Review Article

Acute pulmonary oedema in pregnant women

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Summary

Acute pulmonary oedema in pregnant women is an uncommon but life-threatening event. The aims of this review are to address why pulmonary oedema occurs in pregnant women and to discuss immediate management. We performed a systematic literature search of electronic databases including MEDLINE, EMBASE and the Cochrane Library, using the key words obstetrics, pregnancy, acute pulmonary oedema, pregnancy complications, maternal, cardiac function and haemodynamics. We present a simple clinical classification of acute pulmonary oedema in pregnancy into pulmonary oedema occurring in normotensive or hypotensive women (i.e. without hypertension), and acute pulmonary oedema occurring in hypertensive women, which allows focused management. Pre-eclampsia remains an important cause of hypertensive acute pulmonary oedema in pregnancy and preventive strategies include close clinical monitoring and restricted fluid administration. Immediate management of acute pulmonary oedema includes oxygenation, ventilation and circulation control with venodilators. Pregnancy-specific issues include consideration of the physiological changes of pregnancy, the risk of aspiration and difficult airway, reduced respiratory and metabolic reserve, avoidance of aortocaval compression and delivery of the fetus.

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Acute pulmonary oedema in pregnant women is a life-threatening event. Despite improvements in the management of congestive heart failure in non-pregnant adults, it continues to cause significant morbidity and mortality in pregnancy. This is due to the superimposed issues of the physiological changes of pregnancy and the presence of the fetus, as well as the contributory effect of poorly understood pathophysiology of pregnancy-related disease such as pre-eclampsia. The objective of this review is to present an overview of the physiology and pathophysiology underpinning acute pulmonary oedema in pregnancy and to consider the management issues specific to pregnancy, including risk reduction and preventative strategies.

Methods

The criteria for consideration of the literature that was reviewed included any systematic review, randomised controlled trial, observational study, case report or expert or consensus statement pertaining to pregnant women and their cardiovascular physiology, cardiovascular pathophysiology, acute pulmonary oedema, and management and interventions in pregnant women with acute pulmonary oedema. Electronic search strategies included searching the databases MEDLINE (until October 2011), EMBASE (until October 2011) and the Cochrane Library using the following key words: obstetrics; pregnancy; acute pulmonary oedema; pregnancy complications; maternal; cardiac function;

haemodynamics. Literature in languages other than English was included in the searches. The web-based resources of relevant colleges were examined for any relevant publications, including the Royal College of Obstetricians and Gynaecologists, the American College of Obstetricians and Gynecologists, the Canadian Society of Obstetricians and Gynecologists, the Society of Obstetric Medicine of Australia and New Zealand, the International Society of Obstetric Medicine, the World Health Organization, the International Federation of Gynecologists and Obstetricians, the Obstetric Anaesthetists' Association, the Society of Obstetric Anesthesiologists and Perinatologists, the American Heart Association and the European Society of Cardiology. Where appropriate, we determined levels of evidence according to the National Institute for Health and Clinical Excellence (NICE) 2005 levels of evidence for intervention studies scale (Table 1).

Pulmonary oedema

Acute pulmonary oedema is a significant cause of morbidity and mortality in pregnant and recently

pregnant women [1, 2]. It is characterised by sudden-onset breathlessness, may be accompanied by agitation, and is often the serious clinical manifestation of a variety of pathophysiological processes. The Scottish Confidential Audit of Severe Maternal Morbidity, one of the largest maternal morbidity audits, reported that acute pulmonary oedema was the fourth most common form of maternal morbidity [1]. It is also frequently the reason for intensive care admission [3], and may occur during the antenatal, intrapartum or postpartum periods. Risk factors and predisposing conditions are shown in Table 2.

Estimated rates of acute pulmonary oedema in pregnancy vary from as low as 0.08% to as high as 0.5% [4–7]. The wide ranges reported are due the poor reporting of maternal morbidity and lack of minimal reporting datasets of key outcomes in pregnancy and the postpartum period [8].

Conceptualising cardiac function and acute pulmonary oedema

The forces determining the rate of fluid transfer to the lungs and hence whether acute pulmonary oedema

Table 1 National Institute for Health and Clinical Excellence (NICE) 2005 levels of evidence for intervention studies.

Level	Intervention
1++	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1−	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2++	High-quality systematic reviews of case–control or cohort studies; high quality case–control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is casual
2+	Well-conducted case–control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is casual
2−	Case–control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not casual
3	Non-analytical studies (e.g. case reports, case series)
4	Expert opinion, formal consensus

RCT, randomised clinical trial

Table 2 Risk factors for the development of acute pulmonary oedema in pregnancy.

Category	Specific risk factors
Pre-existing pre-pregnancy conditions	Cardiovascular disease (hypertension, ischaemic heart disease, congenital heart disease, valvular heart disease, arrhythmias, cardiomyopathy) Obesity Increased maternal age Endocrine disorders (phaeochromocytoma and hyperthyroidism)
Specific diseases in pregnancy	Pre-eclampsia Cardiomyopathy Sepsis Preterm labour Amniotic fluid embolism Pulmonary embolism
Pharmacological agents	β-Adrenergic tocolytic agents Corticosteroids Magnesium sulphate Illicit drugs including cocaine
Iatrogenic intravenous fluid therapy	Positive fluid balance > 2000 ml
Fetal conditions	Multiple gestation

occurs are the same in both pregnant women and non-pregnant adults. The differences between the groups, and the reasons for separate consideration, are the underlying physiological differences between pregnant and non-pregnant adults, the specific pathophysiology of the important pregnancy-specific condition of pre-eclampsia and the management of a critically ill pregnant woman with the considerations of a fetus. To understand these differences, it is first important to outline the fundamental principles of why pulmonary oedema occurs in adults in general.

Acute pulmonary oedema may be caused by a variety of perturbations of any one of the key determinates of cardiovascular function and fluid flow into the pulmonary interstitium [9]. Hydrostatic pressures, colloid osmotic pressures and capillary permeability determine the amount of fluid within the pulmonary interstitium and are described by Starling's equation [10]:

$$\text{Transcapillary fluid filtration rate} \propto$$
$$K_f[(P_{mv} - P_t) - (COP_{mv} - COP_t)]$$

where: K_f is the ultrafiltration coefficient, capillary permeability; P_{mv} is microvasculature pressure, which approximates to arterial pressure–venous pressure; P_t is tissue hydrostatic pressure; COP_{mv} is microvasculature colloid osmotic pressure; and COP_t is tissue colloid osmotic pressure.

Hydrostatic pressures are determined by cardiac function in which the key components are preload, heart rate, heart rhythm, contractility, lusitropy and afterload. Hydrostatic pressures are also determined by arterial and venous tone through nervous system activity and circulating vasoactive substances [11]. The systemic and pulmonary circulations function in parallel, with cardiac output equalling venous return. The Frank-Starling mechanism enables matching of the stroke volumes of the two ventricles. This coupling mechanism means that neither acute pulmonary oedema nor complete empty-ing of the pulmonary circulation can occur, both of which can be fatal [12–16]. A system in balance is represented by cardiac output achieved at the lowest left ventricular end-diastolic pressure that meets the meta-bolic needs of the tissues and that equals venous return. Acute pulmonary oedema or acute congestive cardiac failure represents a system out of balance and unable to meet the metabolic needs to the tissues which, if left untreated, leads to death.

It follows that factors that increase hydrostatic pressure (leading to elevated left ventricular end-diastolic pressure), factors that decrease colloid osmotic pressure, or factors that increase capillary permeability, will predispose a woman to the development of acute pulmonary oedema [17–19]. It is now recognised that not only is fluid accumulation and retention a mecha-nism for acute pulmonary oedema, but so too is fluid redistribution from the systemic circulation to the pulmonary circulation due to venoconstriction or vaso-constriction in a person who is euvolaemic [18, 19]. Therapies for the treatment of acute pulmonary oedema reverse one or more of these factors, with re-absorption of pulmonary oedema both a passive and an active process [20]. Frequently, more than one risk factor is present, with iatrogenic fluid administration a major preventable factor [8]. Specific aetiologies causing acute pulmonary oedema have an increased likelihood of occurring during specific time periods; for example, tocolytic therapy in the antenatal period [21], and fluid overload in combination with pre-eclampsia in the postpartum period [6, 8, 22, 23]. Other contributory factors include baroreceptor-mediated arginine vaso-pressin release, leading to fluid accumulation and hyponatremia, a situation that occurs in some women with pre-eclampsia.

From a clinical perspective, it is useful to classify the condition into acute pulmonary oedema without hypertension (i.e. a normotensive or hypotensive woman) or acute pulmonary oedema with hypertension. This allows the appropriate pharmacological therapy to be chosen.

Acute pulmonary oedema; represents a form of decompensated acute cardiac failure, and is a system out of balance. Classifications of acute cardiac failure have used the terms diastolic and systolic failure to describe whether the cardiac failure occurs in the presence of normal or impaired ventricular function, respectively. Systolic cardiac failure refers to a failure of adequate myocardial contractility [24]. Diastolic failure refers to a failure of adequate myocardial relaxation (lusitropy), usually due to structural changes within the myocardium secondary to hypertension (left ventricular hypertrophy). This leads to reduced compliance, ele-

vated end-diastolic pressure and impaired left ventricular filling [25]. The associated elevated pulmonary venous pressure at rest reduces lung compliance, increases the work of breathing and results in the subjective feeling of breathlessness. These symptoms are made worse by exercise [26]. With respect to understanding diastolic cardiac failure, the presence of a preserved or normal ejection fraction does not imply an adequate cardiac output, and the terms ejection fraction and cardiac output should not be used synonymously. This is shown in Table 3, adapted from Andrew et al. [27], where the values in diastolic failure show a normal ejection fraction, but a markedly reduced cardiac output, compared with the values for normal cardiac function with a similar ejection fraction.

Cardiac failure with preserved ejection fraction may be associated with acute pulmonary oedema with hypertension. The cardiac output in this situation, despite an ejection fraction within the normal reference range, represents a level that is inadequate to meet the requirements of the metabolising tissues. There is reduced oxygen delivery, as the presence of pulmonary oedema limits respiratory gas exchange and leads to hypoxaemia. Following this, in the more chronic heart failure setting, mechanisms are activated to correct this imbalance. The main response is through the renin-angiotensin-aldosterone system and the sympathetic nervous system, which attempt to increase cardiac output through increasing heart rate, cardiac contractility, fluid redistribution and fluid retention to increase stroke volume [26–30].

Table 3 The relationship between ejection fraction and cardiac output (from Andrew et al. [27]).

Variable	Normal	Diastolic failure	Systolic failure
LVEDV; ml	120	100	250
LVESV; ml	50	50	200
LVSV; ml	70	50	50
HR; beats.min^{-1}	60	60	60
EF; %	60	50	20
CO; l.min^{-1}	4.2	3.0	3.0

LVEDV, left ventricular end-diastolic volume; LVESD, left ventricular end-systolic volume; LVSV, left ventricular stroke volume; HR, heart rate; EF, ejection fraction; CO; cardiac output.

$$EF = [(LVEDV - LVESV)/LVEDV] \times 100$$

Diagnosis

There are a number of commonly associated clinical symptoms (breathlessness, orthopnoea, agitation, cough) and signs (tachycardia, tachypnoea, crackles and wheeze on chest auscultation, cardiac S_3 gallop rhythm and murmurs, decreased oxygen saturation). Typical chest X-ray features include upper lobe redistribution, Kerley-B lines and pulmonary infiltrates. Arterial blood gases (decreased P_aO_2), ECG and echocardiography may help establish the diagnosis. Serum concentration of B-type natriuretic peptide, released from the cardiac ventricles in response to stretching of the myocardium, is not widely utilised in pregnancy, in contrast to the non-pregnant emergency setting [24, 31, 32]. Further work is required to define its place in acute cardiac failure in pregnant women [25, 30, 33].

Transthoracic echocardiography is the key diagnostic and management tool [1, 6, 24, 31, 34–38]. This enables measurement of left ventricular outflow tract velocity and septal tissue Doppler systolic movement to assess cardiac systolic function. The mitral valve inflow Doppler velocities (E-wave and A-wave) and septal tissue Doppler diastolic movements of the myocardium (e′ and a′), in addition to volume and pressure changes in the ventricle, enable diastolic function to be assessed [39, 40]. The ratio of the peak early mitral valve inflow velocity divided by the tissue Doppler mitral annular early-diastolic velocity correlates closely with left ventricular end-diastolic pressure. A ratio of ≥ 15 in non-pregnant adults with depressed ejection fraction, or a ratio of ≥ 13 in adults with a normal ejection fraction, indicates elevated left ventricular end-diastolic pressure. A ratio of < 8 indicates low left ventricular end-diastolic pressure and normal diastolic function [41]. Preliminary work in pregnancy indicates that threshold values may be lower, with ratios of > 9.5 associated with significant diastolic impairment [33, 42, 43]. Recent work has reported that interstitial lung fluid may also be detected using echocardiography directed through the lungs [19]. The role of this technique in pregnancy requires further evaluation.

Cardiac function in healthy pregnancy

Pregnancy is a time of rapid physiological and, at times, pathological change. Cardiovascular changes can be

broadly divided into four categories: the effects of circulating hormones; mechanical pressure of the enlarging uteroplacental fetal unit; increasing metabolic demands of the uteroplacental fetal unit; and the presence of the uteroplacental circulation. Labour imposes additional cardiovascular stress due to uterine contraction, pain, positioning, bleeding, fatigue and uterine involution. Postpartum fluid shifts, autotransfusion and hormonal changes further alter cardiovascular system function [44].

Compared with non-pregnant adults, healthy pregnant women demonstrate an increased cardiac output, increased heart rate, increased blood volume, physiological anaemia, decreased systemic vascular resistance and decreased blood pressure. Using transthoracic echocardiography, the reference range for cardiac output in healthy term pregnant women is approximately 4.4–8 l.min^{-1}; the peak value may be achieved at a range of different gestations from 28 to 38 weeks [45–48]. Researchers have also reported a reduction in both systolic and diastolic function near term [40, 49, 50], supporting the hypothesis that there is mild impairment of systolic and diastolic function [47–49]. In addition, healthy pregnancy is associated with a low colloid osmotic pressure to left ventricular end-diastolic pressure gradient, thereby predisposing even healthy pregnant women to the risk of acute pulmonary oedema [51]. The extent to which a woman is able to compensate for the physiological and pathological changes of pregnancy depends on three important factors: her underlying cardiovascular reserve; her cardiac function; and the extent of the disease burden. Acute pulmonary oedema may develop secondary to one major cardiovascular insult, such as critically high blood pressure in pre-eclampsia or cardiogenic shock associated with myocardial ischaemia. Alternatively, acute pulmonary oedema may develop with the accumulation of smaller insults, such as increased age, obesity and pre-existing hypertension, in combination with excessive intravenous fluid administration. Echocardiography in healthy pregnant women enables the detection of subclinical reduced systolic and/or diastolic function, and may thereby identify women at risk of acute pulmonary oedema. It also assists in determining underlying cardiac function at the time of acute pulmonary oedema [34].

Cardiac pathophysiology

The following section considers the two broad classifications of acute pulmonary oedema in pregnancy:

1 Acute pulmonary oedema without hypertension.
2 Acute pulmonary oedema with hypertension.

The management of women with acute pulmonary oedema without hypertension follows similar principles to the management of this condition in non-pregnant adults with some special considerations due to pregnancy. Acute pulmonary oedema in the presence of hypertension, as it occurs in pre-eclampsia, is a unique disease of pregnancy, the mechanism of which is frequently misunderstood and which requires special consideration and management specific to this disease state.

Acute pulmonary oedema without hypertension

The most common associated factors and causes are tocolysis, sepsis, pre-existing cardiac disease, pregnancy-associated cardiac disease (cardiomyopathy, ischaemic heart disease), amniotic fluid embolism with left ventricular systolic failure, aspiration and iatrogenic intravenous fluid administration. These women may be either normotensive or hypotensive. Important risk-reduction strategies include early antenatal recognition of known high-risk women, early multidisciplinary referral and management, and careful fluid balance, with rational administration of intravenous fluids based on haemodynamic indices and end-organ function [1, 52, 53]. The development of acute pulmonary oedema in these circumstances is due to the same underlying alteration in forces controlling pulmonary interstitial fluid – hydrostatic pressure, colloid osmotic pressure and capillary permeability – that occur in non-pregnant adults. However, due to reduced physiological reserve in pregnancy, there is reduced ability to tolerate these changes that might be compensated for in non-pregnant women.

Iatrogenic causes remain an important factor for acute pulmonary oedema without hypertension. The management of preterm labour with the use of tocolytic agents such as β-adrenoceptor antagonists (terbutaline and salbutamol) has been associated with acute pulmonary oedema. Important mechanisms in this setting include β-adrenoceptor effects on capillary permeability, reduced myocardial contractility, fluid administration

during tocolytic therapy and the concurrent use of steroid medication [52]. Newer single agents such as nifedipine are associated with less acute pulmonary oedema [54] (level 1++ evidence). Magnesium sulphate and corticosteroids have both been implicated as precipitators of acute pulmonary oedema in pregnant or postpartum women. Women in whom magnesium sulphate infusions are administrated for fetal neuroprotection in preterm labour [55] (level 1++ evidence) need to be carefully monitored and their fluid balance meticulously recorded.

Acute pulmonary oedema with hypertension

Hypertensive disease of pregnancy affects approximately 15% of pregnant women [44]. Any form of sustained hypertension (systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg) in pregnancy is abnormal, as the healthy physiological response to pregnancy is a reduction in blood pressure. In addition to chronic hypertension, gestational hypertension, pre-eclampsia and pre-eclampsia superimposed on chronic hypertension, women may present with critically high blood pressure after intake of illicit drugs including cocaine, or if they have an underlying endocrine disorder such as hyperthyroidism or phaeochromocytoma.

Pre-eclampsia is a multisystem major cardiovascular disease of pregnancy with hypertension its main clinical manifestation [56, 57]. Acute pulmonary oedema, which signifies severe disease, is a leading cause of death in women with pre-eclampsia [58, 59], and is a frequent cause for admission to an intensive care unit [60]. Pulmonary oedema may occur in up to approximately 3% of women with pre-eclampsia, with 70% of cases occurring after birth. It is associated with excessive fluid administration and disease severity, including the presence of haemolysis, elevated liver enzymes and low platelets (HELLP), and eclampsia [22, 61]. In addition to the usual management goals of stabilising the woman and treating the acute pulmonary oedema, consideration needs to be given to delivery of the fetus if acute pulmonary oedema occurs in the antenatal period. The underlying mechanism for the hypertension in this disease state remains unknown. Compared with healthy pregnant women, women with pre-eclampsia demonstrate a range of cardiac abnormalities, from increased

cardiac output and mildly elevated systemic vascular resistance [62–66], to low cardiac output with elevated systemic vascular resistance [22, 67–72]. Diastolic cardiac function is impaired, with increased left ventricular mass and pericardial effusion more common [33, 40, 43]. Figure 1 shows the effect of pregnancy and pre-eclampsia on the heart, illustrated by pressure–volume loops. In healthy pregnant women, there is an upward displacement of the diastolic resting tension curve, with a downward displacement of the systolic curve, compared with healthy non-pregnant women. In pre-eclamptic women, there is further upward displacement of the diastolic curve, showing that the same left ventricular end diastolic volume is associated with an increased left ventricular end-diastolic pressure. The systolic curve is either shifted upward (increased systolic function) or downward (decreased systolic function), compared with non-pregnant adults.

Pre-eclampsia also leads to a reduction in plasma colloid osmotic pressure, altered endothelial permeability, and a reduction in colloid osmotic pressure to left ventricular end-diastolic pressure gradient (Fig. 2) [71]. Studies in women with pre-eclampsia at the time of acute pulmonary oedema are few in number and show large variability in haemodynamic profile. This may be explained by the heterogeneity of the women in these case series, small sample size, varying gestations and differing treatment interventions [66, 71–73].

The underlying mechanism of acute pulmonary oedema in these circumstances depends on the underlying haemodynamic state of the pregnant woman. Not only are there cardiac structural and functional abnormalities, but there are also alterations in fluid balance associated with hypoproteinuria. There are many similarities with acute pulmonary oedema associated with hypertensive crises in non-pregnant patients [42–44], although this is a poorly characterised condition [30, 74]. As stated earlier, there is often preserved left ventricular ejection fraction, indicating significant cardiac reserve; however, the heart is still unable to generate a large enough cardiac output to deliver oxygen to the vital organs [28, 30].

The acute hypertensive crisis that precipitates the acute pulmonary oedema may occur through sympathetic nervous system activation, causing acute venoconstriction and vasoconstriction, which leads to increased
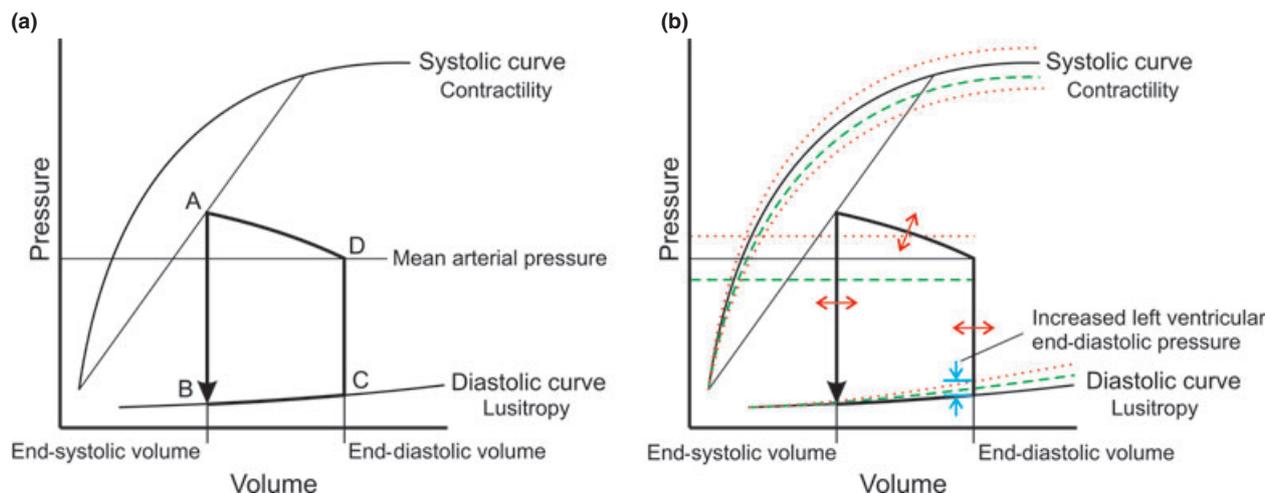
Figure 1 Pressure-volume loops, showing a single cardiac cycle (points A, B, C, D).
(a) Healthy non-pregnant woman: the aortic valve closes (A) and ventricular pressure falls with active relaxation of the left ventricle during the isovolumetric relaxation period and the first phase of diastole. The heart then fills from an end-systolic volume (B) to an end-diastolic volume (C) along the diastolic (or resting tension) curve. The mitral valve closes and the ventricular pressure rises (C). This time period (the isovolumetric contraction time) is the first phase of left ventricular systole. The aortic valve opens when left ventricular pressure exceeds aortic pressure (D), and the stroke volume is ejected. Left ventricular contraction is governed in part by factors intrinsic to the myocardium and is related to the systolic curve of the left ventricle. The aortic valve closes when the left ventricular pressure falls below aortic pressure. This completes left ventricular systole.
(b) Non-pregnant adult (black lines) with superimposed curves for a healthy pregnant woman (dashed green lines) and one with pre-eclampsia (dotted red lines). The healthy pregnant women has an upward displacement of the diastolic resting tension curve, and a downward displacement of the systolic curve. The mean arterial pressure in decreased. In pre-eclampsia, there is further upward displacement of the diastolic curve; i.e. the same left ventricular end-diastolic volume is associated with an increased left ventricular end-diastolic pressure (blue arrows). The systolic curve is either shifted upwards (increased systolic function) or downwards (decreased systolic function) compared with non-pregnant adults. The mean arterial pressure is increased compared with healthy pregnant women. The location of the pressure-volume loop on the diastolic curve may alter with gestation and there is no consistent agreement in healthy pregnant women or women with pre-eclampsia (hence not shown with certainty (red arrows) in this Figure).

afterload and redistribution of fluid from the peripheral circulation to the pulmonary vessels. This causes alveolar fluid accumulation and reduced oxygenation and concurrently increases cardiac output as a compensatory mechanism due to reduced renal oxygen delivery [75]. Unfortunately, the diversity of reported haemodynamic changes means that the research data are not generalisable to the individual woman with this condition.

Despite uncertainty as to the mechanism of the hypertension, knowledge regarding the adverse effects of intravenous fluid therapy in women with pre-eclampsia is increasing. Unrestricted intravenous fluid therapy is recognised as a significant risk factor for the development of acute pulmonary oedema [22, 76] (level 3 evidence). Historically, the use of intravenous fluids was thought to improve maternal cardiovascular parameters;

however, in one large trial [59] (level 1+ evidence) and a systematic review [58] (level 1++ evidence), volume expansion was not beneficial. Intravenous fluid therapy may also exacerbate acute respiratory distress syndrome, leading to hypoxaemia, high airway pressures and difficulty with ventilation. The postpartum period is high-risk for the development of acute pulmonary oedema. The use of intravenous fluids to increase plasma volume or treat oliguria, which is multifactorial in nature, in a woman with normal renal function and stable serum creatinine levels, is therefore not recommended [58] (level 1++ evidence). Antenatal fluid therapy may be indicated if there are concerns about placental perfusion; however, communication with the obstetric team and cautious use should occur, with close monitoring of cardiovascular and respiratory function.
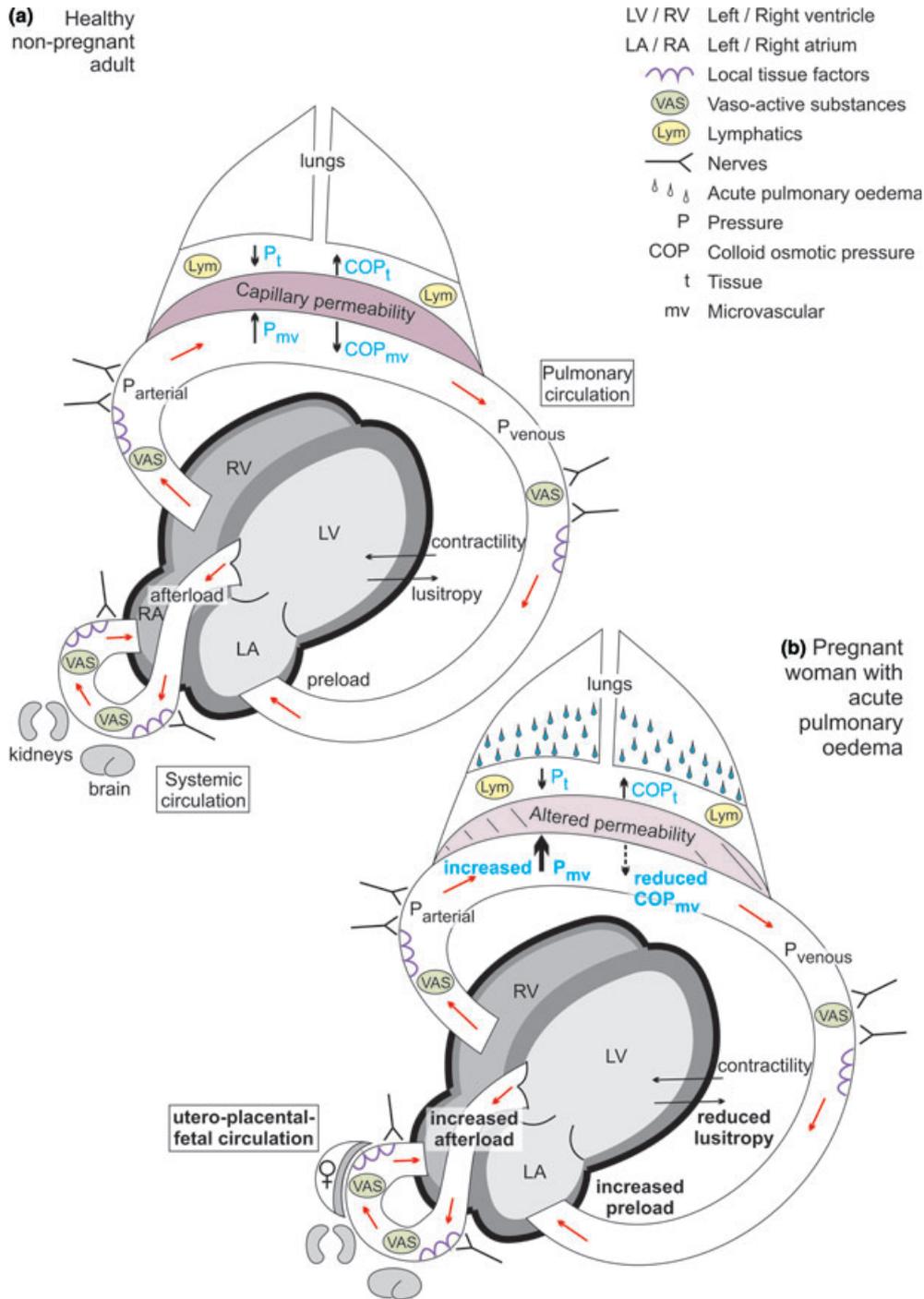
Figure 2 Filtration forces in a healthy non-pregnant adult (a) and in a woman with pre-eclampsia and acute pulmonary oedema (b). There is increased afterload caused by hypertension and reduced lusitropy due to left ventricular structural changes such as left ventricular hypertrophy. This leads to increased microvascular forces and increased preload. Reduced colloid osmotic pressure combined with alterations in capillary permeability further increases the chance of acute pulmonary oedema.

Table 4 Strategies to reduce the risk of acute pulmonary oedema in pregnant women.

Category	Risk-reduction strategy
Planning and communication	Multidisciplinary team involvement [1, 2] (level 3 evidence) Effective verbal and written communication and handover [1, 2] (level 3 evidence)
Close observation	Close monitoring and recording of observations (including conscious state, blood pressure, respiratory rate, heart rate, oxygen saturation, temperature and fluid balance) [1, 2] (level 3 evidence) Close monitoring and recording of biochemical parameters (haematological, renal, metabolic and respiratory) [1, 2] (level 3 evidence)
Avoidance of precipitants	Avoidance of non-steroidal anti-inflammatory drugs [77] (level 3 evidence) Restricted fluid administration and minimisation of additional intravenous fluids by the use of undiluted solutions of magnesium sulphate and reduced volume Syntocinon® infusions [1, 8] (level 3 evidence)
Early intervention	Critical hypertension (systolic blood pressure > 150 mmHg requires antihypertensive therapy; systolic blood pressure >180 mmHg is a medical emergency requiring urgent reduction) [1, 78] (level 1++ evidence)

A recent one-year retrospective individual patient data review conducted at two similar tertiary referral obstetric hospitals demonstrated that acute pulmonary oedema in hypertensive pregnant women was strongly associated with increased intravenous fluid administration in the unit that had unrestricted fluid policies for women undergoing labour, caesarean section and magnesium sulphate seizure prophylaxis (0/472 vs 19/408 cases) [8] (level 3 evidence). The relative risk of developing acute pulmonary oedema with 5000 ml of peripartum fluid administration was 1.9, and the relative risk with 10 000 and 15 000 ml was 4.0 and 9.2, respectively. This is consistent with work from other groups that have reported acute pulmonary oedema in the postpartum period to be associated with positive fluid balances of > 5500 ml [4, 23] (level 3 evidence).

The unit with restricted fluid policies had a median total fluid administration of 2100 ml in the peripartum period, and there were no reports of adverse outcomes related to undiluted magnesium sulphate administration or acute renal failure [8] (level 3 evidence).

Strategies to reduce the risk of acute pulmonary oedema in pregnant women are shown in Table 4.

The management of hypertensive acute pulmonary oedema in pregnancy

The goals of treatment are:

1 Reduce left ventricular preload.
2 Reduce left ventricular afterload.
3 Reduce/prevent myocardial ischaemia.
4 Maintain adequate oxygenation and ventilation with clearance of pulmonary oedema.

Immediate management

The occurrence of acute pulmonary oedema in a hypertensive pregnant or recently pregnant woman is a medical emergency and should trigger an emergency response (Fig. 3) aimed at rapidly assembling an experienced team of staff [79, 80] (level 3 evidence). Further deterioration may occur, leading to cardiac arrest, and staff should be prepared to institute advanced life support and consider peri-mortem caesarean section. Transthoracic echocardiography can assist in differentiating a low cardiac output from a high cardiac output state, as well as exclude other important causes of acute pulmonary oedema.

Electrocardiography, chest X-ray, blood pressure, oxygen saturation, heart rate, respiratory rate, temperature and fluid balance monitoring should be considered mandatory. Pulmonary artery catheters for haemodynamic monitoring are rarely required and have significant side effects [81] (level 1++ evidence).

Despite the risks of aspiration [82], non-invasive ventilation should be tried as the initial technique before tracheal intubation, as it provides increased inspired oxygen concentration, displaces fluid from the alveoli into the pulmonary and subsequently systemic circulation, decreases the work of breathing, and decreases the need for tracheal intubation [31, 83] (level 1++ evidence). The use of non-invasive ventilation also avoids the complications associated with tracheal intubation in pregnant or recently pregnant women who are hypertensive, such as intracerebral haemorrhage [83,
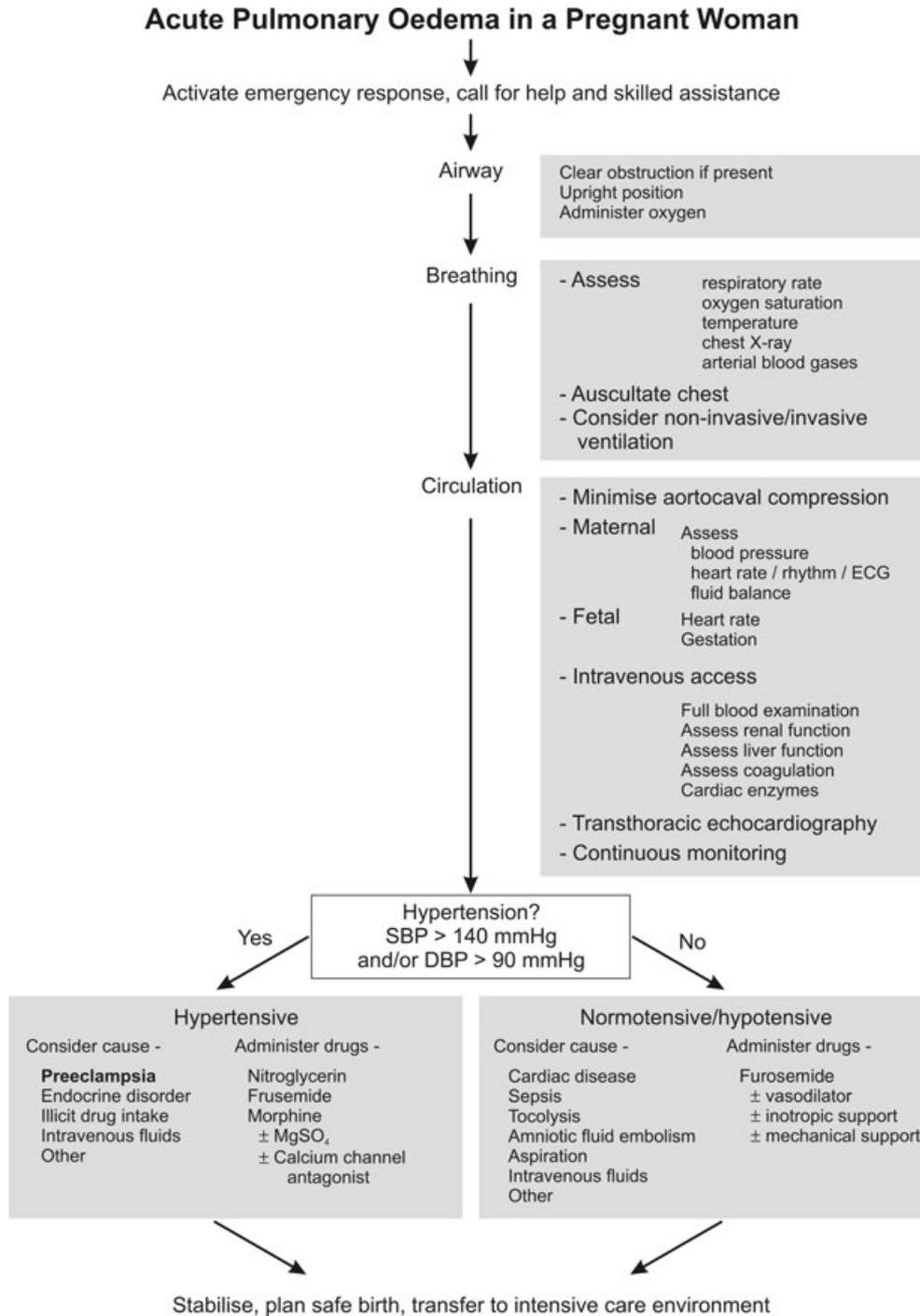
Acute Pulmonary Oedema in a Pregnant Woman

Activate emergency response, call for help and skilled assistance

Airway
- Clear obstruction if present
- Upright position
- Administer oxygen

Breathing
- Assess
  - respiratory rate
  - oxygen saturation
  - temperature
  - chest X-ray
  - arterial blood gases
- Auscultate chest
- Consider non-invasive/invasive ventilation

Circulation
- Minimise aortocaval compression
- Maternal
  - Assess
    - blood pressure
    - heart rate / rhythm / ECG
    - fluid balance
- Fetal
  - Heart rate
  - Gestation
- Intravenous access
  - Full blood examination
  - Assess renal function
  - Assess liver function
  - Assess coagulation
  - Cardiac enzymes
- Transthoracic echocardiography
- Continuous monitoring

Hypertension?
SBP > 140 mmHg
and/or DBP > 90 mmHg

Yes ← → No

Hypertensive

Consider cause -
Preeclampsia
Endocrine disorder
Illicit drug intake
Intravenous fluids
Other

Administer drugs -
Nitroglycerin
Frusemide
Morphine
± MgSO₄
± Calcium channel antagonist

Normotensive/hypotensive

Consider cause -
Cardiac disease
Sepsis
Tocolysis
Amniotic fluid embolism
Aspiration
Intravenous fluids
Other

Administer drugs -
Furosemide
± vasodilator
± inotropic support
± mechanical support

Stabilise, plan safe birth, transfer to intensive care environment

Figure 3 Flow chart for management of pregnant woman with acute pulmonary oedema. SBP, systolic blood pressure; DBP, diastolic blood pressure.

84]. Mechanical ventilation strategies incorporating the known cardiorespiratory and metabolic changes of pregnancy need to be considered when ventilating the lungs of a pregnant or recently pregnant woman, as well as the lung protective strategies of low tidal volumes and

low peak pressures [38]. Avoidance of aortocaval compression is essential.

Urgent reduction of critically high blood pressure with an intravenous antihypertensive agent is necessary. Nitroglycerin (glyceryl trinitrate) is recommended as the

drug of choice in pre-eclampsia associated with pulmonary oedema [44] (level 3 evidence). It is given by intravenous infusion starting at 5 $\mu g.min^{-1}$, gradually increasing every 3–5 min to a maximum of 100 $\mu g.min^{-1}$. Nitroglycerin can also be administered by sublingual spray (400 μg, 1–2 puffs every 5–10 min). An alternative agent, sodium nitroprusside, is recommended in severe heart failure and critical hypertension; however, it should be used only with caution and by experienced clinicians. The typical dose by infusion is 0.25–5.0 $\mu g.kg.min^{-1}$ [31] (level 4 evidence). Reduction in systolic and diastolic blood pressure should occur at a rate of approximately 30 mmHg over 3–5 min followed by slower reductions to blood pressures of approximately 140/90 mmHg.

Intravenous furosemide (bolus 20–40 mg over 2 min) is used to promote venodilation and diuresis, with repeated doses of 40–60 mg after approximately 30 min if there is an inadequate diuretic response (maximum dose 120 $mg.h^{-1}$) [31] (level 1 evidence).

If hypertension persists despite the combination of nitroglycerin or sodium nitroprusside and furosemide, then a calcium channel antagonist such as nicardipine or nifedipine may be considered (especially if diastolic dysfunction is diagnosed). Prazosin as well as hydralazine [78] (level 1++ evidence) may also be considered; however, reflex tachycardia may be deleterious in this setting. Intravenous morphine 2–3 mg may also be given as a venodilator and anxiolytic [31] (level 1 evidence). High dependency care and close observation are essential (Table 5).

Long-term management

Women who suffer from severe pre-eclampsia and experience acute pulmonary oedema are at increased risk of cardiovascular complications in later life, including hypertension, ischaemic heart disease, stroke and renal disease [86–88]. They should be closely monitored with control of blood pressure until resolution of the initial disease process and then followed up regularly, with observation for the long-term complications of the disease. Angiotensin-converting enzymes, whilst contraindicated in pregnancy, are safe to use in the postpartum period. Risk reduction strategies should be offered, such as weight reduction and smoking cessation programs, dietary modification, encouragement of regular exercise

Table 5 Short-term management strategies in pregnant women with acute pulmonary oedema.

Planning and communication	Multidisciplinary team management [1] (level 3 evidence)
Close observation	High dependency care and close monitoring with one-to-one nursing/midwifery staff [1, 2] (level 3 evidence) Continuous monitoring of vital signs [1, 2] (level 3 evidence) Serial monitoring of respiration, cardiac, renal and haematological function [1, 2] (level 3 evidence) Assessment of fetal wellbeing and multidisciplinary planning for safe birth if acute pulmonary oedema occurs antenatally [1, 2] (level 3 evidence)
Avoidance of precipitants	Strict fluid balance and fluid restriction [8] (level 3 evidence)
Early intervention	Control of blood pressure [84] (level 1++ evidence)
Prevention of further complications	Eclampsia prophylaxis with magnesium sulphate if woman has pre-eclampsia [85] (level 1++ evidence) Prevention of deep vein thrombosis and pulmonary embolism Prevention of stress ulceration of the gastrointestinal tract

and control of hypertension [89]. In women who require long-term treatment, the aims are to modify the underlying cardiac function or structural pathology.

Conclusion

Acute pulmonary oedema is an indicator of significant morbidity and may lead to mortality in pregnant women. It is paramount to identify the at-risk patient, recognise signs of critical illness and manage these women with a skilled multidisciplinary team. Special consideration needs to be given to both the mechanical effects and the metabolic requirements of the fetus, the altered physiology that affects circulatory and respiration function, stabilisation of the woman and planning for safe birth. Risk reduction strategies should include an emphasis on the importance of fluid balance and recording regular clinical observations. Appropriate long-term follow-up is necessary to reduce the chance of further complications in later life. Future work needs

to focus on the implementation of simplified algorithms for critically ill pregnant women, applicable across all disciplines, concentrating on the importance of clinical symptoms and signs. Finally, the use of transthoracic echocardiography should be encouraged, both as an educational tool and to aid diagnosis and management.

Acknowledgement

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