



# Genetics Information Sheet

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Please note that genetics fact sheets # 1, 2, 3, 5 and 12 should accompany this information sheet. These are available at

[www.genetics.com.au](http://www.genetics.com.au)

## MOWAT-WILSON SYNDROME

### ALSO KNOWN AS

- ❖ MWS
- ❖ MICROCEPHALY, MENTAL RETARDATION, AND DISTINCT FACIAL FEATURES, WITH OR WITHOUT HIRSCHSPRUNG DISEASE
- ❖ HIRSCHSPRUNG DISEASE SYNDROME
- ❖ HIRSCHSPRUNG DISEASE-MENTAL RETARDATION SYNDROME

### GENERAL INFORMATION ABOUT MOWAT-WILSON SYNDROME

Mowat-Wilson syndrome is a rare genetic condition that may be evident at birth (*congenital*) or during infancy. Some cases may not be recognised until childhood or adulthood especially when Hirschsprung disease is not present.

The major symptoms include intellectual disability, distinctive facial characteristics and seizures. Additional features may include Hirschsprung disease (disorder of the colon), microcephaly (smaller than normal head size), congenital heart disease, male genital abnormalities, kidney anomalies and short stature.

Mowat-Wilson syndrome results from new genetic changes (*mutations*) in the ZFHX1B gene located on chromosome 2.

### MORE INFORMATION ABOUT MOWAT-WILSON SYNDROME

Mowat-Wilson syndrome is characterised by the following facial features:

- Square shaped face (infancy)
- Long face (adolescence)
- Prominent but narrow triangular chin
- Hypertelorism (wide set eyes)
- Deep set but large eyes
- Broad nasal bridge
- Prominent rounded nasal tip
- Open mouth
- High arched palate
- Full or everted lower lip
- Medially sparse broad eyebrows
- Uplifted ear lobes with a central depression

Moderate to severe intellectual disability is usual. Most people with Mowat-Wilson syndrome have a happy demeanour with frequent smiling. Speech is often very delayed or absent although comprehension is usually much better. Some children communicate well using signing techniques. Motor milestones are always very delayed. Most children cruise for longer than expected before walking independently. Seizures are common, occurring in approximately 90% of individuals by 10 years of age. Seizures can be difficult to control in childhood but are not usually a major problem in adults. Cerebral imaging (MRI or CT) sometimes demonstrates absence of the corpus callosum, a structure connecting the two hemispheres of the brain or smaller brain size (especially frontal lobes).

Short stature is usual although some people have normal stature.

Hirschsprung disease has been present in approximately 60% of individuals diagnosed so far. Hirschsprung disease (HSCR) is a rare condition of the colon usually diagnosed soon after birth with symptoms of bowel obstruction or severe constipation. Milder forms of HSCR might not be diagnosed in infancy. A history of significant constipation warrants investigation for possible mild HSCR (rectal biopsy).

Additional features may include congenital heart disease, problems with the development of the kidneys and/or the male genitalia, ptosis (droopy eyelids), strabismus (crossed eyes), pigmented spots in the iris, calcaneovalgus (foot position alteration, a bit similar to flat feet), slender fingers and toes, and rarely cleft palate.

## **WHAT CAUSES MOWAT-WILSON SYNDROME?**

Mowat-Wilson syndrome usually occurs as a result of new genetic changes in a gene called zinc finger homeobox 1B (ZFHX1B), which is located on chromosome 2 in the region known as 2q22. These changes lead to loss of function of one copy of the gene. The genetic change causing MWS is almost always sporadic, meaning that in nearly all cases, the genetic change has occurred at the time of formation of the egg or sperm for that child only, and no other family member will be affected. Gene testing is available on a limited basis at present, but can be useful to confirm the diagnosis and to aid in genetic counselling.

MWS is distinguished from other syndromic forms of HSCR by the characteristic facial appearance. One such form of syndromic HSCR is called Goldberg-Shprintzen syndrome (GSS). In GSS the facial features are different and there may be additional features such as coloboma of the iris or retina. GSS is thought to be inherited in an autosomal recessive manner, as in reported cases, there have been some recurrences within families and a higher proportion of consanguinity (related parents) than expected. The chromosome locus, or the gene, causing GSS has not been identified. Mutations in the ZFHX1B gene have not yet been found in children with GSS.

Some MWS children have been thought to have Angelman syndrome because both conditions share features such as a happy personality, microcephaly, seizures and poor balance. The facial appearance is quite different in Angelman syndrome, and an experienced clinical geneticist should be able to recognise the difference.

*For more information about genes, chromosomes and genetic deletions please refer to Genetics Fact Sheets 1, 2, 3 and 12.*

## **WHO IS AFFECTED BY MOWAT-WILSON SYNDROME?**

Mowat-Wilson syndrome has been identified in more males than females so far. This is probably because the initial cases were identified because of the presence of HSCR and HSCR is more common in males. In cases identified because of the facial features and intellectual disability the ratio of males to females is 1:1.

This syndrome was first recognised as a distinct cause of syndromic HSCR in 1998. The gene involved, ZFH1B (previously called SIP1) was identified in 2001. Since then there have been more than 100 confirmed cases with mutations within the ZFH1B gene reported in the literature.

As this is a newly described condition it is likely that many more cases will be recognised over the next few years. MWS may be responsible for up to 50% of syndromic HSCR. The exact incidence of MWS is unknown, although it is likely to be a rare condition (less than 1 in 20,000). Cases without HSCR are more difficult to recognise unless the doctor is familiar with the characteristic facial features of MWS.

### ***What is the chance of recurrence for a couple who have one affected child?***

The chance of recurrence in subsequent children for parents who have one affected child is approximately 1%. There have been two instances where this has happened reported in the medical literature. This rare occurrence happens when one parent has a proportion of cells in the ovaries or testes that have the gene change (mutation) which causes MWS. This is called germline mosaicism and is a well-recognised phenomenon in a range of other genetic conditions. There is no test for this situation prior to having a pregnancy. Testing during a pregnancy (prenatal testing) may be available and is best discussed directly with a genetic specialist.

## **IS THERE ANY TREATMENT FOR MOWAT-WILSON SYNDROME?**

### ***Diagnosis***

Mowat-Wilson syndrome is usually diagnosed during infancy or childhood, based upon a thorough clinical evaluation, identification of characteristic physical findings and facial appearance, and information from a variety of specialised tests. Such testing may include imaging techniques, such as computerised tomography (CT) scanning or magnetic resonance imaging (MRI) of the brain. Standard chromosome testing is usually normal in MWS. The clinical diagnosis can be confirmed by DNA testing or FISH directed at the ZFH1B gene. As MWS is rare, all children with suspected MWS should be referred to a clinical geneticist, who will be able to organise the specialised testing if necessary.

### ***Treatment***

The treatment of Mowat-Wilson syndrome is directed toward the specific symptoms that are apparent in each individual. Such treatment may require the coordinated efforts of a team of medical professionals.

In some cases seizures have been resistant to treatment in childhood, but appear to be more easily managed in adolescents and adults.

Treatment of Hirschsprung disease usually consists of surgery to relieve bowel obstruction. A temporary bowel opening of the colon in the abdominal wall (colostomy) is usually performed. A second operation is performed later to remove the non-functioning section of the colon, and rejoin the healthy sections of bowel.

It is important to distinguish this condition from other similar syndromes that may have a different mode of inheritance. Since Mowat-Wilson syndrome occurs sporadically, the recurrence risk is low. To help understand this, families may benefit from genetic counselling.

*For more information about genetic counselling, please refer to Genetics Fact Sheet # 5.*

## RESOURCES

To join the Australian Mowat-Wilson Parent Discussion Group, Email: [MWparents@topica.com](mailto:MWparents@topica.com) or [cfitzsimons@bigpond.com](mailto:cfitzsimons@bigpond.com)

The following website may provide additional information:

<http://www.mowatwilson.org/>

General peer support is available from:

Association of Genetic Support of Australasia (AGSA)

66 Albion Street, SURRY HILLS NSW 2010

Phone: (02) 9211 1462 Fax: (02) 9211 8077

E-mail: [agsa@ozemail.com.au](mailto:agsa@ozemail.com.au)

Home Page: <http://www.agsa-geneticsupport.com.au>

The following overseas group may be able to provide additional information and support for MWS patients with Hirschsprung disease:

International Foundation for Functional Gastrointestinal Disorders

PO Box 170864

Milwaukee WI 53217

Phone: 414 964 1799

E-mail: [iffgd@iffgd.org](mailto:iffgd@iffgd.org)

Home page: <http://www.iffgd.org>

### For information regarding local genetic counselling services:

The Centre for Genetics Education

PO Box 317

ST LEONARDS NSW 1590

Phone: (02) 9926 7324 Fax: (02) 9906 7529

E-mail: [genetics@med.usyd.edu.au](mailto:genetics@med.usyd.edu.au)

Home Page: <http://www.genetics.com.au>

## REFERENCES

This information sheet is based on information available from **NORD** (see below) which was current in **1997** and **OMIM** (see below) which was current in **07/2004**.

**NORD** National Organization for Rare Disorders (NORD)

Home Page: [www.rarediseases.org](http://www.rarediseases.org)

**OMIM** MENDELIAN INHERITANCE IN MAN ON-LINE:

Home Page: <http://www.ncbi.nlm.nih.gov/Omim>

Parisi MA. Updated: July 28, 2004. Hirschsprung Disease Overview. In.: *GeneReviews at GeneTests: Medical Genetics Information Resource (database online)*. Copyright, University of Washington, Seattle. 1997-2004. Available at <http://www.genetests.org>. Accessed: November 1, 2004.

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