



## The Arc of Therapy: From Cure to Humbling Legacy

Gene Bishop, MD<sup>1</sup>

In June 1965, at the age of 18, I sat in a room with my parents and heard an oncologist tell me that I had Hodgkin lymphoma. If I shared that diagnosis with people, he said, they would look at me as if I were dying because almost no one with this disease survived, but I would. With breathtaking confidence, the oncologist said a new treatment—radiation—would cure me.

In October 2018, at the age of 71, I sat in an oncologist's office as he told me I had stage IV non-small-cell lung cancer, presumably, a result of that radiation in 1965. He offered palliative therapy. His goal: "more good days than bad." He called me "our humbling legacy." I reflect now on that arc: from optimistic cure, through a mounting problem list of likely consequences of radiation, to the almost certainty that I will die of the treatment of a cancer I had in 1965.

I received the best treatment there was in 1965 and am getting the best treatment there is in 2019, but I am no longer being promised a cure. Both my oncologist and I are living with the reminder that no treatment does only what we want it to do and that one year's miracles may have serious consequences even 50 years later. And although some of these may be known, or theoretically possible, many are not even imagined until one, two, three, or many case reports begin to appear and random events turn into warnings and known consequences.

For the patient seeking cure and life, an unknown but potentially dangerous future is hard to imagine. Some new miracle will come along.<sup>1</sup> Physicians, waiting for data, recruiting patients for the next clinical trial, or facing pressure from patients for positive results, can also be focused more on immediate results. They may minimize the known or unknown future. How will physicians be both wise and humble?

The first oncologist was right. I was cured of lymphoma. I graduated, went to medical school, and had a family and a full life. I shared the story with friends, patients, and colleagues when I thought it was appropriate or helpful. "Look," I said to families facing radiation. "I had radiation and here I am, alive and well." A little hope never hurt anyone. I never thought of myself as a cancer survivor on an ongoing journey. I thought of myself as a cure. And I certainly didn't think about the difference until many years later.<sup>2</sup> If oncologists were no longer interested in me, then cancer was over.

There was no concept or field of study of adult survivors of childhood cancer. Certainly, no physician—neither the oncologists I saw initially nor the internists

who later followed me when the oncologists' interest—raised the issue. Why and when did I even begin to consider that I might be at some kind of risk? In 1979, 14 years after my treatment, the worst domestic nuclear power accident in US history occurred at the Three Mile Island nuclear plant in Pennsylvania. I was more than sympathetic to the nuclear disarmament movement, and although I understood that nuclear war and my radiation treatment were considerably different, I did begin to wonder if the treatment could have had unexpected consequences. I began to ask questions of physicians, with very few answers. Thus began almost 20 years of symptoms and consequences of being in the earliest cohort, not part of any study, before the age when anyone could request, if it occurred to them, weekly updates from the National Library of Medicine on consequences of earlier cancer treatment.

In 1981 (at age 34), I asked whether I should start mammograms early, and my internist asked the mammographers. We don't know, I was told, but it might be a good idea. In 1985, seeking answers to a persistent tachycardia, cardiopulmonary testing and a Holter monitor showed a baseline heart rate in the 90s. I was told I was deconditioned and anxious. In 1986, a physician studying effects of radiation on the heart—he had a 7-year follow-up at that point—told me the only known effect was constrictive pericarditis, which I did not have. Don't worry, I was told.

Both were correct. I was anxious. But my ectopy and tachycardia were not symptoms of anxiety, they were the cause of the anxiety. I was anxious about the effects of radiation. I never tried to be my own doctor, but only I looked through the lens of a radiation treatment survivor. Not until 2006 did I find early consensus-based guidelines, of which my physicians were unaware.<sup>3</sup> In the late 1980s, I was denied life insurance because of a new right bundle branch block, but not until 2001, 36 years after my initial treatment, did a cardiologist name it radiation-induced heart disease.

I imagined it as static, rather than dynamic. Not only was my heart not static but the entire field of radiation-induced heart disease was evolving. I didn't have a permanent scar, I had ongoing damage, and neither I nor my doctors had the evidence for where it was heading. I found a cardiologist who focused on cardiac consequences of cancer treatment. When I mentioned that hiking in the Canadian Rockies and trekking in Vietnam had ceased to be fun, the cardiologist found critical aortic stenosis. My already-damaged conduction system did not survive an aortic valve replacement, and I now had both a pacemaker and a new aortic valve.

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In 2015 (at age 68), I read a published report of abnormal exercise response in long-term survivors of Hodgkin lymphoma treated with thoracic irradiation. I recognized myself in graphic detail.<sup>4</sup> No amount of training at the gym would get my heart rate below 90. That article appeared 50 years after radiation and 30 years after I first sought help, one of several sobering lessons in the length of time it can take to discover the effects of medical treatment.

The truth is, in my own therapy arc, I was lucky. Every consequence, until the lung cancer, was treatable, with the promise of a good outcome. I saw the article recommending breast magnetic resonance imaging for those who had received mantle radiation, appealed my insurance denial, and found my breast cancer early. However, two medical oncologists, two breast surgeons, and three radiation therapists all had vastly different treatment recommendations for my situation, reflecting the murky state of knowledge on treatment of Hodgkin survivors. A huge thyroid nodule was benign, but out came my thyroid, with a different small focus of cancer.

I faced each challenge, albeit with some depression and fear, with the knowledge that I would get better. Cure was still the operative word. In the arc of my disease, radiation had consequences, but they were not insurmountable.

As I reached more than 50 years out, I think I breathed an inward sigh of relief. I expected to have progressive cardiac disease. I imagined I would develop congestive heart failure. I worried about lung cancer—it had been reported 40 years out—but there were few studies on 50 years out. I thought I was done with my cancers.

When I developed a sudden and persistent cough, I began to worry. I could hear gurgles high in my midchest, but my doctors heard nothing. I doubted the pulmonologist's diagnosis of cough variant asthma, newly present in a 70-year-old. My doctors began gently suggesting what they do when a patient has unexplained symptoms. Perhaps you are anxious, they said. The classically trained psychiatrist noted he hadn't seen a conversion symptom in a long time, but thought I might never have really thought through what it meant having cancer at age 18. Several unexplained symptoms and normal computed tomography scans later, I contemplated what a nonphysician would do.

What if I weren't thinking like a doctor, but more like my fellow survivors? Off I went to Facebook, an unimaginable resource in 1965. I typed "Hodgkin's survivors" in the search box, and up popped a closed group: Hodgkins Lymphoma Disease Survival and Late Effects 1960s-early 2000s. Here were 500 people from around the world who had received radiation, chemotherapy, or both. It was hardly a tidy cohort. Their treatments for Hodgkin spanned the years from mantle radiation to chemotherapy, splenectomy, improved imaging, and actual staging.

As befits a social media site, they were seeking support, medical advice, and shared experiences. I was one of only

two survivors on the site who were more than 50 years post treatment. Initially, I felt lucky, at least until the lung cancer diagnosis. The number of valve replacements, arrhythmias, pacemakers, and stents was extensive. Many had severe neck contractures from radiation. Breast cancer seemed to be an everyday occurrence; the question of prophylactic mastectomies frequently was raised. Cough, lung disease, and esophageal reflux with aspiration all appeared. I briefly let myself be reassured that my pulmonologist was correct, and my cough had a reflux component, even if I never had a classic reflux symptom and a gastroenterologist was doubtful.

If the medical world has been slow to recognize cancer survivorship, this nonrandom group has not. Many of them travel hundreds of miles to find survivorship clinics in various countries around the world. The more recently treated ones had both the good fortune to benefit from the new field of cancer survivorship, but the bad fortune to be beset constantly by worries about what the future holds. As with much of the lay public, many believe that screening and early diagnosis are always beneficial and are unaware that the evidence in our cohort is scant.<sup>5</sup>

I found myself alternately fascinated, riveted, terrified, and reassured, but refrained from diagnosing myself from Facebook. I also knew I had found my peeps—a cohort more aware of their risk factors than much of the medical world.

One woman expressed relief when her new oncologist said, "This is all our fault." Others chimed in they had never heard a physician acknowledge that. My new oncologist had fancier words: "You are our humbling legacy."

I am the living—or perhaps I should say dying—history of one of our more successful efforts to treat and cure cancer in the last 50 years. There are now numerous other efforts, especially to treat childhood malignancies. Awareness of long-term consequences, the concept of survivorship, and the concept of shared decision making are but a few of the inflections in the arc of therapy. Many patients make difficult decisions, choosing extremely toxic therapies that will extend life only months, with imminent consequences that are known. But many also make decisions on the basis of limited information, filled with hope. In early 2019, should an American woman wait while the Food and Drug Administration continues to investigate textured breast implants, or imagine she lives in France, where sales have been halted because of reports of an association with a rare lymphoma? What will be the effects of the successful immunotherapy in 10, 20, or 50 years? Of course, physicians are focused on near-term cure; yet, they must also acknowledge the uncertainty regarding possible late effects of the very treatment that is now saving their patients' lives.

But if I am a humbling legacy, humility is needed. We need clinicians to provide guidance and information to patients as they find themselves in unknown and often frightening

terrain years or decades after completing their course of treatment. In my primary care practice, I often told patients I had left my crystal ball at home, along with my magic wand. But I was usually referring to when they could return to work after a viral illness, not whether they would get a terminal illness 50 years later.

I try to imagine my 18-year-old self and the doctor peering into his crystal ball. *You will have symptoms no one will believe. You will happily marry and successfully have one child.* (As long as he has a crystal ball, I might as well learn everything.) *You will develop heart disease and require an artificial valve and a pacemaker. You will develop three other cancers, two of which will be treatable, but the third, at age 72, will be the cause of your death. Would you like the radiation and cure we can offer you now?*

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