The Molecular Genetics Laboratory at Children’s Mercy Hospital is now performing testing for Rett syndrome (RTT). RTT, an X-linked dominant neurodevelopmental disorder, is the second most common cause of mental retardation in females, affecting about 1 in 10,000. It is most often recognized between 6-18 months in females who show a plateau in developmental progress, followed by loss of purposeful hand skills coincident with the onset of stereotyped hand movements. Classic RTT is defined by the following diagnostic criteria:

**Necessary criteria**
1. Apparently normal prenatal and perinatal history
2. Apparently normal psychomotor development through first 6 months
3. Normal head circumference at birth
4. Appearance of gait apraxia and truncal apraxia/ataxia between ages 1-4
5. Deceleration of head growth between 3 - 48 months
6. Loss of acquired purposeful hand skills between 6 - 30 months, associated with communication dysfunction, loss of learned words, cognitive impairment, and emerging social withdrawal
7. Development of severely impaired expressive and receptor language; severe psychomotor retardation
8. Stereotypic hand movements such as hand wringing/squeezing, clapping/tapping, mouthing and washing/rubbing automatisms

**Supportive criteria:**
1. Disturbed breathing while awake (hyperventilation, breath-holding, air swallowing, etc.)
2. Bruxism
3. Impaired sleep pattern from early infancy
4. Abnormal muscle tone successively associated with muscle wasting and dystonia
5. Peripheral vasomotor disturbances
6. Scoliosis/kyphosis progressing through childhood
7. Growth retardation
8. Hypotrophic small and cold feet; small, thin hands

*Atypical* RTT often presents with a milder course and may include preserved speech, early onset seizures, or delayed onset of symptoms (forme fruste). In addition, a congenital form also exists, characterized by absence of a period of normal development.

Although there is no cure for RTT, diagnosis is important for several reasons: Since 99.5% of cases are due to sporadic mutations, there is a very low recurrence risk for RTT. Families should be referred for genetic counseling to discuss these risks. A diagnosis also gives the family more accurate expectations for the patient's prognosis, and provides an opportunity to join support groups, like the International Rett Syndrome Association ([www.rettsyndrome.org/main/rettbase.htm](http://www.rettsyndrome.org/main/rettbase.htm)). Finally, ending the search for a diagnosis also ends the need for invasive and expensive diagnostic tests.

**Molecular Diagnosis:** RTT is caused by mutations in the MECP2 gene. Since mutations can lie anywhere in the gene, the entire coding region (exons 1-4) must be sequenced. This method will identify a mutation in approximately 80-85% of classic RTT patients. The 4 most important diagnostic criteria (5-8; in bold), when present together, give a positive predictive value (PPV) of ~90.6% (ref 1). Omitting acquired microcephaly gives a PPV of 64%; however, substituting acquired microcephaly for stereotypic hand movements reduces the PPV to 34%.

**Specimen Requirements:** 3 cc whole blood in an EDTA tube. The turn-around time is 2-4 weeks.
Did you know?  We store any left-over DNA from patients tested in our lab, making repeat sampling unnecessary for most add-on tests. Please check with the lab before drawing blood on your patient! Phone: 816-234-3588

References for Rett Syndrome:

News from Central Processing

The Outpatient Laboratory

By Marilyn S. Hamilton, MD, PhD

The Outpatient Laboratory is located on the ground floor of the Outpatient Center and is open 8-5:30. It consists of two phlebotomy rooms which are kept very busy with 90-100 patients on an average day. These patients come not only from CMH but also from community physicians and from commercial labs that may have tried to collect a specimen and not been able to – so they send them to the experts in pediatric phlebotomy. Maxine Baskin, a Lab Tech and phlebotomist who has been with CMH 16 years and with the Outpatient Laboratory since it opened, and Shaunte Howard, a phlebotomist, are in the Outpatient Laboratory full time. During peak times an additional phlebotomist is also available. They are trained in pediatric phlebotomy and provide containers for urine and stool collection. They also perform sweat testing by appointment. Specimens are transported via Translogic Tube to the Main Lab. If a respiratory specimen needs to be collected the patient will be sent to the Main Lab and a Respiratory Therapist will be called to collect the specimen.

In addition to patient services the Outpatient Laboratory provides clinical training to Care Assistants in the CMH Basic Phlebotomy class and occasionally to student nurses, technologists from various fields, nurses and residents. Phlebotomy students from Penn Valley Community College and St Luke’s Hospital also receive clinical training in the CMH Outpatient Laboratory.

The Outpatient Laboratory depends on all CMH staff to help make it run smoothly. Working together we can make the Outpatient Laboratory a positive experience for our patients and their families.

1. Have the orders correctly entered on the correct account in the computer before the patient arrives for specimen collection. Time spent phoning for orders and the associated follow-up significantly delays all the waiting patients.
2. If the patient is coming to the Lab before a clinic appointment try to make sure sufficient time is allowed for collection and testing before the appointment. Patients with diabetes have their hemoglobin A1C results by the time they see the doctor.
3. Sweat testing takes an hour and really cannot be done without an appointment.

CME Series

**Sponsored by Department of Pathology & Laboratory Medicine**

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