A 30-year-old Negro female, gravida VI, para IV, with two previous abortions, was admitted to the hospital complaining of increasingly severe lower abdominal pain associated with syncope. Slight vaginal bleeding, which had begun two days previously, was accompanied by nausea but no vomiting. The last normal menses was eight weeks prior to admission.

Physical examination revealed a moderately distended and diffusely tender abdomen. Upon manipulation, tenderness was also present in the cervix, uterus, and right and left adnexa. Bowel sounds were active. A serous discharge was found upon vaginal examination. A culdocentesis aspirated blood from the cul-de-sac (pouch of Douglas). The pregnancy test was negative.

A laparotomy was performed. The abdominal cavity contained 500 ml. of clotted and unclotted blood. The left ovary had a corpus luteum of pregnancy. The ampulla of the right uterine tube was a bulbous hemorrhagic mass showing active bleeding. A right salpingectomy was performed and the clots and free blood evacuated. The postoperative course was uneventful and the patient was discharged on the fifth day.

The pathology report follows:
1. Gross description: The distal 8 cm. of the right uterine tube is enlarged, with a patent fimbriated end. There is one small, smooth-lined, clear-filled paratubal cyst. The opened cyst contains a fetus having a crown rump (CR) length of 2 cm.
2. Microscopic description:
   A. Proximal portion right uterine tube. The lumen is patent. A scattering of inflammatory cells are within the muscularis.
fertilization and implantation as a tubal pregnancy. At ovulation (Fig. 1) the secondary oocyte, with an eccentrically placed second polar spindle, is surrounded by a plasma (vitelline) membrane, outside of which lies the first polar body. This secondary oocyte and first polar body are within the zona pellucida; the latter is surrounded by the corona radiata. Upon ovulation the oocyte is swept into the fimbriated end of the uterine tube, which is closely applied to and partially covers the ovary.

Fertilization normally occurs in the outer third of the uterine tube. As sperms approach the oocyte, their acrosomal caps dissolve, releasing hyaluronidase, which causes a separation of the cells composing the corona radiata and facilitating penetration of the zona pellucida. The sperm adhere to the oocyte through an antigen-antibody-type reaction that occurs between fertilizing at the surface of the oocyte and anti-fertilizing in the acrosomal cap. Subsequently, the oocyte is activated and forms a fertilization membrane around the fluid-filled perivitelline space. The fertilization membrane prevents entry of additional sperms. The second polar spindle now completes division, with the formation and extrusion of the second polar body and the formation of the female pronucleus. The head of the sperm forms the male pronucleus. The nuclear membranes of the female and male pronuclei disappear, and with their centrioles the pronuclei migrate towards the center of the cell where their chromosomes become arranged around the equator just prior to the first cleavage division. Thus, fertilization results in: (1) restoration of the diploid number of chromosomes; (2) determination of the chromosomal sex of the individual; and (3) the initiation of cleavage.

Cleavage is a rapid succession of mitotic divisions resulting in the production of an increased number of smaller cells, called blastomeres. The principal consequences of cleavage are: (1) division of the protoplasm of the zygote amongst the blastomeres; and (2) increased mobility of this protoplasm. In addition, the fertilized ovum is considerably larger than the average adult cell, and cleavage results in an approximation in size of the developing cells to that size characteristic of the definitive cells of the organism. During this initial period of cleavage, certain unknown factors influence the implantation and further development of the embryo in an abnormal position, e.g., tubal.

Etiology

What factors may contribute to the formation of ectopic, particularly tubal, pregnancies? Factors that delay or prevent tubal transport of the fertilized ovum, such as (1) gonorrhea; (2) postabortion; (3) puer-
B. Distal portion right uterine tube and placenta. Immature chorionic villi and blood clots are present. The blood clots are between the placenta and the epithelial lining of the tube.

DIAGNOSIS

Right tubal pregnancy.

DISCUSSION

Ectopic pregnancy occurs on the average in 5 of 1,000 deliveries with variations between different races and socioeconomic groups. Ectopic pregnancy was first described by Albusciss in the eleventh century, while in 1604 Riolanus the younger detailed one of the earliest cases of tubal gestation with classical symptomatology of tubal rupture. In 1899 Mauriceau and Vassal described a pregnancy in a rudimentary uterine horn, and in 1883 Sänger performed the first amputation of a rudimentary uterine horn containing a pregnancy.

Embryology

Describe the development of the ovum from ovulation through

![Diagram of embryology process](image)
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[Table continues with various activities and assignments]

**Notes:**
- All lectures and activities are compulsory.
- Labs and quizzes are given to assess understanding.
- Tests are cumulative and cover material from the previous weeks.

**Additional Information:**
- Students must submit assignments on time.
- Late submissions will be penalized.
- Attendance will be recorded for each week.

**Course Logistics:**
- **Instructor:** Dr. Johnson
- **Office Hours:** Monday 3-5 PM, Wednesday 10-12 AM
- **Contact:** johnson@example.edu
peral infection; (4) hormonal influence; (5) conception genital abnormalities; and (7) chronic inflammatory thing that impairs tubal function.
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*Note: The table contains placeholder text (Yeast example) and a diagram.*
quence; (5) conceptus itself; (6) con-

tronic inflammatory disease, or any-

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* Postnatal age
† Methods of measurement
✨ Gross features: young embryo lacking a relatively straight body. White pigmentation; a complete count should also be made.
4

Trophoblastic Disease

A 38-year-old gravida III, para II female was admitted to University Hospital in May, 1970, complaining of excessive vaginal bleeding of less than one day's duration. Her last menstrual period (LMP) was January, 1970. Prior to this time she had menstruated regularly. Gynecologic examination in April, 1970, revealed a uterus corresponding to a normal three-month pregnancy. Examination at the present admission disclosed an intrapelvic and intra-abdominal mass located in the midline and corresponding to a uterine enlargement of a six-month pregnancy (an apparent uterine growth of three months' pregnancy occurring within one month's time). The cervix was soft, and the os cervix was dilated.

DIAGNOSIS

Missed abortion, hydatidiform mole, or multiple pregnancy?

TREATMENT

Bioassays revealed HCG excretion above 50,000 I.U./24 hours (a peak excretion of 7,000 to 500,000 I.U./24 hours normally occurs between the tenth and fourteenth week; if after the sixteenth week, hydatidiform mole is probable). Fetal ECG verified the absence of fetal heart sounds; spontaneous expulsion of a small portion of tissue with a grapelike appearance, combined with ultrasound, confirmed the diagnosis of hydatidiform mole (a cystic, hydropic swelling of the chorionic villi, accompanied by variable hyperplastic and anaplastic changes in the chorionic epithelium with no apparent embryo). Curettage of
The mole; the sac did not result in avoided death. Two normal increased.


The future embryo and some extraembryonic membranes attach eccentrically to the inner aspect of the outer layer of cells of the blastocyst. The outer layer is now termed the trophoblast (Fig. 2).

One week after ovulation, the trophoblastic cells attach to the uterine epithelium by erosion and penetration of the underlying endometrial stroma. The cells composing the trophoblast differentiate into two types: (1) the cytotrophoblast, an inner layer adjacent to the developing embryo; and (2) the syncytiotrophoblast (syncytiotrophoblastic), an outer layer adjacent to the uterine epithelium. The above two cell layers will form the chorion, and by differentiation the latter gives rise to the chorial plate.

Nine to eleven days after ovulation, isolated vacuoles appear within the syncytiotrophoblast. Subsequently, these vacuoles become confluent, forming lacunae which are the beginning of the future intervillous space of the placenta.

The uterine wall is composed of an endometrial, a myometrial, and
the uterine cavity was performed to remove the remainder of the mole. Close examination of the mole revealed a small choriocarcinoma and the cavity was opened and found to be empty.

Quantitative determination of HCG was done weekly and results were normal for three consecutive weeks. The determinations were repeated monthly for one year, during which time pregnancy was excluded. Simultaneously, chest x-rays to detect lung metastases were obtained. After two years postoperatively the patient was well, the lung fields were clear, as determined by x-rays, and there was no evidence of HCG.

DISCUSSION

In the United States, hydatidiform mole (molar pregnancy) occurs in 1/1,500 pregnancies. Although Actius wrote about hydatidiform mole in the sixth century, von Graefenberg (1565) is credited with the first classical description. Gieson (1847) was the first to attempt to distinguish between hydatidiform mole and consider it to be a result of changes in the decidua of pregnancy. Sänger (1889) suggested that hydatidiform mole was a specialized tumor derived from the decidua of pregnancy, while Marchand (1897) demonstrated that tumors in the placenta were the sequel of normal pregnancy, abortion, and hydatidiform mole. Despite the non-neoplastic nature of the trophoblast, its potential malignancy (choriocarcinoma) is real and is approximately parallel to the degree of hyperplasia and

Embryology

Discuss normal placentation. The zygote (Fig 2), composed of a double-layered ball of cells (morula), surrounded by the zona pellucida, enters the uterine cavity and approximately the sixth day following fertilization. At this time the endometrium is in the luteal phase and the uterine cavity is lined by mucus. The morula is suspended in this mucus, two to three days, during which time it develops into a spherical cyst by the following modifications: (1) the zona pellucida dissolves; (2) nutrition (embryotroph) occurs via fluid passing from the uterine cavity into the intercellular spaces between the double layers of cells composing the blastocyst (at this time the inner cell mass has not yet formed); (3) the intercellular spaces become confluent as a result of the increased amount of fluid, giving rise to a single cavity, the blastocyst; and (4) the inner cell mass then
by fusion of the decidua capsularis with the decidua parietalis. Subsequently, the decidua capsularis thins and disappears, leaving the deci-
dua basalisis to form the maternal portion of the placenta.

Chorionic villi, the essential structure of the definitive placenta, begin to form at the third week of gestation (Fig. 4A). The cytotropho-
blast extends into the syncyti um to form primary villi as the first step in the development of chorionic villi. As extension occurs, a core of
mesodermal tissue extends into the primary villi, which are now known

![Image of placental structure]

Fig. 4 Enlargement of placental site in Figures 2 and 3; A, Third to fifth week of gestation; B, Second month of gestation; C, Middle of second trimester.

as secondary villi. These villi become united distally to form a cho-
-rician shell that is penetrated by maternal vessels. This penetration
 aids in anchoring fetal to maternal portions of the placenta.

In the fourth to fifth week of gestation, the secondary villi are
penetrated by blood vessels and are now called tertiary villi (hemato-
rophic nutrition). These villi will branch and fuse with one another (Fig. 4B).

By the fourth prenatal month, the cytotrophoblastic cells begin to
retrogress, probably the result of a reduction in mitotic rate, leaving
villi covered predominantly by syncyti um. Concurrently septa from the
de cidua basalisis extend into the intervillous spaces dividing the placenta
into 15 to 20 units called cotyledons (Fig. 4C). The septa do not ex-
tend to the chorionic plate, thus communications between cotyledons
remain. The placenta rapidly decreases in growth toward the end of
the fourth month.
zona compacta and the zona spongiosa constitute the decidua undergoes a decidual reaction in response to the trophoblast and is shed at parturition. The decidua consists of three topographical regions up to the fourth month: (1) the decidua basalis; (2) the decidua capsularis; an decidua parietalis. Twelve days following ovulation, the cavities of the decidua basalis become congested and dilated and form the decidua parietalis. The syncytium implants into the decidua, and blood flows from the sinusoids to the developing lacunae (horns of nutrition). As implantation continues, larger maternal vessels appear and the syncytium becomes directly continuous with the endotrophoblast of these vessels. By the fifth month, the uterine cavity is completely obliterated.
on of hyde- 
levelontology established is either core within any maternal id transfers since there distending site of the within the
Cause

Discuss the development of hydatidiform mole. Form tidiform mole begins between the third and fifth week or at the time the fetochorionic circulation normally becomes. However, no chorionic circulation develops, since the fetus absent, defective, or dead, and dissolution of the mesoderm the villi results. Concomitantly, the trophoblast, nourished blood within the intervillous spaces, survives and secretes products from this maternal blood into the chorionic villi if there is no chorionic circulation the liquid products accumulates and converting the villi into cysts. The chorionic villi, in defective intrinsic blood supply, continue to grow rapidly uterine cavity, giving rise to a hydatidiform mole.
5

Teratoma

A 29-year-old woman previously having had four normal deliveries was in labor and admitted to the emergency room. The infant's head, upper limbs, and trunk were delivered normally, at which time labor became obstructed by the buttocks and lower limbs. Traction failed to complete delivery and a cesarean section was performed and the infant extracted.

EXAMINATION

The female infant weighed 3,600 gm. and appeared active and well at birth. A raised skin-covered mass devoid of hair and 20 cm. in diameter protruded from the coccygeal region, slightly displaced to the left of the midline. X-ray studies of the pelvis revealed a soft tissue mass in the gluteal area and no calcification of the coccygeal vertebra. Pelvic extension of the mass could not be determined and surgery was performed at age 48 hours.

DIAGNOSIS

Provisional diagnosis: benign sacrococcygeal teratoma.
Sacrococcygeal teratoma.
fant was discharged at 8 days of age. At 15 months after surgery the female infant is healthy and well developed with no evidence of tumor recurrence.

DISCUSSION

The earliest written record of sacrococcygeal teratoma is found on a cuneiform tablet of Babylonian origin from Chaldea around 2000 B.C.¹ The first successful surgical extirpation of a sacral teratoma was reported by Blizard in 1841.² Descriptive and speculative investigation of teratomas has led to a vast accumulation of literature.³ ⁴ ⁹

Definition of Teratoma

Give a generalized definition or description of teratoma that includes all clinical manifestations. Teratomas occur primarily in the female and are present in 1/35,000 live births.¹¹ Teratomas are tumors arising from pluripotential embryonic cells; these cells have escaped the influence of an organizer and occupy a preaxial median or a closely paramedian position. The tumors usually arise from more than one germ layer and form a variety of tissues foreign to the area in which they develop. These tumors generally are of two types: (1) a benign cystic or solid mass which grows at the same rate as the embryo, fetus, or infant and is asymptomatic only because of its size or by its displacement of adjacent organs, or (2) a rapidly growing, invasive or metastatic mass, generally arising from one layer. In teratomas of the newborn (congenital), any of the involved tissues may become malignant.

Embryology

From the generalized definition of a teratoma, suggest how these tumors might develop. These benign or malignant tumors may arise from detached embryonic cell nests (e.g., neuroenteric canal, postanal gut, proctodeal membrane, anal plate) or from embryonic misplacement of tissues, which retain some or all of their totipotentiality (capable of forming a new individual) and for reasons unknown grow, despite an apparent lack of the required organizer. The median or paramedian location suggests an origin from embryonic cells of the primitive streak or primitive knot.

In general, discuss briefly what the primitive streak and the primitive knot are. Discuss formation of the intraembryonic mesoderm and the notochordal process. The primitive streak is an ectodermal area at the caudal edge of the bilaminar embryo, and early in the third week.
Fig. 5 Removal of a sacrococcygeal teratoma via an inverted V-shaped incision.

TREATMENT

The teratoma, an encapsulated tumor beneath the subcutaneous tissues, was excised through an inverted V incision (Fig. 5) over the sacrum and buttocks. Prior to removal of the tumor, the main artery and vein and the lateral sacral vessels supplying it were tied. The tumor was separated from the rectum and the coccyx was left attached to the tumor, after which the wound was closed.

Histological sections of the tumor showed cysts lined by epithelium; fat, muscle, and connective tissue; acini resembling salivary glands; cartilaginous material, sebaceous glands; hair follicles and sweat glands, which confirmed the provisional diagnosis of a benign sacrococcygeal teratoma. The postoperative course was uneventful, a
of gestation (Fig 6A) the primitive streak appears as a proliferation of cells that bulge into the amniotic cavity in this caudal region. Cells migrate laterally from the streak between the ectoderm and entoderm to form the third germ layer of the embryo, the intraembryonic mesoderm. A further thickening of ectoderm at the cephalic end of the streak forms the primitive knot (Hensen's node), in the center of which occurs an inward movement of surface cells resulting in the development of the primitive pit (blastopore) (Fig 6B). Surface cells migrate through the blastopore between the ectoderm and entoderm forming the notochordal or head process. As the embryo increases in length, the primitive streak and knot are carried caudally and persist until the end of the somite stage (5 mm), when they undergo retrogressive change and rapidly diminish (Fig 6C).

Discuss briefly how germinal and somatic cells might give rise to a teratoma. In the early stages of development and segmentation of the zygote, the first blastomeres are totipotent; later these same blastomeres are multipotent (capable of forming all three germ layers). These multipotent blastomeres give rise to two definitive cell types: (1) germinal cells, which normally develop into spermatozoa or ova, and (2) somatic cells, which develop into the remaining body cells proper. If either germinal or somatic cell is detached and stimulated to grow outside of its normal location, a teratoma may arise.

Specificity of the Germ Layers

What is the germ layer theory of specificity? Does the histological
Fig 6 Development of the primitive streak: A. Sagittal section, 25-"we Sagittal section, 3-week-old embryo: C. Dorsal view, 4-week-o
ute this theory? The ile of differentiating nstances. After gas-
issue becoming more m, mesoderm, ento-
vers is of two types:
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1895.
appearance of a teratoma help to substantiate or; cells of an embryo prior to gastrulation are cap into widely diverse tissues under appropriate cir-
trulation this plasticity is progressively lost, each restricted to one of the three germ layers (ecto-
derm). The developmental potential of the germ (1) actual, what the germ layers will form unt and (2) total, what the germ layers are capable of. But diversified, conditions or under experi-
teratoma represents the area of total potential or supports the theory of specificity, because teratoma associations of structures occurring under normal tilage with respiratory epithelium, bone with te with hair.

Absolute adherence to the germ layer theory perimental findings regarding the origin of certain musculature of the iris, branchial cartilages, menin-gent cells.

Sites of Teratomas

Teratomas are found in diverse areas of the pineal, face, thyroid, mediastinum, stomach, gonad peritoneal.

Differential Diagnosis

What malformations of the sacrococcygeal regi with a teratoma? A sacrococcygeal teratoma may lead: perirectal abscess, pilonidal cyst, meningocele, chy cyst, or hemangioma.

Associated Malformations

A random distribution of congenital malforma with teratomas.

REFERENCES


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