AOK for AFE

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Amniotic fluid embolism (AFE)

- Life-threatening emergency\(^1\)
  - Embolism can occur at any time throughout pregnancy
  - Most typically occurs during:
    - Labor and vaginal delivery
    - Cesarean section delivery

- Mortality rate reported between 40-80%

- Because so little fetal material is embolized, chemical mediators are thought to be central to the body’s lethal response
Incidence

- 2-8:100,000 pregnancies\textsuperscript{1,6}

- Actual incidence is unknown due to inaccurate diagnoses and inconsistent reporting of nonfatal cases

- Approximately 4,000,000 pregnancies annually in the United States

\[
\frac{4,000,000}{100,000} \times (2, 8) = 40 - 320 \text{ AFE/yr}_{\text{United States}}
\]
Risk factors for AFE$^{2,3,4,5}$

- Multiparity
- Advanced maternal age
- Induction of labor
- Cesarean section
- Abruption
- Placenta previa
- Cervical laceration
- Uterine rupture
Symptoms of AFE

- Restlessness and/or confusion → decorticate posturing
- Dyspnea → cyanosis → respiratory arrest
- Cardiovascular
  - Hypotension
  - Arrhythmia
    - PEA (25%), bradycardia (20%), asystole, ventricular fibrillation, normal
- Uterine atony
- Consumptive coagulopathy (DIC)
  - Low fibrinogen and platelet count
  - High fibrin split products
  - Abnormal PT and PTT
- Fetal distress → fetal death
Review of decerebrate posturing

- Alpha and gamma motor neuron mediated rigidity
- Decerebrate posturing indicated that there is brainstem involvement
  - Particularly true with reticular formation and vestibulospinal tract
- Decerebration is commonly considered to be near-fatal
Small amount of fetal material embolizes pulmonary arteries
- Blood clot, marrow, fat, hair, etc

- **Pulmonary artery spasm**
- **Pulmonary hypertension**

  - Increased right ventricular pressure

  - **HYPOXIA**

    - Extends cardiac and pulmonary insult

      - **Left heart failure**
      - **Acute resp failure**

    - **Platelets degranulate**

      - **Serotonin released**
      - **Thromboxane A₂ released**

      - **Vagal response**

      - **Activation and aggregation of platelets**

      - **Amplification of hemostatic mechanisms**

- “Prior to labor, there were prominent changes in the myometrial fibers that reflected shearing, shrinkage, edema, and particularly apoptosis; endothelial cells of thin-walled vessels prominent in the biopsies displayed marked nuclear biotinylation, and the vascular lumen contained fibrin and platelet thrombi, microparticles, desquamated endothelial cells, amniotic squamous cells, and mucoid material.”

- Foreign material was present across samples from the study, indicating fetal-maternal transfer occurs commonly

- Logically, physiologic mediators must be involved
Seconds following amniotic fluid embolism, the patient begins to exhibit restlessness and confusion

- Impending sense of doom

Extreme dyspnea is apparent as the patient experiences pulmonary artery spasm and an acute increase in pulmonary artery pressures.
**Phase I:**

- RV pressures increase → leads to hypoxia
  - Manifested as cyanosis

**Phase II:**

- Cellular mediators released
  - Serotonin – increases pulmonary symptoms
  - Thromboxane A$_2$ – causes inappropriate clotting of blood

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Activation and aggregation of platelets

Vagal response

Amplification of hemostatic mechanisms
Analysis of vulnerable points

- Vagal response
- Serotonin
- Thromboxane A₂

ATROPINE
ONDANSETRON
KETOROLAC

AOK for AFE 😊
Case study 1

- 41 year old G₈P₃
- 39 week induction of labor
- Forceps delivery
- 31 min ACLS
- AOK for AFE
- Led to palpable pulse and stable vital signs at $T_{0+2\text{min}}$
- DIC began 1 hour later
- Survived with minimal neurological deficits
Case study 1

- Traditional CPR for 31 minutes
- AOK for AFE given

Heart rate (BPM) vs. Minutes

Persistent pulse and perfusion after AOK
Case study 2

- 28 year old, G$_2$P$_1$
- 39 week elective Cesarean
- Following uterine incision → tachypnea, restlessness, gasp, decerebrate posturing, apnea, PEA
- ACLS, including vasopressin 40 units → remains pulseless
- AOK for AFE at T$_{0+5\text{min}}$
- T$_{0+6\text{min}}$, patient has strong pulse and 105/80 NIBP
- DIC began 1 hour later
- Survived, neurologically intact
Case study 2

- Heart rate (BPM)
- Minutes
- AOK for AFE given
- Traditional CPR
- Persistent pulse and perfusion after AOK
Hypothesis

- The emergent treatment of amniotic fluid embolism should include therapy that targets serotonin and thromboxane A2
  - Atropine 1mg
  - Ondansetron 8mg
  - Ketorolac 30mg

Why should these drugs be effective in treatment of amniotic fluid embolism?
A is for atropine

- Competitive, reversible muscarinic antagonist that when bound causes parasympathectomy\(^7\)
  - Muscarinic receptors are found throughout the body in multiple subtypes
  - When bound to acetylcholine, muscle contraction occurs
    - Results in **vagal mediated pulmonary artery spasm and pulmonary hypertension**

- Beneficial effects of atropine for treatment of AFE:\(^8\)
  - Decreases vasoconstriction in pulmonary vasculature
  - Ameliorates symptomatic bradycardia and heart blocks commonly observed in Phase I of AFE
O is for ondansetron

- Ondansetron is a 5-HT3 receptor antagonist\(^7\)
  - 5-HT3 receptors are a specific subtype of serotonin, which is a physiologic neurotransmitter with multiple functions
  - 5-HT3 receptors are in abundance in the vagal efferent terminals in the heart and lungs → not only acetylcholine/MAchR mediated function
    - Approximately 50% of efferents are serotonergic in heart and lung\(^9\)

- Beneficial effects of ondansetron for treatment of AFE:\(^{10}\)
  - Contributes to vagotomoy via 5-HT3 antagonism, which can prevent cardiovascular collapse
K is for ketorolac

- Ketorolac is an intravenous non-steroidal anti-inflammatory, which is known to inhibit the production of prostaglandins, specifically thromboxane $A_2^{7,11}$

  - Thromboxane A2 functions:
    1. Role in the activation and aggregation of platelets, which is a component of primary hemostasis
    2. Central to the amplification of the hemostatic mechanism
  - Overproduction of thromboxane A2 occurs during even a normal pregnancy
  - An abundance of thromboxane A2 can lead to the cascade of inappropriate clotting seen with DIC

- Beneficial effects of ketorolac for treatment of AFE:\textsuperscript{12}
  - Inhibits formation of clots and the extension of clots in situ
  - Decreases the cascade of inappropriate clotting
Case study 3

- 34 year old G3P2
- 39 weeks, induction and vaginal delivery
- Gasp, dyspnea → progresses to respiratory arrest quickly
- ACLS
- AOK for AFE at $T_{0+3\text{min}}$
- $T_{0+5\text{min}}$ vital signs stabilized
- Discharged to floor
- PE 48 hours post-delivery
AOK for AFE Rescue Pack

- It is suggested that a separate AOK for AFE rescue pack be placed in the crash cart of each L&D unit.

- Each pack should consist of:
  - Atropine 1mg
  - Ondansetron 8mg
  - Ketorolac 30mg
## Cost of AOK for AFE Rescue Pack

<table>
<thead>
<tr>
<th>Medication</th>
<th>Cost</th>
</tr>
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<tbody>
<tr>
<td>Atropine 1mg/ml</td>
<td>$4.85</td>
</tr>
<tr>
<td>Ondansetron 8mg/2ml</td>
<td>$0.65</td>
</tr>
<tr>
<td>Ketorolac 30mg/ml</td>
<td>$0.75</td>
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</table>

**Total cost** $6.05

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What is the value of a healthy mother and child?