Gynecology and Obstetrics

by

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This book is dedicated to that always delightful but sometimes enigmatic biological phenomenon: The Human Female

Preface

This book has been designed to meet the need for a text which will give the student a summation of accepted present-day concepts in gynecology and obstetrics. The combination of the two subjects in one work is not novel, but the arrangement of the chapters in accordance with the growth and regression of the genitalia, as presented here, is new. This arrangement permits the reader to integrate the age of the human female, from conception to senescence, with the steps in the development of her genitalia, the physiologic processes which they manifest and the morbid conditions which affect them.

It is my hope that this book has avoided the sometimes mechanical exposition of principles guiding the health of women, that it has its foundations in biology and its canopy of coverage in the natural history of woman.

The evolution of textbooks ot gynecology and obstetrics has taken a most interesting course. For many centuries the teaching of those subjects trailed after that of other branches of medicine. With the exception of the work of Soranus of Ephesus in the second century and of Aëtius of Amida in the sixth century practically nothing was written about obstetrics until after the Renaissance was in full flower. Gynecology did not achieve medical status until the elder Van Roonhuyse's work in the seventeenth century. The authors, in preparing their commentaries on the work of the masters, combined all medical subjects in one treatise or in huge encyclopedias. The first printed book on obstetrics, Röslin's *Rosengarten*, 1513, was, for the most part, a paraphrase of the the work of Soranus. Ambroïse Paré described podalic version, but included gynecology and obstetrics in his work on surgery.

The seventeenth and eighteenth centuries saw an awakening of interest in gynecology and obstetrics. VanDeventer of The Hague, the father of modern obstetrics, wrote the first modern textbook on the subject. Smellie developed bedside obstetrical teaching to a high degree. His *A Sett of Anatomical Tables* and Hunter's *Anatomy of the Human Gravid Uterus* graphically portrayed human gestation for the first time. Most of the textbooks on diseases of women, of which those by Astruc and Gifford are examples, and others after them, combine both gynecologic and obstetric subjects under one cover. All of them tend to separate problems of parturition from disorders of the genitalia. In recent years the combined books of obstetrics and gynecology, such as the monumental three-volume work edited by Arthur Curtis, have had a distinct division between the two subjects.

This text deviates from the patterns of its predecessors in that gynecology and obstetrics are not divided by a bundling-board, but are, instead, wedded in an indissoluble union. An awareness of the need for integration of the two subjects has been recently emphasized by the amalgamation of the separate departments at several major medical schools in the United States.

There are many reasons why it is not a popular practice for one author to write on all facets of a major medical specialty. Herbert Evans has said that it is no longer possible for one person to cover the whole field of a given science. I am sure that this is true of gynecology and obstetrics if the essayist attempts to explore and present his subject in depth. But one author can portray the sequential development, physiologic processes and morbid affections of the female genitalia as a broad diorama. He sees the project as a unit, he can eliminate or stress certain points, and he can reduce the duplication of subject matter which often occurs when many contributors join together in one project. No effort has been made in this book to present all aspects of obstetrics and gynecology. It does attempt to answer two questions about the normal and abnormal changes which occur in the female genitalia during life: *what* happens to them, and *why* does it happen?

Treatment is described, but emphasis is placed,

for the most part, on the principles which guide gynecologic and obstetric management. The indications for and contraindications to surgical procedures are discussed, but the technical details and illustrations of the operations are omitted.

I feel very strongly that a book is not the place to learn how to perform an operation and that obstetric and gynecologic surgical skills can be acquired only in the delivery and operating rooms. A resident and I, as we talk on rounds, can discuss the principles which led to a specific operation, but I cannot teach him how to use his hands or his instruments except at the workbench of our specialty. Once upon a time, experience was often gained through a teaching do-it-yourself program. The result was a few fine surgeons and a great many unfortunate patients. Today, experience means specialized hospital training. Such training is a prerequisite to the performance of obstetric and gynecologic operations. As I have noted in several places in this text, an attendant should have the necessary experience before he starts a surgical procedure. If he does not, he should get help from a confrere who does.

I have drawn freely from many sources for the subject matter of this book. The purpose in writing each chapter has been to present things as simply as possible to the student. Multiple references to source material in the text defeat this purpose. In some places, therefore, I have taken concepts, even phrases, but, more often, paraphrased matter without giving line credit to the source. In each instance there has been a sincere effort to include the origin in the list of references.

There are many to whom I would express my appreciation for their help in the preparation of this volume. There are those who have permitted me to use illustrations and whose kindliness is acknowledged in the legends. Also, I am indebted to others who worked for longer or shorter periods on the manuscript, the reference lists and the illustrations.

I wish, in particular, to thank Mr. John Dusseau of the W. B. Saunders Company, whose encouragement and kindly counsels have made my task less onerous.

I am deeply indebted to Mrs. Edward Peth for her unswerving loyalty and patience in typing the text in finished form and for the many hours she spent in checking the references, and also to Miss Sheila Lechin for her assistance in completing the manuscript. I am also indebted to Miss Mildred Milligan, in the Gynecologic Laboratory of Northwestern University Medical School, who prepared the beautiful histologic sections from which many of the photomicrographs were made. Dr. Mark Wheelock and his confreres in the Department of Anatomic Pathology of Passavant Memorial Hospital, and Dr. Joseph Boggs in the Department of Pathology of Children's Memorial Hospital have been most helpful in supplying material for photomicrography.

It is a pleasure and an obligation to express my appreciation to the W. B. Saunders Company, and particularly to Mr. John Shaw, who edited the manuscript and prepared the index; and to Mr. E. J. Hoguet and Mr. S. J. Mink for their cooperation in the preparation and publication of this volume.

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Contents

chapter 1

Applied Embryology

A new individual is created when the elements of a potent sperm merge with those of a mature ovum. Before this union both gametes undergo a series of migrations and developmental changes in preparation for their specialized roles in fertilization (Fig. 1). Considering the complex evolution of the mammalian embryo and the intricate mechanism required for its preservation, it is remarkable that so many embryos experience an uneventful intrauterine life and that so few of them have major developmental abnormalities. Reproductive failure may be attributable to the male's inability to place potent spermatozoa within the female genital tract at a time when one of them will meet a viable oocyte, to barriers within the female genital tract which prevent the migration of spermatozoa to a point where they will meet the ovum, to failure of the female to shed a viable egg, to failure of union of the sperm and the egg or to abnormal development or death of the conceptus.

GAMETOGENESIS

SPERMATOGENESIS

The epithelium of the seminiferous tubules of the adult functioning testis contains *sustentacular (Sertoli) cells* and *spermatogonia.* The latter arise from the primordial sex cells of the germinal epithelium. They carry and pass on the chromosomes, which eventually unite with those of the ovum.

Formation of a mature gamete begins with mitotic division of the spermatogonium. Some of the daughter cells enlarge to form *primary spermatocytes,* which are irregularly shaped and somewhat larger than a spermatogonium. The nucleus of a primary spermatocyte contains twenty-two pairs of *autosomes* and two sex chromosomes. The latter consist of the female *X-chromosome* and the male *Y-chromosome.* A centriole, situated between the Golgi apparatus and the nucleus, first appears in the primary spermatocyte.

The primary spermatocyte is pushed or migrates near the lumen of the seminiferous tubule, where it divides to form two *secondary spermatocytes.* This division, unlike that of a spermatogonium, is *meiotic* or heterotypical. As a result, the number of chromosomes in each cell is halved, each secondary spermatocyte containing twenty-two autosomes or simple chromosomes and either an X- or Y-chromosome.

Division of the secondary spermatocyte, the next phase in spermatogenesis, results in the formation of two *spermatids.* During this division each chromosome splits longitudinally. As a result, each spermatid contains twenty-two autosomes and one sex chromosome. The nucleus of each spermatid forms the nuclear head of a *spermatozoon.*

Spermatozoa develop from the spermatids by a process of maturation without division. The spermatid becomes embedded in a sustentacular cell and undergoes radical change with rearrangement of its cellular constituents. The nucleus becomes the sperm head. A portion of the Golgi apparatus spreads out over the apical surface of the nucleus to form the anterior cap or acrosome. The flagellum grows from the centrioles, which move to the side of the cell away from the acrosome. The centrioles, with the flagellum, then move through the cytoplasm to the nucleus. The anterior centriole remains between the nucleus and the flagellum. The other moves down the flagellum to become the ring centriole at the flagellar end of the middle piece. The middle piece between the two centrioles contains the mitochondrial material. The portion of the cytoplasm which is not cast off becomes a thin layer about the surface of the nuclear head and extends along the middle piece and the flagellum.

When spermatogenesis is complete, groups of nonmotile spermatozoa separate from the sustentacular cells. They are carried out of the seminiferous tubules into the epididymis, where maturation is completed and separation occurs. There is little definitive knowledge of the factors in the human being which preserve or activate sperm potency or of the means by which the sperm is transported from the vagina to the outer portion of the uterine tube, where it meets the ovum. These factors have been investigated in other species, and many of the inferences from those studies can be applied to man. Motility is presumably stimulated by activating

Fig. 1. Semidiagrammatic drawing illustrating, *left*, gametogenesis in testis and, *right*, in ovary

agents in the secretions of the accessory glands. Although it is an expression of sperm potency, it is not necessarily correlated with the capacity for fertilization. In species other than man it has been shown that motility may exist for a considerable time after the power of fertilization has been lost. The potential energy which the sperm has at the time it is deposited in the vagina is rapidly dissipated by the effort of motility. Spermatozoa live for some time in the epididymis in what might be called a state of suspended animation. They have remained motile in saline solution for a number of days at room temperature and in a state of hibernation at a lower temperature. In the human female genital tract, however, their motile life is probably not over two or three days; their fertilizing ability is probably not present for more than twenty-four or thirty-six hours.

A normal motile sperm will travel between 1.5 and 3 mm. per minute. Movement of a sperm from the vagina to the infundibulum of the uterine tube should not require more than one and a half hours. Spermatozoa in vitro do not necessarily travel in a straight line. Despite this, it is probable that sperm transportation in the human being is largely due to the spermatozoon's own motility aided by unknown directional stimuli. It has been suggested that the male cells leave the acid vagina for the more friendly alkaline cervix. Spermatozoa in vitro have rheostatic properties which make them direct themselves against a feeble current; such a current is present in the cervix. Muscular movements of the cervix concomitant with orgasm have been reported. It is presumed that these movements aspirate seminal fluid into the uterus and that peristaltic activity within the uterine tube subsequently forces the spermatozoa outward. The frequent occurrence of pregnancy both after coitus without orgasm and after human and animal artificial insemination makes untenable any suggestion that orgasm is necessary for the transportation of spermatozoa. It is possible that movements of cilia and muscular contraction of the uterine tube, heightened at ovulation, may assist in the joining of the sperm and the egg.

OOGENESIS

In an ovarian follicle destined to contain a ripening egg one cell differentiates and outgrows the other follicular cells. This cell, the *oogonium*, becomes the *primary oocyte*, comparable to the primary spermatocyte of the spermatogenic scheme. The fully developed primary oocyte has an investing membranous *zona pellucida* separating it from the surrounding follicular cells of the *cumulus oophorus*. Its cytoplasm contains scattered, nutrient, *fatty yolk granules*. The *mitochondria* and *Golgi* apparatus are dispersed about the nucleus, within which is a distinct nucleolus and the chromatin material. Because of an increase in the volume of the cytoplasm, the actual size of the maturing oocyte becomes greater. It contains twenty-two pairs of autosomes and two female X-chromosomes.

The fully developed primary oocyte divides by meiosis before ovulation. As a result of this reduction division the two daughter cells each receive twenty-two autosomes and one X-chromosome. One of the daughter cells, the *secondary oocyte*, contains the cytoplasmic mass and most of the cellular constituents; it is destined to become the ovum. The

other, the *polar body*, is a much smaller secondary oocyte. Denied the opportunity to develop, the polar body soon degenerates and disappears.

The secondary oocyte has reached full development when it is extruded at *ovulation* from the ruptured follicle. It is surrounded by an adherent mass of follicular cells, the *corona radiata*. The zona pellucida forms a translucent, refractive surface membrane covering the egg. The Golgi apparatus and the mitochondria are dispersed throughout the cytoplasm. Many of the fat granules have disappeared. Although the second polar body does not separate until after conception, a second polar spindle is present at ovulation.

The exact manner in which the ovum finds its way into the uterine tube is not known. Reported observations indicate that in lower mammals, and also in human females, there are movements of the infundibular portion of the tube and ovary at ovulation. These movements bring the fimbriae into contact with the surface of the ovary in a funnel-like fashion. Muscular contractions in the tube and the action of the tubal ciliated cells then sweep the ovum into the tubal lumen. Tubal peristaltic-like contractions, always present, are most active immediately after ovulation. Once within the lumen, most of the cells of the corona radiata separate from the ovum, exposing areas of the zona pellucida (Fig. 2). The ovum is carried into the outer interstitial portion of the tube, where it meets the spermatozoa, and fertilization occurs.

The life span of the unfertilized human ovum and the length of time required for tubal migration are unknown. In lower mammals, however, the period during which an egg is capable of fertilization is measured in hours. The time for tubal migration is a matter of three or four days. It is probable that the same holds true for man.

FERTILIZATION

Fertilization is the merging of the male and female gametes. It is initiated when a spermatozoon penetrates the zona pellucida of the secondary oocyte (conception) and is completed when the chromosomes of the male and female pronuclei are conjoined. If fruitful coitus has occurred, the outer third of the tube is soon invaded by large numbers of actively motile spermatozoa. The remaining cells of the corona radiata are dispersed by substances within the sperm plus, as Shettles has shown, a fibrinolytic effect from the tubal mucosa. Spermatozoa cover almost the entire surface of the zona pellucida after the ovum has been denuded (Fig. 3). A number of spermatozoa penetrate the zona pellucida and the perivitelline space. Several may possibly enter the ooplasm, but only one becomes the fertilizing organism (Fig. 4, *B*).

The last phase of maturation does not occur until the spermatozoon has penetrated the secondary oocyte. Subsequently the second maturation division takes place with separation of the second polar body. This second division is an equal one; there is splitting of the chromosomes similar to that in mitosis. In contrast to a reduction division, there is no decrease in the number of chromosomes; both the *ootid* or mature ovum and the second polar body have twenty-two autosomes and one X-chromosome. The second polar body, like the first, soon degenerates. The nuclear material of the ootid is now known as the *female pronucleus*.

After the sperm has entered the egg the tail and middle piece are detached and disappear (Fig. 4, *C*). The mitochondria and Golgi apparatus become scattered throughout the ovular cytoplasm. The sperm head, enlarging as it travels toward the

Fig. 2. Photomicrograph of a section of a human ovum showing the second maturation spindle and extruded first polar body. (Reproduced from J. Anat., Vol. 78, by the courtesy of Prof. W. J. Hamilton.)

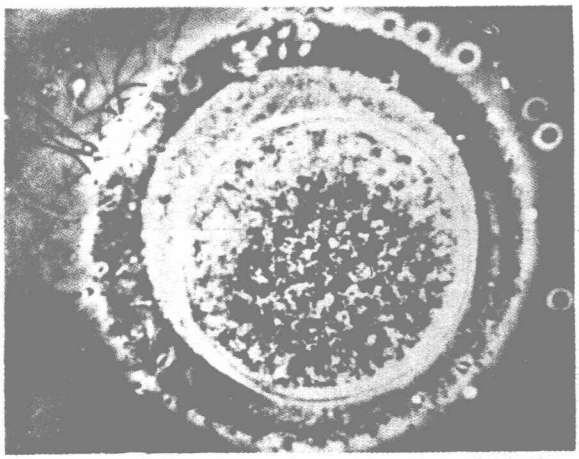

Fig. 3. A denuded ovum with spermatozoon penetration. (Reproduced from Am. J. Obst. & Gynec., Vol. 69, by the courtesy of L. B. Shettles.)

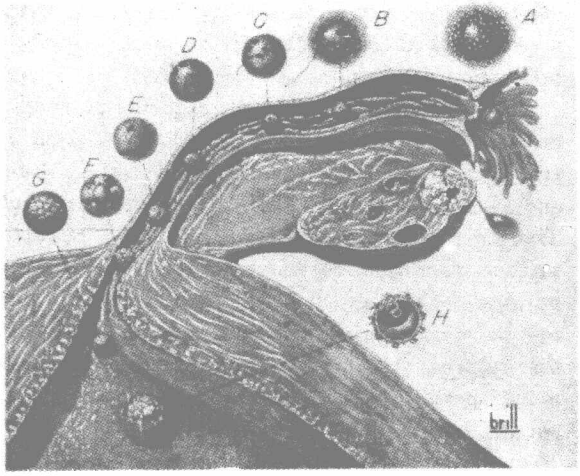

Fig. 4. Drawing illustrating progressive steps in fertilization and development of the young conceptus. *A*, Ovum covered by corona radiata in tubal infundibulum; *B*, denuded tubal ovum, after being surrounded by many spermatozoa, is penetrated by one fertilizing spermatozoon; *C*, the spermatozoon loses its tail and middle piece, while its head becomes the male pronucleus; *D*, the 2 pronuclei have met, the chromosomes in each of them have split, and the halves are moving along a spindle toward their respective centrosomes to form 2 cells; *E*, 2-celled embryo; *F*, the solid multicelled morula; *G*, the vesicular blastocyst; *H*, the implanted conceptus.

female pronucleus, becomes a typical nucleus, the *male pronucleus*.

The two pronuclei meet in the center of the ootid. In each the chromatin material organizes into chromosomes; the female pronucleus has twenty-two autosomes and an X-chromosome; the male pronucleus, twenty-two autosomes and an X- or a Y-chromosome. The nuclear membranes disappear. A *centrosome* appears and divides into two daughter centrioles. These arrange themselves at either end of

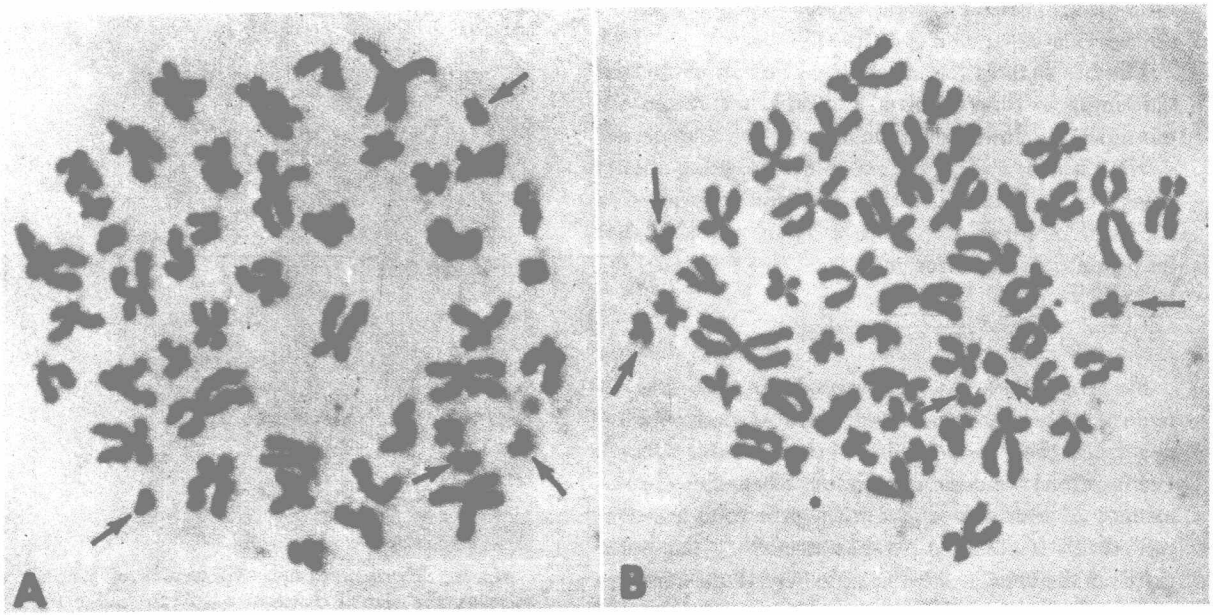

Fig. 5. Chromosomes at metaphase in human myeloid cells after colchicine treatment. Acetic-orcein squash preparations. *A*, From a female; 4 small acrocentric chromosomes are indicated by arrows. *B*, From a male; 5 small acrocentric chromosomes indicated by arrows. (Reproduced from Nature, Vol. 181, by the courtesy of C. E. Ford et al.)

a spindle upon which the chromosomes divide again, the halves gaining their respective centrosomes (Fig. 4, *D*). The fertilized ovum, or zygote as it is now called, divides into two equal-sized daughter cells, forming a two-celled embryo (Fig. 4, *E*). This mitotic division gives each daughter cell forty-four autosomes, half of which are of maternal and half of paternal origin. There are now two sex chromosomes, either an X and a Y (male) or an X and X (female), depending upon the constituents which the paternal gamete brought to the union. As a result, the species number of chromosomes is duplicated in the new individual, sex is determined and cleavage begun.

Before 1956 it was generally believed that man normally had forty-eight paired or diploid chromosomes which were formed by doubling of the primary chromosomes of the gametes at the time of fertilization. In recent years Tjio and Levan, Ford and his co-workers and others have demonstrated that the basic human diploid chromosomal number is forty-six (Fig. 5). Variations in the number of somatic chromosomes are found, however. It is believed that some of the additional ones, which are occasionally noted, are supranumerary bodies which have little genetic effect. The presence or absence of the small acocentric Y-chromosome determines the sex of an individual.

DEVELOPMENT OF THE EMBRYO

There are four phases of anatomic development during prenatal growth: (1) that of a flat disklike presomite embryo; (2) that of a segmented somite embryo; (3) that of an embryo undergoing organ system differentiation; and (4) that of fetal growth.

The first phase lasts approximately three weeks. It may be conveniently broken down into nine stages, based on the developmental grouping devised by Streeter for the classification of young embryos: stage I, the one-celled ovum; stage II, the segmenting egg; stage III, the free blastocyst; stage IV, the implanting ovum; stage V, the implanted avillous ovum; stage VI, the ovum with primitive villi and distinct yolk sac; stage VII, the ovum with branching villi and axial differentiation; stage VIII, the appearance of Hensen's node and the primitive groove; and stage IX, the presence of neural folds and elongated notochord. It should be understood that such a grouping is not definitive and that these stages should not be identified on a time basis. As Streeter points out in calling them "developmental horizons," they are levels through which the living embryo develops from a simple to a more complex form.

FERTILIZATION TO IMPLANTATION

In recent years Rock and Hertig have gathered and presented a remarkable collection of very young embryos. From their material and from the material in the monkey it is possible to reconstruct, with a considerable degree of accuracy, the changes which occur in the early embryo between fertilization and nidation. The time required for the human embryo to traverse the tube is unknown. It probably reaches the uterine cavity about seventy-two hours after fertilization. During its passage through the tube the embryo changes from a two-celled body to a solid, multicellular, mulberry-like *morula* (Fig. 4, *F*). In 1950 Hertig and Rock reported a two-celled human embryo recovered from the uterine tube. It contained two equal-sized blastomeres and two polar bodies (Fig. 6). In the monkey the larger of the two cells next divides, and a three-celled stage occurs. The smaller cells then divide and undergo division at unequal rates. In the eight-celled embryo the cells derived from the larger blastomere of the two-celled zygote are at one pole and the four cells derived from the smaller blastomere are at the

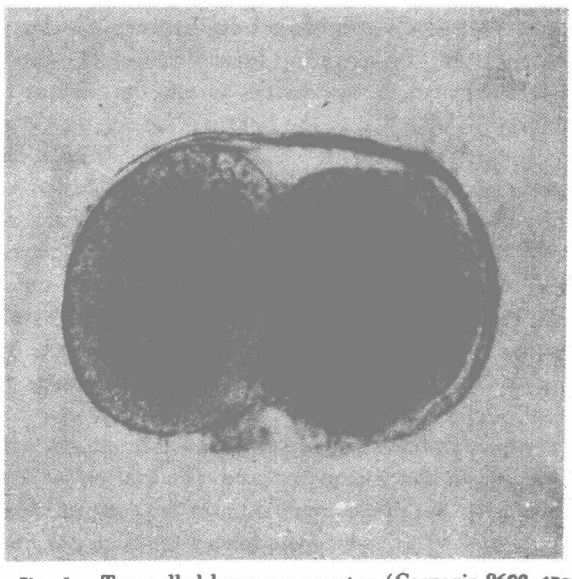

Fig. 6. Two-celled human conceptus (Carnegie 8698, seq. 12) recovered from the uterine tube approximately 1½ days after conception. (Hertig, Rock, Adams and Mulligan, Contrib. to Embryol., No. 240, 1954, reproduced by the courtesy of the Carnegie Institution of Washington.)

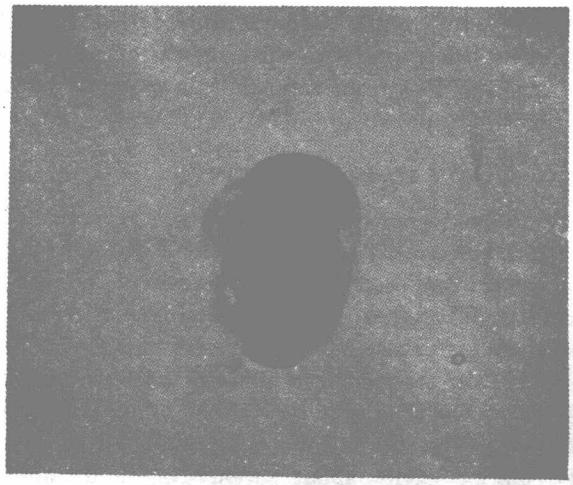

Fig. 7. An 8-cell human morula (Carnegie 8450, Seq. 11); intact specimen oriented to show flattened shape of morula. (Hertig, Rock, Adams and Mulligan, Contrib. to Embryol., No. 240, 1954, reproduced by the courtesy of the Carnegie Institution of Washington.)

other pole. Rock and Hertig also describe an eight-celled conceptus (Fig. 7). At this stage the fertilized ovum is a solid ball of rapidly multiplying cells. The sixteen-celled morula consists of a centrally placed *inner cell mass* and a superficial layer of cells. The latter develop into the *trophoblast.* The entire structure is encompassed by the zona pellucida.

When it enters the uterus, or shortly thereafter, the morula becomes a vesicular structure, the *blastocyst* (Fig. 4, *G*). Fluid collects between the inner cell mass and the covering layer of cells. The inner cell mass, which eventually forms the definitive embryo, is attached to the inner surface of the outer cells at one point known as the *embryonic pole.* Increase in the amount of fluid causes distention of the vesicle and flattening of the surface cells. The cells forming the thin membranous wall of the cyst-like blastocyst become the *trophoblast.* The inner cell mass becomes the formative cells of the embryonic disk. A portion of the trophoblast overlying the formative cells of the inner cell mass consists of small, irregularly shaped cells which become the *extraembryonic* structures. These structures will function in the anchoring and penetration of the blastocyst into the endometrium at the time of nidation and later in the formation of the placenta and membranes.

The conceptus lies unattached in the uterine cavity for a short time, probably less than twenty-four hours. Just before its attachment it appears as a minute, globular-like vesicle (Fig. 8). The formative cells at the embryonic pole multiply to form the *embryonic disk.* The actively proliferating, thickened polar trophoblast makes up the outer surface of the disk. The trophoblastic wall is continuous with it and forms the single-layered surface of the distended vesicle. The zona pellucida disintegrates, exposing the trophoblast. On the inner surface of the embryonic disk, but separated from it, the *primary endoderm* becomes evident as a distinct layer of cells. It probably originates by spreading from the trophoblast. The inner cell mass or embryonic disk will form the *primary ectoderm,* which gives rise to the *embryonic ectoderm* and later the *secondary mesoderm.*

The conceptus makes contact with the endometrium when it is five or six days old. The blastocystic cavity collapses. The *syncytial trophoblast,* or that portion of the trophoblastic tissue covering the inner cell mass, proliferates and invades the maternal tissues (Fig. 4, *H*).

IMPLANTATION TO VILLUS FORMATION

A blastocyst at the time of attachment has not been observed. It is likely that the same things occur in man as in other primates. The blastocyst comes in contact with the endometrium in the upper portion of the uterus. The polar trophoblast

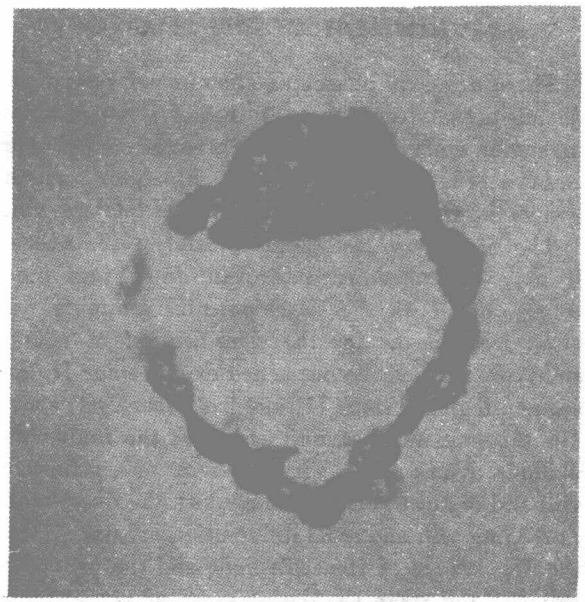

Fig. 8. 107-cell human blastula; section through blastocyst (Carnegie No. 8663, sect. 9). (Hertig, Rock, Adams and Mulligan, Contrib. to Embryol., No. 240, 1954, reproduced by the courtesy of the Carnegie Institution of Washington.)