February 24, 2016

To: SHC & LPCH Medical Staff

From: Stanford Hospital and Clinics Clinical Laboratory

Subject: Change in creatinine measurements to the isotope dilution mass spectrometry (IDMS) reference method for serum, plasma, urine, and fluid specimens and implementation of Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation on April 6, 2016.

The Chemistry section of the Stanford Healthcare Clinical Laboratory performs serum, plasma, urine, and fluid creatinine testing on the Siemens Dimension RxL and ExL instruments. The current method used for creatinine determinations in specimens is a modification of the kinetic Jaffe reaction. For routine creatinine testing, the National Kidney Disease Education Program (NKDEP) recommends that clinical laboratories use methods that are calibrated and traceable to the isotope dilution mass spectrometry (IDMS) reference method. Standardization with the IDMS reference method will improve detection, diagnosis, and treatment of chronic kidney disease by reducing the inter-laboratory bias in creatinine results and yield more accurate estimated glomerular filtration rates (eGFR) when using the IDMS-traceable Modification of Diet in Renal Disease (MDRD) Study or the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations.

IDMS traceable creatinine method on Serum/Plasma Creatinine concentrations

The new Siemens creatinine assay is enzymatic (improved specificity for creatinine; IDMS) and compared to the current kinetic Jaffe method (Non-IDMS), the serum/plasma creatinine concentrations will be ~ 0.1 to 0.3 mg/dL lower. Accordingly, the serum/plasma creatinine reference ranges will be changed and there will be separate reference ranges for male and female patients (see below) and lower reference range limit values. Because of the improved precision of the enzymatic creatinine assay, serum/plasma creatinine values will be reported to 2 decimal places.

New Serum/Plasma Creatinine Reference Intervals (mg/dL)

Age	Current	Male	Female
0-6 days	< 1.2	0.30-1.00	0.30-1.00
7 days-1 month	< 0.8	0.10-0.60	0.10-0.60
1 month-1 yr	< 0.4	0.10-0.40	0.10-0.40
1-12 yrs	< 0.8	0.10-0.70	0.10-0.60
12+ yrs	< 1.2	0.50-1.20	0.40-1.00

IDMS traceable creatinine method on Estimated Glomerular Filtration Rate (eGFR)

Since we began reporting eGFR, Stanford Healthcare has used the MDRD Study 4-variable equation to calculate eGFR. Due to the change to an IDMS-traceable creatinine method, we can also use a more accurate equation called CKD-EPI (see below) to calculate eGFR values above 60 mL/min/1.73 m^2.

GFR (mL/min/1.73 m^2) = 141 × min (S_{cr} /κ, 1)$^{\alpha}$ × max (S_{cr} /κ, 1)$^{-1.209}$ × 0.993^{Age} × 1.018 [if female] × 1.159 [if black]

Where: S_{cr} is serum creatinine in mg/dL, κ is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of S_{cr} /κ or 1, and max indicates the maximum of S_{cr} /κ or 1.

The reported CKD-EPI eGFR values will include values for both African-American and non-African American patients. Therefore, the healthcare provider can decide on which eGFR value to use for their patients.

In patients with decreased renal function, the change in eGFR with the IDMS-traceable creatinine method is minor and not likely to change the stratification of patients' kidney damage.

IDMS traceable creatinine method on 24 hour creatinine clearance

As stated above, the measured plasma/serum creatinine concentrations will be lower with the IDMS-traceable method but the urine creatinine concentration will be marginally affected. This will result in a calculated creatinine clearance that will be slightly higher with the new IDMS-traceable creatinine method. There is no IDMS-traceable version for the Cockcroft-Gault equation.

Urine excretion (mg/24 hr) reference interval with the IDMS-traceable creatinine method

There will be no change in the reference interval for urine excretion with the new IDMS traceable creatinine method.

IDMS traceable creatinine method on pediatric patients

In general, pediatric patients have lower creatinine concentrations compared to adults. The change to the IDMS-traceable enzymatic method for creatinine determinations requires the use of the IDMS-traceable bedside Schwartz equation for calculating eGFR.

The IDMS-traceable bedside Schwartz equation is:

eGFR (mL/min/1.73 m^2) = (0.41 x height in cm) / (Plasma creatinine in mg/dL)

IDMS traceable creatinine method on drug dosage

It is important to recognize that the Cockcroft-Gault equation for calculating creatinine clearance has not been adjusted or standardized to account for the accuracy shift in IDMS traceable plasma creatinine values as compared to non-IDMS traceable creatinine. Plasma creatinine values obtained with the IDMS-traceable methods may impact the dosage estimates obtained based on the use of drug dosing algorithms published by pharmaceutical manufacturers as part of the product labeling for certain drugs. In some instances, the use of creatinine values obtained with IDMS-traceable creatinine methods may result in calculated doses for a given drug higher than doses calculated using non-IDMS traceable creatinine results.

Clinical practice guidelines with limitations for use of the CKD-EPI equation and drug dosage guidelines with use of the CKD-EPI equation when reporting eGFR can be found on the NKDEP website (http://www.niddk.nih.gov).

The IDMS-traceable creatinine method will be implemented on April 6, 2016.

If you have any questions about this change, please contact me at your earliest convenience.

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