Clinical Embryology for Medical Students

Second Edition

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Clinical Embryology for Medical Students

By the same author

Clinical Anatomy for Medical Students

To My Students—Past, Present, and Future

Preface

Embryology provides a basis for understanding gross anatomy and an explanation of many of the congenital anomalies that are seen in clinical medicine. The purpose of this book is to give the student a concise account of the development of the human body. At the end of all pertinent chapters there is a description of the more common congenital anomalies that a practicing physician is likely to encounter. References to embryological literature are included so that students can acquire a deeper knowledge of specific areas of interest, should they so desire.

In this second edition, the simple illustrations have been retained and photographs of clinical cases have been added. Clinical problems requiring embryological knowledge for their solution are also presented at the end of each chapter.

This book has not been written with the idea of replacing the larger reference textbooks of embryology. From extensive teaching experience in medical schools in the United States and in Great Britain, and from conversations with senior medical students and faculty colleagues, I have become aware of the need for a concise, simplified account of human development from the clinical point of view. This need has become particularly important in recent years because of the extensive curriculum revisions taking place in many medical schools.

I thank the many students, colleagues, and friends who have consciously or unconsciously stimulated me to write this book. I am most grateful to the following clinical colleagues at The George Washington University Medical Center who have provided me with photographic examples of congenital anomalies: Dr. John P. Adams, Professor and Chairman of Orthopaedic Surgery; Dr. Gordon Avery, Professor of Child Health and Development; Dr. Mervyn Elgart, Associate Professor of Dermatology and of Child Health and Development; Dr. David S. Friendly, Assistant Professor of Ophthalmology and of Child Health and Development; Dr. Pandit Klug, Assistant Professor of Medicine; Dr. Lawrence S. Lessin, Associate Professor of Medicine and of Pathology (Hematology); Dr. Harry Miller, Professor and Chairman, Department of Urology; Dr. Ronald J. Neviaser, Associate Professor of Orthopaedic Surgery; Dr. Mark M. Platt, Associate Professor of Neurology and of Child Health and Development; Dr. Judson G. Randolph, Professor and Director

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I am also greatly indebted to Dr. Robert Chase, Emile Holman Professor of Surgery and Chairman, Department of Surgery, Stanford University School of Medicine, Stanford, California, for additional photographs of clinical cases. I wish to extend my sincere thanks to my artists, Mrs. Terry Dolan, Mrs. Virginia Childs, and Mr. Kenneth Finan, for their careful interpretation of my rough sketches for the illustrations, and for their patience in executing the final artwork, and to the librarians of The George Washington University School of Medicine for their help in procuring for me much-needed reference material. I am greatly indebted to Miss Sonia Malitsky for her skill in typing the manuscript.

R. S. S.

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SPERMATOGENESIS

The term *spermatogenesis* is applied to the sequence of events by which spermatogonia are transformed into spermatozoa within the testes.

The Testes and Their Ducts

The testes are paired ovoid organs situated in the scrotum (Fig. 1-1). The descent of the testes from the abdominal cavity into the scrotum (Chap. 16) is important, since it has been found that spermatogenesis will only take place normally if the testes are at a lower temperature than that of the abdominal cavity. Each testis has a thick fibrous capsule, the *tunica albuginea* (Fig. 1-2), which is thickened posteriorly to form the *mediastinum testis*. Extending from the inner surface of the capsule to the mediastinum is a series of fibrous septa which divide the interior of the organ into about 250 lobules. Lying within each lobule are one to three coiled *seminiferous tubules*. Each tubule is in the form of a loop, the ends of which are continuous with a *straight tubule*. The straight tubules open into a network of channels within the mediastinum testis called the *rete testis*. Situated within each lobule between the seminiferous tubules are delicate connective tissue and groups of rounded *interstitial cells* that produce the male sex hormone *testosterone*.

The rete testis is drained by *efferent ductules* into the long much-coiled duct, the *epididymis* (Figs. 1-1 & 1-2), which is situated on the posterior surface of the testis. The duct of the epididymis becomes continuous with the thick-walled *vas deferens*. This emerges from the lower end or *tail* of the epididymis and passes up through the inguinal canal into the abdomen. On reaching the posterior surface of the bladder, it joins the duct of the *seminal vesicle* to form the *ejaculatory duct,* and this in turn opens into the prostatic part of the *urethra*.

Seminiferous Tubule

The wall of the seminiferous tubule (Fig. 1-2) has a basement membrane lined by an epithelium consisting of a number of layers of cells. The basal layer of cells is of two types: the scattered, tall, pyramid-shaped *Sertoli cells,* which extend from the basement membrane to the lumen of the tubule, and, lying between these cells, the numerous germinal cells, the *spermatogonia*. The spermatogonia are of two types, A and B. Type A spermatogonia are the stem cells, which undergo mitotic division to form additional

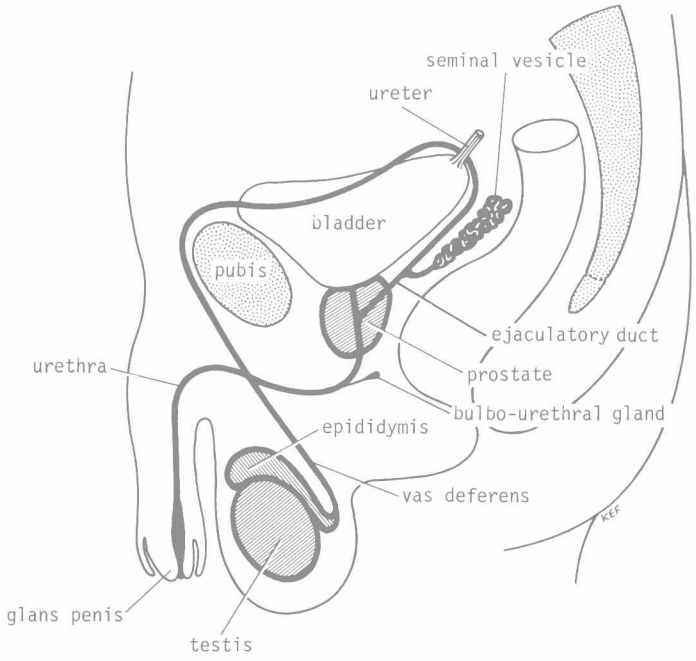

Fig. 1-1. Male reproductive system as seen in sagittal section.

type A spermatogonia and a more differentiated type B spermatogonia. After this division, type B spermatogonia now divide by mitosis into *primary spermatocytes*. The latter cells migrate toward the middle zone of the seminiferous epithelium and then undergo meiotic division into smaller *secondary spermatocytes,* each containing half the number of chromosomes of the primary cell. The secondary spermatocytes soon divide to form the smallest cells, the *spermatids,* which become embedded in the cytoplasm of the free ends of Sertoli cells. The spermatids now undergo a series of morphological changes with the ultimate formation of *spermatozoa.* The nucleus of the spermatid condenses and becomes slightly flattened and elongated in shape. It forms most of the sperm head. Granules within the vacuoles of the Golgi apparatus coalesce to form the *acrosomic granule.* This granule then spreads out over the surface of the nucleus as a thin membrane called the *acrosomal cap*. The centrioles move to the side of the nucleus opposite the acrosomal cap. There, one of the centrioles gives rise to an *axial filament* that grows out and penetrates the cell surface. At the same time the mitochondria migrate toward the axial filament and become arranged around it in the form of a sheath or collar. At the distal end of the mitochondrial collar is a ring-like structure, the *terminal ring*. The collar and terminal ring lie within the *middle piece* or *body* of the spermatozoon. The remainder of the cytoplasm is cast off from the developing spermatozoon and degenerates. The fully formed spermatozoon now leaves the Sertoli cell and becomes free within the lumen of the seminiferous tubule. It has been estimated that the total duration of spermatogenesis is 64 days. The spermatozoon moves successively through the straight tubules, rete testis, and efferent ductules to the epididymis. It is believed that contractile elements in the

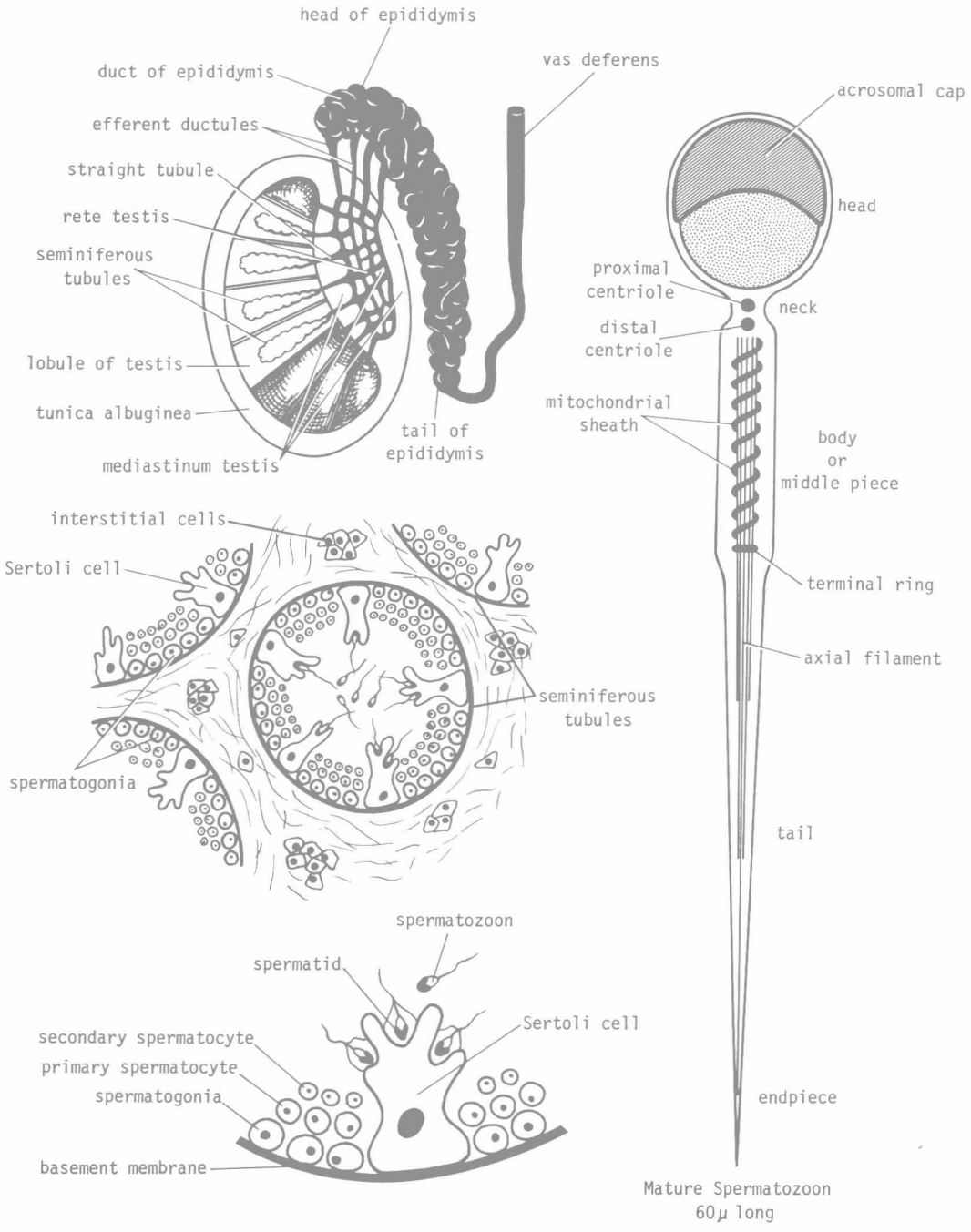

Fig. 1-2. Spermatogenesis.

walls of these tubes are responsible for this movement. The spermatozoon, while lying within the epididymis, undergoes further maturation as seen by the increase in motility and fertilizing power.

Spermatogenesis begins at about 14 years of age, but it does not start at that time unless the testes are in the scrotum. Not all seminiferous tubules are actively producing spermatozoa at the same time. Moreover, areas of germinal epithelium in a single tubule may be active while other areas may be temporarily dormant. Spermatogenesis continues into advanced old age, but after middle age, increasing numbers of atrophic tubules are found.

Mature Spermatozoon

The mature spermatozoon measures about 60 μ in length. The structure of a mature spermatozoon is seen in Figure 1-2. It consists of a *head, neck, body,* and *tail*. The head is formed largely by the condensed nucleus and is covered by the cell membrane. Covering the anterior half of the nucleus under the membrane is the acrosomal cap. Behind the head is the neck containing the two centrioles. The axial filament arises from the distal centriole, and in the body consists of a pair of central fibrils surrounded by two concentric rings of nine fibrils. Outside the concentric rings, a further ring of coarse fibrils is present. Mitochondria are arranged spirally around the axial filament within the middle piece or body. The spiral collar of mitochondria ends distally at a terminal ring. The tail contains the pair of central fibrils surrounded by the two concentric rings of nine fibrils. The outer coarse fibrils are present only at the proximal end of the tail. The fibrils of the tail are enclosed in a sheath of transversely oriented fibrils. Near the end of the tail the sheath is absent. The spermatozoon is covered by a thin layer of cytoplasm and a cell membrane. It is thus seen that the head of the spermatozoon contains the structures responsible for the transmission of genetic information and the remainder of the spermatozoon is concerned with locomotion.

OOGENESIS

The term *oogenesis* is applied to the sequence of events by which oogonia are transformed into ova within the ovaries.

Ovary

The mature ovaries are paired ovoid organs situated within the pelvis (Fig. 1-3). Each is suspended from the posterior surface of the *broad ligament* of the uterus by a short mesentery, the *mesovarium* (Fig. 1-4). The ovaries are surrounded by a thin fibrous capsule, the *tunica albuginea*. This is covered externally by a single layer of cuboid cells called the germinal epithelium. The term *germinal epithelium* is a misnomer, since it does not give rise to ova (for further details see p. 224). The germinal epithelium is a modified area of peritoneum and is continuous with the squamous mesothelial cells of the general peritoneum at the hilum of the ovary where the mesovarium is attached. The ovary has an outer *cortex* and an inner *medulla,* but the division between the two is ill defined. Embedded in the connective tissue of the cortex are the *ovarian follicles* in different stages of development. The medulla consists of very vascular connective tissue.

Ovarian Follicles

During early fetal development primordial germ cells migrate from the yolk sac into the developing ovaries. These cells then differentiate into *oogonia*. By the third prenatal month, the oogonia start to undergo a number of mitotic divisions within the cortex of the ovary to form the *primary oocytes*. The oocytes now enter the prophase of their first meiotic division, and by the time of birth they are in a late stage of prophase of their

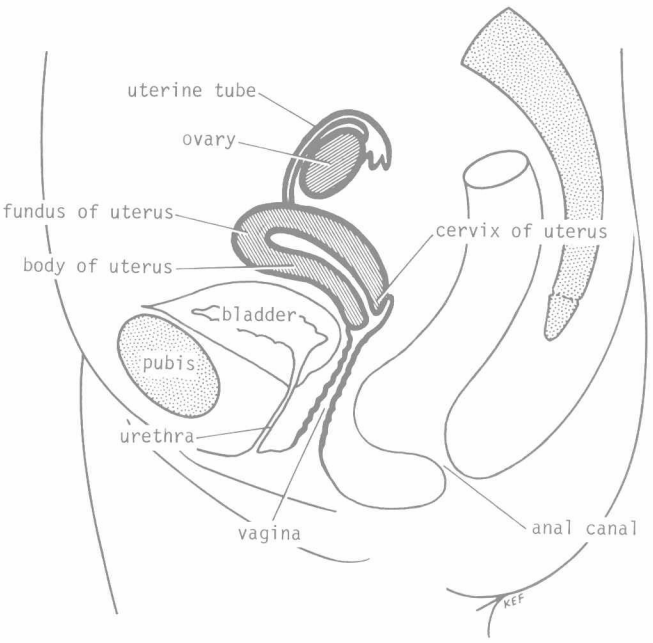

Fig. 1-3. Female reproductive system as seen in sagittal section.

meiotic division. The primary oocytes become surrounded by a single layer of flattened cells and are known as *primordial follicles*. The surrounding cells are termed *granulosa cells*. Many oogonia and primary oocytes degenerate during the fifth and sixth months of fetal life (for details see Chap. 16). The surviving primordial follicles mainly occupy the periphery of the cortex. The nucleus of the oocyte is large, pale, and centrally placed. Little chromatin is seen, but the nucleolus is prominent. The cytoplasm is pale, and yolk granules are evenly dispersed throughout it. At birth there may be over 700,000 follicles present in the two ovaries. The number diminishes with age so that about 40,000 survive to puberty.

At puberty, as a result of hormonal stimulation from the pituitary, the ovarian cycles begin. With each cycle, many follicles in both ovaries start to enlarge, but gradually one follicle only gains ascendancy and reaches maturity, while the remainder degenerate and become *atretic follicles*. As a result, one ovum normally ovulates during each ovarian cycle. It has been estimated that only from 300 to 400 follicles come to full maturity and liberate ova from the ovaries during the reproductive life of a woman.

The primordial follicles increase in size after puberty in response to the *follicle-stimulating hormone* (FSH) of the pituitary. The granulosa cells become cuboid in shape and begin to divide so that the oocyte is surrounded by a number of layers of granulosa cells. These cells now secrete around the oocyte a hyaline material consisting of glycoproteins. This material forms the *zona pellucida*. As the oocyte increases in size, irregular spaces filled with clear fluid, the *liquor folliculi,* appear among the granulosa cells. These spaces later coalesce to form a single cavity, the *follicular antrum*. The granulosa cells, which line the cavity, make up the *membrana granulosa*. The oocyte, still surrounded by granulosa cells, the *cumulus oophorus,* projects into the antrum from one side. At this stage of development the follicle is known as a *graafian follicle*. While the follicle has been increasing in size, the sur-

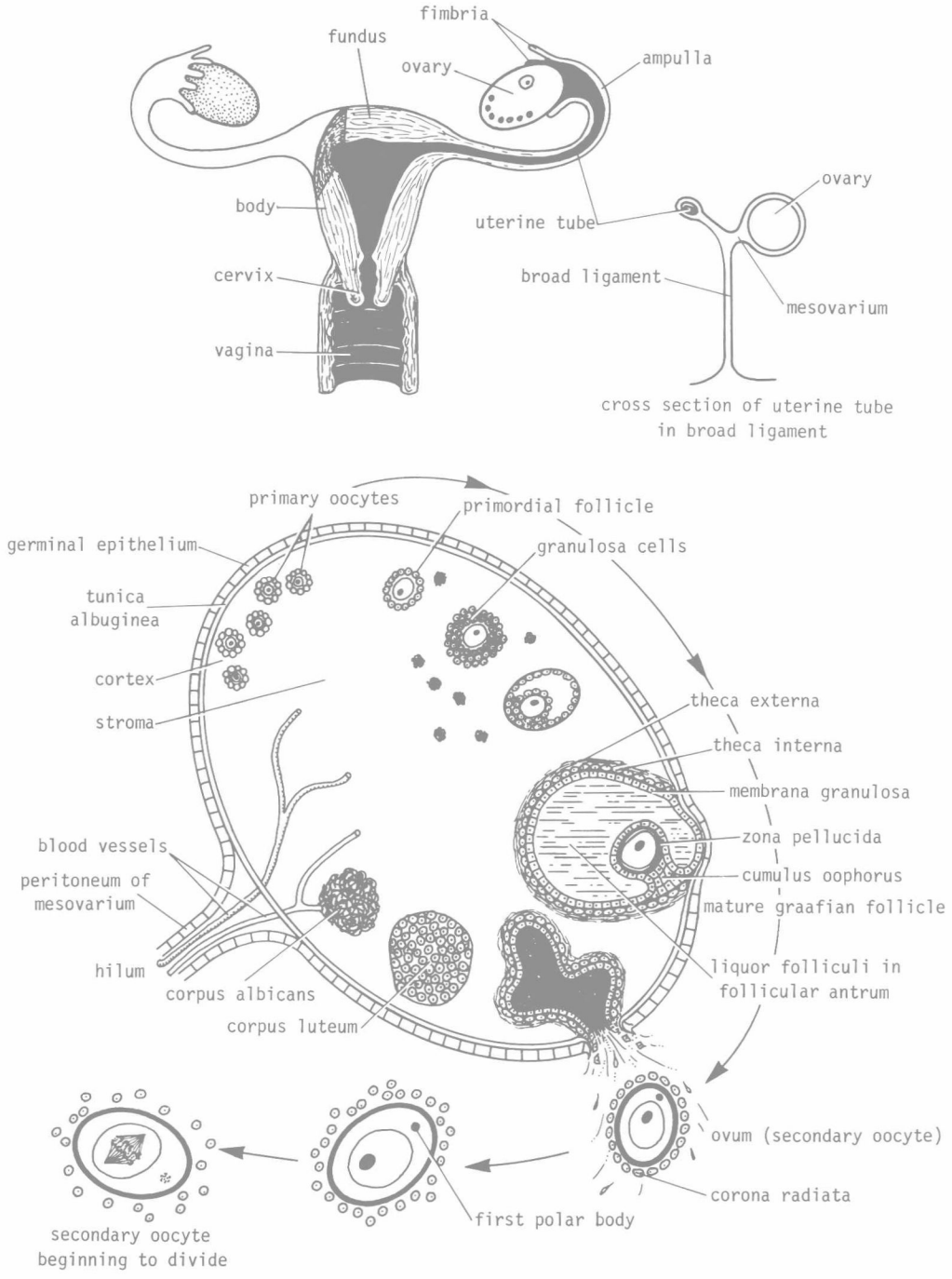

Fig. 1-4. Maturation of an ovarian follicle.

rounding stroma has been differentiating into an inner vascular layer of secretory cells, the *theca interna,* and an outer connective tissue layer, the *theca externa.* After 10 to 14 days of growth, the follicle measures about 10 mm in diameter and bulges slightly from the free surface of the ovary.

As the ovarian follicles mature under the influence of the FSH of the pituitary, the ovary begins to elaborate *estrogens.* The exact site of origin of these hormones is not known, but the cells of the theca interna and the granulosa cells are probably responsible for their genesis.

Ovulation

The meiotic division of the primary oocyte which began during the third month of fetal development is finally completed a few hours before ovulation occurs, and the *secondary oocyte* and the *first polar body* are formed. The first polar body, which receives only a little cytoplasm, lies between the zona pellucida and the cell membrane of the secondary oocyte (Fig. 1-4). As a result of the continued accumulation of liquor folliculi, the tense graafian follicle now ruptures, and the secondary oocyte, the zona pellucida, and the cumulus oophorus, now known as the *corona radiata,* escape into the peritoneal cavity. Immediately after ovulation the secondary oocyte undergoes the second meiotic division to form the *mature ovum* and the *second polar body;* however, this division is not completed until after fertilizaton has taken place. When the second polar body is formed, the first and second polar bodies undergo rapid breakdown and disappear. The mature ovum has a diameter of about 120 μ.

Following ovulation, the walls of the follicle collapse and the cells of the membrana granulosa are thrown into folds. Blood from the ruptured capillaries of the theca interna fills the remains of the antrum and clots. The cells of the membrana granulosa and the theca interna are stimulated by the *luteinizing hormone* (LH) of the pituitary. They enlarge and their cytoplasm accumulates lipid. Later a yellow pigment appears in the cytoplasm. These modified cells are known as *luteal cells,* and together they form the *corpus luteum.* The luteinized theca interna cells continue to produce estrogens, and the luteinized granulosa cells start to produce progesterone. As the result of continued hormonal stimulation from the pituitary, the corpus luteum enlarges for about 10 days after ovulation, reaching a diameter of about 2 cm, when it may be seen on the surface of the ovary as a yellowish projection surrounded by an area of hyperemia. If fertilization does not occur, the LH of the pituitary decreases in amount and the corpus luteum begins to involute. The secretion of progesterone diminishes, and the corpus luteum is finally converted into a fibrous scar, the *corpus albicans.*

Recently, it has been shown that the administration of progesterone will inhibit the process of ovulation. This finding has led to the preparation of contraceptive compounds that may be taken orally and that completely arrest the process of maturation of the follicles. It is of clinical interest to note that the ovaries may be artificially stimulated to ovulate by the administration of the pituitary FSH followed by the chorionic gonadotropic hormone or by treatment with the synthetic nonsteroid *clomiphene.* This may be of value in cases of sterility resulting from anovulation.

CHROMOSOMAL CHANGES DURING SPERMATOGENESIS AND OOGENESIS

In the human somatic cell there are 46 chromosomes, consisting of 22 pairs of *autosomes* and one pair of *sex chromosomes* (XY or XX). The different pairs of autosomes vary in size, but the two members of any