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Commentary

Cancer in the Shadow of the AIDS Epidemic in Southern Africa

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Disclosures of potential conflicts of interest may be found at the end of this article.


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This essay considers the possibilities for and challenges of oncology in southern Africa, where there is a cancer epidemic rapidly emerging, part of the cancer pandemic escalating across the global south. Already, more than half of all new cancer cases and two thirds of cancer deaths occur in the developing world, and epidemiologists tell us that these figures are steadily rising [1]. This epidemic will profoundly shape the future of oncology, raising fundamental challenges for patients, their clinicians, and the research community. This is not an epidemic that will be solved by a magic bullet, or by a simple program of technology transfer. It is a multidimensional, long-term problem that will necessitate dynamic, sustainable, context-specific solutions—solutions that take social and economic realities fully into account. These dynamics are magnified in southern Africa, especially given that cancer there is emerging in the shadow of HIV/AIDS.

My window into the epidemic is a 20-bed cancer ward and its associated clinic in Botswana's central referral hospital, located in the capital city, Gaborone. Between 2006 and 2009, I worked for long periods in the ward doing ethnographic research for my book, *Improvising Medicine: An African Oncology Ward During an Emerging Cancer Epidemic* [2]. This ward was perpetually full, and the oncologist faced tremendous pressure to turn over beds rapidly, in order to provide care to the greatest number of patients possible. This meant a triage that discharged those for whom active treatment was no longer possible, in favor of those whose lives could somehow be extended. This oncologist faced long queues in the clinic. Patients and their accompanying relatives, many of whom had already traveled great distances from their village homes, waited several hours for their consultation and chemotherapy from a doctor who, much to his frustration, could spare very little time with each patient. This often meant sacrificing the time-consuming humanistic side of medicine in order to serve all who needed care. The oncologist was training doctors in primary hospitals to diagnose and treat uncomplicated cases of the most common cancer encountered there, Kaposi's sarcoma, through basic chemotherapy algorithms. Nonetheless patient volume in this, the country's only oncology ward, continued to grow.

Botswana's cancer ward offers an ad hoc solution to a serious problem, even as Botswana in many ways presents a best-case scenario for health care in the region. Botswana is a middle-income country with a robust social contract between state and citizens, and a forward-thinking Ministry of Health. These features are evidenced by its steady investment in infrastructure and social services, and its system of universal health care. Problems nonetheless remain. Botswana is now home to large numbers of political and economic migrants (mainly from Zimbabwe), the majority of whom do not qualify for these benefits of citizenship. Needless to say, such patients are ill-equipped to pay for their oncology care out of pocket. While the GDP has steadily risen over the past four decades, the United Nations Development Programme estimates that about a third of Batswana (as citizens of Botswana are called) live below the poverty line, as the gap between rich and poor expands across the globe [3]. Human resources are uneven and strained in the health system, and, as in many medical systems, bureaucratic requirements often hamper delivery of efficient, effective care. Nonetheless, given the degree of state commitment to health, in recent years Botswana has become a site where new health policies and clinical modalities are developed and piloted, including, most notably, the first public antiretroviral (ARV) program on the African continent. From Botswana we can begin to see the thicket of intellectual, infrastructural, technical, and ethical challenges that this cancer epidemic poses. And we can see the complex relationship between the ongoing epidemics of cancer and HIV.

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Beginning in the mid-1990s, Botswana, like the rest of southern Africa, was engulfed by HIV/AIDS. Responding to the scale of the epidemic and the promise of new treatments, the government, as the majority funder, partnered with the Gates Foundation and Merck to establish the national ARV program in Africa, which began in 2002. This is enormously important in a country where nearly a quarter of adults are HIV positive. Unlike many other places in the region, Batswana do not have to cobble together insufficient, yet vitally necessary, health care amid a shifting archipelago of nongovernmental organization, private, and research-driven programs. Instead, their care, including antiretrovirals, is provided as a basic right of citizenship. The ARV program is also important in setting a precedent for what is possible in Africa. Recall that when protease inhibitors were first developed, most international experts deemed them too expensive for Africa, and Africans too "backwards" to take them properly. Batswana have proved such attitudes facile, unethical, and wrong-headed.

This vital ARV program is directly caught up in Botswana's cancer epidemic, both as a driver of cancers, and also by creating a platform in which extant but previously undiagnosed cancers are increasingly becoming recognized. Virus-associated cancers have become a significant problem in Botswana as they are across east and southern Africa. This secondary epidemic tracks through populations now gaining access to antiretroviral drugs. Patients who would previously have died of AIDS-related infections are now living long enough to endure opportunistic cancers facilitated by their immunosuppression (especially Kaposi's sarcoma, genital cancers, non-Hodgkin's lymphoma, and head and neck tumors).

A minority—but given the scale of HIV infection a significant number—of patients will develop a virus-associated cancer before beginning antiretroviral therapy, or during the process of partial immune reconstitution. This was expected. As a result, the Botswana Ministry of Health converted a small piece of the accident and emergency department of the central referral hospital to a cancer ward just as they began the ARV program. Experience in the U.S. had already demonstrated the synergy between HIV and cancer. This relationship was evidenced by the fact that three viral-associated cancers, Kaposi's sarcoma (KS), non-Hodgkin's lymphoma, and cervical cancer, served as AIDS-indicator illnesses. In 2003 program officials at the National Cancer Institute predicted this new African epidemic, and African oncologists and other enlightened members of the international oncology community have been warning of rising rates of incidence for some time [4-6]. From its inception, CD4 counts were used to triage patients in need of ARVs as Botswana's program scaled up. The program began by initiating patients on highly active antiretroviral therapy if their CD4 count was 200 or below or they had an AIDS indicator illness. The cutoff point was then raised to 250 and then 300. In practice, this also means that people need to be tested before they are symptomatic, and also that the CD4 machines are functioning properly (they break down regularly). It also means that doctors and nurses in the HIV clinics need to be able to recognize AIDS-defining cancers, which in practice, it seems they often do not. Even if African AIDS programs can overcome the infrastructural, financial, and other obstacles to initiate patients with much higher counts, experience in the U.S. has shown that the cancer problem will shift shape rather than simply disappear. In the U.S., while ARVs have brought a crucial reduction in the numbers of HIV- positive patients with AIDS-defining cancers, over time there has also been a rise in those with non-AIDS-defining cancers.

The implications of HIV infection go beyond etiology, as HIV coinfection also appears to complicate prognoses for nonvirus-associated cancers in ways that we still do not fully understand. And of course patients and their accompanying relatives arrive in oncology already reeling from the existential angst and long-term pressures on familial caregiving resources that the HIV/AIDS epidemic has wrought.

The presence of AIDS care has made cancer visible. But cancer is not merely a subset of HIV/AIDS in Botswana. Indeed, one of the side effects of establishing the oncology service has been to unearth a hidden cancer epidemic already present and growing in the country, given its shifting demographic and ecological norms. Preliminary results from an ongoing study suggest that approximately two thirds of cancer patients receiving treatment in Botswana's oncology service are infected with HIV [7]. We do not yet know the extent to which HIV coinfection might draw a patient into the health system and thereby improve the chances that her cancer is diagnosed and counted. Nor are all HIV-positive patients afflicted with cancers that stem directly from their HIV disease. In other words, it would be a serious mistake to imagine that virus-associated cancers are the only problem in Botswana. Throughout the developing world, just as in the global north, poverty and political marginality renders people particularly vulnerable to environmental and occupational exposure to known carcinogens. Experience in the ward and in village communities suggests significant burdens of breast, esophageal, and bone cancers, to name only three among the many cancers present in the country that currently appear not to have any viral associations.

Given this situation, Botswana's small cancer ward is a promising development. Yet, at present, it remains an improvised solution in a broader context of widespread need. Currently the field of oncology is structured such that cutting-edge research keeps edging up cost and therapeutic intensity, while the problems of patients in impoverished contexts are, for the most part, ignored for lack of funds. In middle-income countries like Botswana, patients receive treatment from already overloaded clinicians who are straining to provide care amid an ever-growing volume of patients.

On the one hand, an extension of resources in the form of technologies, goods, and expertise is necessary. Most cancer patients in Africa have a hard time accessing care at all. For example, the International Atomic Energy Agency estimates that only 20% of African patients have any potential access to radiotherapy if needed [8]. Of course, access is not the same thing as quality treatment. Many machines are ill-maintained, or run at higher doses for shorter courses in order to handle the volume of patients, and many patients (unlike in Botswana) live in contexts where they must pay out of pocket for such services, which renders them unobtainable.

Palliation is grossly insufficient. An international network of laws designed to prevent the illicit trade in narcotics also prevents most terminally ill African patients from access-

ing vitally necessary opioid analgesics. An ethic of palliation established by the oncologist holds in Botswana's cancer ward, where oral morphine and codeine are used regularly, as long as they are in stock in the hospital pharmacy. This ethic, unfortunately, does not extend through the rest of the hospital or broader health system. The more powerful antiemetics are costly, and therefore, by and large not available to African patients, which compromises their ability to complete their course of chemotherapy. In Botswana the off-patent metoclopramide is used, but this is often insufficient, such that the ward echoes with the sound of patients bent over their vomitus, retching their guts out.

But even if care is available, as it is in Botswana, cancer in Gaborone differs from cancer in Boston, where it lies at the heart of highly capitalized biotechnical research. The biological, epidemiological, sociocultural, and technical contexts of southern Africa differ from the evidentiary basis of most current oncology research, with its emphasis on ever-newer drugs and techniques, such as the turn to precision or personalized medicine. Fewer studies address the challenges of effectively administering chemotherapy to patients like many in Botswana who have simultaneous HIV and tubercular coinfections alongside their cancer. Newer "smart" drugs like Herceptin are too expensive to use, as are important support interventions like Neupogen, such that patients with neutropenia are regularly sent away and asked to try again the following week for their chemotherapy. Surgical and laboratory capacity necessary to support timely and accurate diagnosis and treatment are often overstretched or lacking. Nursing capacities are also different. Isolation conditions are not available, the use of ports or feeding tubes is uncommon, and the necessary support care to enable concurrent radiotherapy and chemotherapy (the standard of care for many cancers) is not possible.

In most African countries, though thankfully not in Botswana, structural adjustment policies imposed by the International Monetary Fund and World Bank essentially privatized public health care into collapse beginning in the late 1980s. Left with hollowed out health infrastructure, patients must purchase their drugs and other medical supplies themselves, usually from private pharmacies. As I have witnessed in neighboring countries, often patients cannot afford the entire chemotherapeutic regimen, so they might, for example, return from the pharmacy with either doxorubicin or cisplatin, but not both, for the oncologist to administer. What is the best way for an oncologist to proceed in such a setting? Even in Botswana, where patients receive oncology care, including drugs and radiation, as a right of citizenship, there are problems of supply. Evidence-based protocols published in the leading oncology journals do not say what to do when etoposide, fluorouracil, bleomycin, or cisplatin suddenly go out of stock—as each did for some time during my research stints in the ward. Even when the off-patent drugs in Botswana's basic arsenal are in stock, the oncologist must figure out how best to deploy them in a hospital that lacks MRI, endoscopy, or mammography; where the oncologist must also act as his own cytologist; where tumor markers are unavailable, the waiting times for biopsy and then histology are long; and where often there are not enough platelets for all the patients who are bleeding.

Needless to say, being effective in such a context is a challenge and requires a high degree of intellectual and institutional creativity and energy. In 2010 I sat with an oncologist at a large public hospital in Zimbabwe as she combed through medical journals from the 1960s and early 1970s that sat next to the latest issues of *Lancet Oncology or the Journal of the National Cancer Institute* on her shelf, trying to determine the best course of treatment for her patient, given the available drugs and technologies on that day. In other words, oncologists in these settings have to keep as up to date as possible while also dipping back into an older store of knowledge in order to be effective for their patients, in institutions where the technological field is uncertain and continually shifting. There is much to learn from these oncologists. Despite their creativity, given such circumstances it is not surprising that a recent study by International Agency for Research on Cancer noted that the lifetime risk of dying from a cancer is nearly twice as high for women in Africa than in developed countries [1].

Donating goods and techniques developed in the West to Africans is not an adequate solution, as seen in the case of the HPV vaccines for cervical cancer. Aside from the logistical challenges of administering a three-part vaccine, without genotyping, it becomes difficult to know whether or not Gardasil (Merck, Whitehouse Station, NJ) and Cervarix (GlaxoSmithKline, Middlesex, UK), which were originally developed with American consumers in mind, will be biologically appropriate for southern African women. Gardasil and Cervarix address only the two oncogenic viral subtypes (16 and 18) associated with the major burden of cervical cancer and dysplasia in the U.S. Preliminary studies from urban Zambia, however, found that oncogenic HPV strains 52, 58, and 53 were much more common than HPV 16 or 18 in women with high-grade squamous intraepithelial lesions or squamous cell carcinoma [9]. Preliminary results from a small study in Botswana on 30 HIV-positive women with stage 2 or 3 cervical cancer found that 50% of patients were infected with HPV 16 or 18 (or both), but also that 83% of women carried other high-risk HPV types [10]. Similarly, another preliminary study among HIV-infected women in Botswana found that HPV 58 was the most prevalent HPV genotype [11]. Larger systematic studies are ongoing. Even where a vaccine targeting strains 16 and 18 is biologically appropriate, questions remain as to whether the suppression of prevalent oncogenic viral subtypes through vaccination might provide an opportunity for selective pressure by other currently less-prevalent oncogenic subtypes within a given population, particularly in contexts where HPV and HIV are locked in a deadly synergy [12].

This is not to say that there is no room for technological innovation; only that innovation must be driven by local conditions rather than metropolitan profits, and it must be high standard. Clinical oncology asks a tremendous amount from very sick people. It is a dangerous and sometimes iatrogenic, though absolutely vital, pursuit. Third-rate and hand-me-down oncology has the potential to be more dangerous than no oncology at all. While oncology developed within a system of universal care and cost constraint has the potential to better balance the kinds of extremes in therapeutic intensity and cost that afflict American oncology and the urgent need for care that marks most of Africa. A good example is the new

see-and-treat program using visual inspection with acetic acid and then cryotherapy for cervical cancer. The first such program in Botswana is currently being piloted by Dr. Doreen Ramagola-Masire in her women's health clinic in the referral hospital in Gaborone, part of the Botswana–University of Pennsylvania partnership. This program eliminates a central problem of laboratory capacity, and potentially shortens the delays patients face in receiving treatment [13].

Sustainable supplies of pharmaceuticals, equipment, expertise, and infrastructure are all needed. So too is knowledge that is developed specifically for these patients and their particular epidemiological and institutional circumstances, research that will require partnering with African oncologists and nurses who know these issues best. Equally necessary elsewhere in the region is a revision of the social contract, to provide broad-based, social medicine, like there is in Botswana. It makes no sense epidemiologically or in economic terms that the poorest people are those who have to pay. It is also ethically dangerous to do clinical research in settings where people's only access to medical care is gained by offering themselves up as experimental subjects. Palliation, including access to effective antiemetics, will need to be central to oncology in Africa, just as it is in the West. Not as a substitute for meaningful care, but as a vital, ethical component of it. All of this will require oncology to change as much as African health systems. Perhaps we can even hope that, in learning from Botswana, patients in the U.S. too will someday have a system of universal care to rely upon, as a first ethical principle of biomedical progress and care.

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Editor's Note: See the related editorial on page 777.