Management of Three Uncommon but Potentially Detrimental Anesthesia Emergencies;

Local Anesthetic toxicity,
Intraoperative Myocardial Infarction
Amniotic Fluid Embolism

Claston Reid, Naomi Moneyheffer and Sarah Bringas

Local Anesthetic Systemic Toxicity (LAST)

- Local anesthetics (LA) are weak bases
- Two main classes of LA; esters and amides
- Function by diffusing to the interior of the neuron and reversibly antagonizing voltage gated sodium channels preventing the propagation of an action potential at the nodes of *Ranvier*
- Termination of effect is directly related to the degree of protein binding.
  - Which serum protein do LA bind to primarily ? Is this protein affect by pregnancy? How?
  - The greater the protein binding the greater the duration of action.
- LA diffuse away from site of action and are metabolized
  - What is responsible for the metabolism of LA?

History and Incidence

- LAST has been an issue ever since the first LA were used for surgical procedures beginning in 1884
  - Does anyone know which LA was first used for surgical procedures?
- Bonica et al., reported an incidence of over 3% in obstetrical patients who developed systemic toxicity prior to 1981. Epidurals were responsible for the majority of the incidences
- Incidences were reported to the FDA at rates of 100/10000
- More recently the incidence has fallen significantly. Numerous statistics exist;
  - Tanaka et al. reported a frequency of 11 per 10,000 without the use of epinephrine
  - Brown et al.5 reviewed the Mayo Clinic experience and reported an incidence of 1.2per 10,000 epidural anesthetics with epinephrine usage
- Decades ago the result of LAST was either death from cardiopulmonary failure or permanent brain damage from intractable seizure

History and Incidence

- The American Society of Regional Anesthesia and Pain Medicine evaluated closed claims data from 1979-2009 and identified 93 separate LAST events.
- 77 of these cases were a result of single injection
- 14 of these cases were a result of continuous infusion
- 2 of the 93 were a result of a combination

Occurrence

Type of Regional Block	Rate of occurrence (%)
Epidural	33
Axillary	17
Interscalene	13

Signs of LAST

- Typically occurs as a progression of subjective symptoms such as agitation, tinnitus, circumoral numbness, blurred vision, and a metallic taste in your mouth
- As it progresses muscle twitching begins, followed by loss of consciousness
- As blood concentrations get higher seizures begin to become evident followed by cardiovascular and respiratory arrest

Signs of LAST

- Timing and onset of symptoms after a single injection varied from 30 seconds to 60 minutes
  - **Over 50% of reported cases occur within 50 seconds**
- However, signs usually occur rather rapid as most incidences occur with inadvertent intravascular injection

Neurological Signs

- Agitation, tinnitus, circumoral numbness, blurred vision, metallic taste seizure then with greater blood concentration unconsciousness and coma
  - What?? How does this happen??
- Excitation occurs before depression because the cortical inhibitory pathways (which are less resistant) in the brain are affect by the LA first allowing for unopposed firing of action potentials and hence excitation
- As blood levels increases the excitatory pathways (more resistant to LA) then become blocked by the LA leading to unconsciousness and coma
- The presentation mentioned above is the typical presentation and occurs at a rate of 60% of reported cases
- However, note that early signs may be absent and first sign noted may be convulsion or cardiac arrest

Cardiovascular Signs

- LA cardiotoxicity especially with bupivacaine involves life threatening arrhythmias as well as depression of contractility
  - Which would be of bigger concern, arrhythmias or cardiac depression?
- Cardiac toxicity is related to the action of local anesthetics on the cardiac action potential, and their membrane-stabilizing effects
  - Which phase of the cardiac action potential do they affect?
- Most LA cause relaxation of vascular smooth muscle leading to wide spread vasodilation. This results in decreases in Preload and hence CO
- Electrocardiograph (ECG) changes include prolonged PR and QRS intervals and a prolonged refractory period

Cardiovascular Signs

- Local anaesthetics also have a non-selective blocking action on calcium and potassium channels, reducing current amplitude
- Local anesthetics inhibits carnitine acylcarnitine translocase resulting in exhaustion of the heart's ATP supply
- Bupivicaine dissociates most slowly from sodium channels prolonging its effects
- Laboratory data suggest the toxicity associated bupivicaine occurs because of the dextro (R) enantiomer.

Cardiotoxic Profile of Common Local Anesthetics From Greatest to Least

- **Bupivacaine>Etidocaine>Ropivacaine**

Treatment and Management

- For mild symptoms :
  - Keen observation and Monitor using standard ASA monitors

Treatment and Management

- Moderate to Severe symptoms:
  - Airway management: 100% O_2
  - Control Seizures preferably with Benzodiazepines
  - Begin BCLS as well as ACLS if indicated
    - Note that resuscitation efforts may be prolonged. Why?
    - Adjust Medication doses and avoid Vasopressin, calcium channel blockers or beta blockers

    1. **How would you treat Ventricular tachycardia or SVT?**
  - Consider and prepare for cardiopulmonary bypass

Treatment and Management

- Avoid propofol
  - Why?

- Lipid emulsion therapy.
  - Relatively new therapy and still being investigated, and debated. The treatments and protocols are still being developed and refined.
- In 2006, the first published Human case report detailed the successful resuscitation of local anesthetic toxicity using intravenous (IV) lipids

Treatment and Management

- Lipid therapy first introduced in 1998 by Weinberg et al.
  - Demonstrated successful resuscitation of bupivacaine overdose in rats
- Prior to Lipid therapy LAST resulted in death or permanent brain damage unless cardiopulmonary bypass was instituted
- The mechanism of action is not fully understood. Proposals include:
  - LA is neutralized by the lipid emulsion or that the lipid emulsion actually sequesters the local anesthetic
  - lipid emulsion enhances metabolism of the local anesthetic via a mitochondrial mediated process
  - that lipid emulsion simply increases calcium concentration in myocytes leading to improved contractility

Treatment and Management

- ASRA recommends 20% Lipid Emulsion
  - Some literature recommend 10% or 30%. Does anyone knows what ASRA stands for?
- **Bolus with 1.5ml/kg**
- Continuous infusion at 0.25ml/kg
- Repeat bolus once or twice for refractory CV collapse
- Double infusion rate if desired response not obtained
- Continue infusion for at least 10 minutes after attaining cardiovascular stability

Measures for Preventing LAST

- Be sure to continue to observe and monitor patient up to 60 minutes after LA injection
- Exercise vigilance and constantly assess patient for signs and symptoms of LAST
- Be sure not to over-sedate patient prior to procedure because this can
  - Why?

Measures for Preventing LAST

- Use lowest effective dose
- Practice incremental dosing
  - 3-5mL at a time waiting 15-30 seconds
- Always aspirate prior to injection LA especially in vessel rich areas
- Use Epinephrine unless contraindicated
  - When is Epinephrine contraindicated?
- Always ensure patient is fully monitored
- Use technology assistants, for example, ultrasound and peripheral nerve stimulator for proper mapping of anatomy

Perioperative Myocardial Infarction

NAOMI MONEYHEFFER

Incidence

- Perioperative myocardial ischemia continues to be a major contributor of mortality and morbidity in patients after non-cardiac related surgeries with mortality rates up to 25%
- Some sources: Incidence anywhere from 1-17 %

  - may be an underestimation because it does not account for silent or undiagnosed intraoperative ischemia.
- Generally, with Acute myocardial infarction, more than half of deaths occur within the first hour due to cardiac arrhythmias especially v. fib.

Diagnostic Criteria

- WHO diagnostic criteria for perioperative MI include at least 2 of the 3 conditions below
  1. Clinical symptoms of MI
  2. Deviation in a standard 12 lead EKG
  3. increases in serum biomarkers

Risk Factors

- Known history of CAD
- Compensated or history of congestive heart failure
- History of TIA or CVA
- Diabetes
- Renal insufficiency

PMI

- General or regional anesthesia is not a risk factor even for high risk cardiac patients when administered without complications.
- If an intraoperative MI is to occur, it will most likely peak during emergence and early postoperative period
- Postoperative stress especially during emergence is what causes ischemia, infarction and mortality

PMI

- Most PMIs occurs within 3 days after surgery and are thought to be as a result of a combination of imbalance of myocardial oxygen supply and demand , plaque rupture and coronary blockage

- This postoperative myocardial ischemia is usually seen as ST depression and less likely ST elevation, is mostly silent (non-Q wave).

Pathophysiology

- Ischemia results when oxygen demand by the myocardium exceeds supply
- Myocardial oxygen delivery is a function of coronary perfusion pressure and oxygen content of blood.
- In normal coronary circulation, an increase in oxygen demand triggers local regulatory mechanisms (adenosine and nitric oxide in the smooth muscles of the vessels) causing vasodilation.

Pathophysiology

- In diseased coronary arteries (CAD), these mechanisms are impaired.
- An unstable atherosclerotic plaque ruptures causing a thrombus that blocks a coronary vessel hence blood supply to a particular portion of the heart muscle.
- Can cause transmural infarcts – which involve the full thickness of the ventricular wall or subendocardial infarcts which involve the inner 1/3-1/2 of the wall.

Pathophysiology

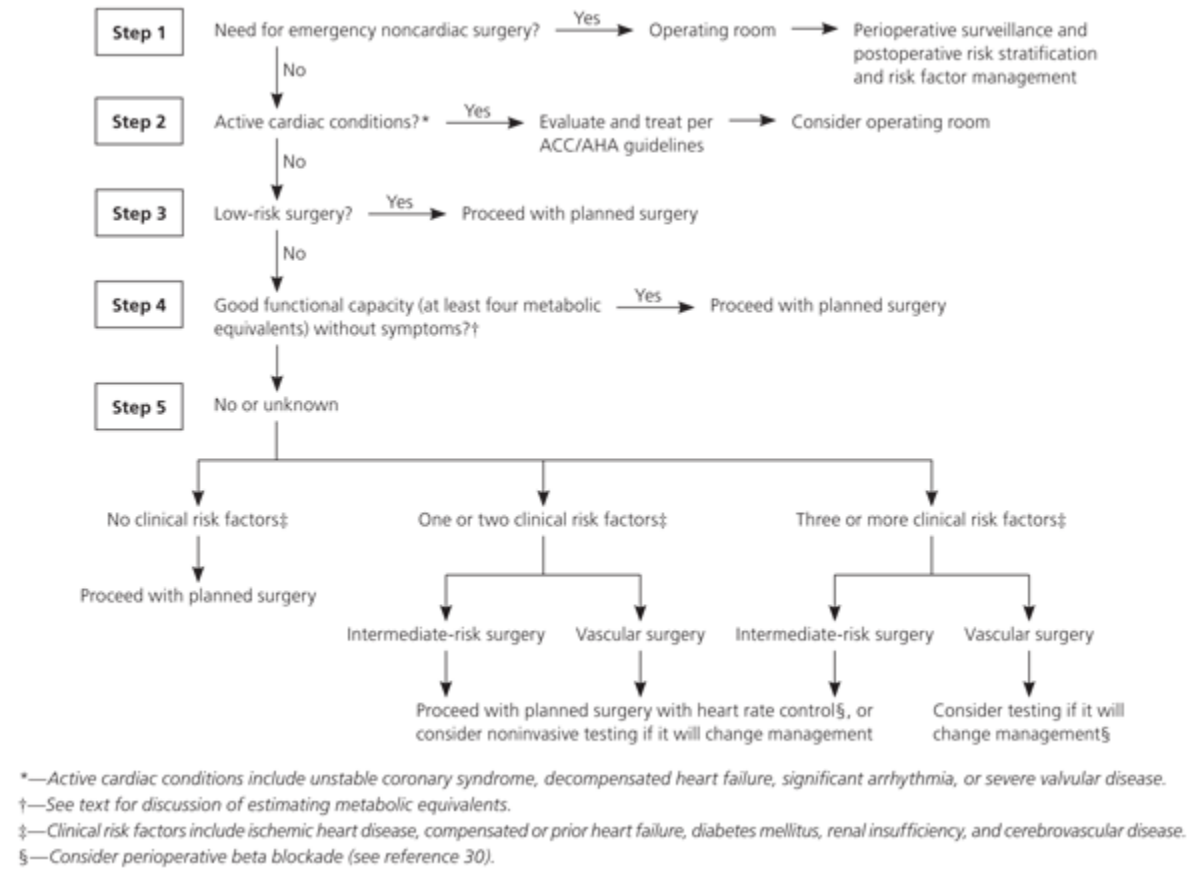
- Most MI occur in patients with more than one severely narrowed coronary artery (>75%)
- Critical narrowing of coronary arteries that result in MI by frequency

  LAD- 40-50%

  RCA- 30-40%

  LCX - 15-20%
- No correlation between severity of preoperative coronary blockage or plaque size and the possibility of getting a perioperative myocardial infarction (according to one source)

AHA Framework to Evaluate Cardiac Risk



*—Active cardiac conditions include unstable coronary syndrome, decompensated heart failure, significant arrhythmia, or severe valvular disease.
†—See text for discussion of estimating metabolic equivalents.
‡—Clinical risk factors include ischemic heart disease, compensated or prior heart failure, diabetes mellitus, renal insufficiency, and cerebrovascular disease.
§—Consider perioperative beta blockade (see reference 30).

Li, S., Wang, D., Wu, X., Li, N., & Xie, Y. (2013). Perioperativeacute myocardial infarction increases mortality following noncardiac surgery. *Journal of Cardiothoracic and Vascular Anesthesia*, doi: 1053-0770/2601-000136.00/0

- In a Chinese retrospective study analyzing 117,856 patients undergoing non-cardiac surgeries over 9 years, perioperative myocardial ischemia frequently occurred in male patients over 60 who had such risk factors as hypertension, diabetes and dyslipidemia. In the same study, 77% of patients with hemodynamic instability intraoperatively especially with blood pressure labiality and increased heart rate suffered from myocardial ischemia or infarction within 72 hours of surgery

Detection

- In the operating room classic MI symptoms are masked by general anesthesia. Even with readily available monitors, it may not always be possible to detect ischemia

- Myocardial ischemia should always be suspected in patients that are hemodynamically unstable with cardiac risks

Myocardial Ischemia criteria

- For men 40 years of age and older, the threshold value for abnormal J-point elevation should be 0.2 mV (2 mm) in leads V2 and V3 and 0.1 mV (1 mm) in all other leads.
- –For men less than 40 years of age, the threshold values for abnormal J-point elevation in leads V2 and V3 should be 0.25 mV (2.5 mm).
- –For women, the threshold value for abnormal J-point elevation should be 0.15 mV (1.5 mm) in leads V2 and V3 and greater than 0.1 mV (1 mm) in all other leads
- –For both sexes of all ages, abnormal J-point depression is 0.5 mm in V2-3 and 1 mm in all other leads

Signs and symptoms

- Left ventricular wall abnormalities seen on the transesophageal echocardiogram are more foretelling of myocardial infarction than using EKG and can be used for diagnosis in the OR.
- Suspicion should also be raised with arrhythmia, conduction abnormalities, unexplained tachycardia, bradycardia and elevation of cardiac filling pressures

Detection

We commonly use lead II only in routine surgeries. However, lead II has fairly low sensitivity to detect ischemia compared to 12 lead – only 33 %

- In a study by London et. al, leads 2 and V5 increased detection of ST changes by 80% while using leads 2, V4 and V5 increased sensitivity by 96%

- Computerized analysis by the monitors is more sensitive than visual inspection but this was dependant on proper lead placement, preoperative EKG changes and default settings

Complications

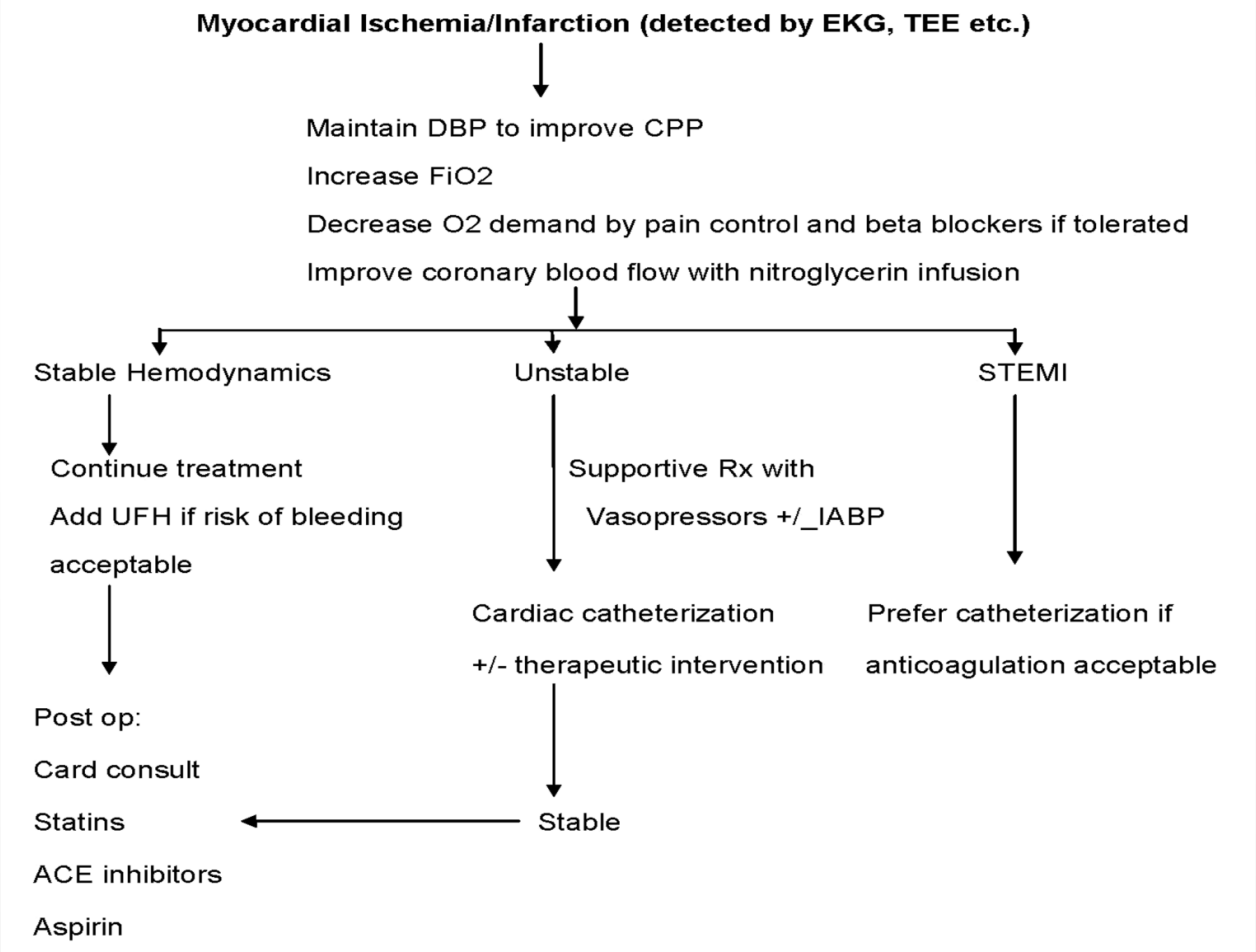
- Sudden death due to fatal arrhythmias
- Cardiogenic shock especially with large infarcts that affect more than 40% of the left ventricle.
- Mitral regurgitation- when the papillary muscles are affected
- Thromboembolism – stasis of blood due to an ineffective pump

PMI

- If Ischemia or infarction is detected before incision, delay the case until patient is stable.

- If during surgery, inform the surgeon to expedite the procedure the goal for the anesthesia provider should be improving coronary blood flow and oxygen delivery while reducing oxygen demand

Algorithm


Myocardial Ischemia/Infarction (detected by EKG, TEE etc.)
Maintain DBP to improve CPP
Increase FiO2
Decrease O2 demand by pain control and beta blockers if tolerated
Improve coronary blood flow with nitroglycerin infusion
Stable Hemodynamics
Unstable
STEMI
Continue treatment
Add UFH if risk of bleeding acceptable
Supportive Rx with Vasopressors +/_IABP
Cardiac catheterization +/- therapeutic intervention
Prefer catheterization if anticoagulation acceptable
Post op:
Card consult
Statins
ACE inhibitors
Aspirin
Stable

Management

- After myocardial ischemia/infarction is identified – CALL FOR HELP
- Oxygen demand should be decreased by; increasing FIO2 to 100%, use of pain control and beta blockers to slow the heart rate. Beta blockers should be held for bradycardia or hypotension.

- Diastolic blood pressure should be maintained to improve coronary perfusion pressure. Nitroglycerin can be used to achieve this as long as the patient is not hypotensive

Management

- Treat hypotension or hypertension accordingly. Consider placing an arterial line and central line, check labs including CK/ troponins and treat anemia with packed red blood cells.
- If hemodynamics are stable and surgical bleeding is acceptable, a post op cardiac consult, statins, ACE inhibitors and aspirin can be started after surgery
- * Ck rises 4-8 hrs, myoglobin -1 hr(not cardiac sensitive) trops- rise in 3 hrs.

Management

- If the patient is hemodynamically unstable, blood pressure support with vasopessors and assessment/ placement of intra-aortic balloon pump is indicated.
- If the patient has an ST elevated myocardial infarction then cardiac catheterization is preferred if coagulation is acceptable

Conclusion

- Prevention of perioperative myocardial events begins with understanding the pathophysiology of myocardial ischemia, good preoperative assessment to evaluate cardiac risk, use of sensitive diagnostic tools to identify the event and reduction of intraoperative cardiac stressors especially during emergence.

Amniotic Fluid Embolism

Sarah Bringas

Pathophysiology

- Amniotic Fluid Embolism (AFE) is also known as the Anaphilactoid Syndrome or Sudden Obstetric Collapse Syndrome
- The presence of bradykinin, leukotriene, tryptase, complement activation and antigen-antibody response were determined to be closely related in the pathogenesis process
- Humoral, hemodynamic and coagulopathic changes occur in the maternal circulation with the presence of AFE
- Previously associated with 80% of mortality rates but a recent decline to 40-20% shows to be the lowest reported

Risk Factors

- Advanced maternal age
- Placental abnormalities such as Placenta Previa and placental abruption
- Forceps or vacuum assisted cesarean deliveries

Signs & Symptoms

Frequently present during labor or immediately post-partum

- Sudden cardiovascular collapse
- Altered mental status with respiratory compromise
- Fetal distress
- Development of disseminated intravascular coagulopathy (DIC)
- Compromised cardiopulmonary systems, respiratory failure, neurologic symptoms and hypotension

Diagnosis

- Symptoms occurring during delivery with high likelihood of collapse and incipient disseminated intravascular coagulation
- CXR may show pulmonary edema, acute respiratory distress syndrome (ARDS), right atrial enlargement and a prominent pulmonary artery
- ECG and arterial blood gases are not helpful

Diagnosis

- Postmortem will reveal fetal squamous cells and hair (lanugo) in the maternal pulmonary circulation

- In the future, the measurement of complement, which may be activated following amniotic fluid embolism (AFE), or the fetal antigen sialyl-Tn may help to diagnose the condition. The last one can be measured serologically or by immunocytochemistry on lung tissue but, as yet, is not usually available

Outcomes and Management

Implementations of several actions and therapies can prevent catastrophic events:

- Emergency delivery after successfully securing patient's airway
- Hysterectomy
- Recombinant factor VIIa is generally the treatment to help achieve hemostasis
- Nitric oxide administration secondary to its strong vasodilator effect

Outcomes and Management

Management of AFE relies on the prompt diagnosis and rapid aggressive hemodynamic support. Some measures include:

- ACLS protocol implementation
- Correction of coagulopathy
- Immediate cesarean section
- Extracorporeal membrane oxygenation
- Uterine embolization
- Cardiopulmonary bypass and exchange transfusions

Pharmacological Support

- Dopamine, if a pulmonary artery catheter can be inserted (coagulopathy may prevent this)
- Otherwise, rapid digitalization needs to be implemented
- Management of coagulopathy with:
  - Fresh frozen plasma (FFP) for a prolonged aPTT.
  - Cryoprecipitate for a fibrinogen level < 100 mg/dL
  -Transfuse platelets for platelet counts less than 20 x 109 dL

Prognosis

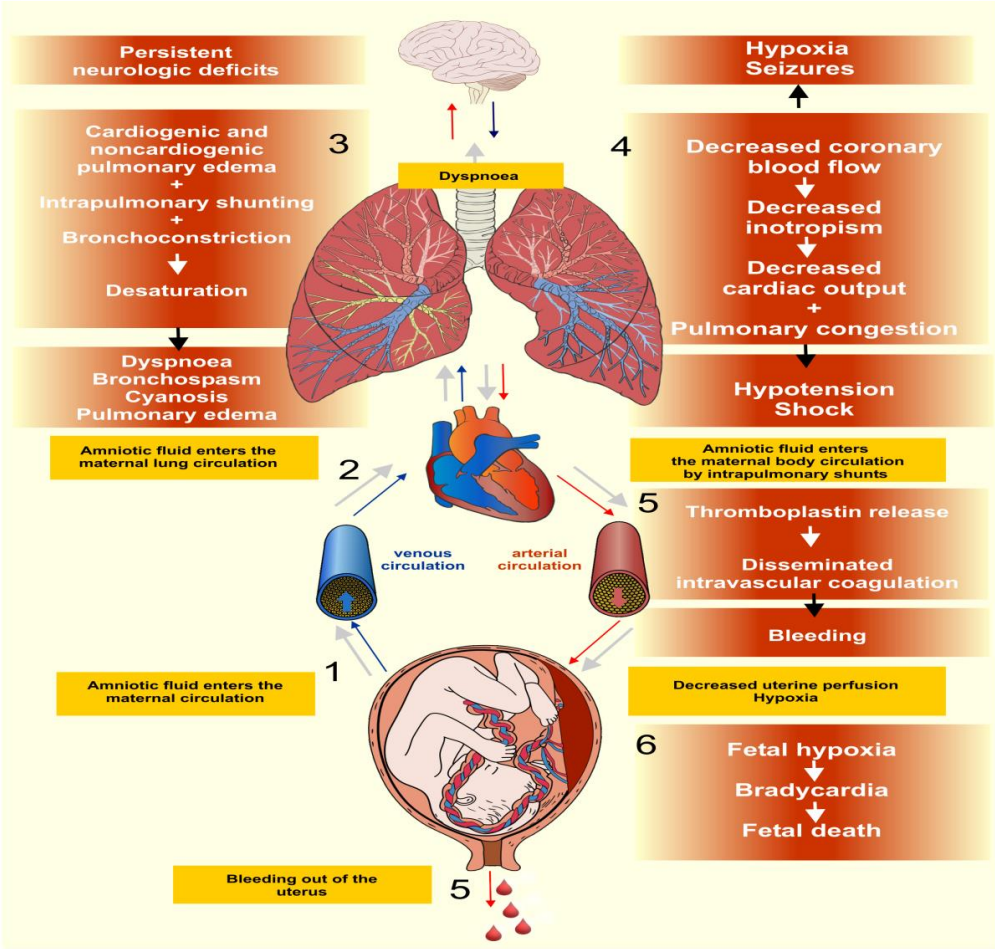
- The prognosis of amniotic fluid embolism can always be improved with early diagnosis and prompt interventions
- Awareness between clinicians and anesthesia providers is crucial in the progression of the incident and in the avoidance of all catastrophic events that can take place if adequate management of the emergency is not attained.

Mortality and Morbidity

- AFE causes a high level of morbidity for mother and baby. If the patient survives, disseminated intravascular coagulation is a common complication. Typical findings among survivors include: cardiac arrest, hysterectomy, further laparotomies, subglottic stenosis, persisting neurological impairment and admission to intensive care units.

- The majority of women will survive but hypoxic ischemic encephalopathy and cerebral palsy are frequently found amongst surviving neonates.

Flowchart


Persistent neurologic deficits
Hypoxia Seizures
Cardiogenic and noncardiogenic pulmonary edema + Intrapulmonary shunting + Bronchoconstriction
Desaturation
3
Dyspnoea
4
Decreased coronary blood flow
Decreased inotropism
Decreased cardiac output + Pulmonary congestion
Dyspnoea Bronchospasm Cyanosis Pulmonary edema
Hypotension Shock
Amniotic fluid enters the maternal lung circulation
2
Amniotic fluid enters the maternal body circulation by intrapulmonary shunts
5
Thromboplastin release
Disseminated intravascular coagulation
venous circulation
arterial circulation
Bleeding
1
Amniotic fluid enters the maternal circulation
Decreased uterine perfusion Hypoxia
6
Fetal hypoxia
Bradycardia
Fetal death
Bleeding out of the uterus
5

References

- Abenhaim, H. A., Azoulay, L., Kramer, M. S., & Leduc, L. (2008). Incidence and risk factors of amniotic fluid embolisms: a population-based study on 3 million births in the United States. American Journal of Obstetrics & Gynecology, 199, 49e1-49e8. http://dx.doi.org/10.1016/j.ajog.2007.11.061
- Beecroft, C., & Davies, G. (2013). Systemic toxic effects of local anaesthetics. *Anaesthesia and Intensive Care Medicine. 24*, 146-149
- Berrio Valencia, M., & Silva, J. (2013). Protocoal and importance of using the kit for local anesthetic systemic toxicity. *Colombian Journal of Anesthesiology. 1*, 1-6. http://dx.doi. org/ 10. 1016/j.rca.2013.06.005
- Chu, L., & Fuller, A. (2012). *Manual of clinical anesthesiology*. (1 ed., pp. 1332-1333). Philadelphia, PA: Wolters Kluwer/ Lippincott Williams & Wilkins

References

- Conde-Agudelo, A., & Romero, R. (2009). Amniotic fluid embolism: an evidence- based review. American Journal of Obstetrics & Gynecology, 201, 445.e1-13. http://dx.doi.org/10.1016/j.ajog.2009.04.052
- Dean, L. S., Rogers III, R. P., Harley, R. A., & Hood, D. D. (2012). Case scenario: amniotic fluid embolism. Anesthesiology, 116(1), 186-192
- Didier, M. & Sinead A. (2010). Management of local anesthetic toxicity. *International Anesthesiology Clinics*, *48*, *4*, 117-140
- Fleisher, L. A., Beckman, J. A., Brown, K. A., Calkins, H., Chaikof, E., & Fleischmann, K. E…Robb, J. (2007). ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for non-cardiac surgery. *Circulation*, *116*, e418-e500. doi: 10.1161/CIRCULATIONAHA.107.185699

References

- Goyal, C. R., & Shukla, C. R. (2012). Local anesthetic systemic toxicity (LAST) – Should we not be concerned? *Medical Journal Armed Forces India*, *68*, 371-375. http://dx.doi.org/10.1016/j.mjafi.2012.02.011
- Landesberg, G. (2003). Perioperative myocardial infarction: Facts and perspective. *Journal of Cardiothoracic and Vascular Anesthesia*, *17*(1), 90-100. Retrieved from adu.edu/science/article/pii/S105307700247718X
- Li, S., Wang, D., Wu, X., Li, N., & Xie, Y. (2013). Perioperative acute myocardial infarction increases mortality following noncardiac surgery. *Journal of Cardiothoracic and Vascular Anesthesia*, doi: 1053-0770/2601-000136.00/0
- Mato, J. (2008). Suspected amniotic fluid embolism following amniotomy: a case report. AANA Journal, 76(1), 53-59. Retrieved from www.aana.com/aanajournal.aspx

References

- McDonnell, N. J., Chan, B. O., & Frengley, R. W. (2007). Rapid reversal of critical hemodynamic compromise with nitric oxide in the parturient with amniotic fluid embolism. International Journal of Obstetric Anesthesia, 16, 269-273. http://dx.doi.org/10.1016/j.ijoa.2006.10.008
- Mulroy, M. F. (2003). Systemic toxicity and cardiotoxicity from local anesthetics: Incidence and preventive measures. *Regional Anesthesia and Pain Medicine*, *27*, *6*, 556-561. doi:10.1053/rapm.2002.37127
- Nagelhout, J., & Plaus, K. (2013). Nurse anesthesia. (5 ed., pp. 125-144). St Louis: Elsevier.

References

- Singh, A., & Antognini, J. F. (2011). Perioperative hypotension and myocardial ischemia: Diagnostic and therapeutic approaches. *Annals of Cardiac Anesthesia*, *14*(2), 127-130. doi: 10.4103/0971-9784.81569
- Toledo, P. (2011). The role of lipid emulsion during advanced cardiac life support for local anesthetic toxicity. *International Journal of Obstetric Anesthesia*, *20*, 60-63. doi:10.1016/j.ijoa.2010.09.005
- Tuffnell, D. J., & Togobo, M. (2011). Amniotic Fluid Embolism. Obstetrics, Gynecology and Reproductive Medicine, 21(8), 217-220

QUESTION???