

Management of Miscarriage and Early 2nd Trimester Intrauterine Fetal Demise

Summary & Recommended Management:

Overview

- SAB = approx. 25% of pregnancies
- Most common 1st tri complication
- 50% chromosomal
- Unlikely to be recurrent
- Usually unexplained and not preventable
- Modifiable RF: tobacco and substance cessation, folate supplementation, optimization of chronic medical conditions (e.g. improved BG control in DM)

Options

- Expectant, medical, and surgical
- Hemorrhage and infection rates low for all groups
- No difference in future birth rates

Expectant

- >80% will complete w expectant management alone
- May require follow up for 4wks or more to complete
- Antibiotics not needed
- Success with completion likely decreasing with increasing GA, especially beyond 8wks

Medical

- Up to 90% success w medical management
- Ideal dose not known, **misoprostol 800mcg PV or buccal may be the most efficient**
- Mifepristone 200mg PO 24hrs before misoprostol administration should be considered if available
- An additional 800mcg misoprostol dose may be repeated 3hrs to 7days after initial misoprostol
- Increased success with higher misoprostol doses, more time, and lower GA
- Antibiotics not needed
- Confirmation of complete SAB may be a clinical diagnosis, no clear US criteria exist

Surgical

- Successful >99%, immediate resolution
- D+C <14wks, D+E >=14wks GA
- US assist intraoperatively may help if: anomalies, challenging dilation, perforation suspected, concern about incomplete procedure, later GA
- US recommended at D+E, especially for less-experienced providers

- **Antibiotic prophylaxis recommended: 200mg IV doxycycline pre-op, alternate regimen: single dose 500mg PO/IV metronidazole, single dose azithromycin 500mg; consider 1g PO azithromycin due to high +CT rates in Alaska in patients with RF**
- Ensure completion with examination of POC before sending to pathology
- Complications include hemorrhage, infection, and incomplete procedures

Cervical preparation

- Medication (misoprostol and or mifepristone) or osmotic dilators (laminaria, dilapan)
- Decreases complications in some patients
- **Consider <12wks adolescents or nulliparous, history of cervical surgery, obstructive cervical pathology, or prior difficult dilations**
- **Recommended for all women 12-14wks GA**
- **Strongly recommended >14wks prior to D+E**
- **Misoprostol buccal 400mcg 2hrs prior to procedure is recommended regimen**
- Same day preparation adequate <16wks generally
- Can give higher doses of misoprostol or lengthen or shorten interval to procedure depending on clinical circumstances (parity, GA, et al)
- Advanced GA ≥ 16 wk, consider 2-day dilation and/or use of multiple agents
- Advanced GA D+E should be undertaken by surgeons familiar with these procedures

Contraception

- Initiate immediately after complete AB confirmed in patients desiring birth control
- Post-surgical placement of LARC is recommended
- May have higher IUD expulsion rates, but overall complications rates are low

2nd trimester

- Expectant management not recommended, but delay in initiation of IOL or D+E reasonable in medically stable patients
- D+E is preferable if experienced provider available with faster completion and fewer complications, but does not allow for intact fetus or autopsy
- Multiple regimens for medical IOL: **recommended regimen of 400mcg q6hrs** (alternate regimens: load w 800mcg, can decrease respective doses to 200mcg if side effects, can vary dosing interval to q3-6hrs)
Adding Mifepristone 200mg PO 24hrs before misoprostol administration should be considered if available (can decrease IOL time)
- Alternate medical regimens including prostin (PGF2) and Pitocin.
- IOL with misoprostol is safe <28wks, even in patients with history of uterine scar
- Retained placenta is a common complication

Follow up

- Pelvic rest for 2 weeks, or as long as patient is having vaginal bleeding
- Initiate contraception immediately in patients requesting BC
- Delay trying to conceive for one menstrual period for patients desiring pregnancy
- BHC referral as needed
- Discuss and improve modifiable RF and preconception counseling

Literature Review and Discussion:

Definition

Pregnancy loss refers to pregnancies <20 weeks gestation that end in spontaneous abortion, or miscarriages. Pregnancy loss can also apply to intrauterine fetal demise \geq 20wks, or stillbirths. WHO defines miscarriage as any pregnancy with fetal or embryonic loss <500g, fetal death as any pregnancy with fetal demise >500g and <28wks, and reserves the term stillbirth for pregnancies with fetal demise \geq 28wks. This guideline focuses on the management of miscarriage as defined as the common US definition of spontaneous abortion, pregnancy loss in the first trimester and early second trimester <20wks. There is brief discussion of management of intrauterine fetal demise >20wks GA. Late second trimester fetal demise at gestational ages >24wks GA are managed similarly to stillbirth. **Stillbirth** is discussed in a separate guideline. **First trimester vaginal bleeding** with diagnosis and management of pregnancies of undetermined location is reviewed in a separate guideline. **Recurrent pregnancy loss** is discussed in a separate guideline.

Background

Spontaneous abortion, or SAB, is the most common first trimester pregnancy complication. Up to 25% of pregnancies end in miscarriage, although many of these are too early to be commonly recognized and diagnosed formally. Incidence of SAB decreases with increasing gestational age. <1% of SAB occur beyond 15wks GA (in chromosomally and structurally normal feti). Most SAB occur in patients with no risk factors. The most common associated risk factors are increasing maternal age, prior SAB, and tobacco use. Associated risk factors are other substance use, increasing gravidity, low folate intake, extremes in weight, and fever. The most common etiology of SAB is a chromosomal abnormality, accounting for 50% of miscarriage, although many losses remain unexplained. Other causes include other fetal congenital anomalies, traumatic invasive intrauterine procedures (after CVS or amnio), maternal co-morbidities, uterine anomalies, and infectious or teratogenic exposures. Many patients will associate other causes with the occurrence of SAB, most commonly recent falls and trauma, stress, heavy lifting or exertional exercise, and prior contraceptive use. There is no evidence to support these correlations. Therefore, reassurance should be provided to help dispel myths, and relieve the patient's feeling of responsibility, if they associate these events with the SAB. Primary prevention of SAB is with prenatal care and preconception counseling, although since most are chromosomal, most SABs cannot be prevented. PNV are recommended to all women, with folate doses between 400-800 mcg recommended to prevent neural tube defects. However, taking PNV has not been shown to decrease SAB rate. Similarly, progesterone addition in early pregnancy has not been found to be generally helpful in the prevention of SAB. The indications and workup

for recurrent miscarriage, or “habitual aborter,” is discussed in the **Recurrent pregnancy loss** separate guideline.

Diagnosis and Definitions

The diagnosis of SAB is generally made after patients present with vaginal bleeding and cramping, and increasingly the diagnosis is made incidentally in asymptomatic women as there is increased access to early ultrasound for gestational dating. Confirmed spontaneous abortions fall into subcategories: incomplete abortions have some or all products of conception passed, inevitable abortions will have vaginal bleeding with an open cervix, finally “missed abortion” is better defined as either an anembryonic gestation (or “blighted ovum”) if the GS is empty, or an embryonic (<10wk) or early fetal demise (>10wk) if the FP has no heartbeat. Septic abortion refers to spontaneous abortion with associated intrauterine infection. Spontaneous abortion is complete with passage of all intrauterine tissue. However, many women presenting with vaginal bleeding and cramping will be diagnosed with threatened abortions: normal ultrasounds with a closed cervix. These are managed expectantly with interval follow up in the next 1-2 week for repeat US. Bedrest has not been shown to be helpful in pregnancies with threatened abortions, but pelvic rest may be considered. Differential diagnosis should consider other causes of early pregnancy bleeding including normal physiologic bleeding of early pregnancy (“implantation bleeding”), subchorionic hemorrhage, lower genital tract pathology, GTD, and ectopic. Clarification of the diagnosis of early pregnancy failure and loss with ultrasound criteria for diagnosis is discussed in the **First trimester bleeding guideline**.

Workup

Upon confirmed diagnosis, history should be completed as well as pelvic exam and US to clarify gestational age. Decisions regarding the management of the pregnancy are based upon the US GA and not the GA by LMP. Rh testing should be confirmed for all patients. Rh isoimmunization can occur from pregnancies resulting in SAB. For Rh negative patients, microgram can be given to patients <12wk6d GA, and full dose Rhogam should be given to patients \geq 13wk GA. Other tests may be completed as appropriate: e.g. STD screening if risk factors, RPL labs if indicated, IUFD labs if indicated. The diagnosis of SAB can be emotionally overwhelming for patients. However, as 50% of pregnancies are unplanned, some may receive the diagnosis with an element of relief. Even those patients who had planned termination of pregnancy may experience grief response. The diagnosis is best made expeditiously, directly, empathically, and ideally in-person. The patient should be offered options as soon as possible, but may choose to take time to decide how to respond. This is reasonable as long as the patient is medically stable. BHC should be offered. The patient’s pregnancy plan for the next year should be addressed as soon as the patient chooses her management option, and patients that desire contraception should have methods initiated immediately after the pregnancy is complete.

Management Options

The management of confirmed SAB is either: expectant, medical, or surgical. There is conflicting data regarding expectant management patients. Meta-analysis showed expectant management and medical management have similar success and complication rates; however, some trials have shown up to 40% of expectant management patients required surgical intervention, while medical management patients needed surgical interventions up to 13% of the time. There may be increased bleeding and pain reported in patients with expectant and medical

management, but this varies with clinical scenario. Hemorrhage rates are low for all groups, with transfusions reported in 2% of expectant, 1% of medical, and <1% of surgical management patients. Completion rates are highest with surgical management, >99%, and can resolve pregnancy more quickly. Expectant, medical, and surgical management have equal and very low infection rates. There is no difference in birth rates in expectant, medical, or surgical management groups at 5 years.

Expectant Management

Expectant management is reasonable in patients <14wks GA with stable vital signs, no evidence of infection, and no active hemorrhage. Expectant management is successful in 80-90% of patients, with increased success with more time. Higher rates are also reported for incomplete abortions and in patients who are already experiencing vaginal bleeding and cramping at SAB diagnosis. Expulsion of the pregnancy tissue increases with time and with pregnancy type. 30% are complete at 2wks from diagnosis. At 4wks from diagnosis, 90% of incomplete, 75% of missed, and 66% of anembryonic SABs will be complete. An additional 10% of SABs take 6-8wk to complete. There is not good data on expectant management greater than 8wks, thus it is not recommended. Although data is conflicting, increasing GA may decrease success of expectant management.

Medical Management - 1st Trimester, Overview

Medical management can be considered as first line for SAB management, or after failed expectant management. Stable patients may be managed outpatient if they can follow up if they have hemorrhage or severe pain. Some patients may be candidates for medical management in an inpatient or emergency setting with observation for completion in case of need for urgent surgical intervention. Medical management may be less optimal in patients with infection, severe anemia, an inability to follow up, and actively anti-coagulated or with bleeding disorders, and those with organ failure. Contraindications to medical therapies include allergy to prostaglandin medications and in patients with suspected GTD.

Medical Management - 1st Trimester, Regimen

Varying regimens for medical management of SAB have been described using multiple different pharmacologic agents, doses, routes, and timing. The ideal dosing for first trimester medical management of SAB is not known, but recommendations do exist. Misoprostol (PGE1) is the most well-studied agent. Misoprostol can be administered via multiple routes: PO, buccal, SL, PV, or PR resulting in varying absorption, plasma levels, and side effects. may be the most effective route, but sublingual and buccal administration has similar pharmacokinetics to vaginal administration. Regardless of route, larger doses of misoprostol are more effective than lower doses. Very high doses are associated with more side effects. Common misoprostol side effects are gastrointestinal (N/V/D), fever, and mild rigors. Vaginal Misoprostol, at doses used for medical management of SAB (as well as for dilation and cervical preparation prior to D+C, D+E - see below), and for IOL less than 28wks GA, is considered safe in women with prior uterine scars, including prior cesarean deliveries. The dose, route, and frequency of misoprostol probably effects success. Rates as low as 13% up to as high as >90% have been reported. Vaginal overall appears to have higher success rates. Buccal and sublingual administration is as effective vaginal, but possibly has higher side effects. Duration of awaiting effect of misoprostol also effects success with 70% by day 3, and 85% by day 8 in missed SAB pregnancies. The type

of pregnancy also may effect success rates, with anembryonic SAB achieving completion with medical management 80% of the time, versus almost 90% success with incomplete SAB. Induced medical abortion rates for termination of pregnancy have success rates as higher than 95%, but with increased failure rates with increasing GA; in comparison, GA of SAB has more conflicting data. There may be decreased success rates at higher GA. Overall, first trimester pregnancy termination has a success rate similar to medical management for first trimester SAB with misoprostol alone, approximately 80-90% success. For induced first trimester abortion, addition of mifepristone (progesterone antagonist) 24-48hrs prior to misoprostol, increases success rates to 95-98%. The addition of 200mg mifepristone 24 hrs before misoprostol administration significantly improves treatment efficacy as demonstrated by an RCT in 2018, leading to higher completion rates without need for surgical intervention. Thus the combination of mifepristone with misoprostol is superior to misoprostol alone and should be offered preferentially when mifepristone is available. (Of note: mifepristone is contraindicated in women taking high-dose systemic steroids). Methotrexate and tamoxifen have also been studied alone or in combination with misoprostol, but do not show superiority in effecting complete SAB. High success rates with overall low side effect profiles have been described with the following regimens: ACOG: 800mcg misoprostol vaginally for one dose, with repeat dose no sooner than 3hrs, but up to 7 days later. SFP: concurs with ACOG recommendation, with buccal route as alternative; Up-to-date: 400mcg misoprostol vaginally every 4 hrs for 4 doses (patient self-administration), with success rates of 70-90% at 24hrs; 2007 WHO Consensus: For missed SAB, 800mcg misoprostol vaginally once, 600mcg misoprostol sublingually once, or for incomplete SAB, 600mcg orally once. Antibiotics are not recommended for medical SAB management.

Follow-up after Expectant or Medical Management

Strict pelvic rest is advised until SAB completion is confirmed. Pain and bleeding is expected during pregnancy passage, but should not exceed 2-3 hrs of soaking pads with uterine bleeding and passage of large clots. Continued heavy bleeding beyond 2-3hrs, uncontrolled pain, or continued orthostatic symptoms should prompt follow up. Fever can occur as a misoprostol side effect, especially at higher doses. However, fever accompanied by malodorous discharge, worsening pelvic or abdominal pain, or worsening systemic infection symptoms should also prompt follow up. Confirmation of complete SAB after expectant or medical management varies with provider. Patients will often describe an episode of bleeding and cramping, with passage of tissue, and then improvement and then resolution of symptoms. With this descriptive history, most SABs will be complete; however, some patients may still have retained pregnancy tissue. If patients can keep tissues and bring them, they can be submitted to pathology. Pelvic exam can confirm uterine involution, resolution of bleeding, and that the cervix is closed. HCG levels can help to determine pregnancy resolution, with decline >50% from baseline at 48hrs consistent with resolving SAB. HCG levels may take over 4wks to return to zero. Unless GTD is suspected, serial measurements of HCG until zero are not recommended for routine follow up of expectantly or medically managed asymptomatic SAB patients. Follow up ultrasound is not universally recommended for patients, especially those who are asymptomatic; however, if ultrasound is performed, then it can be used to diagnose completion if the GS is no longer present, and the EMS is thin, and mostly homogeneous. There are no universally defined criteria of an empty uterus. Specific measurements of EMS thickness for defining complete SAB vary from, from <10mm to <30mm EMS. If the patient is asymptomatic, the EMS is homogeneous, and the EMS is <15mm, with declining HCG levels then routine surgical intervention is not

indicated. If SAB is not complete at follow up, then continued expectant management for another 1-2 week, repeat medical management, or surgical management may all be options.

Surgical Management - Overview

Surgical management of SAB results in immediate completion in >99% of patients. Surgical management is preferred for unstable patients, and those with septic abortions, hemorrhage, coagulopathy, or who do not have access to emergency follow up. Surgical management results in shorter time to completion, decreased bleeding, decreased risk of transfusion, and decreased need for unexpected readmission. Surgical SAB management complication rates are very low, approximately 1%.

Surgical Management - Technique

Surgical SAB management is achieved with dilation and curettage (D+C) <14wks GA, and dilation and extraction (D+E) ≥14wks GA. Cervical dilation, either mechanical or by other means, is followed by suction of the intrauterine contents, finally concluding with curettage. Extraction may be needed in the second trimester as the fetus is more calcified and with the presence of larger fetal parts (especially the calvarium). Suction for D+C can be provided by either electric vacuum aspirator machine, or by manual vacuum aspiration (MVA). [MVA picture]. The MVA is a hand-held suction device, originally developed for low-resource settings, but is now in use frequently in well-resourced settings, sometimes preferred for its quieter suction, especially for outpatient use. D+C can be performed safely in the outpatient setting or in the operating room. Office D+C procedures can be done with the MVA with local paracervical block alone, or with mild sedation (PO or IM). D+C is most commonly performed in the OR w IV sedation, with or without paracervical block. If a block is performed, various preparations and doses have been shown to be equally effective. Deep paracervical block (>2cm) with fewer injection sites has been shown to provide superior pain relief. Ultrasound guidance may be used at the time of D+C if uterine anomalies are present, a challenging dilation is encountered, if perforation is suspected, if there is question of completion of procedure, and at increasing GA in less-experienced providers, particularly for D+ E. Choice of D+ C technique depends on provider and experience. Overall, MVA is equivalent to EVA at <10wk GA with no difference in complications such as infection, hemorrhage, or pain. MVA is quieter and may cause less pain and perforation, although this may be provider proficiency related. EVA and MVA utilize the same pressure, although the flexible cannulas often used with MVA may be less traumatic and lead to fewer uterine perforations. D+C with suction is less associated with uterine scarring than D+C with sharp curettage alone.

Surgical Management - Antibiotics

ACOG recommends preoperative antibiotics prior to surgical management of SAB. Doxycycline 200mg IV or PO 1hr prior to procedure is recommended, however, alternative regimens can be considered. These include single dose metronidazole 500mg or single dose azithromycin 500mg. High chlamydia rates in Alaska may guide antibiotic therapy. If the patient has chlamydia risk factors and has not already been screened negative, 1g of azithromycin is recommended prior to surgical first trimester abortion. This can also be applied to surgical management of SAB.

Cleansing the vagina with antiseptic solution prior to D+C has not been shown to affect the risk of post-procedure infection. Chlorhexidine may be more effective than betadine at reducing bacteria within the vagina.

Surgical Management - Dilation

Cervical dilation can be achieved with mechanical dilators (Pratt, Hagar, or Denniston surgical instruments), osmotic dilators (dried seaweed laminaria, or synthetic dilapan - absorb water from the cervix and increase in size), or pharmacologic agents (misoprostol and mifepristone). The latter two methods take time, either hours or days, prior to achieving dilation. None of these methods increases infection risk. Especially at higher GA, the amount of dilation achieved with each method is variable, much like labor induction. Differences in multiple cm may be observed from woman to woman despite matched parity, GA, and medication regimen. Increasing parity, multiple agents, and increasing time with medical and osmotic dilators generally achieve more cervical relaxation and dilation. Adequate dilation required for successful uterine contents removal at D+C depends on the GA of the pregnancy by US, not by LMP. (e.g. SAB with GA 12wk by LMP with growth consistent with 8wks GA missed SAB will usually require dilation more consistent with 8wks GA). The cannula needed for removal of pregnancy products of conception roughly correlates dilation in mm with GA. (e.g. 8wks GA = size 8 cannula = 8mm dilation = #23-25 pratt dilator). At <7wks, in a multiparous patient at early GA, and in patients where are already bleeding at early GA, mechanical dilation may not be needed. Between 7-13wks, patients usually do require dilation, and \geq 14wk almost always need cervical dilation, including cervical preparation prior to dilation. Intraoperative challenges in dilation can be managed with US guidance to help prevent false passage or perforation. If intrauterine access is not successful, then the procedure may need to be delayed. Challenging dilation can be generally be avoided by adequate preoperative cervical preparation. Cervical preparation prior to mechanical dilation is recommended for some women before D+C, and in all women before D+E.

Surgical Management - Cervical Preparation

Cervical preparation aims to ease dilation to decrease risk of cervical trauma, decrease risk of perforation, and to decrease risk of inadequate dilation leading to incomplete procedure. Cervical preparation options include pharmacologic or osmotic means. Cervical preparation, as with cervical dilation as discussed above, is highly variable from patient to patient. SFP, RCOG, and WHO all have discussion of research related to cervical preparation and recommendations. No single protocol is recommended in all clinical situations. Overall, cervical preparation should be considered for women <12wks if they are adolescents or nulliparous. Cervical preparation is also recommended in women with a history of cervical procedures (excision w LEEP or CKC, or cerclage), obstructive cervical pathology (stenosis or fibroid), or prior difficult dilations, and for surgeons with less experience. Cervical preparation is recommended for all women 12-14wks GA. Cervical preparation is strongly recommended $>$ 14wks prior to D+E procedures in order to accommodate instruments for removal and achieve adequate dilation. Misoprostol alone, 2-4hrs before procedure, can result in adequate cervical preparation prior to D+C. Doses from 200mcg-800mcg has been used, but 400mcg at least 2hrs prior to procedure is recommended. Dilapan osmotic dilators are equally effective to misoprostol for same-day cervical preparation, but may be more uncomfortable. At GA \geq 14wk but <16wks, same day cervical preparation is adequate in most patients. However, for D+E $>$ 14wks, 200mg mifepristone given 24hrs prior to procedure

in addition to 400mcg misoprostol 2 hrs prior to procedure provides more dilation than misoprostol alone and can be considered. For D+E at GA >16wks, a two-day procedure may be preferable to achieve more dilation. Laminaria or dilapan may be placed the day before the procedure, with or without addition of misoprostol the day of the procedure. Mifepristone 24hrs prior to procedure along with misoprostol the day of the procedure achieves similar dilation to osmotic dilators. The addition of multiple agents results in a synergistic effect. If osmotic dilators are used, the number should be recorded, and all should be accounted for at time of removal and surgery. The addition of mifepristone may increase cost and may be limited in availability. Repeat doses of and higher doses of misoprostol can also be given with greater effect, but may lead to increased side effects at doses >1000mcg. At GA>20wks, adequate cervical preparation often requires multiple agents and may take more than 2 days. [Table 1].

Surgical Management - Procedure Completion

A complete D+C procedure is confirmed with a gritty intrauterine texture in all quadrants (uterine cri), decreased vaginal bleeding, no further tissues removed on passes inside of the uterus, uterine involution, and complete tissue on POC exam. POC can be examined and will show villi and gestational sac in early GA pregnancies that can be floated in saline or water. After in 12wks, fetal parts can be identified. Between 12-14wks, and with all D+E procedures, examination should be performed on POC for confirmation of removal of all fetal parts. POC can be rinsed in saline or water, and villi will float. [Table 2]. In later gestations, fetal foot length can be correlated with gestational age. All removed POC are then sent to pathology. If an incomplete procedure is suspected, then intraoperative US can be performed initially. If retained POC are suspected, then repeat suction or extraction is indicated. If retained POC are unable to be retained due to lack of dilation (most commonly retained calvarium or larger calcified POC), then repeat dosing of cervical preparation agent can be administered (e.g. misoprostol) with an interval reattempt at extraction, which is generally effective. At earlier GA if continued retained POC is suspected, then pathology can be followed up, and repeat post-operative HCG levels can be drawn. These should decline by 50% in 48hrs.

Surgical Management – Complications

Overall, surgical management has a very low complication rate/ 1-5% of procedures encounter minor complications including infection, cervical trauma, retained products, hematometra or increased bleeding. Major complications are encountered <=1% of surgical procedures and include significant hemorrhage, perforation, sepsis, and maternal mortality. Mortality events are almost universally anesthesia-related, or rarely the result of AFE. Hemorrhage at D+C is most commonly caused by incomplete procedure or uterine atony. Significant hemorrhage at D+C should be treated similarly to PPH. IVF and labs are indicated, and blood transfusion considered. Please see the **Post-Partum hemorrhage guideline** or more extensive discussion. Excessive bleeding at D+C is usually the result of incomplete uterine evacuation and retained pregnancy tissue. Respiration is indicated in this case. US can be used to assist with D+C completion. The tissue can be examined to ensure it is complete. If products are retained and cannot be extracted, especially at advanced gestation, then misoprostol can be used intraoperative or postoperatively to increase dilation and allow for tissue passage. If complete uterine evacuation is confirmed, then atony should be considered next. Bimanual massage should be performed, bladder emptied, and uterotonics administered. Methergine 0.2mg IM or intracervical, Misoprostol 1g PR, Oxytocin 20-40U IV or 10U IM, or vasopressin 4-6U intracervical can be given. If bleeding does

not respond to uterotonic agents, and the uterus remains enlarged and boggy, then placement of an intrauterine 30cc foley balloon can be considered. If bleeding continues in the setting of a well-contracted uterus, then the cervix and lower genital tract should be examined for laceration or uterine perforation. Cervical laceration (usually at the tenaculum site) can be observed, compressed with pressure from ring forceps, cauterized with silver nitrate or bipolar cautery, rendered hemostatic with clotting agents such as Monsie's solution or hemostatic products (Floseal, e.g.), injected with vasopressin (4-6U IC), or sutured. If perforation is suspected, then intraoperative US is indicated to clarify the location of the perforation site. If the procedure is complete, the patient is stable, and bleeding is minimal, then some perforations can be managed conservatively. However, if pelvic organ injury is suspected, especially in cases where suction may have entered the intrauterine cavity, or if the patient is unstable, then laparoscopy or laparotomy may be indicated. Perforation is more likely in patients at higher gestational ages, with inadequate cervical preparation, or in cases of septic abortion. If bleeding continues in the setting of a well-contracted uterus, then other less-common causes of hemorrhage should be considered. Labs should be ordered to rule out coagulopathy, or suspicion of accreta or AVM. If the bleeding cannot be controlled with these measures, then the massive transfusion protocol should be initiated with consideration for UAE or laparotomy for possible hysterectomy. If molar pregnancy is suspected, then preoperative preparation for hemorrhage at time of D+E should be undertaken. Delayed atony may result in hematometra. Patients exhibiting high levels of pain with a boggy, enlarged uterus on exam and US showing intrauterine clotted blood may require respiration and uterotonic therapy. Infection will occur in up to 20% of patients undergoing D+C if they do not receive preoperative antibiotics. The incidence is much lower, $\approx 5\%$, if preoperative antibiotics are administered, as discussed above. After continued retention of POC is ruled out, stable patients with postoperative endometritis can be managed outpatient similarly to PID treatment. The recommended course is ceftriaxone 250mg IM x1, and doxycycline 100mg BID x 14 days, +/- metronidazole 500mg BID for 14 days. Recommended inpatient treatment of postoperative endometritis is IV cephalosporin and IV doxycycline for 24-48hrs afebrile. If a post-surgical IUD is in place, then it should be removed if the patient does not clinically improve after treatment. Scarring after D+C is uncommon. Intrauterine adhesions or synechiae or cervical agglutination are uncommon, but may more likely result if infection complicates D+C. If women persist with post-surgical amenorrhea, hormonal effect – either contraceptive or endocrine abnormality – should be ruled out. If persistent, then hysteroscopy may be indicated.

Surgical Management - Postoperative Contraception

If the patient desires contraception, this should be initiated right away. Confirmed ovulations have been reported in women as soon as 4 days after SAB. Follow up rates can be low, in some populations less than $<50\%$ after D+C surgery. Added follow up barriers such as access, school and childcare issues, and unique challenges to Alaska (geographic, weather, transportation, and access) may lead to poor follow up for contraception initiation. Additionally, initiation of hormonal contraception decreases post-procedure vaginal bleeding. LARC are considered first-line contraceptive methods. Implants can be placed in the operating room after completion of D+C. IUDs can be placed immediately post-D+C. Expulsion rates are higher, up to 20%, but this is still lower than the highest follow up rates. Infection, bleeding, and pain are equivalent in patients with immediate post-D+C IUD placement vs delayed placement. Other hormonal contraceptives can be initiated immediately without increased side effects or complication rates.

Management of 2nd Trimester Pregnancy Loss – D&E

Expectant management is not generally recommended for 2nd trimester pregnancy losses due to risk of DIC and uncontrolled complication. However, interventions are not emergent, and patients may take days or even weeks to proceed with surgery or medical induction, provided they are medical stable. 2nd trimester pregnancy loss management depends on provider experience. At GA ≥ 14 wk and < 16 wk, surgical management with D+E is preferable, leading to completion faster, with less pain, less bleeding, fewer infections, and decreased risk of retained placenta or pregnancy tissues, and fewer overall complications. At GA > 16 wks, medical management or D+E can be considered, depending on provider experience. Again, complications are lower with surgical management than medical management, but D+E should only be performed > 16 wks GA by providers experienced in these procedures due to increasing risks of perforation and cervical injury. IUFD pregnancies > 20 wks GA and ≤ 24 wks can be managed surgically only by providers experienced in 2nd trimester abortion and advanced D+E. D+E, no matter the GA, requires preoperative cervical preparation, as discussed above. Pregnancy loss > 24 wks is managed similarly to stillbirth.

Medical Management of 2nd Trimester Pregnancy Loss

2nd trimester SAB medical management has been well-studied. The recommended regimen for medical management of 2nd trimester SAB is 200mg of mifepristone 24-48hrs prior to misoprostol. Addition of mifepristone results in 50% reduction in time to complete SAB in the second trimester. Dosage for 2nd trimester pregnancy SAB management is 400mcg vaginally every 3hrs until delivery. A single 800mcg loading dose increases effectiveness and decreases time to completion. Misoprostol can be given via alternative sublingual or buccal routes. Doses up to 800mcg at a time or in intervals up to 12hrs can also be effective. Decreased doses of 200mcg can be given if patients do not tolerate side effects, or in cases of prolonged induction. As discussed prior, these doses do not significantly increase risk of scar disruption in patients with prior uterine scarring < 28 wks GA. Multiple agents decrease time of induction, with osmotic dilators and misoprostol having equivalent efficacy to mifepristone and misoprostol. If misoprostol alone is used due to cost or access issues with mifepristone, then misoprostol alone can be effective if given enough time. 85% of patients undergoing medical management of second trimester pregnancy loss will complete the procedure by 24hrs. Alternate medical regimens including prostin (PGF₂) have slightly less effectiveness than misoprostol, but are more expensive, offer no alternate dosing routes, and do not store easily as misoprostol. High dose oxytocin can also be used for medical management, but has an increased rate of side effects, requires an IV, and takes longer. Doses as high as 300U over 3hrs have been described, but generally 20U-30U in 500mL of saline is effective with fewer side effects. The management of the placenta should be considered in 2nd trimester pregnancy losses.

Management of the Placenta in 2nd Trimester Pregnancy Loss

Retained placenta is common after 2nd trimester pregnancy managed medically. The placenta may deliver with the fetus, but may be delayed. Usually the placenta will deliver at 30 minutes to 1hr after fetal delivery, but waiting for up to 4 hrs without surgical intervention is reasonable if the patient is stable with minimal bleeding. Automatic curettage is not indicated for all placentae after 2nd trimester medical management of pregnancy loss. If the placenta does not deliver immediately with the fetus, oxytocin is recommended at delivery in 3rd stage dosing. If the

placental delivery is delayed, then other uterotonic drugs can be administered, including hemabate and methergine. If delivery is delayed up to 4hrs, or sooner with heavy vaginal bleeding and no response to uterotonic agents, or if the cervix has completely closed around the cord (uterine relaxant such as nitroglycerine can be attempted in this case), then curettage is indicated. Of note, pregnancies ≥ 14 wk GA should have US assessment of placentation in women with a history of uterine scar (prior myomectomy or cesarean delivery). Presence of previa may still be managed either surgically or medically, but surgical interventions may be preferable. If accreta is suspected, then management may require hysterectomy.

Follow up After Pregnancy Loss

Generally, patients are advised to be on pelvic rest for 2 weeks after surgical procedures. Restrictions include: no tampons, no tub baths, no douching, no swimming, and no vaginal intercourse. However, no specific studies have shown pelvic rest to decrease risk of infection. However, reasonable advice is recommending pelvic rest for as long as patients are having vaginal bleeding after expectant, medical, or surgical SAB management, as this is generally a sign of continued healing and the possibly of minimal cervical dilation. Contraception should be addressed, and in patients not actively trying to conceive, initiated immediately after complete SAB as ovulation has been confirmed as soon as 4 days after complete SAB, and spermatozoa can survive in the body for over 7 days. In patients trying to conceive, a prolonged delayed inter-pregnancy interval has not been shown to decrease adverse pregnancy outcomes; however, for practical purposes a delay in attempting conception until after the next normal menstrual cycle is a reasonable recommendation. Some patients, especially those with a history of depression or psychiatric illness or poor social support, may have more risk of depression. BHC referral should be offered to all patients. Providers should have a nonjudgmental discussion of modifiable risk factors (e.g. tobacco cessation, diabetic blood sugar control) and given reassurance that SAB is common (25% if pregnancies) and not generally preventable (50% chromosomal). Workup for RPL is discussed elsewhere, and is indicated in very few patients after SAB. Recurrence of SAB is approximately 14% after 1 SAB, and $< 30\%$ after 2 or 3 SABs. Other poor pregnancy outcomes are not associated with a single episode of SAB. However, PTB, recurrent IUFD, and stillbirth are all more common after pregnancies complicated by 2nd trimester pregnancy loss, and may require further testing as is discussed elsewhere.

Appendices:

Table 1
Cervical Preparation

D+C < 14 wk GA	Cervical Preparation Recommended: 400mcg buccal miso 2hrs pre-procedure
< 12 wks	Consider for: <ul style="list-style-type: none"> • Adolescents, nulliparous • H/o cervical surgery • Cervical pathology • Known prior difficult dilation • Less experienced surgeons
12-14wk	<ul style="list-style-type: none"> • Recommended
D+E > 14 wk GA	Cervical Preparation:

>14-16wks	400mcg-800mcg buccal miso at least 1hr pre-procedure +/- addition of osmotic dilator Same day <ul style="list-style-type: none"> • Strongly recommended for all women
>16wks	400mcg-800mcg buccal miso at least 1hr pre-procedure + addition of osmotic dilator 2 day <ul style="list-style-type: none"> • Strongly recommended for all women

Table 2

POC Examination

Tissue Type	Expected Findings
Gestational sac	Thin, transparent, identified in pregnancy <12wk <ul style="list-style-type: none"> • 6wk = dime size • 7wk = nickel size • 8wk = quarter size
Chorionic villi	Transparent w frond-like projections, will float, turns bone-white with heated water or vinegar
Fetal parts	<ul style="list-style-type: none"> • <9-10wk: villi, GS • 10-13wk: villi, GS, some fetal parts • 12-13+wks: villi, placenta, GS, all fetal parts – calvarium, spine, four extremities
Decidual tissue	Opaque, red-brown-grey, does not float
Fetal foot length	See chart, UpToDate online

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