GENEReviews

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Alpha-Thalassemia X-Linked Mental Retardation Syndrome

[*ATRX Syndrome; Alpha Thalassemia/Mental Retardation, X-Linked; XLMR-Hypotonic Face Syndrome*]

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Summary

Disease characteristics. Alpha-thalassemia X-linked mental retardation (ATRX) syndrome is characterized by distinctive craniofacial features, genital anomalies, and severe developmental delays with hypotonia and mental retardation. Craniofacial abnormalities include small head circumference, telecanthus or ocular hypertelorism, small nose, tented upper lip, and prominent or everted lower lip with coarsening of the facial features over time. Although all affected individuals have a normal 46,XY karyotype, genital anomalies range from hypospadias and undescended testicles to severe hypospadias and ambiguous genitalia, to normal-appearing female genitalia. Global developmental delays are evident in infancy and some affected individuals never walk independently or develop significant speech.

Diagnosis/testing. The diagnosis of ATRX syndrome is established in individuals with a recognizable pattern of somatic abnormalities, mental retardation, hypotonia, and a family history consistent with X-linked inheritance. *ATRX* is the only gene associated with ATRX syndrome. Approximately 90% of the known *ATRX* mutations can be detected using sequence analysis of the zinc finger domain (exon 7, exon 8, proximal area of exon 9) and helicase domains. Such testing is clinically available.

Management. *Treatment of manifestations:* calorie-dense formula and/or gavage feeding as needed for adequate nutrition; anticholinergics, botulinum toxin type A injection of the salivary glands, and/or surgical redirection of the submandibular ducts for excessive drooling; early intervention programs and special education. *Prevention of secondary complications:* antiobiotic prophylaxis and vaccination to prevent pneumococcal and meningococcal infection in those with asplenia. *Surveillance:* regular assessment of growth in infancy and childhood; regular monitoring of developmental progress. *Other:* Anemia rarely requires treatment.

Genetic counseling. ATRX syndrome is inherited in an X-linked manner. Affected individuals do not reproduce. The mother of a proband may be a carrier or the affected individual may have a *de novo* gene mutation. Carrier women have a 50% chance in each pregnancy of transmitting the *ATRX* mutation; offspring with a 46,XY karyotype who inherit the *ATRX* mutation will be affected; offspring with a 46,XX karyotype who inherit the mutation are unaffected female carriers. Carrier testing in at-risk females and prenatal testing are possible when the disease-causing mutation in the family is known.

Diagnosis

Clinical Diagnosis

Alpha-thalassemia X-linked mental retardation (ATRX) syndrome may be suspected on the basis of characteristic craniofacial, genital, skeletal, and other somatic findings. Of greatest importance clinically is the failure to achieve developmental milestones on schedule. Cognitive function is usually profoundly impaired, although individuals with less severe intellectual disabilities have been reported.

Because phenotypic findings overlap with those of other syndromes, clinical diagnosis should be confirmed by molecular genetic testing.

Testing

Hematologic Studies—Demonstration of hemoglobin H (HbH)

- **Affected individuals.** Most individuals with *ATRX* mutations have evidence of alpha-thalassemia. HbH inclusions (β-globin tetramers) in erythrocytes can be demonstrated following incubation of fresh blood smears with 1% brilliant cresyl blue (BCB). The proportion of cells with HbH inclusions ranges from 0.01% to 30% [Gibbons et al 1995].

  Note: (1) HbH inclusions may be demonstrated readily in some individuals, found only in an occasional erythrocyte in some, or observed only after repeated testing in others. (2) The absence of HbH inclusions in 10%-20% of affected individuals and paucity of laboratories that maintain the required reagents diminish the utility of this testing in most clinical settings.

- **Carriers.** HbH inclusions are found in only about 25% of carriers [Gibbons et al 1995].

Hemoglobin electrophoresis. HbH may also be demonstrated by hemoglobin electrophoresis. The test is not highly sensitive and may fail to identify many cases.

Red blood cell indices. Although microcytic hypochromic anemia may be seen in some affected individuals, many have red cell indices in the normal range [Gibbons et al 1995].

Molecular Genetic Testing

Molecular Genetic Testing —Gene. *ATRX* is the only gene known to be associated with ATRX syndrome.

Clinical testing

- **Sequence analysis and mutation scanning of select exons.** Approximately 90% of the known *ATRX* mutations can be detected using sequence analysis of the zinc finger domain (exon 7, exon 8, proximal area of exon 9) and helicase domains (exons 17-20) [Villard & Fontes 2002; Badens, Lacoste et al 2006; Argentaro et al 2007].
- **Sequence analysis and mutation scanning of all exons and splice junctions** are used to detect the less common mutations located outside the zinc finger and helicase domains. Deletions and duplications have been reported, but no data are available on mutations in the promoter regions.
- **Deletion/duplication analysis.** Array CGH or targeted MLPA detects deletions and duplications in affected males and carrier females. Only a few such genomic alterations have been identified.

- **X-chromosome inactivation studies.** The finding that carrier females have marked skewing of X-chromosome inactivation (>90:10) has been used as a nonspecific and presumptive test for carrier detection. Non-random X-chromosome inactivation is not unique to ATRX syndrome; thus, the finding of skewed X-chromosome inactivation is not diagnostic and must be used in the context of clinical findings.

Table 1 summarizes molecular genetic testing for this disorder.

Table 1. Molecular Genetic Testing Used in Alpha-Thalassemia X-Linked Mental Retardation Syndrome

Test Method	Mutations Detected	Mutation Detection Frequency [1, 2]	Test Availability
Sequence analysis of exon 7, exon 8, proximal area of exon 9, and the helicase domains	*ATRX* sequence variants in specific regions	85% of known mutations	Clinical Testing
DNA and RNA sequence analysis and mutation scanning	*ATRX* coding region sequence variants and splice junctions	95% of known mutations	
Array-CGH, MLPA, qPCR deletion/ duplication analysis	*ATRX* deletions/duplications	<5% of known mutations	
X-chromosome inactivation study	Skewed X-chromosome inactivation	Most carrier females	

1. Proportion of affected individuals with a mutation(s) as classified by test method
2. Approximately 25% of individuals tested on the basis of suggestive clinical findings have the diagnosis confirmed by gene testing [Badens, Lacoste et al 2006].

Interpretation of test results. For issues to consider in interpretation of sequence analysis results, click here.

Testing Strategy

To confirm the diagnosis in a proband

- Sequencing of the *ATRX* zinc finger domain (also designated the PHD and ADD domain) and helicase domain detects in excess of 80% of mutations.
- A second level of molecular testing includes full gene sequencing or RNA sequencing to detect exonic and splice mutations outside the zinc finger and helicase domains. Array CGH and MLPA detect genomic alterations including deletions and duplications.
- Although staining of erythrocytes with BCB to identify HbH inclusions has been a helpful and inexpensive adjunct to diagnosis in the past, its utility is diminished by the fact that 10%-20% of affected individuals do not have these inclusions and few laboratories can perform the test; however, the test may be useful in supporting the diagnosis in individuals with clinical findings of ATRX syndrome but negative molecular genetic testing.

Carrier testing for at-risk relatives requires prior identification of the disease-causing mutation in the family.

Note: Female carriers are heterozygous for ATRX syndrome but rarely develop clinical findings.

Prenatal diagnosis and preimplantation genetic diagnosis for at-risk pregnancies require prior identification of the disease-causing mutation in the family.

Genetically Related (Allelic) Disorders

ATRX mutations have been found in several named X-linked mental retardation (XLMR) syndromes (Carpenter-Waziri syndrome, Holmes-Gang syndrome, Chudley-Lowry syndrome), XLMR with spastic paraplegia, XLMR with epilepsy, and nonsyndromic XLMR [Lossi et al 1999, Stevenson 2000, Yntema et al 2002]. These entities should be considered to be in the phenotypic spectrum of ATRX syndrome; there are no compelling reasons to maintain the syndromic names.

ATRX mutations have also been identified in families reported as having Juberg-Marsidi syndrome and Smith-Fineman-Myers syndrome [Villard, Ades et al 1999]. Because *ATRX* mutations have not been reported in the original families with Juberg-Marsidi syndrome and Smith-Fineman-Myers syndrome, the relationship between ATRX syndrome and these two syndromes is unclear [Schwartz, personal communication 2005].

Clinical Description

Natural History

A more or less distinctive phenotype has emerged from the study of individuals with alpha-thalassemia X-linked mental retardation (ATRX) syndrome. Craniofacial, genital, and developmental manifestations are prominent among the most severely affected individuals [Gibbons et al 1995; Stevenson, Schwartz et al 2000; Badens, Lacoste et al 2006]. As clinical experience with the condition has increased and additional individuals/families have been evaluated using molecular genetic testing, the range of phenotypic variability has broadened, particularly on the mild end of the spectrum. Findings by Guerrini et al (2000) and Yntema et al (2002) confirm this. Both describe families within which affected males have mild, moderate, or profound mental retardation. Adults in the family described by Yntema et al (2002) appeared to have nonsyndromic XLMR, although childhood photographs showed evidence of facial hypotonia.

A recognizable pattern of craniofacial findings includes small head circumference, upsweep of the frontal hair, telecanthus or ocular hypertelorism, small triangular nose with retracted columella, tented upper lip, prominent or everted lower lip, and open mouth. Irregular anatomy of the pinnae, wide spacing of the teeth, and tongue protrusion are supplemental findings, the latter two adding to a coarseness of the facial appearance, particularly after the first few years of life.

The external genitalia are usually abnormal. The anomalies are often minor, including first-degree hypospadias, undescended testes, and underdevelopment of the scrotum. More severe defects are second- and third-degree hypospadias, micropenis, and ambiguous genitalia. Although all individuals with ATRX syndrome have a normal 46,XY karyotype, occasionally gonadal dysgenesis results in inadequate testosterone production and ambiguous genitalia or even normal-appearing female external genitalia. Although the spectrum of possible genital anomalies in ATRX syndrome is broad, the type of genital anomaly appears to be consistent within a family.

Short stature is typical and may be accompanied by minor skeletal anomalies (brachydactyly, clinodactyly, tapered digits, joint contractures, pectus carinatum, kyphosis, scoliosis, dimples over the lower spine, varus and valgus foot deformation, and pes planus). Stature is less than two standard deviations (SD) below the mean in two-thirds of individuals using standard growth charts; syndrome-specific growth charts are not available.

Major malformations are not common, but ocular coloboma, cleft palate, cardiac defects, inguinal hernia, heterotaxy, and asplenia [Leahy et al 2005] have been reported.

The severe developmental impairment and mental retardation are the most important clinical manifestations. From the outset, developmental milestones are globally and markedly delayed. Speech and ambulation occur late in childhood. Some affected individuals never walk independently or develop significant speech.

Hypotonia is a hallmark of the condition, contributing to the facial manifestations, drooling, and developmental retardation. Seizures occur in approximately one-third of individuals [Gibbons et al 1995].

The majority of affected individuals have gastrointestinal symptoms that contribute significantly to morbidity. Approximately three-fourths have gastroesophageal reflux and one-third have chronic constipation. Gastric pseudo-obstruction resulting from abnormal suspension of the stomach and constipation resulting from colon hypoganglionosis have been observed [Martucciello et al 2006]. Aspiration, presumably related to gastroesphageal reflux, has been a fatal complication in some.

Although the neurobehavioral phenotype has not been extensively delineated, most individuals appear affable, but some are emotionally labile with tantrums and bouts of prolonged crying or laughing.

Alpha-thalassemia. A microcytic, hypochromic anemia may be seen, but many individuals have normal red cell indices and normal hematocrit/hemoglobin. The mutated *ATRX* gene apparently down-regulates α-globin gene expression in those individuals with HbH inclusions.

Genotype-Phenotype Correlations

Badens, Lacoste et al (2006) found that mutations in the *ATRX* zinc finger domain produce severe psychomotor impairment and urogenital anomalies, whereas mutations in the helicase domains cause milder phenotypes.

Heterozygous females rarely show clinical manifestations.

- Badens, Martini et al (2006) reported a girl conceived by in vitro fertilization (IVF) who had craniofacial features, growth retardation, and developmental impairment typical of ATRX syndrome. Leukocyte studies showed marked skewing of X-chromosome inactivation with her mutation-bearing X chromosome being the active X chromosome. The role of IVF in this unique case of female expression is not known.
- Wada et al (2005) reported moderate mental retardation without other phenotypic features of ATRX syndrome in a female carrier with random X-chromosome inactivation.

Penetrance

Penetrance is presumed to be 100% in males as *ATRX* mutations have not been reported in normal males.

Nomenclature

"Alpha-thalassemia X-linked mental retardation syndrome" and "ATRX syndrome" are the two most widely accepted terms for this disorder.

Carpenter-Waziri syndrome, Holmes-Gang syndrome, and Chudley-Lowry syndrome are allelic, each reported in a single family, and clinically similar to ATRX syndrome [Abidi et al 1999; Stevenson, Abidi et al 2000; Abidi et al 2005]; they are now considered to be in the

phenotypic spectrum of ATRX syndrome and thus no compelling reason remains to retain their names.

Such is not the case for Juberg-Marsidi syndrome and Smith-Fineman-Myers syndrome; *ATRX* mutations have not been found in the original families with Juberg-Marsadid syndrome or Smith-Fineman-Myers syndrome; thus, allelism between these and ATRX syndrome cannot be considered proven.

Prevalence

The prevalence is not known. Approximately 200 affected individuals are known to the laboratories conducting molecular genetic testing; substantial under-ascertainment, especially of those with milder phenotypes, is probable.

No racial or ethnic concentration of individuals has been reported.

Differential Diagnosis

For current information on availability of genetic testing for disorders included in this section, see GeneTests Laboratory Directory. —ED.

Coffin-Lowry syndrome, (CLS) is characterized by severe to profound mental retardation in males and normal intelligence to profound retardation in heterozygous females. Older males have a characteristic facial appearance, and short, soft, and fleshy hands, often with remarkably hyperextensible tapering fingers. Short stature, microcephaly, and dental anomalies are common. Childhood-onset **s**timulus-**i**nduced **d**rop **e**pisodes (SIDEs) may affect 10%-20% of individuals; unexpected tactile or auditory stimuli or excitement triggers a brief collapse but no loss of consciousness. Progressive kyphoscoliosis and early mortality are seen. Mutations in the *RSK2* gene are causative. Inheritance is X-linked.

***MECP2* duplication syndrome.** Duplication of *MECP2* and adjacent genes in Xq28 has been associated with a syndrome of severe mental retardation, spasticity, hypotonia, absent or limited speech, seizures, and recurrent respiratory infections [Friez et al 2006]. Gastrointestinal symptoms with gastroesophageal reflux and swallowing dysfunction occur in most. Half of affected males die by early adulthood. Marked skewing of X-chromosome inactivation occurs in carrier females. The face is not as characteristically hypotonic as in ATRX syndrome, nor does microcephaly occur as commonly. Molecular testing should be used to confirm the diagnosis in each syndrome.

Alpha-thalassemia mental retardation chromosome 16 (ATR-16) is the association of alpha-thalassemia and mental retardation in individuals with a contiguous gene deletion involving the distal short arm of chromosome 16. Such deletions produce alpha-thalassemia by deleting the two genes in *cis* configuration at 16p13 that encode α-globin chains. Because the chromosomal deletions and rearrangements giving rise to ATR-16 are large and variable, no specific clinical phenotype is observed in ATR-16; this is in contrast to ATRX syndrome, in which the phenotype is more predictable.

Alpha-thalassemia results from reduced production of the α chains of adult hemoglobin (designated Hb α_2 β_2). In individuals of Mediterranean origin with developmental delay, it is appropriate to determine the α-globin genotype. Individuals with ATRX syndrome have a normal α-globin genotype (αα/αα), whereas those with alpha-thalassemia have deletions of one α-globin gene (α-/αα), two α-globin genes ([α-/α-] or [- -/αα]), or three α-globin genes (- -/-α). Mental retardation is not a component of isolated alpha-thalassemia.

Management

Evaluations Following Initial Diagnosis

To establish the extent of disease in an individual diagnosed with alpha-thalassemia X-linked mental retardation (ATRX) syndrome, the following evaluations are recommended:

- Review of medical history for developmental progress and seizures
- Assessment of growth in infants and children
- Physical examination including assessment of facial features, muscle tone, and deep tendon reflexes
- Auscultation of the heart for evidence of structural defect
- Examination of the genitalia for cryptorchidism and other anomalies
- Assessment of feeding in early childhood for swallowing difficulties, gastroesophageal reflux, and/ or recurrent vomiting
- Ophthalmologic evaluation for strabismus, visual acuity problems, or structural eye defects if indicated by clinical assessment

Treatment of Manifestations

The following treatments are recommended:

- Calorie-dense formula and/or gavage feeding to compensate for poor nutritional intake
- If food refusal is an issue, evaluation for gastrointestinal causes such as peptic ulcer disease
- If drooling is a serious problem, treatment with anticholinergics, botulinum toxin type A injection of the salivary glands and/or surgical redirecting of the submandibular ducts
- Treatment in the usual manner for gastroesophageal reflux, recurrent respiratory and urinary tract infections, seizures, severe behavior problems, anomalies (e.g., cleft palate, cardiac malformations, cryptorchidism, ambiguous genitalia, hypospadias)
- Early intervention programs and special education

Prevention of Secondary Complications

Antiobiotic prophylaxis and vaccination to prevent pneumococcal and meningococcal infection are reasonable precautions in the rare patient with asplenia [Leahy et al 2005].

Surveillance

Growth should be followed regularly in infancy and childhood and plotted on age-appropriate growth charts. (Syndrome-specific growth charts are not available.)

Developmental progress should be monitored throughout infancy and childhood.

Testing of Relatives at Risk

See Genetic Counseling for issues related to testing of at-risk relatives for genetic counseling purposes.

Therapies Under Investigation

Search ClinicalTrials.gov for access to information on clinical studies for a wide range of diseases and conditions. Note: There may not be clinical trials for this disorder.

Other

Anemia, if present, is mild and rarely requires treatment.

Genetics clinics are a source of information for individuals and families regarding the natural history, treatment, mode of inheritance, and genetic risks to other family members as well as information about available consumer-oriented resources. See the GeneTests Clinic Directory.

Support groups have been established for individuals and families to provide information, support, and contact with other affected individuals. The Resources section (below) may include disease-specific and/or umbrella support organizations.

Genetic Counseling

Genetic counseling is the process of providing individuals and families with information on the nature, inheritance, and implications of genetic disorders to help them make informed medical and personal decisions. The following section deals with genetic risk assessment and the use of family history and genetic testing to clarify genetic status for family members. This section is not meant to address all personal, cultural, or ethical issues that individuals may face or to substitute for consultation with a genetics professional. To find a genetics or prenatal diagnosis clinic, see the GeneTests Clinic Directory.

Mode of Inheritance

Alpha-thalassemia X-linked mental retardation (ATRX) syndrome is inherited in an X-linked manner.

Risk to Family Members

Parents of a proband

- In a family with more than one affected individual, the mother of an affected individual is an obligate carrier.
- In families with only one affected individual, the mother may be a carrier or the affected individual may have a *de novo* gene mutation. No data on the frequency of *de novo* gene mutations in this condition are available.

Sibs of a proband

- The risk to sibs of a proband depends on the carrier status of the mother.
- If the mother of the proband has a disease-causing mutation, the chance of transmitting it is 50% in each pregnancy. Sibs with a 46,XY karyotype who inherit the mutation will be affected; sibs with a 46,XX karyotype who inherit the mutation are female carriers and will not be affected. Thus, with each pregnancy, a woman who is a carrier has a 25% chance of having an affected child.
- Germline mosaicism has been demonstrated in this condition. Thus, even if the disease-causing mutation has not been identified in the mother's DNA, sibs of the proband are still at increased risk of inheriting the disease-causing mutation.

Offspring of a proband. No affected individual has reproduced.

Other family members of a proband. The proband's maternal aunts and their offspring may be at risk of being carriers or being affected.

Carrier Detection

Carrier testing of at-risk female relatives is available on a clinical basis if the disease-causing mutation has been identified in the family.

Related Genetic Counseling Issues

Assisted reproduction technologies (ART). Donor eggs may be utilized by carrier females to avoid the risk of transmitting an *ATRX* mutation. Although experience with ART in ATRX syndrome is limited, one female conceived by IVF had total inactivation of her normal X chromosome and the physical and psychomotor findings typical of ATRX syndrome in males [Badens, Martini et al 2006].

Family planning. The optimal time for determination of genetic risk, clarification of carrier status, and discussion of the availability of prenatal testing is before pregnancy. It is appropriate to offer genetic counseling (including discussion of potential risks to offspring and reproductive options) to young adults who are carriers or at risk of being carriers.

DNA banking. DNA banking is the storage of DNA (typically extracted from white blood cells) for possible future use. Because it is likely that testing methodology and our understanding of genes, mutations, and diseases will improve in the future, consideration should be given to banking DNA of affected individuals. DNA banking is particularly relevant in situations in which the sensitivity of currently available testing is less than 100%. See Testing for a list of laboratories offering DNA banking.

Prenatal Testing

Prenatal testing is possible for pregnancies at increased risk for ATRX syndrome.

High-risk pregnancies. For pregnancies in which the mother has been identified as being heterozygous for the disease-causing *ATRX* mutation identified in the family, the usual procedure is to determine fetal sex on cells obtained from amniocentesis usually performed at approximately 15-18 weeks' gestation or chorionic villus sampling at approximately ten to 12 weeks' gestation. If the fetus has a 46,XY karyotope, DNA can be analyzed to determine if the disease-causing *ATRX* mutation identified in the family is present.

Note: Gestational age is expressed as menstrual weeks calculated either from the first day of the last normal menstrual period or by ultrasound measurements.

Indeterminate-risk pregnancies. Germline mosaicism has been documented in ATRX syndrome [Bachoo & Gibbons 1999]; thus, the mother of a proband who does not demonstrate the *ATRX* mutation in her leukocytes is still at risk of having a second affected child. Prenatal diagnosis as described for high-risk pregnancies should be offered for all XY fetuses.

Preimplantation genetic diagnosis (PGD). Preimplantation genetic diagnosis may be available for families in which the disease-causing mutation has been identified. For laboratories offering PGD, see Testing.

Molecular Genetics

Information in the Molecular Genetics tables is current as of initial posting or most recent update. —ED.

Table A. Molecular Genetics of Alpha-Thalassemia X-Linked Mental Retardation Syndrome

Gene Symbol	Chromosomal Locus	Protein Name
ATRX	Xq13	Transcriptional regulator ATRX

Data are compiled from the following standard references: Gene symbol from HUGO; chromosomal locus, locus name, critical region, complementation group from OMIM; protein name from Swiss-Prot.

Table B. OMIM Entries for Alpha-Thalassemia X-Linked Mental Retardation Syndrome

300032	ATR-X GENE; ATRX
301040	ALPHA-THALASSEMIA/MENTAL RETARDATION SYNDROME, NONDELETION TYPE, X-LINKED; ATRX

Table C. Genomic Databases for Alpha-Thalassemia X-Linked Mental Retardation Syndrome

Gene Symbol	Entrez Gene	HGMD
ATRX	546 (MIM No. 300032)	ATRX

For a description of the genomic databases listed, click here.

Note: HGMD requires registration.

Normal allelic variants: The gene extends over 350 kb and includes 35 exons.

Pathologic allelic variants: Although mutations have been distributed throughout *ATRX*, more than 90% of those reported are in the zinc finger and helicase domains [Villard, Bonino et al 1999; Villard & Fontes 2002; Borgione et al 2003; Badens, Lacoste et al 2006; Argentaro et al 2007; Thienpont et al 2007]. Missense mutations appear more commonly than do frameshift and nonsense mutations. Deletions, insertions, intragenic duplications, and missense, nonsense, and splice mutations have been found. (For more information, see Genomic Databases table.)

Normal gene product: Zinc finger domain functions as a transcription factor; the helicase domains function in the transcription process opening double-stranded DNA. In combination with other chromatin-associated proteins, the ATRX protein appears to play a role in chromatin remodeling, possibly silencing gene expression during development [Xue et al 2003; Ausio et al 2003; Tang, Park et al 2004; Tang, Wu et al 2004].

Abnormal gene product: The mutant ATRX protein down-regulates the α-globin locus, resulting in thalassemia, and probably suppresses expression of other genes by disturbances in transcription and chromatin structure, leading to malformations and mental retardation [Tang, Park et al 2004; Tang, Wu et al 2004]

Resources

GeneReviews provides information about selected national organizations and resources for the benefit of the reader. GeneReviews is not responsible for information provided by other organizations. Information that appears in the Resources section of a GeneReview is current as of initial posting or most recent update of the GeneReview. Search GeneTests*for this disorder and select* Resources *for the most up-to-date Resources information.*—ED.

American Association on Intellectual and Developmental Disabilities (AAIDD)
444 North Capitol Street NW Suite 846
Washington DC 20001
Phone: 800-424-3688; 202-387-1968
Fax: 202-387-2193

Email: anam@aaidd.org
www.aaidd.org

Medline Plus
Mental retardation

Mental Retardation Association of America, Inc (MRAA)
211 East 300 South Suite 212
Salt Lake City UT 84111
Phone: 801-328-1574

References

Medical Genetic Searches: A specialized PubMed search designed for clinicians that is located on the PubMed Clinical Queries page. PubMed

Published Statements and Policies Regarding Genetic Testing

No specific guidelines regarding genetic testing for this disorder have been developed.

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Chapter Notes

Author Notes

Web: www.ggc.org

Dr. Stevenson's work focuses on the clinical and laboratory delineation of mental retardation and birth defects.

Revision History

- 15 October 2007 (me) Comprehensive update posted to live Web site
- 27 October 2006 (cd) Revision: mutation scanning clinically available
- 24 March 2006 (cd) Revision: sequence analysis of all 35 exons and associated splice junctions of *ATRX* clinically available
- 14 June 2005 (me) Comprehensive update posted to live Web site
- 15 April 2003 (me) Comprehensive update posted to live Web site
- 19 June 2000 (me) Review posted to live Web site
- 29 November 1999 (rs) Original submission