TABLE 1

Ref.	Tracer	Sample(s)	Slope —	Y intercept (ml/min)	r —	s.e.e. (ml/min)
(3)	[^{51}Cr]EDTA	2 hr, 3 hr	1.023 ± 0.023	−3.41 ± 1.84	0.989	4.2
(3)	[^{51}Cr]EDTA	1 hr, 3 hr	0.999 ± 0.023	−1.57 ± 1.90	0.988	4.3
(1)	[^{169}Yb]DTPA	1 hr, 3 hr	1.044 ± 0.029	−2.11 ± 2.32	0.984	5.3
(3)	[^{51}Cr]EDTA	3 hr	0.992 ± 0.029	−2.57 ± 2.33	0.982	5.3
(1)	[^{99m}Tc]DTPA	1 hr, 3 hr	1.042 ± 0.029	−2.33 ± 2.38	0.983	5.4
(4)	[^{51}Cr]EDTA	3 hr	1.176 ± 0.035	−10.21 ± 2.82	0.981	6.4
(1)	[^{169}Yb]DTPA	3 hr	1.059 ± 0.039	−4.22 ± 3.12	0.972	7.1
(1)	[^{99m}Tc]DTPA	3 hr	1.127 ± 0.041	−11.30 ± 3.31	0.972	7.5
(2)	[^{125}I/^{131}I]DTZ	2 hr	1.154 ± 0.065	−5.86 ± 5.23	0.936	11.9
(1)	[^{169}Yb]DTPA	2 hr	1.139 ± 0.069	−8.71 ± 5.56	0.927	12.7
(1)	[^{99m}Tc]DTPA	2 hr	1.172 ± 0.071	−18.42 ± 5.76	0.927	13.1

[^{51}Cr]EDTA and then fitting a double exponential function to the tracer disappearance curve. A total of 47 GFR results ranging in value from 20 to 140 ml/min in 37 patients were obtained with a maximum of three determinations for any one subject. Correlations have been sought between these "standard" GFR values (X axis) and values predicted from formulae in the references quoted above using one or two samples only (Y axis). If the various tracers are equivalent and if the one or two sample methods are acceptably accurate, then we would expect the linear correlation regression lines to have unit slope and a zero Y intercept while the correlation coefficients would be close to unity and the standard errors in the estimates, s.e.e., would be small. The results are shown in Table 1 in order of increasing standard error in the estimate.

From the table, it is apparent that [^{51}Cr]EDTA, [^{99m}Tc]DTPA and [^{169}Yb]DTPA are essentially equivalent as evidenced by the slope and Y intercept information for the first five entries. It is also apparent that, as indicated by Russell et al. (*1*), the two sample methods are generally superior while the 3-hr single-sample method gives an acceptable level of accuracy for most purposes. Unfortunately, we have been unable to apply a 3-hr single-sample formula obtained from the DTZ tracer data (*3*) because, although the author states that "for general use the 180-min sampling time may suffice", the necessary coefficients to be incorporated into his general prediction formula are not quoted for this sampling time. We have, however, incorporated our [^{51}Cr]EDTA data into the generally less satisfactory 2-hr prediction equation from the same reference which yields results very similar to those calculated using the 2-hr prediction formulae obtained with [^{99m}Tc] and [^{169}Yb]DTPA (*1*). Therefore, it is likely that all four tracers are equivalent when used for GFR determination.

From our study, it appears that if the added accuracy of a two-sample method is required, there is little to choose between the predictive equations of Refs. *1* and *3*. However, the predictive equations of Morgan et al. (*3*) using 1- and 3-hr and 2- and 3-hr samples are marginally superior to the alternatives; they came at the top of our league table based on lowest s.e.e. when using [^{51}Cr]EDTA tracer and the 1- and 3-hr equation was again marginally superior when used by Russell and associates to predict GFR from [^{99m}Tc] or [^{169}Yb]DTPA data (*1*). An additional advantage of this equation, and those of Ref. *1*, is that the sample time appears in the equation as a continuous variable so that minor variations about the correct sampling times are automatically accounted for without having to alter the "constants" in the equation as is required in some methods (*2*). Where a single-sample method is preferable, then, here again, the 3-hr predictive equation of Morgan et al. (*3*) appeared to be best, although in this case there is no automatic correction for minor variations in sampling time.

The criticism may be made that our data set is too small and that perhaps it would be more practical to perform the analysis on data from a larger number of patients with GFR values in the more clinically relevant range below 60 ml/min. To this end, we would be happy to provide our detailed data to anyone wishing to repeat the analysis with a larger database.

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REPLY: It is interesting that our glomerular filtration rate (GFR) formulas worked so well with chromium-51 EDTA, which is probably better than the agents for which our formulas were derived. Though technetium-99m diethylenetriaminepentaacetic acid ([^{99m}Tc]DTPA) permits imaging and split function measurements (which explains the dose we used), there are quality control problems with this agent (*1–3*). Ytterbium-169 DTPA has not been extensively studied as a GFR agent, and we have noticed some decomposition after

dilution in vitro. We would have used [^{51}Cr]EDTA instead, if it had been available in the United States.

We found a small but statistically significant difference between [^{99m}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.

References

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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 ([^{99m}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 [^{99m}Tc]GH is partly excreted by the biliary route in addition to its main renal pathway of elimination. We investigated the pharmacokinetic behavior of [^{99m}Tc]GH formulated with an in-house prepared Sn(II)GH "kit" and Na^{99m}TcO$_4$ 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 ^{99m}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 [^{99m}Tc]GH could possibly be due to either the presence of more than one ^{99m}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 scintiimages obtained with [^{99m}Tc]GH (*1*). This makes [^{99m}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 [^{99m}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 ^{99m}Tc compounds including ^{99m}Tc radiopharmaceuticals are xenobiotics (*2,3*) and are not associated with any nutritional or useful metabolic role in humans. They are invariable 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., [^{99m}Tc]GH. (The amounts cleared by the biliary pathway in the case of [^{99m}Tc]DTPA is comparatively small). Some of the currently used ^{99m}Tc radiopharmaceuticals could possbily 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 [^{99m}Tc]GH in Adult Wistar Strain Rats

Tissues	Percent administered dose* at different time periods				
	30 min	1.0 hr	2.0 hr	4.0 hr	6.0 hr
Blood†	5.0 ± 1.0	2.5 ± 0.5	1.6 ± 0.2	1.2 ± 0.2	0.9 ± 0.1
Muscle†	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)

* Results expressed as mean ± s.d. ($n \geq 5$, except for data pertaining to 6 hr, $n = 4$).
† Total blood and muscle assumed to be 5.0 and 45.5% body weight, respectively.