***Pregnancy Loss and Spontaneous Abortion***

**Etiology**

• Although spontaneous abortion has multiple etiologies, chromosome abnormalities are present in up to 60% of abortuses in some studies.

• Abortuses after 12 weeks are less likely to be karyotypically abnormal. Factors that are known to increase the risk for spontaneous abortion include advanced maternal age, alcohol, cigarette smoking, previous spontaneous abortion, and uterine anomalies.

**Epidemiology**

• The incidence of spontaneous abortion is believed to be 15% to 20% of all pregnancies. Some have estimated the true incidence to be as high as 50% to 78%.

• Fetal loss is higher in women in their late 30s and older irrespective of reproductive history. The risk of a spontaneous abortion by age group: age 20 to 30 years: 9% to 17%; age 30 to 35 years: 20%; age 35 to 40 years: 40%; age 40 to 45 years: 80%.

***THREATENED ABORTION***

**Laboratory Tests**

• Blood count if bleeding has been heavy.

• Serum β-human chorionic gonadotropin (hCG) level if pregnancy is undocumented or unknown location. Positive tests may occur in nonviable gestations because β-hCG may persist in the serum for several weeks after fetal death.

**Differential Diagnosis**

• Benign and malignant lesions of the genital tract

• Anovulatory bleeding

• Disorders of pregnancy

• Hydatidiform mole

• Ectopic pregnancy

**Clinical Manifestations**

Vaginal bleeding, with or without menstrual-like cramps, in the first 20 weeks of pregnancy is the most common manifestation of threatened abortion. There is frequently no history of passage of tissue or rupture of membranes. Physical exam is normal, except that the speculum exam may reveal a small amount of bleeding with a closed cervix and no more than mild discomfort.

**Treatment**

Traditional treatment is bed rest and abstinence from intercourse; however, controlled studies supporting the efficacy of bed rest are lacking. Symptoms are best managed on an outpatient basis with hospital admission reserved for heavy bleeding and/or pain relief.

**Medications**

* • There is no evidence that any hormones or medications alter or improve the outcome of threatened abortion in the first and early second trimester. However, Progesterone is prescribed in 13-40% of women with threatened miscarriage. Progesterone is the main product of the corpus luteum, and giving progestogen is expected to support a potentially deficient corpus luteum gravidarum and induce relaxation of a cramping uterus. The evidence on progesterone is of low quality given the poor quality of the data, progesterone does not seem to improve outcome in women with threatened miscarriage. However, local application of a progestogen was found to subjectively decrease uterine cramping more rapidly than bed rest alone in one small study.
* • Medications given during the period of organogenesis (days 18 to 55 after conception) may have teratogenic effects on the fetus. This may need to be balanced with the health of the mother.
* • A regimen of bed rest and abstinence from sexual intercourse seems more rational for late threatened abortions (after 12 weeks of gestation), although the efficacy of such has not been confirmed.

***INCOMPLETE ABORTION***

Incomplete abortion in which some tissue has already has passed (by history) or tissue is present in the vagina or the endocervical canal and the cervix is dilated.

**Laboratory Tests**

• Complete blood count.

• Rh typing.

• Consider blood type and cross-match if bleeding is heavy or if vital sign postural changes are present.

• Consider karyotyping products of conception (POC) if there is a history of recurrent losses.

**Diagnosis**

*Differential Diagnosis*

• Threatened abortion: the internal cervical os is closed on ultrasound exam. In this case, the cervix should not be examined with instruments, as bleeding may also occur with a normal pregnancy.

• Complete abortion: positive pregnancy test with a history of abortion symptoms, passage of tissue via vagina and no evidence of tissue or gestational sac in the uterus on ultrasound

• Ectopic pregnancy is a possibility if no tissue is present.

• Incompetent cervix.

***Clinical Manifestations***

Along with cramping and bleeding, the patient may report the passage of tissue. Caution should be taken not to mistake organized clots for tissue. Speculum examination reveals a dilated internal os with tissue present in the vagina or endocervical canal.

**Treatment**

I. Stabilization

• If the patient has signs and symptoms of heavy bleeding, at least one large-bore intravenous catheter suitable for blood transfusion (16 gauge or larger) is started immediately, if she has unstable vital signs.

• Ringer lactate or normal saline with 30 U oxytocin per 1000 mL is started at 200 mL/h and increased if necessary to obtain uterine tone (the uterus is less sensitive to oxytocin in early pregnancy). Such doses may depress urine output because of the antidiuretic hormone–like activity of oxytocin and should be discontinued as soon as appropriate.

• POC should be removed from the endocervical canal and uterus with ring forceps or suction. This maneuver often dramatically decreases the bleeding.

• RHoGAM is administered to Rh-negative, unsensitized patients.

II. Curettage

During curettage, the uterine cavity should be explored for myoma, septa, and other anomalies that may be related to abortion.

III. Postcurettage

• The patient is observed for several hours. Repeat blood count is ordered if bleeding has been excessive or if there is temperature greater than 38°C. One might also observe in the hospital setting.

• Avoid coitus, douching, or the use of tampons for 2 weeks.

• Oral ferrous sulfate is prescribed if blood loss has been moderate.

• Analgesics are rarely required.

• Rh-negative, unsensitized patients are given intramuscular RhoGAM..

• Follow-up is scheduled in 2 weeks.

***COMPLETE ABORTION***

**Diagnosis**

*Differential Diagnosis*

The differential diagnosis is the same as for incomplete abortion.

***Clinical Manifestations***

The passage of POC appears to be complete and bleeding is minimal. The cervix may be closed or minimally dilated and the uterus, on examination, is well contracted and small.

**Treatment**

• Observation without surgical intervention is appropriate if the patient’s vital signs are stable and no fever is present. The passage of tissue appears to be complete and bleeding is minimal. Ectopic pregnancy is not suspected

• If these conditions are not present, then uterine curettage is appropriate.

• Check β-hCG weekly until levels indicate resolution of the pregnancy

• Give RhoGAM (300 mg) if the patient is Rh negative.

***MISSED ABORTION***

**Definition**

Missed abortion is defined as the retention of POC after death of the fetus. There is no definition of the length of time of retention of the POC.

**Laboratory Tests**

Ultrasonography is essential in confirming the diagnosis of missed abortion.

**Clinical Manifestations**

The pregnant uterus fails to enlarge as expected. Amenorrhea may persist, or intermittent vaginal bleeding, spotting, or brown discharge may occur. Rarely disseminated intravascular coagulopathy (DIC) may rarely develop with a missed abortion that extends for more than 4 or 5 weeks.

**Medications**

RHoGAM is administered to Rh-negative, unsensitized patients.

**PROCEDURES**

I. Dilation and curettage

• D&C is available for missed abortions that are less than 12 to 14 weeks’ gestation by fetal size on ultrasound. If the cervix is not dilated, then preoperative dilation is accomplished with laminaria or prostaglandin cervical-dilating agents.

II. Dilation and evacuation

• D&E is available for missed abortions greater than 14 weeks’ gestation by fetal size on ultrasound. The D&E procedure is used rather than D&C when there are fetal bones and associated risk for uterine perforation.

Although surgery is the most rapid mode of treatment, surgical treatment may rarely result in uterine perforation requiring additional surgery, intrauterine adhesions and scarring, or cervical trauma with subsequent cervical incompetence.

Cervical ripening agents aid in patient comfort and reduce the difficulty of uterine evacuation procedures. Available cervical ripening agents include misoprostol, mifepristone, and osmotic dilators. When given at least 2 to 3 hours prior to procedure, misoprostol produced better results with fewer side effects when administered vaginally or sublingually rather than orally. However, when compared with mifepristone, 200 mg, given 24 hours prior to the evacuation procedure, the use of misoprostol by any route was less effective.

III. Misoprostol

Misoprostol may be used for outpatient treatment of missed or incomplete abortion patients with:

• Stable vital signs

• No evidence of infection

• Good reliability

• Fetus measuring less than 13 weeks’ gestation

• POC with no fetal pole on transvaginal ultrasound

The American College of Obstetrics and Gynecology (ACOG) endorses a protocol for medical management of women with an incomplete abortion and a uterus less than 12 weeks in size that utilizes misoprostol, 600 \_g orally or 400 \_g sublingually. For missed abortion, misoprostol can be increased to 800 \_g vaginally or 600 \_g sublingually. Doses can be repeated every 3 hours for up to three total doses. This dose is repeated once after 24 hours if there are no results.In women with gestations at 7 to 17 weeks, the 800-\_g vaginal misoprostol regimen resulted in an 80% success rate when measured by complete expulsion within 3 days of treatment. The efficacy is similar among all modes of administration, although gastrointestinal (GI) side effects (nausea, diarrhea) are more common when misoprostol is administered orally or sublingually.

When counseling women about expectations with misoprostol use, it is important to discuss common side effects. GI distress is the most frequently reported side effect, but patients also commonly note fever or chills. Oral analgesics are given for pain. The bleeding pattern 16

experienced with tissue passage is typically described as heavier than the patient’s usual menstrual flow and lasts approximately 3 or 4 days. This is followed by a transition to vaginal spotting that may last for a week or longer. One common concern among providers who are considering treating outpatients with misoprostol is the possibility of acute blood loss resulting in hemodynamic instability and return to the emergency room. Up to 30% of patients treated with misoprostol may require surgical evacuation

***HABITUAL ABORTION***

***Definition***

Habitual abortion, also known as recurrent pregnancy loss (RPL), is defined as three or more consecutive spontaneous abortions of clinical, previable pregnancies (documented by ultrasound or histopathology).

***Etiology***

Up to 75% of cases of RPL will not have a clearly defined etiology. General etiological categories of RPL include anatomic, immunological, genetic, endocrine, and infectious factors.

I. Uterine anatomic defects that are implicated causes (note that if one of these anatomic causes is found, it should be treated before proceeding with other treatments):

• Double uterus

• Septate uterus

• Asherman syndrome

• Endometrial polyps

• Leiomyomas that impinge on the endometrial cavity

II. Cervical anatomic defects:

• Incompetent cervix (15 weeks and beyond)

• Antiphospholipid syndrome (APS) is the only immunological condition in which pregnancy loss is a diagnostic criterion for the disease. Up to 15% of patients with RPL may have APS.

• Genetic abnormalities: Approximately 4% of couples with RPL have a major chromosomal rearrangement (vs. 0.7% of the general population); usually a balanced translocation. One or both partners may harbor lethal genes in a heterozygous or balanced combination that does not affect them but causes pregnancy loss when inherited by the embryo in a homozygous or unbalanced state.

III.Other possible causes that are less well documented:

• Endocrine factors such as thyroid dysfunction, luteal phase defect, hyperprolactinemia, and

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• Some infections, such as *Listeria monocytogenes, Toxoplasma gondii*, and cytomegalovirus, are known to cause sporadic pregnancy loss, but no infectious agent has been proven to cause RPL.

• Maternal–fetal human leukocyte antigen (major histocompatibility complex).

***Epidemiology***

Habitual abortion accounts for approximately 5% of all spontaneous abortions. Cytogenetic studies of abortion specimens have demonstrated chromosomal anomalies in 20% to 60% of abortuses. Approximately 95% of chromosomally abnormal fetuses are less than 8 weeks of developmental age, although they often are retained in utero for much longer periods of time.

**Evaluation**

***Laboratory Tests***

• Submit tissue for pathologic examination.

• Chromosomal studies using banding techniques are recommended for both the father and mother.

• The minimum immunology work-up for women with RPL is measurement of anticardiolipin antibody (IgG and IgM) and lupus anticoagulant. Lupus anticoagulant and fetal loss rates secondary to placental thrombosis and infarction.

**Clinical Manifestations**

Uterine anomalies may present with unique nonobstetrical manifestations. Incompetent cervix may present with a history of repeated mid-trimester losses with painless cervical dilation. The diagnosis is difficult and relies on previous obstetrical history and/or history of cervical surgery or trauma.

**Treatment**

• Patients with repeated abortions beyond 12 weeks of gestation should be investigated for known maternal causes of abortion.

• Sonohysterogram, hysterosalpingography, or hysteroscopy should be performed to evaluate uterine anatomy.

• There is no generalized treatment for habitual abortion. Specific treatment is directed to any identified causes.

• Whether low-dose aspirin (60 to 80 mg/d), low-dose heparin, or prednisone (20 to 60 mg/d) improves outcomes is controversial and depends on the specific etiology of each patient’s series of habitual abortion. When indicated for specific thrombophilias,

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subcutaneous low-dose heparin and aspirin have been shown to have equally successful outcomes, with fewer complications compared with prednisone.

***Teratology and Drugs in Pregnancy***

A *teratogen:* is an agent that interferes with the normal growth and development of the fetus, and is used to describe drugs or chemicals that cause major or gross birth defects.

The food and Drug Administration (FDA) lists five categories of labeling

for drug use in pregnancy.

*Category A :* no fetal risk shown in controlled human studies.

*Category B :* no human data available and animal studies shown no fetal risk or animal studies show a risk but human studies do not show fetal risk.

*Category C :* no controlled studies on fetal risk available for humans or animals or fetal risk shown in controlled animal studies but no human.

data available (benefit of drug use must clearly justify potential fetal risk in this category).

*Category D :* studies show fetal risk in humans ( use of drug may be acceptable even with risks such as in life threatening illness or where safer drugs are ineffective).

*Category X :* risk to fetus clearly outweighs any benefits from these drugs.

***Social Drug Exposure***

*1. Smoking :* Smoking is associated with decreased birthweight and increased prematurity. Risks of complications and of the associated perinatal loss increase with the no. of cigarettes smoked. Discontinuation of smoking or reduction in the no. the no. of cigarettes smoked during pregnancy can reduce the risk of complications and perinatal mortality, especially in women at high risk for other reasons.

*2. Alcohol:* Fetal alcohol syndrome has been reported in offspring chronically alcoholic mothers and includes the features of gross physical retardation that begins prenatally and continues after birth.

*3. Caffeine:* There is no evidence of any teratogenic effect of caffeine in humans. Concomitant consumption of caffeine with cigarette smoking may increase the risk of low birth weight. Maternal coffee intake decreases iron absorption and may increase the chance of anemia.