Chronic Disease: Infectious Cause?

Nothing is more exorcised in medicine than the notion of the “magic bullet.” Yet that is, in part, the allure that draws the public and researchers to seek an infectious cause for chronic disease. Who would not like to eliminate cancer or heart disease with a pill or a vaccine?

When the federal Centers for Disease Control and other public health and infectious disease organizations held the First Annual Conference on Emerging Infectious Diseases in Atlanta, Ga, earlier this year, it was that search for a magic bullet that made the issue of chronic disease and infections was one of the plenary topics.

Gail Cassell, PhD, formerly of the University of Alabama School of Medicine and now a vice president with Eli Lilly & Co in Indianapolis, Ind, gave that lecture. She said that perhaps it all began with acquired immune deficiency syndrome. “AIDS was an eye opener,” she said. “It was something unimaginable: an infectious agent that could lie dormant for so long and then cause such a devastating infection.”

Now, she said, a growing body of knowledge indicates that a variety of infectious agents may be associated with chronic diseases. The best known of these is the Helicobacter pylori story, in which Australian physician Barry J. Marshall, MD, fought an uphill battle to have the association between the bacterium and ulcers recognized. As recently as the mid-1980s, peptic ulcers were blamed on stress and other environmental factors. Drugs to reduce the flow of stomach acid were among the most prescribed drugs in the United States and many areas of the developed world. But Dr Marshall and his colleagues found that treatment with antibiotics and some bismuth-containing compounds cured the acute ulcer and even seemed to prevent it from returning. At the time, most medical experts scoffed. Dr Marshall, failing to find an animal model for the infection, drank a pure culture of H pylori in 1984, which resulted in the type of severe acute gastritis associated with the finding of many H pylori in the digestive tract. This finding netted Marshall a Lasker Award in 1995 and eventual vindication in the medical community.

Although the ulcer–infectious disease connection was largely unsuspected, other chronic diseases had long been thought to have an infectious component, said Dr Cassell. For example, she said, rheumatoid arthritis has long been thought to have an infectious origin. The same sorts of suspicions have long lingered about cardiovascular disease. "There are compelling preliminary data." The promises of such findings are great. It is unlikely that the discovery of a link between chronic disease and a variety of infectious agents will lead to elimination of the long-term disorders in question; however, such a discovery could lead to treatments that would, in part, prevent primary disease and recurrence. In some instances, treatment might even prevent the infection in the first place. That, said Dr Cassell, could decrease the long-term burden of chronic disease on the population.

H pylori is itself associated with gastric cancer as well as mucosa-associated lymphoid tissue lymphoma. Schistosoma haematobium is associated with bladder cancer and Opisthorchis viverrini with cholangiocarcinoma. Hepatitis B and C have been shown to be causal factors in hepatocellular cancer, she said. Human Papillomavirus is strongly associated with cervical cancer; human herpes virus 8 and Kaposi sarcoma are similarly associated. All these findings have major implications for treatment, prevention, and research, said Dr Cassell. Research to pinpoint the exact risks posed by these infectious agents and to determine who is at risk will not be inexpensive, she warned. "It will require long-term, sustained studies," she said.

One agent will not be found to be the single cause of all cancer or arthritis, said Dr Cassell. Many agents could contribute to the development of heart diseases. "You could culture 50 patients and find nothing," she stated. "We would need something on the order of a Framingham study to sort it all out."

Simply treating patients with antibiotics willy-nilly is unlikely to work and raises a whole new specter of creating resistant infectious agents. "Lots of antibiotics will not kill the organisms that are implicated," Dr Cassell said. "Patients [with chronic infections] would have to be treated over a long period of time." The treatment might be something like that currently prescribed for tuberculosis, she said.

Dr Cassell argues that the best course will be to look for multiple agents to be involved in chronic diseases. On the basis of current knowledge, she said, thousands of patients would have to be followed up for many years by both clinical epidemiologists and laboratory personnel with the ability and willingness to look for a host of virtually undetectable organisms. Information about the genetic backgrounds and immune systems of the patients will also play a crucial role in this task of molecular epidemiology, she said.

Such studies will require inordinate cooperation among a host of groups. "But I think it will happen," said Dr Cassell. "There are compelling preliminary data."

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