



Saint Luke's Regional Laboratories Clinical Laboratory Letter

January 2014

Microalbumin Update

The two most important laboratory tests for chronic kidney disease (CKD) are estimated glomerular filtration rate (eGFR) and urine albumin. For many people, albuminuria is the earliest sign of CKD. The 2012 clinical practice guidelines developed by the Kidney Disease Improving Global Outcomes (KDIGO) Chronic Kidney Disease Work Group include an increased role for measurement of albuminuria in the evaluation and management of CKD (*Kidney International Supplements 2013, 3:19-62*). Measurement of urinary albumin is preferred over measurement of total protein because it is the single most important protein in urine. Also, analytical methods for albumin have been standardized and have better accuracy and precision at the lower threshold for early CKD. Normal values of urine albumin are usually expressed as the albumin excretion rate (AER). KDIGO chose a urinary AER of ≥ 30 mg per 24 hours sustained for >3 months as the threshold for chronic kidney disease. This value is three times higher than the normal value in young adult men and women.

Although the reference point remains an accurately timed 24 hour specimen, inaccuracies in collection often contribute to errors in estimation of protein loss. For this reason KDIGO recommends collection of an early morning urine sample. Because hydration status and urine flow rate can influence albumin concentration in a random urine sample, KDIGO recommends that laboratories report the ratio of albumin to creatinine (ACR). Creatinine excretion is fairly constant throughout the day and corrects for variations in urine concentration. An ACR value of ≥ 30 ug/mg in a random urine sample is equivalent to an AER of ≥ 30 mg per 24 hours.

Even though albuminuria is a continuous risk factor for cardiovascular and all cause mortality, KDIGO divided ACR into 3 categories to simplify clinical practice.

Category	ACR	Interpretation
A1	<30	Normal- mild increase
A2	30-300	Moderate increase
A3	>300	Severe increase

The 300 ug/mg cut-off correlates with the lower limit of sensitivity of the traditional urine dipstick for albumin. Category A3 includes the nephrotic syndrome in which albumin excretion is >2200 mg per 24 hours or an ACR of >2200 ug/mg.

KDIGO guidelines recommend at least annual measurement of GFR and albuminuria. They also provide a guide to the frequency of monitoring based on the eGFR and albuminuria categories. For example, a patient with eGFR of 40 mL/min/1.73m² and an ACR of 200 ug/mg should be tested three times a year.

Albumin excretion also plays a role in determining the blood pressure target in patients with CKD and hypertension. For example, target blood pressure is $\leq 140/90$ in patients with an ACR <30 ug/mg and $\leq 130/80$ in patients with an ACR ≥ 30 ug/mg.

Several studies have reported that ACR values obtained with first morning urine samples correlate more closely with the results of 24 hour urine collections than random urine samples collected later in the day. In fact random urine samples yield values that are $\sim 50\%$ higher than first morning samples near the decision threshold of 30 ug/mg. For this reason, KDIGO recommends measuring ACR in a first morning urine sample. However, collection of random sample is often more convenient for the patient and avoids the need for a repeat visit. If a patient has an elevated ACR on a random urine sample, KDIGO recommends repeat testing with a first morning void sample. With this sequential testing strategy, fewer than 50% of patients with an elevated ACR on a random sample will be confirmed. Repeat testing is very important to confirm a persistent increase in urinary excretion of albumin.

Previous guidelines for detection of diabetic nephropathy recommended the use of different ACR thresholds for males (0-16 ug/mg) and females (0-24 ug/mg) to account for differences in creatinine excretion. However, KDIGO guidelines recommend a single threshold of 30 ug/mg. Saint Luke's Regional Laboratories has changed its reference range for ACR to 0-30 ug/mg.

Anaerobic Cultures

Anaerobic infections are usually caused by leakage of normal flora into a sterile body site, following disruption of a mucosal barrier. The most commonly isolated gram-negative anaerobic pathogens include *Bacteroides*, *Fusobacterium*, *Prevotella*, and *Porphyromonas*. Gram-positive anaerobic pathogens include *Anaerococcus* and a variety of *Clostridium* species. The most frequent sites of infection include skin and soft tissue, pleuropulmonary and abdominal spaces, and female genital tract. Anaerobic infections are characterized by suppuration or abscess formation and tissue necrosis. **When anaerobes are suspected to be the causative agent of an infection, physicians must specifically request an anaerobic culture.**

Specimens for anaerobic culture should be collected only from an acceptable site and in such a way as to avoid contamination with normal flora. This is best accomplished by aspiration with a needle and syringe or with tissue or biopsy samples. Swabs are strongly discouraged since they provide a limited quantity of specimen, allow exposure to oxygen that is lethal to anaerobes, and are often contaminated with normal flora. For these reasons, swabs should only be used during surgery and only when aspiration or biopsy is not possible.

In the instance that a swab must be collected, the eSwab transport system should be utilized.

New Flu-only PCR

New to Saint Luke's Microbiology test menu, and available in-house immediately, is PCR testing for influenza viruses only. In addition to influenza B, the flu A/B PCR detects influenza A H1 and H3 subtypes and differentiates 2009 H1N1. Sensitivity averages 90% with specificity near 100%. Nasopharyngeal or nasal swabs submitted in viral transport media or nasal washes are the only acceptable specimen types for flu A/B PCR.

In addition to influenza, the respiratory PCR panel detects coronavirus, human metapneumovirus, rhinovirus, parainfluenza, RSV, adenovirus, *Bordetella pertussis*, *Mycoplasma pneumoniae*, and *Chlamydia pneumoniae*. The predominant influenza subtype detected by PCR testing this season is influenza A 2009 H1. Coronavirus, rhinovirus, metapneumovirus, RSV, and *Mycoplasma* are also detected frequently. The respiratory PCR panel can be performed on bronchoscopy specimens in addition to nasal swabs or washes. All respiratory PCR testing is performed in the central Microbiology lab at Saint Luke's Hospital, and is completed as specimens are received.

Rapid antigen testing, available throughout Saint Luke's Health System laboratories, detects and differentiates both influenza A and B. Compared to PCR, the rapid antigen's detection rate for this season's predominant strain has been 60-80%. Rapid antigen testing is also available for RSV.

Test Name	Detects	Specimen	Transport
Rapid Flu A/B Antigen	Influenza A & B	NP/nasal swab Nasal wash	Flocked swab in VTM Flocked swab - saline Eswab in Amies
Flu A/B PCR	Influenza A & B, 2009 H1N1	NP/nasal swab Nasal wash	Flocked swab in VTM
Respiratory panel PCR	7 viruses, influenza subtypes, <i>Bordetella</i> , <i>Mycoplasma</i> , <i>Chlamydia</i>	NP/nasal swab Nasal wash Bronchoscopy wash/ lavage	Flocked swab in VTM