The Source of Fecal Gallium—Clinical Implications: Concise Communication

Andrew Taylor, Neil Chafetz, Jot Hollenbeck, and Wallace Hooser

Veterans Administration Hospital and the University of California, San Diego, California

Bowel preparation before gallium-67 scanning often consists of cathartics, enemas, and a liquid or low-residue diet. Since human bile has approximately one third the gallium concentration of the liver, the diet is presumably designed to minimize biliary excretion of gallium into the gut. To determine the actual biliary contribution to fecal gallium, the bile ducts of 15 rats were ligated and severed. Following the i.v. injection of Ga-67 citrate, the 72-hr fecal excretion of gallium was compared with that of 15 control rats with only a sham operation. Tissue distribution studies were also performed, and an additional 14 rats were gavaged with Ga-67 citrate to assess intestinal absorption. The organ distribution of gallium was similar in both groups and there was no appreciable intestinal absorption. The 72-hr fecal excretion of gallium in the control animals was not significantly different from that in the group with ligated bile duct: 13.1% compared with 12.9%, respectively. The data suggest that galium reaches the feces primarily through the bowel mucosa rather than by biliary excretion, and for that reason it is probably unnecessary to deprive a patient of solid food. Furthermore, a liquid or low-residue diet is unlikely to facilitate gallium transit through the bowel.

J Nucl Med 19: 1214–1216, 1978

The localization of gallium-67 in neoplastic and inflammatory lesions is well documented. In the abdomen and pelvis, however, it may be difficult to identify a pathologic process by scanning, owing to the physiologic accumulation of gallium in the bowel (*1–5*). Attempts to minimize this problem have included cathartics and enemas (*1,4,6*); oral EDTA to chelate gallium (*7*); oral and rectal administration of technetium sulfur colloid to outline the bowel (*8*); computer subtraction studies following technetium sulfur colloid administration (*9*); low-residue diets (*10*); and early imaging (4 hours after injection) before bowel activity becomes a major problem (*2,11*). In attempting to cleanse the bowel of gallium, some hospitals use the standard barium enema preparation, which incorporates a liquid diet, a variable whose effect on gallium excretion has not been evaluated. Before attempting to study additional techniques for reducing gallium concentration in the gut, we decided to review the mechanism by which gallium enters the feces.

In humans, the liver accumulates approximately 5% of the injected dose of gallium and the concentration of Ga-67 in the bile is about one third of the gallium concentration in the liver (*12*). These observations indicate elimination of Ga-67 in the bile, and, in fact, after the first 24 hr, the liver is reported to be the major route of gallium excretion (*11*). If gallium reaches the bowel primarily by biliary excretion, a low-fat or liquid diet followed by 24-hr imaging might reduce biliary emptying and improve the diagnostic quality of the scan. Based on these considerations, animal studies were undertaken to resolve the question of biliary excretion.

MATERIALS AND METHODS

Thirty female Sprague-Dawley rats with weights

Received Apr. 7, 1978; revision accepted June 9, 1978.

For reprints contact: Andrew Taylor, Department of Nuclear Medicine (115), Veterans Administration Hospital, 3350 La Jolla Village Dr., San Diego, CA 92161.

ranging from 270 to 401 g were divided into experimental and control groups of 15 animals each. The bile ducts of all rats in the experimental group were doubly ligated and severed to prevent any bile from reaching the gut. On each control rat a sham operation was performed in which the abdomen was opened, the abdominal contents handled, the bile duct identified and the abdomen closed.

Immediately following surgery, control and experimental rats received a tail-vein injection of 20–30 μCi of Ga-67 citrate. All rats were placed in metabolic cages and urine and feces collected at 24-hr intervals for 72 hr. Five rats from each group were killed at the end of each 24-hr period, and selected organs were removed, weighed, and counted in an automated well counter using the 184-keV peak of gallium.

A second group of 14 female Sprague-Dawley rats, with weights ranging from 361 to 466 g, were used to examine absorption of gallium from the bowel. Under ether anesthesia, all rats were gavaged with 25μCi of Ga-67 citrate in 0.5 cc of normal saline. Immediately afterwards, the rats were housed in metabolic cages and allowed free access to food and water. Urinary and fecal gallium excretion was monitored at 8, 24, 32, 48, 56, and 72 hr, at which time the animals were killed and studied as described above.

RESULTS

During the first 24 hr, the sham-operated control animals excreted about 5 times as much gallium in their feces as did the experimental rats, ($p \leq 0.05$, Table 1); in contrast, however, the fecal excretion of gallium in the 48- and 72-hr stool collections was slightly higher in the rats with ligated bile ducts. Furthermore, the total fecal excretion at 72 hr was essentially the same for both groups: 13.1% for the controls and 12.9% for the bile-duct-severed group. Urinary excretion of gallium was essentially the same for both groups of rats at all three time periods, with the total 72-hr excretion averaging 12.4% for the controls and 13.5% for the experimental group.

The 14 rats gavaged with Ga-67 citrate did demonstrate different rates of gallium excretion in their feces, but there was no evidence of significant tracer absorption. By 72 hr, four rats had excreted 100% of the administered dose in the feces and all rats had excreted at least 70% of the dose (average 87%). Their total urinary excretion at 72 hr averaged less than 1%, even though the urine was contaminated with feces. In the gavaged rats, the highest tissue accumulation of gallium was found in the liver, but it amounted to only 0.03% of the administered dose compared with 8.7% in the livers of control rats receiving i.v. gallium.

DISCUSSION

As stated above, the mean gallium excretion in the feces of the control animals was 5 times that of the bile-duct-ligated rats during the first 24 hr. Similarly, the mean fecal weight for the control animals during the first 24 hr was also 5 times as great—4.0 and 0.8 g, respectively ($p \leq 0.05$). After the first 24 hr, the mean fecal excretion was not significantly different. In retrospect, although we had thought the sham operation was a satisfactory control, we handled the gut of the bile-duct-ligated rats for a longer time during surgery. This handling and the longer operative time probably resulted in decreased fecal excretion of gallium during the first 24 hr.

Since no bile could reach the bowel directly in the experimental animals, the fecal accumulation of gallium must have occurred by some other route—presumably transit through the bowel wall like that described for pertechnetate (*13*). Further evidence of this conclusion is provided indirectly. During the first 72 hr, about 12% of the administered dose was excreted in the feces of the control animals. If the liver excreted up to 10% of the administered dose by way of the bile, the liver concentration of gallium should have diminished with time, especially since

TABLE 1. FECAL EXCRETION OF Ga-67 (% ADMINISTERED DOSE) IN CONTROL* AND EXPERIMENTAL† RATS KILLED AT 24, 48, AND 72 HR

	Rats killed at 24 hr		Rats killed at 48 hr		Rats killed at 72 hr	
	Control	Experimental	Control	Experimental	Control	Experimental
24-hr fecal collection	5.2 ± 0.8	1.0 ± 0.1	5.4 ± 0.8	0.4 ± 0.4	3.9 ± 2.4	0.9 ± 0.9
48-hr fecal collection	—	—	4.8 ± 0.9	5.7 ± 1.6	5.0 ± 1.4	6.8 ± 1.6
72-hr fecal collection	—	—	—	—	4.2 ± 1.9	5.2 ± 2.2
Total	5.2	1.0	10.2	6.1	13.1	12.9

* Bile ducts of experimental rats were ligated and severed. Control animals underwent sham operations.

† Mean of five animals at each time period, one s.d.

gallium levels in the blood dropped to less than 1% of the administered dose during the 72-hr study period. In fact, gallium accumulation in the liver of the control animals was essentially unchanged at 24, 48, and 72 hr, a finding that suggests minimal if any biliary excretion.

Tissue levels of gallium in the experimental animals were slightly higher than those in the control group, which is probably because less gallium was eliminated during the first 24 hr in the experimental rats, leaving more gallium available for tissue accumulation. The fact that the rats gavaged with Ga-67 citrate did not absorb any appreciable gallium from the gut argues against an enterohepatic circulation of Ga-67 and suggests that once the tracer reaches the bowel lumen, it remains there until it is excreted.

It is interesting to note that formed fecal material in the colon of the control rats at 24 hr contained (1.3 ± 0.4) % of the administered dose compared with (0.4 ± 0.2) % in the washed colon wall. At 48 hr, formed colon feces contained 0.9% of the dose compared with 0.2% in the wall, and at 72 hr the values were 1.1% against 0.3%, thus maintaining a ratio of roughly 4:1 between formed feces and colon wall.

CONCLUSION

In summary, our data strongly suggest that most of the intravenously administered Ga-67 that reaches the feces is excreted by the intestinal mucosa rather than the liver. Our data do not identify which segment of the bowel is most important in this excretion, nor do they indicate whether transport is active or passive.

The findings also suggest that it is probably unnecessary to deprive a patient of solid food, since the biliary contribution to gut excretion was found to be minimal and a liquid diet would be unlikely to facilitate gallium transit through the bowel. If any diet is indicated, it would probably be one with a high fiber content to accelerate the passage of gallium and fecal material through the bowel.

ACKNOWLEDGMENTS

This work was supported by Veterans Administration Research Funds, MRIS 8330 and a grant from the Academic Senate, University of California, San Diego.

REFERENCES

1. LITTENBERG RL, TAKETA RM, ALAZRAKI NP, et al: Gallium-67 for localization of septic lesions. *Annals of Internal Medicine* 79: 403–406, 1973

2. DELAND FH, SAUERBRUNN BJL, BOYD C, et al: ^{67}Ga-citrate imaging in untreated primary lung cancer: Preliminary report of cooperative group. *J Nucl Med* 15: 408–411, 1974

3. JOHNSTON GS, GO MF, BENUA RS, et al: Gallium-67 citrate imaging in Hodgkin's disease: Final report of cooperative group. *J Nucl Med* 18: 692–698, 1977

4. HARVEY WC, PODOLOFF DA, KOPP DT: ^{67}Gallium in 68 consecutive infection searches. *J Nucl Med* 16: 2–4, 1975

5. MURATA A, NAKAMURA K, SUGIYAMA M, et al: Clinical evaluation of ^{67}Ga-citrate scanning. *J Nucl Med* 13: 196–201, 1972

6. BAKSHI SP, PARTHASURATHY KL: Combination of laxatives for cleansing of Ga-citrate activity in the bowel. *J Nucl Med* 15: 470, 1974

7. HURWITZ SR, HAGAN PL, ALAZRAKI NP: Distribution of ^{67}Ga following intravenous administration: Effects of disodium edetate therapy. *J Nucl Med* 16: 280–283, 1975

8. VAN KIRK O, CHAFETZ N, COOKE S, et al: Imaging the bowel with technetium—An aid in gallium studies. *J Nucl Med* 18: 69–70, 1978

9. DAMRON JR, BEIHN RM, SELBY JB, et al: Gallium-technetium subtraction scanning for the localization of subphrenic abscess. *Radiology* 113: 117–122, 1974

10. HANDMAKER H, O'MARA R: Gallium imaging in pediatrics. *J Nucl Med* 18: 1057–1063, 1977

11. HOPKINS GB, KAN M, MENDE GW: Early ^{67}Ga scintigraphy for the localization of abdominal abscesses. *J Nucl Med* 16: 990–992, 1975

12. NELSON B, HAYES RL, EDWARDS CL, et al: The distribution of gallium in human tissues after intravenous administration. *J Nucl Med* 13: 92–100, 1972

13. TAYLOR AT, ALAZRAKI N, HENRY JE: Intestinal concentration of ^{99m}Tc-pertechnetate into isolated loops of rat bowel. *J Nucl Med* 17: 470–472, 1976