

Twenty Years In: The Long Goodbye

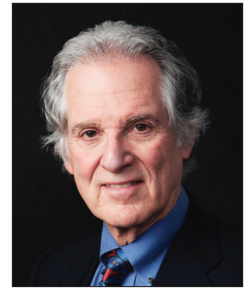
*Some cause happiness wherever they go; others
whenever they go.*

—Anonymous; often misattributed to Oscar Wilde

What shall I get for Steve and Paul, the publishers of *Clinical Advances in Hematology & Oncology*, to celebrate the 20th anniversary of the journal? To get some ideas, I googled “20th anniversary gift.” The traditional gift turns out to be china, but I think we have received enough gifts from China during the past two years.

The invitation to contribute to this special issue, as the first and longest-lasting editor-in-chief, offered an opportunity to relive times that were important to me. The first thing I did was to pore through my file of 168 “Letters From the Editor,” written over a period of 14 years (all but the oldest are available online at www.hematologyandoncology.net). My letters were almost a form of therapy for me, and I hope they brought a smile to—and inspired thought in—the readers. Many of them started and/or ended with a quote that seemed relevant to that space in time. When re-reading the letters, I was immediately overwhelmed by memories. Some of these memories were whimsical, such as my recollections of interviewing candidates for fellowships. Some were about notable people, such as Bob Dylan and his Nobel Prize, and Lance Armstrong and his ignoble (reputational) demise. Some of the memories were happy ones, such as vacation adventures and the discovery of onotherapy (that is, donkey riding as therapy) in Lisbon; others were sad ones, such as the death of our dogs, first Ellie and then Annie.

It has been a rather incredible two decades—scientifically, politically, professionally, and personally. Some things have changed, whereas others have remained the same. When I first assumed my role as editor-in-chief, rituximab—the first antibody used to treat a human cancer—had just shown activity that would revolutionize the lymphoma world forever. This success heralded the end of the development of standard chemotherapy agents. However, it took a while to get things going. The field went through a period not unlike the old days of lymphoma chemotherapy, in which we mixed and matched various drugs that provided no benefit. Years were spent trying to find the best chemotherapy backbone for rituximab in



treating the various histologic types. Clinical trial resources were squandered comparing the radioimmunotherapeutics yttrium ⁹⁰Y ibritumomab tiuxetan and iodine ¹³¹I tositumomab (now gone). While that was going on, our Cancer and Leukemia Group B (now Alliance) Lymphoma Committee began a program of combining targeted agents in the absence of chemotherapy, creating such regimens as R² (rituximab plus lenalidomide), which is now FDA approved for follicular lymphomas. We were considered a bit mad back then. Now, new chemo drugs are no longer in sight. Now, we target receptors, pathways, and the microenvironment with kinases, cellular therapies, and immunotherapies, alone and in combinations.

As a result, chemotherapy is now only a bad memory in some diseases—namely, chronic lymphocytic leukemia, marginal zone lymphoma, and Waldenström macroglobulinemia—with others soon to follow. In other histologic types, however, replacing chemotherapy with targeted agents has been more challenging. No agent to date has accomplished much when added to R-CHOP to treat patients with diffuse large B-cell lymphoma. However, substituting the antibody-drug conjugate polatuzumab vedotin for vincristine has been shown to improve progression-free survival—although not overall survival—according to results of the POLARIX study that were presented at the most recent ASH meeting. A gaggle of bispecific agents are causing excitement by bringing effector cells into proximity to tumor cells, creating a fatal form of hooking up. Positive studies favoring CAR T-cell therapy over high-dose chemotherapy that requires stem cell support have demonstrated that the immune system is more powerful than alkylating agents. We have gone from total empiricism in our selection of treatments to the potential for choosing them according to molecular and genetic direction. Indeed, this possibility was predicted in an article on genomics and the coming of personalized medicine published in the January 2007 issue of this journal. The author was a relatively unknown (at the time) senator from Illinois—Barack Obama.

Unfortunately, the political landscape has seen little progress. Although four administrations have come and gone during the lifetime of this journal, inequity reigns. In January of 2015, violent extremists killed 12 people at the *Charlie Hebdo* headquarters in Paris because of the satirical cartoons they published. We continue to fight the

suppression of speech not only overseas but also on our own turf—suppression that assaults us in every direction, from schools to the voting booth.

In our lifetime, nothing has altered the world more than ... climate change. (You thought I was going to say something else!) Our plans to visit Antarctica were stalled because of COVID. I hope we can get to the continent while it is still covered with ice. In a previous time, we had a minor brush with SARS, and a bit later, a few cases of Ebola in the United States caused what I viewed at the time as hysteria. I am no longer as sanguine about a few cases of a deadly viral infection. After all, COVID in the United States began as just a few cases. Now we are almost two years in, and we have contended with everything from spending months nearly homebound to having our ears constantly pulled forward by elastic straps. Worst of all is the number of people who have died—and are continuing to die—of this illness.

During this hiatus from normalcy, we were zoned out and Zoomed in. My ties and braces and pressed trousers gave way to more casual attire, at least from the waist down. Nevertheless, hibernation gave me the chance to play more often with my guitar, my fountain pen collection, and my puppy. I tried in vain to organize my wine cellar, which encompasses everything from Petite Petit to Château Lafite. I am not so sure that my spending so much time at home was on my wife's wish list. On the downside were the countless hours spent chatting in front of a faux background and electronically pushing a button to raise my hand. I had to remember to unmute and mute at the appropriate times, often failing at both—which could be quite embarrassing. I found the hours of Zooming to be a rather mind-numbing experience. The worst part of it was my virtual lectures, during which I often wondered, Where is the audience? Who are they? Was my joke funny? Is anyone paying attention?

Yet there is hope! Now that COVID vaccinations are up (no thanks to NFL player Aaron Rodgers or to Eric Clapton) and cases are down, people are starting to get together again and meetings are going live once more, or at least hybrid. Despite the current plague, the Lymphoma Research Foundation recently held its 15th anniversary Lymphoma Research Ride. We had an abridged version last year, in which most riders cycled with others in their own neighborhoods. This year, all possible precautions were exercised, and it was a pedaling success. The seven million dollars raised thus far for the Lymphoma Research Foundation goes toward several programs critical to the progress of lymphoma research. In fact, the LRF was the only foundation of its kind that was able to fund fellowship grants this year. They were even kind enough to honor me by establishing a fellowship in my name.

Whereas many of my colleagues prefer the safety of their offices, I miss the dynamic of personal interactions. I look forward to reconnecting with old friends at ASH 2021. Although the Oncotones took a break because the ASCO meeting was virtual in 2020, I am optimistic that we will rock again at the House of Blues in Chicago in 2022. Yet we will experience many changes at the meetings. One of my favorite letters rated the giveaways at the pharmaceutical exhibit booths at ASH and ASCO. Now compliance is incredibly strict, with nary a pen, or a pad of paper in sight—as if those Post-it Notes from companies developing drugs for pancreatic cancer would really redirect my treatment paradigm for CLL.

Perhaps the best example of things changing yet remaining the same was my retirement last year, which was followed soon after by a return to practice (by patient popular demand), albeit at a new venue. I recalled a quote from Camus' *The Plague*: "I have no idea what's awaiting me, or what will happen when this all ends. For the moment I know this: there are sick people and they need curing." The relationships are quite bidirectional; my patients still teach me important lessons about life and the alternatives. I am grateful to all of them, and this special bond is what powers my pedals. Unfortunately, my re-emergence is but temporary, given the inexorable process of aging. I previously wrote about my aging (and eventually dying) parents, and how the child becomes father to the man. Now, 20 years later and older, I sense the positions slowly reversing. Back then, I railed against the policies of AARP. Now I am a card-carrying member, getting my discounts at Disney World and making use of Medicare Part D.

As I write this epistle, it is almost a new year, a time when I routinely give thanks to those who have influenced my life. To Steve, Paul, and Devon for the opportunity to make a James Brown-like comeback to the journal I raised from a pup. To Meg and the staff at the LRF, who have given me ample opportunities to continue to affect patients and lymphoma research. New friends include Ralph Boccia, who gave me the chance to return to care for my patients again; our administrator, Careen; and Natalie and her gang in the protocol office, who have made my re-entry a smooth one. Numerous pharmaceutical companies deserve thanks for bringing us a tsunami of exciting new, novel, and non-chemo agents to improve the lives of our patients.

I am thankful for the new friends I made over these years. And I also remain grateful to those who are no longer in my life but whose memory remains important to me. Most notable is Gary Ford, who was one of the co-founders of the Lymphoma Research Ride. He and his wife cycled throughout Europe with my wife and me and shared many a lovely bottle of wine with us at home.

He was devoted to the cause of the Ride, first because of his wife—my patient Lisa—but then because of all the friends he made along the way. I will always remember his kindness, smarts, and generosity, and that he was a truly good person. He sadly lost his fight with esophageal cancer this year. I also appreciate the friendship of Pier Luigi and Michel Meignan, and those in the Lugano Classification group: Franco Cavalli, Emanuele Zucca, Larry Schwartz, Rich Fisher, Sally Barrington, and Andrew Lister. Together, we made an important contribution to clinical research, and we will soon start working on Lugano 2.0.

I am grateful to my family, notably my daughter Sara and my granddaughters Madeline and Samantha, now 9 and 11, respectively, who make their Poppy smile. I am also fortunate still to have my big sister Sheri, who has always loved me (except when I was a little kid, and she and her friends used to beat me up). For reasons I cannot comprehend, she remains proud of her little brother.

Few events cause such intense grief as the death of a long-loved (but never long enough) pet. I was bereft when Ellie and then Annie died; could I ever have the same feelings for a successor? Certainly not, because feelings for each of them are quite different. But now we are lucky to have our cute little three-year-old golden retriever, Miss Abbie Rose. She is very funny and special in her own right, and we love her dearly. Not a hand can be dangled without her furry head rubbing against it, or a walk taken anywhere without someone wanting to pet

her. My final and most sincere gratitude and appreciation go to my wife, Christine, who continues to put up with me through these years, who is everything to me, and whom I will always love.

Six years ago, my final letter as editor-in-chief concluded with a list of goodbyes from various favorites of mine from the worlds of music, TV, and literature. As I do not expect to be around, at least with all my faculties, for the 30th anniversary of *Clinical Advances in Hematology & Oncology*, I bid the readers farewell one last time.

You and I will meet again / When we're least expecting it / Somewhere in some far-off place / I will recognize your face / I won't say goodbye, my friend / For you and I will meet again.

—Tom Petty

Don't cry because it's over. Smile because it happened.

—Anonymous; often misattributed to Dr Seuss

How lucky I am to have something that makes saying goodbye so hard.

—Anonymous; often misattributed to A. A. Milne

Sincerely,



Bruce D. Cheson, MD

Dr Cheson was the editor-in-chief of *Clinical Advances in Hematology & Oncology* from 2002 through 2016. He was the head of hematology at Medstar Georgetown University Hospital, Lombardi Comprehensive Cancer Center from 2002 to 2020, and is currently practicing community oncology at The Center for Cancer and Blood Disorders in Bethesda, Maryland.