Treating the Untreatable

As a kid, Anush sensed that something was wrong with his vision. He found difficulty navigating dimly lit areas. Dark spots appeared in his central vision and gradually spread, eventually affecting even his peripheral vision. Anush was diagnosed with retinitis pigmentosa (RP), a progressive genetic disease that often leads to severe vision loss and blindness, many a time before the person turns 30.

While RP affects 1 in every 3000-7000 births globally, in rural South India the prevalence is 1 in 1000, making it a major cause of blindness in the region.

The other 10%

In the eye care world, we often focus on the 90% of people with avoidable vision loss—and rightly so. But the remaining 10%, those with irreparable sight loss, deserve equal attention. It would be a travesty if they cannot live life to their full potential. At LVPEI, our Institute for Vision Rehabilitation (IVR) ensures that people with irreversible vision loss can live full, independent, and meaningful lives.

Anush is a testament to this. With specialist training at IVR, he mastered screen-reading software, high-contrast displays and other computer tools that empowered him to work and learn effectively. It is fascinating to watch him navigate webpages, listening to an electronic voice reading out the content (at high speeds!) and making choices rapidly using keyboard shortcuts and a mouse.

While these technologies and software are heartening and offer hope, a fundamental question remains: *should we accept the fact that those with irreparable retinal disease will never regain vision*? After all, several medical conditions once considered untreatable--both life - and sight-threatening--are now managed and treated effectively in clinical medicine.

Understanding Inherited Retinal Diseases

RP is part of a larger group called *inherited retinal diseases* (IRDs)—conditions caused by mutation in one or more genes impairing the retina. The retina is the light-sensitive tissue at the back of the eye that converts light into electrical signals that are then sent to the brain. While we have made many advances in treating retinal conditions, sight lost to IRDs is often irreparable.

These diseases present complex challenges for clinicians trying to slow progression, and for rehabilitation specialists trying to understand how structural eye defects translate into functional difficulties for patients. Further, the disease patterns vary by geography and community. In southern India, for example, where the practice of consanguinity and long runs of inter-community marriages between people with shared genetic ancestry are culturally accepted, the prevalence is higher.

In India, some of the earliest work on characterising these retinal diseases happened at LVPEI. Dr Chitra Kannabiran, our molecular genetics expert, has played a transformative role in helping us understand the genetic underpinnings of these diseases in the Indian population.

A good example is the RPE65 gene, responsible for producing specific proteins essential for the 'rod' photoreceptor-cells in the retina that help us see in dim light. When this gene malfunctions (due to a mutation), the production of these special proteins is disrupted. Over time, these photoreceptor cells progressively degenerate leading to vision loss and blindness. This is one of the reasons Anush has spotty vision; it is analogous to random tiny LED bulbs burning out and dying on a TV screen—imagine watching your TV with several black spots on it.

Because IRDs are rare, understanding them is scientifically demanding and financially intensive. Much of the world's research comes from high-income countries. This makes work like Chitra's especially vital: it helps define these diseases within low-income and diverse genetic populations.

Treating the untreatable

Although most IRDs have no curative treatment today, progress is accelerating. Genetic counselling is an integral part of management of such diseases and is gaining ground in India. The first US FDA approved gene therapy for a form of RP is now available and several others are under clinical trials. However, these treatments remain prohibitively expensive and are out of reach for most patients even in the United States. We need solutions tailored to low-resource settings for these therapies to work in India.

LVPEI is actively strengthening efforts to characterise, and potentially treat, a range of these untreatable inherited eye diseases. Because of their higher prevalence in Indian contexts, I am looking to formalise various initiatives to tackling them. My colleagues are exploring affordable gene therapy and stem cell based solutions that work in our contexts, to treat IRDs. These therapies rejuvenate or replenish degenerated cells with working copies of the mutated cell. Many parts of the eye that are currently untreatable will hopefully respond to such a treatment strategy. If they don't, then, somewhere in the future lies the holy grail: a whole eye transplant.

A couple of years ago, Anush graduated with a bachelor's degree in science, and joined IVR as an IT instructor and helpline counsellor. His confident baritone voice guides patients calling our helpline, seeking to face the same fears he had once experienced. He also trains others to use tools like the screen-reading software that transformed his life. Every day, he turns up to work knowing that he is helping others with vision loss and low vision reclaim independence and dignity.

Rehabilitation remains essential today, but the future holds promise. In good time, we will be able to do more than offer comfort and coping strategies to the 10%.

-Prashant Garg