



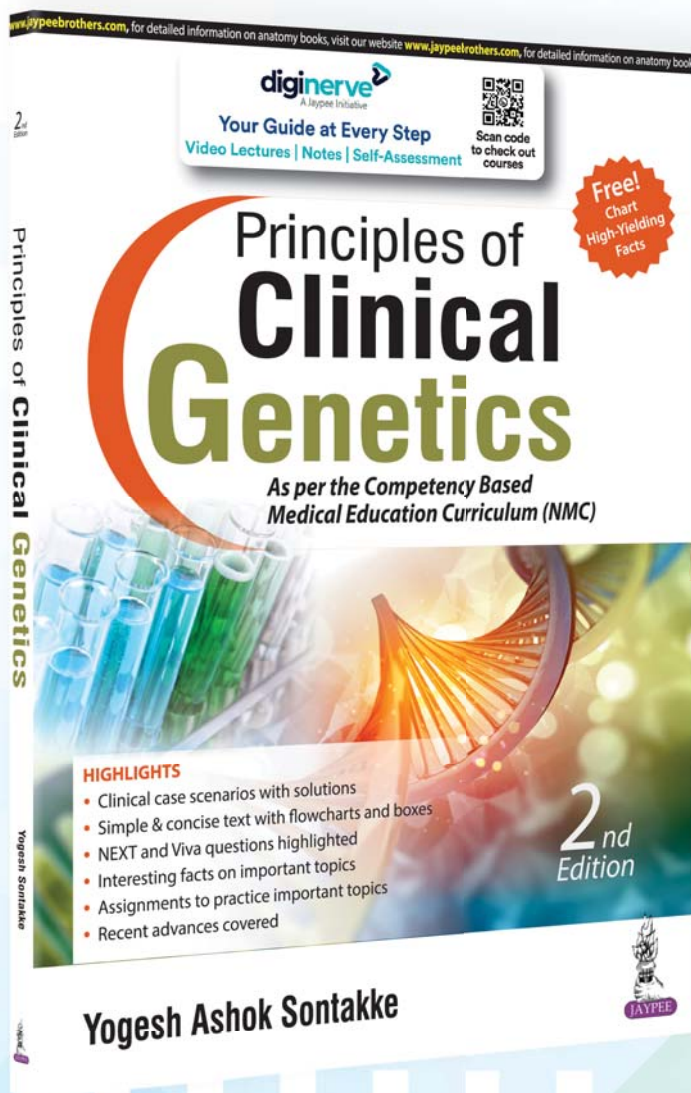
Principles of Clinical Genetics

As per the Competency Based
Medical Education Curriculum (NMC)

2nd
Edition

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Yogesh Ashok Sontakke



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Why to Buy this Book ?

- As per the **Competency Based Medical Education Curriculum (NMC)**.
- Each Chapter has **Competencies, Clinical Case scenarios** with their solutions.
- **Next and Viva marking** for the preparation of various upcoming examinations.
- Some **interesting facts** are highlighted in brown boxes.
- Some important topics covered in the Annexures - Polymerase Chain Reaction, Recombinant DNA Technology, DNA Fingerprinting or Profiling, Developmental Genetics, SRY Gene, Blood Group Genetics, Immunogenetics, Cloning, Genetic Mosaicism and Chimeras.
- Recent Techniques in **Genetic Diagnostics** (Chapter No. 16).
- **Free Chart High-Yielding Facts** with the Book.

SAMPLE PAGES

Competencies are provided at the beginning of each chapter.

COMPETENCIES

- AN73.1 Describe the structure of chromosomes with classification.
- AN73.3 Describe the Lyon's hypothesis.

CLINICAL CASE



CLINICAL CASE

A physician made a call to a genetic center for obtaining the information regarding a 19-year-old female patient with primary amenorrhea with the absence of Barr body on buccal smear. The physician inquired about the reasons for the absence of Barr body. How will you respond to this query?

STRUCTURE OF CHROMOSOMES

Morphology of the chromosomes can be best studied during metaphase of cell division. In other phases (prophase, anaphase and telophase), chromosomes are either not completely condensed or over condensed.

Number

- The number of chromosomes in the given species is constant.
- Diploid (2n) number:** The number of chromosomes in each of the somatic cells (46).
- Haploid (n) number:** The number of chromosomes in each of the gametes (sperm or ovum). They are 23 in human.

Clinical Cases are provided to highlight the complexity of case-based learning.

Next and Viva markings are given for the preparation of various upcoming examinations.

Chromatid^{Viva}

- At mitotic metaphase, each chromosome shows **two symmetrical** structures called **sister chromatids**.
- Both chromatids are attached to each other at the **centromere**.
- Sister chromatids get separated at centromere in anaphase and migrate to the opposite poles (structure and nomenclature of parts of chromosome is shown in Fig. 2.1).

Q. Classify the chromosome (Box 2.3).

- Each chromosome has two arms—short arm or p-arm (*petit* = small) and long arm or q-arm (*q* is next alphabet to *p*).^{NEXT}
- Both the arms are connected with each other by centromere.
- According to the position of centromere, chromosomes are classified as metacentric, submetacentric, acrocentric and telocentric chromosomes (Fig. 2.3).

Q. Classify the chromosome (Box 2.3).

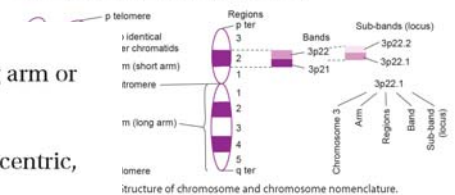
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of the chromosome to which sister chromatids are attached forms a thin segment of the chromosome called **kinetochore**.

NA sequences that bound to specific proteins and thus, provide attachment site for the kinetochore and provide attachment site for the spindle fibers during anaphase.

acentric as they contain only one centromere. acrocentric (no centromere) or dicentric (two centromeres).



Solutions for Clinical Case Scenarios are provided at the end of each chapter.



SOLUTION FOR CLINICAL CASE

The nucleus of diploid cells shows the presence of dense dark-staining spot at the periphery of the nucleus that represents inactive X chromosome. This darkly stained zone is called as Barr body. Number of Barr bodies = Number of X chromosomes - 1. Thus, normal female with 46,XX karyotype shows the presence of single Barr body. In the present case, as the female patient with the absence of Barr body and primary amenorrhea indicates a case of Turner syndrome (45,X). For confirmation of the condition, karyotyping should be advised.

Chromosomes 11

Telocentric Chromosome

- Chromosome with centromere at the one end (have only one arm) is called telocentric chromosome.
- In human, telocentric chromosomes are absent.

Box 2.3: Facts about chromosomes.

- Chromosomes are also classified as sex chromosomes (X and Y chromosomes) and autosomes (1-22 chromosomes).
- Chromosomal nomenclature is based on centromeric position.¹⁰¹⁷

24 Chromosomal Aberration



- Low ledge of nose
 - Small chin (micrognathia)
 - Macroglossia
 - Hypotonia
 - Simian crease (Fig. 4.6)
 - Larger space between big toe and second toe
 - Incurving of the fifth finger (clinodactyly). Brush field spot (in 35-80% cases) - small white spots on the iris due to aggregation of connective tissue.
- Causes**
- Increased maternal age (specifically after 35 years of age)¹⁰¹⁷

Some Interesting Facts

- In Down syndrome, *DYRK1*, a kinase gene located on the long arm of chromosome 21 produces mental retardation.^{NEXT}
- Life expectancy in Down syndrome is increased to 60 years due to health sector developments.
- The region 21q22 (distal part of long arm of chromosome 21) is 'critical region' for Down syndrome. Trisomy of this region produces typical facial features of Down syndrome.

- Down syndrome**
- Described first by Henry Turner (1938).

Some Interesting Facts given in the brown Boxes

Each chapter contains a series of questions and answers to provide deeper understanding.

Q. Write a short note on deletion.

- It is also called as deletion mutation.
- In deletion, part of a chromosome is lost during DNA replication.
- There are three types of deletion aberrations:
 - Terminal deletion:** A terminal segment of the chromosome is lost. For example, deletion of terminal part of the short arm of chromosome 5 → Cri-du-chat syndrome.
 - Interstitial or intercalary deletion:**
 - A segment of chromosome between two breaks is lost.
 - For example, a deletion of segment of long arm of chromosome 15 (15q11-13) → Prader-Willi syndrome.^{NEXT}
 - Microdeletion:**
 - It involves deletion of small segment of chromosome usually less than 5 million base pairs (5 mb).
 - For detection of microdeletion high-resolution banding karyotype or fluorescent in situ hybridization (FISH) technique is required.
 - Examples of microdeletion are listed in Table 4.1.

18 Chromosomal Aberration

Box 4.3: Classification of structural Chromosomal aberrations.

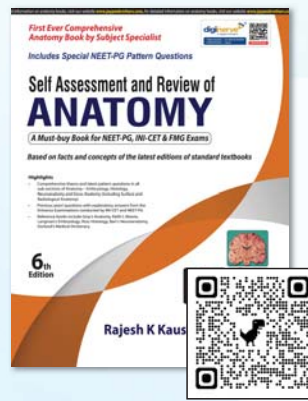
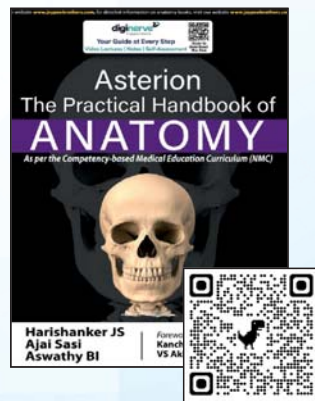
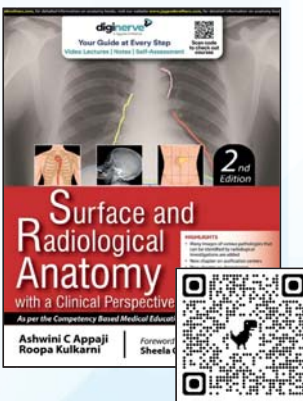
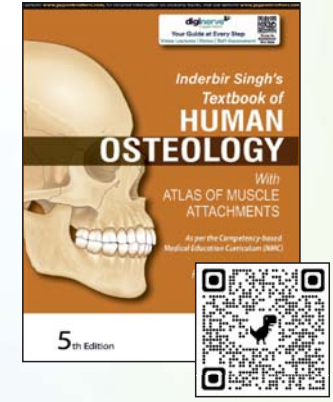
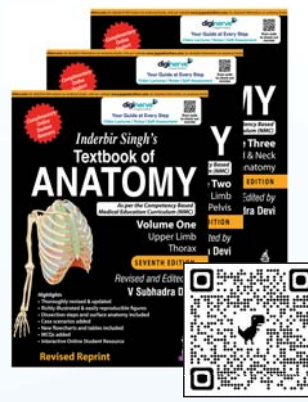
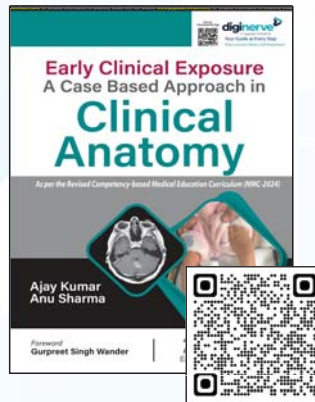
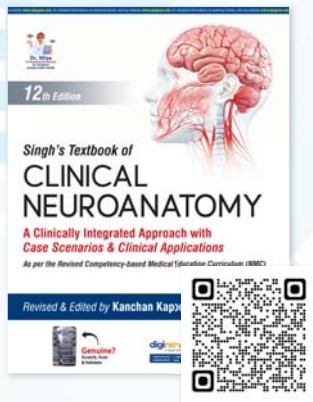
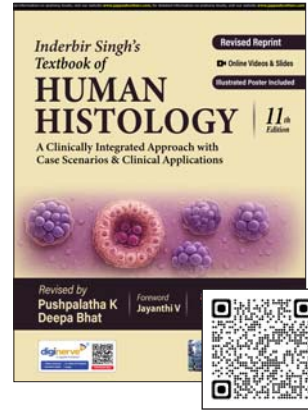
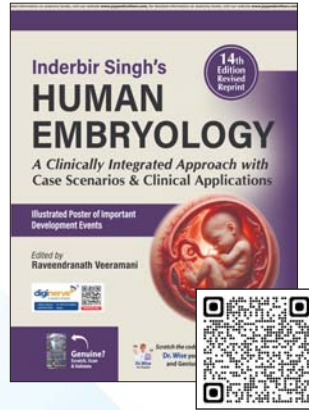
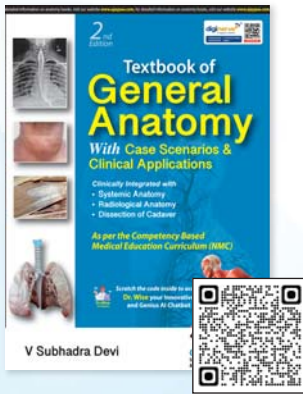
- Deletion—terminal, interstitial, microdeletion
- Translocation—Robertsonian, reciprocal
- Insertion
- Inversion—pericentric, paracentric
- Sex chromosome
- Ring chromosome

Smith-Magenis syndrome 17p11.2

DiGeorge syndrome 22q11.2

Few genes from these segments get deleted in the syndromes.

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