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Amniotic Fluid Embolism

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Course Description:

Amniotic Fluid Embolism (AFE) is a high acuity, low occurring process that when recognized may be life-saving. The course will help by giving understanding of the disease and its management.

Approximate Time to Complete: 40 minutes

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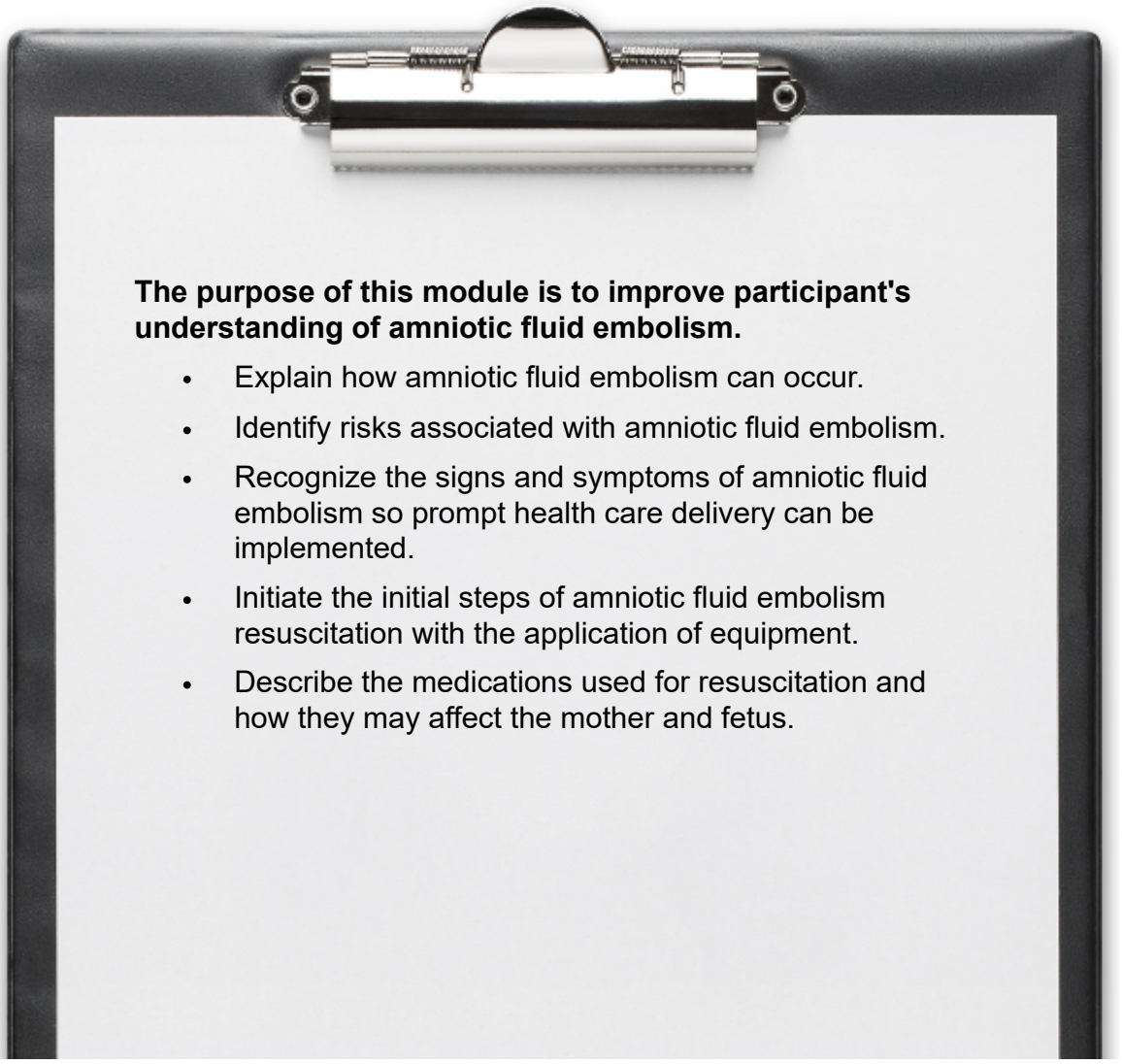


The purpose of this module is to improve participant's understanding of amniotic fluid embolism.

- Explain how amniotic fluid embolism can occur.
- Identify risks associated with amniotic fluid embolism.
- Recognize the signs and symptoms of amniotic fluid embolism so prompt health care delivery can be implemented.
- Initiate the initial steps of amniotic fluid embolism resuscitation with the application of equipment.
- Describe the medications used for resuscitation and how they may affect the mother and fetus.

Amniotic Fluid Embolism (AFE)

- *A rare, sporadic, unpredictable condition that can occur in pregnancy or immediately postpartum and may lead to cardiovascular collapse [1-3].*
- *Also called anaphylactiod syndrome of pregnancy.*
- *AFE is believed to be triggered by the abnormal release of trophoblasts or other material into the maternal circulation.*
- *Other cells from the fetal compartment can cause the AFE, rather than only amniotic fluid as the name implies.*

- First reported in 1926.
- Not widely recognized until 1941.
- In 1941, autopsies from a series of eight women who died from sudden shock during labor reported squamous cells and mucin of fetal origin in the maternal pulmonary vasculature [4,5].
- These same fetal squamous cells have been described in the vascular beds of maternal kidneys, liver, spleen, pancreas and brain [6].

- The condition typically presents with hemodynamic and respiratory compromise in addition to disseminated intravascular coagulopathy (DIC).
- The incidence is between 1-12 cases per 100,000.
- However, due to the lack of international consensus regarding diagnostic criteria, estimates of both incidence and mortality rates associated with AFE vary widely [56].

AFE appears to involve complex events triggered in certain women by entrance into the maternal circulation of material from the fetal compartment, resulting in an abnormal proinflammatory mediator system activation similar to the systemic inflammatory responses syndrome (SIRS) [56].

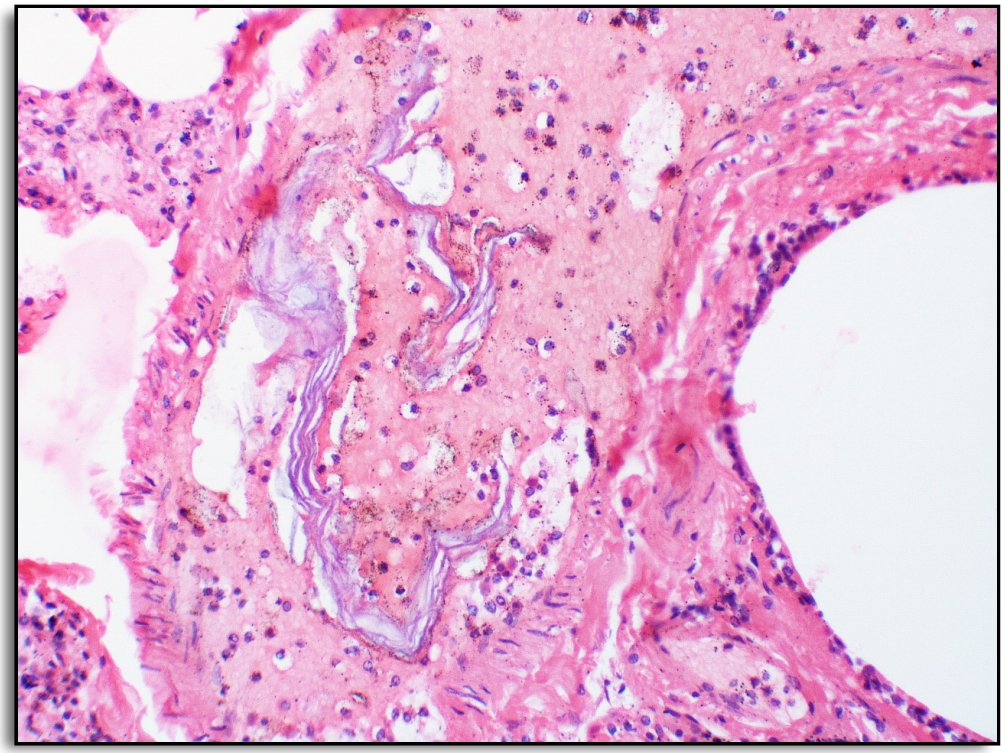
Occurrence

Several factors have been associated with AFE [7,12,13], including, but not limited to:

- Precipitous or tumultuous labor
- Advanced maternal age
- Cesarean and instrumental delivery
- Placenta previa, placental abruption, placenta acreta, percreta, or increta
- Grand multiparity (≥ 5 live births or stillbirths)
- Cervical lacerations
- Fetal distress
- Eclampsia
- Medical induction of labor
- Uterine rupture
- Polyhydramnios
- Miscarriage or abortion
- Amniocentesis

AFE is best considered unpreventable and unpredictable.

- The pathogenesis of AFE is thought to involve the amniotic fluid or other fetal compartment cells entering the maternal circulation through endocervical veins, the placental insertion site or a site of uterine trauma [14].
- Once the amniotic fluid or other fetal compartment cells reaches the maternal circulation, it can precipitate cardiogenic shock, respiratory failure and most likely, an inflammatory and anaphylactoid response.



Example of amniotic fluid embolism

Figure A: Proposed Pathophysiology of Amniotic Fluid Embolism (AFE)

Click each box for more information.

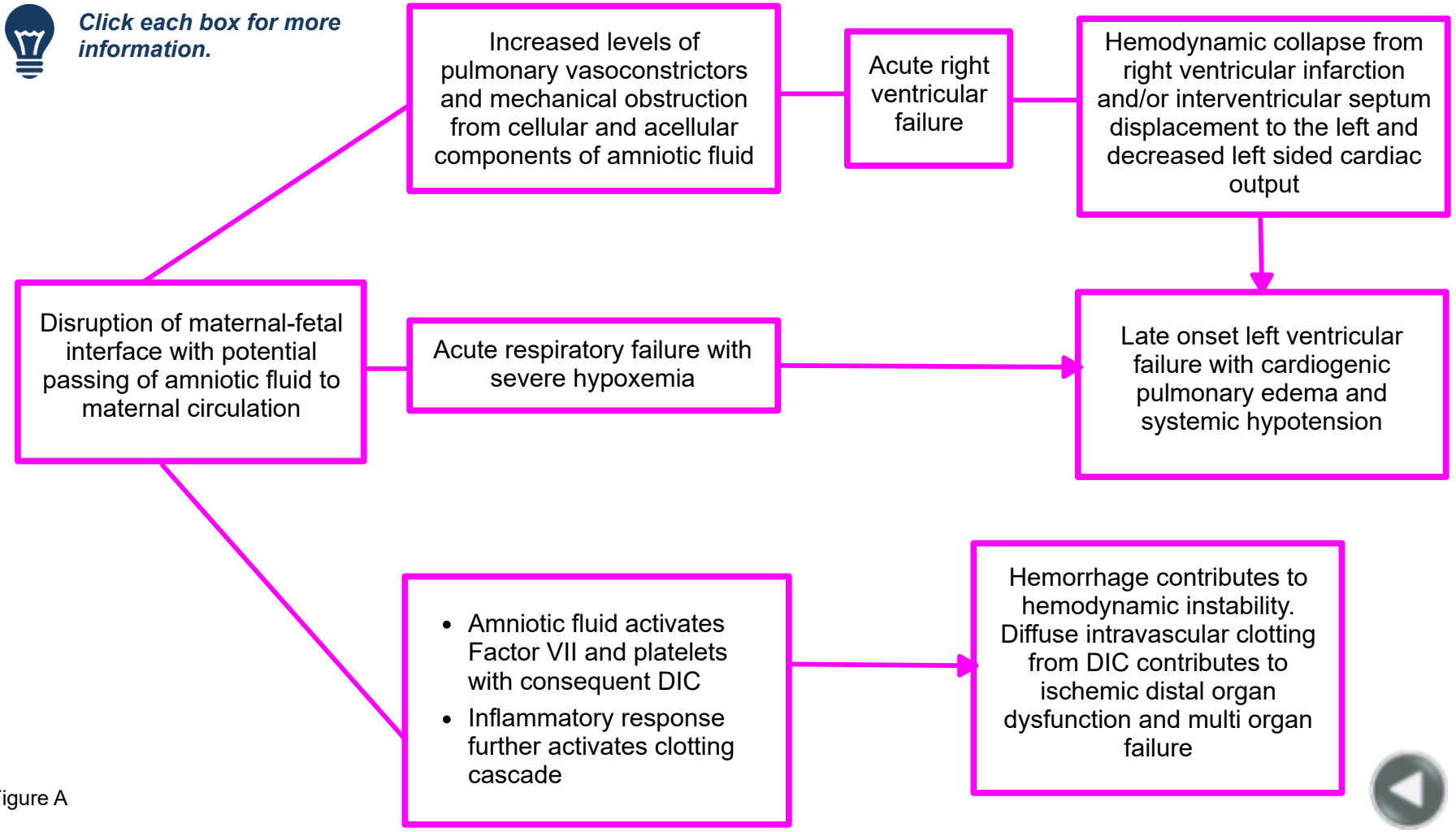
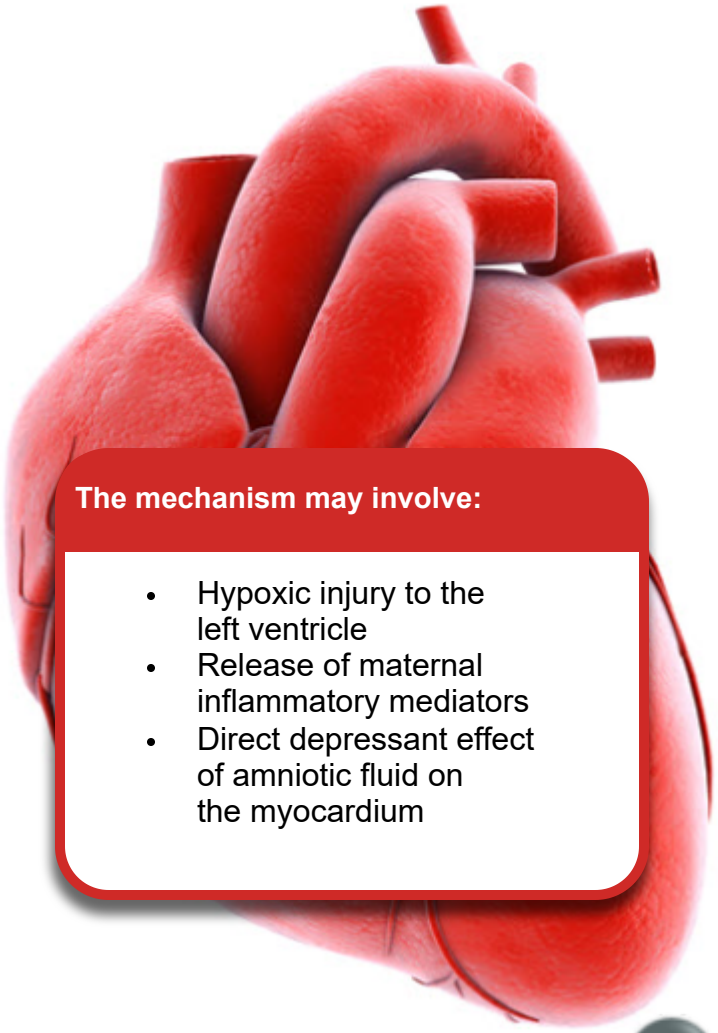


Figure A

- Amniotic fluid has been shown to cause occlusion and vasospasm of the maternal pulmonary vasculature with animal studies, resulting in rapid development of pulmonary hypertension, acute cor pulmonale and systemic hypotension [15-17].
  - In women with AFE, invasive hemodynamic studies seem to contradict these animal studies [18,19].
  - When elevated pulmonary arterial pressure, elevated pulmonary capillary wedge pressure, decreased cardiac output and decreased cardiac index are combined, it suggests the principal hemodynamic alteration in humans is left ventricular failure, rather than pulmonary hypertension and right ventricular failure.

- To reconcile the human and animal observations, a biphasic pattern of cardiogenic shock in AFE has been proposed [2,15,19].
- Initial acute pulmonary hypertension and right ventricular failure (usually lasting 15-30 minutes), according to the hypothesis, is followed by left ventricular dysfunction [20,21].
- Studies utilizing transesophageal echocardiography to non-invasively measure the hemodynamic parameters early during AFE, demonstrate vasospasm of the pulmonary vasculature, elevated pulmonary arterial pressure and right ventricular failure, thus supporting the bi-phasic hypothesis [20,21].
- The late phase of left ventricular dysfunction is poorly understood.



Mouse over the heart to see what the mechanism may involve.

- Among patients with AFE, hypoxemia is the most common manifestation of the resultant respiratory failure.
- Hypoventilation can also occur.
- The primary cause of hypoxemia involves severe ventilation/perfusion (V/Q) mismatching.

Factors contributing to the V/Q mismatch [2] :

- Acute pulmonary hypertension during the first phase of cardiogenic shock
- Cardiogenic pulmonary edema during the second phase

Other contributors may include [8, 22] :

- Bronchospasm (about 15% of patients)
- Noncardiogenic pulmonary edema

- In 70% of patients who survive the first several hours, noncardiogenic pulmonary edema occurs [22].
- It generally develops as left ventricular dysfunction improves.
- Damage to the endothelial-alveolar membrane and capillary leak syndrome likely to lead to to high protein concentration in edematous fluid and the presence of amniotic debris in sputum and alveolar spaces.
- Widespread damage to the alveolar-capillary membrane causes non-cardiogenic edema to occur in AFE; it usually does not produce the clinical pattern typical of acute respiratory distress syndrome (ARDS).
- Women who survive the first few hours of AFE usually recover quite rapidly, whereas the course of ARDS tends to be protracted.

- Obstruction of the pulmonary vasculature seems unlikely to be the lone cause of AFE, since there is often a lag of many hours between the entry of amniotic fluid into the the maternal circulation and onset of symptoms and signs of AFE.
- Propositions have brought up how the lag may reflect evolution of AFE as an immunologic response or inflammatory reaction to the amniotic fluid.
- Support is evident by reports of decreased complement and increased inflammatory markers in some patients with AFE, including elevated serum tryptase levels and pulmonary mast cell activity [23-28].
- It is hypothesized that AFE is caused by a breach in the normal physiologic barrier between the mother and fetus.
- The clinical manifestations and the severity may be related to the degree of immunologic stimulation or the balance of arachidonic acid metabolites such as leukotrienes in the amniotic fluid [29,30].

- The symptoms and signs associated with AFE have a typical onset during labor and delivery, or immediately postpartum [2].
- In rare instances, it has been reported following first or second trimester abortion, amniocentesis, or abdominal/uterine trauma, and as late as 48 hours after cesarean delivery or post partum, [8, 31-35].
- Most women present with rapid cardiorespiratory collapse [10].
- Preceding the onset of dyspnea and hypotension may be nonspecific symptoms such as chills, nausea, vomiting and agitation [8,10].
- A less severe presentation of AFE, may present with only some of the major symptoms and signs [15,36,37].
    - These patients with partial AFE generally present with sudden onset of milder dyspnea and hypotension.
    - In this situation, the clinical course tends to be abbreviated and the prognosis much better compared to those who have the full syndrome.

The major clinical findings are the abrupt and fulminant onset of:

Click the terms in blue to learn more.

- **Hypotension due to cardiogenic shock**
- **DIC**
- **Hypoxemia and respiratory failure**
- **Coma or seizures**

- A prominent feature of AFE is hypotension due to cardiogenic shock.
- When AFE occurs in women, approximately 85% die from cardiogenic shock or its complications [10].
- The management of cardiogenic shock may be complicated by cardiac dysrhythmias.
- The cardiac dysrhythmia could include pulseless electrical activity, bradycardia, ventricular fibrillation, and asystole [8].
- Management of the cardiogenic shock and dysrhythmias is supportive.

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- A common early finding of AFE is profound hypoxemia.
- Hypoxemia is most commonly detected by pulse oximetry, but clinical findings include confusion, agitation, somnolence, dyspnea, tachycardia, tachypnea, cyanosis, and acidemia.
- Evidence may include crackles and radiographic air space disease when cardiogenic or noncardiogenic pulmonary edema is present.
- Wheezing is occasionally detected.
- Approximately 50% of the deaths are caused by profound hypoxemia and occur within the first hour of the AFE.
- Prolonged hypoxemia may lead to permanent, severe neurologic impairment or maternal brain death [8].

The major clinical findings are the abrupt and fulminant onset of:

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- Nearly 80% of women with AFE develop DIC [1,2,8].
- DIC can begin 10-30 minutes after the onset of cardiopulmonary signs and symptoms. However, DIC may also be delayed by as many as four hours [2,38-41].
- The most common manifestations of DIC are prolonged bleeding from sites of invasive interventions, such as intravenous (IV) sites, and bruising.
- However, in some cases, major hemorrhage may be the clinical manifestation.
- When hemorrhage occurs, it can delay the diagnosis of AFE since an exhaustive search for structural causes of hemorrhage will likely occur [42].

The major clinical findings are the abrupt and fulminant onset of:

Click the terms in blue to learn more.

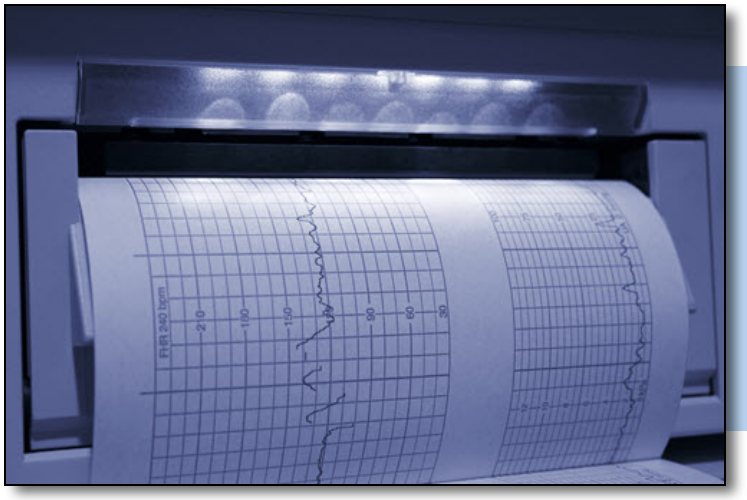
- Hypotension due to cardiogenic shock
- DIC
- Hypoxemia and respiratory failure
- **Coma or seizures**

Encephalopathy (which may progress to a coma) associated with AFE is thought to be secondary to hypoxia and includes a spectrum of symptoms ranging from altered mental state to seizures. Tonic-clonic seizures are seen in 10-50% of patients [55].

AFE is diagnosed based on the collection of clinical findings, rather than isolated signs and symptoms.

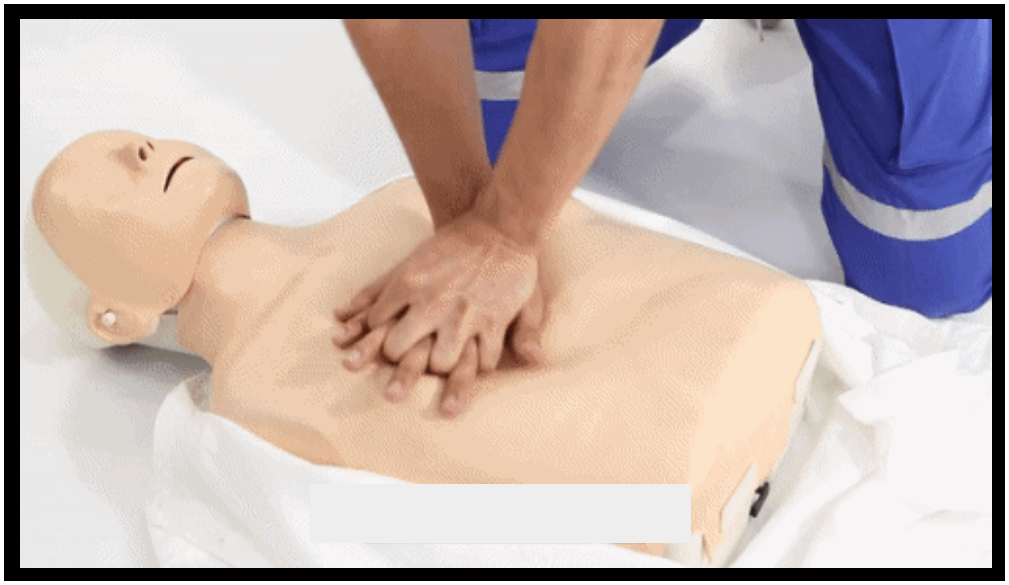
- AFE should be suspected whenever shock and/or respiratory compromise develops during labor or immediately postpartum.
- Other causes of sudden intrapartum or postpartum cardiorespiratory failure must be excluded.
- Amniotic fluid debris is common in maternal circulation without AFE, so finding the amniotic fluid debris alone should not be considered diagnostic [43].

- There is no specific treatment for AFE.
- The therapeutic goal is to correct hypoxemia and hypotension so that ischemic consequences (i.e. hypoxic brain injury, acute kidney injury) are prevented in the mother and adequate oxygen delivery occurs to the fetus.



- Monitoring of maternal oxyhemoglobin saturation, heart rate and rhythm, and respiratory rate should be immediately initiated in all patients with suspected AFE.
- It is important to monitor the blood pressure non-invasively at frequent intervals until continuous blood pressure monitoring is established.
- Continuous monitoring of the fetal heart rate is recommended.

High quality cardiopulmonary resuscitation (CPR) in pregnancy is needed.



Components [56]:

- rapid chest compressions (100 times per minute)
- perform hard compressions, achieving a depth of at least 2 inches
- assure adequate chest recoil between compressions
- minimize interruptions of chest compressions
- avoid prolonged pulse checks (5-10 seconds at the most)
- switch provider of compressions every 2 minutes to avoid fatigue
- lateral displacement of uterus during resuscitation.

- If the patient is not delivered, the maternal oxygen status dictates fetal oxygen status.
- The delivery of fetal oxygen is directly related to umbilical vein oxygen tension, umbilical vein oxyhemoglobin saturation, fetal hemoglobin concentration, and maternal cardiac output.
- Healthy pregnant women have increased fetal hemoglobin concentration and maternal cardiac output. These compensate for low umbilical vein oxygen tension, so as to maintain sufficient fetal oxygen delivery.
- In the setting of a birth center, having an AED may be beneficial to apply. Certainly, supplemental oxygen use, if available, to keep the SpO2 >95%.

For those delivering within hospitals:

- For women who are intravascularly normovolemic or hypervolemic, a vasopressor is the preferred initial therapy.
- If the intravascular volume is unknown, it is recommended to begin empiric therapy with a vasopressor.
  - This recommendation is based on the observations showing hypotension in AFE is almost always due to cardiogenic shock and coexisting intravascular hypovolemia is rare.

- When vasopressor therapy is warranted, norepinephrine and dopamine are the typical drugs of first choice.
- The inotrope, dobutamine, may be added and would likely be beneficial since it increases the low cardiac output and decreases the high afterload that is characteristic of cardiogenic shock.
- However, until the vasopressors have improved blood pressure, dobutamine should not be used.
- Dobutamine, when used alone, tends to reduce blood pressure by causing a drop in the systemic vascular resistance that is out of proportion to the increase in cardiac output.

Vasoactive Drugs

Vasopressors

Stimulates smooth muscle contraction of the capillaries & arteries

↓

Vasoconstriction

Ionotropes

Increase the force of contraction of myocardial muscle

↓

Positive ionotropism

↓ ↓

Rise in Mean Blood Pressure

↓

Improved tissue perfusion and oxygenation

- Vasopressors are used to treat hypotension in AFE even though they may diminish uteroplacental perfusion pressure.
- The rationale is that untreated shock diminishes uteroplacental perfusion pressure and has numerous additional potential adverse consequences.

These include:

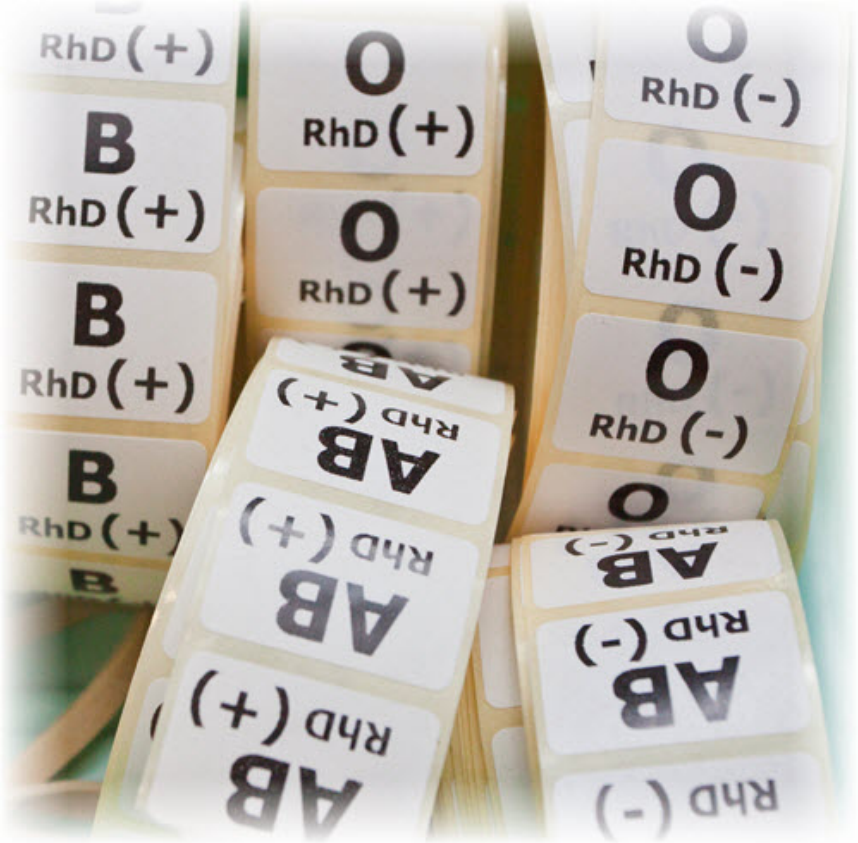
- Decreasing fetal oxygen delivery
- Increasing the mother's risk of ischemic complications
- Acute kidney injury
- Hypoxic brain injury
- Increasing mother's risk of death

IV Fluids

- Pulmonary edema is common in AFE so a cautious approach is necessary whenever a trial of IV fluid is selected.
- When IV fluid is given, it is necessary to be administered in small boluses with recurrent assessment being required.
- The IV fluids should be discontinued when the intravascular volume has been replenished.
- The IV fluids should be promptly discontinued when new or worsening pulmonary edema occurs.
- When the pulmonary edema worsens with a trial of IV fluids, these women should be regarded as having uncertain intravascular volume and may be better managed with vasoactive agents.

The development of DIC is common in the setting of AFE. If DIC is noted, massive transfusion protocols should be administered as supportive care.

For those delivering outside a hospital, while waiting for the patient transfer, monitoring for bleeding is key. DIC should be suspected when bleeding occurs from places such as IV sites.

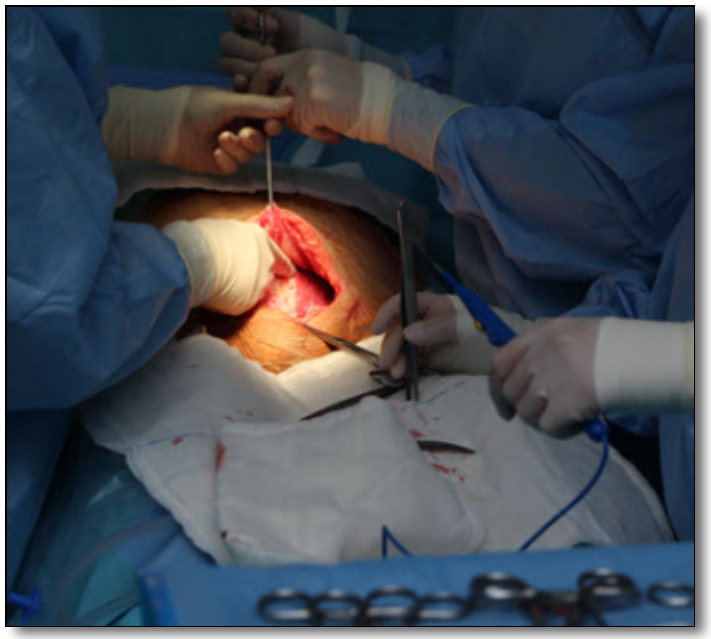


When AFE presents intrapartum, the need for immediate delivery must be determined.

Need for immediate delivery is determined on an individual basis; however, factors supporting delivery include:

- Non-reassuring fetal heart race tracing
- Rapid and progressive deterioration of the mother's condition
- The opinion that delivery of the fetus may facilitate maternal resuscitative efforts
- If the cervix is fully dilated and the fetal head is +2 station, operative vaginal delivery should be considered
- Otherwise, an emergency cesarean delivery is indicated.

- Consideration for peri-mortem cesarean is warranted when shock and cardioplumonary resuscitative efforts fail to restore maternal circulation.
- Because brain damage begins at 5 minutes of anoxia, the procedure should be initiated at 4 minutes to deliver the healthiest fetus.
- If a mother has a resuscitatable cause of death, then her life may be saved as well by a prompt and timely cesarean delivery during CPR.
- Sadly, the clinicians are too often paralyzed by the horror of the maternal cardiac arrest and instinctively CPR is performed too long before turning to the perimortem delivery.
- This quick procedure may actually improve the situation for the mother and can potentially save the infant's life [45].



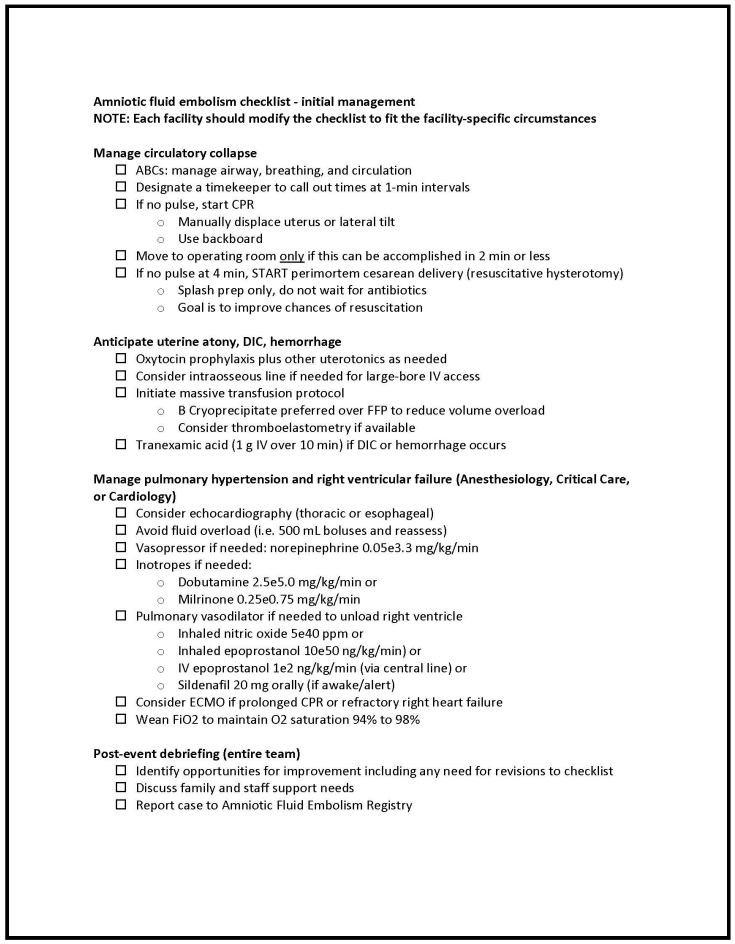
- There is significant risk of major maternal morbidity or death when a cesarean is performed in the presence of coagulopathy.
- Blood, fresh frozen plasma, platelets, and cryoprecipitate should be available and administered if there is any evidence of impaired coagulation:
  - Persistent bleeding without clotting from the incision
  - Needle site bleeding

- Maternal mortality rate due to AFE has been reported between 10 to 90% [1,7,8,50-53], although more recent data suggest overall mortality rates may be closer to 20 percent [7,11,12].
- Even those surviving AFE generally have a poor outcome with as many as 85% suffering significant neurologic injury due to cerebral hypoxia [2,8].
- AFE is one of the leading causes of maternal mortality and is reported to cause ten percent of all maternal deaths in developed countries [53].

The Society of Maternal Fetal Medicine (SMFM) [57] has a checklist with further information to delineate what needs to be modified for each facility.

Here is a sample:

Click on the picture to download a copy of the checklist.



Amniotic fluid embolism checklist - initial management
NOTE: Each facility should modify the checklist to fit the facility-specific circumstances

Manage circulatory collapse
- ☐ ABCs: manage airway, breathing, and circulation
- ☐ Designate a timekeeper to call out times at 1-min intervals
- ☐ If no pulse, start CPR
  - ○ Manually displace uterus or lateral tilt
  - ○ Use backboard
- ☐ Move to operating room only if this can be accomplished in 2 min or less
- ☐ If no pulse at 4 min, START perimortem cesarean delivery (resuscitative hysterotomy)
  - ○ 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
  - ○ B Cryoprecipitate preferred over FFP to reduce volume overload
  - ○ Consider thromboelastometry if available
- ☐ Tranexamic acid (1 g IV over 10 min) if DIC or hemorrhage occurs

Manage pulmonary hypertension and right ventricular failure (Anesthesiology, Critical Care, or Cardiology)
- ☐ Consider echocardiography (thoracic or esophageal)
- ☐ Avoid fluid overload (i.e. 500 mL boluses and reassess)
- ☐ Vasopressor if needed: norepinephrine 0.05e3.3 mg/kg/min
- ☐ Inotropes if needed:
  - ○ Dobutamine 2.5e5.0 mg/kg/min or
  - ○ Milrinone 0.25e0.75 mg/kg/min
- ☐ Pulmonary vasodilator if needed to unload right ventricle
  - ○ Inhaled nitric oxide 5e40 ppm or
  - ○ Inhaled epoprostanol 10e50 ng/kg/min) or
  - ○ IV epoprostanol 1e2 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% to 98%

Post-event debriefing (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

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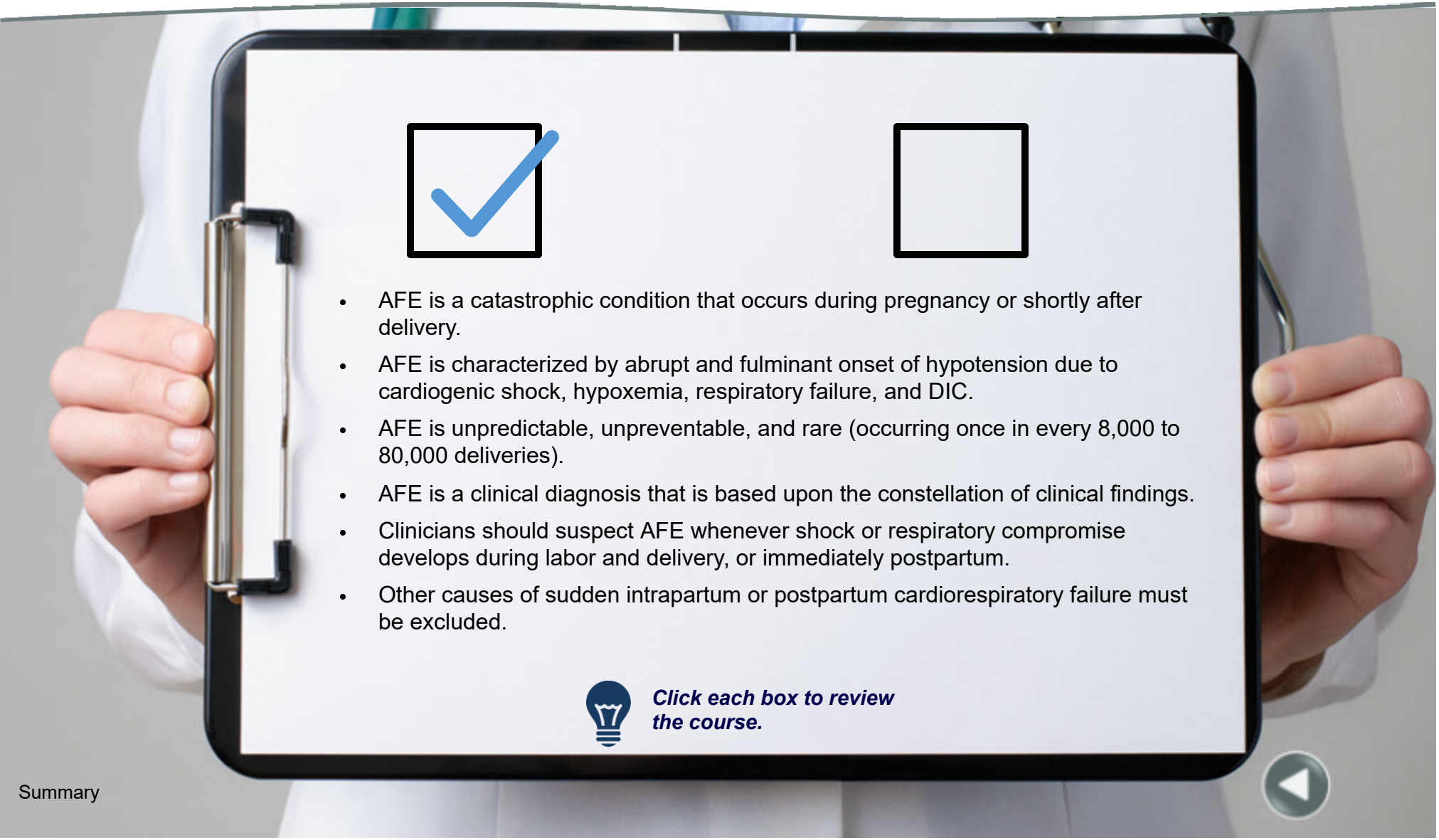
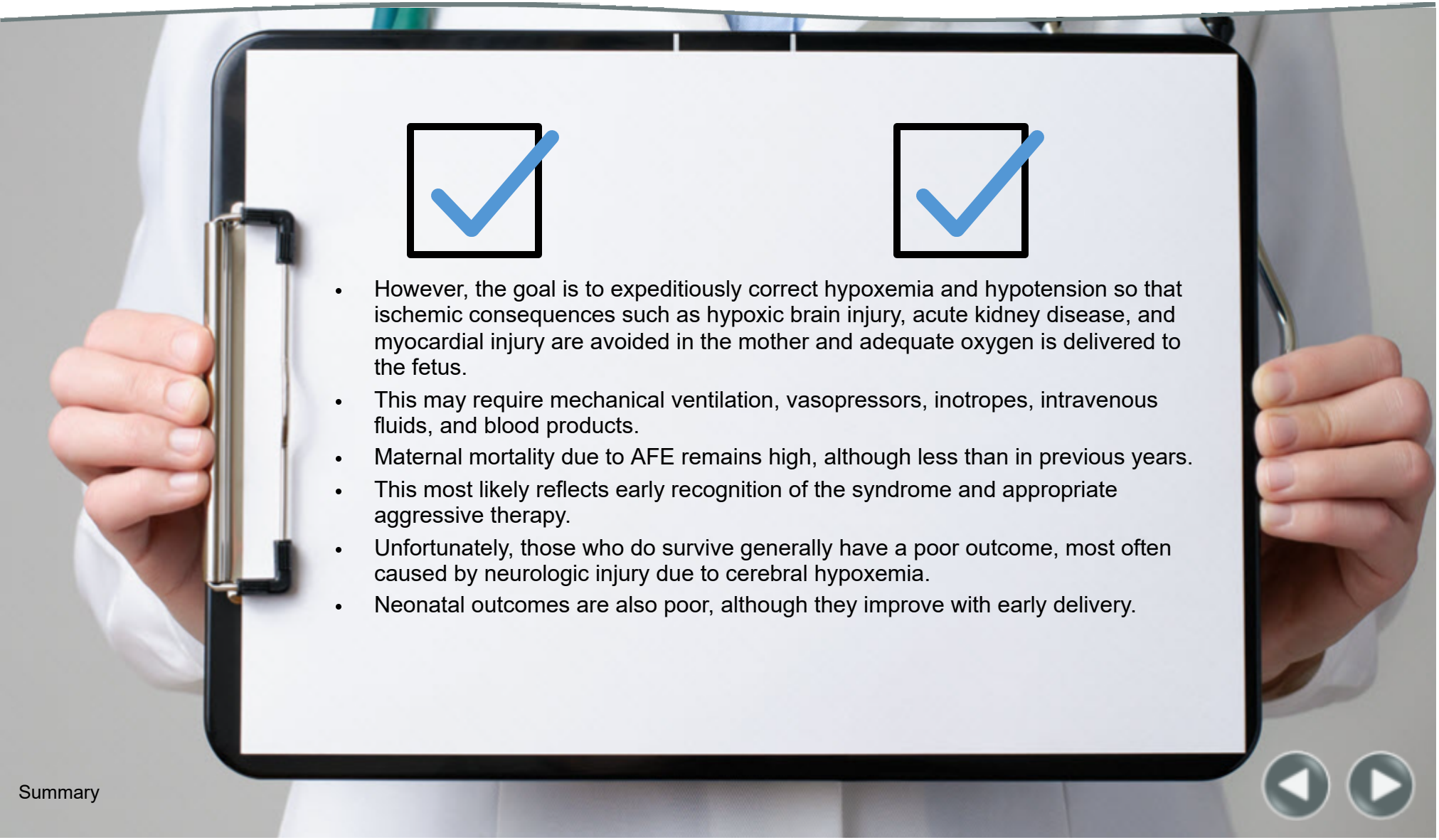


- AFE is a catastrophic condition that occurs during pregnancy or shortly after delivery.
- AFE is characterized by abrupt and fulminant onset of hypotension due to cardiogenic shock, hypoxemia, respiratory failure, and DIC.
- AFE is unpredictable, unpreventable, and rare (occurring once in every 8,000 to 80,000 deliveries).
- AFE is a clinical diagnosis that is based upon the constellation of clinical findings.
- Clinicians should suspect AFE whenever shock or respiratory compromise develops during labor and delivery, or immediately postpartum.
- Other causes of sudden intrapartum or postpartum cardiorespiratory failure must be excluded.

Click each box to review the course.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However, the goal is to expeditiously correct hypoxemia and hypotension so that ischemic consequences such as hypoxic brain injury, acute kidney disease, and myocardial injury are avoided in the mother and adequate oxygen is delivered to the fetus.
This may require mechanical ventilation, vasopressors, inotropes, intravenous fluids, and blood products.
Maternal mortality due to AFE remains high, although less than in previous years.
This most likely reflects early recognition of the syndrome and appropriate aggressive therapy.
Unfortunately, those who do survive generally have a poor outcome, most often caused by neurologic injury due to cerebral hypoxemia.
Neonatal outcomes are also poor, although they improve with early delivery.
Summary

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Congratulations!

You have successfully completed this module.

Click on the above 'X' to take the post-test for this course.
If you do not attain a passing score after two attempts at the post-test the entire program must be repurchased.

1. Gilmore DA, Wakim J, Secrest J, Rawson R. Anaphylactoid syndrome of pregnancy: a review of the literature with latest management and outcome data. AANA J 2003; 71:120.

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