22q11.2 SA
Deletion Syndrome Foundation

UNDIAGNOSED…

Have you considered testing for the 22q11.2 Deletion or Duplication Syndrome?

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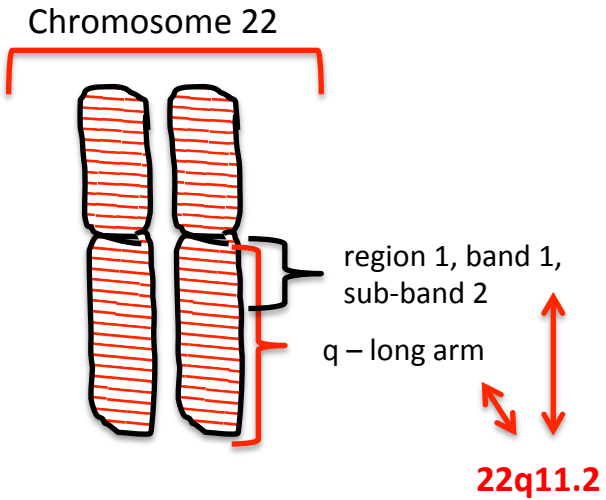
What does 22q11.2 mean?

It refers to the location within a specific chromosome

Humans have 23 pairs of chromosomes - numbered 1 to 23

Chromosomes are made from long strands of DNA molecules

Genes are sections of DNA…and they contain instructions for coding proteins... So DNA contains our genetic information



Chromosomes have short arms known as ‘p’ and long arms known as ‘q’

The area of 22q11.2 holds between 30-40 genes...and the deletion or duplication could vary in size between 1.5Mb to 3Mb, therefore the variability of the syndrome

But, 22q11.2 means a deletion or duplication in only one of the two chromosomes ‘22’

The deletion or duplication of a piece of chromosome 22 will happen within the long arm ‘q’, in region 1, band 1, sub-band 2… hence 22q11.2

How common is the 22q11.2 deletion or duplication?

22q11.2 Deletion:

Statistics vary considerably, but the deletion occurs in approximately 1 in every 1,000 to 4,000 live births, although this is likely an underestimate of its prevalence.
It is thought to be almost as common as Down Syndrome.

22q11.2 Duplication:

The duplication has not been researched as extensively as the deletion, but current statistics indicate the duplication to be about half as common as the deletion.

What does that mean for South Africa:

- Estimated that about 1million babies will be born in South Africa during 2018 (StatsSA)
- The infant mortality rate for 2018 is estimated at 36.4 per 1000 live births (StatsSA)
    - if we work on an estimate of +- 960 000 (surviving) births for 2018…
    - and apply the average 22q11.2 deletion statistics of 1 in 3000 live births…
    - We should have at least 300+ new birth diagnoses of 22q11.2 deletion syndrome during 2018
    - Therefore, we should have about 150 new birth diagnoses of 22q11.2 duplication syndrome during 2018

22q11.2 facts

22q11.2 Deletion:

- The second most common genetic cause of intellectual disabilities and the most common micro-deletion syndrome
- Mainly de novo / spontaneous mutations
- Individuals diagnosed will have all, some or none of the problems associated with the syndrome
- Many different names have been used to describe the same syndrome, including Velo-Cardio-Facial Syndrome ("VCFS"), Shprintzen Syndrome, DiGeorge Syndrome
- Facial features could include elongated face, prominent nasal bridge and nasal tip, almond shape eyes, small ears and some individuals will have tapered fingers
- Extensive international research and regular published guidelines on dealing with patients

22q11.2 Duplication:

- About half as common as the 22q11.2 Deletion Syndrome
- Mainly familial / hereditary
- Identified when genetic tests confirm an extra copy of a small piece of no.22 chromosome
- Individuals diagnosed will have all, some or none of the problems associated with the syndrome
- To date, no extensive research and limited published guidelines on dealing with patients…recommendations are to follow 22q11.2 Deletion guidelines until more data becomes available

Key characteristics include

- cardiac abnormalities or heart defects at birth
- cleft palate or other palate abnormalities
- low immunity or immune deficiencies
- chronic upper respiratory and middle ear infections
- feeding, swallowing, breathing problems
- infant nasal regurgitation
- gastrointestinal issues including reflux
- chronic constipation
- seizures
- thyroid problems and other endocrine issues
- calcium deficiencies
- kidney abnormalities
- hernia
- scoliosis
- speech and language delays; hypernasal speech
- developmental delays
- learning challenges and differences
- behavioural challenges and differences, autism, ADHD, OCD, anxiety,
- mental illness

22q11.2 Deletion

- TBX1 gene omitted…
- Impacts pharyngeal pouches
  - Thymus and parathyroid... Hypoplasia...deficiency in mature T Cells
  - Hypocalcemia

22q11.2 Duplication

- Anomalies / problems not as prominent / severe as in deletion

Recommended genetic testing

FISH is still commonly used: Fluorescence in situ hybridization (FISH) provides researchers with a way to visualize and map the genetic material in an individual's cells, including specific genes or portions of genes. This may be used for understanding a variety of chromosomal abnormalities and other genetic mutations.

However, new more favourable tests and recommendations have been published...

22q11.2 Deletion:

- Methods that can tell the size of the deletion:
  - "Genome-wide" methods such as comparative genomic hybridization - single nucleotide polymorphism (SNP) microarray or multiplex ligation-dependent probe amplification (MLPA) tests
- A standard cytogenetic test (karyotype) is not recommended as it only detects about 25% of cases

22q11.2 Duplication:

- Array genomic hybridization (array GH) or
- Multiplex ligation-dependent probe amplification (MLPA)
- 22q11.2 Duplication Syndrome is not detectable by routine genetic testing (karyotyping)

Closing thoughts…

The very variable expression of 22q11.2 Deletion Syndrome makes for clinical challenges especially in the absence of more serious symptoms like congenital heart disorders, immune complications, and palatal anomalies. However, delayed diagnosis for families means delayed access to resources and crucially, early intervention services and much-needed parental knowledge on developmental, educational, behavioural and mental health issues.

What is the solution…

- more education and awareness?
  - Who is the audience / target market?

- New born screening?
  - at what / whose cost?
  - when is specific new born screening justifiable?

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Resources

Information obtained from:

- www.massgeneral.org
  - The 22q11 Deletion Syndrome Clinic at Massachusetts General Hospital
- https://www.ncbi.nlm.nih.gov
  - NCBI (National Center for Biotechnology Information) - PMC
- www.22q.org
  - The International 22q11.2 Foundation Inc.
- www.22q.org.au
  - 22q Foundation Australian & New Zealand
- www.22qireland.org
  - 22q11 Ireland Support Group

Thank you

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