Diagnostic Imaging Obstetrics

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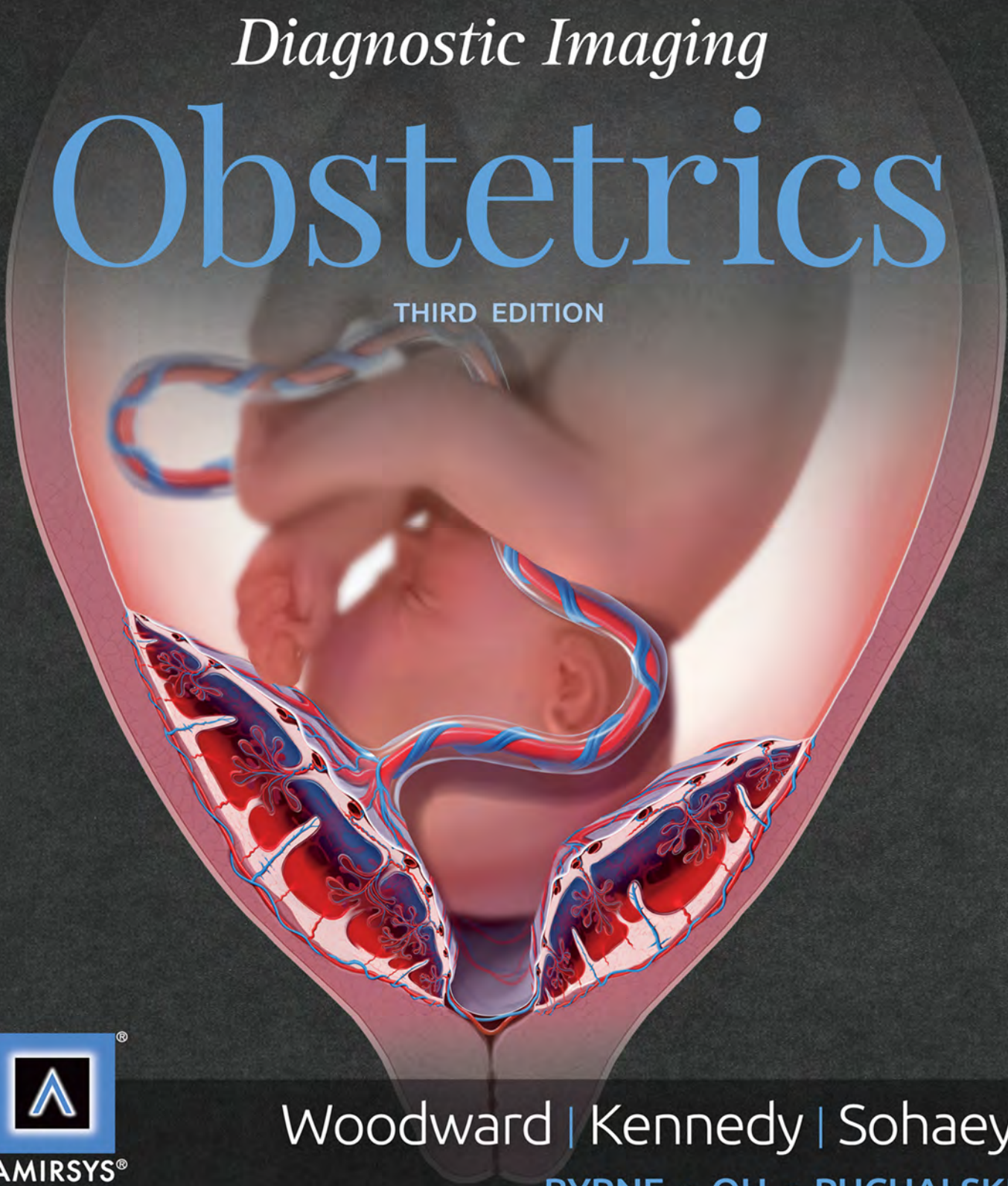

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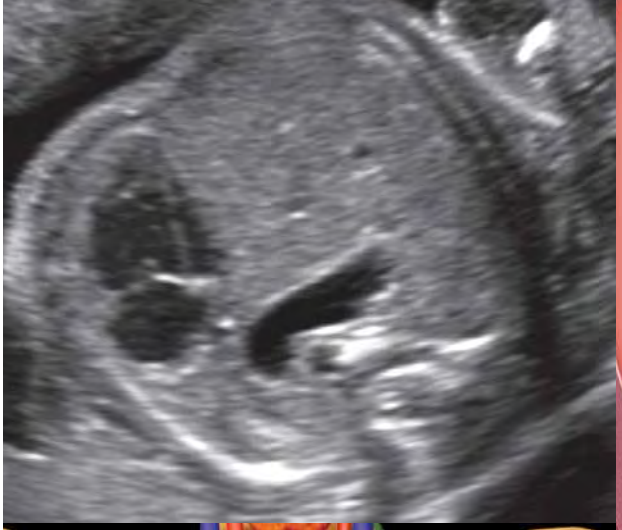

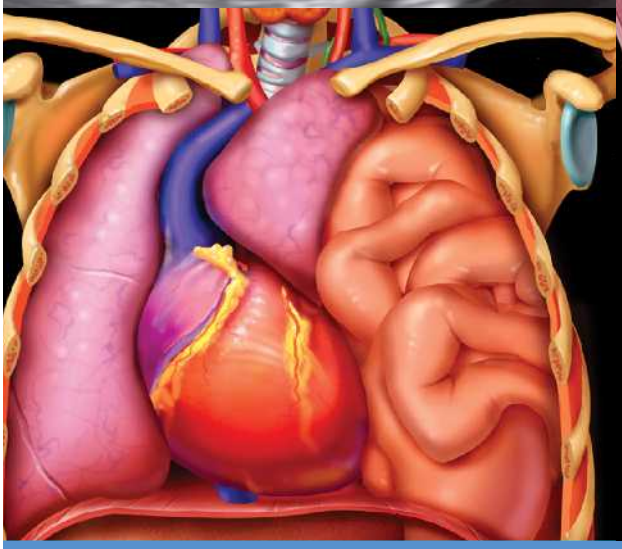

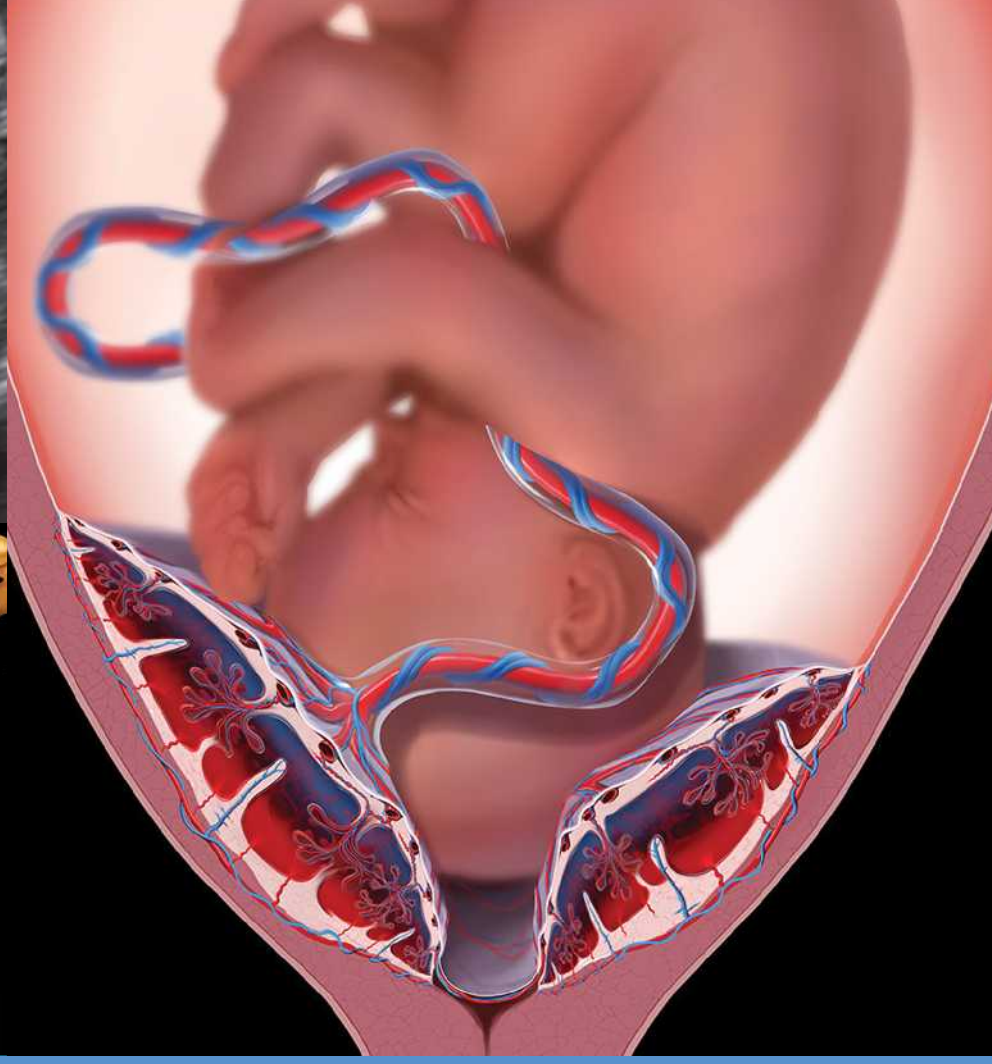

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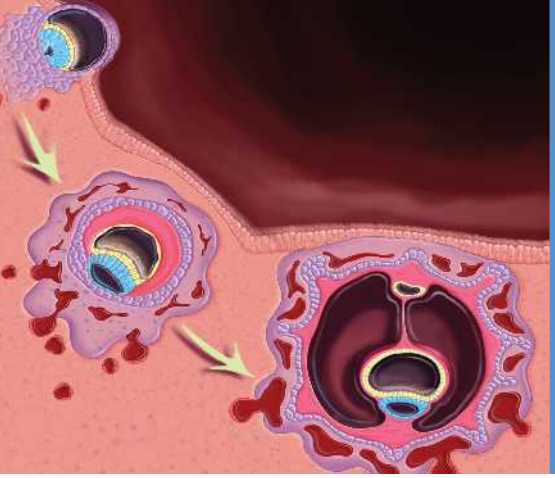

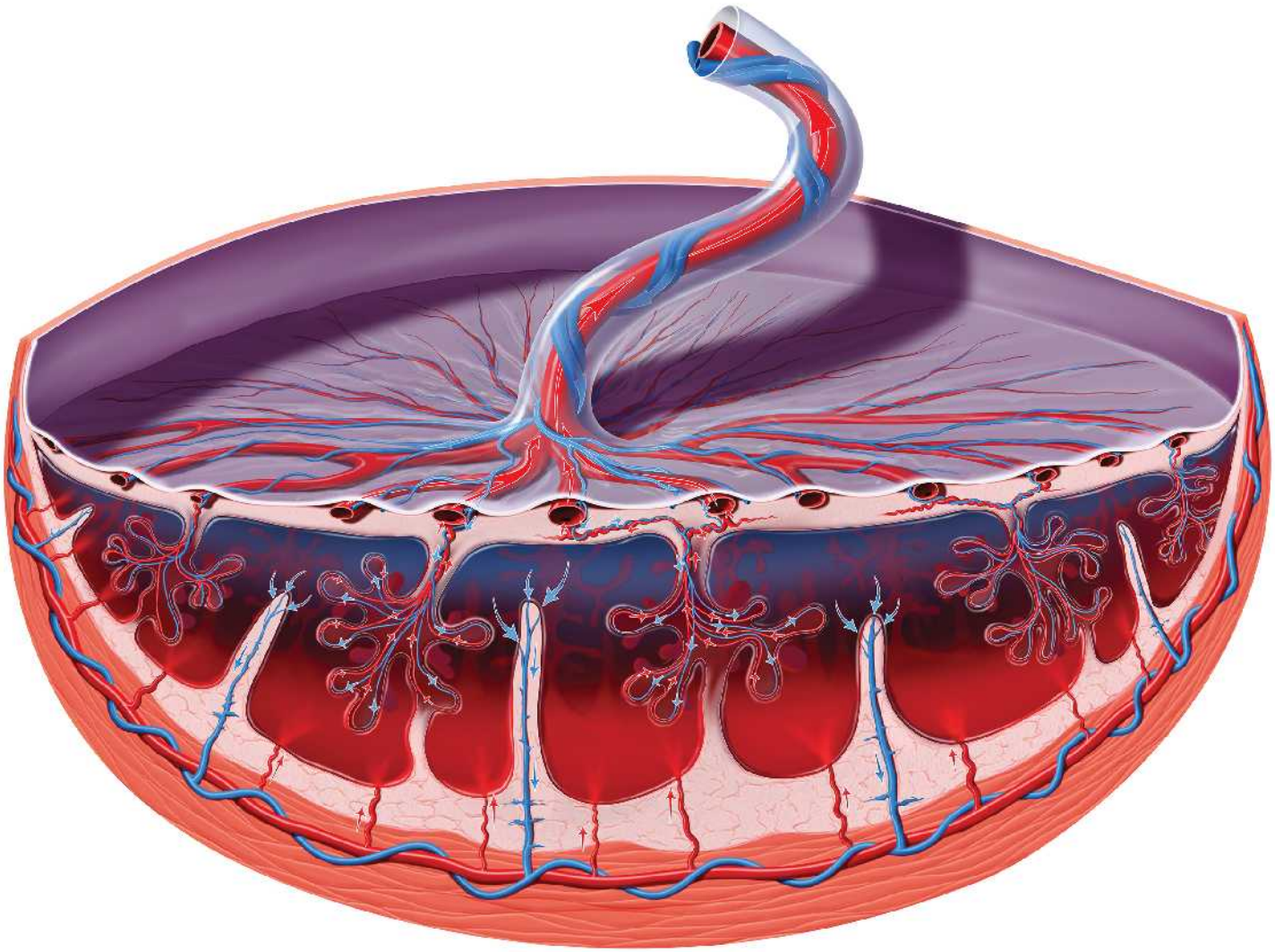

Diagnostic Imaging

Obstetrics

THIRD EDITION

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Dedications

The Past: To my parents—your support is my confidence, your encouragement is my achievements, your love is the person I am. The Present: To the FWCCM family—a mix of wonderful souls woven together with laughter and love. Proof family is what you make it. The Future: To Anthony—a bundle of excitement, joy, and delight. When viewing the world through your eyes, there is hope and promise in all things.

PJW

This one is for my mum and mothers everywhere. The umbilical cord is cut but the bond is never severed.

AK

To my David, whose generous love and spirit gives me strength and shelter.

RS

To all my wonderful patients who, often in times of great stress, have allowed me the privilege of photographing their children.

To Drs. Theresa Werner and Mark Dodson: With cancer survivors, there comes a point when you have to re-define your purpose in life. Often, it's when you discover that there's more to survival than just being alive—you have to go on living.

JLBB

To my families, both at home and at work—thank you for your support, guidance, and collaboration. I am ever grateful for your presence in my life.

KYO

To Brenda, for your neverending love and faith in me, I reach higher because of you. To Luli and Tristan, thank you for the love and laughter you bring into my life and for reminding me to see the world through a child's eyes.

MDP

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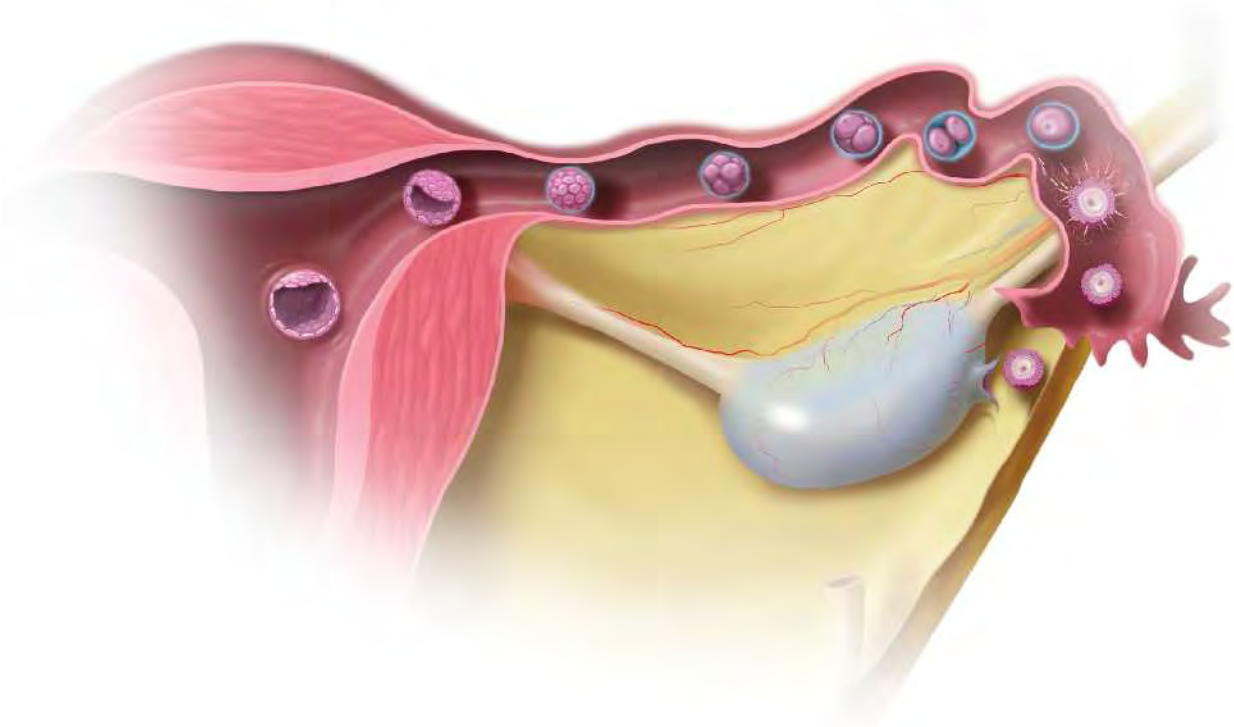

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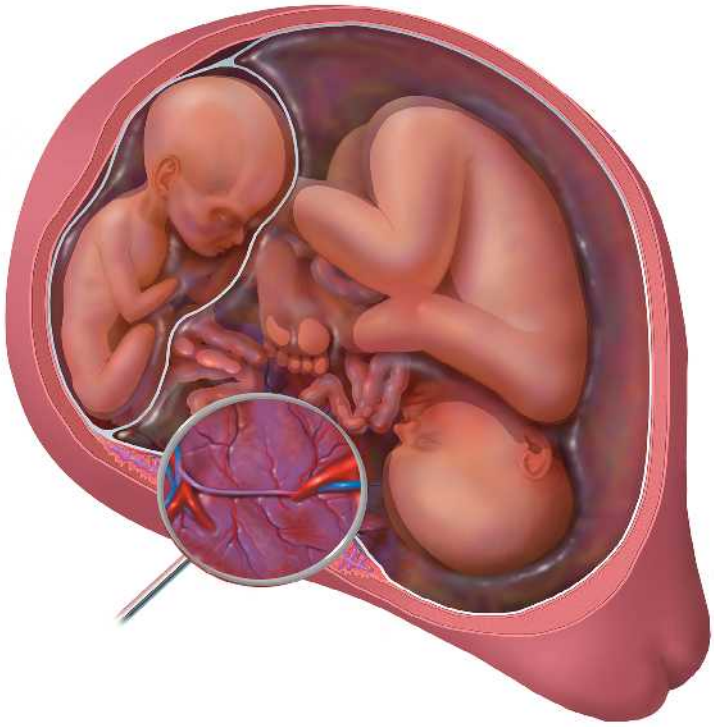

Preface

Truly, the third time is THE CHARM!

I have never been so excited about spearheading a project. My extraordinary team (and dear friends) includes a diverse group of fetal imaging experts, including authorities in radiology, perinatology, cardiology, and clinical genetics. The collaborative effort among the team members elevates each chapter to its highest attainable level of excellence. We are all dedicated to advancing the understanding and diagnosis of fetal diseases and remain humbly aware of how devastating these diagnoses can be for the affected family. This is why we, like you, carry a passion for making the correct diagnosis and providing the most complete information possible to patients and their families. Each chapter was written with the excitement of sharing our collective knowledge and life's work with you.

The first edition was revolutionary in that it offered a totally new style of textbook. Each chapter followed a highly structured, information-dense, bulleted style that yielded more "pearls per pound" than a standard prose-style textbook. This allowed for extensive image galleries, far more than in any other text of comparable size. In the second edition, we built on that foundation, adding section introductions, embryology, and anatomy chapters. Our first two editions were well received (thank you), and a question may rise, "Why write a third edition?" or better yet, "Why buy a third edition?" Realistically, our field has changed greatly in the last few years. The advent of new fetal testing and better fetal imaging equipment coupled with the patient's and referring physician's desire for earlier and more specific diagnoses has led to a need and call for "an update." We have been moved, like you, to not "rest on our laurels." No doubt, the third edition is different, bigger, and better. Here are just a few of the highlights:

- **New Pertinent Differential Diagnoses Sections:** Sometimes you have a finding but not a clear diagnosis. The cavum is absent, the kidneys look big, the head shape is funny—what could that mean? Each anatomic area now has a list of Pertinent Differential Diagnoses designed to address that very problem. Each chapter begins with an ordered list (most to least common). For each finding, there are imaging and clinical pearls, not to mention extensive image galleries, helping to distinguish the various entities. We feel this provides the user with a pragmatic approach to imaging findings.

- **Updated and New Chapters:** All previous chapters have been meticulously "revamped" and reflect the most up-to-date information and references. New chapters have been added where appropriate. Since the second edition, multiple specialty society consensus panels have convened and numerous guidelines have been published, all included in this third edition. These guidelines are considered new "standards of care." We have added many new tables for rapid reference to the most important information.

- **Updated Image Galleries:** Most importantly, all of the image galleries have been updated and are richly illustrated with multiple new graphics: 3D, grayscale, and Doppler ultrasound; fetal MR; and extensive clinical &/or pathologic correlation. There are more than 3,500 images, making this textbook, along with the digital gallery, one of the most comprehensive imaging reference resources on the market.

In addition to the physicians who worked on this book, it is important to acknowledge the talented sonographers and MR technologists for their fine work, which is used extensively throughout this text. I would also like to thank the wonderful Elsevier Salt Lake City editorial staff—with a special shout out to Jeff—and the medical illustrators who make this book truly special (Lane, you rocked it). I am most grateful to my co-leads, Anne and Roya—if I could put all our names as first author, you know I would.

It is with a great deal of pride that we present to you the third edition of *Diagnostic Imaging: Obstetrics*.

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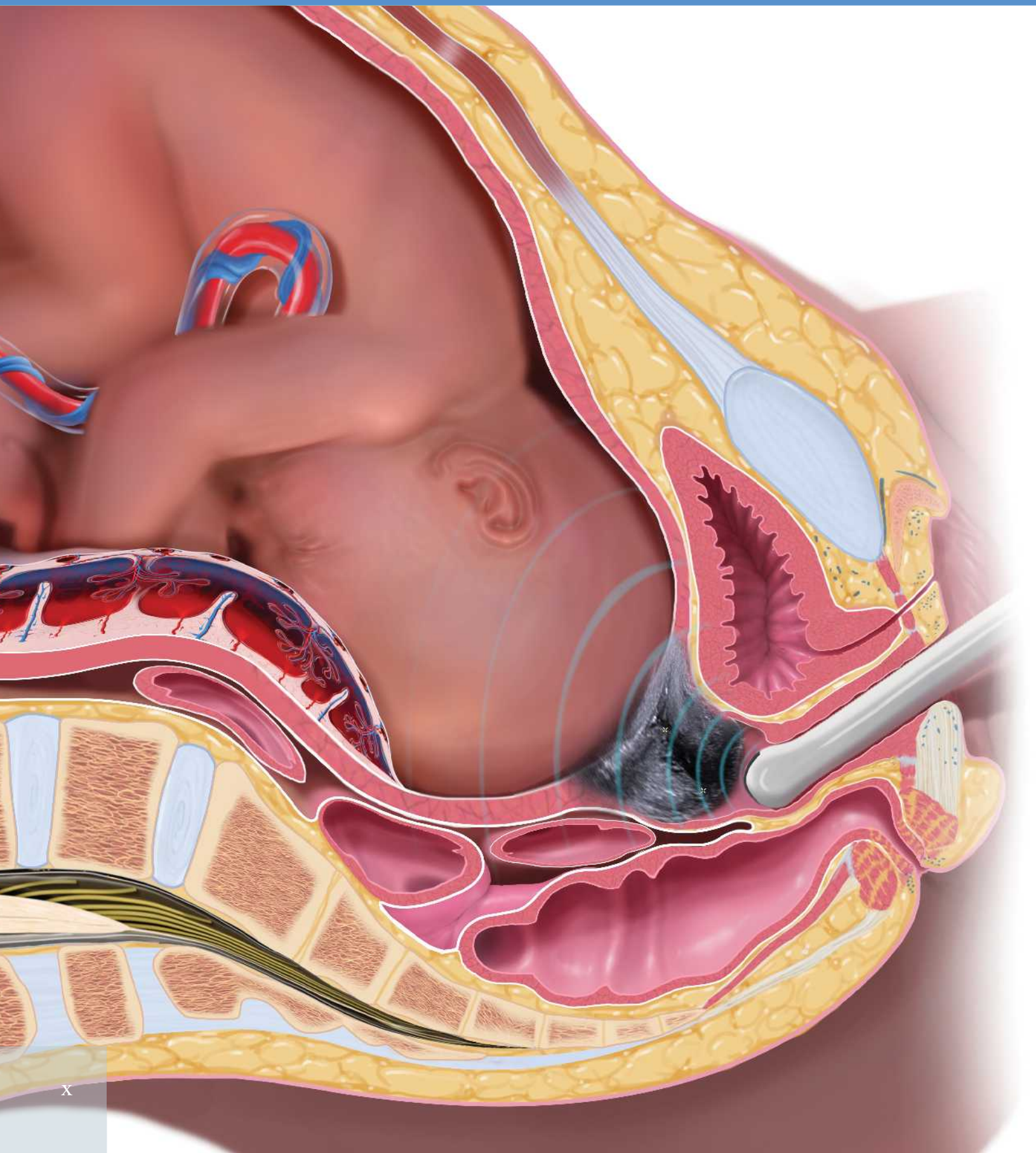

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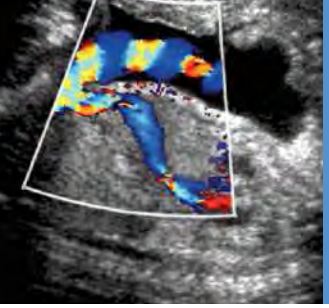

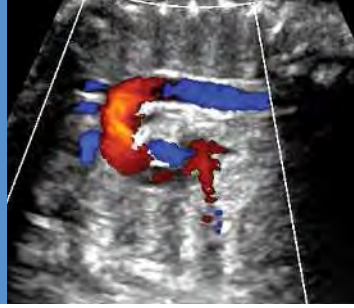

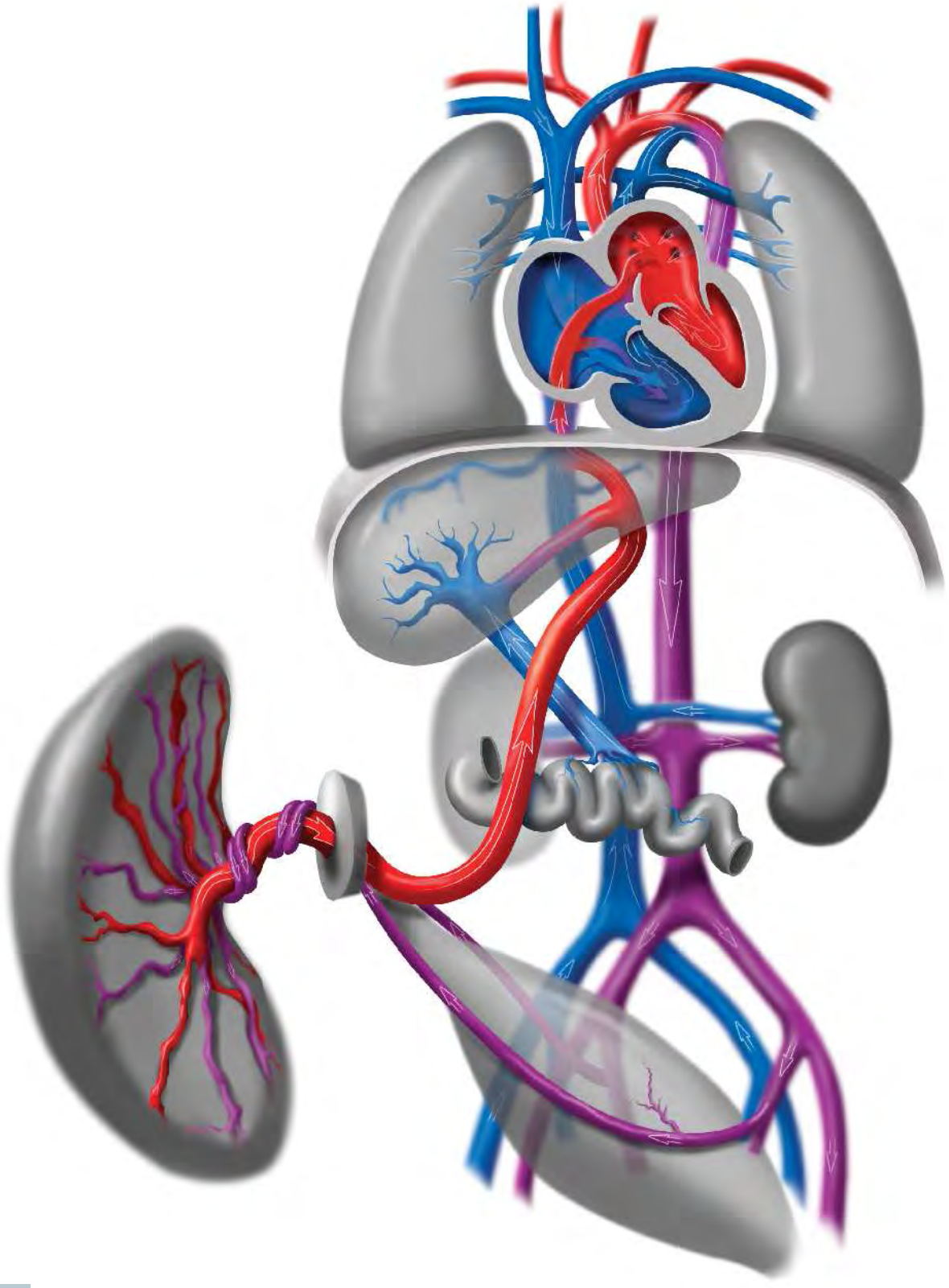

Sections

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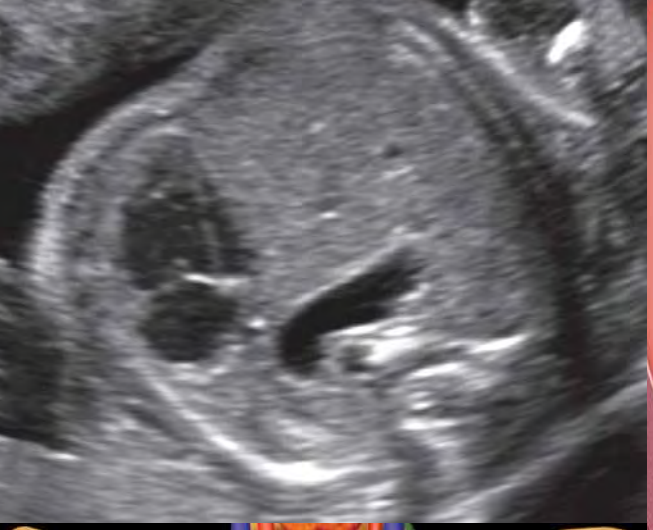

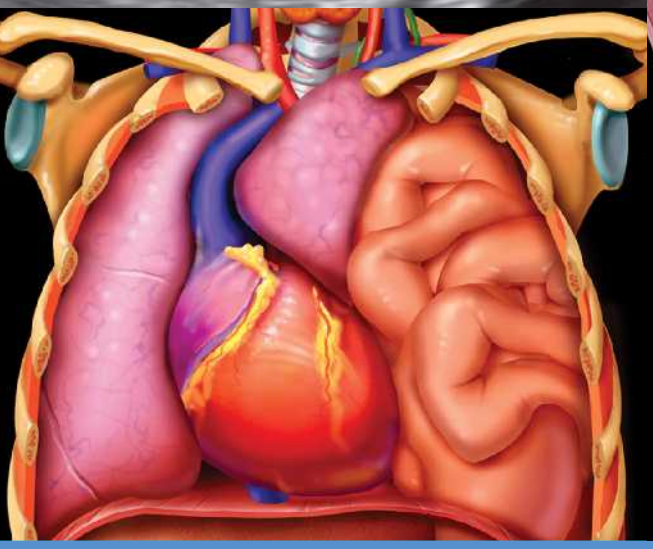

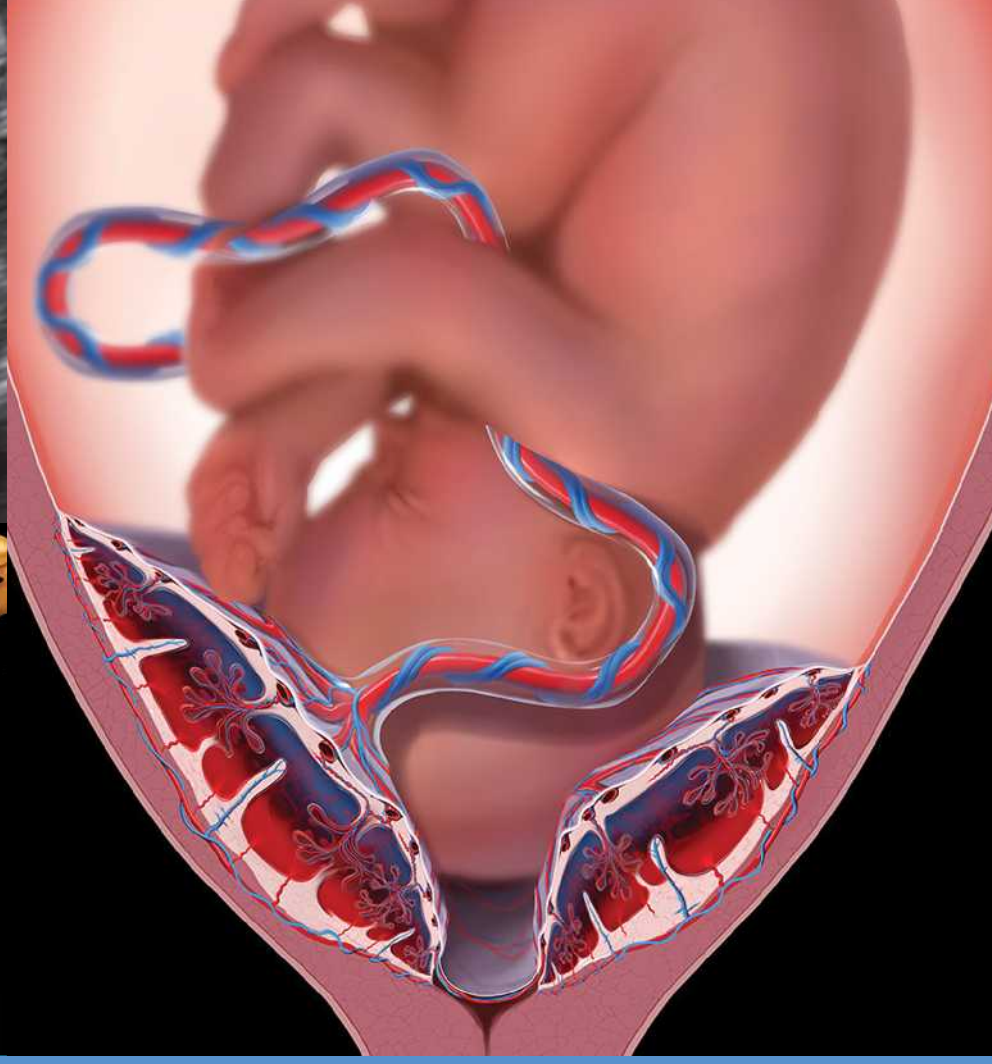

Diagnostic Imaging

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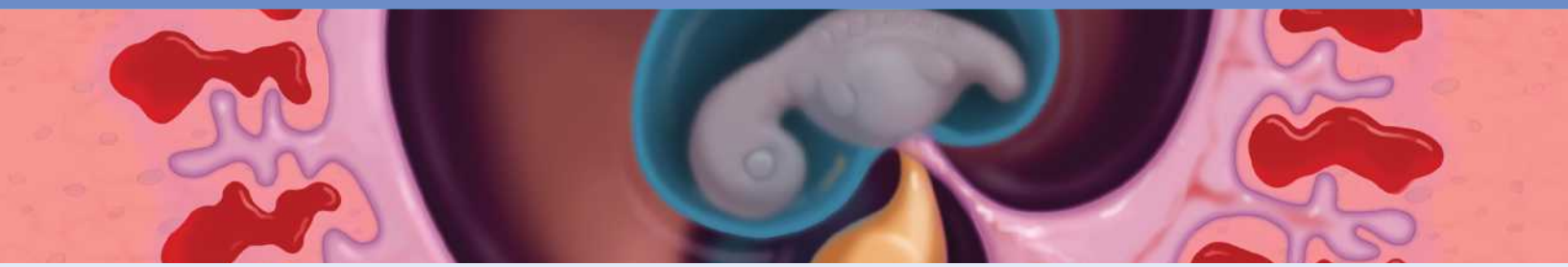
SECTION 1

First Trimester



TERMINOLOGY

Definitions

- 1st trimester covers time from 1st day of last menstrual period to end of 13th postmenstrual week

EMBRYOLOGY

Embryologic Events

- 1st trimester includes
  - Ovulation
  - Fertilization
  - Cleavage
  - Implantation
  - Embryonic development
  - Organogenesis
  - Placental development
  - Umbilical cord development

Ovulation

- Primordial follicles → 5-12 primary follicles per cycle
- All but 1 degenerate, leaving single dominant follicle
- Pituitary gonadotrophin surge → ovulation → oocyte extruded onto ovarian surface
- Oocyte surrounded by tough zona pellucida as well as layers of cumulus cells
- Fimbria sweep oocyte into fallopian tube
- Remaining "empty" follicle becomes corpus luteum producing estrogen and progesterone

Fertilization

- Occurs in fallopian tube
- Oocyte can be fertilized for ~ 24 hours
- Sperm penetrates oocyte, cell membranes fuse → zygote
- Spermatozoon and oocyte nuclei become male and female pronuclei
- Nuclear membranes disappear, chromosomes replicate in preparation for zygote cleavage

Cleavage

- Zygote → 2 cells → 4 cells → 8 cells → morula → blastocyst
- Several cell divisions result in smaller parts called blastomeres
- At 8 cell stage, compaction occurs with some cells → inner cell mass or embryoblast, some cells → peripheral trophoblast
  - Inner cell mass/embryoblast = embryonic pole of blastocyst
- 16-32 blastomeres = morula
- Morula absorbs fluid → central cavity called blastocoele within blastocyst

Implantation

- Blastocyst "hatches" from zona pellucida
- "Naked" blastocyst then interacts directly with maternal endometrium
- Trophoblast cells give rise to membranes and placenta, not embryo proper
  - Trophoblast cells at embryonic pole → syncytiotrophoblast, which burrows into endometrial lining
  - Remaining trophoblast cells become cytotrophoblast
- Maternal endometrial cells differentiate into decidual cells in response to
  - Progesterone secreted by corpus luteum
  - β human chorionic gonadotrophin produced by syncytiotrophoblast

Embryonic Development

- Bilaminar embryonic disc forms when embryoblast splits into epiblast and hypoblast
- Hypoblast = primitive endoderm
  - Hypoblast cells migrate around cavity of blastocyst to create primary yolk sac
  - Hypoblast + primary yolk sac give rise to extraembryonic mesoderm (loosely associated cells filling blastocyst cavity around primary yolk sac)
  - 2nd wave of migrating hypoblast cells create secondary yolk sac, which displaces primary yolk sac
  - Extraembryonic mesoderm splits into 2 layers, creating chorionic cavity (extraembryonic coelom)
  - Chorionic cavity separates embryo/amnion/yolk sac from chorion (outer wall of blastocyst)
- Epiblast contributes to embryo and gives rise to amnion
  - Fluid collects between epiblast and overlying trophoblast → cavity
  - Layer of epiblast differentiates into amniotic membrane separating new cavity from cytotrophoblast
- Trilaminar disc
  - Develops by process of gastrulation, which moves cells to new locations with resulting induction
  - 3 primary germ layers = ectoderm, mesoderm, endoderm
  - Body axes also determined by gastrulation
- Disc elongates and folds → series of tubular structures → major organ systems
- Ectoderm → neural plate → neural tube + neural crest cells
  - Neural tube → brain and spinal cord
  - Neural crest cells migrate from neural tube → many differing structures and cell types
- Mesoderm
  - Head mesoderm → muscles of face, jaw, and throat
  - Notochordal process
  - Cardiogenic mesoderm
  - Somites → most of axial skeleton
  - Intermediate mesoderm → genitourinary system
  - Lateral plate mesoderm → abdominal wall and gut walls
- Endoderm
  - Foregut, midgut, hindgut (oropharyngeal membrane → mouth)

Organogenesis

- **Central nervous system**
  - Arises from neural folds → neural tube + neural crest
    - Cranial/rostral 2/3 of neural tube → brain
    - Caudal 1/3 of neural tube → spinal cord, nerves
    - Neural crest → peripheral nerves, autonomic nervous system
- **Cardiovascular system**
  - Arises from cardiac tube → heart and great vessels
  - Cardiogenic precursors form 1° heart field at cranial end of embryo

- Lateral endocardial tubes brought together by embryonic folding → primitive heart tube
- Looping, remodeling, septation of primitive heart tube → definitive 4-chamber heart
- Conotruncus = primitive outflow tract that splits → ventricular outflow tracts

- **Respiratory system**
  - Foregut → respiratory diverticulum → 1° bronchial buds → 3 right + 2 left 2° bronchial buds → terminal bronchioles → respiratory bronchioles → primitive alveoli
- **Gastrointestinal system**
  - Early embryonic folding → endodermal tube → foregut, midgut, hindgut
  - Foregut (blind-ending at oropharyngeal membrane) → esophagus, stomach, proximal duodenum
    - Liver, gallbladder, cystic duct, and pancreas arise from duodenal diverticula
  - Midgut (initially open to yolk sac) → distal duodenum to proximal 2/3 transverse colon
    - Future ileum elongates rapidly → 1° intestinal loop, which herniates into base of umbilical cord rotating 90°
    - During retraction into peritoneal cavity, additional 180° rotation secures normal bowl orientation with cecum right, duodenojejunal flexure left
  - Hindgut (blind-ending at cloacal membrane) → distal 1/3 transverse colon to rectum
    - Terminal expansion of primitive hindgut tube → cloaca
    - Urorectal septum divides cloaca into urogenital sinus + dorsal anorectal canal
- **Genitourinary system**
  - Intermediate mesoderm → pronephros, mesonephros, metanephros
    - Mesonephros → rudimentary kidneys connected to cloaca by mesonephric ducts
    - Mesonephric ducts → ureteral bud → collecting system
    - Ureteral bud connection to metanephric blastema → induction of nephron formation
  - Bladder arises from cloaca and allantois
  - Bladder separated from rectum by urogenital sinus
- **Musculoskeletal system**
  - Upper and lower extremities develop from individual limb buds

Placental Development

- Chorionic sac initially covered in villi, atrophy of those adjacent to uterine cavity → chorion laeve
- In villi adjacent to implantation site, burrowing syncytiotrophoblast develops trophoblastic lacunae
  - Adjacent maternal capillaries expand → maternal sinusoids, anastomose with trophoblastic lacunae
  - Budding/proliferation of cytotrophoblast into syncytiotrophoblast and maternal lacunae → mature tertiary villi
  - Tertiary villi contain fully differentiated blood vessels for gas exchange in chorion frondosum
- Chorion frondosum + decidua basalis = placenta

Umbilical Cord Development

- Embryonic disc lies between amnion and yolk sac
- Embryo initially connected to chorion by connecting stalk, which arises from extraembryonic mesoderm
  - Allantois (endodermal hindgut diverticulum) arises as outpouching of yolk sac
  - Allantois and allantoic vessels extend into connecting stalk (become umbilical vessels)
- Embryonic growth and folding result in blind-ended foregut and hindgut tubes with midgut open to yolk sac
  - As body wall forms by lateral folding and midgut becomes tubular, yolk sac is "pinched off"
  - Narrow elongated neck of yolk sac = vitelline duct, which connects yolk sac to closing midgut tube
- As embryo enlarges and folds, amniotic cavity expands to encompass embryo completely except at umbilical ring
  - Connecting stalk, allantois, vitelline duct become incorporated as umbilical cord
  - Amnion continues to enlarge and forms tubular covering over incorporated cord elements → dense epithelial covering
- Progressive cord elongation and coiling occur with embryonic/fetal growth and movement

ANATOMY IMAGING ISSUES

Questions

- Developmental milestones (in weeks post LMP)
  - Gestational sac (intradecidual sac sign) usually visible by 4.0-4.5 weeks
  - Yolk sac usually visible by 5.0-5.5 weeks
  - Distinct embryo with cardiac activity usually visible by 6.0-6.5 weeks
- Developmental milestones based on mean sac diameter (MSD)
  - Embryo should be visible if MSD > 25 mm EV
- Embryo of > 7 mm in length must have cardiac activity
  - If embryo seen within visible amnion, cardiac activity should be present (expanded amnion sign)
- Gestational age assessment most accurate in 1st trimester
  - Biological variations take effect after 13 weeks
- Determination of chorionicity best done in multiple pregnancies
  - Most important factor in prognosis
- Is there evidence of increased risk for aneuploidy
  - 11- to 13-week scan can be used to adjust priori risk of aneuploidy, determine need for invasive testing
- Is anatomy normal
  - Organogenesis is complete by end of 13th week
  - Use EV sonography for best resolution
- 1st trimester is time of complex cell multiplication and differentiation
  - Great potential for error if normal processes are not clearly understood

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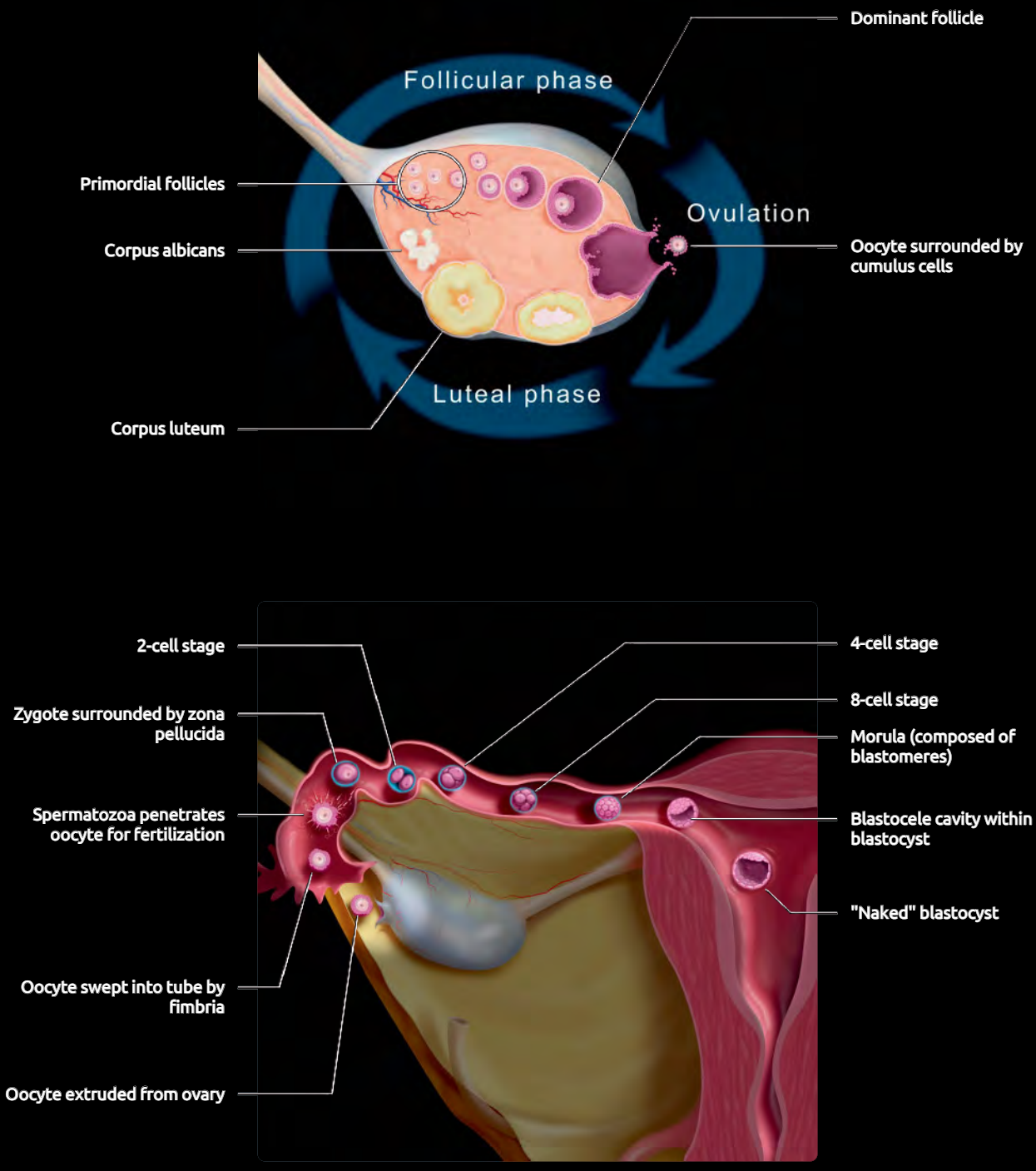
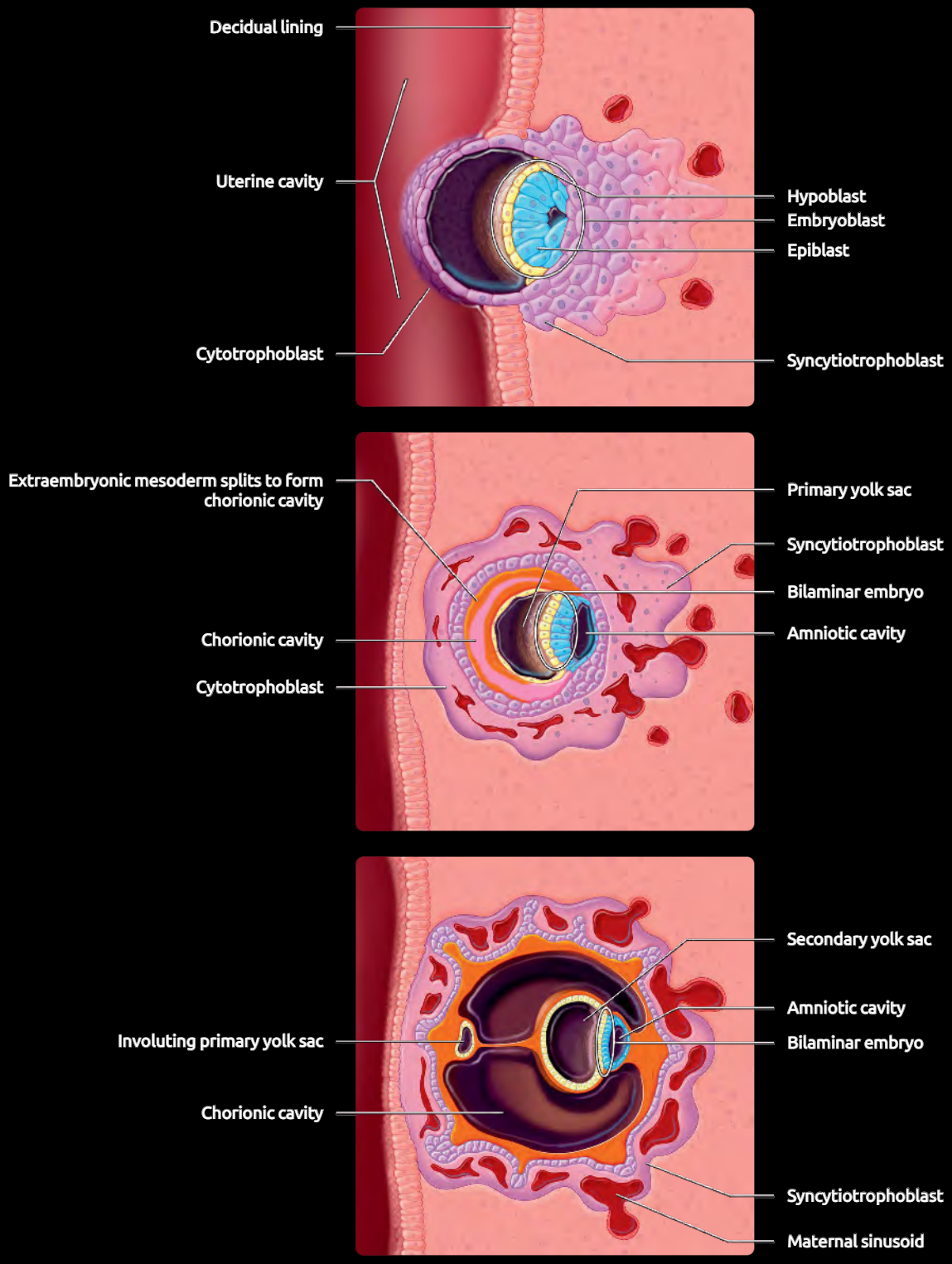
OVULATION AND FERTILIZATION



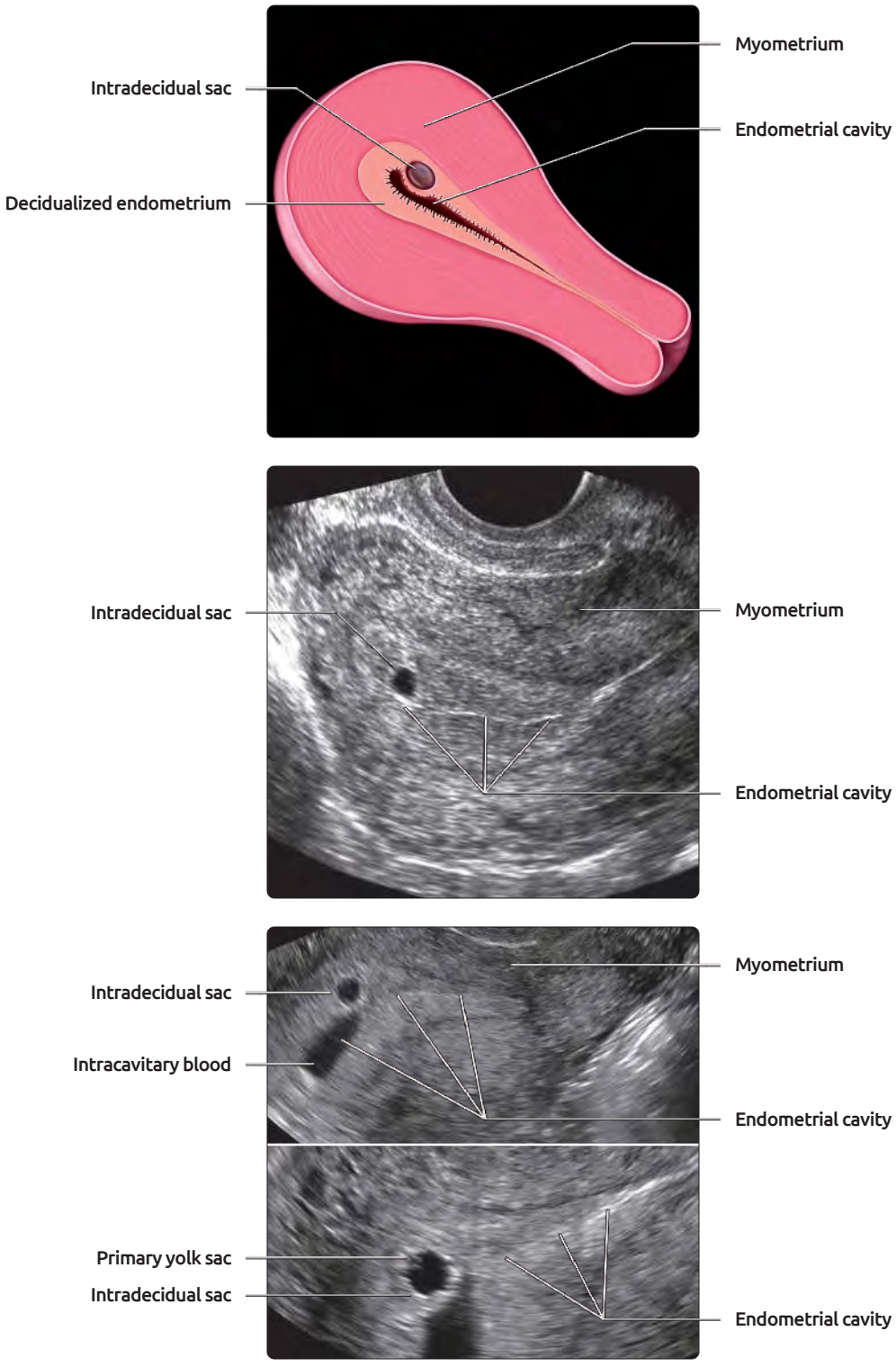
(Top) *During the follicular phase of the menstrual cycle, several follicles begin to develop; 1 becomes dominant and eventually a mature oocyte is extruded from the ovarian surface at the time of ovulation. The remaining follicle becomes the corpus luteum, which produces progesterone and helps to maintain the early pregnancy until the placenta is formed. If fertilization does not occur, the corpus luteum degenerates into a corpus albicans.* **(Bottom)** *The oocyte is swept into the fallopian tube where it is fertilized. The fertilized ovum divides repeatedly during passage along the tube such that by the time it reaches the endometrial cavity, a blastocyst has formed. The blastocyst "hatches" from the zona pellucida and implants into the maternal endometrium.*

CLEAVAGE AND IMPLANTATION



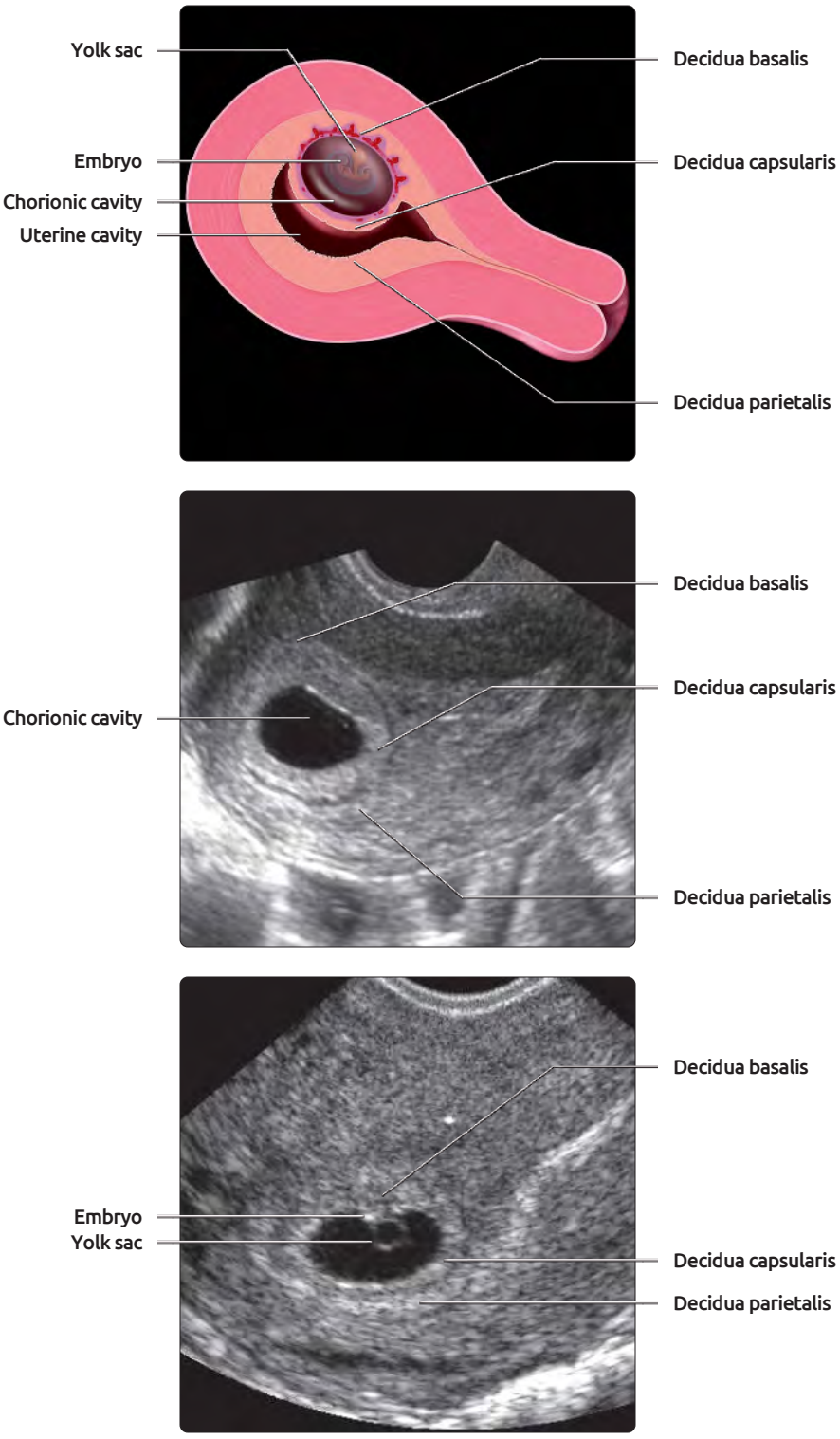
(Top) *While the dividing zygote is still in the fallopian tube (8-cell stage), cells differentiate into embryoblast and trophoblast. Syncytiotrophoblast interacts with the endometrium to form the placenta; the remainder is the cytotrophoblast. Embryoblast cells will give rise to the embryo, amnion, and yolk sac.* **(Middle)** *The embryoblast splits into 2 layers: Epiblast and hypoblast. The hypoblast gives rise to the primary and secondary yolk sacs and extraembryonic mesoderm. The latter splits, forming the chorionic cavity. The epiblast gives rise to the embryo and the amnion.* **(Bottom)** *As the primary yolk sac involutes, the secondary yolk sac develops. It is the secondary yolk sac that is visible sonographically; however, by convention, it is usually referred to as simply the yolk sac on ultrasound images. The chorionic cavity enlarges. The embryo is still a bilaminar disc.*

INTRADECIDUAL SAC SIGN



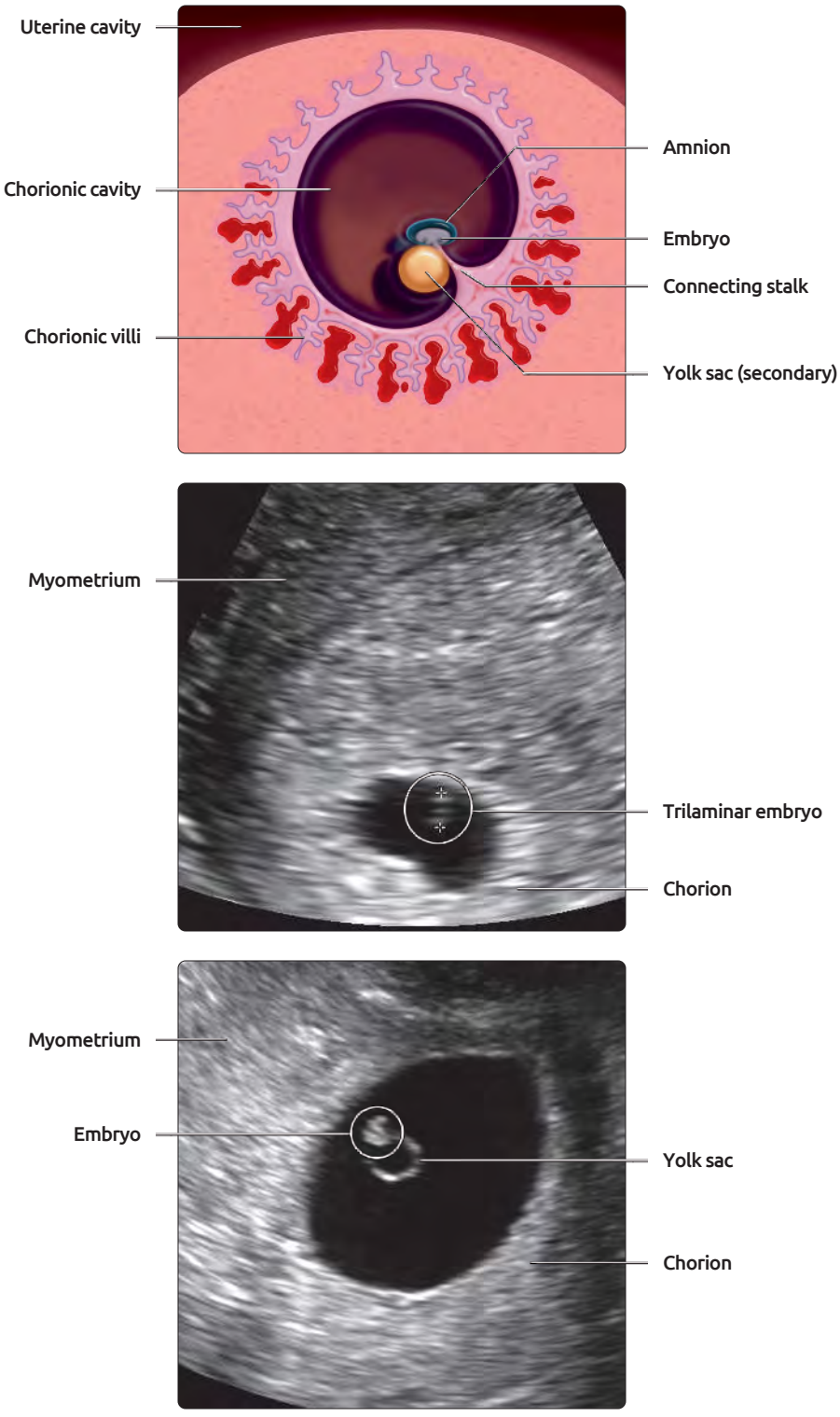
(Top) *The graphic illustrates the earliest sonographic manifestation of the embryological development illustrated previously. The gestational sac has burrowed into the decidualized endometrium, creating an asymmetrically placed echogenic ring with a lucent center. This was initially described as the intradecidual sac sign (IDSS). It is not always visible in early pregnancy and it is subject to considerable interobserver variability.* **(Middle)** *The intradecidual gestational sac is an echogenic ring eccentric to the line created by apposition of the endometrial surfaces. Currently, recommended terms for such an observation are intrauterine sac-like structure or probable intrauterine pregnancy.* **(Bottom)** *This is an example of the IDSS. In this example, bleeding has resulted in accumulation of blood in the endometrial cavity. Again, note the eccentric location of the 4-mm diameter sac. In the lower image, a tiny circular structure within the gestational sac is likely the primary yolk sac, which can be seen with high-resolution modern transducers.*

DOUBLE DECIDUAL SAC SIGN



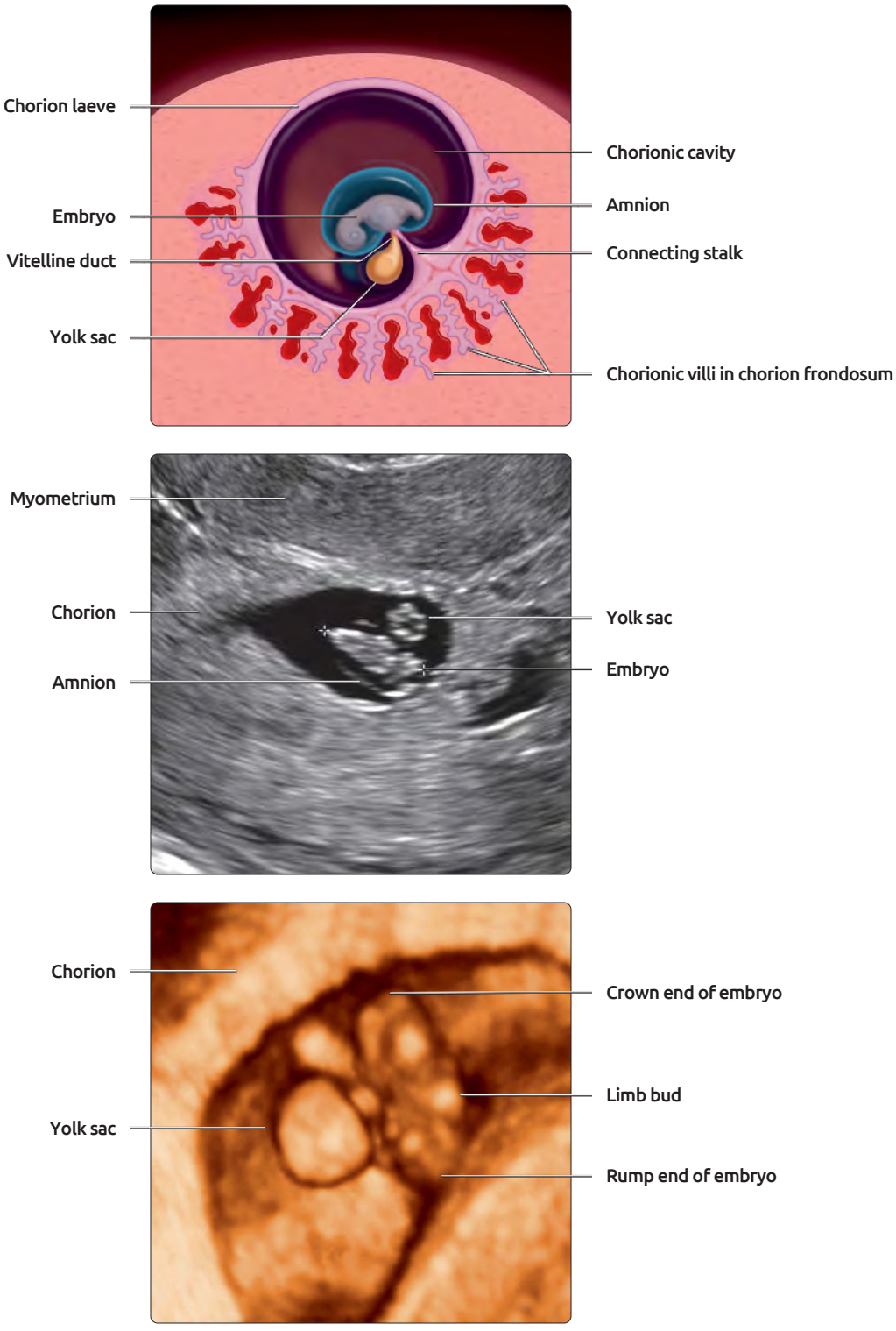
(Top) *This graphic illustrates the double decidual sac sign (DDSS). This is seen when the enlarging gestational sac protrudes from the site of implantation and starts to expand into the uterine cavity, exerting mass effect on the opposite uterine wall. The decidua covering the expanding sac is decidua capsularis; that which is being pushed ahead of the expanding sac is the decidua parietalis. The decidua basalis is where the sac is adherent to the uterine wall and marks the site where the placenta will develop. Internal structures may be seen on transvaginal scans.* **(Middle)** *The decidual layers are easily seen on this transvaginal scan. The concentric rings created by the decidua capsularis and parietalis create the DDSS. This finding is characterized as a probable intrauterine pregnancy.* **(Bottom)** *In this example, the embryo and yolk sac are visible in addition to the DDSS; this indicates a definite intrauterine pregnancy. It would also be a pregnancy of uncertain viability if there was no cardiac activity in an embryo < 7 mm in length.*

EMBRYONIC DEVELOPMENT: 6 WEEKS



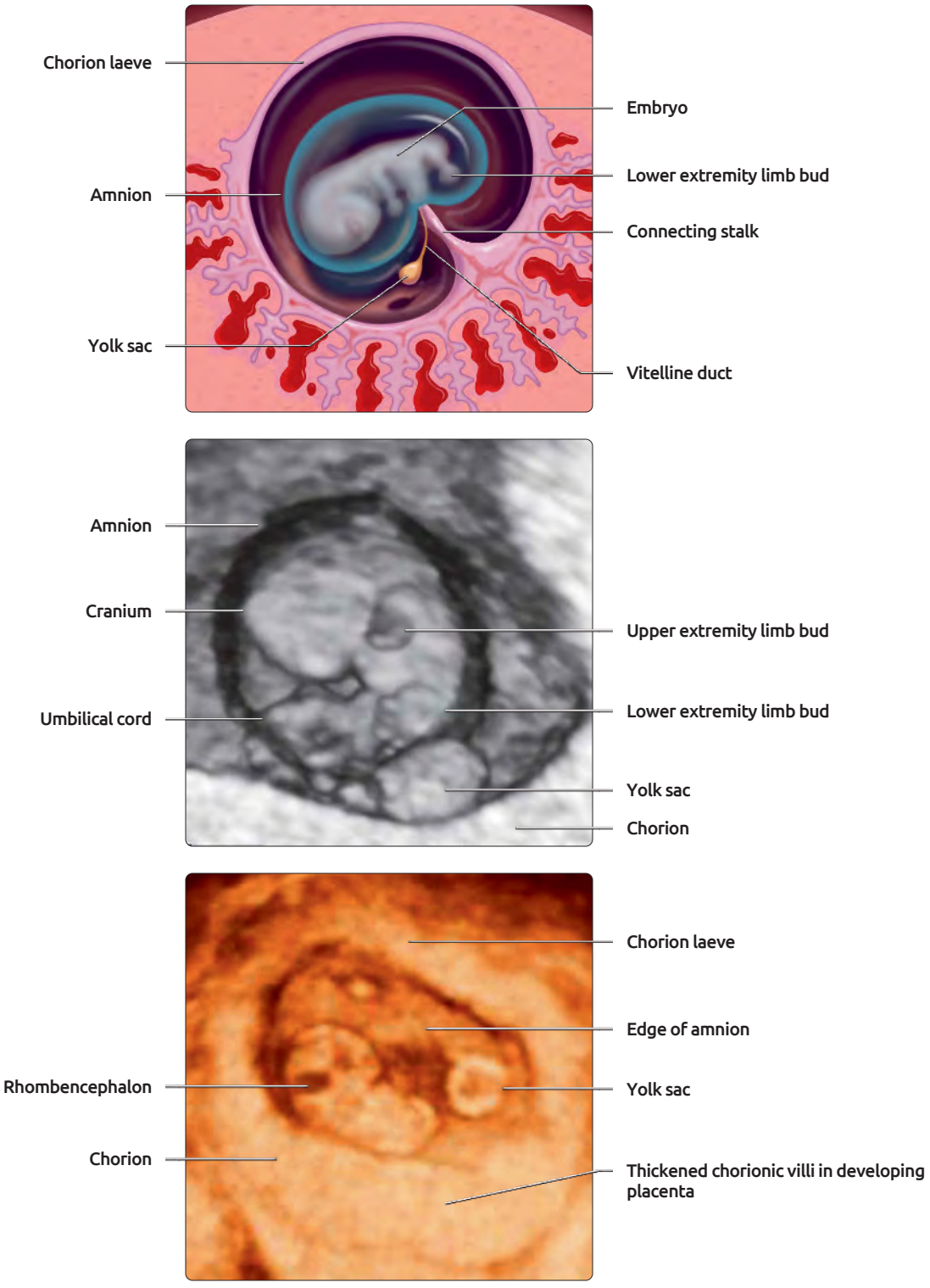
(Top) *The graphic illustrates normal early development. The embryo is intimately associated with the yolk sac such that the amnion and yolk sac appear as a double bleb with the embryo sandwiched between them. The embryo is within the amniotic sac; both the embryo and yolk sac are inside the chorionic sac.* **(Middle)** *Vaginal ultrasound at 5 weeks, 5 days from last menstrual period shows a 2-mm embryo. There are 3 linear echoes, which resemble an Oreo cookie. The process of gastrulation results in cellular movement with creation of the 3 primary germ layers; the endoderm, the mesoderm, and the ectoderm. Despite the tiny size of this embryo, cardiac activity was visible in real time.* **(Bottom)** *Vaginal ultrasound shows the embryo immediately adjacent to the yolk sac. The amnion is not yet visible. At this gestational age, the abdominal wall is still open, and the midgut is in continuity with the yolk sac. After the abdominal wall closes, the "discarded" yolk sac is compressed between the expanding amnion and the chorion.*

EMBRYONIC DEVELOPMENT: 7-8 WEEKS



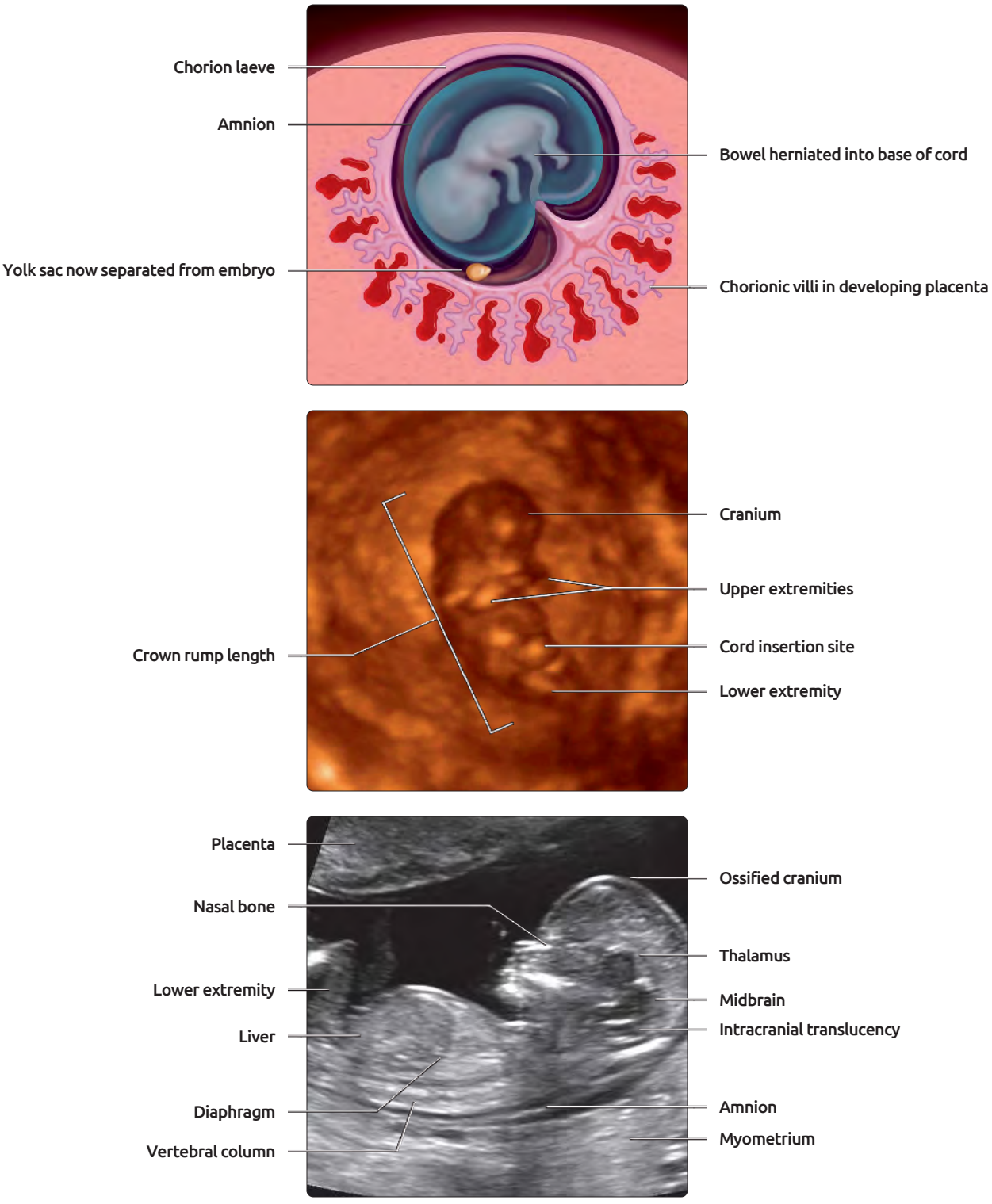
(Top) *Curvature and folding of the embryo result in closure of the abdominal wall and pinching off of the yolk sac. The elongated neck forms the vitelline duct. Eventually the yolk sac separates from the embryo, dropping into the chorionic cavity. At the same time, it becomes clear which end of the embryo is which, and limb buds start to form. The chorion adjacent to the uterine cavity is now completely smooth. Chorionic villi in the developing placenta become more complex in structure.* **(Middle)** *Vaginal ultrasound at 7 weeks, 4 days from LMP shows the yolk sac is separate from the embryo. It lies outside the amnion, which is now expanded enough to be just visible as it surrounds the embryo. Remember that the yolk sac will always be outside the amnion; the embryo lies inside the amniotic sac.* **(Bottom)** *3D surface-rendered ultrasound shows the yolk sac separate from the embryo, which now has an elongated configuration with defined cranial or crown and pelvic or rump ends. The crown rump length is measured to confirm menstrual dating.*

EMBRYONIC DEVELOPMENT: 8-9 WEEKS



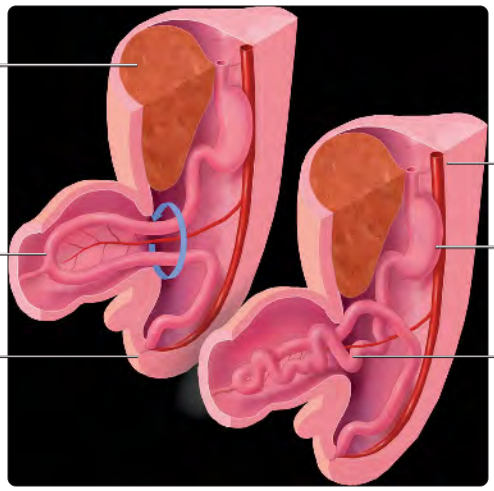
(Top) *The graphic illustrates continued embryonic development; the limb buds are evident, the head has grown dramatically, and the embryo is assuming a recognizable human form. The umbilical cord forms as a result of fusion of the vitelline duct, allantois, and connecting stalk. Once formed, it elongates rapidly until the embryo is suspended within the enlarging amniotic sac. Cord elongation allows for free mobility of the developing fetus.* **(Middle)** *3D surface-rendered ultrasound of an 8-week embryo show the short limb buds and the relatively thick umbilical cord. The crown end is assuming a more recognizable head shape and the embryo is curling into the typical fetal position.* **(Bottom)** *Another 3D ultrasound in the sagittal plane shows the rhombencephalic vesicle in the cranial part of the embryo. This fluid-filled space is a precursor of the 4th ventricle and should not be confused with a pathological intracranial cyst.*

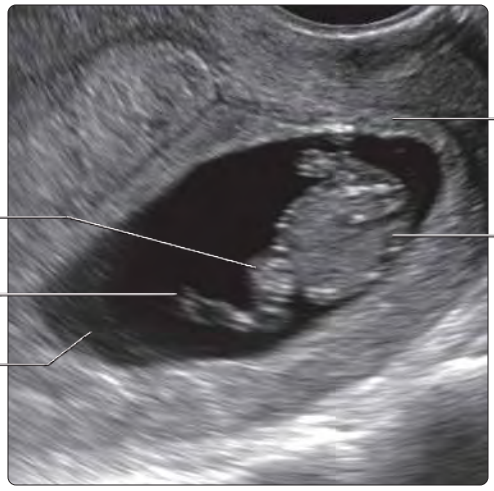
EMBRYONIC DEVELOPMENT: 10-13 WEEKS

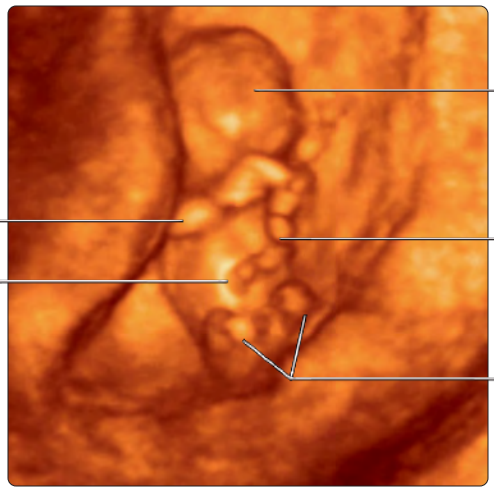


(Top) *Toward the end of the 1st trimester, the amnion fills the chorionic cavity. The membranes do not "fuse" until 14-16 weeks. The placenta continues to grow, and the chorionic villi develop an increasingly complex branching pattern.* **(Middle)** *3D surface-rendered ultrasound at 10 weeks shows increasingly recognizable fetal anatomy with a well-developed cranium and extremities. The abdominal wall cord insertion site is quite broad due to the physiologic herniation of bowel into its base. This occurs as the peritoneal cavity is too small to accommodate the rapidly growing bowel at this gestational age.* **(Bottom)** *Sagittal transabdominal ultrasound at 12 weeks, 6 days from LMP shows recognizable anatomic features. Organogenesis is completed by the end of the 13th week. Growth and maturation of the various organ systems occurs during the remainder of gestation.*

ABDOMINAL WALL AND GI TRACT

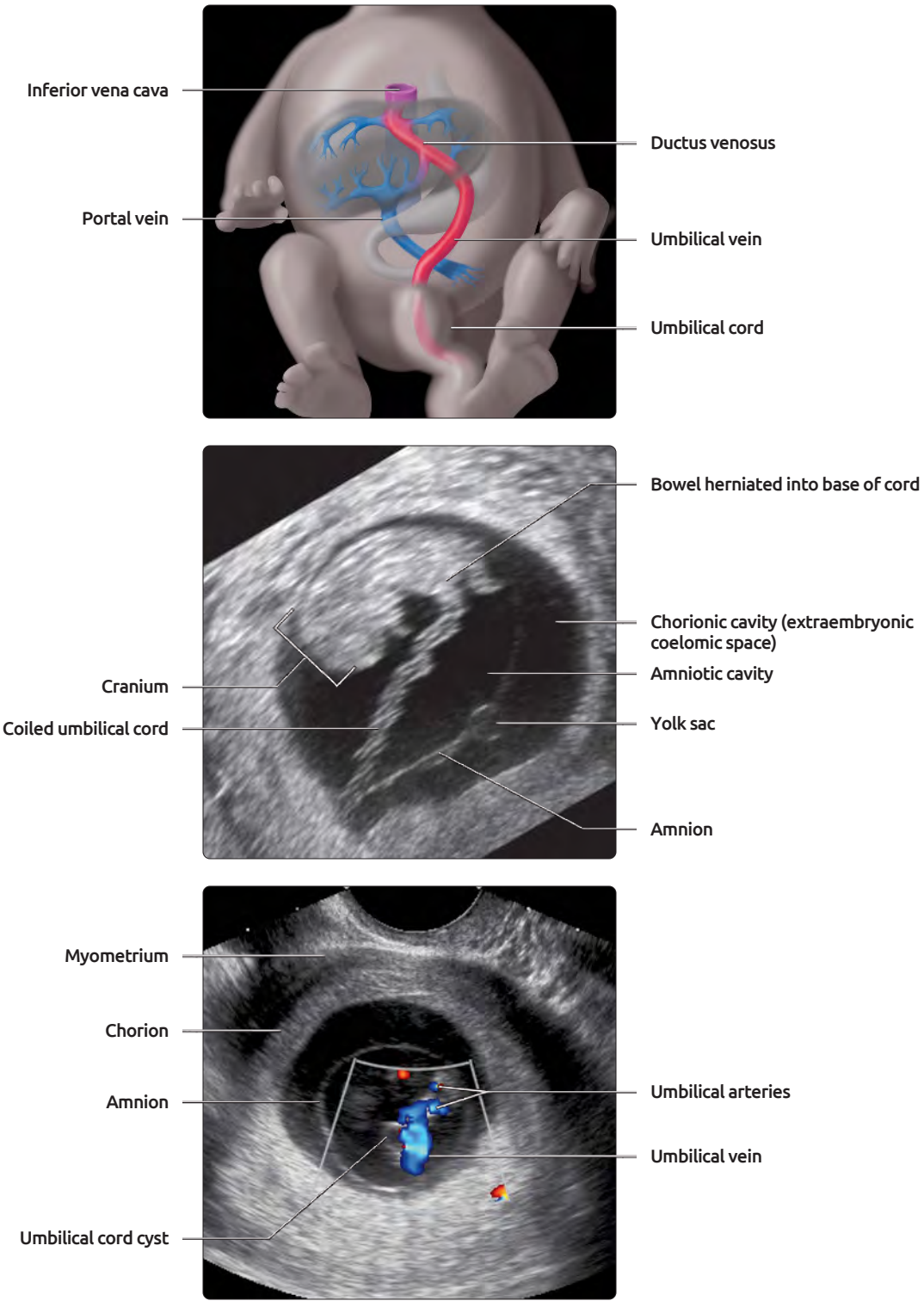






(Top) *The graphic illustrates herniation of bowel into the base of the cord in the 1st trimester. This happens as the gut tube elongates before there is adequate room to accommodate it in the peritoneal cavity. The gut undergoes a 90° counterclockwise rotation as it herniates and an additional 180° rotation as it is retracted into the peritoneal cavity. Only the gut herniates; liver is never normally seen at the base of the cord.* **(Middle)** *Vaginal ultrasound at 10 weeks, 3 days shows echogenic bowel at the base of the umbilical cord. This is normal at this gestational age and should not be misinterpreted as a bowel-containing omphalocele.* **(Bottom)** *3D surface-rendered ultrasound of a 12-week fetus shows a normal abdominal wall contour. The cord insertion is normal, and there is no residual bowel herniation. Three of the extremities are seen, the cranial contour is normal, and the cord is already coiled.*

UMBILICAL CORD DEVELOPMENT



(Top) *The graphic illustrates fetal circulation in which oxygenated blood from the placenta returns to the fetus via the umbilical vein. The umbilical vein courses through the left lobe of the liver to the left portal vein, across the ductus venosus into the inferior vena cava. The umbilical cord also contains 2 arteries, which arise from the internal iliac arteries.* **(Middle)** *At 10 weeks, there is some residual herniation of bowel into the base of the cord. The embryo is freely suspended within the amniotic sac by the cord, which already shows evidence of coiling. The yolk sac will be obliterated as the amnion apposes to the chorion.* **(Bottom)** *Color Doppler ultrasound shows a small umbilical cord cyst as an avascular area adjacent to the cord vessels. As a 1st-trimester finding this is usually of no significance; the cysts form at 8-9 weeks and usually resolve by ~ 12 weeks.*

Imaging Techniques and Normal Anatomy

Transvaginal ultrasound (TVUS) is the imaging modality of choice in the evaluation of the first-trimester pregnancy. In rare instances, a transabdominal ultrasound (TAUS) may be sufficient. For example, in cases where there is a known intrauterine pregnancy (IUP), but fetal cardiac activity is not heard, TAUS may be used to verify that the embryo is still alive.

The sonologist performing the examination must be familiar with the appearance of a normal early pregnancy, ectopic gestation, and failed pregnancy. Misunderstanding of normal anatomy and developmental milestones may lead to an incorrect diagnosis and incorrect treatment. Administration of methotrexate to a patient with an IUP must be avoided.

In 2013, the Consensus Panel on Diagnostic Criteria for Nonviable Pregnancy Early in the First Trimester published guidelines for determination of pregnancy failure and established definitions for terms that, though commonly used, were often misunderstood. As defined by the Consensus Panel, a viable pregnancy is one that can potentially result in a liveborn baby.

Additionally, new descriptive terms have been suggested for use in early pregnancy. The term probable IUP is defined as an intrauterine echogenic sac-like structure without a yolk sac or embryo. The term definite IUP is defined as an intrauterine sac-like structure with a yolk sac or embryo, whether or not there is cardiac activity.

The consensus panel discouraged the use of the terms intradecidual sac sign (IDSS) and double decidual sac sign (DDSS), as they are not present in all early pregnancies and are subject to interobserver error. Nonetheless, they are described below, and both fit under the umbrella term probable IUP.

The IDSS manifests as a spherical, cystic structure eccentric to the central echo of the uterine cavity. Embryologically, it corresponds to the time of implantation when the early embryo burrows into the decidualized endometrium.

The expanding gestational sac creates two echogenic rings or the DDSS. The decidual capsularis is the outward expansion of the trophoblastic tissue; it creates the inner ring, whereas the decidual parietalis of the surrounding uterine cavity creates the second peripheral, outer ring. The focal thickened decidua at the site of implantation is referred to as the decidua basalis.

When a gestational sac without a yolk sac is seen in the uterus, the lack of a live embryo 14 days later is diagnostic of pregnancy failure.

Following visualization of the DDSS, the next visible sonographic milestone is the yolk sac**.** The amnion forms embryologically before the yolk sac, but it is such a thin, delicate membrane that it is resolved later, even with TVUS. The yolk sac has a distinct wall, smooth outline, and spherical shape with a maximum diameter of 6 mm. An intrauterine sac with a yolk sac is considered a definite IUP. When a yolk sac is seen, the lack of a live embryo 11 days later is diagnostic of pregnancy failure.

The embryo is first resolved as a focal thickening at the circumference of the yolk sac. Cardiac activity may be seen as a flickering in this area before the embryo is sufficiently large enough to allow accurate measurement. Once the embryo is discretely resolved, the longest axis is measured and referred to as the crown rump length.

When the abdominal wall closes during the process of gastrulation, the yolk sac is pinched off the embryo and will eventually be compressed between the amnion and chorion at the time of membrane fusion. Thus, if the yolk sac is seen separate from the embryo, that embryo has undergone the process of gastrulation and should have a visible heart beat. Lack of cardiac activity in this setting is called the yolk stalk sign.

Initially, the embryo fills the amnion. As the pregnancy progresses, the embryo becomes suspended from the umbilical cord within the enlarging amniotic sac. This is a very important observation; the embryo is always inside the amnion, and the yolk sac is always outside the amnion. If the amnion is visible, the embryo should also be visible. If not, this is the empty amnion sign. If an embryo is present within a visibly expanded amniotic cavity, it should manifest cardiac activity. If absent, this is the expanded amnion sign. Although not included in the consensus guidelines, the empty amnion, expanded amnion, and yolk stalk signs of failed pregnancy are described in peer-reviewed articles.

The embryo visibly changes shape from a dot to a grain of rice to a more kidney bean-shaped structure. Then, limb buds develop, and the head, torso, and extremities can be resolved. At 10 weeks post last menstrual period (LMP), the embryo officially becomes a fetus. By 13 weeks post LMP, organogenesis is complete.

Approach to the First Trimester

Where Is the pregnancy?

Many patients present to the sonologist with a history of a positive pregnancy test and vaginal bleeding. In this situation, the differential diagnosis includes a normal IUP vs. abnormal pregnancy vs. complete abortion vs. ectopic pregnancy.

The term pregnancy of unknown location (PUL) has been coined to describe the situation in which there is a chemical pregnancy with no evidence of either an IUP or an ectopic by TVUS. Thus, it is vital that the sonologist knows the signs of IUP as well as those of ectopic pregnancy. In particular, it is important to evaluate the adnexa carefully for mass, tubal ring, and echogenic free fluid. The normal corpus luteum should not be mistaken for an ectopic pregnancy. Prominent flow around the corpus luteum is a normal observation and should not be confused with the ring of fire sign of trophoblastic flow around an ectopic gestation. Blood products may appear as an oval or flattened fluid collection placed centrally in the uterine cavity in association with an ectopic pregnancy. The term pseudosac of ectopic pregnancy is discouraged as it is imprecise and can be misleading. The shape of the fluid collection should be characterized as round/oval or pointy edged with the former much more likely to represent an IUP than the latter.

If the patient is stable, it is always wise to be conservative. Normal early pregnancies develop in a standard manner with rapid changes in a short time frame. In the case of PUL, either an IUP or an ectopic gestation should become visible within days.

In heterotopic pregnancy, an IUP coexists with an ectopic gestation. This is rare in the normal population but is not uncommon in patients with risk factors, such as tubal scarring or a history of assisted reproduction. Medical management is contraindicated in heterotopic pregnancy as systemic methotrexate administration would be harmful to the IUP.

Nomenclature in First Trimester

Recommended Terminology	Definition
Viable pregnancy	One that may potentially result in liveborn baby
Nonviable pregnancy	One that cannot possibly result in liveborn baby; examples include ectopic and failed intrauterine pregnancies (IUPs)
Pregnancy of unknown location	Positive pregnancy test (urine or serum) with no signs of intrauterine or extrauterine gestation on transvaginal ultrasound
IUP of uncertain viability	IUP with embryo < 7 mm without cardiac activity or mean sac diameter < 25 mm without embryo
Definite IUP	Intrauterine gestational sac with yolk sac ± embryo ± cardiac activity
Probable IUP	Intrauterine echogenic sac-like structure without yolk sac or embryo
Definite ectopic	Extrauterine gestational sac with yolk sac ± embryo ± cardiac activity
Probable ectopic	Inhomogeneous adnexal mass or extrauterine sac-like structure

Use of consistent terminology is important to avoid confusion and to collect accurate information for outcome studies.

Terminology reproduced from Doubilet PM et al: Diagnostic criteria for nonviable pregnancy early in the first trimester. N Engl J Med. 369(15):1443-51, 2013 and from Barnhart K et al: Pregnancy of unknown location: a consensus statement of nomenclature, definitions, and outcome. Fertil Steril. 95(3):857-66, 2011.

First-Trimester Milestones

Embryo Should Be Visible	
	When mean sac diameter is ≥ 25 mm by transvaginal ultrasound (TVUS)
Cardiac Activity Should Be Present	
	If embryo is ≥ 15 mm in length by transabdominal ultrasound
	If embryo is ≥ 7 mm in length by TVUS
	≥ 14 days from visualization of a gestational sac without yolk sac
	≥ 11 days from visualization of a gestational sac with yolk sac

Reproduced from Doubilet PM et al: Diagnostic criteria for nonviable pregnancy early in the first trimester. N Engl J Med. 369(15):1443-51, 2013.

Criteria to Change Menstrual Dating

Gestational Age by Last Menstrual Period	Use Sonographic Dates if Difference Is
≤ 8 6/7 weeks	> 5 days
9 0/7 weeks to 15 6/7 weeks	> 7 days
16 0/7 weeks to 21 6/7 weeks	> 10 days
22 0/7 weeks to 27 6/7 weeks	> 14 days
28 0/7 weeks onward	> 21 days

Sonographic gestational age is assessed by crown rump length to 13 6/7 weeks. Thereafter, use head circumference, biparietal diameter, femur length, and abdominal circumference.

Committee opinion no. 611: method for estimating due date. Obstet Gynecol. 124(4):863-6, 2014.

How Many Embryos Are There?

Once the diagnosis of IUP is established, it is essential to scan the entire pelvis to document the number of embryos. Müllerian duct anomalies are a possible pitfall; if an incomplete scan is performed, a bicornuate or septate uterus may not be appreciated. Multiple pregnancies may occur with implantation in one or both horns.

Perigestational hemorrhage (PGH) should not be confused with an IUP. A PGH is usually crescentic in shape and located deep to the echogenic ring of chorionic tissue; there will be neither an embryo nor a yolk sac.

Determination of chorionicity is crucial in all multiple gestations. The chorion forms a thick echogenic ring that completely encompasses the embryo. If more than one embryo is seen within a single chorionic ring, the pregnancy is monochorionic. The next step is to determine amnionicity. As mentioned, the amnion is a very delicate membrane that may not be seen in early gestation. However, the number of yolk sacs often parallel the number of amnions; therefore, if there are two embryos and two yolk sacs, it is likely that the pregnancy is a monochorionic diamniotic twin gestation. If only one yolk sac is seen after a complete sweep through the gestational sac in longitudinal and transverse planes, the pregnancy may be monoamniotic or the embryos may be conjoined. Conjoined twins maintain a fixed relationship to each other and have an area of contiguous skin covering differentiating them from monoamniotic twins that move

independently of each other and are completely separate, even if mobility is limited by cord entanglement.

What Is the Gestational Age?
The normal menstrual cycle is 28 days, and the assumption is made that conception occurs on day 14 of the cycle. In the absence of a menstrual history, a first-trimester ultrasound is the most accurate way to determine gestational age as there is little biological variation in the first trimester. Correct gestational age is essential for assessment of growth in the second and third trimesters.

Is the Pregnancy Normal?
Modern equipment provides exquisite resolution and allows for a quite detailed anatomic assessment by the end of the first trimester. Between 11 and 13 weeks, nuchal translucency, facial angle, tricuspid regurgitation, ductus venosus flow, and nasal bone assessment can be used to select a group of fetuses at higher risk for aneuploidy. The availability of cell-free fetal DNA testing has changed prenatal screening for aneuploidy; however, early anatomy scans have the additional benefit of allowing detection of structural abnormalities, such as abdominal wall defects, limb reduction abnormalities, and central nervous system malformations, including neural tube defects and alobar holoprosencephaly. None of these major birth defects can be detected by cell-free fetal DNA testing.

In multiple gestations, evaluation of nuchal translucency and ductus venosus flow can be used to detect monochorionic pairs at increased risk for complications, such as twin-twin transfusion syndrome as well as for aneuploidy screening.

Assessment of uterine artery Doppler waveforms may be helpful to select patients at increased risk for preeclamptic toxemia, thus allowing more intensive surveillance.

What About the Uterus and Adnexa?
The first-trimester scan is not restricted to evaluation of the embryo/fetus. It is important to look at the uterine contour, document fibroid size and location, assess for possible müllerian duct anomalies, and note the presence of nabothian cysts or Gartner duct cysts that might cause a confusing appearance on a TAUS evaluation of the cervix later in gestation.

The majority of adnexal masses seen in pregnancy are benign. However, particularly with advancing maternal age, ovarian neoplasms may be detected. Even a benign neoplasm, such as teratoma, may undergo torsion. If the presence of an adnexal mass is known, the evaluation of a patient with acute onset of abdominal or pelvic pain in pregnancy is much simplified.

The appearance of the corpus luteum is highly variable from a small, crenulated, involuting, thick-walled cyst to the complex appearance seen with hemorrhage. Corpus luteal cysts may reach several centimeters in diameter; they should resolve by 16 weeks post LMP.

Clinical Implications

First-trimester scans provide accurate information on gestational age, assist in screening for aneuploidy, exclude several major malformations, and are vital in determination of chorionicity in multiple pregnancies. It behooves all US practitioners to use stringent standards in the determination of embryonic demise or early pregnancy failure. "First do no harm...to early pregnancies" is a good rule of thumb to practice.

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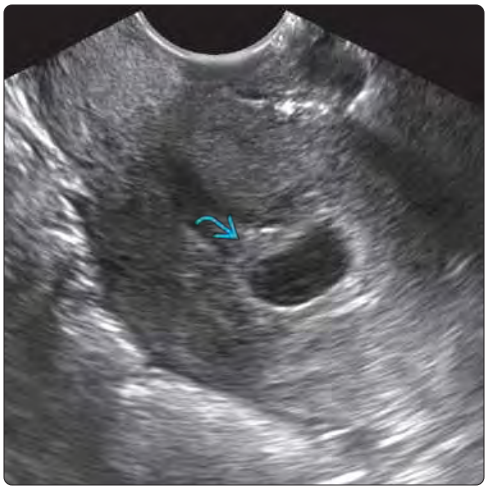
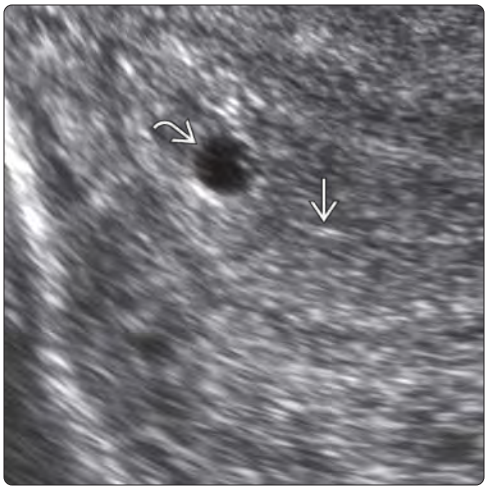
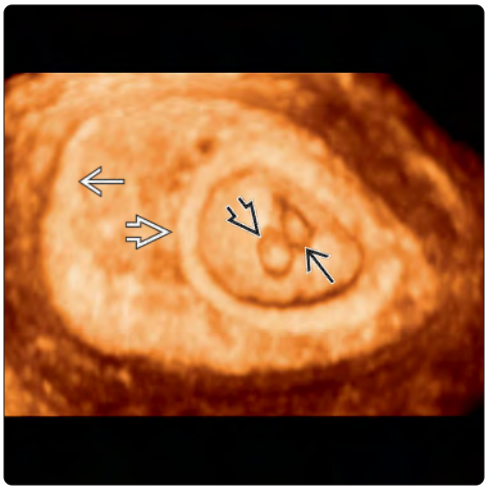
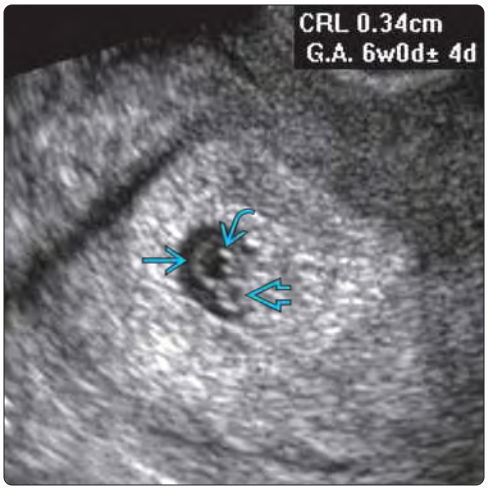


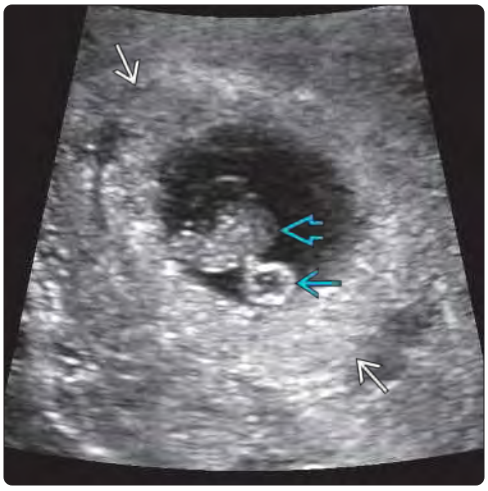


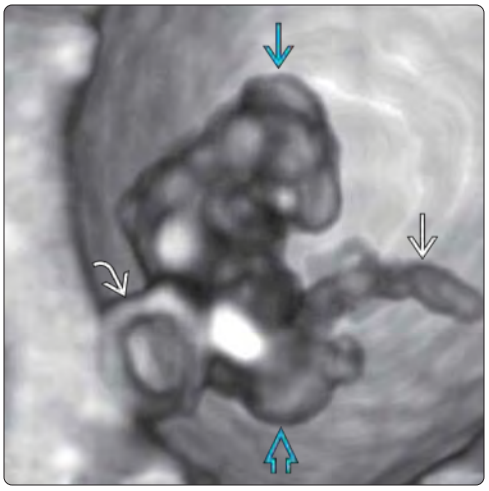
(Left) *TVUS shows an intrauterine sac-like structure. In the setting of a positive pregnancy test, this finding is statistically most likely to represent an intrauterine pregnancy (IUP). This example is of a normal pregnancy in which the DDSS is not appreciated. Recommended description for this sort of finding is probable IUP.* **(Right)** *TVUS shows the IDSS with a small, round fluid collection eccentric to midline uterine cavity echo. The more generic term, intrauterine sac-like structure, is now preferred to describe this observation.*



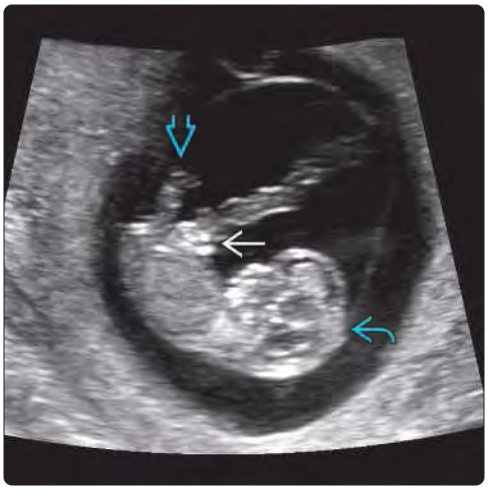


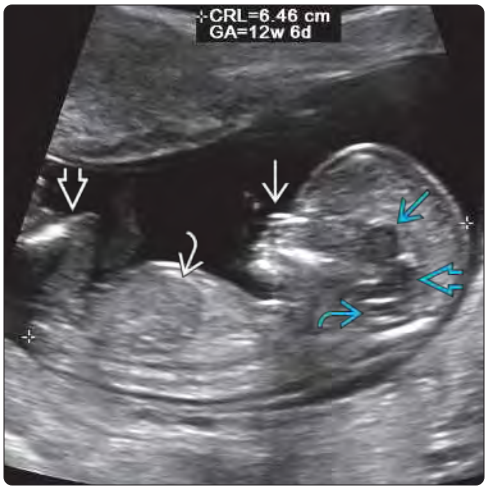
(Left) *3D US shows the layers of the DDSS sign. The inner decidua capsularis is surrounded by the outer decidua parietalis. The amnion and yolk sac are inside the gestational sac. The generic term, intrauterine sac-like structure, is now recommended rather than DDSS.* **(Right)** *TVUS shows a more advanced definite IUP in which the yolk sac is adjacent to the amnion, which surrounds the more elongated embryo. The embryonic shape is now closer to a grain of rice than a dot.*





(Left) *TVUS shows a definite IUP: An intrauterine gestational sac with a yolk sac and an embryo. Note that neither an embryo nor cardiac activity is a prerequisite for use of this descriptor.* **(Right)** *3D US shows the more kidney bean-shaped embryo with a defined crown or head end and a smaller tail or rump end. Note the separated yolk sac and elongated umbilical cord.*





(Left) *TVUS shows bowel herniation into the base of the umbilical cord. This is a normal embryological event. Note how clearly the cranial structures and facial profile are seen, whereas the rump end of the embryo looks smaller, and the lower extremities are still quite short.* **(Right)** *At 13 weeks, organogenesis is complete. In this fetus, the nose, diaphragm, and a lower extremity are clearly visible, as are the thalamus, midbrain, and the early 4th ventricle a.k.a. intracranial translucency.*

Failed First-Trimester Pregnancy

KEY FACTS

TERMINOLOGY

- Pregnancy is considered viable if it can potentially result in live birth
- Nonviable pregnancy is one that will not result in live birth

IMAGING

- Criteria for nonviable pregnancy on transvaginal sonography
  - Mean sac diameter > 25 mm without embryo
  - Crown rump length ≥ 7 mm without cardiac activity
  - Cessation of previously documented cardiac activity regardless of crown rump length
- Time follow-up intervals for definitive diagnosis of failure
  - Lack of live embryo 11 days after demonstration of gestational sac **with** yolk sac (YS)
  - Lack of live embryo 14 days after demonstration of gestational sac **without** YS
- Other published signs of failed pregnancy
  - Empty amnion sign
  - Expanded amnion sign
  - Yolk stalk sign

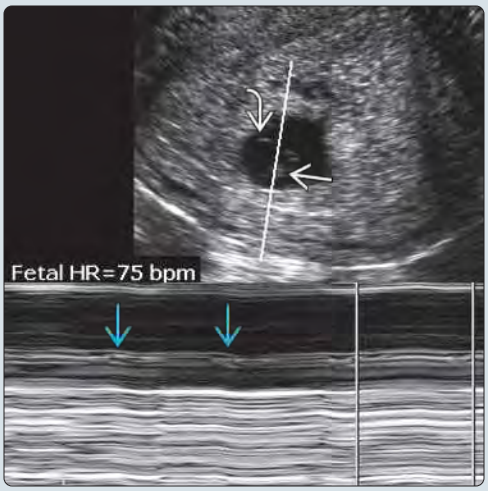
TOP DIFFERENTIAL DIAGNOSES

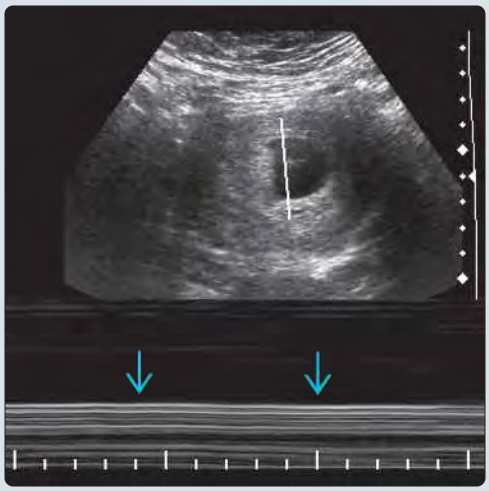
- Probable intrauterine pregnancy (IUP)
  - Intrauterine sac-like structure without yolk sac or embryo
- Intrauterine pregnancy of uncertain viability
- Retained products of conception
- Gestational trophoblastic disease

DIAGNOSTIC CHECKLIST

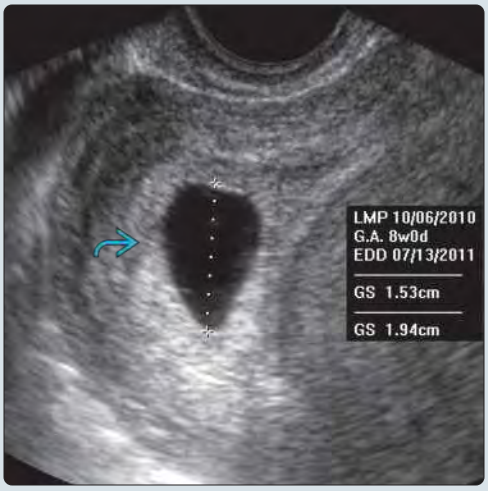
- Failed 1st-trimester pregnancy simplifies terminology
- Positive pregnancy test with intrauterine fluid collection with rounded edges is statistically most likely to be IUP
  - Probable IUP if no YS or embryo
  - Definite IUP if YS or embryo visible
- If in doubt, wait and see

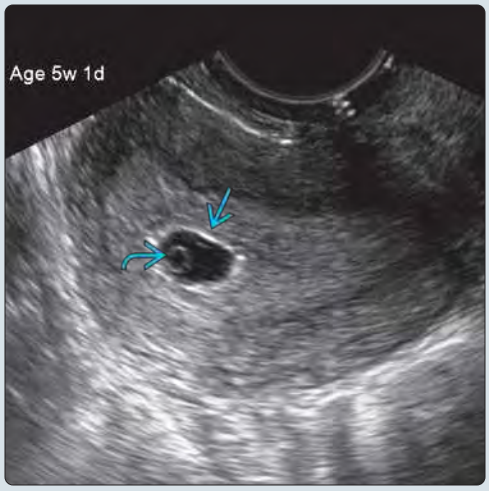
(Left) *M-mode ultrasound shows embryonic bradycardia with heart rate of 75 beats per minute in this tiny embryo seen immediately adjacent to the yolk sac. Cardiac activity is often visible before the crown rump length (CRL) can be measured accurately. Embryonic bradycardia is associated with poor outcome.* **(Right)** *Follow-up 1 week later in the same patient shows cessation of cardiac activity. This is diagnostic of embryonic demise regardless of the CRL.*





(Left) *TVUS shows an oval gestational sac smaller than expected for menstrual dates with mean sac diameter 17.2 mm. This is not indicative of pregnancy failure. Lack of a live embryo 14 days after demonstration of a sac without a yolk sac indicates a nonviable pregnancy.* **(Right)** *TVUS shows a gestational sac with a yolk sac in a patient with pain and bleeding. This is not indicative of pregnancy failure. Lack of a live embryo 11 days after demonstration of a sac with a yolk sac indicates a nonviable pregnancy.*





TERMINOLOGY

Definitions

- Pregnancy is considered viable if it can **potentially** result in live birth
- Nonviable pregnancy is one that will not result in live birth
- Intrauterine pregnancy (IUP) of uncertain viability
  - Intrauterine gestational sac, no embryonic heartbeat but no definite signs of pregnancy failure on transvaginal ultrasound (TVUS)

IMAGING

General Features

- Criteria for definite diagnosis of nonviable pregnancy are now based on TVUS

Ultrasonographic Findings

- Grayscale ultrasound
  - **Nonviable pregnancy**
    - Mean sac diameter (MSD) ≥ 25 mm without embryo
    - Embryo with crown rump length (CRL) ≥ 7 mm without cardiac activity on TVUS
      - Although new criteria are on TVUS, CRL ≥ 15 mm without cardiac activity on TAUS can be used to call demise
    - Lack of live embryo 11 days after demonstration of gestational sac **with** yolk sac (YS)
    - Lack of live embryo 14 days after demonstration of gestational sac **without** YS
    - Cessation of cardiac activity in embryo of any size
  - **Expanded amnion sign**
    - Amnion visible surrounding embryo without cardiac activity implies embryonic demise regardless of CRL
  - **Empty amnion sign**
    - Gestational sac with visible amnion, without visible embryo
  - **Yolk stalk sign**
    - Embryo without cardiac activity with visible YS separate from embryo
  - Other findings of concern for abnormal gestation
    - Abnormal sac contour (e.g., pointed edges)
    - Poor decidual reaction
    - Sac positioned low in uterus
      - Beware scar implantation if prior cesarean section
- Color Doppler
  - Poor color Doppler signal around sac
    - Use Doppler to support abnormal diagnosis

Imaging Recommendations

- Be sure to scan through entire uterus in longitudinal and transverse planes
- Measure MSD by averaging 3 planes; do not include chorion
- Verify date of last menstrual period/cycle length/regularity
  - When was 1st positive pregnancy test
- If possible normal early pregnancy, follow-up at intervals timed to normal milestones
- Know anatomy and developmental stages
  - Intrauterine sac-like structure = **probable IUP**
    - Round or oval shape more likely normal early IUP
    - Fluid collection with "pointed" edges less likely to be IUP
      - More likely blood or decidual cast in association with ectopic
  - Gestational sac with YS = **definite IUP**
  - Double bleb: Embryonic disc between amnion and YS
    - As pregnancy progresses embryo and amnion enlarge
      - Embryo initially fills amniotic cavity
      - As umbilical cord forms embryo "suspended" by cord within expanded amniotic sac
      - YS lies outside amniotic cavity
      - YS eventually compressed between amnion and chorion as membranes "fuse"
  - Normal YS round in shape, ≤ 6 mm diameter

DIFFERENTIAL DIAGNOSIS

Probable Intrauterine Pregnancy (Intrauterine Sac-Like Structure)

- Intradecidual sac sign (IDSS) and double decidual sac sign (DDSS) are classic descriptors for developing sac
  - IDSS
    - Spherical, echogenic ring "burrowed" into decidualized endometrium
  - DDSS
    - 2 thick echogenic rings (decidual capsularis, parietalis) project into uterine cavity
- Not all normally developing sacs show IDSS or DDSS
  - **Intrauterine sac-like structure** now preferred generic descriptor for rounded fluid collection in endometrial cavity
    - No yolk sac or embryo
- Term pseudosac of ectopic pregnancy no longer recommended
  - Was used to described central fluid collection in uterus without features of IDSS or DDSS
  - Due to decidual cast/blood products in setting of ectopic pregnancy
  - Often angular shape with pointed edges
  - Potential for incorrect administration of methotrexate to normal early IUP

Intrauterine Pregnancy of Uncertain Viability

- Definite IUP with MSD < 25 mm without embryo
- Definite IUP with embryo < 7 mm without cardiac activity

Pregnancy of Unknown Location

- Positive pregnancy test, no signs of intra- or extrauterine pregnancy on TV scans
  - Could be normal early, ectopic, or failed pregnancy
  - Requires laboratory analysis and follow-up scanning for definitive diagnosis

Retained Products of Conception

- Disorganized material in uterine cavity
- If echogenic with flow on color Doppler → most likely retained products of conception
- Retained clot is usually hypoechoic, nonperfused

Gestational Trophoblastic Disease

- Classic 2nd-trimester hydatidiform mole has Swiss cheese appearance

Ultrasound in Failed Pregnancy

Findings Diagnostic for Pregnancy Failure	Findings Suspicious for Pregnancy Failure
No heartbeat in embryo ≥ 7 mm crown rump length (CRL)	No heartbeat in embryo < 7 mm CRL
No embryo with mean sac diameter (MSD) ≥ 25 mm	No embryo with MSD 16-24 mm
Absence of embryo with heartbeat ≥ 14 days after demonstration of gestational sac without yolk sac	Absence of embryo ≥ 6 weeks post last menstrual period
Absence of embryo with heartbeat ≥ 11 days after demonstration gestational sac with yolk sac	Absence of embryo with heartbeat 7-13 days after demonstration of gestational sac without yolk sac
	Absence of embryo with heartbeat 7-10 days after demonstration gestational sac with yolk sac
	Empty amnion sign
	Enlarged yolk sac (> 7 mm)
	Embryo to sac size discrepancy (< 5 mm difference between MSD and CRL)

Reproduced from: Diagnostic Criteria for Nonviable Pregnancy Early in the First Trimester. N Engl J Med. 2013 Oct 10;369(15):1443-51.Diagnostic criteria are based on TVUS measurements.

- Early in 1st trimester may just see amorphous tissue or abnormal-appearing gestational sac
- May see associated ovarian theca lutein cysts

PATHOLOGY

General Features

- Etiology
  - Failure of implantation vs. failed embryonic development vs. early embryonic demise
  - 60% of spontaneous abortions < 12 weeks due to abnormal chromosomes

CLINICAL ISSUES

Presentation

- May be asymptomatic
- Vaginal bleeding, pain, contractions suggest imminent spontaneous abortion

Demographics

- Epidemiology
  - 30-60% documented elevations of β-hCG end as failed pregnancy
  - Up to 20% of confirmed 1st-trimester pregnancies fail
  - Increased incidence of early pregnancy failure with
    - Advanced maternal age
    - History of recurrent abortions
    - Poor diabetic control

Treatment

- Most will spontaneously abort without treatment
- Vaginal misoprostol → successful evacuation of uterus in majority of patients
  - Many patients prefer definitive treatment to expectant management
  - Some will require curettage but overall expect 50% reduction in need for surgical management
- Suction curettage
  - Small associated risk of excessive bleeding, uterine perforation, synechiae development

DIAGNOSTIC CHECKLIST

Consider

- Abnormalities common in early pregnancy
- Diagnosis of failed pregnancy depends on knowledge of normal early pregnancy milestones

Image Interpretation Pearls

- 1st, do no harm
  - If in doubt regarding viability, wait and see

Reporting Tips

- Positive pregnancy test with intrauterine fluid collection with rounded edges is statistically most likely to be IUP
  - Probable IUP if no YS or embryo
  - Definite IUP if YS or embryo visible
- Term failed 1st-trimester pregnancy simplifies terminology
  - Avoids confusion with terms such as blighted ovum, missed abortion
- Live intrauterine pregnancy more accurate than viable as fetus < 24-weeks gestation not viable independent of mother
- Empty amnion, expanded amnion, yolk stalk signs are described in peer-reviewed literature but are not part of 2013 consensus panel statement

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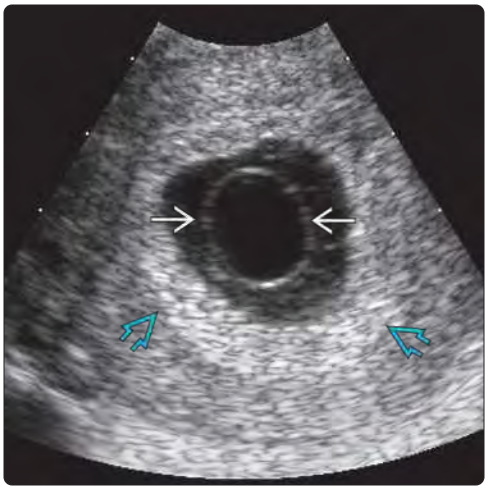
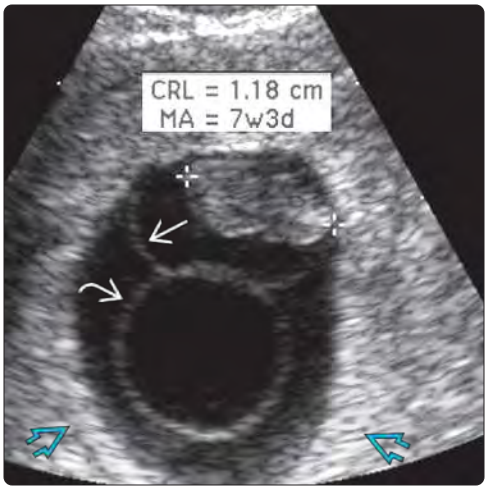
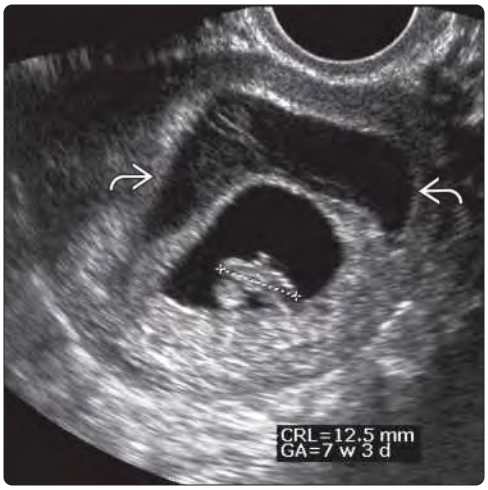
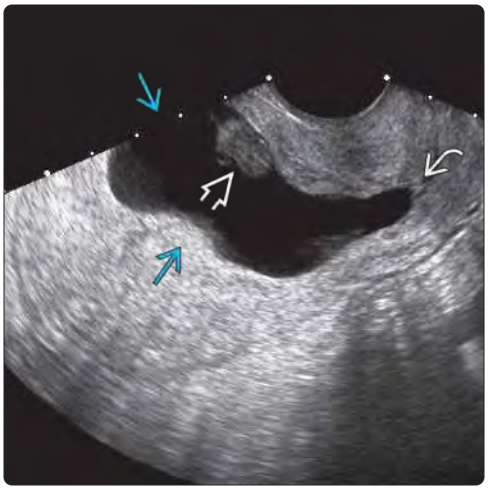


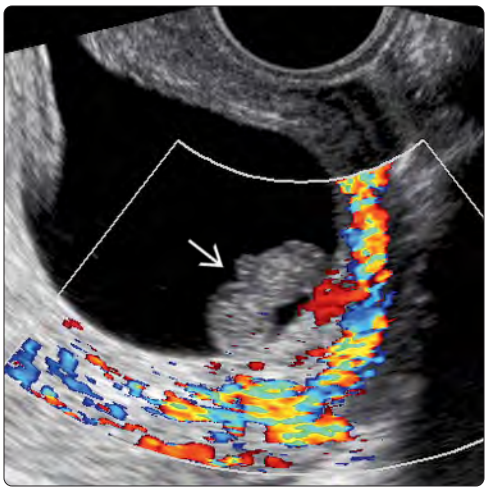


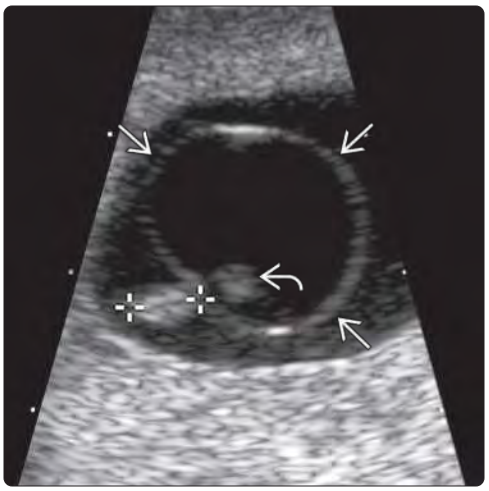
(Left) *TVUS shows an example of the empty amnion sign in which the amnion is visible inside the gestational sac. No embryo is present. Do not confuse this sign with the finding of a sac with a yolk sac.* **(Right)** *TVUS shows an 11.8-mm dead embryo (calipers) surrounded by visible amnion. This is the expanded amnion sign. The yolk sac is abnormal. Normal diameter is < 6 mm, but this one measured 9 mm. The embryo is inside the amnion, and the yolk sac is outside the amnion, inside the chorion.*





(Left) *TVUS shows a 12.5-mm embryo (calipers). There was no visible heart motion. Note the large perigestational hemorrhage in this patient who presented with pelvic pain and vaginal bleeding.* **(Right)** *TVUS shows a large irregular gestational sac collapsing in on itself as the cervical canal dilates. There was no cardiac activity in the embryo, which was 11 mm in length. This case shows definite pregnancy failure.*





(Left) *Color Doppler shows lack of cardiac motion in this embryo, which measured 13 mm.* **(Right)** *TVUS shows the expanded amnion sign with a dead embryo and a collapsed yolk sac (calipers). Embryologically, if the amnion has expanded enough to be visible around the embryo, there should be cardiac activity. The collapsed yolk sac was incorrectly measured as the crown rump length. Remember, the embryo is inside the amnion and the yolk sac is outside.*

Perigestational Hemorrhage

KEY FACTS

TERMINOLOGY

- Perigestational hemorrhage (PGH): Hematoma in subchorionic space adjacent to gestational sac

IMAGING

- Acute hematoma is echogenic
- Subacute hematoma is complex, more hypoechoic
- Old hematoma approaches sonolucent
- PGH has no blood flow on color Doppler

TOP DIFFERENTIAL DIAGNOSES

- Diamniotic twinning in early 1st trimester
- Chorioamniotic separation in late 1st trimester

PATHOLOGY

- Large PGH
  - > 50% of gestational sac surrounded by blood
  - PGH volume > 30 cc

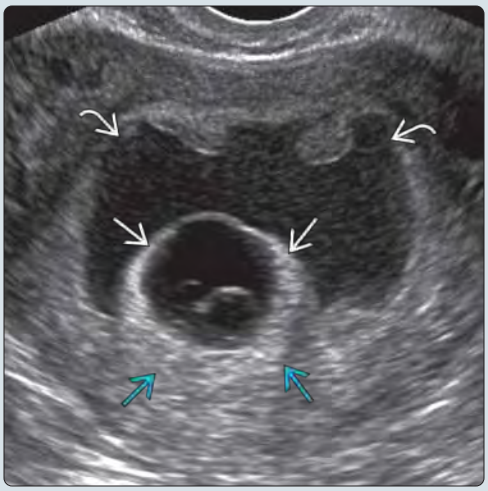
CLINICAL ISSUES

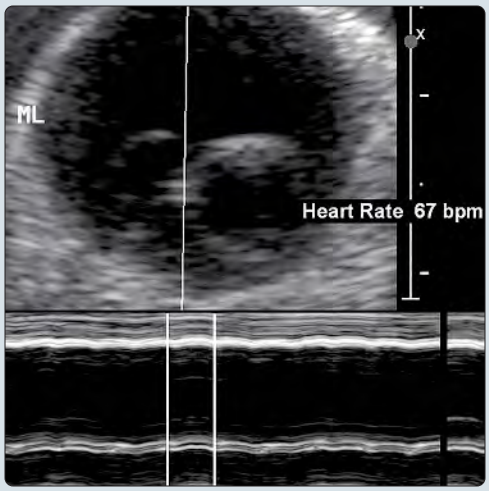
- Presence of living embryo with normal heart rate is most reassuring sign
- Most resolve without sequelae
- 2% of all 1st-trimester patients have PGH
- 20% of patients with vaginal bleeding have PGH
- PGH associated with 2nd- and 3rd-trimester complications
  - Elevated maternal serum α-fetoprotein
  - 2nd-/3rd-trimester abruption
  - Preterm delivery
- > 90% pregnancy success rate if living embryo + small PGH
- Guarded prognosis if embryonic bradycardia
- Guarded prognosis with large PGH

DIAGNOSTIC CHECKLIST

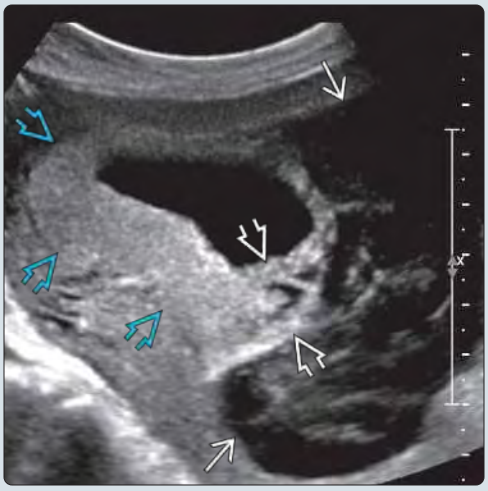
- Beware of twins mimicking PGH and vice versa

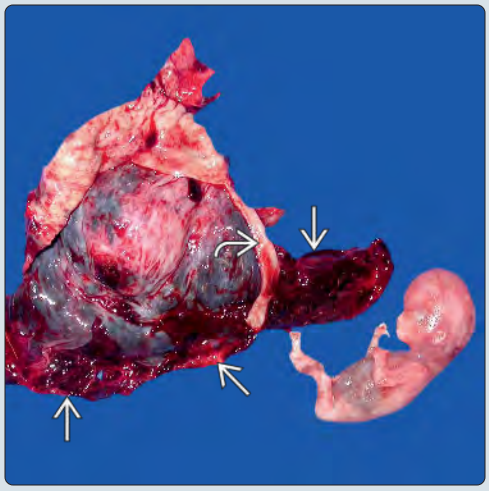
(Left) *A large perigestational hemorrhage (PGH) surrounds an early gestational sac (GS). The GS is attached posteriorly with 2/3 of the circumference of the sac surrounded by blood.* **(Right)** *A living embryo was seen within the gestational sac, but the heart rate was slow. The combination of embryonic bradycardia and PGH is associated with a poor prognosis, and this pregnancy failed shortly after the scan.*





(Left) *In this 12-week pregnant patient from the fertility center, a large PGH with complex echogenicity lifts the inferior edge of the chorionic frondosum (CF), or early placenta. The majority of the CF is otherwise well attached, and the fetus survived.* **(Right)** *In a case of an 11-week pregnancy loss from subchorionic hemorrhage, gross pathology shows a large perigestational hemorrhage that extends from behind the membranes and placenta.*





TERMINOLOGY

Abbreviations

- Perigestational hemorrhage (PGH)

Synonyms

- Subchorionic hematoma

Definitions

- Hematoma in subchorionic space adjacent to gestational sac (GS)
- Bleeding from chorionic frondosum (CF) later in 1st trimester

IMAGING

General Features

- Best diagnostic clue
  - Crescentic fluid collection between GS and uterine wall

Ultrasonographic Findings

- PGH appearance depends on age of bleed
  - Acute hematoma is echogenic
    - Isoechoic to GS or CF
  - Progression to hypoechoic/anechoic with time
    - Complex fluid collection
    - Fibrin strands resemble septations
  - Most PGH resolves, with delivery of normal infant
- Shape is variable
  - Round, mass-like bleed
  - Curvilinear/lenticular follows contour of uterus
- Findings associated with poor prognosis
  - Large hematoma
    - > 50% of sac circumference, > 30 cc volume
    - Misshapen GS, abnormal intrasac anatomy
  - Bradycardia: Embryo heart rate ≤ 90 beats/minute
  - Cervical os dilatation → miscarriage
- Color Doppler can help identify PGH separate from GS

DIFFERENTIAL DIAGNOSIS

Twin Gestation

- 2nd GS can mimic PGH
- Follow-up to see yolk sac/embryo development in sac

Pseudogestational Sac (Ectopic Pregnancy)

- This term now discouraged as it is imprecise and may lead to confusion
- Represents blood centrally located in endometrial cavity
- Look for adnexal mass and echogenic cul-de-sac fluid

Chorioamniotic Separation

- Amnion seen separate from uterine wall
- Placental edge remains attached

PATHOLOGY

General Features

- Etiology
  - Bleeding from area of trophoblastic tissue implantation

Staging, Grading, & Classification

- Compare PGH to GS size
  - Small PGH surrounds < 20% of sac circumference
  - Medium PGH surrounds 20-50% of sac circumference
  - Large PGH surrounds > 50% of sac circumference
- PGH volume estimation (length x width x depth/2)
  - > 30 cc associated with 50% loss rate
  - > 60 cc associated with 93% loss rate

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
  - Asymptomatic (incidentally seen PGH)
  - Threatened abortion/miscarriage
  - Post procedure (chorionic villus sampling)

Demographics

- Epidemiology
  - 2% of all 1st-trimester pregnancies have PGH
  - 20% of patients with vaginal bleeding have PGH
  - 2x higher incidence with in vitro fertilization pregnancy

Natural History & Prognosis

- Excellent prognosis if living embryo + small PGH
  - > 90% pregnancy success rate
- Guarded prognosis with large PGH
  - 25% loss rate even if living embryo seen
  - > 50% GS/CF detachment has greatest loss rate
- Poor prognosis if associated embryonic bradycardia
  - 80% loss rate
- Failed pregnancy if cervix is open
  - Regardless of appearance of PGH
  - Clinical diagnosis but may see with US
- Associated maternal/fetal morbidity
  - Placental abruption (2.6-5.7x ↑ risk)
  - Preterm delivery (1.3x ↑ risk)
  - Elevated maternal serum α-fetoprotein

Treatment

- Surveillance and maternal support
- Short-term follow-up for early and large PGH
  - Look for signs of viable pregnancy
  - Hematoma should ↓ in size and echogenicity
- Follow-up growth scans for large PGH
  - ↑ risk for placental insufficiency

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

- Presence of living embryo is most reassuring sign
- Look for usual signs of viable pregnancy
- Beware of twins mimicking PGH and vice versa

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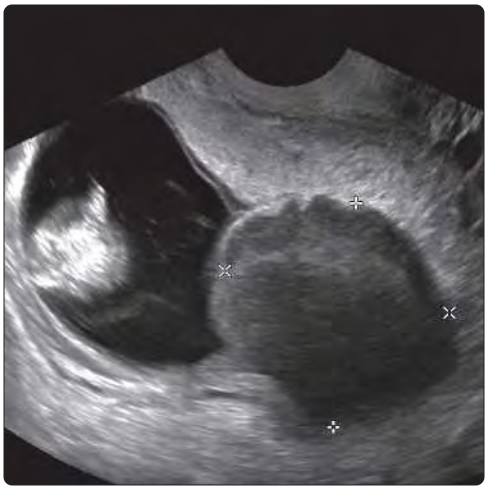
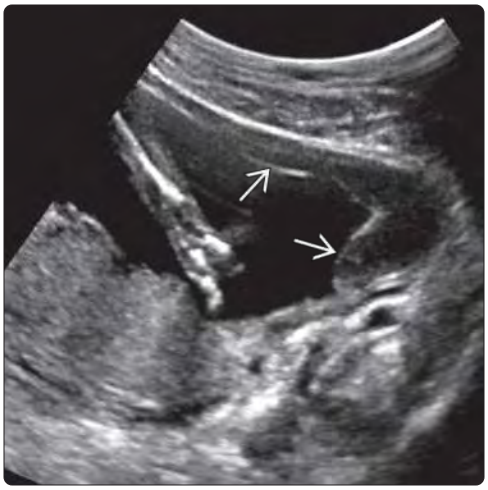
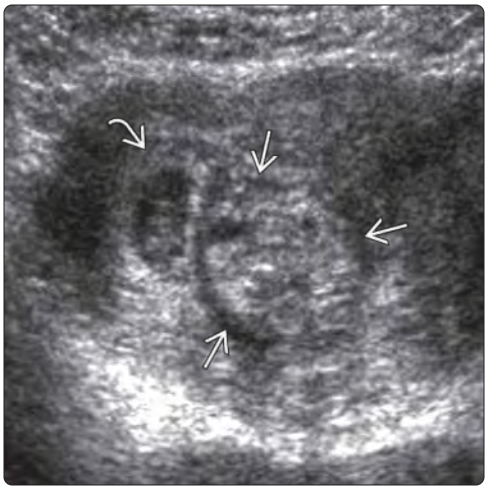
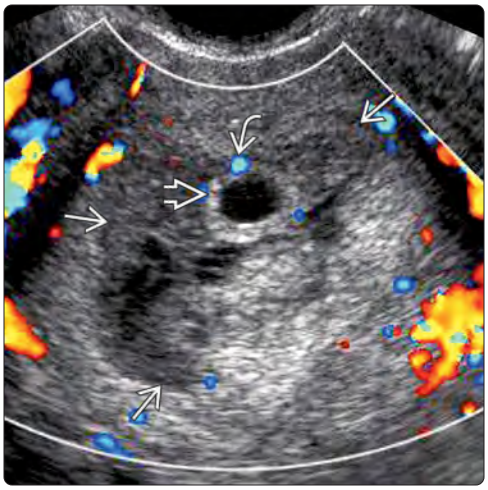
(Left) *Calipers measure a large, mass-like, round PGH. Although this appearance can mimic a myoma in pregnancy, the lack of internal blood flow and the symptomatic presentation favored the diagnosis of PGH.* **(Right)** *On follow-up several weeks later, the subchorionic hematoma is now smaller, almost anechoic, lenticular, and follows the uterine contour.*



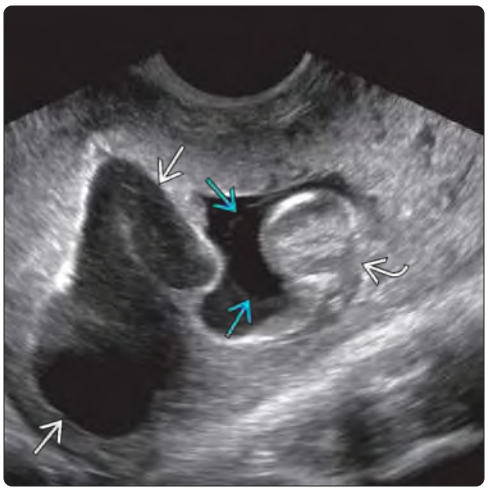


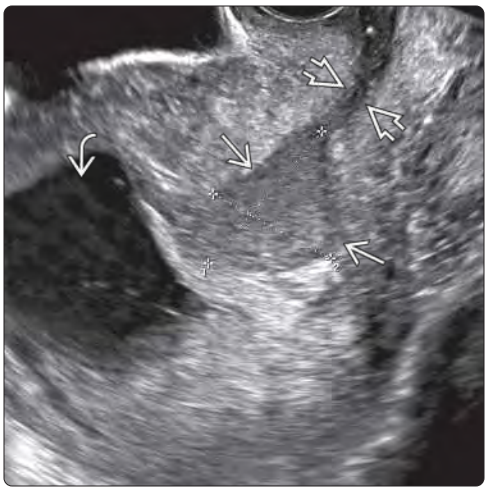
(Left) *Transverse US shows an echogenic, mass-like, acute PGH. The GS is compressed by the hematoma. There was a living embryo at the time of this study, and the pregnancy was successful. The round echogenic PGH is a blood clot that eventually retracted and resolved.* **(Right)** *Color Doppler shows a large avascular hemorrhage surrounding a gestational sac. A small chorionic vessel is seen at the attachment site. Surprisingly, this pregnancy was also successful.*

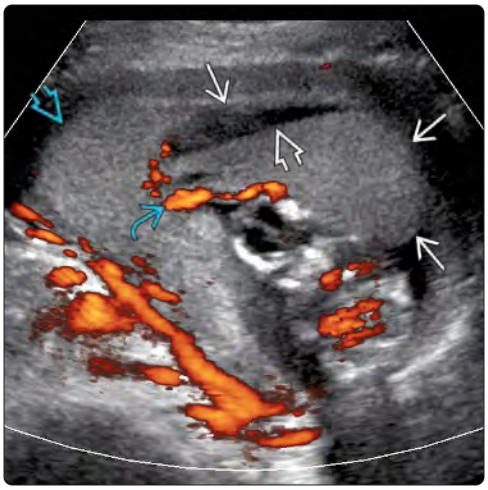


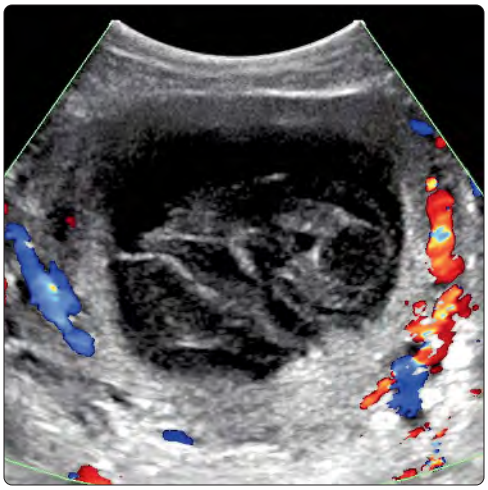


(Left) *This early GS is misshapen by hypoechoic and echogenic hematomas, most likely from hemorrhages occurring at different times. Intrasac anatomy is abnormal with a thin, echogenic line probably representing an empty amnion. This pregnancy failed.* **(Right)** *Sagittal TVUS shows a PGH extending through a mildly dilated cervical canal. The sac is misshapen and contains neither an embryo nor a yolk sac. The patient miscarried a few hours later.*

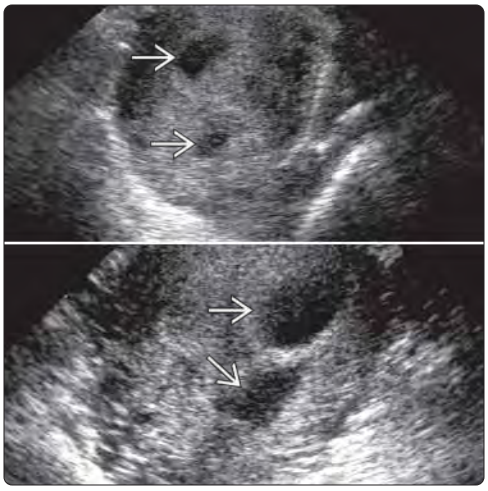


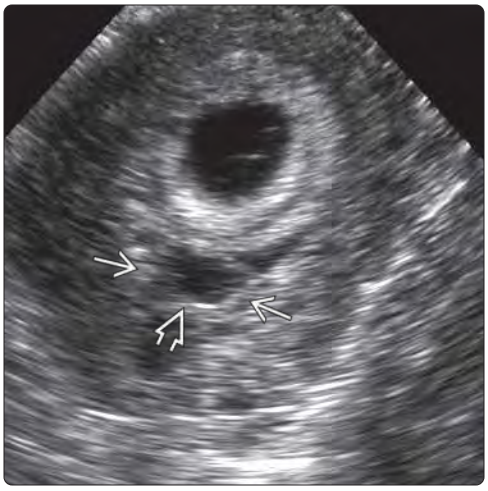




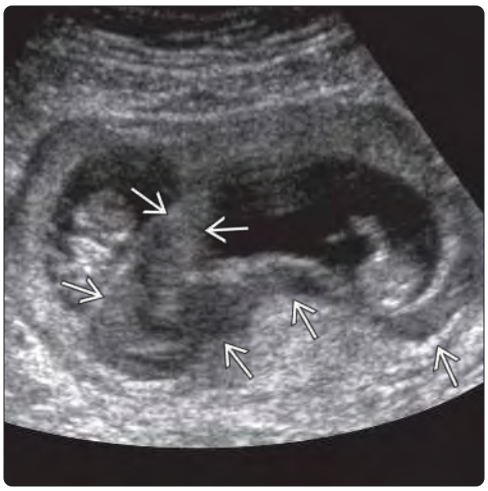


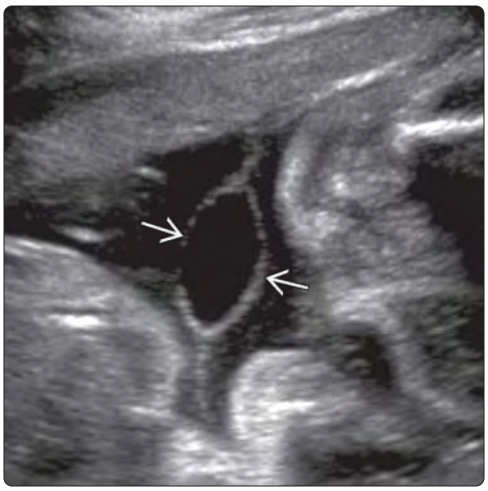
(Left) *This atypical subchorionic hematoma is located in the preplacental subchorionic space, near the placental cord insertion, and has a fluid-fluid level and no flow with power Doppler. The uteroplacental attachment is normal. This patient was asymptomatic.* **(Right)** *In another case with a large PGH, color Doppler helps show that the hematoma has no blood flow. Color and power Doppler help differentiate hematoma from placenta and myometrium.*





(Left) *US images from a transabdominal scan show 2 fluid collections within the uterus mimicking the appearance of a twin gestation. The inferior posterior collection is the PGH.* **(Right)** *The PGH mimics a misshapen dichorionic GS with a yolk sac. On follow-up, the PGH was more anechoic and lenticular. A PGH may mimic a twin gestation and vice versa.*





(Left) *In this case of dichorionic twinning, a subacute PGH is seen extending along the posterior uterus and between the 2 sacs.* **(Right)** *Later, in the same pregnancy, a sonolucent fluid collection was seen between the membranes that separate the dichorionic diamniotic twins. Presumably, this is old anechoic blood products from the PGH that occurred earlier in the pregnancy.*

Chorionic Bump

KEY FACTS

IMAGING

- Focal protrusion of chorion
  - Continuous with surface of chorion
  - Margins form acute angles with chorionic plate surface
- Central hypoechogenic area in 20%
- Low-level swirling echoes seen in central area on real-time evaluation in 27%

TOP DIFFERENTIAL DIAGNOSES

- Failed 1st-trimester pregnancy
- Abnormal yolk sac
- Perigestational hemorrhage

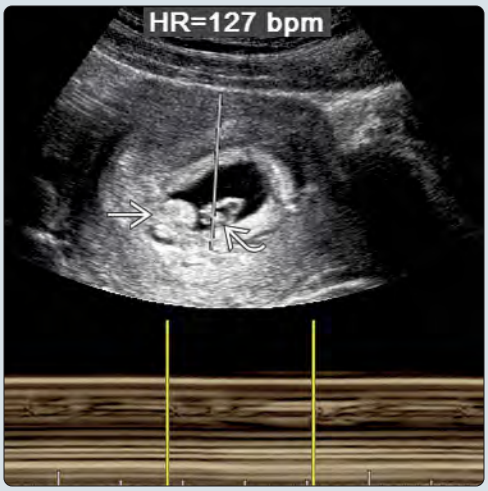
CLINICAL ISSUES

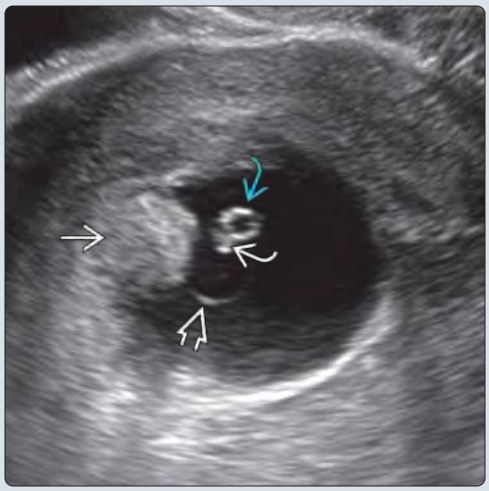
- Prevalence 0.15% in retrospective case-control study
- Thought to be arterial hematoma arising from developing intervillous space or chorionic plate
- In continuing pregnancy, chorionic bump becomes smaller, less echogenic, eventually resolves
- Enlarging CB associated with increased chance of failure
  - Strong association with partial mole in failed pregnancies where tissue obtained
- Prognosis
  - 50% failure rate documented in initial cohort
    - 80% survived if embryo with normal heart rate seen
  - Subsequent studies have shown better outcome
    - Sana et al: Live birth rate 62% with ~ 2x loss rate in CB group vs. controls
    - Arleo et al: Overall live birth rate 65%
      - If live embryo at some point → live birth rate 83%
  - In 1 series, all pregnancies with multiple bumps were nonviable
- No specific therapy

DIAGNOSTIC CHECKLIST

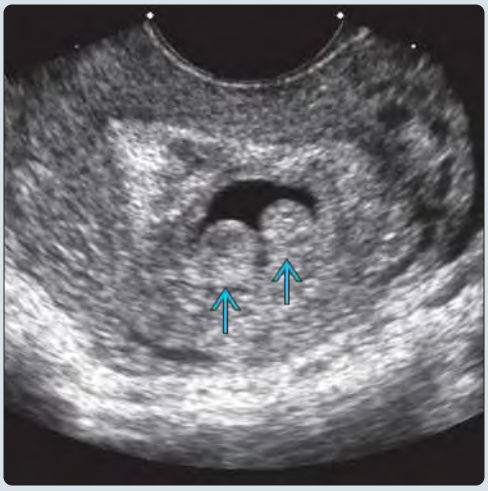
- Must know normal appearance of early pregnancy
  - Avoid confusion with embryonic demise
  - Avoid confusion with abnormal yolk sac

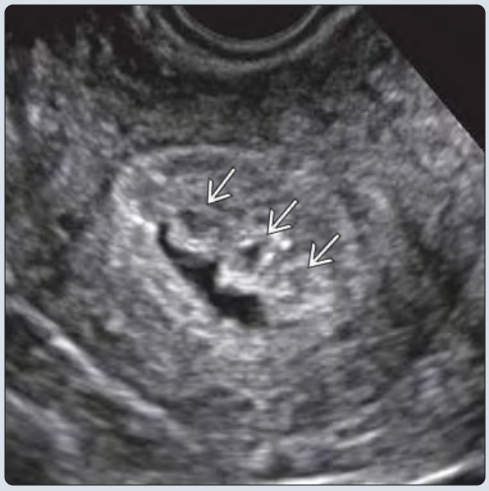
(Left) *TVUS show a chorionic bump. In this case, there was a live embryo the size of which was concordant with menstrual dates. This was a successful pregnancy.* **(Right)** *TVUS shows a chorionic bump with a visible embryo, which is far smaller than expected for menstrual dates, which were confirmed on an earlier scan. The embryo is surrounded by the expanded amnion. The yolk sac is normal. This is a failed 1st-trimester pregnancy with a dead embryo.*





(Left) *TVUS shows multiple chorionic bumps. No normal early pregnancy structures (e.g., yolk sac, embryo, amnion) were ever visible. Dilation and curettage confirmed triploidy in this case.* **(Right)** *TVUS shows multiple chorionic bumps with hypoechoic centers in a patient who presented with vaginal bleeding. This case ended in complete, spontaneous abortion.*





TERMINOLOGY

Abbreviations

- Chorionic bump (CB)

IMAGING

General Features

- Best diagnostic clue
  - Persistent focal protuberance from chorion into gestational sac
- Size
  - Reported size ranged from 0.5-3.8 cm max diameter; volumes 0.04-11.2 mL
  - No correlation between size and outcome
- Morphology
  - Continuous with surface of chorionic plate
  - Margins form acute angles with chorionic plate surface

Ultrasonographic Findings

- Grayscale ultrasound
  - Focal protrusion of chorion
    - Echogenicity usually similar to that of chorion
      - Central hypoechogenic area in 20%
    - Low-level swirling echoes seen in central area on real-time evaluation in 27%
    - Avascular on Doppler interrogation
    - Persistent throughout duration of scan
  - Usually single but can be multiple

DIFFERENTIAL DIAGNOSIS

Failed 1st-Trimester Pregnancy

- Chorionic sac may be flattened or irregular in contour
  - CB projects into round or oval sac
- In embryonic demise, dead embryo is inside amnion, not flush with chorion

Abnormal Yolk Sac

- Seen outside amnion, in extraembryonic coelomic space, not flush with chorion
- Yolk sac has more distinct linear echo

Perigestational Hemorrhage

- Occurs in decidua or cytotrophoblastic shell
  - Venous bleed so low pressure → crescentic or oval shape on myometrial side of chorion
  - Hypoechoic
  - CB round, often similar echogenicity to chorion

PATHOLOGY

General Features

- Focal round shape suggests arterial rather than venous bleed
- Thought to be arterial hematoma arising from developing intervillous space or chorionic plate

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
  - Often asymptomatic
  - May present with vaginal bleeding

Demographics

- Epidemiology
  - Prevalence 0.7% in index cohort
    - Mean gestational age at demonstration was 6.7 weeks
  - 0.15% in retrospective case-control study

Natural History & Prognosis

- 50% failure rate documented in initial cohort of patients with assisted reproduction
  - Presence of embryo with normal heart rate conferred better prognosis (80% survived)
- Subsequent studies have shown better outcome
  - Sana et al: Live birth rate 62% with ~ 2x loss rate in CB group vs. controls
  - Arleo et al: Single institution/single reader review 1st-trimester scans for any indication
    - 52 pregnancies with CB → overall live birth rate 65%
    - 41 with live embryo at some point → live birth rate 83%
      - 6 with gestational sac with yolk sac but no embryo → 4 live births
      - 8 with gestational sac only → 2 live births
      - 3 with gestational sac with yolk sac + embryo but no cardiac activity → 0 live births
      - 18 nonviable (7 anembryonic, 11 early demise)
- In 1 series, all pregnancies with multiple bumps were nonviable
- Serial changes over follow-up suggestive of focal hematoma
  - In continuing pregnancy, CB becomes smaller, less echogenic, eventually resolves
- Enlarging CB associated with increased chance of failure

Treatment

- No specific therapy
- Consider tissue analysis of failed pregnancies
  - Strong association with gestational trophoblastic disease, particularly partial mole

DIAGNOSTIC CHECKLIST

Consider

- Must know normal appearance of early pregnancy
  - Avoid confusion with embryonic demise
  - Avoid confusion with abnormal yolk sac

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Complete Hydatidiform Mole

KEY FACTS

TERMINOLOGY

- Trophoblastic proliferation (both cytotrophoblast and syncytiotrophoblast) and vesicular swelling of placental villi associated with absent fetus

IMAGING

- Classic findings described as "Swiss cheese" or "cluster of grapes" endometrium
  - No fetus or embryo
  - Increased vascularity on color Doppler
  - Areas of hemorrhage common
- 1st-trimester CHM
  - Very different appearance than seen later
  - Thickened, irregular endometrium
  - Appearance may mimic retained products of conception or anembryonic pregnancy
- Ovarian theca lutein cysts in 50% of cases
  - Result from ovarian hyperstimulation due to ↑ hCG
  - Rare < 13 weeks
  - Occur more frequently with invasive mole and choriocarcinoma than in CHM
- Must distinguish CHM with coexistent fetus (dizygotic twin pregnancy) from partial mole (triploidy)

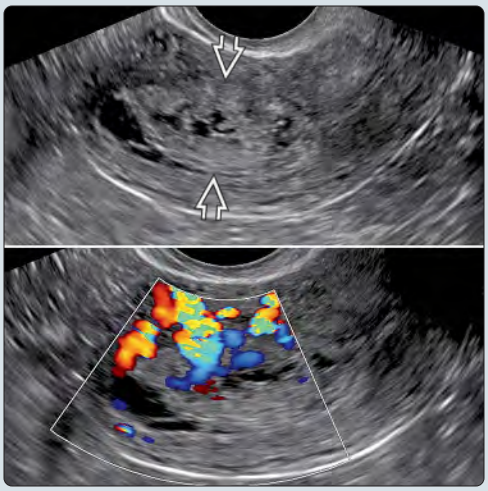
TOP DIFFERENTIAL DIAGNOSES

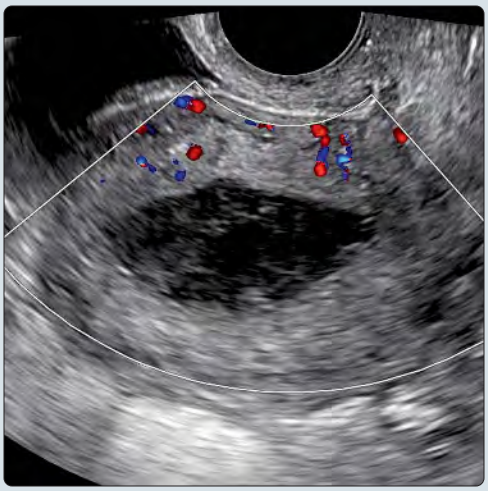
- Placental hydropic degeneration
- Triploidy
- Placental mesenchymal dysplasia

CLINICAL ISSUES

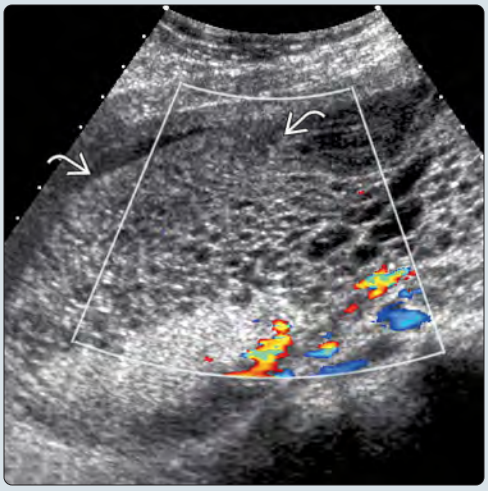
- Normal hCG levels do not rule out CHM if < 13 weeks
- Treatment
  - Evacuation with suction curettage
  - Measure hCG weekly until undetectable for 3 weeks and then monthly for 6 months
- Invasive mole in 12-15%
- Choriocarcinoma in 5-8%
  - Excellent prognosis even with metastases

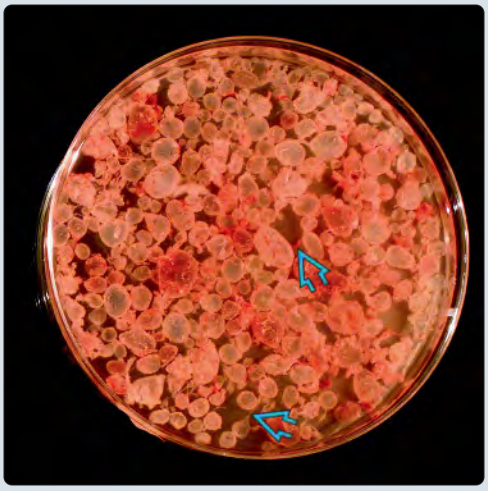
(Left) *Do not expect the classic bunch of grapes appearance of a complete hydatidiform mole (CHM) in the 1st trimester. It often appears a thickened endometrium & can mimic retained products of conception or an anembryonic pregnancy. In this case, the endometrium is thickened, with a few scattered lucencies and significant flow on color Doppler.* **(Right)** *This is another CHM in the 1st trimester that is hypovascular. The 1st-trimester appearance is quite variable and it is essential to compare with the hCG levels.*





(Left) *By the 2nd trimester, a CHM will have a more classic Swiss cheese appearance. This longitudinal transabdominal ultrasound shows a large cystic endometrial mass with multiple small cystic areas representing the hydropic villi.* **(Right)** *This Petri dish is filled with hydropic villi from a CHM. They are attached by thin fibrous strands. Evidence of prior hemorrhage is typically present.*





TERMINOLOGY

Abbreviations

- Complete hydatidiform mole (CHM)

Definitions

- Trophoblastic proliferation (both cytotrophoblast and syncytiotrophoblast) and vesicular swelling of placental villi associated with absent fetus
- Most common (~ 76% of all cases) type of gestational trophoblastic disease, which also includes
  - Partial mole (triploidy)
  - Invasive mole (chorioadenoma destruens)
  - Choriocarcinoma
  - Placental-site trophoblastic tumor
  - Epithelioid trophoblastic tumor

IMAGING

General Features

- Best diagnostic clue
  - Enlarged uterus with "Swiss cheese" or "cluster of grapes" endometrium
    - "Snowstorm": Older term used before technology was capable of discerning individual cysts
  - Bilateral, complex ovarian cysts (theca lutein cysts)
  - No fetus or embryo

Ultrasonographic Findings

- Uterine findings
  - **1st-trimester CHM**
    - Very different appearance than classic 2nd-trimester CHM
      - Only 1/2 will show cysts in 1st trimester
    - Thickened, irregular endometrium similar to retained products of conception
    - Can look identical to anembryonic gestation
  - **Late 1st-/2nd-trimester CHM**
    - Hydropic villi appear as multiple anechoic spaces, 1-30 mm in size, within echogenic intrauterine mass ("Swiss cheese" endometrium)
    - No embryo or fetus
- Ovarian theca lutein cysts
  - Bilateral multiseptated cysts
  - Enlarged ovaries, sometimes massive
  - Only in 50% of all CHM
  - Rare < 13 weeks
    - β-hCG not extremely elevated yet
- Doppler findings
  - Mass is vascular
    - Color Doppler easily shows flow
  - High-velocity, low-resistance flow
    - Mean resistive index (RI) of 0.55
    - Normally, uterine arcuate artery flow is low velocity until 3rd trimester
      - Normal RI often > 0.66 if < 20 weeks
- **CHM with coexistent fetus**
  - Dizygotic twin pregnancy
    - 1 normal fetus, 1 CHM
    - Normal fetus has normal placenta
  - Must differentiate from partial mole (triploidy)
- CHM often associated with hemorrhage
  - Adjacent sonolucent hematoma
    - Mimics perigestational hemorrhage
  - Hemorrhage within mass
    - Disrupts typical appearance

CT Findings

- CECT
  - Limited role in evaluation of CHM
  - Heterogeneously enhancing endometrial mass
    - Enhancing septa give uterine contents reticular appearance
  - Usually performed when metastatic disease suspected

MR Findings

- T1WI
  - Uterine mass isointense to myometrium
    - Areas of hemorrhage are hyperintense
- T2WI
  - Markedly hyperintense mass distends endometrial cavity
- Avidly enhancing with gadolinium
  - Excellent modality to evaluate for myometrial invasion

DIFFERENTIAL DIAGNOSIS

Placental Hydropic Degeneration

- Hydropic change without proliferation
- Seen after pregnancy failure
  - Embryonic demise
  - Anembryonic gestation
- Can look identical to CHM
  - Need histologic diagnosis
- Less vascular than CHM
  - ↓ velocity, ↓ resistance
- ↓ hCG levels

Triploidy (Partial Mole)

- Fetus is present but abnormal
  - Severe growth restriction
  - Multiple anomalies
- 3 complete sets of chromosomes
  - 2 paternal + 1 maternal (diandry)
    - Placenta is cystic
    - Most likely aneuploidy to be confused with CHM
  - 2 maternal + 1 paternal (digyny)
    - Placenta normal or small
- Must differentiate from twin pregnancy with 1 CHM
  - Normal fetus and placenta + CHM

Placental Mesenchymal Dysplasia

- Also called pseudopartial mole
- Thickened, cystic placenta
- Associated with maternal/fetal morbidity
  - Fetal growth restriction
    - Often early onset and severe
    - Preterm labor and fetal death common
  - Preeclampsia
- Absence of trophoblastic proliferation differentiates it from partial mole
- ~ 20% have Beckwith-Wiedemann syndrome

Complete Hydatidiform Mole

PATHOLOGY

General Features

- Etiology
  - Risk factors
    - Pregnancy at very young or advanced reproductive ages and in grand multiparas
    - Risk of recurrence in future pregnancy is 1.2-1.4%
      - Increases to 20% after 2 moles
      - *NLRP7* and *KHDC3L* gene mutations found in this group
- Genetics
  - Diploid karyotype of paternal origin
    - Single haploid sperm fertilizing ovum lacking maternal genes followed by duplication
      - 90% of cases
      - (46, XX) karyotype
      - Abnormal ovum more likely at both ends of reproductive years
    - 2 haploid sperm fertilizing ovum lacking maternal genes
      - 10% of cases
      - (46, XX) or (46, XY) karyotype
    - May be tetraploid
- Associated abnormalities
  - Ovarian theca lutein cysts
    - Result from ovarian hyperstimulation due to hCG
    - Usually not seen in 1st trimester
    - Occur more frequently with invasive mole and choriocarcinoma than in CHM

Gross Pathologic & Surgical Features

- Large mass, sometimes consisting of > 500 mL of bloody tissue
- Classic bunch of grapes appearance
  - Large villi forming transparent vesicles of variable size (1-30 mm) attached to one another by thin fibrous strands
  - Size of villi ↑ as gestation progresses
- Absent fetus
- No normal placental tissue

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
  - Most CHM present in late 1st trimester
  - Vaginal bleeding
  - Absence of fetal heart tones
  - Rapid uterine enlargement
  - Hyperemesis
  - ↑ hCG levels
    - hCG may not be elevated < 13 weeks
  - Preeclampsia
- Other signs/symptoms
  - Enlarged ovaries with theca lutein cysts
  - Preeclampsia
  - Thyroid storm

Demographics

- Age
  - Young or advanced maternal age
- Ethnicity
  - Higher incidence in Asia (3.2-9.9 per 1,000 gestations) compared with Western countries (0.6-1.1 per 1,000 gestations)

Natural History & Prognosis

- Excellent prognosis
  - Evacuation often curative
- Invasive or metastatic disease may develop
  - Invasive mole in 12-15%
  - Choriocarcinoma in 5-8%
    - Excellent prognosis even with metastases

Treatment

- Evacuation with suction curettage
  - Measure hCG weekly until undetectable for 3 weeks and then monthly for 6 months
  - If serum hCG levels plateau or rise, there is concern for invasive mole or choriocarcinoma
    - Requires work-up for metastatic disease
  - Should not become pregnant during monitoring period
    - Cannot interpret hCG results; complicates management
    - Options include hormonal contraception or barrier methods
    - Intrauterine device should not be used because of risk of uterine perforation
- Hysterectomy if childbearing has been completed

DIAGNOSTIC CHECKLIST

Consider

- CHM with atypical anembryonic gestation
- Rule out CHM when hCG levels are ↑
- Normal hCG levels do not rule out CHM if < 13 weeks
- Careful evaluation for invasive disease
  - Color Doppler of myometrium

Image Interpretation Pearls

- Repeat imaging if hCG levels ↑ after treatment
  - Ultrasound to look for myometrial vascular cysts
  - MR for local invasion
- CHM can look identical to anembryonic pregnancy

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