a 6-to-12-month duration of effect, oligonucleotide therapeutics might become competitive not only with biologics, but also with orally administered drugs, an outcome that was unforeseeable only a short while ago. Of course, the future of inclisiran and oligonucleotide therapeutics is completely dependent on the demonstration of their safety.

Conjugated oligonucleotides are chemically defined "large small molecules" that can be synthesized in an advanced oligonucleotide lab within a day. They are assembled from standard building blocks, phosphoramidites, in an automatic fashion using solid-phase chemistry. The cost of oligonucleotides is driven mainly by the cost of its precursors and is expected to be in the low hundreds of dollars per gram on a commercial scale. With a yearly dose of 300 to 500 mg, the manufacturing cost for this class of drugs is on par with that of small-molecule drugs and is probably much lower than that of monoclonal antibodies. Although the manufacturing cost accounts for only a minority of the initial market price of the drug, the relative simplicity of the manufacturing process and the room-temperature stability of the dried oligonucleotides, which can be brought to solution at the point of care, might eventually make this class of therapeutics widely available for a broad population.

Disclosure forms provided by the author are available at NEJM.org.

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1. Khvorova A, Watts JK. Oligonucleotide therapeutics: from chemistry advances to clinical utility. Nat Biotechnol (in press).
2. International nonproprietary names for pharmaceutical substances (INN). WHO Drug Information 2016;30(3):504 (http://www.who.int/medicines/publications/druginformation/innlists/RL76.pdf?ua=1).
3. Nair JK, Willoughby JL, Chan A, et al. Multivalent N-acetylgalactosamine-conjugated siRNA localizes in hepatocytes and elicits robust RNAi-mediated gene silencing. J Am Chem Soc 2014;136:16958-61.
4. Hawkins PN, Ando Y, Dispenzeri A, Gonzalez-Duarte A, Adams D, Suhr OB. Evolving landscape in the management of transthyretin amyloidosis. Ann Med 2015;47:625-38.

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A View from the Edge — Creating a Culture of Caring

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In 2008, an occult adenoma in my liver ruptured, and I effectively bled to death in my own hospital. I lost my entire blood volume into my abdomen, triggering what's known in trauma as the Triad of Death — a kind of suicidal spiral of the blood in which it becomes too acidic and too cold to clot. I would receive more than 26 units of blood products that night — packed red cells, platelets, cryoprecipitate, fresh frozen plasma. I would go into multisystem organ failure, my liver and kidneys would shut down, I would be put on a ventilator, have a stroke and a complete hemodynamic collapse. The baby I was 7 months pregnant with would not survive, but I would — thanks to the incredible skill and grace of the teams of professionals who cared for me.

My recovery involved five major operations including a right hepatectomy. I had to relearn to walk, speak, and do many other things I had taken for granted. But in the process, as a patient, I learned things about us — physicians and other medical professionals — that I might not have wanted to know. I learned that though we do so many difficult, technical things so perfectly right, we fail our patients in many ways.

As a patient, I was privy to failures that I'd been blind to as a clinician. There were disturbing deficits in communication, uncoordinated care, and occasionally an apparently complete absence of empathy. I recognized myself in every failure.

When I overheard a physician describe me as "trying to die on us," I was horrified. I was not trying to die on anyone. The description angered me. Then I cringed. I had said the same thing, often and thoughtlessly, in my training. "He was trying to die on me." As critical care fellows, we had all said it. Inherent in that accusation was our common attribution of intention to patients: we subconsciously constructed a narrative in which the doctor–patient relationship was antagonistic. It was one of many revelatory moments for me.

I heard my colleagues say

things to me in ways that inflicted more suffering, even when they believed they were helping.

"We're going to have to find you a new liver, unless you want to live here forever."

"Are you sure your pain is an eight? I just gave you morphine an hour ago."

"You should hold the baby," someone said. "I don't want to be graphic, but after a few days in the morgue, their skin starts to break down and you won't be able to anymore, even if you change your mind."

Small things would gut me. Receiving a bill for the attempted resuscitation of the baby, for example. My husband took on the task of reconciling the bill with the lack of a baby. The billing department explained that the bill was generated when we had failed to enroll her in our insurance plan. No one could explain, of course, at what exact juncture we should have called our insurance company, seeing as how she'd never technically been alive. It took four phone calls to settle the charges. A trivial oversight, by a department ostensibly not involved in patient care, had the potential to bring me to my knees.

My experience changed me. It changed my vision of what I wanted our organization to be, to embody. I wanted the value of empathetic, coordinated care to spread through our system. I shared my story openly. I wanted the system leaders and every employee to know that everything matters, always. Every person, every time.

How do you build and maintain a culture of shared purpose in the infinitely complex arena of health care? How do you ensure that you engender in employees a dedication and commitment to doing what's right? Identifying the gaps between the stated mission and values of an institution and its actual delivery of care is critical. As systems, we have to recognize and acknowledge our mistakes, our shortcomings, just as individual physicians do. We need to reflect on times when our care has deviated from what we intended — when we haven't been who we hoped to be. We have to be transparent and allow the failure to reshape us, to help us reset our intention and mold our future selves.

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Bravely, my institution responded to my experience by radically revising the way in which we introduce every new employee to our organizational culture — colloquially referred to as "onboarding." Our institutional leaders had already launched a "Culture of Caring" curriculum for nursing. But they understood that to truly change the culture, all new employees, including physicians, needed to internalize our institution's values. So they expanded their efforts, incorporating the failures and successes of my patient story to illuminate our shared purpose and build an engaged culture.

Through the training that was developed, participants learn to articulate their purpose as distinct from their job. Transporters hear how meaningful it was to me when one of their own — having seen me break down when questioned by someone in radiology — took it upon himself to warn the technicians performing various tests not to ask about the baby whose small pink wristband was still in my chart. He asked his colleagues to do the same. In an 800-bed hospital, the transporters had united to form a protective enclosure around one patient.

Similarly, radiology technicians learn what a kindness it was that they stopped trying to awaken my exhausted husband to move him from my bedside for my portable x-ray, instead throwing a lead cover over him and letting him sleep. The power of these stories shows new employees that they have a purpose and that they are valued.

In addition, new employees are taught to recognize different forms of suffering: avoidable and unavoidable. Our goal is to find ways to mitigate suffering by re-

sponding to the unavoidable kind with empathy and by improving our processes and procedures to avoid inflicting the avoidable kind whenever possible.

Our failures are analyzed, and our successes shared. Consider the power of that choice. Early on, all new employees hear about how we recognize and admit to our failures. How we partner to ensure that transparency keeps us from repeating our errors. How we hold each other accountable. By illuminating our failures, we can begin an authentic conversation about shared purpose, resilience, and building an engaged culture.

We believe that by focusing on our missteps, we can ensure that the path ahead is one of compassionate, coordinated care. When we are ashamed, we can't tell our stories. They become inaccessible to us. In the wake of painful experience, we all seek meaning. It is the human thing to do, but it is also the job of great organizations. The stories we tell do more than restore our faith in ourselves. They have the power to transform.

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