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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. AFE is a detrimental disease process that is life threatening for the women it effects. The AFE module will provide knowledge for this low occurring process.

Approximate Time to Complete: 40 minutes

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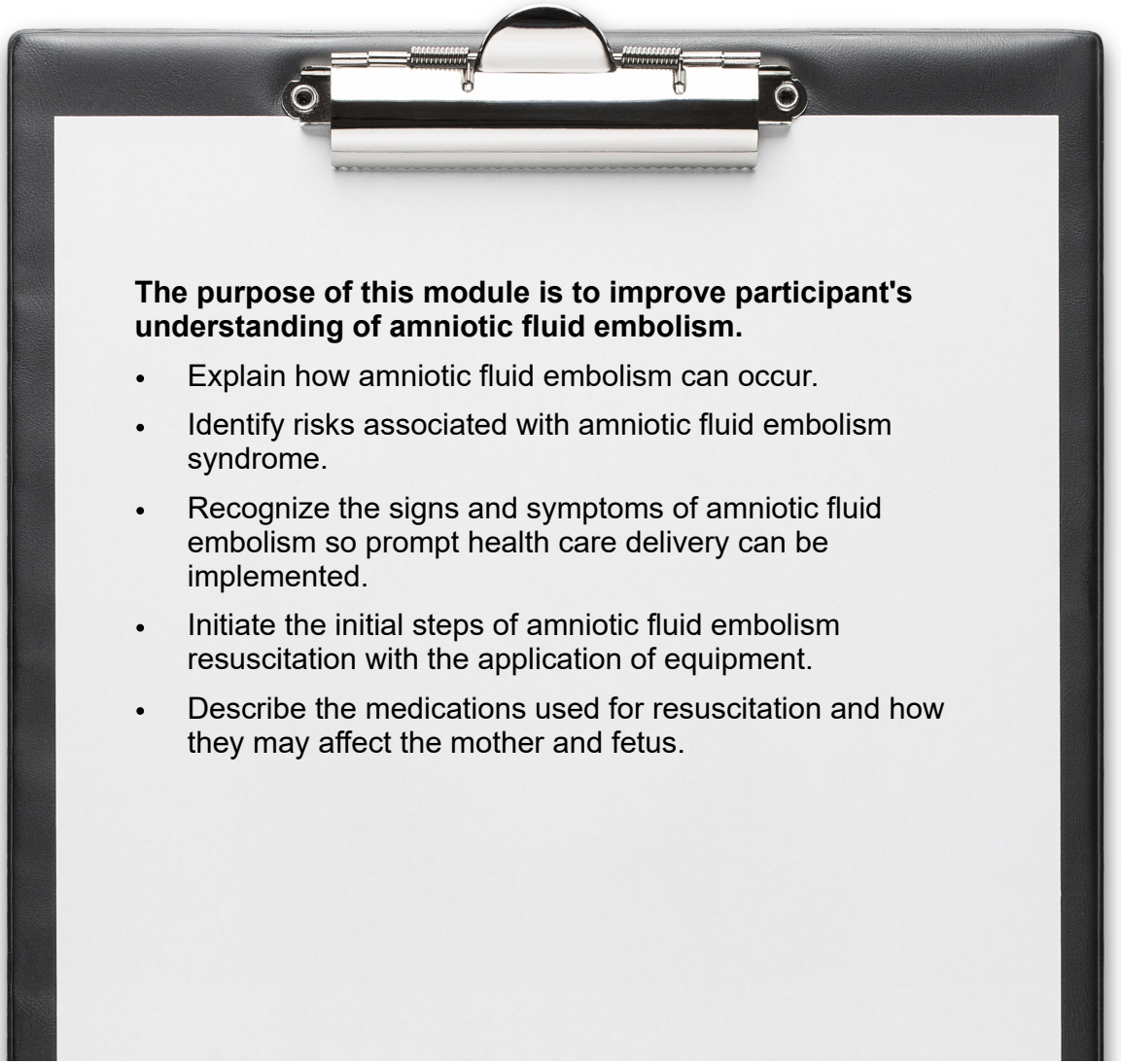

The purpose of this module is to improve participant's understanding of amniotic fluid embolism.

- Explain how amniotic fluid embolism can occur.
- Identify risks associated with amniotic fluid embolism syndrome.
- 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.

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- Amniotic Fluid Embolism
  - AFE
  - Occurrence
  - Risk Factors
  - Etiology
- Symptoms and Clinical Presentation
  - Cardiogenic Shock
  - Respiratory Failure
  - Inflammation
  - Clinical Presentation
- Diagnosis and Management
  - Diagnosis
  - Management
  - Invasive Monitoring
  - Oxygen
  - Hemodynamics
  - Vasoactive Agents
  - IV Fluids
  - Blood Products
  - Delivery
  - Prognosis and Complications
- Summary
  - Summary
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Amniotic Fluid Embolism (AFE)

- *A rare, sporadic, unpredictable condition that can occur in pregnancy or immediately postpartum that can lead to cardiovascular collapse [1-3].*
- *Also called anaphylactiod syndrome of pregnancy.*

- 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 renals, liver, spleen, pancreas and brain [6].

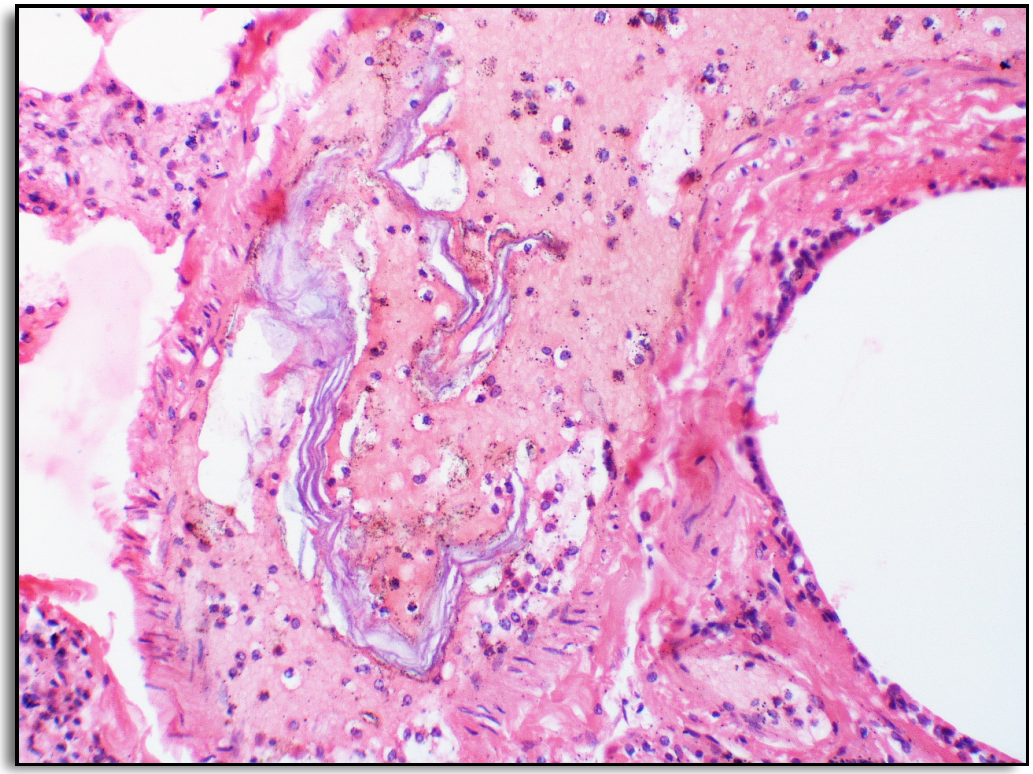
- The condition typically presents with hemodynamic and respiratory compromise in addition to disseminated intravascular coagulopathy.
- The incidence is between 1-12 cases per 100,000.

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.

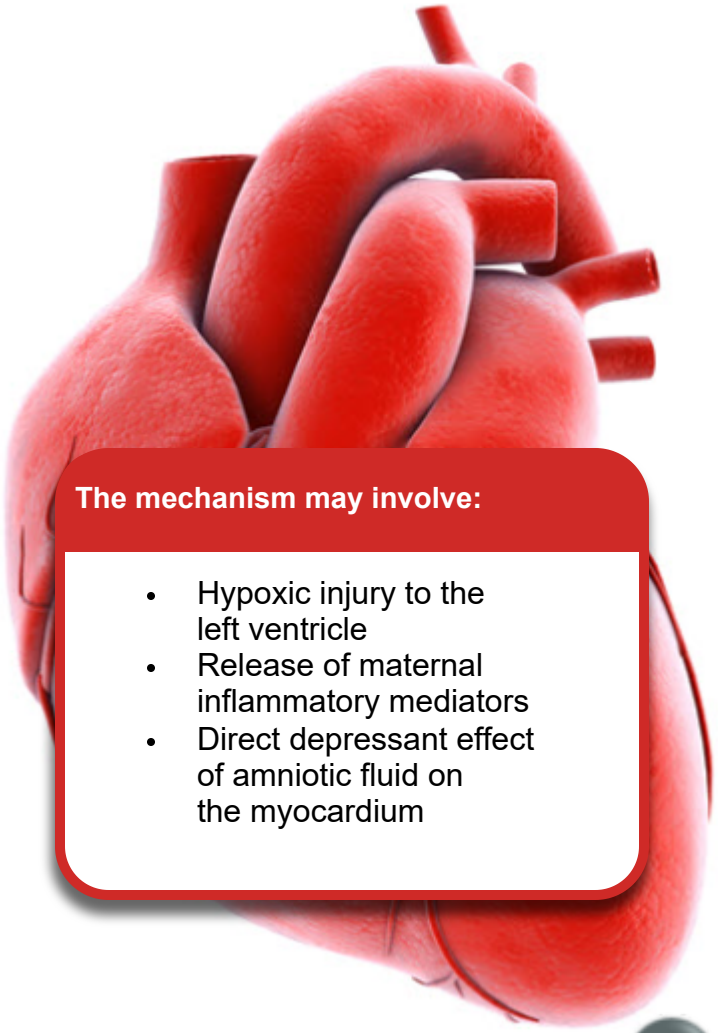
- The pathogenesis of AFE is thought to involve the amniotic fluid entering the maternal circulation through endocervical veins, the placental insertion site or a site of uterine trauma [14].
- Once the amniotic fluid reaches the maternal circulation, it can precipitate cardiogenic shock, respiratory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



Example of amniotic fluid embolism

- 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 AFES, 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 amniotic fluid embolism 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**
- **Disseminated intravascular coagulation (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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- Hypoxemia and respiratory failure
- Coma or seizures

- 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 disseminated intravascular coagulation (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 AFES since an exhaustive search for structural causes of hemorrhage will likely occur [42].

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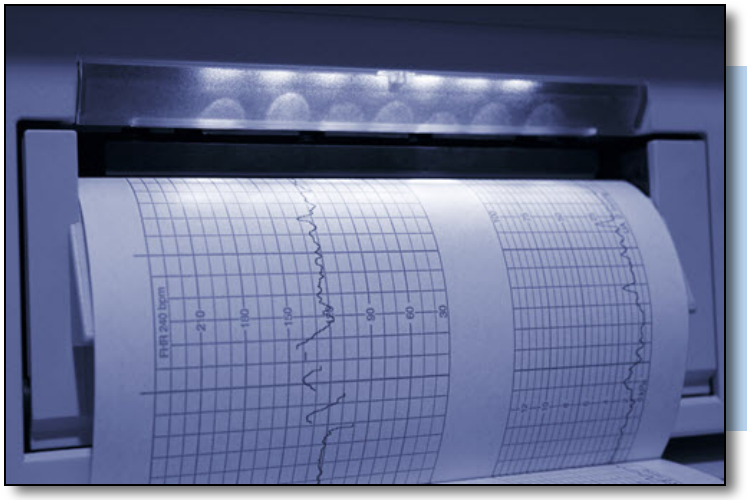
- Disseminated intravascular coagulation (DIC)
- Hypoxemia and respiratory failure
- **Coma or seizures**

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 collective 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.

Invasive Monitoring

- As clinical suspicion for AFE arises, plans should be made for both an arterial and a central venous catheter to be inserted.
- Additional management measures should not be delayed for catheter insertion as these procedures can be time consuming.
- An arterial catheter can be used to continuously monitor blood pressure.
- It also provides access to arterial blood for frequent measurement of arterial blood gases.

Invasive Monitoring

The central venous catheter can be used to:

- Infuse IV fluids
- Infuse medications (i.e. vasopressors, inotropics, etc.)
- Infuse blood products
- Draw venous blood
- The central line can be used for limited hemodynamic monitoring by measuring the central venous pressure and the central venous oxyhemoglobin saturation.

Invasive Monitoring

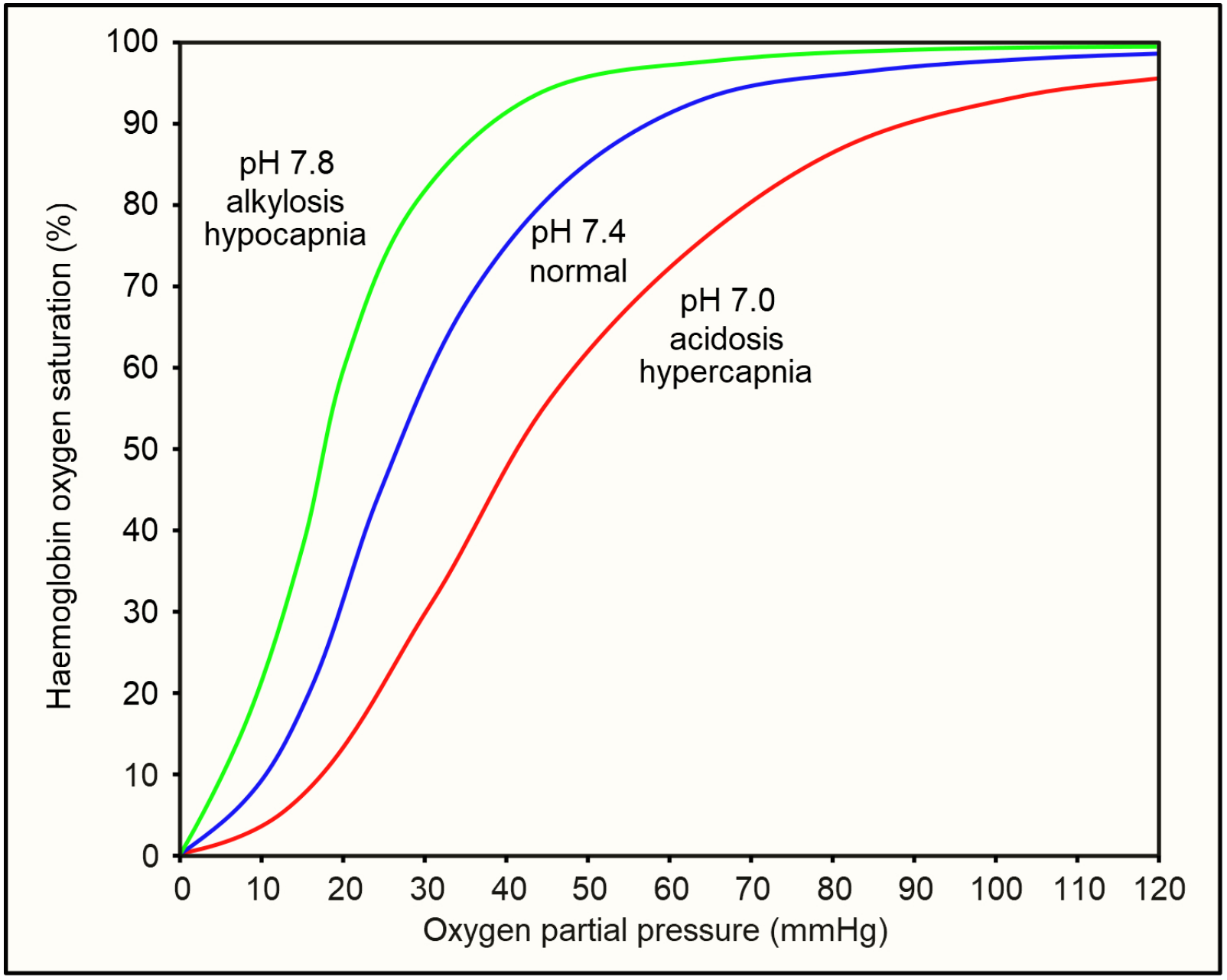
- Hemodynamic monitoring via a pulmonary arterial catheter should not be performed routinely.

- Supplemental oxygen should be provided to all patients.
- Reaching a maternal oxygen tension (PaO2) above 65 mmHg is a reasonable goal.
- To reach this goal, it often requires high flow rates of supplemental oxygen by facemask or invasive mechanical ventilation.
- If mechanical ventilation is required, the following parameters can be adjusted:
  - Increasing the fraction of inspired oxygen
  - Increasing the positive end-expiratory pressure
  - Prolonging or inversing the inspiratory to expiratory ratio.
  - Due to the associated high risk of aspiration, non-invasive positive pressure ventilation should be avoided during pregnancy.

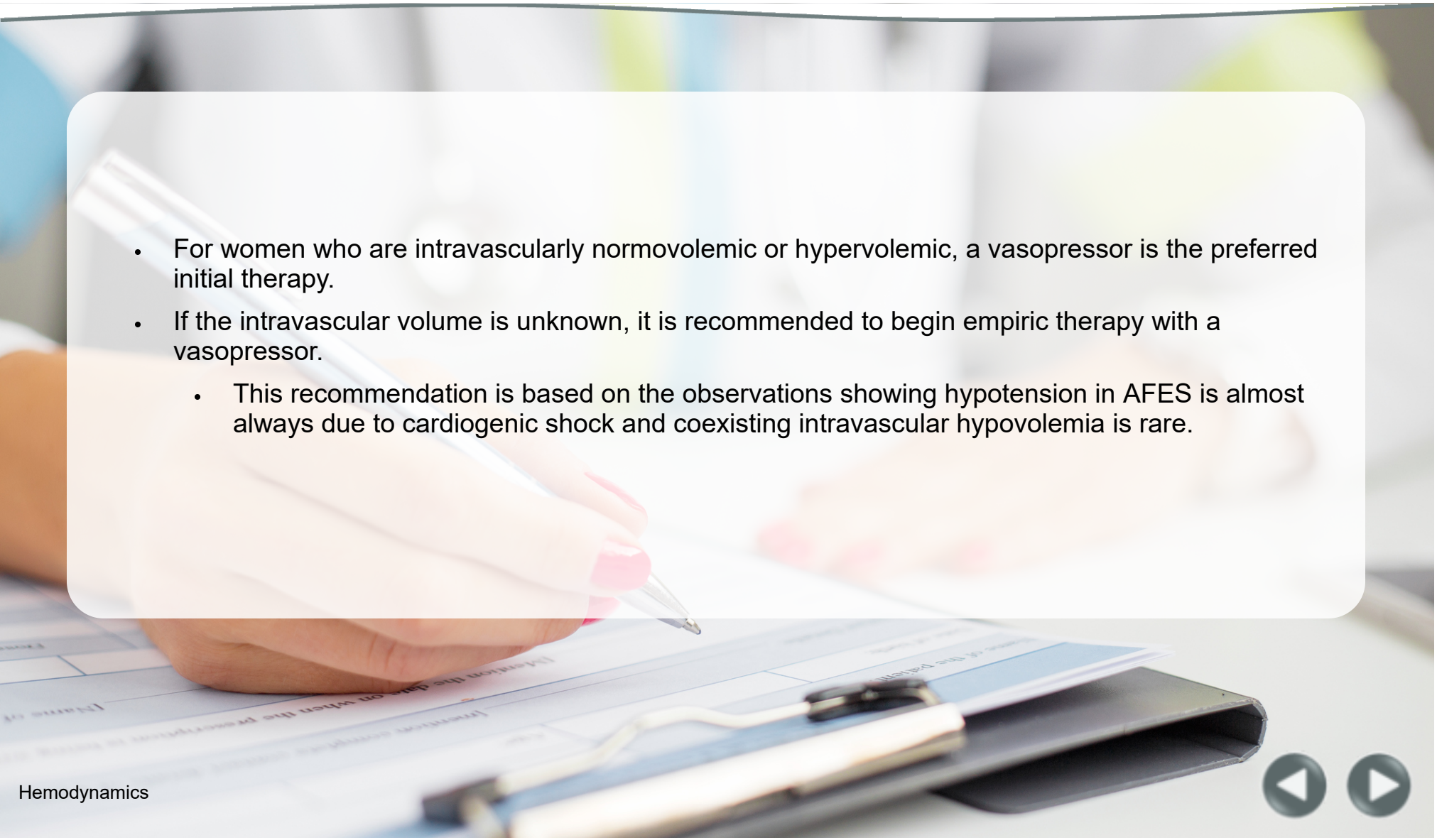
- Factors impairing oxygen delivery to the fetus such as anemia or diminished cardiac output should be corrected.
- This may involve red blood cell transfusions and inotropic agents.
- If the woman has delivered, these factors (i.e. anemia, dimished cardiac output) should be corrected if there is evidence of persistent hypoperfusion despite optimization of the PaO2.
- Common signs of hypoperfusion include:
  - Cool, vasoconstricted skin due to redirection of blood flow to core organs (however, warm flushed skin may be present early on in phases of sepsis)
  - Obtundation or restlessness
  - Oliguria or anuria
  - Lactic acidosis

- It is, however, similar for women who have delivered, but the primary concern shifts from end organ oxygen delivery to delivery of oxygen for the fetus.
- If the patient is not delivered, the maternal oxygen status dictates fetal oxygen status.
- 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.

- The compensatory increase of fetal hemoglobin and maternal cardiac output may not be adequate to maintain the fetal oxygenation in pregnant women who have an even lower umbilical vein oxygen tension due to systemic hypoxemia.
- The level has not been determined at which the compensatory mechanisms become inadequate for the degree of maternal hypoxemia.
  - In a study on exposing healthy pregnant women to low fractions of inspired oxygen, a maternal PaO_2 below 47mmHg was associated with a decline in umbilical vein oxygen tension [44].
  - This PaO_2 is on the steep portion of the hemoglobin dissociation curve, where small changes in PaO_2 may cause large changes in oxyhemoglobin saturation and oxygen delivery.
  - The maternal oxygen tension should be maintained at a level that lies on the flat portion of the hemoglobin dissociation curve (i.e. > 65mmHg). This is assuming there are no complicating abnormalities in maternal cardiac output, hemogobin or pH.



Peter Southwood [CC0]: https://commons.wikimedia.org/wiki/File:Oxygen-Haemoglobin_dissociation_curves.svg



- 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 AFES 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:

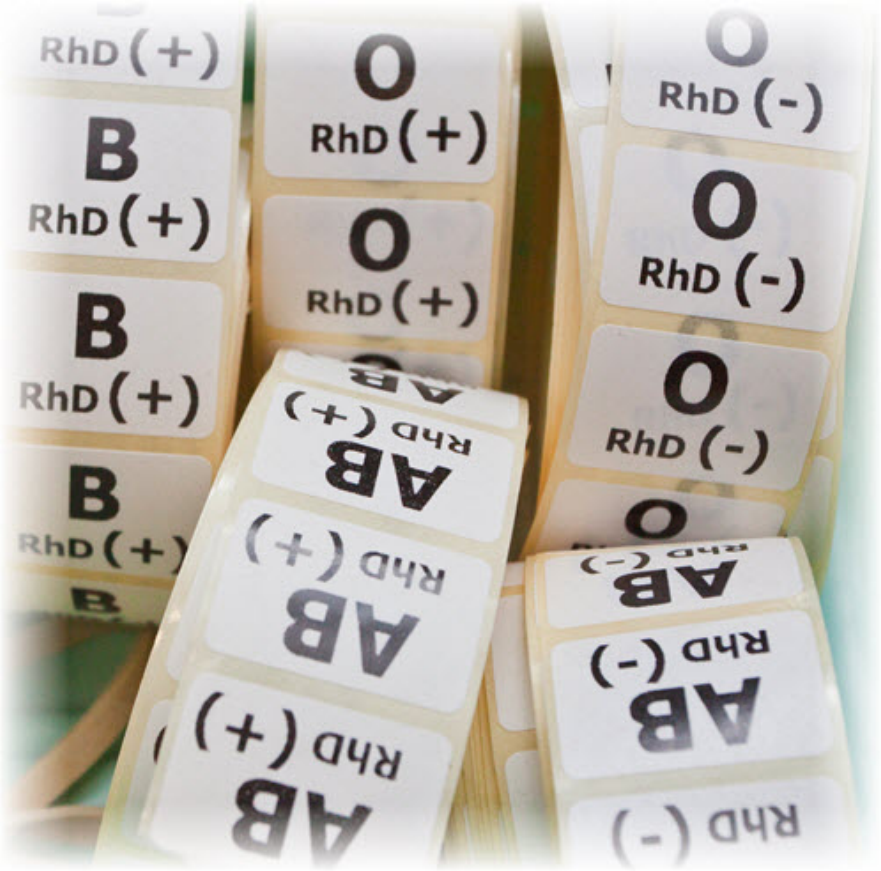
- Decreasing fetal oxygen delivery
- Increasing the mother's risk of ischemic complications
- Acute kidney injury
- Hypoxic brain injury
- Increasing mother's risk of death

IV Fluids

- Pulmonary edema is common in AFES 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.

Some studies have investigated the use of recombinant factor VIIa in the setting of AFE; however, the use of this product has unclear benefit and some studies have demonstrated worse outcomes.

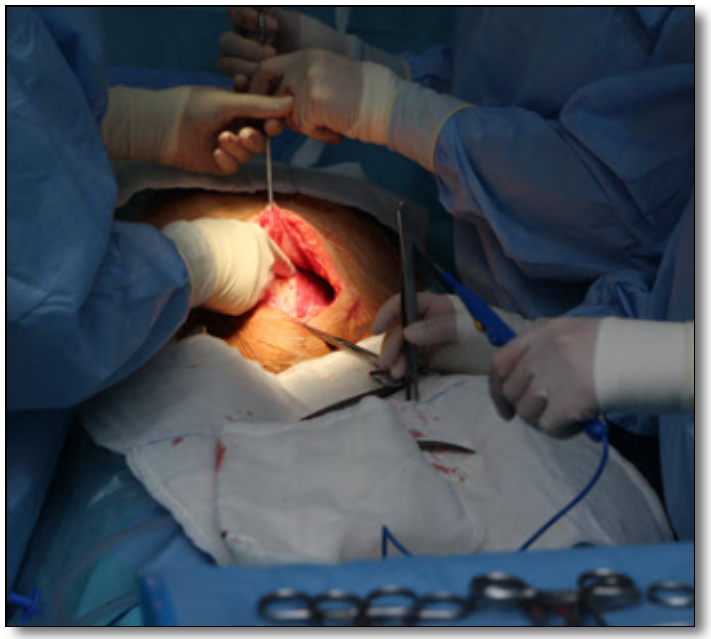


When AFE presents intrapartum, the need for immediate delivery must be determined.

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

Case reports have described novel interventions that have been successfully used in patients with AFE:

- A right ventricular device and inhaled nitric oxide have been used in patients with right ventricular failure and pulmonary hypertension [46,47].
- In patients with severe left ventricular failure and hypoxemia, the following have been utilized: cardiopulmonary bypass, intraaortic balloon pump counterpulsation and extracorporeal membrane oxygenation (ECMO) [21,48].
- The use of recombinant human factor VIIa (rVIIa) may be utilized when severe coagulopathy and bleeding, especially in those undergoing surgery to control postpartum hemorrhage. [47,49].
- Unfortunately, rVIIa use in AFE may be associated with thrombotic morbidity and mortality (i.e. stroke and pulmonary embolism).

Maternal | **Neonatal**

Click the blue buttons to learn more.

- Neonatal outcomes are also poor.
  - The mortality rate is estimated to be between 20 and 60% [8,9].
  - Only 50% of survivors are neurologically intact.
- When the mother sustains an an AFE-induced cardiac arrest, overall neonatal outcomes are improved with prompt delivery of the fetus [54].

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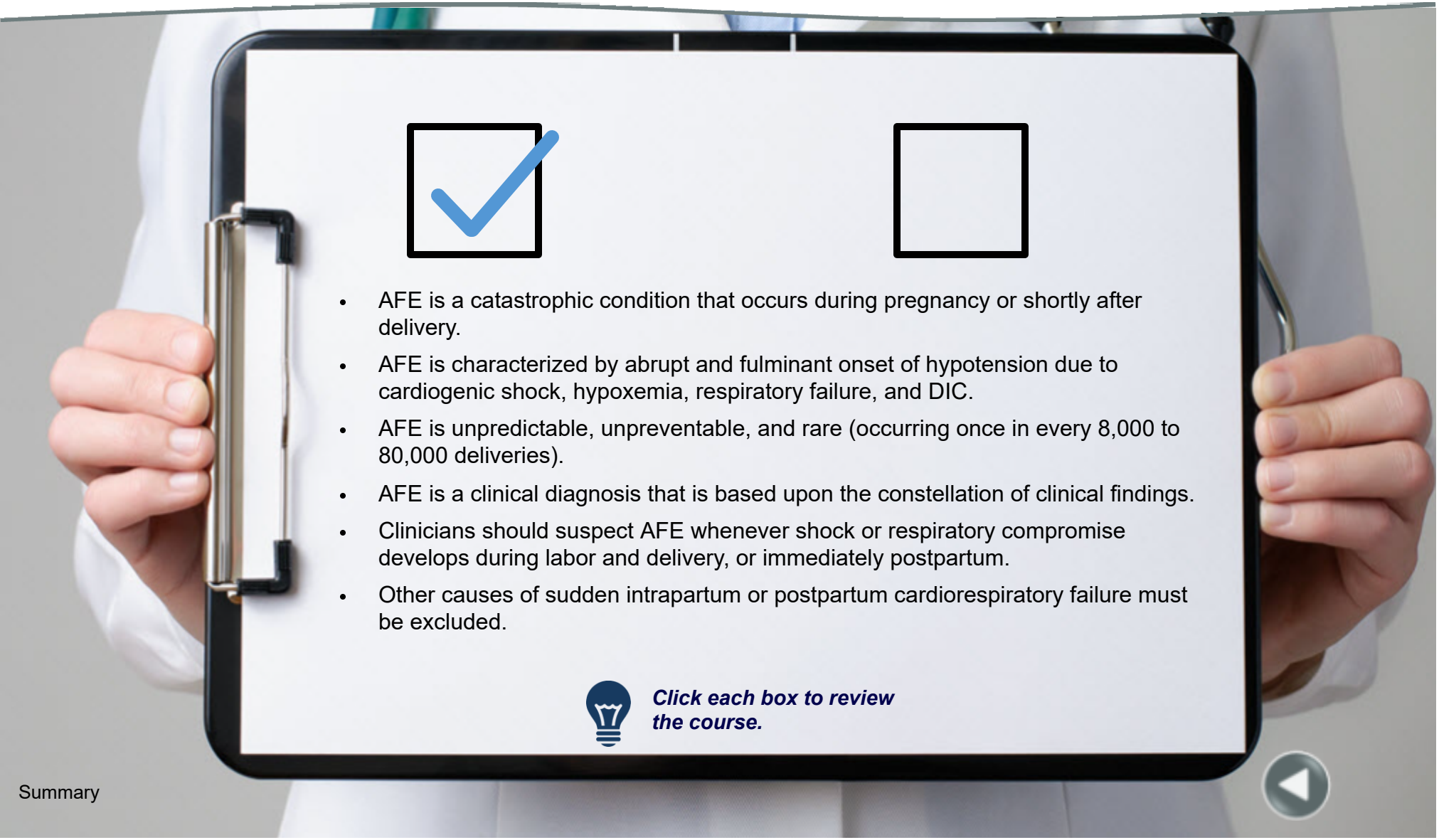
Maternal **Neonatal**

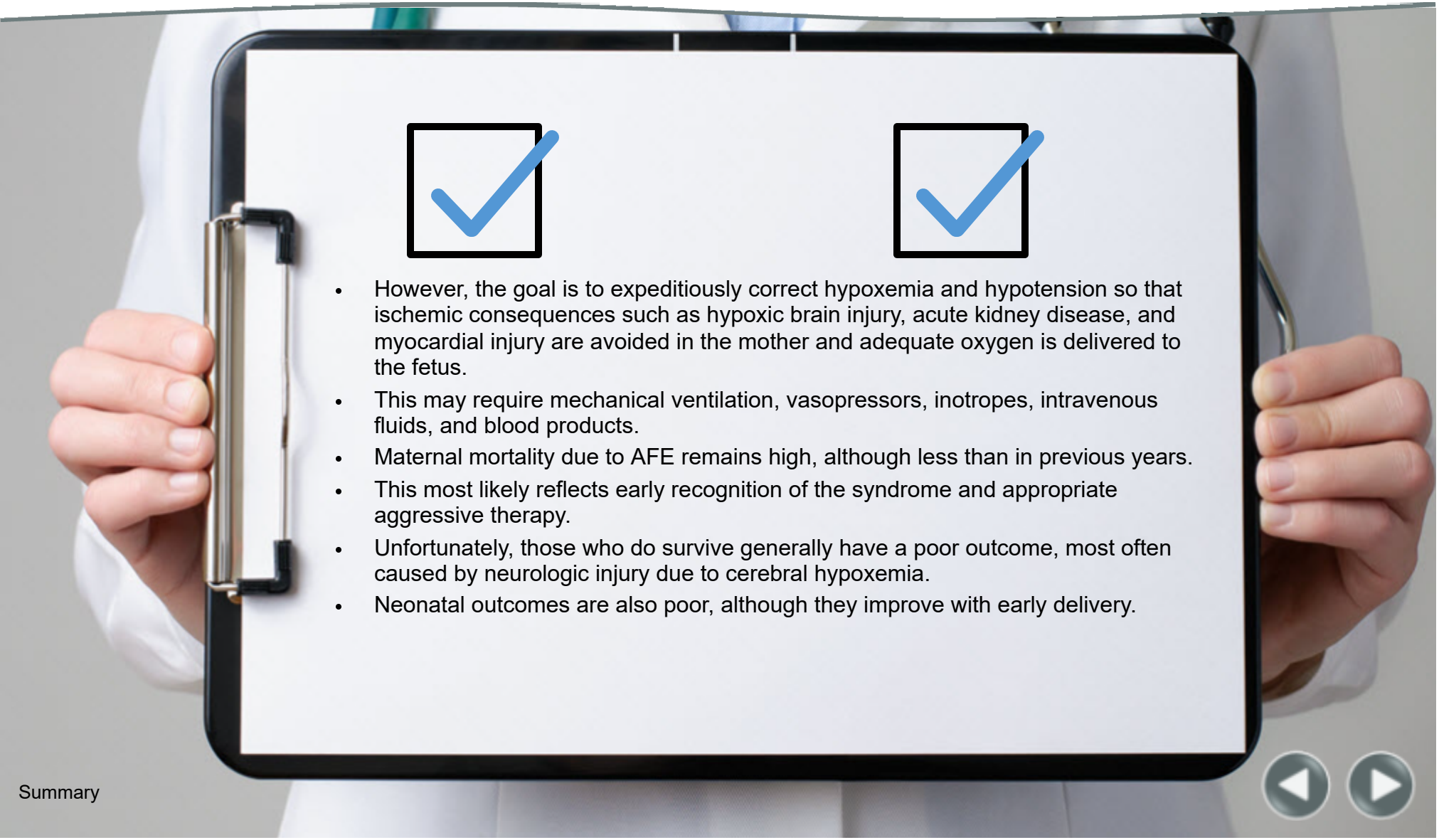
Click the blue buttons to learn more.

- Maternal mortality rate due to AFES 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 AFES generally have a poor outcome with as many as 85% suffering significant neurologic injury due to cerebral hypoxia [2,8].
- AFES is one of the leading causes of maternal mortality and is reported to cause ten percent of all maternal deaths in developed countries [53].



- 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.

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