NKDEP LABORATORY WORKING GROUP
ESTIMATION OF KIDNEY FUNCTION
PHARMACY OBJECTIVES
JULY 2005

1) Describe how pharmacists currently use estimated GFR to make clinical decisions (current situation).

Assessment of GFR is a key component for the assessment and design of drug dosage regimens for patients with kidney disease. Pharmacists assess GFR routinely when evaluating drug therapy in order to estimate clearance and to avoid potential drug toxicity. Many pharmacists currently estimate GFR by determining creatinine clearance using various prediction equations, most commonly of which, is the Cockcroft-Gault (C-G) equation. Also, there are many computerized dosing programs which are often based on predicted creatinine clearance derived from the C-G (or other) equation. Regardless which prediction equation is utilized, the clinician must have an understanding of the limitations and applicability of the equation utilized. A common limitation of prediction equations includes lack of validation in certain populations (e.g., obese, elderly, patients with alterations in muscle mass, or patients with unstable renal function).

For many pharmacists, the C-G equation has long been a popular method for predicting renal function in order to design appropriate drug dosage regimens. Interestingly, no consensus exists regarding which weight variable, if any, should be utilized in the C-G equation when calculating creatinine clearance in obese patients or if results should be normalized to body surface area of 1.73 m^2. Furthermore, there appears to be no consensus regarding the need, if any, to adjust serum creatinine values to account for alterations in muscle mass (e.g. 'rounding up' serum creatinine values in elderly patients).

Drug dosing recommendations put forth by pharmaceutical manufacturers are often based on creatinine clearance as estimated by the C-G equation, however, a universal standard is lacking. When reviewing package labeling for many medications, it is difficult to determine what method of GFR estimation was utilized to estimate drug dosage in kidney disease. To further complicate the issue, glomerular filtration is only one component of renal elimination. Tubular secretion and reabsorption also play a role, but there is no practical method for assessing these and their impact on drug dosing.

With the development of the MDRD equation, the pharmacy profession has now been presented with another tool to assess GFR. However, its impact on drug dosage regimen design for patients with kidney disease is yet to be

determined since many drug dosing guidelines have been derived from creatinine clearance estimates, rather than GFR determination.

It is worthy to note that GFR estimation to determine staging of chronic kidney disease presents another opportunity for pharmacists to improve patient care. Utilization of the MDRD equation will help pharmacists target patients for pharmacotherapeutic interventions to slow disease progression, avoid drug-induced nephrotoxicity, and optimize medical management. Pharmacists in hospitals and other health care systems are in a unique position to collaborate physicians and laboratory departments in developing processes which identify and treat patients at risk.

2) Discuss issues surrounding use of a new estimating equation (impact of transition).

A new estimating equation would likely have significant implications for drug dosage regimen design. If current dosing guidelines are based on creatinine clearance, it will need to be determined if current methods could be used interchangeably with the new method. Furthermore, any changes would have a profound impact on computerized dosing applications since many programs utilize creatinine clearance as basis for automated rules. Pharmacists are wondering if the MDRD equation should be the universal method for estimating renal function to determine drug dosage, and, most importantly, if it can be applied to current drug dosage guidelines.

It would be helpful to work with the FDA to develop universal standards for pharmaceutical manufacturers as they develop drug dosage guidelines for their specific products when used in patients with kidney disease. At minimum, clinicians should be aware of which method should be applied for the specific drug(s) which are being prescribed.

As described in objective number one, there are controversies and limitations to the current methods of estimating GFR, so clinicians would need a clear understanding those issues with the new method for estimating GFR.

3) Identify recommendations for educating pharmacists about the changes in creatinine and estimating equation.

Collaboration with key pharmacy organizations such as the American Society of Health System Pharmacists (ASHP), the American College of Clinical Pharmacy (ACCP), and the American Pharmaceutical Association (APhA) will be an important step for pharmacist education. These organizations could collaborate with others to identify and develop methods for educating pharmacists. This may include publication of articles in key pharmacy journals, development of educational programs at professional meetings and

continuing education offerings. Professional pharmacy organizations could also reach out to state and local chapters to disseminate information.

Pharmacy schools will also need to be made aware of changes so that adjustments can be made with school curricula.