Section 1   Preconception and conception

Chapter

1

Assisted conception

The treatment of infertility has developed rapidly, and the anaesthetist may be involved in many aspects of the patient's treatment, which may be complex. The harvesting of oocytes needs to take place within a defined period of time, or ovulation may have occurred and oocytes will be lost. Couples presenting for infertility treatment are generally anxious and often the women are emotional at the time of oocyte retrieval. It is therefore particularly important for the anaesthetist to understand the couple's anxieties, and to be able to explain the effects of the anaesthetic technique that is to be used.

Problems/special considerations

All of the techniques involve extraction of oocytes from the follicles, either laparoscopically or, with the development of transvaginal ultrasonography, via the transvaginal route (ultrasound directed oocyte retrieval, UDOR). The techniques differ in the site of fertilisation and/or replacement of the gamete/zygote:

- *In vitro fertilisation (IVF):* This term is often (incorrectly) used to encompass all aspects of infertility treatment. However, the process involves fertilisation in the laboratory and the developing embryo is transferred into the uterus via the cervix, usually 48 hours after oocyte retrieval. Embryo transfer is performed with the patient awake, although there are occasions when the help of the anaesthetist may be required to provide sedation. The success rate is approximately 15–25%.
- *Gamete intrafallopian transfer (GIFT):* This involves retrieval of oocytes which are placed together with sperm into the fallopian tube, laparoscopically, although an ultrasound-guided transvaginal procedure may sometimes be used. The success rate is approximately 35%.
- *Zygote intrafallopian tube transfer (ZIFT) or pronuclear stage transfer:* This process involves oocyte retrieval and IVF, with the zygote then being placed in the fallopian tube as for GIFT. The success rate is approximately 30–40%.
- *Intracytoplasmic sperm injection (ICSI):* Fertilisation occurs in the laboratory via injection of sperm into the oocytes, and the developing embryo is transferred into the uterus as for IVF. This technique is used for male infertility. The success rate is approximately 30%.

The main considerations for laparoscopy are the type of anaesthesia, the pneumoperitoneum and the effects of the anaesthetic agents on fertilisation and cell cleavage. The length of exposure to the drugs is also important. The effects of nitrous oxide and volatile anaesthetic agents on fertilisation and cleavage rates have been extensively examined. It is generally recognised that all volatile agents and nitrous oxide have a deleterious effect, although opinion is divided as to the

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extent of the problem. It is also recognised that the carbon dioxide used for the pneumoper-itoneum causes a similar effect, and it is difficult to separate the effects of the anaesthetic agents from those of the carbon dioxide.

Of the intravenous agents, the effect of propofol on fertilisation and cleavage appears to be minimal. Propofol accumulates in the follicular fluid, and the amount in the follicular fluid may become significant if there are a large number of oocytes to retrieve. Propofol decreases the fertilisation rates but there is no significant effect on the cell division rates.

All assisted conception techniques carry the risk of ovarian hyperstimulation (see Chapter 2, Ovarian hyperstimulation syndrome), and multiple or ectopic pregnancy.

Management options

Most women who present for assisted conception techniques are healthy and in their 30s–40s. However, it is now recognised that some women may also have a number of associated comorbidities with increasing age. Therefore, a multidisciplinary approach is necessary.

It would be logical to use regional anaesthesia whenever possible, although this is not well suited for laparoscopy. The development of the transvaginal route for oocyte retrieval has increased the possibility of using regional anaesthesia.

For patients requiring laparoscopy, it would seem sensible to minimise the use of drugs. This has led to the increased use of propofol as the main agent in total intravenous anaesthesia.

For UDOR, which has become the most common method used for oocyte retrieval, the main anaesthetic techniques are intravenous sedation and regional anaesthesia. It is important to remember that patients requiring UDOR are day cases and the basic principles of day-case anaesthesia apply. There has been a considerable amount of work to date on the use of propofol with alfentanil, and this combination of drugs would appear to be the technique of choice for intravenous sedation. Propofol may be administered by intermittent boluses or by continuous infusion, with the patient breathing oxygen via a Hudson mask. Many anaesthetists find that they are using levels of sedation close to anaesthesia. It is essential that the sedation is administered in a suitable environment with resuscitation facilities and anaesthetic monitoring. Often the assisted conception unit is some distance from the main theatre suite; therefore it may be difficult for the staff working in an isolated environment to maintain their skills in resuscitation.

The aim of minimising the drugs administered to women undergoing ultrasound-guided techniques has led to the use of regional anaesthesia. The main problem has been to develop techniques that allow the woman to go home the same day. Epidural and spinal anaesthesia have both been used with success, particularly where early ambulation is not essential. The low-dose spinal that is used for labour analgesia has been shown to give good operating conditions and to satisfy the criteria needed for day-case anaesthesia; it may be some way to achieving an ideal in this difficult group of patients.

Analgesia following the procedure may be provided with a combination of codeine and paracetamol. Non-steroidal anti-inflammatory drugs such as diclofenac are considered less suitable as these are thought to interfere with embryo implantation, owing to a disruption in prostaglandin levels.

Key points

- Oocyte retrieval may involve laparoscopy requiring general anaesthesia, although intravenous sedation and regional anaesthesia are suitable for transvaginal ultrasound-directed techniques.
- Couples are usually very anxious and require constant reassurance.

Further reading

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Yasmin E, Dresner M, Balen A. Sedation and anaesthesia for transvaginal oocyte collection: an evaluation of practice in the UK. *Hum Reprod* 2004; **19**: 2942–5.

Chapter

2 Ovarian hyperstimulation syndrome

Ovarian hyperstimulation syndrome is a complication of ovarian induction that may be caused by any agent that stimulates the ovaries. Over the last ten years, the incidence has increased owing to the development of IVF treatments, where the ultimate goal is to produce enough oocytes and embryos. The condition may become severe enough to warrant intensive care admission.

Ovarian hyperstimulation syndrome occurs 3–8 days after treatment with human chorionic gonadotrophin (hCG), and the effects continue throughout the luteal phase. The active ingredient causing the syndrome via increased capillary permeability is thought to be secreted from the ovaries, and both histamine and prostaglandins have been implicated.

Problems/special considerations

Clinical manifestations of the syndrome are:

- Enlargement of the ovaries
- Pleural effusion
- Ascites.

Table 2.1 Grading of ovarian hyperstimulation syndrome

Grade	Features	Incidence
1	Abdominal distension and discomfort	8–23%
2	Grade 1 plus nausea, vomiting and diarrhoea	
3	Grade 2 plus ascites (detected by ultrasonography)	1–8%
4	Grade 3 plus clinical ascites and shortness of breath	
5	Grade 4 plus clinical hypovolaemia, haemoconcentration, coagulation defects, decreased renal perfusion – therefore urea and electrolyte disturbance, thromboembolic phenomena	1–1.8%

Additional complications that may occur are:
- Hypovolaemic shock
- Renal failure
- Acute lung injury
- Thromboembolism
- Cerebrovascular disorders.

Women undergoing ovarian stimulation who develop ovarian hyperstimulation syndrome may be classified by placing them in one of five grades according to presenting symptoms and signs (Table 2.1).

Management options

When a large number of eggs (> 20) have been retrieved ovarian hyperstimulation should be suspected and the patient monitored. This may involve hospital admission.

Once suspected, the diagnosis of ovarian hyperstimulation syndrome can be confirmed by:
- A rapid increase in plasma oestradiol concentration
- The presence of multiple ovarian follicles on ultrasound examination
- An increase in body weight.

Immediate treatment is to stop hCG administration and to aspirate the enlarged follicles. Mild forms of ovarian hyperstimulation syndrome will be self-limiting, but those women graded 3 or worse will require intravenous fluids to correct the hypovolaemia and haemoconcentration. The intravenous administration of 1000 ml of human albumin is recommended at the time of oocyte retrieval if hyperstimulation is suspected.

In women graded 4 and 5, dopamine has been given to improve renal perfusion. In addition, it may be advisable to drain the ascitic fluid and to consider anticoagulation. Ultrafiltration and intravenous reinfusion of ascitic fluid has been used in severe cases.

Monitoring is tailored to the severity of the syndrome, and the following progression is recommended:
- Urea and electrolytes
- Full blood count and packed cell volume
- Plasma/urine osmolality
- Clotting screen

- Chest radiography
- Central venous pressure if large volumes of fluids are needed.

Key points
- Hyperstimulation comprises ovarian enlargement, pleural effusion and ascites, which may be relentless.
- Severe protein loss may result in shock and renal failure.
- The most severe form occurs in 1–2% of cases treated with human chorionic gonadotrophin.

Further reading

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Chapter

3

Anaesthesia before conception or confirmation of pregnancy

Many women will require anaesthesia when they are pregnant and many will be unaware that they are pregnant at the time of the anaesthetic, especially in the first 2–3 months of their pregnancy. The thalidomide catastrophe initiated the licensing arrangements for new drugs and their use in pregnancy; the current cautious stance of the pharmaceutical industry is reflected in the *British National Formulary*'s statement that no drug is safe beyond all doubt in early pregnancy. The anaesthetist should have a clear knowledge of the time scale of the developing fetus in order to balance the risks and benefits of any drug given to the mother. A *teratogen* is a substance that causes structural or functional abnormality in a fetus exposed to that substance.

Problems/special considerations
The possible effect of a drug can be considered against the stage of the developing fetus:
- *Pre-embryonic phase (0–14 days post-conception):* The fertilised egg is transported down the Fallopian tube and implantation occurs at around 7 days post-conception. The conceptus is a ball of undifferentiated dividing cells during this time and the effect of

drugs on it appears to be an all-or-none phenomenon. Cell division may be slowed with no lasting effects or the conceptus will die, depending on the severity of the cell damage.

- *Embryonic phase (3–8 weeks post-conception):* Differentiation of cells into the organs and tissues occurs during this phase and drugs administered to the mother may cause considerable harm. The type of abnormality that is produced depends on the exact stage of organ and tissue development when the drug is given.
- *Fetal phase (9 weeks to birth):* At this stage, most organs are fully formed, although the cerebral cortex, cerebellum and urogenital tract are still developing. Drugs administered during this time may affect the growth of the fetus or the functional development within specific organs.

Management options

The anaesthetist should always consider the possibility of pregnancy in any woman of child-bearing age who presents for surgery, whether elective or emergency, and should specifically enquire in such cases. If there is doubt, a pregnancy test should be offered. If pregnancy is suspected, the use of nitrous oxide is now generally considered acceptable, despite its effects on methionine synthase and DNA metabolism, as there is little evidence that it is harmful clinically. Similarly, although the volatile agents have been implicated in impairing embryonic development, clinical evidence is lacking. Some drugs cross the placenta and exert their effect on the fetus, e.g. warfarin, which may cause bleeding in the fetus.

Key points

- The possibility of pregnancy should be considered in any woman of childbearing age.
- No drug is safe beyond all doubt in pregnancy.

Further reading

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Chapter

4

Ectopic pregnancy

There are approximately 11 000 ectopic pregnancies per year in the UK (just over 1% of all pregnancies), and the incidence is thought to be increasing as a result of pelvic inflammatory disease. There are many risk factors, with tubal pathology and/or surgery and the use of an intrauterine device the most important; other risk factors are infertility, increased maternal age and smoking. About 3–5 women die as a consequence in the UK per year, representing about 3–6% of all direct maternal deaths (~1 per 2500 ectopics). Most ectopic pregnancies occur in the Fallopian tube, but up to 5% occur elsewhere within the genital tract or abdomen. Typically, the tube initially expands to accommodate the growing zygote, but when it is unable to do so any more, there may be bleeding from the site of implantation or even rupture of the tube.

Problems/special considerations

The main risk of ectopic pregnancy is sudden severe haemorrhage, which may be intra-abdominal and thus concealed until sudden decompensation and collapse occur. A common theme in deaths associated with ectopic pregnancy is the failure to consider the diagnosis before collapse. Ectopic pregnancy may present with non-specific abdominal signs including diarrhoea or constipation, thus mimicking other intra-abdominal conditions (e.g. appendicitis). Mortality rates from misdiagnosis of an ectopic pregnancy have risen since 1997 and the Confidential Enquiries into Maternal Deaths report recommends that an ectopic pregnancy should be considered as a diagnosis in any women of reproductive age who presents with severe gastrointestinal symptoms.

Diagnosis may be difficult. Signs and symptoms of an ectopic pregnancy vary; early symptoms include a brown discharge, bleeding that can be light to heavy – although a significant proportion of women do not have any bleeding (20%) – and abdominal pain. Most ectopic pregnancies present early in pregnancy and thus many of the physiological changes of pregnancy are absent or mild – the patient may even be unaware that she is pregnant. However, even at this early stage there may be features of the physiological changes of pregnancy. Abdominal ultrasound has low specificity and transvaginal ultrasound has been shown to be better. If ultrasound is not convincing, then diagnosis is aided by blood tests and laparoscopy. Serum levels of human chorionic gonadotrophin (hCG) and progesterone are often measured but these measurements often resemble those levels seen in a normal pregnancy. Previously, the gold standard for diagnosis of an ectopic pregnancy was a laparoscopy; however, its accuracy in diagnosing an ectopic pregnancy has been questioned.

The implications for the current and future pregnancies pose a great psychological stress on the patient and her partner. There may be a previous history of ectopic pregnancy since its occurrence is itself a risk factor for subsequent ectopics.

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Management options

Initial management is directed at treating and preventing massive haemorrhage; thus the patient requires at least one large-bore intravenous cannula and careful observation at least until the diagnosis has been excluded. Similarly, once the decision to operate has been made, it needs to occur as soon as possible, since the risk of tubal rupture is always present.

Operative management usually involves laparoscopy unless there is severe haemodynamic instability, in which case laparotomy is performed. Traditionally, laparoscopy was performed purely for diagnostic purposes, but laparoscopic removal of the zygote with or without tubal resection has become routine in many units.

Anaesthetic management is as for any emergency surgery, given the above considerations. Haematological assistance and admission to the intensive care unit should be available if required. In severe cases, anaesthesia must proceed as for a ruptured aortic aneurysm: full preoperative resuscitation may be impossible and the patient is prepared and draped before induction of anaesthesia, which may be followed by profound hypotension.

In some countries, medical management is increasingly used as the first-line treatment of early ectopic pregnancies, with intramuscular methotrexate, and guidelines regarding the use of methotrexate have been published by the American College of Obstetricians and Gynecologists. The drug antagonises folic acid and prevents further growth of the trophoblast, which is especially vulnerable at this early stage. Similar outcome to that following surgical management has been claimed. Local injection of hyperosmolar glucose, prostaglandin and potassium chloride have also been used. Finally, expectant management has been used in selected patients, although women whose pregnancies are self- limiting cannot yet be identified reliably.

Key points

- Ectopic pregnancy accounts for 3–6% of all direct maternal deaths in the UK.
- Severe haemorrhage and/or cardiovascular collapse is always a risk.

Further reading

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Chapter
5

Evacuation of retained products of conception

Evacuation of retained products of conception (ERPC) may be required at any stage of pregnancy, but it occurs most commonly in early pregnancy following incomplete miscarriage or early fetal demise. It is also required during the puerperium following retention of placental tissue (see Chapter 38, Removal of retained placenta and perineal suturing).

Problems/special considerations

- ERPC following spontaneous abortion at 8 weeks' gestation may be a minor routine gynaecological emergency for the anaesthetist, but the mother may have lost a much-wanted baby.
- The urgency of the procedure varies greatly. The majority of ERPCs are performed as scheduled emergencies in fit young women, and this may lull the inexperienced anaesthetist into a false sense of security. Death may occur from spontaneous abortion; blood loss may be heavy and is frequently underestimated.
- The possibility of co-existing uterine or systemic sepsis must always be considered, especially in postpartum ERPC or in a repeat procedure following incomplete evacuation.

Management options

- Diagnostic ultrasound scanning is frequently used to confirm a non-viable early pregnancy or the presence of retained placental tissue. Transabdominal and transvaginal ultrasonography are now considered to be complementary to each other, with most women requiring a transvaginal ultrasound. Most units now operate a policy of fully assessing mothers on the day of admission in an early pregnancy advisory unit (EPAU), allowing them home and re-admitting them the following day for planned ERPC. This facilitates planning of medical and nursing staffing levels, reduces prolonged periods of waiting and starvation for the mother, and can be economically advantageous. Medical treatment is increasingly used and this enables women to be allowed home after treatment with prostaglandin analogues to await events. Some of these women will need surgical management if the products of conception are not fully expelled.
- Preoperatively, a full assessment is required. Assessment of blood loss may be difficult; fit young women may lose a significant proportion of their blood volume without becoming hypotensive. Tachycardia should alert the anaesthetist to possible hypovolaemia. Signs of sepsis should be sought, and prophylactic antibiotics may be considered.
- General anaesthesia is most commonly used in the UK, although in the absence of uncorrected hypovolaemia or other contraindications, regional anaesthesia is entirely

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suitable. The puerperal mother in particular may wish to stay awake if offered a choice, and she should be advised to do so if at risk of regurgitation.

- Rapid sequence induction of general anaesthesia is indicated for the non-fasting mother requiring urgent surgery (uncommon) and for the mother who is at risk of regurgitation (see Chapter 54, Aspiration of gastric contents). Anaesthesia using a laryngeal mask airway or facemask using any standard day-case anaesthetic technique is appropriate for the majority of women needing ERPC. Sedative premedication is rarely needed. Intravenous anaesthesia, e.g. with propofol or inhalational anaesthesia, is acceptable, though if the latter is used high concentrations of volatile anaesthetic agents (> 1 minimum alveolar concentration) should be avoided because of the uterine relaxation that may ensue.

- Oxytocic drugs may be requested by the surgeon, although there is little evidence for their efficacy at gestations of less than 15 weeks. A single intravenous bolus of 5 U Syntocinon usually suffices. Ergometrine causes increased intracranial and systemic pressure, and nausea and vomiting, and should not be used routinely.

- Spinal anaesthesia produces more rapid and dense anaesthesia than epidural anaesthesia, and an anaesthetic level of at least T8 is recommended. Clinical experience shows that the traditionally taught anaesthetic level of T10 is insufficient to prevent pain occurring when the uterine fundus is manipulated or curetted.

- Postoperatively, the aim is rapid recovery and discharge home. Requirement for postoperative analgesia rarely exceeds simple non-opioid drugs. Non-steroidal anti-inflammatory agents may be beneficial in relieving uterine cramps. Routine administration of antiemetics should be considered since these women are at risk of postoperative nausea and vomiting.

Key points

- A sensitive and sympathetic approach to the mother is necessary.
- Prolonged preoperative waiting and starvation reflects poor communication and inefficiency.

Further reading

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