Aspiration of gastric contents is a rare but potentially serious adverse event. As such, the subject does not lend itself to rigorous investigation by randomised controlled trial since meaningful studies would require prohibitively large numbers. They would also probably be unethical because of the outcomes involved. Much of our best evidence therefore emerges from mortality reports and the investigation of surrogate outcomes such as the measurement of gastric volumes and pH. As the evidence is sparse, many possible interpretations emerge as does the possibility of misinterpretation. In some cases, clinicians may be tempted to implement clinical practices contrary to established norms in the absence of positive supportive evidence. The priority must always be to attempt to deliver the safest anaesthetic care, balancing all relevant risks.

This document deals with antacid prophylaxis prior to anaesthesia and surgery. It covers the specific clinical circumstances in pregnant patients requiring elective or emergency surgery and procedures in the immediate postpartum period. The related specific issues of oral intake in labour and the details of anaesthetic techniques during pregnancy and in the peripartum period are covered elsewhere.

1. MORTALITY AND MORBIDITY FROM ASPIRATION

An appropriate clinical risk-management strategy is to identify the population most at risk and those factors which are likely to be associated with adverse outcomes. In this regard, all pregnant women must be considered to be at some risk of requiring anaesthetic intervention. Outcomes recorded in birth centres caring for even low risk pregnancies, where all women were allowed to eat and drink as they desired, have shown 15.4% required transfer to another hospital and 4.4% required caesarean delivery (Rooks et al 1989, Level IV). Risk of aspiration is a function of those factors which influence
gastric volume and pH, opioid effects, the experience and expertise of the anaesthetist managing the airway, as well as maternal obesity (Lewis 2007; McClure & Cooper 2005).

1.1 Incidence

The incidence of aspiration has changed over recent decades and is now rare. In this context, attempts at stating a specific incidence and defining possible underlying factors are problematic. As a starting point, it is widely accepted that parturients are at increased risk from aspiration of gastric contents secondary to hormonal and mechanical factors. Significant risk factors for aspiration include the presence of food and opioid analgesia in labour (Murphy et al 1984, Level III-2; O’Sullivan 1987, Level III-2; Wright 1992, Level II). Loss of consciousness and sedation contribute to these risks. The National Sentinel Caesarean Section Audit showed that 1 in 29 women (3.4%) having caesarean section in England and Wales were unconscious during childbirth (Thomas & Paranjothy 2001).

Mendelson first reported maternal death and severe morbidity due to aspiration of stomach contents under general anaesthetic in 1946 (Mendelson 1946, Level IV). This sentinel paper highlighted that there is an increased risk of aspiration of both solids and liquids into the lungs during obstetric anaesthesia. In a series of 44,016 pregnancies, 45 patients aspirated either solid or liquid stomach contents (approximately 1:1000); all had received general anaesthesia. Two deaths were recorded which resulted from obstruction through aspiration of solid material. Significant morbidity was additionally recorded in 40 patients who became “critically ill” from aspiration of liquids. They developed pyrexia, asthma-like symptoms, cyanosis, tachycardia, dyspnoea and expiratory wheezing. Two patients developed pneumonia and two developed lung abscess. This retrospective observational series highlighted firstly the impact of solid material obstruction of the airway and secondly the dangers of fluid aspiration.

Aspiration when it occurs remains an important cause of death and morbidity. In the US between 1979 and 1990, 23% of maternal deaths were found to be due to aspiration (Hawkins et al 1997, Level IV). Some of the most useful data come from the UK maternal mortality triennial reports (now identified as CEMACH) which in various forms go back to the 1950’s (McClure & Cooper 2005). These reports continue to highlight airway problems which frequently precipitate pulmonary aspiration as the commonest causes of anaesthetic death in mothers. In addition, American Society of Anesthesiologists closed-claims data identify aspiration pneumonia as the cause of maternal injury in 6% of obstetric files compared to 2% of non-obstetric files reviewed (Chadwick et al 1996, Level IV). In relation to the timing of the actual aspiration episodes reported, it is noted that women have encountered airway complications after regional blockade and also at the time of emergence and extubation from general anaesthesia, not just at the time of intubation. Also, there may be a requirement to convert a planned regional anaesthetic for caesarean section to a general anaesthetic. This may be less than 1% (Letson & Simmons 2008, Level IV) but may be as high as 3% (Bloom et al 2005, Level IV).
Over the last 50 years, the introduction of several measures designed to reduce the risk of aspiration have been associated with a profound effect in reducing mortality from aspiration. Fasting in labour, antacid premedication, cricoid pressure, intubation with cuffed endotracheal tubes and popularisation of regional anaesthesia have all been identified as contributing to the dramatic fall in maternal mortality (Cooper et al. 2002).

1.2 Risk factors

Critical values for volume and acidity

Gastric content values of volume and pH are considered surrogate measures of risk for pneumonitis should aspiration occur. The accepted criterion for defining the risk of pneumonitis is a combination of pH less than 2.5 and a volume greater than 25 mL of stomach contents. These arbitrarily set critical values, originally extrapolated from animal work by Mendelson’s 1946 rabbit experiment, were validated by Roberts and Shirley (1974, Level III-2). This work set critical values of gastric contents for an adult human female as a pH value of <2.5 and a volume of >0.4 mL/kg.

The clinical significance of these criteria has not been well investigated. The introduction of solid undigested food into the lungs produces complete obstruction. The introduction of 20 mL of 1/10 HCL or unneutralized liquid vomitus produced demise within hours and histological changes including perivascular oedema, peribronchial haemorrhage and necrotic bronchiolar epithelium (Mendelson 1946).

Opioids

Administration of parenteral opioids during late pregnancy and labour is associated with delayed gastric emptying (Nimmo et al. 1975, Level III-2; Murphy et al. 1984, Level III-2; La Salvia & Steffen 1950, Level III-2). Opioids administered epidurally or intrathecally in labour may also have this effect, although it would appear to be dose-dependent. Porter et al. (1997, Level II) showed that gastric emptying was only delayed in women who had received more than 100 μg fentanyl by epidural infusion.

Obesity

The decline in incidence of aspiration and maternal mortality needs to be considered against the background of changing population demographics. Obesity is a major public health issue and a major obstetric and anaesthetic risk factor. Problems may arise due to increased difficulty with tracheal intubation and respiratory problems including regurgitation and aspiration. Patient weight has been found to be a significant factor in gastric content volume during labour with those patients over 72 kg having a significantly higher gastric volume in labour than those below that weight (Roberts & Shirley 1974).
Obese patients featured prominently in a recent CEMACH report in which respiratory problems following anaesthesia resulted in death (Lewis 2007, Level IV). Aspiration was not cited as the direct cause of death in these particular cases but with greater risk of airway problems, aspiration is a prominent danger. It is noteworthy that the body mass index (BMI) of women described in this report is by current norms relatively low, with 27% of mortalities involving a BMI of only 30 or greater.

2. EFFECTS OF AVAILABLE PREPARATIONS

Preventative strategies aim to raise pH and/or reduce intragastric volume. There are a number of preparations available which may influence one or both of these factors and they are often used in combination (Paranjothy et al 2008). Antacids work by direct neutralisation of gastric contents. Other agents reduce gastric secretions by H2- receptor antagonism, proton pump inhibition or have a prokinetic effect.

2.1 Antacids

In the context of aspiration prophylaxis, clinical use is now confined to non-particulate formulations such as sodium citrate. Particulate antacids such as those containing magnesium or aluminium (e.g. Mylanta®) are likely to be associated with more severe pneumonitis should aspiration occur (Eyler et al 1982; Gibbs et al 1979). Clinicians should be aware that symptoms of indigestion and heartburn are common in pregnancy and these types of preparations are often used by pregnant women. Should symptom control be desired during labour or in the immediate pre-operative period, the use of these particulate agents should ideally be discontinued in favour of other preparations.

Sodium citrate

Sodium citrate is the most effective agent for immediate neutralisation of acidic gastric contents (Gibbs et al 1982) and appears to be equally effective in emergency and elective cases and with either general or regional anaesthesia (Dewan et al 1985, Level II; Lin et al 1996, Level II; Stuart et al 1996, Level III-3). It is usually presented as a 0.3 M (8.8%) solution in a volume of 30 mL and is readily commercially available.

The reported effects on gastric volume are inconsistent with either no change (Dewan et al 1985, Level II) or a slight increase (Jasson et al 1989, Level II; Yau et al 1992; Level II). This variability is probably a function of the sensitivity of the measurement techniques used, the power of the studies and the clinical context; typically the range of gastric volumes reported is very large. The addition of either ranitidine or omeprazole alone to sodium citrate has been associated with smaller gastric aspirate volumes (Yau et al 1992; Level II) and this may be enhanced with the added presence of metoclopramide (Stuart et al 1996, Level III-3).

In a study involving 32 healthy term parturients undergoing elective caesarean section and given 30 mL of 0.3 M sodium citrate, the mean gastric
pH measured immediately after delivery was 5.0 (+/- 1.5), compared with 1.8 (+/- 2.7) in the control (Dewan et al 1985, Level II). Significantly, all the women who did not receive sodium citrate had a pH of less than 2.5 compared with only 9% of women who had received it within 60 minutes of sampling. In addition, no-one in the citrate group had a combination of pH <2.5 and gastric volume of > 25 mL. The neutralising effect was, however, relatively short lived. In another group of women in the same study, who received the citrate more than 60 minutes in advance, only 50% had a pH less than 2.5.

The acid neutralising effect appears to be very rapid in onset and certainly within a few minutes. Jasson et al (1989, Level II) demonstrated a significant elevation of pH when measured 10 minutes after administration. Others have shown similar significant rises in the very short interval between arrival in the operating room and immediately after endotracheal intubation (Gibbs et al 1982, Level IV; Ormezzano et al 1990, Level II; Rout et al 1993, Level II).

Almost all studies of sodium citrate have used a volume of 30 mL. However, as little as 15 mL has also been shown to be effective at raising pH to what is believed to be an acceptable level although possibly not to the same degree. In the study by Ormezzano et al (1990, Level II) the mean pH shortly after tracheal intubation at caesarean section was 4.38 (+/- 1.44) and 13.8% of women had a pH of <2.5.

Sodium citrate has been noted to promote nausea amongst caesarean section patients (Kjaer et al 2006, Level II) and may be quite unpalatable, but this may be reduced by chilling of the solution (Gibbs et al 1982).

**Other oral antacids**

There are other commercially available alkalinising solutions, e.g. Ural® (sodium citrotartrate) but these either have not been specifically evaluated, are inferior to sodium citrate, or have some particulate content. Effervescent oral rantidine has some acid-neutralising properties due to the added presence of sodium citrate and sodium bicarbonate. The tablets must be fully dissolved which can take up to five minutes and the final molarity diminishes significantly with volumes of diluent greater than 30 mL (Glaxo Wellcome , pers. com. 1997). In a study of 15 fasting healthy males, Watson et al (1996, Level III-2) showed a clinically relevant rise in pH at 10-20 minutes after administration of 150 mg of effervescent ranitidine that was not seen with the standard preparation. Even within the effervescent group, however, this direct effect was transient with the period from approximately 30-60 minutes after administration being at an unacceptably low pH before a second rise in pH became evident.

**2.2 H₂-receptor antagonists**

Ranitidine has been the most extensively studied (Escolano et al 1996, Level II; Lin et al 1996, Level II; Rout et al 1992, Level II). To date, no other agent has been consistently demonstrated to be more effective than ranitidine and most are more expensive.
Ranitidine

A number of studies have been done in the non-obstetric elective surgery setting. Maltby et al (1990, Level II) showed that 150 mg of oral ranitidine when given two to three hours before surgery resulted in a mean gastric pH of 5.86 (+/- 1.73) and with only one out of 49 patients having an ‘at risk’ combination of pH <2.5 plus gastric volume of >25 mL. Also, when given this far in advance there was no extra benefit on pH by adding sodium citrate or metoclopramide or both compared with ranitidine alone. Other studies have demonstrated a similar effect at only 60 minutes after a single 150 mg oral dose (Escolano 1996, Level II). However this would appear to be approaching the lower limit of the time needed for an adequate response. In a similar population evaluated at only 30 to 60 minutes after an oral tablet and using a larger dose of 300 mg, the proportion of patients with a gastric pH less than 2.5 may be as high as 35% (Jacobs et al 1991, Level II). The effervescent oral formulation is absorbed more rapidly in healthy males and produces a more rapid rise in gastric pH (Watson et al 1996, Level III-2). There is also no significant difference between 150 mg and 300 mg, with both taking around 60 minutes to achieve a sustained increase in pH which then lasts for approximately five hours. The transient acid-neutralising effect of the effervescent form is noted above.

When used in obstetric patients, these effects may be less predictable particularly in the context of active labour or concurrent opioid use (Murphy et al 1984, Level III-2), or in the presence of particulate material in the stomach of non-fasted patients (Rout et al 1993, Level II), or with emergency as compared to elective surgery (Lim & Elegbe 1992, Level III-2). Oral ranitidine has been studied in the context of regular dosing during labour, using 50 mg 6-hourly (Yau et al 1992, Level II) or in single doses of 300 mg (Lin et al 1996, Level II). The effects on gastric pH and volume in these studies are consistent with those found in the non-obstetric population. However, there are no properly designed randomised controlled trials specifically comparing different oral doses across a range of clinical circumstances.

The intravenous route has been more extensively studied and has been shown to have a faster rate of onset. In the context of emergency general anaesthesia for casearean section, Tripathi et al (1995, Level II) found that all patients had a gastric pH >2.5 and volume <25 mL by 45 minutes after 50 mg of IV ranitidine. In this setting also the combination of IV ranitidine and sodium citrate has been shown to be more effective than sodium citrate alone (Rout et al 1993, Level II) with less than 1% of women having the ‘at risk’ combination at 30 minutes.

There have been a few individual case reports of anaphylactoid reactions with ranitidine (Barry et al 1992; Kaneko & Maruta 2003; Powell & Maycock 1993), but given the widespread usage of this drug over a long period this must be described as rare.
Other H₂-receptor antagonists

There are several other agents available, most of which have not been specifically investigated. Famotidine has been studied in the obstetric setting. A single oral dose of 40 mg three hours before elective caesarean section has been shown to be as effective as 300 mg oral ranitidine (Lin et al 1996; Level II).

2.3 Proton pump inhibitors

Omeprazole has been the agent most extensively studied in this population. It can be given orally or by intravenous injection and has been studied at doses of 40 mg and 80 mg. The onset of effect after IV administration is similar to that of ranitidine and should be considered to be at least 40 minutes (Tripathi et al 1995, Level II). In the setting of emergency caesarean section, a single IV dose of omeprazole 40 mg results in the same percentage of patients with the combination of pH <2.5 and volume > 25 mL as ranitidine 50 mg IV when combined with sodium citrate (Tripathi et al 1995, Level II; Stuart et al 1996, Level III-3). When given orally, regularly every 12 hours during labour, omeprazole alone is not as effective as when combined with sodium citrate or the combination of ranitidine with sodium citrate (Yau et al 1992, Level II). There appears to be no additional benefit in using 80 mg compared with 40 mg (Levack et al 1996, Level II).

2.4 Prokinetic agents

Metoclopramide increases the rate of gastric emptying, is an antiemetic and increases lower oesophageal sphincter tone. It has been studied alone and in combination with other agents in obstetric patients at a dose of 10 mg IV (Murphy et al 1984, Level III-1; Stuart et al 1996, Level III-3) and after intramuscular (IM) injection. Reported effects are inconsistent which may be a function of a range of factors including patient selection and concurrent opioid use. When given intramuscularly in labour, both a decrease in gastric volume (Howard & Sharp 1973, Level II) and no change have been observed (Nimmo et al 1975, Level III-2). It is possible that some of this difference may be due to the variable presence of opioids and the relatively small dose of metoclopramide used. After IV administration Murphy et al (1984, Level III-2) showed accelerated gastric emptying across a range of contexts including elective caesarean section and also when in established labour irrespective of the added administration of opioids.

3. GESTATIONAL AGE AND PERIPARTUM CONSIDERATIONS

Pregnant women occasionally require anaesthesia during pregnancy for a range of indications and also in the immediate postpartum period commonly as a result of a complication of the birth or for tubal ligation. The surgical procedure may itself increase aspiration risk through the adoption of lithotomy or Trendelenberg positions or the creation of a pneumoperitoneum. Numerous studies have been conducted at various stages of pregnancy and the puerperium although generally with very low numbers and of an observational or non-interventional design. Outcomes reported include
gastric pH and volume, lower oesophageal sphincter tone, and gastric emptying using a variety of techniques including paracetamol absorption, real time ultrasound, applied potential tomography, test meals, x-rays and radio-isotopes. A comprehensive listing of this work dating back to the 1930s has been compiled by O’Sullivan et al (2005).

3.1 Pregnant state

It is commonly believed that the pregnant patient is at increased risk of aspiration because of gastro-oesophageal reflux and delays in gastric emptying. Gastro-oesophageal reflux is common in pregnancy and can be demonstrated even in the absence of symptoms. There is no difference in basal and evoked gastric acid secretion in pregnancy but there is a reduction in lower oesophageal barrier pressure which is likely to be a progesterone effect present from early pregnancy (Bainbridge et al 1984; Van Thiel et al 1977). In the non-obstetric population there is a significant positive correlation between obesity and symptomatic reflux (Nocon et al 2007). Current evidence is inconclusive in relation to intra-abdominal pressure and anatomical displacement during pregnancy as contributors to reflux.

A consistent finding is that pregnancy in itself does not significantly delay gastric emptying. However there are a number of factors that have each in at least one study been shown in different contexts to be associated with significant delays in gastric emptying and it is possible that combined effects may be greater. Hence it is likely that a pregnant woman will exhibit delayed gastric emptying when she is not fasted, in labour, obese, in pain, or has recently received opioids.

More than two decades ago, considerable controversy was generated in the literature from a study in which 75 women undergoing elective surgical abortion at 15 weeks gestation were given a general anaesthetic with a ‘tight-fitting face mask’ and without aspiration prophylaxis (White et al 1983). There were no instances of aspiration.

3.2 Labour and immediately postpartum

Gastric emptying is slowed in labour and there are typically additional risk factors evident, such as food intake or the effect of opioids. The use of prophylactic drugs routinely in normal labour to reduce gastric aspiration has been the subject of a recent Cochrane systematic review (Gyte & Richens 2006, Level I). Whilst this analysis found no evidence to support this practice, the rare outcomes of maternal mortality and significant morbidity render this analytical approach somewhat problematic.

Studies in the postpartum period have demonstrated no significant difference in gastric emptying compared with non-pregnant controls by 18 hours (Whitehead et al 1993).
4. CLINICAL PRACTICE IMPLICATIONS

There is an absence of specific high-level evidence to guide decision making in this area. Norms of clinical practice are likely to be heavily influenced by local custom. In our region, difficult and failed intubation is reported more frequently in the obstetric population than non-obstetric (Sinclair et al 1999, Level IV) and the consequences of aspiration when it occurs may be severe. Clinical practice has favoured a low threshold for use of these measures based on the perceived benefit of reduced mortality and morbidity in the context of a very low incidence of side-effects (Kluger & Willemsen 1998, Level IV, Burgess & Crowhurst 1989, Level IV). These surveys also suggested that there is a preference for elective cases to be managed in the same manner as emergency cases when pregnancy alone was the consideration.

Therefore, it is reasonable to conclude that aspiration prophylaxis prior to anaesthesia and surgery as a result of pregnancy alone should be used in all women from the second trimester. This is reflected in standard texts as approximately 18-20 weeks gestation (Naughton & Cohen 2004). In the postpartum period this applies up to 18 hours post delivery. These limits should be extended if the woman is in labour, there is symptomatic reflux or when any other factors prevail that are likely to be associated with delayed gastric emptying. This should always be in the context of the usual considerations for pre-operative fasting. Every woman in labour who requires anaesthesia should receive antacid prophylaxis with sodium citrate and ranitidine or equivalent. The addition of metoclopramide is most likely to be effective when given intravenously in the presence of opioids. In addition, prophylactic administration of ranitidine or equivalent should be considered in those women who have a significant risk of requiring general anaesthesia or surgical intervention. This includes contraindications to regional blockade, BMI >30, previous caesarean delivery, diabetes, and extremes of fetal weight (Chu et al 2008; Patel et al 2005; Sherrard et al 2007).

KEY MESSAGES

1. Pulmonary aspiration of solids or liquids is a rare but significant cause of morbidity and mortality for pregnant women (Level IV).

2. Multiple changes in anaesthetic and obstetric practice including the widespread adoption of regional techniques, fasting in labour, use of antacids, use of cuffed endotracheal tubes and cricoid pressure have been associated with a dramatic reduction in maternal mortality from aspiration over the last 50 years (Level IV), but the independent effects of each of these is difficult to establish.

3. From early pregnancy, there is a reduction in lower oesophageal barrier pressure and symptomatic reflux is common but the rate of gastric emptying and basal gastric acid production due to pregnancy alone are unaltered.

4. Labour, food in the stomach, obesity and the use of opioids are all associated with delayed gastric emptying.
5. Particulate antacids which are commonly available over the counter are associated with more severe pneumonitis should aspiration occur.

6. Sodium citrate 0.3 M, 30 mL given orally is the most effective means of immediate neutralisation of gastric acidity; it is effective within a few minutes and lasts up to one hour (Level II).

7. Ranitidine is effective in a dose of 50 mg IV or 150 mg orally. There is no additional benefit from 300 mg. The onset is more rapid after IV administration, being approximately 45 minutes (Level II), while at least one hour should be allowed after oral administration (Level II). The duration of action is at least five hours.

8. The effervescent formulation of ranitidine exhibits a biphasic action on reducing acidity and some women will have unacceptably low levels of pH at approximately 30 to 60 minutes after administration (Level III-2).

9. The combination of sodium citrate plus ranitidine is the most effective means of reducing gastric acidity (Level II).

10. Proton pump inhibitors are no more effective than ranitidine and are generally more expensive (Level II).

11. Metoclopramide increases the rate of gastric emptying in some cases and is more effective after IV administration than intramuscular (Level II, III-2).

12. Aspiration prophylaxis should be used in all women of greater than 18-20 weeks gestation, and in the postpartum period up to 18 hours post delivery (Level IV). These limits should be extended when any other factors prevail that are likely to be associated with delayed gastric emptying or there is symptomatic reflux.

13. Routine prophylaxis with ranitidine in labour should be considered in those women who have a significant risk of requiring general anaesthesia or surgical intervention including contraindications to regional blockade, BMI >30, previous caesarean delivery, diabetes, and extremes of fetal weight. The usual schedule in this context is six-hourly dosing.

REFERENCES


