

Please contact us for further information

The Dalglish Family
Hearts and Minds Clinic



for Adults with
22q11.2 Deletion Syndrome

The Dalglish Family Hearts and Minds Clinic For Adults with 22q11.2 Deletion Syndrome

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For more information, please visit our website:

www.22q.ca

For referral information, please visit:

<http://22q.ca/medicalprofessionals/referral-information/>

Information for health professionals

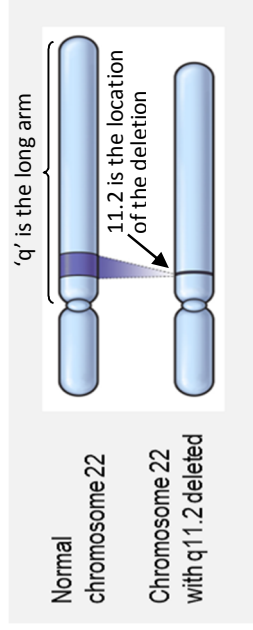
This pamphlet is about:

- Clinical features of 22q11.2DS
- Genetics and testing for individuals with suspected 22q11.2DS
- Specialized help for adults with 22q11.2DS



What is 22q11.2DS?

Individuals with **22q11.2 deletion syndrome (22q11.2DS)** are missing a part of region q11.2 of one of the two chromosome 22s in each cell of their body. The most common deletion, which accounts for about 80% of the cases, eliminates approximately 3 megabases (Mb) of DNA, or about 45 genes. Deletions of other sizes also exist.



Usually 22q11.2 deletions occur as a new genetic change in a family. Only about 1 out of 10 people with the 22q11.2 deletion have a parent who is also affected. Each child of an adult with the deletion has 50% chance of inheriting the deletion. Advanced maternal age does not appear to be a risk factor.

Individuals with 22q11.2DS can have many physical and mental health problems. The number and severity of features vary from person to person, even among affected members of the same family. Many adults with 22q11.2DS have not yet been diagnosed because of the wide range of possible features. Also, some health professionals may not recognize the features as 22q11.2DS.

22q11.2DS has also been known by many other names, including DiGeorge syndrome, Shprintzen syndrome, and velocardiofacial syndrome (VCFS). Now that researchers have found the unifying genetic cause of these conditions, the standard name **22q11.2 deletion syndrome** is preferred.

Resources for 22q11.2DS / intellectual and developmental disabilities

- Bassett AS *et al.* and the International 22q11.2 Deletion Syndrome Consortium. (2011). **Practical guidelines for managing patients with 22q11.2 deletion syndrome.** *Journal of Pediatrics.* 159(2): 332-339.e1. doi: 10.1016/j.jpeds.2011.02.039
- Fung WLA *et al.* (published electronically January 8, 2015). **Practical guidelines for managing adults with 22q11.2 deletion syndrome.** *Genet Med.* doi: 10.1038/gim.2014.175.
- Sullivan WF *et al.* and Colloquium on Guidelines for the Primary Health Care of Adults with Developmental Disabilities. (2011). **Primary care of adults with developmental disabilities: Canadian consensus guidelines.** *Canadian Family Physician, 57*(5):541-53, e154-68.

Websites for 22q11.2DS

- The Dalglish Family Hearts and Minds Clinic for Adults with 22q11.2 Deletion Syndrome - www.22q.ca
- 22q Clinic at The Hospital for Sick Children - <http://www.sickkids.ca/genetics/what-we-do/22q-deletion-syndrome-clinic/index.html>
- The International 22q11.2 Foundation Inc. - <http://www.22q.org/>
- VCFS 22q11 Foundation – www.vcfsfa.org.au
- The Dempster Family Foundation - <http://dempsterfamilyfoundation.org/>

Requisition for microarray testing (for all ages)

- Hospital for Sick Children
Cytogenetics – Genomic SNP Microarray with Billing Form
http://www.sickkids.ca/pdfs/Paediatric%20Laboratory%20Medicine/External-Requisitions/57104-GenomicSNPMicroArrayExt_05ff.pdf

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Where can adults with 22q11.2DS get specialized help?

Individuals aged 17 and older with a **confirmed or suspected** 22q11.2 deletion can ask their doctors to refer them to The Dalglish Family Hearts and Minds Clinic, which is located at Toronto General Hospital. This is a specialty clinic with a team of health care professionals who are familiar with 22q11.2DS. **See back cover for referral information.** Younger individuals with confirmed 22q11.2DS can be referred to the 22q Deletion Syndrome Clinic at the Hospital for Sick Children in Toronto.

Depending on the individual's needs, he or she may have appointments with one or more of these health care providers:

- **Genetics expert in 22q11.2DS**
- **Psychiatrist**
- **Endocrinologist**
- **Neurologist**
- **Social Worker**
- **Registered Dietitian**

Cardiologists from the Toronto Congenital Cardiac Centre for Adults (TCCCA) are an important part of the Dalglish Clinic team.



The health care providers involved will:

- Provide timely and effective care for individuals with 22q11.2DS.
- Provide regular and careful monitoring of their health.
- Connect them with local resources and peer support as needed.
- Help co-ordinate care.

How common is 22q11.2DS?

22q11.2DS has an estimated prevalence of around 1 in 2,000 live births. Although detection is increasing, 22q11.2DS is still under-recognized.

Chronic genetic condition	How common is it?
Down syndrome	1 in 1,000 live births
22q11.2DS	1 in 2,000 live births
Cystic fibrosis	1 in 3,600 live births
Phenylketonuria	1 in 10,000 to 15,000 live births

Biau N, van Spronsen FJ, Levy HL. (2010). **Phenylketonuria**. *Lancet* 376 (9750):1417–1427. doi: 10.1016/S0140-6736(10)60961-0.
Fung WLA et al. (published electronically January 6, 2015). Practical guidelines for managing adults with 22q11.2 deletion syndrome. *Genet Med*. doi: 10.1038/gim.2014.175.
Dupuis A, Hamilton D, Cole DE, Corey M. (2005) Cystic fibrosis birth rates in Canada: a decreasing trend since the onset of genetic testing. *J Pediatr*. 147(3):312-5. doi: 10.1016/j.jpeds.2005.06.043
World Health Organization: **Genes and human diseases—Down Syndrome**. <http://www.who.int/genomics/public/geneticdisorders/en/index1.html>

“The 22q11.2 deletion is the second most common cause of developmental delay and major congenital heart disease after Down syndrome, accounting for approximately 2.4% of individuals with developmental disabilities and approximately 10% to 15% of individuals with tetralogy of Fallot.”

– Bassett et al. 2011

The number of individuals diagnosed with this syndrome is expected to increase because:

- Pediatric surgical and medical advances have led to an increase in the number of individuals with 22q11.2DS who survive congenital heart defects. These individuals in turn have children of their own, 50% of whom will inherit the deletion.
- Individuals who were never tested because of the unavailability of genetic testing are now being properly diagnosed.
- Atypical 22q11.2 deletions previously missed due to the limitations of FISH (Fluorescence in situ hybridization) are now detectable by newer technologies.

Features of 22q11.2DS

There are many possible features associated with 22q11.2DS. There is no established correlation between the extent of the deletion and the clinical features. The presence of one feature does not predict the presence of any other feature. Possible features include, but are not limited to:

- **Intellectual and developmental disabilities**
- **Congenital heart defects**
- **Palate abnormalities** (feeding and speech difficulties)
- Abnormal facial features (variable, often mild)
- Immune system related disease (recurrent infections, autoimmune diseases, seborrhea, dermatitis)
- Endocrine related diseases (**hypocalcemia**, **hypothyroidism**, hypoparathyroidism, abnormal thyroid hormone levels, obesity)
- Growth faltering
- Neuromuscular and musculoskeletal abnormalities (scoliosis, spine deformities, leg pains)
- Blood disorders (thrombocytopenia) and cancers
- Gastroenterological abnormalities (dysmotility, dysphagia, reflux gallstones, constipation)
- Genitourinary abnormalities (improperly formed urinary tract, dysfunctional voiding)
- Sensory abnormalities (problems with smell, vision, hearing)
- Neuropsychiatric disorders (attention deficit and hyperactivity disorder, autism spectrum disorder, **anxiety and mood disorder**, **schizophrenia and other psychotic disorders**)
- Neurologic (recurrent **seizures**, **epilepsy**, deterioration or early onset Parkinson's disease)
- Dental (enamel disturbances, cavities)

Individuals can be diagnosed at any stage of their lives. Those with cardiac anomalies or severe feeding problems tend to be diagnosed in infancy. Those with less severe and/or less typical congenital abnormalities or who were born before genetic testing became widely available may be diagnosed later in life or may not be diagnosed at all.

Health concerns may change with age. As young people with 22q11.2DS approach adulthood, the focus usually shifts from mainly physical and developmental issues to neuropsychiatric, social, and employment challenges.

Strategies for communicating with adults with 22q11.2DS

Work with the patient and his/her caregivers...

- Understand the specific level of cognitive and practical functioning as well as any learning disabilities the patient has
- Use the patient's preferred terminology for his/her disability, even if not technically correct
- Involve caregivers in counseling sessions
- Elicit patient's feelings and attitudes related to the decisions

...using suitable language and tools

- Use non-judgemental language
- Use simple diagrams and visual aids
- Avoid discussing probabilities
- Avoid using analogies
- Provide handouts
- Repeat and reinforce concepts over multiple sessions
- Provide a written summary to patient and caregivers
- Summarize and confirm the patient's decisions

Early detection of psychiatric issues

The diagnosis and treatment of psychiatric disorders can be challenging in adults with intellectual disability and communication limitations. Physicians are advised to be aware of the patient's suggestibility, intellectual level, and his/her baseline state and functioning.

Emotional outbursts may be a feature of untreated or undertreated anxiety or psychotic illnesses. Changes in emotions, thinking, physical state, behaviour, and functioning may be indicative of early signs of psychiatric illnesses. Monitoring these signs will help in early diagnosis and effective management.

Periodic investigations

- 22q11.2DS-relevant laboratory tests (annual)
 - complete blood count (CBC) and differential, electrolytes, thyroid-stimulating hormone, pH-corrected ionized calcium, magnesium, parathyroid hormone, creatinine, liver function tests (especially alanine aminotransferase), lipid profile, glucose, and HbA1C
- Electrocardiography (if not previously performed)
- Transthoracic echocardiography (if not previously performed)
- Abdominal ultrasound (if not previously performed)
- Electroencephalography (if not previously performed)

Other management/assessments

- Contraception and safe sex counselling
- Counselling on internet safety
- Dental assessment
- Audiology assessment
- Vocational counselling and employment support
- Diet and exercise counselling
- Life skills training
- Financial management

We recommend that all individuals with 22q11.2DS receive routine assessment at a specialty clinic, where possible. It is useful to anticipate and proactively deal with health and other issues associated with 22q11.2DS. For further information, please consult Table 1 of “**Practical guidelines for managing adults with 22q11.2 deletion syndrome**” by Fung *et al.*, 2015. However, each individual also requires a **personalized approach** to management of 22q11.2DS and the accompanying health problems.

Who should be screened for 22q11.2DS?

Genome-wide genetic testing (e.g. aCGH—see below) is recommended for all individuals with one or more of the following:

- Intellectual and developmental disabilities
- Autism spectrum disorders
- Any developmental delay, including a delay in gross motor, fine motor, learning, and/or speech & language
- Multiple congenital anomalies, especially of the heart or palate (velopharyngeal insufficiency)

How is screening done?

Genetic tests require a **blood sample** from the individual being tested to be sent to a **genetics lab**.

Fluorescence in situ hybridization (FISH) involves the use of fluorescence microscopy to find out whether a patient’s chromosome contains **specific** DNA sequences in the 22q11.2DS region. However, this method may miss some deletions and cannot provide information on the length or exact position of a deletion.

The first-tier genetic diagnostic test for 22q11.2DS is now **array comparative genomic hybridization (aCGH)**, also known as “**microarray**”. It screens the **whole genome** at the same time to identify gains or losses of **any chromosomal region**. All 22q11.2 deletions, regardless of size and location, can be identified with the same confidence. Other chromosomal aberrations that result in a change in copy number can also be found using the same assay.

When a genetic test does not reveal the basis for a patient’s symptoms, it does not rule out the possibility of a genetic cause. In that case, the patient may need other diagnostic options such as dysmorphological investigation, metabolic screening tests, neurological examinations etc. A referral to a clinical geneticist may be advisable.

Recommended assessments and monitoring for adults with 22q11.2DS

Why should we test individuals with suspected 22q11.2DS?

Knowledge about the deletion will provide an opportunity to:

- Access to specialized clinics and better medical care
- Recognition and intervention for treatable problems that have been mild or hidden. For example:
 - cardiac anomalies
 - psychiatric illnesses
 - learning disabilities
 - endocrinologic disorders
- Minimization of complications and costs of treatment
- Provision of anticipatory care, such as calcium and vitamin D supplementation to offset propensity for hypocalcemia
- Better interaction with health professionals, including more respect and attention
- Optimization of educational and social support
- Achievement of greater understanding and certainty of oneself or affected family members, thereby reducing stigma and blaming
- Gain of a sense of purpose, hope for others, and a platform for advocacy
- Obtainment of reproductive counselling
- Assessment for possible familial cases

Genetic/general management

- Consultation with medical geneticist and clinicians experienced with 22q11.2DS
- Genetic counselling
- Family planning and prenatal counselling

Clinical assessments

- Comprehensive medical history
- Systems review
- Psychiatric assessment
- Cognitive and capacity assessments
- Neurological assessment (as needed)
- Ophthalmological assessment
- Orthopedic assessment (as needed)
- Family history
- Physical examination (including for hygiene and care)
- Body mass index (BMI) / growth / nutritional assessment