U.S. National Library of Medicine
National Center for Biotechnology Information

NLM Citation: Van Esch H. *MECP2* Duplication Syndrome. 2008 Jan 18 [Updated 2020 May 21]. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024.
Bookshelf URL: https://www.ncbi.nlm.nih.gov/books/

MECP2 Duplication Syndrome

Hilde Van Esch, MD, PhD[1]

Created: January 18, 2008; Updated: May 21, 2020.

Summary

Clinical characteristics

MECP2 duplication syndrome is a severe neurodevelopmental disorder characterized by early-onset hypotonia, feeding difficulty, gastrointestinal manifestations including gastroesophageal reflux and constipation, delayed psychomotor development leading to severe intellectual disability, poor speech development, progressive spasticity, recurrent respiratory infections (in ~75% of affected individuals), and seizures (in ~50%). *MECP2* duplication syndrome is 100% penetrant in males. Occasionally females have been described with a *MECP2* duplication and a range of findings from mild intellectual disability to a phenotype similar to that seen in males. In addition to the core features, autistic behaviors, nonspecific neuroradiologic findings on brain MRI, mottled skin, and urogenital anomalies have been observed in several affected boys.

Diagnosis/testing

The diagnosis of *MECP2* duplication syndrome is established in an individual by identification of a heterozygous whole-gene duplication of *MECP2* on molecular genetic testing.

Management

Treatment of manifestations: Routine management of feeding difficulties, constipation, developmental and speech delays, spasticity, and seizures. Physical therapy to maintain range of motion to reduce likelihood of contractures. Prompt antibiotic treatment for respiratory infections; all vaccines should be given; consider gastrostomy tube if aspiration is present. Social work and care coordination as indicated.

Surveillance: Routine monitoring for growth, feeding issues, constipation, reflux, loss of speech, progressive spasticity, seizure disorder and response to anti-seizure medication, infections, and autistic-like features.

Author Affiliation: 1 Center for Human Genetics, University Hospitals Leuven, Leuven, Belgium; Email: hilde.vanesch@uzleuven.be.

Genetic counseling

MECP2 duplication syndrome is inherited in an X-linked manner. The majority of affected males have inherited the *MECP2* duplication from a heterozygous mother; however, *de novo* genetic alterations have been reported. If the mother of the proband has a *MECP2* duplication, the chance of transmitting it in each pregnancy is 50%. Males who inherit the *MECP2* duplication will be affected; females who inherit the *MECP2* duplication are typically asymptomatic but may exhibit clinical manifestations ranging from mild nonspecific intellectual disability to a severe phenotype similar to that observed in males. If the mother of the proband has a balanced structural chromosome rearrangement involving the Xq28 region, the risk to sibs depends on the specific chromosome rearrangement. Once the *MECP2* duplication has been identified in an affected family member (and/or the mother of the proband is found to be a carrier of a balanced translocation), prenatal testing for a pregnancy at increased risk and preimplantation genetic testing are possible.

Diagnosis

Suggestive Findings

MECP2 duplication syndrome **should be considered** in males with the following clinical findings:

- Severe-to-profound intellectual disability with limited or absent speech
- Early-onset hypotonia with very slow motor development
- Progressive spasticity predominantly of the lower limbs
- Predisposition to infections manifest as recurrent respiratory infections (in 75% of affected males)
- Epileptic seizures (in 50%)
- Other variably present features including autistic features, gastrointestinal dysfunction, and mild facial dysmorphism

Note: *MECP2* duplication syndrome occurs rarely in females because of skewing of X inactivation against the X chromosome that carries the duplicated fragment (see Clinical Characteristics, Heterozygous Females). In rare instances, however, females can be as severely affected as males and similar clinical findings can be observed.

Establishing the Diagnosis

The diagnosis of *MECP2* duplication syndrome **is established** in an individual with suggestive findings and a heterozygous whole-gene duplication of *MECP2* identified by molecular genetic testing (see Table 1).

Molecular genetic testing in a child with developmental delay or an older individual with intellectual disability typically begins with chromosomal microarray analysis (CMA). Note: Single-gene testing is rarely useful and typically NOT recommended.

Chromosomal microarray analysis (CMA) uses oligonucleotide or SNP arrays to detect genome-wide large deletions/duplications (including *MECP2* duplications).

Note: Routine G-banded cytogenetic analysis only detects duplications of Xq28 (the chromosomal locus of *MECP2*) larger than approximately 8 Mb; therefore, this testing is not considered first-tier testing and individuals with *MECP2* duplication syndrome may have a normal G-banded karyotype.

An intellectual disability multigene panel that includes duplication analysis of *MECP2* and other genes of interest (see Differential Diagnosis) is most likely to identify the genetic cause of the condition while limiting identification of variants of uncertain significance and pathogenic variants in genes that do not explain the underlying phenotype if CMA were not performed. Note: (1) The genes included in the panel and the diagnostic sensitivity of the testing used for each gene vary by laboratory and are likely to change over time. (2) Some

multigene panels may include genes not associated with the condition discussed in this *GeneReview*. (3) In some laboratories, panel options may include a custom laboratory-designed panel and/or custom phenotype-focused exome analysis that includes genes specified by the clinician. (4) Methods used in a panel may include sequence analysis, deletion/duplication analysis, and/or other non-sequencing-based tests. For this disorder an intellectual disability multigene panel that also includes deletion/duplication analysis is recommended (see Table 1).

For an introduction to multigene panels click here. More detailed information for clinicians ordering genetic tests can be found here.

Comprehensive genomic testing does not require the clinician to determine which gene(s) are likely involved. **Exome array** (when clinically available) may be considered to detect (multi)exon duplications.

For an introduction to comprehensive genomic testing click here. More detailed information for clinicians ordering genomic testing can be found here.

Table 1. Molecular Genetic Testing Used in *MECP2* Duplication Syndrome

Gene [1]	Method	Proportion of Probands with a Pathogenic Variant [2] Detectable by Method
MECP2	Gene-targeted duplication analysis [3]	100% [4]
	CMA [5]	100% [6]

1. See Table A. Genes and Databases for chromosome locus and protein.
2. See Molecular Genetics for information on allelic variants detected in this gene.
3. Gene-targeted deletion/duplication analysis detects intragenic deletions or duplications. Methods used may include a range of techniques such as quantitative PCR, long-range PCR, multiplex ligation-dependent probe amplification (MLPA), and a gene-targeted microarray designed to detect single-exon deletions or duplications.
4. Duplications ranging from 0.3 to 4 Mb are found in 100% of affected males [Van Esch et al 2005, del Gaudio et al 2006, Smyk et al 2008, Clayton-Smith et al 2009, Lugtenberg et al 2009]. The duplications occur in the chromosome region Xq28, which includes all of *MECP2*.
5. Chromosomal microarray analysis (CMA) uses oligonucleotide or SNP arrays to detect genome-wide large deletions/duplications (including *MECP2*) that cannot be detected by sequence analysis. The ability to determine the size of the deletion/duplication depends on the type of microarray used and the density of probes in the Xq28 region. CMA designs in current clinical use target the Xq28 region.
6. Sanlaville et al [2005]

Clinical Characteristics

Clinical Description

MECP2 duplication syndrome is an X-linked disorder, mainly affecting males. The core phenotype includes developmental delay / intellectual disability, infantile hypotonia, speech and motor delay, recurrent infections, seizures, and gastrointestinal dysfunction. Additional, less frequent clinical features have been described.

More than 300 affected males have been reported to date and the clinical findings are consistent in all reports [Meins et al 2005, Van Esch et al 2005, del Gaudio et al 2006, Friez et al 2006, Smyk et al 2008, Clayton-Smith et al 2009, Echenne et al 2009, Kirk et al 2009, Lugtenberg et al 2009, Prescott et al 2009, Velinov et al 2009, Breman et al 2011, Sanmann et al 2012, Tang et al 2012, Lim et al 2017, Miguet et al 2018, Pascual-Alonso et al 2020].

Table 2. Select Features of *MECP2* Duplication Syndrome

Feature	% of MALES w/Feature	Comment
Developmental delay / Intellectual disability	100%	Most males have moderate-to-severe intellectual disability.
Infantile hypotonia	95%	

Table 2. continued from previous page.

Feature	% of MALES w/Feature	Comment
Feeding issues	60%	
Constipation	61%	
Walk independently or w/support	55%	
Spasticity	65%	Can be an underestimation given that this feature is age related
Seizures	~50%	
Recurrent infections	>75%	Most often affecting the respiratory tract
Nonspecific anomalies on brain imaging	69%	

Feeding/gastrointestinal manifestations. During the first weeks of life, feeding difficulties resulting from hypotonia may become evident in affected males. Children with *MECP2* duplication syndrome are very hypotonic and may also exhibit difficulty with swallowing, gastroesophageal reflux, failure to thrive, and extensive drooling. In some cases, nasogastric tube feeding becomes necessary. In some affected individuals, fundoplication or permanent gastrostomy becomes necessary later in life to improve feeding conditions and prevent aspiration of fluids. Clinically important constipation is reported in more than one third of affected individuals.

Development. As a result of hypotonia, motor developmental milestones including sitting and crawling are severely delayed. Walking is also severely delayed; some individuals have an ataxic gait. One third of affected individuals never walk independently. Speech development is severely delayed; the majority of affected individuals (>60%) do not develop speech. In some individuals who were able to speak some words in early childhood, speech was progressively lost in adolescence. Most affected males function at the level of moderate-to-severe intellectual disability.

In 65% of affected males, hypotonia gives way to spasticity in childhood. The spasticity is more pronounced in the legs; mild contractures may develop over time. Often the use of a wheelchair is necessary in adulthood.

Seizures are seen in nearly 50% of affected individuals with a median age at onset of six years. Multiple seizure types have been observed, the most frequently reported include atonic, tonic-clonic, tonic, and atypical absence seizures [Marafi et al 2019]. There is no specific electroclinical phenotype or specific effective monotherapy or polytherapy. Seizures resistant to treatment have been reported in about 82% of affected males with epilepsy [Marafi et al 2019]. Often it is noted that the onset and the severity of the seizures correlate with neurologic deterioration, characterized by loss of speech, hand use, and/or ambulation.

Recurrent infections. Recurrent respiratory infections, especially recurrent pneumonia that may require assisted ventilation, occur in 75% of affected individuals. Other types of infections have also been described. Recurrent infections may be fatal; death before age 25 years is reported in almost 50% of affected individuals.

Mild dysmorphic features including brachycephaly, midface retrusion, large ears, and depressed nasal bridge may be present.

Growth measurements at birth, including head circumference, are usually normal. Growth throughout childhood, including head circumference, is usually within the normal range.

Other associated findings that can be observed include the following:

- Nonspecific neuroradiologic findings on brain MRI including hypoplasia of the corpus callosum, enlarged ventricles, nonspecific changes in the white matter, and cerebellar hypoplasia [Friez et al 2006, Philippe et al 2013, El Chehadeh et al 2016]

- Autistic features including anxiety, stereotypic hand movements, and decreased sensitivity to pain/temperature [Miguet et al 2018, Giudice-Nairn et al 2019, Pascual-Alonso et al 2020]
- Mottled appearance of the skin
- Urogenital anomalies including bladder dysfunction, cryptorchidism, and small penis [Clayton-Smith et al 2009, Miguet et al 2018]

Heterozygous Females

Most females heterozygous for *MECP2* duplication show extreme-to-complete skewing of X-chromosome inactivation and are asymptomatic. However, neuropsychiatric symptoms including depression, anxiety, and autistic features have been described in heterozygous females with normal intellectual abilities [Ramocki et al 2009].

More recently, several symptomatic females with an Xq28 duplication without skewing of X-chromosome inactivation have been reported. In the majority of these females, the duplication arises from an unbalanced X-autosomal translocation or a genomic insertion elsewhere in the genome, explaining the absence of skewing of the aberrant X chromosome and leading to a complex and severe phenotype. To date, about 20 females have been described with an interstitial Xq28 duplication including *MECP2*. In about half of them, the duplication arose *de novo*, often on the paternal allele. In the other half the duplication was inherited from an apparent asymptomatic mother. The phenotype in females with an interstitial Xq28 duplication is more variable and broader than in affected males, ranging from mild nonspecific intellectual disability to a severe phenotype similar to that observed in males. Studies show that the clinical severity in affected females did not necessarily correlate with the X chromosome inactivation pattern in blood [Bijlsma et al 2012, Shimada et al 2013, Fieremans et al 2014, Novara et al 2014, Scott Schwoerer et al 2014, San Antonio-Arce et al 2016, El Chehadeh et al 2017].

Genotype-Phenotype Correlations

No clear genotype-phenotype correlation has been identified to date. However, the following have been noted:

- Individuals with a large, cytogenetically visible Xq28 duplication have growth deficiency, microcephaly, and urogenital anomalies in addition to those findings described in Heterozygous Females [Lachlan et al 2004, Sanlaville et al 2005].
- A more important correlation with clinical severity is *MECP2* copy number, as triplication of the *MECP2* region apparently results in a more severe phenotype [del Gaudio et al 2006, Tang et al 2012].

Penetrance

MECP2 duplications are believed to be completely penetrant in males.

Prevalence

To date, more than 300 affected individuals have been reported [Meins et al 2005, Van Esch et al 2005, del Gaudio et al 2006, Friez et al 2006, Smyk et al 2008, Clayton-Smith et al 2009, Echenne et al 2009, Kirk et al 2009, Lugtenberg et al 2009, Prescott et al 2009, Velinov et al 2009, Honda et al 2012, Sanmann et al 2012, Tang et al 2012, Lim et al 2017, Miguet et al 2018, Pascual-Alonso et al 2020]. The exact prevalence of *MECP2* duplication syndrome is unknown, but data from several large array-based studies suggest a prevalence of approximately 1% in males with moderate-to-severe intellectual disability. A recent Australian study calculated that the birth prevalence of *MECP2* duplication syndrome in Australia was 0.65:100,000 for all live births and 1:100,000 for males, with a median age at diagnosis of 23.5 months (range: birth - 13 years) [Giudice-Nairn et al 2019]. When a clear X-linked inheritance pattern is present, the likelihood of detecting a *MECP2* duplication is higher.

Genetically Related (Allelic) Disorders

Other kinds of pathogenic variants and intragenic rearrangements of *MECP2* are associated with a spectrum of phenotypes in females ranging from **classic Rett syndrome** to **variant Rett syndrome** with a broader clinical phenotype (either milder or more severe than classic Rett syndrome) to mild learning disabilities; the spectrum in males ranges from severe neonatal encephalopathy to pyramidal signs, parkinsonism, and macroorchidism syndrome to severe syndromic/nonsyndromic intellectual disability.

Differential Diagnosis

Because the phenotypic features associated with *MECP2* duplication syndrome are not sufficient to diagnose this condition, all disorders with intellectual disability without other distinctive findings should be considered in the differential diagnosis. See OMIM Autosomal Dominant, Autosomal Recessive, Nonsyndromic X-Linked, and Syndromic X-Linked Intellectual Developmental Disorder Phenotypic Series.

Int22h1/int22h2-mediated Xq28 duplication syndrome. Several other recurrent duplications involving the X chromosome and resulting in X-linked intellectual disability in males have been identified. On chromosome fragment Xq28, the int22h1/int22h2-mediated Xq28 duplication syndrome has been described, caused by 0.5-Mb duplication in Xq28 located telomeric to the *MECP2* locus and extending from 154.1 to 154.6 Mb. Cognitive impairment and recurrent infections are common in both syndromes. However, the cognitive impairment in int22h1/int22h2-mediated Xq28 duplication syndrome is less severe and infantile hypotonia, spasticity, and seizures have not been observed.

Management

Evaluations Following Initial Diagnosis

To establish the extent of disease and needs in an individual diagnosed with *MECP2* duplication syndrome, the evaluations summarized in Table 3 (if not performed as part of the evaluation that led to diagnosis) are recommended.

Table 3. Recommended Evaluations Following Initial Diagnosis in Individuals with *MECP2* Duplication Syndrome

System/Concern	Evaluation	Comment
Gastrointestinal/ Feeding	Gastroenterology / nutrition / feeding team eval	• To incl eval of aspiration risk & nutritional status • Consider eval for gastric tube placement in those w/ dysphagia &/or aspiration risk.
Development	Developmental assessment	• To incl motor, adaptive, cognitive, & speech/language eval • Eval for early intervention / special education
Musculoskeletal	Orthopedics / physical medicine & rehab / PT & OT eval	To include assessment of: • Gross motor & fine motor skills • Contractures, spasticity • Mobility, activities of daily living, & need for adaptive devices • Need for PT (to improve gross motor skills) &/or OT (to improve fine motor skills)
Neurologic	Neurologic eval	Consider EEG if seizures are a concern.
Immunologic	Clinical assessment for history & risk of recurrent infections	

Table 3. continued from previous page.

System/Concern	Evaluation	Comment
Psychiatric/ Behavioral	Neuropsychiatric eval	For persons age >12 mos: screening for behavior concerns incl ADHD, anxiety, &/or traits suggestive of ASD
Genetic counseling	By genetics professionals [1]	To inform affected persons & families re nature, MOI, & implications of *MECP2* duplication syndrome to facilitate medical & personal decision making
Family support & resources	Assess need for: • Community or online resources such as Parent to Parent; • Social work involvement for parental support; • Home nursing referral.	

ADHD = attention-deficit/hyperactivity disorder; ASD = autism spectrum disorder; MOI = mode of inheritance; OT = occupational therapy; PT = physical therapy
1. Medical geneticist, certified genetic counselor, certified advanced genetic nurse

Treatment of Manifestations

Table 4. Treatment of Manifestations in Individuals with *MECP2* Duplication Syndrome

Manifestation/Concern	Treatment	Considerations/Other
Poor weight gain / Failure to thrive	• Feeding therapy • Gastrostomy tube placement may be required for persistent feeding issues.	Low threshold for clinical feeding eval &/or radiographic swallowing study if clinical signs or symptoms of dysphagia
Bowel dysfunction	Monitor for constipation.	Stool softeners, prokinetics, osmotic agents, or laxatives as needed
Developmental delay / Intellectual disability	See Developmental Delay / Intellectual Disability Management Issues.	
Spasticity	Orthopedics / physical medicine & rehab / PT & OT incl stretching to help avoid contractures & falls	• Consider need for positioning & mobility devices, disability parking placard. • PT w/attention to stretching exercises can help maintain joint range of motion & prevent secondary contractures, thus prolonging ability to walk.
Epilepsy	Standardized treatment w/ASMs by experienced neurologist	• Many ASMs may be effective; none has been demonstrated effective specifically for this disorder. • Seizure treatment may require multidrug therapy. • Education of parents/caregivers [1]
Recurrent infections	• Treat infections (esp respiratory tract) immediately w/appropriate antibiotics. • All vaccines should be given. • If aspiration occurs, consider placement of a permanent gastrostomy.	Consider evaluating post-vaccination titers for pneumococcus; if they are not sufficient, additional vaccination may be required.

Table 4. continued from previous page.

Manifestation/Concern	Treatment	Considerations/Other
Family/Community	• Ensure appropriate social work involvement to connect families w/local resources, respite, & support. • Coordinate care to manage multiple subspecialty appointments, equipment, medications, & supplies.	Ongoing assessment of need for palliative care involvement &/or home nursing

ASM = anti-seizure medication; OT = occupational therapy; PT = physical therapy
1. Education of parents/caregivers regarding common seizure presentations is appropriate. For information on non-medical interventions and coping strategies for children diagnosed with epilepsy, see Epilepsy Foundation Toolbox.

Developmental Delay / Intellectual Disability Management Issues

The following information represents typical management recommendations for individuals with developmental delay / intellectual disability in the United States; standard recommendations may vary from country to country.

Ages 0-3 years. Referral to an early intervention program is recommended for access to occupational, physical, speech, and feeding therapy as well as infant mental health services, special educators, and sensory impairment specialists. In the US, early intervention is a federally funded program available in all states that provides in-home services to target individual therapy needs.

Ages 3-5 years. In the US, developmental preschool through the local public school district is recommended. Before placement, an evaluation is made to determine needed services and therapies and an individualized education plan (IEP) is developed for those who qualify based on established motor, language, social, or cognitive delay. The early intervention program typically assists with this transition. Developmental preschool is center based; for children too medically unstable to attend, home-based services are provided.

All ages. Consultation with a developmental pediatrician is recommended to ensure the involvement of appropriate community, state, and educational agencies (US) and to support parents in maximizing quality of life. Some issues to consider:

- IEP services:
  - An IEP provides specially designed instruction and related services to children who qualify.
  - IEP services will be reviewed annually to determine whether any changes are needed.
  - Special education law requires that children participating in an IEP be in the least restrictive environment feasible at school and included in general education as much as possible, when and where appropriate.
  - PT, OT, and speech services will be provided in the IEP to the extent that the need affects the child's access to academic material. Beyond that, private supportive therapies based on the affected individual's needs may be considered. Specific recommendations regarding type of therapy can be made by a developmental pediatrician.
  - As a child enters the teen years, a transition plan should be discussed and incorporated in the IEP. For those receiving IEP services, the public school district is required to provide services until age 21.
- A 504 plan (Section 504: a US federal statute that prohibits discrimination based on disability) can be considered for those who require accommodations or modifications such as front-of-class seating, assistive technology devices, classroom scribes, extra time between classes, modified assignments, and enlarged text.
- Developmental Disabilities Administration (DDA) enrollment is recommended. DDA is a US public agency that provides services and support to qualified individuals. Eligibility differs by state but is typically determined by diagnosis and/or associated cognitive/adaptive disabilities.

- Families with limited income and resources may also qualify for supplemental security income (SSI) for their child with a disability.

Motor Dysfunction

Gross motor dysfunction

- Physical therapy is recommended to maximize mobility and to reduce the risk for later-onset orthopedic complications (e.g., contractures, scoliosis, hip dislocation).
- Consider use of durable medical equipment and positioning devices as needed (e.g., wheelchairs, walkers, bath chairs, orthotics, adaptive strollers).
- For muscle tone abnormalities including hypertonia or dystonia, consider involving appropriate specialists to aid in management of baclofen, Botox®, or orthopedic procedures.

Fine motor dysfunction. Occupational therapy is recommended for difficulty with fine motor skills that affect adaptive function such as feeding, grooming, dressing, and writing.

Oral motor dysfunction should be assessed at each visit and clinical feeding evaluations and/or radiographic swallowing studies should be obtained for choking/gagging during feeds, poor weight gain, frequent respiratory illnesses, or feeding refusal that is not otherwise explained. Assuming that the child is safe to eat by mouth, feeding therapy (typically from an occupational or speech therapist) is recommended to help improve coordination or sensory-related feeding issues. Feeds can be thickened or chilled for safety. When feeding dysfunction is severe, an NG-tube or G-tube may be necessary.

Communication issues. Consider evaluation for alternative means of communication (e.g., augmentative and alternative communication [AAC]) for individuals who have expressive language difficulties. An AAC evaluation can be completed by a speech-language pathologist who has expertise in the area. The evaluation will consider cognitive abilities and sensory impairments to determine the most appropriate form of communication. AAC devices can range from low-tech, such as picture exchange communication, to high-tech, such as voice-generating devices. Contrary to popular belief, AAC devices do not hinder verbal development of speech, but rather support optimal speech and language development.

Social/Behavioral Concerns

Children may qualify for and benefit from interventions used in treatment of autism spectrum disorder, including applied behavior analysis (ABA). ABA therapy is targeted to the individual child's behavioral, social, and adaptive strengths and weaknesses and typically performed one on one with a board-certified behavior analyst.

Consultation with a developmental pediatrician may be helpful in guiding parents through appropriate behavior management strategies or providing prescription medications, such as medication used to treat attention-deficit/hyperactivity disorder, when necessary.

Concerns about serious aggressive or destructive behavior can be addressed by a pediatric psychiatrist.

Surveillance

Table 5. Recommended Surveillance for Individuals with *MECP2* Duplication Syndrome

System/Concern	Evaluation	Frequency
Feeding	• Measurement of growth parameters • Eval of nutritional status & safety of oral intake	At each visit
Gastrointestinal	Monitor for constipation & reflux.	
Development	Monitor developmental progress & educational needs.	
Musculoskeletal	Physical medicine, OT/PT assessment of mobility, self-help skills	
Neurologic	• Monitor those w/seizures as clinically indicated. • Assess for new manifestations such as seizures, changes in tone, spasticity.	
Immunologic	Assess frequency & type of infections.	
Psychiatric/ Behavioral	Behavioral assessment for anxiety, attention, & autistic-like features	
Miscellaneous/ Other	Assess family need for social work support (e.g., palliative/respite care, home nursing, other local resources) & care coordination.	

OT = occupational therapy; PT = physical therapy

Evaluation 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 in the US and EU Clinical Trials Register in Europe 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.

Genetic Counseling

Genetic counseling is the process of providing individuals and families with information on the nature, mode(s) of 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; it is not meant to address all personal, cultural, or ethical issues that may arise or to substitute for consultation with a genetics professional. —ED.

Mode of Inheritance

MECP2 duplication syndrome is inherited in an X-linked manner.

Risk to Family Members

Parents of a male proband

- The father of an affected male will not have *MECP2* duplication syndrome nor will he be hemizygous for the *MECP2* duplication; therefore, he does not require further evaluation/testing.
- In a family with more than one affected individual, the mother of an affected male is either an obligate heterozygote for an interstitial *MECP2* duplication or a carrier of a balanced translocation involving Xq28.

Note: If a woman has more than one affected child and no other affected relatives and if the *MECP2* duplication (or a predisposing balanced translocation) cannot be detected in her leukocyte DNA, she most likely has germline mosaicism.

- If a male is the only affected family member (i.e., a simplex case), the mother may be heterozygous for a *MECP2* duplication or have a balanced translocation involving Xq28; or the causative genetic alteration may have occurred *de novo* in the affected male.

  In the majority of males who have an interstitial *MECP2* duplication (not an X/Y rearrangement, or insertion elsewhere in the genome), the duplication is inherited from a heterozygous mother. However, *de novo* duplications have been described in several males [Giudice-Nairn et al 2019, Pascual-Alonso et al 2020].

- Recommendations for the evaluation of the mother of a male proband include molecular genetic testing for the *MECP2* duplication identified in the proband and chromosome analysis to determine if a balanced chromosome rearrangement involving the Xq28 region is present.

- Typically, mothers who are heterozygous for a *MECP2* duplication show extreme-to-complete skewing of X-chromosome inactivation and are asymptomatic. However, neuropsychiatric symptoms including depression, anxiety, and autistic features were described in heterozygous females with normal intellectual abilities [Ramocki et al 2009] (see Clinical Characteristics, Heterozygous Females).

Sibs of a male proband. The risk to sibs depends on the genetic status of the mother:

- If the mother of the proband has an interstitial *MECP2* duplication, the chance of transmitting it in each pregnancy is 50%.
  - Males who inherit the *MECP2* duplication will be affected.
  - Females who inherit the *MECP2* duplication will be heterozygous and will typically be asymptomatic (with extreme to complete skewing of X-chromosome inactivation). However, heterozygous females may rarely exhibit clinical manifestations ranging from neuropsychiatric symptoms and mild nonspecific intellectual disability to a severe phenotype similar to that observed in males [El Chehadeh et al 2017]. It is not possible to correctly predict clinical outcome in a heterozygous female as clinical severity does not necessarily correlate with the X-chromosome inactivation pattern in blood [El Chehadeh et al 2017].
- If the mother of the proband has a balanced structural chromosome rearrangement involving the Xq28 region, the risk to sibs is increased. The estimated risk depends on the specific chromosome rearrangement.
- If a male proband represents a simplex case (i.e., a single occurrence in a family) and if testing of maternal leukocyte DNA does not detect a *MECP2* duplication or chromosome rearrangement involving the Xq28 region, the risk to sibs is low but greater than that of the general population because of the theoretic possibility of germline mosaicism.

Offspring of a male proband. No affected male has reproduced.

Other family members. If a *MECP2* duplication or chromosome rearrangement is identified in the mother of a male proband, the proband's maternal aunts may be at risk of also having the genetic alteration and the aunts' offspring, depending on their sex, may be at risk of being heterozygous or hemizygous for the genetic alteration.

Heterozygote Detection

Molecular genetic testing of at-risk female relatives to determine their genetic status is most informative if the causative genetic alteration has been identified in the proband.

Note: Females who are heterozygous for a *MECP2* duplication will typically be asymptomatic (with extreme-to-complete skewing of X-chromosome inactivation). However, heterozygous females may rarely exhibit clinical manifestations ranging from neuropsychiatric symptoms and mild nonspecific intellectual disability to a severe phenotype similar to that observed in males [El Chehadeh et al 2017] (see Clinical Characteristics, Heterozygous Females).

Related Genetic Counseling Issues

Family planning

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

Prenatal Testing and Preimplantation Genetic Testing

Once the *MECP2* duplication has been identified in an affected family member (and/or the mother of the proband is found to be a carrier of a balanced translocation), prenatal testing for a pregnancy at increased risk and preimplantation genetic testing are possible.

Note: X-inactivation analysis of amniotic cells is not informative because the X-inactivation pattern in amniotic cells may not correlate with X inactivation in the fetal body and brain.

Differences in perspective may exist among medical professionals and within families regarding the use of prenatal testing. While most centers would consider use of prenatal testing to be a personal decision, discussion of these issues may be helpful.

Resources

GeneReviews staff has selected the following disease-specific and/or umbrella support organizations and/or registries for the benefit of individuals with this disorder and their families. GeneReviews is not responsible for the information provided by other organizations. For information on selection criteria, click here.

- **MECP2 Duplicatie Syndroom**
  Netherlands
  MECP2 duplicatie syndroom
- **American Epilepsy Society**
  www.aesnet.org
- **CDC - Developmental Disabilities**
  Phone: 800-CDC-INFO
  Email: cdcinfo@cdc.gov
  Intellectual Disability
- **Epilepsy Foundation**
  Phone: 301-459-3700
  Fax: 301-577-2684
  www.epilepsy.com
- **Unique: Understanding Rare Chromosome and Gene Disorders**
  United Kingdom

Phone: +44 (0) 1883 723356
Email: info@rarechromo.org
rarechromo.org

Molecular Genetics

Information in the Molecular Genetics and OMIM tables may differ from that elsewhere in the GeneReview: tables may contain more recent information. —ED.

Table A. MECP2 Duplication Syndrome: Genes and Databases

Gene	Chromosome Locus	Protein	Locus-Specific Databases	HGMD	ClinVar
MECP2	Xq28	Methyl-CpG-binding protein 2	MECP2 @ LOVD CCHMC - Human Genetics Mutation Database (MECP2) RettBASE	MECP2	MECP2

Data are compiled from the following standard references: gene from HGNC; chromosome locus from OMIM; protein from UniProt. For a description of databases (Locus Specific, HGMD, ClinVar) to which links are provided, click here.

Table B. OMIM Entries for MECP2 Duplication Syndrome (View All in OMIM)

300005	METHYL-CpG-BINDING PROTEIN 2; MECP2
300260	INTELLECTUAL DEVELOPMENTAL DISORDER, X-LINKED, SYNDROMIC, LUBS TYPE; MRXSL

Molecular Pathogenesis

MECP2 encodes MeCP2, a chromatin-bound nuclear protein that binds methylated DNA and hence plays an important role in gene regulation. In addition to the well-accepted role of MeCP2 as transcriptional repressor, recent studies have shown MeCP2 to be involved in RNA processing and active transcription as well. Studies have shown that hundreds of genes may be regulated by MeCP2 in a cell-specific manner [Shahbazian & Zoghbi 2002, Chahrour et al 2008, Skene et al 2010, Connolly & Zhou 2019]. While MeCP2 is ubiquitously present in various human tissues, it is expressed abundantly in the brain [Shahbazian & Zoghbi 2002], and within the brain, neurons express the highest levels. During embryogenesis, the neuronal level of MeCP2 is initially low, increases during the course of postnatal development, and reaches its maximum with maturation [Skene et al 2010]. Both loss of *MECP2* (see Genetically Related Disorders) and duplication of *MECP2* lead to intellectual disability syndrome, indicating that a correct dose of the protein is essential for normal brain development.

Overexpression of the MeCP2 protein could have detrimental effects on brain development and function as shown in mouse models [Collins et al 2004] and in the human [Van Esch et al 2005, Ramocki & Zoghbi 2008]. A more recent human neuronal in vitro model, using the induced pluripotent stem (iPS) cell technology, showed that human iPS-derived neurons, carrying the duplication, have an abnormal morphology and altered electrophysiologic behavior [Nageshappa et al 2016].

Mechanism of disease causation. The genomic duplication involving *MECP2* leads to increased protein expression.

***MECP2*-specific laboratory technical considerations.** As this is a copy number variation (CNV), it can only be diagnosed by using a quantitative method such as chromosomal microarray analysis (CMA) or CNV calling using whole-genome data.

Chapter Notes

Author Notes

Hilde Van Esch is a clinical geneticist and researcher with focus on genetics of intellectual disability and brain malformations.

Acknowledgments

The author's research has received funding from Fonds voor Wetenschappelijk Onderzoek, Vlaanderen.

Revision History

- 21 May 2020 (sw) Comprehensive update posted live
- 9 October 2014 (me) Comprehensive update posted live
- 24 June 2010 (me) Comprehensive update posted live
- 18 January 2008 (me) Review posted live
- 12 October 2007 (hve) Original submission

References

Literature Cited

Bijlsma EK, Collins A, Papa FT, Tejada MI, Wheeler P, Peeters EA, Gijsbers AC, van de Kamp JM, Kriek M, Losekoot M, Broekma AJ, Crolla JA, Pollazzon M, Mucciolo M, Katzaki E, Disciglio V, Ferreri MI, Marozza A, Mencarelli MA, Castagnini C, Dosa L, Ariani F, Mari F, Canitano R, Hayek G, Botella MP, Gener B, Mínguez M, Renieri A, Ruivenkamp CA. Xq28 duplications including MECP2 in five females: Expanding the phenotype to severe mental retardation. Eur J Med Genet. 2012;55:404–13. PubMed PMID: 22522176.

Breman AM, Ramocki MB, Kang SH, Williams M, Freedenberg D, Patel A, Bader PI, Cheung SW. MECP2 duplications in six patients with complex sex chromosome rearrangements. Eur J Hum Genet. 2011;19:409–15. PubMed PMID: 21119712.

Chahrour M, Jung SY, Shaw C, Zhou X, Wong ST, Qin J, Zoghbi HY. MeCP2, a key contributor to neurological disease, activates and represses transcription. Science. 2008;320:1224–9. PubMed PMID: 18511691.

Collins AL, Levenson JM, Vilaythong AP, Richman R, Armstrong DL, Noebels JL, David Sweatt J, Zoghbi HY. Mild overexpression of MeCP2 causes a progressive neurological disorder in mice. Hum Mol Genet. 2004;13:2679–89. PubMed PMID: 15351775.

Connolly DR, Zhou Z. Genomic insights into MeCP2 function: a role for the maintenance of chromatin architecture. Curr Opin Neurobiol. 2019;59:174–9. PubMed PMID: 31430649.

Clayton-Smith J, Walters S, Hobson E, Burkitt-Wright E, Smith R, Toutain A, Amiel J, Lyonnet S, Mansour S, Fitzpatrick D, Ciccone R, Ricca I, Zuffardi O, Donnai D. Xq28 duplication presenting with intestinal and bladder dysfunction and a distinctive facial appearance. Eur J Hum Genet. 2009;17:434–43. PubMed PMID: 18854860.

del Gaudio D, Fang P, Scaglia F, Ward PA, Craigen WJ, Glaze DG, Neul JL, Patel A, Lee JA, Irons M, Berry SA, Pursley AA, Grebe TA, Freedenberg D, Martin RA, Hsich GE, Khera JR, Friedman NR, Zoghbi HY, Eng CM, Lupski JR, Beaudet al Cheung SW, Roa BB. Increased MECP2 gene copy number as the result of genomic duplication in neurodevelopmentally delayed males. Genet Med. 2006;8:784–92. PubMed PMID: 17172942.

Echenne B, Roubertie A, Lugtenberg D, Kleefstra T, Hamel BC, Van Bokhoven H, Lacombe D, Philippe C, Jonveaux P, de Brouwer AP. Neurologic aspects of MECP2 gene duplication in male patients. Pediatr Neurol. 2009;41:187–91. PubMed PMID: 19664534.

El Chehadeh S, Faivre L, Mosca-Boidron AL, Malan V, Amiel J, Nizon M, Touraine R, Prieur F, Pasquier L, Callier P, Lefebvre M, Marle N, Dubourg C, Julia S, Sarret C, Francannet C, Laffargue F, Boespflug-Tanguy O, David A, Isidor B, Le Caignec C, Vigneron J, Leheup B, Lambert L, Philippe C, Cuisset JM, Andrieux J, Plessis G, Toutain A, Goldenberg A, Cormier-Daire V, Rio M, Bonnefont JP, Thevenon J, Echenne B, Journel H, Afenjar A, Burglen L, Bienvenu T, Addor MC, Lebon S, Martinet D, Baumann C, Perrin L, Drunat S, Jouk PS, Devillard F, Coutton C, Lacombe D, Delrue MA, Philip N, Moncla A, Badens C, Perreton N, Masurel A, Thauvin-Robinet C, Des Portes V, Guibaud L. Large national series of patients with Xq28 duplication involving MECP2: delineation of brain MRI abnormalities in 30 affected patients. Am J Med Genet A. 2016;170A:116–29. PubMed PMID: 26420639.

El Chehadeh S, Touraine R, Prieur F, Reardon W, Bienvenu T, Chantot-Bastaraud S, Doco-Fenzy M, Landais E, Philippe C, Marle N, Callier P, Mosca-Boidron AL, Mugneret F, Le Meur N, Goldenberg A, Guerrot AM, Chambon P, Satre V, Coutton C, Jouk PS, Devillard F, Dieterich K, Afenjar A, Burglen L, Moutard ML, Addor MC, Lebon S, Martinet D, Alessandri JL, Doray B, Miguet M, Devys D, Saugier-Veber P, Drunat S, Aral B, Kremer V, Rondeau S, Tabet AC, Thevenon J, Thauvin-Robinet C, Perreton N, Des Portes V, Faivre L. Xq28 duplication including MECP2 in six unreported affected females: what can we learn for diagnosis and genetic counselling? Clin Genet. 2017;91:576–88. PubMed PMID: 27761913.

Fieremans N, Bauters M, Belet S, Verbeeck J, Jansen AC, Seneca S, Roelens F, De Baere E, Marynen P, Froyen G. De novo MECP2 duplications in two females with intellectual disability and unfavorable complete skewed X-inactivation. Hum Genet. 2014;133:1359–67. PubMed PMID: 25037250.

Friez MJ, Jones JR, Clarkson K, Lubs H, Abuelo D, Bier JA, Pai S, Simensen R, Williams C, Giampietro PF, Schwartz CE, Stevenson RE. Recurrent infections, hypotonia, and mental retardation caused by duplication of MECP2 and adjacent region in Xq28. Pediatrics. 2006;118:e1687–95. PubMed PMID: 17088400.

Giudice-Nairn P, Downs J, Wong K, Wilson D, Ta D, Gattas M, Amor D, Thompson E, Kirrali-Borri C, Ellaway C, Leonard H. The incidence, prevalence and clinical features of MECP2 duplication syndrome in Australian children. J Paediatr Child Health. 2019;55:1315–22. PubMed PMID: 30756435.

Honda S, Satomura S, Hayashi S, Imoto I, Nakagawa E, Goto Y, Inazawa J; Japanese Mental Retardation Consortium. Concomitant microduplications of MECP2 and ATRX in male patients with severe mental retardation. J Hum Genet. 2012;57:73–7. PubMed PMID: 22129561.

Kirk EP, Malaty-Brevaud V, Martini N, Lacoste C, Levy N, Maclean K, Davies L, Philip N, Badens C. The clinical variability of the MECP2 duplication syndrome: description of two families with duplications excluding L1CAM and FLNA. Clin Genet. 2009;75:301–3. PubMed PMID: 19018795.

Lachlan KL, Collinson MN, Sandford RO, van Zyl B, Jacobs PA, Thomas NS. Functional disomy resulting from duplications of distal Xq in four unrelated patients. Hum Genet. 2004;115:399–408. PubMed PMID: 15338277.

Lim Z, Downs J, Wong K, Ellaway C, Leonard H. Expanding the clinical picture of the MECP2 duplication syndrome. Clin Genet. 2017;91:557–63. PubMed PMID: 27247049.

Lugtenberg D, Kleefstra T, Oudakker AR, Nillesen WM, Yntema HG, Tzschach A, Raynaud M, Rating D, Journel H, Chelly J, Goizet C, Lacombe D, Pedespan JM, Echenne B, Tariverdian G, O'Rourke D, King MD, Green A, van Kogelenberg M, Van Esch H, Gecz J, Hamel BC, van Bokhoven H, de Brouwer AP. Structural variation in Xq28: MECP2 duplications in 1% of patients with unexplained XLMR and in 2% of male patients with severe encephalopathy. Eur J Hum Genet. 2009;17:444–53. PubMed PMID: 18985075.

Marafi D, Suter B, Schultz R, Glaze D, Pavlik VN, Goldman AM. Spectrum and time course of epilepsy and the associated cognitive decline in *MECP2* duplication syndrome. Neurology. 2019;92:e108–e114. PubMed PMID: 30552298.

Meins M, Lehmann J, Gerresheim F, Herchenbach J, Hagedorn M, Hameister K, Epplen JT. Submicroscopic duplication in Xq28 causes increased expression of the MECP2 gene in a boy with severe mental retardation and features of Rett syndrome. J Med Genet. 2005;42:e12. PubMed PMID: 15689435.

Miguet M, Faivre L, Amiel J, Nizon M, Touraine R, Prieur F, Pasquier L, Lefebvre M, Thevenon J, Dubourg C, Julia S, Sarret C, Remerand G, Francannet C, Laffargue F, Boespflug-Tanguy O, David A, Isidor B, Vigneron J, Leheup B, Lambert L, Philippe C, Béri-Dexheimer M, Cuisset JM, Andrieux J, Plessis G, Toutain A, Guibaud L, Cormier-Daire V, Rio M, Bonnefont JP, Echenne B, Journel H, Burglen L, Chantot-Bastaraud S, Bienvenu T, Baumann C, Perrin L, Drunat S, Jouk PS, Dieterich K, Devillard F, Lacombe D, Philip N, Sigaudy S, Moncla A, Missirian C, Badens C, Perreton N, Thauvin-Robinet C. AChro-Puce R, Pedespan JM, Rooryck C, Goizet C, Vincent-Delorme C, Duban-Bedu B, Bahi-Buisson N, Afenjar A, Maincent K, Héron D, Alessandri JL, Martin-Coignard D, Lesca G, Rossi M, Raynaud M, Callier P, Mosca-Boidron AL, Marle N, Coutton C, Satre V, Caignec CL, Malan V, Romana S, Keren B, Tabet AC, Kremer V, Scheidecker S, Vigouroux A, Lackmy-Port-Lis M, Sanlaville D, Till M, Carneiro M, Gilbert-Dussardier B, Willems M, Van Esch H, Portes VD, El Chehadeh S. Further delineation of the MECP2 duplication syndrome phenotype in 59 French male patients, with a particular focus on morphological and neurological features. J Med Genet. 2018;55:359–71. PubMed PMID: 29618507.

Nageshappa S, Carromeu C, Trujillo CA, Mesci P, Espuny-Camacho I, Pasciuto E, Vanderhaeghen P, Verfaillie CM, Raitano S, Kumar A, Carvalho CM, Bagni C, Ramocki MB, Araujo BH, Torres LB, Lupski JR, Van Esch H, Muotri AR. Altered neuronal network and rescue in a human MECP2 duplication model. Mol Psychiatry. 2016;21:178–88. PubMed PMID: 26347316.

Novara F, Simonati A, Sicca F, Battini R, Fiori S, Contaldo A, Criscuolo L, Zuffardi O, Ciccone R. MECP2 duplication phenotype in symptomatic females: report of three further cases. Mol Cytogenet. 2014;7:10. PubMed PMID: 24472397.

Pascual-Alonso A, Blasco L, Vidal S, Gean E, Rubio P, O'Callaghan M, Martínez-Monseny AF, Castells AA, Xiol C, Català V, Brandi N, Pacheco P, Ros C, Del Campo M, Guillén E, Ibañez S, Sánchez MJ, Lapunzina P, Nevado J, Santos F, Lloveras E, Ortigoza-Escobar JD, Tejada MI, Maortua H, Martínez F, Orellana C, Roselló M, Mesas MA, Obón M, Plaja A, Fernández-Ramos JA, Tizzano E, Marín R, Peña-Segura JL, Alcántara S, Armstrong J. Molecular characterization of Spanish patients with MECP2 duplication syndrome. Clin Genet. 2020;97:610–20. PubMed PMID: 32043567.

Philippe O, Rio M, Malan V, Van Esch H, Baujat G, Bahi-Buisson N, Valayannopoulos V, Gesny R, Bonnefont JP, Munnich A, Froyen G, Amiel J, Boddaert N, Colleaux L. NF-κB signalling requirement for brain myelin formation is shown by genotype/MRI phenotype correlations in patients with Xq28 duplications. Eur J Hum Genet. 2013;21:195–9. PubMed PMID: 22805531.

Prescott TE, Rødningen OK, Bjørnstad A, Stray-Pedersen A. Two brothers with a microduplication including the MECP2 gene: rapid head growth in infancy and resolution of susceptibility to infection. Clin Dysmorphol. 2009;18:78–82. PubMed PMID: 19057379.

Ramocki MB, Zoghbi HY. Failure of neuronal homeostasis results in common neuropsychiatric phenotypes. Nature. 2008;455:912–8. PubMed PMID: 18923513.

Ramocki MB, Peters SU, Tavyev YJ, Zhang F, Carvalho CM, Schaaf CP, Richman R, Fang P, Glaze DG, Lupski JR, Zoghbi HY. Autism and other neuropsychiatric symptoms are prevalent in individuals with MeCP2 duplication syndrome. Ann Neurol. 2009;66:771–82. PubMed PMID: 20035514.

San Antonio-Arce V, Fenollar-Cortés M, Oancea Ionescu R, DeSantos-Moreno T, Gallego-Merlo J, Illana Cámara FJ, Cotarelo Pérez MC. *MECP2* duplications in symptomatic females: report on 3 patients showing the broad phenotypic spectrum. Child Neurol Open. 2016.:3.

Sanlaville D, Prieur M, de Blois MC, Genevieve D, Lapierre JM, Ozilou C, Picq M, Gosset P, Morichon-Delvallez N, Munnich A, Cormier-Daire V, Baujat G, Romana S, Vekemans M, Turleau C. Functional disomy of the Xq28 chromosome region. Eur J Hum Genet. 2005;13:579–85. PubMed PMID: 15741994.

Sanmann JN, Bishay DL, Starr LJ, Bell CA, Pickering DL, Stevens JM, Kahler SG, Olney AH, Schaefer GB, Sanger WG. Characterization of six novel patients with MECP2 duplications due to unbalanced rearrangements of the X chromosome. Am J Med Genet A. 2012;158A:1285–91. PubMed PMID: 22581587.

Scott Schwoerer J, Laffin J, Haun J, Raca G, Friez MJ, Giampietro PF. MECP2 duplication: possible cause of severe phenotype in females. Am J Med Genet A. 2014;164A:1029–34. PubMed PMID: 24458799.

Shahbazian MD, Zoghbi HY. Rett syndrome and MeCP2: linking epigenetics and neuronal function. Am J Hum Genet. 2002;71:1259–72. PubMed PMID: 12442230.

Shimada S, Okamoto N, Ito M, Arai Y, Momosaki K, Togawa M, Maegaki Y, Sugawara M, Shimojima K, Osawa M, Yamamoto T. MECP2 duplication syndrome in both genders. Brain Dev. 2013;35:411–9. PubMed PMID: 22877836.

Skene PJ, Illingworth RS, Webb S, Kerr AR, James KD, Turner DJ, Andrews R, Bird AP. Neuronal MeCP2 is expressed at near histone-octamer levels and globally alters the chromatin state. Mol Cell. 2010;37:457–68. PubMed PMID: 20188665.

Smyk M, Obersztyn E, Nowakowska B, Nawara M, Cheung SW, Mazurczak T, Stankiewicz P, Bocian E. Different-sized duplications of Xq28, including MECP2, in three males with mental retardation, absent or delayed speech, and recurrent infections. Am J Med Genet B Neuropsychiatr Genet. 2008;147B:799–806. PubMed PMID: 18165974.

Tang SS, Fernandez D, Lazarou LP, Singh R, Fallon P. MECP2 triplication in 3 brothers - a rarely described cause of familial neurological regression in boys. Eur J Paediatr Neurol. 2012;16:209–12. PubMed PMID: 21821449.

Van Esch H, Bauters M, Ignatius J, Jansen M, Raynaud M, Hollanders K, Lugtenberg D, Bienvenu T, Jensen LR, Gecz J, Moraine C, Marynen P, Fryns JP, Froyen G. Duplication of the MECP2 region is a frequent cause of severe mental retardation and progressive neurological symptoms in males. Am J Hum Genet. 2005;77:442–53. PubMed PMID: 16080119.

Velinov M, Novelli A, Gu H, Fenko M, Dolzhanskaya N, Bernardini L, Capalbo A, Dallapiccola B, Jenkins ES, Brown WT. De novo 2.15 Mb terminal Xq duplication involving MECP2 but not L1CAM gene in a male patient with mental retardation. Clin Dysmorphol. 2009;18:9–12. PubMed PMID: 19090026.

License