Section 1 – Preconception and Conception

1 ASSISTED CONCEPTION

There have been rapid developments in the treatment of infertility. 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 will 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):* fertilisation occurs 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):* the oocytes and sperm are placed together in the Fallopian tube, usually laparoscopically although an ultrasound-guided transvaginal procedure may also be used. The success rate is approximately 35%.
- *Zygote intrafallopian tube transfer (ZIFT):* fertilisation occurs in the laboratory and, before cell division occurs, the zygote is placed in the Fallopian tube as for GIFT. The success rate is approximately 28%.
- *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 28%.

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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 the volatile agents and nitrous oxide have a deleterious effect, although opinion is divided as to the extent of the problem. It is also recognised that the carbon dioxide used for the pneumoperitoneum 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, p. 3), and multiple or ectopic pregnancy.

Management options

It would be logical to use regional anaesthesia wherever possible, although this is often 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 drug combination would appear to be the technique of choice for intravenous sedation. The 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 is important 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 lay in developing 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 technique 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.

Post-procedure analgesia may be provided with non-steroidal anti-inflammatory drugs such as diclofenac.

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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Viscomi CM, Hill K, Johnson J, Sites C. Spinal anaesthesia versus sedation for transvaginal oocyte retrieval: reproductive outcome, side effects and recovery profiles. *Int J Obstet Anesth* 1997; **6**: 49–51.

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.

2 OVARIAN HYPERSTIMULATION SYNDROME

Ovarian hyperstimulation syndrome is associated with the medical stimulation of ovulation necessary for in vitro fertilisation. It 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.

Additional complications that may occur are:

- Hypovolaemic shock
- Renal failure
- Acute lung injury
- Thromboembolism
- Cerebrovascular disorders.

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	1–1.8%
5	Grade 4 plus clinical hypovolaemia, haemoconcentration, coagulation defects, decreased renal perfusion – therefore urea and electrolyte disturbance, thromboembolic phenomena	

Women undergoing ovarian stimulation who develop ovarian hyperstimulation syndrome can be assessed 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 anti-coagulation. 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
- Pulmonary artery catheter if the woman is severely affected.

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

Shanbhag S, Bhattacharya S. Current management of ovarian hyperstimulation syndrome. *Hosp Med* 2002; **63**: 528–32.

Whelan JG 3rd, Vlahos NF. The ovarian hyperstimulation syndrome. *Fertil Steril* 2000; **73**: 883–96.

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 child-bearing age.
- No drug is safe beyond all doubt in pregnancy.

FURTHER READING

Koren G, Pastuszak A, Ito S. Drugs in pregnancy. *N Engl J Med* 1998; **338**: 1128–37.

Section 2 – Pregnancy

I Procedures in early/mid-pregnancy

4 CERVICAL SUTURE (CERCLAGE)

Cervical suture (Shirodkar or McDonald cerclage) is performed to reduce the incidence of spontaneous miscarriage when there is cervical incompetence. Although it can be done before conception or as an emergency during pregnancy, the procedure is usually performed electively at 12–16 weeks' gestation; it generally takes 10–20 minutes and is performed transvaginally on a day-case basis. A non-absorbable stitch or tape is sutured in a purse-string around the cervical neck at the level of the internal os; this requires anaesthesia since the procedure is at best uncomfortable, although the suture can usually be removed easily without undue discomfort (usually at 37–38 weeks' gestation unless in preterm labour); spontaneous labour usually soon follows.

In patients with a grossly disrupted cervix, e.g. following surgery, placement of the suture via an abdominal approach may be required. Delivery is usually by elective Caesarean section in these cases.

Problems/special considerations

Women undergoing cervical suturing may be especially anxious since previous pregnancies have ended in miscarriage. Otherwise anaesthesia is along standard lines, bearing in mind the risks of anaesthesia in the pregnant woman and monitoring of, and possible effects of drugs on, the fetus (see Chapter 7, Incidental surgery in the pregnant patient, p. 12).

Cerclage may be difficult if the membranes are bulging; the head-down position and/or tocolysis may be requested to counter this.

Management options

Many authorities advocate spinal anaesthesia as the technique of choice since only a small amount of a single drug is administered, although epidural anaesthesia is also acceptable. If spinal or epidural anaesthesia is chosen, standard techniques are used. The procedure itself requires a less extensive block than Caesarean section

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(from T8–10 down to and including the sacral roots) and thus smaller doses are required; however, the reduction is offset by the greater requirements at this early stage of pregnancy compared with the term parturient. Thus the doses required for regional anaesthesia are in the order of 75% of those used for Caesarean section. Low-dose techniques have also been used, as for Caesarean section; the women have more sensation (though painless) but have less motor block.

General anaesthesia may also be used; an advantage is the relaxing effect of volatile agents on the uterus, but it does usually involve administration of more than one drug, and the effects on the fetus of many agents in current use are not clear. There may also be an increased risk of regurgitation and aspiration of gastric contents, depending on the gestation and severity of symptoms (see Chapter 56, Aspiration of gastric contents; p. 138).

Paracervical and pudendal block and/or intravenous analgesia/sedation may also be used, but most authorities would recommend avoiding paracervical block because of the potential adverse effects on uteroplacental perfusion.

Key points

- Cervical suture is usually performed at 12–16 weeks' gestation.
- Patients may be especially anxious because of previous miscarriage.
- Standard techniques are used; spinal anaesthesia may be preferable.

FURTHER READING

Drakeley AJ, Roberts D, Alfirevic Z. Cervical stitch (cerclage) for preventing pregnancy loss in women (Cochrane Review). In: *The Cochrane Library*, Issue 4, 2003. Chichester, UK: John Wiley & Sons, Ltd.

5 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 or surgery and use of an intrauterine device the most important; others 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 unable to do so any more, there may be bleeding from the site of implantation or even rupture of the tube. Thus the classic presentation is with abdominal pain, which may be sudden in onset, accompanied by a history of amenorrhoea (although there is vaginal bleeding

at presentation in ~80% of cases). There may be sudden collapse if the tube ruptures, caused by reflex vagal activity or hypovolaemia if bleeding is severe, or both.

Problems/special considerations

The main risk of ectopic pregnancy is sudden severe haemorrhage, which may be intra-abdominal and thus concealed until rapid 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), although with serial measurement of plasma human chorionic gonadotrophin (hCG; doubles every 2–3 days in normal pregnancy) and use of pelvic ultrasonography this should be unusual. The potential severity of the condition is not always appreciated by other hospital staff, the patient herself or her relatives. Ectopics outside the Fallopian tubes are more likely to be associated with massive haemorrhage, with abdominal pregnancies the most hazardous, especially when the placenta is removed.

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.

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.

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 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 aspects of the procedure itself are as for any laparoscopic operation.

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. 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

Pisarska MD, Carson SA, Buster JE. Ectopic pregnancy. *Lancet* 1998; **351**: 1115–20.
Tay JI, Moore J, Walker JJ. Ectopic pregnancy. *BMJ* 2000; **320**: 916–19.

6 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 41, Removal of retained placenta, p. 107).

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 coexisting uterine or systemic sepsis must always be considered, especially in postpartum ERPC or in a repeat procedure following incomplete evacuation.