SECTION 1 BASIC CONSIDERATIONS IN INFECTIOUS DISEASES

144 Approach to the Patient with an Infectious Disease

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HISTORICAL PERSPECTIVE

The origins of the field of infectious diseases are humble. The notion that communicable diseases were due to a *miasma* ("bad air") can be traced back to at least the mid-sixteenth century. Not until the work of Louis Pasteur and Robert Koch in the late nineteenth century was there credible evidence supporting the germ theory of disease—i.e., that microorganisms are the direct cause of infections. In contrast to this relatively slow start, the twentieth century saw remarkable advances in the field of infectious diseases, and the etiologic agents of numerous infectious diseases were soon identified. Furthermore, the discovery of antibiotics and the advent of vaccines against some of the most deadly and debilitating infections greatly altered the landscape of human health. Indeed, the twentieth century saw the elimination of smallpox, one of the great scourges in the history of humanity. These remarkable successes prompted noted scholar Aidan Cockburn to write in a 1963 publication entitled *The Evolution and Eradication of Infectious Diseases*: "It seems reasonable to anticipate that within some measurable time . . . all the major infections will have disappeared." Professor Cockburn was not alone in this view. Robert Petersdorf, a renowned infectious disease expert and former editor of this textbook, wrote in 1978 that "even with my great personal loyalties to infectious diseases, I cannot conceive a need for 309 more [graduating trainees in infectious diseases] unless they spend their time culturing each other." Given the enormous growth of interest in the microbiome in the past 5 years, Dr. Petersdorf's statement might have been ironically clairvoyant, although he could have had no idea what was in store for humanity, with an onslaught of new, emerging, and re-emerging infectious diseases.

Clearly, even with all the advances of the twentieth century, infectious diseases continue to represent a formidable challenge for patients and physicians alike. Furthermore, during the latter half of the century, several chronic diseases were demonstrated to be directly or indirectly caused by infectious microbes; perhaps the most notable examples are the associations of *Helicobacter pylori* with peptic ulcer disease and gastric carcinoma, human papillomavirus with cervical cancer, and hepatitis B and C viruses with liver cancer. In fact, ~16% of all malignancies are now known to be associated with an infectious cause. In addition, numerous emerging and re-emerging infectious diseases continue to have a dire impact on global health: HIV/AIDS, pandemic influenza, and severe acute respiratory syndrome (SARS) are but a few examples. The fear of weaponizing pathogens for bioterrorism is ever present and poses a potentially enormous threat to public health. Moreover, escalating antimicrobial resistance in clinically relevant microbes (e.g., *Mycobacterium tuberculosis*, *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Plasmodium* species, and HIV) signifies that the administration of antimicrobial agents—once thought to be a panacea—requires appropriate stewardship. For all these reasons, infectious diseases continue to exert grim effects on individual patients as well as on international public health. Even with all the successes of the past century, physicians must be as thoughtful about infectious diseases now as they were at the beginning of the twentieth century.

GLOBAL CONSIDERATIONS

Infectious diseases remain the second leading cause of death worldwide. Although the rate of infectious disease–related deaths has decreased dramatically over the past 20 years, the absolute numbers of such deaths have remained relatively constant, totaling just over 12 million in 2010 **(Fig. 144-1*A*)**. As shown in **Fig. 144-1*B***, these deaths disproportionately affect low- and middle-income countries **(Chap. 13e)**; in 2010, 23% of all deaths worldwide were related to infectious diseases, with rates >60% in most sub-Saharan African countries.

Given that infectious diseases are still a major cause of global mortality, understanding the local epidemiology of disease is critically important in evaluating patients. Diseases such as HIV/AIDS have decimated sub-Saharan Africa, with HIV-infected adults representing 15–26% of the total population in countries like Zimbabwe, Botswana, and Swaziland. Moreover, drug-resistant tuberculosis is rampant throughout the former Soviet-bloc countries, India, China, and South Africa. The ready availability of this type of information allows physicians to develop appropriate differential diagnoses and treatment plans for individual patients. Programs such as the Global Burden of Disease seek to quantify human losses (e.g., deaths, disability-adjusted life years) due to diseases by age, sex, and country over time; these data not only help inform local, national, and international health policy but can also help guide local medical decision-making. Even though some diseases (e.g., pandemic influenza, SARS) are seemingly geographically restricted, the increasing ease of rapid worldwide travel has raised concern about their swift spread around the globe. The world's increasing interconnectedness has profound implications not only for the global economy but also for medicine and the spread of infectious diseases.

UNDERSTANDING THE MICROBIOTA

Normal, healthy humans are colonized with over 100 trillion bacteria as well as countless viruses, fungi, and archaea; taken together, these microorganisms outnumber human cells by 10–100 times **(Chap. 86e)**. The major reservoir of these microbes is the gastrointestinal tract, but very substantial numbers of microbes live in the female genital tract, the oral cavity, and the nasopharynx. There is increasing interest in the skin and even the lungs as sites where microbial colonization might be highly relevant to the biology and disease susceptibility of the host. These commensal organisms provide the host with myriad benefits, from aiding in metabolism to shaping the immune system. With regard to infectious diseases, the vast majority of infections are caused by organisms that are part of the normal flora (e.g., *S. aureus*, *S. pneumoniae*, *Pseudomonas aeruginosa*), with relatively few infections due to organisms that are strictly pathogens (e.g, *Neisseria gonorrhoeae*, rabies virus). Perhaps it is not surprising that a general understanding of the microbiota is essential in the evaluation of infectious diseases. Individuals' microbiotas likely have a major impact on their susceptibility to infectious diseases and even their responses to vaccines. Site-specific knowledge of the indigenous flora may facilitate appropriate interpretation of culture results, aid in selection of empirical antimicrobial therapy based on the likely causative agents, and provide additional impetus for rational antibiotic use to minimize the untoward effects of these drugs on the "beneficial" microbes that inhabit the body.

WHEN TO CONSIDER AN INFECTIOUS ETIOLOGY

The title of this chapter may appear to presuppose that the physician knows when a patient has an infectious disease. In reality, this chapter can serve only as a guide to the evaluation of a patient in whom an