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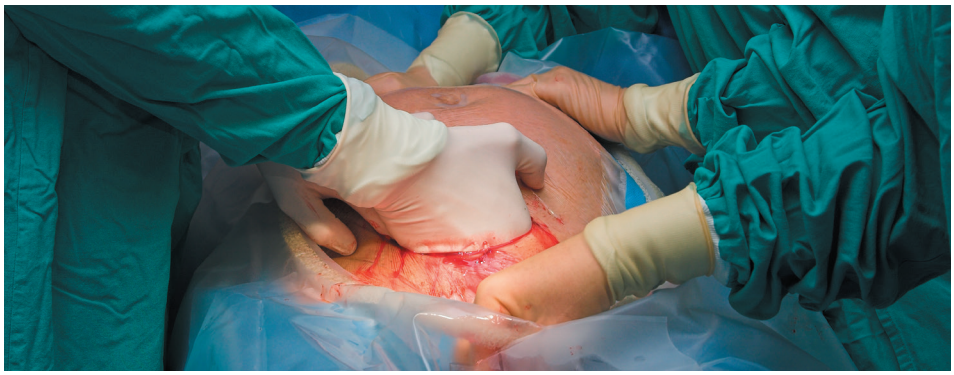
Recognition and Management of Amniotic Fluid Embolism: A Critical Role for Anesthesia Professionals on Labor and Delivery

by David E Arnolds, MD, PhD

Amniotic fluid embolism (AFE) is a catastrophic complication unique to the obstetric patient characterized by acute cardiovascular collapse and a profound coagulopathy.[1] While AFE is rare, with an incidence of 1–2/100,000 pregnancies, it is associated with a mortality or permanent neurologic injury rate of 30–40%.[1,2] AFE is the second leading cause of maternal death on the day of delivery in the United States.[3] Early recognition and goal-directed treatment of suspected AFE is critical to successful management and decreasing morbidity. Women who die of AFE are less likely than those who survive to have an obstetrician or anesthesia professional present at the time of AFE,[2] highlighting the critical role for early recognition. Despite being recognized as a syndrome for nearly 100 years, the etiology of AFE remains elusive, the diagnosis remains clinical, and management is entirely supportive. The goal of this article is to review the presentation, differential, and initial management of AFE as well as to discuss potential avenues to further our understanding and management of this rare, but potentially fatal syndrome. Given the critical need for timely and focused intervention for AFE, the development of facility-specific cognitive aids is recommended to assist in initial management.[4]

The historical lack of consistent criteria for diagnosing AFE has made it challenging to define the true incidence of the syndrome and has hampered efforts to evaluate treatment strategies. AFE is a clinical diagnosis based on cardiorespiratory collapse and coagulopathy in the absence of other conditions sufficient to explain these symptoms: there are no serum or histologic findings specific to AFE. The need to rely on clinical criteria has likely resulted in both over- and underdiagnosis, with underdiagnosis of mild cases as well as inappropriate diagnosis of AFE in women who become critically ill from other causes. Given that AFE is considered the least preventable cause of maternal mortality,[5] there may be additional medical legal pressure to diagnose AFE in some cases of maternal mortality. Furthermore, international criteria for diagnosis of AFE vary considerably,[2] and some definitions include the presence of fetal epithelial cells in post-mortem histopathologic samples from maternal lungs, despite evidence that the presence of fetal epithelial cells in the maternal pulmonary circulation is neither specific nor sensitive for AFE.[6,7] In an effort to standardize diagnosis and reporting of AFE for research purposes, an expert panel convened by the Society for Maternal-Fetal Medicine and the Amniotic Fluid Embolism Foundation has proposed diagnostic criteria (commonly referred to as the Clark Criteria) for amniotic fluid embolism for research purposes (Table 1).[8]



AFE must be distinguished from other life-threatening causes of cardiovascular collapse in obstetric patients. In an analysis of cases submitted to the United States AFE Registry, obstetric hemorrhage was the most common actual diagnosis in cases misdiagnosed as AFE.[9] While severe obstetric hemorrhage may cause life-threatening hypotension and hemostatic derangements, it can be distinguished from AFE by both the antecedent event as well as by the absence of respiratory compromise. Sepsis is associated with hypotension and can cause both hypoxia and a coagulopathy, but typically is insidious in onset and is associated with maternal hyper- or hypothermia. Anaphylaxis can cause hypotension and hypoxia, but is not associated with a coagulopathy and occurs in association with exposure to an allergen, such as a medication, latex, or chlorhexidine skin prep. Anesthetic complications, such as a high neuraxial block, can be associated with hypotension and respiratory compromise, but do not include a coagulopathy and can further be distinguished from AFE by the association with neuraxial anesthesia. While pulmonary venous or air embolism can cause hypotension and hypoxia, they are not typically associated with a coagulopathy. Similarly, hemodynamic collapse from a primary cardiac etiology, such as an acute myocardial infarction, does not present with a coagulopathy and typically occurs in the clinical context of patients with known risk factors or recognized cardiac pathology.

The criteria described in Table 1 are biased towards specificity as opposed to sensitivity and thus some cases of AFE may not meet these strict criteria. A slightly more liberal definition was agreed on through a Delphi process by an expert panel assembled by the International Network of Obstetric Surveillance Systems (INOSS): acute cardiorespiratory collapse within 6 hours after labor, delivery or ruptured membranes, with no other identifiable cause, followed by acute coagulopathy in those women who survive the initial event.[10] In an analysis of cases submitted to the United States AFE registry, 12% of cases were considered atypical in that they did not meet the full research criteria, but nevertheless were felt upon expert review to represent AFE.[9] In con-

Table 1: Diagnostic Criteria for Research Reporting of Amniotic Fluid Embolism.[8]

1. Sudden onset of cardiorespiratory arrest, or both hypotension (systolic blood pressure <90 mm Hg) and respiratory compromise (dyspnea, cyanosis, or peripheral capillary oxygen saturation [SpO_2 < 90%).
2. Overt disseminated intravascular coagulation (DIC)* following appearance of these initial signs or symptoms. Coagulopathy must be detected prior to loss of sufficient blood to itself account for dilutional or shock-related consumptive coagulopathy.
3. Clinical onset during labor or within 30 min. of delivery of placenta
4. No fever (>38° C) during labor

*A score >3 is considered compatible with overt DIC in pregnancy

Platelet count >100,000/mL = 0, <100,000/mL = 1, <50,000/mL = 2

Prolonged prothrombin time or international normalized ratio (from baseline): <25% increase = 0, 25–50% increase = 1, >50% increase = 2

Fibrinogen level: >200 mg/dL = 0, <200 mg/dL = 1

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trast, the INOSS found that 31% of cases[2] collected by member institutions met INOSS, but not Clark Criteria, with a lack of evidence for DIC being the most common reason for not meeting the Clark Criteria. At a practical level, while obtaining laboratory studies to assess coagulation status can be essential in the management of a critically ill patient, it may not occur, or may not occur in the appropriate time frame, in the context of ongoing resuscitation.

Some patients with AFE will present with cardiac arrest as their first recognized symptom: for these patients, initial management should focus on providing high-quality advanced cardiac life support as outlined in the American Heart Association Scientific Statement on Cardiac Arrest in Pregnancy.[11] Key considerations in pregnant patients of greater than 20 weeks of gestational age include left uterine displacement, prioritization of oxygenation and airway management, and perimortem cesarean delivery (resuscitative hysterotomy) to relieve aortocaval compression and aid in maternal resuscitation within 5 minutes of arrest if return of spontaneous circulation (ROSC) has not been achieved, regardless of fetal viability. For patients with AFE who do not present with cardiac arrest or in whom ROSC is achieved, acute pulmonary hypertension and right ventricular failure is typically the primary initial presentation.[12] Right ventricular failure may progress to left ventricular failure with ongoing clinical deterioration. Focused cardiac ultrasound (either transthoracic or transesophageal) is within the scope of appropriately trained anesthesia professionals, provides valuable diagnostic information, and can be used to guide therapy.[13,14] Norepinephrine or epinephrine may be appropriate depending on the extent of circulatory collapse, with consideration for use of dobutamine or milrinone for inotropic support and inhaled nitric oxide or epoprostanol as pulmonary vasodilators.[4,12] As these agents are not routinely available on most labor and delivery units, phenylephrine and epinephrine may be appropriate in the initial phases of resuscitation, and the locations of, and processes to rapidly obtain advanced inotropic support and pulmonary vasodilators should be identified in institutional-specific planning sessions and clearly featured on cognitive aids. Similarly, extracorporeal membrane oxygenation (ECMO) can be considered early if it is institutionally available, and cognitive aids should include ECMO contact information. Overzealous fluid administration should be avoided in the presence of right ventricular failure.

Patients who survive the initial cardiorespiratory collapse associated with AFE go on to develop a profound coagulopathy. Viscoelastic testing may help guide rational management of blood products and clotting factor concentrates,[15] although empiric ratio-based resuscitation may be necessary in the face of massive ongoing hemodynamically significant hemorrhage. Several case reports and case series suggest hyperfibrinolysis during AFE,[16,17] and tranexamic acid administration (1 g IV over 10 minutes, with the possibility of an additional 1g dose after 30 minutes with ongoing bleeding) is recommended[4] based on extrapolation from the WOMAN trial[18] despite the lack of specific evidence for efficacy in AFE. Administration of a concentrated source of fibrinogen (fibrinogen concentrate or cryoprecipitate) has also been associated with improved outcomes,[2] consistent with the established role for treating hypofibrinogenemia in obstetric hemorrhage. Uterine atony should be anticipated and prophylactically treated to further limit blood loss following delivery.

While multiple "treatments" for amniotic fluid embolism have been proposed in case reports or suggested in discussions of the syndrome, none have been universally accepted or are supported by evidence. Proposed treatments include hydrocortisone,[19] lipid emulsion,[20] C1 esterase inhibitor,[21] and the combination of atropine, ondansetron, and ketorolac, often referred to as "A-OK."[22,23] While hydrocortisone is effective in the treatment of adrenal insufficiency and plays a role in managing allergic reactions, lipid emulsion is effective for local anesthetic systemic toxicity, and C1 esterase inhibitor is effective for treatment and prevention of hereditary angioedema, there is no evidence supporting use of any of these agents to treat AFE. Similarly, atropine is an effective antidote in cases of cholinergic poisoning, but there is no evidence for the effectiveness of atropine, ondansetron, and ketorolac in treatment of AFE. Unless or until additional research demonstrates the effectiveness of any case-reported treatments for AFE, they should not distract from prioritizing effective supportive care.

AFE is a rare and potentially catastrophic event. As with all such events, postevent debriefing sessions are crucial to offer support to affected staff members and identify opportunities for improvement. In addition, contacting the Amniotic Fluid Embolism Foundation (https://afesupport.org/) for all suspected cases is recommended as it provides an additional source of support for the patient and their family. Furthermore, the AFE Foundation supports a registry and biorepository that facilitates research on this rare syndrome with the goal of transforming AFE into a predictable, preventable, and treatable condition. Until such advances occur, early recognition and high-quality supportive care are essential to decrease the morbidity from AFE.

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