

dilution in vitro. We would have used [<sup>51</sup>Cr]EDTA instead, if it had been available in the United States.

We found a small but statistically significant difference between [<sup>99m</sup>Tc]DTPA and [Yb]DTPA, even after correcting for protein binding (2). This was a paired study in the same patients, and therefore more sensitive to small differences than another experimental design might be.

The important point, on which agreement seems general, is that virtually all of these methods are far more reliable than creatinine clearance.

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#### Biliary Propensities of Technetium-99m Glucoheptonate

It was reported by Tyler and Powers (1) that scinti-imaging of the anterior right upper abdominal quadrant region of fasted patients having normal hepatobiliary and renal function and administered with technetium-99m glucoheptonate ([<sup>99m</sup>Tc]GH) resulted in the visualization of the gall-bladder. This was in addition to the visualization of the kidneys (imaging in posterior position). This finding indicates that [<sup>99m</sup>Tc]GH is partly excreted by the biliary route in addition to its main renal pathway of elimination. We investigated the pharmacokinetic behavior of [<sup>99m</sup>Tc]GH formulated with an in-house prepared Sn(II)GH "kit" and Na<sup>99m</sup>TcO<sub>4</sub> in rats. We

found that ~10.0% of the administered dose is excreted by the biliary route (Table 1). Since the rat does not have a gallbladder the <sup>99m</sup>Tc activity present in the small + large intestinal tract constitutes the fraction cleared by the biliary route. It is evident from the data (Table 1) that a considerable amount (10%) of the injected dose is transported through the biliary route from the small to the large intestines over a period of 6 hr.

The supposedly anomalous *in vivo* behavior of [<sup>99m</sup>Tc]GH could possibly be due to either the presence of more than one <sup>99m</sup>Tc complex species in the formulated preparation (the major component(s) being excreted via the kidneys, the minor one being eliminated through the biliary route), or caused by *in vivo* metabolic products, or both. The biliary contribution could possibly result in the misinterpretation of kidney scintigrams obtained with [<sup>99m</sup>Tc]GH (1). This makes [<sup>99m</sup>Tc]GH a nonideal radiopharmaceutical for kidney imaging. However, it could still be used for imaging the kidneys in the posterior position with due caution. The use of [<sup>99m</sup>Tc]GH for brain (pathology) imaging should be avoided since the administration of ~20 mCi (740.0 MBq) amounts could result in a small avoidable contribution of radiation dose (especially to the kidneys, as well as gut of the patient). Technetium-99m diethylenetriaminepentaacetic acid (DTPA) could serve as a better substitute for this purpose.

All <sup>99m</sup>Tc compounds including <sup>99m</sup>Tc radiopharmaceuticals are xenobiotics (2,3) and are not associated with any nutritional or useful metabolic role in humans. They are invariably excreted out at some point of (early or delayed) time by any one or more of the excretory pathways. The amounts cleared by each pathway depends primarily on the chemical characteristics of the individual complexes as well as on the physiologic (normal compared with diseased) status of the *in vivo* species, e.g., [<sup>99m</sup>Tc]GH. (The amounts cleared by the biliary pathway in the case of [<sup>99m</sup>Tc]DTPA is comparatively small). Some of the currently used <sup>99m</sup>Tc radiopharmaceuticals could possibly contain two or more different chemical species. Technetium-99m agents serve a useful purpose in diagnostic nuclear medicine only when they are accumulated in sufficiently high concentrations in select organ system(s)/tissue(s) during their transitory resident phase prior to their elimination by any one or more of the excretory pathways.

TABLE 1  
Pharmacokinetics of i.v. Injected [<sup>99m</sup>Tc]GH in Adult Wistar Strain Rats

Tissues	Percent administered dose <sup>*</sup> at different time periods				
	30 min	1.0 hr	2.0 hr	4.0 hr	6.0 hr
Blood <sup>†</sup>	5.0 ± 1.0	2.5 ± 0.5	1.6 ± 0.2	1.2 ± 0.2	0.9 ± 0.1
Muscle <sup>†</sup>	12.6 ± 3.3	6.2 ± 1.0	3.2 ± 0.6	1.9 ± 0.8	1.7 ± 0.4
Liver	2.2 ± 0.5	1.6 ± 0.3	1.1 ± 0.1	1.1 ± 0.1	0.9 ± 0.1
Kidneys	17.8 ± 1.9	21.0 ± 1.0	18.9 ± 1.2	20.8 ± 1.4	20.5 ± 1.0
Urine	45.2	58.7	65.0	65.8	62.9
Small intestines	3.6 ± 0.8	4.9 ± 1.3	5.5 ± 1.7	2.5 ± 0.8	1.0 ± 0.5
Large intestines	0.6 ± 0.2	0.2 ± 0.1	0.2 ± 0.1	5.2 ± 1.4	8.3 ± 2.1
(Total gut)	(4.2)	(5.1)	(5.7)	(7.7)	(9.3)

<sup>\*</sup> Results expressed as mean ± s.d. (n ≥ 5, except for data pertaining to 6 hr, n = 4).

<sup>†</sup> Total blood and muscle assumed to be 5.0 and 45.5% body weight, respectively.

## ACKNOWLEDGMENT

This study was supported in part by the International Atomic Energy Agency, Vienna.

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**REPLY:** Noronha has measured the distribution of technetium-99m ( $^{99m}\text{Tc}$ ) glucoheptonate in various organ systems in a rat model. His results are similar to those obtained by Arnold et al. in 1975 using a rabbit model (1). While this group did not examine the small bowel in this phase of their study, they did report a value of 0.25% for that organ in a dog model. Discrepancy between this measurement and the value report by Noronha ( $4.9 \pm 1.3\%$ ) could well be due to the fact that Arnold et al. apparently did not include gallbladder activity in their measurement.

Numerous studies attest to the efficacy of [ $^{99m}\text{Tc}$ ]glucoheptonate in the evaluation of renal function. The radiopharmaceutical is admirably suited for this purpose if reasonable precautions are observed as pointed out by us (2) and Noronha. However, we find it difficult to agree with his statement that glucoheptonate should not be used for brain scanning because of the radiation dose to the kidneys and GI tract. Glucoheptonate has been shown to be superior to [ $^{99m}\text{Tc}$ ] diethylenetriaminepentaacetic acid for the detection of intracranial pathology (3) making it the agent of choice for brain scanning.

### References

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## Peripheral Versus Axial Skeleton Absorptiometry in Osteoporosis

**TO THE EDITOR:** In their letter of November 1985, Vogel and Wasnich (1) posit a similarity of single-photon absorptiometry (SPA) of the peripheral skeleton and dual-photon absorptiometry (DPA) of the axial skeleton for diagnosis and monitoring of osteoporosis. They contrast these nuclear medicine procedures to quantitative computed tomography (QCT), which they deem to be less cost-effective. In doing so, however, they neglect to mention research which has shown that direct measurements of osteoporotic fracture sites (hip and spine) are needed to define fracture risk. Many investigators in osteoporosis research no longer believe the peripheral skeleton can be used as an indicator of the axial skeleton. Numerous reports have shown that measurements at sites like the distal radius and os calcis show a standard error of estimate of 15% in predicting axial density in normals (2). The 95% confidence interval in bone disease ranges from 25 to 50%. The study of Nilas et al. (3) confirmed this. In a recent review of methods by the American College of Physicians (4) DPA and QCT were selected as preferred methods. In regard to effectiveness DPA, QCT and other (albeit experimental) methods measuring the axial skeleton share more in common than they do with peripheral measurements.

Readers must note that the conclusions of Vogel and Wasnich regarding the os calcis are based on their unique, and as yet unreplicated, study (5) of 26 nonosteoporotic fractures (including six wrist, eight rib, ten foot/lower leg). The authors were able to generate a monotonic relationship of fracture rate to os calcis density but this relationship was critically dependent on a few fracture cases. There is no evidence that os calcis density is superior to body weight, let alone site-specific density, for spine or hip fractures. This same study showed that all fracture cases were below the "fracture threshold" of 1.0 g/cm<sup>2</sup> for spinal density (or 2 s.d. below the mean in normal U.S. whites) while half of the fracture cases had normal os calcis density (above 275 mg/cm<sup>3</sup>). Thus the spine was a better discriminator of risk than peripheral sites, even for these nonosteoporotic fractures. The os calcis is particularly suspect because it is so dramatically influenced by body weight and physical activity. Even if os calcis measurements could predict long-bone fractures, there would be no basis for extrapolating to hip and spine fractures since peripheral fractures, including Colles fractures of the distal radius, are unrelated to those of the axial skeleton (6,7). In contrast measurement of the spine, by either DPA or QCT, directly reflect fracture risk; fracture rate increases as density decreases (8).

We agree that a screening procedure for osteoporosis that can be broadly applied, at low-cost, is needed. However, all studies on peripheral skeletal sites show a high proportion of false negatives (9), particularly in younger patients where preferential axial osteopenia has not yet been reflected by generalized skeletal loss (10). In their own study of spinal osteoporosis (11) the Hawaiian investigators found that the os calcis was not more sensitive than the distal radius or the radius shaft. All these sites exhibited over 50% false negatives (compared with the usual rate of <5% for spinal density). Scans of only one vertebra by DPA or QCT, rather than the usual four lumbar vertebrae, can provide a low-cost alternative with few false negatives.