Introduction: What Should We Do Now about H. pylori?

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Cancer is widely seen as a problem of industrialized countries, reflecting the consequences of affluent lifestyles and exposure to chemical carcinogens, such as those in tobacco smoke. In low- and middle-income countries, where infectious diseases and child survival are dominant concerns, cancer tends to receive relatively little attention. However, at least half of the roughly seven million deaths annually caused by cancer worldwide now occur in the low- and middle-income countries. By 2025, as decreasing fertility and improved childhood survival lead to relatively more aged populations and as the consequences of the worldwide epidemic of tobacco-induced lung cancer are fully manifested, the global number of cancer deaths will increase to >10 million, of which more than two thirds will be in the low- and middle-income countries (1, 2). Cancer already accounts for 10% of all deaths in the low- and middle-income countries and in many of the lowest income countries, particularly those that have been spared the brunt of the HIV epidemic, cancer is one of the three leading causes of adult mortality (along with cardiovascular disease and injury).

Severely constrained resources in the developing world pose a major challenge to the implementation of rational policies for cancer control (3, 4) and many approaches to cancer screening and treatment that are accepted as standard practice in the United States and Western Europe could not be provided feasibly or equitably in low-income countries. Primary prevention strategies, however, may be cost-effective even when resources are scarce (5). In this regard, prevention of tobacco uptake is likely to be the most cost-effective approach and should be a part of any nation’s cancer control plans (WHO Framework Convention on Tobacco Control, http://www.who.int/tobacco/framework/en/). Measures to address specific infectious causes of cancer, including hepatitis B virus (hepatocellular cancer) and human papilloma virus (cervical cancer), cannot be too far behind tobacco control in their potential importance as part of a cancer policy.

Control of Helicobacter pylori, a bacterium that is the major cause of gastric cancer, may soon be added to the list of high-priority cancer prevention strategies. H. pylori seems to have evolved together with humans over tens of thousands of years (6) and arguably has accounted for more deaths from cancer than has any other single carcinogen. Gastric cancer was the principal cause of worldwide cancer deaths, before being replaced by lung cancer at the end of the twentieth century. It was also the leading cause of cancer death in the United States until about 1940 (7), and its decline in frequency since then probably represents an important and largely unappreciated consequence of the sanitary revolution. Mortality rates for gastric cancer now vary profoundly around the world, with the greatest effect seen in much of Asia and Latin America (1). Some countries with a high prevalence of chronic H. pylori infection, such as South Africa and India, have low rates of gastric cancer and even within high-risk countries, such as China, Colombia, and Costa Rica, rates can vary greatly. The reasons for these findings are not fully understood, but they may in part reflect variations in the distribution of the more virulent strains of H. pylori (8).

This issue of CEBP includes a series of review articles on H. pylori and gastric cancer that grew out of two symposia held in 2004: the first celebrated the opening of the new Public Health Sciences Building at the Fred Hutchinson Cancer Research Center in Seattle and the second was organized by the Southwest Oncology Group in Huntington Beach, CA. The authors of these reviews cover topics that range from the basic biology of H. pylori to human host factors that may influence the consequences of infection and to the development of preventive and therapeutic vaccines. The reviews together portray how far we have come in our understanding of H. pylori and also illustrate the growing promise of effective methods for control of gastric cancer. As we learn more about the pathogenesis of H. pylori-induced cancer and about the immunologic mechanisms that contribute to chronicity of infection, the prospects for vaccine-based prevention strategies become increasingly bright. If we can prevent the acquisition of H. pylori infection, which in high-risk countries usually occurs in early childhood, we may virtually eliminate gastric cancer as an important cause of cancer death.

But what of the hundreds of millions of people who are already chronically infected with H. pylori? For them, another prevention strategy is necessary. Screening endoscopy has been reported to be effective in detecting early gastric neoplasms; however, no clinical trial has yet shown that it prevents gastric cancer death, and potential biases complicate the interpretation of the epidemiologic studies of this issue (9). Furthermore, the costs and complexity of screening make this an unfeasible strategy for most of the world and particularly for many of the nations with the highest burden of gastric cancer.

Eradication of infection with antibiotic therapy seems to offer more promise, and the results of two clinical trials have provided encouraging, although not conclusive, evidence that antibiotic treatment of adults may prevent gastric carcinogenesis (10, 11). H. pylori is notoriously difficult to treat, and the need to use a multidrug regimen over extended periods, as well as the emergence of resistant organisms, has complicated research and, ultimately, implementation programs aimed at eradication. However, the recent report of the effectiveness of a single-day regimen of combined antibiotic therapy in eradicating infection (12) provides some encouragement that mass treatment programs may be feasible in future. Towards this end, investigators in the Southwest Oncology Group and several comprehensive cancer centers (e.g., Fred Hutchinson Cancer Research Center, Arizona Cancer Center, Lee Moffitt Cancer Center, Memorial Sloan Kettering Cancer Center) are now exploring the possibility of conducting randomized trials of antibiotic therapy for cancer prevention that would involve tens of thousands of patients followed for ≥10 years in China and in Latin America.

As the reviews in this issue so well illustrate, much has been accomplished since the initial description of H. pylori two decades ago (13), but much also remains to be done. Let’s do it!
References

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