cessing as mentioned above, we measured FT$_3$ by Immulite 2000 and ACS 180 plus (Bayer Corporation), as an alternative instrument, and triiodothyronine (T$_3$) only by Immulite 2000 (Table 1). A significant group effect was shown by repeated-measures ANOVA in SST results obtained by Immulite 2000 and ACS 180 plus ($F = 107.25$; $P < 0.001$). T$_3$ values gradually increased in both types of tubes with time, and repeated-measures ANOVA showed a significant time effect ($F = 8.450$; $P < 0.001$).

Additionally, we compared two types of evacuated gel-containing tubes, Vacutainer (SST) and Vacuette (16 × 100 mm; Greiner) for FT$_3$ on the Immulite 2000 (n = 6). FT$_3$ was higher in the SSTs than in the Vacuette (Table 1). A significant group effect was shown by repeated-measures ANOVA ($F = 4.320$; $P = 0.044$).

Finally, to determine the magnitude of the effect of relatively short-term storage at room temperature on FT$_3$, we measured FT$_3$ by Immulite 2000 at 4-h intervals up to 12 h. Repeated-measures ANOVA showed a significant group effect ($F = 34.809$; $P < 0.001$) but not a significant time effect or group–time interaction ($P > 0.05$).

Although the mechanism of the FT$_3$ increase remains unresolved, the following mechanisms could be envisioned: (a) in gel-containing tubes, the barrier gel could displace FT$_3$ from binding proteins such as thyroxine-binding globulin, albumin, and transthyretin; (b) the barrier gel could enhance binding of labeled analog to binding proteins; and (c) the barrier gel could show FT$_3$-like activity or interfere with the indicator chemiluminescent reaction under assay conditions.

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**Reference**


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**More Accurate Alternatives to Serum Creatinine for Evaluating Glomerular Filtration Rate**

To the Editor:

The timely reports by Laterza et al. (1) and Filler et al. (2) in the same issue of the Journal discuss the use of serum analytes other than creatinine as surrogates for glomerular filtration rate (GFR). They describe the advantages as well as the limitations of these factors in special adult circumstances and in the pediatric age group, respectively. Recent publications by the Work Group of the National Kidney Foundation (3) also reaffirm the limitation of basing GFR only on serum creatinine. Levey et al. (4) reviewed data from 1628 patients enrolled in the Modification of Diet in Renal Disease Study (MDRD). Their stated purpose was “to develop an equation from MDRD Study data that could improve the prediction of GFR from serum creatinine”. Of the 1628 patients selected, data from 1070 were used to derive the equations, and data from 558 were used to verify the equations. They concluded that GFR calculated from serum creatinine, albumin, urea, and basic patient demographic data closely approximates the GFR determined from direct methods such as renal clearance of [125I]iodothyramine (4). Their prediction equations 6 and 7 decreased unexplained variance from measured GFR by more than one-half when compared with measured creatinine or urea clearance or the Cockcroft–Gault equation, i.e., from 19.6% to a range of 8.8–9.7%.

I would appreciate the authors’ comments regarding the calculated GFR as opposed to use of a separate, additional serum analyte such as cystatin C. The calculated GFR is based on widely available and relatively inexpensive serum analytes and requires a single blood specimen. With the ubiquitous use of computers in the clinical chemistry laboratory, no human intervention for calculation is required for reporting relative to an individual test result. Consequently, the incremental cost relative to measuring serum creatinine by itself is less than US $1.00. Perhaps the authors have data for calculation and comparison of this approach to GFR with the proposed cystatin C or other low-molecular weight analytes that they have studied.

We now provide our medical staff with an orderable calculated GFR based on equation 7 from Levey et al. (4). This closely approximates equation 6, but does not require a urine specimen. We also include the calculated GFR in our basic metabolic chemistry panel because the analytes required for its calculation are already being measured.

The automated measurement of serum albumin, creatinine, and urea with the aid of computerized calculations and reporting will most likely make the calculated GFR the standard of care for evaluating renal function. Solo measurement of serum creatinine for this purpose may become an anachronism.

**References**

4. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine:
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Individuals been validated, such as diabetic individuals, have been released after submission of our data. Indeed, these recommendations are to be commended, I feel compelled to raise several laboratory issues that may complicate wide implementation of the recommendation.

First, at our institution ~85% of patient registrations list race as “unknown”. Presumably this is because of telephone and electronic registrations and the lack of race as a “required” field in our registration software. Although this problem could likely be overcome, it is not clear what to do with Asians, Native Americans, Hispanics, and other races.

Second, there are significant analytical issues surrounding measurement of SCr that are discussed in the guidelines and that have plagued the accuracy of 24-h creatinine clearance estimates of GFR (2, 3).

The guidelines point out that between- and within-method differences in SCr values can be 40% for individuals with SCr values <20 mg/L and that there is a lack of standardization of different SCr methods (3). This is confirmed by examining SCr values from different methods in the College of American Pathologists (CAP) surveys. Similar variability also exists among albumin methods where mean values from some albumin methods differed by 12–34% for the five samples in 2002 CAP survey set CA. If an estimated GFR using the full equation is calculated using the upper and lower 2 SD ranges of SCr and albumin values for the samples in this CAP survey (assuming the samples are from a 60-year-old white male), the resulting estimated GFR values will differ by 26–41%.

International standardization of SCr methods, which is recommended in the guidelines immediately after the recommendation to report an estimated GFR (2, 3), will greatly improve this situation. However, even standardization will not change the susceptibility of picrate-based SCr methods to marked interference from common drugs and metabolites, such as cephalosporins and ketones (6).

Reference intervals for the estimated GFR using these equations are suggested (2). However, it will be necessary for each laboratory to carefully establish its own reference intervals based on the SCr method(s) used at the institution.

Finally, the recommendations state that “laboratories should mind the importance of calibrating their serum creatinine to the same level as the laboratory in which the equations was developed” (3). Unfortunately, the method cited in the original 1999 study (4) is for the Beckman Astra analyzer, which has not been in common use in this country for at least 10 years and has not appeared as a method on CAP reports since at least 1997.

An improved means for estimating GFR will clearly benefit patients, and I hope that these recommendations will emphasize the critical importance of standardization for creatinine or other potential markers of GFR, such as cystatin C.

Dr. Mitchell G. Scott responds:

To the Editor:

I thank Lupovitch for his comments on our recent review article (1) about cystatin C (cysC) as a marker for glomerular filtration rate (GFR). I read with great interest the recent recommendation by the Working Group of the National Kidney Foundation (2, 3) that clinical laboratories should report an estimated GFR calculated from serum creatinine (SCr), albumin, blood urea nitrogen (BUN), age, and race or from an abbreviated equation that does not include albumin and BUN but that performs nearly as well (4).

Although Filler et al. (5) showed that a calculated GFR in children based on the Schwartz equation was essentially equivalent to cysC, I am not aware of any studies that directly compare cysC with the estimated GFR recommended in the guidelines from the National Kidney Foundation. Indeed, these recommendations were released after submission of our article, and it will be important to determine how cysC performs compared with the estimated GFR, particularly in those populations where SCr values can be misleading (1) and in which the estimated GFR has not been validated, such as diabetic individuals (2, 3).

Although the desire and efforts of the National Kidney Foundation to provide a more accurate assessment of GFR are to be commended, I feel compelled to raise several laboratory issues that may complicate wide implementation of the recommendations. The guidelines point out that between- and within-method differences in SCr values can be 40% for individuals with SCr values < 20 mg/L and that there is a lack of standardization of different SCr methods (3). This is confirmed by examining SCr values from different methods in the College of American Pathologists (CAP) surveys. Similar variability also exists among albumin methods where mean values from some albumin methods differed by 12–34% for the five samples in 2002 CAP survey set CA. If an estimated GFR using the full equation is calculated using the upper and lower 2 SD ranges of SCr and albumin values for the samples in this CAP survey (assuming the samples are from a 60-year-old white male), the resulting estimated GFR values will differ by 26–41%.

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References

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