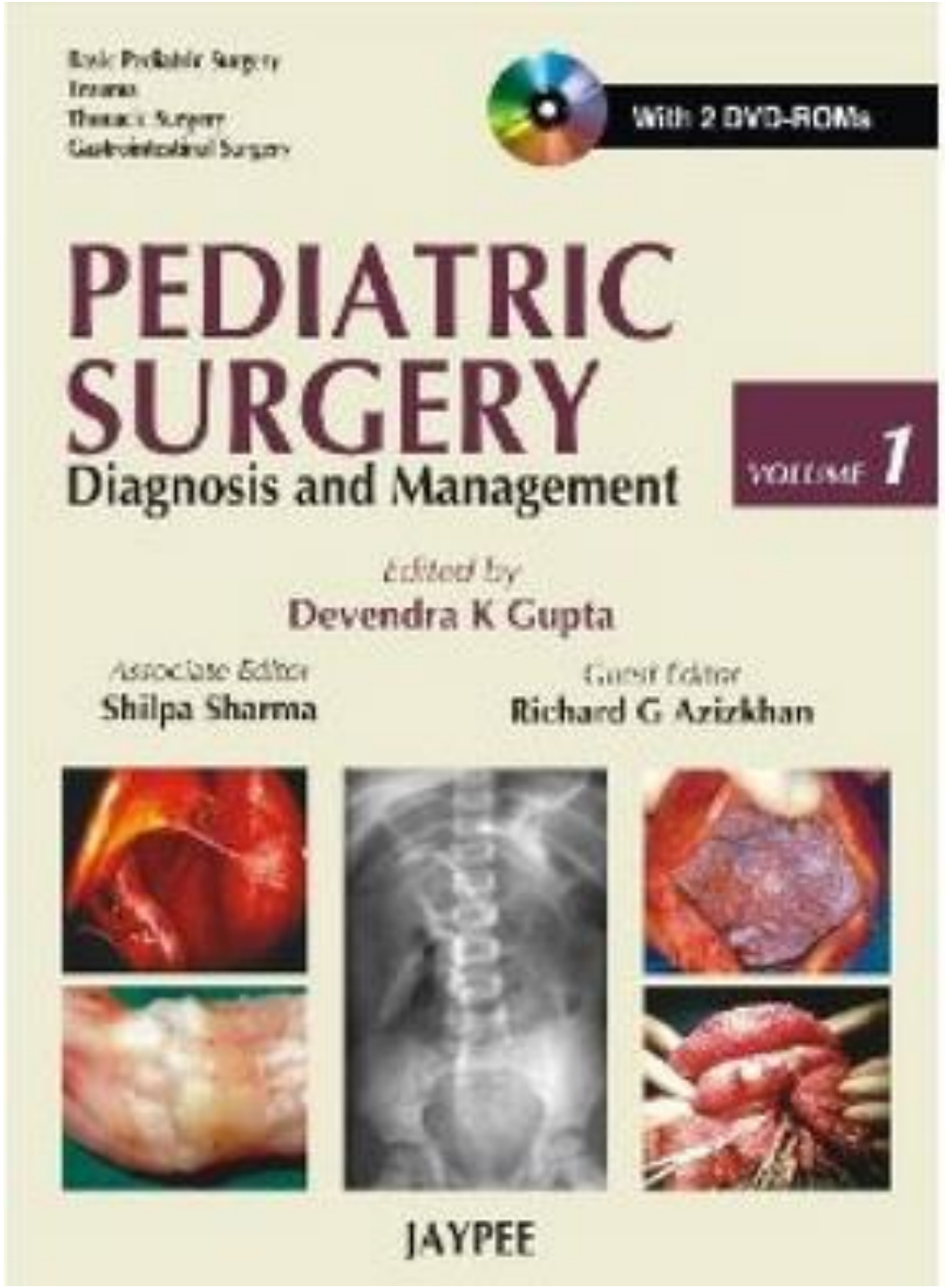

Coverage includes:
Overview of the Specialty, Ventilatory Support, Pediatric Anesthesia, Nuclear Imaging, Interventional Radiology, Postoperative Care, Management of Terminal Illnesses, Trauma, Thoracic Surgery, Gastrointestinal Surgery, Neurosurgery, Vascular Disorders, Head and Neck Surgery, Pediatric Surgical Specialties, Recent Advances

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CHAPTER 3

Molecular Biology and the Pediatric Surgeon

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We are presently in the era of Molecular Medicine and for a busy Pediatric Surgeon it is difficult to be updated on molecular biology concepts and applications. For better understanding of the following text, it is imperative to understand the commonly used terms in Molecular Medicine. Therefore, the glossary given at the end of this chapter has commonly referred terms.

There are several pediatric surgical conditions where we encounter defects at the genetic and the molecular level. For example, duodenal atresia may be seen in Down's syndrome, which is one of the commonest chromosomal abnormality. There are numerous other situations, where study of molecular biology may enhance our basic understanding of the disease, structure diagnostic tests, and identify appropriate molecular therapeutic targets. The DNA for molecular diagnosis may be obtained from a variety of living tissues including peripheral and umbilical blood lymphocytes, epithelial cells lining the buccal mucosa, chorionic villus and amniotic fluid. The principal limitation in using these molecular techniques for diagnosis is the heterogeneity of genetic changes that underlie the inherited disorder.

The *gene* is the basic unit of heredity and contains the information for a particular *protein* and/or *RNA* (ribonucleic acid) molecule. This gene consists of a continuous *stretch of DNA* (deoxyribonucleic acid), which in turn forms part of a larger microscopically visible genetic unit associated with acidic and basic proteins, the *chromosome*. Even bacteria and virus require thousands of different genes and their products to carry out its biological function.

The term gene was first used by Danish geneticist Wilhelm Johannsen in 1911. Thomas Hunt Morgan predicted that these genes were carried on chromosomes. The three-dimensional structure of DNA was elucidated in 1953 in an exciting way by James Dewey Watson and Francis Harry Compton Crick in collaboration with Maurice Hugh Frederick Wilkins and Rosalind Franklin. They demonstrated (using X-ray diffraction studies) that DNA existed as a *double helix* consisting of 2 *polynucleotide* chains held together by hydrogen bonds. The key components of the DNA molecule with respect to its role as the carrier of transmissible information were the four *nitrogenous bases* which were the alphabets of heredity and reproduction - A, T, G, C - and it was the sequence of the bases along one of the two polynucleotide chains (the coding strand) that carried the information in the form of a *genetic code*, and was the essential blueprint of life.

The two complementary strands of the double helix are held together by specific number of hydrogen bonds (with low bond energy) between A-T and G-C (Table 3.1). The complementary nature of the two strands ensures that the information stored within a gene can be transmitted to the next generation by the process of DNA replication with complete fidelity.

Genes are the blueprints for all RNA and protein molecules within a cell. Some genes encode RNA as the final product (genes for r RNA, t RNA, sn RNA) whereas others encode polypeptide chains, which are synthesized by way of the intermediate m RNA. These blueprints may be modified by *mutation*, which alters the genetic information encoded by the gene through alteration of the base sequence of the DNA.

The genetic information stored within a gene is downloaded in a couple of sequential processes: *transcription*, whereby a linear portion of the gene is copied into a single-stranded RNA molecule, and