Before We Are Born

Basic Embryology and Birth Defects

Second Edition

Keith L. Moore

Illustrated primarily by
Glen Reid

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The illustration on the front cover is a photograph of an embryo of about 51 days.

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To our second grandchild
KRISTIN ELIZABETH SEMCHUK
daughter of Karen and Bob

Our first grandchild, Melissa Moore,
is featured in the author's other text,
The Developing Human.

PREFACE

This book is designed to arouse the beginning student's interest in embryology and its clinical application. The illustrations, many in color, are designed to help the student visualize developmental processes and time sequences.

In preparing this edition, each chapter has been carefully reviewed and revised to ensure that the material is up to date and suitable for the students to whom it is directed. Students desiring more details about any of the subjects should refer to the author's textbook *The Developng Human: Clinically Oriented Embryology,* 3rd edition, 1982.

The wide acceptance of this book would indicate that it meets the requirements of many students in acquiring a basic understanding of human development and of the common congenital malformations. Since the first edition was published, there has been an increased interest in embryology and in the vulnerability of the developing embryo to radiation, drugs, and chemicals. In this edition the common and medically important congenital malformations of organs are discussed immediately after the normal development. This provides a better understanding of normal and abnormal development. The summaries of the chapters have been improved so that students can easily review the important points covered in the chapters.

Besides new illustrations and additions to the text, a number of figures have been redrawn or modified in the light of teaching experience. A few have been omitted. Color has also been added to several more drawings to facilitate understanding. For this work I owe thanks to Dorothy Irwin; Glen Reid prepared most of the illustrations in the first edition of this book.

The *Nomina Embryologica*, approved by the Tenth International Congress of Anatomists in Tokyo, 1975, has been followed and, in accordance with international agreement, the terminology departs from strict Latin in most cases by anglicizing the terms. There is also some use of eponyms (e.g., Meckel's diverticulum and Down syndrome) because students will need to recognize these terms when they are used in specialty texts and by clinical teachers.

While working on this edition, I have had the benefit of receiving helpful criticism from students from many parts of North America, and suggestions from a number of embryologists who have kindly written to me or sent reprints of their publications. To all these people I express my most sincere thanks.

Mrs. Jill Weinheimer and my wife, Marion, have carefully and cheerfully typed changes and new additions to the text. Dorothy Irwin modified many of the drawings and prepared all the new illustrations. Robert Kangilaski, Medical Editor, W. B. Saunders Company, and Walter Bailey, President and General Manager of the W. B. Saunders Company of Canada, have given me much help with this edition. To all the above, I express my sincere thanks.

KEITH L. MOORE

CONTENTS

1

INTRODUCTION

Human development begins when an ovum from a female is fertilized by a sperm from a male. Development is a process of change that transforms the fertilized ovum or *zygote* into a multicellular human being.

Most developmental changes occur during the embryonic and the fetal periods, but important changes also occur during the other periods of development: infancy, childhood, adolescence, and adulthood.

STAGES OF DEVELOPMENT

Development can be divided into *prenatal* and *postnatal* periods, but it is important to understand that *development is a continuous process*. Birth is a dramatic event during development, but important developmental changes occur after birth (e.g., in the teeth and the female breasts).

The developmental stages occurring before we are born are illustrated in the *Timetables of Human Prenatal Development* (Figs. 1–1 and 1–2). The following list explains the terms used in these timetables and other commonly used ones.

Zygote. This cell is the *beginning* of a human being. It results from the fertilization of an ovum by a sperm. The expression "fertilized ovum" refers to the zygote.

Cleavage. Division or cleavage of the zygote by mitosis[1] forms daughter cells called *blastomeres*. The blastomeres become smaller and smaller at each succeeding cell division (see Fig. 3–3).

Morula. When 12 to 16 blastomeres have formed, the ball of cells is called a morula because it resembles the berry-like fruit known as a mulberry (L. *morus*, mulberry).

Blastocyst. After the morula passes from the uterine tube into the uterus, a cavity forms in it, known as the *blastocyst cavity* (see Fig. 3–3*E*). This converts the morula into a blastocyst.

Embryo. The cells of the blastocyst which give rise to the embryo appear as an *inner cell mass* (see Fig. 3–3*E*). The term embryo is not usually used until the *embryonic disc* forms (day 8). The *embryonic period* extends until the end of the eighth week, by which time the beginnings of all major structures are present. By the end of this period characteristics are present that mark the embryo as definitely human.

Fetus. After the embryonic period, the developing human is called a fetus. During the *fetal period* (ninth week to birth), many systems develop further. Although developmental changes are not so dramatic as those occurring during the embryonic period, they are very important. The rate of body growth is remarkable, especially during the third and fourth months, and weight gain is phenomenal during the terminal months.

Conceptus. This term is used when referring to the embryo and its membranes, i.e., the *products of conception*.

Abortion (L. *abortio*, miscarriage). This term refers to the birth of an embryo or of a fetus before it is viable (mature enough to survive outside the uterus). All terminations of pregnancy that occur before 20 weeks are called *abortions*. About 15 per cent of all recognized pregnancies end in *spontaneous abortions* (ones that occur naturally), usually during the first 12 weeks. Legal *induced abortions* are brought on purposefully, usually by *suction curettage* (evacuation of the embryo and its membranes from the uterus). *Therapeutic abortions* are induced owing to the mother's poor health, or to prevent the birth of a severely malformed child.

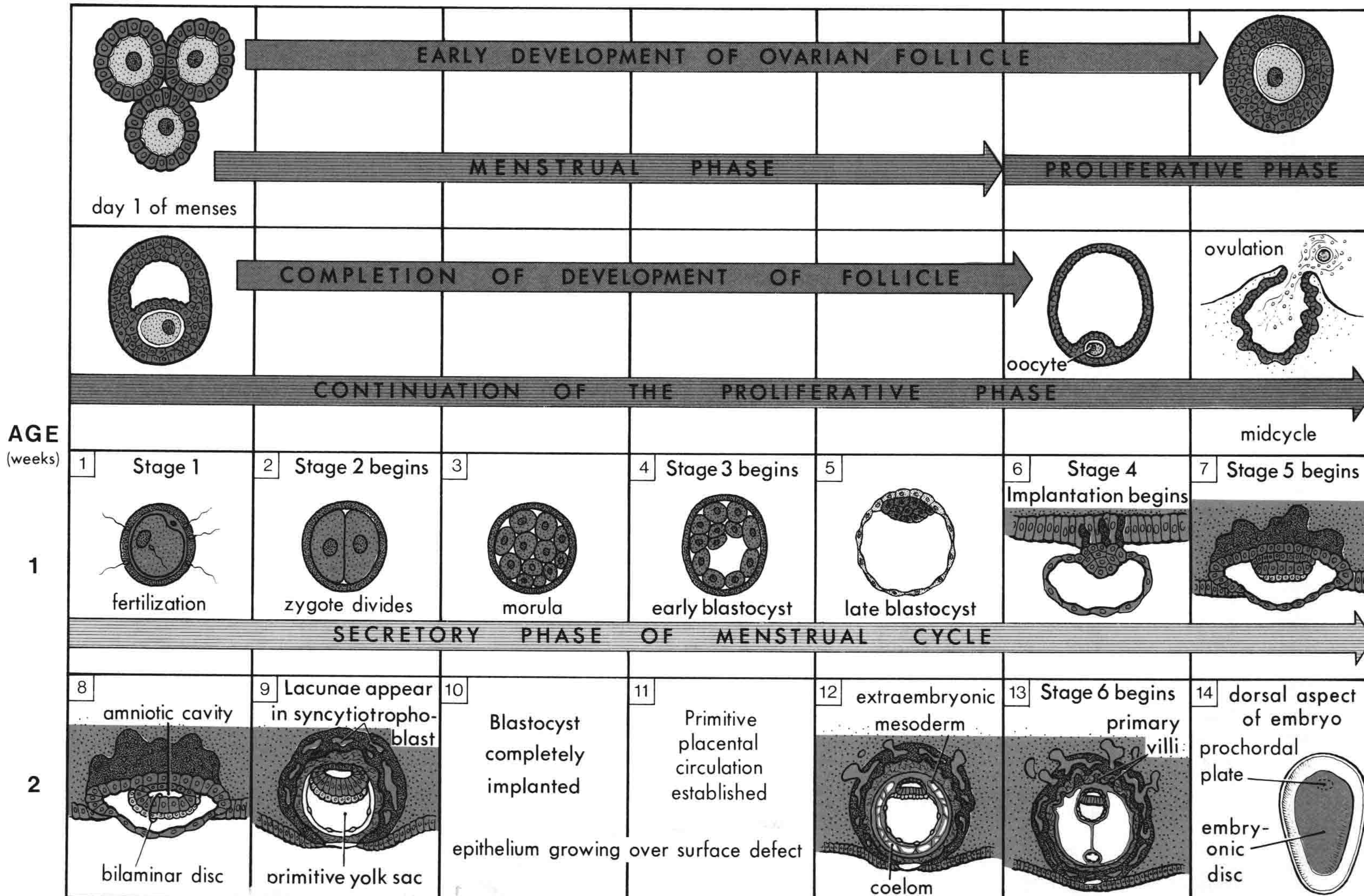
Abortus. This term describes any product or all products of an abortion. An embryo or a *nonviable fetus* and its membranes weighing less than 500 gm is called an *abortus* (see Fig. 8–3).

Primordium (L. *primus*, first + *ordior*, to begin). This term refers to the first trace or

Text continued on page 6

[1] A method of division of a cell by means of which two daughter cells receive identical complements of chromosomes. For details of this process, see a histology or a biology textbook.

TIMETABLE OF HUMAN PRENATAL DEVELOPMENT
1 to 6 weeks



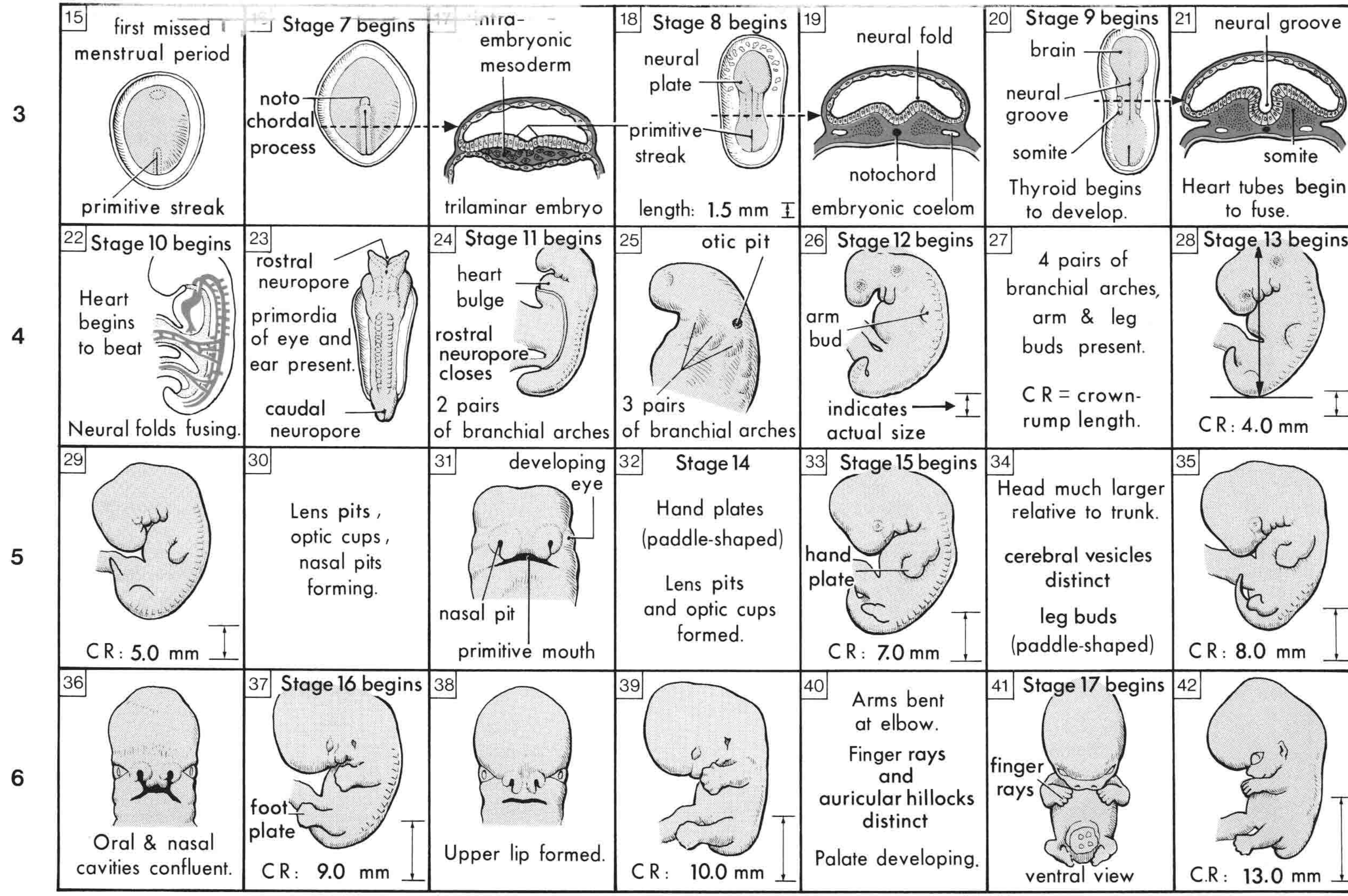
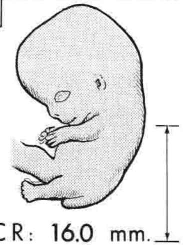
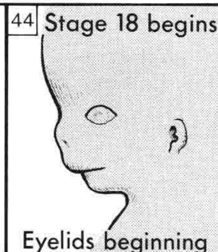
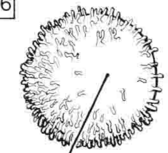
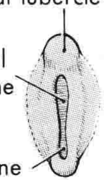
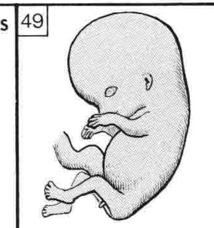
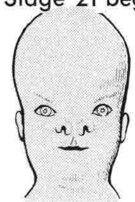
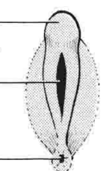
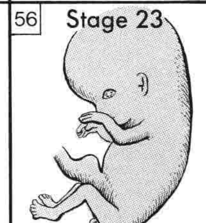
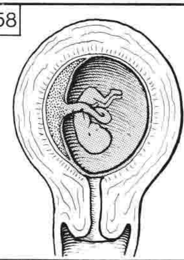
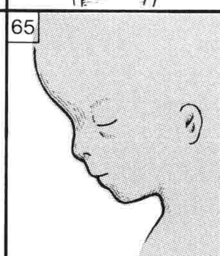
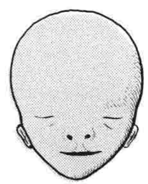
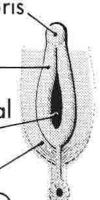
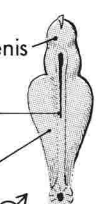
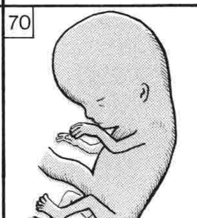
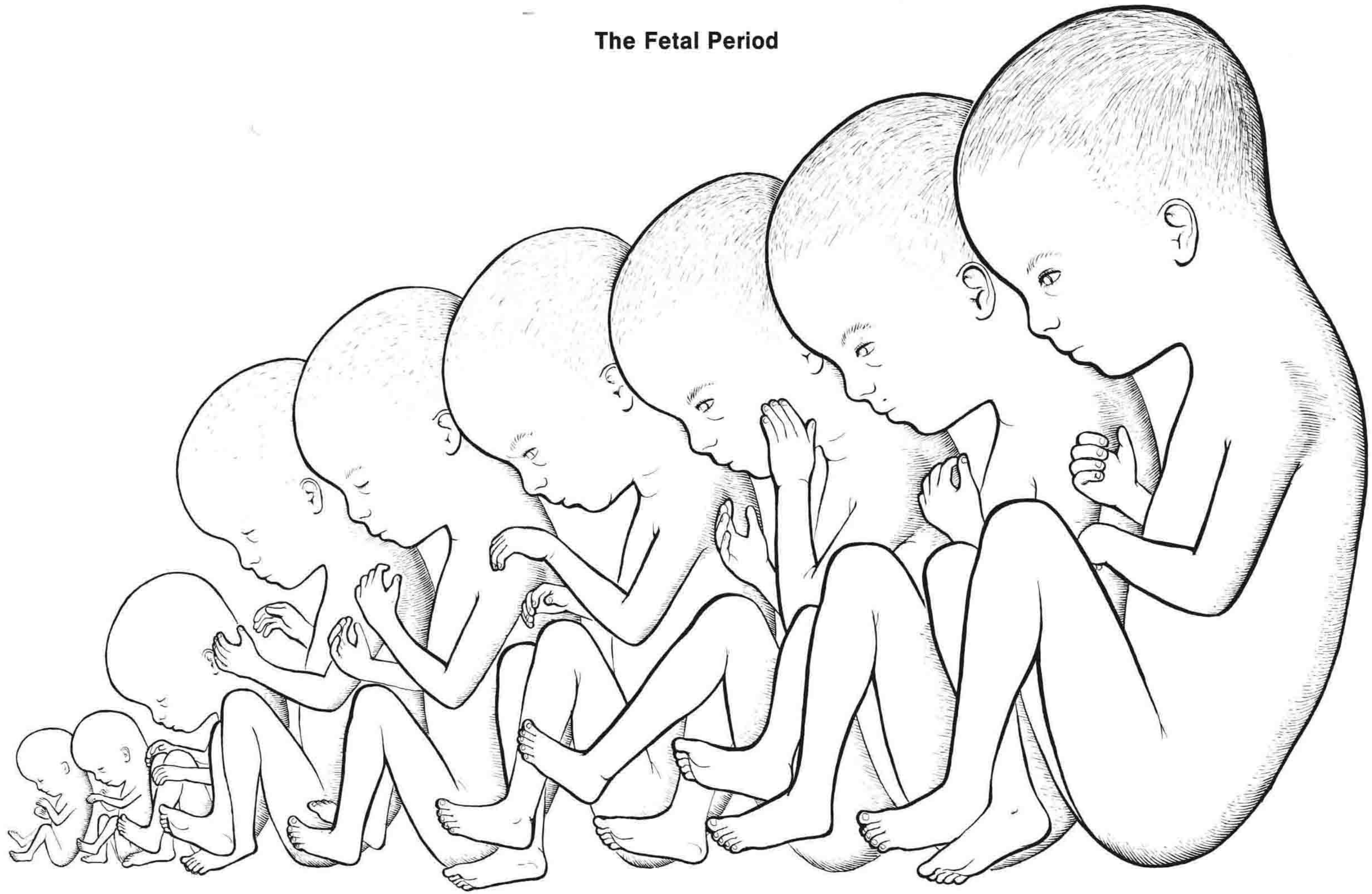


Figure 1–1 Development of an ovarian follicle containing an oocyte, ovulation, and the phases of the menstrual cycle are illustrated. *Development begins at fertilization*, about 14 days after the onset of the last menstruation. Cleavage of the zygote in the uterine tube, implantation of the blastocyst, and early development of the embryo are also shown. The main features of developmental stages in human embryos are illustrated. For a full discussion of embryonic development, see Chapter 6.

TIMETABLE OF HUMAN PRENATAL DEVELOPMENT
7 to 38 weeks

AGE (weeks)							
7	43  C R: 16.0 mm.	44 Stage 18 begins  Eyelids beginning	45 Tip of nose distinct. Toe rays appear. Ossification may begin. C R: 17.0 mm	46  Loss of villi. Smooth chorion forms.	47  genital tubercle, urogenital membrane, anal membrane. ♀ or ♂	48 Stage 19 begins. Trunk elongating and straightening	49  C R: 18 mm
8	50 Upper limbs longer & bent at elbows. Fingers distinct	51 Anal membrane perforated. Urogenital membrane degenerating. Testes and ovaries distinguishable.	52 Stage 21 begins 	53 Stage 21. External genitalia still in sexless state but have begun to differentiate.	54 Stage 22 begins  genital tubercle, urethral groove, anus. ♀ or ♂	55 Beginnings of all essential external & and internal structures are present.	56 Stage 23  C R: 30 mm
9	57 beginning of fetal period	58 	59 Genitalia show some ♀ characteristics but still easily confused with ♂.	60  phallus, urogenital fold, labioscrotal fold, perineum. ♀	61 Genitalia show fusion of urethral folds. Urethral groove extends into phallus.	62  phallus, urogenital fold, labioscrotal fold, perineum. ♂	63  C R: 50 mm
10	64 Face has human profile. Note growth of chin compared to day 44.	65 	66  Face has human appearance.	67  clitoris, labium minus, urogenital groove, labium majus. ♀	68 Genitalia have ♀ or ♂ characteristics but still not fully formed.	69  glans penis, urethral groove, scrotum. ♂	70  C R: 61 mm

The Fetal Period



9 12 16 20 24 28 32 36 38 FULL TERM

Figure 1–2 The embryonic period ends at the end of the eighth week; by this time, the beginnings of all essential structures are present. The fetal period, extending from the ninth week until birth, is characterized by growth and elaboration of structures. Sex is clearly distinguishable by 12 weeks. The above 9- to 38-week fetuses are about half actual size. For more information, see Chapter 7.

indication of an organ or structure, i.e., its earliest stage of development. The term *anlage* has a similar meaning.

Miscarriage. This word is used colloquially to refer to any interruption of pregnancy that occurs before a fetus is viable (i.e., a spontaneous abortion). In medical description, it is most accurate to use the term *spontaneous abortion* for the birth of an embryo or a fetus prior to about 20 weeks; thereafter the event is called a *premature birth.*

Trimester. Obstetricians commonly divide the nine calendar months, or period of gestation (stages of intrauterine development), into three 3-month periods called *trimesters.*

THE IMPORTANCE OF EMBRYOLOGY

The study of prenatal stages of development, especially those occurring during the embryonic period, helps us to understand the normal relationships of adult body structures and the causes of congenital malformations. The embryo is extremely vulnerable during the first three months to large amounts of radiation, viruses, and certain drugs (see Chapter 9). The physician's knowledge of normal development and the causes of congenital malformations aid in giving the embryo the best possible chance of developing normally. Much of the modern practice of obstetrics involves what might be called "applied developmental biology."

The significance of embryology is readily apparent to pediatricians because many of their patients have disorders resulting from maldevelopment, e.g., spina bifida and congenital heart disease. Progress in surgery, especially in the pediatric age group, has made knowledge of human development more clinically significant. The understanding of most congenital malformations (e.g., cleft palate and cardiac defects) depends upon an understanding of normal development and the deviations that have occurred.

HISTORICAL HIGHLIGHTS

If I have seen further, it is by standing on the shoulders of giants.

Sir Isaac Newton
English mathematician, 1643–1727

This statement emphasizes that each new study of a problem rests on a base of knowledge established by earlier investigators. Every age gives explanations according to its knowledge and experience, and so we should be grateful for their ideas and neither sneer at them nor consider them as final. Man has always been interested in knowing how he originated, how he was born, and why some people develop abnormally.

The Greeks made important contributions to the science of embryology. The first recorded embryological studies are in the book of Hippocrates, the famous Greek physician of the fifth century B.C. In the fourth century B.C., Aristotle wrote the first known account of embryology, in which he described development of the chick and other embryos. Galen (second century A.D.) wrote a book entitled *On the Formation of the Foetus* in which he described the development and nutrition of fetuses.

Growth of science was slow during the Middle Ages, and few high points of embryological investigation are known to us.

It is cited in the *Koran*, The Holy Book of the Muslims, that human beings are produced from a *mixture of secretions* from the male and the female. Several references are made to the creation of a human being from a *droplet,* and it is also suggested that the resulting organism settles in the woman like a seed, six days after its beginning. (The human blastocyst begins to implant about six days after fertilization.) Reference is also made to the

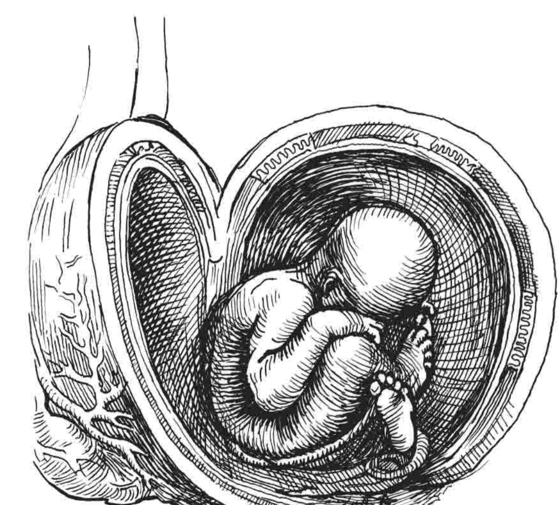


Figure 1–3 Reproduction of Leonardo da Vinci's drawing (15th century) showing a fetus in an opened uterus.

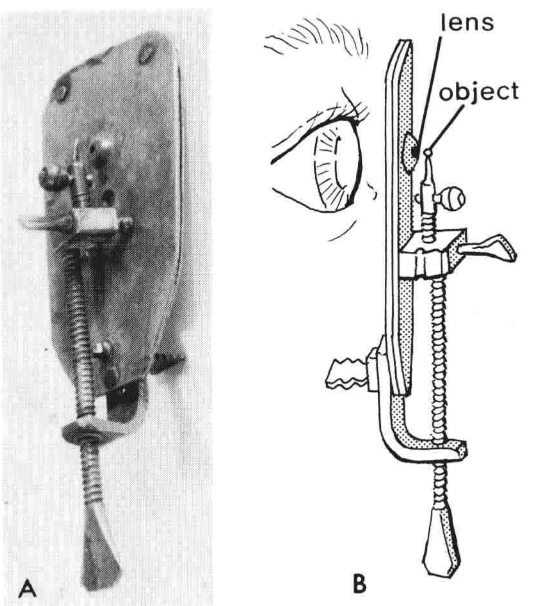


Figure 1–4 *A*, Photograph of a *1673 Leeuwenhoek microscope. B*, Drawing of a lateral view illustrating its use. The object was held in front of the lens on the point of the short rod, and the screw arrangement was used to adjust the object under the lens.

leech-like appearance of the early embryo. (The embryo of 22 to 24 days resembles a leech, or bloodsucker, in appearance.) The embryo is also said to resemble "a chewed substance" like gum or wood. (The somites shown in Figure 6–5*B* somewhat resemble the teethmarks in a chewed substance.)

The Koran also states that the embryo develops within "three veils of darkness." This probably refers to (1) the maternal abdominal wall, (2) the uterine wall, and (3) the amniochorionic membrane.

In the fifteenth century, Leonardo da Vinci made accurate drawings of dissections of the pregnant uterus and associated fetal membranes (Fig. 1–3).

In 1651 Harvey studied chick embryos with simple lenses and made observations on the circulation of blood. Early microscopes were simple (Fig. 1–4), but they opened a new field of observation. In 1672 de Graaf observed little chambers (undoubtedly what we now call blastocysts) in the rabbit's uterus and concluded that they came from organs he called ovaries.

Malpighi, in 1765, studying what he believed to be unfertilized hen's eggs, observed early embryos. As a result, he thought the egg contained a miniature chick. In 1677 Hamm and Leeuwenhoek, using an improved microscope, first observed human sperms, but they did not understand the sperm's role in fertilization: they thought it contained a miniature human being (Fig. 1–5).

In 1775, Spallanzani showed that both the ovum and the sperm were necessary for initiation of a new individual. From his experiments, he concluded that the sperm was the fertilizing agent.

Great advances were made in embryology when the *cell theory* was established in 1839 by Schleiden and Schwann. The concept that the body was composed of cells and cell products soon led to the realization that the embryo developed from a single cell, the zygote.

The *principles of heredity* were developed in 1865 by an Austrian monk named *Gregor Mendel*, but medical scientists and biologists did not understand the significance of these principles in the study of mammalian development for many years.

Flemming observed chromosomes in 1878 and suggested their probable role in fertili-

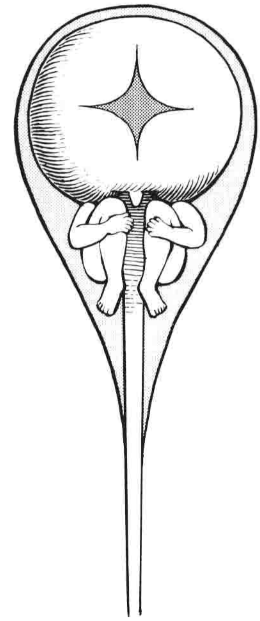


Figure 1–5 Copy of a seventeenth century drawing by Hartsoeker of a sperm. The miniature human being within it was thought to enlarge after it entered an ovum.