

Genetic Fact Sheets 1, 2, 3, 4, 5 and 13 should accompany this Information Sheet.
Fact Sheets are available to download from www.genetics.edu.au

MOWAT-WILSON SYNDROME

Also referred to as: Hirschsprung disease-mental retardation syndrome

Mowat-Wilson syndrome (MWS) is a rare genetic condition associated with a range of physical symptoms as well as intellectual disability. Most people with MWS have a severe intellectual disability, though a small number have milder features and only moderate intellectual disability. People who have MWS typically have a distinctive facial appearance, absent or severely limited speech, a significant degree of intellectual disability and often have seizures. Some physical problems may present at birth or infancy. These include an intestinal disorder (*Hirschsprung disease - HSCR*) in about half, problems with development of the kidneys and male genitalia (*hypospadias*), congenital heart defects, eye problems and absence of the area of the brain which connects the two cerebral hemispheres (*agenesis of the corpus callosum*). Later features may include small head size (*microcephaly*) and short stature. Chronic constipation may occur even in those who do not have Hirschsprung disease.

The distinctive facial appearance of people with MWS is the most consistent feature of this condition, and can be recognised by an experienced medical specialist. Common features include a high forehead, broad eyebrows that are wide apart centrally, wide spaced eyes (*hypertelorism*) that are large and deep set, uplifted ear lobes with a central depression, relatively small nose (in babies) with a prominent rounded nasal tip, prominent portion between nostrils (*columella*), open mouth with M-shaped upper lip, and a prominent but narrow and triangular pointed chin. These features may not all be obvious in babies. Some facial features become more obvious with time, so a diagnosis of MWS is easier to make in older children.

Children with MWS make their developmental progress (such as sitting, crawling, and walking) at a significantly slower rate than average. Speech is often delayed or absent. Comprehension is usually better than speech ability and children may communicate in non-verbal ways such as signing. They usually have a happy demeanour and smile frequently.



WHAT CAUSES MOWAT-WILSON SYNDROME?

Mowat-Wilson syndrome is caused by a change (*mutation*) in a gene called the *ZEB2 gene* (previously called *ZFH1B* or *SIP1*). The *ZEB2 gene* is located on chromosome 2 in the region 2q22.3. The *ZEB2 genes* provide the instructions for making a protein that plays a critical role in the formation of many organs and tissues of the body before birth. When a mutation occurs in one copy of this gene, the protein produced may be faulty, inefficient, or absent. This affects the development of many organs and tissues throughout the body especially the brain.

MWS almost always occurs as a new (*sporadic* or *de novo*) condition. This means that in nearly all cases, the gene mutation has occurred at the time of formation of the egg or sperm for that child only, and no other family member will be affected. It is usually not inherited from, or “carried” by a healthy parent.

In a very small number of families, more than one child has been affected with MWS. Of the 200 or so families described in the literature, recurrence of MWS has only been reported in 5 families. The chance of recurrence for parents who have a child with MWS is thus approximately 2% or less. This could happen if one parent has a proportion of cells in their ovaries or testes that have a mutation which causes MWS. This is called *germ-line mosaicism*.

In rare cases, one parent may have a particular chromosome rearrangement in or around the MWS gene *ZEB2*. This increases the risk of having a child with MWS, however this risk is also very small. Testing during subsequent pregnancies is available for couples for further reassurance if they wish, if the genetic change in *ZEB2* has been found in their affected child.

There have been no reports of individuals with MWS reproducing.

There is another inherited condition associated with HSCR and intellectual disability called Goldberg-Shprintzen syndrome. This condition is inherited in a different way and caused by mutations in a different gene (called the *KIAA1279 gene*). Individuals with Goldberg-Shprintzen syndrome have a different facial appearance to those with MWS, which can be distinguished by an experienced geneticist.

Genes, chromosomes and genetic conditions

Inside all the cells of our body, our genetic information is found on structures called *chromosomes*. There are usually 23 pairs of chromosomes, making a total of 46 chromosomes in each cell. One of each pair is passed on to us from our mother and the other from our father. 22 of these chromosome pairs are numbered. These numbered pairs are known as the *autosomal chromosomes*. The 23rd pair is made up of the *sex chromosomes* called X and Y. Males have an X and a Y chromosome and females have two copies of the X chromosome.

We have many thousands of genes on our chromosomes that provide information for our body to grow, develop and remain healthy. The gene sends messages to the cell to make important chemical products such as proteins.

Genetics Fact Sheets 1, 2 and 3 provide more information on genes, chromosomes, and genetic conditions.

www.genetics.edu.au

RNS Community Health Centre. Royal North Shore Hospital.
St Leonards NSW 2065

☎ (02) 9462 9599 📠 (02) 9906 7529

✉ contact@genetics.edu.au

Page 2 of 5



Everyone has variations (changes) in their genes, which is why we are all unique. Variations can either be harmless or at times, can cause a gene to be faulty. Variations that make a gene faulty are called *mutations*.

Faulty genes do not work as they should in the body and are unable to provide the correct information to our cells. Sometimes a faulty gene has been passed down (*inherited*) from one or both parents. Other times, it has occurred as a new faulty gene during the making of an egg or sperm or at conception. Once a faulty gene is present in an individual, it can be passed on to future generations. This is referred to as *genetic inheritance*.

Mowat-Wilson syndrome almost always occurs sporadically because of a new genetic mutation. There is usually no other affected family member. In a very small number of families, MWS may be inherited as a result of hidden germ-line mosaicism in one parent. Genetic counselling can provide more explanation and discussion of options for couples concerned about germ-line mosaicism and recurrence.

Genetics Fact Sheet 13 provides more information on Complex Patterns of Inheritance

WHO IS AFFECTED BY MOWAT-WILSON SYNDROME?

Mowat-Wilson syndrome affects both males and females. It is estimated to occur in 1 in 50,000-100,000 births. MWS has been described in many different countries and ethnic groups around the world.

HOW IS MOWAT-WILSON SYNDROME DIAGNOSED AND TREATED?

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. Many of these features become more pronounced with time and so the diagnosis is easier to make in older individuals.

Checking for features may include imaging techniques such as computerised tomography (CT) scanning or magnetic resonance imaging (MRI) of the brain, kidney ultrasound or heart ultrasound.

Standard chromosome testing is usually undertaken in MWS to exclude a chromosome rearrangement involving chromosome 2q22, which is rare. The clinical diagnosis can be confirmed by gene (DNA) testing using different techniques to detect small or large changes in the *ZEB2* gene. A mutation in the *ZEB2* gene is found in almost all children diagnosed with MWS by an experienced clinician.

www.genetics.edu.au

RNS Community Health Centre, Royal North Shore Hospital.
St Leonards NSW 2065

☎ (02) 9462 9599 📠 (02) 9906 7529

✉ contact@genetics.edu.au

Page 3 of 5



Treatment

The treatment of individuals with MWS should be directed towards the needs of each individual. It may be necessary for a team of specialists to work together and plan for the best strategy to enable each individual to reach their full potential. Just like each individual will be different, the treatment plan will be unique and best discussed with the health professionals involved in the care plan.

In MWS, associated conditions including HSCR, heart abnormalities and seizures require intervention of relevant specialists, such as neurologists, cardiologists, and surgeons. Physical therapy, occupational therapy and speech therapy may all be useful in helping children with developmental delay reach their full potential.

Genetic Testing Options

Genetic testing is available for MWS in a number of laboratories around the world and is usually organised by a clinical geneticist. Testing is initially carried out on affected individuals. If the mutation is identified for a particular family, testing on an unborn baby (*prenatal testing*) or on an embryo conceived by IVF (*pre-implantation genetic diagnosis (PGD)*) is possible. Contact a genetic counselling service for the most appropriate and accurate information and to discuss your specific options and questions.

For more information on genetic counselling, prenatal testing and PGD, please refer to Genetics Fact Sheets 3, 17 and 18.

MORE INFORMATION AND SUPPORT

If you would like to discuss support options and possible contact with other affected individuals or families, please contact:

Association of Genetic Support of Australasia (AGSA)

Telephone: (02) 9211 1462

E-mail: info@agsa-geneticssupport.org.au

Web: <http://www.agsa-geneticssupport.org.au>

For more information about genes, inheritance patterns, genetic testing and genetic services discussed in this information sheet please contact:

Centre for Genetics Education (CGE)

Telephone: (02) 9462 9599

E-mail: contact@genetics.edu.au

Web: www.genetics.edu.au

Additional information and support may be available from the following sources:

Mowat-Wilson Support Groups

Web: www.mowatwilson.org

Web: www.mowatwilsonsyndrome.com

www.genetics.edu.au

RNS Community Health Centre. Royal North Shore Hospital.
St Leonards NSW 2065

☎ (02) 9462 9599 📠 (02) 9906 7529

📧 contact@genetics.edu.au

Page 4 of 5



This is a resource developed by NSW Health's Centre for Genetics Education and is intended for educational purposes only. All efforts are made to ensure that information and resources provided by the Centre are based on current accurate information. Client referrals to genetics services, genetic support groups and community services are based on current listings. The Centre assumes no responsibility for the type, amount or quality of assistance, support or service provided by other agencies. This Information Sheet is in no way to be seen or taken to be a substitute for individual advice concerning diagnosis or treatment from an appropriately skilled genetics specialist.

This document is based on information obtained from the following sources:
National Organization for Rare Disorders (NORD) - www.rarediseases.org
Online Mendelian Inheritance in Man - www.ncbi.nlm.nih.gov/omim
GENE TESTS (Gene Reviews) – www.genereviews.org

END OF DOCUMENT

www.genetics.edu.au

RNS Community Health Centre. Royal North Shore Hospital.
St Leonards NSW 2065

☎ (02) 9462 9599 📠 (02) 9906 7529

✉ contact@genetics.edu.au

Page 5 of 5

