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Clinical Guidelines

# Induction of fetal demise before abortion

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## Abstract

For decades, the induction of fetal demise has been used before both surgical and medical second-trimester abortion. Intracardiac potassium chloride and intrafetal or intra-amniotic digoxin injections are the pharmacologic agents used most often to induce fetal demise. In the last several years, induction of fetal demise has become more common before second-trimester abortion. The only randomized, placebo-controlled trial of induced fetal demise before surgical abortion used a 1 mg injection of intra-amniotic digoxin before surgical abortion at 20–23 weeks' gestation and found no difference in procedure duration, difficulty, estimated blood loss, pain scores or complications between groups. Inducing demise before induction terminations at near viable gestational ages to avoid signs of life at delivery is practiced widely. The role of inducing demise before dilation and evacuation (D&E) remains unclear, except for legal considerations in the United States when an intact delivery is intended. There is a discrepancy between the one published randomized trial that used 1 mg intra-amniotic digoxin that showed no improvement in D&E outcomes and observational studies using different routes, doses and pre-abortion intervals that have made claims for its use. Additional randomized trials might provide clearer evidence upon which to make further recommendations about any role of inducing demise before surgical abortion. At the current time, the Society of Family Planning recommends that pharmacokinetic studies followed by randomized controlled trials be conducted to assess the safety and efficacy of feticidal agents to improve abortion safety. © 2010 Elsevier Inc. All rights reserved.

## Background

Induced abortion is the second most common surgery for reproductive-aged women in the United States, after cesarean delivery [1,2]. The safety of this common procedure is well-established [3]. Surgical and medical methods of abortion can be performed safely in the second trimester, and even in the third trimester when pregnancy termination usually is completed by medical induction for lethal fetal anomalies or other significant medical conditions affecting the pregnant woman [4].

During the past three decades, many modalities for causing fetal demise (often described as "feticide" in the medical literature) have been used. In the last several years, induction of fetal demise has become more common before second-trimester abortion, as well as for selective fetal reduction. Improved methods of inducing ovulation, and treatments such as in vitro fertilization (IVF) and gamete intrafallopian transfer (GIFT), have increased the rate of multiple pregnancies; almost 70% of twins and 99% of all higher-order multiple pregnancies are now iatrogenic [5]. In addition, since the Supreme Court of the United States

upheld the case of *Gonzalez v. Carhart* — affirming the constitutionality of the Partial-Birth Abortion Ban Act of 2003 (the Act) — many abortion providers have begun to induce and document fetal demise before an abortion begins, to avoid any potential accusations of intending to violate the law.

Since the early 1980s, various modalities of inducing fetal demise have been documented. Aberg et al. [6] published the first successful selective termination in 1978 by intracardiac puncture, and soon thereafter many techniques for multifetal pregnancy reduction, selective termination and inducing demise in singletons were investigated. However, most of these cases and studies did not precede abortion.

### Mechanical methods

The first documented selective termination was performed on a single fetus of a twin pregnancy discordant for Hurler's disease [6]. This occurrence led to research for better techniques to terminate selectively pregnancies found to be discordant for anomalies, as well as to reduce higher-order multiple gestations to triplets, twins or singletons in

order to decrease morbidity and improve fetal survival. Techniques have included cardiac puncture and exsanguination [6–15] or air embolization [9–11,16–20]. Cardiac puncture and exsanguination techniques require a great deal of skill to induce cardiac injury while keeping the patient comfortable. Air embolization injection techniques are efficacious, but produce an "air artifact" on ultrasound that makes it more difficult to discern asystole. Other methods of selective reduction that are outside the scope of this review have included hysterotomy, fetoscopic cord ligation and transection, intrafunic steel coil placement and gestational sac aspiration. Although complications from infection [21] and accidental intravascular injection of a feticidal agent [22] during selective termination and multifetal pregnancy reduction have occurred, with the exception of extramural deliveries, there have been no significant complications reported in the abortion literature in conjunction with injections to induce fetal demise.

### Sclerotic agents

The injection of sclerotic chemicals or adhesive and occlusive agents has been described in several case reports [23–28] and in one case series of 12 women. These modalities are no longer recommended because the published techniques of intrafunic and intrahepatic injections of ethanol or enbucrilate were difficult technically and achieved demise in only 48% of attempted cases in one small series [29].

### Pharmacologic agents

The most frequently studied methods involve chemical injections to induce demise pharmacologically including normal and hypertonic saline injections [9,30–32], hyper-osmolar urea and other pharmaceuticals [33]. Hypertonic saline injections have been reviewed in the literature as abortifacients, but they have not been studied specifically as agents to cause fetal demise independently and have been associated with disseminated intravascular coagulation, hemorrhage and electrolyte abnormalities with significant sequelae when used for induction terminations, along with some instances of failure to achieve demise [34–40]. In 1984, calcium gluconate was used to induce demise in a pregnancy of 19 weeks [41]. Lidocaine has also been used to induce fetal asystole [42,43]. In 1988, the first induced demise by potassium chloride (KCl) was described [44] and since that time numerous case series totaling thousands of patients have reported different doses, routes and techniques of KCl injections [8–11,18,45–64]. Asystole generally is reported within several minutes of injection. There has been one case report of maternal cardiac arrest [22] when inadvertent intravascular injection occurred and one case report of sepsis by *Clostridium perfringens* 2 days after a feticidal injection [21].

Beginning in the 1980s, some abortion providers began describing the use of digoxin injections to induce fetal demise before dilation and evacuation (D&E). Various techniques and routes have been described without any reported major feticide-related complications and without any clinically significant cardiac events [65–69]. Only one study of eight subjects described postinjection electrocardiographic (ECG) monitoring, during which no digoxin-associated arrhythmias were reported for. The most common reactions to digoxin injection noted were mild signs of digoxin toxicity, such as increased vomiting [68] and the onset of miscarriage before the patient's scheduled procedure [69].

### Umbilical cord transection

Transecting the umbilical cord at the beginning of or during a D&E procedure and awaiting cessation of fetal cardiac activity potentially could eliminate concern that an intentional medical act violated the definitions of the Partial-Birth Abortion Ban Act of 2003, which applies only when the fetus has cardiac activity. Although some providers perform amniotomy and divide the cord the day before D&E [70], this intervention has not been described recently in the medical literature as a technique before abortion. However, this method would fulfill the requirement of the Act that a provider not "deliberately and intentionally" deliver a living fetus to certain anatomic landmarks before causing demise. With documentation of fetal cardiac asystole, a surgical abortion of any type does not violate the Act.

Although numerous methods have been used over the years to achieve fetal demise, data remain scarce documenting the effect of these techniques upon the safety of the abortion itself. Acknowledging this significant limitation, the goal of these guidelines is to assess the current evidence and make recommendations for the use of feticidal agents in the provision of abortion care.

## Clinical questions and recommendations

### 1. Outside of legal concerns, what are the medical reasons providers induce fetal demise before abortion?

The most commonly reported use of feticidal agents is for selective termination and multifetal pregnancy reduction [71]. Since the advent of ovulation stimulation, IVF and GIFT, many women treated for infertility get pregnant with multiple gestations. There have been no randomized controlled trials (RCTs) comparing pregnancy reduction to carrying multiple gestations to delivery with respect to any fetal or maternal outcomes. The reduction of higher-order gestations to twins — or twins to a singleton in a retrospective case series [72] — significantly reduces morbidity for the surviving fetuses [51].

In the literature describing induction termination, there have been multiple case reports of unintended live births [47,52,54,59]. Less commonly, this outcome can occur before or during D&E if the patient begins laboring before

the surgical extraction begins or has enough cervical dilation to allow the fetus to be removed largely intact. By ensuring demise before the termination is begun, live birth cannot occur, thus avoiding entirely the problem that faces the provider, the team of caregivers and the patient undergoing induction or D&E if the patient were to expel the fetus with signs of life [73]. Patients and members of the medical care team prefer to avoid delivery of a nonviable fetus with signs of life when the original intent was pregnancy termination [74]. This issue can arise more frequently when multiple days of osmotic dilators are used and labor occurs before the D&E procedure, or in induction abortion that was not preceded by the use of a feticidal agent. Providers are also concerned about potential legal ramifications from an unintended live birth [54].

### 2. Do patients having a surgical abortion prefer to have fetal demise induced before abortion?

Some patients may prefer to have fetal demise induced before the abortion procedure begins. The prevalence of this preference is difficult to assess precisely, because it may be influenced by counseling and education and because patients may believe that stating such a preference is more socially acceptable. One study that assessed this preference was conducted in conjunction with a 126-subject, double-blinded trial of 1 mg intra-amniotic digoxin dose [68]. In a questionnaire that subjects completed after their procedure, 92% reported a strong preference for fetal demise before abortion. Among the women who preferred feticidal injection before their abortion procedure (*n*=107), 29% believed the injection would make the procedure easier and 19% less painful for the woman having the termination [68]. However, the generalizability of this result is limited. This question was posed to patients within the context of a clinical trial in which many of them believed the injection might make their abortion safer. Also, the social acceptability of a positive response may have skewed the results. In one induction termination study, the authors' discussion included the statement, "feticide was perceived as the most difficult moment confronted by the women during the termination process." However, their method of drawing this conclusion was not elucidated [59].

### 3. Does induction of fetal demise have any benefit related to fetal perception of pain during an abortion?

It is difficult to determine whether or not a fetus has the ability to perceive pain, which by its definition requires cortical interpretation of noxious stimuli. A multidisciplinary review of the medical evidence concluded that a fetus cannot experience pain until 29 weeks of gestation at the earliest, when thalamocortical connections are first present [75]. In the past, withdrawal reflexes and the release of hormonal stress hormones have been indicated as evidence of fetal pain perception. This review shows evidence that both withdrawal reflexes and hormonal stress hormones can be elicited by nonpainful stimuli and can occur without conscious cortical processing. Therefore, the best indicator as to when a fetus has potentially the capacity to experience pain is the development of the thalamocortical axons, which do not occur until at least 29 weeks of gestational duration; however, their functionality within the intrauterine environment has not been determined. With the difficulty of establishing any clear way to measure fetal pain and the lack of specific markers for fetal pain, any potential pain of the means of inducing fetal demise cannot be assessed either. By inducing fetal demise the issue of whether the fetus could experience pain during the abortion can be circumvented [73], which is another reason feticide may be offered by some providers.

### 4. How could inducing fetal demise protect providers from violating provisions of the Partial-Birth Abortion Ban Act?

In April 2007, the United States Supreme Court upheld the Partial-Birth Abortion Ban Act of 2003 in the *Gonzales v. Carhart* decision [76]. This ban makes illegal the "partial-birth abortion" procedure, which is not a precise or medically defined procedure. The Act [77] defines it as an abortion in which the person performing the abortion:

> (A) deliberately and intentionally vaginally delivers a living fetus until, in the case of a head-first presentation, the entire fetal head is outside the body of the mother, or, in the case of breech presentation, any part of the fetal trunk past the navel is outside the body of the mother for the purpose of performing an overt act that the person knows will kill the partially delivered living fetus; and

> (B) performs the overt act, other than completion of delivery, that kills the partially delivered living fetus….

To be in violation of the law, an abortion provider must therefore perform the banned procedure "deliberately and intentionally" as described above. As the Supreme Court affirmed in *Gonzales v. Carhart*, if the fetus is "delivered past the critical point by accident or inadvertence" or if the fetus is not delivered "for the purpose of performing an overt act that the [doctor] knows will kill [it]," then the procedure does not violate the law. By electing to use an agent with established feticidal properties at a dose and by a route that have been established to ensure cardiac asystole in most cases, there is no intention of performing the banned abortion procedure.

Similarly, transection of the umbilical cord with subsequent documentation of cardiac asystole fulfills the requirement of the Act. Documentation also shows the physician's intent not to deliver a living fetus to the specified anatomical points. Therefore, using a feticidal agent or dividing the cord could demonstrate the abortion provider's intention to avoid the banned procedure and allows documentation of the absence of cardiac activity, thus protecting the provider.

The Supreme Court's decision explicitly permits providers to complete a "standard D&E," a definition that can include multiple passes with the use of extracting forceps. On the other hand, serial dilation or osmotic dilators with adjuvant misoprostol may be viewed as intent to perform the banned procedure.

Those providers electing not to use the injection of a feticidal agent before performing a standard D&E should know that they still may be protected against performing the banned procedure by documenting their intended procedure as long as they have not performed any dilatory procedures that show intent to perform the banned procedure. The "standard dilation and evacuation" is defined by the Supreme Court decision in part by multiple passes required to complete a destructive procedure. The standard D&E is not an attempt to "deliver" a "living fetus"; this is especially true considering the landmarks demarcated by the Act. By its Supreme Court definition, a "standard D&E" excludes the deliberate and intentional delivery of an intact fetus. If delivery of a more intact fetus were to occur during an intended "standard D&E," it was neither a deliberate nor an intentional act.

Because the terms "Partial Birth Abortion" and "Standard D&E" are not defined or recognized medically, nor do they have clear surgical definitions, the Society of Family Planning is not able to make any evidence-based legal recommendations.

## 5. What techniques and agents are used currently for induction of fetal demise before abortion?

Pharmacologic agents are the most commonly used methods for inducing fetal demise. In the United States, KCl is used generally by specialists in infertility and maternal-fetal medicine, whereas digoxin is used more commonly by abortion providers. No randomized trials compare modalities of inducing demise; however, many case series of single agents exist.

### Potassium chloride

Potassium chloride achieves its effect by disrupting the balance of intra- and extracellular potassium ions, decreasing the conduction of action potentials in cardiac myocytes, thus leading to bradycardia and, eventually, asystole. Because it must be administered by intracardiac injection for maximum effect on the myocardium, KCl injection requires more technical skill than intrafetal or intra-amniotic digoxin injection [51].

In a 1994 series of 183 cases of selective termination, demise was achieved with air embolization in 24 cases, by exsanguination in 3 cases and by injection of KCl in 156 cases. In all of the cases the induction of demise was successful [10]. By 1996, selective termination and multifetal pregnancy reduction were performed almost exclusively by transabdominal injection of intracardiac KCl, especially after the first trimester [78].

The most common technique of KCl administration is via transabdominal intracardiac injection performed with ultrasound guidance. Concentrated KCl (2 mEq/mL) is injected in aliquots of 2–3 mL until asystole is observed for 2–5 min [71]. Typically, a total of 6–10 mEq is needed. An ultrasound may be repeated 30 min to 1 h later to confirm the absence of cardiac activity. In addition to verifying asystole, ultrasound is crucial in determining intracardiac placement of the injection needle. This technique was advocated by the Royal College of Obstetricians and Gynaecologists (RCOG) before medical termination at 22 weeks of gestation or greater and before all induction terminations [79,80]; however, the more recently published and more general RCOG guidelines for abortion care include no recommendation about the use of potassium injection before abortion, because "the nature of the procedure ensures that there is no risk of a live birth" [81].

There are no RCTs comparing routes of administering concentrated KCl. A large retrospective review compared 846 transabdominal procedures to 238 transcervical procedures. All cases were ultimately successful, although 1% required a second injection to achieve cardiac asystole. Their study focused on delivery rates after selective termination or multifetal pregnancy reduction. However, little data were reported about the feticidal injection itself [10].

### Digoxin

Abortion providers in the United States use digoxin more often than KCl to induce fetal demise [66,69]. Digoxin functions by inhibiting the sodium-potassium ATPase — which regulates sodium and calcium concentrations indirectly — increasing cardiac contractility, eventually leading to AV block. Its use was first reported in a large case series in conjunction with hyperosmolar urea. Digoxin can be administered via intra-amniotic injection or intrafetal routes, thus less skill is required than to achieve intracardiac or intrafunic placement of a needle for KCl injections [67]. Intrafetal injections typically use up to 2 mg of digoxin injected on the day of dilator placement, 1 to 2 days before the D&E [66,67,69]. Intrafetal injections of at least 1 mg digoxin have been extremely effective at inducing demise with a minimum of reported side effects, although no formal pharmacokinetic or safety studies currently exist.

In 2001, a series of 1677 consecutive patients, all with demise induced by intrafetal digoxin injections of 1.5–2 mg, reported no failures of causing demise, no injection-related complications and no signs of toxicity or clinically significant cardiac events [66]. Serial multiple laminaria were placed over 2 days, and the abortion procedure was performed on the third day. The median gestational duration was 22 weeks, ranging from 18 to 34 weeks. In patients 24 weeks and beyond, 40 g of hyperosmolar urea was injected intrafetally after the digoxin. The author concluded that intrafetal digoxin caused cervical priming and softening of the fetus, which led to additional research about feticidal agents in abortion care.

A pharmacokinetic study was performed to describe patient serum absorption after 1 mg intra-amniotic digoxin injection. Eight patients received baseline coagulation labs and had a Holter cardiac monitor placed before their digoxin injection. They were observed in the hospital overnight, and serial serum digoxin levels were drawn during the 24 h preceding their abortion. No digoxin-associated arrhythmias or clinically significant cardiac events occurred, and patient serum digoxin levels were not within a toxic range [65].

There has been one randomized trial of intra-amniotic digoxin vs. placebo, in which 126 women were randomized to receive a dose of 1 mg digoxin or normal saline via amniocentesis. The injection occurred before laminaria were placed, 24 h before the abortion. There was a failure rate of 8% to achieve cessation of cardiac activity, documented by ultrasonography before the D&E [68]. The retrospective cohort analysis by Molaei et al. [69] assessed varying doses of intra-amniotic digoxin (from 0.125 to 0.5 mg) and found an overall failure rate of 31% by this route.

The same study assessed varying doses of intrafetal digoxin and reported no failure to induce demise at a 1 mg dose among any of 107 patients. Overall, the failure rate of various doses of intrafetal digoxin was 5%. They reported no adverse events suggesting digoxin toxicity, and there was no increase in anti-emetic medicines prescribed, but information was not collected from patients about these side effects [69].

*Transection of umbilical cord*

Dilation of the cervix and transection of the umbilical cord were first described in the English medical literature in 1972 [70]. Recently, some providers have had success with umbilical transection techniques performed during multifetal pregnancy reduction and selective termination endoscopic procedures [82–91] or under sonographic guidance alone [92–94]. Although these techniques described in the selective reduction literature are far more invasive and bear more risk than other methods of feticide before an abortion is performed, they relate an important concept. After the umbilical cord has been divided, fetal cardiac activity ceases. This suggests an additional method of inducing demise before abortion that has yet to be investigated rigorously: the feasibility of direct cord transection before surgical termination of pregnancy.

*6. What is the effectiveness of feticidal agents in achieving fetal demise?*

Data are summarized in Table 1. In recent literature, KCl has shown excellent efficacy at achieving fetal

Table 1
Efficacy

| Author | Year | Regimen | Dose | *n* | Gestation | First injection failure rate |
|---|---|---|---|---|---|---|
| Molaei et al. [69] | 2008 | Intra-amniotic digoxin | 0.125 mg | 22 | 17–24 | 46% |
| | | Intra-amniotic digoxin | 0.25 mg | 20 | 17–24 | 70% |
| | | Intra-amniotic digoxin | 0.375 mg | 53 | 17–24 | 26% |
| | | Intra-amniotic digoxin | 0.5 mg | 36 | 17–24 | 8% |
| Jackson et al. [68] | 2001 | Intra-amniotic digoxin | 1.0 mg | 62 | 20–23 | 8% |
| Drey et al. [65] | 2000 | Intra-amniotic digoxin | 1.0 mg | 8 | 19–23 | 0% |
| Molaei et al. [69] | 2008 | Intrafetal digoxin | 0.125 mg | 98 | 17–24 | 14% |
| | | Intrafetal digoxin | 0.25 mg | 466 | 17–24 | 6% |
| | | Intrafetal digoxin | 0.5 mg | 993 | 17–24 | 4% |
| | | Intrafetal digoxin | 1.0 mg | 107 | 17–24 | 0% |
| Hern [66] | 2001 | Intrafetal digoxin[a] | 1.5–2 mg[a] | 1677 | 18–34 | 0% |
| Hern et al. [67] | 1993 | Intrafetal digoxin[a] | 1.5–2 mg[a] | 118[b] | 15–34 | 0% |
| Pasquini et al. [57] | 2008 | Intracardiac KCl | 6–10 mEq | 124 | 20–36 | 0% |
| Hern [53] | 2004 | Intracardiac KCl | 6–40 mEq | 4 | 32+ | 0%[c] |
| Bhide et al. [47] | 2002 | Intracardiac KCl | 8–40 mEq | 73 | 18–35 | 0% |
| Eddleman et al. [48] | 2002 | Intracardiac KCl | 6–18 mEq | 200 | 12–24 | 0%[d] |
| Bhide et al. [47] | 2002 | Intrafunic KCl | 6–16 mEq | 21 | 17–33 | 9%[f] |
| Senat et al. [58] | 2002 | Intrafunic KCl | 20 mEq | 10 | 22–38 | 0% |
| Gill et al. [52] | 1994 | Intrafunic KCl | 5–10 mEq | 60 | 18–32 | 13% |
| Evans et al. [51] | 1999 | Intracardiac or intrafunic KCl | Not reported | 369 | 9–25+ | Not reported |
| Berkowitz et al. [46] | 1997 | Intracardiac or Intrafunic KCl | 3–10 mEq | 100 | 12–23 | Not reported |
| Evans et al. [50] | 1996 | Intrathoracic KCl[e] | Not reported | 1789 | Not reported | Not reported |
| Evans et al. [10] | 1994 | Intrathoracic KCl[e] | Not reported | 1084 | 6–11 | Not reported |
| Evans et al. [95] | 1993 | Intrathoracic KCl | Not reported | 463 | 6–14 | 0%[d] |

[a] Study administered 40 g intrafetal hyperosmolar urea after digoxin in patients over 24 weeks of gestation.
[b] Exact number of total patients to receive interventions was not stated.
[c] Demise was induced in all cases; however, 75% required a second injection.
[d] Induction of demise was 100% successful, but required one or more injections when the first failed to cause asystole, and the number of re-injections required was not reported.
[e] Includes transabdominal, transcervical and transvaginal routes of intrathoracic KCl.
[f] In one case, demise was not achieved. In a second case, demise was achieved with a second injection.

demise, although occasionally a second injection is required. One cohort of 239 patients who received feticidal KCl injection before second-trimester induction abortion had no failures. The authors used an intracardiac injection of 1–2 mL KCl (2 mEq/mL) and observed asystole for at least 2 min, then repeated the ultrasound 30 min later to confirm demise. There were no injection-related complications [57].

During an international collaborative experience with selective terminations, there were no failed inductions of fetal demise by intrafetal or intrafunic injection of KCL in 402 cases, which included gestational durations from 9 weeks until after 24 weeks. Because the study focused on the neonatal outcome of the surviving twin, little attention was given to the technique of inducing fetal demise. However, it is notable that the intrafetal and intrafunic injections conferred a 100% success rate [51]. In subsequent publications on the international experience of selective termination by this collaborative group, all attempts ultimately achieved fetal demise. Study methods indicated that any case that did not result in cardiac asystole was ascertained by repeat ultrasound and received an additional intracardiac injection, a technique described in current maternal–fetal medicine textbooks [51].

Intrafunic KCl has also been studied, although it requires greater technical skill than intracardiac injection [10,46,47,52]. Among the publications of the collaborative international data, when direct umbilical vein injection was not successful, the practitioner would then use an intracardiac injection. There were no published data on the occurrence of conversions to intracardiac injection; however, the end point of fetal demise was still universally achieved [10]. Other studies that attempted intrafunic injections alone reported failure rates of 5–13% [47,52]. In a retrospective analysis, 73 women who received intracardiac KCl were compared to 21 women who received intrafunic injections. The volume of KCl required to achieve cardiac asystole was lower in the intrafunic group (5 vs. 10 mL, p<.001). However, there was one failed intrafunic injection resulting in a fetus born with signs of life, which prompted a change in protocol to repeat the ultrasound 20 min after the feticidal injection. There were no other complications reported [47].

In contrast to KCl, intra-amniotic digoxin has mediocre efficacy at low doses. A retrospective cohort study reviewed 1795 terminations of various doses and routes of digoxin administration. Of the 36 women who received 0.5 mg of intra-amniotic digoxin, 8% of injections did not achieve demise. At doses lower than 0.5 mg, failure rates were documented of up to 70% [69]. In the only RCT of digoxin, 126 women were randomized to receive either 1 mg intra-amniotic digoxin (n=62) or placebo (n=64). At 24 h, there was a failure rate of 8%, consistent with the large observational study utilizing 0.5 mg digoxin [68].

Intrafetal digoxin has had better efficacy in achieving demise. A dose of 0.5 mg intrafetal digoxin was associated with a 4% failure rate, but no failures occurred at 1 mg (n=107) [69]. In a report of 1677 consecutive cases, 1.5–2 mg digoxin was injected intrafetally on the day of intracervical dilator placement. In patients over 24 weeks' gestation, 40 g of hyperosmolar urea was injected intrafetally after the digoxin. No failures were noted in this series [66].

## 7. Is there any surgical benefit to inducing fetal demise before D&E?

The only RCT comparing feticide to placebo evaluated intra-amniotic digoxin and used procedure duration as a proxy for ease of abortion. With 1 mg intra-amniotic digoxin, there was no difference in procedure time (p=.60) or physician-reported case difficulty (p=.64) [68]. There was no difference in estimated blood loss, pain scores or complications either; however, this study was not powered to determine whether there was a difference in these outcomes.

The use of a feticidal agent at the time of dilator placement has been reported to promote cervical ripening and fetal maceration. A 2001 case series of 1677 late second-trimester abortions employed intrafetal digoxin administered 2–3 days before the D&E procedure. Only three major complications occurred (0.2%), and the minor complication rate was 6%. The author reported a subjective softening of products of conception that could account for the low complication rate [66]. The injection of digoxin before multiple osmotic dilator placements in a nonblinded series caused demise 2–3 days before the abortion procedure [66], whereas in the previously mentioned RCT, digoxin was used to cause demise only 24 h before the abortion [68]. The measured time interval between induced demise and the abortion procedure has not yet been addressed specifically and may affect fetal maceration or cervical priming, which has the potential to increase or decrease the ease and safety of procedures. Increasing the interval between injection and abortion also would be expected to result in more extramural deliveries.

## 8. Is there any procedural benefit to inducing fetal demise before induction termination?

### Induction-to-abortion interval

A recent retrospective review of 68 women undergoing termination by labor induction compared women receiving feticidal injections to those who did not [49]. Women received vaginal suppositories of 20 mg prostaglandin $E_2$ placed every 4 h until products of conception were expelled. Seventeen women had KCl injections before $E_2$ suppositories were placed and 51 served as the control group. Those who had received a KCl injection had a significantly shorter induction-to-abortion interval than those who had not: 570 vs. 890 min (p=.006). The KCl group received two doses, compared to the control group, which received an average of three doses (p<.001). These results are consistent with two other retrospective chart reviews that assessed abortion interval in pregnancy terminations with and without

spontaneous, noniatrogenic fetal demise [96,97]. A more recent chart review using similar methodology found no difference in induction-to-abortion times for women with induced fetal demise vs. those who did not receive a feticidal injection. However, the fetal demise group had a significantly earlier gestational duration. Because earlier gestation is a conservative bias that could favor shorter induction-to-abortion interval, there appears to be conflicting evidence as to whether this effect is real [59].

### Potential for decreased blood loss

A small retrospective chart review of a subset of women with complete placenta previa having second-trimester induction terminations suggested that using a feticidal agent reduces blood loss (*n*=15) [98]. Of women who terminated pregnancies with complete placenta previa, the first nine cases did not receive a feticidal agent and the last six cases received intracardiac KCl to induce demise 2–14 days (mean 7 days) before induction termination. Hemorrhage was defined as blood loss requiring a transfusion. There was no statistically significant difference in the number of patients with hemorrhage (four who did not have feticide vs. 0 who did have feticide; p>.05). The mean difference in hemoglobin levels before and after the termination was then compared, and the group that had not received a feticidal injection had a larger hemoglobin drop (2.5 vs. 1.0 g/dL, p=.03); estimated blood loss was not a reported outcome. Their results suggested blood loss may be lower in at least a subset of women whose induction terminations are preceded by a feticidal injection [98]. This assertion requires more rigorous study.

As discussed above, avoiding the medical, ethical and emotional consequences of signs of life at the time of delivery is a widely recognized benefit of fetal demise before induction termination [54,73].

### 9. What are the side effects and complications of inducing demise?

Data are summarized in Table 2.

### Vomiting

The most common side effect of intra-amniotic digoxin is vomiting. In the double-blinded RCT, 16% of women receiving a 1 mg intra-amniotic digoxin injection experienced vomiting vs. 3% who had received placebo (p=.02)

[68]. This effect has not yet been described with any doses of intrafetal digoxin injections or KCl. One study of intrafetal digoxin used anti-emetics dispensed in the recovery room as a proxy for nausea and vomiting; however, it is not clear whether these data were collected routinely [69].

### Early labor or extramural deliveries

One of the concerns of iatrogenic demise is that the patient will go into labor and have an extramural delivery before her scheduled abortion procedure. This has occurred in several case series [47,52,69,73] (Table 2). Of 1796 digoxin cases, 0.5% had contractions for which they were sent to the hospital or experienced extramural delivery (1.5% or 2/131 intra-amniotic, and 0.4% or 7/1775 intrafetal) [69]. Unscheduled delivery can cause a major ethical dilemma if the woman must go to the nearest hospital instead of the clinic where she is receiving abortion care [73]. The use of a feticidal agent can circumvent the ethical dilemma of administering hopeless resuscitative measures or withholding care [54,73]. When demise has already been induced, the care of the woman in very premature labor may be more standardized and available at hospitals than the specialized care an abortion clinic provides.

### Infection

The most adverse case of serious infection directly related to a feticidal injection in the literature occurred in a 41-year-old woman at 22 weeks who received a selective termination by intrafunic KCl injection and developed sepsis 2 days later. She presented to the hospital febrile with signs of chorioamnionitis and expelled the pregnancy 2 h later. Broad spectrum antibiotics were administered and she was transferred to intensive care for 1 day. After another 6 days, she was discharged in good condition without needing a hysterectomy. Blood and fecal cultures grew *C. perfringens* [21]. Other cases of infection have been documented in patients who received a feticidal injection (see Table 2), but none as serious as the previous case. One case of amnionitis was reported in 1996 involving selective termination that resolved with antibiotics [55]. In another series of multifetal pregnancy reduction there were two cases of amnionitis, one of which resolved with antibiotics, and the other required immediate uterine evacuation, neither of which had any further sequelae [61].

Table 2
Complications

| Author | Year | Regimen | Dose | Gestation | Complication | Resolution |
|---|---|---|---|---|---|---|
| Molaei et al. [69] | 2008 | Intrafetal digoxin | | | 7 extramural deliveries | 7/1665 total=0.4% |
| Molaei et al. [69] | 2008 | Intra-amniotic digoxin | | | 2 extramural deliveries | 2/131 total=1.5% |
| Coke et al. [22] | 2004 | Intracardiac KCl | 5 mEq | 22 | Maternal cardiac arrest | ACLS protocol without further sequelae |
| Li Kim Mui et al. [21] | 2002 | Intrafunic KCl | | 22 | *Clostridium perfringens* sepsis | Broad-spectrum antibiotics |
| Lipitz et al. [55] | 1996 | Intracardiac KCl | 3–5 mEq | 28 | Amnionitis | Resolved |
| Timor-Tritsch et al. [61] | 1993 | Transcervical KCl | 2–4 mEq | 13 and 10 | Infection | 3/134 total=2.2%. Two resolved with oral antibiotics; one required evacuation |

## Cardiac events

In one case report, KCl was administered inadvertently into maternal vasculature resulting in the patient's cardiac arrest. She was resuscitated successfully in conformity with the standard ACLS protocol without further sequelae [22]. Cardiac arrhythmia or arrest has not been reported from any other feticidal agent. In a pharmacokinetic study of the safety of 1 mg intra-amniotic digoxin, women had a Holter monitor placed 1 h before their digoxin injection and wore it for 24 h until their D&Es. No clinically significant cardiac events or digoxin-related arrhythmias were noted [65].

## Coagulopathy

Consumptive coagulopathy has been reported after a single fetal death in multiple gestation pregnancies [99,100]. This outcome, however, is very rare when demise occurs with retention of dead fetus for less than 5 weeks [101]. In a retrospective review of first- and second-trimester terminations, one group found rates of coagulopathy per 100,000 procedures to be 8 for D&C, 191 for D&E and 658 for saline instillation abortion [102].

## Pain from injection

The injection of a feticidal agent can be uncomfortable. Pain may be controlled with local anesthetic administered before the injection, although some providers use deep sedation for injections [69] or oral medications for pain control and anxiolysis.

## Emotional distress

Not enough is known about patients' feelings surrounding feticidal injection. In the RCT of intra-amniotic digoxin, 92% of women preferred fetal demise before the abortion procedure [68]. However, it may be difficult to ascertain more information about this subject because of social desirability implicit in the question itself or because women may believe that inducing fetal demise may make the abortion safer.

## 10. How can the risk and severity of complications from induction of fetal demise be reduced?

### Use of ultrasound

To decrease the possibility of complications related to intrafetal and intra-amniotic injections and to guide intracardiac and intrafunic injections, ultrasonographic guidance has been used. Ultrasound may allow the needle's location to be visualized before any drug is administered to avoid intravascular, intramyometrial or intraplacental administration [22], although no data have been published to document its utility or importance.

### Plan for extramural delivery

After having received feticidal injections, some patients begin laboring before returning for the scheduled abortion. The possibility of extramural delivery should be addressed with patients. This discussion should include an individualized plan if labor begins while the patient is at home, including where the patient should present herself for evaluation.

### Dose and route of injection

If a feticidal agent is indicated, the smallest effective dose should be used. Although intra-amniotic digoxin has increased vomiting when compared to placebo [68], it is unclear whether this occurs with intrafetal digoxin as well. There have been no known studies comparing various routes of digoxin injection that were powered to find a difference in feticide-associated complications. No authors have reported using anti-emetics for this side effect.

### Infection or coagulopathy

Sterile technique is routinely recommended for injection. No data exist about the use of prophylactic antibiotics; the incidence of postinjection infection is very low. Similarly, data do not support monitoring for coagulopathy because of the brief period of fetal demise between injection and the abortion.

## Conclusions and recommendations

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

Level A: Recommendations are based primarily on good and consistent scientific evidence.

- One milligram of intra-amniotic digoxin is no better than placebo to decrease procedure time or provider-reported technical difficulty. Patients have increased vomiting after intra-amniotic digoxin injections.

Level B: Recommendations are based primarily on limited or inconsistent scientific evidence.

- Intrafetal injections require less digoxin than intra-amniotic injections to achieve demise effectively. Intrafetal injection of at least 1 mg digoxin is required to ensure fetal demise consistently.
- Although technically challenging and thus requiring skilled technicians, intracardiac KCl injections are a generally safe and effective method to induce fetal demise, although rare complications could occur.
- A 1 mg intra-amniotic digoxin dose has been established as generally safe by a pharmacokinetic trial and by observational studies, although this cannot exclude the possibility of more rare complications.
- Feticide may decrease the induction-to-abortion time when completing a medical abortion in the second trimester.

Level C: Recommendations are based primarily on consensus and expert opinion.

○ Inducing fetal demise before induction termination avoids signs of live birth that may have beneficial emotional, ethical and legal consequences.

○ Intrafetal digoxin injections up to 2 mg appear to be usually safe, although no established pharmacokinetic data exist.

○ Inducing demise may lead to fetal maceration and cervical priming.

○ In the United States, if a provider intends to obtain greater cervical dilation to achieve a more intact surgical abortion, ensuring fetal demise either by cord transection or by feticidal injection can be considered.

### Important questions to be answered

Although we have primarily observational data about the safety and effectiveness of feticidal injections, there is a paucity of the highest level of evidence — RCTs — about the effect of inducing fetal demise on the safety, speed and risks of the abortion procedure itself, before either D&E or induction termination. We currently have inadequate data to recommend this intervention to increase the safety of D&E. In order to study the safety and absorption of digoxin and KCl, we need more pharmacokinetic data about the varying doses and routes by which the drugs are being administered.

Most of the data that exist about feticidal agents document their efficacy in causing fetal demise. The only RCT of their efficacy in improving D&E safety assessed a single dose and route of digoxin (1 mg intra-amniotic 24 h before D&E) and did not show improvement in markers of abortion safety.

To demonstrate whether second-trimester abortion is made safer by different doses or routes of feticidal agents or by a longer time interval between the feticidal intervention and D&E, additional RCTs are necessary. Before such investigations can be pursued, pharmacokinetic data should be described for any dose and route of interest. If RCTs were to demonstrate that feticidal agents improved the safety of second-trimester D&E, large observational studies will be needed to quantify the risks of the intervention. These risks include extramural expulsions, infection and possible changes in abortion safety. To justify the harm of the documented increase in spontaneous labor and extramural delivery, along with an increase in vomiting seen in the one blinded digoxin RCT, in addition to any more infrequent risks, a significant increase in D&E safety would seem warranted. We also need more data from blinded RCTs about the effect of feticidal agents on the speed and safety of induction termination.

To avoid the risks and side effects of feticidal agents, the feasibility and effectiveness of cord transection at the time of D&E should be studied and documented for those US abortion providers who feel that their abortion technique might violate the requirements of the Partial-Birth Abortion Ban Act of 2003.

### References

[1] Jones RK, et al. Abortion in the United States: incidence and access to services, 2005. Perspect Sex Reprod Health 2008;40:6–16 [Evidence Grade: III].

[2] Martin JA, et al. Births: final data for 2005. Natl Vital Stat Rep 2007;56:1–03 [Evidence Grade: III].

[3] Bartlett LA, et al. Risk factors for legal induced abortion-related mortality in the United States. Obstet Gynecol 2004;103:729–37 [Evidence Grade: III].

[4] Grimes DA, Schulz KF. Morbidity and mortality from second-trimester abortions. J Reprod Med 1985;30:505–14 [Evidence Grade: III].

[5] Evans MI, Britt DW. Fetal reduction. Semin Perinatol 2005;29:321–9 [Evidence Grade: III].

[6] Aberg A, et al. Cardiac puncture of fetus with Hurler's disease avoiding abortion of unaffected co-twin. Lancet 1978;2:990–1 [Evidence Grade: III].

[7] Beksac MS, et al. Selective feticide in dichorionic pregnancies with intracardiac blood aspiration: report of nine cases. J Perinat Med 2009;37:85–6 [Evidence Grade: III].

[8] Boulot P, et al. Multifetal pregnancy reduction: a consecutive series of 61 cases. Br J Obstet Gynaecol 1993;100:63–8 [Evidence Grade: III].

[9] Dommergues M, et al. Embryo reduction in multifetal pregnancies after infertility therapy: obstetrical risks and perinatal benefits are related to operative strategy. Fertil Steril 1991;55:805–11 [Evidence Grade: III].

[10] Evans MI, et al. Transabdominal versus transcervical and transvaginal multifetal pregnancy reduction: international collaborative experience of more than one thousand cases. Am J Obstet Gynecol 1994;170:902–9 [Evidence Grade: III].

[11] Golbus MS, et al. Selective termination of multiple gestations. Am J Med Genet 1988;31:339–48 [Evidence Grade: III].

[12] Iberico G, et al. Embryo reduction of multifetal pregnancies following assisted reproduction treatment: a modification of the transvaginal ultrasound-guided technique. Hum Reprod 2000;15:2228–33 [Evidence Grade: III].

[13] Kanhai HH, et al. Selective termination in quintuplet pregnancy during first trimester. Lancet 1986;1:1447 [Evidence Grade: III].

[14] Kerenyi TD, Chitkara U. Selective birth in twin pregnancy with discordancy for Down's syndrome. N Engl J Med 1981;304:1525–7 [Evidence Grade: III].

[15] Redwine FO, Petres RE. Selective birth in a case of twins discordant for Tay Sachs disease. Acta Genet Med Gemellol (Roma) 1984;33:35–8 [Evidence Grade: III].

[16] Rodeck CH, et al. Selective feticide of the affected twin by fetoscopic air embolism. Prenat Diagn 1982;2:189–94 [Evidence Grade: III].

[17] Birnholz JC, et al. Selective continuation in gonadotropin-induced multiple pregnancy. Fertil Steril 1987;48:873–6 [Evidence Grade: III].

[18] Chitkara U, et al. Selective second-trimester termination of the anomalous fetus in twin pregnancies. Obstet Gynecol 1989;73:690–4 [Evidence Grade: III].

[19] Pijpers L, et al. Selective birth in a dyzygotic twin pregnancy with discordancy for Down's syndrome. Fetal Ther 1989;4:58–60 [Evidence Grade: III].

[20] Shalev E, et al. Ultrasound-guided selective feticide of hydrocephalic fetus in triplet pregnancy. J Clin Ultrasound 1988;16:41–3 [Evidence Grade: III].

[21] Li Kim Mui SV, et al. Sepsis due to *Clostridium perfringens* after pregnancy termination with feticide by cordocentesis: a case report. Fetal Diagn Ther 2002;17:124–6 [Evidence Grade: III].

[22] Coke GA, et al. Maternal cardiac arrest associated with attempted fetal injection of potassium chloride. Int J Obstet Anesth 2004;13:287–90 [Evidence Grade: III].

[23] Dommergues M, et al. Twin-to-twin transfusion syndrome: selective feticide by embolization of the hydropic fetus. Fetal Diagn Ther 1995;10:26–31 [Evidence Grade: III].

[24] Dumler EA, Kolben M, Schneider KT. Intracardiac fibrin adhesive for selective feticide in twin pregnancy: report of three cases. Ultrasound Obstet Gynecol 1996;7:213–5 [Evidence Grade: III].

[25] Grab D, Schneider V, Keckstein J. Twin, acardiac, outcome. Fetus 1992;2:11–3 [Evidence Grade: III].

[26] Denbow ML, et al. Selective termination by intrahepatic vein alcohol injection of a monochorionic twin pregnancy discordant for fetal abnormality. Br J Obstet Gynaecol 1997;104:626–7 [Evidence Grade: III].

[27] Holzgreve W, et al. A simpler technique for umbilical-cord blockade of an acardiac twin. N Engl J Med 1994;331:56–7 [Evidence Grade: III].

[28] Sepulveda W, et al. Ablation of acardiac twin by alcohol injection into the intra-abdominal umbilical artery. Obstet Gynecol 1995;86:680–1 [Evidence Grade: III].

[29] Denbow ML, et al. High failure rate of umbilical vessel occlusion by ultrasound-guided injection of absolute alcohol or enbucrilate gel. Prenat Diagn 1999;19:527–32 [Evidence Grade: III].

[30] Bolodar A, et al. Invasive intrauterine procedures in twin pregnancies discordant for fetal malformation. Acta Chir Hung 1990;31:39–42 [Evidence Grade: III].

[31] Farquharson DF, et al. Management of quintuplet pregnancy by selective embryocide. Am J Obstet Gynecol 1988;158:413–6 [Evidence Grade: III].

[32] Wittmann BK, et al. The role of feticide in the management of severe twin transfusion syndrome. Am J Obstet Gynecol 1986;155:1023–6 [Evidence Grade: III].

[33] Hern WM. Serial multiple laminaria and adjunctive urea in late outpatient dilatation and evacuation abortion. Obstet Gynecol 1984;63:543–9 [Evidence Grade: III].

[34] Berkowitz RL. Electrolyte changes and serious complications after hypertonic saline instillation. Mod Treat 1971;8:114–26 [Evidence Grade: III].

[35] Dominguez de Villota E. Complication of hypertonic saline induction of abortion. Heart Lung 1973;2:116–21 [Evidence Grade: III].

[36] Gustavii B. Studies on accidental intravascular injection in extra-amniotic saline induced abortion and a method for reducing this risk. J Reprod Med 1972;8:70–4 [Evidence Grade: III].

[37] Mirchandani HG, Mirchandani IH, Parikh SR. Hypernatremia due to amniotic fluid embolism during a saline-induced abortion. Am J Forensic Med Pathol 1988;9:48–50 [Evidence Grade: III].

[38] Radonov D, Mirchev N, Madzharov N. Sodium chloride poisoning during abortion. Akush Ginekol (Sofiia) 1989;28:77–9 [Evidence Grade: III].

[39] Reches A, et al. Reversible hypernatremic coma following therapeutic abortion with hypertonic saline. Harefuah 1975;89:209–11 [Evidence Grade: III].

[40] Reid DE, Frigoletto Fd J, Goodlin RC. Hypernatremia from intravascular saline infusion during therapeutic abortion. JAMA 1972;220:1749 [Evidence Grade: III].

[41] Antsaklis A, et al. Selective survival of only the healthy fetus following prenatal diagnosis of thalassaemia major in binovular twin gestation. Prenat Diagn 1984;4:289–96 [Evidence Grade: III].

[42] Senat MV, et al. The use of lidocaine for feticide in late termination of pregnancy. BJOG 2003;110:296–300 [Evidence Grade: III].

[43] Brandes JM, et al. Reduction of the number of embryos in a multiple pregnancy: quintuplet to triplet. Fertil Steril 1987;48:326–7 [Evidence Grade: III].

[44] Westendorp AK, et al. Selective fetocide by direct intracardiac injection of isotonic potassium chloride. Arch Gynecol Obstet 1988;244:59–62 [Evidence Grade: III].

[45] Appelman Z, Caspi B. Chorionic villus sampling and selective termination of a chromosomally abnormal fetus in a triplet pregnancy. Prenat Diagn 1992;12:215–7 [Evidence Grade: III].

[46] Berkowitz RL, Stone JL, Eddleman KA. One hundred consecutive cases of selective termination of an abnormal fetus in a multifetal gestation. Obstet Gynecol 1997;90:606–10 [Evidence Grade: III].

[47] Bhide A, et al. Comparison of feticide carried out by cordocentesis versus cardiac puncture. Ultrasound Obstet Gynecol 2002;20:230–2 [Evidence Grade: III].

[48] Eddleman KA, et al. Selective termination of anomalous fetuses in multifetal pregnancies: two hundred cases at a single center. Am J Obstet Gynecol 2002;187:1168–72 [Evidence Grade: III].

[49] Elimian A, Verma U, Tejani N. Effect of causing fetal cardiac asystole on second-trimester abortion. Obstet Gynecol 1999;94:139–41 [Evidence Grade: III].

[50] Evans MI, et al. International, collaborative experience of 1789 patients having multifetal pregnancy reduction: a plateauing of risks and outcomes. J Soc Gynecol Investig 1996;3:23–6 [Evidence Grade: III].

[51] Evans MI, et al. Selective termination for structural, chromosomal, and mendelian anomalies: international experience. Am J Obstet Gynecol 1999;181:893–7 [Evidence Grade: III].

[52] Gill P, et al. Induction of fetal demise in advanced pregnancy terminations: report on a funic potassium chloride protocol. Fetal Diagn Ther 1994;9:278–82 [Evidence Grade: III].

[53] Hern WM. Selective termination for fetal anomaly/genetic disorder in twin pregnancy at 32+ menstrual weeks. Report of four cases. Fetal Diagn Ther 2004;19:292–5 [Evidence Grade: III].

[54] Isada NB, et al. Fetal intracardiac potassium chloride injection to avoid the hopeless resuscitation of an abnormal abortus: I. Clinical issues. Obstet Gynecol 1992;80:296–9 [Evidence Grade: III].

[55] Lipitz S, et al. Late selective termination of fetal abnormalities in twin pregnancies: a multicentre report. Br J Obstet Gynaecol 1996;103:1212–6 [Evidence Grade: III].

[56] Lynch L, et al. First-trimester transabdominal multifetal pregnancy reduction: a report of 85 cases. Obstet Gynecol 1990;75:735–8 [Evidence Grade: III].

[57] Pasquini L, Pontello V, Kumar S. Intracardiac injection of potassium chloride as method for feticide: experience from a single UK tertiary centre. BJOG 2008;115:528–31 [Evidence Grade: III].

[58] Senat MV, Fischer C, Ville Y. Funipuncture for feticide in late termination of pregnancy. Prenat Diagn 2002;22:354–6 [Evidence Grade: III].

[59] Silva LV, et al. Feticide does not modify duration of labor induction in cases of medical termination of pregnancy. Fetal Diagn Ther 2008;23:192–7 [Evidence Grade: III].

[60] Tabsh KM. A report of 131 cases of multifetal pregnancy reduction. Obstet Gynecol 1993;82:57–60 [Evidence Grade: III].

[61] Timor-Tritsch IE, et al. Multifetal pregnancy reduction by transvaginal puncture: evaluation of the technique used in 134 cases. Am J Obstet Gynecol 1993;168:799–804 [Evidence Grade: III].

[62] Wapner RJ, et al. Selective reduction of multifetal pregnancies. Lancet 1990;335:90–3 [Evidence Grade: III].

[63] Donnenfeld AE, et al. Fetal exsanguination following intrauterine angiographic assessment and selective termination of a hydrocephalic, monozygotic co-twin. Prenat Diagn 1989;9:301–8 [Evidence Grade: III].

[64] Donner C, de Maertelaer V, Rodesch F. Multifetal pregnancy reduction: comparison of obstetrical results with spontaneous twin gestations. Eur J Obstet Gynecol Reprod Biol 1992;44:181–4 [Evidence Grade: III].

[65] Drey EA, et al. Safety of intra-amniotic digoxin administration before late second-trimester abortion by dilation and evacuation. Am J Obstet Gynecol 2000;182:1063–6 [Evidence Grade: III].

[66] Hern WM. Laminaria, induced fetal demise and misoprostol in late abortion. Int J Gynaecol Obstet 2001;75:279–86 [Evidence Grade: III].

[67] Hern WM, et al. Outpatient abortion for fetal anomaly and fetal death from 15–34 menstrual weeks' gestation: techniques and clinical management. Obstet Gynecol 1993;81:301–6 [Evidence Grade: III].

[68] Jackson RA, et al. Digoxin to facilitate late second-trimester abortion: a randomized, masked, placebo-controlled trial. Obstet Gynecol 2001;97:471–6 [Evidence Grade: I].

[69] Molaei M, et al. Effectiveness and safety of digoxin to induce fetal demise prior to second-trimester abortion. Contraception 2008;77:223–5 [Evidence Grade: II-3].

[70] Davis G, Liu DT. Mid-trimester abortion. Lancet 1972;2:1026 [Evidence Grade: III].

[71] Bush MC, Eddleman KA. Multifetal pregnancy reduction and selective termination. Clin Perinatol 2003;30:623–41 [Evidence Grade: III].

[72] Evans MI, et al. Fetal reduction from twins to a singleton: a reasonable consideration? Obstet Gynecol 2004;104:102–9 [Evidence Grade: III].

[73] Fletcher JC, et al. Fetal intracardiac potassium chloride injection to avoid the hopeless resuscitation of an abnormal abortus: II. Ethical issues. Obstet Gynecol 1992;80:310–3 [Evidence Grade: III].

[74] Dommergues M, et al. Feticide during second- and third-trimester termination of pregnancy: opinions of health care professionals. Fetal Diagn Ther 2003;18:91–7 [Evidence Grade: III].

[75] Lee SJ, et al. Fetal pain: a systematic multidisciplinary review of the evidence. JAMA 2005;294:947–54 [Evidence Grade: III].

[76] Gonzales v. Carhart. 2007, 127 S.Ct.

[77] Partial-birth Abortion Ban Act, U.S.C. §1531, Editor. 2003. [Evidence Grade]

[78] Berkowitz RL, et al. The current status of multifetal pregnancy reduction. Am J Obstet Gynecol 1996;174:1265–72 [Evidence Grade: III].

[79] RCOG. Termination of Pregnancy for Fetal Abnormality in England, Wales and Scotland. London: RCOG Press; 1996 [Evidence Grade: III].

[80] RCOG. Further Issues Relating to Late Abortion, Fetal Viability and Registration of Births and Deaths. London: RCOG Press; 2001 [Evidence Grade: III].

[81] RCOG. The Care of Women Requesting Induced Abortion. Guidelines No. 7. London: RCOG; 2004 [Evidence Grade: III].

[82] Hammond C, Chasen S. Dilation and evacuation. Management of Unintended and Abnormal Pregnancy: Comprehensive Abortion Care. Hoboken: Wiley-Blackwell; 2009. p. 157–77. [Evidence Grade: III].

[83] Ilagan JG, et al. Pregnancy outcomes following bipolar umbilical cord cauterization for selective termination in complicated monochorionic multiple gestations. Fetal Diagn Ther 2008;23:153–8 [Evidence Grade: III].

[84] Lopoo JB, et al. Cord ultrasonic transection procedure for selective termination of a monochorionic twin. Fetal Diagn Ther 2000;15:177–9 [Evidence Grade: III].

[85] Middeldorp JM, et al. Twin-to-twin transfusion syndrome after 26 weeks of gestation: is there a role for fetoscopic laser surgery? BJOG 2007;114:694–8 [Evidence Grade: III].

[86] Middeldorp JM, et al. Fetoscopic laser surgery in 100 pregnancies with severe twin-to-twin transfusion syndrome in the Netherlands. Fetal Diagn Ther 2007;22:190–4 [Evidence Grade: III].

[87] Moise Jr KJ, et al. Radiofrequency ablation for selective reduction in the complicated monochorionic gestation. Am J Obstet Gynecol 2008;198:198.e1–5 [Evidence Grade: III].

[88] Porreco RP, Barton SM, Haverkamp AD. Occlusion of umbilical artery in acardiac, acephalic twin. Lancet 1991;337:326–7 [Evidence Grade: III].

[89] Quintero RA, et al. Brief report: umbilical-cord ligation of an acardiac twin by fetoscopy at 19 weeks of gestation. N Engl J Med 1994;330:469–71 [Evidence Grade: III].

[90] Quintero RA, et al. In utero percutaneous umbilical cord ligation in the management of complicated monochorionic multiple gestations. Ultrasound Obstet Gynecol 1996;8:16–22 [Evidence Grade: III].

[91] Robyr R, Yamamoto M, Ville Y. Selective feticide in complicated monochorionic twin pregnancies using ultrasound-guided bipolar cord coagulation. BJOG 2005;112:1344–8 [Evidence Grade: III].

[92] Bebbington MW, et al. Selective feticide in twin transfusion syndrome using ultrasound-guided insertion of thrombogenic coils. Fetal Diagn Ther 1995;10:32–6 [Evidence Grade: III].

[93] Gallot D, Laurichesse H, Lemery D. Selective feticide in monochorionic twin pregnancies by ultrasound-guided umbilical cord occlusion. Ultrasound Obstet Gynecol 2003;22:484–8 [Evidence Grade: III].

[94] Nicolini U, et al. Complicated monochorionic twin pregnancies: experience with bipolar cord coagulation. Am J Obstet Gynecol 2001;185:703–7 [Evidence Grade: III].

[95] Evans MI, et al. Efficacy of transabdominal multifetal pregnancy reduction: collaborative experience among the world's largest centers. Obstet Gynecol 1993;82:61–6 [Evidence Grade: III].

[96] Srisomboon J, Pongpisuttinun S. Efficacy of intracervicovaginal misoprostol in second-trimester pregnancy termination: a comparison between live and dead fetuses. J Obstet Gynaecol Res 1998;24:1–5 [Evidence Grade: II-2].

[97] Triolo O, et al. Therapeutic abortion intrauterine fetal death in the second trimester. Treatment with a gemeprost-sulprostone combination. Minerva Ginecol 1997;49:383–91 [Evidence Grade: II-3].

[98] Ruano R, et al. Second- and third-trimester therapeutic terminations of pregnancy in cases with complete placenta previa—does feticide decrease postdelivery maternal hemorrhage? Fetal Diagn Ther 2004;19:475–8 [Evidence Grade: II-3].

[99] Romero R, et al. Prolongation of a preterm pregnancy complicated by death of a single twin in utero and disseminated intravascular coagulation. Effects of treatment with heparin. N Engl J Med 1984;310:772–4 [Evidence Grade: III].

[100] Skelly H, et al. Consumptive coagulopathy following fetal death in a triplet pregnancy. Am J Obstet Gynecol 1982;142:595–6 [Evidence Grade: III].

[101] Lurie S, Feinstein M, Mamet Y. Disseminated intravascular coagulopathy in pregnancy: thorough comprehension of etiology and management reduces obstetricians' stress. Arch Gynecol Obstet 2000;263:126–30 [Evidence Grade: III].

[102] Kafrissen ME, et al. Coagulopathy and induced abortion methods: rates and relative risks. Am J Obstet Gynecol 1983;147:344–5 [Evidence Grade: III].

## Sources

The MEDLINE database was used to identify references published between 1955 and January 2009. The database was searched for the following terms: feticide, feticidal, abortion, termination, induced abortion, induction, demise, selective termination, pregnancy reduction and multifetal pregnancy reduction. Abstracts of all languages were included. The abstracts were reviewed and relevant articles obtained. Citations from these journals were reviewed, as well as contemporary textbooks.

## Authorship

These guidelines were prepared by Justin Diedrich, MD, and Eleanor Drey, MD, EdM, and reviewed and approved by the Board of Directors of the Society of Family Planning.

**Conflict of interest statement**

Justin Diedrich, MD reports no significant relationships with industry and Eleanor Drey, MD, EdM, is a trainer for Schering Plough. The Society of Family Planning receives no direct support from pharmaceutical companies or other industries.

**Intended audience**

This guideline has been developed under the auspices of the Society of Family Planning for its fellows and for any physicians and other clinicians who perform surgical abortions or who care for women undergoing these procedures. This guideline may be of interest to other professional groups that set practice standards for family planning services. The purpose of this document is to review the medical literature evaluating common means and goals of inducing fetal demise before pregnancy termination. This evidence-based review should guide clinicians, although it is not intended to dictate clinical care.