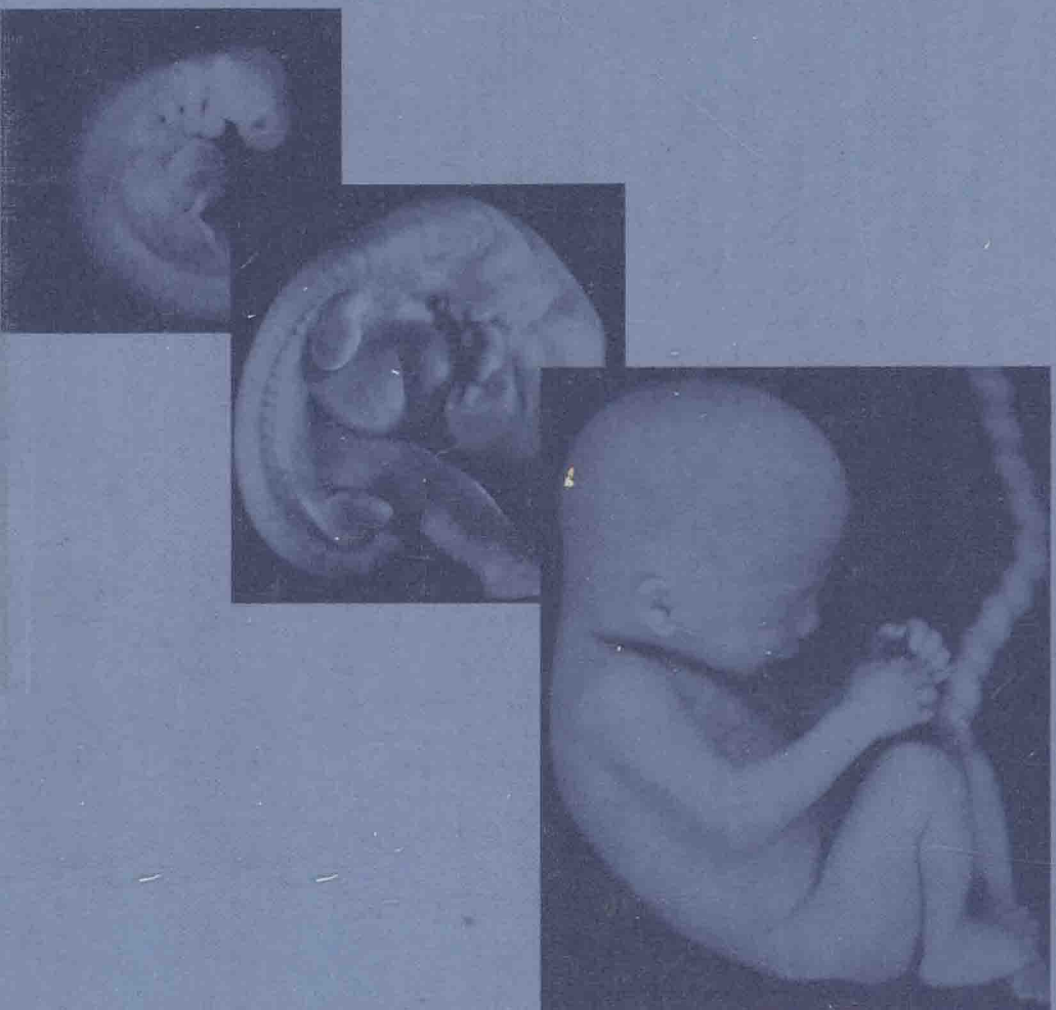
LANGMAN'S MEDICAL EMBRYOLOGY

Fifth Edition

T. W. SADLER



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LANGMAN'S MEDICAL EMBRYOLOGY

Fifth Edition

To Jan Langman

for his inspiration as a teacher, colleague, and friend

Preface to the Fifth Edition

The success of previous editions of *Medical Embryology* is due in part to the unique approach of the book in presenting human embryology in a concise yet comprehensive format. It is also due in part to the incorporation of the spirit and style of the original author found within its pages. The goal with the forthcoming editions will be to maintain the excellence originally imparted to the book, while keeping abreast of new scientific observations and techniques. Therefore, in this edition several sections have been rewritten, modified, and added to reflect new developments in the medical field. Increased numbers of scanning electron micrographs have been included to demonstrate with embryos what has previously been depicted only in the illustrations. Several new charts have been included which are designed to provide summaries of principles found in the text. Those charts inside the rear cover offer an overview of abnormal development and are designed to complement the normal pattern of organogenesis illustrated at the beginning of the book. Finally, in tribute to the original author, the title of the text has been changed to *Langman's Medical Embryology*.

I wish to express my thanks to Pat Horton for her assistance in proofreading and typing the text and to Dr. Kathy Sulik who provided the scanning electron micrographs. My special thanks to Dr. Langman for his confidence in me as his successor to the authorship and for his tutelage and especially his friendship over the years.

T.W.S.
Chapel Hill, North Carolina
November 1984

Preface to the Fourth Edition

The worldwide acceptance of the previous editions of *Medical Embryology*, as reflected in its many foreign translations, indicates that the book continues to fill a great need among students preparing themselves for a medical career. As a result of recommendations from students and colleagues, this edition has been changed considerably. In the first place, the medically important congenital abnormalities are now interwoven with the normal development, and not discussed in separate subchapters. This provides a better coordination and integration between normal and abnormal development. Secondly, a summary has been added at the end of each chapter so that the student quickly can review the important points covered in the foregoing pages. Thirdly, and maybe most importantly, the material has been rearranged to correlate better with gross anatomy. Therefore, some chapters have been shortened and a few new ones have been added. This change makes it easier to integrate the gross structures of the thorax, head and neck, abdomen and pelvis with its normal and abnormal development. A fourth important change is the addition of color to almost all drawings. We have tried to give a particular color to each of the germ layers and to maintain this color for most of its derivatives throughout the book, thus making it easier to recognize the origin of certain organs and structures. The fifth change concerns the addition of photographic charts at the beginning and end of the book. The first chart gives a day-to-day recapitulation of the important facts of the first seven weeks of development. The other charts make it possible to correlate normal and abnormal development and to determine on what day or week an abnormality has developed.

Hence, the changes in this edition, which even concern its outside appearance, will make this a better illustrated, more integrated, more concise and, hopefully, a better book to study normal development and its clinical applications.

As in the previous editions almost all the illustrations were made by Miss Jill Leland; the new drawings and photographs were made by Betsy Cochran and Barbara Haynes. In particular, I wish to express my thanks to Rudolf Johannes Müller from Berlin who did the color work and some new drawings in an outstanding manner. I also wish to express my great gratitude to Sara Finnegan, Vice President and Editor-in-Chief of the Williams & Wilkins Co., who for so many years has spared no effort to

make this book a success in its field. Thanks also to Nan Tyler, George Stamathis and Patrick Hudson for their excellent cooperation and outstanding qualities in the production of this edition. My special thanks to Dr. Thomas W. Sadler, who will become my co-author with the fifth edition of *Medical Embryology*.

Charlottesville, Virginia
November 1980

Preface to the First Edition

Recent advances in embryology, radioautography, and electron microscopy have been so overwhelming that the medical student often has difficulty in grasping the basic facts of development from the highly complicated picture presented to him. The aim of this book, therefore, is to give the future doctor a concise, well illustrated presentation of the essential facts of human development, clarifying the gross anatomical features without omitting the recent advances or changing concepts in the basic sciences. Furthermore, since embryology has become of great practical value because of the enormous progress made in surgery and teratology, each chapter on the development of the organ systems has been complemented by a description of those malformations important to the student in his further training. As a further reflection of the increased clinical importance of embryology an entire chapter has been developed to the etiology of congenital defects.

Of the many colleagues who have been of help in the writing of this book, I particularly wish to thank Dr. C. P. Leblond for his continuous interest and encouragement; Dr. F. Clarke Fraser, for his help in discussing the various aspects of the congenital malformations; and my friends, Dr. Harry Maisel, Dr. Robert van Mierop, and Dr. Yves Clermont, who have spared no effort in assisting with the design of the drawings and the checking of the text.

I wish to express my sincere thanks to Miss Jill Leland, who prepared all the illustrations in this book, and to Mrs. E. Dawson, who has been of such excellent support to me in setting up the manuscript.

Contents

PART 1

General Embryology

chapter 1

Gametogenesis

The development of a human being begins with fertilization, a process by which the **spermatozoon** from the male and the **oocyte** from the female unite to give rise to a new organism, the **zygote.** In preparation for fertilization, both male and female germ cells undergo a number of changes involving the chromosomes as well as the cytoplasm. The purpose of these changes is twofold:

①To reduce the number of chromosomes to half that in the normal somatic cell, *i.e.,* from 46 to 23. This is accomplished by the **meiotic** or **maturation** divisions and is necessary, since otherwise fusion of a male and a female germ cell would result in an individual with twice the number of chromosomes of the parent cells.

②To alter the shape of the germ cells in preparation for fertilization. The male germ cell, initially large and round, loses practically all of its cytoplasm and develops a head, neck, and tail. The female germ cell, on the contrary, gradually becomes larger as the result of an increase in the amount of cytoplasm. At maturity the oocyte has a diameter of about 120 μ.

The human somatic cell contains 23 pairs or a diploid (diploos-double) number of chromosomes. One chromosome of each pair is originally derived from the mother and the other from the father. The members of a chromosome pair are generally not in close proximity to each other either in the resting cell or during the mitotic division. The only time that they come in intimate contact with each other is during the meiotic or maturation divisions of the germ cells.

To make the events occurring during the meiotic divisions easier to understand, the most important features of these divisions are compared with those of a mitotic division. Similarly, although reduction in the number of chromosomes and the cytoplasmic changes are both integral parts of germ cell maturation, each process is described separately.

Chromosomes During Mitotic Division

Before a normal somatic cell enters mitosis, each chromosome replicates its DNA and in fact becomes doubled. During the DNA-duplication phase the chromosomes are extremely long, diffusely spread through the cytoplasm, and cannot be recognized with the light microscope. With the onset of mitosis, the chromosomes begin to coil, contract, and condense, but the two paired subunits (chromatids) still cannot be recognized as individual units (Fig. 1-1*A*). Only in the prometaphase when the chromosomes become compact rods are the chromatids distinguishable (Fig. 1-1*B*). During the metaphase, the chromosomes line up in the equatorial plane and their doubled structure is clearly visible (Fig. 1-1*C*). Soon afterwards, each chromosome undergoes a longitudinal division of the centromere and separates into two daughter chromosomes which migrate to opposite poles of the cell (Fig. 1-1*D, E*). Each daughter cell receives one half of all the doubled chromosome material and thus maintains the same number of chromosomes as the mother cell.

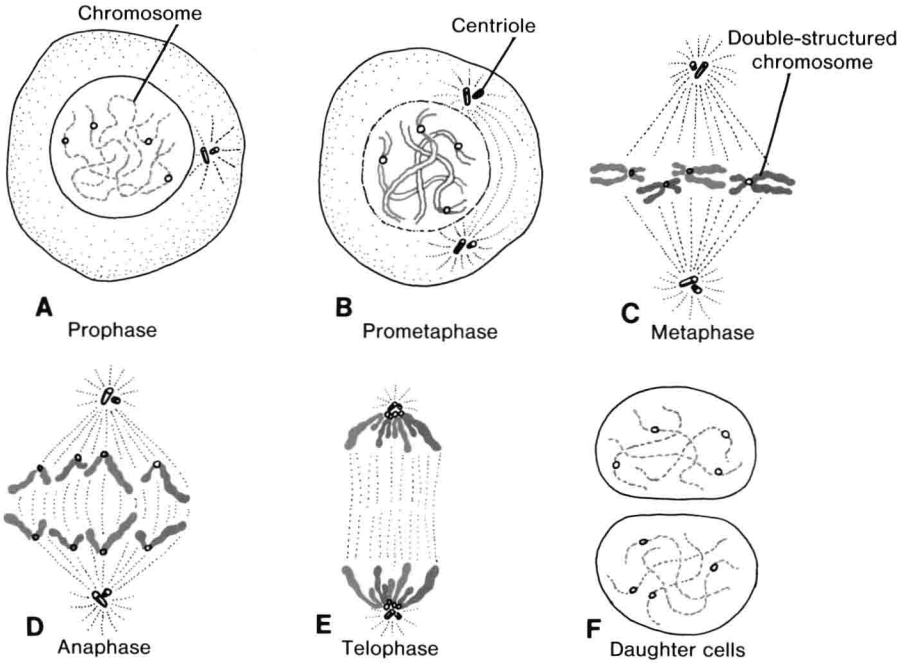

Figure 1-1. Schematic drawing of the various stages of the mitotic division. In the prophase the chromosomes are visible as slender threads. The doubled chromatids become clearly visible as individual units during the prometaphase. At no time during the division do the members of a chromosome pair unite. Blue—paternal chromosomes; red—maternal chromosomes.

Chromosomes During Meiotic Divisions

FIRST MEIOTIC DIVISION

Similarly, as in a mitotic division, the female as well as the male primitive germ cells (primary oocyte and primary spermatocyte) replicate their DNA just before the first meiotic division begins. Hence, at the beginning of the maturation divisions, the germ cells contain double the normal amount of DNA (4n) and each of the 46 chromosomes is a double structure (Fig. 1-2).

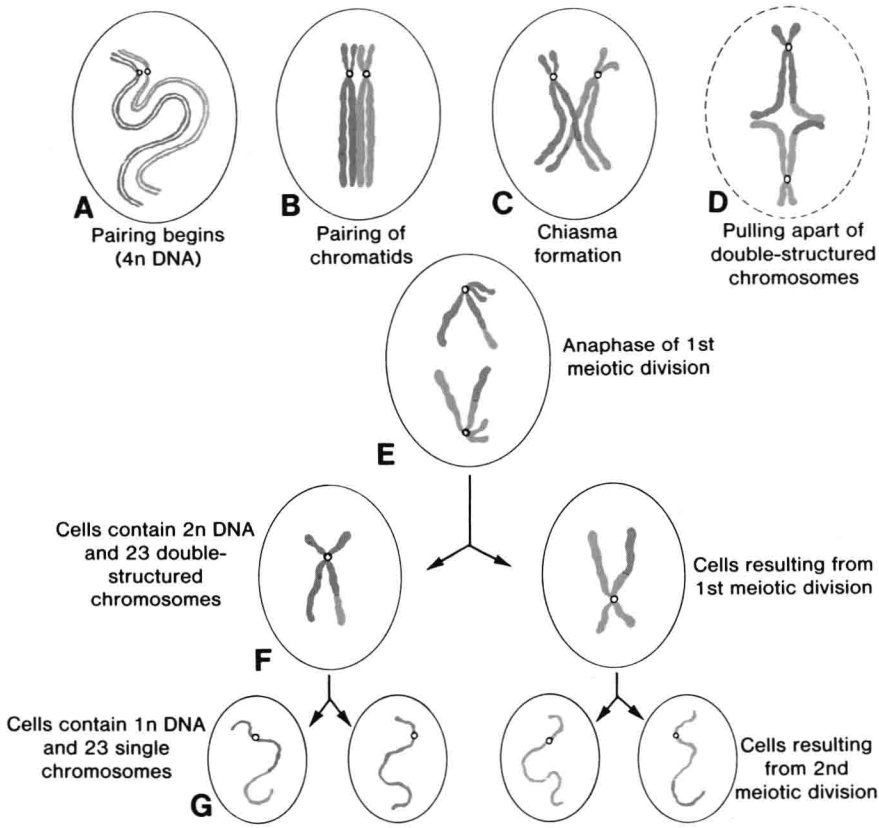

Figure 1-2. Schematic representation of the first and second meiotic divisions. (*A*) The homologous chromosomes approach each other. (*B*) The homologous chromosomes pair and each member of the pair consists of two chromatids. (*C*) The intimately paired homologous chromosomes interchange chromatid fragments. Note the chiasma. (*D*) The double-structured chromosomes pull apart. (*E*) Anaphase of the first meiotic division. (*F* and *G*) During the second meiotic division the double-structured chromosomes split at the centromere. At completion of the division the chromosomes in each of the four daughter cells are different from each other.

The *first characteristic feature* of this meiotic division is the **pairing of the homologous chromosomes** (Fig. 1-2*A*). The pairing is exact and point for point, except for the X-Y combination. The centromere regions of the homologous chromosomes do not pair. Since each individual chromosome is double-structured and contains two chromatids, the homologous pair consists of four chromatids (Fig. 1-2*B*). In a mitotic division the homologous chromosomes never pair.

The *second characteristic feature* of the first meiotic division is the **interchange of chromatid segments** between the two paired homologous chromosomes (cross over) (Fig. 1-2*C*). When, subsequently, each (double-structured) member of the homologous pair splits longitudinally, one or more transverse breaks occur in the chromatids and an interchange of chromatid segments between two homologous chromosome occurs (Fig. 1-2*C*). During the separation of the homologous chromosomes, the points of interchange temporarily remain united and the chromosomal structure has then an X appearance, known as a **chiasma** (Fig. 1-2*C*). During the chiasma stage, blocks of genes are exchanged between homologous chromosomes. In the meantime, the separation continues and the two members of each pair become oriented on the spindle (Fig. 1-2*D*). In subsequent stages the members migrate to the opposite poles of the cell (Fig. 1-2*E*).

After the first meiotic division has been completed, each daughter cell contains one member of each chromosome pair and thus has 23 double-structured chromosomes (Fig. 1-2*F*). Since each chromosome is still double-structured except at the centromere, the amount of DNA in each daughter cell equals that of a normal somatic cell (2n).

SECOND MEIOTIC DIVISION

Immediately after the first meiotic division, the cell begins its second maturation division. In contrast to the first meiotic division, **no DNA synthesis occurs in advance of this division.** The 23 double-structured chromosomes divide at the centromere and each of the newly formed daughter cells receives 23 chromatids (Fig. 1-2*G*). The amount of DNA in the newly formed cells is now half that of the normal somatic cell. Hence, the purpose of the two meiotic or maturation divisions is twofold: (*a*) to enable the members of the homologous chromosome pair to exchange blocks of genetic material (first meiotic division); and (*b*) to provide each germ cell with both a haploid number of chromosomes and half the amount of DNA of a normal somatic cell (second meiotic division).

As a result of the meiotic divisions, one primary oocyte eventually gives rise to four daughter cells, each with 22 + 1 X-chromosomes (Fig. 1-3*A*). Only one of these develops into a mature gamete, the oocyte; the other three, the **polar bodies**, receive hardly any cytoplasm and degenerate during subsequent development.

The primary spermatocyte gives rise to four daughter cells; two with 22

+ 1 X-chromosomes and two with 22 + 1 Y-chromosomes (Fig. 1-3*B*). All four develop into mature gametes.

ABNORMAL MEIOTIC DIVISIONS

The events occurring during the meiotic divisions apparently are not without hazards. No sooner was the normal chromosome pattern in man established when it became evident that some people possessed an abnormal number of chromosomes.

Chromosomal abnormalities originate during the meiotic divisions. Normally the two members of a homologous chromosome pair separate during the first meiotic division so that each daughter cell receives one component of each pair (Fig. 1-4*A*). Sometimes, however, separation does not occur (**nondisjunction**), and both members of a pair then move into one cell (Fig. 1-4*B*). As a result of the nondisjunction of the chromosomes, one cell receives 24 chromosomes and the other 22, instead of the normal 23 chromosomes. When, at fertilization, a gamete having 23 chromosomes fuses with a gamete having 24 or 22 chromosomes, the result will be an individual with either 47 chromosomes (trisomy), or 45 chromosomes (monosomy). Nondisjunction is thought to occur during the first or second meiotic division of the female germ cells rather than during the divisions of the male germ cells (Fig. 1-4*C*). For further details see Chapter 8.

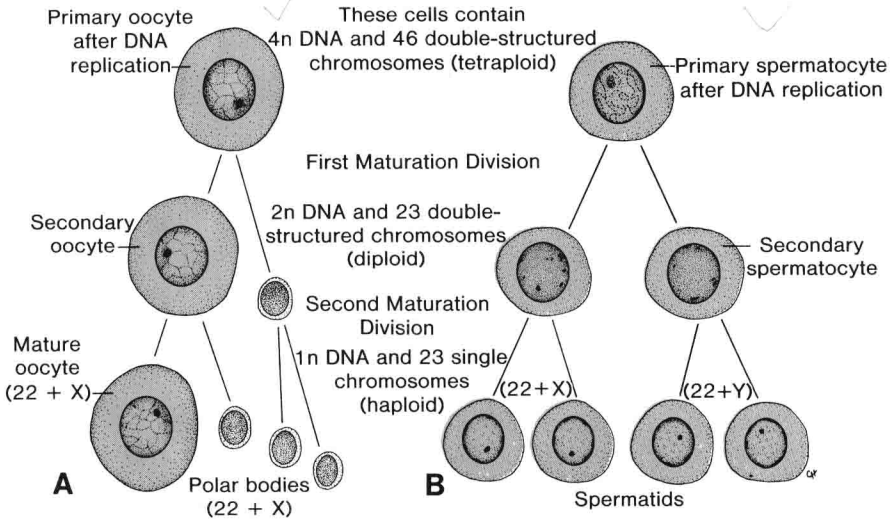

Figure 1-3. Schematic drawing showing the events occurring during the first and second maturation divisions. (*A*) The primitive female germ cell (primary oocyte) produces only one mature gamete, the mature oocyte. (*B*) The primitive male germ cell (primary spermatocyte) produces four spermatids, all of which develop into spermatozoa.