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Infectious Complications of Abortion

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This article reviews the infectious complications of abortion (both spontaneous and induced) and the management of this condition. The key points are: (1) Making abortion illegal does not reduce its incidence or prevalence; rather, it only makes abortions unsafe, increasing the likelihood of infectious complications. (2) Timely recognition of developing sepsis in the pregnant patient is critical. This requires constant vigilance and a high index of suspicion. (3) Rapid intravenous administration of broad-spectrum antibiotics targeted to the likely intrauterine source of infection as soon as sepsis is diagnosed is critical to prevent severe sepsis, septic shock, and multisystem organ failure. (4) The mainstay of treatment is prompt evacuation of any residual products of conception from within the uterine cavity under broad-spectrum antibiotic cover targeting the likely intrauterine source of infection. (5) Prompt engagement of specialists in both critical care and obstetrics-gynecology is necessary to optimize outcomes in patients with septic abortion.

Keywords. septic abortion; induced abortion; infectious complications of abortion; spontaneous abortion.

The recent Supreme Court ruling in the case of Dobbs v. Jackson Women's Health Organization held that there is no constitutionally protected right to abortion throughout the United States as a whole [1]. In overturning the constitutional precedent set by Roe v. Wade establishing that right nearly 50 years ago, the court referred such matters back to the individual states, many of which have already established Draconian anti-abortion laws that effectively outlaw most, if not all, abortions within their jurisdictions [2-4]. Some states are attempting to prevent women from traveling to other states to seek abortion services, to prohibit counseling women on why and how to seek abortion, and to outlaw websites that provide information on self-managed abortions. Some states are even establishing legal frameworks to promote citizen vigilantism against women who seek abortion and those who provide abortion services. Some states are going as far as establishing mechanisms that would allow individual citizens to sue clinicians who provide abortion care to residents in other states. Many states are attempting to restrict the delivery of Food and Drug Administration-approved medications that may be used to produce medical abortions in early pregnancy, and

women—are refusing to fill prescriptions for drugs that might be used to produce an abortion, even when those drugs have other, well-established, legitimate medical uses. A patchwork of state abortion laws is developing in the United States that will mean that while elective abortion is freely available in some states, it is beyond the reach of most women in many others.

Without question, these actions will increase abortion-related morbidity and mortality as desperate women confront

pharmacists—some fearful of incurring legal liability and oth-

ers who wish to impose their own moral views on pregnant

related morbidity and mortality as desperate women confront the prospect of forced birth under the diktats of right-wing legislatures in the states in which they happen to live [5-8]. Increasingly harsh and intrusive legal environments will hinder the provision of appropriate care to women requiring pregnancy terminations due to medical complications of pregnancy. At the same time, some women in desperate personal circumstances will attempt to terminate their unwanted pregnancies using unsafe methods. The World Health Organization defines an unsafe abortion as "a procedure for terminating an unwanted pregnancy either by persons lacking the necessary skill or in an environment lacking the minimum medical standards or both" [9]. Such abortions are certain to increase in the nowpunitive environment that is developing. Obstetricians, gynecologists, and other clinicians who provide reproductive health care are aghast at the prospect of the nation returning to the status quo ante of the early 20th century before Roe v. Wade, in which the wards of public hospitals were full of young women suffering from the serious, life-threatening complications that resulted from illegal, unsafe abortions [5–8]. Those days are now quite likely to return [8, 10–13]. Richard Schwarz's classic book, Septic Abortion, long out of print, is now sadly relevant again [14].

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This is not alarmist hysteria-mongering. There is abundant evidence that making abortions illegal does little to reduce their incidence and prevalence; rather, when abortion becomes illegal, abortion services are driven underground, abortion practices become unsafe, and there is a dramatic increase in unnecessary injury and death to women of reproductive age, many of whom will live with lingering health consequences into their postreproductive years. When abortion is legalized and becomes safe, maternal mortality drops [15]. A vivid 20th century historical example of the effects that harsh, restrictive anti-abortion policies have on women's health must be heeded.

Abortion in Romania: A Cautionary Tale

Nicolae Ceausescu became the dictator of Communist Romania in 1965. At the time of his ascension to power, Romania had a maternal mortality rate comparable to other East European countries [16]. In 1966, however, without advance warning, Ceausescu outlawed abortion in Romania except under extraordinarily strict conditions. He also banned the importation of contraceptives in order to increase the country's population as part of his master economic development program, and for the next 23 years he pursued "the world's most rigidly enforced pronatalist population policy," while also establishing the most repressive totalitarian government in Eastern Europe [16].

The Romanian government's intrusion into reproductive life was ubiquitous and breathtaking. Employed women had to undergo monthly gynecological examinations, and those who refused lost their access to medical and dental care as well as their pensions and social security. Factories had a required monthly birth quota, and the supervising factory physicians had their salaries reduced if these quotas were not met. Unmarried individuals over age 25 were subjected to a special 10% surtax. Taxes were also increased for childless couples who had been married for over 2 years unless they could document a medical reason for their lack of fertility. A special police unit was established to investigate alleged illegal abortions, and agents were placed in every maternity ward and obstetrical and gynecological clinic. Self-induced abortion became punishable by a prison term of up to 2 years. Physicians convicted of performing illegal abortions could be imprisoned for up to 12 years, with loss of their medical licenses [16].

Initially, these policies led to a brief upturn in births, but the birth rate soon fell to previous levels. At the same time, maternal mortality skyrocketed as women sought to terminate unwanted pregnancies by any means possible. Surveys confirmed that three-quarters of Romanians wanted families with only 1 or 2 children. Between 1981 and 1989, maternal mortality doubled, and Romania had the highest maternal mortality ratio in Europe at 159 maternal deaths per 100 000 live

births, roughly 20 times higher than the US maternal mortality ratio during the same time period [17]. It was estimated that 87% of these maternal deaths were due to unsafe, illegal abortions. During Ceausescu's rule, at least 10 000 women died from abortion complications [15]. It was also estimated that 20% of Romania's women had been rendered infertile from infectious and other complications of these unsafe practices [15, 16].

In addition to the toll on female reproductive health, staggering damage was inflicted upon the nation's children. The infant mortality rate in 1989 was 26.9 deaths per 1000 live births and 25.3 deaths per 1000 infants within the first 6 months of life. Thousands of children were abandoned by mothers who could not care for them, leaving them living in truly appalling conditions as wards of the state. It was estimated that only 2% of children in Romanian orphanages were truly "orphans": The vast majority had been abandoned at birth by families who either did not want them or who could not afford to care for them. As many as 200 000 "orphans" were living in horribly substandard institutions when the regime finally fell [18].

In December 1989, increasing popular discontent led to a revolution that overthrew the Ceausescu government. Ceausescu and his wife, Elena, attempted to flee, but were captured and executed on Christmas Day, 1989. The next day, the new provisional government overturned the prohibitions on the importation of contraceptives and made abortion legal again as of January 1, 1990. Almost immediately clinical facilities were overrun with women seeking contraception and abortion services. Over 1 million safe abortions were performed in Romania in 1990, triple the number of live births. At the same time, maternal mortality dropped by 50%, decreasing to 83 deaths per 100 000 live births in 1990 [16, 18]. By 2017, maternal mortality in Romania was 19 deaths per 100 000 live births —the same as in the United States [19]. (Both countries, however, continue to have maternal mortality 5 times higher than Sweden, at 4 maternal deaths per 100 000 live births [19].) Almost every country that has legalized abortions has seen similar trends in falling maternal mortality, as also happened in the United States after the initial Roe decision [15, 16, 18, 20]. As Stubblefield and Grimes wrote nearly 30 years ago, "The most important effect of the legalization of abortion on public health in the United States was the near elimination of deaths from illegal abortion" [20]. The United States now seems likely to reverse this trend.

Complications of Unsafe Abortion

Worldwide, ~6 out of 10 unintended pregnancies are terminated by induced abortion, 45% of which are unsafe and 97% of which take place in low-resource, developing nations [9, 21–24]. Estimates suggest that nearly 50 000 women die each year from complications of unsafe abortion, primarily as the result of

hemorrhage, infection, or both, and this accounts for 8%–13% of total world maternal deaths [23, 24]. Treating complications of unsafe abortions also imposes huge social and economic burdens on the health care systems of countries where abortions are illegal and generally unsafe [24–27].

When performed in safe, medically supervised environments, first trimester abortion is extremely safe compared with the risks of delivering a pregnancy at term. In the United States between 1998 and 2005, the pregnancy-associated mortality rate for women who delivered live neonates was 8.8 per 100 000 live births, but the mortality rate for induced abortions was only 0.6 deaths per 100 000 abortions. The risk of death from child-birth is 14 times higher than that associated with safe abortion, and the rates of morbidity are similarly greatly increased after childbirth at term [28]. The number of unsafe abortions in the United States will certainly increase as a result of the changes currently taking place in state abortion laws [2–8].

This means that practitioners of internal medicine and specialists in infectious diseases increasingly will be consulted to help manage the infectious complications of abortion, both spontaneous and induced. Because the most important management of septic abortion is surgical—prompt evacuation of the infected products of conception under broad-spectrum antibiotic coverage—infectious disease specialists will not be the primary clinicians managing such cases, but they will be called upon increasingly to help manage the most difficult cases of severe sepsis and septic shock. This review provides background information needed for such care.

The relevant obstetrical terminology is given in Table 1.

Although sepsis can complicate pregnancy at any point in gestation, the developing medico-legal environment in the United States suggests that there will be an uptick in 2 particular types of cases.

The first group of cases will likely be those in which women who are desperate to end an unwanted pregnancy and who are denied access to safe, legal abortion procedures as the result of restrictive abortion laws will resort to unsafe abortions on their own or at the hands of unqualified practitioners. The more invasive the abortion technique used, the more likely it is to disrupt the pregnancy, but also the more likely it is to cause dangerous complications, such as perforation of adjacent organs, hemorrhage, and sepsis—sometimes all together. The greater the gestational age of the pregnancy when such procedures are performed, the greater the likelihood of serious complications.

A wide variety of unsafe methods have been used in attempts to procure abortions [29]. These include the insertion of unclean objects such as coat hangers or knitting needles into the cervix and uterus; ingestion of toxic substances such as bleach, turpentine, or quinine or injecting such substances into the uterine cavity; physical violence to the abdomen with the intention of disrupting the placenta; and the placement of caustic

Table 1. Terminology Related to Abortion

- Abortion—Disruption of an embryo or fetus implanted in the uterus.
 Abortions may be spontaneous or induced. A pregnancy does not begin until after the implantation of the blastocyst, ~7 d after fertilization.
- Induced abortion—An abortion that is deliberately caused for elective or therapeutic medical reasons.
- Spontaneous abortion—An abortion that is not induced but occurs without
 obvious external cause. Most spontaneous abortions—especially early in
 pregnancy—are the result of lethal genetic defects in the developing
 embryo. The death of the embryo or fetus before 20 wk of gestation is
 usually classified as a spontaneous abortion, whereas after 20 wk of
 gestation it is usually classified as a stillbirth or intrauterine fetal death.
 Induced abortions are referred to as abortions at all gestational ages.
- Threatened abortion Vaginal bleeding occurring before 20 wk of gestation without dilatation of the cervix, indicating that a spontaneous abortion may be about to occur.
- Inevitable abortion Vaginal bleeding occurring before 20 wk of gestation with rupture of the amniotic membranes and/or dilatation of the cervix.
- Incomplete abortion—An abortion in which some, but not all, of the
 products of conception (including placenta and amniotic membranes) remain
 in the uterus. Women with incomplete abortions are at increased risk of
 infection or hemorrhage if the products of conception are not removed
 promptly.
- Complete abortion An abortion in which all of the products of conception have been expelled.
- Missed abortion—A pregnancy in which the death of the embryo or fetus
 has occurred but which has not yet caused bleeding. In early pregnancy, this
 is sometimes also referred to as a blighted ovum or an anembryonic
 pregnancy. The term intrauterine fetal death is also used, depending on the
 qestational age.
- Septic abortion—Infection of the uterus and its contents before, during, or after an abortion (either spontaneous or induced). In such cases, systemic sepsis may develop explosively, progressing rapidly to septic shock. If not treated promptly and effectively, a fatal outcome may result.
- Chorioamnionitis—Infection of the amniotic fluid and fetal membranes (chorion and amnion), usually arising from an ascending polymicrobial infection from the lower genital tract, especially when the membranes have ruptured. Subclinical chorioamnionitis is often suspected as a cause of premature labor or spontaneous abortion.

chemicals such as potassium permanganate into the vagina, which, although ineffective in producing abortion, nonetheless can cause severe chemical burns that may erode through the vagina into the rectum [29]. Injection of substances such as liquid soap or disinfectant into the uterine cavity are particularly dangerous and may lead to extensive uterine necrosis [30]. Infectious complications may occur with any and all such unsafe techniques and will vary according to the characteristics of particular cases.

The second group of cases involves women with previable or periviable fetuses who develop preterm, prelabor rupture of the amniotic membranes. Many of these cases will occur as tragic complications of planned, wanted pregnancies, but the women involved may be denied termination of their nonviable pregnancies because of anti-abortion laws that prohibit any intervention in the presence of a fetal heartbeat. This has been the practice in Catholic hospitals in the United States for many years (largely unknown to the general public), but with the increasing instantiation of Roman Catholic theology into the legal system by aggressive conservative legislatures, this will be an increasing problem for clinicians working in non-Catholic

hospitals who are now subject to these new legal restrictions [31–33].

Once the amniotic membranes have ruptured, the risk of chorioamnionitis, sepsis, and septic shock increases with increasing duration of rupture of the membranes [34, 35]. The internationally recognized standard of care is prompt intervention with broad-spectrum antibiotic coverage and removal of the products of conception to prevent infectious complications [11, 20, 22, 36–42]. Delay in such cases can be fatal. As Grimes, Cates, and Selik noted in 1981,

Incomplete abortion is a powerful risk factor for death from infection. The death-to-case ratio for women with incomplete abortion is over 50 times higher than that for those who have adequate evacuation of the products of conception; the comparative mortality ratio is approximately 18 times higher. Retained tissue provides a nidus for the development of local infection, which then leads to generalized sepsis. [43]

Pathophysiological Considerations in Septic Abortion

It is important to understand the underlying physiology that makes septic abortion such a dangerous complication of pregnancy.

Pregnancy begins with the implantation of the blastocyst into the endometrial lining of the uterus. The placenta develops at the point of implantation, becoming the primary interface with the woman's body and the seat of the fetal-maternal communication system that regulates pregnancy. The embryo/fetus develops inside a membranous sac within the uterine cavity. This membranous sac is full of amniotic fluid, which provides the liquid environment necessary for fetal development but which is also a potentially nutritious culture medium for bacterial growth. At term, the amniotic fluid volume around the fetus is ~800 mL [44, 45].

The fetal and maternal circulatory systems are separate and normally do not intermix. The transfer of nutrients from the maternal to the fetal side and the transfer of waste matter from the fetal to the maternal side take place across the placenta. There are roughly 15 square meters of surface area through which these interchanges take place [46]. Effective gas exchange and the transfer of nutrient and waste matter across the placenta are dependent upon the enormous volume of blood flow going to the uterus and placenta. The nonpregnant uterus receives roughly 2% of cardiac output, but in pregnancy uterine blood flow increases almost 10-fold, with nearly 20% of the cardiac output flowing through the uterus and placenta at term [46]. This blood flows from uterine spiral arterioles into lacunar spaces beneath the placenta that bathe the placental villi across which nutrient/waste exchanges take place before the blood drains away through the engorged uterine venous system [47].

The infectious agents that produce septic abortion arise from the polymicrobial environment of the vagina and lower genital tract, reaching the uterine cavity through ascending infection [16, 29, 41, 42]. Devitalized tissue is often present in the uterine cavity in septic abortions, allowing anaerobic bacteria to flourish. Because of the extreme vascularity of the uterus and the placental circulation, septic abortion results in very high rates of bacteremia (up to 60% of cases). When bacteria gain access to the maternal bloodstream, they can spread rapidly to every organ system in the body [10]. The confluence of these physiological and microbiological factors explains why infection of the amniotic fluid and membranes (chorioamnionitis) can explode in such a fulminant way, progressing from chorioamnionitis to sepsis, to severe sepsis, and to potentially fatal toxic shock in only a few hours.

Many of the bacteria found in septic abortions produce potent endotoxins that can result in damage to distant organ systems, affecting the pulmonary, renal, cardiac, and coagulation systems [40]. One study of 63 patients admitted to an intensive care unit with septic abortions found that 73% developed acute renal failure, 31% developed disseminated intravascular coagulopathy, 13% developed acute lung injury or acute respiratory distress syndrome, 32% developed septic shock, and 48% developed multiple organ failure [48].

This is why every modern review emphasizes 4 key actions in the diagnosis and management of septic abortion: (1) timely recognition of developing sepsis (which requires constant vigilance and a high index of suspicion); (2) rapid intravenous administration of broad-spectrum antibiotics targeted to the potential/likely intrauterine source of infection as soon as sepsis is diagnosed; (3) prompt evacuation of any residual products of conception from within the uterine cavity under antibiotic cover; and (4) prompt involvement of clinicians experienced in critical care in the management of patients with septic abortion [7–43]. An overview of the steps that should be taken in a case of septic abortion is given in Table 2.

Prompt diagnosis, speedy intervention, and rapid escalation of care are of critical importance. One cohort study of admissions of pregnant women with sepsis to an obstetric critical care unit found that in nearly 60% of those who died, there had been a delay of more than an hour in initiating antibiotic therapy after the diagnosis of sepsis had been made. The need for vasopressors to combat septic shock carried with it an odds ratio of 26.4 for dying [49]. In another study of 63 women with septic abortions admitted to an intensive care unit, 92% of those who died had developed septic shock [48].

Most women who die from septic abortions are otherwise healthy, without significant underlying medical comorbidities. The fact that the overall population of pregnant women is young and generally healthy can lull the unwary clinician into complacency until disaster suddenly intrudes in the form of severe sepsis and septic shock. The Society of Maternal-Fetal Medicine

Table 2. Steps in Clinical Management of Septic Abortion (Based on [10, 20, 25–32])

- Confirm pregnancy and document gestational age.
- Document any previous or attempted uterine instrumentation, length and time of vaginal bleeding, history suspicious for rupture of membranes, length of fever, and any other symptoms.
- Features suggestive of possible sepsis include fever and/or chills, diarrhea and/or vomiting (possible toxic shock), rash (associated with Streptococcus infection), abdominal/pelvic pain/tenderness, foul-smelling vaginal discharge, productive cough, urinary tract symptoms.
- Evaluate uterine cavity by ultrasound for retained products of conception.
- Vital signs: temperature, pulse, blood pressure, respiration, oxygen saturation.
- · Physical examination, to include:
 - o Vaginal speculum examination to look for trauma to the vaginal/cervix/ uterus, foul-smelling discharge, presence of foreign bodies;
 - Exploration of the cervix/uterus with ring forceps to look for retained products of conception;
 - Cervical and uterine cultures, both aerobic and anaerobic, including assessment of sexually transmitted infections such as gonorrhea, chlamydia, and trichomoniasis;
 - Bimanual pelvic examination (including digital rectal examination), with special attention to the presence of cervical motion or uterine tenderness, presence of adnexal masses;
- o Abdominal examination for direct and rebound tenderness.
- Blood and urine cultures. The most common serious infection in pregnant
 patients is acute pyelonephritis, which may present similarly to septic
 abortion and which can also progress rapidly to urosepsis, acute respiratory
 distress syndrome, and septic shock.
- Laboratory studies, to include complete blood count, serum lactate, coagulation studies, renal function tests, blood type, and screen for possible transfusion (Rh-factor is especially important in pregnancy).
- Radiographic studies including abdominal flat plate and/or CT scan to look for free air in the abdomen, which may indicate organ perforation or gas in the myometrium, suggesting the presence of clostridial infection.
- Intravenous fluids and initial broad-spectrum antibiotics (typically ampicillin and gentamicin with clindamycin or metronidazole). Antibiotics should be administered promptly, intravenously, and in advance of uterine evacuation.
- Antibiotics can be changed later depending on clinical responsiveness and the results of culture and sensitivity testing, but it is essential to provide prompt initial broad-spectrum antibiotic coverage as soon as sepsis is suspected.
- Uterine curettage to remove retained products of conception. Suction
 curettage with anesthesia is usually preferred, but manual vacuum
 aspiration may be done on the ward if the patient is clinically stable. This is
 especially useful in low-resource settings. Due to the risk of bacteremia
 during curettage, broad-spectrum intravenous antibiotics must be on board
 before the procedure. Sharp curettage may heighten the risk of bacteremia
 and should be avoided if possible.
- Pathological examination of curettings with culture of any products of conception.
- Advanced intensive medical treatment in the presence of septic shock, including vasopressors, central venous monitoring, and ventilator support as clinically indicated. Patients with septic abortions may develop multisystem organ failure including acute respiratory distress syndrome, disseminated intravascular coagulopathy, acute renal failure, and septic cardiomyopathy that require aggressive management in a well-equipped intensive care unit.

Abbreviation: CT, computed tomography.

emphasized this point in their 2019 guidelines on sepsis in pregnancy and the puerperium, writing,

Among women who died from sepsis, the majority had a delay in care and a delay in escalation of care. Most were afebrile, possibly delaying the recognition of the presence of sepsis. Even after the diagnosis, 73% of women were started on antibiotics that provided inadequate coverage.... The early involvement of consultant with expertise in infectious disease may expedite treatment of sepsis and help improve outcomes. [41]

Large-scale maternal mortality reviews from the United Kingdom have reached similar conclusions [36–38].

Microbial Pathogens in Septic Abortions

As noted previously, most bacteria involved in septic abortions are found in the normal vaginal flora, which ascend to cause infections of the uterus and upper genital tract, if favorable conditions for growth are present [16, 29, 36–42]. Anaerobic bacteria are commonly present. Cervical and uterine cultures, cultures of the placenta and of any evacuated products of conception, and blood cultures should all be part of the microbiological investigation of such cases. It is also particularly important to obtain urine cultures in these cases, as acute pyelonephritis is the most common serious infectious complication of pregnancy. Acute pyelonephritis may present similarly to septic abortion and may also progress rapidly to urosepsis and multisystem organ involvement [50–52].

Cultures are especially important in identifying bacteria that may produce endotoxins, such as *Clostridum* spp., group A *Streptococcus* (the pathogen of classic puerperal sepsis), *Staphylococcus aureus* (associated with toxic shock syndrome), and various toxin-producing strains of *E. coli*, but *it is critically important to start patients on broad-spectrum antibiotics that cover these infections as soon as infection is suspected. Delay in starting intravenous antibiotics may be fatal. When culture results become available, the antibiotic focus may be narrowed if indicated [41].*

The initial choice of antibiotics is empirical but must be broad-spectrum [49]. The 2 most commonly used regimens employ triple antibiotic therapy to attain broad-spectrum microbial coverage: ampicillin 2 g intravenously (IV) every 4 hours, gentamicin 5 mg/kg/d IV, plus clindamycin 900 mg IV every 8 hours. A reasonable alternative to clindamycin is metronidazole 500 mg IV every 8 hours. Specific cases may require case-specific adjustments. Once patients have been afebrile and asymptomatic on intravenous antibiotics, they can be discontinued. Although some authors prefer to place patients on oral antibiotics to complete a 10-day course of treatment, there is evidence that this is not necessary [40, 42, 53].

Role of Surgery in Septic Abortion

As noted previously, prompt evacuation of the infected uterine contents under broad-spectrum antibiotic therapy is the mainstay in the treatment of septic abortion [12, 16, 29]. This can usually be done with suction curettage or a blunt curette; however, if patients do not respond promptly to uterine evacuation

and intravenous antibiotics, more aggressive surgical intervention may be required. Exploratory laparotomy is indicated if there is evidence of organ perforation and/or tissue necrosis in a septic abortion. The presence of gas in the myometrium on radiologic studies is strongly suggestive of anaerobic *Clostridium* infection, which frequently requires hysterectomy to remove the nidus of infected tissue. Prompt surgical intervention, including hysterectomy, may be lifesaving, whereas delay may be fatal [14, 40, 53–59].

Case Study: The Death of Savita Halappanavar From Septic Abortion

The unnecessary death of Savita Halappanavar from a septic abortion in Ireland in 2012 outraged the world and was an important factor in the subsequent amendment of the Irish constitution several years later to permit abortions [60–63]. The case is instructive because the factors that led to Savita's untimely death are now likely to become increasingly prevalent in the United States as abortion access becomes much more restricted. Because individual states have now outlawed abortions irrespective of the surrounding circumstances, even in pregnancies occurring in girls as young as 10 who have been raped or under circumstances where a pregnancy has occurred as the result of rape or in which the pregnant woman's life is in jeopardy, clinicians are increasingly uncertain as to whether they will face prosecution for intervening, even when it is obvious what "the right thing to do" clinically is in such cases.

In 2012 when Savita Halappanavar's death occurred, Irish law recognized the "equal right to life" of both mother and fetus, except under extraordinary (and previously unspecified) circumstances. The result was that most doctors felt that they could not intervene in a complicated pregnancy if a fetal heartbeat was present, unless there was a clear and immediate danger to the life of the pregnant woman. The criteria to determine whether such a danger was present had never been clarified, leading to much medico-legal confusion.

Savita Halappanavar was a 31-year-old married dentist from India living in Ireland with her husband, when she became pregnant in the summer of 2012 with a much-wanted pregnancy [62]. She registered for prenatal care and had an unremarkable pregnancy until 17 weeks, when she presented to the gynecology ward at University Hospital Galway on October 21, 2012, with complaints of back pain. Initially she was diagnosed with sciatica (without undergoing a pelvic examination) and sent home with analgesia and an appointment for physical therapy. She returned several hours later, upset and crying, in worsening pain. A pelvic examination revealed ballooning amniotic membranes, bulging almost to the vaginal introitus. She was admitted with a diagnosis of inevitable abortion. A fetal heartbeat was present. She was afebrile at admission but had an elevated white blood count of 16 900 per microliter. The potential significance of this laboratory finding was ignored by the admitting team.

Because intra-amniotic infection is a common cause of premature labor, it is likely that Savita was already infected at this time. She was admitted to the hospital for observation and expectant management. Early the following morning, she had spontaneous rupture of the membranes. In this scenario, with a previable 17-week fetus and ruptured membranes, the risk of maternal infection is high, and the risk accelerates progressively with each hour the patient is not delivered. The inquest into Savita's death confirmed that international best obstetric practice in such cases mandates prompt delivery of the previable fetus to preserve the woman's life, irrespective of the presence of a fetal heartbeat [63, 64].

In light of these facts, Savita and her husband both requested that her pregnancy be terminated expeditiously, but this was denied them because a fetal heartbeat was still present. They were told that such a course of action was not possible because "Ireland is a Catholic country," and "theoretical" risk was not enough to justify the procedure. The attending gynecologist told them that because "we can't predict who is going to get an infection," no intervention was possible [63]. They protested that they were both practicing Hindus from India and that in their circumstances they regarded termination of the pregnancy as standard medical care, especially considering that the fetus was not viable. Their requests were ignored.

Savita's clinical care over the next few days was substandard, marred by poor communication among clinicians, lack of follow-up with appropriate laboratory studies, and inattention to her deteriorating clinical condition. The inquest into her subsequent death noted that there "was an apparent overemphasis on the need not to intervene until the fetal heart stopped altogether with an under-emphasis on the need to focus appropriate attention on monitoring for and managing the risk of infection and sepsis in the mother" [63]. Because she was a healthy, 31-year-old woman, the risk of her developing fulminant sepsis, which might speedily turn into fatal septic shock, was discounted, if not ignored, because of the persistent presence of a fetal heartbeat and medico-legal fears about performing an abortion.

Early in the morning of Wednesday, October 24, the patient complained of being cold. When the midwife gave Savita a blanket, she noticed that her teeth were chattering, even though her temperature was normal. A few hours later, she vomited and spiked a fever to 39.6°C (103.3°F). She was now tachycardic with a pulse of 160 beats per minute, a blood pressure of 94/55 mmHg, a foul-smelling vaginal discharge, and diffuse abdominal tenderness. Blood cultures were obtained, a serum lactate was drawn (but subsequently lost), and she was started on intravenous amoxicillin/clavulanate. Somewhat later, metronidazole was added.

A fetal heartbeat was still present at noon, but Savita's condition was deteriorating. Her blood pressure was 76/46 mmHG. She was having trouble breathing, complained of

diffuse myalgias, and was noted by the midwives to be "very unwell." Her antibiotics were changed to piperacillin/tazobactam and gentamicin after consulting with the hospital microbiologist. Metronidazole was continued.

Arrangements were made to move her to the high dependency unit (one tier below intensive care), but a bed was not readily available. She was taken to the gynecology operating room, where a central venous catheter was placed. While in the operating room, she spontaneously delivered a stillborn female fetus along with the placenta, which appeared to be intact.

From this point on, Savita Halappanavar received excellent medical care, but it was too little, too late. She continued to deteriorate and was finally admitted to the intensive care unit with a diagnosis of septic shock. There she was intubated and placed on a ventilator. Vasopressors were needed to maintain her blood pressure. A trans-esophageal echocardiogram showed a dilated right ventricle, severe triscupid regurgitation, a hypokinetic left ventricle, and a possible pulmonary embolism. She developed disseminated intravascular coagulopathy and was heparinized. Her blood cultures, which had earlier shown the presence of a gram-negative bacillus, grew out extended-spectrum beta-lactamase-producing *E. coli*.

Savita Halappanavar had a cardiac arrest at 12:45 AM on October 28, 2012, and was pronounced dead after failed resuscitation at 1:09 AM that morning.

A postmortem examination on October 30 and the subsequent coroner's inquest concluded that the cause of her death was "fulminant septic shock from *E. coli* bacteremia, ascending genital tract sepsis, and miscarriage at 17 weeks' gestation associated with chorioamnionitis" [63]. There were no comorbidities.

Two extensive investigations into these events by the Irish government determined that there had been gross clinical mismanagement of the case from the beginning, which led to inadequate medical treatment, insufficient monitoring of the patient's clinical status, and inappropriate delays in treatment, all stemming from an excessive concern about the persistent presence of a fetal heartbeat [63, 64]. Similar cases are now likely to occur in the United States [65].

As noted earlier, the kinds of restrictive and medically inappropriate policies that led to the death of Savita Halappanavar are the norm in Roman Catholic hospitals and health systems in the United States and have been so for years, even though the general public is largely unaware of this fact [31–33]. What is happening now is that policies based on Catholic theological presuppositions are being forced upon all hospitals in the states in which these laws are being passed, including secular hospitals and Jewish hospitals, which operate under very different ethical assumptions. These laws are a direct violation of the religious freedoms of Jews and others who view the status of the fetus differently from anti-abortion radicals. As Rabbi Israel Margolies wrote over 50 years ago,

Until a child is born into the world, it is literally part of its mother's body, and belongs to her and her mate. It does not belong to society at all, nor has it been accepted into any faith. Its existence is entirely and exclusively the business and concern of its parents, whether they are married or not. It is men and women who alone must decide whether or not they wish their union to lead to the birth of a child, not the synagogue or chuch, and certainly not the state. [66]

We must do everything possible to prevent the intrusion of these radical theological beliefs into the practice of medicine. The recent constitutional referendum in Kansas, which resoundingly *protected* the right to abortion access, demonstrates that the loudest, most radical voices against abortion rights are not representative of the opinions of the majority of the population [67].

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Patient details of the clinical case study are in the public domain due to the Irish Government's investigation of the case and the publication of the inquest documents, cited in the references.

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Patient consent. As this is a review article, no patient consent was required. As noted in the article and in the references, all of the information concerning the case of Savita Halappanavar is widely accessible in the public record, and no consent was required to access this information. As a review article, institutional approval from an Institutional Review Board was not required.

References

- Supreme Court of the United States. Dobbs, State Health Department Officer of the Mississippi Department of Health et al. v. Jackson Women's Health Organization et al., Certiorari to the United States Court of Appeals for the Fifth Circuit. No. 19–1392. Available at: https://www.supremecourt.gov/ opinions/21pdf/19-1392_6j37.pdf. Accessed September 8, 2022.
- Jimenez L. 60 days after Dobbs: state legal developments on abortion. Brennan Center for Justice, New York University. Available at: https://www. brennancenter.org/our-work/research-reports/60-days-after-dobbs-state-legal-developments-abortion. Accessed September 8, 2022.
- New York Times. Tracking states where abortion is now banned. New York Times.
 October 13, 2022. Available at: https://www.nytimes.com/interactive/2022/us/abortion-laws-roe-v-wade.html. Accessed September 8, 2022.
- Guttmacher Institute. State legistlation tracker: major developments in sexual and reproductive health. Available at: https://www.guttmacher.org/state-policy. Accessed September 8, 2022.
- Stevenson AJ. The pregnancy-related mortality impact of a total abortion ban in the United States: a research note on increased deaths due to remaining pregnant. Demography 2021; 58:2019–28.
- Tolentino J. We're not going back to the time before Roe. We're going somewhere
 worse. New Yorker. July 4, 2022. Available at: https://www.newyorker.com/
 magazine/2022/07/04/we-are-not-going-back-to-the-time-before-roe-we-aregoing-somewhere-worse. Accessed September 8, 2022.
- Gold RB. Lessons from before Roe: will past be prologue? Guttmacher Policy Rev
 2002; 6:1. Available at: https://www.guttmacher.org/gpr/2003/03/lessons-roe-will-past-be-prologue. Accessed September 8, 2022.
- Kaufman E. I'm a doctor who worked an 'infected abortion' ward in 1960. I worry that they're coming back. Los Angeles Times. June 24, 2022. Available at: https://

- www.latimes.com/opinion/letters-to-the-editor/story/2022-06-24/doctor-who-worked-an-infected-abortion-ward-in-1960-roe-vs-wade. Accessed September 8, 2022.
- World Health Organization. Safe Abortion: Technical and Policy Guidance for Heath Systems. World Health Organization; 2003.
- Studdiford WE, Douglas GW. Placental bacteremia: a significant finding in septic abortion accompanied by vascular collapse. Am J Obstet Gynecol 1956; 71: 842–58
- Tenney B, Little AB, Wamsteker EM. Septic abortion. New Engl J Med 1957; 257: 1022–4.
- Reid DE. Assessment and management of the seriously ill patient following abortion. JAMA 1967; 199:141–8.
- Minkoff H, Gibbs RS. Preparing for a post-Roe world. Am J Obstet Gynecol 2019; 220:249:e1-3.
- 14. Schwarz RH. Septic Abortion. J.B. Lippincott; 1968.
- Benson J, Andersen K, Samandari G. Reduction in abortion-related mortality following policy reform: evidence from Romania, South Africa and Bangladesh. Reprod Health 2011; 8:39.
- Hord C, David HP, Donnay F, Wolf M. Reproductive health in Romania: reversing the ceausescu legacy. Stud Fam Plann 1991; 22:231–240.5.
- Centers for Disease Control and Prevention. Maternal mortalilty—United States, 1982–1996. MMWR Morb Mortal Wkly Rep 1998; 47:705–7.
- Stephenson P, Wagner M, Badea M, Serbaescu F. Commentary: the public health consequences of restricted induced abortion—lessons from Romania. Am J Pub Health 1992; 82:1328–31.
- WHO, UNICEF, UNFPA, World Bank Group, and the United Nations Population Division. Trends in Maternal Mortality: 2000 to 2017. World Health Organization; 2019.
- 20. Stubblefield PG, Grimes DA. Septic abortion. New Engl J Med 1994; 331:310-4.
- Ganatra B, Gerdts C, Rossier C, et al. Global, regional, and subregional classification of abortions by safety, 2010–2014: estimates from a Bayesian hierarchical model. Lancet 2017; 390:2372–81.
- World Health Organization. Abortion Fact Sheet. World Health Organization;
 2021.
- Say L, Chou D, Gemmeill A, et al. Global causes of maternal death: a WHO systematic analysis. Lancet Glob Health 2014; 2:e323–33.
- Ahman E, Shaw IH. New estimates and trends regarding unsafe abortion mortality. Int J Gynecol Obstet 2011; 115:121–6.
- Singh S. Hospital admissions resulting from unsafe abortion: estimates from 13 developing countries. Lancet 2006; 368:1887–92.
- Vlassoff M, Walker D, Shearer J, Newlands D, Singh S. Estimates of health care system costs of unsafe abortion in Africa and Latin America. Int Perspect Sexual Reprod Health 2009; 35:114–21.
- Levin C, Grossman D, Berdichevsky K, et al. Exploring the costs and economic consequences of unsafe abortion in Mexico City before legalization. Reprod Health Matters 2009; 17:120–32.
- Raymond EG, Grimes DA. The comparative safety of legal induced abortion and childbirth in the United States. Obstet Gynecol 2012; 119:215–9.
- Grimes DA, Benson J, Singh S, et al. Sexual and reproductive health 4: unsafe abortion—the preventable pandemic. Lancet 2006; 368:1908–19.
- Janovski NA, Weiner L, Ober WB. Soap intoxication following criminal abortion. NY State J Med 1963: 63:1463–87.
- Freedman LR, Landy U, Steinauer J. Where there's A heartbeat: miscarriage mismanagement in Catholic-owned hospitals. Am J Pub Health 2008; 98:1774–8.
- 32. Raghavan R. A piece of my mind: a question of faith. JAMA **2007**; 297:1412.
- Sawicki NN. Religious hospitals and patient choice. Hastings Center Report 2016;
 46:8–9.
- Sklar A, Sheeder J, Davis AR, Wilson C, Teal SB. Maternal morbidity after preterm premature rupture of membranes at<24 weeks' gestation. Am J Obstet Gynecol 2022; 226:e1-11.
- Nambiar A, Patel S, Santiago-Munoz P, Spong CY, Nelson DB. Maternal morbidity and fetal outcomes among pregnant women at 22 weeks' gestation or less with complications in two Texas hospitals after legislation on abortion. Am J Obstet Gynecol. 2022; 227(4):648–650.e1.
- 36. Harper A. Genital tract sepsis. In: Lewis G, ed. Saving Mothers' Lives: Reviewing Deaths to Make Motherhood Safer, 2003–2005. The Seventh Report of the Confidential Enquiries into Maternal Deaths in the United Kingdom. Confidential Enquiry into Maternal and Child Health; 2007.
- 37. Knight M, Tuffnell D, Kurinczuk JJ; on behalf of the Sepsis Chapter-Writing Group. Message for the prevention and treatment of sepsis. In: Knight M, Tuffnell D, Shakespare J, Kenyon S, Kurinczuk JJ, eds. Saving Lives, Improving Mothers' Care: Lessons Learned to Inform Maternity Care From the UK and Ireland Confidential Enquiries Into Maternal Deaths and Morbidity 2013–2015. National Perinatal Epidemiology Unit, University of Oxford; 2017; 59–66.

- Royal College of Obstetricians and Gynaecologists. Green-Top Guideline No. 64a, Bacterial Sepsis in Pregnancy. Royal College of Obstetricians and Gynaecologists;
 2012
- 39. Morgan J, Roberts S. Maternal sepsis. Obstet Gynecol Clin NA 2013; 40:69-87.
- 40. Eschenbach DA. Treating spontaneous and induced septic abortions. Obstet Gynecol 2015; 125:1042–8.
- Plante LA, Pacheco LD, Louis JM. Society for Maternal-Fetal Medicine consult series #47: sepsis during pregnancy and the puerperium. Am J Obstet Gynecol 2019; 220:87–10
- Prager S, Micks E, Dalton V. Septic abortion: clinical presentation and management. UpToDate. October 19. 2022.
- Grimes DA, Cates W, Selik RM. Fatal septic abortion in the United States, 1975– 1977. Obstet Gynecol 1981; 57:739–44.
- Ross MG, Beall MH. Amniotic fluid dynamics. In: Resnick R, Lockwood CJ, Moore TR, Green MF, Copel JA, Silver RM, eds. Creasy and Resnick's Maternal-Fetal Medicine. 8th ed. Elsevier. 2019; 62–7.
- Moore KL, Persaud TVN. The placenta and fetal membranes. In: The developing human: clinically oriented embryology. Saunders Elsevier; 2008:110–44.
- Monga M. Maternal cardiovascular, respiratory, and renal adaptation to pregnancy. In: Resnick R Lockwood CJ, Moore TR, eds. Creasy and Resnick's Maternal-Fetal Medicine. 8th ed. Elsevier; 2019:141–7.
- Wang Y, Zhao S. Placental blood circulation. In: Vascular Biology of the Placenta.
 Morgan & Claypool Life Sciences; 2010. ncbi.nlh.gov/books/NBK53254/.
 Accessed November 1, 2022.
- Finkielman JD, De Feo FD, Heller PG, Afessa B. The clinical course of patients with septic abortion admitted to an intensive care unit. Intensive Cae Med 2004; 30:1097–102.
- Holanda AMC, Ramos de Amorim MM, Bezerra SMB, Aschoff LMS, Katz L. Risk factors for death in patients with sepsis admitted to an obstetric intensive care unit: a cohort study. Medicine (Baltimore) 2020; 99:e23566.
- Hill JB, Sheffield JS, McIntire DD, Wendel GD Jr. Acute pyelonephritis in pregnancy. Obstet Gynecol 2005: 105:18–23.
- Jolly JA, Kim S, Wing DA. Acute pyelonephritis and associated complications in 2006 in US hospitals. J Maternal-Fetal Neonatal Med 2012; 25:2494–8.
- Wing DA, Fassett MJ, Getahun D. Acute pyelonephritis in pregnancy: and 18-year retrospective review. Am J Obstet Gynecol 2014; 210:219.e1–e6.
- Fouks Y, Samueloff O, Levin I, Many A, Amit S, Cohen A. Assessing the effectiveness of empiric antimicrobial regimens in cases of septic/infected abortions. Am J Emerg Med 2020; 38:1123–8.
- 54. Savaris RF, de Moraes GS, Cristovam RA, Braun RD. Are antibiotics necessary after 48 hours of improvement in infected/septic abortions? A randomized controlled trial followed by a cohort study. Am J Obstet Gynecol 2011; 204:301.e1–5.
- Singhal PC, Kher VK, Dhall GI, et al. Conservative vs. surgical management of septic abortion with renal failure. Int J Gynaecol Obstet 1982; 20:189–94.
- Rivlin ME, Hunt JA. Surgical management of diffuse peritonitis complicating obstetric/gynecologic infections. Obstet Gynecol 1986; 67:652–6.
- Barrett JP, Whiteside JL, Boardman LA. Fatal clostridial sepsis after spontaneous abortion. Obstet Gynecol 2002; 99:899–901.
- Nanda S, Sangwan K, Agarwal U. The ugly face of septic abortion. Eur J Obstet Gynecol Reprod Biol 2002; 105:71–2.
- Eaton CJ, Peterson EP. Diagnosis and acute management of patients with advanced clostridial sepsis complicating abortion. Am J Obstet Gynecol 1971; 109:1162–6.
- O'Connor A. How the death of Savita Halappanavar changed the abortion debate.
 Irish Examiner. October 28. 2017.
- Specia M. How Savita Halappanavar's death spurred Ireland's abortion rights campaign. New York Times. May 27, 2018.
- 62. Holland K. Savita: The Tragedy That Shook a Nation. Transworld Ireland; 2013.
- 63. Health Service Executive. Investigation of Incident 50278 From Time of Patients Self-Referral to Hospital on the 21st of October, 2012 to the Patient's Death on the 28th of October, 2012. Irish Health Services Executive; 2013. Available at: https://www.lenus.ie/handle/10147/293964. Accessed September 1, 2022.
- 64. Health Information and Quality Authority. Investigation Into the Safety, Quality and Standards of Services Provided by the Health Service Executive to Patients, Including Pregnant Women, at Risk of Clinical Deterioration, Including Those Provided in University Hospital Galway, and as Reflected in the Care and Treatment Provided to Savita Halappanavar. Health Information and Quality Authority; 2013. Available at: https://www.hiqa.ie/sites/default/files/2017-01/Patient-Safety-Investigation-UHG.pdf. Accessed September 1, 2022.
- Wall LL. The ghost of Savita Halappanavar comes to America. Obstet Gynecol 2022;140(5):724-8.
- Margolies IR. A reform rabbi's view. In: Hall RE, ed. Abortion in a Changing World. Vol. I. Columbia University Press; 1970; 30–3.
- Doan A. The Kansas abortion vote shows the loudest voices in this debate are not representative ones. BMJ 2022; 378:o2024.