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Dear 'Chromosome 6' parents,

We have understood that there is some confusion about the clinical relevance of some of the duplications and deletions found in your group. Some of you have been told that the chromosome 6 aberration found in your child is most likely not the cause of your child's problems. We understand that this is frustrating and confusing for you and would like to offer you some information on this complex topic.

What are chromosomes and genes?
The human body is made up of millions of cells. Our cells each contain thousands of genes. Genes act like a set of instructions, controlling our growth, development and how our body works. They are responsible for many of our characteristics, such as eye colour, blood type or height.

Genes are located on thread-like structures called chromosomes. Usually, there are 46 chromosomes in each cell, arranged as 23 'pairs' of chromosomes. A child inherits chromosomes from both its parents – 23 from the mother and 23 from the father – resulting in two sets of 23 chromosomes, or 23 pairs. Because genes are located on the chromosomes, a child inherits two copies of most genes, one copy from each parent.

Chromosome analysis
Detailed chromosomal analysis can pinpoint a change in the number, size or structure of the chromosomes. Such a change may result, for example, in a learning disability, developmental delay, or health problems. Changes in chromosome structure can take the form of either an addition (duplication) or loss (deletion) of chromosomal material.

A *deletion* means that part of a chromosome has been lost or deleted. A deletion can happen on any chromosome, and along any part of a chromosome. The deletion can be of any size, small or large. If the genes located on the deleted part of the chromosome contain important information (instructions), that person may have a learning disability, developmental delay, or other health problems. The seriousness of these problems will depend on how many genes have been deleted and how important their function is.

A *duplication* means that the chromosome has duplicated part of itself, so that there is too much chromosomal material present. If important genes are duplicated, this may also result in a learning disability, developmental delay, or health problems in a child.

Such changes in chromosome structure may be very subtle and hard to detect in the laboratory. Even when a change is found, it is often hard to predict what effect the change will have on an individual child. This can be very frustrating for the parents, who are keen to have as much information about their child and his/her future development and health as possible.

Detailed chromosome analysis
Nowadays, chromosome studies are performed by very sensitive methods. This means that very small chromosomal aberrations can also be detected. Such small aberrations do not necessarily contain important genes and they may thus have no effect on the health and development of the child.

These detailed chromosome tests are called: oligo array, SNP array, microarray or whole genome array. When an array test is done, several different results are possible.

1. Normal array pattern
This means that no deletions or duplications are found above a specific size limit. This does not necessarily mean that there is no genetic cause for the child's observed problems. If a deletion or duplication is very small, or if there is a very small change within a gene, this will not be detected by array analysis.

2. Deletion or duplication that explains the clinical problems
If a deletion or duplication has also been found in other people who have a similar condition, it is likely to be the cause of the problems. A child can be born with a deletion or duplication even though both parents' chromosomes are normal. This is called a *'de novo'* change or mutation (from Latin, meaning *new*), or a new rearrangement. When a deletion or duplication is a new rearrangement, it is more likely to be the cause of the child's observed problems.

3. Deletion or duplication that gives an increased risk for developmental delay or behavioural problems
Certain deletions or duplications are known to be risk factors for developmental delay or behavioural problems. Such a risk factor might be traced in a parent who does not have these problems.

4. Deletion or duplication that has no clinical effect
When a variant is thought to be harmless (and not the cause of the condition), it is called a polymorphism or benign variant. Many people have small deletions or duplications, but have no apparent health or behavioural problems. Such chromosome changes are usually *inherited* from a parent. When such a chromosomal rearrangement is found in a healthy parent, geneticists think it is unlikely to be the cause of the child's problems.

If a variant is found but it is not yet known what it means, your health professional may be able to give you more information later, in a few years' time, as our knowledge improves.

While having a genetic diagnosis for your child can be hard to accept, many people feel that having an answer to the question as to what caused the condition is helpful. For

some people, the worst outcome is to have the test performed but not get a definite result. If this happens to you, it is natural to feel frustrated and disappointed.

Best wishes,

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