Critical Care in Obstetrics:
An Innovative and Integrated Model for Learning the Essentials
Amniotic Fluid Embolism

Gary A. Dildy, M.D.
Professor
Vice Chairman of Quality & Patient Safety
Division Director, Maternal-Fetal Medicine
Department of Obstetrics & Gynecology
Baylor College of Medicine

Chief Quality Officer, Obstetrics & Gynecology
Service Chief, Maternal-Fetal Medicine
Texas Children’s Hospital

Society for Maternal-Fetal Medicine

MATERNAL PULMONARY EMBOLISM BY AMNIOTIC FLUID
AS A CAUSE OF OBSTETRIC SHOCK AND UNEXPECTED DEATHS IN OBSTETRICS
PAUL E. STEINER, M.D., Ph.D.
AND
C. C. LUSHBAUGH, B.S.
CHICAGO

JAMA 1941; 117: 1245-1254 & 1341-1345.
Search term *preeclampsia* yields 35,610 citations

Key Points

- Classic triad:
  - Hypoxia
  - Hypotension or hemodynamic collapse
  - Coagulopathy

- Remains poorly understood: unpredictable, rare, acute, and lacks a gold standard diagnosis

- There probably are *formes fruste* of AFE
Incidence & Outcomes
Incidence

- Incidence (per 100,000 maternities)
  - Australia, Canada, the Netherlands, UK & USA
  - Retrospective discharge database: 5.5-6.1
    - ~ 1:17,000
  - Validated case identification: 1.9-2.5
    - ~ 1:45,000

If the difference between the above 2 rates is due solely to false positives in the former, the incidence of AFE is overestimated by 62% in retrospective discharge database studies. (GAD)

## HCA, 2000-2006

<table>
<thead>
<tr>
<th>CAUSE OF DEATH</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complications of Preeclampsia</td>
<td>15</td>
<td>16</td>
</tr>
<tr>
<td>Amniotic fluid embolism</td>
<td>13</td>
<td>14</td>
</tr>
<tr>
<td>Obstetric hemorrhage</td>
<td>11</td>
<td>12</td>
</tr>
<tr>
<td>Cardiac disease</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td>Pulmonary Thromboembolism</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Nonobstetric infection</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Obstetric infection</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Accident/suicide</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Medication error or Reaction</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Ectopic pregnancy</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td>11</td>
<td>12</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>95</td>
<td>100</td>
</tr>
</tbody>
</table>

Outcomes

Maternal Outcome

Fetal Outcome


### Outcomes

- **Maternal Mortality (MM)**

<table>
<thead>
<tr>
<th>Publication</th>
<th>Years</th>
<th>Population</th>
<th>Methodology</th>
<th>AFE (N)</th>
<th>MM (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morgan 1979</td>
<td>1941-1978</td>
<td>English lit.</td>
<td>Literature Review</td>
<td>272</td>
<td>86</td>
</tr>
<tr>
<td>Clark 1995</td>
<td>1983-1994</td>
<td>USA</td>
<td>Registry</td>
<td>46</td>
<td>61</td>
</tr>
<tr>
<td>Tuffnell 2005</td>
<td>1997-2004</td>
<td>UK</td>
<td>Registry</td>
<td>44</td>
<td>30</td>
</tr>
<tr>
<td>Knight 2010</td>
<td>2005-2009</td>
<td>UK</td>
<td>UKOSS</td>
<td>60</td>
<td>20</td>
</tr>
<tr>
<td>Stolk 2012</td>
<td>2004-2006</td>
<td>Netherlands</td>
<td>Registry</td>
<td>9</td>
<td>11</td>
</tr>
<tr>
<td>Guillaume 2013</td>
<td>2000-2010</td>
<td>France</td>
<td>Chart Review</td>
<td>11</td>
<td>27</td>
</tr>
</tbody>
</table>
Pathophysiology & Etiology
Proposed Pathophysiology

Anaphylaxis (IgE) → Sepsis (Endotoxin) → Amniotic Fluid Embolism (various fetal elements) → Endogenous mediator release → Clinical manifestations

Proposed Pathophysiology

- **Phase I**
  - Vasoactive substance(s)
  - Pulmonary vasospasm
  - Profound hypoxia
    - Pulmonary injury
    - Myocardial injury
  - Resolved in 15-30 min

- **Phase II**
  - Left heart failure
  - Pulmonary edema / ARDS
  - Coagulopathy

Maternal Death Following Cardiopulmonary Collapse After Delivery: Amniotic Fluid Embolism or Septic Shock Due to Intrauterine Infection?

Roberto Romero¹,², Nicholas Kadar, Edi Vaisbuch¹,³, Sonia S. Hassan¹,³

- 2 cases of maternal death attributed to AFE
- Supra-lethal levels maternal plasma TNF-α (> 0.1 ng/mL) at admission
  - 29 yo G3P1 at 41+ weeks 1 ng/mL
  - 30 yo G3P2 at 28+ weeks 10 ng/mL

As illustrated in this case, uterine hypertonicity followed the initial signs and symptoms of AFE.

Etiology: ? Induction of Labor

- Kramer et al. Lancet 2006
  - Canada 1991-2002
  - Association: yes

  - USA 1999-2003
  - Association: no

- Knight et al. Obstet Gynecol 2010
  - UK 2005-2009
  - Association: yes
FDA & PGE & AFE

- Cytotec Package Insert (2009) – “A major adverse effect of the obstetrical use of Cytotec is...amniotic fluid embolism.”

- Prepidil Package Insert (2009) – “The Clinician should be alert that the intracervical placement of dinoprostone gel may result in inadvertent disruption and subsequent embolization of antigenic tissue causing in rare circumstances the development of Anaphylactoid Syndrome of Pregnancy (Amniotic Fluid Embolism).”

- Cervidil Package Insert (2010) – “The Clinician should be alert that use of dinoprostone may result in inadvertent disruption and subsequent embolization of antigenic tissue causing in rare circumstances the development of Anaphylactoid Syndrome of Pregnancy (Amniotic Fluid Embolism).”
Diagnosis
AFE Registry Entry Criteria

- Acute hypotension or cardiac arrest
- Acute hypoxia
- Coagulopathy
- Onset during labor, delivery, or 30 minutes postpartum
- Absence of any other explanation
- Occurrence within 5 years of registry opening

Proposed diagnostic criteria for the case definition of amniotic fluid embolism in research studies

Steven L. Clark; Roberto Romero; Gary A. Dildy; William M. Callaghan; Richard M. Smiley; Arthur W. Bracey; Gary D. Hankins; Mary E. D’Alton; Mike Foley; Luis D. Pacheco; Rakesh B. Vadhera; J. Patrick Herlihy; Richard L. Berkowitz; Michael A. Belfort

- Working group 2/2/16 under the auspices of:
  - Society for Maternal-Fetal Medicine
  - Amniotic Fluid Embolism Foundation
- Task was to develop uniform diagnostic criteria for the research reporting of AFE

**Modified ISTH Score: Overt DIC In Pregnancy**

**International Society on Thrombosis and Haemostasis (ISTH)**

<table>
<thead>
<tr>
<th>Score</th>
<th>Platelets</th>
<th>PTT or INR</th>
<th>Fibrinogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>&gt;100,000</td>
<td>&lt;25%</td>
<td>&gt;200</td>
</tr>
<tr>
<td>1</td>
<td>50,000-100,000</td>
<td>25-50%</td>
<td>&lt;200</td>
</tr>
<tr>
<td>2</td>
<td>&lt;50,000</td>
<td>&gt;50%</td>
<td></td>
</tr>
</tbody>
</table>

*Score ≥3 is compatible with overt DIC in pregnancy*

Differential Diagnosis

- Acute myocardial infarction
- Anaphylactic shock
- Anesthetic accident
- Aspiration pneumonia
- Placental abruption
- Pulmonary thromboembolism
- Septic shock
Histologic Findings of AFE
Evaluation & Treatment
Initial Evaluation

- CBC & platelets
- Fibrinogen and FSP
- PT, PTT, and INR
- Blood type & cross
- Arterial blood gas

- Serum electrolytes
- Cardiac enzymes
- Chest X-ray
- 12-lead EKG
- Echocardiogram
Treatment

- Initial treatment is supportive
  - CPR, High FiO2
- Treat left ventricular failure
  - Volume expansion, inotropes
- Fetal management
  - Cardiac arrest: perimortem C/S (ABC’s + D)
  - Hemodynamically unstable: individualize
Perimortem Cesarean

Maternal Arrest-to-Delivery Interval
Intact Versus Impaired Neonatal Survival

Treatment: case reports

- Cardiopulmonary bypass
- Hemofiltration
- Recombinant Factor VIIa
- Nitric oxide
- High-dose corticosteroids


# Recurrence Risk

- 1992 Clark AJOG 0/2
- 1995 Burrows ANZJOG 0/1
- 1998 Duffy AIC 0/2
- 1998 Collier AIC 0/1
- 2000 Stiller JRM 0/1
- 2005 Demianczuk JOGC 0/1
- 2005 Abecassis IJOA 0/1

**TOTAL** 0/9

**Maximum Risk with 95% CL: “Rule of 3”** \( \frac{3}{n} \times 100 = 33\% \)

AFE Registry at BCM

- AFE Foundation & BCM partnership
  - The AFE Registry opened 2 August 2013
  - Cases are collected and abstracted
  - Cases are categorized (Classic v Atypical v Unlikely AFE)

- Future Plans
  - AFE families Bio-Bank (store serum/plasma and DNA)
  - Network for collection of specimens from acute AFE cases
Summary

- Thought to follow maternal exposure to fetal antigens
- Pathophysiology similar to anaphylaxis & septic shock
- Treatment is generally supportive
- Maternal-fetal morbidity & mortality are frequent
- OB team should be prepared for acute emergencies
- Team training & simulation training may be helpful
- Better predictive and diagnostic tests are needed
- Current efforts are being invested in improved diagnostic tests and treatment

All recommendations are GRADE 1C.
All recommendations are GRADE 1C (strong recommendation, low-quality evidence).
Thank You for Your Attention!

Planning Committee

Mike Foley, Director
Helen Feltovich, co-Director
Loralei Thornburg, Content co-Chair
Suneet Chauhan, Testing Chair
Daniel O’Keeffe
Barbara Shaw

Shad Deering, co-Director
Bill Goodnight, co-Director
Deirdre Lyell, Content co-Chair
Mary d’Alton
Andrew Satin

Society for Maternal • Fetal Medicine
Summary
Copper, Otto & Leighton. SOAP 2013 Abstract S47

- ondansetron (5-HT3 antagonist) 8 mg
- metoclopramide (5-HT3 antagonist) 10 mg
- atropine (vagolytic) 1 mg
- ketorolac (cyclooxygenase inhibitor) 30 mg

OMAK ?
MAKO ?
AMOK ?
AMNIOTIC FLUID EMBOLISM
Case Presentation

- 26 year old Para 1-0-0-1
- Diamniotic-Monochorionic twins
- Presented at 28 weeks
- C/O back pain & uterine contractions
- U/S: TTTS and IUFD x 2
11:59  Admission labs
- HCT = 40, PLT = 178, WBC = 9
- F = 378; PT / PTT / INR = WNL
12:00  Admit BP = 124/60, P = 88
14:30  Epidural placed
17:30  SROM □ clear AF
17:30  Maximum oxytocin @ 21 mU/min
AMNIOTIC FLUID EMBOLISM

Case Presentation

- 20:40  Cervix complete
- 21:18  Delivery “A” 999 gm
- 21:19  Tachypnea, “I don’t feel right”
- 21:24  Code Blue, given FiO2 1.0
- 21:33  Delivery “B” 1594 gm
- 21:35  Delivery placenta
- 21:45  ABG 7.20, pCO2 48, pO2 17, SaO2 16
- 21:52  Vaginal bleeding  Hemabate
- 22:04  Code called
AMNIOTIC FLUID EMBOLISM
Case Presentation

- Autopsy
  - No evidence of pulmonary embolism
  - No microscopic evidence of AFE
  - Head not examined

- Clinical diagnosis?
  - Amniotic fluid embolism
AMNIOTIC FLUID EMBOLISM
Case Presentation

- 38 y.o. Gravida 5 Para 0-1-3-1
- Spontaneous labor @ 41 weeks
- Previous low transverse C/S for breech
- 4 cm: continuous lumbar epidural
- 7 cm: amniotomy no AF
- FHR decels to 70’s x 3
- 30 minute Stage II

Case: NEJM 9-1998
AMNIOTIC FLUID EMBOLISM
Case Presentation

- Immediately after delivery brisk bleeding with EBL of 500 mL
- Placenta would not deliver, plus another EBL of 500 mL
- BP = 60/20 mm Hg, P = 115
- Fluid bolus and ephedrine
- Another gush of 200 mL EBL

Case: NEJM 9-1998
Manual exploration of uterus
  - Rent in anterior wall c/w rupture
  - No placental cleavage plane
CPR; BP = 100/60 mm Hg, P = 160
ST [ ] SB [ ] asystole
Incision: minimal intra-abdominal blood
Hysterectomy performed
AMNIOTIC FLUID EMBOLISM
Case Presentation

- Arterial blood gas during CPR
  - pH = 8.01
  - PaO2 = 337 mm Hg
  - PaCO2 = 19 mm Hg
- Pronounced dead after CPR x 1 hour

Case: NEJM 9-1998
AMNIOTIC FLUID EMBOLISM
Case Presentation

- Clinical Diagnoses
  - Uterine rupture
  - Amniotic fluid embolism

- Anatomic Diagnoses
  - Amniotic fluid embolism
  - Uterine rupture
  - Placenta accreta with focal placenta increta

Case: NEJM 9-1998