Amniotic fluid embolus

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A case report of a 27-yr-old healthy patient for Caesarean section under epidural anaesthesia is presented. The patient suffered an acute cardiorespiratory collapse when the infant's head was being delivered through the anterior abdominal wall. The patient remained cyanosed after proper tracheal intubation and pulmonary ventilation with 100% O₂. Hypotension was difficult to treat but returned to normal 25 min after the event. A pulmonary artery catheter inserted three hours after the event showed normal pressures and a high cardiac output. The patient suffered permanent neurological damage. The differential diagnosis is discussed and current concepts of the aetiology and management of amniotic fluid embolism reviewed.

Il s'agit du cas d'une patiente bien portante subissant une césarienne sous anesthésie épidurale. La patiente présente une collapsus cardiorespiratoire aigu au moment où la tête de l'enfant est dégagée à travers la paroi abdominale antérieure. La patiente reste cyanosée après une intubation trachéale (correcte) et une ventilation pulmonaire avec 100% d'O₂. L'hypotension est difficile à traiter mais revient à la normale 25 minutes plus tard. Un cathéter Swann-Ganz inséré trois heures après l'évènement donne des pressions normales et un débit cardiaque élevé. La patiente a subi une atteinte neurologique définitive. Le diagnostic différentiel est discuté et les concepts habituels de l'étiologie et du traitement de l'embolie amniotique sont revus.

Case report

In 1987, a 27-yr-old healthy woman presented for an elective Caesarean section. She had had a previous Caesarean section under general anaesthesia without difficulty. There were no problems found on history or physical examination. The patient decided after discussion with her general practitioner and anaesthetist to have an epidural an-

aesthetic for pain control. Haemoglobin and urinalysis were normal. She was given 30 ml Na citrate outside the OR.

At 08:00 a continuous epidural catheter was inserted with the patient in the seated position with no difficulty. The patient was positioned with a wedge under her right hip. Intermittent injections to a total of 22 ml lidocaine 2% with epinephrine were placed in the epidural space. One litre of normal saline was given *iv*. The monitors were a hard copy blood pressure (BP) showing normal fluctuating BP and pulse and an ECG. The epidural level was tested and found to be at the T₅₋₆ level. Surgery started 20 min after the epidural was inserted. The patient was carrying on a normal social conversation.

At 08:45 (as the head of a normal crying infant was delivered through the anterior abdominal wall) the mother suddenly complained of shortness of breath (SOB), began to hyperventilate, coughed and became cyanosed. The blood pressure decreased, the sinus heart rate increased, and she may have suffered a seizure (there was thrashing of both arms). Almost immediately BP and pulse on the Dinemapp recorder were undetectable (Table I – 8:48) but the ECG showed sinus tachycardia. The airway was managed initially with mask and oxygen and then the trachea was intubated without difficulty. Breathing was managed initially with mask ventilation with oxygen and continued with bag ventilation through the endotracheal tube. There was no bronchospasm and air entry was equal bilaterally.

Circulation was managed by the infusion of fluid, drugs which included ephedrine, epinephrine, NaHCO₃, isuprel and atropine, and cardiac massage. Other drugs given included Na citrate preoperatively, succinylcholine, atracurium, thiopentone, and oxytocin. At various times another anaesthetist, two intensive care physicians and nurses were in the operating room observing and helping with the resuscitation. These manoeuvres were successful in returning blood pressure but the patient remained cyanosed in spite of an adequate blood pressure and positive pressure ventilation with 100% O₂.

The blood pressure decreased a second time (Table I – 9:01) and again the patient was resuscitated. The first inadequate blood pressure (taken from the Dinemapp) was recorded at 08:48 (only one reading at this level). The total time between adequate blood pressures was seven minutes. The total time of inadequate blood

Key words

ANAESTHESIA: obstetric;
EMBOLISM: amniotic fluid.

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Accepted for publication 25th June, 1993.

TABLE I Dinemapp recording

Time	BP	Heart rate
8:33	149/88	74
8:36	114/87	94
8:41	69/43	88
8:45	76/49	115
8:48	00/00	0
8:52	86/45	147
8:54	93/34	125
8:57	49/33	156
8:59	53/23	0
9:01	00/00	0
9:03	36/22	0
9:05	00/00	0
9:08	96/68	153
9:10	133/76	159
9:12	154/91	153

pressure as recorded by the Dinemapp therefore could be as short as 15 sec (since it takes that long to make a recording) or as long as seven minutes. The second inadequate blood pressure was recorded at 09:01 (three readings at low levels) with a total time between adequate blood pressures of nine minutes. This total time of inadequate blood pressure as recorded by the Dinemapp therefore could be as short as five min or as long as nine minutes. Finally, the patient "pinked up," the operation was completed and the patient was sent to the ICU.

In the ICU there was good urine output at all times. The first blood gas analysis indicated a mild respiratory, more severe metabolic acidosis and no hypoxaemia (pH 7.12, PaCO₂ 45 mmHg, and PaO₂ 470 mmHg). The chest x-ray was normal. Three hours later, a pulmonary artery catheter was inserted (11:30) and the results were normal except for a high cardiac output (pulmonary artery pressure (PPA) 24/7 mmHg, cardiac output ($\dot{Q}$) 8.4 L · min⁻¹ and pulmonary wedge pressure (Pw) 12 mmHg) at a time when the heart rate was 130 min⁻¹ and blood pressure was 143/90 mmHg. The patient developed disseminated intravascular coagulation (DIC – fibrin degradation products (FDP) > 40 µg · ml⁻¹ (normal < 10),

GLOSSARY OF TERMS

PPA – Pulmonary artery pressure (mmHg)

Pw – Pulmonary wedge pressure (mmHg)

Pmv – Pulmonary microvascular pressure (mmHg)

Pla – Left atrial pressure (mmHg)

 $\dot{Q}$ – Cardiac output (L · min⁻¹)

PT – Prothrombin time (sec)

PTT – Partial thromboplastin time (sec)

FDP – Fibrin degradation products (µg · ml⁻¹)

AFE – Amniotic fluid embolus

partial thromboplastin time (PTT) 87 sec ($n = <35$), prothrombin time (PT) 17.7 sec ($n < 14$), Fibrinogen 1.9 g · L⁻¹ ($n > 4$), platelet count decreased from 383,000 × 10⁹ · L⁻¹ preoperatively to 145,000 × 10⁹ · L⁻¹ post-operatively) and she bled vaginally. Blood loss was replaced and coagulation factors infused. A blood sample was not taken to identify if "squames" were present. A lung scan was ordered but once the patient stabilized and before the scan was done she was transferred to a teaching hospital where mechanical ventilation was continued.

At the teaching hospital an EEG showed diffuse changes. A CAT scan showed no definite infarct. There were ECG changes described first as consistent with anterior ischaemia and then borderline flat T waves in leads V₂ and V₃ (two days later). In one week the ECG was normal. The patient was left with severe diffuse neurological impairment. No new diagnoses were made.

Discussion

Several possible diagnoses were considered in this patient.

(a) *Anaesthesia related problems* (Table II):

Total spinal anaesthesia would have occurred immediately after the local anaesthetic was injected (Table II) and would result in *immediate* loss of consciousness and apnoea. Heart rate would approach that of a denervated heart (72 · min⁻¹) and BP might decrease depending on the intravascular volume status. Positive pressure ventilation with 100% O₂ should correct the cyanosis. None of these occurred.

Intravenous bolus of local anaesthetic would create symptoms immediately after the local anaesthetic was injected and result in confusion, loss of consciousness, convulsions, possible decrease in BP and apnoea. None of these occurred at the appropriate time.

Slow absorption of local anaesthesia over time (10–30 min) from the epidural space would create hyperexcitability, confusion, convulsions, and loss of consciousness. The events would come on gradually after a dose of lidocaine of > 500 mg (total given 440 mg) and is unlikely in the presence of epinephrine. This could not account for the cyanosis, the suddenness, the SOB, or massive decrease in BP. A witnessed cardiac arrest created by this mechanism would not likely result in neurological problems.

High epidural block either because too much drug has been given or because it had been placed in the subdural space (Table II) may block the muscles of breathing and

TABLE II Effects of AFE, high epidural, subdural and total spinal

Disorder	AFE	High epidural	Subdural	Total spinal
<i>Lab results</i>	AFE debris (False +ve and -ve) PaO ₂ decreased PaCO ₂ increased	PaO ₂ decreased PaCO ₂ increased	PaO ₂ decreased PaCO ₂ increased	Xylocaine in brain CSF PaO ₂ decreased PaCO ₂ increased
<i>Timing</i>	*After uterine veins open *Sudden onset	Variable time after injection Slow onset	Variable time after injection (15 min) Slow onset	Within 5 min of xylocaine injection Fast onset
<i>CNS</i>	Loss of conscious. *Movement Distress *Convulsions *Few survivors (14%) *Brain damage (10%) *If brain damage pupils fix and dilate	No loss of conscious. Some movement Distress No convulsions Do survive No brain damage Pupils small	No loss of conscious. Some movement Distress No convulsions Do survive No brain damage Pupils small	Loss of conscious. No movement No distress No convulsions Do survive No brain damage Pupils fixed and dilated
<i>Respiratory system</i>	*Hyperventilation Respiratory distress *Hypoxaemia with high FiO ₂ and IPPV *Cough	Hypoventilation Respiratory distress No hypoxaemia with high FiO ₂ & IPPV Can't cough	Hypoventilation Respiratory distress No hypoxaemia with high FiO ₂ & IPPV Can't cough	Hypoventilation No distress No hypoxaemia with high FiO ₂ and IPPV Can't cough
<i>CVS</i>	*Blood pressure very low or 0 Heart rate increase *Cardiac arrest common *Difficult to resusc. (86% die) *PPA up for 30 min. May produce left & right heart failure *Jug. veins distended *CVP high	Blood pressure - reduced or no change Heart rate variable Card arrest uncommon Easy to resuscitate PPA not increased Heart normal Jug. veins collapsed CVP low	Blood pressure - reduced or no change Heart rate slow Card arrest uncommon Easy to resuscitate PPA not increased Heart normal Jug. veins collapsed CVP low	Blood pressure - reduced or no change Heart rate - 72 Card arrest uncommon Easy to resuscitate PPA not increased Heart normal Jug. veins collapsed CVP low
<i>Haematology system</i>	*DIC	No DIC	No DIC	No DIC

*Occurred in patient's case and different than other 3 diagnoses.

the patient will complain of gradually increasing SOB. But, the anaesthetic level was only at T₅₋₆. This problem is usually associated with a decrease in BP that occurs slowly (over ten minutes) and that responds to fluid infusion. Fluid was infused and a slow decrease in BP did not occur. The decrease in BP should be associated with pale or white skin and not cyanosis. The patient would not be able to cough since her muscles of breathing would be too weak. Positive pressure ventilation with 100% O₂ should correct the cyanosis.

Allergic reactions to the anaesthetic drugs used in this case are *extremely* rare, are usually associated with bronchospasm, and if life threatening, with hypotension.

Inadequate administration of O₂ Since the patient was resuscitated without changing the anaesthetic machine

and O₂ was administered by the anaesthetist this is ruled out.

(b) *Non-anaesthesia related problems*

Ruptured intracranial aneurysm was eliminated by the CAT scan.

Cerebral embolus is possible but would have been small or it would have shown up on the CAT scan. Amniotic fluid embolus to the brain may give rise to the CAT scan picture seen and be confused with global ischaemia since the emboli are small. Whether this patient had a cerebral embolus or global brain ischaemia cannot be determined but one (or both) must have occurred.

Myocardial Infarct has occurred in this type of setting

because of the increased coagulability and heart stress of late pregnancy. Although there were ECG changes, a myocardial infarct severe enough to create cyanosis is unlikely since the chest x-ray was clear and the Pw normal postoperatively.

Blood loss was not seen.

Sepsis is possible but unlikely to create a sudden event and to be corrected without the use of antibiotics and DIC is likely after severe sepsis. However, cardiac arrest and cyanosis are very unlikely after sepsis and it should have responded more quickly to the infusion of fluids given and the drugs applied.

Aspiration of stomach contents could create all of the problems but the normal postoperative chest radiographs rule it out.

Pulmonary embolism: the sudden timing of the event is typical of a pulmonary embolus. The patient would complain suddenly of SOB, hyperventilate, cough, be cyanosed, and have a decrease in blood pressure and increase in heart rate, seizures proceeding to cardiac arrest that is difficult to resuscitate and might produce neurological damage in a witnessed cardiac arrest. There are several possible embolic elements (blood clot, air and amniotic fluid).

Blood clot is possible in the pregnant patient but is unlikely with the normal pulmonary vascular pressures found three hours postoperatively.

Air is possible and air emboli have been described at Caesarean section by Doppler ultrasonography. Air is entrained into the open veins in the uterus at Caesarean section and could result in all of the presenting symptoms and the late findings since the air would be rapidly absorbed from the lungs and pulmonary artery pressures postoperatively would be normal. Although DIC is possible it is unlikely.

Amniotic fluid embolus (AFE) is the most likely diagnosis as the findings almost exactly match the expected effects of an AFE (Table II).⁸

Amniotic fluid embolism literature review

The primary defect created by an AFE is mechanical blockage of a part of the pulmonary arteries and vasoconstriction of the remaining vessels perhaps through the release of undefined chemicals such as prostaglandins, leukotrienes, serotonin or histamine.⁸⁻¹⁴ As a result, *pulmonary artery pressure (PPA)* increases. The initial

rise in PPA has never been documented in patients since no patient has even had a Swan Ganz catheter in place until after the AFE occurred.^{9,10,15-22} (Table III) but in animals PPA returns to normal within 30 min of an AFE²³⁻²⁵ (Table IV). One patient has been described with AFE but with low pulmonary artery pressures, as in the present case, five hours after the event.²¹

The two major defects created by the increased PPA are a decrease in O₂ transferred in the lungs and cyanosis, and a decrease in BP from the right ventricle outflow obstruction.

Hypoxaemia

The most important causes are lung and heart shunts.

LUNG SHUNT

$\dot{V}/\dot{Q}$ abnormalities: If an embolus reaches the lung it obstructs the vessels and stops perfusion to that part of the lung. Blood flow is reduced and dead space is created. This probably occurred in this case since the first PaCO₂ was 45 mmHg while the lungs were hyperventilated and which should have reduced the PaCO₂ into the 20 mmHg range. Therefore the PaCO₂, although normal, supports the diagnosis of AFE. However, while it is known that *hypoxaemia* occurs in pulmonary embolism the reason is not agreed upon. There are several possibilities. First, areas of the lung that have not been obstructed by embolus or vasoconstriction receive too much blood flow and overwhelm the amount of ventilation to that area so that insufficient O₂ is picked up by the blood going through the lung causing hypoxaemia and cyanosis.²⁶ Second, obstruction in the pulmonary circulation (either mechanical or vasoconstrictive) results in a decrease in cardiac output that reduces the O₂ content in the venous blood returning to the heart and lungs and thus magnifies the first effects. Third, emboli, or chemicals, pass through the pulmonary circulation into the coronary circulation and depress the heart leading to heart failure and pulmonary oedema.²¹

HEART SHUNT

The foramen does not completely close after birth in 35% of the normal population and may open with the AFE induced increase in PPA and allow blood containing AFE into the systemic circulation where it will travel to the brain. This blood that passes through the foramen has a venous O₂ content so that arterial O₂ concentrations decrease and this may damage the brain. Since opening of the foramen is dependent on the pressure gradient between the left and right atria any increase in PPA may be sufficient to cause this and even small numbers of emboli could create brain damage. The PPA must be

TABLE III Human data with PPA and amniotic fluid emboli

First author	Time to first PPA measure	First PPA (mmHg)	Pw (mmHg)	P. ed. before PA cath?	Fluid balance	Did patient survive?
Masson 1979 ¹⁵	24 hrs	41/26	22	Yes	++ colloid	Yes
Duff 1983 ¹⁶	50 min	26.6	18	Yes	+7160 ml	Yes
Dolyniuk 1983 ¹⁷	48 hrs	23	14	Yes	?	Yes
Schaerf 1977 ¹⁸	2 hrs	15	10	No	+1000 ml	Yes
Clark 1985 ¹⁰	70 min	29	19	Yes	?	No
Quance 1988 ¹⁹	2 hours	75/34	32	Yes	?	No
Shah 1986 ²⁰	AFE			No	?	Yes
	- Before	35/9	14			
	- After	38/16	?			
Clark 1988 ⁹ (4 cases)	Within 1-2 hrs	18	16	?	?	?
		42	31			
		21	16			
		25	14			
Girard 1986 ²¹	5 hrs	16	12	Yes	Not excessive	Yes
Moore 1982 ²²	20 hrs	27	21	Yes	+3000 ml	Yes

TABLE IV Animal data with continuous PPA reported after AFE

Authors	Source of AFE	Recip of AFE	AFE vol	Increase in mean PPA (peak) (time to)	Maximum time to return to normal mean PPA
Reeves 1974 ²³	Cow	Calf	100 ml · kg ⁻¹	1cr. 8 mmHg 2 min	10 min
Attwood 1965 ²⁴	Human	Dog	50 ml	Incr. 9 mmHg 1 min	30 min
Reis 1969 ²⁵	Sheep	Sheep	150 ml	Incr. 18 mmHg 1 min	30 min

lowered to correct this cause of reduced blood O₂ content reaching the tissues.

The hypoxic effect of cardiac or lung shunts may be improved by increasing venous O₂, for example by increasing cardiac output. However, increased cardiac output will increase PPA in the now noncompliant pulmonary vascular bed and may not increase venous O₂ levels if the heart consumes more O₂ to increase cardiac output.²⁷ The correct objective is to decrease the amount of shunt by reducing PPA.

Reduced blood pressure

The increase in PPA causes a reduction in cardiac output and therefore in blood pressure. If the pulmonary vessels are partially blocked or constricted, insufficient blood reaches the left heart and so preload will decrease. With inadequate preload, stroke volume, cardiac output and blood pressure may fall even if the heart keeps beating and at a more rapid rate. If the blockage is severe enough the heart will arrest. This type of cardiac arrest with a rapid heart rate is unusual. The pump cannot produce an adequate cardiac output without sufficient blood returning to the left heart. Since the problem is the obstructed, vasoconstricted pulmonary vessels, it will be difficult, if not impossible, to improve cardiac output until

PPA falls. Drugs may not improve cardiac output and CPR is useless since there is insufficient blood in the left ventricle to pump out. In this setting, the heart working maximally is far more effective than CPR. The outcome will be determined by how long the PPA is increased: if the PPA remains high, neurological damage may occur first and death may result regardless of the treatment applied.

The solution to the problem is to unblock the pulmonary vessels but there is no known way to remove AFE. Isuprel^{11,28,29} has been suggested to decrease PVR but it may also decrease arterial blood pressure. Since stroke volume is low increased heart rate improves cardiac output. This was done with ephedrine but, even then the blood pressure was abnormal. If pulmonary vessel obstruction and vasoconstriction are severe even heart rate increases cannot maintain cardiac output since cardiac output is limited by how much blood can pass through the lungs.

Although epinephrine is more potent than ephedrine it is not certain which is more effective. In this case 25 mg ephedrine were given and the heart rate increased to 147 · min⁻¹ at 8:52 and to 156 · min⁻¹ at 8:57 (Table I). The maximum effective heart rate is 160 · min⁻¹; at higher rates the heart is beating so rapidly that it has

no time to fill between beats. Vasopressors may also increase myocardial contractility and myocardial contractility increases when heart rate increases. Both ephedrine and epinephrine increase SVR. If BP is low, an increase in SVR might increase coronary perfusion and decrease perfusion to organs that are temporarily unnecessary (e.g., skin, muscle, gut and kidney). The effect of epinephrine is impeded in acidosis; epinephrine constricts pulmonary vessels and in the presence of hypoxaemia and acidosis epinephrine may result in ventricular fibrillation.

If cardiac output can be improved, hypoxaemia might be reduced and coronary and cerebral perfusion might be increased. The available data are from animal studies and with emboli other than AFE but they provide suggestions that might be useful in the treatment of AFE. Dog experiments with starch microemboli²⁷ found that volume infusions were effective in increasing cardiac output but also increased lung water: volume infusions worsened right ventricular dysfunction when PPA was increased.³⁰ Nitroprusside was effective²⁷ with volume, in increasing cardiac output but could not be used in the face of extreme hypotension. Dobutamine increased cardiac output²⁷ by increasing heart rate, but did not increase venous O₂ levels because the increased O₂ consumption of the heart used up the O₂ provided and it increased PPA. Angle *et al.*³¹ found that norepinephrine increased cardiac output and blood pressure after blood clot emboli in dogs. This was associated with an improvement in right ventricular performance, perhaps from increased coronary perfusion to the right ventricle. No measurements of pulmonary oedema were made. The suggestion that systemic vasoconstriction with neosynephrine is helpful has been made by State *et al.*³² Alpha vasoconstriction may be helpful after AFE as coronary perfusion pressures to a stressed right ventricle may improve and blood flow to organs such as the skin, gut, and kidneys is reduced, but is improved to the brain and heart. The 30-min time course of pulmonary hypertension after AFE found in animals is short enough to suggest that reduced perfusion to gut and kidney by alpha vasoconstriction may not create permanent damage.

The difficulty in treating severe pulmonary hypertension after AFE, results from the effect of maximally distended pulmonary vessels that now behave like rigid pipes. The only way to increase flow through rigid pipes is to increase the driving pressure, PPA, but the high PPA is the major problem in AFE. Even nitroprusside increased PPA when cardiac output increased.²⁷ In the most serious cases of AFE probably a combination of increased myocardial contractility, heart rate, volume infusions and increased SVR will all be needed. Epinephrine will provide most of these and alpha vasopressors

appear to be beneficial in animal experiments. No matter which therapy is chosen the result will not only depend on the therapy but on the degree of obstruction of the pulmonary vessels created by the emboli and therefore on the PPA.

The *cause of the reduced BP* (ending in a cardiac arrest) of an amniotic fluid pulmonary embolus is also debated. The cause may be (1) obstruction in the pulmonary vessels preventing blood from getting to the left side of the heart (2) hypoxaemia or chemicals reducing the heart's ability to function, (3) emboli in the coronary circulation creating ischaemic heart muscle, or (4) the same, or other, chemicals that create pulmonary vasoconstriction may also cause myocardial damage.²¹

Diffuse intravascular coagulation (DIC) is very common in documented cases of amniotic fluid embolism. The mechanism may relate to tissue damage caused by the effects of hypoxaemia and a low cardiac output but since DIC is not as common in patients after cardiac arrest from causes other than amniotic fluid embolism the DIC probably results from the chemical changes induced by the amniotic fluid embolus. This patient had DIC.

Brain damage is very common in any patient who survives an amniotic fluid pulmonary embolus in spite of immediate intensive resuscitation. Current data⁸ state that 86% of patients will die after an amniotic fluid embolus and permanent brain damage is common in the survivors. There are three possible causes of damage to the brain:

- 1 The AFE may pass through an existing foramen ovale. Once in the left heart they are distributed throughout the body in proportion to blood flow. As the brain receives a higher proportion of the cardiac output it will also receive a higher proportion of the emboli. Also, the first large vessels that come off the aorta pass to the brain. Other organs are protected from emboli by vasoconstriction and they may not be detected.
- 2 The AFE may go through the lungs themselves. Byrick *et al.*³³ showed in dogs, that within two hours fat emboli move out into the lung to obstruct progressively smaller vessels. This reduces PPA and may account for the rapid reduction in PPA after emboli. They also found fat emboli in the brain and kidneys of a size that could pass through the lungs in dogs who did not possess a patent foramen ovale. This suggests that the less viscous material in an AFE is even more likely to pass through the lungs and be responsible for diffuse brain damage.
- 3 Thirdly, brain damage after AFE may result from the combination of a low PaO₂ and low cardiac output which reduce O₂ transport to the brain. Normally, if resuscitation is successful within five minutes of cardiac arrest the brain survives because the blood bathing it

contains O₂ which can be used until perfusion with oxygenated blood is resumed. The contraction of hypoxaemia and poor perfusion leads to early brain damage. There is little time for resuscitation, CPR is ineffective and the increased PPA prevents filling of the left ventricle. Until PPA decreases manoeuvres will be ineffective in preventing brain damage.

There are no data concerning brain damage in the few patients who survive an AFE. We analyzed all cases of AFE described since 1977 in which there was a description of the neurological result.^{10,14-18,20-22,34,35} Permanent neurological injury occurred in 8% if the patient survived and 25% if the patient died because the neurological damage was so severe.

Subgroups of patients with AFE

Since the number of emboli are variable in an AFE there will be a spectrum of presentations. There are three categories of patients who suffer AFE. The first two (emboli through the lungs or foramen ovale) should create brain damage and the third problem is pulmonary oedema.

1 Emboli through the lungs

It is likely that AFE, like fat emboli,²³ will pass through the lungs.

2 Foramen ovale – paradoxical emboli

Although the incidence of foramen ovale has been quoted as 35% (0.6 to 1 cm foramen ovale in 6% and 0.2 to 0.5 cm foramen ovale in 29% of unselected autopsies) by Thomson and 25% by Hagan *et al.*³⁷ clinical studies consistently suggested a lower incidence, but the difference has been explained by Konstadt *et al.*³⁸ who found an overall incidence of foramen ovale of 26% in patients *without atrial septal defects*, in contrast to 6 and 18% reported by others.³⁹⁻⁴² The higher figure agreed with the autopsy data of Hagen *et al.*³⁷ and Thompson *et al.*³⁶ They found that when right-sided heart pressures were increased the incidence of foramen ovale increased from 10% to 22% and after adding Doppler recordings it increased further to 26%. The AFE are small (microscopic) and so can pass through a hole as small as 0.2 cm.

Harvey *et al.*⁴³ studied 286 patients after a stroke who were *thought not to have a foramen ovale*. In eleven <50 yr, a CAT scan showed no evidence of haemorrhagic stroke, heart valve defects, or clots inside their hearts, ECG was unchanged and there was no evidence of atherosclerotic cerebrovascular disease, and chest x-rays and cerebral physical findings were normal. *Eight of the eleven patients were shown to have a foramen ovale*. The authors conclude "we found an unexpectedly high association between interatrial defects and stroke in eleven

young patients, raising the possibility that paradoxical cerebral embolization is commoner than is usually believed."

Fat emboli may pass through lung capillaries to reach the systemic circulation. Thus, it is likely that AFE which is less viscous than fat will also pass through the lungs which is corroborated by the reports of AFE in the brain, heart, liver, and kidney. In some studies,^{24,44-46} a foramen ovale was not looked for. There are only two ways for emboli to reach the systemic circulation, either through the lungs or through a foramen ovale.

3 Pulmonary oedema

Clark⁴⁷ suggested that after the initial AFE problems due to PPA (phase one) a secondary event, left ventricular failure, may lead to pulmonary oedema (phase two). However, in most of the cases reported^{10,15-17,19,21,22} pulmonary oedema was present before the catheter was inserted (Table III). In the remaining two reports^{18,20} there were other reasons for inserting the catheter and pulmonary oedema did not occur.

The reported incidence of pulmonary oedema varies from 24% to 70%.⁴⁶ However, pulmonary oedema is difficult to detect even when based on lung weight at post mortem. Until there is a 60% increase in lung water we have difficulty seeing it on chest x-ray, or hearing it with a stethoscope, and blood gases and oxygenation will be normal.⁴⁸ A 60% increase in lung weight from 600 g takes us to 1000 g. Therefore Peterson⁴⁶ found only three cases of 40 with sufficient pulmonary oedema that it could have been detected clinically. Another 48% of patients had smaller (clinically undetectable) increases in lung water in the interstitial phase.

Peterson⁴⁶ and then Clark¹⁰ suggest that large increases in pulmonary oedema that can be detected clinically are unusual.

If pulmonary microvascular pressure (Pmv)

$$Pmv = Pla + 0.4(PPA - Pla)^{49}$$

is increased pulmonary oedema will, over time, increase.⁵⁰ Pulmonary oedema will not accumulate for several hours because it must overcome several safety factors built into the lungs to keep them dry. First, protein in blood and the surrounding tissues holds fluid inside vessels, second, the lung can carry away, through lymphatics, a 30-fold increase in the production of pulmonary oedema. But if Pmv stays high enough, long enough, pulmonary oedema will eventually result. Thus, delayed pulmonary oedema after AFE will show up following (a) the infusion of large amounts of fluid to increase Pmv or (b) left ventricular dysfunction.

In those reports of AFE in which the details of fluid administration, PA catheter information, and the presence

of pulmonary oedema are complete (Table III), three of four patients had excessive fluid administered and high Pmv.^{15,16,22} In a fourth patient²¹ treatment for pulmonary oedema with furosemide was given before the PA catheter was inserted. None of the mechanisms that create pulmonary oedema can account for the initial reduced PaO₂ after AFE since it occurs too rapidly. Only later can pulmonary oedema play a role in reducing PaO₂.

Pulmonary oedema may occur after AFE for the same reasons as it occurs in other situations, i.e., by an increase in Pmv. Whether pulmonary oedema occurs will depend on how much fluid is infused and the heart damage done by the AFE. Most, 76%, of 272 patients did not develop pulmonary oedema after AFE.

Relationship to patient

The sudden onset of dyspnoea, cyanosis, hypotension, convulsions and DIC are typical of AFE (or air emboli) in a pregnant patient. In 1987 neither pulse oximetry nor end-tidal CO₂ were available to aid in the diagnosis. The haemodynamic profile (Table I) indicates that the patient had an AFE before 08:41. If a convulsion occurred, emboli may have passed through a foramen ovale. The administration of O₂, tracheal intubation and ventilation were not effective in correcting the shunt. By 08:52 the combination of reduced PPA, fluid and ephedrine resulted in an improved BP at near maximum heart rates. At 08:57 a second AFE obstructed more pulmonary vasculature. The obstruction to blood flow and the lack of further cardiac reserves resulted in undetectable BP. The improvement in BP at 09:08 (Table I) may have been due to a reduction in PPA.

After oxygenation and blood pressure returned to normal the heart rate remained elevated because an O₂ debt has to be paid back to tissues. The Swan-Ganz catheter inserted one hour later found normal values which was compatible with both an AFE and other patient data.²¹ The chest x-rays and breath sounds were normal. Pulmonary oedema was not seen but it is possible that some pulmonary oedema (<60% increase) was present but this amount of oedema would not be heard by stethoscope or seen on chest x-ray and would not modify blood gases. Whether clinicians should accept the risk of pulmonary oedema by infusing large fluid volume loads in an attempt to increase venous return to the left heart after AFE is debatable. On balance, aggressive fluid volume infusions and high-dose inotropes (epinephrine, norepinephrine, isuprel, dobutamine and/or dopamine) in an attempt to improve cardiac output rapidly at the point of highest initial PPA and lowest cardiac output might have an opportunity for success. Of these, norepinephrine has provided benefits in animal experiments. The pulmonary oedema that might result could then be dealt with later

(once the AFE obstruction of the pulmonary vascular bed has abated).

The only diagnostic tool missing is a sample of pulmonary artery blood for "squames." But, the value of this test has been questioned since "squames" occur in the pulmonary venous blood of pregnant patients without symptoms of AFE.^{51,52} Other tests, ECG, lung scan, chest x-ray and pulmonary angiograms are not helpful in most cases because even small amounts of emboli can create a large amount of damage.

We should recognize⁵³ that the patient outcome may not be changed by therapy regardless of how aggressive it may be. Rather outcome will be determined by the number of emboli reaching the pulmonary, brain or coronary vascular beds. Nevertheless, we must be prepared to deal with this sudden, unheralded, and potentially catastrophic event in any pregnant patient.

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