



## Embolic complications in the parturient

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Embolic events are the current predominant cause of maternal death (~20%) in the United States<sup>(1)</sup>. They are also the most common cause of acute hemodynamic and respiratory collapse during pregnancy<sup>(2)</sup>. Embolized materials during pregnancy include: thrombus, air, amniotic fluid, and trophoblastic tissue. While the risk factors, presentation, course, and prognosis are all somewhat different with these embolic events, they tend to follow a similar initial course with obstruction of the pulmonary vasculature and/or pulmonary outflow tract leading to V/Q mismatch and compromise of cardiac output through mechanical obstruction, release of vasoactive mediators - all of which ultimately result in clinically-significant hypoxemia. Additionally, a disseminated intravascular coagulation (DIC) picture may develop with either air or amniotic (especially prominent) embolism. In contrast to other embolic events, trophoblastic embolization uniquely carries the risk of malignant spread in any seeded tissue bed<sup>(3)</sup>.

### VENOUS THROMBOEMBOLISM (VTE)

Pregnancy is associated with a 5- to 10-fold increase in risk in VTE<sup>(2)</sup>. Venous thrombosis occurs in 0.5 – 3 per 1,000 deliveries; and when untreated, up to 24% of these women may develop pulmonary embolism, with a cumulative mortality of 15%<sup>(4)</sup>. VTE may occur at any time during pregnancy or the puerperium. The presence of Virchow's triad of hypercoagulability, venous stasis, and trauma in all pregnant females leads to this increased risk. The hypercoagulability is secondary to increases in Factor II, VII, X, and fibrin; along with decreases in Antithrombin III, protein C, and in protein S<sup>(5,6)</sup>. Venous stasis occurs secondary to the well-known phenomenon of aortocaval compression. Venous trauma may occur secondary to vaginal birth, cesarean section, antepartum surgical procedures, or injury to varicosities. Other risk factors for VTE include: familial hypercoagulable states, prolonged bed rest, sepsis, advanced maternal age, obesity, preeclampsia, and multiparity<sup>(7)</sup>.

Symptoms suggestive of VTE include dyspnea, chest pain, cough and apprehension<sup>(8)</sup>. Symptoms may be absent in a large number of patients. Clinical signs include: tachycardia, tachypnea, and arterial desaturation. Laboratory findings are non-specific and include hypoxemia, widened A-a gradient, respiratory alkalosis, normal CXR, and nonspecific EKG changes. Advanced clinical testing is warranted if suspicion is high. CXR, V/Q scanning, and pulmonary angiography may all be performed as necessary. Total fetal exposure to radiation in these cases is approximately 0.5 rad<sup>(9)</sup>.

Treatment for symptomatic VTE is largely supportive and includes oxygen, fluids, inotropes. Central invasive monitoring and/or an A-line may be warranted in patients receiving significant circulatory support. Specific therapy includes heparin therapy (unfractionated or fractionated) and treatment with thrombolytics.

### VENOUS AIR EMBOLISM (VAE)

VAE's are the most common embolic events occurring during cesarean section with estimated incidences between 40-97% of all sections<sup>(10,11)</sup>. Fortunately, serious consequences of VAE are relatively rare-being responsible for perhaps 1% of all maternal deaths<sup>(12)</sup>. Nevertheless, the clinical significance of VAE is probably under-appreciated both as a cause of chest pain and dyspnea commonly seen in women undergoing cesarean section and as in many cases, lead to transient desaturations<sup>(13)</sup>. VAE may occur during either cesarean section<sup>(14)</sup> or vaginal delivery<sup>(15)</sup>, and has also been reported to result from forceful vaginal air insufflation during oral sex in pregnancy<sup>(16)</sup>.

Risk factors for VAE are present during every delivery. These include a source of gas (generally room air), open veins or sinusoids (placental implantation site), and a pressure gradient (uterine exteriorization or bearing down on gas pocket during delivery). Two factors that increase this gradient - uterine exteriorization and Trendelenburg position - are most

likely to occur with obese parturients<sup>(17-19)</sup>. VAE's that occur during cesarean section usually occur between initial hysterectomy and closure of the uterine incision. However, it may also occur as the uterus is returned to the abdominal cavity. Other risks for VAE include hemorrhage and general anesthesia-both of which are often associated with an increased gradient secondary to a real or relative hypovolemia<sup>(20)</sup>. General anesthesia may also exacerbate VAE as a result of the rapid diffusion of nitrous oxide into the air bubbles followed by their marked enlargement<sup>(21)</sup>.

As with VTE, symptoms of VAE include chest pain, dyspnea, restlessness and apprehension. Clinical signs include tachypnea, tachycardia, cyanosis, and a classic wheel-mill murmur. It may also present as acute cardiorespiratory collapse, especially in the patient undergoing general anesthesia. Decreases in peripheral saturation may also be present. Unlike the usual case with VTE, VAE may present with a DIC-like picture, although this is relatively rarer<sup>(22)</sup>. In the patient undergoing general anesthesia either a decrease in end-tidal CO<sub>2</sub> or an increase in end-tidal N<sub>2</sub> may occur, with end-tidal N<sub>2</sub> being more sensitive. The diagnosis may also be assisted with precordial Doppler or with transesophageal echocardiography which can visualize as little as 0.2 ml of air<sup>(23)</sup>.

Treatment and/or prevention of VAE is largely preventative and supportive. Initial efforts are aimed at minimizing the occurrence, size and impact of VAE and include: placing the operative site below the level of the heart<sup>(10)</sup> (at CCF I recommend a reflex position with slight Trendelenburg for all cesarean sections), encouraging *in situ* uterine repair *versus* exteriorization, flooding the surgical field with saline, maintaining normovolemia and/or CVP with crystalloid or colloid, and discontinuing nitrous oxide if the patient is receiving general anesthesia<sup>(23)</sup>. Supportive measures include oxygen, inotropes and/or vasopressors, and pain control. CPR and assisted ventilation may be useful in dispersing bubbles into the distal pulmonary vasculature and through the capillary beds. Left lateral tilt (as much as possible) will favor movement of the air out of the pulmonary outflow tract where it may be essentially causing a "vapor-lock" in the heart. Placement of a multiorifice catheter into the right atrium may successfully remove enough air to reverse a potentially fatal outcome. However, experiments with dogs suggest that CPR and left tilt should be the initial steps, with catheter placement occurring thereafter<sup>(24)</sup>. Finally, treatment with hyperbaric oxygen may be useful especially in patients with neurological or cardiac symptoms secondary to paradoxical embolism<sup>(25)</sup>.

### AMNIOTIC FLUID EMBOLISM (AFE)

AFE is a protean clinical syndrome characterized by the abrupt onset of hypotension, hypoxia, and disseminated

intravascular coagulopathy (DIC). AFE is a relatively rare syndrome occurring between 1:8,000 to 1:80,000 pregnancies<sup>(19)</sup>. A survey of national registry data indicates that most cases occur during labor (70%) and delivery (30% - includes both vaginal and cesarean births)<sup>(26)</sup>. Rare cases have occurred during first trimester abortions, after abdominal trauma, and in the postpartum period<sup>(27)</sup>. Despite its rarity, the consequences of AFE are disastrous with an overall mortality of 60 to 86%; with a large proportion of survivors exhibiting severe neurologic injury<sup>(19,27)</sup>.

The clinical presentation is often dramatic, with a rapid onset of dyspnea, hypotension, and hypoxemia followed by cardiopulmonary arrest. These symptoms are probably secondary to both direct mechanical obstruction of the pulmonary vascular system, along with release of vasoactive and cardiodepressant substances<sup>(28)</sup>. Coagulopathy is a common finding, and may even be the presenting symptom<sup>(28)</sup>. This is probably due to tissue factor present in the amniotic fluid<sup>(29)</sup>. Both the hemodynamic and coagulopathic effects of amniotic fluid appear to be worsened by the presence of meconium<sup>(30,31)</sup>. In addition to the symptoms seen with all other embolic phenomena, AFE may also be associated with a bad taste in the mouth.

The initial diagnosis, as with other embolic phenomena, rests on a number of non-specific signs in association with the appropriate clinical picture. Additionally, pulmonary edema<sup>(28)</sup> and DIC<sup>(28,29)</sup> are prominent in the clinical picture. Specific diagnosis is made by the post-mortem demonstration of fatal debris in the pulmonary vasculature<sup>(32)</sup>. Noninvasive methods of AFE diagnosis have been suggested to include zinc coproporphyrin<sup>(33)</sup> and monoclonal antibodies to an amniotic fluid-specific antigen<sup>(34)</sup>. Recently, *in vitro* models of AF-induced coagulopathy have been developed which may ultimately permit quantitation of AF entering the circulation<sup>(35,36)</sup>.

Therapy is again supportive and invasive hemodynamic monitoring is almost always warranted. In addition to hemodynamic support, vigorous therapy of DIC may also be required.

### TROPHOBLASTIC EMBOLIZATION (TE)

TE is a rare phenomenon, which may occur during evacuation of a molar pregnancy by dilation and curettage<sup>(37)</sup> or with removal of an invasive mole by hysterectomy<sup>(38)</sup>. Presentation and therapy are similar to that for other embolic disorders. Oxytocin administration prior to any manipulation of the molar pregnancy is believed by some to decrease the incidence of this condition<sup>(39)</sup>. Follow-up B-HCG levels are mandatory for any patient surviving a TE as they have the potential of developing malignant gestational trophoblastic neoplasia, which is then treated with methotrexate<sup>(40)</sup>.

## REFERENCES

- Kaunitz AM, Hughes JM, Grimes DA, Smith JC, Rochat RW, Kafrisen ME. Causes of maternal mortality in the United States. *Obstet Gynecol* 1985;65:605-12.
- Gei AF, Vadhera RB, Hankins GD. Embolism during pregnancy: thrombus, air, and amniotic fluid. *Anesthesiol Clin North America* 2003;21:165-82.
- Orr JW Jr, Austin JM, Hatch KD, Shingleton HM, Younger JB, Boots LR. Acute pulmonary edema associated with molar pregnancies: a high-risk factor for development of persistent trophoblastic disease. *Am J Obstet Gynecol* 1980;136:412-5.
- Ie S, Rubio ER, Alper B, Szerlip HM. Respiratory complications of pregnancy. *Obstet Gynecol Surv* 2002;57:39-46.
- Stirling Y, Woolf L, North WR, Seghatchian MJ, Meade TW. Haemostasis in normal pregnancy. *Thromb Haemost* 1984;52:176-82.
- Weiner CP, Kwaan H, Hauck WW, Duboe FJ, Paul M, Wallemark CB. Fibrin generation in normal pregnancy. *Obstet Gynecol* 1984;64:46-8.
- ACOG. Thromboembolism in pregnancy. *ACOG Bulletin No. 234*, 1987.
- Wilin AG, Mattar FM, Saade GR, Van Hook JW, Sibai BM. Presentation of venous thromboembolism during pregnancy. *Am J Obstet Gynecol* 1999;181:1118-21.
- Spritzer CE, Evans AC, Kay HH. Magnetic resonance imaging of deep venous thrombosis in pregnant women with lower extremity edema. *Obstet Gynecol* 1995;85:603-7.
- Fong J, Gadalla F, Druzin M: Venous emboli occurring cesarean section: the effect of patient position. *Can J Anaesth* 1991;38:191-5.
- Leu TW, Tay DH, Thomas E. Venous air embolism during cesarean section: More common than previously thought. *Anesth Analg* 1993;77:448.
- Lowenwirt IP, Chi DS, Handwerker SM. Nonfatal venous air embolism during cesarean section: a case report and review of the literature. *Obstet Gynecol Surv* 1994;49:72.
- Kawahito S, Kitahata H, Kimura H, et al. Hypoxemia during cesarean section - evaluation of venous air embolism by transthoracic echocardiography. *Masui* 1995;44:10.
- Fong J, Gradalla F, Pierri MK, et al. Are Doppler-detected venous emboli during cesarean section air embol. *Anesth Analg* 1990;71:254.
- Flanagan J, Slimack J, Black D, et al. The incidence of venous air embolism in the parturient. *Reg Anesth* 1990;15:A10.
- Kaiser RT. Air embolism death of a pregnant woman secondary to orogenital sex. *Acad Emerg Med* 1994;1:555-8.
- Handler JS, Bromage PR. Venous Air embolism during cesarean delivery. *Reg Anesth* 1990;15:170.
- Bromage PR, Hohman WA. Uterine posture and incidence of venous air embolism (VAE) during cesarean section. *Reg Anesth* 1991;15:529.
- Skerman JH, Huckaby T, Oherson WN. Embolism pregnancy. In: Datta S. (ed) *Anesthetic and obstetrical management of high risk pregnancy* St. Louis, Mosby-Yearbook 1991.
- Naulty JS, Ostheimer GW, Datta S, et al. Incidence of venous air embolism during epidural catheter insertion. *Anesthesiology* 1982;57:410.
- Presson RG Jr., Kirk KR, Haselby KA, et al. Effect of ventilation with soluble and diffusible gases on the size of air embol. *J Appl Physiol* 1991;70:1068.
- Collins KA, Davis GJ, Lantz PE. An unusual case of maternal & fetal death due to vaginal insufflation of cocaine am S. *Forensic Med Pathol* 1994;15:335.
- Sharma SK, Joshi GP. Pulmonary embolism In *Gambling Dr, Douglas MJ. (ed) Obstetric anesthesia and uncommon disorders*. Philadelphia, W.B. Saunders Company, 1998.
- Alvaran SB, Toung JK, Graff TE, Benson DW. Venous air embolism; Comparative merits of external cardiac massage intracardiac aspiration, and left lateral decubitus position. *Anesth Analg* 1978;57:1660.
- Tibbles PM, Edelsberg JS. Hyperbaric-oxygen therapy. *N Engl J Med* 1996;334:1642-8.
- Clark SL, Hankins GD, Dudley DA, Duldy GA, Porter TF. Amniotic fluid embolism: analysis of the national registry. *Am J Obstet Gynecol* 1995;172:1158-67.
- Malinow AM. Embolic disorders. In: Chestnut DA (ed). *Obstetric Anesthesia. Principles and Practice*, 2nd Edition St. Louis, Mosby, Inc., 1999.
- Clark SL. Amniotic fluid embolism. *Crit Care Clin* 1991;7:877-82.
- Lockwood CJ, Bach R, Guha A, Zhou XD, Miller WA, Nemerson Y. Amniotic fluid contains tissue factor, a potent initiator of coagulation. *Am J Obstet Gynecol* 1991;165:1335-41.
- Petroianu GA, Altmannsberger SH, Maleck WH, Assmus HP, Friedberg C, Bergler WF, Rufer R. Meconium and amniotic fluid embolism: effects on coagulation in pregnant mini-pigs. *Crit Care Med* 1999;27:348-55.
- Hankins GD, Snyder RR, Clark SL, Schwartz L, Patterson WR, Butzin CA. Acute hemodynamic and respiratory effects of amniotic fluid embolism in the pregnant goat model. *Am J Obstet Gynecol* 1993;168:1113-29.
- Courtney LD. Amniotic fluid embolism. *Obstet Gynecol Surv* 1974;29:169-77.
- 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.
- Kobayashi H, Ohi H, Terao T. A simple, noninvasive, sensitive method for diagnosis of amniotic fluid embolism by monoclonal antibody TKH-2 that recognizes NeuAc alpha 2-6 GalNAc. *Am J Obstet Gynecol* 1993;168:848-53.
- Dolak JA, Dubsy JA, Waters JH. A novel in vitro model of amniotic fluid-induced hypercoagulability. *Anesthesiology* 2004;Suppl 1:A105.
- Dolak JA, Dubsy JA, Waters JH. Increases in clot initiation and rate of fibrin formation are responsible for amniotic fluid-induced hypercoagulability. *Anesthesiology* 2004;Suppl 1:A104.
- Chantigian RC, Chantigian PDM. Problems of early pregnancy. In: Chestnut DH. (ed) *Obstetric anesthesia: principles and practice*. 2nd Edition, St. Louis, Mosby, Inc., 1999.
- Garner EI, Chang-Lee WY, Lu KH, Goldstein DP, Berkowitz RS. Trophoblastic pulmonary embolization after hysterectomy for invasive complete mole. A case report. *J Reprod Med* 1999;44:908-12.
- Cotton DB, Bernstein SG, Read JA, Benedetti TJ, D'Ablaing G, Miller FC, Morrow CP. Hemodynamic observations in evacuation of molar pregnancy. *Am J Obstet Gynecol* 1980;138:6-10.
- Kohorn EI. Clinical management and the neoplastic sequelae of trophoblastic embolization associated with hydatidiform mole. *Obstet Gynecol Surv* 1987;42:484-8.