

Principles of ear nose and throat surgery for pregnant women

Management of the pregnant surgical patient is challenging. The surgical procedure is usually postponed until the postpartum period, although this may not be possible in emergency situations. This article highlights the optimal management of the pregnant woman requiring ear nose and throat surgery.

Ear nose and throat surgery may become necessary during pregnancy. Elective surgical procedures can generally wait until after the baby is born and sometimes until after breast-feeding is completed, but this is not the case for most ear nose and throat emergencies. The ear nose and throat surgeon may need to operate on pregnant women in emergency conditions such as airway obstruction, neck abscesses and severe epistaxis, and also relatively urgent situations such as thyroid malignancies and parathyroid adenomas.

Between 0.75% and 2% of pregnant women require non-obstetric surgery (Rosen, 1999). A Swedish study on 5405 pregnant women undergoing non-obstetric surgery during pregnancy reported 419 (7.7%) ear, nose and throat surgeries in their cohort (Mazze and Kallén, 1989) – an incidence of 0.06% ear nose and throat surgeries in pregnant women overall. As operating on pregnant women is relatively uncommon, the ear nose and throat surgeon may find him-/herself in uncharted territory. Several factors need to be considered in the optimum ear nose and throat surgical management of the pregnant woman. This article highlights important facets of the perioperative management of the pregnant woman who needs ear nose and throat surgery and provides an overview of the main principles involved.

Surgical and anaesthetic considerations

Surgery during pregnancy is challenging as maternal and fetal safety are both important considerations. The surgical and anaesthetic teams need a thorough understanding of physiological and pharmacological changes during pregnancy to circumvent the risks of non-obstetric anaesthesia in pregnant women. In addition to the

risks of the primary surgery itself, there are direct risks to the mother during non-obstetric surgery associated with the physiological changes of pregnancy. (General and ear nose and throat-related physiological changes in pregnancy are comprehensively discussed in Soma-Pillay et al (2016).) Also, there are risks to the fetus such as fetal asphyxia and loss, preterm labour and congenital defects. In general, perioperative fetal safety can be enhanced by the avoidance of teratogenic drugs and maintenance of adequate intraoperative uteroplacental perfusion, and obstetric support to monitor fetal wellbeing and manage preterm labour and delivery should it happen during or after surgery.

The goals of the anaesthetist in the management of the pregnant woman undergoing non-obstetric surgery are summarized by Walton and Melachuri (2006) as:

1. Optimize and maintain normal maternal physiological function
2. Optimize and maintain utero-placental blood flow and oxygen delivery
3. Avoid unwanted drug effects on the fetus
4. Avoid stimulating the myometrium (oxytocic effects)
5. Avoid awareness during general anaesthesia
6. Use regional anaesthesia if possible.

To achieve maternal and fetal safety, a multidisciplinary approach with senior involvement is needed early in the management. Although detailed discussion of the anaesthetic concerns during pregnancy is outside the scope of this article it will touch upon the main issues relevant to the surgeon during decision making and perioperative care.

Will the surgery and anaesthesia affect the pregnancy?

The patient will ask both the surgeon and the anaesthetist this question. An increase in fetal loss has been reported in women who undergo non-obstetric surgery during pregnancy. This could be a result of both surgical and anaesthetic factors that could potentially cause intrauterine death, premature labour or congenital anomalies. Two large studies have attempted to shed light on these outcomes. Duncan et al (1986) studied 2500 Canadian women who had undergone surgery during pregnancy and a similar number of pregnant women who had not and compared the outcomes. They found no increase in the

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rate of congenital anomalies but reported an increased rate of spontaneous abortion in women who had received general anaesthesia for non-obstetric surgery during the first trimester and second trimester. Interestingly, women undergoing surgery under regional or local anaesthesia in the early trimesters did not have increased rates of abortion. These authors concluded that in addition to the surgical procedure, general anaesthesia itself increased the rate of abortions. The other study was conducted in Sweden and enrolled over 5000 pregnant women (Mazze and Kallén, 1989). This study also did not note any increase in congenital anomalies following non-obstetric surgery and anaesthesia, but reported an increase in low birth weight and perinatal death. Curiously perinatal death occurred even in the absence of a temporal association with the surgical procedure. In contrast to the Canadian study, the Swedish study did not find general anaesthesia to have an increased risk of adverse events. They concluded that the nature of the illness requiring surgery during pregnancy was a determinant of the fetal outcome and not the method of anaesthesia itself (Mazze and Kallén, 1989).

What is the best time to operate?

Surgery during pregnancy may become essential during any trimester. Mazze and Kallén (1989) found that 42% of surgeries during pregnancy happened in the first trimester, 35% in the second trimester and 23% in the third. Some reports suggest that surgery in early pregnancy is associated with an increased rate of miscarriage (Brodsky et al, 1980; Duncan et al, 1986). This is in contrast to Cohen-Kerem et al (2005) who reported a miscarriage rate of 10.5% after non-obstetric surgery during the first trimester. This rate is comparable to the baseline miscarriage rate, so does not implicate non-obstetric surgery in the first trimester as resulting in increased miscarriage.

An increased risk of teratogenicity is also perceived to be associated with surgery in the first trimester as this is the critical period for organogenesis. This is not supported by the literature – the reported incidence of birth defects following first trimester surgery ranged from 2–3.9% (Cohen-Kerem et al, 2005), similar to the baseline incidence of 1–3% for the general population. There is some evidence in animal studies of neuronal damage upon exposure to anaesthetic agents, but these phenomena have not been demonstrated in human fetuses.

Elective surgery is best avoided in the first trimester of pregnancy in view of the possible risk of miscarriage and defects in neural development reported in animal studies. However, urgent or emergency surgery may be required in any trimester in pregnancy and the primary goal then is to preserve the life of the mother. Surgeries in the third trimester are thus confined to emergencies. In order to maximize fetal safety in the third trimester, a decision is usually made with the obstetric team as to whether delivery of the baby by trial of vaginal delivery or caesarean section is needed before the non-obstetric surgery. Issues such as antenatal morbidity, closeness to term and the potential

of ear nose and throat surgery to compromise placental blood flow are likely to influence decision making in this situation. Steroids are administered for 48 hours before delivery if possible, to allow maturation of the fetal lung and decrease the risk of hyaline membrane disease.

As a general rule surgery in the second trimester is considered to be the safest when preterm contractions and spontaneous abortion are least likely (ACOG Committee on Obstetric Practice, 2011).

What kind of anaesthesia will be appropriate?

The type of anaesthesia depends on the type and site of surgery, maternal factors and the experience of the anaesthetist. It is imperative that the anaesthetic team includes a senior anaesthetist with obstetric experience. Physiological changes associated with pregnancy can make airway management more difficult. The general antenatal population presenting for caesarean section has a ten times higher incidence of difficult intubation than the non-obstetric population (Rocke et al, 1992; Hawthorne et al, 1996; McKeen et al, 2011).

As pregnancy, especially in the third trimester, is associated with a higher risk of aspiration of gastric contents the requirement for intubation is even higher. There is an increased risk of airway bleeding and swelling as a result of the upper airway mucosa becoming more vascular and oedematous during pregnancy. These changes result in an increasing Mallampati score as pregnancy progresses, and also during labour and delivery (Kodali et al, 2008). This can result in the challenging can't intubate can't oxygenate situation that could require emergency cricothyroidotomy or tracheostomy (Kinsella et al, 2015; Mushambi et al, 2015). Coupled with a ear nose and throat-related airway pathology, management of the airway in the pregnant woman can become extremely challenging and requires advance planning. Additionally pregnancy carries an increased risk of reflux and aspiration. This is a real anaesthetic worry, and in the third trimester would always necessitate tracheal intubation in order to protect the airway, most likely with a cricoid pressure-type of induction. This is made more tricky as these patients have a higher incidence of difficult intubation.

Regional or local anaesthesia is preferred over general anaesthesia during pregnancy but is not suitable for many ear nose and throat surgeries. Local anaesthesia is appropriate for small procedures such as drainage of superficial abscesses but complex surgeries such as thyroidectomies are best done under general anaesthesia. Pregnancy can alter the response to local anaesthetic agents and a 25–30% lower total dose of local anaesthetics during pregnancy is recommended (Butterworth et al, 1990). It is also important to remember that the use of adrenaline infiltration during surgery could be potentially hazardous because of the risk of placental circulatory vasoconstriction and fetal hypoxia.

All general anaesthetic drugs cross the placenta. Sevoflurane and isoflurane are used commonly during pregnancy and are considered safe. Nitrous oxide has been

shown to be teratogenic during the organogenic period in animal studies as it interferes with the synthesis of thymidine. There are no studies in humans demonstrating this effect but as nitrous oxide is no longer considered an essential component of anaesthesia its use can easily be avoided.

Another area to be considered is hypotensive anaesthesia which is commonly used to create a 'bloodless' operating field in ear surgery and nasal surgery. Hypotensive anaesthesia could compromise fetal integrity, so is preferably avoided. Increased bleeding in the intraoperative field in the absence of hypotensive anaesthesia could make surgery more challenging but still manageable in experienced hands. In many ear nose and throat cases requiring bloodless fields, remifentanyl is often used as an infusion to augment intraoperative analgesia (it has a short duration of action and is hydrolysed quickly once the infusion is turned off at the end of surgery) and assist with cardiovascular stability (obtunding pressor responses very well). However, it should be used with caution and infusion rates titrated very carefully in the obstetric patient as its propensity to cause a reduction in both heart rate and blood pressure could compromise placental blood flow.

Is there a difference in preoperative preparation?

The pregnant woman should undergo all investigations deemed necessary, as for non-pregnant patients. Precautions are required with investigations requiring exposure to radiation. Fasting guidelines in pregnancy are the standard adult fasting guidelines in practice (i.e. 6 hours for solid food). Pregnancy carries a higher risk of aspiration because of reduced gastric barrier pressure and a lower oesophageal sphincter tone (Wong et al, 2007). Prophylaxis against aspiration pneumonitis should be administered with H₂-receptor antagonists and non-particulate antacids. A rapid sequence induction with cricoid pressure reduces the risk of aspiration of gastric contents during induction. The need for preoperative antibiotic prophylaxis depends on the specific procedure and selection of the appropriate antibiotic depends on the safety profile to the patient and the fetus. In certain situations prophylactic glucocorticoids could be indicated to increase fetal lung maturity. Administration of antenatal glucocorticoids 24–48 hours before surgery between 24 and 34 weeks of gestation can reduce perinatal morbidity and mortality if preterm birth occurs and can be initiated after discussion with the obstetric team.

How should the patient be positioned?

Patient positioning is critical during surgery in pregnant women to avoid aortocaval compression. Compression of the inferior vena cava by the gravid uterus in the supine position reduces venous return to the heart and this can decrease cardiac output by 20%. In turn this leads to vasoconstriction that diverts blood away from the uterus and can precipitate fetal distress. Pressure on the aorta can also compromise uterine blood flow, can result in supine hypotension and prove hazardous. Aorto-caval compression becomes significant after 20 weeks of pregnancy and can

be effectively managed intraoperatively by the use of left lateral position (15° tilt), uterine displacement through wedging or manual displacement. Most ear nose and throat surgeries also require a reverse Trendelenburg position which should be acceptable in pregnant women. Addition of 15° reverse Trendelenburg tilt to the supine with pelvic tilt position in obese pregnant women has been reported to marginally improve aortocaval compression (Saravanakumar et al, 2016).

How to ensure fetal safety?

Intraoperative fetal monitoring is an area of controversy. The fetal heart rate can be monitored during the surgery from 24–26 weeks of gestation as the fetus would be considered viable at this stage. Fetal heart rate and its variability can be affected by anaesthetic agents in the absence of any fetal distress, so interpretation could be unreliable and can result in unnecessary interventions. There are no long-term data showing improved fetal outcome with intraoperative fetal heart rate monitoring. Cardiotocography has been suggested as a viable alternative but may not be available in all units. The American College of Obstetricians and Gynecologists lists situations where intraoperative fetal heart rate monitoring would be applicable, but recommends that the decision is individualized depending upon the gestational age, type of surgery and the available facilities (ACOG Committee on Obstetric Practice, 2011). A practical approach is to collaborate with the obstetric team to check fetal heart rate pre- and postoperatively and be prepared to recognize and manage premature labour.

Should anticoagulation prophylaxis be started?

Pregnancy is associated with a hypercoagulable state because of increased pro-coagulant factors such as fibrinogen, factors VII, VIII, X and XII and fibrin degradation products. The incidence of thromboembolic complications is at least five times greater during pregnancy. Therefore thromboprophylaxis is essential during the perioperative period (Barron, 1985). This can be in the form of mechanical prophylaxis (early mobilization, anti-embolism stockings, calf compression devices) and pharmacological prophylaxis (subcutaneous low molecular weight heparin). Thrombosis and thromboembolism remain the leading cause of direct maternal death (Knight et al, 2016). However, the introduction of guidelines by the Royal College of Obstetricians and Gynaecologists has led to a vast improvement in outcome, highlighting the need for adequate risk assessment and guideline orientated thromboprophylaxis (Royal College of Obstetricians and Gynaecologists, 2015). Most ear nose and throat procedures do not have a significantly heightened risk of bleeding with thromboprophylaxis; routine pharmacological thromboprophylaxis can be instituted preoperatively or at the earliest opportunity postoperatively (usually the same day as surgery). The evidence regarding thromboprophylaxis in ear nose and throat procedures is limited (O'Hanlon et al, 2006).

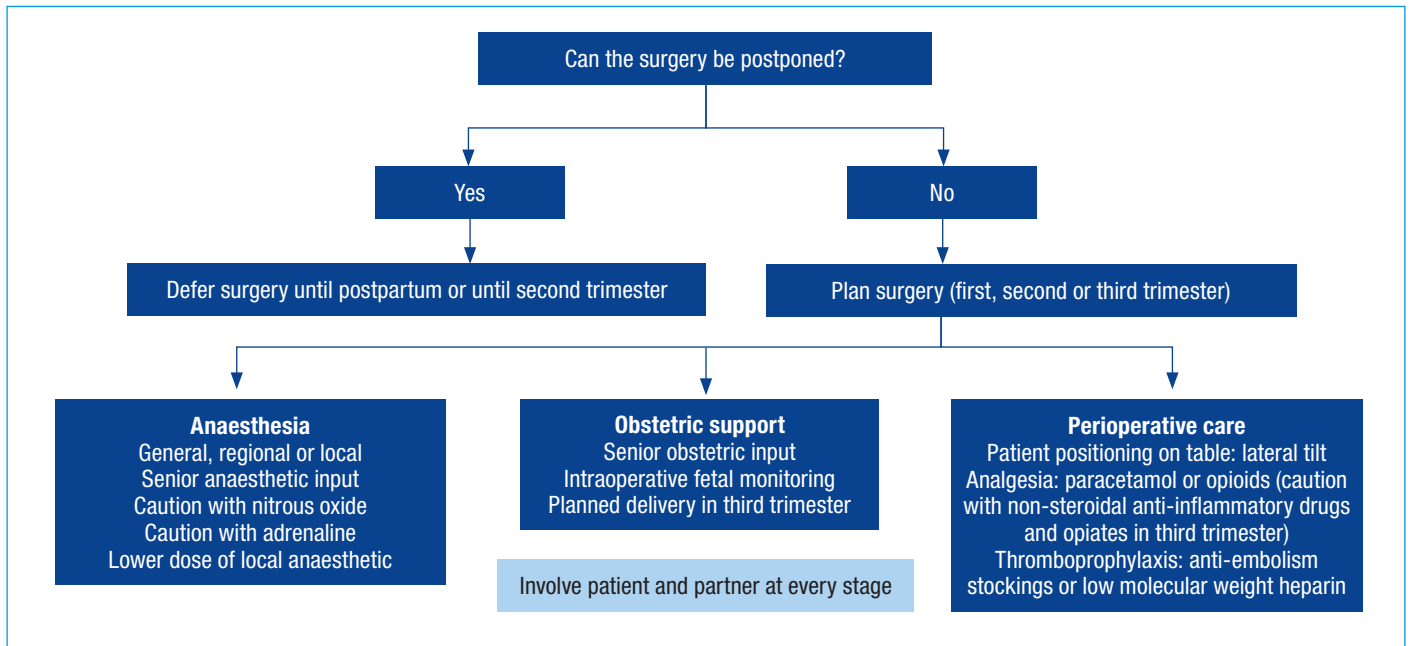


Figure 1. Management of the pregnant patient requiring ear nose and throat surgery.

What is the appropriate postoperative care and analgesia?

Close monitoring is required during recovery from anaesthesia. This is particularly true of the airway, because most severe anaesthetic complications as a result of hypoventilation or airway obstruction occur during extubation and recovery (Upadya and Saneesh, 2016). It is important to liaise with the obstetric team to plan postoperative fetal monitoring. Pain can increase sympathetic outflow and circulating catecholamines that can impair uteroplacental circulation, so adequate analgesia is vital following non-obstetric surgery during pregnancy. Limited data are available on the adverse effects of common analgesics on human pregnancy. Non-steroidal anti-inflammatory drugs such as ibuprofen and diclofenac are best avoided in the third trimester because of the risk of premature closure of the ductus arteriosus. Paracetamol crosses the placenta and is considered safe for short-term use, although some studies suggest a link between intra-partum use of paracetamol and the development of asthma in the child as well as a possible effect on the immune system (Shaheen et al, 2002; Thiele et al, 2013). High doses and long-term use of opioid analgesics especially in the third trimester is not recommended as these can cause neonatal respiratory depression, fetal growth retardation and withdrawal symptoms. However, opioids may be safe in second trimester surgeries and no structural teratogenicity has been reported with morphine in animal studies (Fujinaga and Mazze, 1988).

To reiterate, the management of the pregnant woman requiring ear nose and throat surgery is multidisciplinary. Awareness of potential complications and good preoperative planning are essential for maternal and fetal safety. The key steps in planning surgery in the pregnant woman are

summarized in *Figure 1* and *Table 1*. In addition to the general surgical and anaesthetic concerns discussed above certain situations present special conundrums to the ear nose and throat surgeon, as discussed below.

General otorhinolaryngological procedures during pregnancy

Limited data are available on the gamut of general otorhinolaryngological procedures performed on pregnant women. Ear nose and throat emergencies can present in any stage of pregnancy and can require urgent surgical intervention. One important example is otogenic abscesses. Jacob et al (2009) report a cerebellar abscess secondary to chronic suppurative otitis media in a 23-year-old woman

Table 1. Perioperative checklist for the pregnant patient requiring ear nose and throat surgery

Involve senior most anaesthetist with obstetric experience
Involve obstetric team
Decide regarding general vs local or regional anaesthesia
Consider difficult intubation and risk of aspiration
Consider intraoperative fetal monitoring
Remember intraoperative patient positioning to avoid aorto-caval compression
Limit adrenaline infiltration and limit hypotensive anaesthesia
Consider Royal College of Obstetricians and Gynaecologists guidelines on thromboembolism for venous thromboembolism prophylaxis
Minimize postoperative pain (safe analgesia)
Postoperative monitoring (patient airway and fetal stability)

at 35 weeks of pregnancy. The patient underwent a caesarean section to safely deliver the baby followed by the neurosurgical and ear procedures in the same theatre setting.

Physiological changes during pregnancy lead to an increased incidence of epistaxis and worsening of any sinonasal pathology (Incaudo, 2004). Management of epistaxis in pregnancy follows the same principles as in non-pregnant patients, using nasal cauterization and anterior nasal packing. Care should be taken with the use of BIPP (bismuth iodoform paraffin paste) which is contraindicated in pregnancy and the use of Flowseal, whose safety in pregnancy has not been demonstrated. Surgery should be the last resort. Embolization during pregnancy may not be considered a safe procedure for the baby or the mother in refractory epistaxis and surgery may be the better option in this situation. Goldstein and Govindaraj (2012) describe endoscopic nasal cauterization for persistent epistaxis in a pregnant woman. Crunckhorn et al (2014) describe a case of torrential epistaxis in the third trimester that required theatre on two occasions and prolonged posterior nasal packing. Considerations during endoscopic surgery for epistaxis in pregnancy include avoidance of cocaine and judicious use of adrenaline to decongest nasal mucosa. Epistaxis could also result from nasal haemangiomas that can present during pregnancy and can be amenable to excision under local anaesthesia (Noorizan and Salina, 2010).

Complications of sinusitis could also require surgical intervention irrespective of the trimester of pregnancy. Domville-Lewis et al (2013) describe surgical management in a 35-week pregnant woman who presented with Potts puffy tumour, epidural empyema and periorbital cellulitis. The patient underwent an endoscopic sinus drainage under general anaesthesia and the baby was delivered safely 3 days later. Boztas et al (2016) describe endoscopic sinus surgery to remove a left optic mass causing loss of vision in a 27-week pregnant woman.

In addition to the difficult intubation scenario during pregnancy discussed earlier, pregnant women can develop other airway pathologies. Acute epiglottitis, recurrent laryngeal papillomatosis, laryngeal rhinoscleroma, tracheitis and intratracheal tumours have all been reported as presenting with airway obstruction during pregnancy and have been successfully managed with tracheostomy (Glock and Morales, 1993; Armstrong et al, 1995; Amir et al, 2002; Sholapurkar et al, 2002; Scurry and McGinn, 2008). In addition, thyroid enlargement could also be a cause of airway obstruction during pregnancy. Hendrie and Kumar (2013) described a 32-week pregnant woman with airway obstruction secondary to compression by an enlarged thyroid that necessitated a caesarean section and a total thyroidectomy. Further facets of thyroid-related conditions during pregnancy are discussed below.

Thyroid surgery during pregnancy

Thyroid surgery can become necessary during pregnancy for the following reasons: large retrosternal thyroid glands causing airway compression, thyroid malignancy,

or thyrotoxicosis that fails medical therapy. Airway compression as a result of large thyroid glands presents a special case in pregnancy. Physiological changes of pregnancy create a hyperdynamic circulation that can lead to significant enlargement of the gland. If significant symptoms of stridor develop, thyroidectomy may be indicated before term to prevent difficult airway management at term. A risk–benefit assessment will need to be undertaken between ear nose and throat, obstetric and anaesthetic teams.

Surgery for thyroid malignancy is delayed until delivery of the baby whenever possible. This is almost always the case with well-differentiated thyroid cancers unveiled in the third trimester, the exception being thyroid malignancy causing airway compromise. Authors differ in the approach to well-differentiated thyroid malignancies discovered early in pregnancy (first and second trimesters). Well-differentiated non-aggressive thyroid malignancies can be left untreated until after delivery. However, surgery could be performed in the second trimester if there are issues such as a large tumour, rapid growth or maternal concern. Medullary cancer discovered early in pregnancy is treated in most cases with a thyroidectomy in the second trimester as its behaviour tends to be aggressive compared to well-differentiated thyroid cancers. There are comprehensive discussions in reviews and published guidelines (Owen et al, 2010; Stagnaro-Green et al, 2011; Perros et al, 2014).

The safety of thyroid surgery during pregnancy is an important issue. Several studies report no maternal or fetal complications following thyroid surgery in pregnant women (Doherty et al, 1995; Nam et al, 2005; Vannucchi et al, 2010). However, Kuy et al (2009) compared 201 pregnant women who underwent thyroid or parathyroid surgery with 31 155 non-pregnant women undergoing similar surgery and found a higher rate of complications in the pregnant group with longer hospital stays and costs. Concerns with thyroid surgery during pregnancy include the adverse effects of complications such as maternal haematoma and maternal hypoparathyroidism on the fetus. Delaying surgery for well-differentiated thyroid cancers until the second trimester or until delivery has not been shown to adversely affect the disease prognosis in the mothers in several studies (Choe and McDougall, 1994; Tan et al, 1996). However, Vannucchi et al (2010) reported that the presence of oestrogen alpha-receptors in the thyroid tumour may worsen prognosis with pregnancy as a result of oestrogen-mediated tumour growth, although this is difficult to assess preoperatively.

Thyroid hormone replacement during the postoperative period is important and thyroxine is started as soon as possible following thyroidectomy. Maternal hypoparathyroidism can sometimes occur following thyroid surgery. Hypocalcaemia can increase uterine irritability and cause preterm labour or abortion and is therefore potentially dangerous. However, calcium

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replacement and calcitriol therapy are safe and effective in managing hypoparathyroidism in pregnancy (Callies et al, 1998).

Parathyroid surgery in pregnancy

Primary hyperparathyroidism in pregnancy is a rare presentation. Potential problems for the mother include nephrolithiasis, bone disease, pancreatitis, hyperemesis, mental status changes and hypercalcaemic crises (Carella and Gossain, 1992). The effects on the fetus are equally worrying and include intrauterine growth retardation, low birth weight, preterm delivery, intrauterine death, postpartum neonatal tetany and permanent hypoparathyroidism, and can affect up to 80% of fetuses.

There have been illuminating studies on operative *vs* conservative management for primary hyperparathyroidism during pregnancy. Norman et al (2009) reported on 77 pregnancies in 32 women with primary hyperparathyroidism. Sixty-two pregnancies were managed conservatively and fetal death occurred in 32 (48%), mostly in the late first and early second trimester. In contrast, parathyroidectomy was performed in the second trimester in 15 pregnancies and no fetal loss occurred, favouring surgical removal of the offending parathyroid during pregnancy.

Planning parathyroid surgery in pregnancy is very important. Preoperative localization of the parathyroid makes surgery easier, although this can be difficult in the pregnant woman. Risks to the fetus exclude the use of sestamibi scanning and computed tomography scanning for preoperative localization. Similarly, risk of fetal death and teratogenicity excludes the use of methylene blue for intraoperative localization (Kidd et al, 1996). Ultrasound and magnetic resonance imaging are safe investigations that can help preoperative localization of the parathyroid during pregnancy. Local anaesthesia may be a good option for parathyroid exploration if the gland has been localized preoperatively. If not, the best approach would be exploration under general anaesthesia with intraoperative parathyroid hormone assay and frozen section.

Future directions and conclusions

Research is ongoing to improve maternal and fetal safety with anaesthesia during pregnancy. Kargaran et al (2015) focussed on the neurotoxic effects of anaesthetic agents on the developing brain in rats and mechanisms to counteract them. A lot of this work is on experimental models and human applications are awaited. Of note, advances in surgical and anaesthetic techniques have allowed for advanced procedures such as the EXIT technique in the management of airway obstruction in babies still attached to placental circulation (Laje et al, 2013, Nnamani, 2015).

However, optimal management of the pregnant woman requiring surgery will always depend on a multidisciplinary effort and good preoperative planning. Awareness of the

KEY POINTS

- General otolaryngological emergencies, thyroid and parathyroid surgery may necessitate surgery during pregnancy.
- A multidisciplinary approach involving a senior anaesthetist with obstetric anaesthesia experience and a senior obstetrician is essential.
- Good preoperative and perioperative planning is required to ensure maternal and fetal safety.

fetal–maternal physiology and the key goals of the surgery are essential to ensure a safe outcome for the mother and baby. **BJHM**

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- ACOG Committee on Obstetric Practice (2011) Nonobstetric surgery during pregnancy. Committee Opinion No. 474. *Obstet Gynecol* **117**: 420–421. <https://doi.org/10.1097/AOG.0b013e31820eede9>
- Amir R, Danahey D, Ferrer K, Maffee M (2002) Inflammatory myofibroblastic tumor presenting with tracheal obstruction in a pregnant woman. *Am J Otolaryngol* **23**(6): 362–367. <https://doi.org/10.1053/ajot.2002.128041>
- Armstrong WB, Peskind SP, Bressler KL, Crockett DM (1995) Airway obstruction secondary to rhinoscleroma during pregnancy. *Ear Nose Throat J* **74**(11): 768–773.
- Barron WM (1985) Medical evaluation of the pregnant patient requiring nonobstetric surgery. *Clin Perinatol* **12**(3): 481–496.
- Boztas N, Ozkardesler S, Akan M, Sari M (2016) The anesthetic approach for a 27-week pregnant woman undergoing endoscopic sinus surgery. *Obstet Gynecol cases Rev* **3**: 095. <https://doi.org/10.23937/2377-9004/1410095>
- Brodsky JB, Cohen EN, Brown BW Jr, Wu ML, Whitcer C (1980) Surgery during pregnancy and fetal outcome. *Am J Obstet Gynecol* **138**(8): 1165–1167. [https://doi.org/10.1016/S0002-9378\(16\)32785-5](https://doi.org/10.1016/S0002-9378(16)32785-5)
- Butterworth JF 4th, Walker FO, Lysak SZ (1990) Pregnancy increases median nerve susceptibility to lidocaine. *Anesthesiology* **72**(6): 962–965.
- Callies F, Arlt W, Scholz H, Reincke M, Allolio B (1998) Management of hypoparathyroidism during pregnancy report of twelve cases. *Eur J Endocrinol* **139**(3): 284–289. <https://doi.org/10.1530/eje.0.1390284>
- Carella MJ, Gossain VV (1992) Hyperparathyroidism and pregnancy. *J Gen Intern Med* **7**(4): 448–453. <https://doi.org/10.1007/BF02599166>
- Choe W, McDougall R (1994) Thyroid cancer in pregnant women: diagnostic and therapeutic management. *Thyroid* **4**(4): 433–435. <https://doi.org/10.1089/thy.1994.4.433>
- Cohen-Kerem R, Railton C, Oren D, Lishner M, Koren G (2005) Pregnancy outcome following non-obstetric surgical intervention. *Am J Surg* **190**(3): 467–473. <https://doi.org/10.1016/j.amjsurg.2005.03.033>
- Crunkhorn RE, Mitchell-Innes A, Muzaffar J (2014) Torrential epistaxis in the third trimester: a management conundrum. *BMJ Case Rep* pii: bcr2014203892. <https://doi.org/10.1136/bcr-2014-203892>
- Doherty CM, Shindo ML, Rice DH, Montero M, Mestman JH (1995) Management of thyroid nodules during pregnancy. *Laryngoscope* **105**(3): 251–255. <https://doi.org/10.1288/00005537-199503000-00006>
- Domville-Lewis C, Friedland PL, Santa Maria PL (2013) Potts puffy tumour and intracranial complications of frontal sinusitis in pregnancy. *J Laryngol Otol* **127**(S1) Suppl 1: S35–S38. <https://doi.org/10.1017/S0022215112001673>
- Duncan PG, Pope WDB, Cohen MM, Greer N (1986) Fetal risk of

- anesthesia and surgery during pregnancy. *Anesthesiology* **64**(6): 790–794. <https://doi.org/10.1097/0000542-198606000-00019>
- Fujinaga M, Mazze RI (1988) Teratogenic and postnatal developmental studies of morphine in Sprague-Dawley rats. *Teratology* **38**(5): 401–410. <https://doi.org/10.1002/tera.1420380502>
- Glock JL, Morales WJ (1993) Acute epiglottitis during pregnancy. *South Med J* **86**(7): 836–838. <https://doi.org/10.1097/00007611-199307000-00026>
- Goldstein G, Govindaraj S (2012) Rhinologic issues in pregnancy. *Allergy Rhinol* **3**(1): 13–15. <https://doi.org/10.2500/ar.2012.3.0028>
- Hawthorne L, Wilson R, Lyons G (1996) Dresner M. Failed intubation revisited: 17-yr experience in a teaching maternity unit. *Br J Anaesth* **76**(5): 680–684. <https://doi.org/10.1093/bja/76.5.680>
- Hendrie MA, Kumar MM (2013) Airway obstruction, caesarean section and thyroidectomy. *Int J Obstet Anesth* **22**(4): 340–343. <https://doi.org/10.1016/j.ijoa.2013.06.002>
- Incaudo GA (2004) Diagnosis and treatment of allergic rhinitis and sinusitis during pregnancy and lactation. *Clin Rev Allergy Immunol* **27**(2): 159–178. <https://doi.org/10.1385/CRIAI:27:2:159>
- Jacob CE, Kurien M, Varghese AM, Aleyamma TK, Jasper P, Prabu K, Poonnoose SI (2009) Treatment of otogenic brain abscess in pregnancy. *Otol Neurotol* **30**(5): 602–603. <https://doi.org/10.1097/MAO.0b013e3181b04d6b>
- Kargarani P, Lenglet S, Montecucco F, Mach F, Copin JC, Vutskits L (2015) Impact of propofol anaesthesia on cytokine expression profiles in the developing rat brain. *Eur J Anaesthesiol* **32**(5): 336–345. <https://doi.org/10.1097/EJA.0000000000000128>
- Kidd SA, Lancaster PA, Anderson JC, Boogert A, Fisher CC, Robertson R, Wass DM (1996) Fetal death after exposure to methylene blue dye during mid-trimester amniocentesis in twin pregnancy. *Prenat Diagn* **16**(1): 39–47. [https://doi.org/10.1002/\(SICI\)1097-0223\(199601\)16:1<39::AID-PD789>3.0.CO;2-P](https://doi.org/10.1002/(SICI)1097-0223(199601)16:1<39::AID-PD789>3.0.CO;2-P)
- Kinsella SM, Winton AL, Mushambi MC, Ramaswamy K, Swales H, Quinn AC, Popat M (2015) Failed tracheal intubation during obstetric general anaesthesia: a literature review. *Int J Obstet Anesth* **24**(4): 356–374. <https://doi.org/10.1016/j.ijoa.2015.06.008>
- Knight M, Nair M, Tuffnell D, Kenyon S, Shakespeare J, Brocklehurst P, Kurinczuk JJ, eds on behalf of MBRRACE-UK (2016) *Saving Lives, Improving Mothers' Care - Surveillance of maternal deaths in the UK 2012-14 and lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2009-14*. National Perinatal Epidemiology Unit, University of Oxford, Oxford
- Kodali BS, Chandrasekhar S, Bulich LN, Topulos GP, Datta S (2008) Airway changes during labor and delivery. *Anesthesiology* **108**(3): 357–362. <https://doi.org/10.1097/ALN.0b013e31816452d3>
- Kuy S, Roman SA, Desai R, Sosa JA (2009) Outcomes following thyroid and parathyroid surgery in pregnant women. *Arch Surg* **144**(5): 399–406, discussion 406. <https://doi.org/10.1001/archsurg.2009.48>
- Laje P, Howell LJ, Johnson MP, Hedrick HL, Flake AW, Adzick NS (2013) Perinatal management of congenital oropharyngeal tumors: the ex utero intrapartum treatment (EXIT) approach. *J Pediatr Surg* **48**(10): 2005–2010. <https://doi.org/10.1016/j.jpedsurg.2013.02.031>
- Mazze RI, Kallén B (1989) Reproductive outcome after anesthesia and operation during pregnancy: A Registry study of 5405 cases. *Am J Obstet Gynecol* **161**(5): 1178–1185. [https://doi.org/10.1016/0002-9378\(89\)90659-5](https://doi.org/10.1016/0002-9378(89)90659-5)
- McKeen DM, George RB, O'Connell CM, Allen VM, Yazer M, Wilson M, Phu TC (2011) Difficult and failed intubation: incident rates and maternal, obstetrical, and anesthetic predictors. *Can J Anaesth* **58**(6): 514–524. <https://doi.org/10.1007/s12630-011-9491-9>
- Mushambi MC, Kinsella SM, Popat M, Swales H, Ramaswamy KK, Winton AL, Quinn AC, Obstetric Anaesthetists' Association; Difficult Airway Society (2015) Obstetric Anaesthetists Association and Difficult Airway Society guidelines for the management of difficult and failed tracheal intubation in obstetrics. *Anaesthesia* **70**(11): 1286–1306. <https://doi.org/10.1111/anae.13260>
- Nnamani N (2015) From OOPS to EXIT: a review of the origins and progression of ex utero intrapartum treatment. *J Anesth Clin Res* **6**: 540. <https://doi.org/10.4172/2155-6148.1000540>
- Nam KH, Yoon JH, Chang HS, Park CS (2005) Optimal timing of surgery in well-differentiated thyroid carcinoma detected during pregnancy. *J Surg Oncol* **91**(3): 199–203. <https://doi.org/10.1002/jso.20327>
- Noorizan Y, Salina H (2010) Nasal septal haemangioma in pregnancy. *Med J Malaysia* **65**(1): 70–71.
- Norman J, Politz D, Politz L (2009) Hyperparathyroidism during pregnancy and the effect of rising calcium on pregnancy loss: a call for earlier intervention. *Horumon To Rinsho* **71**(1): 104–109. <https://doi.org/10.1111/j.1365-2265.2008.03495.x>
- O'Hanlon S, Andrews PJ, Harcourt JP (2006) Thromboprophylaxis in ENT patients: a national survey. *Int J Clin Pract* **60**(10): 1250–1253. <https://doi.org/10.1111/j.1742-1241.2006.01031.x>
- Owen RP, Chou KJ, Silver CE et al (2010) Thyroid and parathyroid surgery in pregnancy. *Eur Arch Otorhinolaryngol* **267**(12): 1825–1835. <https://doi.org/10.1007/s00405-010-1390-0>
- Perros P, Boelaert K, Colley S et al (2014) Guidelines for the management of thyroid cancer. *Clin Endocrinol* **81**: 1–122. <https://doi.org/10.1111/cen.12515>
- Rocke DA, Murray WB, Rout CC, Gouws E (1992) Relative risk analysis of factors associated with difficult intubation in obstetric anesthesia. *Anesthesiology* **77**(1): 67–73. <https://doi.org/10.1097/0000542-199207000-00010>
- Rosen MA (1999) Management of anesthesia for the pregnant surgical patient. *Anesthesiology* **91**(4): 1159–1163. <https://doi.org/10.1097/0000542-199910000-00033>
- Royal College of Obstetricians and Gynaecologists (2015) Reducing the risk of thrombosis and embolism during pregnancy and the puerperium. RCOG Green-top Guideline No. 37a. www.rcog.org.uk/globalassets/documents/guidelines/gtg-37a.pdf (accessed 17 March 2017)
- Saravanakumar K, Hendrie M, Smith F, Danielian P (2016) Influence of reverse Trendelenburg position on aortic caval compression in obese pregnant women. *Int J Obstet Anesth* **26**: 15–18. <https://doi.org/10.1016/j.ijoa.2015.09.007>
- Scurry WC Jr, McGinn JD (2008) Recurrent respiratory papillomatosis in pregnancy: a case of emergent airway management. *Ear Nose Throat J* **87**(6): E8–E11.
- Shaheen SO, Newson RB, Sherriff A, Henderson AJ, Heron JE, Burney PG, Golding J; ALSPAC Study Team (2002) Paracetamol use in pregnancy and wheezing in early childhood. *Thorax* **57**(11): 958–963. <https://doi.org/10.1136/thorax.57.11.958>
- Sholapurkar SL, Slack RWT, Avery AF, Tonge HM, Dunster GD (2002) Acute tracheitis with severe upper airway obstruction complicating pregnancy. *BJOG* **109**(2): 221–222. <https://doi.org/10.1111/j.1471-0528.2002.00048.x>
- Soma-Pillay P, Nelson-Piercy C, Tolppanen H, Mebazaa A (2016) Physiological changes in pregnancy. *Cardiovasc J Afr* **27**(2): 89–94. <https://doi.org/10.5830/CVJA-2016-021>
- Stagnaro-Green A, Abalovich M, Alexander E et al; American Thyroid Association Taskforce on Thyroid Disease During Pregnancy and Postpartum (2011) Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. *Thyroid* **21**(10): 1081–1125. <https://doi.org/10.1089/thy.2011.0087>
- Tan GH, Gharib H, Goellner JR, van Heerden JA, Bahn RS (1996) Management of thyroid nodules in pregnancy. *Arch Intern Med* **156**(20): 2317–2320. <https://doi.org/10.1001/archinte.1996.00440190059007>
- Thiele K, Kessler T, Arck P, Erhardt A, Tiegs G (2013) Acetaminophen and pregnancy: short- and long-term consequences for mother and child. *J Reprod Immunol* **97**(1): 128–139. <https://doi.org/10.1016/j.jri.2012.10.014>
- Upadya M, Saneesh PJ (2016) Anaesthesia for non-obstetric surgery during pregnancy. *Indian J Anaesth* **60**(4): 234–241. <https://doi.org/10.4103/0019-5049.179445>
- Vannucchi G, Perrino M, Rossi S et al (2010) Clinical and molecular features of differentiated thyroid cancer diagnosed during pregnancy. *Eur J Endocrinol* **162**(1): 145–151. <https://doi.org/10.1530/EJE-09-0761>
- Walton NKD, Melachuri VK (2006) Anaesthesia for non-obstetric surgery during pregnancy. *Contin Educ Anaesth Crit Care Pain* **6**(2): 83–85. <https://doi.org/10.1093/bjaceaccp/mkl008>
- Wong CA, McCarthy RJ, Fitzgerald PC, Raikoff K, Avram MJ (2007) Gastric emptying of water in obese pregnant women at term. *Anesth Analg* **105**(3): 751–755. <https://doi.org/10.1213/01.ane.0000278136.98611.d6>