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PREGNANCY COMPLAINTS AND COMPLICATIONS: CLINICAL PRESENTATIONS
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Chapter
Bleeding in Early Pregnancy

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DEFINITION

Vaginal bleeding during pregnancy is any discharge of blood from the vagina. It can happen anytime from conception (when the egg is fertilized) to the end of pregnancy. Bleeding during pregnancy can cause maternal anxiety and emerging evidence suggests that it may be associated with poor fetal and maternal outcomes.

INTRODUCTION

First trimester bleeding is a matter of great concern to a large group of the obstetric population. One-quarter of pregnant woman will experience vaginal bleeding during the first trimester. About half of these will end in miscarriage within 20 weeks of gestation and those women who remain pregnant have an increased risk of developing other complications later in pregnancy.¹

Bleeding can be in the form of spotting, light, or heavy bleeding. Spotting is bleeding reported by the patient as scant or traces of blood or visualized by clinician as scant or no blood in the vagina and at the cervix. It is considered a spotting when a woman notices a few drops of blood occasionally in her underwear, or if a woman wipes herself with tissue and sees a little blood on the paper. Light bleeding is reported by the patient as like a “menses”. It is visualized by the clinician as a small amount of blood in the vagina or at the cervix. Heavy bleeding is reported by the patient as more than a “menses”. It is visualized as a moderate to heavy amount of blood in the vagina or at the cervix.

It is not always possible to make a diagnosis at the first presentation. In some cases, the need for follow-up
Causes of first-trimester vaginal bleeding includes obstetric and non-obstetric etiologies. The most frequent etiologies are miscarriage and ectopic pregnancy. Rarer causes include cervical and vaginal lesions (e.g., malignancy, cervical ectropion, polyps, infection) and uterine infection. Gestational trophoblastic disease (GTD) should always be considered, particularly in the setting of an abnormally raised serum human chorionic gonadotropin (hCG) or suggestive ultrasound findings. Establishing the site of the pregnancy is a crucial step, as failure to correctly diagnose an ectopic pregnancy can have potentially life-threatening consequences.

The early weeks of (4–12 weeks) pregnancy is the period of organogenesis. Various factors may disturb the pregnancy during this period, which has a subsequent effect on obstetric outcome. First-trimester vaginal bleeding is an independent risk factor for adverse obstetric outcome that is directly proportional to the amount of bleeding. Heavy vaginal bleeding subjects are more likely to have intrauterine growth restriction, preterm delivery, preterm premature rupture of membranes, and placental abruption.

Local hemostatic factors in the uterus during implantation, decidualization, and early pregnancy, for example, tissue factor expressed in cytotrophoblasts and systemic factors in the women during the ongoing pregnancy seem to play distinct roles in a successful pregnancy. Dysfunction of any of these factors could lead to an adverse outcome.

It is hypothesized that first-trimester bleeding may indicate an underlying placental development dysfunction, which manifest later in pregnancy causing adverse pregnancy outcome.

Impaired invasion of cytotrophoblasts and remodeling of spiral arteries in early placentation have been demonstrated in pregnancies ending in miscarriage and also those pregnancies complicated by preterm delivery, premature preterm rupture of membranes (PPROM), placental abruption. An iron excessive deposit may also provoke a production of excessive oxidative stress, which has been linked to preterm delivery, PPROM, and pre-eclampsia. Subchorionic hematoma can result in a nidus, which may become infected and cause preterm rupture of membranes and preterm delivery.

Also, decidual bleeding will generate an excess amount of thrombin, which is a uterotonic agent and may cause preterm labor during late pregnancies and spontaneous abortion during the early weeks of gestation.

As bleeding may be an early marker of placental dysfunction, few studies have evaluated the association between bleeding and development of pre-eclampsia in later pregnancy. A 40% increased risk of pre-eclampsia was found in women with light bleeding during the first trimester in comparison to women without bleeding, whereas women with heavy bleeding did not have this elevated risk.

Ultrasound is the primary imaging modality in the evaluation of patients presenting with bleeding in the first trimester of pregnancy. It is a safe and non-invasive diagnostic technique, which helps in the timely diagnosis of bleeding per vagina in the first trimester with the advent of transvaginal ultrasonography, a developing fetus can be detected within 5 weeks of conception. Moreover, the obstetric literature indicates that visualizing an intrauterine pregnancy (IUP) with fetal heart beat has a significant predictive value. Patients with first-trimester complications whose ultrasonographic findings reveal an IUP with detectable cardiac motion, (or a LIUP : live IUP) have a 90% or higher chance of delivering a live infant.

With the advent of improved technology and high-resolution transvaginal probes, fetal heart movement can now be detected 2 to 3 weeks earlier than previously with a transabdominal approach.

**ASSESSMENT**

Bleeding in early pregnancy is probably the most common condition that gynecologists face in daily clinical practice. The initial assessment of a woman in these cases must first consider hemodynamic stability, the degree of bleeding, and the associated pain. Immediate transfer to the emergency department could be necessary in a hemodynamically unstable patient. It is important to recognize that young women may suffer significant blood loss before any signs of hemodynamic instability are evident. History, speculum examination, and transvaginal ultrasound are first important steps in the assessment of the origin of bleeding, the differential diagnosis process, and the consequent management.

**History**
It is important to assess the likely gestational age of the pregnancy, the amount of blood loss, and any associated pain symptoms. Syncope, chest pain, and shortness of breath may point to anemia from significant blood loss, and shoulder tip pain may be associated with intra-abdominal bleeding. Then, consider the possible risk factors for ectopic pregnancy (use of an intrauterine device (IUD), pregnancy as a result of assisted reproduction, a past history of pelvic infection or sexually transmissible infections (STIs) or tubal surgery, previous ectopic pregnancy). In addition, cervical smear history is relevant, particularly if any abnormal bleeding has also been occurring outside of pregnancy. Certain medical conditions, such as poorly controlled diabetes and thyroid disease, are sometimes associated with an increased risk of miscarriage and thus early bleeding.

**Examination**

Following initial assessment for any diagnosis of hemodynamic instability and anemia, *abdominal examination* may reveal areas of tenderness, guarding or rigidity, and signs of distension. The fundus will be palpable above the symphysis pubis when the uterus reaches the size appropriate for a 12-week gestation. It may be palpable earlier than this in the case of a multiple pregnancy, gestational trophoblastic disease (GTD), or if other pelvic or uterine masses such as fibroids or ovarian cysts are present.

*Speculum examination* is performed to assess the amount and origin of ongoing bleeding. The vagina and cervix should be inspected for other possible causes of bleeding (e.g., polyps, cervix/vaginal lesions). Tissue present in the open cervical os must always be removed and should be sent for histopathological examination. Bimanual examination allows assessment of uterine size, dilatation of the cervical os, pelvic tenderness, and cervical motion tenderness.

**Complementary investigations**

A combination of ultrasound assessment (transvaginal/transabdominal) and measurement of serum hCG is often required to determine the location and viability of an early pregnancy, when the woman has presented with bleeding. Testing for maternal blood group and antibody status will determine the need for Rh D immunoglobulin administration.

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**OBSTETRIC CAUSES**

Early pregnancy loss (EPL) is a term often used interchangeably with spontaneous abortion and miscarriage and refers to pregnancy loss during the first trimester. It is the most common cause of early pregnancy bleeding and is usually associated.\(^8\),\(^9\)

Threatened early pregnancy loss, often considered a type of early pregnancy loss, refers vaginal bleeding in the presence of an intrauterine pregnancy and a closed cervix. The presence of fetal heart rate largely determines whether the pregnancy will progress to a viable outcome.

**Implantation bleeding**

In early pregnancy, some harmless light bleeding could be observed, called “spotting”. This is when the developing embryo implants in the uterine cavity. This type of bleeding often happens around the time the menstrual period would have been due.\(^9\)

**Threatened miscarriage**

If a pregnancy ends before the 22nd week, it is called a miscarriage. Around 1 in 5 pregnancies ends this way. Many early miscarriages (before 12 weeks) happen because there are chromosome errors. There can also be other causes of miscarriage, such as hormone or blood-clotting problems.\(^10\)

Two important clinical risk factors for miscarriage are a history of previous miscarriages and vaginal bleeding in the current pregnancy. Moreover, the risk of miscarriage increases in line with the number of previous miscarriages a woman has suffered.\(^11\)

A recent meta-analysis showed that the risk of miscarriage increases along a sequential biological gradient from an 11% risk of miscarriage in those women with a history of no previous miscarriage, to a 65% risk of miscarriage in those
women with a history of six or more previous miscarriages. Progesterone supplementation in early pregnancy has therefore been attempted in these two contexts of increased miscarriage risk: the first is to prevent miscarriages in asymptomatic women with a past history of recurrent miscarriages, and the second is to rescue a pregnancy in women who have started to bleed in early pregnancy. It is important to consider that approximately half of all miscarriages, including pregnancy losses in women with recurrent miscarriage, are due to numeric chromosome errors with trisomy being the most frequent, especially with advancing maternal age, followed by polyploidy and monosomy X. A study by Ogasawara et al. demonstrated that "aneuploid" miscarriages occur on a random basis, meaning that the risk of subsequent aneuploid miscarriage is not increased according to the number of previous miscarriages. Conversely, "euploid" miscarriages are more frequently diagnosed with increasing number of previous miscarriages. Therefore, the potential therapeutic opportunity for any drug or treatment is greatest in women with a large number of previous miscarriages. These data are important in the context of the latest clinical trial data on the effectiveness of progesterone to prevent miscarriage in both recurrent and threatened miscarriage.

Table 1 Common symptoms of threatened miscarriage/miscarriage.

<table>
<thead>
<tr>
<th>Symptoms</th>
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</thead>
<tbody>
<tr>
<td>Cramping and pain in lower abdomen</td>
</tr>
<tr>
<td>Discharge or fluid from vagina</td>
</tr>
<tr>
<td>Discharge of tissue from vagina</td>
</tr>
<tr>
<td>No longer experiencing the symptoms of pregnancy, such as breast tenderness and feeling sick</td>
</tr>
</tbody>
</table>

The scientific literature has plenty of treatment proposals for threatened miscarriage, all aimed to succeed in a term viable fetus. Very few of them have been validated over the years with randomized controlled trials.

Vaginal micronized progesterone 800 mg/day is now recommended for pregnant women with first-trimester vaginal bleeding and one or more previous miscarriages, from the time when bleeding till 20 weeks.

Vaginal bleeding during the first trimester as well as two or more previous miscarriages are considered as a risk factor for very early preterm birth. Therefore, it is reasonable to continue vaginal micronized progesterone 200 mg/day till 36 weeks in these patients.

In patients with recurrent pregnancy loss (RPL), vaginal progesterone supplementation is recommended from the preconceptional stage (during the luteal phase, 2–3 cycles before the conception) at a dosage of 800 mg/day till 20 weeks. (Table 2).

Table 2 Evidence-based treatment of threatened miscarriage.

<table>
<thead>
<tr>
<th></th>
<th>Treatment</th>
<th>Timing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding during the first trimester (if at least one previous miscarriage)</td>
<td>Micronized vaginal progesterone 800 mg/day</td>
<td>Till 20 weeks</td>
</tr>
<tr>
<td>Previous miscarriages and bleeding during the first trimester</td>
<td>after 20 weeks: 200 mg/day</td>
<td>Till 36 weeks</td>
</tr>
<tr>
<td>Recurrent pregnancy loss</td>
<td>800 mg/day from luteal phase</td>
<td>Till 20 weeks</td>
</tr>
</tbody>
</table>

Subchorionic hematoma

A hematoma in the uterus or intrauterine hematoma is an effusion of blood that accumulates inside the uterine cavity during gestation. Hematomas, especially subchorionic hematomas, appear most often during the first trimester of pregnancy and can occur with or without vaginal bleeding. They are always a major cause of concern for pregnant women.
In normal pregnancies, the earliest stages of placental development take place in a low oxygen (O$_2$) environment. This physiological hypoxia of the early gestational sac protects the fetus against the teratogenic effects of O$_2$ free radicals and stimulates cytotrophoblast proliferation while inhibiting trophoblast invasion. As the second trimester approaches, a rise in pO$_2$ occurs as maternal blood flow starts, triggering trophoblast from the proliferative state to the invasive state, leading to a secondary wave of trophoblast invasion of maternal spiral arterioles. This results in a high-flow, low-impedance uteroplacental circulation. This coordination of trophoblast and endothelial cell development, proliferation, invasion, and differentiation is mediated by locally acting growth factors, which are probably regulated by oxygen tension and mechanical stimuli. Vaginal bleeding during early pregnancy most commonly originates from developing placenta and is an outcome of impaired placenta, which results in synthesis and release of altered angiogenic and antiangiogenic factors in the maternal circulation. Regulation of normal placentation involves the interaction of various pro- and anti-angiogenic factors, angiopoietins and matrix metalloproteinases. In early pregnancy failure, the development of the placenta-decidual interface is severely impaired, leading to premature and excessive entry of maternal blood inside the placenta, which has two effects on the villous tissue. First a direct mechanical effect of large intervillous blood thrombi, which progressively embed the villi and secondly an indirect O$_2$-mediated oxidative damage, leading to apoptosis and necrosis of the villous trophoblast. This leads to placentation degeneration with loss of syncytiotrophoblast function and detachment of the placenta from the uterine wall. The premature perfusion of the intervillous space results in subchorionic hemorrhage (SCH). Shallow trophoblast invasion and impaired angiogenesis, resulting in friable blood vessels, may be a predisposing factor of subchorionic hemorrhage, as well as subsequent adverse outcomes. The presence of a hematoma may create an area of weakness, where further separation of the placenta from the uterine wall may occur, resulting in placental abruption, which is more common with a retroplacental type of hemorrhage. The presence of an SCH and detachment of the gestational sac from the endometrium may result in miscarriage.

**Focus on the role of progesterone in early pregnancy**

As previously mentioned, progesterone has a crucial significance in the support of pregnancy. The role of progesterone in the maintenance of pregnancy comprises the modulation of maternal immune response, the suppression of the pro-inflammatory cascade, the inhibition of uterine contractility, and its beneficial effects on utero-placental perfusion. In recent years, researches reached important advances in biochemical progesterone formulations and routes of administration (for example, vaginal soft capsules, dry effervescent tablets, pessaries, and even suppositories are now available). This improved knowledge continues to stimulate experts to deepened their bioequivalence profile in order to define the “best therapeutic way” in terms of efficacy and safety, daily dose, adverse event, cost-effectiveness, patient compliance, and tolerability. The standard management of threatened miscarriages, recurrent pregnancy loss, and threatened preterm birth are based now on progesterone administration, mainly vaginally applied. If progesterone supplementation reduces the risk of repeat miscarriage, the scientific basis for its use may be related in part to its role in the regulation of inflammatory mediators in pregnancy. Progesterone deficiency leads to increased levels of pro-inflammatory interleukin 8 (IL-8), cyclo-oxygenase-2, and monocyte chemoattractant protein-1, which destabilize the endometrium. Successful pregnancy is associated with the down-regulation of pro-inflammatory T helper cell type 1 (Th-1) cytokines and up-regulation of anti-inflammatory T helper cell type 2 (Th-2) cytokines. A 34-kDa protein, progesterone-induced blocking factor (PIBF) prevents inflammatory reactions by blocking Th-1 cytokines and natural killer cells’ degranulation and increasing asymmetric non-toxic blocking antibodies.

**ECTOPIC PREGNANCY**

An ectopic pregnancy is when a fertilized egg implants outside the uterus – for example, in the fallopian tube. It can cause bleeding and, sometimes, an acute abdomen that needs to be managed with an urgent surgery approach. When the clinical features are stable an expectant management or pharmacological therapy are reasonable options. Symptoms and signs of an ectopic pregnancy tend to variably develop between 4 and 12 weeks (Table 3).

**Table 3** Symptoms of ectopic pregnancy.*
Symptoms

<table>
<thead>
<tr>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tummy pain low down on one side</td>
</tr>
<tr>
<td>Vaginal bleeding or a brown, watery discharge</td>
</tr>
<tr>
<td>Pain in the tip of shoulder</td>
</tr>
<tr>
<td>Discomfort when peeing or pooing</td>
</tr>
</tbody>
</table>

* These symptoms are not specific and other possible diagnosis could be taken into consideration.

The tubal mass, sometimes, but not always, ruptures during the clinical course, usually after 7 weeks of gestation. The rupture may occur because of the limitations of the growing ectopic mass imposed by the tubal lumen. When a rupture is present, severe abdominal distention and marked tenderness may be present due to peritoneal irritation caused by massive hemoperitoneum. When these physical signs are obvious and the woman has a tendency of hypotension and tachycardia, immediate fluid reinfusion should be selected to maintain a sufficient volume flow through the circulation and surgical management to arrest the hemorrhage. The accuracy of diagnosing tubal pregnancy has been greatly improved by technical advances in diagnostic tools and techniques. However, discriminating earlier spontaneous pregnancy is unavoidable. Differentiating spontaneous abortion from tubal pregnancy is also necessary. In addition, early diagnosis of tubal pregnancy is important to prevent maternal mortality and potential massive hemorrhage of a ruptured tubal pregnancy.

Ultrasonography is the first diagnostic tool used when a tubal pregnancy is suspected. Transvaginal ultrasonography (TVS) for diagnosis of tubal pregnancy is considered superior to transabdominal ultrasonography (TAS). The first step in diagnosing tubal pregnancy is differentiating it from spontaneous pregnancy and miscarriage by visibility and viability of an intrauterine gestational sac using TVS. If the gestational sac is not visible on TVS after 5 weeks of gestation, other findings should be carefully evaluated when a tubal pregnancy is suspected. However, in some cases of tubal pregnancy, a pseudo-sac appears in the intrauterine cavity, leading to a misdiagnosis of spontaneous pregnancy on TVS. In addition, although spontaneous heterotopic pregnancy is considered very rare with an incidence of 1 in 30,000 pregnancies, the incidence of heterotopic pregnancy following ART is increased and has been reported to occur in approximately 0.8% of pregnancies following infertility treatment. It is known that previous surgery is one of the risk factors of heterotopic tubal pregnancy: approximately two-thirds of patients report previous surgery including salpingectomy for previous tubal pregnancy. An anechoic free fluid in the pouch of Douglas on TVS is generally detected in not only intrauterine but also ectopic gestations. The presence of echogenic fluid has been found in 28–56% of women with tubal pregnancy. The echogenic appearance reflects the condition of tubal pregnancy and correlates well with the surgical findings of hemoperitoneum. The presence of fluid in the Morrison's pouch observed via TAS indicates that severe hemoperitoneum may have occurred by rupture of the tubal pregnancy.

**Table 4 Management of ectopic pregnancy.**

<table>
<thead>
<tr>
<th>Expectant management β-hCG level &lt;1000 mIU per mL and decreasing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ectopic or adnexal mass ≤3 cm or not detected</td>
</tr>
<tr>
<td>Minimal pain or bleeding</td>
</tr>
<tr>
<td>No embryonic cardiac activity</td>
</tr>
<tr>
<td>No evidence of tubal rupture</td>
</tr>
<tr>
<td>Patient reliable for follow-up and has no barriers to accessing health care</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Absence of embryonic cardiac activity β-hCG level &lt;2000 mIU per mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ectopic mass ≤3.5 cm</td>
</tr>
<tr>
<td>No medical contraindication (hematologic dysfunction; liver, kidney, or pulmonary disease; immunodeficiency; peptic</td>
</tr>
</tbody>
</table>
ulcer disease; breastfeeding; sensitivity to methotrexate; alcohol abuse)

Patient reliable for follow-up and has no barriers to accessing health care

Stable vital signs and few symptoms

**Surgical management** (the laparoscopy approach should be first line)

**Advanced ectopic pregnancy** (high $\beta$-hCG level, large mass, embryonic cardiac activity)

Contraindications to observation or methotrexate

Patient unreliable for follow-up or has barriers to accessing health care (individualization of intervention)

Uncertain diagnosis

Unstable vital signs or signs of hemoperitoneum

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**GESTATIONAL TROPHOBLASTIC DISEASE**

It refers to pregnancy-related tumors that be either cancerous or non-cancerous. This etiology is extremely rare with non-cancerous gestational trophoblastic neoplasia found in 23 to 1299 cases per 100,000 pregnancies and cancerous forms with a tenfold lower incidence.

The hypervascular and friable nature places the patient at risk for significant hemorrhage. Vaginal hemorrhage caused by gestational trophoblastic disease (GTD) may be a challenging event in the management of these patients. Traditionally, gauze packing and surgery, such as abdominal hysterectomy or uterine artery ligation, were the treatment of choice for controlling intractable hemorrhage. Recently, selective arterial embolization (SAE) has been shown to be a safe and highly effective alternative procedure for massive genital bleeding. Similar to the case of postpartum hemorrhage, interventional therapies play a key role in the management of patients with gynecological hemorrhage. Most of the reports in the literature have been in the setting of postpartum hemorrhage, but the same principles apply in the management of gynecological malignancy, such as GTD embolization can be more complicated in cases of GTD compared to embolization in postpartum hemorrhage. GTD can destroy blood vessel walls and connect arteries and veins, thereby facilitating the formation of uterine arteriovenous malformations (AVMs). If there is a large fistula in the AVMs, SAE should proceed cautiously. In the large fistula, coils are initially used to embolize the feeding arteries because gelatin sponge may cross the fistula and result in complications. The vessels that cause bleeding from the female genital tract are usually predictable. The uterine artery supplies the uterus and cervix and accounts for the majority of bleeding; however, the tumor often extends outside of these structures into the pelvis, and other anterior division vessels are recruited to supply the tumor. It seems logical that the presence of collaterals to the uterus increases the risk of rebleeding. Owing to their remarkable sensitivity to chemotherapy, the cure rates are almost 100% in the low-risk group and nearly 80% in the high-risk group with current chemotherapy regimens. Chemotherapy is the primary modality of treatment in patients with GTD. Some physicians are unwilling to accept SAE, and did so only when the patient had life-threatening hemorrhage. They thought that embolizing a tumor-feeding artery might block release of the chemotherapeutic drugs into the tumor tissue, which has never been shown.

**RUPTURED CORPUS LUTEUM CYST IN PREGNANCY**

Appropriate evaluation of hemoperitoneum is an important clinical issue in obstetric practice because of the potential need for emergent surgical intervention. A ruptured corpus luteum cyst (RCLC) is the major cause of gynecological hemoperitoneum and can be a life-threatening surgical condition, which can occur at all stages of a woman's reproductive life, including pregnancy. The diagnosis is mainly based on high clinical suspicion, laboratory data, and ultrasound findings. Most ruptures are associated with unilateral lower abdominal pain, thought due to blood seeping into the ovary and stretching the ovarian cortex. Pain often begins during strenuous physical activity, such as exercise or sexual intercourse. Ectopic pregnancy, ruptured tubo-ovarian abscess, ovarian mass torsion, and other cystic ovarian...
disorders are the major differential diagnoses for RCLC. Ultrasonography and magnetic resonance (MR) imaging can often aid in diagnosis and risk assessment. The clinical presentation of RCLC is variable, ranging from a benign asymptomatic state to clinical shock. While mild cases of RCLC require only clinical observation and support, surgical intervention is necessary for severe cases of RCLC with hemodynamic instability.

General recommendations for RCLC in pregnancy include conservative management of stable light hemoperitoneum and/or uncomplicated RCLC and surgical management of complicated RCLC involving abnormal vital signs, significant hemoperitoneum by clinical or radiological exam, or abnormal laboratory values. Other surgical indications include cysts greater than 5 cm in diameter, a failure of a cyst to resolve or decrease in size spontaneously, complex or solid cysts indicative of suspected malignancy, history of anticoagulation therapy, severe persistent abdominal pain, and complications such as ovarian torsion, active hemorrhage, or infarction.

GYNECOLOGICAL ETIOLOGIES

Cervical polyps
Cervical polyps are uncommon in pregnancy, and they are often asymptomatic and small. Thus, some cervical polyps can be misdiagnosed, but sometimes they cause bleeding in pregnancy. A vaginal speculum examination (VSE) prior to transvaginal ultrasound is useful as part of early bleeding assessment in pregnancy, because it could reveal the presence of cervical polyps. In these cases, experts suggest not removing the polyp during gestation, if bleeding is stopped or under control. Cervical polyps are often spontaneously destroyed and eliminated during vaginal delivery. It is reasonable to suggest a gynecological visit after about 6 weeks from delivery.

Cervical cancer
The diagnosis of invasive cervical cancer during pregnancy brings much angst to the patient, family, obstetrician-gynecologist, and other health-care providers. Although most cancer cases are diagnosed at an early stage, difficult decisions are needed that impact both the mother and the fetus, which may be in conflict. There is significant evidence that delay in treatment of early stage cancer is not likely to have a deleterious effect on the mother, and that delay of treatment until fetal maturity in a desired pregnancy is a reasonable course of action. In more advanced-stage disease, special issues regarding imaging and treatment of the gravid patient can be complicated, and little data are available to guide adequate counseling. Most women diagnosed with cervical cancer during pregnancy are found to have early stage disease. Microinvasive carcinoma (FIGO stage IA1 and IA2) and visible lesions limited to the cervix (stage IB1 and IB2) complicating pregnancy have been studied extensively under the category of early stage disease. Decisions regarding timing of treatment and delivery are weighted by the trimester in which the diagnosis is made and more importantly the desirability of the pregnancy for the affected woman and her family.

Blood loss and transfusion requirements are greater than in the non-pregnant or early pregnant states. Invasive cervical cancer diagnosed within the first and second trimesters can be a bit more challenging. Counseling regarding gestations less than 20 weeks (before any definition of fetal viability) is easier than when the diagnosis and impending treatment occurs within the gray zone of fetal viability (22 to 24 weeks). If the gestation is 20 weeks and the pregnancy is undesired, termination can ensue followed by appropriate treatment. If enough data are known to warrant proper surgical intervention, treatment can occur simultaneously as in type II or type III radical hysterectomy with pelvic lymphadenectomy leaving the fetus in situ for stages IA2 or IB cervical cancer. If the extent of the disease is not known, then termination should be completed and further evaluation performed, such as cervical cone biopsy for anticipated microinvasive carcinoma.

There are no case reports of metastatic cervix cancer to the fetus or placenta. Treatment for stage IIB-IVA should be directed toward curative intent, and maternal outcome should weigh greater than fetal well-being. Chemoradiation is the mainstay of therapy and should be initiated promptly. Non-viable fetuses abort with radiation. There are no data to suggest fetal loss occurs sooner with chemoradiation. Although radiation should have lesser fetal effects in the third trimester, a live fetus spontaneously delivered after radiation in the third trimester has been described, demonstrating microcephaly and mental retardation. Multidisciplinary counseling is paramount. Newer technologies are under development that allow women a choice of fertility-sparing procedures designed to treat early-stage cervical cancer. Their use following pregnancy has not been studied. Often, gravid women desire future fertility, and preservation of both
ovarian function and the uterine fundus is critical to achieve this outcome. In highly select patients, delayed surgical therapy by radical trachelectomy and pelvic lymphadenectomy may be a valid option after delivery and postpartum recovery. Patients should understand the relative novelty of the procedure in the non-gravid state and the lack of outcomes data in this scenario. With careful counseling, however, options for more conservative therapy may be acceptable.

NON-GYNECOLOGICAL ETIOLOGIES

Hematological disorders

von Willebrand disease (VWD) is the most common inherited bleeding disorder, found in approximately 1% of the general population, without ethnic differences. VWD is the result of a deficiency or defect in von Willebrand factor (VWF), the large multimeric protein, which mediates platelet adhesion and serves as a carrier protein for factor VIII (FVIII). There are three major types. Type 1 is the result of a partial, quantitative deficiency of a structurally normal VWF, and accounts for 70–80% of all VWD patients. Type 2 (20% of VWD patients) includes several qualitative defects in VWF that affect its multimeric structure or function. Patients with type 3 VWD (<10% of VWD patients) are homozygous or doubly heterozygous for two mutant VWF alleles, with a resulting complete deficiency of VWF and a secondary severe deficiency of FVIII. Although the autosomal inheritance pattern predicts that both sexes should be equally affected, there is a higher frequency of symptomatic VWD in women because of the hemostatic challenges of menses, pregnancy, and delivery. Pregnant women with VWD are at risk from a variety of bleeding complications, as a result of invasive prenatal diagnostic and monitoring procedures, spontaneous or elective abortions, and the hemostatic challenge of delivery. There are no prospective studies defining the risk of bleeding in these settings; estimates are based on surveys and small case series.

Since FVIII and VWF levels do not increase significantly until the second trimester, women with VWD remain at risk from bleeding in early pregnancy. In one series, first-trimester vaginal bleeding occurred in 33% of pregnancies. Antepartum hemorrhage is uncommon but may occur after spontaneous miscarriage or elective termination, occasionally as the initial presentation of VWD. In one study, 10% of spontaneous or elective abortions were complicated by excessive bleeding requiring transfusion. Intermittent bleeding 2 weeks after miscarriage occurred in 30% of cases. In another series, 3.8% of women with VWD had bleeding at the time of abortion.

Antifibrinolytics, such as ε-aminocaproic or tranexamic acid (TA) are often used in VWD patients to control bleedings. The basis for their use is the rich fibrinolytic activity of mucosal tracts – the source of most bleedings in VWD. Antifibrinolytics alone may be sufficient to control less severe forms of bleedings or can be used as adjuncts to desmopressin or factor concentrates. Both women suffering from HMB or PPH may benefit from using antifibrinolytic drugs. A recent report from an international, randomized, double-blind, placebo-controlled trial named WOMAN assessed the efficacy of TA in reducing postpartum morbidity, mortality, and hysterectomy rates. Authors concluded that TA significantly reduces bleeding. They also stressed the importance of giving TA as soon as possible after bleeding onset.

Desmopressin is a type 2-vasopressin receptor agonist and it causes release of VWF from deposits. Desmopressin has no uterotonic effect and can be safely used in pregnant women before invasive procedures (amniocentesis or villus sampling) to avoid bleeding complications. Recent systematic review also confirmed its safety and efficacy among women with bleeding disorders. Desmopressin may cause hyponatremia if combined with abundant fluid intake, and thus electrolytes should be monitored carefully. Patients are more likely to respond adequately to desmopressin stimulation, if they have normal VWF structure, e.g., if they belong to type 1. Moreover, one may expect satisfactory response if preinfusion levels of FVIII and VWF are at least 10–20% of normal. Therefore, desmopressin is contraindicated in patients with type 2B, as it results in secretion of dysfunctional VWF, which rapidly binds to platelets causing thrombocytopenia. In addition, the drug should be used with caution in patients with severe atherosclerosis. Upon desmopressin stimulation larger VWF multimers release and they may become highly thrombogenic under high shear-stress conditions (atherosclerotic plaques). Individual response to desmopressin is usually constant over time and therefore giving a test dose is probably a suitable approach to estimate how an exact patient responds. The main effect lasts for 8–10 hours, which determines the mode of administration – every 12–24 hours. Initially, plasma-derived VWF/FVIII factor concentrates were developed for the treatment of hemophilia. Today, they prove to be the treatment of choice in VWD patients, unresponsive to desmopressin. However, there are several concerns related to plasma-derived...
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Obstetrics - V6 - Pregnancy complaints and complications: clinical presentations - Chapter - Bleeding in Early Pregnancy

#brinogen levels, which nearly double in value. Although the guidelines for prehospital trauma care generally apply, Most coagulation factor levels rise throughout pregnancy, although laboratory values remain unchanged, except for Gradual growth and stretching of the peritoneal cavity seems to desensitize the pregnant patient to peritoneal irritation. dilated. Abdominal tenderness, rebound, and guarding may be absent in the trauma patient with signiﬁcant injury. superiorly, so that the bladder becomes an intra-abdominal organ. In addition, the renal pelvis and ureters become in the supine position, the uterofetoplacental unit may compress the inferior vena cava and decrease preload to the point that it significantly diminishes cardiac output. This diminished cardiac output may cause significant hypotension. Pulmonary and acid-base changes are adaptations to the increasing metabolic demands and oxygen delivery to the fetus. Overall, oxygen consumption increases by 15% to 20% during pregnancy. Progesterone stimulates the medullary respiratory center, initially leading to hyperventilation and a respiratory alkalosis. After metabolic compensation caused by renal bicarbonate excretion, there still remains a slight alkalemia. The carbon dioxide partial pressure (pCO₂) of the pregnant patient usually ranges from 27 to 32. The tidal volume and minute ventilation increase about 40% as the respiratory rate returns to baseline. The gradual 4-cm elevation of the diaphragm and increasing thoracic anteroposterior diameter contribute to a 20% to 25% decrease in functional residual capacity. This combination of changes, in addition to increasing levels of 2,3-diphosphoglycerate, facilitates oxygen release to the fetus. These changes, however, leave the pregnant patient with a diminished oxygen reserve and buffering capacity. Hypoxemia occurs earlier than in non-pregnant patients, and, when it does occur, the patient is ill prepared to compensate for the ensuing acidosis. Fetal arterial oxygen pressure (PaO₂) decreases minimally provided that maternal PaO₂ remains above 60 mm Hg; however, it will drop precipitously below this level. When fetal oxygen saturation drops by 50%, the so-called fetal “diving reflex” shunts fetal blood flow to the heart, brain, and adrenal glands, leaving other organ systems at risk for insult. In addition to the cardiovascular and pulmonary systems, other organ systems also undergo signiﬁcant changes. The potential for aspiration is markedly increased because of decreased gastric tone, delayed gastric emptying, cephalad displacement of intra-abdominal organs, and an increase in baseline gastric acid production. The pregnant trauma patient is more susceptible to genitourinary injury. The uterus displaces the bladder anteriorly and superiorly, so that the bladder becomes an intra-abdominal organ. In addition, the renal pelvis and ureters become dilated. Abdominal tenderness, rebound, and guarding may be absent in the trauma patient with signiﬁcant injury. Gradual growth and stretching of the peritoneal cavity seems to desensitize the pregnant patient to peritoneal irritation. Most coagulation factor levels rise throughout pregnancy, although laboratory values remain unchanged, except for fibrinogen levels, which nearly double in value. Although the guidelines for prehospital trauma care generally apply,
there are specific issues related to the traumatized pregnant patient. Upon initial assessment, emergency medical service personnel should follow standard guidelines for trauma care.

A sterile speculum examination is an integral aspect of the pregnant trauma evaluation. The source of vaginal fluid may be difficult to discern, but ferning and blue discoloration of nitrazine paper may aid in distinguishing alkaline amniotic fluid from urine. Vaginal bleeding may herald placental abruption, uterine rupture, pelvic fracture with vaginal injury, or other injuries. The cervix should be visually inspected for evidence of dilation and effacement. A bimanual examination is an integral part of the secondary survey that is sometime overlooked. Emphasis should be placed on the abdominal examination, because signs of significant peritoneal injury may be masked. Trauma panels or order sets performed in many emergency departments can be excessive, wasting time and money, but the pregnant patient may warrant more laboratory testing than other trauma patients. These laboratory tests should include hemoglobin, hematocrit, typing and crossmatching, and a gross inspection of the urine. A serum bicarbonate level, blood gas analysis, or lactate level may be considered, because there is evidence that maternal acidosis may be linked to fetal outcome.

Prenatal laboratory tests may be helpful for comparison. A fibrinogen level that is normal in a non-pregnant patient may be an early indicator of DIC and placental abruption in a pregnant trauma patient. A Kleihauer–Betke (KB) test may be considered in an Rh-negative patient with significant trauma. Routine use of KB is not indicated in the emergency department and may not be indicated at all for most patients. Multiple studies, mostly retrospective chart reviews, have attempted to identify variables that may aid in predicting fetal outcome in trauma. Few factors were isolated, particularly those that may be identified in the emergency department. Hypotension seems intuitive and seems predictive in some studies, but other studies have not validated these data.

The factor most consistently identified (the Injury Severity Score) may be helpful to the trauma surgeon, but unfortunately it is not available to the emergency physician. No single variable is unquestionably predictive for the emergency physician. In cases of recent maternal death with potential fetal viability, perimortem cesarean section should be performed. When performed early in maternal cardiac arrest, it yields good fetal survival and may improve maternal hemodynamics, as well, given the chance of survival to the woman.

**Diagnosis**

The evaluation of the pregnant trauma patient should focus on the identification of maternal injuries and the evaluation of fetal well-being. In general, diagnostic studies should be obtained in the pregnant trauma patient for the same indications as in non-pregnant patients. Some special management options, however, should be considered in pregnant patients to assure good outcomes. Initial plain radiographs of the cervical spine, chest, and pelvis should be obtained in traumatized pregnant patients as usual. Chest radiographs must be interpreted in the context of pregnancy-related changes. Increased AP diameter, mild cephalization of pulmonary vasculature, cardiomegaly, and a slightly widened mediastinum are seen in normal pregnancy. Similarly, pelvis radiographs reveal widening of the sacroiliac joints and the pubic symphysis. Radiographic studies should not be withheld because of concerns about radiation exposure. The risk of radiation to the fetus depends on multiple variables, including gestational age, shielding of the uterus, techniques used, and specific studies obtained. As a general rule, it is assumed that the earlier in gestation and the higher the dose, the greater the risk from radiation. The most sensitive time for the fetus to be exposed to significant radiation is from 2 to 7 weeks, during organogenesis. Unfortunately, at this period of highest risk, the pregnancy may be unsuspected by the patient. A radiation dose of less than 1 cGy (rad) is believed to carry very little risk. Exposures of 15 cGy, however, carry a 6% chance of mental retardation, a 3% chance of childhood cancer, and a 15% chance of microcephaly. Typically, a plain pelvis radiograph will expose a fetus to approximately 1 cGy. Plain radiographs of the cervical spine and the chest hold very little exposure risk, especially if the uterus is shielded. After 20 weeks’ gestation, radiation is unlikely to cause any fetal anomalies, particularly if cumulative exposure is less than 10 cGy. Computed tomography (CT) is widely used in the evaluation of traumatic injuries, particularly in head, chest, and abdominal/pelvic trauma. The specific radiation doses used vary depending on the technique of the study and the type of machine used. Newer CT scanners tend to use less radiation than their predecessors, but even the newer machines expose the fetus to a significant dose. A typical abdominal CT will expose a fetus to 5 to 10 cGy. Head and chest CT scans are generally safer, with minor exposures with uterine shielding. As a general rule, abdominal CT should be avoided in early pregnancy; other diagnostic modalities, such as ultrasound and diagnostic peritoneal lavage, are acceptable alternatives. CT, however, does afford a better visualization of retroperitoneal and intraperitoneal injuries. Head and chest CT may be used when indicated, because the radiation is much less and because there are few, if any, alternative diagnostic modalities. Diagnostic peritoneal lavage
(DPL) is still commonly used in trauma centers to identify intra-abdominal injury. DPL has proven to be a safe and accurate alternative to diagnostic imaging for identification of peritoneal injury using the usual criteria. If used in pregnancy, a supraumbilical approach is indicated when the gravid uterus is palpable above the pubis. Although the percutaneous, wire-guided Seldinger technique is commonly used in non-pregnant patients, the open-technique or the minilaparotomy technique should be employed in all pregnant patients. This technique carries a lower risk of complications, particularly inadvertent uterine and fetal injury. Proponents of DPL emphasize the increased sensitivity for identifying hollow-viscous injuries and early identification of the need for immediate laparotomy in the case of massive hemoperitoneum. With the use of ultrasonography and with the judicious use of observation with serial abdominal examinations in trauma patients, DPL may become even less common. The focused abdominal sonogram of trauma (FAST) has been shown to be sensitive in identifying peritoneal fluid. Clearly, the use of an invasive test with significant complications such as bowel perforation or vascular injury should be abandoned, if a safer and equally sensitive alternative such as FAST examination becomes commonplace. The pregnant trauma patient, however, may be one of the few remaining indications for DPL. The first-trimester pregnant patient with an equivocal FAST examination may be a candidate for DPL, avoiding exposure to large amounts of radiation. Later in pregnancy, DPL may help differentiate between massive peritoneal bleeding from an ureteroplacental source, once again in a patient with an equivocal FAST examination.

In a stable patient, a trauma and obstetric ultrasound evaluation should be performed in the emergency department as soon as possible. The use of the FAST examination has become routine in recent years at many trauma centers. It is widely used by trauma surgeons and emergency physicians, who, after minimal training, are able to reproduce the high sensitivity and accuracy for identification of free intraperitoneal fluid. Rapid ultrasound in the pregnant trauma patient yielded comparable sensitivity and specificity.

**Blunt trauma**

Most cases of blunt trauma are related to motor vehicle accidents, followed by falls and direct assaults. Motor vehicle accidents account for nearly 60% of blunt traumas. Only falls do not seem to be evenly distributed throughout pregnancy, with more than 80% occurring after 32 weeks' gestation in one series. In blunt-trauma patients, the most common cause of fetal death is maternal death. Maternal mortality is moreover uncommon and often, as in non-pregnant patients, is a result of significant head trauma.

**Penetrating trauma**

Several key factors should be considered in the management of penetrating abdominal trauma in the pregnant patient. Penetrating trauma in pregnancy is usually the result of gunshot or knife wounds. Gunshot wounds, which are more common than knife wounds, have a higher mortality for both mother and fetus. As pregnancy advances into the second trimester, the gravid uterus moves out of the relatively protected position in the bony pelvis into the abdominal cavity, and a pregnancy-specific pattern of injury develops. Superiorly displaced visceral organs are less likely to be injured overall, but they are at greater risk when penetrating trauma involves the upper abdomen. Maternal visceral injuries are less common during pregnancy, complicating only 19% of cases and carrying a maternal mortality of 3.9%. The disparity probably results from the protective effect of the large, muscular uterus on visceral organs. Gunshot wounds cause transient shock waves and cavitations as they impart their kinetic energy to the high-density tissues of the body, thus causing more severe injury patterns than low-velocity knife wounds. The fetus is at high risk, and fetal injuries complicate 66% of gunshot injuries to the uterus. Fetal mortality ranges from 40% to 70% in cases of penetrating trauma and generally results from either premature delivery or direct fetal injury by the missile. Stab wounds to the abdomen are less common than gunshot wounds in the pregnant patient, and they have a lower mortality for both mother and fetus. Stab wound location is even more crucial in the management of the pregnant patient. The management of penetrating abdominal injuries is a controversial issue at this time. Management options include immediate surgical exploration, DPL, laparoscopy, contrast-enhanced CT scanning, local wound exploration, and observation. Because the uterus seems to provide some protection from missile injury, a more individualized approach may be appropriate in the gravid victim. If the entrance wound of the bullet is below the uterine fundus, and the bullet remains in the body of the uterus, the incidence of visceral injury is less than 20%. Because penetrating trauma to the upper abdomen is worrisome for maternal bowel injury, many authorities strongly believe that upper abdominal injuries should be operatively managed. Because trauma over the uterus has a higher risk of fetal injury, an individualized approach has been
advocated and may be better suited for lower abdominal injuries. The evaluation of penetrating trauma in the pregnant patient needs to be a coordinated, multidisciplinary effort. Amniocentesis may provide additional information on the viability and possible injury of the fetus. Amniocentesis, however, does carry a significant risk to fetal well-being. The decision to use operative or non-operative management should be made by the consulting trauma surgeon and obstetrician.

**Domestic violence**

For emergency physicians, diagnosing domestic abuse may be more crucial than diagnosing a placental abruption. The pregnant patient seems to be at increased risk for domestic violence. This apparent increased risk may be a result of increased incidence, or it may be a result of greater health-care use and better detection. Common sites of physical abuse in pregnancy include the face, head, breasts, and abdomen. Domestic abuse may be a risk factor for low birth weight and delay in prenatal care. The prevalence of domestic violence to range from 0.9% to 20.1%. The most effective strategies for identifying domestic violence tended to incorporate multiple in-person interviews by highly trained individuals asking specific questions. Using a simple three-question screening tool, McFarlane et al. found a 17% prevalence of physical or sexual abuse during pregnancy, a more than twofold increase from previous studies. Sixty per cent of abused pregnant women reported two or more occurrences. A heightened index of suspicion and a concise screening tool may afford the emergency physician the unique opportunity to identify, intervene, and prevent reoccurrence of domestic violence. If domestic violence is suspected, consultation with social services should not be delayed.

**Excessive blood loss and disseminated intravascular coagulation (DIC)**

Incomplete miscarriage, with heavy bleeding, should be treated with surgical evacuation promptly. Risks of delayed intervention include excessive blood loss subsequently requiring transfusion of blood products or DIC. Obstetrical DIC is relatively rare in first-trimester miscarriages but can occur in mild trimester losses, especially if there are fetal demise and retention in utero for a long period. DIC can follow placental abruption or septic abortion and may lead to severe hemorrhage and possibly amniotic fluid embolism. Severe DIC can lead to multiple organ failure and even mortality. In extreme cases even hysterectomy may be required. These can be prevented by prompt diagnosis and treatment. The clinical presentation of DIC is acute bleeding combined with the following laboratory changes: decreased platelet count, prothrombin time prolongation, decreased fibrinogen levels, and increased markers of fibrin breakdown such as D-dimer. Management of DIC related to incomplete abortion or septic abortion includes the following four steps: treating the underlying condition predisposing to DIC – including the surgical removal of retained products of conception and broad-spectrum intravenous antibiotics in the case of suspected sepsis. Tranexamic acid is widely used for the treatment and prevention of obstetrical hemorrhage. However, there is no evidence regarding its safety and efficacy in the scenario of incomplete or septic abortion. Recombinant activated factor VII (rFVIIa) was originally developed for the treatment of hemophilia. Similarly to tranexamic acid, there is lack of high-quality evidence regarding its efficacy and safety in the setting of DIC complicating incomplete or septic abortion. There is concern regarding the possibility of arterial thrombosis. Recent guidelines for the treatment of PPH stated that rFVIIa may be used as an adjunct to other surgical treatments.

**MATERNAL BLOOD GROUP AND MANAGEMENT OF RHESUS-NEGATIVE PATIENTS**

Studies evaluated transvaginal bleeding (TVB) as a risk factor for Rhesus isoimmunization during pregnancy. The majority of experts suggest that blood-group assessment is essential and prophylaxis with anti-D gammaglobulin should be given to all non-immunized Rhesus-negative pregnant woman with TVB at any stage of pregnancy.

Rh D immunoglobulin (RhIg) is indicated for the prevention of Rh D sensitization in Rh D negative women. RhIg can be obtained through emergency departments or blood banks; RhIg is required for a first-trimester sensitizing event such as miscarriage, ectopic pregnancy, termination of pregnancy, and chorionic villous sampling, although the risk of alloimmunization is estimated to be 1.5% to 2% in this setting. This should be given within 72 hours of the sensitizing event, though administration of RhIg up to 9 to 10 days later may provide some protection.
CONCLUSIONS

Early pregnancy bleeding is a very distressing symptom for which a woman seeks reassurance that she has an ongoing pregnancy. It is not always possible to make a diagnosis at the first presentation. In some cases, the need for follow-up investigations or referral to an obstetrician is required. As health-care providers, we should continue to review and update our knowledge in the management of this common presentation in order to optimize our care of these patients (see Practice Recommendations).

PRACTICE RECOMMENDATIONS
Having established the first emergency measures, proceed with:

ACCURATE HISTORY

- LMP and cycle characteristics
- positive pregnancy test, previous beta-hCG values and previous ultrasound scans
- characteristics of the blood loss (quantity, bright or dark red color, recurrence)
- any pelvic pain (location, intensity, irradiation, temporal relationship with bleeding)
- highlight the possible presence of risk factors for:
  - ectopic pregnancy (previous ectopic, PID, sexual promiscuity, infertility, endometriosis. FMA, Previous pelvic surgery, cesarean section, fibromyalgia, previous acute or chronic peritonitis, exposure to DES in utero, IUD or progestogen-only contraceptives up to the periconceptional period; frequent use vaginal douches, age> 35 yrs, block ncc)
  - mola (D at the extremes of fertile age <15 or >45 yrs, African race, Southeast Asia & Latin America, advanced paternal age, E/P use, beta-carotene deficiency, presence of maternal symptoms accentuated with nausea and severe hyperemesis, gestational hypertension – preeclampsia arising in 1tr, signs and symptoms of hyperthyroidism)
- Maternal systemic diseases (infectious, endocrine, diabetes, PCOS, haematological, autoimmune, uterine abnormalities)

OBJECTIVE EXAMINATION

BP, HR, treatability of the abdomen to exclude acute abdominal condition in which there is indication for surgery regardless of cause (ectopic, appendicitis, PID, ovarian cyst torsion, endometrial hemorrhage secondary to follicle dehiscence or hemorrhagic corpus luteum or gastric ulcer perforation etc...)

↓

Sudden pain with a dagger strike in the lower abdominal quadrant then spread to the whole abdomen, shoulder pain, imperious urge to defecate, signs of parietal irritation with defense contumency, meteorism, parailetic ileus and signs of cardio-circulatory collapse

OBSTETRIC EXAMINATION WITH BIMANUAL VISIT AND SPECULUM

1. Confirmation of blood loss from the cervical canal, extent and characteristics:
   - poor, dark red and intermittent → ectopic, threatened abortion, spontaneous abortion
   - abundant, bright red → unavoidable and ongoing abortion
   - expulsion of clots and ovarian tissue → abortion
   - expulsion of molar vesicles → grading wedge
   - Deciduous expulsion + Arian-Stellwag reaction → ectopic

2. Assessment of the state of the cervix (external vs. internal os):
   - cervix closed → ectopic, mola, internal abortion and threatened abortion
   - cervix open → abortion unavoidable

3. Exclusion of gynecological causes of bleeding

4. With bimanual examination, evaluation of the size, consistency and shape of the uterus:
   - uterus increased in size in proportion to amenorrhea with decreased consistency → ectopic and threatened abortion
   - uterine size < amenorrhea → abortion in progress, complete or incomplete and retained abortion
   - uterine size > amenorrhea with ↑ consistency, with increased size growth → mola

5. Assessment of tenderness in mobilization of the uterus

6. Painful unilateral adnexal swelling → ectopic

7. Very painful posterior vaginal fornix on pressure (Douglas curl) → ectopic

8. Non-painful stretched elastic formations found in the case of functional ovarian cysts or in mild ovarian hyperstimulations and echo-bulbar ovarian cysts (present in 50% of cases of mola)

LABORATORY EXAMS

1. Beta hCG dosage:
   - at the lower or lower limits for gestational age (GA) → pregnancy begun later or abortion or ectopic.
   - It is necessary to evaluate the beta hCG trend in several successive measurements at a distance of 48–72 hours:
     - if ↓ <50% → abortion
     - if no doubling in 48–72 hours or ↓ <60% in the absence of intrauterine pregnancy → ectopic
     - if value much higher than those expected for the GA → suspected mola (values in case of chromosomal pathologies and/or twin pregnancies)

2. Progesterone dosage:
   - >25 ng/ml → pregnancy in good evolution
   - <5 ng/ml → unfavorable → abortion
**ULTRASOUND SCAN**

All these data combined with an ultrasound TV scan can make an accurate diagnosis

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<tr>
<td>- light and intermittent bleeding, dark red in color</td>
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<td>- discontinuous mild pelvic and lumbosacral pains that arise after the appearance of blood loss</td>
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<td>- uterus ↑ in volume as per amenorrhea, ↓ consistency, closed and softened cervix</td>
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<tr>
<td>- beta hCG at the lower limits for the GA and ↑ abnormally &lt;normal</td>
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<tr>
<td>- a live and viable embryo / fetus at echo TV scan</td>
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↓ DIAGNOSIS OF THREATENED ABORTION

Rest is recommended, abstaining from intercourse up to 7 days. Progesterone therapy (see Table 2)

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<td>- abundant bright red blood loss mixed with clots and decidual chorionic material</td>
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<tr>
<td>- cramping pains in the pelvic and lumbosacral areas, even accentuated, which occur after blood loss</td>
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<td>- uterus of volume &lt;comparred to amenorrhea and a patent cervix on the finger</td>
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<td>- beta hCG with low values for the gestational age and in decrease</td>
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↓ DIAGNOSIS OF IMPENDING UNAVOIDABLE ABORTION

- Full: subtle endometrial thickness to echo TV → no treatment
- Incomplete: lack of embryo / fetus, thick and / or deformation of the gestational chamber and / or thick endocavitary echoes of inhomogeneous appearance → waiting and / or misoprostol and / or curettage

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<tr>
<td>- little dark red blood loss, sometimes absent</td>
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<tr>
<td>- mild pelvic pain (usually onset after blood loss)</td>
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<tr>
<td>- closed cervix with uterus with pregnancy characteristics with ↑ volume &lt;amenorrhea</td>
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<td>- beta/hCG values &lt;those expected for the GA and in decrease</td>
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↓ DIAGNOSIS OF INTERNAL ABORTION

If the ultrasound shows:
- Absence of BCF in embryo with CRL ≥5mm (TV) or ≥10mm (TA) ○
- Absence of embryo in CO ≥20 mm (TV) or ≥25 mm (TA)
- Repeat Eco TV + beta hCG at seven days
- If gestational age <13 wk → waiting;
- If abortion residues persist beyond 7/15 days from diagnosis or EG> 14 wk. → misoprostol and / or RCU

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<td>- blood loss of variable entity from spotting to profuse bleeding, intermittent and worsening up to causing anemia, or intermittent leaking of dark liquid from the genital tract</td>
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<td>- abdominal distension</td>
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<td>- severe hyperemesis</td>
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<td>- signs and symptoms of hyperthyroidism</td>
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<td>- sometimes preclampsia</td>
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<td>- uterus much ↑ in size compared to GA with reduced consistency and sometimes snap growth with closed cervix</td>
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<td>- ↑ volume of the ovaries with echogenic cysts, even very large, not painful</td>
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<td>- high beta hCG + values for the GA, even ↑ 20 times</td>
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<tr>
<td>- ultrasound image typical of a beehive or a snowstorm picture (picture also present in internal abortion believed for a long time, septic abortion and fibroids in necrosis)</td>
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↓ SUSPICION OF GESTATIONAL TROPHOBLAST DISEASE

Definitive diagnosis only by histological examination after curettage

(in doubtful cases with abortive hydrosalpinx, perform immunohistochemical staining for p57 kip2)

Curettage followed by beta hCG monitoring until normalization


CONFLICTS OF INTEREST

The authors of this chapter declare that they have no interests that conflict with the contents of the chapter.
REFERENCES


