Cancer in the Developing World: How Should Care Be Delivered and Research Conducted?

Second of a two-part series.

The development of specific types of cancer within individuals and populations is in large measure a reflection of lifestyle factors and exposures to carcinogens and infectious agents. These factors differ between regions—for example, infectious diseases cause far more cancers in developing countries than in developed countries—and change over time.

“The tobacco epidemic started in Western countries and is now spreading worldwide, particularly to Asia,” noted Paul Kleihues, M.D., director of the International Agency for Research on Cancer (IARC) in Lyon, France. “The Western lifestyle, which is responsible for several major tumor types, including breast, prostate, colon, and endometrium cancer, is also increasingly acquired by developing countries. While the overall mortality from cancer is now declining in North America and some European countries, a steep increase can be predicted for many other regions.”

As the picture of cancer incidence on the world map changes, and with a growing cancer burden expected to befall resource-poor nations, many experts believe cancer research should move toward globalization. Affluent nations, for which cancer has long been a feared and burdensome disease, continue to invest heavily in cancer research, and there have been tangible returns on the investment. But how can cancer research be exported to the developing world?

“One cannot assume that all advances made in affluent nations can be applied without further testing to developing countries,” said Ian Magrath, M.D., president and medical and scientific director of the International Network for Cancer Treatment and Research in Brussels, Belgium. “The cancers may be biologically different—the people and their com-

morbidities certainly are—and facilities, including supportive care, differ quite dramatically. What works in New York may not be ideal for Dar es Salaam.”

Prevention and Screening

There are some interventions that could be readily used in resource-poor nations. “From a public health point of view, there is already a sound basis of knowledge about preventive strategies, and there is plenty of opportunity for operational research into how they can be applied,” said Max Parkin, M.D., chief of IARC’s Unit of Descriptive Epidemiology. For example, Parkin is working on the Gambian Hepatitis Intervention Study, unusual for its application of a primary preventive strategy in a high-risk, low-resource population. It is one of two randomized studies evaluating the efficacy of the hepatitis B virus (HBV) vaccine in preventing invasive cancer. The vaccine (which is currently a recommended vaccination for children in the United States) has already been proven effective in protecting inoculated children against chronic HBV infection, and the expectation is that it also will have a strong protective effect against hepatocellular carcinoma, which has been associated with chronic HBV infection.

Parkin said he and his colleagues are following some 60,000 children who were vaccinated between 1986 and 1991 and a comparably sized group of children who were born during that period but not vaccinated. As liver cancer cases are documented in a cancer registry established in The Gambia as part of the study, they are also cross-referenced to the study database.

There have been concerns that the HBV vaccine would be too expensive to be a practical intervention in resource-poor countries, and some countries with endemic HBV do not provide the vaccine to children. In the case of The Gambia, Parkin said that all newborns in the country are being vaccinated with vaccine donated by different agencies, including the Global Vaccine Initiative.

Cancer screening technology may not be as readily exportable. “For cancers where early detection is a mainstay of control in Western countries—for example breast and cervical cancer—there is an urgent need to review approaches to mass screening, both from a technological point of view as well as organizational,” said Parkin. This is particularly true for cervical cancer; more than 80% of women dying from cervical cancer live in developing countries, Kleihues said. He stressed that early detection strategies that can be used in settings where resources are limited are essential if the burden of cervical cancer is to be lessened.

An IARC colleague, Rengaswamy Sankaranarayanan, M.D., research scientist with the Unit of Descriptive Epidemiology, is investigating alternatives to cytology for cervical cancer screening. Studies are under way in India and several African countries to compare traditional Pap smears with DNA testing for human papillomavirus (the infectious agent responsible for most cases of cervical cancer), and with direct visualization techniques. “Our studies in India and Africa indicate that VIA [visual inspection with acetic acid] and VILI [visual inspection with Lugol’s iodine] are simple and accurate alternatives for cervical cancer early detection,” said Sankaranarayanan. Magrath asserted that
“the sensitivity of direct visualization techniques, which cost very little, are not greatly different [from]—in fact, probably better [than]—cytology, which costs quite a bit and requires a highly skilled cytologist.”

When it comes to exporting the benefits of cancer research, distribution may be the rate-limiting factor. Rafael Bengoa, M.D., director for Management of Noncommunicable Diseases at the World Health Organization, described how a national concern for many developed countries is also a global one: “The richer countries are putting enormous amounts of resources into cancer research to identify its causes and to improve the efficacy of early detection and treatment approaches. … Unfortunately, globally there is not a similar amount of resources to implement these evidence-based interventions in a systematic and comprehensive way. This gap between knowledge and practice is especially dramatic in less developed countries and within underprivileged communities in richer countries where the cancer problem is also rising and access to appropriate services [is] limited.”

‘Global Laboratory’

Some feel that affluent nations are missing opportunities not only to provide humanitarian assistance to resource-poor countries and stimulate goodwill within the world community, but also to understand more about cancer for the common good. “Tunnel vision—in this context, a national view of health rather than a global view—it is easy to see, would greatly limit our horizons and slow progress. Such a perspective results in ineffective use of available resources, reduces concerted efforts so necessary to our global civilization in general, and global health in particular, and tends to create competition where there should be collaboration,” said Magrath. “There are unique scientific opportunities in developing countries and … this is a part of the global laboratory which is underused to the detriment of all.”

Parkin noted that any movement toward doing more epidemiologic work in developing countries has been slow.

“The etiology of some cancers that are common in some developing countries—for example, cancers of the esophagus and biliary tract—offer opportunities for epidemiological studies, including work on biomarkers of exposure or susceptibility,” said Parkin.

Magrath said that to a limited degree, “the advances in genetics and epidemiology have led some to try to take advantage of scientific opportunities in these areas that exist particularly in developing countries [that] have a much broader range of environments, and, because of frequent cousin marriages and larger families, genetic markers of disease predisposition may be more apparent.”

Some pharmaceutical companies are showing interest in conducting clinical trials in developing countries to increase the number of study participants, thereby reducing costs and time for drug development, Magrath added. Alan Goldhammer, Ph.D., associate vice president for regulatory affairs for the Pharmaceutical Research and Manufacturers of America (PhRMA), does not yet see a major push by its members to do more clinical studies in developing countries, but he anticipates that as disease patterns change, PhRMA members “will do clinical trials where the patients are located to get them done as quickly as possible to benefit everyone.”

PhRMA’s guidelines for conducting clinical studies indicate that its members abide by the Declaration of Helsinki, an internationally accepted statement by the World Medical Association of ethical principles for medical research involving human subjects. The declaration includes
provisions stating that study populations must “stand to benefit from the results of the research,” and new interventions must be compared with the “best current” interventions. They are guidelines, however, and communities that would like to participate in clinical trials are free to negotiate what they will accept based on their own interpretations of “benefit” and “best current.” Magrath pointed out that “there is much to be gained [by both developing and developed countries], but in a world driven largely by economic considerations rather than altruism, the possibility of exploitation is always there” and must be prevented.

**Training New Researchers**

Training scientists from developing countries is widely promoted as a key component of the globalization of cancer research. “This is very important indeed,” said Kleihues, pointing to IARC’s 30-year history of providing fellowships for young scientists in the developing world. There may be room for improving the training process by conducting training in concert with building research capacity. Magrath cited one drawback associated with bringing people from developing countries to affluent countries for training: “many trainees never go back, or go back and are disgruntled because of limited resources and facilities, only to leave again. Even many of those trained in developing countries, once they are trained, may seek greener (or more lucrative) pastures elsewhere.” He proposed that this effect can be mitigated by “maximiz[ing] training in place, and coupl[ing] training, wherever possible, with ongoing research projects in which trainees participate.”

Magrath listed several reasons for which the research element is critical: “one cannot necessarily directly transfer research results from rich to poor countries, and … the problems faced may be different, such that only local research will suffice. In addition, research creates a different attitude of mind—one much more likely to lead to sustainable development—and even in a non-research context, results in a more curious person more able to analyze situations. Also, being able to conduct useful research in unique situations may be one incentive to young professionals to stay in, or return to, their country of origin.”

Magrath recognizes that there are many challenges associated with conducting research in resource-poor environments while research capacity is under construction. There are few investigators in the developing world experienced with the grant application process, and they may have difficulty competing for funds with highly trained researchers from affluent countries. Research projects may take longer and the quality of the work may not reach the highest standard, initially. He feels that the challenges can and should be met. “The advantage is that once such capacity is built, a whole new world may open up,” he said. “It’s a simple issue of investing in people and the future.”

—Stacye Bruckbauer and Christine Theisen