CASE 1 A Patient of Ashkenazi Jewish Ancestry Presents for Preconception Counseling

Emily R. Rosen

History of Present Illness

A 30-year-old nulligravid patient presents to the clinic for preconception counseling. She is recently married and is planning to start a family. She is worried about conceiving as her sister had a child diagnosed with cystic fibrosis (CF) earlier this year. She wants to make sure that she is as healthy as possible before becoming pregnant and asks to discuss any testing or recommendations to have a healthy pregnancy. She currently has an intrauterine device (IUD) in place for contraception. Her gynecologic history is otherwise unremarkable. She denies any medical or surgical history. There is no family history of birth defects, developmental delay, or cancer. She does not take any medications and has no known drug allergies.

Physical Examination

General appearance: Alert, in no distress
Vital signs:

Temperature: 37.1°C
Pulse: 76 beats per minute
Blood pressure: 110/65 mmHg
Respiratory rate: 15 breaths per minute
Body mass index (BMI): 26.1 kg/m^2

Abdomen: Soft, non-tender, non-distended, no masses
Pelvic: Normal external genitalia, normal vaginal epithelium without lesions or discharge, cervix normal in appearance, 8 week–sized anteverted mobile uterus, normal adnexa without tenderness or masses palpated
Laboratory studies:

Cervical cytology: Negative for intraepithelial lesion or malignancy
Human papillomavirus (HPV): Not detected

How Would You Manage This Patient?

This patient presents for preconception counseling. A thorough review of her personal and family genetic histories is completed and reveals a niece with CF. This patient was counseled on maintaining a healthy lifestyle, and recommendations to minimize health risks were discussed. After genetic counseling, the patient elected for expanded carrier screening given her family history and Ashkenazi Jewish ancestry. Genetic testing was positive for CF– and Canavan disease–carrier status. Subsequent testing of her husband was negative. She received appropriate post-test counseling, her IUD was removed, and she started a prenatal vitamin. She represented three months later with a viable intrauterine pregnancy.

Preconception Counseling

Preconception counseling can be completed at any patient encounter with a patient of reproductive potential and should occur multiple times during a patient's lifespan (Table 1.1). The goal of preconception counseling is to educate patients about healthy pregnancies, adjust risk factors, and identify and treat any underlying conditions to promote maternal health and decrease the risk of maternal and neonatal morbidity and mortality [1].

Comprehensive Health Assessment

Starting with a thorough medical history is imperative to identify and subsequently decrease any risk factors for pregnancy. Certain medical conditions, such as hypertension, diabetes, and thyroid disease, are associated with pregnancy-related complications. Optimizing management of known medical illnesses can improve pregnancy outcomes [1]. A review of all the patient's prescription and nonprescription medications as well as supplements should be performed to assess their safety and potential teratogenicity. In a shared decision-making model, there should be a discussion of the risks and benefits of use, and a determination of which medications should be continued. Patients should be questioned about the use of alcohol, tobacco, and illicit substance use, counseled appropriately, and provided resources as indicated. Assessment for intimate partner violence is also recommended during preconception counseling [2].

Lifestyle Modifications

Lifestyle and behavioral assessments are vital. Nutritional status and physical activity should be discussed. Since low and high BMI are associated with both maternal and fetal complications, patients should be encouraged to achieve a BMI in the normal range between 18.5 and 24.9 kg/m^2 [3]. Preventative care, including offering testing for sexually transmitted infections (STIs), performing cervical cancer screening, and confirming immunization status, is recommended. It is important to review the patient's immunization states for tetanus, diphtheria, and pertussis (Tdap); measles, mumps, and rubella (MMR); hepatitis B; varicella; and HPV vaccination in accordance with the current guidances, and to offer any pending vaccinations to ensure completion of the recommended vaccination series. Annual influenza and COVID-19 vaccinations to patients of reproductive age are recommended at a preconception visit if they are not already completed [1]. Lastly, pre-pregnancy folic acid

Table 1.1 Overview of preconception counseling recommendations

History	**Medical**: Address any chronic medical conditions **Family**: Obtain a complete history **Social**: Inquire about use of alcohol, tobacco, or illicit substances **Psychiatric**: Assess for mental health concerns
Lifestyle	**Diet/exercise**: Encourage a normal BMI **Environmental and occupational exposures:** Assess for teratogen exposure (e.g. pesticides, heavy metals, radiation, etc.)
Preventative care	**Immunizations**: Assess immunization status for Tdap, MMR, hepatitis B, varicella, and HPV vaccines; recommend annual influenza and COVID-19 vaccination **Cervical cancer screening**: Confirm patient is up to date **STI screening:** Offer STI testing **Screening for intimate partner violence**
Medications	Review prescription and nonprescription medications and potential risks/benefits in pregnancy Encourage pre-pregnancy folic acid supplementation
Genetic testing	Identify individuals at increased risk of inherited conditions Offer screening for CF and SMA to all patients Offer additional screening based on patient risk and patient preference after counseling

supplementation to reduce the risk of neural tube defects should be recommended [1].

Genetic Counseling and Screening

In addition to ensuring optimal maternal health, a genetic history and ethnic background of the patient, her partner, and their families should be discussed. Education about carrier screening should be given to every patient. The purpose of carrier screening is to identify asymptomatic individuals who carry a pathogenic variant allele within a gene that is associated with a specific diagnosis. Ideally, carrier testing is completed prior to pregnancy to provide patients with an understanding of their genetic risks so they may consider the full spectrum of reproduction options, including preimplantation genetic testing.

The increasing complexity and accessibility of genetic testing have made counseling more complicated. Pre-test counseling including result possibilities, risks, benefits, costs, and limitations should be discussed prior to testing, and appropriate timely post-test counseling is needed [4]. If a patient is identified as a carrier for a specific disease, the patient's partner should be tested. If both individuals are positive for the same genetic condition, referral for genetic counseling should be provided [5].

Screening for spinal muscular atrophy (SMA) and CF should be offered to all women who are pregnant or who are considering pregnancy [5]. Certain populations, including individuals of Eastern and Central European Jewish descent, are at increased risk of carrying a pathogenic variant for clinically significant autosomal recessive conditions [6]. For example, the carrier risk of SMA and CF in the Ashkenazi Jewish population is 1:41 and 1:24 versus 1:117 and 1:58 in the Hispanic white population, respectively. Sickle cell trait is present in approximately 10% of African American patients, and a hemoglobin electrophoresis should be completed if there is a suspicion of hemoglobinopathy based on ethnicity or complete blood count (CBC) indices [5]. Although different organizations have recommended specific carrier screening in unique populations, other experts have advocated for a more universal approach to carrier screening that is not limited to specific racial or ethnic populations. More research on benefits, feasibility, and opinions of patients and providers is needed before expanded carrier screening is offered to the general population [7].

Contraception to Conception

Time to ovulation is variable depending on the type and mechanism of action of contraceptive being used (whether the method prevents ovulation, thickens cervical mucus, or acts as a spermicide). It is possible to become pregnant immediately after discontinuation of certain forms of contraception, or it may take many months before a patient's cycle returns to normal. Discussion of the menstrual cycle including the follicular and luteal phases should be provided so that patients can understand their unique cycle patterns to optimize conception. Education that ovulation occurs fourteen days prior to menses can help patients predict the timing of ovulation and time intercourse on the most fertile days.

Fertility Concerns and Infertility Evaluation

The diagnosis of infertility is made after not having conceived after 12 months of regular intercourse without the use of contraception in patients under the age of 35 and after 6 months of the same in patients aged 35 and older. The majority of couples will conceive in the first year, but the rates of conception decrease over time and with increasing age of the female partner.

Infertility affects up to 15% of couples [8]. Infertility can have any number of causes. Female factors including ovulatory dysfunction, tubal damage, endometriosis, and uterine factors should be considered. Male factors can contribute to 30–50% of the causes of infertility. Between 10 and 30% of cases of infertility will remain unexplained after a thorough workup [8]. If a patient is unable to conceive in the anticipated time frame, further evaluation and workup are recommended. If a patient has a condition known to cause infertility, early evaluation is warranted.

Health Equity and Preconception Care

It is imperative to consider the social, structural, and environmental determinants of health that affect reproductive health care to address health disparities and provide equitable care for all individuals [9].

Although LGBTQIA+ and gender-nonconforming individuals are an increasingly recognized community, many barriers in accessing equitable health care remain [10]. Inquiring about a patient's gender identity, assigned sex at birth, pronouns, and preferred name can establish an inclusive and affirmative medical setting. Family building can occur through

multiple modalities, and it is important to discuss any desire for genetically related children and physically carrying a pregnancy to provide comprehensive counseling and care [11]. Information on timing, implications, and the limited research of testosterone treatment on conception and pregnancy should be discussed, as well as consideration of embryo or oocyte cryopreservation. It is also important to review any surgical treatments that may affect the ability to carry or contribute genetically to a child [11]. Additional medical considerations for this population include delivery preferences, chest-/breast-feeding, and postpartum care.

In addition to medical needs, there are many psychological considerations. There is often a discordance between one's identity and the idea of what a pregnant or gestational parent is, as defined by societal norms. Additionally, in a population with an increased rate of depression and suicide, mental health care from preconception through parenting is crucial [11].

Additional training for health care professionals, enhanced social understanding, and further research are needed to provide inclusive, equitable, and comprehensive reproductive health care to the entire health community.

Key Teaching Points

- Preconception counseling should be offered to all reproductive-aged patients.
- Providing preconception education, adjusting risk factors, and optimizing maternal health can reduce maternal and fetal reproductive complications.
- All women should receive genetic counseling and be offered genetic testing.

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CASE 2 A Patient with a Subchorionic Hematoma Presents with Early Vaginal Bleeding

Rima Rana

History of Present Illness

A 25-year-old primigravid patient at 8 2/7 weeks by her last menstrual period presents to the emergency department with vaginal bleeding. She reports that the vaginal bleeding started two days ago; initially, it was bright red, and now it is dark brown. She initially noticed it as red spotting on her underwear and has required one pantyliner per day. She denies abdominal pain or cramps. She reports increased nausea since she missed her period, but she has been able to tolerate small meals. She denies dizziness, lightheadedness, or shortness of breath. She decided to come in today because the bleeding continued, and she was worried. She reported having intercourse 1 week ago. This is an unplanned but desired pregnancy. She took a home pregnancy test that was positive 3 weeks ago. Her initial prenatal visit is scheduled for next week.

She denies any medical problems or surgeries in the past. She denies any allergies. She is not currently taking any medications or vitamins. This is her first pregnancy. Her prior gynecologic history is significant for a normal pap smear one year ago, and no history of sexually transmitted diseases, ovarian cysts, or fibroids. She is sexually active with one male partner. She drinks alcohol socially and occasionally uses marijuana but has stopped both since her positive pregnancy test. She denies any other substance use.

Physical Examination

General appearance: Well-developed, well-appearing, in no acute distress

Vital signs:

Temperature: 36.9°C
Pulse: 74 beats per minute
Blood pressure: 106/72 mmHg
Respiratory rate: 12 breaths per minute
BMI: 23.9 kg/m^2

Cardiopulmonary: Regular rate and rhythm, lung sounds clear to auscultation bilaterally

Abdomen: Soft, non-tender, non-distended. No rebound, tenderness, or guarding. No masses palpated

Pelvic: Normal-appearing bilateral labia majora and minora. On speculum exam, the vaginal wall rugae are normal in appearance, and there is scant dark brown blood in the vagina. The cervix appears without lesions and appears closed, no active bleeding noted.
On bimanual exam, the uterus is anteverted, mobile, and measures about 10 cm with no masses or tenderness. The adnexa are non-palpable and non-tender bilaterally.

Neurological/psychological: Normal affect, appears anxious, good insight and judgment

Laboratory studies:

Urine pregnancy test: Positive
WBC: 7,000/μL
Hgb: 9.4 g/dL
Beta-human chorionic gonadotropin (beta-hCG): 67,000 IU/L
Blood type: B Positive

Imaging:

Transvaginal ultrasound shows an intrauterine gestational sac and yolk sac. There is an embryo with a crown rump length (CRL) of 1.5 mm consistent with a gestational age of 8 weeks and 3 days. Fetal cardiac activity is identified and is 138 beats per minute. The cervix is closed. There is an 11 mm × 5 mm × 4 mm subchorionic hematoma.

How Would You Manage This Patient?

This patient is presenting with first-trimester vaginal bleeding. The differential diagnosis includes threatened abortion, incomplete or complete abortion, ectopic pregnancy, subchorionic hematoma, normal pregnancy, cervical lesion or polyp, trauma, and infection. A complete history and physical were obtained. Questions focused on determining the characteristics of the bleeding, including quantity, if it is intermittent or constant, and whether it was associated with pelvic pain, cramps, or contractions. The history included a detailed obstetric and gynecologic history, including prior pregnancies, history of sexually transmitted infections (STIs) or pelvic inflammatory disease, or other risk factors for ectopic pregnancies.

Vital signs were reviewed to assess hemodynamic stability. An abdominal exam was performed, assessing each quadrant. A speculum exam was performed to assess the amount of bleeding, the color of the blood, whether there was active bleeding, and whether there were blood clots or tissue present. The appearance of the cervix was assessed. Important laboratory testing for patients presenting with first-trimester bleeding includes a CBC, quantitative beta-hCG, and a type and screen. A transvaginal ultrasound was obtained and showed an intrauterine pregnancy with fetal cardiac activity. The ultrasound also showed a subchorionic hematoma.

Given that the patient was hemodynamically stable, with light bleeding that was not active, no pain, a closed cervix, and a viable intrauterine pregnancy, the patient was counseled on the slightly increased risk of pregnancy loss associated with a subchorionic hematoma. Given the small size of the hematoma, she was advised to start prenatal vitamins and follow up with her routine prenatal visit. Instructions and precautions were reviewed. This patient followed up for a routine ultrasound at 12 weeks' gestation, and the hematoma was reduced in size. She had not had any further bleeding. At her 20-week anatomy ultrasound, the subchorionic hematoma had completely resolved.

Table 2.1 Four types of hematomas in the maternal-placental-fetal unit

Types of hematomas	Location
Retroplacental hematoma	Between placenta and decidua
Marginal hematoma	At placental periphery between chorion and decidua, known as subchorionic hemorrhage
Subchorial thrombosis	Beneath chorionic plate
Subamniotic hematoma	Beneath amnion, of fetal vessel origin

Subchorionic Hematoma

A subchorionic hematoma, also known as a subchorionic hemorrhage, refers to a collection of blood found on a first-trimester ultrasound. It is a finding that can be a cause of anxiety among expecting patients. The developing fetus and its surrounding amniotic fluid are surrounded by fetal membranes. The inner membrane is the amnion, and it lines the amniotic cavity. The outer membrane is the chorion, which is opposed to the maternal decidua [1]. A subchorionic hematoma is one of several types of hematomas that can develop in the maternal-placental-fetal unit (Table 2.1) [2]. Subchorionic hematoma refers to a collection of blood between the chorionic membrane and the decidua due to a separation of these layers [3]. The causes of subchorionic hematoma are not completely understood. Risk factors are also not well-defined, although some association exists with in vitro fertilization [4].

A subchorionic hematoma is diagnosed with imaging studies, usually on a first-trimester ultrasonography performed for vaginal bleeding or on a routine obstetric ultrasound with an incidence of 3.1–18.4% [3]. Other studies report the incidence at 0.5–22% [5]. The diagnosis can also be made with computed tomography (CT) and magnetic resonance imaging (MRI), however, ultrasound is the most common imaging modality used when a subchorionic hematoma is identified [5]. On ultrasound, a subchorionic hematoma appears as a crescent-shaped area behind the fetal membranes and is hyperechoic to isoechoic in the first week, then becomes hypoechoic at 1–2 weeks, and anechoic after 2 weeks [5,2]. Typically, these are small on ultrasound and have no clinical consequence [2]. A systematic review and meta-analysis concluded that a subchorionic hematoma in the first trimester was associated with a one- to three-fold increased risk of miscarriage and no significant association with preterm delivery, fetal growth restriction, preeclampsia, or cesarean delivery [3]. Other studies show that patients with subchorionic hematomas are at slightly increased risk for early and late pregnancy loss, preterm premature rupture of membranes, preterm delivery, and an increased risk of placental abruption. Currently, no specific interventions exist to prevent these outcomes [5].

According to Naert et al., most subchorionic hematomas diagnosed in the first trimester resolve by the second trimester and are not associated with adverse pregnancy outcomes at 20 weeks' gestation. The size of the subchorionic hematoma also does not correlate with negative pregnancy outcomes. In this study, 90.7% of subchorionic hematomas resolved by the second trimester [6]. Despite a slight increased risk of pregnancy loss and other adverse pregnancy outcomes, most subchorionic hematomas resolve and result in healthy live births. Patients should be reassured of this. Typically, patients with subchorionic hematomas do not have life-threatening bleeding. Oftentimes the bleeding is light, without pain, and the patient is hemodynamically stable. Patients should be counseled on the risks of pregnancy loss and preterm delivery. There are no specific interventions to prevent these outcomes, and conservative management with follow-up is sufficient. There is no evidence that bed rest, pelvic rest, and increased frequency of monitoring with ultrasound or nonstress tests result in improved obstetrical outcomes [7]. Larger hematomas can be followed more closely, as the larger size may have an increased risk of miscarriage. However, this is not based on evidence, and currently, no guidelines exist in the follow-up and management of subchorionic hematoma [8]. Patients should be counseled to return to the emergency room if bleeding occurs with greater than one to two pads soaked every hour for more than two consecutive hours or with severe pain. If the patient is Rh negative, consideration should be given to administering Rho(D) immune globulin (RhoGAM).

Key Teaching Points

- Subchorionic hematoma is a common ultrasound finding for patients presenting with first-trimester vaginal bleeding or incidentally identified on a routine pregnancy ultrasound.
- It is associated with a slightly increased risk of pregnancy loss and preterm delivery, although most spontaneously resolve and result in healthy live births.
- Conservative management with follow-up ultrasonography is appropriate.
- Patients should be counseled and treated with empathy and provided reassurance.

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CASE 3 A 25-Year-Old with a Twin Gestation at 9 Weeks

Tara A. Nielsen

History of Present Illness

A 25-year-old gravida 3 para 1 at 9 0/7 weeks' gestational age by her last menstrual period presents to your office for her first prenatal visit. She complains of daily nausea with emesis one to two times per week. She has gained a total of 4 pounds since finding out she was pregnant. She denies bleeding, pelvic pain, or any vaginal complaints. She otherwise feels well. She has a history of one prior missed abortion requiring a suction dilation and curettage at 6 weeks and one prior spontaneous vaginal delivery (SVD) at term of a 7-pound 4-ounce infant. She denies a history of gestational diabetes, gestational hypertension, preeclampsia, or postpartum hemorrhage. She takes a prenatal vitamin daily, and vitamin B6 with doxylamine as needed for nausea. She is allergic to sulfa medications, which cause a rash.

Physical Examination

General appearance: Well-appearing, no acute distress

Vital signs:

Temperature: 36.7°C
Pulse: 86 beats per minute
Blood pressure: 105/65 mmHg
Respiratory rate: 19 breaths per minute
BMI: 23.29 kg/m^2

Cardiopulmonary: Regular rate and rhythm without murmur, rub, or gallop. Lungs clear to auscultation bilaterally

Abdomen: Soft, non-distended, non-tender to palpation, three-finger diastasis recti noted

Pelvic: Normal-appearing external genitalia without lesions, vagina well estrogenized, cervix with Chadwick's sign, uterus 8–10 weeks in size, mobile, non-tender, adnexa without masses or tenderness

Imaging:

Bedside ultrasound reveals two fetuses separated by a thick dividing membrane with the presence of the twin peak sign. Crown-rump-length measurements of 9 0/7 weeks' gestational age and 9 1/7 weeks' gestational age. A 2.2 cm × 3.4 cm corpus luteal cyst is seen in the left ovary. The right ovary is normal in appearance.

How Would You Manage This Patient?

This patient was diagnosed with a dichorionic-diamniotic (DCDA) pregnancy at 9 weeks' gestation. She was counseled on nutritional needs, weight gain goals, neonatal and obstetrical risks, recommended antenatal testing, and delivery recommendations for DCDA pregnancies. She had a low-risk noninvasive perinatal screening and declined further diagnostic testing. She received third-trimester growth ultrasounds with a 5% growth discordance noted. She developed preeclampsia without severe features at 37 weeks' gestation and was delivered via primary low transverse cesarean section due to fetal malpresentation. The neonates Apgar scores were 8, 9, and 7, 9. Her postpartum course was uncomplicated. The patient and her babies were discharged home on postoperative day three.

Twin Gestations

Zygosity refers to the genetic composition of a twin pregnancy. Dizygosity results from two separate ova being fertilized by two separate spermatozoa in a single ovulatory cycle, often referred to as fraternal twins. Monozygosity refers to a fertilized ovum that has split, resulting in identical twins. Chorionicity or type of placentation is determined by the mechanism of twinning specific to monozyotic twins and the timing of the split. If cleavage occurs within the first 72 hours of fertilization, two embryos, two amnions, and two chorions develop, resulting in a monozygotic, DCDA twin pregnancy. Cleavage occurring between days 4 and 7 results in a monozygotic, monochorionic-diamniotic (MCDA) twin pregnancy. Cleavage between days 8 and 12 will result in a monozygotic, monochorionic-monoamnionic (MCMA) twin pregnancy. Although rare, cleavage after this point will result in conjoined twins. Dizygotic gestations will always be DCDA.

It is estimated that 1–1.5% of natural conceptions result in dizygotic twin pregnancies. Monozygotic twin pregnancies are estimated to occur in 0.4% of all natural conceptions. Risk factors for dizygotic twin gestations include advancing maternal age, maternal family history, and race, particularly women of African descent. Risk factors for monozygotic twin pregnancies are less understood, and rates apart from the use of assisted reproductive technologies (ART) are consistent across all variables [1]. The incidence of twin gestations drastically increased from the 1980s until the early 2000s largely due to ART and an increase in maternal age at childbirth. However, the National Vital Statistics show a steady decrease in twin births in the United States from 2014 to 2022. This is hypothesized to be due to refinements and regulations in ART. However, numbers are recently on the rise again, showing a 2% increase in twin gestations from 2020 to 2021. In 2021, the incidence of twin births in the United States was 31.2 per 1,000 live births [2].

Compared to singleton gestations, twin pregnancies are associated with increased maternal risk of hyperemesis, gestational diabetes, hypertensive diseases of pregnancy, anemia, cesarean delivery, postpartum hemorrhage, and

postpartum depression. All twin pregnancies are at increased risk of fetal complications including prematurity, fetal congenital anomalies, and growth restriction, as well fetal and neonatal mortality. Due to an imbalance of blood supply to each fetus caused by arteriovenous malformations within the placenta and the potential imbalance of oxygenation and nutrients, a condition known as twin-to-twin transfusion syndrome, monochorionic pregnancies are at even higher risk of complications, leading to additional interventions and antenatal testing [3,4]. Table 3.1 shows data from the Birth in Brazil Study, a large population-based survey conducted between 2011 and 2012. Data collected from 266 hospitals across Brazil, including 23,746 singleton and 277 twin gestations, demonstrated an increased percentage of both maternal and neonatal complications for twin gestations [3].

First-trimester ultrasonography is clinically important for determining chorionicity, assisting with risk counseling, and delivery timing. Imaging beyond the early second trimester becomes less reliable for accurate diagnoses. If an ultrasound assessment clearly shows two separate gestational sacs separated by a thick membrane ≥2 mm, different sexes, or two distinct placentas, the pregnancy is DCDA. If only one placenta is observed, it is helpful to look for a twin peak sign, also called a delta or lambda sign. This will have the same echogenicity of the placenta, extending from the placental interface in a triangular-like projection into a hair-like dividing membrane, suggesting a DCDA pregnancy. The absence of a twin peak sign is predictive of a monochorionic pregnancy. Early in MCDA pregnancies, two separate yolk sacs and/or an inter-twin membrane without involving chorion may be observed. The inter-twin membrane in an MCDA gestation will appear more like a "T" rather than a "Y," as seen in the twin peak sign (Figure 3.1).

Table 3.1 Maternal and neonatal outcomes for twin and singleton gestations [3]

	Twin gestations (n=277 [%])	Singleton gestations (n=23,746 [%])
Maternal complications		
Hypertensive disorders of pregnancy	51 (18.5)	2,584 (10.9)
Eclampsia	3 (1.1)	135 (0.6)
Gestational diabetes	27 (9.7)	1,955 (8.2)
Emergency cesarean	89 (38.5)	3,043 (24.9)
Neonatal complications		
Low birth weight (<2,500 g)	353 (63.7)	2,116 (8.9)
Small for gestational age	202 (36.5)	1,822 (7.7)
Fetal growth restriction	103 (18.6)	746 (3.1)
Neonatal ICU admission	172 (31)	1497 (6.3)
Stillbirth	6 (1.1)	263 (1.1)
Neonatal death	27 (4.9)	241 (1.0)

Ultrasound imaging of MCMA pregnancies, the highest risk of all twin gestations, often shows cord entanglement with the absence of an inter-twin membrane. If monochorionicity is determined, monozygosity is confirmed. If dichorionicity is present with the same sex of each fetus, genetic testing would be indicated to definitively determine zygosity [1].

All patients should be offered genetic screening for aneuploidy. Options for screening include first-trimester screen, quad screen, sequential, or integrated screening. Nuchal translucency measurements can further evaluate each individual fetus. Noninvasive perinatal screening or cell-free fetal DNA has a sensitivity for trisomy 21 that may be similar to singleton gestations for completed tests. However, a high rate of test failure is present, and the detection rate for trisomy 18 and 13 is yet to be determined [4].

Patients with twin pregnancies must be counseled on adequate nutritional needs and weight gain specific to their twin gestation. It is well known that twin pregnancies are associated with low birth weights and prematurity. While these contributions are largely multifactorial, recognizing nutritional differences for twin gestations can be beneficial to reducing neonatal morbidity. Patients can expect to gain more weight than those carrying a singleton due to an increase in

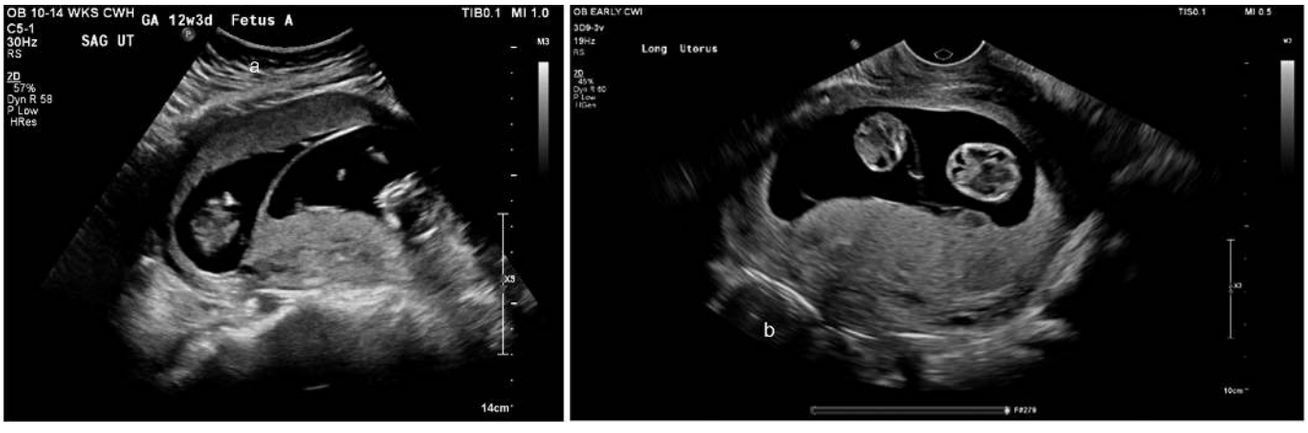

Figure 3.1 Ultrasound imaging of twin gestations. (a) A thick dividing membrane or twin peak sign is observed between an anterior and posterior placenta, demonstrating a DCDA gestation. (b) A thin dividing membrane with a single placenta denotes an MCDA gestation.

both maternal tissue and intrauterine contents. The National Academy of Medicine recommends patients with a normal body mass index (BMI) (18.5–24.9 kg/m^2) can expect a cumulative weight gain between 17 and 25 kg [5,6]. To do this, patients carrying twins need an additional 300 kcal/day from those carrying a singleton, or a total of 600 kcal/day in addition to the standard 2,000 kcal/day for a nonpregnant individual. Micronutrient recommendations for twin gestations include calcium 1,500–2,500 mg/day, vitamin D 1,000 IU/day, magnesium 400–800 mg/day, zinc 15–30 mg/day, DHA/EPA 300–500 mg/day, folic acid 1 mg/day, vitamin C 500–1,000 mg/day, and vitamin E 400 IU/day. A single multivitamin with 30 mg elemental iron is recommended in the first trimester, whereas two vitamins can be taken during the second and third trimesters to meet growing micronutrient demands later in advancing gestation. Due to the potential teratogenic effects of excess vitamin A supplementation, care is taken to avoid excesses of >8,000 IU/day [5].

The stillbirth rate increases with gestational age for twin gestations. While there is no known evidence-based recommendation for fetal growth surveillance, most guidelines recommend serial growth ultrasounds after 20 weeks for DCDA gestations. Discordant growth is defined as >20% difference in estimated fetal weights (EFWs). Discordant growth has been associated with an increase in adverse perinatal outcomes and may warrant further evaluation and surveillance. While there is not an established optimal age for initiating antenatal testing in patients with dichorionic pregnancies, in the absence of other risk factors, initiation of weekly testing may be considered at 36 0/7 weeks' gestation, with delivery at 38 0/7–38 6/7 weeks' gestation.

This rate of stillbirth is significantly greater for those with monochorionic pregnancies. Due to the risk of twin-to-twin transfusion syndrome in MCDA and MCMA pregnancies, ultrasound evaluation is generally recommended every 2 weeks, starting at 16 weeks' gestation, with antenatal testing recommended to start at 32 0/7 weeks' gestation. In the absence of complications, MCDA gestations undergo delivery between 34 0/7 and 37 6/7 weeks' gestation, and uncomplicated MCMA gestations are recommended for delivery between 32 0/7 and 34 0/7 weeks' gestation [4].

The route of delivery for DCDA and MCDA pregnancies is determined by the presenting twin and the experience of the delivering clinician. It is generally acceptable to consider a vaginal delivery if the EFWs are concordant, gestational age is >32 0/7 weeks' gestation, and the presenting twin is cephalic, regardless of the second twin's presentation. Patients with MCMA gestations should be delivered by cesarean section due to the risk of cord-related complications [4,7].

Key Teaching Points

- First-trimester and early second–trimester ultrasound is important in establishing chorionicity and determining risk assessment.
- Compared to singleton gestations, twin pregnancies are associated with an increased risk of both maternal and neonatal morbidity and mortality.
- Twin gestations should be offered genetic testing.
- Twin gestations have unique weight gain recommendations and micronutrient needs.
- Due to the increased risk of stillbirth with advancing gestational age, twin gestations are delivered earlier than singleton gestations.
- The route of delivery for DCDA and MCDA gestations is largely dependent on the presenting twin and the experience of the delivering clinician.
- MCMA gestations should be delivered by cesarean section.

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Section 1 Antepartum (Early Pregnancy)

CASE 4

A 35-Year-Old with HSIL Cervical Cytology at 10 Weeks

Margaret E. Long

History of Present Illness

A 35-year-old gravida 3 para 2 at 10 1/7 weeks is found to have a high-grade squamous intraepithelial lesion (HSIL) on cervical cytology with positive high-risk human papilloma virus (HPV) types other than 16 or 18 on her recent screening. She has no prior abnormal cervical cancer screening but has not undergone screening since the birth of her child 7 years ago, and these results are unavailable. She has no previous HPV testing. She recalls having the HPV vaccine in college. She reports previous tobacco use but none since her first pregnancy. She denies any vaginal bleeding or abnormal discharge. She is concerned about her cervical cancer risk but does not want to do anything that might cause harm to her pregnancy.

Physical Examination

General appearance: Alert, in no apparent distress
Vital signs:

Temperature: 37.2°C
Pulse: 73 beats per minute
Blood pressure: 114/74 mmHg
Respiratory rate: 16 breaths per minute
BMI: 26.2 kg/m^2

Inguinal lymph nodes: No inguinal adenopathy
Pelvic exam: Parous cervix without gross lesions
Laboratory studies:

Cervical cytology: Satisfactory for evaluation, endocervical component present. Epithelial cell abnormality: HSIL. High-risk HPV nucleic acid amplification test: positive for types other than 16 or 18

Imaging:

Viable, single intrauterine pregnancy. Unremarkable uterus and cervix

How Would You Manage This Patient?

Colposcopy was recommended, and this was performed at 13 weeks' gestation. During colposcopy, the complete transformation zone was visualized. The colposcopic impression was high-grade due to the presence of acetowhite changes and a focus of mosaicism. There were no findings suspicious for cancer. A single ectocervical biopsy revealed cervical intraepithelial neoplasia (CIN) 2. An endocervical brushing was negative.

After discussing with the patient, she decided to proceed with surveillance colposcopy during pregnancy. During follow-up colposcopy at 32 weeks' gestation, she was found to have a stable lesion, and biopsies were not performed. Diagnostic cotesting noted HPV+/HSIL. She had an uncomplicated vaginal delivery at 40 weeks' gestation. At her 6-week postpartum visit, diagnostic cotesting revealed HPV+/low-grade squamous intraepithelial lesion (LSIL). At 11 weeks' postpartum, colposcopic evaluation included two biopsies of lesions and an endocervical curettage (ECC). The ECC was negative, and the biopsies returned as CIN 1. She was advised to undergo HPV-based testing and colposcopy in 6 months as conservative follow-up of her initial CIN 2 [1]. Once her annual surveillance phase was satisfactorily completed, she was recommended to have follow-up that included HPV-based testing every 3 years until 25 years after her CIN 2 biopsy.

Cervical Dysplasia Management during Pregnancy

The goal of cervical cancer screening is to prevent cervical cancer by identifying and treating lesions that pose a risk for cancer. Outside of pregnancy, all CIN 3 lesions and many CIN 2 lesions are to be promptly treated. Care during pregnancy requires attention to short- and long-term maternal health while minimizing pregnancy complications.

Survival is improved when cervical cancer is diagnosed in pregnancy compared to 6 months after delivery. Cervical cancer diagnosed during pregnancy has similar survival rates to age-matched nonpregnant controls [2]. However, the risk of progression from CIN 2 or 3 to cancer in pregnancy is very low. For those with histologic HSIL (CIN 2–3), the rate of progression to cancer during pregnancy was 1% (95% CI 0–2%) in a meta-analysis of 10 studies [3]. Increased risk of complications has been observed with cervical excisional procedures performed during pregnancy, including bleeding, infection, and preterm labor [4]. The meta-analysis also noted regression rates of 59% (95% CI 54–65%) for CIN 2 and 29% (95% CI 25–33%) for CIN 3, while persistence rates were 40% (95% CI 35–45%) and 70% (95% CI 65–73%), respectively, at postpartum follow-up [3]. Given the low risk of progression to cancer during pregnancy, the high rate of disease regression, and the possibility of short-term harm from an excisional procedure, treatment of histologic HSIL is not recommended during pregnancy [1].

The 2019 American Society for Colposcopy and Cervical Pathology (ASCCP) management guidelines rely on current HPV and cytology results, biopsy results, and prior screening history to recommend management based on risk thresholds [1]. Human papillomavirus-based testing (cotesting [cytology and HPV] or primary HPV testing with reflex cytology) is preferred for cervical cancer screening in individuals 30 years and older and for surveillance of abnormal results in