



## CHRONIC KIDNEY DISEASE AND THE ESTIMATED GLOMERULAR FILTRATION RATE (eGFR)

Chronic Kidney Disease (CKD) is defined by either kidney damage or an eGFR of <60 mL/min/1.73 m<sup>2</sup> for 3 months or longer. The US National Kidney Foundation (NKF) defines four stages of CKD as shown in the table below. It follows that the diagnosis of Stages 1 and 2 requires evidence of kidney damage as well as an eGFR measurement.

| NKF Stage | Description                                 | eGFR (mL/min/1.73m <sup>2</sup> ) |
|-----------|---|-----------------------------------|
| 1         | Kidney damage with normal or elevated GFR   | 90                                |
| 2         | Kidney damage with mildly depressed GFR     | 60 - 89                           |
| 3         | Kidney damage with moderately depressed GFR | 30 - 59                           |
| 4         | Severely depressed GFR                      | 15 - 29                           |
| 5         | Kidney Failure                              | < 15                              |

As an aid to improve the detection of early CKD, MDS will report the eGFR whenever a serum creatinine is measured by applying the recently updated Modification of Diet in Renal Disease (MDRD) equation using the patient's age and gender together with the creatinine.

Serum creatinine levels do not accurately reflect glomerular filtration rate (GFR) as an indicator of renal function but the MDRD formula permits estimation of the GFR. The eGFR is a

much better indicator of renal function than serum creatinine alone and may allow detection of chronic kidney disease in an early stage.

An illustration of the value of the eGFR is presented here for two individuals, each with a serum creatinine of 93 µmol/L.

### A 25 year old male

eGFR 91 ml/min/1.73 m<sup>2</sup>

### A 65 year old female

eGFR 56 ml/min/1.73 m<sup>2</sup>

Although the eGFR provides a more accurate estimation of GFR than a serum creatinine value, it is not a panacea and the following limitations must be recognized:

- It does not reliably predict GFR for those at extremes of weight and age, vegetarians, amputees, and for those with a sudden change of GFR.
- It does not reliably predict GFR in those with creatinine clearance above 60 ml/min.
- Some medications including trimethoprim, sulphamethoxazole, ciprofloxacin and fenofibrate may interfere with creatinine measurements and therefore the eGFR
- Standard guidelines for dosing medication for those with impaired renal function use estimated creatinine clearance expressed as ml/min not the eGFR expressed as ml/min/1.73 m<sup>2</sup>.
- For those of African descent the reported value is multiplied by a correction factor of 1.21.

A decrease in eGFR should be confirmed by repeat testing and CKD documented by an abnormality persisting three months or longer.

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## Assessment and Management of Patients with a Low eGFR Value

There is concern that the value of reporting the eGFR may be diminished by unnecessary investigation and referral of patients to specialists on the basis of the reported value alone.

It is important to remember criteria for Stage 1 and 2 Chronic Kidney Disease (CKD) require evidence of kidney damage **as well as** eGFR. Evidence of kidney damage includes the laboratory findings of proteinuria and an elevated urine albumin to creatinine ratio.

Slightly more than 30% of the US population 20 yrs or older have an eGFR 60-89 mL/min/1.73 m<sup>2</sup> and the percentage increases with age. The prevalence of Stage 2 CKD however is only 3-4%. This mild decrease in eGFR may be considered "normal for age" in older adults without evidence of kidney damage and is also frequent in infants. Screening for evidence of kidney damage for those with an eGFR of greater than 60 mL/min/1.73 m<sup>2</sup>, is indicated only for those at high risk for CKD including diabetics, hypertensives and those with a family history of CKD. General screening is not indicated.

As a rule of thumb, patients with a low eGFR should be referred to a nephrologist when:

- 1) The eGFR is less than 30 ml/min/1.73 m<sup>2</sup>
- 2) The eGFR declines by more than 20%.
- 3) There is significant proteinuria.

When MDS reports eGFR results the following messages will be appended:

|   |  |
|---|--|
| • eGFR > 90 mL/min/1.73 m <sup>2</sup>    | Normal eGFR.   |
| • eGFR = 60-89 mL/min/1.73 m <sup>2</sup> | Mildly decreased eGFR is seen in approx. 30% of adults 20 years or older. Recommend exclusion of kidney damage in those at high risk for chronic kidney disease. |
| • eGFR = 30-59 mL/min/1.73 m <sup>2</sup> | Consistent with moderate chronic kidney disease if result confirmed by repeat with persistence for 3 months or more.   |
| • eGFR = 15-29 mL/min/1.73 m <sup>2</sup> | Results consistent with severe chronic kidney disease.   |
| • eGFR =< 15 mL/min/1.73 m <sup>2</sup>   | Results consistent with kidney failure.  |

The following websites provide useful additional information:  
[www.oaml.com](http://www.oaml.com)

[http://www.kidney.org/professionals/kdoqi/guidelines\\_ckd/toc.htm](http://www.kidney.org/professionals/kdoqi/guidelines_ckd/toc.htm)

<http://www.healthservices.gov.bc.ca/msp/protoguides/gps/title.html>

# ONTARIO CERVICAL SCREENING PRACTICE GUIDELINES

Practice guidelines released in May 2005 replaced the interim guidelines issued in 1996. The guidelines were formulated using a rigorous process based on the best available evidence at the time.



These guidelines state that liquid-based cytology, which is offered by MDS, is the preferred tool for cervical cytology screening. The full guideline document should be consulted by practitioners but it is instructive to highlight a few points.

## ASCUS (atypical cells of uncertain significance)

Human Papillomavirus (HPV) testing is recommended for women age 30 or older with an interpretation of ASCUS. Women 30 or older, whose result is positive for high-risk oncogenic strains, should be referred for colposcopy, while women who are negative should have cytology repeated in 12 months.

HPV testing, which is currently not an insured benefit, may be obtained through MDS either as a reflexive test on residual cytological material or as a separate test obtained using a special collection kit.

In the absence of HPV testing, repeat cytology in 6 months is acceptable.

Because there is a high rate of positivity for oncogenic strains of HPV in women under the age of 30 and a high rate of spontaneous clearance of the virus, HPV triage is not indicated in women in this age group. Women under the age of 30 should have a repeat cytology in 6 months. If this is abnormal they should then be referred for a colposcopy.

### **LSIL (Low Grade Squamous Intraepithelial Lesion)**

Either colposcopy or repeat cytology in 6 months is recommended for women with LSIL. When repeat cytology is used and the result is abnormal, women should be referred for colposcopy. If the cytology is negative, women should have repeat cytology in another 6 months. After 2 negative cytology interpretations, the patient should return to routine screening.

The highlighted recommendations represent an evolution from those of 1996. It should be emphasized that these are minimum guidelines only and that certain clinical situations may require management which differs from the guidelines. ■

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## **REFERENCE VALUES AND "ABNORMAL" LABORATORY RESULTS. - To flag or not to flag?**

Laboratory results are reported together with the reference ranges in the case of numerical values and with reference values in the case of qualitative data. These are provided to aid in the interpretation of the patient result but it is important to understand how reference ranges are established. They are set so that 95% of apparently normal individuals fall within the reference interval (for a gaussian distribution). Conversely 5% of normal people will generate results which fall outside of the reference range.

The chance for a normal individual, of a result falling outside of the reference interval, obviously increases with the number of tests performed. Reference ranges must be determined by a laboratory for the population served. The reference values may differ depending on gender, age and other parameters such as the stage of the gestation. MDS periodically undertakes an extensive study to set reference ranges and performs reference range studies when new tests or methodologies are introduced.

MDS flags results which deviate from reference values but it is important to appreciate that flagged results do not necessarily indicate an abnormality or disease state. When considered on a statistical basis these are more likely to be abnormal than those which lie within the reference range. It is best to regard the flag as a convenient way of bringing a result to your attention for consideration in the context of the clinical picture and risk factors rather than necessarily indicating an abnormality.

For instance the presence of hemoglobin and red cells flagged in a urinalysis specimen may be explained by menstruation or instrumentation of the lower urinary tract but may on occasion be an indication of undetected renal disease. It is easy enough to exclude the first two possibilities by considering the clinical history. A grouping of results outside of the reference range for tests associated with the disease state is clearly important. When risk factors or other clinical features warrant it, follow-up testing is indicated. It is however important to appreciate that the level for "clinical action" or investigation may differ from the upper or lower limit of the reference interval.<sup>1</sup>

In summary, flagging can be a useful tool but an understanding of the significance of laboratory results requires consideration of clinical context. ■

### **REFERENCES**

1. What information on quality specifications should be communicated to clinicians, and how? M. Plebani, Clinica Chimica Acta Vol 346 25-35 2004

## PATIENT SAFETY: THE UNIQUE IDENTIFICATION OF SAMPLES.

All patient samples including tubes of blood, urine, stool samples, swabs, cytology specimens and tissue biopsies must be clearly labeled using two (2) unique identifiers. The first of these is the patient's full first and second name and the second most appropriately the date of birth or health card number. Not only does the presence of two clearly legible unique identifiers reduce the chance of misidentification but these are required for compliance with the Specimen Handling Standards as stated in Ontario Laboratory Accreditation (OLA) requirements.

When samples are procured in an MDS Patient Service Centre the dual unique identification is standard. Currently some physician offices do not meet this requirement as a routine. Because MDS will be forced to reject all specimens received without two unique identifiers we urge all physicians to ensure that labeling procedures in their office include the use of two unique identifiers on tubes and specimen containers as well as on the laboratory requisition. Irreplaceable specimens, not uniquely identified, such as tissue biopsies and cytology samples will be returned to your office for proper identification.

Please ensure that all physicians working in your office as well as your staff understand the importance of correct labeling of specimens. ■

## MODIFICATION OF ANTIBIOTIC REPORTS

The antibiotics reported for significant bacterial infections have been modified due to an update in our susceptibility testing methodology. An increased number of oral antibiotics have been added to help guide therapeutic choices. These changes will be implemented over December-January. The key changes include:

|   | Addition  | Removal                                  |
|---|---|--|
| Gram negative organisms (eg. <i>E. coli</i> )               | Amoxicillin-clavulanic acid<br>Cefixime<br>Cephalothin* (non-sterile sites)<br>Cefotaxime | Ceftriaxone<br>Piperacillin<br>Cefazolin |
| Gram positive organisms (eg. <i>Staphylococcus aureus</i> ) | Linezolid (upon request)  | Fusidic acid                             |

If you have any questions, please contact Dr. D. Yamamura or Dr. A. Sarabia.

## FOLLOW-UP OF ABNORMAL CYTOLOGY BY MDS

### - The Quality of Care Information Protection Act 2004

Laboratories undertaking interpretation of Cytology are required to correlate subsequent clinical and pathologic findings with Cytology. This correlation contributes to the overall quality management process within the laboratory and may on occasion influence the management of individual patients and result in the issuing of an additional report. Some physicians are concerned that recently enacted Privacy Legislation in Ontario (PHIPA) prevents them from providing such information.

The Quality of Care Information Protection Act 2004 Chapter 3, Schedule B, Section 3 permits disclosure of such information to the MDS Quality of Care Committee which has the responsibility for correlating the data you provide with the Cytological Interpretation. Laboratories are recognized health care providers covered by this Act.

We appreciate the effort required to provide the follow-up which is important to our Cytology Laboratory Quality Management Program. ■

\* Cephalothin is a first generation oral cephalosporin. Susceptibility results (S, I, R) can be used to predict the activity of cephalixin and cefaclor. In addition, if susceptible (S) to cephalothin, the isolate is susceptible to cefazolin; however, isolates can be resistant (R) to cephalothin but susceptible to cefazolin. In this instance if required, results for cefazolin can be requested from the laboratory.

#### For more information, CONTACT:

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