New genetic forms of craniosynostosis

This information sheet from Great Ormond Street Hospital (GOSH) explains the causes, symptoms and treatment of two new genetic forms of craniosynostosis and where to get help.

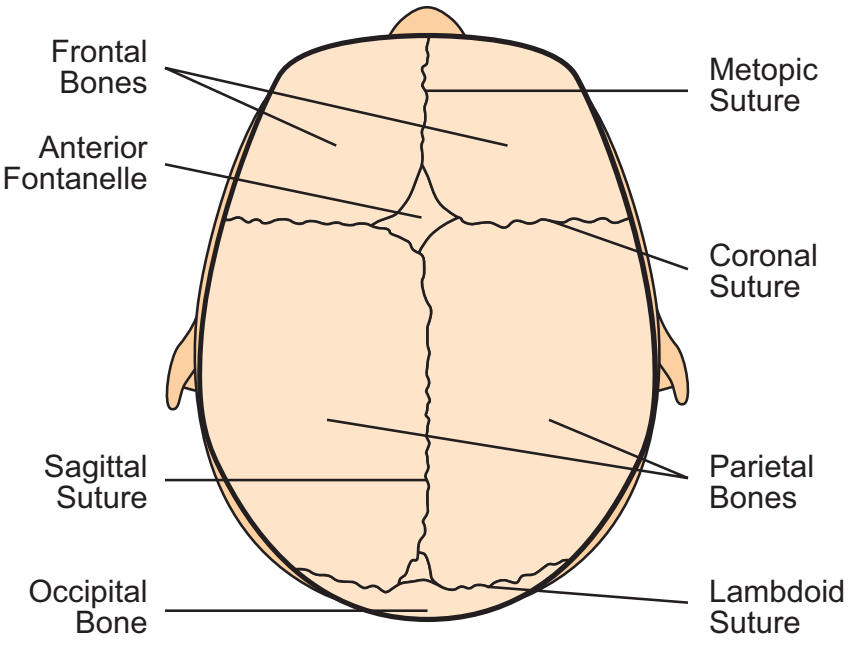
What are the two new genetic forms of craniosynostosis?

The skull is made up of several 'plates' of bone which, when we are born, are not tightly joined together. The seams where the plates join are called 'sutures'.

As we grow older, the sutures gradually fuse (stick) together, usually after all head growth has finished. When a child has craniosynostosis, the sutures fuse before birth. It can affect one suture or several.

When more than one suture is affected, it is called 'complex craniosynostosis'. This may happen as part of a syndrome (collection of symptoms often seen together), and so may be referred to as 'syndromic' as well.

Normal Skull of the Newborn



In the past few years, researchers have identified two new genetic mutations that cause craniosynostosis.

What causes these new forms of craniosynostosis?

Around 25 per cent of all cases of craniosynostosis are thought to have a genetic basis. In many cases, a mutation (change) of a specific gene leads to a child developing craniosynostosis in the womb.

Research has identified two new genetic mutations on the genes called ERF and TCF12. Both are thought to play a part in how certain cells in the body – including bone cells – grow, divide and die. Gene mutations can be passed on from parent to child but in many cases develops sporadically (out of the blue). It is not yet clear how the mutation is passed on from parent to child. In time, further research will identify this mechanism.

As these two new genetic mutations are newly identified, it is possible that children with the mutations have previously been diagnosed with other forms of craniosynostosis. There have been some instances where family members who had not been diagnosed or treated for craniosynostosis in childhood have now been diagnosed with one or other of these gene mutations.

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What are the signs and symptoms of these new forms of craniosynostosis?

Both gene mutations cause children to have a characteristic appearance due to the problems with the skull plates fusing too soon.

If the mutation affects the ERF gene, multiple sutures fuse early. Children also have widely spaced eyes (hypertelorism), a short nose and prominent eye sockets and forehead. They may also have a problem called Chiari malformation where the base of the brain (cerebellum and brain stem) is pushed downwards out of the base of the skull. Children also seem to have behavioural problems, particularly struggling to concentrate, and may start speaking at a later age than expected.

Children with a mutation in the TCF12 gene have a flattened forehead and eye sockets, affecting either one side of the skull (unilateral) or both (bilateral). This is caused by either one or both coronal sutures fusing too soon. Some children with the TCF12 mutation have learning disabilities although these vary in severity.

In both cases, there appears to be a spectrum of severity, with some children being very mildly affected and some more severely. We currently are unable to predict the severity from the genetic tests alone. For this reason, children are followed up regularly as outpatients.

How are they diagnosed?

Children with craniosynostosis tend to have a characteristic appearance so no specific diagnostic tests are needed. However, genetic testing is now routinely carried out, both to increase knowledge of craniosynostosis in general, monitor for long term effects of craniosynostosis and to allow for planning of future pregnancies. Imaging scans, such as x-ray, CT or MRI may be suggested to monitor bone growth before, during and after surgical treatment.

How are they treated?

As craniosynostosis can affect various areas of the body, treatment is best delivered at a specialist centre where a multidisciplinary team approach can be taken. The multidisciplinary team will usually comprise craniofacial (skull and face) surgeons, neuro (brain) surgeons, ear, nose and throat (ENT) surgeons, audiologists (hearing specialists), dentists and orthodontists, geneticists and speech and language therapists with other specialists brought in as needed.

Depending on the severity of the skull fusion, treatment soon after birth may be needed if pressure inside the brain is raised or there is a risk of eye damage. Early surgery is more likely in children with the TCF12 gene mutation.

Children with the ERF gene mutation may not need surgery initially, but will be monitored regularly as complications, such as raised pressure inside the brain (intracranial pressure) seems to develop in early childhood, around the age of four or five years. If this occurs, skull re-shaping surgery will be needed. This will involve cutting through the fused sutures in the skull and re-shaping them to give a more normal skull shape. Chiari malformation (if present) can be treated by widening the opening at the base of the skull).

As the bone continue to grow during childhood and adolescence, further surgery may be needed to make corrections to the skull shape.

What happens next?

The outlook for children with these new forms of craniosynostosis is generally good with the vast majority growing up to lead a normal life, working and raising a family, although it will vary depending on any other medical conditions present. Children may have learning disabilities, although the severity of these is variable. Most will benefit from support in education and day to day life although a degree of independence may be possible.

Further information and support

Headlines – the Craniofacial Support Group – is the main support organisation in the UK for families of children and young people affected by a craniofacial disorder. Visit their website at www.headlines.org.uk.

Changing Faces is another organisation that will be able to offer help and support to anyone living with a condition that affects their appearance. Visit their website at www.changingfaces.org.uk or telephone their helpline on 0845 4500 275.

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