

Nonfatal Amniotic Fluid Embolism

Three Possible Cases and a New Clinical Definition

Michael D. Benson, MD

Three obstetrical patients who experienced cardiovascular collapse followed by disseminated intravascular coagulation were cared for by the author during residency training and 5 years of private practice. All patients survived. Their clinical courses were strongly reminiscent of those of patients described in the medical literature who ultimately died with the diagnosis of "amniotic fluid embolism." Paradoxically, the mere fact of survival is generally regarded as proof that a given individual did not have an amniotic fluid embolism. Proposed herein is a new clinical definition of amniotic fluid embolism syndrome that could apply to patients who survive as well as to those who die. With this definition in mind, the prevalence and prognosis of amniotic fluid embolism syndrome is reexamined. Finally, the traditional assumption that this syndrome is a result of amniotic fluid leakage into the maternal circulation is challenged. A new source is suggested and some new thoughts regarding treatment are provided. (Arch Fam Med. 1993;2:989-994)

The clinical description of amniotic fluid embolism first appeared in the medical literature in a Spanish-language report in 1926 by Meyer.¹ The next major description of this syndrome occurred in a 1941 article that appeared in the *Journal of the American Medical Association*.^{2,3} Steiner and Lushbaugh² described eight maternal deaths at Chicago (Ill) Lying-In Hospital consistent with amniotic fluid embolism syndrome (AFES), all of whom had a large amount of fetal squames in their lungs at the time of autopsy. They estimated the frequency of this illness to be one per 8000 pregnancies and indicated that the diagnosis could only be confirmed at autopsy. An alternative estimate of one per 80 000 pregnancies in the United Kingdom was made by Lewis⁴ in a 1964 obstetrics text. This prevalence rate of one in 8000 to one in 80 000 has been frequently cited in obstetric articles, but it has not

been reassessed in three decades.^{5,6} Other authors have described an 80% to 90% mortality rate although the denominators for this statistic are characteristically vague.⁷

While there has been no clinical definition of AFES offered for patients who survive, the case reports in the medical literature share some features. Characteristically, all of these patients suddenly became very ill without an obvious precipitating cause. Their symptoms included nausea, vomiting, abdominal cramping, anxiety, tachypnea, and shock.⁸⁻¹¹ Forty percent of patients with AFES suffer disseminated intravascular coagulation (DIC) and many suffer adult respiratory distress syndrome.^{12,13} It is worth noting, however, that many of these symptoms, and DIC and adult respiratory distress syndrome in particular, are described in case reports in which the patient ultimately dies. Up to this point, the mere fact of survival has generally cast doubt on the diagnosis of AFES.

From Highland Park (Ill) Hospital and Northwestern University Medical School, Chicago, Ill.

In contrast to the experiences described in the medical literature, I have cared for three patients who experienced sudden shock and DIC in late pregnancy, all of whom survived. The clinical courses and outcomes of these patients suggest that some widely accepted views regarding AFES may need to be revised. Specifically, its diagnosis, possible prevalence rate, treatment, prognosis, and cause will be reexamined here. The term *amniotic fluid embolism syndrome* is used to denote a group of patients who have similar clinical characteristics (although not necessarily identical) presumably caused by the same pathophysiologic process.

SUDDEN MATERNAL CARDIOVASCULAR COLLAPSE FOLLOWED BY DIC

Case 1

A 32-year-old gravida 4 para 3-0-0-3 (three term infants, three living children) black woman presented at 32 weeks' gestation with preterm premature rupture of membranes. She had undergone three cesarean sections, and another cesarean section was planned when she went into labor. Approximately 12 hours after being admitted for bed rest and observation, she experienced rapid labor and delivered within 45 minutes of feeling the first contraction. The infant was delivered using outlet vacuum extraction for a severe variable since the fetus was crowning. Her rapid, sudden labor made cesarean delivery impractical. Approximately 10 minutes following birth, manual exploration of the uterus was done to check the scar and see if the placenta had separated. The scar had separated, but the patient had no visible bleeding and was in no distress.

One minute after uterine exploration, the patient suddenly complained of light-headedness and experienced a precipitous drop in her blood pressure to 60/0 mm Hg with a rise in pulse to 140 beats per minute. Her respiratory rate increased only slightly. She was placed in Trendelenburg's position and her intravenous infusion rate was increased. When a more vigorous effort to remove the placenta yielded only placental fragments, the decision to proceed with laparotomy was made. The patient's shock was attributed to concealed hemorrhage.

During the laparotomy, no concealed blood was discovered, which was remarkable since it was believed that the patient had both an accreta and a uterine dehiscence. However, on exploration of the uterus through the old scar, bleeding was scant, although the remainder of the placenta, which was firmly attached to the posterior wall of the uterus, could not be extracted. At this point, the uterus was removed since it appeared that the patient had placenta accreta (confirmed by the subsequent pathology report).

Approximately 30 minutes into surgery and 60 minutes after the initial onset of shock, the anesthesiologist

noted nasal hemorrhage and obtained an intraoperative surgical consultation for nasal packing. The patient had no apparent coagulopathy at the wound site for another 30 minutes. By then, the uterus had been removed, but the patient had begun bleeding diffusely at the surgical site. A bilateral salpingo-oophorectomy was done in an unsuccessful attempt to reduce bleeding. Eventually, the patient's wound site was closed, but hemostasis was not achieved since she was experiencing florid DIC.

Eight hours after surgery, continuous blood replacement had failed to increase the patient's hematocrit, which was nearly 0.30. This, coupled with her steadily increasing abdominal girth prompted a surgical reexploration of the abdomen. By now her coagulopathy was resolving. Six liters of clotted blood was removed from the abdominal cavity but no active bleeding was noted. A bilateral hypogastric artery ligation was performed as a precaution. Subsequently, the upper abdomen underwent exploration. Immediately following this exploration, bleeding was noted from the region of the spleen. A splenectomy was done and the patient's wound site was closed.

The following day, the patient still required blood transfusions to maintain her hematocrit. At her third abdominal exploration, the splenic bed was oversewn and the tail of the pancreas was removed to achieve hemostasis. The patient was discharged approximately 1 month after admission with a pancreatic-abdominal fistula. She had received 108 U of blood products.

Case 2

A 29-year-old gravida 4 para 3-0-0-3 white woman in good health with known polyhydramnios experienced a sudden cardiorespiratory arrest at 40 weeks' gestation, which was witnessed by her husband, a former marine corps officer. She fell off her chair, hit the floor, and turned blue. Her husband immediately performed cardiopulmonary resuscitation and sent for the paramedics. Approximately 30 minutes after her collapse, she arrived at Highland Park (Ill) Hospital with a pulse of 140 beats per minute and a slightly increased respiratory rate. She was dilated 5 cm although she was unaware of her contractions, and fetal heart rate tracing demonstrated repetitive late decelerations during 5 minutes of monitoring. The patient underwent an emergency cesarean section with the working diagnosis of AFES.

During delivery, the amniotic fluid was diffusely bloody, but the patient had no clinical evidence of a coagulopathy. The patient's wound site was closed uneventfully but florid DIC developed immediately after the patient's arrival in the intensive care unit. This was evident by the profuse aural, nasal, oral, incision site, and intravenous line placement bleeding. The emergency department physician was asked to apply military antishock trousers (MAST), which remained in place for 4 hours, at which time the patient's coagulopathy started to resolve. A hematologist

who had been consulted transfused 4 U of packed red blood cells and 4 U of fresh-frozen plasma. The patient was in stable condition within 6 hours of arrival and was discharged on postoperative day 5.

The neonate did not do as well, however. She had an Apgar score of 2/5 at 1 and 5 minutes and has severe cerebral palsy. Of interest is the fact that the newborn had a large amount of clotted blood in her trachea at the time of intubation. This has never been satisfactorily explained since the infant had normal coagulation study findings and there were no clots in the amniotic fluid.

Case 3

A 32-year-old gravida 3 para 2-0-0-2 white woman delivered a healthy boy at 39 weeks' gestation via outlet vacuum extraction for maternal exhaustion after a 1-hour second stage. She was delivered of the placenta spontaneously 10 minutes later. One to 2 minutes after the third stage, the patient complained of sudden light-headedness and nausea. At that moment, her pulse rose to 140 beats per minute and her blood pressure dropped to 60/40 mm Hg. The continuous lumbar epidural infusion (which had been administered at a constant dosage for several hours) was stopped, and the patient was placed in Trendelenburg's position. Her intravenous infusion rate was increased. She had no clinically evident coagulopathy. Her episiotomy was repaired without difficulty. The sudden shocklike symptoms were initially attributed to a transient and self-limited vasovagal episode, although continuous maternal pulse monitoring failed to demonstrate a bradycardia. When the patient continued to feel poorly and had a sustained pulse rate in the 150s, 4 hours post partum, AFES was suspected. Electrocardiography demonstrated sinus tachycardia, and a chest roentgenogram was normal. The patient's PO_2 was 106 mm Hg while breathing room air. However, her platelet count, which had been $156 \times 10^9/L$ on admission, dropped to 108×10^9 and the fibrin degradation products were higher than 40 mg/L. Since the patient had no clinical coagulopathy, no treatment was given and her pulse steadily improved over the next day. She was discharged on postpartum day 2 in good health and feeling well.

COMMENT

In presenting these three patients, a critical issue emerges. Was AFES the only reasonable explanation of their clinical courses or could alternative (and more commonplace) pathologic processes be operative? It is worth noting that fainting, vasovagal reactions, and relatively large and sudden episodes of blood loss are common in term pregnancies. However, each of these patients shared three clinical features that were not ordinary: sudden blood pressure drop with immediate significant tachycardia, sustained tachycardia, and clinical or compelling laboratory evidence of a coagulopathy.

The diagnosis of AFES in the first patient is potentially the most controversial since she had other diseases, specifically a uterine dehiscence and a placenta accreta. However, AFES has been linked to both precipitous labor and uterine rupture.^{7,14} Above all, it is not the events themselves but their sequence that makes some type of embolic event a likelihood. She experienced sudden shock in the absence of ongoing hemorrhage either visible externally or internally at the time of initial laparotomy. She then experienced DIC within 60 minutes, something not traditionally associated with either uterine dehiscence or placenta accreta. An alternative hypothesis was that her coagulopathy was caused by massive blood replacement. However, clotting difficulties occurred prior to receiving large amounts of blood products and were first evident through the loss of 2 L of blood around her nasogastric tube, not at the site of the uterus.

In the second case, the patient's relatively good clinical course is attributable to the immediate application of a MAST suit with the appearance of a coagulopathy. When she went into shock at the time of her coagulopathy, Swan-Ganz catheter placement to aid with fluid management was considered but was decided against in the presence of florid DIC. Unfortunately, the patient's fetus could not be helped more than by prompt delivery.

Colleagues who have not been persuaded by the AFES hypothesis for this patient have suggested that the patient merely fainted, fell off her chair, and suffered an abruption. This alternative explanation seems doubtful for two reasons. Abruption caused by trauma does not usually occur without a physical force sufficient to damage other abdominal viscera. A simple fall off a chair would not be expected to cause a massive abruption. A more important objection to the abruption theory is that this misfortune is not characteristically associated with cardiorespiratory arrest.

Another hypothesis is that the patient suffered a massive pulmonary embolism. While this is possible, it seems doubtful because the patient's pulmonary status was not much of a problem after the initial insult. Her respiratory rate never exceeded 24 breaths per minute, a blood gas study done in the emergency department showed a PO_2 of 210 mm Hg (while receiving 10 L of oxygen by face mask), and two chest roentgenograms obtained the first day were completely normal. Her condition was not believed to warrant either a ventilation/perfusion scan or angiography. Also, DIC is not an expected sequela of a pulmonary embolus.

The benign clinical course of the third patient may be the most difficult to link to AFES. Perhaps the patient merely fainted or her tachycardia could be explained by a somewhat higher than average blood loss of 600 mL associated with the excision and repair of some redundant vaginal mucosa after the delivery. As noted previously, this was not a vasovagal reaction since there was no antecedent bradycardia. Her epidural anesthesia was

probably not an etiologic factor since she had been receiving a constant infusion of medication for hours via a computerized pump. The somewhat greater than average blood loss was not remotely sufficient to explain a tachycardia of greater than 140 beats per minute 4 hours later. Finally, fainting, vasovagal reactions, and postpartum blood loss do not cause intrapartum thrombocytopenia and increased fibrin degradation products.

While to some, the mild course of the third patient's illness is proof that a significant pathologic process did not occur, careful attention to the specific timing of the hospital course suggests that alternative hypotheses are not truly satisfactory. It is possible that she may have suffered an embolic event of some sort, which was the most compelling reason to present these cases. How could she have an amniotic fluid embolism and not require any treatment other than intravenous fluids? Is AFES as fatal as the literature claims? How could one physician have three cases in only 2000 patients?

DIAGNOSIS OF AFES

The medical literature maintains that the only way AFES can be definitively diagnosed is through demonstration of massive fetal squames in the maternal pulmonary circulation at the time of autopsy or through recovery of squames at the time of central line placement, although this second method is deemed inconclusive by some.¹⁵⁻¹⁹ Of course, this places the clinician in a difficult situation if the patient survives. As for recovery of fetal squames through a central line, this can be a dangerous procedure for patients experiencing DIC. Clearly, an alternative method of diagnosis is called for if this illness is to be better understood. Based on these cases and those described in the literature, a clinically based definition of AFES seems appropriate and the following is suggested: (1) *Sudden* onset of cardiovascular collapse in a pregnant woman or in a patient who has delivered within the past 48 hours as defined by a pulse greater than or equal to 140 beats per minute *and* a diastolic blood pressure of less than or equal to 40 mm Hg *or* a systolic blood pressure of less than or equal to 60 mm Hg; (2) *Sustained* tachycardia (greater than or equal to 140 beats per minute) for 4 hours; (3) *Absence* of other illnesses that would explain signs and symptoms (eg, sepsis, pulmonary embolism, myocardial infarction). This does *not* preclude the coexistence of other maternal diseases.

The definition should also distinguish between type 1 AFES with DIC (laboratory or clinical) and type 2 AFES without DIC. Disseminated intravascular coagulation as defined herein must include thrombocytopenia and elevated fibrin degradation products and also must occur within 4 hours of the initial cardiovascular collapse.

While this definition may seem arbitrary to some, it can serve as a starting point for future reporting and investigation. It is no coincidence that each of the three patients described herein met this definition of AFES. How-

ever, whether or not one accepts embolic phenomenon as an explanation for these particular cases, the idea of establishing an easy to comprehend, clinical definition of AFES remains valid.

For the past six decades, physicians have been able to make a secure diagnosis of AFES only after the patient has died. The difficulty of establishing a diagnosis in patients who survive has tended to focus attention away from possible cases that might be more mild and numerous, skewing perceptions of cause, prevalence, and appropriate treatment.

HIGHLY FATAL?

If one uses a clinical definition of AFES and does not require an autopsy to confirm the diagnosis, the mortality rate is bound to fall. It is more reasonable to believe that this malady has varying degrees of severity with only the most tragic outcomes heretofore identified. The clinical definition provided herein should permit the inclusion of a larger number of patients who survive.

TREATMENT

Recommended treatment has been largely supportive. Monitoring with use of a Swan-Ganz catheter has also been advised since there appears to be left ventricular dysfunction.^{20,21} Swan-Ganz catheter placement also facilitates recovery of fetal squames from the maternal pulmonary circulation, previously thought to aid in diagnosis.^{22,23} However, the literature fails to address two critical issues. First, Swan-Ganz catheter monitoring is at least relatively contraindicated in patients with laboratory or clinical evidence of DIC.²⁴

The second omission is more important. The MAST suit has been well established to be helpful in obstetric DIC although none of the reports reviewed mentioned its use in their treatment protocols.²⁵ The application of a MAST suit appeared to allow the second patient to survive, and it kept her blood replacement to a minimal 8 U. The clinically evident coagulopathy that occurred in two of the patients started to resolve within 4 to 6 hours, an observation cited previously in the medical literature.²⁶ During this critical time, a MAST suit is ideal for maintaining blood pressure and reducing hemorrhage. A significant, practical obstacle to MAST suit use is that while many family practitioners are familiar with its use, most obstetricians have never seen one in application. In the case described herein, I only knew of the theory and simply had the emergency department physician and nurse supervise its placement.

CAUSE

All descriptions of AFES, including the suddenness of onset, the cardiovascular collapse with or without tachypnea, the subsequent development of adult respiratory

distress syndrome or DIC, resemble an immediate, generalized allergic reaction, ie, anaphylaxis.²⁷ Each of these symptoms and signs has been reported with anaphylactic shock.²¹ For both syndromes, the overriding characteristic is the suddenness of cardiovascular collapse. Interestingly, the connection with anaphylaxis was mentioned in passing in only a single report.²⁸ However, if AFES is an anaphylactic reaction, this possibility suggests that more than just supportive therapy may be needed, such as immediate high-dosage steroids, antihistamines, and even epinephrine.

a MAST suit should be considered

A less obvious insight is the fact that amniotic fluid per se may have nothing at all to do with this clinical syndrome. There are three striking issues raised in the medical literature that might stir skepticism about the role of amniotic fluid in this illness. First, no animal model corresponds to the pattern of illness seen in humans.^{15,27} Although injecting amniotic fluid into various species can indeed cause death, this typically occurs when the injection is heterologous. Two studies have failed to demonstrate the toxic effects of autologous amniotic fluid in primates.^{29,30} Second, the onset of illness in relation to the presumed leak of amniotic fluid into the maternal circulation is highly variable. Amniotic fluid embolism syndrome has been reported to occur in first and second trimester abortions, in term patients not in labor, during labor, and even 48 hours post partum.³¹⁻³⁹ This suggests that a simple one-time leak of amniotic fluid might be too limited to explain the array of clinical circumstances in which AFES has been reported. Third, the wide array of symptoms described above casts doubt on a single etiologic agent.

The high degree of variability in clinical features and timing among these patients suggest that the clinical syndrome of sudden cardiovascular collapse in pregnancy may actually reflect the response to a variety of inciting agents, although perhaps arising from a common immunologic mechanism. The idea that AFES results from a toxic reaction to a one-time leak of amniotic fluid into the maternal circulation no longer seems entirely credible.

An alternative explanation is that some type of pregnancy-associated antigen, perhaps on fetal trophoblast or blood cells, gains access to the maternal circulation and incites a massive immune response. Fetal trophoblast, nucleated red blood cells, and squamous cells have all been demonstrated in the maternal circulation at various points in pregnancy.^{15,40-42} Perhaps the clinically evident reaction occurs only after previous subclinical events, much like rhesus factor isoimmunization, become clinically evident in the second pregnancy and drug allergies tend to worsen with each exposure. This concept suggests that AFES is not the result of a toxic reaction to amniotic fluid but rather an immune response to some type of pregnancy-associated antigen. As with anaphylaxis, this may be an IgE-mediated

immune reaction. The clinical picture is so variable, perhaps because the specific antigen and the timing and quantity of antigen exposure may vary.

Disruption of the integrity of the placental-maternal interface has been associated with coagulation abnormalities. Specifically, in a study of the safety of chorionic villosus sampling, there was a demonstrable increase in the levels of fibrinopeptide A following the procedure.⁴³ The authors suggested that this was evidence of coagulation activation. This could be construed as evidence that some types of pregnancy-associated antigens can affect the coagulation cascade when they enter the maternal circulation in abnormal quantities. Perhaps this mechanism, on a larger scale, is operative in those patients with clinically evident DIC.

SUMMARY

The three patients described herein all had sudden cardiovascular collapse followed by DIC in the absence of other obvious explanations. A clinical definition useful in patients who survive has been presented. If widely used, the prevalence of recognized AFES might increase significantly. One would also expect a corresponding drop in the mortality rate for this condition. Traditional recommendations for treatment should be viewed with skepticism. Specifically, for DIC, a MAST suit should be considered while central monitoring may not be necessary or desirable. Finally, this disorder may have an underlying immunologic source that involves the presentation of a pregnancy-associated antigen to the maternal circulation. Amniotic fluid leakage into the maternal circulation per se seems an unlikely cause given the absence of a satisfactory animal model, the variable timing of symptoms after the presumed "leak," and the highly variable clinical presentation of patients. An attractive alternative may be an immunologically mediated response to some type of pregnancy-associated antigen leaking into the maternal circulation.

Accepted for publication June 3, 1993.

The author is interested in hearing from readers who may have cases of definite or suspected amniotic fluid emboli. Anyone who would like to share his or her experiences in this area may contact Dr Benson at 834 Forest Ave, Deerfield, IL 60015, or call him at 708-945-9470.

Reprint requests to 834 Forest Ave, Deerfield, IL 60015 (Dr Benson).

REFERENCES

1. Meyer JR. Embolia pulmonar amnio caseosa. *Brasil-Medico*. 1926;2:301-303.
2. Steiner PE, Lushbaugh CC. Maternal pulmonary embolism by amniotic fluid as a cause of obstetric shock and unexpected death in obstetrics. *JAMA*. 1941; 117:1245-1254, 1340-1345.
3. Sperry K. Amniotic fluid embolism: to understand an enigma. *JAMA*. 1986; 255:2183-2186.

4. Lewis TL. *Progress in Clinical Obstetrics and Gynecology*. 2nd ed. New York, NY: Churchill Livingstone Inc; 1964:48.
5. Dashow EE, Cotterill R, Benedetti TJ, Myhre S, Kovanda C, Sarrafan A. Amniotic fluid embolus: a report of two cases resulting in maternal survival. *J Reprod Med*. 1989;34:660-665.
6. Killam A. Amniotic fluid embolism. *Clin Obstet Gynecol*. 1985;8:32-36.
7. Suidan JS. Amniotic fluid embolism. *Middle East J Anesthesiol*. 1989;10:279-290.
8. Amniotic fluid embolism. *Lancet*. 1979;2:398-400. Editorial.
9. Turner R, Gusack M. Massive amniotic fluid embolism. *Ann Emerg Med*. 1984;13:359-361.
10. Mulder JI. Amniotic fluid embolism: an overview and case report. *Am J Obstet Gynecol*. 1985;152:403-405.
11. Dodgson J, Martin J, Boswell J, Goodall HB, Smith R. Probable amniotic fluid embolism precipitated by amniocentesis and treated by exchange transfusion. *BMJ*. 1987;294:1322-1323.
12. Duff P, Engelsbjerg B, Zingery LW, Huff RW, Montiel MM. Hemodynamic observations in a patient with intrapartum amniotic fluid embolism. *Am J Obstet Gynecol*. 1983;146:112-115.
13. Clark SL, Montz FJ, Phelan JP. Hemodynamic alterations associated with amniotic fluid embolism: a reappraisal. *Am J Obstet Gynecol*. 1985;151:617-621.
14. Kool MJ. Successful treatment of postpartum shock caused by amniotic fluid embolism with cardiopulmonary bypass and pulmonary artery thromboembolism. *Am J Obstet Gynecol*. 1991;164:701-702.
15. Clark SL. New concepts of amniotic fluid embolism: a review. *Obstet Gynecol Surv*. 1990;45:360-367.
16. Chatelain SM, Quirk JG Jr. Amniotic and thromboembolism. *Clin Obstet Gynecol*. 1990;33:473-481.
17. Clark SL, Cotton DB, Gonik B, Greenspoon J, Phelan JP. Central hemodynamic alterations in amniotic fluid embolism. *Am J Obstet Gynecol*. 1988;158:1124-1126.
18. Girard P, Mal H, Laine JF, Petitpretz P, Rain B, Duroux P. Left heart failure in amniotic fluid embolism. *Anesthesiology*. 1986;64:262-265.
19. Roche WD, Norris HJ. Detection and significance of maternal pulmonary amniotic fluid embolism. *Obstet Gynecol*. 1974;43:729-731.
20. Clark SL. Amniotic fluid embolism. *Crit Care Clin*. 1991;7:877-882.
21. Vanmaele L, Noppen M, Vincken M, De Catte L, Huyghens L. Transient left heart failure in amniotic fluid embolism. *Intensive Care Med*. 1990;16:269-271.
22. Resnik R. An obstetric emergency: amniotic fluid embolism. *Contemp Obstet Gynecol*. 1987;29:17-18.
23. Dolyniuk M, Orfei E, Vania H, Kariman R, Tomich P. Rapid diagnosis of amniotic fluid embolism. *Obstet Gynecol*. 1983;61(suppl):28S-30S.
24. Swan HJC. The pulmonary artery catheter. *Dis Mon*. 1991;37:475-543.
25. Pearse CS, Magrina JF, Finley BE. Use of MAST suit in obstetrics and gynecology. *Obstet Gynecol Surv*. 1984;39:416-422.
26. Resnik R, Swartz WH, Plumer MH, Benirschke K, Stratthaus ME. Amniotic fluid embolism with survival. *Obstet Gynecol*. 1976;47:295-298.
27. Kaplan AP. Anaphylaxis. In: Wyngaarden JB, Smith LH Jr, Bennette JC, eds. *Cecil Textbook of Medicine*. 19th ed. Philadelphia, Pa: WB Saunders Co; 1992:1462-1465.
28. Azegami M, Mori N. Amniotic fluid embolism and leukotrienes. *Am J Obstet Gynecol*. 1986;155:1119-1124.
29. Adamsons K, Mueller-Heubach E, Myer RE. The innocuousness of amniotic fluid infusion in the pregnant rhesus monkey. *Am J Obstet Gynecol*. 1971;109:977-984.
30. Stolte L, Van Kessel H, Seelen J, Eskes T, Wagatsuma T. Failure to produce the syndrome of amniotic fluid embolism by infusion of amniotic fluid and meconium into monkeys. *Am J Obstet Gynecol*. 1967;98:694-697.
31. Steingrub JS, Lopez T, Teres D, Steingart R. Amniotic fluid embolism associated with castor oil ingestion. *Crit Care Med*. 1988;16:642-643.
32. Thomsen RJ. Pregnancy in the presence of an intrauterine contraceptive device and amniotic fluid embolism: a possible association. *Am J Obstet Gynecol*. 1975;127:279-280.
33. Esposito RA, Grossi EA, Coppa G, et al. Successful treatment of postpartum shock caused by amniotic fluid embolism with cardiopulmonary bypass and pulmonary artery thromboembolism. *Am J Obstet Gynecol*. 1990;163:572-574.
34. Sprung J, Rakic M, Patel S. Amniotic fluid embolism during epidural anesthesia for cesarean section. *Acta Anaesthesiol Belg*. 1991;42:225-231.
35. Meier PR, Bowes WA Jr. Amniotic fluid embolus-like syndrome presenting in the second trimester of pregnancy. *Obstet Gynecol*. 1983;61(suppl):31S-34S.
36. Cromey MG, Taylor PJ, Cumming DC. Probable amniotic fluid embolism after first-trimester pregnancy termination: a case report. *J Reprod Med*. 1983;28:209-211.
37. Less A, Goldberger SB, Bernheim J, Ben-Nun I, Fejgin MD. Vaginal prostaglandin E₂ and fatal amniotic fluid embolus. *JAMA*. 1990;263:3259-3260.
38. Cates W Jr, Boyd C, Halvorson-Boyd G, Holck S, Gilchrist TF. Death from amniotic fluid embolism and disseminated intravascular coagulation after a curettage abortion. *Am J Obstet Gynecol*. 1981;141:346-348.
39. Price TM, Baker VV, Cefalo RC. Amniotic fluid embolism: three case reports with a review of the literature. *Obstet Gynecol Surv*. 1985;40:462-474.
40. Mueller UW, Hawes CS, Wright AE, et al. Isolation of fetal trophoblast cells from peripheral blood of pregnant women. *Lancet*. 1990;336:197-200.
41. Elias S, Price J, Dockter M, Wachtel S, Tharapel A, Simpson JL. First trimester prenatal diagnosis of trisomy 21 in fetal cells from maternal blood. *Lancet*. 1992;340:1033.
42. Price JO, Elias S, Wachtel SS, et al. Prenatal diagnosis with fetal cells isolated from maternal blood by multiparameter flow cytometry. *Am J Obstet Gynecol*. 1991;165:1731-1737.
43. Al-Gailani F, Elias S, Simpson JL, Green D. Fibrinopeptide A increases after chorionic villus sampling. *Prenat Diagn*. 1987;7:557-660.