

22q11 Deletion Syndrome

[del 22q11, Includes: Shprintzen Syndrome, DiGeorge Syndrome (DGS), Velocardiofacial Syndrome (VCFS), Conotruncal Anomaly Face Syndrome (CTAF), Caylor Cardiofacial Syndrome, Opitz G/BBB]

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Summary

Disease characteristics. Individuals with 22q11 deletion syndrome (del 22q11) have a range of findings, including congenital heart disease (74% of patients), particularly conotruncal malformations (tetralogy of Fallot, interrupted aortic arch, and truncus arteriosus); palatal abnormalities (69%), particularly velopharyngeal incompetence (VPI), submucosal cleft palate, and cleft palate; characteristic facial features (present in the majority of individuals); and learning difficulties (70 - 90%). Hypocalcemia and immune deficiency are typical but less common.

Diagnosis/testing. Del 22q11 is diagnosed in individuals with a submicroscopic deletion of chromosome 22 detected by fluorescence in situ hybridization (FISH) using DNA probes from the DiGeorge chromosomal region (DGCR). Such FISH testing is widely available for the clinical and prenatal diagnosis of del 22q11. Fewer than 5% of patients with the clinical symptoms of del 22q11 have normal routine cytogenetic studies and negative FISH testing. They are presumed to have variant deletions of DGCR which may be detectable on a research basis only.

Genetic counseling. Del 22q11 is inherited as a deletion syndrome. About 94% of probands have a *de novo* deletion of 22q11 and 6% have inherited the 22q11 deletion from a parent. Prenatal testing is possible for fetuses determined to be at 50% risk by family history and for fetuses not known by family history to be at increased risk for del 22q11 but with findings of congenital heart disease and/or cleft palate detected by ultrasound examination.

Diagnosis

The 22q11 deletion syndrome (del 22q11) is suspected in individuals with characteristic clinical findings and confirmed in more than 95% of cases by detection of submicroscopic deletion of chromosome 22 by fluorescence in situ hybridization (FISH) using DNA probes from the DiGeorge chromosomal region (DGCR) [Driscoll, Budarf et al 1992; Wilson et al 1992; Driscoll et al 1993; Desmaze et al 1993]. Such FISH testing is widely available for the clinical and prenatal diagnosis of del 22q11 [Driscoll, Chen et al 1995].

Clinical Diagnosis

The diagnosis of del 22q11 is suspected in patients with a range of findings that may include some combination of the following: congenital heart disease (particularly conotruncal malformations), palatal abnormalities [especially velopharyngeal insufficiency (VPI)], hypocalcemia, immune deficiency, learning difficulties, and, at times, characteristic facial features. Del 22q11 is detected by FISH testing in the vast majority of cases with this combination of findings [Driscoll et al 1993].

Testing

Cytogenetic testing. When del 22q11 is suspected in a patient, it is recommended that routine cytogenetic analysis be performed at the time of FISH testing because a small percentage of patients with clinical findings of del 22q11 have chromosomal rearrangements involving 22q11, such as a translocation between chromosome 22 and another chromosome.

Molecular Genetic Testing

The 22q11 deletion syndrome (del 22q11) is diagnosed in individuals with a submicroscopic deletion of chromosome 22 detected by fluorescence in situ hybridization (FISH) using DNA probes from the DiGeorge chromosomal region (DGCR) [Driscoll, Budarf et al 1992; Wilson et al 1992; Driscoll et al 1993; Desmaze et al 1993]. Such FISH testing is widely available for the clinical and prenatal diagnosis of del 22q11 [Driscoll, Chen et al 1995].

A few patients with clinical symptoms of del 22q11 show normal routine cytogenetic studies and negative FISH testing when the commercially available probes are used, but have variant deletions of the DGCR detected with probes that are available on a research basis only.

Table 1: Testing Used in the Diagnosis of the 22q11 Deletion Syndrome

% of Patients	Genetic Mechanism	Test Type	Test Availability
> 95%	Deletion of 22q11 DGCR	FISH	Clinical GENEtests
< 5%	Smaller 22q11 deletion or point mutation	FISH	Research
< 1%	Unbalanced translocation	Chromosomal analysis	Clinical

[Yamagishi et al \[1999\]](#) recently suggested that the gene responsible for the features of the 22q11 deletion syndrome had been determined. The gene that they implicated, *UFD1L*, was originally described by [Pizzuti et al \[1997\]](#). This gene is one of many genes deleted in all of the individuals who test positive in the FISH testing using the commercially available probes N25 or TUPLE 1. The discovery should not alter the methodology by which testing is currently performed, as the majority of patients have the same large deletion of the DGCR.

Clinical Description

Before the identification of the 22q11 submicroscopic deletion in 1991, 1992, and 1993 [[Scambler et al 1991](#); [Carey et al 1992](#); [Driscoll, Budarf et al 1992](#); [Driscoll, Spinner et al 1992](#); [Driscoll et al 1993](#)], patients with del 22q11 were often described as having either DiGeorge syndrome (DGS) or velocardiofacial syndrome (VCFS). DGS was originally described as a developmental field defect of the third and fourth pharyngeal pouches with a conotruncal cardiac anomaly and aplasia or hypoplasia of the thymus gland and parathyroid glands. VCFS was originally described as the combination of velopharyngeal incompetence (VPI), congenital heart disease (usually a ventricular septal defect or tetralogy of Fallot), characteristic facial features, and developmental delay or learning difficulties.

It is now recognized that the 22q11 deletion syndrome encompasses the phenotypes previously described as DGS and VCFS and that the clinical descriptions of DGS and VCFS resulted from an ascertainment bias. The majority of patients with DGS were identified in the neonatal period with a major congenital heart defect, hypocalcemia, and immunodeficiency, whereas patients with VCFS tended to be diagnosed in cleft palate or craniofacial centers when speech and learning difficulties became evident as children reached school age [[Wilson et al 1993](#); [Wulfsberg 1996](#); [McDonald-McGinn, Zackai et al 1997](#); [Thomas and Graham 1997](#)]. In addition, microdeletions of chromosome 22q11 have also been detected in patients identified as having the conotruncal anomaly face syndrome (CTAF) [[Matsuoka et al 1994](#)], some cases of "Opitz" G/BBB syndrome [[McDonald-McGinn et al 1995](#), [Fryburg et al 1996](#), [LaCassie and Arriaza 1996](#)], and Cayler cardiofacial syndrome [[Giannotti et al 1994](#)].

Findings in 250 patients (48% male; 52% female) with del 22q11 ascertained through the Children's Hospital of Philadelphia are summarized below [[McDonald-McGinn, Kirschner, Goldmuntz, Sullivan et al 1999](#)]. The clinics from which the patients were ascertained were genetics (59%), cardiology (25%), cleft palate (10%), neurology and child development (3%), immunology and rheumatology (2%), and endocrinology (1%). Fifty-six percent of patients were five years of age or younger. Twelve percent of patients were over the age of 16 years, the majority of whom were parents of affected children. Six percent of patients were deceased, 90% of whom succumbed to complications of cardiac disease. Seventy-seven percent of the patients were Caucasian; 14% of the patients were African-American. Because African-American patients lacked many of the "typical facial characteristics" of del 22q11, they were under-represented when compared to the hospital's patient population of African-Americans, which was 42% [[McDonald-McGinn et al 1996](#)]. Six percent of cases were familial with marked inter- and intra-familial variability.

Heart. Congenital heart disease was present in 74% of patients. The primary cardiac malformations are reported in Table 2. Associated cardiac features are not included. Seventy-five percent of patients were ascertained through the mid-Atlantic region. The remainder were self-selected individuals from throughout the US, Canada, Europe, and the Middle East who sought care at our institutions.

Table 2: Cardiac Findings in 222 Patients with Del 22q11

Cardiac Finding	% of Patients
Tetralogy of Fallot (TOF)	22%
Interrupted aortic arch (IAA)	15%
Ventricular septal defect (VSD)	13%
Truncus arteriosus (TA)	7%
Vascular ring	5%
Atrial septal defect	3%
Aortic arch anomaly	3%
VSD; ASD	4%
Other ¹	4%
Normal	26%

1. Hypoplastic left heart syndrome; pulmonary valve stenosis; double outlet right ventricle/interrupted aortic arch; bicuspid aortic valve; heterotaxy/A-V canal/interrupted aortic arch

Palate. One hundred and eighty-one patients had palatal evaluations performed by a plastic surgeon and speech pathologist using standard history, physical examination, and speech evaluation. Patients underwent videofluoroscopy and/or nasendoscopy when indicated. Velopharyngeal incompetence was not ruled out until objective evaluations by a speech pathologist and plastic surgeon were obtained and until the child was old enough to provide an adequate speech sample.

Sixty-nine percent of patients had a definitive palatal abnormality (Table 3). Of the 27% with confirmed VPI, several patients were initially diagnosed with del 22q11 because of their cardiac defect and were subsequently found to have unrecognized but clinically significant VPI [McDonald-McGinn, LaRossa et al 1997]. Only 17% of patients were determined to have no palatal involvement.

Table 3: Palatal Findings in 181 Patients with Del 22q11

Palatal Finding	% of Patients
Velopharyngeal incompetence (VPI)	27%
Submucosal cleft palate (SMCP)	16%
Overt cleft palate	11%
Bifid uvula	5%
Cleft lip/cleft lip and palate ¹	2%
Infantile VPI ²	8%
Need follow-up ³	14%
Normal	17%

1. Either unilateral or bilateral

2. "Infantile VPI" or occult submucosal cleft palate diagnosed by history (nasal regurgitation and frequent otitis media), physical examination, or nasendoscopy (incomplete closure of the velopharyngeal mechanism during crying and swallowing) in patients too young to provide an adequate speech sample for definitive diagnosis

3. No overt abnormality, but patients too young to provide an adequate speech sample

Feeding. Thirty percent of patients had a history of feeding difficulties, a component of del 22q11 that has not been previously appreciated. Seventy-five children had a history of severe dysphagia. Of these, 45% required gastrostomy tube placement and 50% required nasogastric tube feedings. Sixty percent of these patients had a cardiac defect and 24% had palatal anomalies; however, feeding difficulties were independent of other structural anomalies. Evaluation by barium swallow in 23 patients revealed a preponderance of nasopharyngeal reflux, prominence of the cricopharyngeal muscle, abnormal cricopharyngeal closure, and/or diverticulum. Thus, the underlying feeding problem in many of the patients appears to be due to dysmotility in the pharyngoesophageal area, which is derived from the third and fourth pharyngeal pouches.

Immune function. Nineteen infants had T-cell studies at birth and again at one year of age. Compared to control patients without the deletion, newborns with del 22q11 had significantly fewer cells of thymic lineage; however, improvement in T-cell production did occur. Patients with the most significant deficiencies in T-cell production improved most in the first year of life [Sullivan et al 1999]. Sixty patients over the age of six months had immunological evaluations. In all patients, T-cell production and gross T-cell function were evaluated. In those over one year of age, immunoglobulin production and function, as well as more sensitive studies of T-cell function, were evaluated. Of the 60 patients, 77% were considered to be immunodeficient regardless of their clinical presentation. Sixty-seven percent had impaired T-cell production, 19% had impaired T-cell function, 23% had humoral defects, and 13% had IgA deficiency [Sullivan et al 1998, Smith et al 1998].

Parathyroid function. Forty-nine percent of 158 patients had confirmed hypocalcemia. Calcium homeostasis typically normalizes with age, although recurrence of hypocalcemia in later childhood has been reported. Two patients (ages eight and twelve years) who were receiving ongoing follow-up by an endocrinologist for their hypocalcemia, which had presented in infancy, were not diagnosed with the 22q11 deletion until school age.

Craniofacial. Craniofacial findings included auricular abnormalities, hypoplastic alae nasae leading to the appearance of a bulbous nasal tip, prominent nasal root [Gripp et al 1997], and "hooded eyelids". However, the presence of these features as well as other facial findings such as a long face and malar flatness, were quite variable. In fact, some patients offered no clues to their underlying diagnosis based on their facial features, especially African-American patients [McDonald-McGinn et al 1996].

Eyes. A prospective evaluation for ocular abnormalities in 33 patients revealed hooding of the upper lid (41%), ptosis (9%), hooding of the lower lid (6%), epicanthal folds (3%), and distichiasis (3%). Other findings included posterior embryotoxon (69%), isolated corneal nerves (3%), sclerocornea (3%), deep iris crypts (10%), tortuous retinal vessels (58%), small optic nerves (7%), and tilted discs (3%). Strabismus was observed in 13% and amblyopia in 6%.

Although posterior embryotoxon was observed in 12 to 32% of controls, the incidence in this group of patients with del 22q11 was almost as high as that seen in Alagille syndrome (89%) [Krantz et al 1997]. The incidence of astigmatism, myopia, and hyperopia were comparable to the incidence in the general population. No patient had cataracts or colobomas.

Ear, nose, and throat. Ear abnormalities included overfolded or squared off helices; cupped, microtic, and protuberant ears; preauricular pits or tags, and narrow external auditory meati. A prominent nasal root, bulbous nasal tip, hypoplastic alae nasae, and a nasal dimple/bifid nasal tip were common [Gripp et al 1997]. Stridor due to vascular ring, laryngomalacia, and laryngeal webs were observed. Chronic otitis media and chronic sinusitis were common.

Central nervous system. Although the majority of patients had a history of hypotonia in infancy and learning disabilities [Moss et al 1995], specific neurologic manifestations were rare. Seizures were seen in some patients and were most often associated with hypocalcemia. Several patients had asymmetric crying facies [Cayler 1969, Giannotti et al 1994, Levin et al 1982, Sanklecha et al 1992, Silengo et al 1986]. Three patients were ataxic, one of whom had atrophy of the cerebellum [Lynch et al 1995]. Additional CNS abnormalities included multicystic white matter lesions of unknown significance and perisylvian dysplasia [Bingham et al 1997]. Overall, the pattern of CNS abnormalities was diffuse and overlapped with that seen in some cases of Opitz G/BBB syndrome [Guion-Almeida and Richieri-Costa 1992, MacDonald et al 1993, Neri et al 1987].

Psychosocial development and IQ. Patients can be divided into three categories based on age: toddler, preschooler, and school-aged.

In a series of 28 toddlers assessed using the Bayley Scale of Infant Development, the mean Mental Developmental Index was 70±15. The mean Psychomotor Developmental Index was 60±12. In mental development 21% were average, 32% were mildly delayed, and 46% were significantly delayed; in motor development 8% were average, 13% were mildly delayed, and 79% were significantly delayed. Language assessment using the Preschool Language Scale-Revised revealed total language 73±14, expressive language 71±16, and receptive language 78±12.

In a series of 12 preschoolers assessed using the WPPSI-R, the Full Scale IQ was 78±11, the mean Performance IQ was 78±14, and the mean Verbal IQ was 82±15. For the 12 preschoolers, 33% were average, 33% were mildly delayed, and 33% were significantly delayed. The mean language scores for the 12 preschool-age patients were: total language 73±18, expressive language 76±16, and receptive language 77±16. In total language, 16% were average, 44% were mildly delayed, and 40% were significantly delayed; in expressive language, 9% were average, 38% were mildly delayed, and 53% were significantly delayed; and in receptive language, 26% were average, 48% were mildly delayed, and 26% were significantly delayed [Solot et al 1998].

In a series of 55 school-age patients with del 22q11 assessed with the age-appropriate Weschler IQ battery, 13% attained full scale IQ scores in the average range, 26% in the low average range, 35% in the borderline range, and 27% in the retarded range. However, detailed analysis of the battery became important. As an example, one patient had a verbal IQ of 111, which is above the average range, but a performance IQ of 65, which falls in the retarded range, bringing his full scale IQ down to 87, which is in the low average range. This split between verbal and performance IQ was consistent with a nonverbal learning disability. This nonverbal learning disability was seen in 66% of patients with a mean split between verbal comprehension and perceptual organization of 11 points [Moss et al 1995]. Therefore, the full scale IQ scores alone did not accurately represent the abilities of many of these patients; for each patient verbal and performance IQ scores should be considered separately.

On memory testing, verbal learning was superior to visual memory ($p=.01$) and was even superior to VIQ ($p=.001$). On scholastic testing, all individual reading skills were significantly stronger than all individual math skills. Overall reading was therefore much stronger than overall math ($p<.0001$), perhaps reflecting the strong rote verbal memory skills. The evidence of stronger verbal than visual memory skills and stronger reading than math skills also supports the presence of a nonverbal learning disorder. These findings are of particular importance because the cognitive remediation, behavior management, and parental counseling are specific to this type of non-verbal learning disability, which is rare in the general population [Wang et al 1998].

Psychiatric illness. Psychiatric illness has been implicated in some individuals and has included schizophrenia, rapid cycling bipolar disorder, and depression. The prevalence and exact nature of these findings are still being investigated [Yan et al 1998, Bassett et al 1998, Shprintzen et al 1992, Chow et al 1994]

Growth. In a series of 95 patients between the ages of one and 15 years, 41% were below the 5th percentile in height, four of whom were significantly below the 5th percentile. Evaluation revealed low levels of growth factors IGF1 and IGFBP3 in all four patients. Three had evidence of growth hormone deficiency, three had a small pituitary gland on MRI, and two responded to growth hormone therapy [[Weinzimer et al 1998](#)].

Musculoskeletal system. Polyarticular juvenile rheumatoid arthritis (JRA) occurs in children with del 22q11 at a frequency 150 times that of the general population rate. The age of onset of JRA has ranged from 17 months to five years. HLA types that are permissive for the development of JRA are observed [[Sullivan et al 1997](#), [Keenan et al 1997](#)].

Of 108 patients evaluated for skeletal abnormalities, 6% had upper extremity anomalies, including pre- and post-axial polydactyly, and 15% had lower extremity anomalies including post-axial polydactyly, club foot, overfolded toes, and 2,3 syndactyly [[Ming et al 1997](#)].

Of 63 patients on whom chest films were examined, 19% had vertebral anomalies including butterfly vertebrae, hemivertebrae, and coronal clefts. Rib anomalies, most commonly supernumerary or absent ribs, occurred in 19%. Other anomalies, such as hypoplastic scapula, were seen in 1.5% of patients [[Ming et al 1997](#)].

Kidneys. A prospective evaluation using renal ultrasonography in 67 patients with del 22q11 who had no prior history of uropathy revealed renal or GU abnormalities in 37%. These included single kidney, echogenic kidney, multicystic dysplastic kidney, small kidneys, calculi, bladder wall thickening, horseshoe kidney, duplicated collecting system, and renal tubular acidosis. This high incidence of renal abnormalities is similar to that reported by [Devriendt et al \[1996\]](#).

Other. Other findings included: abnormal lung lobation; imperforate anus; hypospadias and undescended testes; hematologic abnormalities including idiopathic thrombocytopenia and, in one patient, Bernard-Soulier syndrome [[Budarf et al 1995](#)]; umbilical and inguinal hernia; significant constipation; bed wetting; leg pain; and craniosynostosis [[McDonald-McGinn et al 1995](#), [McDonald-McGinn et al 1999](#)].

Genotype-Phenotype Correlations

The majority of patients have the same large deletion of the DGCR; the size of the deletion remains unchanged with parent to child transmission. The great inter- and intrafamilial clinical variability makes genotype-phenotype correlations difficult [[Driscoll, Randall et al 1995](#)].

Prevalence

Estimates of prevalence vary from one in 4000 [[Wilson et al 1994](#)] to one in 6395 [[Devriendt et al 1998](#)]. Given the variable expression of del 22q11, the incidence is probably much higher than previously estimated.

Differential Diagnosis

It is appropriate to evaluate patients with a combination of the characteristic abnormalities or with single abnormalities such as conotruncal cardiac anomalies (interrupted aortic arch, truncus arteriosus, tetralogy of Fallot), VPI, unexplained hypocalcemia, or a non-verbal learning disability for 22q11 deletion.

In screening 251 patients based solely on their cardiac lesions, del 22q11 was found in 50% of patients with an interrupted aortic arch type B, 34.5% of patients with truncus arteriosus, 33% of patients with a conoventricular septal defect, and 16% of patients with tetralogy of Fallot [[Goldmuntz et al 1993](#)]. The frequency of del 22q11 did not vary with the presence of pulmonary atresia as compared to pulmonary stenosis with tetralogy of Fallot. There may be an increased frequency of del 22q11 in patients with tetralogy of Fallot and absent pulmonary valve syndrome [[Johnson et al 1995](#)]. This latter study supports evaluating patients with these specific cardiac anomalies in order to provide appropriate recurrence risk counseling and clinical management for these patients and their families.

It is important to note that the 22q11 deletion should now be included in the differential diagnosis of many disorders, such as [Smith-Lemli-Opitz syndrome](#) (when polydactyly and cleft palate are present) and [Alagille syndrome](#) (when butterfly vertebrae, congenital heart disease, and posterior embryotoxon are present), VATER, and oculo-auriculo vertebral syndrome (Goldehar). Furthermore, it should be noted that routine cytogenetic studies should be performed on all individuals suspected of having del 22q11 because they may have a chromosome abnormality involving some other chromosomal region.

Management

Depending on the age and presenting problems of the child, a multidisciplinary evaluation involving healthcare providers from the following specialties is often necessary: genetics, plastic surgery, speech pathology, otolaryngology, audiology, dentistry, cardiology, immunology, child development, child psychology, neurology, and general pediatrics. Some patients also require evaluation by healthcare providers specializing in feeding, endocrinology, rheumatology, gastroenterology, neurosurgery, general surgery, orthopedics, urology, hematology, psychiatry, and ophthalmology.

- In the neonatal period, it is appropriate to measure serum calcium concentration and absolute lymphocyte count and to perform a renal ultrasound. Low serum calcium concentration warrants calcium supplementation.

- A low absolute lymphocyte count necessitates evaluation of T and B cell subsets and referral to an immunologist. Infants with lymphocyte abnormalities should not be immunized with live vaccines (i.e., oral polio, MMR) and should have reevaluation of their immune status before receiving a live vaccine during childhood. In addition, antibody studies to assess results of immunizations are warranted.
- A baseline cardiac evaluation is recommended for all infants diagnosed with the del 22q11 syndrome.
- A baseline renal ultrasound examination is recommended due to the ~30% incidence of structural renal abnormalities.
- Children with growth failure should be evaluated by an endocrinologist for possible growth hormone deficiency.
- Early educational intervention is suggested to include speech therapy, due to the incidence of speech and language delay, beginning at age one year.
- Speech and language assessment may aid in diagnosis of a palatal abnormality or VPI. Referral to a craniofacial team for management is recommended.
- Magnetic resonant angiography (MRA) should be considered in individuals who are candidates for pharyngeal surgery to identify ectopic internal carotid arteries that may pose a risk for surgery.
- Strategies for feeding difficulties include modification of spoon placement when eating, treatment for G-E reflux with acid blockade, and prokinetic agents, postural therapy, and medication therapy for gastrointestinal dysmotility and facilitating bowel evacuation. [Dinulos and Graf 1998]

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 or cultural issues that individuals may face or to substitute for consultation with a genetics professional. To find a genetics or prenatal diagnosis clinic, see [GENETests](#). -ED.

Mode of Inheritance

The 22q11 deletion is inherited as a deletion syndrome.

Risk To Family Members

Parents of a proband. About 94% of probands have a *de novo* deletion of 22q11 and 6% have inherited the 22q11 deletion from a parent; thus, both parents of an individual with del 22q11 should have FISH testing.

Offspring of a proband. Offspring of individuals with the 22q11 deletion have a 50% chance of inheriting the 22q11 deletion.

Sibs of a proband. If the parents of an individual with del 22q11 have normal FISH studies, the recurrence risk is quite small, assuming a very low, and as yet undefined, risk of germline mosaicism.

Prenatal Testing

High-risk pregnancies. Prenatal testing using FISH analysis is possible for fetuses at 50% risk. Chromosome preparations obtained from fetal cells obtained by amniocentesis at 14-16 weeks' gestation or CVS at about 10-12 weeks' gestation can be analyzed using FISH in the same manner described in [Molecular Genetic Testing](#). In addition, high-risk fetuses may be evaluated between 18 and 22 weeks' gestation by high-resolution ultrasound examination for palatal anomalies and by echocardiography for cardiac anomalies.

Low-risk pregnancies. In some fetuses not known by family history to be at increased risk for del 22q11, findings of congenital heart disease and/or cleft palate detected by routine ultrasound examination may suggest the diagnosis in particular in those patients with conotruncal cardiac anomalies such as interrupted aortic arch, truncus arteriosus, tetralogy of Fallot, and ventricular septal defect. Chromosome preparations obtained from fetal cells can be analyzed using FISH. Establishing the diagnosis of the 22q11 deletion even late in gestation can be useful for perinatal management.

Molecular Genetics

Table 4. Molecular Genetics of 22q11 Deletion Syndrome

Critical Region	Locus	Normal Gene Product	Genomic Databases
DGCR	22q11	Unknown	OMIM LocusLink

- **Critical region name:** DGCR (DiGeorge chromosomal region)
- **Chromosomal locus:** 22q11
- **Normal allelic variants:** A number of genes have been mapped within the 22q11 deletion region (see [Table 5](#)).
- **Disease-causing allelic variants:** Although the overwhelming majority (>85%) of patients are deleted for the same ~3 Mb region, a minority of patients have variant deletion endpoints, and recurrent, smaller, nested deletions have been identified. In addition, several reports have described individual patients with atypical shorter deleted segments nested within the large typically deleted region (TDR) [[Levy et al 1995](#), [Kurahashi et al 1996](#), [O'Donnell et al 1997](#), [McQuade et al 1999](#)]. Recently, a small 20 Kb deletion within the typically deleted region was reported in a patient with a classic VCFS/DGS phenotype [[Yamagishi et al 1999](#)]. This smaller deletion disrupts the *UFD1L* and *CDC45L* genes. Several additional patients have been described whose deletions do not overlap the typically deleted region in that their deletions begin distal to it and extend telomerically. The location of duplicated sequence blocks in the vicinity of the 22q11 deletion endpoints strongly implicates them in the events leading to the typical and atypical deletions. Finally, a small number of patients have the deletion as the result of unbalanced translocations that delete the 22pter → q11 region.
- **Normal gene product:** Several of the gene products from within the deletion have been identified and are being further characterized. See [Table 5](#) for a list of genes and their relevant gene products.
- **Abnormal gene product:** Unknown

Resources

GeneClinics provides information about selected national organizations and resources for the benefit of the reader. GeneClinics is not responsible for information provided by other organizations. -ED.

- **Velo-Cardio-Facial Syndrome Education Foundation**
Jacobson Hall Room 707
University Hospital
750 East Adams Street
Syracuse, NY 13210
Phone: 315-464-6590
Fax: 315-464-5321
Email: vcfsef@hscsyr.edu
www.vcfsef.org
- **Chromosome Deletion Outreach, Inc**
PO Box 724
Boca Raton, FL 33429-0724
Phone: 888-CDO-6880 (888-236-6680); 561-391-5098 (family helpline)
Fax: 561-395-4252 (family helpline)
Email: cdo@worldnet.att.net
members.aol.com/cdousa/cdo.htm
- **International DiGeorge/VCF Support Network**
c/o Family Voices of New York
46 1/2 Clinton Avenue
Cortland, NY 13045
Phone: 607-753-1621 (day); 607-753-1250 (eve)
Fax: 607-758-7420
- **The 22q11 Group**
PO Box 1302
MK13 0LZ, United Kingdom
Phone: 19-08-32-08-52
Email: 22q11@melcom.cix.co.uk
www.vcfs.net
- **NCBI Genes and Disease Webpage**
www.ncbi.nlm.nih.gov/disease/DGS.html
- **Canadian 22q Group**
320 Cote Street Antoine
West Montreal, Quebec H3Y 2J4
Email: hsugarmill@aol.com
- **Australian 22q Group**
19 Eleanor Crescente/Rooty Hill
Sydney, NSW 2766 Australia
Phone: 61 2 625 3710
Email: vcfsfa@pnc.com.au

References

[MEDLINE](#) Articles on 22q11 Deletion Syndrome

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Literature Cited

- Auerbach AD (1993) Fanconi anemia diagnosis and the diepoxybutane (DEB) test. *Exp Hematology* 21:731
- Bassett AS, Hodgkinson K, Chow EW, Correia S, Scutt LE, Weksberg R (1998) 22q11 deletion syndrome in adults with schizophrenia. *Am J Med Genet* 81:328-37 [[Medline](#)]
- Bingham PM, Zimmerman RA, McDonald-McGinn D, Driscoll D, Emanuel BS, Zackai E (1997) Enlarged Sylvian fissures in infants with interstitial deletion of chromosome 22q11. *Am J Med Genet* 74:538-43 [[Medline](#)]
- Budarf ML, Konkle BA, Ludlow LB, Michaud D, Li M, Yamashiro DJ, McDonald-McGinn D, Zackai EH, Driscoll DA (1995) Identification of a patient with Bernard-Soulier syndrome and a deletion in the DiGeorge/velo-cardio-facial chromosomal region in 22q11.2. *Hum Mol Genet* 4:763-6 [[Medline](#)]
- Carey AH, Kelly D, Halford S, Wadey R, Wilson D, Goodship J, Burn J, Paul T, Sharkey A, Dumanski J, et al (1992) Molecular genetic study of the frequency of monosomy 22q11 in DiGeorge syndrome. *Am J Hum Genet* 51:964-70 [[Medline](#)]
- Cayler GG (1969) Cardiofacial syndrome. Congenital heart disease and facial weakness, a hitherto unrecognized association. *Arch Dis Child* 44:69-75 [[Medline](#)]
- Chow EW, Bassett AS, Weksberg R (1994) Velo-cardio-facial syndrome and psychotic disorders: implications for psychiatric genetics. *Am J Med Genet* 54:107-12 [[Medline](#)]
- Demuth I, Wlodarski M, Tipping A, Morgan NV, deWinter J, Thiel M, Grasl S, Schindler D, D'Andrea AD, Altay C, Kayserili H, Zatterale A, Kunze J, Ebell W, Mathew C, Joenji H, Sperling K, Digweed M (2000) Spectrum of mutations in the Fanconi Anemia Group G gene, FANCG/XRCC9. *Eur J Hum Genet* 8:861
- Desmaze C, Scambler P, Prieur M, Halford S, Sidi D, Le Deist F, Aurias A (1993) Routine diagnosis of DiGeorge syndrome by fluorescent in situ hybridization. *Hum Genet* 90:663-5 [[Medline](#)]
- Devriendt K, Fryns JP, Mortier G, van Thienen MN, Keymolen K (1998) The annual incidence of DiGeorge/velocardiofacial syndrome [letter] *J Med Genet* 35:789-90 [[Medline](#)]
- Devriendt K, Swillen A, Fryns JP, Proesmans W, Gewillig M (1996) Renal and urological tract malformations caused by a 22q11 deletion. *J Med Genet* 33:349 [[Medline](#)]
- deWinter JP, Waisfisz Q, Rooimans MA van Berkel CG, Bosnoyan-Collins L, Alon N, Carreau M, Bender O, Demuth I, Schindler D, Pronk JC, Arwert F, Hoehn H, Digweed M, Buchwald M, Joenje H (1998) The Fanconi anaemia group G gene FANCG is identical with XRCC9. *Nat Genet* 20:281
- Dinulos MB and Graf WD (1998) DiGeorge Syndrome and Velocardiofacial Syndrome. In: Gilman S, Goldstein GW, Waxman SG (eds) Neurobase, v 1.3-present, Arbor Press, Rochester, NY
- Driscoll DA, Budarf ML, Emanuel BS (1992) A genetic etiology for DiGeorge syndrome: consistent deletions and microdeletions of 22q11. *Am J Hum Genet* 50:924-33 [[Medline](#)]
- Driscoll DA, Chen P, Li M, et al (1995) Familial 22q11 deletions: phenotypic variability and determination of deletion boundaries by FISH. *Am J Hum Genet* 57:92 (abstr)
- Driscoll DA, Randall P, McDonald-McGinn DM, et al (1995) Are 22q11 chromosomal deletions a major cause of isolated cleft palate? 52nd Annual Meeting, American Cleft Palate-Craniofacial Association, Tampa
- Driscoll DA, Salvin J, Sellinger B, Budarf ML, McDonald-McGinn DM, Zackai EH, Emanuel BS (1993) Prevalence of 22q11 microdeletions in DiGeorge and velocardiofacial syndromes: implications for genetic counselling and prenatal diagnosis. *J Med Genet* 30:813-7 [[Medline](#)]
- Driscoll DA, Spinner NB, Budarf ML, McDonald-McGinn DM, Zackai EH, Goldberg RB, Shprintzen RJ, Saal HM, Zonana J, Jones MC, et al (1992) Deletions and microdeletions of 22q11.2 in velo-cardio-facial syndrome. *Am J Med Genet* 44:261-8 [[Medline](#)]
- Faivre I, Guardiola P, Lewis C, Dokal I, Ebell W, Zatterale A, Altay C, Poole J, Stones D, Kwee ML, van Weel-Sipman M, Havenga C, Morgan N, de Winter J, Digweed M, Savoia A, Pronk J, de Ravel T, Jansen S, Joenje H, Gluckman E, Mathew CG (2000) Association of complementation group and mutation type with clinical outcome in Fanconi anemia. *Blood* 96:4064

- FANCC is not associated with a severe phenotype in Japanese patients. *Blood* 95: 1493-8.
- Futaki M, Yamashita T, Yagasaki H, Toda T, Yabe M, Kato S, Asano S (2000) The IVS4 + 4 to T mutation of the Fanconi anemia gene FANCC is not associated with a severe phenotype in Japanese patients. *Blood* 95: 1493
- Garcia-Higuera I, Taniguchi T, Ganesan S, Meyn MS, Timmers C, Hejna J, Grompe M, D'Andrea AD (2001) Interaction of the Fanconi Anemia Proteins and BRCA1 in a Common Pathway. *Mol Cell* 7:249
- Gecz J, Hillman MA, Gedeon AK, Cox TC, Baker E, Mulley JC (2001) Gene structure and expression study of the SEDL gene for spondyloepiphyseal dysplasia tarda. *Genomics* 69:242
- Gedeon AK, Colley A, Jamieson R, Thompson EM, Rogers J, Sillence D, Tiller GE, Mulley JC, Gecz J (1999) Identification of the gene (SEDL) causing X-linked spondyloepiphyseal dysplasia tarda. *Nat Genet* 22: 400
- Giannotti A, Digilio MC, Marino B, Mingarelli R, Dallapiccola B (1994) Cayler cardiofacial syndrome and del 22q11: part of the CATCH22 phenotype [letter] *Am J Med Genet* 53: 303-4 [[Medline](#)]
- Gillio AP, Verlander PC, Batish SD, Giampietro PF, Auerbach AD (1997) Phenotypic consequences of mutations in the Fanconi anemia FAC gene: an international Fanconi anemia registry study. *Blood* 90: 105
- Goldmuntz E, Driscoll D, Budarf ML, Zackai EH, McDonald-McGinn DM, Biegel JA, Emanuel BS (1993) Microdeletions of chromosomal region 22q11 in patients with congenital conotruncal cardiac defects. *J Med Genet* 30: 807-12 [[Medline](#)]
- Gripp KW, McDonald-McGinn DM, Driscoll DA, Reed LA, Emanuel BS, Zackai EH (1997) Nasal dimple as part of the 22q11.2 deletion syndrome. *Am J Med Genet* 69:290-2 [[Medline](#)]
- Guion-Almeida ML, Richieri-Costa A (1992) CNS midline anomalies in the Opitz G/BBB syndrome: report on 12 Brazilian patients. *Am J Med Genet* 43:918-28 [[Medline](#)]
- Johnson MC, Strauss AW, Downton SB, Spray TL, Huddleston CB, Wood MK, Slauch RA, Watson MS (1995) Deletion within chromosome 22 is common in patients with absent pulmonary valve syndrome. *Am J Cardiol* 76:66-9 [[Medline](#)]
- Keenan GF, Sullivan KE, McDonald-McGinn DM, Zackai EH (1997) Letter to the editor. Arthritis associated with 22q11: more common than previously suspected. *Am J Med Genet* 71:488 [[Medline](#)]
- Krantz ID, Piccoli DA, Spinner NB (1997) Alagille syndrome. *J Med Genet* 34: 152-7 [[Medline](#)]
- Kurahashi H, Nakayama T, Osugi Y, Tsuda E, Masuno M, Imaizumi K, Kamiya T, Sano T, Okada S, Nishisho I (1996) Deletion mapping of 22q11 in CATCH22 syndrome: identification of a second critical region. *Am J Hum Genet* 58: 1377-81 [[Medline](#)]
- LaCassie Y and Arriaza MI (1996) Letter to the editor. Opitz GBBB syndrome and the 22q11 deletion syndrome. *Am J Med Genet* 62: 318 [[Medline](#)]
- Levin SE, Silverman NH, Milner S (1982) Hypoplasia or absence of the depressor anguli oris muscle and congenital abnormalities, with special reference to the cardiofacial syndrome. *S Afr Med J* 61:227-31 [[Medline](#)]
- Levran O, Erlich T, Magdalena N, Gregory JJ, Batish SD, Verlander PC, Auerbach AD (1997) Sequence variation in the Fanconi anemia gene FAA. *Proceedings of the National Academy of Science, USA* 94: 13051
- Levy A, Demczuk S, Aurias A, Depetris D, Mattei MG, Philip N (1995) Interstitial 22q11 microdeletion excluding the ADU breakpoint in a patient with DiGeorge syndrome. *Hum Mol Genet* 4: 2417-9 [[Medline](#)]
- Liu J, Young NS (1997) Clinical protocol: Retroviral mediated gene transfer of the Fanconi anemia complementation group C gene to hematopoietic progenitors of group C patients. *Hum Gene Ther* 8: 1715
- Liu N, Lamerdin JE, Tucker JD, Zhou, Z-Q, Walter CA, Albala JS, Busch DB, Thompson LH (1997) The human XRCC9 gene corrects chromosomal instability and mutagen sensitivities in CHO UV40 cells. *PNAS* 94:9232
- Lynch DR, McDonald-McGinn DM, Zackai EH, Emanuel BS, Driscoll DA, Whitaker LA, Fischbeck KH (1995) Cerebellar atrophy in a patient with velocardiofacial syndrome [see comments] *J Med Genet* 32: 561-3 [[Medline](#)]
- MacDonald MR, Schaefer GB, Olney AH, Tamayo M, Frias JL (1993) Brain magnetic resonance imaging findings in the Opitz G/BBB syndrome: extension of the spectrum of midline brain anomalies. *Am J Med Genet* 46: 706-11 [[Medline](#)]
- Matsuoka R, Takao A, Kimura M, Imamura S, Kondo C, Joh-o K, Ikeda K, Nishibatake M, Ando M, Momma K (1994) Confirmation that the conotruncal anomaly face syndrome is associated with a deletion within 22q11.2. *Am J Med Genet* 53:285-9 [[Medline](#)]
- McDonald-McGinn DM, Driscoll DA, Bason L, Christensen K, Lynch D, Sullivan K, Canning D, Zavod W, Quinn N, Rome J (1995) Autosomal dominant "Opitz" GBBB syndrome due to a 22q11.2 deletion [see comments] *Am J Med Genet* 59: 103-13 [[Medline](#)]

- McDonald-McGinn DM, Driscoll DA, Emanuel BS, et al (1996) The 22q11 deletion in African American patients: an underdiagnosed population. *Am J Hum Genet* 59:90 (abstr)
- McDonald-McGinn DM, Kirschner R, Goldmuntz E, et al (1999) Craniosynostosis: another feature of the 22q11.2 deletion syndrome. Platform presentation, 56th Annual Cleft Palate-Craniofacial Association Meeting. Craniosynostosis
- McDonald-McGinn DM, Kirschner R, Goldmuntz E, Sullivan K, Eicher P, Gerdes M, Moss E, Solot C, Wang P, Jacobs I, Handler S, Knightly C, Heher K, Wilson M, Ming JE, Grace K, Driscoll D, Pasquariello P, Randall P, Larossa D, Emanuel BS, Zackai EH (1999) The Philadelphia story: the 22q11.2 deletion: report on 250 patients. *Genet Couns* 10:11-24 [[Medline](#)]
- McDonald-McGinn DM, LaRossa D, Goldmuntz E, Sullivan K, Eicher P, Gerdes M, Moss E, Wang P, Solot C, Schultz P, Lynch D, Bingham P, Keenan G, Weinzimer S, Ming JE, Driscoll D, Clark BJ 3rd, Markowitz R, Cohen A, Moshang T, Pasquariello P, Randall P, Emanuel BS, Zackai EH (1997) The 22q11.2 deletion: screening, diagnostic workup, and outcome of results; report on 181 patients. *Genet Test* 1:99-108 [[Medline](#)]
- McDonald-McGinn DM, Zackai EH, Low D (1997) What's in a name? The 22q11.2 deletion [letter; comment] *Am J Med Genet* 72:247-9 [[Medline](#)]
- McQuade L, Christodoulou J, Budarf M, Sachdev R, Wilson M, Emanuel B, Colley A (1999) Patient with a 22q11.2 deletion with no overlap of the minimal DiGeorge syndrome critical region (MDGCR). *Am J Med Genet* 86:27-33 [[Medline](#)]
- Ming JE, McDonald-McGinn DM, Megerian TE, Driscoll DA, Elias ER, Russell BM, Irons M, Emanuel BS, Markowitz RI, Zackai EH (1997) Skeletal anomalies and deformities in patients with deletions of 22q11. *Am J Med Genet* 72:210-5 [[Medline](#)]
- Moss E, Wang PP, McDonald-McGinn, et al (1995) Characteristic cognitive profile in patients with a 22q11 deletion: verbal IQ exceeds nonverbal IQ. *Am J Hum Genet* 57:42 (abstr)
- Nakanishi K, Moran A, Hays T, Kuang Y, Fox E, Garneau D, Montes de Oca R, Grompe M, D'Andrea AD (2001) Functional analysis of patient-derived mutations in the Fanconi anemia gene, FANCG/XRCC9. *Exp Hem* (in press)
- Neri G, Genuardi M, Natoli G, Costa P, Maggioni G (1987) A girl with G syndrome and agenesis of the corpus callosum. *Am J Med Genet* 28:287-91 [[Medline](#)]
- O'Donnell H, McKeown C, Gould C, Morrow B, Scambler P (1997) Detection of an atypical 22q11 deletion that has no overlap with the DiGeorge syndrome critical region [letter] *Am J Hum Genet* 60:1544-8 [[Medline](#)]
- Pizzuti A, Novelli G, Ratti A, Amati F, Mari A, Calabrese G, Nicolis S, Silani V, Marino B, Scarlato G, Ottolenghi S, Dallapiccola B (1997) UFD1L, a developmentally expressed ubiquitination gene, is deleted in CATCH 22 syndrome. *Hum Mol Genet* 6:259-65 [[Medline](#)]
- Pulsipher M, Kupfer GM, Naf D, Suliman A, Lee J-S, Jakobs P, Grompe M, Joenje H, Sieff C, Guinan E, Mulligan R, D'Andrea AD (1998) Subtyping analysis of Fanconi anemia by immunoblotting and retroviral gene transfer. *Mol Med* 4:468
- Sanklecha M, Kher A, Bharucha BA (1992) Asymmetric crying facies: the cardiofacial syndrome. *J Postgrad Med* 38:147-50 [[Medline](#)]
- Scambler PJ, Carey AH, Wyse RK, Roach S, Dumanski JP, Nordenskjold M, Williamson R (1991) Microdeletions within 22q11 associated with sporadic and familial DiGeorge syndrome. *Genomics* 10:201-6 [[Medline](#)]
- Seyschab H, Sun Y, Friedl R, Schindler D, Hoehn H (1993) G2 phase cell cycle disturbance as a manifestation of genetic cell damage. *Hum Genet* 92:61.
- Shprintzen RJ, Goldberg R, Golding-Kushner KJ, Marion RW (1992) Late-onset psychosis in the velo-cardio-facial syndrome [letter] *Am J Med Genet* 42:141-2 [[Medline](#)]
- Silengo MC, Bell GL, Biagioli M, Guala A, Bianco R, Strandoni P, De Sario PN, Franceschini P (1986) Asymmetric crying facies with microcephaly and mental retardation. An autosomal dominant syndrome with variable expressivity. *Clin Genet* 30:481-4 [[Medline](#)]
- Smith CA, Driscoll DA, Emanuel BS, McDonald-McGinn DM, Zackai EH, Sullivan KE (1998) Increased prevalence of immunoglobulin A deficiency in patients with the chromosome 22q11.2 deletion syndrome (DiGeorge syndrome/velocardiofacial syndrome). *Clin Diagn Lab Immunol* 5:415-7 [[Medline](#)]
- Solot C, Gerdes M, McDonald-McGinn D, et al (1998) Developmental profiles in a pre-school population with 22q11 deletion. American Cleft Palate-Craniofacial Association 55th Annual Meeting and Conference Symposium, Baltimore, MD
- Sullivan KE, Jawad AF, Randall P, Driscoll DA, Emanuel BS, McDonald-McGinn DM, Zackai EH (1998) Lack of correlation

between impaired T cell production, immunodeficiency, and other phenotypic features in chromosome 22q11.2 deletion syndromes. *Clin Immunol Immunopathol* 86: 141-6 [[Medline](#)]

- Sullivan KE, McDonald-McGinn D, Driscoll DA, Emanuel BS, Zackai EH, Jawad AF (1999) Longitudinal analysis of lymphocyte function and numbers in the first year of life in chromosome 22q11.2 deletion syndrome (DiGeorge syndrome/velocardiofacial syndrome). *Clin Diagn Lab Immunol* 6: 906-11 [[Medline](#)]
- Sullivan KE, McDonald-McGinn DM, Driscoll DA, Zmijewski CM, Ellabban AS, Reed L, Emanuel BS, Zackai EH, Athreya BH, Keenan G (1997) Juvenile rheumatoid arthritis-like polyarthritis in chromosome 22q11.2 deletion syndrome (DiGeorge anomalad/velocardiofacial syndrome/conotruncal anomaly face syndrome). *Arthritis Rheum* 40: 430-6 [[Medline](#)]
- Thomas JA, Graham JM Jr (1997) Chromosomes 22q11 deletion syndrome: an update and review for the primary pediatrician. *Clin Pediatr (Phila)* 36: 253-66 [[Medline](#)]
- Tiller GE, Hannig VL, Dozier DP, Carrel L, Trevarthen KC, Wilcox WR, Mundlos S, Haines JL, Gedeon AK, Gecz J (2001) A recurrent RNA splicing mutation in the SEDL gene causes X-linked spondyloepiphyseal dysplasia tarda (SEDL). *Am J Hum Genet* (in press)
- Timmers C, Taniguchi T, Hejna J, Reifsteck C, Lucas L, Bruun D, Thayer M, Cox B, Olson S, D'Andrea A, Moses R, Grompe M (2001) Positional cloning of a novel Fanconi Anemia gene, FANCD2. *Mol Cell* 7: 241
- Waisfisz Q, Morgan NV, Savino M, De Winter JP, van Berkel CG, Hoatlin ME, Ianzano L, Gibson RA, Arwert F, Savoia A, Mathew CG, Pronk JC, Joenje H (1999) Spontaneous functional correction of homozygous Fanconi Anaemia alleles reveals novel mechanistic basis for reverse mosaicism. *Nat Genet* 22: 379
- Wang PP, Solot C, Moss EM, Gerdes M, McDonald-McGinn DM, Driscoll DA, Emanuel BS, Zackai EH (1998) Developmental presentation of 22q11.2 deletion (DiGeorge/velocardiofacial syndrome). *J Dev Behav Pediatr* 19: 342-5 [[Medline](#)]
- Weinzimer SA, McDonald-McGinn DM, Driscoll DA, Emanuel BS, Zackai EH, Moshang T Jr (1998) Growth hormone deficiency in patients with 22q11.2 deletion: expanding the phenotype. *Pediatrics* 101: 929-32 [[Medline](#)]
- Whitney MA, Saito H, Jakobs PM, Gibson RA, Moses RE, Grompe M (1993) A common mutation in the FACC gene causes Fanconi anemia in Ashkenazi Jews. *Nat Genet* 4: 202
- Wilson DI, Burn J, Scambler P, Goodship J (1993) DiGeorge syndrome: part of CATCH 22. *J Med Genet* 30: 852-6 [[Medline](#)]
- Wilson DI, Cross IE, Goodship JA, Brown J, Scambler PJ, Bain HH, Taylor JF, Walsh K, Bankier A, Burn J, et al (1992) A prospective cytogenetic study of 36 cases of DiGeorge syndrome. *Am J Hum Genet* 51: 957-63 [[Medline](#)]
- Wilson DI, Cross IE, Wren C, et al (1994) Minimum prevalence of chromosome 22q11 deletions. *Am J Hum Genet* 55: A169 (abstr)
- Wulfsberg EA, Leana-Cox J, Neri G (1996) What's in a name? Chromosome 22q abnormalities and the DiGeorge, velocardiofacial, and conotruncal anomalies face syndromes [see comments] *Am J Med Genet* 65: 317-9 [[Medline](#)]
- Yamagishi H, Garg V, Matsuoaka R, Thomas T, Srivastava D (1999) A molecular pathway revealing a genetic basis for human cardiac and craniofacial defects *Science* 283: 1158-61 [[Medline](#)]
- Yamashita T, Wu N, Kupfer G, Corless C, Joenje H, Grompe M, D'Andrea AD (1996) The Clinical variability of Fanconi Anemia (Type C) results from expression of an amino terminal truncated FAC polypeptide with partial activity. *Blood* 87: 4424
- Yan W, Jacobsen LK, Krasnewich DM, Guan XY, Lenane MC, Paul SP, Dalwadi HN, Zhang H, Long RT, Kumra S, Martin BM, Scambler PJ, Trent JM, Sidransky E, Ginns EI, Rapoport JL (1998) Chromosome 22q11.2 interstitial deletions among childhood-onset schizophrenics and "multidimensionally impaired". *Am J Med Genet* 81: 41-3 [[Medline](#)]

Suggested Readings

- Burn J, Takao A, Wilson D, Cross I, Momma K, Wadey R, Scambler P, Goodship J (1993) Conotruncal anomaly face syndrome is associated with a deletion within chromosome 22q11. *J Med Genet* 30: 822-4 [[Medline](#)]
- de la Chapelle A, Herva R, Koivisto M, Aula P (1981) A deletion in chromosome 22 can cause DiGeorge syndrome. *Hum Genet* 57: 253-6 [[Medline](#)]
- Emanuel BS, Budard ML, Shaikh T, et al (1998) Blocks of duplicated sequence define the endpoints of DGS/VCFS 22q11 deletions. *Am J Hum Genet* 63: A11 (abstr)
- Fryburg JS, Lin KY, Golden WL (1996) Chromosome 22q11.2 deletion in a boy with Opitz (G/BBB) syndrome. *Am J Med Genet* 62: 274-5 [[Medline](#)]

- Kelley RI, Zackai EH, Emanuel BS, Kistenmacher M, Greenberg F, Punnett HH (1982) The association of the DiGeorge anomalad with partial monosomy of chromosome 22. *J Pediatr* 101: 197-200 [[Medline](#)]
- Nickel RE, Magenis RE (1996) Neural tube defects and deletions of 22q11. *Am J Med Genet* 66:25-7 [[Medline](#)]
- Nickel RE, Pillers DA, Merkens M, Magenis RE, Driscoll DA, Emanuel BS, Zonana J (1994) Velo-cardio-facial syndrome and DiGeorge sequence with meningomyelocele and deletions of the 22q11 region. *Am J Med Genet* 52:445-9 [[Medline](#)]
- Nickel RE, Pillers DM, Merkens M, Magenis RE, Driscoll DA, Emanuel BS, Zonana J (1993) Velo-cardio-facial and DiGeorge syndromes with meningomyelocele and deletions of the 22Q11 region. *Eur J Pediatr Surg* 3 Suppl 1:27-8 [[Medline](#)]
- Ryan AK, Goodship JA, Wilson DI, Philip N, Levy A, Seidel H, Schuffenhauer S, Oechsler H, Belohradsky B, Prieur M, Aurias A, Raymond FL, Clayton-Smith J, Hatchwell E, McKeown C, Beemer FA, Dallapiccola B, Novelli G, Hurst JA, Ignatius J, Green AJ, Winter RM, Brueton L, Brondum-Nielsen K, Scambler PJ, et al (1997) Spectrum of clinical features associated with interstitial chromosome 22q11 deletions: a European collaborative study *J Med Genet* 34:798-804 [[Medline](#)]
- Zackai EH, McDonald-McGinn DM, Driscoll DA, et al (1996) Dysphagia in patients with a 22q11 deletion: unusual pattern found on modified barium swallow. *Am J Hum Genet* 59A:600

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