biodistribution of Ga-67 is rather markedly influenced by many different factors (*1*), e.g., age, sex, exposure to ionizing radiation, and pregnancy and lactation, to cite a few. We have identified yet another factor that affects the relative deposition of intravenously administered Ga-67 in various tissues, namely, food intake. The importance of the effect of food intake on the tissue distribution of Ga-67 became even more apparent to us in subsequent irradiation studies, which we report here.

MATERIALS AND METHODS

The animals used were $CD2F_1$ and C57B1/6 mice† and male Buffalo rats.‡ In each experiment the animals were matched as to age and sex to avoid any effects produced on Ga-67 tissue distribution by variations in these factors (*2*). Fed animals were given free access to both water and food pellets.‖ Fasted animals received only water. In tissue-distribution experiments using the rat, food was withdrawn 24 hr before Ga-67 administration. In fasting experiments involving irradiation, food was withdrawn at the start of the irradiation and continued through the termination of the experiment.

In rat tissue-distribution studies, ~ 5 μCi of Ga-67 citrate§ was administered intravenously. In irradiation studies, rats received 30–50 μCi of Ga-67 and mice a like amount, but by the intraperitoneal route. In irradiation experiments, the Ga-67 was administered to mice 24 hr after termination of the irradiation, and to rats 24 hr after the midpoint of the exposure.

To determine the tissue distribution of Ga-67 in the rat, weighed samples of various tissues were counted in a scintillation well counter against an aliquot of the dose injected, and the tissue concentrations were then calculated as percentage administered dose per gram, normalized to a body weight of 250 g.

In irradiation experiments, mice were exposed to 450 R of whole-body x-irradiation in perforated Plexiglas containers on a revolving turntable centered in the beam of a constant-potential x-ray machine¶ (250 kV, 15 mA, filtration 1.0 mm Cu and 1.0 mm Al). The half-value layer was equivalent to 2 mm of Cu, and the exposure rate was 96 R/min. Rats, contained in individual perforated polyethyl-

---

* Poland–U.S. (NCI) Exchange Scientist from Maria Sklodowska-Curie Memorial Institute of Oncology, Warsaw 22, Poland.

Received Feb. 28, 1979; revision accepted April 2, 1979.

For reprints contact: Raymond L. Hayes, Oak Ridge Associated Universities, P. O. Box 117, Oak Ridge, TN 37830.

TABLE 1. EFFECT OF FASTING ON THE 24-HR TISSUE DISTRIBUTION OF Ga-67 IN MALE BUFFALO RATS

Tissue	Fed	Fasted*	Significance
	% administered Ga-67/g†		p
Liver	0.70 ± 0.03‡	1.06 ± 0.01	< 0.001
Spleen	1.00 ± 0.11	1.45 ± 0.07	< 0.001
Kidney	0.63 ± 0.02	0.96 ± 0.02	< 0.001
Lung	0.23 ± 0.02	0.28 ± 0.01	NS
Muscle	0.21 ± 0.01	0.18 ± 0.02	NS
Femur	2.45 ± 0.07	2.41 ± 0.03	NS
Bone marrow	0.85 ± 0.05	1.51 ± 0.07	< 0.001
Blood	0.11 ± 0.00	0.16 ± 0.01	< 0.001

* Food withdrawn 24 hr before Ga-67 administration.
† Normalized to body weight of 250 g; five animals per group.
‡ s.e.

ene containers, were exposed to 550 R in a Cs-137 medium-exposure total-body irradiation facility (*3*). The exposure rate was 3.17 R/min.

To determine the body retention of Ga-67, animals were counted in a small-animal geometry-independent whole-body gamma counter (*4*) immediately after Ga-67 administration, and a similar count was made of an appropriate Ga-67 standard to establish a "zero time" Ga-67 count rate. Determinations of percentage body retention were then made at subsequent intervals by re-counting the animals and the standard.

RESULTS

The effect of fasting on the tissue distribution of Ga-67 in the rat is shown in Table 1. Clearly major alterations were produced by cessation of food intake, namely, highly significant increases in the concentration of Ga-67 in liver, spleen, kidney, bone marrow, and blood ($p < 0.001$).

In subsequent studies of the effect of total-body x-irradiation on the body retention of Ga-67 in tumor-bearing mice, we failed to observe a significant decrease in Ga-67 body retention in control $CD2F_1$ male mice (Table 2), contrary to the earlier experience of Swartzendruber and Hübner (*5*), and the confirming results of other investigators (*6,7*). This led us to repeat the same experiment using C57B1/6 male mice (see also Table 2). We again obtained no significant difference between the irradiated animals and the controls.

Suspecting that our aberrant irradiation results might be caused by a difference in food intake between the irradiated and nonirradiated animals, we carried out fasting-irradiation experiments, the results of which are shown in Table 3. It is apparent that fasting produced an enhanced body retention of Ga-67 and that in turn, when irradiated animals were subjected to a fasting regimen, a markedly decreased body retention in both mice and rats was observed, in keeping with the reports of others on the effects of ionizing radiation on body retention of Ga-67.

DISCUSSION

Table 1 clearly shows that fasting causes considerable increases in the deposition of Ga-67 in the liver, spleen, kidneys, and bone marrow of the rat. In the mouse, fasting caused a significant increase in the body retention of Ga-67 (Table 3).

We feel that the reason we were not at first able to duplicate the original results of Swartzendruber and Hübner (*5*) in our irradiation experiments (Table 2) was possibly because we used mice that had not been given sufficient time to adjust to their new surroundings following their entry into our animal quarters (1–2 weeks previous to our experiments). They were, therefore, probably still experiencing "shipping stress" (*8*) when they were used in our irradiation experiments. The animals used by Swartzendruber and Hübner (*5*) had generally been housed in animal quarters for several months before they were used experimentally. If our irradiated animals reacted to their treatment by severely restricting their food intake, compared with that of

TABLE 2. INITIAL EXPERIMENTS ON THE EFFECT OF X-IRRADIATION ON BODY RETENTION OF Ga-67 BY FED MICE

Strain	Time after irradiation	Control	Irradiated	Significance
	hr	% Ga-67 body retention*		p
$CD2F_1$	48	68.0 ± 2.9†	62.8 ± 0.7	NS
	72	53.6 ± 2.2	54.9 ± 0.8	NS
C57B1/6	48	71.6 ± 4.7	64.1 ± 4.9	NS
	72	56.1 ± 3.9	52.4 ± 3.3	NS

* Ga-67 administered 24 hr after irradiation (see Methods).
† s.e.; six or more animals per group.

TABLE 3. EFFECT OF IRRADIATION ON BODY RETENTION OF Ga-67 IN FASTING MICE AND RATS

Experiment	Time after irradiation	Control, fed	Control, fasted	Irradiated, fasted	Significance
	hr	% Ga-67 body retention*			p
1. C57B1/6 mice	48	69.7 ± 0.9†	80.9 ± 0.8	—	< 0.001
	72	58.6 ± 0.9	68.6 ± 1.0	—	< 0.001
	48	—	80.9 ± 0.8	65.3 ± 3.2	< 0.001
	72	—	68.6 ± 1.0	58.9 ± 2.6	0.01–0.001
2. Buffalo rats	48	—	78.5 ± 0.4	62.3 ± 1.4	< 0.001
	72	—	71.0 ± 0.9	55.2 ± 1.2	< 0.001

* Ga-67 administered 24 hr after irradiation (see Methods).
† s.e.; seven or more animals per group.

the controls, one might expect that the tendency toward a decrease in body retention of Ga-67 produced by irradiation would be offset by the increase in body retention that is caused by restricted food intake. This indeed appears to have happened (Table 2). We have no proof for this contention except for the fact that when both controls and treated animals were manipulated to the same degree (withdrawal of food) we were able to achieve results similar to those observed by Swartzendruber and Hübner (Table 3). In follow-up experiments we were able to achieve a significantly decreased body retention of Ga-67 in fed mice following irradiation, but only after the animals used had been housed in our animal quarters for approximately 2 mo.

The difficulties we experienced in our irradiation studies serve to emphasize the importance that we think should be given to possible changes in food intake in experiments when a treated group of animals differs sharply from the control group. If such does occur, the food intake factor could very obviously produce confusing side effects (cf. Table 2).

We suggest that when food intake may be affected by a particular treatment, it would be best to impose a fasting regimen on both treated and control groups. Although fasting by itself will change the tissue distribution of Ga-67, it will necessarily occur to the same extent in both the control and treated groups.

FOOTNOTES

† Cumberland View Farms, Clinton, TN.

‡ Simonsen Laboratories, Inc., Gilroy, CA, and Microbiological Associates, Inc., Walkersville, MD.

‖ Ralston Purina Co., St. Louis, MO.

§ New England Nuclear Corp., Boston, MA.

¶ Westinghouse Electric Corp., Electronics and X-Ray Div., Baltimore, MD.

ACKNOWLEDGMENT

This investigation was supported by Grant No. CA-11858 awarded by the National Cancer Institute, DHEW. Oak Ridge Associated Universities operates under Contract No. EY-76-C-05-0033 with the U. S. Dept. of Energy.

REFERENCES

1. HAYES RL: The medical use of gallium radionuclides: a brief history with some comments. *Semin Nucl Med* 8: 183–191, 1978
2. HAYES RL, BROWN DH: Biokinetics of radiogallium. In *Nuklearmedizin: Fortschritte der Nuklearmedizin in klinischer und technologischer Sicht*, Pabst HW, Höv G, Schmidt HAE, eds. Stuttgart–New York, FK Schattauer Verlag, 1975, pp 837–848
3. BRUCER M: A total-body irradiator. *Int Appl Radiat* 10: 99–105, 1961
4. GIBBS WD, HODGES HD, LUSHBAUGH CC: Precise geometry-independent radioassay of large biological samples. *J Nucl Med* 9: 264–266, 1968
5. SWARTZENDRUBER DC, HÜBNER KF: Effect of external whole-body x-irradiation on gallium-67 retention in mouse tissues. *Radiat Res* 55: 457–468, 1973
6. FLETCHER JW, HERBIG FK, DONATI RM: ^{67}Ga citrate distribution following whole-body irradiation or chemotherapy. *Radiology* 117: 709–712, 1975
7. BRADLEY WP, ALDERSON PO, ECKELMAN EC, et al: Decreased tumor uptake of gallium-67 in animals after whole-body irradiation. *J Nucl Med* 19: 204–209, 1978
8. STORER JB: Acute responses to ionizing radiation. In *Biology of the Laboratory Mouse*, 2nd ed., Green EL, ed.. New York, McGraw-Hill Book Co., 1966, p 434