

used to guide therapy and inform prognosis for a number of diseases, the use of genotyping is providing a new means to assess the risk of certain diseases as well as variations in response to a number of drugs, and physicians are better understanding the role of certain genes in the causality of common conditions such as obesity and allergies. Despite these advances, the use of complex genomics in the diagnosis, prevention, and treatment of disease is still in its early stages. The task of physicians is complicated by the fact that phenotypes generally are determined not by genes alone but by the interplay of genetic and environmental factors. Indeed, researchers have just begun to scratch the surface of the potential applications of genomics in the practice of medicine.

Rapid progress also is being made in other areas of molecular medicine. *Epigenomics* is the study of alterations in chromatin and histone proteins and methylation of DNA sequences that influence gene expression. Every cell of the body has identical DNA sequences; the diverse phenotypes a person's cells manifest are the result of epigenetic regulation of gene expression. Epigenetic alterations are associated with a number of cancers and other diseases. *Proteomics*, the study of the entire library of proteins made in a cell or organ and its complex relationship to disease, is enhancing the repertoire of the 23,000 genes in the human genome through alternate splicing, post-translational processing, and posttranslational modifications that often have unique functional consequences. The presence or absence of particular proteins in the circulation or in cells is being explored for diagnostic and disease-screening applications. *Microbiomics* is the study of the resident microbes in humans and other mammals. The human haploid genome has ~20,000 genes, while the microbes residing on and in the human body comprise over 3–4 million genes; the contributions of these resident microbes are likely to be of great significance with regard to health status. In fact, research is demonstrating that the microbes inhabiting human mucosal and skin surfaces play a critical role in maturation of the immune system, in metabolic balance, and in disease susceptibility. A variety of environmental factors, including the use and overuse of antibiotics, have been tied experimentally to substantial increases in disorders such as obesity, metabolic syndrome, atherosclerosis, and immune-mediated diseases in both adults and children. *Metagenomics*, of which microbiomics is a part, is the genomic study of environmental species that have the potential to influence human biology directly or indirectly. An example is the study of exposures to microorganisms in farm environments that may be responsible for the lower incidence of asthma among children raised on farms. *Metabolomics* is the study of the range of metabolites in cells or organs and the ways they are altered in disease states. The aging process itself may leave telltale metabolic footprints that allow the prediction (and possibly the prevention) of organ dysfunction and disease. It seems likely that disease-associated patterns will be sought in lipids, carbohydrates, membranes, mitochondria, and other vital components of cells and tissues. Finally, *exposomics* refers to efforts to catalogue and capture environmental exposures such as smoking, sunlight, diet, exercise, education, and violence, which together have an enormous impact on health. All of this new information represents a challenge to the traditional reductionist approach to medical thinking. The variability of results in different patients, together with the large number of variables that can be assessed, creates difficulties in identifying pre-clinical disease and defining disease states unequivocally. Accordingly, the tools of *systems biology* and *network medicine* are being applied to the enormous body of information now obtainable for every patient and may eventually provide new approaches to classifying disease. **For a more complete discussion of a complex systems approach to human disease, see Chap. 87e.**

The rapidity of these advances may seem overwhelming to practicing physicians. However, physicians have an important role to play in ensuring that these powerful technologies and sources of new information are applied with sensitivity and intelligence to the patient. Since “omics” are evolving so rapidly, physicians and other health care professionals must continue to educate themselves so that they can apply this new knowledge to the benefit of their patients' health and well-being. Genetic testing requires wise counsel based on an understanding of the value and limitations of the tests as well as the implications of

their results for specific individuals. **For a more complete discussion of genetic testing, see Chap. 84.**

The Globalization of Medicine Physicians should be cognizant of diseases and health care services beyond local boundaries. Global travel has implications for disease spread, and it is not uncommon for diseases endemic to certain regions to be seen in other regions after a patient has traveled to and returned from those regions. In addition, factors such as wars, the migration of refugees, and climate change are contributing to changing disease profiles worldwide. Patients have broader access to unique expertise or clinical trials at distant medical centers, and the cost of travel may be offset by the quality of care at those distant locations. As much as any other factor influencing global aspects of medicine, the Internet has transformed the transfer of medical information throughout the world. This change has been accompanied by the transfer of technological skills through telemedicine and international consultation—for example, regarding radiologic images and pathologic specimens. **For a complete discussion of global issues, see Chap. 2.**

Medicine on the Internet On the whole, the Internet has had a very positive effect on the practice of medicine; through personal computers, a wide range of information is available to physicians and patients almost instantaneously at any time and from anywhere in the world. This medium holds enormous potential for the delivery of current information, practice guidelines, state-of-the-art conferences, journal content, textbooks (including this text), and direct communications with other physicians and specialists, expanding the depth and breadth of information available to the physician regarding the diagnosis and care of patients. Medical journals are now accessible online, providing rapid sources of new information. By bringing them into direct and timely contact with the latest developments in medical care, this medium also serves to lessen the information gap that has hampered physicians and health care providers in remote areas.

Patients, too, are turning to the Internet in increasing numbers to acquire information about their illnesses and therapies and to join Internet-based support groups. Patients often arrive at a clinic visit with sophisticated information about their illnesses. In this regard, physicians are challenged in a positive way to keep abreast of the latest relevant information while serving as an “editor” as patients navigate this seemingly endless source of information, the accuracy and validity of which are not uniform.

A critically important caveat is that virtually anything can be published on the Internet, with easy circumvention of the peer-review process that is an essential feature of academic publications. Both physicians and patients who search the Internet for medical information must be aware of this danger. Notwithstanding this limitation, appropriate use of the Internet is revolutionizing information access for physicians and patients and in this regard represents a remarkable resource that was not available to practitioners a generation ago.

Public Expectations and Accountability The general public's level of knowledge and sophistication regarding health issues has grown rapidly over the last few decades. As a result, expectations of the health care system in general and of physicians in particular have risen. Physicians are expected to master rapidly advancing fields (the *science* of medicine) while considering their patients' unique needs (the *art* of medicine). Thus, physicians are held accountable not only for the technical aspects of the care they provide but also for their patients' satisfaction with the delivery and costs of care.

In many parts of the world, physicians increasingly are expected to account for the way in which they practice medicine by meeting certain standards prescribed by federal and local governments. The hospitalization of patients whose health care costs are reimbursed by the government and other third parties is subjected to utilization review. Thus, a physician must defend the cause for and duration of a patient's hospitalization if it falls outside certain “average” standards. Authorization for reimbursement increasingly is based on documentation of the nature and complexity of an illness, as reflected by recorded elements of the history and physical examination. A growing “pay-for-performance” movement seeks to link reimbursement to quality of