

What causes Clubfoot?

What is the problem?

'Clubfoot' is an abnormality of the lower legs and feet, that affects about 1 in 500 babies born in the UK (see Figure 1). We have very little idea what causes it. Sometimes, clubfoot runs in families and we know from previous work that genes are involved.

Figure 1 (right): The lower legs and feet of a newborn baby with clubfoot in both feet.



Figure 1

Although clubfoot is normally treatable, by bending the foot round in a series of plaster casts known as Ponseti manipulation (see Figure 2), children with clubfoot have to wear 'boots-and-bar' for up to 6 years, and clubfoot costs the NHS millions every year.



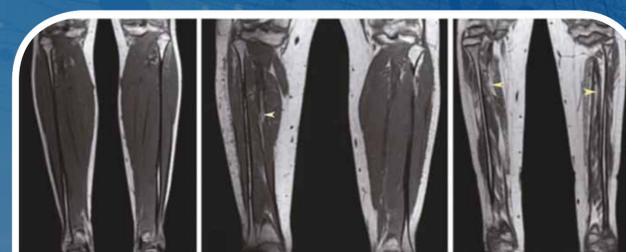
Figure 2

Figure 2: The process of Ponseti manipulation – the foot is pulled over by a series of casts. Lastly, the Achilles tendon is cut, to allow the foot to be placed flat on the ground.

What are we interested in?

We want to know why clubfoot happens – in particular the genes that cause it.

Clubfoot is not a problem of the ankle bones. Our lab has shown before that it is a problem of nerves and muscles in the calf (see Figure 3). If these are not working, the foot bends round during pregnancy. Even after treatment, patients suffer from weak calf muscles into adult life.



NORMAL UNILATERAL CLUBFOOT BILATERAL CLUBFOOT

Figure 3: MRI imaging of the calf muscles of teenagers who: did not have clubfoot at birth (left), had clubfoot on one side (middle), or had clubfoot of both feet. Even after Ponseti manipulation, the muscle weakness (shown by gaps and herring-bone patterns in muscles) persists into later life.

What did we find?

We looked at two types of mice that carry a genetic defect that causes them to be born with clubfoot.

We found that both of them show changes in the expression of a gene (called LIMK1) that stops one branch of the sciatic nerve entering the limb. Loss of nerve stimulation of the calf muscles causes muscle weakness and hence the clubfoot.

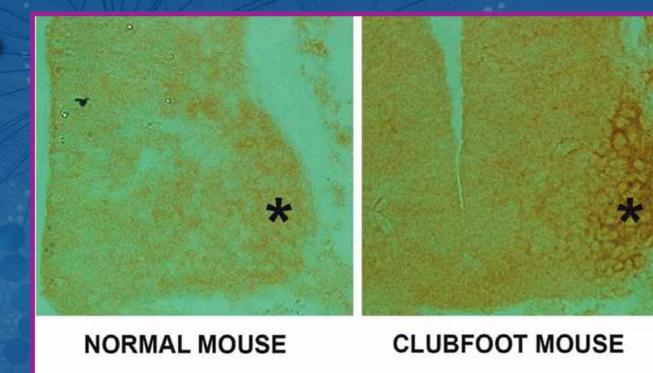


Figure 4: The gene LIMK1 (brown staining) is normally turned on in the neurones of the developing spinal cord that will form the sciatic nerve (asterisk). LIMK1 is present at much higher levels in the clubfoot mouse (darker staining), and this stops the nerve from entering the limb.

Where's the link to human health?

Now we think we know some of the genes that cause clubfoot, it will be possible to screen families and identify people who are at risk of having children with clubfoot. The pathway we have identified can be treated with drugs.

Who am I?

I have recently graduated in Biomedical Sciences at the University of Aberdeen. I held the Medical Research Scotland Vacation Research Scholarship during the summer of 2013 and the experience enhanced my aspirations to do a PhD and then go into the world of medical research and academia.