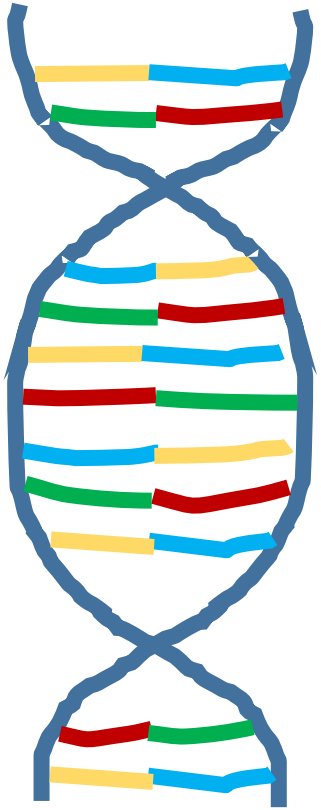
1 Step

What is DNA?

What are Genes?

Genes are sections of DNA.

They contain instructions for coding the proteins humans and other organisms need to live.



DNA stands for deoxyribonucleic acid.

DNA contains our genetic information.

The information is stored in four parts called bases.

The will only ever pair up with their specific partner:

Adenine (A) – Thymine (T)
Guanine (G) – Cytosine (C)

When the bases are paired they form a spiral called a double helix.

DNA is found in a cell's nucleus.

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2 Step

What are chromosomes?

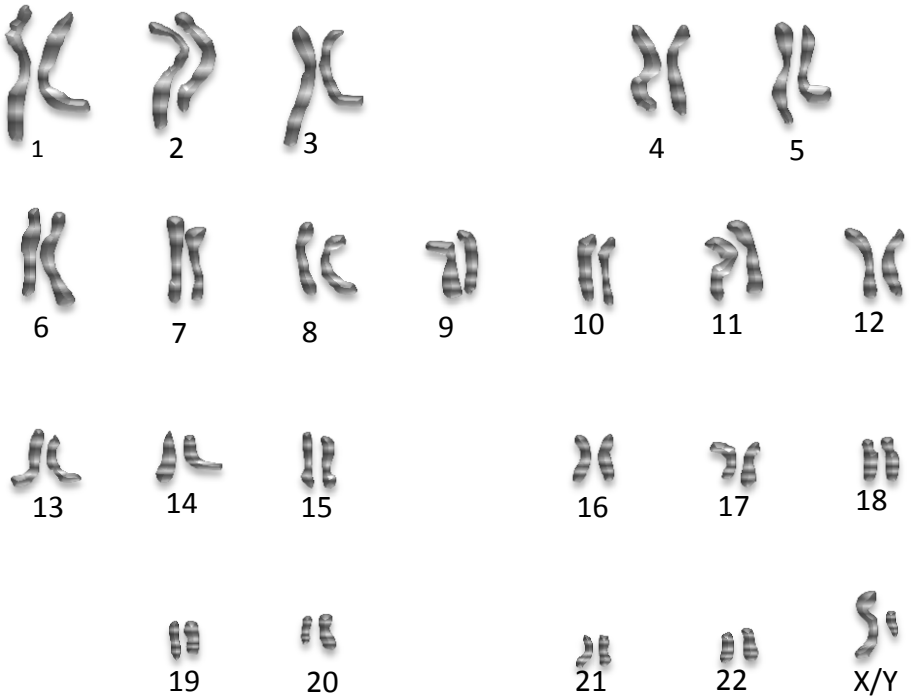
Chromosomes are made from long strands of DNA molecules.

<u>The chromosomes are numbered 1 – 22 in size order from largest to smallest.</u>

The 23rd pair of chromosomes are the sex chromosomes.

Females have two ‘X’ chromosomes (XX).

Males have an ‘X’ and a ‘Y’ chromosomes (XY).



Humans have 23 pairs of chromosomes.

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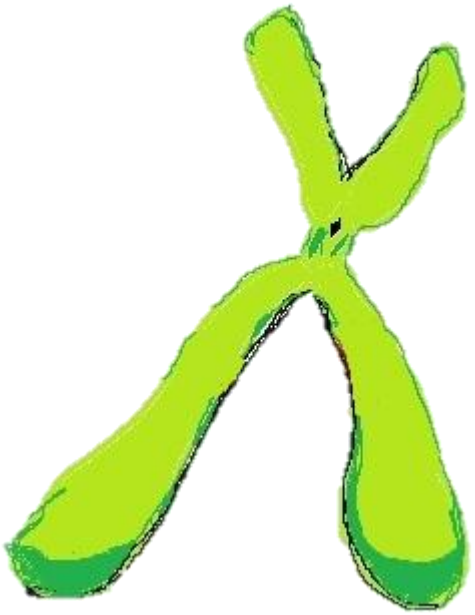
3 Step

Chromosome 22

Chromosome 22 is the second smallest chromosome



Chromosomes have two short arms and two long arms.

The short arms are known as ‘p’ and the long arms are known as ‘q’.

We inherit a short and a long arm of chromosomes 1-22 from each of our parents.

Chromosome 22 represents between 1.6–1.8% of the DNA in our cells.

Chromosome 22 was the first chromosome to be sequenced by Human Genome Project.

Dr Ian Dunham and his team (1999) reported their finding in a very prestigious journal called Nature.

Chromosome 22 was chosen because of its small size.

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4 Step

22q11.2 Deletion: What is a deletion?

DNA is special to everyone.

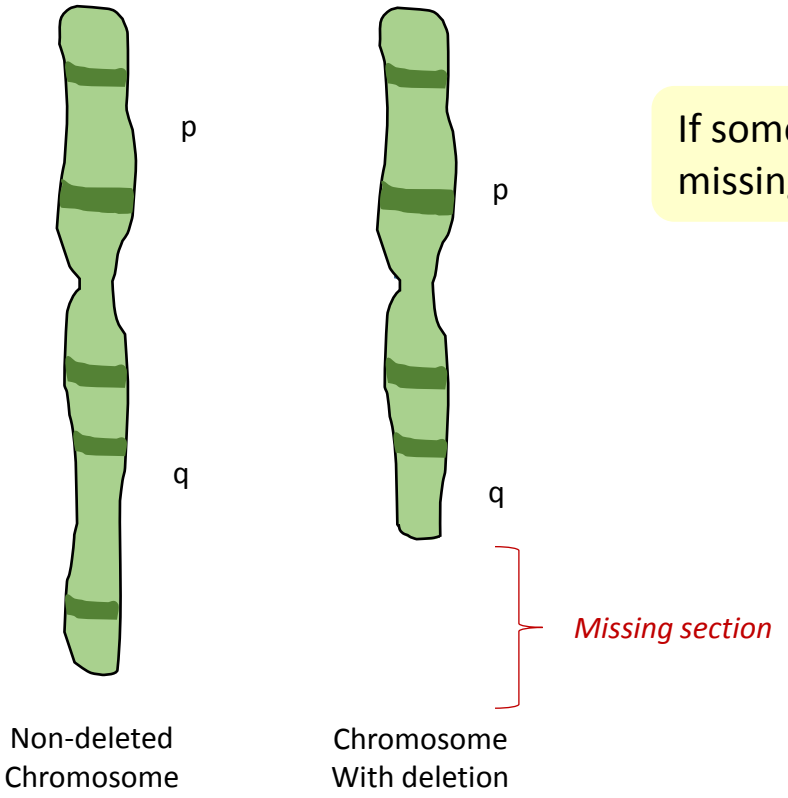
Our DNA is different to other people's DNA (even if we are family members). It is our genetic fingerprint.

It controls how we look, for example, whether we have **blue** or **brown** eyes.

It can also affect how we think and behave.

When compared to others, some people may have a small extra bit of DNA.

Others may have a small bit of DNA missing.



If someone has a small bit of DNA missing, we call this a deletion.

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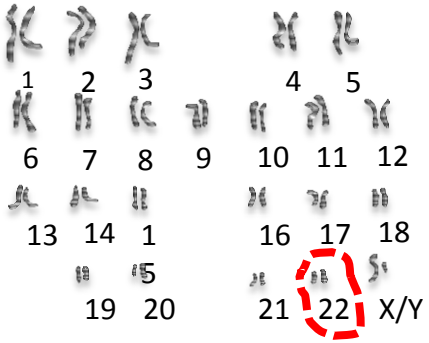
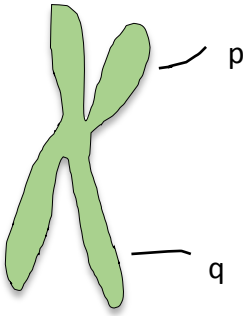
5 Step

22q11.2 deletion: what does the name mean and how common is it?



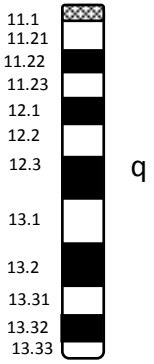
22

Chromosome number



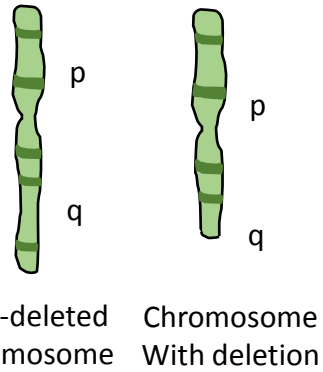
q

Long arm of chromosome



11.2

Location on the long arm



deletion

Information is missing

22q11.2 is one of the most common chromosome disorders.

It is estimated that 22q11.2 deletion is present in 1: 2000/4000 live births.

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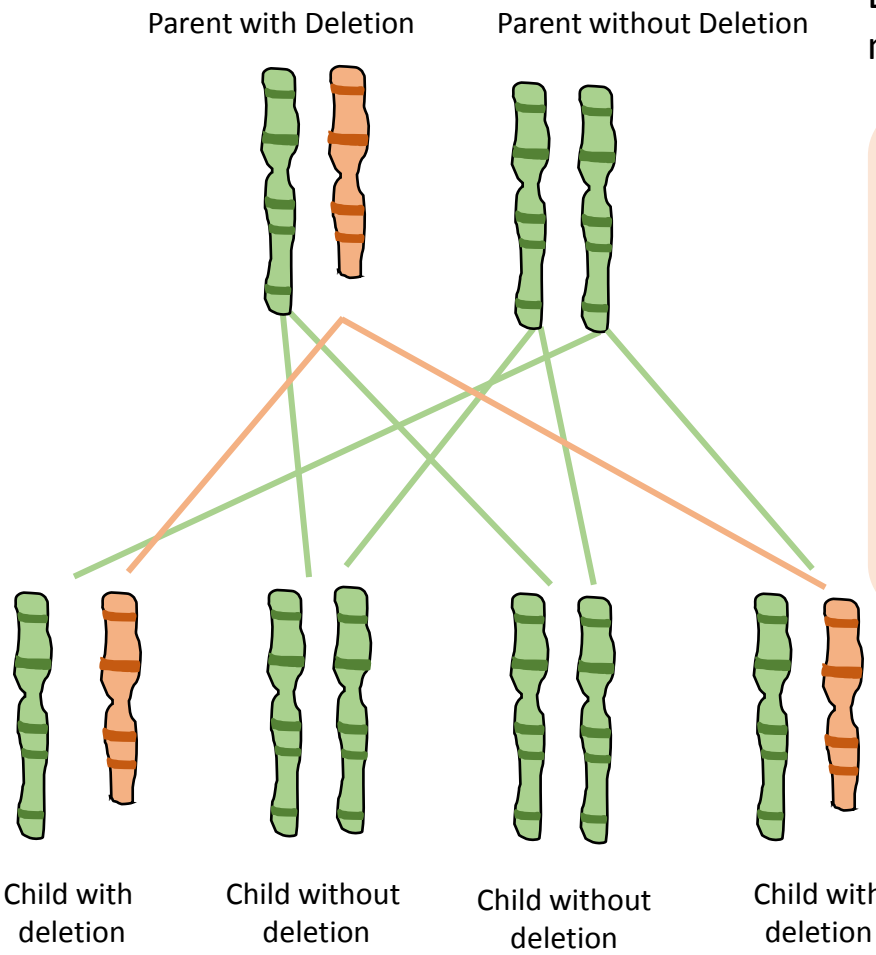
6 Step

Inheritance of 22q11.2 Deletion Syndrome.

Geneticists can test for 22q11.2 deletion by taking a small amount of blood from you and your family members.

The blood then goes through a process called FISH testing or Micro Array.



If a parent has the deletion, they have a 50:50 chance of passing it onto their children.

Deletions such as 22q11.2 deletion mostly occur by chance (De Novo).

They can also be inherited (*see diagram*).

This is when a parent who has the deletion passes their chromosome with the deletion to their child (the parent may have the deletion but be less affected by it).

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7 Step

What does de novo mean and how does the deletion occur?

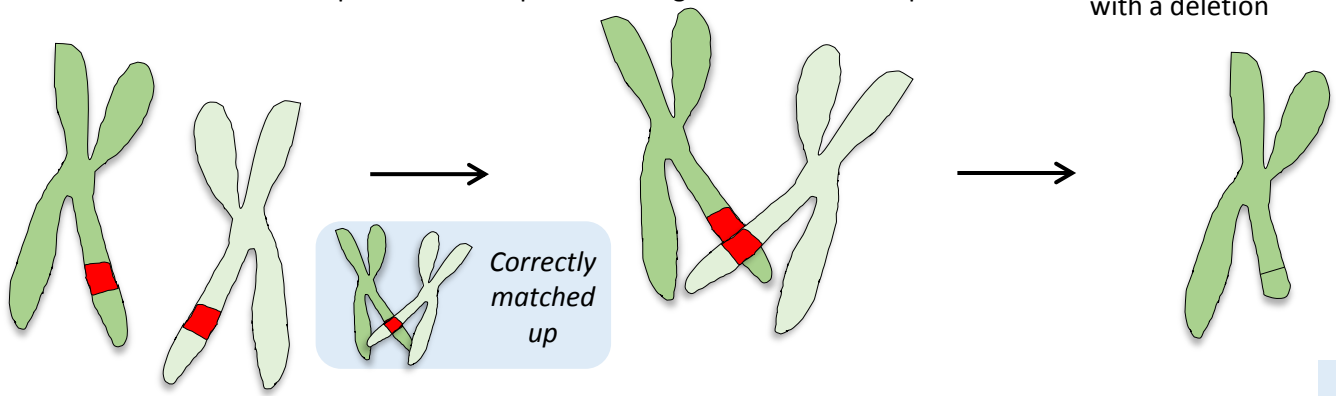
In human fertilisation, a chromosome from each parent crosses over.

This happens for all humans and is why we are all a mixture of our parents' DNA.

De novo is Latin for "from the beginning".

When geneticists use the term 'De Novo' they mean the deletion was not inherited from the parents and occurred by chance.

1. Chromosome 22 from each parent
2. Chromosomes cross over at the wrong place. The regions don't match up.
3. This produces a chromosome with a deletion



Deletions occur when the chromosome cross over at the wrong place. Geneticists refer to this process as 'non-allelic homologous recombination' *(see diagram).*

Why does it happen at the 22q11.2 region? There are areas of DNA either side of the 22q region that are similar in pattern. This makes it more likely for a chromosome to attach to the wrong place so an error occurs.
This is like when you button up your shirt with the wrong buttonholes!

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8 Step

What is missing/deleted from 22q11.2 deletion?

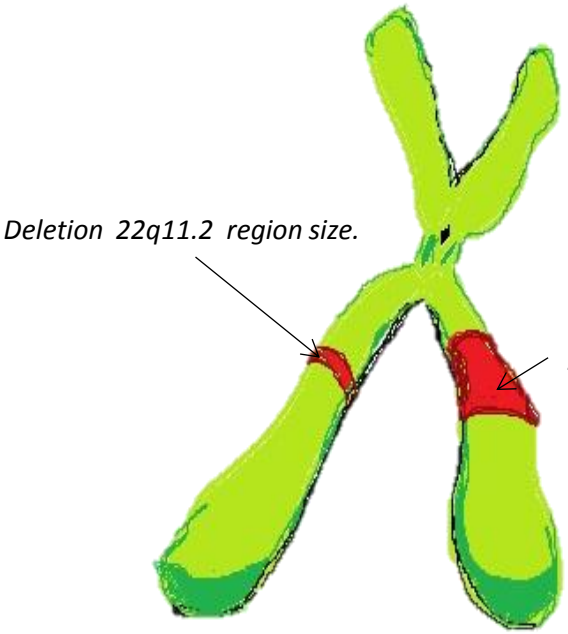
Examples

TBX1

It has been suggested that the cardiac problems found in 22q11.2 deletion are due to missing one copy of the TBX1 gene.

COMT

Scientists are still debating the role that COMT plays, however, it is thought that missing one copy of COMT may contribute to some of the behavioural problems associated with 22q11.2 deletion.



Approximately 30-50 known genes are missing in 22q11.2 deletion.

Scientists have been able to identify some of the missing genes' functions.

However there is still a lot to find out, for example, how the rest of the chromosomes compensate for this deletion.

This could help explain why some people are more affected by the deletion than others which in turn could inform treatment strategies.

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9 Step

Common features: Overview

It is important to remember that everyone is unique!

Not all children with 22q11.2 deletion have the same problems, there is a lot of variability. Some children do not experience problems or have very mild symptoms whereas others can have moderate or severe physical, developmental and behavioural problems.

Some children with 22q11.2 deletion may…

Physical features

- Have heart Problems
- Have immune system difficulties
- Have palate problems

Developmental Features

- Coordination difficulties
- Have trouble learning new skills
- Experience developmental delay
- Have difficulty understanding information
- Need extra help in school

Behavioural features

- Struggle to understand language
- Spend time putting things in a special order
- Have more worries
- Be more anxious
- Find it hard to understand other people's feelings
- Have more difficulty concentrating
- Have ideas or beliefs that other people can't understand
- Hear sounds or voices that other people can't
- Prefer familiar routines
- Find it hard to sit still
- Have more trouble waiting their turn for things
- See things that other people can't see
- Not understand social rules

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10 Step

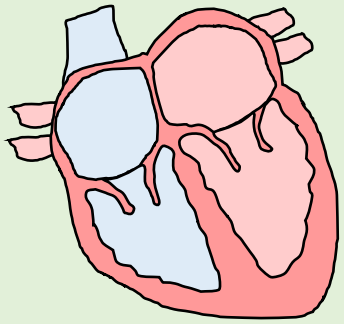
Physical Features

It is important to remember that everyone is unique!

Heart Problems

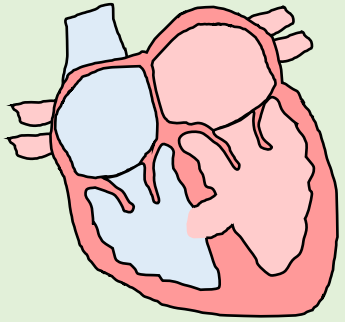
Heart problems occur in around 70% of people with 22q11.2 deletion.

There are two common, non invasive clinical tests for heart problems:
An Echocardiogram- a detailed ultra sound of the heart.
An Electrocardiogram- monitors heart beat.



Heart without septal defect

The most common heart problems in 22q are septal defects (hole in the heart), this is caused by a congenital heart condition called 'tetralogy of fallot'



Heart with septal defect

Immune system difficulties

Some people are more likely to have recurrent infections. This is because people with 22q can have 'partial immunodeficiency'.

The immune system could be weaker in people with 22q because they may have less 'T-lymphocyte' cells (T-cells). These help fight off infection.

Palate problems

Around 70% of children with 22q11.2 deletion have some kind of palate (roof of the mouth) anomaly. This can affect feeding and speech.

22q11.2 deletion is sometimes known as Velo-cardio-facial syndrome. 'Velo' refers to the palate problems children experience.

'Velum' means soft palate.

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11 Step

Developmental Features

It is important to remember that everyone is unique!

Links to LD information help and support

22q11.2 deletion – specific information

- 22Crew http://www.22crew.org/crew-downloads/downloads-education-and-development-1
- MaxAppeal http://www.maxappeal.org.uk/downloads/Consensus_Document_on_22q11_Deletion_Syndrome.pdf

Other

- NHS http://www.nhs.uk/Livewell/Childrenwithalearningdisability/Pages/Copingwithdiagnosis.aspx
- Mencap www.mencap.org.uk
- The Foundation for People with Learning Disabilities www.learningdisabilities.org.uk
- The British Institute of Learning Disabilities (BILD) www.bild.org.uk

Some children with 22q11.2 deletion are slower to reach their developmental milestones (such as crawling, walking and talking) than other children. This is known as 'Developmental Delay'.

Learning Difficulties (LD)

Children with 22q11.2 deletion may need an extra helping hand with their learning. They tend to find spelling and reading words easier than the comprehension of words, maths and problem solving. Usually, children with 22q11.2 deletion have an IQ which is slightly below the average IQ range of 80 and 120.

This doesn't mean that all children with 22q11.2 deletion will need a statement of educational need (SEN) or to go to a special school. Lots of children go to mainstream school but have a little extra support.

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12 Step

Attention Deficit Hyperactivity Disorder (ADHD)

It is important to remember that everyone is unique!

ADHD is a disorder which can include three common symptom areas: a short attention span, hyperactivity and impulsiveness.

It does **NOT** mean ~~**NAUGHTY**~~!

Links to ADHD information, help and support

22q11.2 deletion-specific info

- 22Crew
  www.22crew.org
- MaxAppeal
  www.maxappeal.org.uk
- Unique
  www.rarechromo.org

Other Info

- Young Minds
  www.youngminds.org.uk/assets/0000/1327/WhatIsADHD.pdf
- ADHD Foundation
  www.adhdfoundation.org.uk
- NHS
  www.nhs.uk/Conditions/Attention-deficit-hyperactivity-disorder/Pages/Introduction.aspx

Children with 22q11.2 deletion and ADHD may have more difficulty than other children their age:

- Paying attention (both in school, at home and elsewhere e.g. watching a DVD all of the way through).
- Sitting still or being restful (they are hyperactive and may get up and down from their seat more often e.g. during mealtimes).
- Carefully considering the consequences to their actions. They may often be impulsive and act without thinking (e.g. being unable to wait their turn in games or queueing while shopping).

When should we get help?

The NHS suggest that you should let your child's teacher, their school's special educational needs co-ordinator or GP know your concerns if you think your child has more difficulty than most children their age with attention, hyperactivity and impulsiveness.

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13 Step Anxiety

It is important to remember that everyone is unique!

Feeling anxious from time to time is perfectly normal. However, people with anxiety disorders find it hard to control their fears, worries and feelings of unease.

Links to Anxiety information, help and support

22q11.2 deletion-specific info

- 22Crew
  www.22crew.org
- MaxAppeal
  www.maxappeal.org.uk
- Unique
  www.rarechromo.org

Other Info

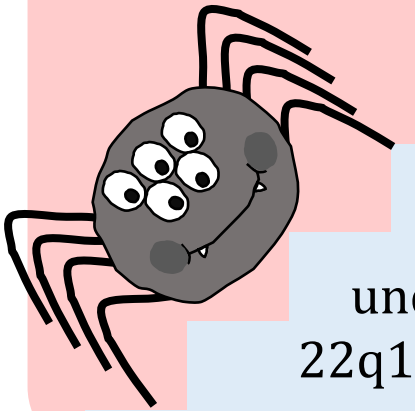
- MIND
  www.mind.org.uk/media/42877/understanding_anxiety_and_panic_attacks_2012.pdf
- No Panic
  www.nopanic.org.uk
- Royal College of Psychiatrists
  http://www.rcpsych.ac.uk/healthadvice/parentsandyouthinfo/parentscarers/worriesandanxieties.aspx

Children with 22q11.2 deletion may have more difficulty than other children coping with anxieties, they may experience:

- Social Anxiety: a fear of speaking to and performing in front of other people e.g. going to parties, speaking up in class and eating in front of other people.
- Specific Phobias: an irrational fear of a particular thing e.g. spiders, heights, the dark. The object is avoided or causes distress if encountered or thought about.
- Generalised Anxiety: a widespread feeling of anxiousness most of the time, without a specific reason.

When should we get help?

The NHS suggest that you should seek help from your GP if anxiety is affecting your child's daily life or causing them distress.



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14 Step

Autistic Features & 22q

It is important to remember that everyone is unique!

Children with 22q may have some symptoms of autism, this can affect how they interact with other people, their interests, behaviour and their communication.

Links to ASD information, help and support

22q11.2 deletion-specific info

- 22Crew
  www.22crew.org
- MaxAppeal
  www.maxappeal.org.uk
- Unique
  www.rarechromo.org

Other Info

- National Autism Society
  http://www.autism.org.uk
- NHS
  http://www.nhs.uk/conditions/autistic-spectrum-disorder/Pages/Introduction.aspx

Symptoms of autism fall into 3 main categories:

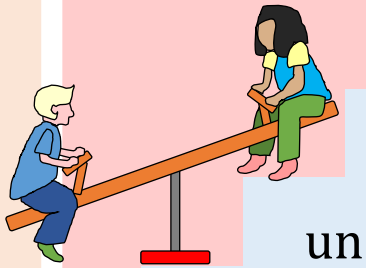
Social interaction: Children may struggle with imaginative play and not have much interest in other children. They can also be more socially naive (e.g. making inappropriate comments) and may struggle to understand other people's feelings and emotions.

Communication: Children may struggle with language, joining in with social chit chat and to a fro conversations. They may only talk about their wants, needs and specific interests.

Restricted, repetitive, stereotyped patterns: Children may have unusual hobbies and spend a lot of time repeating tasks. They may have unusual body movements and they might be overly interested in the sight, smell, feel or touch of things or people.

When should we get help?

The NHS suggest that you should seek help from your GP if you notice any symptoms of autism in your child or if you are worried about their development.



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15 Step

Mood Disorders

It is important to remember that everyone is unique!

It is normal to feel downcast, unhappy or depressed sometimes. However, people with mood disorders find it hard to control their feelings of low mood.

Links to Anxiety Information, Help and Support

22q11.2 deletion-specific info

- **22Crew**
  www.22crew.org
- **MaxAppeal**
  www.maxappeal.org.uk
- **Unique**
  www.rarechromo.org
- Other Info
  - RC of Psychiatrists
    http://www.rcpsych.ac.uk/healthadvice/parentsandyouthinfo/parentscarers/depression.aspx
  - NHS:
    http://www.nhs.uk/conditions/stress-anxiety-depression/pages/low-mood-and-depression.aspx

Children with 22q11.2 deletion may have more difficulty than other children coping with low mood, they may:

- feel tearful
- feel guilt-ridden
- feel irritable
- have no motivation or interest in things
- find it difficult to make decisions
- not getting any enjoyment out of life
- have suicidal thoughts or thoughts of harming themselves
- feel anxious or worried

When should we get help?

The NHS suggest that you should seek help if your child's negative feelings don't go away, or are stopping them from carrying on with everyday life.

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16 Step

Schizophrenia

It is important to remember that everyone is unique!

Schizophrenia is a mental illness that affects thinking, emotions and behaviour. Adults with 22q are at higher risk of schizophrenia with 30% developing it compared to 1% of the general population.

Help, Support and more Information

- **YoungMinds**

Parents' helpline 0808 802 5544 (Mon-Fri, 9.30am-4pm)
Website: www.youngminds.org.uk

- **Rethink Mental Illness**

Phone: 0300 5000 927 (Mon-Fri, 10am-2pm)
Website: www.rethink.org

- **Mind**

http://www.mind.org.uk/media/990900/understanding-schizophrenia-2014-.pdf

- **RC of Psychiatrists**

http://www.rcpsych.ac.uk/healthadvice/parentsandyouthinfo/parentscarers/schizophrenia.aspx

Schizophrenia is more likely to start between the ages of 15 and 35 years, but can sometimes occur in younger children.
Schizophrenia is **not** multiple or split personality disorder (Jekyll/Hyde) and is **not** being a psychopath!

Schizophrenia symptoms

Hallucinations: Hearing voices or seeing things that aren't really there such as voices and people.
Delusions: Holding strong abnormal beliefs. This could include feelings of paranoia that the world is against you or that people are going to hurt you.
Bizarre behaviour:
Acting in strange disorganized ways.

When should we get help?

The NHS advises that If you are concerned about symptoms of schizophrenia, see your GP as soon as possible. The earlier schizophrenia is treated, the more successful the outcome tends to be. Some people can make a complete recovery!!

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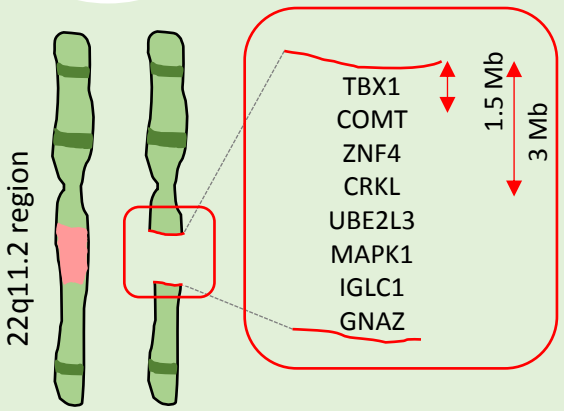
17 Step

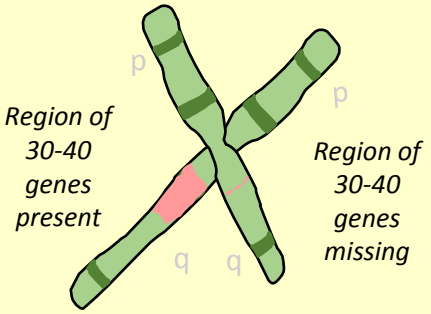
Why is 22q11.2 deletion syndrome so variable? Part One



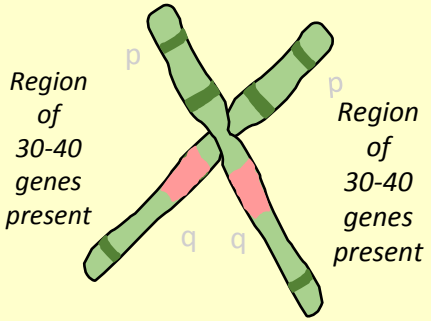
The size of the deletion can vary. Some people will have a 1.5 Mb deletion, others will have a larger 3Mb deletion.

More genes are deleted in the 3Mb deletion than the 1.5Mb deletion which could account for some of the variation in 22q.

In humans, chromosomes are in pairs (one from each parent). The 22q deletion involves a loss of 30 to 40 known genes in one of the two chromosomes '22'. The is leaves only one set of the 30-40 known genes.



Chromosome 22 with one set of 30-40 genes



Chromosome 22 with two sets of 30-40 genes

Genes come in different varieties. The gene version left will be different in different people with 22q. This could explain some of the variation in 22q.

To explain further, imagine gene 1 has versions A & B and gene 2 versions C & D. Either version A or B could be deleted at gene 1 and either C or D at gene 2.

The possible combinations left are AC, AD, BC, BD. Now imagine that for 30 – 40 genes, when calculated that is potentially over a billion combinations!

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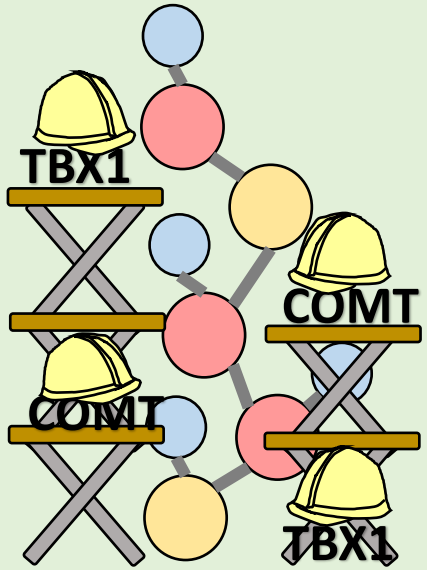
18 Step

Why is 22q11.2 deletion syndrome so variable? Part Two

Genes tell each of your cells what to do and when to do it: "grow hair, make muscle, etc" genes coordinate all this by making proteins. Genes don't work alone, in order to make proteins they work as a team.

Like a team of different experts on a building site, working together.



Everyone has variation in their genetic material. This is what makes us all DIFFERENT.

Though, it is not fully understood why 22q11.2 deletion syndrome is so variable in severity.

- It could be that changes to an affected person's genetic information outside the 22q11.2 region are having an effect. The genes which are missing in 22q function as part of a larger network and the way in which these missing genes are compensated for could vary between people.
- It is possible that people with more severe symptoms have more genetic variations that aren't present in people who have milder symptoms.

Researchers are working hard to understand these mechanisms.

Also, as with many genetic disorders, environmental factors could play a role.

Researchers are investigating how genetic instructions are affected by our environments.

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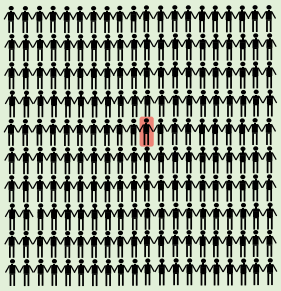
19 Genetic Counselling

Genetic counselling services give support, information and advice about genetic conditions. Care is provided by specialists (genetic counsellors, clinical geneticists and clinical scientists) trained in human genetics and medicine.



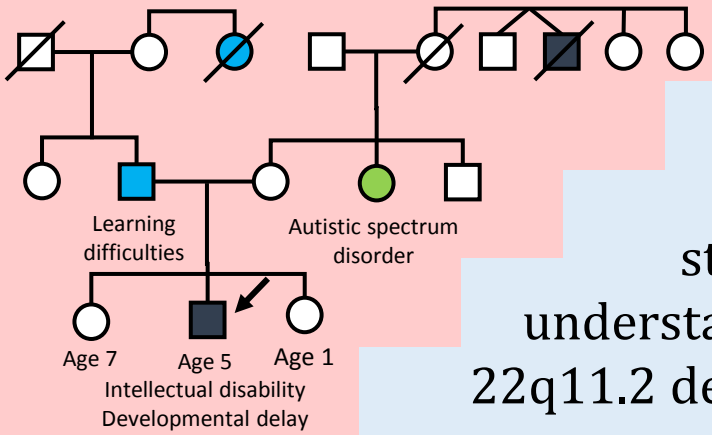
More than 1 in 200 people are born with a chromosome disorder. 22q11.2 deletion syndrome is rare but it is one of the most often diagnosed genetic syndromes.

Appointments with a genetic counsellor may cover many topics, including:

- Learning about the condition, how it's inherited, which family members may be affected.
- Investigating the medical family history and drawing up a family tree.
- Assessing the risk of passing an inherited condition on to children.
- Help and advice if you have a child with a genetic condition and you want another child.
- Discussing genetic tests including the risks, benefits and limitations of genetic testing.
- Understanding results of genetic tests, their impact and adjusting to new circumstances.
- Accessing information about patient support groups.

Because 22q11.2 deletion is rare and variable there is limited information on health problems, how to monitor, treat or prevent them. Parents often express high levels of uncertainty and anxiety.

Genetic counsellors will recognise this. Studies show that helping with effective day-to-day coping strategies may lead to lower anxiety. But we need to understand more about parents' concerns and needs.



22 steps to understanding 22q11.2 deletion

The ECHO Study

#22qAwarenessDays

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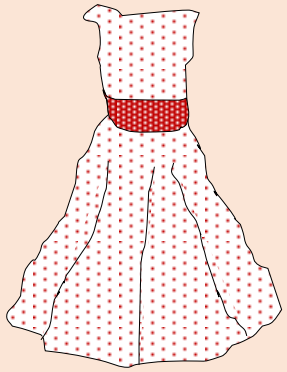
20 Step

People with 22q11.2 deletion in the media

Tessa Koller: *Fashion Designer*



Tessa Koller is a fashion designer from Chicago. Despite having operations from a young age for her congenital heart disease, she was only diagnosed with 22q11.2 deletion when she reached her twenties.

Tessa also campaigns to raise awareness of 22q11.2 deletion. You can find out more about her on her blog: http://tessakoller.blogspot.co.uk/p/about.html

Quinn Bradlee: B*logger*

Quinn Bradlee also had surgery for heart problems when he was younger and was eventually diagnosed with 22q11.2 deletion when he was 14.

Quinn has written a book about his experiences entitled: *A different life: Growing up learning disabled and other adventures.*

He has also set up an online community called *Friends of Quinn* to help support people with learning disabilities (and their families).
http://www.friendsofquinn.com/

22 steps to understanding 22q11.2 deletion

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21 Step

Super Support Groups

These super support groups are doing a great job helping to provide people affected by 22q11.2 deletion with the information and support they need. We hope that they can give you a helping hand too…

www.maxappeal.org.uk

Max Appeal!

Max Appeal want to help people with 22q11.2 deletion to be independent. They have excellent leaflets about challenges people with 22q11.2 may face from their early years through to adulthood.

www.vcfsef.org/index.php

The VCFS Educational Foundation focus on educating the public, scientific community, families and anyone interested in 22q. They work hard to spread awareness and understanding.

www.22crew.org

the 22 crew

The 22 Crew is run by parents of children with 22q11.2 deletion. They have amazing guides to education, medical appointments and more.

www.22q.org

The International 22q11.2 Foundation is a website full of useful information! They aim to bring the 22q community together and improve lives along the way.

www.rarechromo.co.uk

Understanding chromosome disorders Unique

Unique support families affected by rare chromosome disorders. They provide brilliant family-friendly information guides about specific chromosome disorders.

22 steps to understanding 22q11.2 deletion

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22 Step

Our study: Experiences of children with copy number variants (ECHO Study)

Thank you for joining us for 22q Awareness Days. We have really enjoyed sharing our 22 steps to understanding 22q11.2 deletion with you. For our final slide we thought we would tell you a little bit more about ourselves…

We are a team of researchers from Cardiff University who study chromosome disorders. There are lots of parts to our study. Here is a quick overview of some of the ECHO Study's aims and how we are trying to achieve them:

Q1: How many people with a chromosome disorder have problems with their thoughts feelings and behaviours and what sorts of problems do they have?

We visit people at home at a time which is convenient for them and either interview parents about their child's experiences or adults about their own experiences.

Q2: How many people with a chromosome disorder have learning difficulties?

During the home visits we complete some puzzle with children and adults with chromosome disorders. These puzzles let us know what your attention span is like, how you problem solve, your understanding of language, your reaction times and many more.

Q3: Do people with chromosome disorder's brains look different to people without chromosome disorders?

Older children and adults are invited to Cardiff where they have two different types of brain scans: magnetoencephalography (MEG) and magnetic resonance imaging (MRI).

Q4: Do cells from people with chromosome disorders grow differently to cells from people without chromosome disorders?

If you are happy to do so, we take hairs from your head. From the cells found at the root of the hair, we can grow cells in the lab to see whether there are any differences in how cells work in people with and without chromosome disorders.

If you would like more information, please don't hesitate to get in touch!

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02920 688 358

22 steps to understanding 22q11.2 deletion

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