

■ The Genetic Background to Craniosynostosis (*Headlines factsheet*)

■ What are "craniofacial" conditions?

The term "craniofacial malformation syndrome" covers a whole multitude of conditions. Doctors sometimes apply this term to describe patients with abnormality in the development of the face and skull. Some of these conditions are due to altered genes but some have nothing to do with genetic problems. The important thing to recognise about "craniofacial malformation syndrome" is that this is not a diagnosis but a description of the general problems which a given patient has. There are tens, indeed hundreds, of syndromes to which this description may be applied.

What does the word "syndrome" mean? It refers to a situation where a pattern of clinical signs which tend to occur together are found on examination. From previous experience we often recognise conditions by the fact that the clinical examination shows us that the patient has identical features with another patient we examined previously. In this way common syndromes become recognised quickly. Likewise, very rare syndromes may be identified, although the process here is slower. For instance a doctor in Britain may see a patient whose condition he/she does not recognise. By writing about the patient in the medical journals and publishing photographs showing the important aspects of the examination, another doctor elsewhere might look at the details of the case and recognise in it an identical case to one of his patients. The two doctors communicate and a little knowledge about that syndrome starts to accumulate.

If a child is born with features which suggest an abnormality of development of the head and/or face, then doctors might recognise one of the syndromes. Most often the syndromes are known by the name of the doctor who first described the particular condition in the medical literature. Several, though by no means all, of the syndromes are due to genetic causes.

■ What causes the abnormality ?

Most genetically-determined conditions involve abnormalities of chromosomes or changes of a single gene. There are exceptions to this, but discussion of these is beyond the scope of this information leaflet. Everybody has approximately 100,000 genes and these are arranged in chromosomes. Looking down the microscope we can see the chromosomes. Humans have 46 chromosomes, arranged in 23 pairs, of which one in each pair comes from the father and the second from the mother. Sometimes a patient will have an abnormal number of chromosomes. The best example of this is Down's syndrome, where the patient has an extra chromosome 21. Other abnormalities of chromosomes are also found, with material missing from a chromosome or additional material present on a chromosome. Obviously this means that the patient will have genes missing or extra genes present and the clinical effects of these changes on the baby can be very variable from one case to the next. Each case needs to be considered on its own merits and the only general rule for this situation is that parents of a child with a syndrome due to chromosomal abnormality may wish to discuss the case with a clinical geneticist to consider whether a similar problem might occur in a future baby.

■ Which genes are involved?

We cannot see individual genes down the microscope and special laboratory techniques need to be employed to look for changes at this level. Many of the better known syndromes involving malformation of the head and/or face result from changes in individual genes. These changes, resulting in the abnormal development, are called "mutations". Several such syndromes, for instance Crouzon, Apert and Pfeiffer syndromes, have been found to result from mutation in a family of related genes, known as Fibroblast Growth Factor Receptor genes. Although much work remains to be done in identifying genes which are important in causing craniofacial malformations, the genes for other craniofacial syndromes are gradually being found.

■ Why does the abnormality happen?

It is important to understand that many children with craniofacial problems resulting from mutation involving single genes arise as new genetic events. These children's parents have normal genes but in copying of the normal genes prior to fertilisation, a mis-copy occurs when is then passed to the child. With very few exceptions, these parents will have further children who will not have similar genetic mutations. In other cases there may be a risk of a further child being affected, but this depends on the type of problem in the individual case and who else in the family is affected with the condition.

This leaflet is intended as **a very basic general guide only** and there are many exceptions to several of the statements made. For this reason, the leaflet is intended to inform you only until you have the chance to consult with your paediatrician, who may refer you on to a clinical geneticist. Only in such a situation can the individual aspects of your child's case be appropriately considered and it is important to realise that some or all of the information in this leaflet may be not apply to your case.

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