Will we ever… correct diseases before birth?

Some genetic conditions cause irreparable damage at such an early age that scientists are trying to develop ways of treating them in the womb.

Every year, millions of people are born with debilitating genetic disorders, a result of inheriting just one faulty gene from their parents. They may have been dealt a dud genetic hand, but they do not have to stick with it. With the power of modern genetics, scientists are developing ways of editing these genetic errors and reversing the course of many hard-to-treat diseases. These gene therapies exploit the abilities of viruses – biological machines that are already superb at penetrating cells and importing genes. By removing their ability to reproduce, and loading them with the genes of our choice, we can transform viruses from causes of disease into vectors for cures. After a few shaky starts, some of these approaches are beginning to hit their stride. Thirteen children with SCID, an immune disorder that leaves people fatally vulnerable to infections, now have working immune systems. Several British patients with haemophilia, which prevents their blood from clotting properly, can now produce a clotting protein called factor IX, which they once had to inject. A British man and three Americans with inherited forms of progressive blindness can see again. It is still early days as far as trumpeting gene therapy cures are concerned, but even if they do succeed there is still one significant limitation that cannot be overlooked. Treating adults and children in this way will do for some disorders, but genetic disorders cause irreparable organ damage, or even death, very early. “With some of the diseases that we look at, five years old is too late. Sometimes, you don’t get to the age of five,” says Simon Waddington from University College London. “Every single one is a little bit niche but when you list them all out, there’s quite a lot of them.” To treat such conditions, we need to intervene as early as possible, and this means correcting genetic disorders in the womb. There are advantages to such “prenatal gene therapy”. Organs that are hard to target after birth, such as airways blocked with mucus in cystic fibrosis patients, may be easier to reach in the womb. Being smaller, foetuses need a relatively smaller amount of delivery vector. And their immune systems are naive, so they are unlikely to mount an immune response to these vectors. Risk assessment So far, several teams have tested prenatal gene therapy in animals, including mice, monkeys and sheep. The results have been promising. In several cases, the animals produce decent levels of foreign proteins for many months, and their immune systems tolerate the added genes. Some have even been cured of their diseases. Despite these successes, the research has reached an impasse. No one has tried prenatal gene therapy in humans, and no clinical trials are in the works. This is understandable. Altering a foetus’ genes is a sombre prospect, especially as gene therapy is still a relatively immature technology. “It hasn’t been embedded enough yet,” says Waddington. If these treatments can prove their safety and effectiveness in adults, the field will move towards trials in newborn babies, and from there to prenatal tests. For now, there are still many potential risks to address. “We’re still very much looking at which is the right vector to use,” says Anna David, from University College London. Lentiviruses and retroviruses (such as HIV) shunt their genes into those of their host. They would seem to provide an ideal way of correcting a faulty gene, either by overwriting it, or providing a cell with working copies. But if the viruses insert their DNA in the wrong place, they could disrupt other important genes, causing cancers or developmental problems. These fears are well-founded. Five of the twenty children with SCID, who took part in some of the first successful gene therapy trials, developed leukaemia as a result of their treatment. Source: BBC