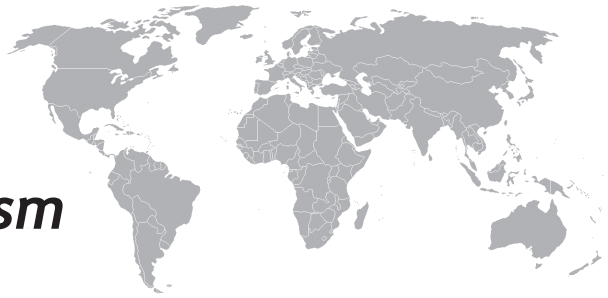
Amniotic Fluid Embolism



Dr. Harun Toy

Harran University, Medical Faculty, Department of Gynecology and Obstetrics, Şanlıurfa, Turkey
Eur J Gen Med 2009;6(2):108-115

Correspondence: *Dr. Harun Toy*
Harran University, Medical Faculty, Department of Gynecology and Obstetrics, Şanlıurfa, Turkey

ABSTRACT

Amniotic fluid embolism (AFE) is a catastrophic syndrome occurring during labor and delivery or immediately postpartum. Amniotic fluid embolism is an important cause of maternal deaths in developed countries. It has high morbidity and mortality rate. The associated mortality and morbidity have decreased dramatically in recent times, such that recent reported maternal mortality is now in the order of 16%. The true incidence is unclear because this syndrome is difficult to identify and the diagnosis remains one of exclusion, with possible under-reporting of nonfatal cases. The pathophysiology of AFE remains unclear. Amniotic fluid embolism occurs when there is a breach in the barrier between the maternal circulation and amniotic fluid. Two separate life-threatening processes seem to occur either simultaneously or in sequence, namely, cardiorespiratory collapse and coagulopathy. The symptoms of AFE commonly occur during labor and delivery or in the immediate postpartum period. Most cases (80%) occur during labor, but it can occur either before labor (20%) or after delivery. About 25% of patients will die within 1 hour of onset. The classic clinical presentation of AFE is that of sudden onset of dyspnea, respiratory failure and hypotension followed by cardiovascular collapse, disseminated intravascular coagulation and death. AFE is poorly understood and diagnosed largely by exclusion. Presently, the AFE diagnosis is not based on any clinical or laboratory finding. The treatment is still not causative but supportive and focuses initially on rapid maternal cardiopulmonary stabilization. The most important goal of therapy is to prevent additional hypoxia and subsequent end-organ failure. The prognosis and mortality of AFE have improved significantly with early diagnosis of AFE and prompt and early resuscitative measures.

Keywords: *Amniotic fluid embolism, cardiorespiratory collapse, coagulopathy, disseminated intravascular coagulation .*

INTRODUCTION

Amniotic fluid embolism (AFE) is a catastrophic syndrome occurring during labor and delivery or immediately postpartum. Although presenting symptoms may vary, common clinical features include shortness of breath, altered mental status followed by sudden cardiovascular collapse, disseminated intravascular coagulation (DIC), and maternal death(1). The syndrome of AFE was first described by Meyer in 1926 (2). It became an established clinical entity in 1941 after Steiner and Luschbaugh (3) published a maternal mortality case series that included eight women who had squamous cells and mucin, presumably of fetal origin, within their pulmonary vasculature. The authors postulated that these histologic findings formed the basis of a clinical syndrome characterized by sudden shock and pulmonary edema during labor that ultimately resulted in maternal death.

Amniotic fluid embolism is an important cause of maternal deaths in developed countries. It has high morbidity and mortality rate. The associated mortality and morbidity have decreased dramatically in recent times, such that recent reported maternal mortality is now in the order of 16% (4). Entry criteria consist of the presence of the following 4 factors:

1. Acute hypotension or cardiac arrest
2. Acute hypoxia
3. Coagulopathy or severe clinical hemorrhage in the absence of other explanations
4. All of these occurring during labor, cesarean delivery, or D&C or within 30 minutes postpartum with no other explanation for the findings(5).

EPIDEMIOLOGY

The true incidence is not known because of inaccuracies in reporting maternal deaths, lack of data from nonfatal cases, and the fact that AFE is difficult to identify and remains a diagnosis of exclusion. In Morgan's series (6) of 272 cases the incidence is reported to range between 1:8000 and 1:80,000, with a maternal mortality of 86%. It is responsible for 10% of all maternal deaths in the United States (7). Burrows and Khoo (8) published a series of ten cases of AFE with a maternal mortality rate of 22%.The syndrome typically occurs during labor, soon after vaginal or cesarean delivery, or during second-trimester dilatation and evacuation procedures. In the national registry, 70% of the cases occurred during labor, 19% were recorded during cesarean delivery, and 11% occurred after vaginal delivery (9). All of the cases noted during cesarean section had their onset soon after delivery of the infant. Despite technological advances in critical care life support, the maternal mortality rate for AFE remains around 61%; a large percentage of survivors have permanent hypoxia-induced neurological damage. The fetal mortality rate, although better than the maternal rate, is a dismal 21%, and 50% of the surviving neonates experience permanent neurological injury (9,10). Recently, the mortality rates of AFE have decreased because of better critical care and early diagnosis. The critical care, multidisciplinary approach to the treatment of AFE is becoming more widely available. The neonatal survival rate was 95% and routine discharge was reported in 72% (8). Neonatal outcome was only marginally better, with a survival rate of undelivered fetuses at the time of AFE of 79%, in which only 50% of those infants were normal at discharge (9).

DESCRIPTION and ETIOLOGY

Normally, amniotic fluid does not enter the maternal circulation because it is contained safely within the uterus, sealed off by the amniotic sac. AFE occurs when the barrier between amniotic fluid and maternal circulation is broken and, possibly under a pressure gradient, fluid abnormally enters the maternal venous system via the endocervical veins, the placental site (if placenta is separated), or a uterine trauma site(11). Why this entry into maternal circulation occurs in some women and not in others is not clearly understood (10). Clark et al.(9) contend that AFE more closely resembles an anaphylactic reaction to fetal debris than an embolic event, and they propose the term "anaphylac-toid syndrome of pregnancy" instead of AFE. The exact mechanism of this anaphylactoid reaction to amniotic fluid is not clearly understood. Predisposing factors once considered to be associated with AFE include placental abruption, uterine overdistention, fetal death, trauma, turbulent labor oxytocin-stimulated labor, multiparity, male fetus, cesarean delivery, advanced maternal age, prolonged gestation, instrumental vaginal delivery, eclampsia, polyhydramnios, fetal distress, large fetal size, high cervical laceration, premature separation of the placenta and rupture of membranes (12-15). The presence of a large or dead fetus and meconium staining of the amniotic fluid are also felt to increase the risk (5) (Table 1).

Table 1. Risk factors of amniotic fluid embolism.

Older age	*Intrauterine fetal death*
Multiparity	
Physiologic intense uterine contractions	*Large fetal size*
Medical induction of labour	*Meconium staining of the amniotic fluid*
Instrumental vaginal delivery	*Placental abruption*
Prolonged gestation	*Eclampsia*
Cesarean section	*Fetal distress*
Uterine rupture	*Trauma to abdomen*
Polyhydramnios	*Surgical intervention*
High cervical tears	*Saline amnioinfusion*
Premature placental separation	*Male fetus meconium*

CLINICAL PRESENTATION

One of the major factors that makes AFE so devastating is its total unpredictability. AFE typically occurs during labor and delivery or in the immediate postpartum period. Exceptions to this timing of onset are rare but cases have been reported in the late postpartum period, after cesarean delivery, amniocentesis, (16) removal of the placenta, or with therapeutic abortions.(17). Other cases have been associated with abdominal trauma,(18) cervical suture removal, ruptured uterus or intrapartum amnioinfusion.

The classic presentation of AFE is described as sudden, profound, and unexpected dyspnea, respiratory failure hypotension followed by cardiovascular collapse disseminated intravascular coagulation and death (3). In Morgan's series, the presenting symptom was respiratory distress in 51% of the patients, hypotension in 27%, coagulation abnormality in 12%, and seizures in 10%. Analysis of Clarke's national registry reveals that of the women presenting before delivery, the presenting symptom was seizures or seizure like activity 30%, dyspnea 27%, fetal bradycardia 17%, and hypotension in 13%. Of those who developed symptoms after delivery, 54% presented with an isolated coagulopathy resulting in postpartum hemorrhage (9) (Table 2).

Table 2. Cardinal criteria of amniotic fluid embolism.

- *Acute hypoxia diagnosed by dyspnea cyanosis, and/ or respiratory arrest*
- *Shock (typically obstructive, cardiogenic, or distributive. Acute hipotansion and/or cardiac arrest)*
- *Coagulopathy severe clinical hemorrhage/ disseminated intravascular coagulation*
- *Altered mental status /hypoxic encephalopathy*
- *All of these occurring during labor, cesarean delivery, or dilatation and evacuation or within 30 minutes postpartum with no other explanatiovn for the findings*
- *Seizure activity, confusion, agitation, constitutional (fever, chills, headache, nausea, vomiting), evidence of fetal distress (late decelerations, bradycardia) , other common presenting signs and symptoms*

There are 3 identified phases of AFE in humans. Phase 1 includes;

1. Respiratory-distress and cyanosis,

2. Hemodynamic-pulmonary edema and hemorrhagic shock,

3. Neurologic- confusion and coma.

These manifestations can occur in combination, separately, and in different magnitudes. If patients survive the initial cardiorespiratory insult, 40% to 50% progress into phase 2, which is characterized by coagulopathy, hemorrhage, and shock. In phase 2, left-sided heart failure is evident and is the most reported sign in humans. Increases in pulmonary capillary wedge pressure, PA pressure and central venous pressure are characteristic of pulmonary edema. In phase 3, acute symptoms have passed and injury to the brain lung and renal systems already established. Phase 3 may last weeks, and patients may die as a result of severe brain and lung injury. Infection and multiple organ system failure also may cause death (19).

PATHOPHISIOLOGY

The pathophysiology of AFE is multifactorial, poorly understood and speculative; various theories have been published. Gei and Hankins (20) proposed a pathophysiological course. Three distinct responses

or a combination of clinical responses to circulating fetal debris are suggested. The initial respiratory reaction possibly begins with transient pulmonary vasospasm (21) may be caused by amniotic microemboli that trigger the release of arachidonic acid metabolitesb (22) and lead to pulmonary hypertension, intrapulmonary shunting, bronchoconstriction, and severe hypoxia (21) Exactly which components of amniotic fluid actually cause this effect is unknown (10). The conventional explanation states that particulate matter such as fetal squamous cells, lanugo, and meconium contained in the amniotic fluid produce pulmonary vascular obstructions that lead to pulmonary hypertension, right- and left-sided heart failure, hypotension, and death. However, current evidence suggests that a mechanical origin is less likely than an immunologic reaction. In this model, pulmonary vasospasm causes a physiologic pulmonary artery obstruction as a reaction to abnormal substances such as leukotrienes and metabolites of arachnoid acid in the amniotic fluid (23). The second manifestation includes negative inotropism and left ventricular failure resulting in increasing pulmonary edema and hypotension quickly leading to shock. The third manifestation is a neurological response to the respiratory and hemodynamic injury, which may include seizures, confusion, or coma(20). About 40% to 50% of patients who survive to this point have severe coagulopathy, usually disseminated intravascular coagulation, which results in uncontrollable uterine bleeding along with bleeding from puncture sites such as insertion sites for intravenous and epidural catheters(20) This coagulopathy is thought to be precipitated by several procoagulant components of amniotic fluid, most notably thromboplastin, which initiate the extrinsic pathway of the clotting cascade and result in excessive fibrinolytic activity (20,24,25,26) (Table 3).

DIAGNOSIS

Immediate recognition and diagnosis of AFE is essential to improve maternal and fetal outcomes.AFE is poorly understood and diagnosed largely by exclusion. Presently, the AFE diagnosis is not based on any clinical or laboratory finding. The differential diagnosis includes air or thrombotic pulmonary emboli, septic shock, acute myocardial infarction, cardiomyopathy, anaphylaxis, aspiration, placental abruption, eclampsia, uterine rupture, transfusion reaction and local anaesthetic toxicity (27))(Table 4). The diagnosis of amniotic fluid embolism should be considered when a pregnant woman with one or more of these risk factors suddenly deteriorates with respiratory distress, bleeding or shock. Several methods have been suggested for the diagnosis of amniotic fluid embolism but no diagnostic test is reliable (28). The initial presenting signs are often seen on the electrocardiogram and the pulse oximeter. The electrocardiogram may show tachycardia with a right strain pattern and ST-T wave changes, and pulse oximetry may reveal a sudden drop in oxygen saturation (5). Although most patients initially present with cardiac and respiratory failure, there is a subset of patients in whom severe

***Table 3**. Pathophysiology of amniotic fluid embolism (10).*

Progression of events:

1. *For reasons not completely understood, amniotic fluid reaches the maternal intravascular compartment (systemic venous system).*
2. *The amniotic fluid enters pulmonary circulation via the pulmonary artery. This contaminated blood crosses to the left atrium through a patent foramen and probably through intrapulmonary shunts once the embolism is significant, as shown in cases of massive amniotic fluid embolism at autopsy.*
3. *The exposure of the pulmonary vasculature to both soluble (leukotrienes, surfactant, thromboxane A2, endothelin, etc.) and insoluble components (squames, vernix, hair, mucin, etc.) of the amniotic fluid and possibly other mediators released locally induces capillary leak, negative inotropism, and bronchospasm. This results in sudden onset of respiratory distress and cyanosis.*
4. *Within minutes, the negative inotropic effect becomes prevalent (probably due to myocardial ischemia). Pulmonary venous pressure (congestion) increases and a drop in cardiac output are manifested by pulmonary edema and hypotension to the point of shock.*
5. *The exposure of the intravascular compartment to amniotic fluid thromboplastin and to other mediators freed in the circulation by the presence of amniotic fluid induces a consumptive coagulopathy in a large proportion of the first-phase survivors. This disseminated intravascular coagulation often results in severe uterine bleeding.*
6. *The resultant systemic hypotension decreases the uterine perfusion. Abnormalities of the fetal heart tracing will rapidly follow and may result in fetal death.*

Table 4. Differential diagnosis of amniotic fluid embolism.

Pulmonary thromboembolism
Air embolism
Transfusion reaction
Hemorrhage
Anaphylaxis
Cardiomyopathy,
Myocardial infarction
Septic shock
Uterine rupture
Eclampsia
Placental abruption
Anesthetic complications
Aspiration of gastric contents
Systemic inflammatory response syndrome

hemorrhage with DIC may be the first sign. The clinical diagnosis is made most frequently in 65-70% of cases during labor and much less frequently, in 11% of cases, in the postpartum patient (29).

There are no specific laboratory tests that confirm the diagnosis of AFE, but some tests may support the diagnosis. Initial laboratory data should include an arterial blood gas to determine adequacy of ventilation and the degree of hypoxemia (29). Diagnostic markers for amniotic fluid embolism based on peripheral blood samples have also been introduced. These include sialyl Tn (STN), zinc coproporphyrin and complement factor consumption (30, 31). Significantly higher serum STN levels were found in patients with clinically apparent AFE than in controls (32). It has recently been demonstrated that the monoclonal antibody THK-2 may be a specific pathologic marker for amniotic fluid embolism (32, 33). Another suggestion is that finding fetal megakarycytes and syncytiotrophoblastic cells in the maternal pulmonary circulation by monoclonal antibodies (CD-61—GPIIIa, β-hCG, and factor VIII-vW hPL antibodies) may be diagnostic (34). The most reliable laboratory test to evaluate the development of DIC are the AT-III level, fibrinopeptide A level, D-dimer level, prothrombin fragment 1.2 (PF 1.2), thrombin precursor protein, and platelet count. More global tests, including the PT, PTT, and fibrinogen level are helpful if abnormal; however, these tests may frequently be normal in DIC (15).

When correlated with clinical signs and symptoms, other diagnostic tools may be employed to support the presumptive diagnosis of AFE. Echocardiography showed severe pulmonary hypertension and right ventricular dilatation, with a displaced intraventricular septum pressing on the left ventricle (35). Transesophageal echocardiography performed during the acute presentation of AFE was reported in case reports. In this reports, the trans-esophageal echocardiography showed right ventricular failure with leftward deviation of the interventricular septum and severe tricuspid regurgitation (36). Chest radiography is a helpful diagnostic tool, but it is limited by a lack of specificity. In mothers with AFE, 24% to 93% show pulmonary edema that presents as acute respiratory distress syndrome on chest radiograph (37). However, multiple patchy, nodular infiltrates and small pleural effusion could occur in chest x-ray (35).

Lung pathology may reveal gross findings of edema or hemorrhage, but the lung may have a normal appearance. Histological examination demonstrates foreign material in the pulmonary capillaries, arterioles, and arteries. Special stains such as TKH-2, a monoclonal antibody to fetal glycopreotein sialyl Tn antigen have been applied to pathologic specimens and also evaluated in maternal serum has not been validated and is not currently recommended for diagnosing the syndrome (38).

TREATMENT

The treatment is still not causative but supportive and focuses initially on rapid maternal cardiopulmonary stabilization. The majority of patients will require intensive care unit admission after initial stabilization(39). The most important goal of therapy is to prevent additional hypoxia and subsequent end-organ failure(29). Despite the decline in mortality, no new therapies have emerged and treatment remains essentially supportive (Table 5). Aggressive resuscitation may be indicated depending on the clinical presentation. Management strategies is improve oxygenation, support circulation, and correct the coagulopathy. When clinically possible, an arterial line and a pulmonary artery catheter should be placed to help guide the therapy (40). If the fetus is sufficiently mature and is undelivered at the time of maternal cardiac arrest, Cesarean section should be instituted as soon as possible (41). Maternal oxygenation up to an arterial oxygen tension of more than 60 mmHg should be achieved by administering oxygen via a face mask to all awake patients. Tracheal intubation and mechanical ventilation using 100% oxygen should be instituted

***Table 5**. General supportive measures in the treatment of amniotic fluid embolism.*

1. *Treat hypoxia with 100% oxygen.*
2. *Treat hypotension by fluid resuscitation with isotonic solutions and vasopressors.*
3. *Treat left ventricular diminished contractility with fluids and inotropic therapy.*
4. *Treat DIC and coagulopathy with FFP, cryoprecipitate, fibrinogen and factor replacement.*
5. *Treat hemorrhage with RBC transfusions and thrombocytopenia with platelets.*

DIC: Disseminated intravascular coagulation; FFP: Fresh frozen plasma; RBC: Red blood cells.

in patients with refractory hypoxemia, seizures, or in comatose patients (42). Vasoactive drug therapy must be tailored to the clinical situation. To enhance cardiac output and support blood pressure, dopamine is suggested, although in severe shock epinephrine or norepinephrine may be ideal agents because of the additional β-adrenerjic effects, which improve cardiac function in addition to the α-adrenerjik vasoconstrictor effects. Inotropic support with dobutamine or milrinone may be needed for inotropic support(29). Other treatment modalities that might have been beneficial for sever pulmonary hypertension include nitric oxide, as a selective pulmonary vasodilator, prostacyclin and sildenafil (43). In less than 4 h, half of the patients who survive the initial phase go on to develop DIC, with massive haemorrhage (3). Therefore, blood products should be prepared ahead of time, and replacement with typed and crossed packed red blood cells, or with O-negative blood, is essential (44). Treatment of DIC requires transfusion of packed red blood cells and blood products. Large-bore intravenous access is essential because massive transfusion may be required (45). Platelets, cryoprecipitate, and fresh frozen plasma should be administered as guided by laboratory assessment of the prothrombin time/ partial thromboplastin time, fibrinogen, and fibrin and fibrin degradation products. In literature, treatment of AFE have described the use of plasma exchange, cardiopulmonary bypass, aprotinin and recombinant activated factor seven (rVIIa) in the management of the associated coagulopathy (46-48). The successful use of uterine arterial embolization to control massive bleeding in two cases of AFE is described (49). During cardiopulmonary resuscitation and chest compressions and before delivery, the uterus should be displaced to the left to avoid compression of the aorta and the inferior cava that compromise maternal venous return to the heart. The uterus can be displaced manually or by placing a wedge under the woman's right hip (29) (Table 6).

***Table 6**. Newer strategies in the treatment of amniotic fluid embolism.*

1. *Intra-aortic balloon counterpulsation (54)*
2. *Extracorporeal membrane oxygenation (54)*
3. *Cardiopulmonary bypass (46)*
4. *Plasma exchange transfusions (55,56)*
5. *Uterine artery embolization (53,57)*
6. *Continuous hemofiltration (56)*
7. *Cell-salvage combined with blood filtration (44)*
8. *Serum protease inhibitors (41)*
9. *Inhaled nitric oxide (41)*
10. *Inhaled prostacyclin (41)*
11. *Application sildenafil (46)*
12. *High-dose corticosteroids (41)*

PROGNOSIS

Patients with AFE have a very poor prognosis .To this date, this syndrome cannot be predicted or prevented. AFE remains one of the most feared and lethal complications of pregnancy. The prognosis and mortality of AFE have improved significantly with early diagnosis of AFE and prompt and early resuscitative measures. Although mortality rates have declined, morbidity remains high with sever sequel, particularly neurologic impairment. Corticosteroid therapy may be administered immediately before amniocentesis and delivery to minimize the theoretical potential of a recurrence (50). Parturient with a known history of atopy or anaphylaxis are also at a high risk of AFE. In the National Amniotic Fluid Embolism Registry, a known history of drug allergy and atopy was found in 41% of the 46 patients with

AFE (9). However, the mainstay of a successful outcome remains the identification of high risk patients. In some cases, death is inevitable despite early and appropriate management. Neonatal survival is reported at 70%. Although there are many new develop-

ments with respect to our knowledge of the diseases, AFE continues to be a catastrophic illness requiring a high index of suspicion, a multidisciplinary approach, and rapid resuscitation efforts in order to have a desirable clinical outcome (29). Ideal management includes prompt evaluation of and intervention for each of the pathologic events found in this complex obstetric condition (1).

FETAL CONSIDERATIONS

In some instances, and of course most favorable for the fetus, AFE does not occur until after delivery. When AFE occurs before or during delivery, however, the fetus is in grave danger from the onset because of the maternal cardiopulmonary crisis. In addition to concern for fetal well-being, delivery of the fetus increases the chances for a good outcome for the mother because the weight of the gravid uterus on the inferior vena cava impedes blood return to the heart and decreases systemic blood pressure (25,51). Therefore, as soon as the mother's condition is stabilized, delivery of the viable infant should be expedited. If resuscitation of the mother is futile, an emergency bedside cesarean delivery may be necessary to save the infant. Undeniably, the sooner after maternal cardiopulmonary arrest that the fetus is delivered, the more favorable is the fetal outcome. (9,52) Therefore, as difficult as it may be, and even though the mother may be viewed as the primary patient, prolonged resuscitation efforts should be discouraged (10).

REFERENCES

1. *Stafford I, Sheffield J. Amniotic Fluid embolism. Obstet Gynecol Clin N Am 2007;34:545-53.*
2. *Meyer JR. Embolia pulmonary amnio caseosa. Bras Med 1926;2:301-3.*
3. *Steiner PE, Lushbaugh CC. Landmark article, 1941: Maternal pulmonary embolism by amniotic fluid as a cause of obstetric shock and unexpected deaths in obstetrics. JAMA 1986;255:2187-203.*
4. *Tuffnell DJ. Amniotic fluid embolism. Curr Opin Obstet Gynecol 2003;15:119-22.*
5. *O'Shea A, Eappen S. Amniotic fluid embolism. Int Anesthesiol Clin 2007;45:17-28*
6. *Morgan M. Amniotic fluid embolism. Anaesthesia 1979; 34:20-32.*
7. *Atrash HK, Koonin LM, Lawson HW, et al. Maternal mortality in the United States, 1979-1986. Obstet Gynecol 1990;76:1055.*
8. *Burrows A, Khoo SK. The amniotic fluid embolism syndrome: 10 years' experience at a major teaching hospital. Aust N Z J Obstet Gynaecol 1995;35:245-50.*
9. *Clarke SL, Hankins GD, Dudley DA, Dildy GA, Porter TF. Amniotic fluid embolism: Analysis of the national registry. Am J Obstet Gynecol 1995;172:1158-67.*
10. *Perozzi KJ, Englert NC. Amniotic Fluid embolism: An obstetric emergency. Crit Care Nurse 2004;24:54-61.*
11. *Bastien JL, Graves JR, Bailey S. Atypical presentation of amniotic fluid embolism. Anesth Analg.. 1998;87:124-6.*
12. *Sisson MC. Amniotic fluid embolism. Crit Care Obstet. 1992;4:667-73.*
13. *Kramer MS, Rouleau J, Baskett TF, Joseph KS. Amniotic-fluid embolism and medical induction of labour: A retrospective, population-based cohort study. Lancet 2006; 368:1444-8.*
14. *Christiansen LR, Collins KA. Pregnancy-associated deaths a 15 year retrospective study and overall review of maternal pathophysiology. Am J Forensic Med Pathol 2006;27:11-9.*
15. *Bick RL, Disseminated intravascular coagulation: A review of etiology, pathophysiology, diagnosis, and management: Guidelines for care. Clin Appl Thrombosis/ Hemostasis 2002;8:1-31.*
16. *Hassart TH, Essed GG. Amniotic fluid embolism after transabdominal aminocentesis. Eur J Obstet Gynecol Reprod Biol. 1983;16:25-30.*
17. *Ray BK, Vallejo MC, Creinin MD, et al. Amniotic fluid embolism with second trimester pregnancy termination: A case report. Can J Anesth 2004;51:139-44.*
18. *Rainio J, Penttila A. Amniotic fluid embolism as a cause of death in a car accident: A case report. Forensic Sci Int 2003;137:231-4.*
19. *Gilmore DA, Wakim J Secrets J, Rawson R. Anaphylactoid syndrome of preganacy: A review of the literature with latest management and outcome data. AANA J 2003;71:120-6.*
20. *Gei G, Hankins GDV. Amniotic fluid embolism: an update. Contemp Ob/Gyn. January 2000;45:53-66.*
21. *Clark SL. New concepts of amniotic fluid embolism: a review. Obstet Gynecol Surv.1990; 45:360-8.*
22. *Reeves WC, Demers LM, Wood MA, et al. The release of thromboxane A2 and prostacyclin following experimental acute pulmonary embolism. Prostaglandins Leukot Med. 1983;11:1-10.*
23. *Rossi SE, Goodman PC, Franquet T. Nonthrombotic pulmonary emboli. AJR 2000;174:1499-508.*
24. *Lewis PS, Lanouette JM. Principles of critical care. In: Cohen WR (ed). Cherry and Merkatz Complications of Pregnancy. 5th ed. Philadelphia, Pa: Lippincott Williams & Wilkins, 2000:763-71.*

25. Martin PS, Leaton MB. Emergency: Amniotic fluid embolism [published correction appears in Am J Nurs. May 2001;101:14]. Am J Nurs. March 2001;101:43-4.

26. Locksmith GJ. Amniotic fluid embolism. Obstet Gynecol Clin North Am 1999;26:435-44.

27. Masson RG. Amniotic fluid embolism. Clin Chest Med 1992;13:657-65.

28. Moore J. Amniotic fluid embolism: On the trail of an elusive diagnosis. Lancet 2006;368:1399-401.

29. Moore J, Baldisseri MR. Amniotic fluid embolism. Crit Care Med 2005;33(10 Suppl):279-85.

30. Kanayama N, Yamazaki T, Naruse H, Sumimoto K, Horiuchi K, Terao T. Determining zinc coproporphyrin in maternal plasma-a new method for diagnosing amniotic fluid embolism. Clin Chem 1992;38:526-9.

31. Harboe T, Benson MD, Oi H, Softeland E, Bjorge L, Guttormsen AB. Cardiopulmonary distress during obstetrical anaesthesia: Attempts to diagnose amniotic fluid embolism in a case series of suspected allergic anaphylaxis. Acta Anaesthesiol Scand 2006;50:324-30.

32. Oi H, Kobayashi H, Hirashima Y, et al. Serological and immunohistochemical diagnosis of amniotic fluid embolism. Semin Thromb Hemost 1998;24:479-84.

33. Kobayashi H, Ooi H, Hayakawa H, et al. Histological diagnosis of amniotic fluid embolism by monoclonal antibody TKH-2 that recognizes NeuAc alpha 2-6GalNAc epitope. Hum Pathol 1997;28:428-33.

34. Lunetta P, Penttila A. Immunohistochemical identification of syncytiotrophoblastic cells and megacaryocytes in pulmonary vessels in a fatal case of amniotic fluid embolism. Int J Legal Med 1996;108:210-4.

35. Hussain SA, Sondhi DS, Munir A, Rosner F. Amniotic fluid embolism with late respiratory failure. Hosp Physician 2001;37:40-3.

36. Porat S, Leibowitz D, Mildwidsky A, Valsky DV, Yagel S, Anteby EY. Transient intracardiac thrombi in amniotic fluid embolism. BJOG 2004;111:506-10.

37. Demianczuk CE, Corbett TF. Successful pregnancy after amniotic fluid embolism: A case report. J Obstet Gynaecol Can 2005;27:699-701.

38. Shapiro JM. Critical care of the obstetric patient. J Intensive Care Med 2006;21:278-86.

39. Gilbert WM, Danielsen B. Amniotic fluid embolism: decreased mortality in a population-based study. Obstet Gynecol 1999;93:973-7.

40. Capan LM, Miller SM. Monitoring for suspected pulmonary embolism. Anesthesiol Clin North Am 2001;19:673-703.

41. Davies S. Amniotic fluid embolus: A review of literature. Can J Anesth 2001;48:88-98.

42. Rodgers L, Dangel-Palmer MC, Berner N. Acute circulatory and respiratory collapse in obstetrical patients: A case report and review of the literature. Am Association Nurse/Anesthetists J 2000;68:444-50.

43. McDonnell NJ, Chan BO, Frengley RW. Rapid reversal of critical haemodynamic compromise with nitric oxide in a parturient with amniotic fluid embolism-case report. Int J of obstetric Anesthesia 2007;16:269-73.

44. Waters JH, Biscotti C, Potter PS, Philipson E. Amniotic fluid removal during cell salvage in the Cesarean section patient. Anesthesiology 2000;92:1531-6.

45. Davies S. Amniotic fluid embolism and isolated disseminated intravascular coagulation. Can J Anaesth 1999; 46:456-9.

46. Stanten RD, Iverson LI, Daugharty TM, Lovett SM, Terry C, Blumenstock E. Amniotic fluid embolism causing catastrophic pulmonary vasoconstriction: Diagnosis by transesophageal echocardiogram and treatment by cardiopulmonary bypass. Obstet Gynecol 2003;102:496-8.

47. Stroup J, Haraway D, Beal JM. Aprotinin in the management of coagulopathy associated with amniotic fluid embolus. Pharmacotherapy 2006;26:689-93.

48. Prosper SC, Goudge CS, Lupo VR. Recombinant factor VIIa to successfully manage disseminated intravascular coagulation from amniotic fluid embolism. Obstet Gynecol 2007;109:524-5.

49. Goldazmidt E, Davies S. Two cases of hemorrhage secondary to amniotic fluid embolus managed with uterine artery embolisation. Can J Anaesth 2003;50:917-21.

50. Stiller RJ, Siddiqui D, Laifer SA, et al. Successful pregnancy after suspected anaphylactoid syndrome of pregnancy (amniotic fluid embolus)- a case report. J Reprod Med 2000;45:1007-9.

51. Martin RW. Amniotic fluid embolism. Clin Obstet Gynecol 1996;39:101-6.

52. Katz VJ, Dotters DJ, Droegemueller W. Perimortem cesarean delivery. Obstet Gynecol 1986;68:571-6.

53. Dorne R, Pommier C, Emery JC, et al. Embolie de liquide amniotique: Evolution favorable après embolisation therapeutique des arteres uterines. Ann Fr Anesth Reanim 2002;21:431-5 .

54. Hsieh YY, Chang CC, Li PC, et al. Successful application of extracorporeal membrane oxygenation and intraaortic balloon counterpulsation as lifesaving therapy for a patient with amniotic fluid embolism. Am J Obstet Gynecol 2000;183:496-7.

55. Awad IT, Shorten GD. Amniotic fluid embolism and isolated coagulopathy: Atypical presentation of amniotic fluid embolism. Eur J Anaesthesiol 2001;18:410 –3.

56. Kaneko Y, Ogihara T, Tajima H, et al. Continuous hemodiafiltration for disseminated intravascular coagulation and shock due to amniotic fluid embolism: Report of a dramatic response. Intern Med 2001;40:945-7.

57. Goldszmidt E, Davies S. Two cases of hemorrhage secondary to amniotic fluid embolism managed with uterine artery embolisation. Can J Anaesth 2004;50:917-21.