MARCHING TO A NEW BEAT

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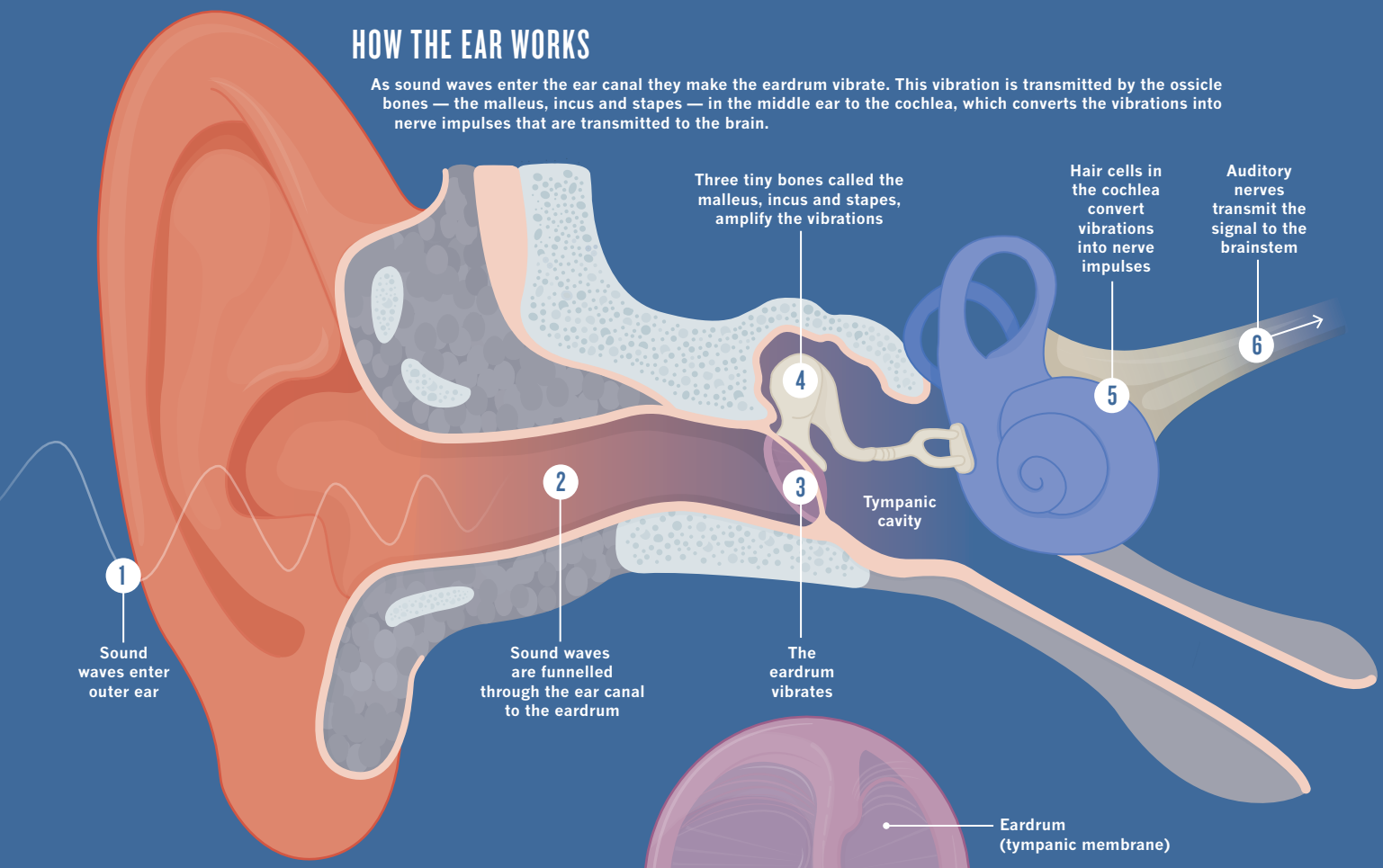
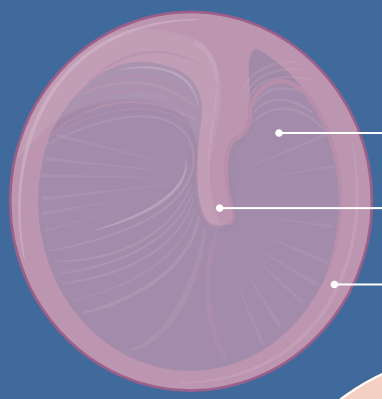
In the most severe cases, a ruptured eardrum can require surgery to put it right, but tissue-engineering techniques might provide a much simpler solution.

By **David Holmes**; illustration by **Lucy Reading-Ikkanda**

HOW THE EAR WORKS

As sound waves enter the ear canal they make the eardrum vibrate. This vibration is transmitted by the ossicle bones — the malleus, incus and stapes — in the middle ear to the cochlea, which converts the vibrations into nerve impulses that are transmitted to the brain.



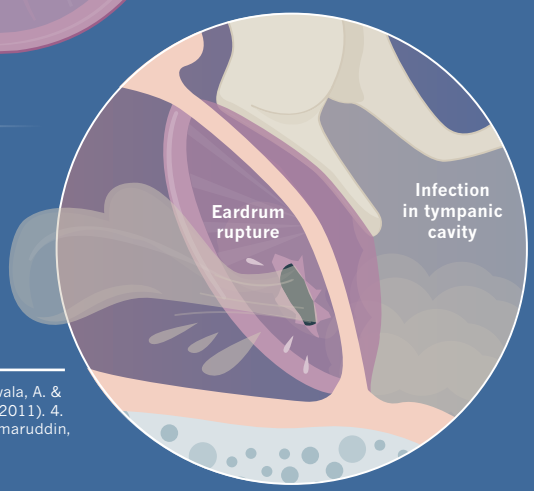


GOOD VIBRATIONS

The eardrum is a thin membrane, just a fraction of a millimetre thick. Attached to the surrounding bone by a fibrocartilaginous ring, it separates the ear canal and the middle ear. It not only acts as a physical barrier, keeping foreign bodies such as bacteria out of the middle ear, but it also performs an essential role in hearing.

PAIN IN THE MEMBRANE

Like a stubbed toe or a paper cut, a ruptured eardrum (also known as a tympanic membrane perforation or perforated eardrum) is a fairly common complaint. It is usually caused by an infection in the middle ear, which leads to a build up of pressure and, subsequently, a tear. But there are many other causes of membrane perforation, including a sudden change of pressure or inserting a cotton bud too far into the ear. A perforated eardrum is painful and associated with hearing loss, which is largely determined by the size of the tear: the larger the hole, the greater the hearing loss.



Sources: 1. *Neurological Regeneration* (ed. Pham, P. V.) (Springer, 2017). 2. Indorewala, S., Adedeji, T. O., Indorewala, A. & Nemade, G. *Iran J. Otorhinolaryngol.* **27,** 101–108 (2015). 3. Kanemaru, S. *et al. Otol. Neurotol.* **32,** 1218–1223 (2011). 4. Hiwatashi, N. *et al. J. Tissue Eng. Regen. Med.* **11,** 1598–1609 (2017). 5. Thilagar, S., Jothi, N. A., Omar, A. R., Kamaruddin, M. Y. & Ganabadi, S. *J. Biomed. Mater. Res. B. Appl. Biomater.* **88,** 12–16 (2009).

PUNCTURE REPAIR

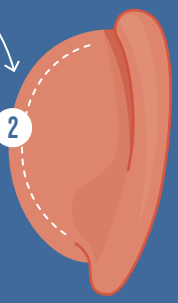
Few small ruptures are reported clinically, and most of these will heal naturally over several weeks. But for the small proportion of tears that fail to heal properly, surgery is the only option.

PATCHING UP

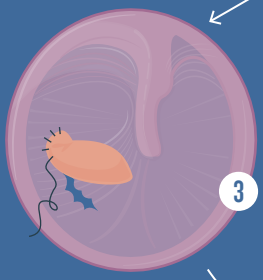
The standard operation, called a tympanoplasty, requires a specialist surgeon to harvest a skin graft from the patient and use this to patch over the damaged eardrum. As with all surgical procedures, cost and a shortage of surgeons — particularly in developing countries — can limit access to treatment.

~150,000 people[1] undergo surgery to repair eardrum perforations each year in the United States.

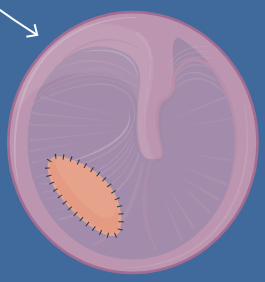
1 Graft material is usually taken from the fascia covering the temporal muscle on the side of the head.



2 The surgeon makes a cut, normally behind the ear, to access the eardrum.



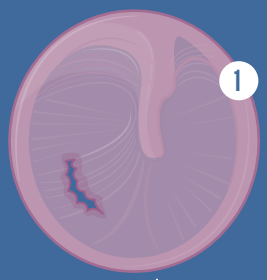
3 The skin graft is stitched over the margins of the perforation and quickly fuses with the eardrum.



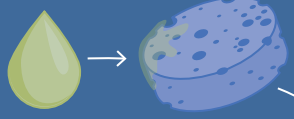
The procedure is effective in 80–90% of patients[2], relieving pain, reducing the risk of infections and improving hearing. But the surgery does have potential complications, including nerve damage and the risks associated with anaesthesia.

AN ENGINEERED SOLUTION

Tissue engineering could be a quick, convenient and effective alternative to surgery. The technique provides cells with a scaffold to grow on and a growth factor to encourage them to proliferate. Researchers in Japan have trialled a technique that infuses basic fibroblast growth factor (bFGF) into a gelatin-sponge scaffold to help the eardrum to regenerate.

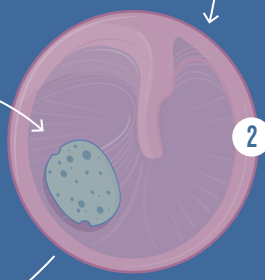


1 A surgical blade is used to break the surface of the tissue around the perforation to expose the cells.

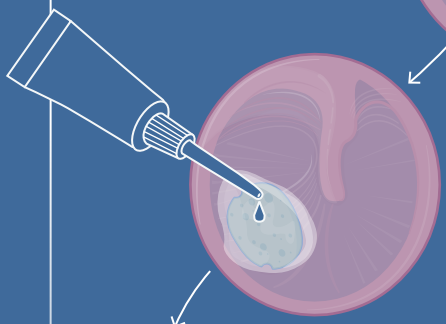


Basic fibroblast growth factor (bFGF)

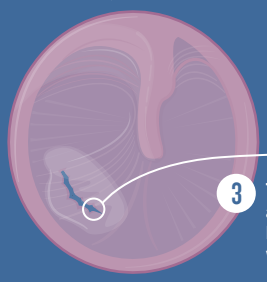
Gelatin sponge 'scaffold'

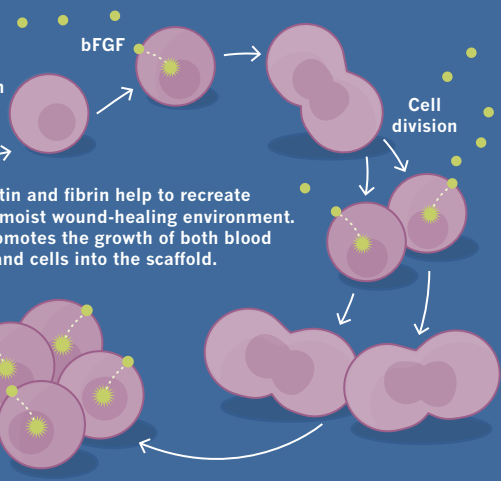


2 Gelatin sponge is cut to size, loaded with bFGF and placed over the perforation.

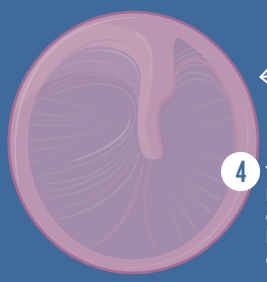


Fibrin glue (a mixture of fibrinogen, which helps to form blood clots, and the enzyme thrombin) is used to form a fibrin clot, which helps to keep the sponge in place, prevents the gelatin sponge from drying out and provides a barrier to infection.

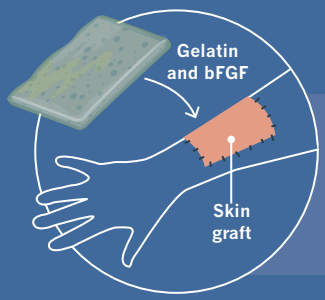




3 The gelatin and fibrin help to recreate a warm, moist wound-healing environment. bFGF promotes the growth of both blood vessels and cells into the scaffold.



4 The gelatin and fibrin are absorbed over three weeks, leaving a new membrane. In a phase II study, 52 out of 53 people who had this procedure had complete healing, compared with only 1 of the 10 in the control group[3].



FROM EAR TO A NEW ERA

The results of a phase III trial completed in July 2016 should reveal whether this simple, outpatient procedure can supplant tympanoplasty. The approach looks set to transform other areas of surgery as well. Preclinical studies have shown that a similar technique using gelatin and bFGF helps vocal-cord scarring to heal[4], and sheets of gelatin and bFGF can reduce healing time for skin grafts[5].