

Lab Focus

April 2004—monthly insert to 'Scope from Fairview Clinical Laboratories

New Reflex-Testing Algorithm for von Willebrand Disease Multimers to Decrease Laboratory Costs

Beginning Apr. 1, the von Willebrand Disease (VWD) work-up will be modified to include a reflex-testing algorithm. The Von Willebrand multimer analysis will be performed only after the screening tests indicate VWD is present to help decrease laboratory costs.

The following tests will be routinely performed when testing for VWD:

- von Willebrand antigen (VWF:Ag)
- von Willebrand ristocetin cofactor (VWF:RCo)
- Factor VIII activity

The VWF multimer analysis will only be performed if:

- The VWF:Ag and/or VWF:RCo is <65% , or
- The ratio of VWF:Ag / Factor VIII is <0.65 , or
- The ratio of VWF:RCo / VWF:Ag is <0.65.

Currently, von Willebrand multimer analysis is performed on every sample submitted for a von Willebrand disease (VWD) panel. The VW multimer test is indicated only to subtype patients with documented VWD. A retrospective analysis of the past year's testing for VWD revealed that in only 23 percent of submitted samples was the VW multimer analysis clinically indicated. Thus, in approximately 77 percent of case, the VW

multimer analysis was clinically not necessary, leading to significant unnecessary patient lab testing costs.

In special cases, VW multimer analysis can be ordered by special request. This change has been discussed and approved by the Fairview Medical Executive Committee.

Karen Meyer

Special Coagulation Supervisor

Agnes Aysolya, MD

University of Minnesota Physicians

Measurement of Cortisol in Saliva Offers Advantages Over Serum Sampling

Salivary cortisol may be used as a substitute for serum cortisol for assessment of adrenal function and of cortisol secretion in children and adults diagnosed with Cushing's syndrome. Salivary cortisol offers ease of sample procurement and flexibility of sampling time over serum cortisol.

Salivary cortisol concentrations have a similar circadian variation as serum cortisol levels and do not vary by gender. Cortisol concentration in saliva corresponds approximately to 2.1-3.5 percent of the total serum cortisol.³

Salivary cortisol responds to ACTH by a three-fold increase at 60 minutes in normal subjects⁴ and is suppressed at 9 a.m. after a 1 mg dexamethasone dose at midnight.⁵

At 9 a.m. and 5 p.m., there are significant overlap of salivary cortisol values between normal and

Cushing's subjects, although Cushing's levels generally are higher. In one study, salivary cortisol levels obtained at 11 p.m. distinguished patients with Cushing's from normal adults with a 100 percent sensitivity and 88 percent specificity at a 90th percentile cutoff of 0.168 ug/dL . In obese adults, a sensitivity of 100 percent also was obtained when using a combination of 11 p.m. and overnight 1 mg dexamethasone salivary cortisol tests.⁵

The efficacy of the use of 11 p.m. salivary cortisol followed by the administration of dexamethasone and a subsequent 9 a.m. salivary cortisol level of less than 0.06 ug/dL indicates Cushing's syndrome in children and adolescents with a sensitivity of 100 percent and specificity of 95.2 percent.⁶ A second report suggests that a midnight salivary cortisol level of >0.27 ug/dL identifies Cushing's syndrome in children and adolescents with an accuracy equivalent to urinary free cortisol expressed per square meter.⁷

In newborn infants, salivary cortisol, as is the case with serum cortisol, does not demonstrate circadian rhythm. Levels ranging from 0.11 to 2.57 ug/dL have been found. These values correlated with simultaneous serum cortisol levels, which ranged between 1.05 and 18.4 ug/dL.¹ Thus the serum/salivary cortisol ratio of the means was approximately 10.5:1. Circadian rhythm of salivary cortisol appears between 9 months and 1 year of age.²

References

1. Francis S J, et al, *Assessment of Adrenocortical Activity in Term Newborn Infants Using Salivary Cortisol Determinations*. J Pediatrics, 1987; 111:129-33.
2. Kiess W, et al, *Salivary Cortisol Levels Throughout Childhood and*

- Adolescence" Relation with Age, Pubertal Stage and Weight*
Pediatric Research, 1975; 37:502-506.
3. Aardal E and Holm A-C, *Cortisol in Saliva: Reference Ranges and Relation to Cortisol in Serum*, Eur.J. Clin Chem Clin Biochem 1995; 33:927-932.
 4. Laudet M H, et al, *Salivary Cortisol Measurement: A Practical Approach to Assess Pituitary-Adrenal Function*. J Clin Endocrinol Metab 1988;1 66:343-348.
 5. Castro M, et al, *Outpatient Screening for Cushing's Syndrome: the sensitivity of the Combination of Circadian Rhythm and Overnight Dexamethasone Suppression Salivary Cortisol Tests*. J Clin Endocrinol Metab 1999; 84:878-882.
 6. Martinelli C E, et al, *Salivary Cortisol for Screening of Cushing's Syndrome in Children*. Clin Endocrinol 1999; 51:67-71
 7. Gafni R I, et al, *Nighttime Salivary Cortisol Measurement as a Simple Non-invasive Outpatient Screening Test for Cushing's Syndrome in Children and Adolescents*. J Pediatrics 2000; 137:30-35

Linda Bailey, CLS
Protein/Endocrine Laboratory

David M Brown, M.D
University of Minnesota Physicians

INSTRUCTIONS FOR COLLECTING SALIVA

Patient Preparation:

1. Do not eat a major meal within 60 minutes prior to sample collection.
2. Avoid dairy products 30 minutes prior to sample collection. Avoid acidic and high sugar foods.
3. Avoid alcohol consumption 24 hours prior to collection. Avoid caffeine for two hours before sampling.
4. Do not apply creams or lotions that contain steroids immediately prior to collection. This is to avoid contamination of the Salivette (Matkon 195332).
5. Avoid activities that can cause the gums to bleed for three hours prior to collection. This would include brushing or flossing teeth. Do not collect sample if the gums or the inside of the mouth is bleeding as blood will invalidate the measurement of Saliva Cortisol.
6. Wash the mouth out with water 10 minutes before collecting the sample.
7. Salivettes are not intended for use with children under the age of three. Children under the age of 10 require adult supervision.

Using a Salivette (Adults and children >3 years old):

1. Remove the cylindrical shaped swab from the insert and place in mouth.
2. Chew swab for 30-45 seconds or until one can no longer prevent swallowing excess saliva and swab is saturated.
3. If the swab cannot be chewed, place under the tongue for 30-45 seconds or until well saturated.
4. After the swab is saturated, the swab is returned to the insert and the Salivette is firmly closed with the stopper. Do not remove the tube that is holding the insert. The Salivette should be returned for processing with the swab inside the insert, the insert inside of the centrifuge

tube and the stopper firmly on top of the insert.

5. Label with patient name and identification number, time and date of collection. Store the sample in the refrigerator.

Collecting saliva from infants:

1. Aspirate saliva from the floor of the infant's mouth using a sterile plastic transfer pipet (Matkon 198719). Saliva flow may be stimulated by gently stroking the pipet over the tongue.
2. Expel the saliva into a 2 mL sterile cryovial (Matkon 182710).
3. Minimum sample requirement is 60 uL.

Sound bites. . . .

New Allergen Available

Allergen testing for whey, casein and egg yolk is now available from the Fairview-University Endocrine Laboratory.

Pyruvic Acid Testing Moves to ARUP Laboratories

Effective Apr. 1, testing for Pyruvic Acid will no longer be performed on site. Testing will now be sent to ARUP Laboratories.

Special handling is required: Immediately after collection, exactly 1 mL whole blood (non-anticoagulated in syringe, purple EDTA tube, or green heparin tube) must be added to a chilled pyruvate collection tube, mixed well for 30 seconds, placed in an ice bath for 10 minutes, and sent to the laboratory immediately.