

Amniotic fluid embolism: Management using a checklist

Because AFEs are rare, with a high mortality rate, using a visual aid that includes several time-critical steps for management can allow for life-saving patient care

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IN THIS ARTICLE

Steps for expediting delivery

page 27

Importance of a debrief

page 28

Checklist

page 29

CASE Part 1: CPR initiated during induction of labor

A 32-year-old gravida 4 para 3-0-0-3 is undergoing induction of labor with intravenous (IV) oxytocin at 39 weeks of gestation. She has no significant medical or obstetric history. Fifteen minutes after reaching complete cervical dilation, she says “I don’t feel right,” then suddenly loses consciousness. The nurse finds no detectable pulse, calls a “code blue,” and initiates cardiopulmonary resuscitation (CPR). The obstetrician is notified, appears promptly, assesses the situation, and delivers a 3.6-kg baby via vacuum extraction. Apgar score is 2/10 at 1 minute and 6/10 at 5 minutes. After delivery of the placenta, there is uterine atony and brisk hemorrhage with 2 L of blood loss.

Management of AFE: A rare complication

This case demonstrates a classic presentation of amniotic fluid embolism (AFE) syndrome—a patient in labor or within 30 minutes after delivery has sudden onset of cardiorespiratory collapse followed by disseminated intravascular coagulation (DIC). AFE is rare, affecting only about 2 to 6 per 100,000 births, but classic cases have a reported maternal mortality rate that exceeds 50%.¹ It is thought to reflect a complex, systemic proinflammatory response to maternal intravasation of pregnancy material, such as trophoblast, thromboplastins, fetal cells, or amniotic fluid. Because the syndrome is not necessarily directly caused by emboli or by amniotic fluid per se,² it has been proposed that AFE be called “anaphylactoid syndrome of pregnancy,” but this terminology has not yet been widely adopted.³

Guidelines from the Society for Maternal-Fetal Medicine (SMFM) recommend several time-critical steps for the initial stabilization and management of patients with AFE.⁴ However, because AFE is rare, most obstetric providers may not encounter a case for many years or even decades after they have received training, so it is unrealistic to expect that they will remember these guidelines when they are needed. For this reason, when AFE occurs, it is important to have a readily accessible cognitive aid, such as a checklist that summarizes the key management steps. The SMFM provides a checklist for initial management of AFE that can be used at your institution; it is



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The authors report no financial relationships relevant to this article.

doi: 10.12788/obgm.0208

presented in the **FIGURE** (page 29) and provides the outline for this discussion.⁵

Provide CPR immediately

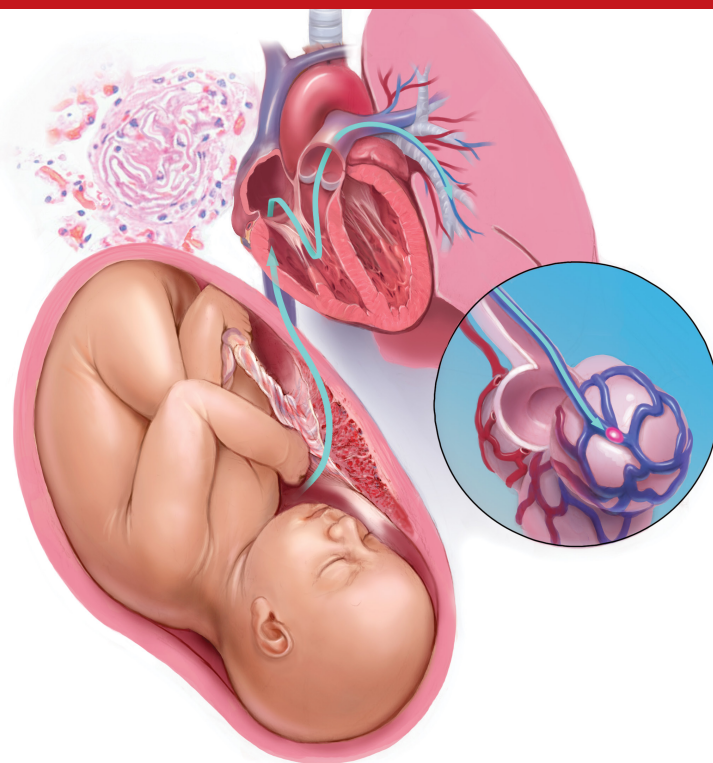
Most AFE cases are accompanied by cardiorespiratory arrest. If the patient has no pulse, call a “code” to mobilize additional help and immediately start CPR. Use a backboard to make cardiac compressions most effective and manually displace the uterus or tilt the patient to avoid supine hypotension. Designate a timekeeper to call out 1-minute intervals and record critical data, such as medication administration and laboratory orders/results.

Expedite delivery

Immediate delivery is needed if maternal cardiac activity is not restored within 4 minutes of starting CPR, with a target to have delivery completed within 5 minutes. Operative vaginal delivery may be an option if delivery is imminent, as in the case presented, but cesarean delivery (CD) will be needed in most cases. This was previously called “perimortem cesarean” delivery, but the term “resuscitative hysterotomy” has been proposed because the primary goal is to improve the effectiveness of CPR⁶ and prevent both maternal and perinatal death. CPR is less effective in pregnant women because the pregnant uterus takes a substantial fraction of the maternal cardiac output, as well as compresses the vena cava. Some experts suggest that, rather than waiting 4 minutes, CD should be started as soon as an obstetrician or other surgeon is present, unless there is an immediate response to electrical cardioversion.^{6,7}

In most cases, immediate CD should be performed wherever the patient is located rather than using precious minutes to move the patient to an operating room. Antiseptic preparation is expedited by simply pouring povidone-iodine or chlorhexidine over the lower abdomen if readily available; if not available, skip this step. Enter the abdomen and uterus as rapidly as possible using only a scalpel to make generous midline incisions.

If CPR is not required, proceed with cesarean or operative vaginal delivery as soon as the mother has been stabilized.



These procedures should be performed using standard safety precautions outlined in the SMFM patient safety checklists for cesarean or operative vaginal delivery.^{8,9}

Anticipate hemorrhage

Be prepared for uterine atony, coagulopathy, and catastrophic hemorrhage. Initiate IV oxytocin prophylaxis as soon as the infant is delivered. Have a low threshold for giving other uterotonic agents such as methylergonovine, carboprost, or misoprostol. If hemorrhage or DIC occurs, give tranexamic acid. Have the anesthesiologist or trauma team (if available) insert an intraosseous line for fluid resuscitation if peripheral IV access is inadequate.

Massive transfusion is often needed to treat DIC, which occurs in most AFE cases. Anticipate—do not wait—for DIC to occur. We propose activating your hospital's massive transfusion protocol (MTP) as soon as you diagnose AFE so that blood products will be available as soon as possible. A typical MTP provides several units of red blood cells, a pheresis pack of platelets, and fresh/frozen plasma (FFP). If clinically indicated, administer cryoprecipitate instead of FFP to minimize volume overload, which may occur with FFP.

CONTINUED ON PAGE 28

CASE Part 2: MTP initiated to treat DIC

The MTP is initiated. Laboratory results immediately pre-transfusion include hemoglobin 11.3 g/dL, platelet count 46,000 per mm³, fibrinogen 87 mg/dL, and an elevated prothrombin time international normalized ratio.

Expect heart failure

The initial hemodynamic picture in AFE is right heart failure, which should optimally be managed by a specialist from anesthesiology, cardiology, or critical care as soon as they are available. An emergency department physician may manage the hemodynamics until a specialist arrives. Avoidance of fluid overload is one important principle. If fluid challenges are needed for hypovolemic shock, boluses should be restricted to 500 mL rather than the traditional 1000 mL.

Pharmacologic treatment may include vasopressors, inotropic agents, and pulmonary vasodilators. Example medications and dosages recommended by SMFM are summarized in the checklist (FIGURE).⁵

After the initial phase of recovery, the hemodynamic picture often changes from right heart failure to left heart failure. Management of left heart failure is not covered in the SMFM checklist because, by the time it appears, the patient will usually be in the intensive care unit, managed by the critical care team. Management of left heart failure generally includes diuresis as needed for cardiogenic pulmonary edema, optimization of cardiac preload, and inotropic agents or vasopressors if needed to maintain cardiac output or perfusion pressure.⁴

Debrief, learning opportunities

Complex emergencies such as AFE are rarely handled 100% perfectly, even those with a good outcome, so they present opportunities for team learning and improvement. The team should conduct a 10- to 15-minute debrief soon after the patient is stabilized. Make an explicit statement that the main goal of the debrief is to gather suggestions as to how systems and processes could be improved for next time, not to find fault or lay blame on individuals. Encourage all personnel involved

in the initial management to attend and discuss what went well and what did not. Another goal is to provide support for individuals who may feel traumatized by the dramatic, frightening events surrounding an AFE and by the poor patient outcome or guarded prognosis that frequently follows. Another goal is to discuss the plan for providing support and disclosure to the patient and family.

The vast majority of AFE cases meet criteria to be designated as “sentinel events,” because of patient transfer to the intensive care unit, multi-unit blood transfusion, other severe maternal morbidities, or maternal death. Therefore, most AFE cases will trigger a root cause analysis (RCA) or other formal sentinel event analysis conducted by the hospital’s Safety or Quality Department. As with the immediate post-event debrief, the first goal of the RCA is to identify systems issues that may have resulted in suboptimal care and that can be modified to improve future care. Specific issues regarding the checklist should also be addressed:

- Was the checklist used?
- Was the checklist available?
- Are there items on the checklist that need to be modified, added, or deleted?

The RCA concludes with the development of a performance improvement plan.

Ultimately, we encourage all AFE cases be reported to the registry maintained by the Amniotic Fluid Embolism Foundation at <https://www.afesupport.org/>, regardless of whether the outcome was favorable for the mother and newborn. The registry includes over 130 AFE cases since 2013 from around the world. Researchers periodically report on the registry findings.¹⁰ If providers report cases with both good and bad outcomes, the registry may provide future insights regarding which adjunctive or empiric treatments may or may not be promising.

Empiric treatments

From time-to-time, new regimens for empiric treatment of AFE are reported. It is important to recognize that these reports are generally uncontrolled case reports of favorable outcomes and that, without a control group, it is

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FIGURE Amniotic fluid embolism: Checklist for initial management

This checklist is a sample only. Each facility should modify it to fit facility-specific circumstances

Manage circulatory collapse

- ABCs: manage Airway, Breathing, and Circulation
- Designate a timekeeper to call out times at 1-minute intervals
- If no pulse, start CPR
 - Manually displace uterus or lateral tilt
 - Use backboard
- Do not move to operating room unless this can be done in ≤ 2 minutes
- Cesarean delivery STAT if no pulse at 4 minutes
 - Splash prep only, do not wait for antibiotics
 - Goal is to improve chances of resuscitation

Anticipate uterine atony, DIC, hemorrhage

- Oxytocin prophylaxis plus other uterotonics as needed
- Consider intraosseous line if needed for large-bore IV access
- Initiate massive transfusion protocol
 - Cryoprecipitate preferred over FFP to reduce volume overload
 - Consider thromboelastometry if available
- Tranexamic acid (1-g IV over 10 minutes) if DIC or hemorrhage

Manage pulmonary hypertension and right ventricular failure (Anesthesiology, Critical Care, or Cardiology)

- Consider echocardiography (thoracic or esophageal)
- Avoid fluid overload (eg, 500-mL boluses and reassess)
- Vasopressor if needed: norepinephrine 0.05-3.3 $\mu\text{g}/\text{kg}/\text{min}$
- Inotropes if needed:
 - Dobutamine 2.5-5 $\mu\text{g}/\text{kg}/\text{min}$ or
 - Milrinone 0.25-0.75 $\mu\text{g}/\text{kg}/\text{min}$
- Pulmonary vasodilator if needed to unload right ventricle
 - Inhaled nitric oxide 5-40 ppm or
 - Inhaled epoprostenol 10-50 ng/kg/min or
 - IV epoprostenol 1-2 ng/kg/min (via central line) or
 - Sildenafil 20 mg orally (if awake/alert)
- Consider ECMO if prolonged CPR or refractory right heart failure
- Wean FiO₂ to maintain O₂ saturation 94%-98%

Postevent debrief (entire team)

- Identify opportunities for improvement including any need for revisions to checklist
- Discuss family and staff support needs
- Report case to Amniotic Fluid Embolism Registry

Version date July 2022

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Use this checklist as an example, but each facility should create its own brief guidelines based on varying and individual facility circumstances

Modified from Patient Safety and Quality Committee, Society for Maternal-Fetal Medicine.⁵

Abbreviations: CPR, cardiopulmonary resuscitation; DIC, disseminated intravascular coagulation; ECMO, extracorporeal membrane oxygenation; FFP, fresh/frozen plasma; FiO₂, inhaled fraction of oxygen; IV, intravenous.

CONTINUED ON PAGE 30

impossible to determine to what extent the treatment contributed to the outcome or was merely incidental. Given the rarity of AFE, it seems unlikely that there will ever be a randomized clinical trial or even a controlled prospective study comparing treatment regimens.

The “A-OK” regimen is an empiric treatment that has garnered some interest after an initial case report.¹¹ It consists of an anticholinergic agent (atropine 0.2 mg IV), a selective 5-HT₃ receptor antagonist (ondansetron 8 mg IV), and a nonsteroidal anti-inflammatory drug (ketorolac 15 mg IV). We have some reservations about this regimen, however, because atropine is relatively contraindicated if the patient has tachycardia (which is common in patients with hemorrhage) and ketorolac may suppress platelet function, which might be harmful for patients with DIC or thrombocytopenia.

Another empiric treatment is the “50-50-500” regimen, which includes an H₁ antihistamine (diphenhydramine 50 mg IV), an H₂ antihistamine (famotidine 50 mg IV), and a corticosteroid (hydrocortisone 500 mg IV). This regimen aims to suppress histamine-mediated and cell-mediated inflammatory responses, based on the notion that proinflammatory responses likely mediate much of the underlying pathophysiology of the AFE syndrome.

We would emphasize that these empiric regimens are not clinically validated, US Food and Drug Administration approved for treatment of AFE, or considered standard of care. Future reports of these and other regimens will be needed to evaluate their efficacy, limitations, and risks. Again, we encourage providers to report all AFE cases to the AFE Foundation registry, regardless of whether the treatments are successful.

CASE Conclusion

The hemorrhage stops after administration of oxytocin, carboprost, 6 units of cryoprecipitate, and a 6-unit platelet pheresis pack. The patient is transferred to the intensive care unit where she eventually requires a total of 10 units of red cells, 8 more units of cryoprecipitate, and another platelet pheresis pack. She is discharged to home in stable condition on postpartum day 4.

Be prepared, have the checklist ready

Because AFE is rare, most members of the health care team will have no prior experience managing a real case. It may have been years or decades since they had any education on AFE or they last read a review article such as this one. It is even possible the anesthesiologist, cardiologist, or critical care specialist has never heard of AFE. Thus if they rely on memory alone, there is substantial risk of forgetting items, getting dosages wrong, or other errors. With this in mind, what is the best way to prepare the team to expeditiously employ the management steps outlined here?

Use of a checklist that summarizes these key steps for early management, such as the SMFM checklist in the FIGURE, will help ensure that all relevant steps are performed in every AFE case. It is designed to be printed on a single sheet of letter-sized paper, and we propose that every labor and delivery (L&D) unit keep laminated copies of this checklist in several places where they will be immediately available should an AFE occur. Copies can be kept on the anesthesia carts in the L&D operating rooms, in an emergency procedures binder on the unit, and on the “crash carts” and hemorrhage supply carts in the L&D unit. Effective implementation of an AFE checklist requires all personnel know where to readily find it and have some familiarity with its contents.

An interdisciplinary team comprising representatives from nursing, obstetrics, and anesthesia should meet to discuss whether the checklist needs to be modified to fit the local hospital formulary or other unique local circumstances. The team should develop an implementation plan that includes where to keep checklist copies, a process to periodically ensure that the copies are still present and readable, a roll-out plan to inform all personnel about the checklist process, and most importantly a training plan that includes incorporating AFE cases into the schedule of multidisciplinary simulations and drills for obstetric emergencies. Other implementation strategies are outlined in the SMFM document.⁵

Ultimately an organized, systematic approach is recommended for management of

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AFE. There is no single best treatment of AFE; it is supportive and directed toward the underlying pathophysiology, which may vary from patient to patient. Therefore, although a check-

list, in conjunction with regular education and simulation activities, may help optimize care and improve outcomes, there is still a high risk of maternal morbidity and mortality from AFE. ●

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