Editorial

Prevention: Toward a Golden Age

Jean-Claude Pechère, MD

According to the World Health Organization reporting office, approximately 52 million human beings died in 1996, including 17 million from infectious diseases, 14 million from cardiovascular conditions, and 6 million from cancer. In 1990 also, there were 17 million deaths by infection. Today, compared to 10 years ago, we have fewer respiratory and diarrheal diseases, less measles, but more tuberculosis (approximately 3 million deaths in 1997, including an increasing number of multidrug-resistant cases), hepatitis B (600,000 deaths in 1997), malaria (probably more than 2 million deaths in 1997, with the increasing burden of resistance to antimalarial remedies), and acquired immunodeficiency syndrome (2,300,000 deaths in 1997). Vancomycin-resistant enterococci, the progressing epidemic of penicillin-resistant pneumococci in the United States, and the increasing number of extended-spectrum β-lactamases illustrate our failure to overcome bacterial antibiotic resistance in developed areas, despite the development of potent new antibacterial agents. In nondeveloped areas, the situation often is even worse, and prevalence of methicillin-resistant *Staphylococcus aureus* or multidrug-resistant pneumococci may surpass 50%. In some privileged, modern, well-equipped institutions, vigorous efforts have maintained an acceptable control of horizontal transmission, but this is not the case in many other places, and nosocomial infections remain a fatal trap for an unknown number of people, probably much higher than we think, in the poorest countries of the world. Life expectancy is progressing in the richest countries, where our populations are getting older, hence more susceptible to cancers and cardiovascular diseases, which bring their concomitant risks of infections. The implication of microbial agents in diseases that were not thought to be infectious is more and more often recognized or suspected: *Helicobacter pylori* in peptic ulcer, retrovirus and superantigen pathogenesis in diabetes and multiple sclerosis, Borna disease virus infection in patients with neuropsychiatric disorders, and *Chlamydia pneumoniae* in severe complications of coronary heart disease are just examples of this situation. Recent data suggest that a variety of syndromes are triggered by acute infectious illnesses, eg, *Campylobacter jejuni* in Guillain-Barré, syndrome. The list of new agents causing infectious diseases lengthens regularly. Altogether, from the public-health viewpoint, we do not progress much, one step forward here, one step backward there.

For meeting the challenge, no magic drugs can be predicted in the foreseeable future, and drug therapy probably will not be the solution. However, new tools are becoming available that open many new avenues in prevention. Research on vaccines has been extraordinarily active and fruitful in the recent years, signaling an actual revolution in the domain. We have learned to design three-dimensional epitopes; to stimulate immune responses towards the most effective directions, depending on the targeted pathogen; and to understand how to elicit long-term immunological memory. Ongoing promising developments are seen in the area of therapeutic vaccines, to be given to asymptomatic-infected individuals before they get sick. Nucleic-acid vaccines, molecular vaccines, microencapsulated vaccines, new adjuvants, mucosal vaccines, vectored vaccines, and edible vaccines are paving the way of products easy to make, for a few cents per dose, easy to administer, stable. Tomorrow, immunization could be as

From the Department of Microbiology, Centre Médical Universitaire, Geneva, Switzerland.
Address reprint requests to Professor Jean-Claude Pechère, MD, CMU, Department of Microbiologie, 9 av de Champel 1211, Geneve 4, Switzerland.

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easy and as cheap as eating a banana. The vaccine pipeline now includes products aimed at protecting against diseases for which no immunizations are presently available, such as rotavirus, the most common cause of severe diarrhea among children, or *H pylori,* associated with peptic ulcer and stomach cancer. In the future, the new vaccine targets may include cancer (cervical neoplasm associated with human papillomavirus infection, as well as vaccines targeted at a variety of tumor-associated antigens) and autoimmune diseases.

Predictive medicine is aiming at the recognition at a pre-clinical stage of genetic configurations predisposing to diseases or defects. Some of these methods permit the detection of such disorders in the fetus during gestation. This should enable us to develop effective preventive measures before the appearance of complications. Such approaches are used already for the early detection of classic patterns of genetic diseases, but can be extended to a great number of conditions out of the classic pattern, from diabetes to cancer to arterial hypertension. Even infectious diseases, which used to be a paradigm of exogenous causality, are modulated by genes of resistance or susceptibility. In a more distant future, when the human genome is sequenced and it is possible to define accurately the genetic risks for certain conditions favoring infectious diseases, it may be conceivable to define new strategies for vaccines.

Epidemiology also is progressing rapidly. Computer-assisted molecular identification of microorganisms has achieved a degree of discrimination allowing a truly clonal epidemiology. Sophisticated mathematical models now are able to predict new epidemiological trends accurately, offering a potent tool for setting active preventive measures. The computer revolution also will help us to take up the immense challenge of education. Prevention is, first, education. Easy and rapid access to information is a key feature. There is no doubt that the new communication networks represent a fantastic advantage for disseminating information in the most remote areas of the world.

The challenge of infectious diseases remains immense, but new concepts and new tools augment considerably our armamentarium for improved prophylactic measures: the 21st century may well be a golden age for prevention.

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