01 - SECTION 1 Basic Considerations in Infectious Diseases

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Approach to the Patient

with an Infectious Disease ■ ■HISTORIC 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 Sir Frank MacFarlane Burnet, a noted immunolo gist and Nobel laureate, to write in a 1962 publication entitled Natural History of Infectious Diseases: “In many ways one can think of the middle of the twentieth century as the end of one of the most impor tant social revolutions in history, the virtual elimination of infectious disease.” Professor Burnet was not alone in this view. Robert Peters dorf, 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 20 years, Dr. Petersdorf’s statement might have been ironi cally clairvoyant, although he could have had no idea what was in store for humanity, with an onslaught of new, emerging, and reemerging 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 cervi cal 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 reemerging infectious diseases continue to have a dire impact on global health: HIV/AIDS, SARS-CoV-2, Ebola, and mpox 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., carbapenem-resistant Enterobacteriaceae and Acinetobacter spp., Candida auris, drug-resistant Mycobacterium tuberculosis, and vancomycin-resistant enterococci) 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.

Infectious Diseases PART 5 ■ ■GLOBAL CONSIDERATIONS Infectious diseases remain the second leading cause of death world wide. Although the rate of infectious disease–related deaths has decreased dramatically over the past 25 years, there were still 9.6 mil lion such deaths in 2019 (Fig. 124-1A). These deaths disproportion ately affect children <1 year of age, adults older than 70 years, and persons living in low- and middle-income countries (Fig. 124-1B and 124-1C; Chap. 487); in 2019, ~17% of all deaths worldwide were related to infectious diseases, with a rate as high as ~69% in sub-Saharan Africa. Given that infectious diseases are still a major cause of global mortal ity, understanding the local epidemiology of disease is critically impor tant in evaluating patients. Diseases such as HIV/AIDS have decimated southern Africa, with HIV-infected adults representing 16–20% of the total population in countries like South Africa, Botswana, and Lesotho, and more than 25% in Eswatini. 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, mpox) are seemingly geographically restricted, the increasing ease of rapid worldwide travel has raised concern about their swift spread around the globe. Indeed, human migration has historically been the source of epidemics: Yersinia pestis spread along trade routes in the fourteenth century, Native American populations were devastated by diseases such as smallpox and Salmonella that were imported by European explorers in the fifteenth and sixteenth centuries, military maneu vers helped facilitate the spread of the 1918 influenza pandemic, and religious pilgrimages (e.g., the Hajj) provide the means for worldwide dissemination of diseases. The continued effects of global travel on the spread of infectious diseases are perhaps best highlighted by the SARS-CoV-2 pandemic (Chap. 204). Although this virus was first identified in Wuhan, China, it quickly spread across the globe and brought an abrupt end to virtually all travel and commerce throughout the world, plunging economies into a deep recession, resulting at one point in more than half the world’s population living under stay-athome orders, and causing the death of ~7 million people

worldwide. Not only can travelers carry person-to-person transmitted infections (e.g., SARS-CoV-2, HIV) anywhere in the world, but they can also introduce vector-borne infections to new geographic areas (e.g., chi kungunya and Zika viruses) and contribute to the worldwide spread of multidrug-resistant organisms. The world’s increasing interconnected ness 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 ~40 trillion bacteria as well as countless viruses, fungi, and archaea; taken together, these microor ganisms outnumber human cells by ~10 times in the human body (Chap. 484). The major reservoir of these microbes is the gastrointesti nal tract, but substantial numbers of microbes live in the female genital tract, the oral cavity, and the nasopharynx. There is increasing interest in the skin and lungs as sites where microbial colonization might be highly relevant to the biology and disease susceptibility of the host. These com mensal 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 microbiota (e.g., Staphylococcus aureus, Streptococcus 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

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