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NON-UNION BONE FRACTURE: A QUICKER FIX

Fractures that fail to heal properly often cause long-term disability, but new cell-based therapies may help.

BY DAVID HOLMES

Bone fractures are an unfortunate fact of life. In the United States alone, around 8 million people each year break a bone. In most cases, the pain subsides and the fracture becomes an inconvenience, soon to be forgotten once the healing process has run its course and the plaster cast is removed. But for 5–10% of individuals with a broken bone, the fracture will fail to heal under the usual treatment. The prolonged pain and disability caused by these non-union bone fractures can have profoundly negative consequences in many areas of life.

Various factors increase the risk of non-union bone fractures: severe fracture; smoking; the use of anti-inflammatory or opioid drugs; poor nutrition; and the use of anticoagulant drugs. Many of these risk factors interfere with the body's ability to produce new blood vessels (the process of vasculogenesis) that are essential for healing. Without vasculogenesis, the body cannot deliver the molecular building blocks and the specialized cells needed to form new bone in the void caused by the fracture.

Current treatment of non-union bone fractures usually involves surgery to stabilize the area and the insertion of a bone graft at the site to stimulate vasculogenesis and osteogenesis (the growth of new bone). The latest research is focusing on ways of improving both the success of surgery and the speed of healing, and regenerative therapies are a particular area of interest. Cells that express the protein CD34, which include endothelial stem cells and haematopoietic progenitor cells, have come to the fore as a potential treatment for a multitude of vascular diseases. The importance of vasculogenesis in normal fracture healing has led some researchers to speculate that therapies based on $CD34^+$ cells might also be a means of stimulating healing in non-union bone fractures.

A 2014 study in Japan showed that patients with non-union bone fractures treated with $CD34^+$ cells isolated from their own peripheral blood tolerated the procedure well (R. Kuroda *et al. Stem Cells Transl. Med.* **3,** 128–134; 2014). A larger three-year multicentre trial of such a therapy will wrap up in 2018, and should shed more light on the utility of $CD34^+$ cells in fracture healing.

RORY WAUDBY-TOLLEY

Whether or not $CD34^+$ cells prove to be a game changer in the treatment of non-union bone fractures, it is clear that fresh therapeutic approaches are needed to deal with what is likely to be a growing problem. There are around 9 million fractures caused by age-related bone fragility each year worldwide, with women at greatest risk — mainly because of the decrease in bone density that occurs after the menopause. As the populations of developed economies continue to age, and the number of fractures rises, the prevalence of conditions that complicate bone healing, such as diabetes, are also expected to increase. Non-union bone fractures look set to be one of the long-term consequences of the changing demographics of the twenty-first century, and regenerative therapies will have a large part to play in dealing with them.

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