# Opinion

RUTH D. WILLIAMS, MD

## Innovators on the Edge

Our family observed a minute of silence on March 11, 2010, the day that Arnall Patz died. Our (now adult) twins were born at 29 weeks and were given oxygen in the NICU. Neither child developed retinopathy of prematurity, and we have Dr. Patz to thank for that.

The interesting part of the story is that few physicians believed Dr. Patz's theory that concentrated oxygen was driving ROP. His idea was met with hostility because neonatologists assumed that decreasing oxygen levels would harm the premature infants. His NIH grant application was rejected as unscientific. Dr. Patz borrowed the money from his brother to fund the study, published in 1952, that was the first prospective controlled clinical trial in ophthalmology. Premature infants were randomized to receive the standard highly concentrated oxygen regimen or a lower concentration of oxygen. Seven of the 28 infants in the high-dose oxygen arm developed severe ROP (grades 3 and 4), but none of the 37 infants receiving the low dose progressed beyond grade 2.[1]

Innovators are often on the edge of their field. The Franciscan friar Richard Rohr calls this prophetic position "on the edge of the inside." He posits that those who operate on the edge are willing to challenge established knowledge or beliefs, while still being part of the system.

Sir Nicholas Harold Lloyd Ridley's ideas were definitely not in the mainstream when he developed the first PMMA intraocular lens, based on his World War II observations that acrylic shards from the shattered windshield of an RAF airplane remained inert inside the eye of its pilot. Dr. Ridley first implanted his IOL in a patient in 1949 and, through the 1950s and '60s, persisted in refining the design and surgical technique despite decades of opposition from the ophthalmic community. He wasn't knighted at the time, nor was his innovation appreciated. Rather, his work was regarded as reckless and dangerous. But by the 1970s, after further evolution, IOL replacement surgery had become commonplace. Harold Ridley, once a pariah, is now honored.

Judah Folkman, the pediatric surgeon who proposed the existence of an angiogenesis factor, was the father of anti-VEGF treatments. His idea—that a tumor could be treated by choking off its blood supply—was derided or ignored by the academic community. He was further criticized for funding his research through industry, with a grant from Monsanto, when he couldn't get support through traditional channels. One of Dr. Folkman's research assistants, Kevin Camphausen, described the difficult early days in the lab, when their work was called "ludicrous or worse." However, he said, "This early criticism probably made Dr. Folkman a better scientist, for he developed an ability to see the weak parts of an experiment, the very results which the reviewers might pick apart, and strengthen the work prior to submission."[2] In 2007, Dr. Folkman gave a stirring talk at the AAO annual meeting Opening Session describing how his work led to saving the vision of countless patients with macular degeneration.

***Ruth D. Williams, MD*** *Chief Medical Editor,* EyeNet

If we want to be open to innovation, how do we distinguish between ideas that have merit and those that are absurd or harmful? Fortunately, the culture of medicine in the United States and many other countries has evolved to protect patients through the FDA and IRBs, as well as carefully designed clinical studies and ethical standards for new treatments. Still, we are also wise to be alert to fresh ideas—and some of them will sound wacky—remembering that the best ones may come from physicians who are "on the edge of the inside."

What is particularly striking about Drs. Patz, Ridley, and Folkman is their persistence in the face of opposition and skepticism. I imagine that each of these great innovators was overflowing with resilience and optimism, as well as commitment to the new idea that defined his career—and profoundly changed medicine for the better.

Let's also be open-hearted and open-minded to new ideas. Let's listen. It might just save the vision of our children.

1 Patz A et al. *Am J Ophthalmol.* 1952;35(9):1248-1253.
2 Camphausen K. *Cell Cycle.* 2002;1(5):296-297.