

# Lab Focus

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## Sound bites. . . .

### Creatinine Reporting Range is Simplified

Creatinine, serum/plasma is now reported to two decimal places, providing more accuracy for the estimation of glomerular filtration rate.

### Creatinine Reference Range

The creatinine reference range for individuals 50 to 60 years and older than 60 years have been deleted and the reference ranges for 20 to 50 years are now used for all adults older than 20 years of age: female 0.6-1.3 mg/dL and male 0.8-1.5 mg/dL. Laboratory leadership made this change in response to physician concerns that creatinine reference ranges were too high.

The revised range more closely represents the "healthy normal" versus the "statistical normal". This change echoes the evolution in thinking over the past decade that those within the cholesterol reference range should be at low risk of cardiovascular disease.

The new range also will correlate more closely to National Kidney Foundation recommended reference values.

*John Eckfeldt, MD, PhD*

### Prostatic Specific Antigen (PSA) Reporting Range.

As of Nov. 19, 2003, the result format for reporting PSA has changed to two decimal places in response to input from clinicians. The lowest reportable result will remain as <0.10 ug/L.

*Linda Bailey, CLS*

### Fibrinogen Name Change

Fibrinogen, Quantitative is now reported as Fibrinogen Activity. This change was made in response to clinician request for clarification.

*Agnes Aysola, MD*

## GFR Now Reported with Creatinine

Glomerular filtration rate (GFR) traditionally is considered the best overall index of renal function in health and disease. A low or decreasing GFR is a good index of chronic kidney disease. Because GFR is difficult to measure in clinical practice, formulas have been developed to estimate creatinine clearance. The Cockcroft and Gault formula<sup>1</sup> has been widely used; however, more recently equations have been developed from the Modification of Diet in Renal Disease (MDRD) Study that improve the prediction of GFR from serum creatinine concentration<sup>2-4</sup>. The abbreviated MDRD Study Equation is an equation for estimating GFR based on a patient's creatinine, age, sex and whether or not they are African-American<sup>3,4</sup>.

### Abbreviated MDRD Study Equation:

Estimated GFR (ml/min/1.73m<sup>2</sup>)

= 186 x (S<sub>Cr</sub>)<sup>-1.154</sup> x (Age)<sup>-0.203</sup> x (0.742 if female) x (1.210 if African-American)

= exp[5.228 - (1.154 x ln(S<sub>Cr</sub>)) - (0.203 x ln(Age)) - (0.299 if female) + (0.192 if African-American)]

S<sub>Cr</sub> = serum creatinine

exp = e raised to the power of a given number

ln = natural logarithm of a number

The GFR is automatically calculated with every serum creatinine result reported by the laboratory computer with

the following exceptions:

- patient is <16 years
- sex is unknown
- creatinine is <0.01

Numerical results will be reported for patients 16 years and older when the computed (estimated) GFR is less than 80 mL/min/1.73m<sup>2</sup>. No pediatric ranges will be reported at this time because of uncertainty in the accuracy of the prediction equation for children. The National Kidney Disease Education Program (NKDEP) ([www.nkdep.nih.gov](http://www.nkdep.nih.gov)) recommends a reportable range for estimated GFR as less than 60 mL/min/1.73m<sup>2</sup>. NKDEP selected 60 mL/min/1.73m<sup>2</sup> because the MDRD Study had few patients without at least a modest decrease in renal function and more importantly because of the significant laboratory to laboratory bias in creatinine analytical measurement. We have confirmed our clinical laboratory method's accuracy against the MDRD study laboratory and feel comfortable in reporting values as high as 80 mL/min/1.73m<sup>2</sup>.

For a reference range, we suggest greater than 80 mL/min/1.73m<sup>2</sup> as being compatible with normal renal function. Values less than 60 mL/min/1.73m<sup>2</sup> may indicate impaired renal function, with values between 60 to 80 mL/min/1.73m<sup>2</sup> as borderline. However, all values should be interpreted with respect to the patient's clinical status and age. Please note that GFR declines with age in healthy people. We welcome any comments or questions about the new estimated GFR reporting. As we have more experience, we will be refining our

criteria and capacity to provide estimates at higher levels of GFR.

#### References:

1. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron* 16:31-41 (1976).
2. Levey AS, Bosch JP, Lewis JB, Greene T. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. *Ann Intern Med* 130:461-70 (1999).
3. Levey AS, Grene T, Kusek JW, Beck GJ. A simplified equation to predict glomerular filtration rate from serum creatinine (Abstract). *J Am Soc Nephrol* 11:A0828 (2000).
4. National Kidney Foundation DOQI. Part 5. Evaluation of laboratory measurements for clinical assessment of kidney disease. *Am J Kidney Dis* 39:S76-92 Suppl (2002).

*John Eckfeldt, MD, PhD  
Michael Steffes, MD, PhD  
University of Minnesota Physicians*

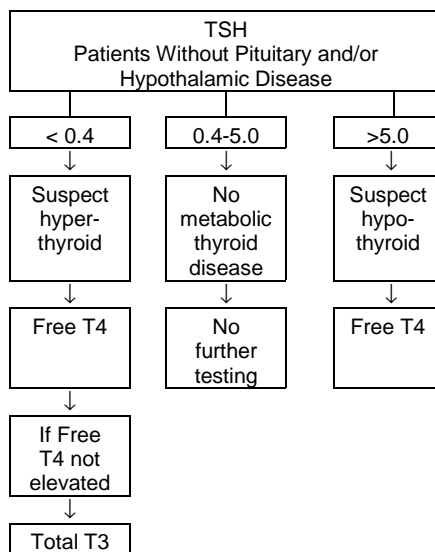
## Evaluation of Thyroid Function

The estimation of “thyroid function” evolved over the past 50 years from true, but not very discriminating tests of function (e.g., respiratory quotient or cholesterol) to measures of thyroid hormones (thyroid binding iodine and total thyroxine—which actually do not measure function, per se). Current testing measures the pituitary production of thyrotropin (TSH), a true response to the function of circulating thyroid hormones. Since the introduction of the measurement of TSH in the early 1970s by radioimmunoassay, the TSH assay has been improved so the modern laboratory can detect the concentration of this hormone in serum or plasma over several orders of magnitude.

TSH now forms the base of contemporary evaluation of thyroid function in the patient

with a normally functioning pituitary gland. Since pituitary disease is relatively rare, in nearly all patients with suspected change in thyroid function, the measurement of TSH allows the detection of suspected hypothyroidism or hyperthyroidism. In hypothyroidism, levels are elevated due to pituitary release of TSH in response to the low levels of thyroid hormone. In hyperthyroidism, low levels result from suppression of TSH production with too much circulating thyroid hormone.

The Thyroid Cascade, first introduced in July 1997, is based on the normal response of the pituitary gland to decreased or increased levels of thyroid hormones, principally triiodothyronine (T3) and thyroxine (T4). University of Minnesota endocrinologists Drs. David Brown, Jack Oppenheimer, Cary Mariash and Charles Sandhofer developed it in collaboration with Mary Fowler, Fairview laboratory manager.



The TSH represents a true test of thyroid function. For the most part, the Thyroid Cascade likely has lowered the numbers of unnecessary tests of thyroid function, although true numbers of reduction cannot be determined accurately. Anecdotally, the inappropriate ordering of Total T3 when suspecting hypothyroidism has been reduced. All these tests may produce different levels in pediatric populations. We suggest consultation with a pediatric endocrinologist for those physicians encountering puzzling results. Reference values for TSH in children 1 month or older: 0.4-5.0 mU/L.

The TSH measure alone also may be useful in following the patient on replacement medication with thyroxine. Over or under treatment will cause a suppression or elevation of the TSH, prompting a change in dosage.

Pituitary and/or hypothalamic hypothyroidism may not be detected using the Thyroid Cascade algorithmic approach and requires both TSH as well as Free T4 measurements, in conjunction with a careful clinical analysis. In most instances for suspected pituitary and/or hypothalamic hypothyroidism, we strongly recommend consultation with an endocrinologist.

*Michael Steffes, MD, PhD.  
David M. Brown, MD  
University of Minnesota Physicians*