

obtaining end-systolic pressure-volume curves to assess LV contractility in selected patients.

We appreciate the comments of Drs. Siegel and Maurer, for they stimulate a discussion of these techniques. Their comments at this early juncture, however, may be overstated regarding the superiority of their method of obtaining individual attenuation-correction factors to obtain LV volumes, as compared with the method we recently analyzed and published in the *Journal*.

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**Re: Filling of the Gallbladder as Studied by Computer-Assisted Tc-99m HIDA Scintigraphy: Concise Communication**

The report by van der Linden and Kempf (1) on "Filling of the Gallbladder as Studied by Computer-assisted Tc-99m HIDA Scintigraphy" concluded that gallbladder filling was not dependent on contraction of the sphincter of Oddi. Their evidence for this conclusion was threefold: (a) half of the patients showed passage of radioactivity into the duodenum; (b) visualization of the gallbladder was not delayed in those subjects having radioactivity in the duodenum; and (c) the gallbladder was visualized before the distal part of the common bile duct. None of these observations justifies their conclusion that filling of the gallbladder is not dependent upon the sphincter of Oddi. First, they did not specifically describe whether duodenal activity appeared before or after gallbladder activity. However, they do quote the report of Weissmann et al. (2), which indicates that the normal gallbladder will be visualized before activity reaches the duodenum. Second, the fact that radioactivity appeared in the gallbladder at the same time after injection, whether or not radioactivity appeared in the duodenum, does not prove that the sphincter of Oddi was not closed during the filling phase of the gallbladder. Third, they correctly point out that bile already present in the duct may prevent radioactivity from reaching the region of the sphincter before filling of

the gallbladder. Nevertheless, they tend to discard this argument on the basis of studies in patients without gallbladders and the fact that bile present in the gallbladder does not prevent the radionuclide from entering. Such an objection cannot be discarded so easily, because fluids will travel the path of least resistance. The least resistance in this case may well be to the gallbladder. In cholecystectomized patients, resistance to biliary flow would be expected to be similar throughout the biliary ducts and probably controlled by the sphincter of Oddi.

It is unfortunate that the authors did not provide data on the relative rate of filling of the gallbladder and the possible relationship between the rate of filling and the rate of discharge of tracer into the duodenum. Since normal subjects will show filling of the gallbladder before emptying into the duodenum, it is likely that the rate of filling of the gallbladder would be similar in normal patients, at least until radioactivity began to appear in the duodenum (i.e., when relaxation of the sphincter of Oddi occurs).

I believe the authors deserve credit for emphasizing that the motor function of the gallbladder is not quiescent during fasting, as others have shown (3,4). However, they should not conclude, on the basis of their data, that contraction of the sphincter of Oddi has no relationship to filling of the gallbladder.

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## Reply

We thank Dr. Shreiner for his interest in the report (1) in which we presented data suggesting that filling of the gallbladder is not dependent on contraction of the sphincter of Oddi. The theory that filling of the gallbladder is due to the pileup of bile above a closed sphincter was contradicted by our data.

In half of our subjects with normally visualized gallbladders, radioactivity had passed into the duodenum. This we interpreted as showing that the sphincter is not permanently closed during fasting and that its opening does not interfere with normal visualization of the gallbladder. Since our data showed that the activity reached the distal part of the duct after it had reached the gallbladder, and the duodenum is distal to the duct, then passage of activity into the gallbladder must precede entrance into the duodenum.

The data showed that visualization of the gallbladder occurred at approximately the same time after injection, irrespective of whether activity appeared in the duodenum. In other words, in some subjects the sphincter had opened, in others it was closed, but this difference did not affect the time interval needed for visualization of the gallbladder. This finding we interpreted as showing

that filling of the gallbladder is not influenced by the state of contraction of the sphincter.

The activity entered the gallbladder before it reached the distal part of the duct. If the theory was correct, it should be the reverse. Shreiner explains this point by surmising that bile already present in the duct prevents the activity from reaching the region of the sphincter. He does not agree with our position that bile already present in the gallbladder is unable to prevent the activity from rapidly reaching the fundus. Nor does he agree with our observation that, in cholecystectomized patients, bile already present in the duct is unable to prevent the activity from rapidly reaching the sphincter (2) because, as he puts it, "in cholecystectomized patients resistance to biliary flow would be expected to be similar throughout the ducts." We found this statement puzzling and speculative. If the resistance really were "similar throughout the . . . ducts," would the activity move at all? Cholescintigraphy enables us to study the flow of activity but provides no information on the forces responsible for that flow.

Dr. Shreiner disregarded our data suggesting that the gallbladder is not quiescent during the interdigestive state. The textbook theory is that filling of the gallbladder occurs passively and that it is due to the gradual pileup of bile against the closed sphincter of Oddi. Motor activity during fasting contradicts the theory.

Finally, Dr. Shreiner considers it "unfortunate that (we) did not provide data on the relative rate of filling of the gallbladder." This data was provided in Figs. 1 and 2 of our paper.

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### Re: A Comparison of Two Cerebral Perfusion Tracers, N-Isopropyl I-123 p-Iodoamphetamine and I-123 HIPDM in The Human

Holman, Lee, Hill, et al. (1) report that the brain uptake of HIPDM is only 50-60% of the uptake of IMP in comparative studies in patients. This value is not consistent with the quantitative measurements for absolute brain uptake of these two compounds previously reported in the literature. This same group (2) reported an uptake of  $7.45 \pm 0.9\%$  for IMP in eight patients. Kuhl et al. (3) measured the uptake of IMP in five patients and reported an average of 5% in brain. As part of a Phase 1 clinical study, we have made a careful evaluation (using conjugate counting) of the brain uptake of HIPDM, and have found an average uptake of  $6.7 \pm 1.4\%$  in seven patients (4). This value has been confirmed by an independent measurement at the University of Michigan (5), where a range of 6.7-7.2% was found for the brain uptake of HIPDM. Thus, the quantitative uptake measurements of both

compounds indicate either an equal uptake or at most a 10 or 15% difference.

No doubt other laboratories have made absolute quantitative measurements of the uptake of IMP and HIPDM in human brain. Since both agents are under Phase 2 clinical trial, we look forward to early publication of these results in the open literature.

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## Reply

We thank Drs. King and Blau for their comments concerning our paper (1). We also express our appreciation and thanks to them for their most gracious and constructive help during the course of the study. We, too, were surprised at the degree of difference in brain uptake between IMP and HIPDM. It was partially for that reason that we investigated that particular point as extensively as we did, with both planar and tomographic studies, as well as a comparison of the two tracers in the same subject. Perhaps as the ligand is further purified, reducing the quantity of lipophobic tracer, the brain uptake of HIPDM will approach that of IMP more closely.

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