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Preface to the Second Edition

This edition of *Textbook of Human Embryology* has been revised to fulfil the requirements of students and teachers as per the latest Competency Based Undergraduate Curriculum for Indian Medical Graduate.¹ The topics are divided in small chapters to generate the confidence in the learner in the pattern of the Miller's pyramid.² It helps to train the students to achieve the required levels of the given competencies: Knows (K), knows how (KH), and shows how (SH), with the help of included domains of learning, Knowledge (K) and skills (S). To fulfil the need for curriculum, requirements of the students and the field of medicine, this textbook characterizes the following features:

- **Concise text** with clinical correlation for quick recapitulation during examination.
- **280 Color atlas 3D illustrations** to provide easy imagining of developing structures.
- **105 Line diagrams** (practice figures) are easy to draw figures for theory examination.
- **110 Flowcharts** help to revise and memorize the text and to overcome the difficulty of summarizing the facts and developmental sequence in theory examinations and consolidation of knowledge.
- **61 Tables** to summarize essential facts.
- **Summary (examination guide)** to overcome the difficulty of summarizing the facts in theory examinations.

- **NEXT, MCQ, Viva, High yielding facts and Clinical facts** markings for preparation of various upcoming academic entrance examinations.
- **81 Boxes** to focus on important topics.
- **Interesting facts** to isolate them from the main text, so that these facts should not be missed by readers and ease the reading burden.
- **40 Scanning electron micrographs** to give real insight into developing structures.
- **76 Clinical cases** for *early clinical exposure* of various clinical anomalies encountered by eminent clinicians (vertical integration).
- **Special topics** such as assisted reproductive techniques (including *in vitro* fertilization) and ultrasonography in embryology, fetal viability, surrogate motherhood, contraception, sex ratio, teratogenesis, abortion, infertility, sterility and pregnancy tests are also included to give orientation toward clinical aspects.

I am hopeful that this book will help to fulfil all the requirements of students and teachers.

Students are suggested to read the book in the following sequence:

Color atlas 3D illustrations → Stages of development → Flowchart → Table → Summary (Examination Guide) → Practice Figure

Any suggestions from the readers are welcome.

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¹Medical Council of India, Competency Based Undergraduate Curriculum for the Indian Medical Graduate, 2018. Vol 1; pg 41–80.

²Miller GE. The assessment of clinical skills/competence/performance. Acad Med 1990;65(9 Suppl):S63–7.

Preface to the First Edition

This *Textbook of Human Embryology* has been written keeping in mind the requirements of students and teachers. Due to the complexity of the subject, readers face difficulty in understanding and imagining the developing human structures. Hence, in the present book, the attempt has been made to provide all necessary information for easy understanding.

User-friendly features of this book with their purposes are as follows:

- **Concise text** is given in easy language; unnecessary details are avoided.
- **3D illustrations** to provide easy imagining of developing structures.
- **Flowcharts** to revise and memorise the developmental sequence.
- **Tables** to summarise essential facts.
- **Summary (examination guide)** to overcome the difficulty of summarising the facts in theory examinations.
- **Neet, MCQ, Viva Voce and Clinical facts** markings for preparation of various upcoming academic entrance examinations.
- **Boxes** to focus on important topics.
- **Interesting facts** to isolate them from the main text, so that these facts should not be missed by readers.
- **40 Scanning electron micrographs** to give real insight in developing structures.
- **70 Clinical cases** for early clinical exposure of various clinical anomalies encountered by eminent clinicians.
- **Special topics** such as assisted reproductive techniques (including *in vitro* fertilisation) and ultrasonography in embryology are also included to give orientation towards clinical aspects.

I am hopeful that this book will help to fulfil all the requirements of students and teachers.

Students are suggested to read in the following sequence:

Illustrations → Stages of development → Flowchart → Table
→ Summary (examination guide) → Practice Figure

Any suggestions from the readers for rectification and improvement are welcome at dryogeshas@rediffmail.com

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Introduction

Chapter Outline

- Basic terminology
- Stages of human life
- Trimesters of pregnancy
- Need of embryology
- Descriptive terms in embryology
- Chromosomes
- Cell division
 - Mitosis
 - Meiosis
- Nondisjunction
- Organizer and induction

Competencies:

- **AN76.1:** Describe the stages of human life.
- **AN76.2:** Explain the terms – phylogeny, ontogeny, trimester, viability.

BASIC TERMINOLOGY

Embryology

- Embryology is a branch of science that deals with the study of formation and development of an organism before birth (*embryon* = Embryo in Greek).

Reproduction

- Sexual reproduction involves fusion of male and female gametes to produce an offspring.
- It helps in maintenance of species.

Reproductive biology

Reproductive biology is the study of reproduction including study of reproductive systems, endocrinology, sexual development and fertility.

Developmental anatomy

It is the study of structural changes that occur in the body throughout the lifespan (from fertilization to maturity).

Ontogeny

- Ontogeny is a branch of science that deals with complete life cycle (prenatal and postnatal growth and development) of an organism.

Phylogeny

- Phylogeny deals with an evolutionary history and relationship among organisms.
- Phylogenetically, organisms are classified as fishes, amphibians, reptiles, birds, and mammals.
- Mammals are classified as protheria (lay eggs), metatheria (produce extremely young offspring that mature in pouch of mother, marsupials), and eutheria (deliver mature young ones, receive nutrition through placenta till birth).
- Humans are *eutherian* or *placental mammals*.
- During human development, it is found that ontogeny recapitulates phylogeny (Ernst Haeckel, 1866).
- It can be explained by the developing human kidney: Pronephric kidney → mesonephric kidney → metanephric kidney.

Development

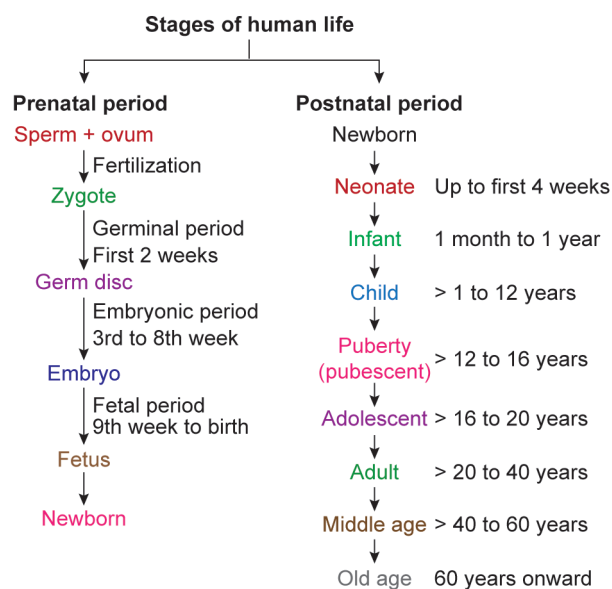
- Development of a human from a single-cell stage of life involves growth and differentiation.
- *Development* is a broad term that involves transformation of a simple single cell into a complex multicellular organism.
- *Growth* is a mere increase in the number and size of cells.
- Growth is of three types:
 1. *Multiplicative growth*: It is an increase in cell number by cell division.
 2. *Auxetic growth*: It is an increase in cell size.

3. **Accretionary growth:** It is an increase in intracellular substances.
4. **Appositional growth:** Formation of new layers on previously formed one.
- **Differentiation** is a process of cell transformation to acquire specific character and function.
- Zygote divides to form many undifferentiated cells as follows:
 1. **Totipotent cells:** Cells of zygote or morula can form all differentiated cell types of an organism. These are called totipotent cells.
 2. **Pluripotent cells:** For example, inner cell mass of blastocyst can form all types of differentiated cells of an organism except placenta.
 3. **Multipotent cells:** For example, adult stem cells can form more than one cell type.
- Differentiation may involve:
 1. Chemo-differentiation
 2. Histo-differentiation
 3. Organogenesis
 4. Functional differentiation
- **Gametogenesis** is a process of formation of gametes (ovum and sperms) from germ cells.

STAGES OF HUMAN LIFE

- Humans undergo continuous physical changes throughout the life. These progressive, orderly, and predictable changes in human begin at conception and continue till death.
- These changes are influenced by genetic, nutritional, environmental, socioeconomic, and many other factors.
- Developmentally, human life is divided into the following stages or periods (Flowchart 1.1):

Flowchart 1.1: Stages of human life



1. **Prenatal period:** Most of the clinicians divide human prenatal period into 3 trimesters: First trimester, second trimester, and third trimester. Each trimester consists of a period of 3 months. Embryologically, prenatal period is divided into the following (Fig. 1.1):
 - A. **Germinal/ovular period:** First 2 weeks of development after fertilization.
 - B. **Embryonic period:** From third to eighth week of development.
 - C. **Fetal period:** From third month till the termination of pregnancy.

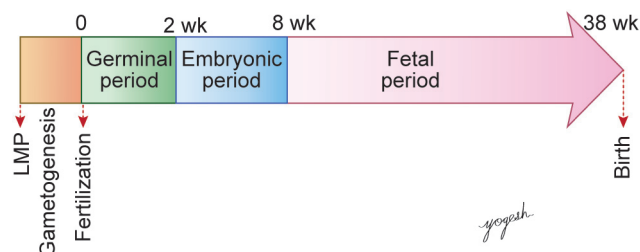


Fig. 1.1: Periods of human embryology. Abbreviations: wk: Week; LMP: Last menstrual period

Period of egg: It extends for 1 week from fertilization to implantation into uterine wall.

Conceptus (product of conception) is also called preimplantation conceptus. In *in vitro* fertilization, *preimplantation conceptus* needs to be transferred to uterus for further growth.

Further, on implantation, conceptus is called *postimplantation conceptus*.

2. **Postnatal period:** It is divided into the following phases:
 - A. **Neonatal period:** First 28 days after birth.
 - B. **Infancy:** From 1 month till 1 year of age.
 - C. **Childhood:** From 1 to 12 years of age.
 - D. **Puberty:** After childhood till 16 years of age.
 - E. **Adolescence:** After puberty till 20 years of age.
 - F. **Adulthood:** From 20 years till 40 years of age.
 - G. **Middle age:** From 40 years till 60 years of age.
 - H. **Old age:** From 60 years of age till death.
 - I. **Death.**

The abovementioned periods are overlapping.

Different ages of fetal (embryonic) period:

Gestational or menstrual age

- Gestation age is measured from the beginning of woman's last menstrual period (LMP).
- Gestation age is mostly used by clinician for assessing pregnancy and fetal wellbeing, for calculation of expected date of delivery, and for taking all decisions (amniocentesis, chorionic villus sampling, termination of pregnancy, and so on).

Fertilization or conceptional age

- Fertilization or conceptional age is measured from the time of fertilization.
- Fertilization age is 2 weeks lesser than the gestational age.

Somite age

- Somite age is a triangular mesenchymal mass in the developing embryo.
- In human, 42 to 44 pairs of somites are present.
- First somite appears on 20th day after fertilization. Everyday its number approximately increases by 3 somites. Thus, somites are useful for determination of fetal age from day 20 to 30. (For details, refer Table 8.1).
- Embryologists use somite age to describe the development events.

TRIMESTERS OF PREGNANCY

- Pregnancy lasts for about 40 weeks, beginning from the first day of the last menstrual cycle (ranges from 37 to 42 weeks).
- Clinically, duration of the pregnancy is divided into 3 trimesters as follows:

First Trimester

- It extends from the first day of the last menstrual cycle to 13 weeks.
- It is the most *crucial period* for organ development.
- Most of the miscarriages occur in the first trimester.
- Mothers may have pregnancy symptoms during the first trimester. It includes nausea, vomiting, and so on.
- In the first trimester, exposure to teratogenic agents, smoking, and alcohol may produce fetal anomalies.
- Ultrasound examination is useful for confirmation of pregnancy, presence, size, location, and number of gestational sacs.

Second Trimester

- It extends from 14th to 26th week of gestation.
- Mothers may have varicose veins, backaches, leg cramps, and so on.
- By the 20th week, mothers may feel fetal movements.
- Ultrasound examination by 18th to 22nd week is usually performed for evaluation of fetal wellbeing, volume of amniotic fluid, cardiac activity, placental position, and fetal morphometry.

Third Trimester

- It extends from the 27th week to termination of pregnancy (37–42 weeks).

Expected Date of Delivery (EDD)

- A normal, full-term pregnancy lasts from 37 to 42 weeks.
- Expected date of delivery can be determined by counting 280 days after the first day of last menstrual period (LMP) or 266 days after conception. *Viva*

- *Naegele's formula* [Franz Karl Naegele, German obstetrician, 1801–1851]

EDD = First day of LMP + 9 months + 7 days = First day of LMP + 280 days

NEED OF EMBRYOLOGY

1. Usually 3–4% of live births children suffer from birth defects. Understanding of this malformation is essential before treatment.
2. All structures in the human body develop from a single cell. Studying embryology will help to understand the gross anatomy and histological structures of body.
3. Deviated growth and development may lead to many diseases. Genes controlling the development may have mutation that results into a disease.
4. In the field of reproductive medicine, embryology helps for better practice for wellbeing of mother and newborn.
5. Knowledge of embryology can be applied in infertility cases (*in vitro* fertilization, intrauterine insemination).
6. Knowledge of embryology is essential for prenatal diagnosis and fetal therapy (amniocentesis, chorionic villus sampling).

Some Interesting Facts

- Aristotle (384–322BC) is the founder of embryology, whereas Karl Ernst von Baer is the father of modern embryology.
- Louise Brown (1978) is the first born test-tube baby.
- Dolly, a female sheep (1996), is the first cloned mammal.
- Y chromosome is acrocentric and smaller in size, whereas X chromosome is large, submetacentric. *NEXT*
- Methods of study of fetal anatomy:
The following methods are useful to study the fetal anatomy:
 1. Ultrasound examination (USG) (For details, refer Chapter 29)
 2. Fetal magnetic resonance imaging (MRI)
 3. Fetal Doppler

DESCRIPTIVE TERMS IN EMBRYOLOGY

- Ventral: Towards the belly or anterior aspect
- Dorsal: Towards the back or posterior aspect
- Cranial or rostral: Towards the head
- Caudal: Towards the tail or coccyx
- Proximal: Close to the root of the structure or towards the trunk
- Distal: Away from the root of the structure or away from the trunk
- Invagination: Projection inside
- Evagination: Projection outside
- Differentiation: An increase in complexity and organization of cells and tissues during development

- Gamete: Sperm or ovum
- Genotype: Genetic makeup of an individual
- Mesenchyme: Loose cellular tissue that arises from mesoderm
- Phenotype: Observable characteristic of an individual
- Teratogen: Substance that may cause birth defect.

Box 1.1: Chromosomes

- Each human cell has 46 chromosomes except ovum (22 + X chromosomes) and sperms (22 + X or 22 + Y chromosomes).
- Out of 46 human chromosomes, 22 pairs are *autosomes* and one pair is *sex chromosomes* (X and Y chromosome).
- Sex chromosomes determine sex characteristics of an individual.
- **Structure** (Fig. 1.2)
 - Each chromosome consists of deoxyribonucleic acid (DNA) tightly coiled around histone proteins.
 - Each chromosome has sister chromatids connected at centromere.
 - Chromosome shows two arms: Short arm (p arm, p for *petit* means small) and long arm (q arm).
 - This typical structure of chromosome appears only during cell division.
 - In interphase, chromosomes form a thin thread-like structure called *chromatin*.

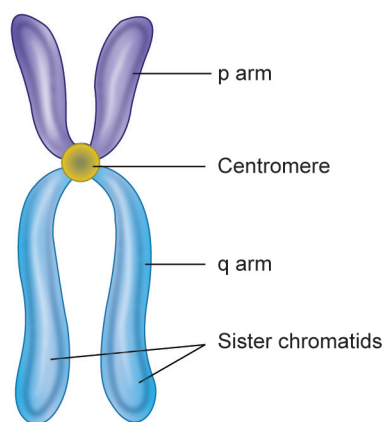


Fig. 1.2: Structure of chromosome

CELL DIVISION

- Cell division is a process of cell multiplication.
- It is of two types: Mitosis and meiosis.

Mitosis

- Mitosis is a cell division that maintains constant number of chromosomes in parent and offspring cells.
- Mitosis is always preceded by S phase where DNA duplicates.

Phases of Mitosis (Fig. 1.3, Flowchart 1.2)

1. **Prophase:** Events – chromosomes condense and become visible; spindle fibres emerge from centrosomes, nuclear envelope breaks down, and centrosome moves toward the opposite pole.
2. **Prometaphase:** Events – continued condensation of chromosomes, centromeres and sister chromatids becomes visible, attachment of microtubules to the centromere.
3. **Metaphase:** Events – chromosomes arranged at metaphase plate, attachment of each centromere to spindle fibres from the opposite pole.
4. **Anaphase:** Events – centromeres split in two, chromatids are pulled towards the opposite poles.
5. **Telophase:** Events – chromosomes arrive at the opposite poles; mitotic spindle breaks, nuclear membrane starts forming.
6. **Cytokinesis:** Event – cleavage furrow appears to separate daughter cells.
 - At the end of one mitotic cycle, two cells are formed from a single cell.

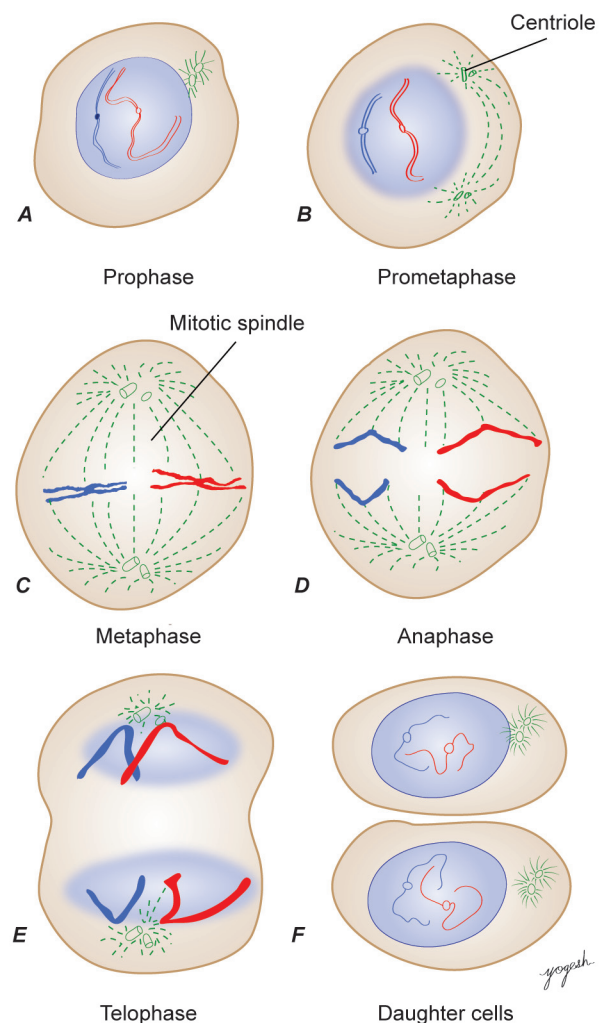
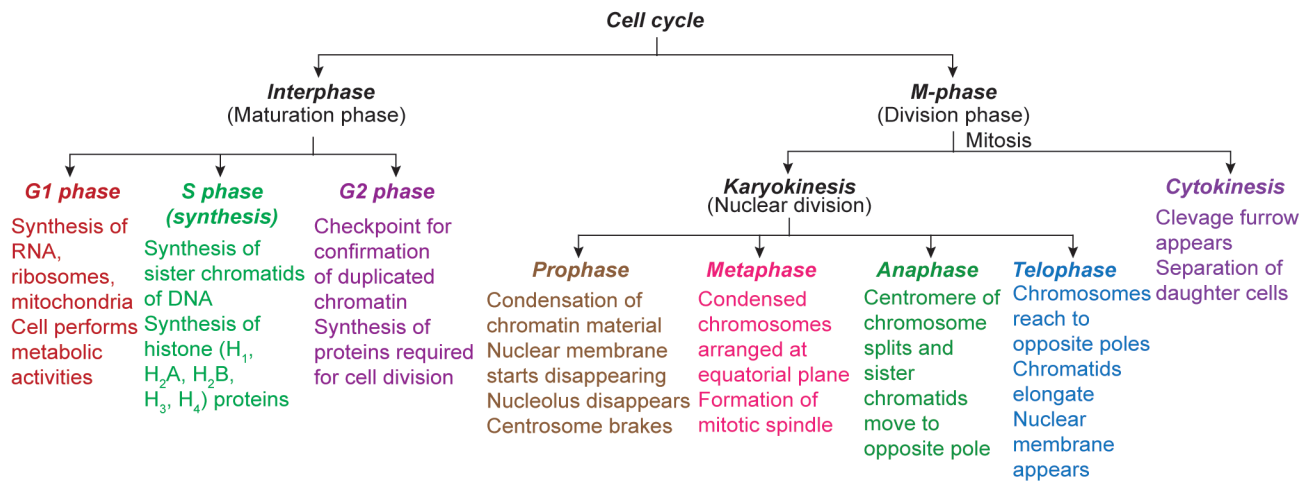


Fig. 1.3: Stages of mitosis

Flowchart 1.2: Cell cycle and mitosis



Significance of Mitosis

- It helps in development and growth of an organism.
- It helps in replacing the damaged body cells.
- It contributes to replace old body cells.
- It produces two daughter cells that are genetically identical to the parent cells.

Meiosis

- Meiosis is the cell division that helps in the formation of gametes with haploid number of chromosomes.
- Meiosis consists of two cell divisions as first meiotic and second meiotic divisions.
- The first meiotic division has prophase I, metaphase I, anaphase I and telophase I, whereas second meiotic division has prophase II, metaphase II, anaphase II and telophase II.

Differences between Mitosis and Meiosis

Q. Write the differences between mitosis and meiosis.

Table 1.1	Differences between mitosis and meiosis	
Event	Mitosis	Meiosis
Occurrence	All cells of body	Only in germ cells
Process	It is an <i>equational</i> division	It is a reductional division
Prophase	No crossover of genetic material No synapsis	<i>Crossover</i> of genetic material takes place <i>Synapsis</i> occurs in zygotene phase
Metaphase	No chiasmata formation Chromosomes arrange at the equator	<i>Chiasmata</i> formation Homologous chromosome arranges on either side of equator
Anaphase	Centromere divides Chromatids move to the opposite pole	No division of centromere Whole chromosome moves to the opposite pole
Telophase	Daughter cells with the same number of chromosomes (46)	Daughter cells with a haploid number of chromosomes (23)
Number of daughter cells	Two	Four

Prophase I

- It is a prolonged phase and consists of the following phases (Fig. 1.4): [NEXT](#)
 1. **Leptotene:** Events – chromosome becomes visible and condensed, sister chromatids of each chromosome are closely placed.
 2. **Zygotene:** Events – synapsis or conjugation (pairing of homologous chromosomes), paired chromosomes are called **bivalent** or **tetrad chromosomes**. [MCQ](#)
 3. **Pachytene:** Events – crossing over (there is an exchange of chromatin material in between approximated chromatids of homologous bivalent chromosomes). The point of contact of chromatids during crossing over is called **chiasmata**. [MCQ](#)
 4. **Diplotene:** Events – homologous chromosomes separate apart from each other.
- Diplotene phase is followed by metaphase I, anaphase I and telophase I. In anaphase I, there is no division of centromere.

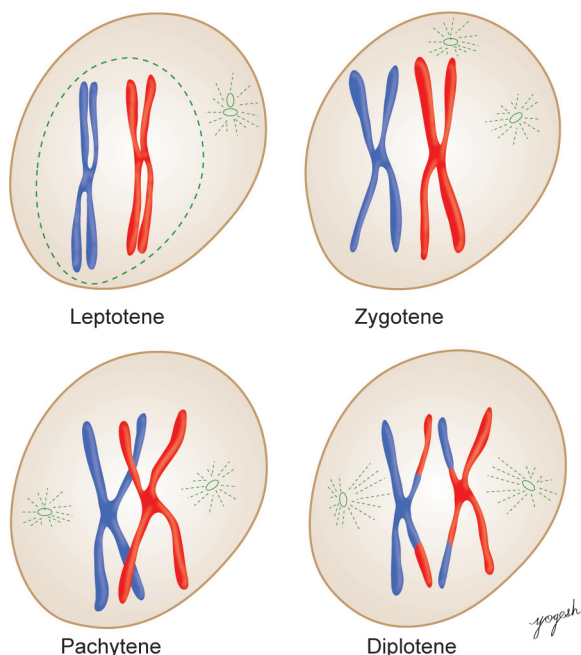


Fig. 1.4: Stages of prophase of first meiotic division

- Homologous chromosome moves towards opposite poles. Hence, resultant daughter cells receive only haploid number of chromosomes.
- The second meiotic division is equivalent of mitosis and just form two cells.
- Thus, at the end of meiosis, four daughter cells with haploid number of chromosomes are produced.

Significance of Meiosis

1. Formation of gametes is the prime aim of meiosis.
2. Meiosis helps to maintain constant chromosome number during sexual reproduction.
3. Exchange of maternal and paternal genes that are carried by homologous chromosomes takes place.
4. Meiosis (crossing over) helps to maintain genetic diversity and mixing of characters.

Box 1.2: Nondisjunction

Nondisjunction

- Usual separation of chromosomes in first meiotic division or sister chromatids in second meiotic division is called disjunction.
- If segregation is not normal, it is called *nondisjunction*.
- On nondisjunction, the resultant cells may receive less number of chromosomes or extra chromosomes.
- Cells of nondisjunction on fertilization may form fetus with an abnormal number of chromosomes (trisomy or monosomy).
- *Examples:*
 - Down syndrome: Trisomy of chromosome 21.
 - Klinefelter syndrome: Extra X chromosome in males (phenotypically male case).
 - Turner syndrome: Lack of Y chromosome (phenotypically female case).

Box 1.3: Organizer and induction

- Organizer is a cluster of cells in developing embryo that can determine differentiation of other regions.
- Primary organizer is a dorsal lip of blastopore that is self-differentiating and its removal results in total failure of embryonic development.
- Influence of an organizer on another area of development is called **induction**.
- Inductors are substances that exert the same effects as that of organizer.
- Hans Spemann was awarded the Nobel Prize in 1935 for his discovery of embryonic induction.

For example:

1. Optic vesicle acts as an organizer and it induces formation of lens on overlying skin.
2. Primary organizer – dorsal lip of primitive streak
Secondary organizer – notochord
Tertiary organizer – neural tube

Some Interesting Facts

Phases of Cell Life (Fig. 1.5, Flowchart 1.2)

- *G₁ phase:* It follows M phase. Events – Cytoplasm increases in volume; damaged DNA gets repaired.
- *S phase:* It follows G₁ phase. Events – DNA gets replicated to form two sister chromatids of each arm of the chromosome. Each cell contains 4n (double 2n) number of chromosomes.
- *G₂ phase:* It follows S phase. Event – it is a check point before mitosis or meiosis for the confirmation of duplicated chromatin.
- *G₀ phase:* It is a nondividing phase of cell cycle.
- *M phase:* It is the cell division phase.

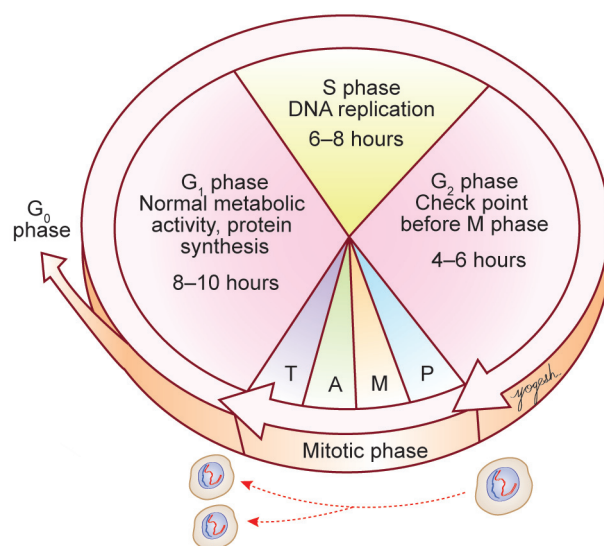


Fig. 1.5: Phases of cell division. Abbreviations: P: Prophase; M: Metaphase; A: Anaphase; T: Telophase