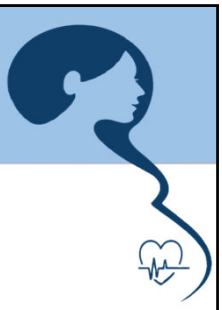
Amniotic Fluid Embolism

Brynn Weise, MD
Kathleen Lorenz, MD

Allina Health

1

Disclosures



- No disclosures

Allina Health

2

Objectives

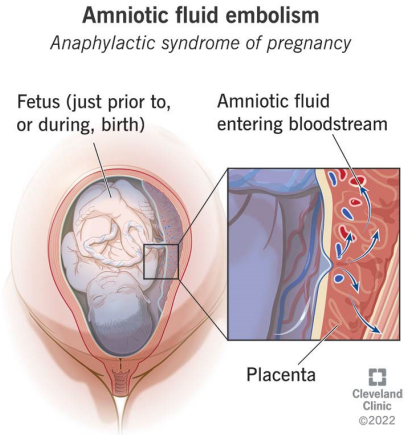
- Definition
- Pathophysiology
- Diagnostic criteria
- Differential diagnosis
- Risk factors
- Classic case presentation
- Textbook management
- Complicated case presentation
- Other management considerations
- Prognosis
- Summary

Allina Health

3

Amniotic Fluid Embolism Defined

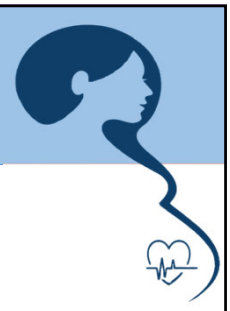
Life threatening obstetric emergency characterized by sudden cardiorespiratory collapse and disseminated intravascular coagulation



Allina Health

4

Amniotic Fluid Embolism Defined



- First described 1941, after finding fetal debris in pulmonary circulation of women who died during labor women in labor
- Occurs in 2-8 per 100,000 deliveries
- Responsible for 10% of maternal mortality in the United States
- Likely more similar mechanism to anaphylaxis than to embolism
  - Term "Anaphylactoid Syndrome of Pregnancy" has been suggested
  - Fetal tissue or amniotic fluid components not universally found in women who present with AFE symptoms
  - Women with AFEs have higher incidence of other allergic reactions

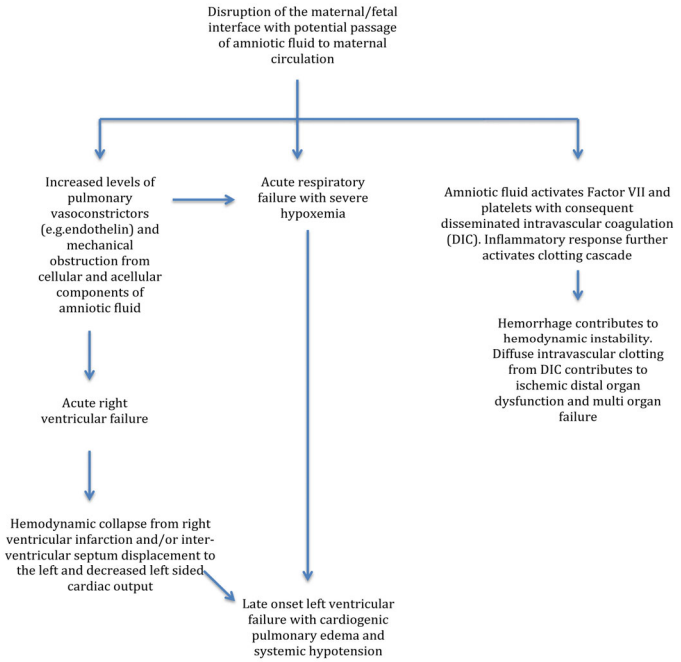
Allina Health

5

Pathophysiology

Phase 1:
Pulmonary vasospasm, pulmonary hypertension, elevated RV pressure -> hypoxia

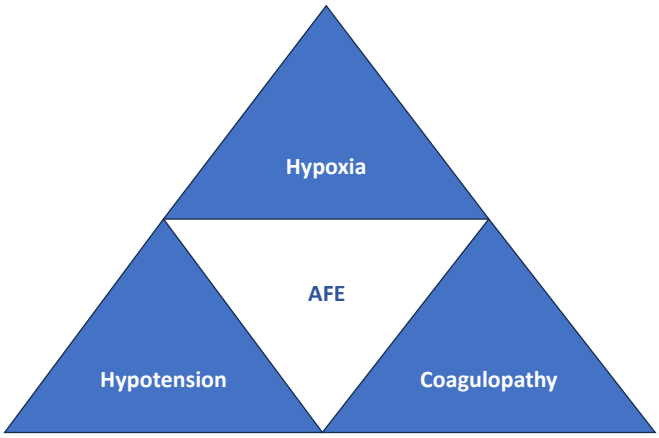
Phase 2:
Massive hemorrhage, atony, DIC



Allina Health

6

Recognition is key: the AFE triad



AllinaHealth

7

AFE Diagnostic Criteria

Diagnostic criteria

1) Sudden onset cardiorespiratory arrest OR hypotension with evidence respiratory compromise
2) Documentation of overt DIC
3) Clinical onset during labor or within 30 mins of delivery
4) Absence of fever during labor

* Some atypical cases may not meet all of the criteria

AllinaHealth

8

Differential Diagnosis

Iatrogenic	Obstetric	Cardiac	Respiratory	Infectious	Hematologic	Hepatic
Anesthesia: High spinal, lidocaine toxicity	Eclampsia	Peripartum cardiomyopathy	Pulmonary embolism	Septic shock	Hemorrhagic shock (OB or other)	Acute fatty Liver (DIC)
Air embolism	Uterine rupture	Myocardial infarction				
Anaphylaxis		Cardiogenic shock				

AFE is a diagnosis of exclusion

Allina Health

9

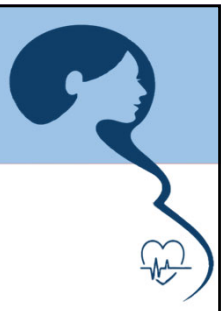
Risk Factors (controversial)

- Advanced maternal age
- Grand multiparity
- Multiples
- Polyhydramnios
- Hypertensive disorders
- Placental issues (previa, abruption)
- PPROM
- Medical induction, cesarean section, operative vaginal delivery
- Abdominal Trauma, uterine rupture, cervical trauma
- Fetal distress, fetal death
- Male fetus

Allina Health

10

Risk factors



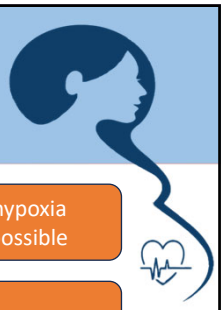
"...as it stands today, no demographic or clinical risk factor has been identified that justifies any prospective alteration of standard obstetric practice to reduce the risk of amniotic fluid embolism"

- Steven Clark, MD

Allina Health

11

Management Overview

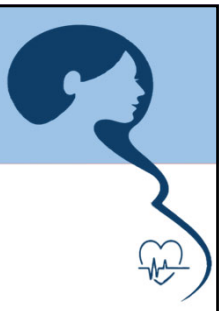


Airway, Circulation, Breathing (Code Blue - ACLS/BLS)	Wide differential - Designate timekeeper - Recognize and manage hypoxia early to mitigate neurologic injury - Alert ECMO team as early as possible
Immediate delivery	If viable fetus or for maternal resuscitation
Consider A-OK (Atropine, Ondansetron, Ketorolac)	Thought to inhibit pathways involved in pathogenesis of AFE
Anticipate Hemorrhage (!!!)	These patients WILL bleed! Activate massive transfusion protocol ideally even before hemorrhage occurs
Transfer to ICU	Supportive care – to be discussed further by Dr. Weise

Allina Health

12

Case 1



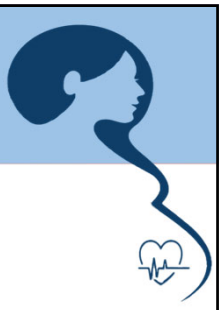
29 yo G5P4004 at 22w6d s/p IOL for fetal demise (hydrops on US)

- SROM
- Breech vaginal delivery initiated
- Head entrapment
- Maternal seizure, treated with lorazepam & magnesium
- Absent maternal pulse
- CPR initiated
- ER physician directed code while OB physician continued delivery
- A-OK given
- Breech vaginal delivery completed
- Retained placenta with manual extraction

Allina Health

13

Case 1

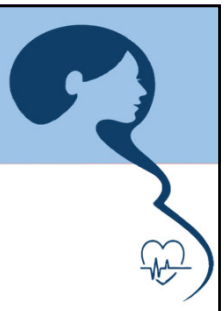


- Postpartum hemorrhage (2.5 L EBL)
- Received all uterotonics
- Jada inserted, then uterine tamponade balloon
- Transfused with 3U PRBCS, 2FFP
- Transferred to Abbott
- Massive transfusion protocol, respiratory support and pressors continued in ICU
- Epidural catheter removed

Allina Health

14

Case 1



ICU course complicated by:

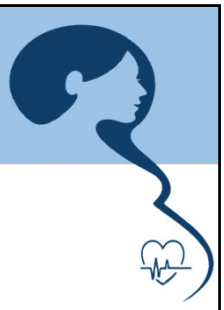
- Shock liver due to ischemic hepatitis
- Acute Kidney Injury due to acute tubular necrosis-> CRRT required
- Pulmonary embolism – anticoagulation held due to coagulopathy
- Severe hypoxic encephalopathy on MRI

Family ultimately elected for comfort care

AllinaHealth

15

Risk Factors

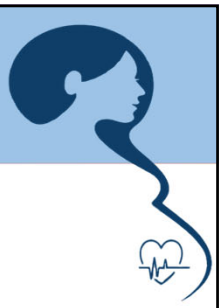


- Advanced maternal age
- Grand multiparity
- Multiples
- Polyhydramnios
- Hypertensive disorders
- Placental issues (previa, abruption)
- PPROM
- Medical induction, cesarean section, operative vaginal delivery
- Abdominal Trauma, uterine rupture, cervical trauma
- Fetal distress, fetal death
- Male fetus

AllinaHealth

16

Initial OB Management



Manage circulatory collapse

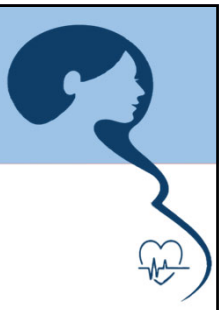
- ☐ ABCs: manage airway, breathing, and circulation
- ☐ Designate a timekeeper to call out times at 1-min intervals
- ☐ If no pulse, start CPR
  - ○ Manually displace uterus or lateral tilt
  - ○ Use backboard
- ☐ Consider move to operating room only if this can be accomplished in 2 min or less
- ☐ If 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

Allina protocol additions:
*Consider LUCAS machine prolonged chest compressions
*Alert ECMO team early

Allina Health

17

Continued OB Management



Allina protocol addition:
*Give A-OK early after recognition of diagnosis: Atropine 1mg IV and Ondansetron 8mg IV and Ketorolac 30mg IV

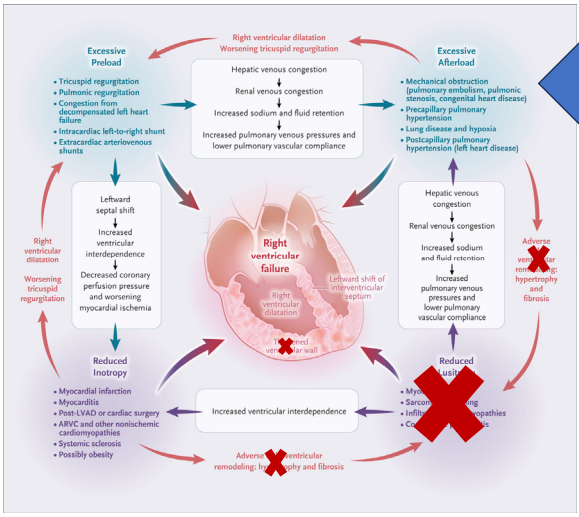
Anticipate uterine atony, DIC, hemorrhage

- ☐ Oxytocin prophylaxis plus other uterotonics as needed
- ☐ Consider intraosseous line if needed for large-bore IV access
- ☐ Initiate massive transfusion protocol
  - ○ 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

Allina Health

18

Critical Care Management



AFE

- Acute onset afterload increase with pulmonary arterial HTN
- Hypoxia
- Thin RV wall
- RV dilation
- Increased preload
- Decrease coronary perfusion
- Reduced inotropy
- Systemic congestion
- Increased pulmonary venous pressure

AllinaHealth

19

Critical Care Management

Disseminated Intravascular Coagulation

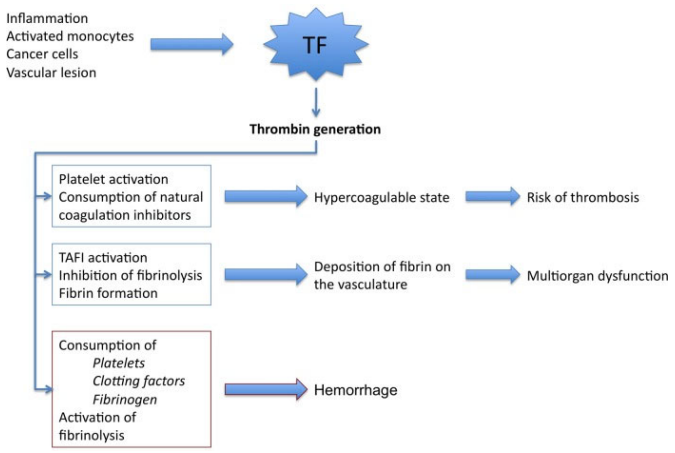
- Fibrinolysis may be first sign of AFE
- Use thromboelastography if available
- Fibrinogen, INR, PT, PTT, PLT, Hgb, D-Dimer

International Society of Thrombosis & Hemostasis (ISTH) DIC score

Test	0 points	1 point	2 points	3 points
INR	≤1.3	1.3-1.7	>1.7	
-or-				
PT prolongation	<3 sec	3-6 sec	>6 sec	
Fibrinogen (mg/dL)	>100	<100		
D-dimer	Normal		Moderately increased (~1-10x upper limit normal)	Severely increased (>10x upper limit normal)
Platelets (b/L)	>100	50-100	<50	

Interpretation of total score:
- ≥5 points: Positive for DIC
- <5 points: Negative, but patients could still have "non-overt DIC" which could evolve into frank DIC. If there is ongoing concern for DIC, coagulation labs may be repeated in 12-24 hours.

Patel P et al. 2019 PMID 30991817 and Bakhtiari K et al. 2004 PMID 15599145



AllinaHealth

20

Case 2

- 37yo G6P2032 presented to OSH at 38w0d for induction
  - Gestational DM on insulin
  - 2 doses misoprostol, by AM was 3cm dilated, had clear fluid on AROM
- Became SOB while on birthing ball, stated "I don't feel well, something is wrong" to partner
- Generalized tonic-clonic seizure x1 at ~ 0845, post ictal but responding to commands, BP normal prior to seizure
- Recurrent seizure
  - 4mg lorazepam, IV magnesium bolus
  - Intubated for emergent C section in OR
  - Acute hypotension, then PEA arrest with 3 minutes of CPR
  - Bedside US w/ severely dilated RV
- MFM called and recommended A-OK protocol, TXA
  - Pt treated with A-OK, started on epinephrine gtt, and given 100mg bolus intralipid
  - EBL 800mL, got carboprost, TXA, rectal misoprostol, routine oxytocin
- Labs:
  - Hgb 11
  - PLT 33
  - Otherwise hemolyzed
- Transferred to ANW

Allina Health

21

Case 2

- Arrival to ANW on vasopressin, norepinephrine, epinephrine
  - Initial blood draw looked very diluted by crystalloid
  - POCUS with dilated RV, underfilled LV
  - Added dobutamine, inhaled epoprostenol
- Resuscitation: 10 RBC, 4 FFP, 6 PLT, 4 cryo
  - BP improved during active transfusion
  - Unable to obtain labs with intralipid interference
  - Transfusion thresholds decided based on clinical picture: initial blood draw consistency, likelihood of DIC with active bleeding from incision site, vagina, and IV sites, urine in Foley red tinged, as well at PLT 33 at OSH
- Seized x2, transitioned to midazolam for sedation
- Worsening abdominal distension prompted discussion of possible exlap
  - POCUS with peritoneal fluid, continued increase in pressors
- VA ECMO team initiated
  - 4 pressor shock, RV dysfunction, POCUS with obstructive shock, if going for exlap would need more cardiac support
- Sudden drop in vasopressor needs that held even when transfusions paused
  - Repeat POCUS with RV:LV ratio ~ 1:1, improved RV function
- AHF, MFM, Intensivist discussion bedside transitioned plan to CT bleed protocol, then cath lab for PAC

Allina Health

22

Case 2

Labs
- 1243: Troponin 515, D-dimer >128
- 1319: fibrinogen 161

CT 1422
Bleed in L rectus sheath, enlarged main pulmonary artery, moderate pulmonary edema

Coronary Angiogram 1526
The right atrial mean pressure is 15. The pulmonary wedge mean pressure is 19. RV pressure is 27/14, 17. PA pressure is 28/18 with a mean of 22. Cardiac index by Fick was 4.36, by thermal dilution was 2.23. The mixed venous saturation was 74%.

SUMMARY OF FINDINGS:
1. Amniotic fluid embolization.
2. Severe RV dysfunction.
3. Cardiogenic shock.
4. Pressor dependent. Hemodynamics currently acceptable and not requiring ECMO insertion.

IR Angiogram 1733
1. Large pseudoaneurysm arising from left inferior epigastric artery was successfully coil embolized.
2. Several small foci of hemorrhage arising from multiple peripheral branches of the right inferior epigastric artery. Successful Gelfoamembolization of right inferior epigastric artery.
3. Completion pelvic angiogram demonstrates no additional sites of bleeding.

Allina Health

23

Case 2

Initial treatment
- Mechanical ventilation
- Inhaled epoprostenol
- EEG with epilepsy consult
- Levetiracetam load and BID dosing
- Magnesium gtt
- Sedation with midazolam, fentanyl
- PAC numbers, O2M guiding epinephrine dosing
- Vasopressin, norepinephrine for BP support
- Hgb, PLT, INR, fibrinogen q6h, transfusion based on labs
- Abx (pip-tazo) for 48h pending cultures

Ongoing treatment
- Extubated next day after weaning O2, epoprostenol, sedation
- Repeat echo showing normal RV and LV at 1444 next day, on day 3 had enlarged RV and LA but normal function and mild TR
- MRI WNL, no venous sinus thrombus
- PM&R, therapies
- F/u with epilepsy, advanced heart failure

Allina Health

24

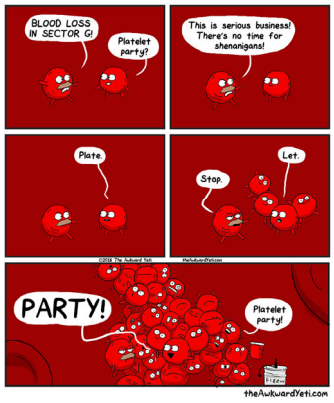
A-OK Protocol

- Serotonin increased in maternal circulation in AFE interacts with thromboxane (also increased) to cause platelet dysfunction
- Serotonin activation of pulmonary vasculature receptors → vasoconstriction and PLT entrapment
- More thromboxane → PLT party
- Serotonin centrally mediated reduction in peripheral vascular tone → CV collapse

Atropine
- Counteracts parasympathetic effects contributing to bradycardia

Ondansetron
- Modulate serotonin effect

Ketorolac
- Decrease thromboxane production



AllinaHealth

25

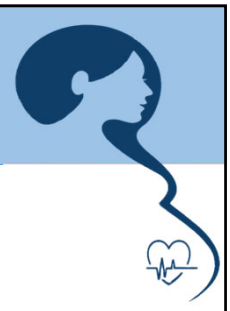
Intralipid

- 1998 paper showing IV lipid emulsion could treat/modulate bupivacaine induced asystole in rats
  - Extrapolated to other toxicities with lipophilic agents
  - "Lipid sink" theory to "lipid shuttle"
- Suspected physiology
  - Reduced local anesthetic level below sodium channel blocking thresholds increase contractility and improves vascular tone
  - Prostaglandin I2 precursors possible way of decreasing pHTN
  - More notable hemodynamic effects than saline, increased aortic flow and BP, not just simple volume expansion causing the inotroy and lusitropy
  - Possible that FFA provide substrate for oxidative phosphorylation
  - Possible activation of voltage gated calcium channels
- Complications
  - AKI, VQ mismatch, VTE, fat embolism, acute pancreatitis, ARDS, CVVHF filter obstruction
  - Made of egg in the US, allergen
- Reports note laboratory interference due to lipidemia despite ultracentrifugation of blood have persisted beyond 25h

AllinaHealth

26

ECMO



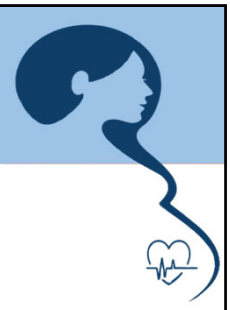
Consider it right away!

- Hemodynamic collapse, call ECMO resource/Intensivist ASAP, in conjunction with beginning resuscitation
- Takes time to set up
- Most peripartum women are candidates
- ECPR also an option
- VA ECMO, maybe VAV, but unlikely VV alone, can always adjust

AllinaHealth

27

Prognosis

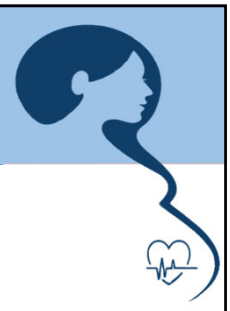


- Historic mortality around 60%, more recently 10-30% in developed countries
- About 50% of mortality occurs within the first hr, and about 66% in the first 5 hours
- Around 60-70% of survivors have have notable neuro, pulmonary, or cardiac sequelae
- While many survivors develop PTSD, around 60% are able to return to their daily life
- Infant mortality is around 30% with increased risk of hypoxic-ischemic encephalopathy, CP, and cognitive disabilities

AllinaHealth

28

Summary

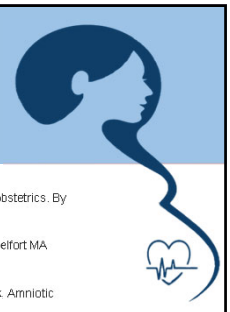


- ❑ Manage circulatory collapse
- ❑ ABCs: manage airway, breathing, and circulation
- ❑ Designate a timekeeper to call out times at 1-min interval
- ❑ If no pulse, start CPR (and call for ECMO activation)
  - ❑ Manually displace uterus or lateral tilt
  - ❑ Consider move to operating room only if this can be accomplished in 2 min or less
  - ❑ If no pulse at 4 min, START perimortem cesarean delivery (resuscitative hysterotomy)
  - ❑ **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**
  - ❑ **Cryoprecipitate preferred over FFP to reduce volume overload**
- ❑ **Consider thromboelastometry if available**
- ❑ **Tranexamic acid (1 g IV over 10 min)**
- ❑ **Manage pulmonary hypertension and right ventricular failure (Anesthesiology, Critical Care, or Cardiology)**
  - ❑ **TTE or TEE**
  - ❑ **Vasopressor**
  - ❑ **Inotropes**
  - ❑ **Pulmonary vasodilator**
  - ❑ **Wean FiO2 to maintain O2 saturation 94% to 98%**
- ❑ **Postevent debrief (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**

Allina Health

29

References



1. Steiner PE, Lushbaugh CC. Landmark article, Oct. 1941: Maternal pulmonary embolism by amniotic fluid as a cause of obstetric shock and unexpected deaths in obstetrics. By Paul E. Steiner and C. C. Lushbaugh. JAMA. 1986 Apr 25;255(16):2187-203. doi: 10.1001/jama.255.16.2187. PMID: 3514978.
2. Fong A, Chau CT, Pan D, et al. Amniotic fluid embolism: antepartum, intrapartum and demographic factors. *J Matern Fetal Neonatal Med*. 2014 Jun 30. 1-6
3. Clark SL, Romero R, Dildy GA, Callaghan WM, Smiley RM, Bracey AW, Hankins GD, D'Alton ME, Foley M, Pacheco LD, Vadhera RB, Herlihy JP, Berkowitz RL, Belfort MA Proposed diagnostic criteria for the case definition of amniotic fluid embolism in research studies. Am J Obstet Gynecol. 2016;215(4):408. Epub 2016 Jun 29.
4. Pacheco, Luis D. et al. Amniotic fluid embolism: diagnosis and managementAmerican Journal of Obstetrics & Gynecology, Volume 215, Issue 2, B16 – B24
5. Irene A. Stafford, Amirhossein Moaddab, Gary A. Dildy, Miranda Klassen, Alexandra Berra, Christine Watters, Michael A. Belfort, Roberto Romero, Steven L. Clark. Amniotic fluid embolism syndrome: analysis of the Unites States International Registry American Journal of Obstetrics & Gynecology MFM,Volume 2, Issue 2,2020
6. Patient Safety and Quality Committee, Society for Maternal-Fetal Medicine. Electronic address: smfm@smfm.org; Combs CA, Montgomery DM, Toner LE, Dildy GA. Society for Maternal-Fetal Medicine Special Statement: Checklist for initial management of amniotic fluid embolism. Am J Obstet Gynecol. 2021 Apr;224(4):B29-B32. doi: 10.1016/j.ajog.2021.01.001. Epub 2021 Jan 6. PMID: 33417901.Akash Mathavan, Akshay Mathavan, Sujay Kamisetty, Ali Ataya, A 35-Year-Old Woman With Placenta Previa and Postpartum Cardiovascular Collapse, CHEST, Volume 166, Issue 2, 2024, Pages e25-e27, ISSN 0012-3692,https://doi.org/10.1016/j.chest.2024.03.001. (https://www.sciencedirect.com/science/article/pii/S0012369224002897)
7. Papageorgiou C, Jourdi G, Adjambri E, Walborn A, Patel P, Fareed J, Elalamy I, Hoppensteadt D, Gerotziafas GT. Disseminated Intravascular Coagulation: An Update on Pathogenesis, Diagnosis, and Therapeutic Strategies. Clin Appl Thromb Hemost. 2018 Dec;24(9_suppl):8S-28S. doi: 10.1177/1076029618806424. Epub 2018 Oct 8. PMID: 30296833; PMCID: PMC6710154.
8. Management of coagulopathy associated with postpartum hemorrhage: guidance from the SSC of the ISTH Collins, P. et al. Journal of Thrombosis and Haemostasis, Volume 14, Issue 1, 205 - 210
9. Society for Maternal-Fetal Medicine Special Statement: Checklist for initial management of amniotic fluid embolism. Combs, C. Andrew et al. American Journal of Obstetrics & Gynecology, Volume 224, Issue 4, B29 - B32
10. Long M, Martin J, Biggio J. Atropine, Ondansetron, and Ketorolac: Supplemental Management of Amniotic Fluid Embolism. Ochsner J. 2022 Fall;22(3):253-257. doi: 10.31486/toj.21.0107. PMID: 36189093; PMCID: PMC9477128.
11. Leaños OL, Hong E, Amezcua JL. Reflex circulatory collapse following intrapulmonary entrapment of activated platelets: mediation via 5-HT3 receptor stimulation. Br J Pharmacol. 1995 Oct;116(3):2048-52. doi: 10.1111/j.1476-5381.1995.tb16410.x. PMID: 8640344; PMCID: PMC1908951.
12. Larsen JB, Aggerbeck MA, Granfeldt A, Schmidt M, Hvas AM, Adelborg K. Disseminated intravascular coagulation diagnosis: Positive predictive value of the ISTH score in a Danish population. Res Pract Thromb Haemost. 2021 Dec 9;5(8):e12636. doi: 10.1002/rth2.12636. PMID: 34938938; PMCID: PMC8660681.
13. Kaestner M, Schranz D, Warnecke G, et al. Pulmonary hypertension in the intensive care unit. Expert consensus statement on the diagnosis and treatment of paediatric pulmonary hypertension. The European Paediatric Pulmonary Vascular Disease Network, endorsed by ISHLT and DGPKHeart 2016;102:ii57-ii66.
14. Rezai S, Hughes AC, Larsen TB, Fuller PN, Henderson CE. Atypical Amniotic Fluid Embolism Managed with a Novel Therapeutic Regimen. Case Rep Obstet Gynecol. 2017;2017:8458375. doi: 10.1155/2017/8458375. Epub 2017 Dec 21. PMID: 29430313; PMCID: PMC5753013.

Allina Health

30