Max Appeal!
Supporting Families affected by DiGeorge Syndrome/VCFS/22q11.2 deletion

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Max Appeal – the official group

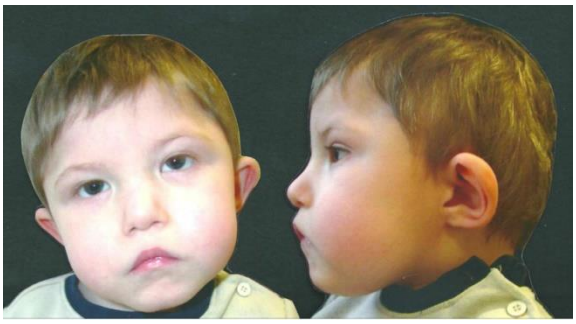
Health & care information you can trust

Information for Students

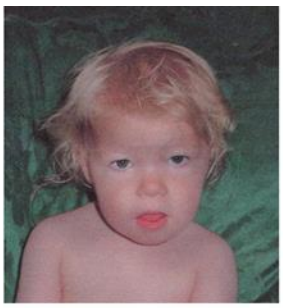
The purpose of this brief leaflet is to introduce medical and other interested students to 22q11.2 Deletion Syndrome (22q11DS). The information has been compiled from the most current and authoritative sources, which are listed at the end. The main sources are the National Consensus for the Diagnosis and Management of 22q11DS and the article in the European Journal of Pediatrics "Towards a safety net for management of 22q11.2 deletion syndrome: guidelines for our times". The leaflet has been produced by Max Appeal, the national charity for people with 22q11DS, in line with its Information Standard production process.

Diagnosing the condition.

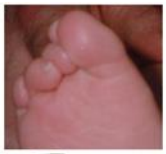
The syndrome is a multisystem disorder with several major features, and many less severe abnormalities which aid detection, in conjunction with typical facial dysmorphia which collectively are not always appreciated by clinicians.



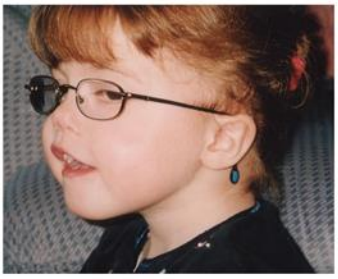
The photographs below have been supplied by Max Appeal families and show some physical and facial characteristics.

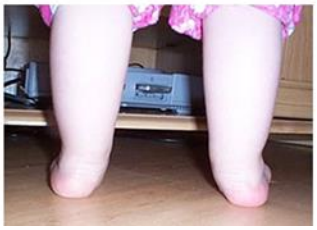


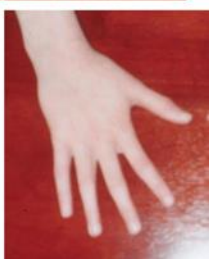
Cyanotic lips
Low set ears
Over-folded toes
Long fingers
Pronated ankles



Open-mouthed expression
Thin top lip/small mouth
Flat cheeks
Slightly puffy eye lids
Small nostrils
Small chin



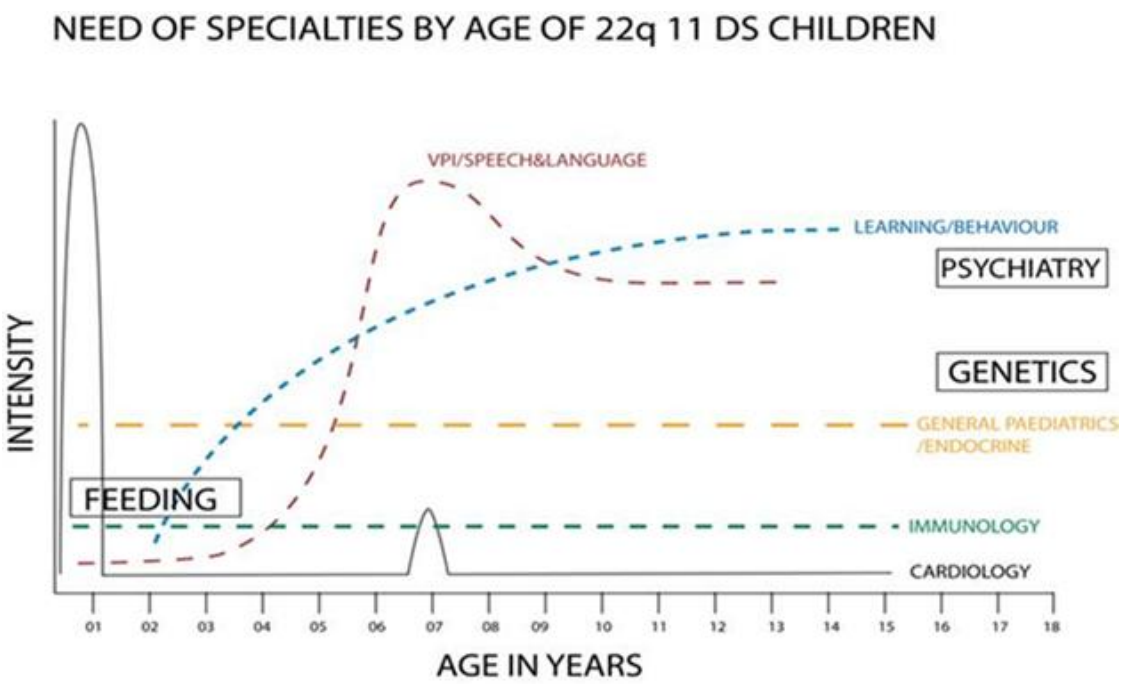




The 22q11.2 deletion is a 1.5- to 3-megabase deletion on the long (q) arm of chromosome 22. The deletion contains TBX1, the major candidate gene, and other genes, controlling the third and fourth pharyngeal arches, brain and skeletal development. Haploinsufficiency results in the principal syndrome phenotype. No correlation between the size or site of the deletion with phenotype has yet been found. The deletion occurs spontaneously in 85–90 % of patients or is inherited from either parent in an autosomal dominant fashion. An unaffected parent may carry the deletion in their egg or sperm (germline mosaicism); their recurrence risk is 1 %. The 22q11DS population prevalence is reported to be one in 4,000 to one in 6,000. Though the VCFSEF (Velo-Cardio-Facial Syndrome Education Foundation) report this as 1 in 2,000.

Diagnosis in 95 % of subjects with the deletion has been by fluorescent in situ hybridisation (FISH), and is being superseded by methods that also reveal the 5 % of atypical deletions which FISH fails to identify. They include array comparative genome hybridisation (aCGH), genome wide microarrays and multiplex ligation-dependent probe amplification (MPLA).
The multitude of combinations can cause diagnostic confusion, a legacy of which has been the nomenclature applied to apparently different syndromes such as DiGeorge, velocardiofacial, conotruncal now known to be usually due to the 22q11.2 deletion as well as some of the problems associated with Opitz G/BBB and Cayler cardiofacial syndromes (ref Children's Hospital of Philadelphia). Rates of detection increase where specialists are familiar with the condition.

How the condition affects people.
With present-day treatment, survival beyond infancy is 90–95 % although life span may be reduced in some as adults. It is likely that only the more severely affected children and a small proportion of adults are currently correctly identified and receiving appropriate support from social, educational and health services.



93% are affected by behavioural and psychiatric disorders, with 24% of adults being affected by schizophrenia.

- Articulation and communication problems occur in 90%, characterised by hypernasal articulation due to VPI (velo pharyngeal insufficiency).
- 70 % or more are affected by congenital heart disease, immune deficiency and learning difficulties with an average IQ in the 70's.
- Those conditions found in 25–50 % include:
    - feeding disorders,
    - early growth faltering,
    - gut dysmotility
    - neurological conditions
    - hearing impairment
    - haematological and autoimmune disorders. hypocalcaemia,
    - structural (renal, skeletal, brain, gastrointestinal, eye and dental) abnormalities

The VCFSEF factsheet lists 188 different anomalies.

22q11.2 *duplication* was first reported in 1999. There appear to be many overlaps in reported symptoms but this is still an emerging condition. (ref; chromosome 22 central)

Management of the Condition/Recommended Schedule of Tests.
(compiled by Hilary Joyce in the Parent/Carer Consensus Document – ref Max Appeal)

	At diagnosis	Infancy <1yr	Pre-School 1-5 yr	School age6-11 yr	Adolescence 12-18yr	Adult >18 yr
Ionised calcium and PTH (Parathyroid hormone)	✓	✓	✓	✓	✓	✓
TSH (thyroid stimulating hormone)	✓		✓	✓	✓	✓
FBC (full blood count and differential) Annual check	✓	✓	✓	✓	✓	✓
Immunologic evaluation	✓		✓			
Opthalmology (eyes)	✓		✓			
Evaluate palate	✓	✓	✓			
Audiology (hearing)	✓	✓	✓			✓
Cervical spine			✓			
Scoliosis	✓		✓		✓	
Dental evaluation			✓	✓	✓	✓
Renal ultrasound	✓					
ECG	✓					✓
Echocardiogram	✓					
Development	✓	✓	✓			
School performance				✓	✓	
Socialisation/functioning	✓	✓	✓	✓	✓	✓
Psychiatric/emotional/behavioural	✓		✓	✓	✓	✓
Systems review	✓	✓	✓	✓	✓	✓
Deletion studies of parents	✓					
Genetic counselling	✓				✓	✓

References and Resources:

The National Consensus Document for the Diagnosis and Management of 22q11DS
http://www.maxappeal.org.uk/knowledge/consensus_document/content.asp?s=44&p=67

"Towards a safety net for management of 22q11.2 deletion syndrome: guidelines for our times" - European Journal of Pediatrics
http://link.springer.com/article/10.1007%2Fs00431-013-2240-z

The Children's Hospital of Philadelphia 22q and You Centre
https://www.chop.edu/service/22q-and-you-center/home.html

The Velo-Cardio-Facial Syndrome Education Foundation.
http://www.vcfsef.org/resources.php

Chromosome 22 Central - re: 22q11 duplications.
http://www.c22c.org/22q11dup.htm

22q11DS growth Charts.
http://www.maxappeal.org.uk/knowledge/early_years/content.asp?s=40&p=74

The 22q Society is the international academic society that is open to clinicians, researchers and academics with an expertise or interest in 22q11DS.
www.22qsociety.org

About Max Appeal.
The charity was founded by parents of children with the condition and gained charitable status in 2001. Max Appeal was initially a fundraising banner but due to the confusion with names for the conditions (DiGeorge syndrome, VCFS, 22q11.2 deletion and so on), Max Appeal was easier for people to connect with and so was adopted as the name of the charity. Max was the son of Paul and Julie Wootton who died in 1999 of septicaemia when he was four months old.

It cannot be over-emphasised how this condition can detrimentally affect every aspect of a person's daily life especially with poor care and support. Max Appeal's mission is to enable people with 22q deletion to lead an independent and economically prosperous life as possible with Max Appeal being the voice to achieve appropriate medical care, social support, employment and empowerment for individuals and their families. The charity offers advice and support to almost 800 families across the UK and is generally regarded as the largest charity for this condition in the world.

The National Consensus Document was initiated by Dr Kumararatne, a trustee of Max Appeal and consultant immunologist at Addenbrooke's Hospital. Max Appeal funded all of the expenditure for the project and facilitated communication between the authors. The authors are recognised experts within their field and have an interest in 22q11DS, and now form the medical panel for the charity.

The article in the European Journal of Paediatrics was written by Dr Alex Habel who is the retired paediatrician from the specialist 22q clinic at Great Ormond Street Hospital, based upon the information within the National Consensus Document. The open access for this article was funded by Max Appeal. Alex Habel is also Max Appeal's medical advisor for the 22q11DS All-party Parliamentary Group being established by Max Appeal to raise awareness of the condition. Max Appeal is the secretariat to the 22q Society.