A-OK

A Novel Treatment for Amniotic Fluid Embolism

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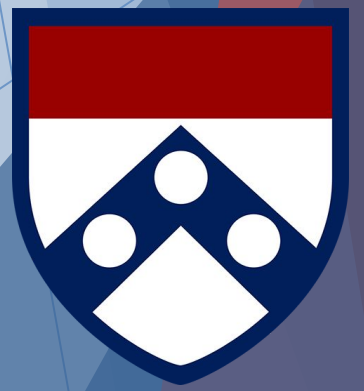


Learner Objectives

- Define Amniotic Fluid Embolism
  - Statistics
  - Pathophysiology
  - Traditional Treatment
- A-OK Protocol Proposed Mechanism of Action
  - Atropine
  - Ondansetron
  - Ketorolac
- Case Study

Statistics

- Amniotic Fluid Embolism (AFE)
- Meyer - 1926

- Incidence: 6.1-7.7 per 100,000
- Case Fatality: 13-26%
- Infant Survival: 70%

- No universally accepted diagnostic criteria

Risk Factors

- **Age > 35 years**
- Multiparity
- Male Fetus
- **Medical Induction of Labor**
- Instrumental Delivery
- Caesarean Delivery
- Cervical Trauma
- Uterine Rupture
- Uterine Hyperstimulation
- Preeclampsia
- Eclampsia
- Placenta Previa
- Placental abruption
- Ethnic Minority

Clinical Presentation

- Hypotension*
- Dyspnea/Cough
- Cyanosis
- Desaturation
- Decrease in ETCO2
- Acute Pulmonary HTN
- LOC/AMS
- Bleeding
- Coagulopathy
- Seizures
- Cardiac Arrhythmias
- ST segment changes
- Cardiac Arrest
- **Fetal Bradycardia and hypoxia***

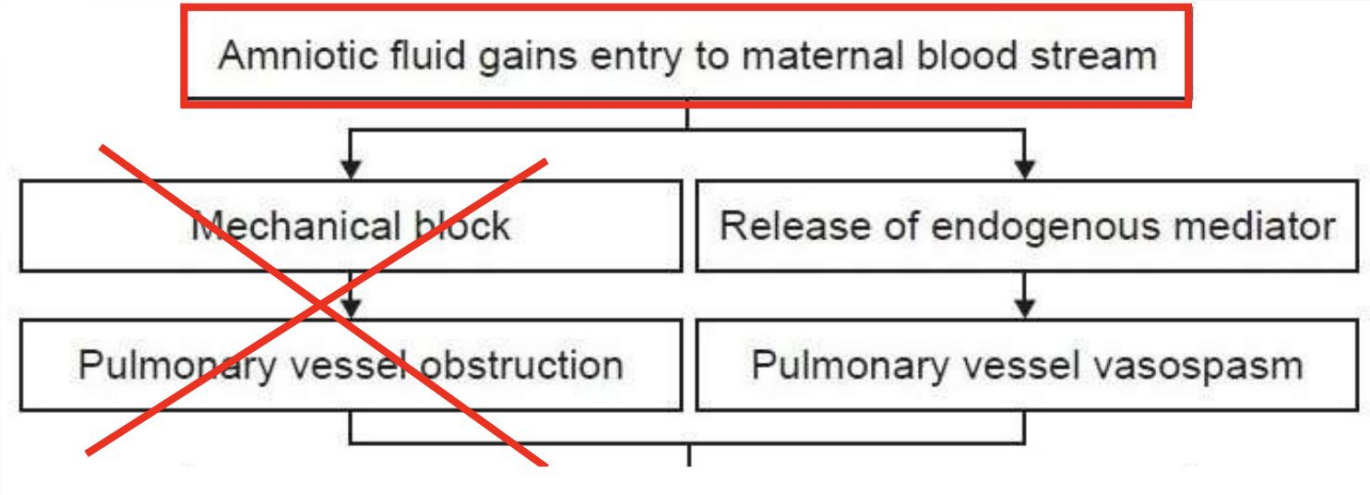
Differential Diagnoses

- Anaphylaxis
- Aspiration
- Aortic Dissection
- Total Spinal Anesthetic
- Hemorrhagic Shock
- LAST
- Myocardial Infarction
- Pulmonary Emboli (air, fat, thrombi)
- Septic Shock
- Tension Pneumothorax
- Uterine Rupture

The Four Cardinal Signs

- Altered Mental Status
- Respiratory Distress
- Hypotension
- DIC

Pathophysiology



Historical Theory

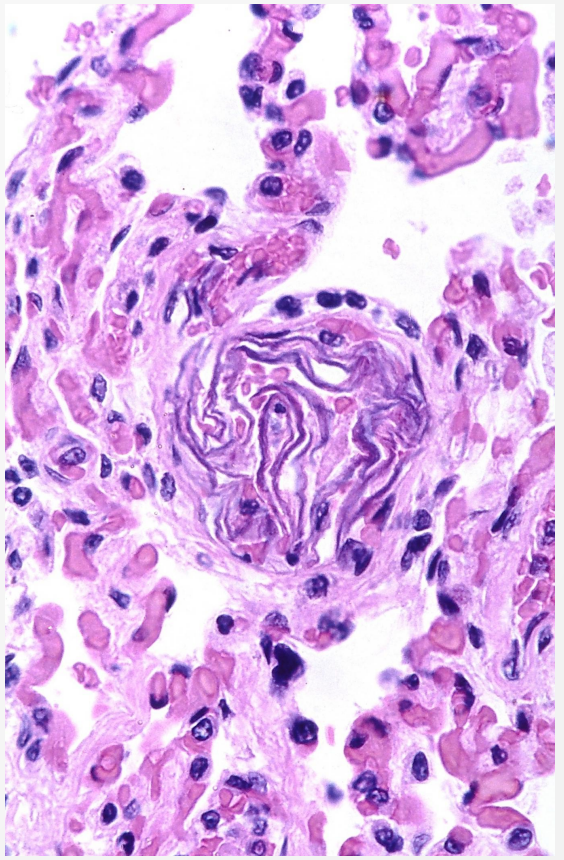
- Steiner & Lushbaugh - 1941
- Mechanical obstruction of pulmonary vessels by amniotic fluid embolus

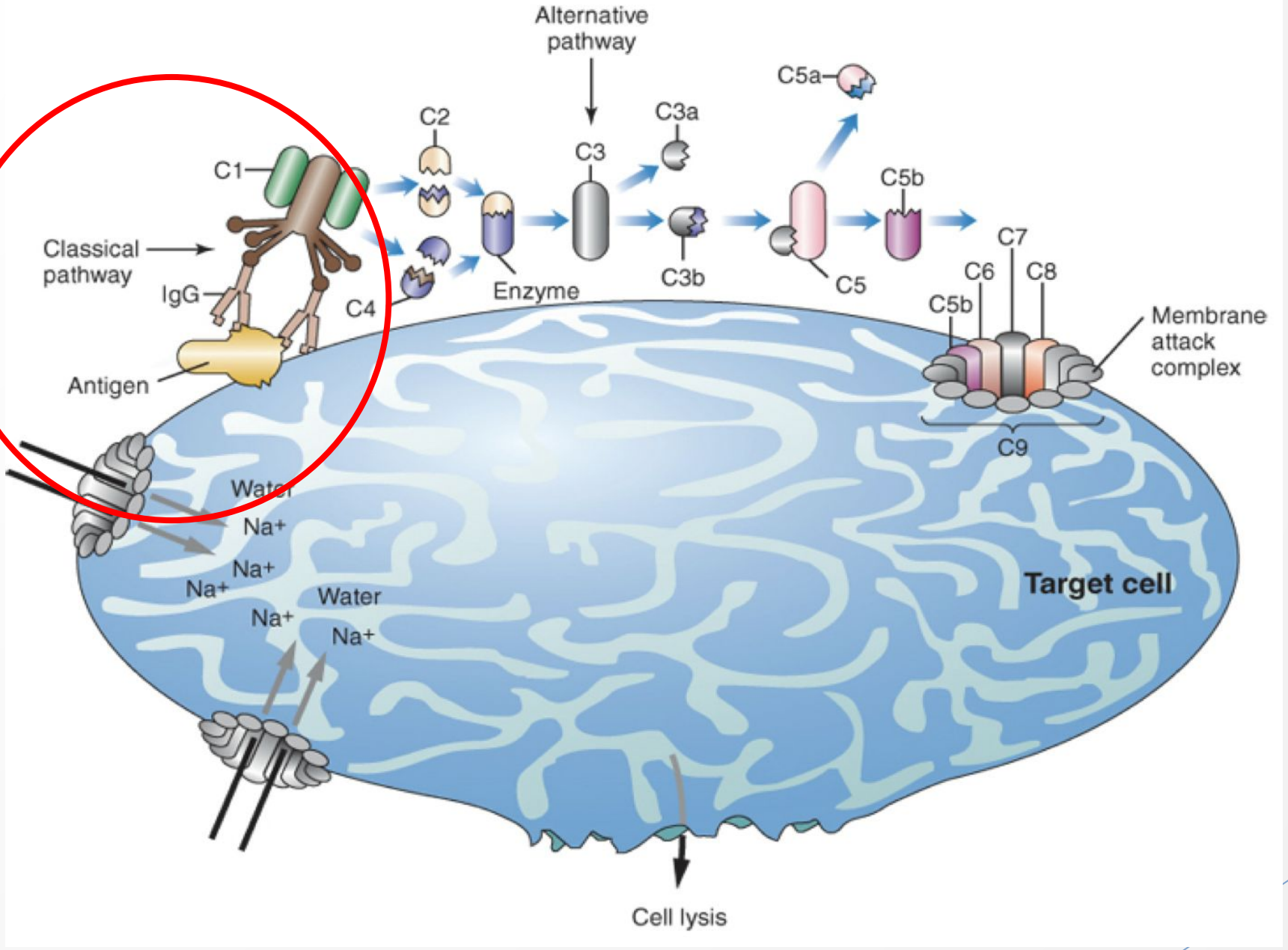
Current Theory

- Attwood - 1956
- Immune-mediated mechanism
- “Anaphylactoid Syndrome of Pregnancy”

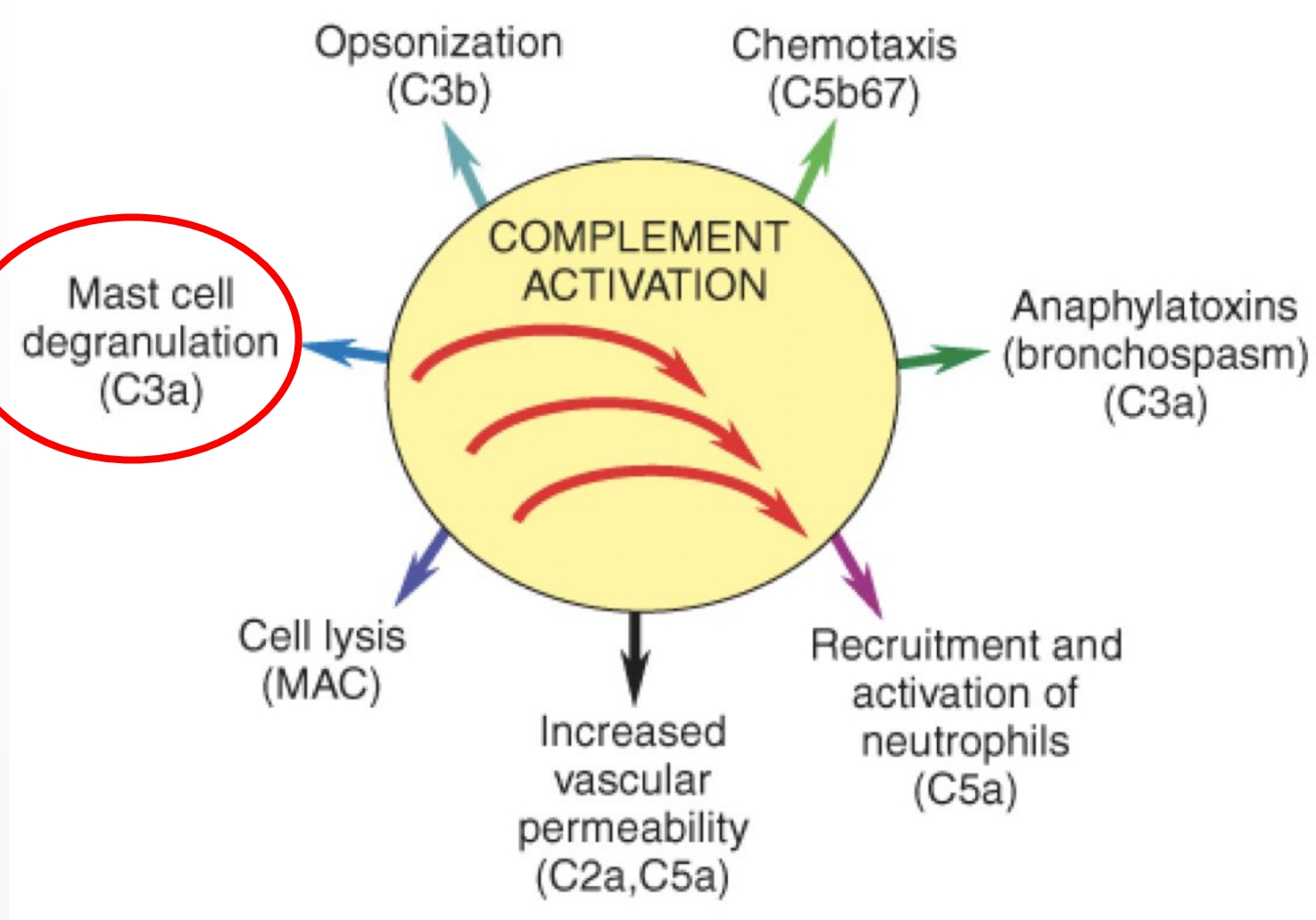
Amniotic Fluid Components

- Platelet Activating Factor
- Interleukin 1
- Tumor Necrosis Factor-Alpha
- Leukotrienes
- Endothelin
- Tissue Factor
- Arachidonic Acid

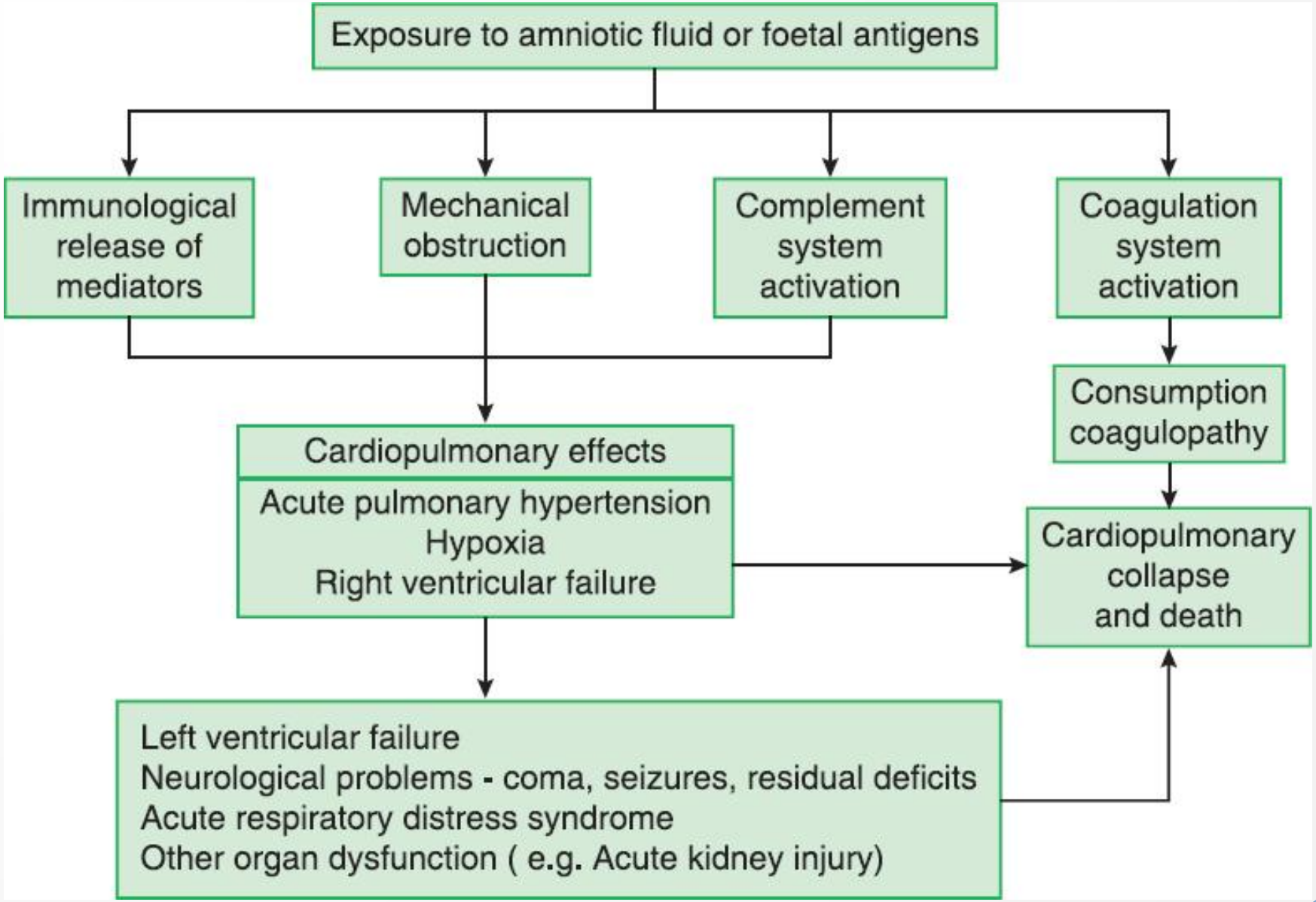




Source: Schindler, L. W. (1991). *Understanding the immune system*. Bethesda, Md.: U.S. Dept. of Health and Human Services, Public Health Service, National Institutes of Health.



Source: Gutierrez, K., & Peterson, P. G. (2007). *Pathophysiology*. St. Louis, MO: Saunders Elsevier.



Source: Sadera, G. & Vasudevan, B. (2015). Amniotic Fluid Embolism. *Journal of Obstetric Anesthesia and Critical Care*, 5(1), 1-8.

Classification of AFE Into Three Major Subtypes

Subtype	Mechanisms	Initial Signs and Symptoms	Onset	Prognosis: Fatal or Non-Fatal	Fetal anti-gens (STN) in maternal serum	Volume of Amniotic Fluid Entering the Maternal Circulation
Classic	mechanical obstruction	pulmonary dyspnea and arrest	immediate (within minutes) onset	Aggressive course: fatal > non-fatal	elevated	much
Anaphylactoid	anaphylaxis	cardiac dysfunction and arrest	intermediate onset	fatal = non-fatal	slightly elevated	moderate
DIC	coagulation and protease attack	coagulopathy	delayed (within hours) onset	Good response to therapy: fatal < non-fatal	slightly elevated	little

Source: Tsunemi T., Oi, H., Sado, T., Naruse, K., Noguchi, T. & Kobayashi, H. (2012). An Overview of Amniotic Fluid Embolism: Past, Present and Future Directions. *The Open Women's Health Journal*, 6, 24-29.

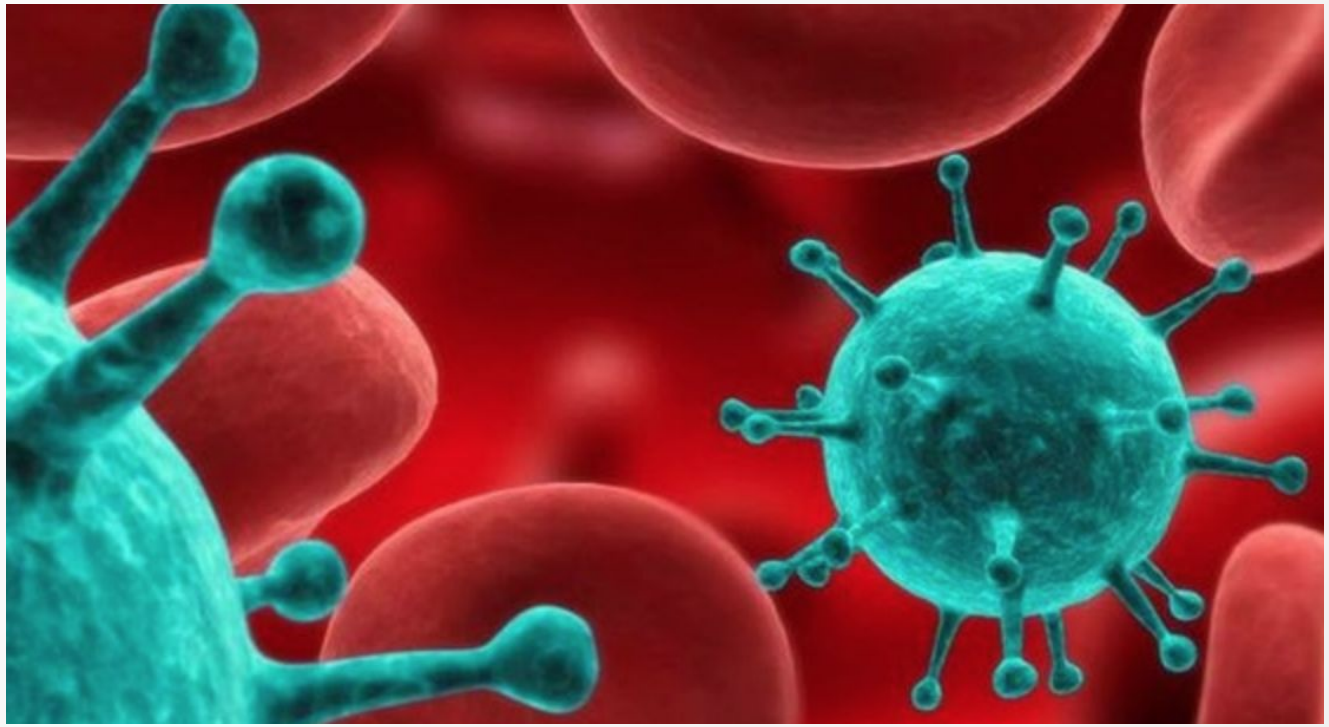
Diagnostic Criteria

"Let us be careful not to make it (the diagnosis of amniotic fluid embolism) a waste-basket for all cases of unexplained death in labor." **- NJ Eastman 1948**

I. Sudden onset of cardiorespiratory arrest, or both hypotension (systolic blood pressure <90 mm Hg) and respiratory compromise (dyspnea, cyanosis, or peripheral capillary oxygen saturation (S_pO_2) <90%)
II. Documentation of overt disseminated intravascular coagulation (DIC)
III. Clinical onset during labor or within 30 minutes of delivery of the placenta
IV. No Fever

Immunology & Diagnosis

- Serum Tryptase
- C3/C4
- STN



Traditional Treatment

- Intensive Care
- Cardiopulmonary Resuscitation (CPR)
- Left Lateral Displacement of the Uterus
- Intubation and Mechanical Ventilation
- Volume Expansion
- Vasopressors & Inotropes
- Invasive monitoring
- Echocardiography
- Cardiac Output Monitors
- Intraaortic Balloon Pump (IABP)
- Extracorporeal Membrane Oxygenation (ECMO)
- Blood Product Transfusion

AMNIOTIC FLUID EMBOLISM

By Stanford Anesthesia Cognitive Aid Group

SIGNS

Consider amniotic fluid embolism if there is the sudden onset of the following in a pregnant or post-partum patient:

1. Respiratory distress, decreased O_2 saturation.
2. Cardiovascular collapse: hypotension, tachycardia, arrhythmias, cardiac arrest.
3. Coagulopathy +/- Disseminated intravascular coagulation (DIC).
4. Seizures.
5. Altered mental status.
6. Unexplained fetal compromise.

1. CALL FOR HELP.
2. CALL FOR CODE CART.
3. INFORM TEAM.

TREATMENT

1. Anticipate possible **cardiopulmonary arrest** and **emergent C-section.**
2. Place patient in left uterine displacement (**LUD**).
3. Increase to **100% O_2**, high flow.
4. Establish large volume **IV access** (upper body best).
5. Support circulation with **IV fluid, vasopressors, and inotropes.**
6. **Prepare for emergent intubation.**
7. When possible, place arterial line. Consider central venous access or IO line in humerus.
8. Anticipate **massive hemorrhage** and DIC. **Go To Hemorrhage – MTG, event #14.**
9. Consider **circulatory support**: IABP/ECMO/CPB.

RULE OUT

Rule out other causes that might present in a similar fashion:

1. Eclampsia.
2. Hemorrhage.
3. Air embolism.
4. Aspiration.
5. Anaphylaxis.
6. Pulmonary embolism.
7. Anesthetic overdose.
8. Sepsis.
9. Cardiomyopathy/cardiac valvular abnormality/MI.
10. Local anesthetic toxicity.
11. Total Spinal.

Stanford Anesthesia Emergency Manual (2016)

1st reported Case Study (2013)

- 41 yo G8P3043 female presented at 39 weeks for labor induction.
- SOB → SpO2 80% → within 1 minute cardiac arrest.
- ACLS was initiated; baby delivered via forceps.
- The patient was still pulseless after **40 minutes** of ACLS.

- Atropine 1mg, ondansetron 8mg, metoclopramide 10mg, and ketorolac 30mg were administered.
- **Pulse regained and stabilized within 2 minutes.**

- DIC → 13u PRBC, 6u FFP, 2u platelets, 30u cryoprecipitate, 2 doses of recombinant Factor VIIa, and an intrauterine Bakri balloon.
- Hemodialysis for 5 days due to acute tubular necrosis (ATN).

- The patient developed speech and memory function difficulties which still persist. DTH on day 13.

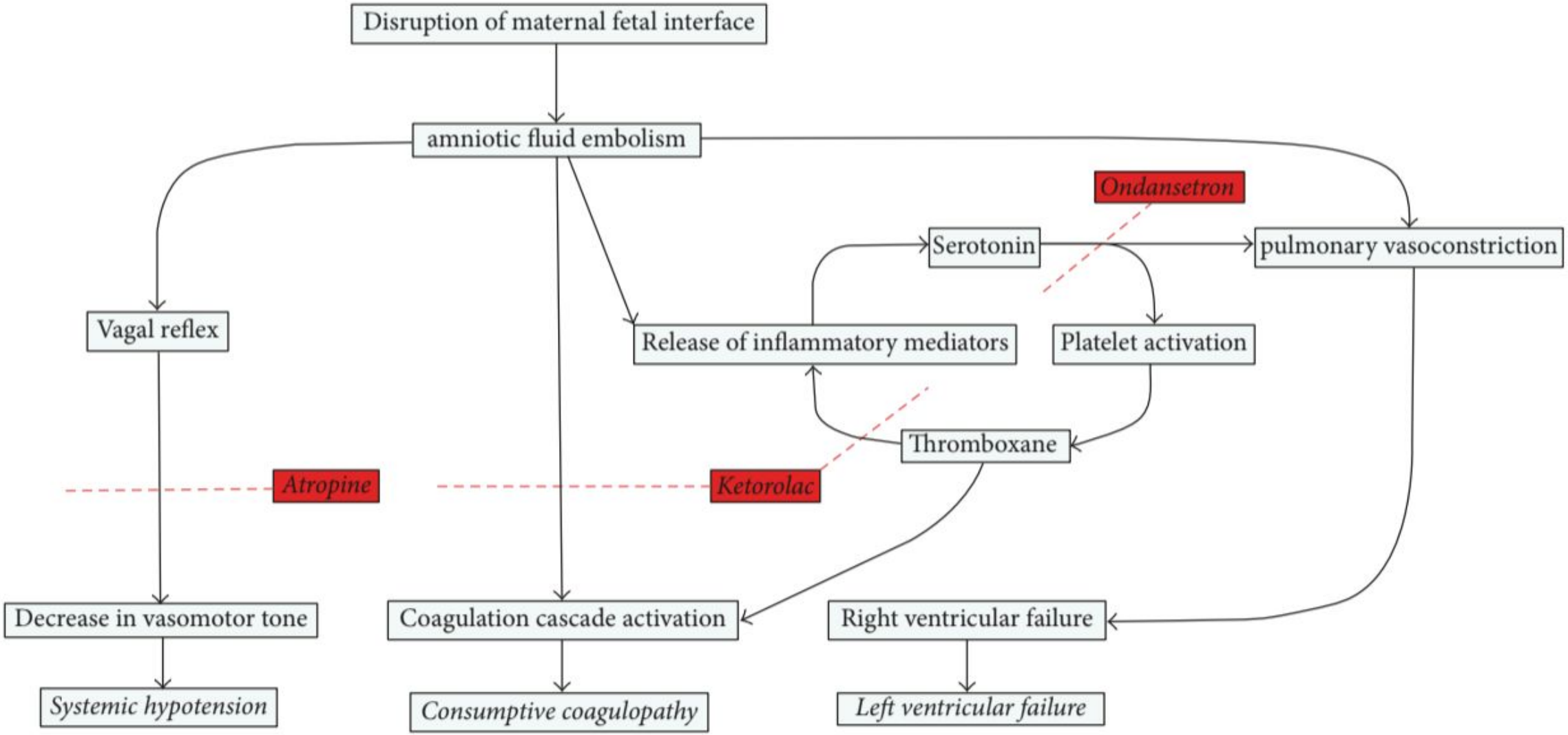


FIGURE 1: Proposed mechanism for Atropine, Ondansetron, and Ketorolac (A-OK) protocol.

Source: Rezai et al. (2017). Atypical Amniotic Fluid Embolism Managed with a Novel Therapeutic Regimen. *Case Rep Obstet Gynecol.*

Limitations

- Limited case studies
- Ketorolac Contraindications
- Inaccurate diagnosis and inconsistent reporting
- No confirmatory laboratory tests
- Difficulty of obtaining human evidence
- Little value from animal studies

Recommendations for Providers

- Cost/Benefit ratio
- Ease of Access
- PUBLISH Findings
- Educate Colleagues

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