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CHAPTER 5

Genetic Disorders

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Genes and Human Diseases

In chapter 1 we discussed the architecture of the normal human genome. Here we build upon that knowledge to discuss the genetic basis of human diseases.

Genetic disorders are far more common than is widely appreciated. The lifetime frequency of genetic diseases is estimated to be 670 per 1000. Furthermore, the genetic diseases encountered in medical practice represent only the tip of the iceberg, that is, those with less extreme genotypic errors that permit full embryonic development and live birth. It is estimated that 50% of spontaneous abortuses during the early months of gestation have a demonstrable chromosomal abnormality; there are, in addition, numerous smaller detectable errors and many other genetic lesions that are only now coming into view thanks to advances in DNA sequencing. About 1% of all newborn infants possess a gross chromosomal abnormality, and serious disease with a significant genetic component develops in approximately 5% of individuals younger than age 25 years. How many more mutations remain hidden?

Before discussing specific aberrations that may cause genetic diseases, it is useful to summarize the genetic contribution to human disease. Human genetic disorders can be broadly classified into three categories:

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