The Development of a Novel Method of Hysteroscopic Sterilisation

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Abstract

For over 100 years gynaecologists have attempted to effect sterilisation via a transcervical approach, however most had limited success. Our aim was to develop a safe and simple method of hysteroscopic sterilisation, which could be performed as an out-patient.

A tubal device based on a self tapping screw was developed as it was felt that such a design would be less likely to become dislodged with time. In-vivo and in-vitro application studies were performed to ensure correct positioning of the screw at the tubal ostia and to test the strength of application. The equipment used to apply the tubal screw initially consisted of a modified hysteroscope, superseded by a cystoscope; the original application technique used a tubular cannula and ‘push-rod’ for screw disimpaction, this was replaced by mounting the screw with a titanium bayonet loosely in a metal coil applicator. The means of providing effective uterine distension evolved from the use of fixed and variable flow hysteromat pumps to the use of a large pressure bag to provide for excellent cornual visualisation.

In women undergoing concurrent laparoscopic sterilisation tubal patency was tested pre and post screw application and to monitor screw retention interval pelvic ultrasonography was performed. If the tubal screws were still present after 1 year they were removed hysteroscopically under local anaesthesia.

The development of the equipment was challenging requiring many changes
to improve the screw application technique; this was manifested in an improvement of screw retention with the final apparatus.

*In-vitro* and *in-vivo* screw application demonstrated that the screws were held firmly at the uterine cornu. However, despite demonstrating effective tubal occlusion with the tubal screws, *in-vivo* screw retention even in the later stages of the development process was poor.

Further refinements of the equipment are essential prior to testing as a method of sterilisation.

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### Contents

<table>
<thead>
<tr>
<th>Acknowledgements</th>
<th>Pages 7-8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Declaration</td>
<td>Pages 8</td>
</tr>
<tr>
<td>Tables</td>
<td>Pages 9-10</td>
</tr>
<tr>
<td>Figures</td>
<td>Pages 11-19</td>
</tr>
</tbody>
</table>

**Chapter 1.** The need for a simple, outpatient method of female sterilisation. Pages 20-45

**Chapter 2.** Review of intrauterine methods of female sterilisation. Pages 46-101

**Chapter 3.** Review of the anatomy of the uterotubal junction, studies of uterine morphology and review of the safety of insertion of a PTFE tubal screw. Pages 102-172

**3A.** Anatomy and physiology of the fallopian tube Pages 102-121

**3B.** Studies performed to derive the deflection required to cannulate the tubal ostia Pages 122-151

**3C.** Review of the safety of insertion of a PTFE screw Pages 152-170
Chapter 4. Developmental changes in the design of the tubal screw and insertion system. 172-237

Chapter 5. In-vitro studies of a new tubal screw sterilisation device. 238-254

Chapter 6. In-vivo hysterectomy studies of the tubal screw sterilisation device. 255-281

Chapter 7. The retention of tubal screws in patients undergoing simultaneous laparoscopic sterilisation. 282-312

Chapter 8. The future of the hysteroscopic tubal screw to effect sterilisation. 313-319

Chapter 9. References 320-369
## Appendix

<table>
<thead>
<tr>
<th>Publication Type</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Publications</td>
<td>371</td>
</tr>
<tr>
<td>Presentations</td>
<td>372</td>
</tr>
<tr>
<td>Protocol for <em>in-vivo</em> hysterectomy studies</td>
<td>373</td>
</tr>
<tr>
<td>Patient information for <em>in-vivo</em> hysterectomy studies</td>
<td>374</td>
</tr>
<tr>
<td>Consent form for <em>in-vivo</em> insertion at hysterectomy</td>
<td>375</td>
</tr>
<tr>
<td>Protocol for sterilisation study</td>
<td>376</td>
</tr>
<tr>
<td>Patient information for sterilisation study</td>
<td>377</td>
</tr>
<tr>
<td>Consent form for sterilisation study</td>
<td>378</td>
</tr>
</tbody>
</table>

CD-ROM of tubal screw insertion: (in back cover)
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This work was carried out solely by myself with the assistance and supervision of my supervisor, Mr Adam Magos BSc MD FRCOG at The Royal Free Hospital between 1\textsuperscript{st} April 1996 and 1\textsuperscript{st} October 1998.
Tables

Chapter 3

Table 3.1 The angle of deflection required for perpendicular approach to the uterine cornu derived from reviewing old hysterosalpingograms.

Table 3.2 Statistics for the angle deflection required for access to the uterine cornu.

Table 3.3 Table of uterine specimens used for extirpated hysterosalpingogram assessment.

Table 3.4 The angle of deflection required in extirpated hysterosalpingogram assessment.

Table 3.5 Statistics for the angle deflection required for access to the uterine cornu performed on extirpated uteri.

Table 3.6 Morphological measurements of uteri as made by ultrasound assessment, in parous women with dysfunctional uterine bleeding.

Chapter 5

Table 5.1 Description of uterine specimens used in the in-vitro application study.

Table 5.2 In-vitro application of tubal screw experimental data
Chapter 6

Table 6.1 The histological assessment study to assess correct placement of in-vivo applied screws.

Table 6.2 The weight study to assess strength of application of in-vivo applied plugs.

Chapter 7

Table 7.1 Method of hysteroscopic tubal screw application, follow-up ultrasound reports and interval screw removal.

Table 7.2 Duration of screw retention or until removal at the time of hysteroscopy (cases 1-20).

Table 7.3 Duration of screw retention or until removal at the time of hysteroscopy (cases 21-35).
Figures

Chapter 1

Figure 1.1 The intratubal screw (from original plans).

Figure 1.2 The intratubal screw mounted on applicator and applied to uterine cornu (from original plans).

Figure 1.3 The intratubal screw mounted on applicator (from original plans).

Figure 1.4 The tubal screw used in the in-vitro-studies.

Chapter 2

Figure 2.1 Intratubal devices and their method of fixation

Figure 2.2 The Essure™ pbc device, Conceptus, San Carlos, USA.

Figure 2.3 The Adiana catheter is inserted into the intramural portion of the fallopian tube, and a mild lesion is created.

Figure 2.4 After the lesion is created, the sheath of the catheter retracts, depositing a matrix into the scarred area, and the catheter is then withdrawn.

Figure 2.5 Surrounding tissue grows into the matrix over the next few weeks, resulting in tubal occlusion.
Chapter 3

Figure 3.1 Diagrammatic representation of the uterus demonstrating the angle of approach required to cannulate the tubal ostia.

Figure 3.2 Position of uterus in the female pelvis. Gray's Anatomy (37th Edition, 1989).

Figure 3.3 Blood supply to uterus and fallopian tube. Gray's Anatomy (37th Edition, 1989).

Figure 3.4 Venous drainage of the fallopian tube via uterine veins to the internal iliac vein. Gray's Anatomy (37th Edition, 1989).

Figure 3.5 Lymphatic drainage of the pelvis. Gray's Anatomy (37th Edition, 1989).

Figure 3.6 Schematic representation of measurements performed on hysterosalpingogram to gauge required deflection for uterine cornual access.

Figure 3.7 Uterus deviated to right.

Figure 3.8 Uterus deviated to right with incorrect uterine axis drawn.

Figure 3.9 Hysterosalpingogram on extirpated uterus. (Poor projection as background is radiolucent and uterus has many fibroids)

Figure 3.10 The uterine cavity ultrasound measurements.

Figure 3.11 Plot representing the angle of deflection required to approach uterine cornu.

Figure 3.12 Scatter of cornual angles as measured by reviewing old hysterosalpingograms.
Figure 3.13 Graph showing the distribution of the angle of deflections required to approach the uterine cornu as demonstrated by hysterosalpingography on uterine specimens immediately after hysterectomy.

Figure 3.14 The difference in angle of deflection required comparing *in-vivo* hysterosalpingograms of subfertile women and hysterosalpingograms performed on extirpated uteri.

Figure 3.15 Plot of uterine morphological measurements.

Figure 3.16 The effect of rotation of the uterus reducing the apparent deflection required to cannulate the tubal ostia by artefact.

Figure 3.17 Demonstration of the projection of the hysterosalpingogram. The cornual angles subtended from the mid-line are dependant on the degree of uterine anteversion.

Figure 3.18 Using the ultrasound study the angle of deflection that would be required to approach the uterine cornu is 16°.

Figure 3.19 Creation of polymer polytetrafluoroethylene (PTFE) from tetrafluoroethylene.

Figure 3.20 Demonstration of the non-stick and non-wettability properties of PTFE which is used in medicine as an inert implant.

Figure 3.21 The medical uses of PTFE.

**Chapter 4**

Figure 4.1 The original design of the tubal screw developed by Adam Magos (British Patent Application no.980634.7)
Figure 4.2  The hysteroscopic tubal screw.

Figure 4.3  A reverse screw thread scored into base of the tubal screw, which is mounted on the applicator with a screw thread.

Figure 4.4  Hexagonal PTFE mounting on applicator and corresponding recessed area in base of tubal screw.

Figure 4.5  Tubal screw with titanium bayonet mounted on coil applicator.

Figure 4.6  Diagrammatic representation of device in applicator showing bayonet pin locking mechanism.

Figure 4.7  Demonstration of the field of view with the $15^\circ$ and $70^\circ$ lens optical hysteroscopes, however with the natural tendency to ‘point’ towards the area being treated the $30^\circ$ hysteroscope was favoured.

Figure 4.8  The original Rimmer Brothers modified single channel hysteroscope.

Figure 4.9  The fixed deflector at the distal end of the Rimmer hysteroscope.

Figure 4.10  Distal end of Rimmer hysteroscope with PTFE cannula and tubal screw demonstrating fixed deflector.

Figure 4.11  Tubal screw mounted on distal end of PTFE cannula with push-rod for disimpaction.

Figure 4.12  Original green PTFE cannula demonstrating water tight seal of push-rod at proximal end to enable disimpaction.

Figure 4.13  Rotation of the Portex tubing by seven $360^\circ$ rotations (© SIMS
Portex Limited) after placement of the screw at the tubal ostia.

Figure 4.14 Demonstrating that a proximal small rotational torque when applied to a curved cannula is amplified distally to describe a large arc.

Figure 4.15 Scoring in outer sheath of hysteroscope.

Figure 4.16 The coil with rubber casing to prevent fluid leakage.

Figure 4.17 Demonstration of the lateral frictional force generated by the natural elasticity of the application cannula.

Figure 4.18 Demonstrating the effect of using a coil mounting to hold the tubal screw.

Figure 4.19 Standard Hamou Hysteromat.

Figure 4.20 Leakage of distending fluid around the oval diameter of the hysteroscope as compared to the conventional hysteroscope.

Figure 4.21 Leakage of distending fluid around rubber seal to the operating channel of the hysteroscope.

Figure 4.22 Distension fluid pours into the application cannula after the tubal device is disimpacted and out of the operating channel of the hysteroscope.

Figure 4.23 Litechnica Statflo Liquid infusion system.

Figure 4.24 The 3 litre pressure bag - the preferred method of uterine distension. VBM Medizintechnik GMBH, Germany.

Figure 4.25 The use of two separate systems to effect deflection towards the tubal ostia. Operating hysteroscope not shown for clarity.

Figure 4.26 The separate deflector used for case 11 in Chapter 7.
Figure 4.27 The technique of altering the angle of deflection with the 'trombone outer sheath'.

Figure 4.28 The 'trombone' outer sheath.

Figure 4.29 The 'trombone' outer sheath overlying the hysteroscope.

Figure 4.30 Tubal screw mounted on cannula, which adopts a predetermined angle of deflection once extruded from the hysteroscope.

Figure 4.31 An active method to alter deflection with a proximal 'joy-stick'.

Figure 4.32 A passive method to alter deflection with a proximal 'joy-stick'.

Figure 4.33 The extra deflecting bridge attachment on the cystoscope with tubal screw mounted on coiled applicator with rubber outer coating.

Figure 4.34 Application of the tubal screw to the tubal ostia.

Figure 4.35 The bayonet mounted tubal screw prior to disimpaction after being screwed into place at the tubal ostia.

Figure 4.36 Bilaterally placed tubal screws demonstrating the bayonet mounting of the tubal screws.

Figure 4.37 The tubal screw with bayonet mounting enabling easy insertion and disimpaction.

Figure 4.38 Developmental changes in the equipment in chronological order.

Figure 4.39 The development of the hysteroscopic plug sterilisation equipment that was used *in-vivo*. 
Chapter 5

Figure 5.1  The uterus fixed on board and suture attached to tubal screw.

Figure 5.2  The applicator to screw tubal screw in place.

Figure 5.3  The applicator with tubal screw mounted prior to performing in-vitro study.

Figure 5.4  The dissecting board and jig system used in the in-vitro weights study

Figure 5.5  Weights attached to the plug suspended by the jig.

Figure 5.6  The weight required to dislodge the tubal screw from the uterine cornu after in-vitro application.

Figure 5.7  The force required to dislodge the tubal screw from the uterine cornu after in-vitro application. (The gravitational force acting upon the weights applied to the screw is assumed to be 10 m/s² downward force).

Chapter 6

Figure 6.1  A prototype pointed tubal screw approximated to the tubal ostia prior to insertion.

Figure 6.2  The push-rod to disimpact the tubal screw.

Figure 6.3  The push-rod to disimpact the tubal screw close-up.

Figure 6.4  Tubal screw in-situ at the uterotubal junction. Note presence of methylene blue around screw suggesting correct placement.
Patient 1 in the histological assessment study.

Figure 6.5 Tubal screw at uterine cornu after serial sections have been performed. Patient 1 in the histological assessment study.

Figure 6.6 Uterine cornu incised and tubal screw transected to confirm correct placement by the methylene blue dye and subsequently by histology (with 1cm scale).

Figure 6.7 Patient 2 in the histological assessment study with uterine cornu bisected after screw placement.

Figure 6.8 Patient 2 with close-up of uterine cornu.

Figure 6.9 Patient 3 in histological assessment study after bisection of the uterus showing tubal screw at uterine cornu.

Figure 6.10 Preparing to perform the weights study on an in-vivo applied tubal screw in the operating theatre.

Figure 6.11 The purpose built weights and their support for the in-vitro and in-vivo weights studies.

Figure 6.12 Graph demonstrating the force required to dislodge the in-vivo hysteroscopically applied tubal screws.

Chapter 7

Figure 7.1 Flow chart showing the changes in the equipment and technique of hysteroscopic screw sterilisation.

Figure 7.2 Ultrasound appearance of a hysteroscopically placed tubal
screw viewed on ultrasound scan 3 months post insertion.

Figure 7.3  Ultrasound appearance of a hysteroscopically placed tubal screw viewed on ultrasound scan 3 months post insertion.

Figure 7.4  Further ultrasound scan demonstrating a single tubal screw

Figure 7.5  Further ultrasound scan demonstrating bilaterally placed tubal screws

Figure 7.6  3-D ultrasonography demonstrating the presence of a tubal screw at the uterine cornu. (Patient number 1)

Figure 7.7  3-D ultrasound scan demonstrating bilateral placement of tubal screws.

Figure 7.8  Life table plot of right tubal screw retention (cases 1-20).

Figure 7.9  Life table plot of left tubal screw retention. (cases 1-20)

Figure 7.10  Life table plot of retention of all tubal screws (cases 1-20).

Figure 7.11  Life table plot of right tubal screw retention (cases 21-35).

Figure 7.12  Life table plot of left tubal screw retention (cases 21-35).

Figure 7.13  Life table plot of retention of all tubal screws (cases 21-35)

Figure 7.14  Log rank test to compare the life table plots between the initial and latter cases.
Chapter 1

The need for a simple, outpatient method of female sterilisation
1.1. Introduction

For well over one hundred years physicians have struggled to effect a surgical technique whereby they render a woman sterile (Blundell, 1823, cited by Bordahl 1985). The driving force behind the technique employed was that it was to be simple and rapid, it was only many years later that concerns of safety in the choice of technique were really addressed (Phillips et al., 1977, Chamberlain and Brown, 1978). Now at the beginning of the 21st century the commonest method of sterilisation is a laparoscopic technique performed under a general anaesthetic.

1.2. History of Tubal Sterilisation

The current technique of occluding the fallopian tubes has its origins in the early 19th century. Ligation of the fallopian tubes was first discussed in 1827, and then subsequently in 1829, by Blundell. Although he did not mention whether he actually performed the procedure it would seem likely (Blundell, 1828 and 1829). He described his technique thus;

"draw up the fallopian tube, which is easily done, first on one side, then the other, cutting out a portion of it, so as to render it impervious, by which the woman would for ever afterwards become sterile".

From then on various doctors advocated sutures around the fallopian tube, single or multiple, and at various points on the fallopian tube to effect a rapid
and simple technique of tubal sterilisation. Reasons for sterilisation were the risk of repeated caesarean section, severe chronic illness and occasionally mental sub-normality (Wilson 1995). The procedure was often performed at the time of caesarean section (Irving 1924).

Although sterilisation was still practised infrequently, the drive for a rapid irreversible method of contraception continued for sinister purposes. From 1907 onwards various US states adopted legislation to practice eugenic sterilisation for people with hereditary diseases (Skajaa, 1932), as indeed was practised by the Nazis from 1933-45. Evidence of this is shown in this extract from the proceedings of the Annual Meeting of the Eugenics Association in New York in 1929:

‘the sterilization of subnormal women to protect racial integrity is regarded much more important by eugenicists than sterilization of the male’

(DeVilbiss, 1935).

Throughout the early part of the 20th century various eponymous techniques to effect surgical ligation for sterilisation were developed. The most widely known being ligation-and-crushing, Madlener technique (Madlener, 1919), the Irving technique (Irving, 1924) where the tubes are divided and proximal stump buried in myometrium, and the Pomeroy technique (Bishop and Nelms, 1930), not reported until after his death.

Other techniques reported included; the Aldridge technique, burying the
fimbrial ends of the tubes in the broad ligament (Aldridge, 1934), cornual resection (Overstreet, 1964), fimbriectomy (Kroener, 1969) and the Uchida procedure, postpartum fimbriectomy (Uchida, 1975).

Baird introduced sterilisation as a technique of family planning in Aberdeen in the 1930s. However they were criticised for their liberal use and hence a woman had to be near 40 years and have more than eight children (Baird, 1965). The first reported case of puerperal sterilisation was in 1939, ‘the Oslo method’ (Adair and Brown 1939), which led to an increase in the practice of sterilisation elsewhere.

The use of electrosurgery to effect laparoscopic tubal sterilisation was first described by Boesch (Boesch et al., 1936) and in 1941 by Power and Barnes using an early laparoscope under local anaesthetic. With the advent of the newer laparoscopes electrocautery became more frequently used initially using high frequency monopolar electrodiathermy but this was superseded by the safer use of bipolar electrodiathermy due to the occurrence of accidental visceral thermal injury with monopolar surgery (Peterson et al., 1983a). After the early laparoscopes of Power and Barnes, Raul Palmer was a pioneer in the development of more advanced laparoscopic techniques and instrumentation (Palmer, 1946; Palmer, 1947). These newer laparoscopes used improved endoscopic lenses and advances in the technology of cold light transmission. Palmer also introduced the Trendelenberg position along with safer methods of peritoneal insufflation and monitoring, to provide a view of the pelvis that was reliable and of high quality (Palmer, 1962). Palmer
performed monopolar electrocoagulation and transection of the fallopian tubes aided by his biopsy drill forceps bearing his name. Steptoe was another pioneer in laparoscopic surgery publishing the first English language textbook in the field containing a report of his experience of electrocoagulation of the fallopian tubes. (Steptoe, 1967).

A modification of the Madlener technique to convert a laparotomy approach to a less invasive laparoscopic procedure was developed by Fragenheim in Germany. This technique used a prolene suture to ligate the fallopian tubes, but this procedure required a high degree of endoscopic expertise and skill to manipulate the instruments (Fragenheim and Kleindienst, 1974; Wortman, 1976). Fragenheim, who had learnt his laparoscopic techniques from Raul Palmer, went on to develop many laparoscopic instruments and made one of the first prototype carbon dioxide insufflators. A milestone in the development of gynaecological laparoscopy was the introduction at the end of the 1950s of electrocoagulation for tubal sterilisation by Palmer in Paris and Frangenheim in Konstanz each working independently. The technique of laparoscopic fulguration of the fallopian tubes involved either inserting the monopolar instrument either down a special channel in the laparoscope or via a secondary entry site after insufflation with 2-4 litres of gas. The fallopian tube was then picked up and either coagulated or transected using a cutting current. A coagulation current causes cellular dehydration and charring without division whilst the intense heat of cutting current causes the tube to divide. Both forms of current are potentially dangerous as they may produce sparks, which could burn adjacent structures. Realising the potential dangers
of using monopolar current Frangenheim developed bipolar electrocoagulation for sterilisation and for controlling bleeding in 1972. The benefit of bipolar diathermy is that the current passes only between the blades of the instrument and does not pass through the patient to a return plate electrode thus minimising sparking. This technique was demonstrated to be as effective as transection of the fallopian tube using monopolar current. Indeed Yuzpe encountered no pregnancies in 335 women followed-up for up to 10 months (Yuzpe, 1974).

A safer method of laparoscopic sterilisation by coagulation and transection of the fallopian tube using monopolar electrodiathermy was developed by Semm and Steptoe (Steptoe, 1976 cited by Wortman, 1976) by using a fulguration instrument, which is heated from the inside using a low voltage and low temperature technique. With this technique there was less risk of thermal injury to surrounding structures, and indeed the remainder of the fallopian tube by thermal spread, leaving the possibility of reversal an option by surgical reanastomosis of the remaining ends.

The Pomeroy method of interval tubal sterilisation by laparotomy, mini laparotomy, culdoscopy or colpotomy was the favoured technique to effect sterilisation at this time (Wortman, 1976). However Clark (Clark, 1972), Loeffler (Loeffler, 1974), Greene (Greene, 1974) and Alexander (Alexander, 1975) described Pomeroy ligation via laparoscopy whereby the fallopian tube was either tied within the abdomen or brought out through the abdominal puncture site for ligation. This technique was difficult to perform and
consequently the approach of mini-laparotomy persisted (Wortman, 1976)

Clips or rings have also been used to effect tubal closure via laparoscopy. The clips that were used initially were made of tantalum, a non-tissue reactive metal. These clips were previously used to provide haemostasis at open surgery. Failure to cause tubal occlusion was as high as 27% (Davidson and Donald, 1972; Wheeless, 1974). The first reported purpose built clip was the Hulka clip (Hulka et al., 1973), the Falope ring was reported by Yoon et al., in 1974 and the Filshie clip was introduced in 1975 and is probably the most widely used clip today (Wilson, 1995).

Until the advent of laparoscopy and culdoscopy the main route to approach the fallopian tube had been via a mini-laparotomy incision 2-3 cm above the symphysis pubis (Osathanondh et al., 1974). Culdoscopy was abandoned as the favoured route for sterilisation due to the high incidence of failures and due to an unacceptably high complication rate (WHO 1982).

1.3. Complications of Tubal Sterilisation

The advent of laparoscopic surgery to gynaecology, as in other surgical specialities, has brought some undisputed benefits to patient care. It is claimed that advantages over laparotomy include reduced postoperative discomfort, shorter hospitalisation, faster recovery all leading to savings in treatment cost, and of course a better cosmetic result. This is undoubtedly true when comparing laparotomy and laparoscopic surgery for certain
indications such as tubal pregnancy in gynaecology and appendicectomy in
general surgery (Vermesh et al., 1989; Kum et al., 1993; Nagele et al., 1996;
Golub et al., 1998). This also follows for a technique as simple and
widespread as sterilisation. However, laparoscopic management can also be
associated with potential disadvantages. It is well documented that
endoscopic procedures can have their unique complications rarely seen at
laparotomy which can be life threatening. Examples include vascular or bowel
trauma from the insertion of trocars; (Bassil et al., 1993; Nordestgaard et al.,
1995; Soderstrom, 1993; Soderstrom, 1997) and electrosurgical and laser
burns to the gastro-intestinal tract; (Tucker, 1995; Harkki-Siren and Kurki,
1997). The complication rate for the procedure of laparoscopic sterilisation is
up to 1.8% (DeStefano et al., 1983).

Although these complication rates are very low it is important to understand
how frequently laparoscopic sterilisation is performed. There are in excess of
50,000 laparoscopic tubal sterilisations performed each year in the UK
(hospital in-patient episode statistics 1997), approximately 1 million annually
in the United States of America (Tulandi, 1997), and enormous numbers are
performed each year in developing countries. Indeed worldwide there were
predicted to have been 159 million sterilisations performed in the 1990s (Ross

Complications in laparoscopic surgery arise with the insertion of the Verres
needle, insertion of the trocar and complications related to the operation itself.
The rate of major complications was 0.33% when studied prospectively in
25,764 laparoscopies performed in 72 hospitals in Holland (Jansen et al., 1997). The commonest complication was laceration of the inferior epigastric vein (0.15%), gastro-intestinal injury (0.11%) and intra-abdominal vascular injury (0.11%). Most injuries occurred during the laparoscopic approach, rather than the procedure proper. When the rates were calculated by type of procedure the rate for diagnostic laparoscopy was 0.27%, for sterilisation 0.45%, and for operative laparoscopy 1.8%. A recent report detailing the different complications rates according to method of laparoscopic sterilisation was produced by the United States Collaborative Review of Sterilization which demonstrated that the spring clip method had the lowest complication rate, 0.47 per 100 procedures. This rate was not significantly lower than the complication rates of other procedures although in adjusted analysis, diabetes mellitus, general anaesthesia, previous abdominal or pelvic surgery and obesity were all independent predictors of complications (odds ratio 4.5, 3.2, 2.0 and 1.7 respectively) (Jameison et al., 2000).

There have been many large scale reviews of the mortality rate for laparoscopic sterilisation, although many relate to the now outmoded practice of monopolar diathermy to the fallopian tubes. The mortality rate of tubal sterilisation is approximately 1.5 per 100,000 procedures as reported by the Centre for Disease Control in the USA (Escobedo et al., 1989). However a more recent survey of 22,966 sterilisations performed in the United States reported one death, deriving a mortality rate of 4 per 100,000 procedures, but only 13% of gynaecological surgeons surveyed replied to the questionnaire (Hulka et al., 1995). Although Hulka himself reported no deaths in 30,480
sterilisations performed (Hulka et al., 1990).

Reports in the literature detail fatality rates of up to 10.2 per 100,000 sterilisations performed (Chamberlain and Brown, 1978). These initial reports of the Royal College of Obstetricians and Gynaecologists and the Collaborative Review of Sterilization in the United States and the International Project / Association for Voluntary Sterilization attributed the high mortality rate to the use of monopolar diathermy to transect fallopian tubes, a practice now rarely used and to the use of general anaesthesia (Chamberlain and Brown, 1978; Aubert et al., 1980; Peterson et al., 1982; Peterson et al., 1983a; Peterson et al., 1983b). However the death rates can be much greater in developing countries due to their use of local anaesthetic with sedation. In one series of 170,000 sterilisations performed over a two-year period, the death rate was 99 per 100,000 procedures (0.1%), 66 times as great as in the developed world (Rosenberg et al., 1982). In the largest series of camp sterilisation deaths Bhatt (1991) reported a mortality rate of 0.02% for 3 million laparoscopic sterilisations performed over three years. The mortality rate was 0.05% for those gynaecologists with less than six months experience and was greatest in higher parity women. However the results were markedly better with a very experienced single operator, being as low as 4.8 per 100,000 (Mehta et al., 1989)

1.4. Failure Rates of Tubal Sterilisation

In a discussion regarding the complications of a surgical technique to effect
sterilisation it is important to report the rate of failure of sterilisation and the subsequent ectopic pregnancy rate if the woman did conceive. The cumulative probability of conceiving 10 years after sterilisation is 1.34% and one third of these failures are ectopic pregnancies (US Collaborative Review of Sterilization, CREST) (Peterson et al., 1996). In this report the failure rate was greatest with laparoscopic spring clip application and least after monopolar tubal coagulation. A subsequent analysis showed that the rate of ectopic pregnancy was greatest in women sterilised when less than thirty years of age by bipolar cautery of the fallopian tubes (Peterson et al., 1997). However the results of laparoscopic sterilisation may be better if performed by experienced operators, 1.7 per 1000 for tubal ring and Filshie clip application at one year using life-table analysis (Sokal et al., 2000). The Royal College Working Party on Sterilisation quote a failure rate for Filshie clip sterilisation of 1 in 200 procedures, as described later in this chapter (RCOG, 1999). Other reported failure rates of tubal sterilisation record the failure rate of tubal sterilisation of approximately one in 100 procedures at between two and eight years; Mumford and Bhiwandiwala (1981) with the majority of procedures performed by monopolar diathermy, Aranda et al, (1985) using the Rocket clip and Koetsawang et al., (1990) who used electrocoagulation, the Hulka clip and the tubal ring to effect sterilisation.

Another important factor in the management of a woman undergoing sterilisation is the incidence of sterilisation regret. It is known that women under 30 are most likely to return requesting reversal of sterilisation (Winston 1977). In a review of 22 studies analysing the incidence of sterilisation regret
the incidence was found to be between 1.5% and 15% (Schwyart and Kutner, 1973). In this study the highest dissatisfaction occurred in women with less than four children and in those women sterilised at the time of termination of pregnancy. The CREST group reported the cumulative incidence of sterilisation regret in a cohort of women followed-up for five years after their sterilisation as 7.0%. They also recorded the incidence of regret in a group of women whose husbands had undergone a vasectomy as 6.1% (Jamieson et al., 2002).

The chance of a successful sterilisation reversal depends upon the length of the remaining fallopian tube, the location of the anastomosis and the experience of the surgeon (Siegler et al., 1985). All methods of tubal sterilisation cause damage to the fallopian tube, either due to excision of a short part of its length, thermal damage or by crushing and pressure necrosis. Hence up to about 40% of patients may have their request for sterilisation reversal denied as their fallopian tubes are too damaged (Antoine et al., 1983). Therefore a technique that potentially causes minimal damage to the fallopian tube, which could in theory be reversible would appear to be very desirable. Several procedures have been described which involved either carefully dividing the fallopian tube, with a view to a potential later anastomosis, or buried the ovary or fallopian tube within a peritoneal fold intended to prevent oocyte transport (Siegler et al., 1985). Hysteroscopic procedures designed to be reversible are described in Chapter 2.
1.5. Guidelines of Royal College of Obstetricians and Gynaecologists for female sterilisation

In 1999, the Royal College of Obstetricians and Gynaecologists (RCOG) published evidence-based guidelines for female sterilisation developed from a multidisciplinary body and after peer review.

1.5.1. Indication and timing of sterilisation.

There are no absolute contraindications to sterilisation providing the patient is able to give adequate consent. Caution is advised for sterilisation at the time of Caesarean section, in association with abortion, in nulliparous women and women under 25 years of age in view of an increased incidence of sterilisation failure and post sterilisation regret. Sterilisation can be performed at any stage of the menstrual cycle providing the woman continues contraceptive precautions until the next period. A pregnancy test is imperative if a woman believes she has missed a period. All women should be offered comprehensive information as to all contraceptive choices available including the use of freely available, impartial and easily understood information. The latter is very important, as in a UK study in 65% of patients had not received any written information regarding their sterilisation (Walsh et al., 1998).

1.5.2. Information

All patients should receive information regarding all alternative long-term
reversible methods of contraception, as some methods are as successful as sterilisation at preventing conception. For instance, the TCu380A intrauterine device, which has a 12-year cumulative pregnancy rate of 1.9/100 women treated (Anonymous, 1997). This is similar to the success of laparoscopic sterilisation (Peterson et al., 1996). It is imperative that couples are aware that male sterilisation is a local anaesthetic, outpatient procedure, which is very successful at preventing conception and is safer. The failure rate of vasectomy is approximately 1 in 1,000 in the first year (RCOG, 1999). The surgeon should ensure that the medical records include a full gynaecological and medical history, and the examination findings are recorded, along with the preoperative counselling for sterilisation:

**Out-patient consultation and counselling:**

Parity and any complex obstetric history
Gynaecological history and current symptoms
Pelvic examination
Discussion of long-term contraceptive alternatives to tubal occlusion
Expected method of access to tubes and method of occlusion (and reason for method of occlusion if not mechanical)
Risk of extended procedure, if non-life-threatening problems occur
Extent of consent to alternative methods of tubal occlusion if first intended method not possible
Failure rate 1 in 200
Risk of ectopic pregnancy
Irreversibility, potential for reversibility with expected method and availability of reversal locally on NHS

Information leaflet given

**Immediate pre-procedure:**

Date of last menstrual period

Pregnancy test result if performed

Confirm outpatient details and other preoperative discussions

Confirm valid consent form with the patient’s name, name of doctor obtaining consent – to be countersigned by surgeon performing the procedure

(Fitness for day case surgery)

**Operation notes:**

Name of operating surgeon(s) including surgeon present in theatre taking overall responsibility

Ease of access to the tubes

Clarity of identification of the tubes

Accurate placement of occlusive method

Additional procedures or unexpected events
Post-procedure:

Method actually used
Discharge letter to GP
Patient informed of method used and any intra-operative findings / events
Whether further contraception advised eg. up to next period, or pending result of tubal patency test.

Royal College of Obstetricians and Gynaecologists
Evidence Based Guidelines on Female Sterilisation, 1999

Prior to undergoing sterilisation of the female partner the surgeon should establish the date of the last menstrual period to ensure she is not pregnant, and perform a pregnancy test if indicated. It is imperative that the operating surgeon ensures that the patient has been appropriately counselled, is aware of the risks of the surgery and the failure rate of the procedure. The patient should be warned that the risk of a laparotomy due to visceral injury is 1.9 per 1,000 and the mortality rate is 1 in 12,000 as described previously (Chamberlain and Brown, 1978; Jansen et al 1997). The woman should be informed about the method of sterilisation performed prior to discharge, any surgical difficulties encountered and if there was any difficulty in clip application or if an extra clip was required. If there is any doubt as to the success of the sterilisation then the woman should be informed postoperatively, and advised to continue contraceptive precautions until a hysterosalpingogram has been performed to assess tubal integrity. The
patient should be warned prior to discharge to attend the emergency
department or her General Practitioner should she suffer abdominal pain or
begins to feel unwell due to the potential late presentation of bowel injury.

The woman should be informed both preoperatively and again prior to
discharge that the risk of sterilisation failure is 1 in 200 women overall lifetime
risk (RCOG, 1999). This figure is based on the CREST study (Peterson et al.,
1996). This prospective study of 10,685 women, described earlier, derived a
ten-year life table probability of failure of 16.6 per 1,000 procedures. This
failure rate is substantially greater than the failure rates previously reported of
3-6 per 1,000 at up to one year (RCOG, 1999). After multivariate analysis the
spring clip (Hulka clip), bipolar coagulation, decreasing age and particularly
women less than 28 years of age were all associated with significantly
increased chances of sterilisation failure. However the Filshie clip was not
available in the USA at the time of the CREST study. The best available
evidence suggests that it has a failure rate of 2-3 per 1,000 at two years
(personal communication, Professor John Guillebaud). The RCOG guidelines
extrapolate this figure using the CREST model to derive a lifetime risk of
sterilisation failure of 1 in 200 for Filshie clip application and the chance of
failure does not diminish with time. With regard to the risk of an ectopic
pregnancy post laparoscopic sterilisation the RCOG Guidelines (1999)
suggest that women should be warned that the risk of an ectopic gestation is
greater if tubal diathermy has been used and less likely if mechanical
occlusion or tubal ligation has been performed. Whilst women who have been
sterilised are at less risk of an ectopic pregnancy than non-sterilised fertile
women, if they conceive their chance of the pregnancy being ectopic is up to nine times greater than a woman who has not been sterilised (RCOG, 1999).

The RCOG review provides reassurance that for women over thirty years of age, tubal occlusion does not cause a significant change to the menstrual cycle. All women should be informed that it is possible to reverse the sterilisation if required, although it should be stressed that sterilisation is intended to be permanent.

The guidelines state that culdoscopy should not be used as an approach to sterilisation, and that laparoscopic mechanical occlusion of the fallopian tubes by either clips or rings as a day case procedure should be is the method of choice in the UK. The guidelines state that ‘transcervical application of chemicals, adhesives or synthetic plugs are still under evaluation and have not been considered for these recommendations on methods of tubal occlusion’.

With regard to analgesia the RCOG guidelines state that it is probable that pain after surgery is greatest after ring application, with diathermy being the least painful and with clip application being intermediate. Of benefit at alleviating pain is; instillation of a local anaesthetic agent over the fallopian tubes, into the mesosalpinx or on the Filshie clip. With regard to sterilisation under local anaesthesia, benefits were noted with regard to postoperative pain and earlier return to normal activities post procedure. It is cheaper, accepted by patients and easy to perform. The largest UK series of local
anaesthetic sterilisation reported that 91% of patients would recommend the procedure to a friend (Mackenzie et al., 1987).

1.5.3. Training in sterilisation

Due to the increasing incidence of litigation against gynaecologists the RCOG recommends that the operator should be properly trained and that the operation should be carried out technically correctly. The Guidelines recommend that a trainee should not perform the laparoscopic sterilisation until they have successfully completed 25 supervised cases and are able to perform a laparotomy unsupervised. It is also advised that trainees learn an alternative method of sterilisation in case it is impossible to apply an occlusive clip at the time of the operation. It is also imperative that sterilisation only takes place in site with properly maintained equipment where there is equipment available to perform a laparotomy if necessary. Regarding audit the working group of the RCOG advocate establishing a national database of failed sterilisations to provide accurate failure rates for counselling patients, and it would also identify an area of substandard practice at an early stage.

1.5.4. Areas for more research

The working party recommends performing long-term studies of the failure rate, risk of ectopic pregnancy and the effect on the menstrual cycle of all sterilisation techniques, particularly Filshie clip sterilisation. A study, of women under thirty years of age, of the effect of tubal occlusion on the menstrual
cycle and risk of hysterectomy should be performed. Interestingly, the RCOG working party made no suggestion that there should be research into the development of a hysteroscopic method of sterilisation.

1.5.5. Compliance of the study with the RCOG guidelines

These guidelines were published after the completion of our study of a novel method of hysteroscopic sterilisation. Despite this fact the preoperative counselling was as described in the Guidelines, however the failure rate of laparoscopic sterilisation quoted to our patients was that the failure rate of the procedure over the long-term was unknown but that it could be as high as one failure in 100 patients. This figure was derived as Vessey et al., reported a failure rate of one per 100 procedures over a seven year period after ring sterilisation. When the CREST study was reported we were obliged to inform our patients that the failure rate of laparoscopic sterilisation maybe higher than the quoted figure of 1% over seven years previously quoted (Peterson et al., 1997). All other facets of the pre-procedure counselling were as recommended in the Guidelines of the working party, including providing the patient the current information leaflet from the Family Planning Association to read prior to their sterilisation.

1.6. The Need for a Simple, Outpatient Method of Sterilisation

In view of the complications of laparoscopy it would appear that the ideal sterilisation technique is a procedure that could be performed rapidly in an
outpatient-setting, avoiding abdominal instrumentation and general anaesthesia. If this technique were highly effective and potentially reversible it would become the ‘gold-standard’ method of female sterilisation. With these aims in mind we developed a ‘tubal screw’, which would be applied hysteroscopically into the uterine ostia and would be immediately effective (Figures 1.1 to 1.4).
Figure 1.1 The intratubal screw (from original plans).
Figure 1.2 The intratubal screw mounted on applicator and applied to uterine cornu (from original plans).
Figure 4: Outer applicator

Figure 1.3 The intratubal screw mounted on applicator (from original plans).
A - B = 15mm
A - C = 3mm

Figure 1.4 The tubal screw used in the in-vitro-studies.
Chapter 2

Review of intrauterine methods of female sterilisation
2.1. Introduction

Due to the risks associated with general anaesthesia and the potential risks of visceral trauma on instrumentation of the abdomen, a permanent method of female contraception avoiding these pitfalls has been sought for many years. However the initial attempts at sterilisation were via a uterine approach as opposed to being an abdominal procedure.

2.2. Initial intra-uterine techniques

Proximal obstructions of the fallopian tubes were first recanalised by Smith in 1849. This was performed using a whalebone guide passed through a silver directing tube, which due to the shape of the uterus he thought ‘would always pass to the ostia’ to treat cornual block.

At around the same time attempts to cause obliteration of the uterine cornu were made by Frioriep (1849). This technique relied on infusing silver nitrate into the uterine cavity towards the cornua via a cannula. Electrocautery was employed by Kocks in 1878, to cause thermal injury and then potentially destruction of the endometrium to prevent implantation of an embryo. Electrocauterity of the tubal cornua remained unchanged over the following years apart from improvements in the controlled delivery of the electric current to cause tissue damage (Risquez and Confino, 1993). Further reports of attempts to occlude the tubal ostia were published in the early 20th century.
Dickinson (1916), as an introduction to his new technique, provides an interesting insight into the background and requirements for a technique of sterilisation almost 100 years ago.

'Section of the vas deferens, though simple, is not accepted by the male...'

'Ovarian shrinkage by X-ray is neither sure nor its duration determined. Chemical slough stricture inside the upper uterine angles as advised by Froriep in 1850 was given up......'

'.various operations on the fallopian tubes involve opening the abdominal cavity....which is never justifiable for this purpose....'

'The only outlook for a simple and sure method, and that without risk or loss of time and with but little pain, seems through closure of the tube, where it enters the uterus...'

Dickinson 1916

It would appear that we are still striving to achieve this ideal almost 90 years later. The technique reported by Dickinson was to apply local anaesthetic into the uterine cavity and to the cervix. Then cauterisation of the cervix was performed. Note was taken of the cervix to see how long scarring and slough took to form. Then with touch only he attempted to find the tubal ostia and repeated this cautery for the same duration of time, using a semi-flexible loop of wire, at the cornua of the uterus. Confirmation of tubal occlusion was confirmed with silver, which produces an X-ray shadow. No results of this
technique are reported although he reported that he had performed 40 procedures between 1916 and 1950 without complication (Dickinson and Gamble, 1950, cited by Hulka and Omran, 1972). At this time Prudnikoff was also performing electrocoagulation of the uterine cornu (1912).

DeVilbiss reported her results in 1935 using a similar technique to Dickinson employing a semi-flexible uterine electrode placed by touch at the uterine cornua. A 3.5 amp current was applied for 15 seconds. Tubal patency was assessed using the Rubin's test, whereby if the uterus holds an air pressure of 150-200 mm Hg for up to 5 seconds the fallopian tubes are presumed blocked. Of 30 patients treated 17 cases were reported with bilateral blocked fallopian tubes, however there were 3 conceptions in this group. She described that the treatment is contraindicated in un-treated syphilis due to the liability to haemorrhage. Two case histories are described below which appear to demonstrate that sterilisation was used as a method of eugenics at this time:

"Case 14.-White paralytic moron, husband when drunk kicked her about. Reported blocked tubes.....returned to the clinic pregnant, with signs of an impending abortion....staff surgeons recommended a hysterectomy."
Case 7.-Colored syphilitic moron, aged twenty-four...5 pregnancies, 4 living children, 1 dead...reported four months pregnant."

DeVilbiss 1935

2.3. The advent of hysteroscopy

The first attempt at visualisation of an abdominal organ was by Bozzini in 1806. This was performed by illumination of the urethra with a candle. However the future of endoscopy was jeopardised as the Medical Faculty of Vienna reprimanded Bozzini for his undue curiosity. After this, procedures were performed by touch rather than with visual guidance until hysteroscopy was developed in 1869 as a diagnostic tool for intrauterine disease (Pantaleoni, 1869, cited by Silander 1962). Illumination was by an external kerosene lamp.

The first report of 'out-patient' hysteroscopy was described in 1908 by David who wrote his thesis on the uses, dangers and contraindications of hysteroscopy, although he did not use this approach to perform sterilisations (David, 1908 cited by Rubin 1925). With development of hysteroscopy for the purpose of cornual electrocoagulation by Rubin in 1925 the possibility of effecting sterilisation by an intra-uterine technique became increasingly a realistic objective. He described the visualisation of the uterotubal ostia with carbon dioxide gas (CO₂) and water and suggested the possibility of sterilisation by cautery. At this time the hysteroscope had a bulb light source
at its distal end.

To reduce the problems, noted by previous hysteroscopists, of poor uterine distension with the uterine wall being too near the objective lens and profuse bleeding interfering with the view of the uterine cavity, Silander in 1962 devised a technique of uterine distension and tamponade. His hysteroscope had at its distal end a balloon, which inflated to distend the uterine cavity to improve visualisation of the endometrium (Silander, 1962).

2.4. Sterilisation by tubal electrocoagulation

Hyams reported his success of cornual electrocoagulation at almost 100%. The procedure was reportedly performed without anaesthesia and perforation of the uterus was thought to be impossible (Hyams, 1934). This technique consisted of blind introduction of an insulated probe to find the uterine cornua. Then a trocar was advanced enabling an electrode to protrude and a current of 200mA was activated for 5 seconds. No anaesthetic was used for this procedure. After one month tubal obliteration was confirmed by performing a hysterosalpingogram. Later the technique was changed to use X-ray screening to aid visualisation of the uterine cornua. Iodine dye was initially injected into the uterus, and then the cauterisation would be performed under X-ray screening (Hyams, 1934).

DeVilbiss reported similarly poor success rates in 30 patients in 1935 using a
blind technique as described above, as 40% of fallopian tubes were patent after the procedure. Schroeder in 1934 described his technique of sterilisation of the intramural portion of the fallopian tubes by electrocoagulation under direct vision in 2 patients. Unfortunately follow-up hysterosalpingograms demonstrated no success. The warmth of the uterus felt through the abdomen determined the intensity and duration of the current required for coagulation. Although it appeared that these techniques were using women in experiments, there were attempts made to perform in-vitro testing on extirpated uteri; for instance, Mickulicz-Radecki and Freund in 1927 used an instrument they called a 'curetoscope'. In their opinion to effect sterilisation they needed to destroy the endosalpinx and part of the myometrium to stop the fallopian tube recanalising. However this degree of thermal damage although, undoubtedly causing severe tubal damage in the in-vivo situation, would potentially lead to severe local visceral thermal injury. If this occurred to the bowel, bladder or ureter then fistulae and peritonitis would ensue.

The most reported method to effect sterilisation via an intrauterine approach at this time was using a thermal modality. Norment and Greensboro in 1956 described their hysteroscope using water as the distension medium and reported 100 cases of hysteroscopy. They attempted sterilisation by cornual fulguration but described too few to cases to report their results (Norment and Greensboro, 1956). Using the Hyams technique, Sheares in 1958 described the results of tubal electrocautery. In 48 patients where an attempt at sterilisation was made he reported a 57% success rate. There was one death
due to peritonitis caused by a bowel injury. He described the new technique whereby he listened for sizzling and crackling over the abdomen with a stethoscope for 15 seconds. At this point it was felt that sufficient thermal injury had occurred to cause sterilisation (Sheares, 1958). The fallopian tubes were tested for occlusion using a CO₂ manometer, the Rubin's test.

Other authors who reported attempts at tubal electrocoagulation were Bowers in 1938 and Porter et al. (1957, cited by Quinones et al., 1973). Yasui in 1952 described 299 patients mostly after termination of pregnancy, using a transcervical procedure, and reported an 80% bilateral occlusion rate. There were 13 pregnancies but no complications. Effective sterilisation was thought to have occurred when a 'vibrational sound' was heard after 20-30 seconds of treatment.

The technique of cornual coagulation under either hysteroscopic or X-ray monitoring was popular in Japan at this time, although success rates were poor (Hayashi, 1972). New electrodes were developed to overcome the curve required to pass to the tubal ostia (Ishikawa and Hayashi parabola electrodes), rather than the straight cone electrodes developed initially by Hyams in 1934. Hayashi reported that using the Hyams’ cones the pregnancy rate in his treated patients was 83%, after refinement by using a round electrode the pregnancy rate was 39% and using a curved electrode the pregnancy rate was 5%. The temperature that was required was 110-120°C for up to 70 seconds (Hayashi, 1972).
Pasricha in 1968 described her blind detection of the uterine cornua and cautery for up to 20 seconds in 89 patients. Initially she followed Dr. Hyams’ technique but due to the difficulties of working in a very busy hospital in New Delhi she felt that she was able to accurately locate the cornua blindly. As described by Sheares in 1958 she would listen with a stethoscope for sizzling followed by crackling where upon sterilisation was presumed to have occurred. A refinement that she described was to place a finger in the rectum and fix the uterus in a retroverted position to aid the cautery procedure. Of 34 patients attending for a follow-up hysterosalpingogram a success rate of 47% was initially reported. The procedure was repeated in those women who had undergone a failed sterilisation and then overall success rate was reported as 76%. Unfortunately several patients suffered serious complications; salpingitis in two patients, 1 patient suffered with profuse bleeding and underwent an emergency hysterectomy, three patients suffered with peritonitis, one patient had a bowel perforation and two patients required a laparotomy (Pasricha, 1968).

In a consensus statement after a hysteroscopic sterilisation workshop of 54 scientists from 9 countries Williams and Sciarra (1973) reported that:

1. The ostia are best visualised in the post menstrual phase
2. A uterine relaxant aids dilatation of the uterine cavity
3. Dextran is advantageous
4. Tubal openings vary from case to case
5. A $45^\circ$ or $60^\circ$ hysteroscope is beneficial

6. Tubal cannulation was possible in all cases

7. Tubal blockage occurs only if the endosalpinx is completely destroyed

8. Thirty watts for 3 or 4 seconds or 40 watts for 2 seconds is sufficient for treatment

9. Side effects were minimal

10. Long term clinical evaluation of the sterilising effect is premature.

Williams and Sciarra, 1973

In their review of the literature Hulka and Omran, in 1972, reported on 603 patients who had been treated worldwide to date with an overall pregnancy rate of 8.4%. All patients underwent a test of tubal patency and the rate of success of successful occlusion at the initial attempt was 40-80%. Most authors recommended a repeat procedure if the initial attempt did not cause bilateral tubal occlusion. This series reported a total major complication rate of 2.5% and a mortality rate of 0.1%.

With the development of fibre optical leads, the light source was held distant to the patient and did not risk thermal injury. These new optics also provided a better view of the endometrial cavity leading to a renewed interest in hysteroscopy. However to effect thermal cautery to the uterine cornua using electrocoagulation, which relies on the heating effect of a monopolar current, it is important to irrigate the uterus with a non-conductive solution. Thirty
percent dextran had been used in Sweden (Edstrom and Fernstrom, 1970) and been found to be an acceptable solution for uterine distension. It is immiscible with blood and highly viscous. Levine and Neuwirth validated this method of hysteroscopy in 1972. They described excellent visualisation of the tubal ostia and the cannulation of the ostia with a Teflon catheter and injection of indigo carmine dye.

The following year using their technique of hysteroscopy with 30% dextran and employing a specially developed serrated cautery tip they reported treating the tubal ostia of 18 patients with a 25% failure rate (Neuwirth et al., 1973). They subsequently tested their technique in Thailand, in order to evaluate the feasibility of a large-scale ambulatory program, (Richart et al. 1973). Their success rate was 84% bilateral tubal closure, 34 of the 44 also had a tubal mesh or plug placed concurrently to the cauterised area of the ostia.

With the development of CO$_2$ hysteroscopy by Lindemann and Mohr in 1970 (Lindemann, 1974 and Lindemann and Mohr, 1976), the modality that Rubin initially described in 1925 was revisited (Rubin 1925). They described their adaptor which, by means of a vacuum attached to the cervix maintained a pneumometra and their 'Hysteroflator 1000', maintained a constant inflation pressure. When they developed CO$_2$ hysteroscopy they performed initial studies on dogs to determine the safe limits of uterine insufflation. They treated 450 women with electrocoagulation of 90° C for 1 minute or 140° C for
7 seconds. They performed follow-up on 267 women and described success in 90.2% of them. Their results were better when performed during the early proliferative phase of the menstrual cycle and when using the lower temperature. They reported two cases of bowel perforation and one case of bowel necrosis (Lindemann and Mohr, 1976).

Quinones et al. (1973) were convinced of the need for accurate hysteroscopic visualisation of the tubal ostia, to gain accurate information as to the amount of thermal injury caused by their interstitial tubal electrocoagulation, and to accurately place their hysteroscopic electrode. Their initial procedure was performed with laparoscopic control. This was a procedure that was performed in the outpatient setting under local anaesthetic only. After initial experiments on hysterectomy specimens they reported an 8.7% failure rate after 3 months, at the time of follow-up hysterosalpingogram. In 1975 they reported the treatment of 350 patients and followed their patients for up to 1 year with hysterosalpingography. Patients were requested to use contraception for one year until tubal occlusion could be confirmed. Initial studies using a coagulating current of 27.8 watts for 4 seconds was superseded by treatment for 6 seconds. The initial treatment produced bilateral tubal closure in 87.8% of patients.

March and Israel in 1975 reported the use of three different types of electrodes placed hysteroscopically into the uterine cornua in 30 women. Fulguration was performed in dextran 40 solution using 30 watts of power.
The study was prematurely terminated due to the serious complications that were being reported in the world literature at this time, although no major complications were reported in this study. In the same year Cibils reported a small series of 22 patients who were treated by dextran and CO$_2$ hysteroscopy. Dextran had the disadvantage that debris occluded the vision, although the clarity of the visualisation of the tubal ostia was greater than with CO$_2$ hysteroscopy. One patient had a uterine perforation and an ileal perforation that was not noted at the time of the surgery and required a small bowel resection. In another patient the tip of the coagulating electrode was subsequently discovered at the time of the follow-up hysterosalpingogram.

Further reports on cornual electrocoagulation were reported in France (Porto, 1974), Singapore (Ng et al. 1976), and from Germany using the Thermo-Probe, with temperatures of 140-160°C, (Rimkus and Semm, 1977). In Japan Sugimoto (1974) cannulated 32 of 38 ostia up to 1cm, and using a coagulating current applied 30 watts of energy for four seconds. Sugimoto also inserted an intratubal device but had a poor success rate with only 12 of 22 tested with the insufflation test demonstrating obstruction.

In 1976 Quinones et al. reported on the follow-up of 800 cases of hysteroscopic sterilisation using a different electrosurgical generator than previously reported Quinones et al. (1973). They applied 25 watts of energy to the uterine cornu and the duration of treatment was increased to 6 seconds. Hysterosalpingograms were performed every 3 months for 1 year.
In those patients that did not demonstrate bilateral tubal occlusion re-treatment was performed, leading to an overall tubal occlusion rate of 98.8% in the 487 patients who attended for follow-up. They reported 5 pregnancies, 3 were cornual and there was one case of uterine perforation. The authors also reported on various factors that they felt affected the success of the treatment. They reported that if the procedure was performed after the eighth day of the menstrual cycle they were less likely to visualise the tubal ostia due to an increased amount of mucus and bleeding. They also felt that the cauterisation of the ostia at this time was less effective. This is similar to that reported by previous authors (Lindemann and Mohr, 1974; Sugimoto, 1974; Cibils, 1975). Quinones et al. reported that their results were better when they replaced their spherical electrode with a cylindrical electrode inserted no further than 5mm into the tubal ostia.

To date in the world literature two patients have died due to peritonitis secondary to tubal electrocoagulation. The first patient was reported by Sheares in 1958 (see above) and the second by Israngkun and Phaosavasdi in 1976 who treated 251 patients, two suffered a bowel perforation, one of which was fatal.

In view of the apparent high rate of complications and poor success rates in some series The Hysteroscopic Sterilisation Registry was established at Columbia University. The results were published as a collaborative study of hysteroscopic sterilisation by cautery from a total of ten centres, from the
United States of America, Thailand, West Germany, India and Singapore (Darabi and Richart, 1977; Darabi et al., 1978). Five hundred and eighty-seven patients were treated in total. Each centre reported their series of between 6 and 298 cases, after exclusions for incomplete information or lack of follow-up test of tubal patency. The overall success with regard to bilateral tubal occlusion was 57% of patients. There was an overall major complication rate of 3.2%, including tubal and cornual ectopic pregnancies, uterine perforation, bowel damage, peritonitis, endometritis and excessive bleeding. The patients who had a failed tubal occlusion were likely to be younger than those who had a successful occlusive procedure. The younger patient was more likely to have a major complication than their older counterparts and burn related complications were more likely if a long treatment was performed (more than 40 seconds) using a medium power output (approximately 21-40 watts). A successful treatment was more likely if it was performed early in the proliferative phase of the menstrual cycle, and if an insulated curved probe was used instead of a straight or non-insulated electrode, and if the distension medium used was CO₂ or dextrose as opposed to dextran. The study concluded that the procedure should not be offered to women less than 30 years of age. Treatment should be for 40-60 seconds in the early proliferative phase of the menstrual cycle, using less than 20 watts of power and that the optimum time to check tubal patency should be after three months has elapsed.
2.5. Sterilisation by use of gels or polymers

Hefanwi et al. in 1967 was the first to report of the use of elastic substances to block the fallopian tubes of rabbits. These elastomeres are thick liquids, which change to a rubber consistency on the addition of a catalyst, which had previously been employed in plastic surgery. 64 rabbits were injected with two different formulations of silicone elastomeres at the time of laparotomy through puncture of the uterine cornua. There was a 33.7% conception rate in the treated uterine horns of the rabbits. The expulsion rates were 8.6% and 15.2% with the two different compounds with the majority of the expulsions being intraperitoneal. In those uterine horns from which the plugs were removed there was a 75% conception rate. Histological examination of the fallopian tubes demonstrated no local inflammation caused by the treatment. These preliminary studies gave hope, that although initial success rates were low in preventing pregnancy, local injury was minimal and this technique was potentially reversible (Hefanwi et al., 1967). At the same time that Hefanwi was performing these experiments in Egypt Rakshit was performing similar experiments in India with various chemicals (see below) and liquid plastic (Rakshit, 1968). Despite only a small number of cases being performed in the rabbit model with a substantial mortality, attributed to the anaesthetic, the procedure was tried in human subjects. Unfortunately the results of these studies were not reported. In 1970 Rakshit reported on a study using a slowly precipitating silicone with a catalyst (stannous octate). This elastomere took 15 minutes to solidify and contained barium for X-ray confirmation of the plug.
In 21 of 37 women a satisfactory block was demonstrated by X-ray examination. Several different radio-opaque liquid silicone plastics were tested to determine the most efficacious compound to solidify and be retained in the fallopian tubes (Rakshit, 1972). However the method of application of the silicone compound and catalyst was ‘blind’ and cumbersome, requiring the uterine cavity to be cleaned after application to ensure that no polymer solidified in the uterine cavity.

The application of silicone elastomers was refined by Erb et al. (1974). He used a more viscous silicone compound, which was applied via an obturator tip, which effectively sealed the cornual region of the uterus to prevent backflow into the uterine cavity. Silver powder was used to make the polymer visible to X-rays. Results of preliminary studies in rabbits demonstrated long term plug retention and a high success rate at preventing pregnancy (94.7%). This technique was potentially reversible with pregnancy rates of 29%, although it was felt that with time due to ciliary re-growth in the fallopian tube that this would increase (Davis et al., 1975). Tests were then performed on extirpated human uteri although no results were reported (Erb et al., 1974).

Interestingly the investigators subsequently reported an increase in the ‘angle subtended by the upper and lower walls of the cornual pocket’ in highly parous women (effectively meaning that a greater degree of deflection would be required to reach the tubal ostia). Consequently they designed four obturator tips to apply their ‘formed-in-place’ silicone compound. Application
was monitored using an image intensifier to ensure correct positioning at the uterine cornu, (Erb 1976). These obturator tips, which were made of silastic, with silver powder and a retrieval loop, sealed with the uterotubal junction. It then became permanently bonded to the plug. It also ensured a practical method for instillation of the polymer and a means of non-surgical removal of the plug, as the plug did not adhere to the tissues. With further refinement of the application system Erb and Reed used the hysteroscope to apply the silicone plugs (Erb and Reed, 1979). They used a variable speed motor drive to aid the delivery of the solution and catalyst, which subsequently set in 4 minutes and 45 seconds. To ensure that each tubal ostia was identified correctly, and was patent, a dilute solution of methylene blue was instilled in the region of the cornu so it could be seen passing into the fallopian tube directly (Reed and Erb, 1979).

An update on the progress of the refinement of the technique was reported in 1981 (Reed et al., 1981). At this time the procedure was being performed as an outpatient procedure with a paracervical nerve block. Dextran 70 was used to distend the uterus by the surgeons in the United States and CO₂ or Dextran 70 by the group in Belgium. A standard hysteroscope and light source were used to carry out the procedure. An X-ray was performed to ensure the plugs had formed normally and these patients were followed-up with further X-ray after three months. If the three-month post procedure hysterosalpingogram was satisfactory then the patients were encouraged to discontinue contraception. In the 239 women who underwent the procedure in
the United States there was a success rate of 71.5% for good plug formation, and in those women with satisfactory plug formation there were no pregnancies after the discontinuation of contraception. Women with ‘diseased fallopian tubes’ on pre-procedure hysterosalpingogram were subsequently found to have poor plug formation and were excluded from involvement in the study. In 1980 they introduced an elastic memory into the guide to enable a marked degree of deflection to improve the results in women with very ‘lateral’ uterine cornu, which were inaccessible with the normal deflecting mechanism. Complications that were reported were three uterine perforations by the guide assembly and one patient developed chronic pelvic pain, which resolved after plug removal. In the Belgian patients there were again no pregnancies in those women with good plug formation (Reed et al., 1981). A further modification that was introduced to enable greater lateral deflection was the addition of ‘kinks’ into the guide at 1cm intervals which provided for greater bending towards the tubal ostia (Reed, 1983). In this report Reed describes the use of a non-steroidal anti-inflammatory premedication to reduce tubal spasm and intravenous glucagon if it is not relieved. After 965 procedures there were 13 pregnancies with one ectopic gestation, 5 uterine perforations, with an overall 82% good bilateral plug formation (Reed, 1983).

A further group reported their results of 415 patients undergoing local anaesthetic hysteroscopic sterilisation with ‘formed-in-place silicone plugs’ (Houck and Cooper, 1982). The procedure was unsuccessful in 75 patients due to one or more of the following; the ostia may have been seen but plug
application was unsuccessful either due to tubal spasm (23) or debris obstructing the ostia (30), or inadequate deflection of the catheter (16), inadequate uterine distension (10), uterine perforation (1) or other factors. Overall 20% of initial procedures were unsuccessful, although a second attempt was often successful. Of those 328 patients with a satisfactory appearing 3-month post-procedure hysterosalpingogram, none conceived subsequently. The authors advocated a hysterosalpingogram two years after the procedure as they felt that the plugs were slowly disintegrating (Houck and Cooper, 1983). They had previously described their technique of relieving tubal spasm with intravenous glucagon to aid plug removal, when the silicone was applied incorrectly, for instance if the distal end passed into the peritoneal cavity (Houck and Cooper, 1982).

In 1984 Franklin Loffer reported his experience of treating 206 patients using this 'Ovabloc' method, 91.3% were sterilised and followed-up for 2910 patient months without a pregnancy (Loffer, 1984). Twenty patients required a repeat procedure and two required a third to demonstrate a successful plug development after three months by X-ray. In 16 patients (7.8%) sterilisation was not effected due to tubal spasm.

With regard to the potential reversibility of the 'Ovabloc' method the silicone polymer induces immediate structural alterations of the epithelial lining in the isthmical part of the fallopian tube (Assaf et al., 1993; van der Leij and van Krimpen, 1995). The authors found no evidence of restoration of tubal
epithelial integrity after removal or expulsion of the polymer, although in their study of 224 patients, one patient of sixteen conceived after a plug that was in situ for one year was removed, however, there is no comment as to the contraceptive use in the other patients.

The most recent report of the success of the Ovabloc system has come from Belgium. Of 392 patients who agreed to be sterilised it was not possible to instil silicone in 13% or the instillation failed in 4% (Ligt-Veneman et al., 1999). Two procedures were needed in 7% and three in 1% of patients. The mean follow-up period was 547 months. The efficacy of the treatment was evaluated by plug appearance on X ray follow-up. The three-month plug retention rate was 96.6% with 93.8% of plugs being retained at one year, two pregnancies occurred during this time. In total of the 325 women treated, two conceived, 20 spontaneously expelled their plugs, and 10 had plugs removed due to complaints or regrets (Ligt-Veneman et al., 1999).

A tissue adhesive has been employed to effect tubal occlusion by using a mixture of gelatin-resorcinol-formaldehyde (GRF) in rabbits (Grode et al., 1971). This compound had previously been demonstrated to be non-toxic, to be biodegradable and to facilitate the in-growth of surrounding tissue into the plug to facilitate tubal blockage. Very good tubal blockage results were demonstrated when the animals were sacrificed. Histological examination of the fallopian tubes showed necrosis of the tube and epithelial invasion of the plug suggesting good long-term results are possible. This technique was
refined with the introduction of formaldehyde and quinacrine into the compound, just prior to delivery, with the aim to cause tubal sclerosis (Falb et al., 1976). Initial studies in rabbits demonstrated that the addition of quinacrine appeared to decrease the effectiveness of the compound and its use was then discontinued. The results of these studies proved this technique to be very effective at preventing pregnancy in rabbits, despite not causing tubal occlusion on histological assessment. If the compound spilled out of the distal end of the fallopian tube it had a tendency to provoke granulomas in adjacent tissue (Falb et al., 1976).

The first reported use of the polymer methylcyanoacrylate was by Corfman et al. in 1965. This solution, which is clear, polymerises after 20 seconds to become solid. It was instilled into the uterus, without visual control via a special balloon, with the intention of avoiding spillage of the liquid into the uterine cavity, which may have caused endometrial adhesions (Stevenson and Taylor, 1972). The solution passed to the uterine cornu and caused tubal damage and fibrosis. The initial studies were performed on hysterectomy specimens and then on women who were awaiting hysterectomy. The short time prior to polymerisation was intended to prevent the solution from reaching the peritoneal cavity. The methylcyanoacrylate was broken down with time and was then removed by phagocytosis, by which time local tissue fibrosis has started to occur (Stevenson and Taylor, 1972). The first report of the procedure being performed under local anaesthetic, with sedation, was reported in 1976 (Stevenson, 1976). Histological assessment of the fallopian
tubes in women treated, who subsequently underwent hysterectomy, demonstrated that tubal occlusion by fibrosis took up to 14 weeks. In the 38 women who volunteered to be sterilised 11 were required to have a further treatment due to unilateral tubal blockage (Stevenson, 1976). To ensure safe, easy cornual application of methylcyanoacrylate a specially developed applicator was developed for this purpose using a balloon, which inflated to fill the uterine cavity. It forced the compound into the fallopian tubes, although no results of treatment were reported, and to enable effective delivery of the compound a piston driven applicator the ‘SAFR’ device was developed (Richart et al., 1977). This evolved into the 'FEMCEPT system' (Neuwirth et al., 1980), X-ray monitoring of the application was performed and three groups were tested with differing concentrations of the methylcyanoacrylate. It rapidly polymerised in contact with bodily fluids, however the best group's bilateral closure rate on subsequent hysterosalpingogram was only 78% (Neuwirth et al., 1980). The equipment has been changed 14 times in total (Bolduc et al., 1983) and bilateral tubal closure has been reported in 87% of patients treated with a two dose regime (Neuwirth et al., 1983), however in 22% of patients pelvic pain persisted for up to 1 month.

Another group reported their results in 1983, of 112 patients treated by 'blind insertion' (de Souza Filho and Coutinho, 1983); they reported that in patients having a single application a 4 month post procedure bilateral tubal closure rate of 74% was achieved and 88% after two injections. There were two uterine perforations and four women conceived after a hysterosalpingogram
appeared to confirm bilateral tubal occlusion. The most recent report of the ‘Femcept’ system was reported in 1989 (Schuber, 1989), although radio-opaque methylcyanoacrylate was not used, of the 34 patients followed-up, 88.2% had complete bilateral tubal occlusion on subsequent hysterosalpingogram.

Another method of administering the methylcyanoacrylate has been direct application by microcatheterisation under X-ray control in rabbits. None of 11 rabbits that were treated and were subsequently involved in mating experiments became pregnant (Berkey et al., 1995). Plugs have also been applied that contain other chemicals in the plug; Vancaillie et al. (1989) caused tubal damage at the uterotubal junction in rabbits with a bipolar electrical current and then inserted a plug (Aqualloy). The plug on one side contained quinacrine and a platelet extract in the other. Histological assessment by serial sections indicated occlusion of the uterotubal junction in all but one case (96% success rate). This was taken further by Sonmez et al. (1997) where rabbits underwent bipolar electrosurgery which provoked tubal damage, and then tube was plugged with a fibrin sealant, with a success in 10 of 14 rabbits.

A further plastic substance that has been used with aim of effecting tubal occlusion is Proplast, an alloplastic composed of polytetrafluoroethylene (PTFE) and carbon fibre (Malinak and Homsy, 1976). The material presented a three-dimensional matrix into which fibroblasts were able to grow to
generate connective tissue throughout the implant. The preliminary studies in three baboons were encouraging although no subsequent results have been reported (Malinak and Homsy, 1976).

Another polymer employed to effect tubal occlusion is paraformaldehyde, a long chain polymer of methanol suspended in ethanol. This caused tubal occlusion by sclerosis of the tubal lumen. It was initially performed by ‘blind’ insertion prior to hysterectomy and then in four healthy volunteers who subsequently had a six-week follow-up hysterosalpingogram. This demonstrated that 7 of the 8 fallopian tubes were blocked (Dafoe, 1976). Problems with this technique were that it occasionally polymerised prior to insertion into the uterine cornu, leading to difficulty in application and that in two patients, of the 25 treated, intravascular particulate embolisation to the lungs occurred.

The P-block is a hydrogelic intratubal device, which has evolved through 10 stages (Brundin 1983, Brundin 1987, Brundin, 1991) (see Figure 2.1). The hydrogelic device has a nylon core and swells 2.5 times its size through absorption of body moisture. As the body of the device swelled over 45 minutes retention wings formed, to prevent expulsion of the device, which became embedded in the surrounding musculature. The porous nature of the device also enables in growth of tissue and fibroblasts. The P-block was inserted under CO₂ hysteroscopic control as an outpatient procedure and check hysteroscopy was performed at 1, 6 and 12 months, and later by the
means of ultrasound. Initial insertions of the P-block were by forceps, then with a polyethylene catheter with a plunger. Both these methods facilitated cannulation of the ostia particularly if the ostia were deviated markedly from the axis of the uterus. A final stiffer catheter was used for plug application. The aim of the P-block was to cause luminal blockage at the intramural part of the fallopian tube, however at the time of hysterosalpingogram the radio-opaque dye could pass the P-block. The Pearl index with the plug in-situ was 0.3 and tubal perforation occurred in 3 cases. Brundin concluded that a non-occlusive intratubal device in the intramural part of the fallopian tube exerts a contraceptive effect (Brundin, 1987). The author advocated this procedure as potentially reversible, with a high patient satisfaction rating (99%) and as a technique that in the future could potentially be applied under ultrasound guidance without the need for hysteroscopy (Brundin, 1991).

A further group studied the effects of combining a hydrogel with a sclerosing agent, sodium tetradecyl sulphate applied under X-ray monitoring, which was thought would lead to eventual closure of the intramural fallopian tube by scarring. In the 8 rabbits that were studied the hydrogel prevented conception in seven of the treated uteri (Maubon et al., 1994).

2.6. Sterilisation by tubal plugs (see Figure 2.1)

Application of tubal plugs to animals has been attempted since 1967 (Hefanwi et al., 1967), although the plugs became dislodged and Dacron was
abandoned as it caused extensive scar formation and epithelial destruction (Omran and Hulka, 1970). One of the first tubal plugs that were applied in humans was applied at the time of concurrent hysteroscopic tubal electrocoagulation (Richart et al., 1973). Richart applied a Tefdek mesh or a Mersilene tape, 1 patient had a uterine perforation and of 44 patients 37 (84%) had bilateral occlusion. Richart et al. (1978) also described two further plugs that were tested on pigtailed monkeys. One was covered ethylene vinyl acetate, the 'microflock device', and the other constructed of titanium-aluminium-vanadium alloy with an etched surface. Some had 10% silver nitrate or 50% quinacrine hydrochloride added for extra contraceptive effect. The microflock device anchored in the tube mechanically, but the aim of the polymeric or metal alloy devices bonding with Fallopian tube epithelium was not achieved. The research workers concluded that a mechanical design approach to intratubal devices was a more productive line of approach than one that assumes a tissue-device bond. This mechanical approach to tubal occlusion was the method we aimed to use with our tubal screw. However with the later development of the STOP device, subsequently renamed ESSURE, this assumption was proven to be flawed (Kerin et al., 2001; Valle et al., 2002).

The following year a silicone plug was described (Porto, 1974) which was 16 mm long and 1.3 mm wide. It had distal and proximal balloons connected to each other via a thin canal. During introduction the first balloon was flattened due to tubal tonus, the air being pushed into the distal balloon. After insertion,
as the pressure equalised, the balloons adopted a similar shape. Porto also
described another silicone plug which was distorted by an external piston
when it was correctly placed, to transfix it in position (Porto, 1974). However
none of these plugs were tested on animals or humans.

To facilitate direct instrumentation of the tubal ostia a new steerable
hysteroscope was developed (Brueschke et al., 1977), he also described the
application of two types of plugs into extirpated uteri. Both were made of
silicone but the original one buckled under the pressure of application and
consequently a flexible metallic stiffening core was added. Three sizes of plug
were applied after visualisation of the ostia; 10 mm x 1.8 mm, 11 mm x 2.0
mm and 12 mm x 2.2 mm. To facilitate retention of the plugs moulded inward
projections were initially used, however these plugs became displaced and
three metal anchors were added at the proximal end to dig into the tubal
interstitium (see Figure 2.1). To ensure good uterine distension a cervical cup
was applied to prevent fluid leakage. Then the out-flow channel from the
uterine cavity was turned off once the cavity became clear. The plugs were
applied on the end of a fine wire and were dislodged from the end of this wire
by a rotational force. In the later experiments application was successful in
80% of cases. Studies in 15 baboons demonstrated successful occlusion in
all cases (Brueschke et al., 1976).

Hosseinian et al. (1976) described another uterotubal junction blocking device
(see Figure 2.1) after performing preliminary studies on the human and
baboon uteri, by the instillation of liquid silicone to clarify the geometry. Their plug was 10 mm long by 2 mm at its base and 1 mm at its tip and was initially made of polyethylene. To fix in place at the uterotubal junction four metallic spikes were located at its base to embed it into the myometrium. The plug was applied or removed by a long grasping forceps that was passed down the length of the hysteroscope. The studies were carried out on seven baboons and after four months patency of only one of 14 fallopian tubes was demonstrated (Hosseinian et al., 1976). After further studies it was felt that the polyethylene was too rigid and consequently may cause a uterine perforation, so the plug was then manufactured from silicone rubber (Hosseinian and Morales, 1983). In 33 subjects who were scheduled for hysterectomy they inserted the plugs and demonstrated that 91% of the fallopian tubes could be occluded. Of the 20 women who had their plugs removed 90% regained tubal patency. Due to their rigid application system through a non-flexible hysteroscope they reported a difficulty in applying 15% of their plugs due to the lateral position of the ostia. In 11 volunteers who underwent the procedure, as an elective method of sterilisation, five conceived. The main cause of failure was attributed to the difficulty in aligning the rigid applicator to the tubal ostia, which was not a problem in their baboon trials due to the different uterine anatomy facilitating easier application of the plugs (Hosseinian and Morales, 1983).

Porous ceramic material was used as it was felt that it would provide a stable supportive matrix for tissue in growth (Craft, 1976) (see Figure 2.1). This plug
was 7 mm long and 2 mm wide at its widest point with a 5mm projection from the base of the plug for application. In 15 patients who were about to undergo hysterectomy the plugs were applied. A major problem reported was the difficulty in aligning the plug with the ostia, there was one uterine perforation, and in 10 of the patients application of the plug was felt to be satisfactory on examination of the extirpated uterus.

Droegemueller et al. (1978) after performing studies on baboons with cryocoagulation injected a collagen plug, 8 mm by 2 mm, into the uterotubal junction and subsequently confirmed tubal blockage, although these plugs were not used further.

Sugimoto in Japan (1974) (see Figure 2.1) developed a silicone rubber intratubal contraceptive device, 10 mm long and 1.2 mm in diameter, with notches every 1.5 mm to prevent expulsion and with two flanges placed distally to prevent the plugs being displaced into the fallopian tube. The plug was mounted on a base enabling the plug to be grasped for removal. To insert the plug it was mounted in a Teflon tube and was dislodged by a wire plunger. The plugs were tested on 32 women prior to hysterectomy. Spontaneous loss of the plug occurred in three cases. In those plugs that were correctly fitted no patency was demonstrated on follow-up hysterosalpingogram. After removal of the plugs tubal patency was restored.
The Popp claw device has been developed and tested in rats along with other prototype plugs based on a cylinder. The Popp claw device consisted of a walking stick like hook, which anchored the plug in the lumen of the uterine cornu (Popp et al., 1984) (see Figure 2.1). Other plugs that were tested by Popp et al. were expanding cylindrical plugs and transversely perforated plastic plugs. Unfortunately these plugs were unsuccessful when tested on rats.

Lindemann was reported to have been developing a method of hysteroscopic sterilisation using a rigid plug, however he reported difficulty in application of this plug, and of the 12 uteri into which these plugs were uterotubal perforation occurred in 5 instances (Sciarrà, 1980).

A technique that appears to have a similar method of action to that of the intrauterine contraceptive device is the surgical nylon thread with an open loop with an elastic memory employed by Hamou et al. (1984) and inserted by microhysteroscopy. The preliminary results were very successful with a preliminary Pearl index of 0.8.

The most recent and perhaps the most important, in terms of offering a realistic alternative method of sterilisation, is the STOP microcoil device, which evolved into the Essure™ pbc system (permanent birth control system (Conceptus, San Carlos, USA) (Kerin et al., 2001, Valle et al., 2001) (Figure
2.2). As this is the most recent innovation in the field of hysteroscopic sterilisation and perhaps the most promising technique it will be discussed in detail.

The Essure device, previously called STOP (Selective Tubal Occlusion Procedure) consists of a flexible stainless steel inner coil, an outer coil made from Nitinol™ (an alloy of nickel and titanium) and fibres of polyethylene terephthalate (PET or Dacron), which run along and through the inner coil. The inner coil attaches the device to a guide wire for placement at the tubal ostia. To reduce the diameter of the device for insertion an outer sleeve is placed over the device, as a release catheter, to keep it in a low profile. Covering the release catheter, the guide wire and the device is placed a hydrophilic catheter to aid access to the fallopian tubes. At the proximal end of the system is a handle enabling single-handed application; via a 5 French operating channel of a 5mm continuous flow hysteroscope, using saline as the distending medium with gravity only to produce the distension pressure. The method of introduction of the hysteroscope into the endometrial cavity is as for standard diagnostic hysteroscopy. The device is advanced into the tubal ostia without the need for a deflecting bridge. It is inserted so as to leave 3-8mm remaining in the endometrial cavity, ensuring that the device spans the intramural portion of the fallopian tube and reaches the isthmic portion of the tube. The hydrophilic outer cannula is then withdrawn. The micro-insert is then released through retraction of the inner catheter, allowing the micro-insert outer coil to expand. If correct placement has been achieved
then the delivery wire is detached by applying five to eight anti-clockwise rotations to the wire. The method by which the device is retained at the uterotubal junction is by the in-growth of the surrounding tissue. Initially there is a moderate inflammatory response caused by the PET with the invasion of macrophages, fibroblasts, foreign body giant cells and plasma cells. This initial response peaks between 2 and 3 weeks and resolves over the ensuing 10 weeks after which extensive fibrosis ensues causing occlusion and anchoring of the device in the lumen of the fallopian tube (Kerin et al., 2001, Valle et al., 2001).

The first study of the use of the STOP microcoil / Essure™ pbc was designed to look at the histological effect of the device when placed at the uterine cornu in 43 women undergoing hysterectomy who were willing to defer their operation for up to three months. Only premenopausal or postmenopausal women, taking hormone replacement, were included provided they did not have markedly distorted uterine anatomy. Seven patients had the device fitted under local anaesthesia the remainder under epidural blockade. Device placement at the utero-tubal junction was successful in 57 of 84 attempts (67.8%). Two patients undergoing sterilisation only had attempted unilateral placement and there were three uterine perforations, which were attributed to a design problem that was subsequently rectified. The poor result of device application was felt to be due to equipment problems only in one instance and the remainder were attributed to uterine factors. The average procedure time was 15 minutes. No patient reported pain whilst wearing the device. At the
time of hysterosalpingogram, prior to hysterectomy, all 57 of the fallopian tubes examined had X-ray confirmation of occlusion. Forty-seven fallopian tubes were examined histologically after hysterectomy. Acute inflammation was predominant at the cornu of those uterine specimens from hysterectomies performed up to four weeks after device placement, consisting mainly of macrophages and mononuclear cells. In those hysterectomy specimens performed between 8-30 weeks, after device placement, chronic inflammation and fibrosis was usually seen with both loose and dense fibrous tissue with, in some instances, smooth muscle infiltrating between the coils. The reaction was limited to the area of the fallopian tube immediately adjacent to the device and did not extend through the wall. The authors concluded that the STOP / Essure™ pbc device, as a method of hysteroscopic sterilisation, is feasible, safe and well tolerated by patients. The histological assessment suggested that the device causes luminal occlusion by fibrosis but that the tubal inflammatory process is well localised (Valle et al., 2001).

The second study of the tubal device, now renamed Essure™ pbc, was a much larger study to evaluate the use of Essure™ pbc as a permanent method of sterilisation. The objectives were to assess the safety and patient tolerance of the procedure and device and its long-term safety and effectiveness at preventing pregnancy. Women included in the study were counselled prior to sterilisation but were only included if they had regular menstrual cycles and had no evidence of any pelvic pathology. All the
procedures were performed under local anaesthesia, with the addition of sedation if required, apart from one patient who requested a general anaesthetic. The women were instructed to use an alternative method of contraception for three months after the procedure to allow for luminal fibrosis to occur to occlude the fallopian tube, which was to be confirmed by a follow-up hysterosalpingogram.

One hundred and thirty women underwent the procedure, 85.3% had bilateral device placement and in 12.3% of patients it was not possible to apply the device to either tube. There was no difference in outcome of device placement according to the stage of the menstrual cycle or parity, although successful application was more likely in older women. Of the 114 women who had a device inserted 96.4% (110 women) had correctly placed devices at the time of hysterosalpingography. Of the 107 women with correctly placed bilateral tubal devices, 105 demonstrated tubal occlusion during hysterosalpingography and were advised to cease alternative contraceptive measures. One woman had unilateral device application, however the contralateral tube was already occluded by cornual adhesions. The two women who had patent fallopian tubes at the time of initial hysterosalpingography underwent repeat examination after a further six months and were now found to have occluded fallopian tubes.

There were nine adverse incidents reported during the study; distal end of device became detached in fallopian tube (1), unsatisfactory device
placement (3), perforation of uterus (2) and three women experienced a break in the outer coil of the device during insertion but were able to rely on the device as a method of contraception. Regarding the contraceptive effectiveness of the device, 108 women have accumulated 1894 months relying on the Essure™ pbc system without a pregnancy and there were no late plug expulsions. After three months 99% of women recorded their tolerance to wearing the device as very good to excellent and 89% reported no pain or unusual symptoms during this time. The authors attribute the success of their technique to the length of the device, as approximately 2.3cm lies within the fallopian tube, which they believe leads to their high plug retention. Other positive attributes of their device they believe are; the conformability of the device to any fallopian tube, the dynamic nature of the coil which enables it to straddle the ‘waist’ of the uterotubal junction limiting its movement, the expanded coils in the uterine cavity limiting distal migration and the growth of the fibroblastic tissue into the coils leading to long term tubal obliteration (Kerin et al., 2001).

It would appear that a safe and reliable method of permanent hysteroscopic sterilisation may have been achieved, although bilateral application was not possible in 15% of women treated in the larger study, however one important issue may require investigation is that of the safety of the application in women with nickel allergy. The outer coil of the Essure™ pbc device is made of Nitinol, which consists of nearly equal atomic nickel-titanium (NiTi) alloy, known for its flexible shape and elastic memory properties. These properties
have been put to use in various other biomedical applications, such as wires for orthodontic tooth alignment and osteosynthesis staples (Wever et al., 1997). The inner coil of the Essure™ pbc device is manufactured from stainless steel.

The commonest stainless steel used in medicine is 316 stainless steel, which is corrosion resistant and flexible. This also contains an amount of nickel of approximately 12% to 14%, but usually the alloying is sufficient and very little nickel is released under normal circumstances. These properties made them popular for making wires for surgical techniques and for wires used in orthodontics. Similarly, because of its ease of fabrication, reasonable expense, and availability, stainless steel is used in the manufacture of cannulas, screws, plates, rods, and various other fracture fixation devices. The early total hip replacements, pacemaker casings and other devices used in heart surgery were made of stainless steel. With the recognition that approximately 15% of the population was allergic to nickel, and that these devices were intended to last the lifetime of the patient, concern was raised. Indeed allergic responses to cannulas, pacemakers, osteosynthesis screws, other osteosynthesis devices, various dental devices, and total joint replacements have all been reported (Merrit and Rodrigo, 1996).

The most common skin sensitivity, however, is to nickel. It is more common in females, which has been attributed to the greater use of jewellery causing skin sensitisation. There are documented incidences where sensitivity
reactions have necessitated premature removal of orthopaedic implants but Merritt and Rodrigo who have researched this area in detail believe that the incidence of severe reaction is probably less than 0.1% (Merrit and Rodrigo, 1996; Milavec-Puretic et al., 1998). With regard to the NiTi alloy Wever et al., in 1997 carried out detailed animal studies to assess its toxicity and allergic potential. Their conclusion was that the NiTi alloy showed no cytotoxic, allergic or genotoxic activity, and was indeed similar to the clinical reference control material, 316 stainless steel. They believed that this promising biological behaviour was most likely due to a minimal release of ions that in turn reflected the good corrosion resistance of the NiTi alloy.

'Given these very good results, together with the good tissue compatibility as shown in several implantation studies in the literature, the NiTi alloy can be regarded as a biologically safe implant material with many promising clinical applications' 

(Wever et al., 1997).

It is important to note, however, that the risk of becoming sensitised to nickel after an implant of stainless steel is approximately 3% (Duchna et al., 1998; Swiontkowski et al., 2001) and indeed Denmark has banned the marketing and import of any alloy that releases more nickel than 0.5 µg/cm² per week,
although it is known that 316 stainless steel releases far less than this.

Consequently the Essure™ pbc device is almost certainly safe as an implant but it may well provoke sensitisation in some patients but whether this will lead to a failed tubal sterilisation remains to be tested.
Figure 2.1 Intratubal devices and their method of fixation.

Legend for figure 2.1

2. Craft porous plug (Craft 1976)
3. Sugimoto plug with notches (Sugimoto 1974)
6. Brundin hydrogelic P-block swollen after absorption of water (Brundin 1987)
7. Popp inflated plug (Popp 1984)
10. Hosseinian plug with metal spikes (Hosseinian and Morales 1983)
11-13. Brundin combination plugs (hydratisation and anchoring protrusions) (Brundin 1987)
17-18. Popp 'claw' device (Popp 1984)
Essure System Overview:
Micro-insert Design

- Fibers (PET)
- Dynamic Expanding Superelastic Outer Coil
- Wound Down Diameter 0.8 mm
- Expanded Diameter 1.5 - 2.0 mm
- Micro-Insert Length = 4cm

Figure 2.2 The Essure™ pbc device, Conceptus, San Carlos, USA.
2.7. Sterilisation by tubal laser

Laser photocoagulation to effect endometrial ablation has been performed for several years after its first use by Goldrath *et al.* (1981). It is relatively easy to perform by passing a flexible optical fibre passed through the operating channel of a hysteroscope and with the limited depth of thermal damage of the Nd:YAG laser, up to 7mm, it was potentially a safe modality. Hence in 1990 Donnez *et al.* described in-vitro experiments on 10 rabbit uteri to effect cornual photovaporisation. In a multi-centre study to assess the effect of the Nd:YAG laser to effect bilateral tubal obstruction the results were so poor, with only four successes out of 17 procedures with one uterine perforation, that the study was abandoned (Brumsted *et al.*, 1991). There were no further reports of the Nd:YAG laser for sterilisation.

The overall likelihood of preventing pregnancy by performing ablation by laser endometrial ablation is approximately as good as performing a laparoscopic sterilisation (Neuwirth 1995). The effect is not solely due to the tubal damage caused by the procedure but also due to the removal of the endometrium preventing implantation of an embryo. Istre *et al.* in 1996 demonstrated that of fifty patients undergoing endometrial ablation, with cornual coagulation, bilateral tubal occlusion was only demonstrated in three patients.
2.8. Sterilisation by cryocoagulation

Cryocaunity has been used in gynaecology for many years (Collins et al., 1967). Its use as a potential method of endometrial ablation and as a technique for effecting tubal sterilisation was first discussed in 1970 (Droegemueller et al.). In this initial study six women were treated with a probe with a freezing area of 3cm, treatment was performed for four to six minutes with temperatures down to -50°C. These patients then underwent hysterectomy at various intervals after treatment up to six weeks. Histological analysis demonstrated coagulative necrosis around the area of treatment. As the interval between treatment and hysterectomy increased this area became fibrosed. These studies encouraged the authors to continue their research with cryocoagulation for endometrial ablation but no results of the use of cryocaunity for sterilisation were reported (Droegemueller et al., 1971a; Droegemueller et al., 1971b). However with time they noticed that the procedure was time consuming and often required multiple probe placements. They undertook studies with baboons and modified their cryoprobe. With three rapid freeze and thaw cycles they discovered that they could produce uniform cylindrical necrosis at the cornu. To facilitate scar formation they then applied a collagen plug to the cornu. This appeared to improve the scar formation. However they did not report their success in human subjects (Droegemueller et al., 1978) and none have subsequently been reported to date. Martens in 1972 reported his results of cryosurgical closure of the fallopian tubes, initially at the time of hysterectomy, and then as the sole
method of sterilisation. His results demonstrated that of 32 fallopian tubes treated only 11 were closed at the time of follow-up hysterosalpingogram after two months (Martens, 1972). Hulka and Omran have also attempted to use cryosurgery to effect sterilisation in rabbits but results of human studies are not reported (Hulka and Omran, 1972), presumably as the Hulka clip was developed and found to be more effective (Hulka et al., 1973).

2.9. Sterilisation by radiofrequency ablation

In vitro studies on animals have been performed using radiofrequency to effect tubal injury by a similar means to that initially described by Phipps (1990) to effect endometrial ablation, but these results have not been encouraging (Manganiello et al., 1998, Hurst et al., 1998). In the study reported by Manganiello et al., nineteen nulliparous purpose-bred cats were maintained in an anovulatory state. After laparotomy, all animals had focal radiofrequency lesions applied to their uterine horns. Ten of 30 treated uterine horns appeared grossly occluded at the time of subsequent post-mortem examination, but histological assessment demonstrated only 6 complete occlusions. In the study involving eight guinea pigs by Hurst et al., 34 lesions were made in the fallopian tubes. Three weeks later the animals were sacrificed and their uterus analysed histologically. Complete occlusion of the tubes was seen at 12 of the 22 sites evaluated by histology. However in the following year Hurst reported a more successful outcome when analysing the effects of using endotubal radiofrequency ablation of the rabbit uterine
cornu by heating the tissue to either $95^0\text{C}$ or $105^0\text{C}$ using different energy levels (Hurst et al., 1999). No pregnancies were observed in any of the uterine horns in which minimal or maximal energy was delivered to the fallopian tubes or uterus, although pregnancy occurred in one horn as a result of the delivery of energy below the radiofrequency minimum of $95^0\text{C}$. They concluded that with adequate tissue heating, 100% sterilisation efficacy was achieved with the new, computer-controlled delivery of radiofrequency energy, whereas pregnancies occurred in all untreated control groups. They believe that if human studies support these results, the goal of a safe, effective means of transcervical sterilisation may be realised.

The method by which the procedure will be performed was reported at a meeting of the Association of Reproductive Health Professionals of America in May 2002 with companies aiming to market a method of intrauterine sterilisation. Adiana, Inc. developed the Adiana procedure, which is a technique for performing transcervical sterilisation by radiofrequency endometrial ablation using a two-step method (Figures 2.3-2.5). First, a catheter is delivered through a hysteroscope into the intramural portion of the fallopian tube. A superficial lesion is created using low-level bipolar radiofrequency energy to remove surface epithelium. The second step is the placement of a porous, non-biodegradable implant (matrix) into the lesion. The aim of the matrix is that it remains implanted within the fallopian tube and the surrounding tissue grows into the matrix over a few weeks. The hypothesis is that this in-growth results in permanent and total occlusion of
the fallopian tube. The Adiana transcervical sterilisation system is an investigational device and is not yet marketed, although the company are meeting the American Food and Drug Administration later this year to discuss a large-scale trial of its use. The company state that:

'Generation of the lesion involves low bipolar radiofrequency energy that prevents secondary damage to surrounding tissues. The biomaterial associated with the implantable matrix has been safely used in clinical applications for many years. No adverse reactions to this procedure have been reported. Adiana has completed studies optimising the lesion and biomaterial in both animal and clinical models. The company has also completed studies demonstrating the ability of this procedure to occlude fallopian tubes as determined by (a) HSG, (b) an in vitro dye-pressure test, and (c) histological analysis of the implant. The histology indicates healthy, stable, space-filling in-growth.

Women participating in the studies have reported little or no discomfort associated with placement and subsequent wearing of the device (up to 12 weeks). The efficacy of the Adiana procedure has been determined by several tubal occlusion assays.'

However there are no published studies as yet as to the efficacy of this method of hysteroscopic sterilisation in women.
A further method of hysteroscopic sterilisation that was presented at this meeting of the Association of Reproductive Health Professionals of America in May 2002 which is in the early stages of development, is the Reversible Tubal Occlusion Device, a nickel-titanium stent that is intended to be implanted transvaginally developed by Berkeley Applied Science and Engineering (BASE). The device is composed of a nitinol frame structure to occlude the fallopian tube by tissue in-growth, aiming to provide radial strength with minimum tissue injury. It is introduced and navigated under direct scope visualization, using a catheter-based delivery system.
Figure 2.3. The Adiana catheter is inserted into the intramural portion of the fallopian tube, and a mild lesion is created.

Figure 2.4 After the lesion is created, the sheath of the catheter retracts, depositing a matrix into the scarred area, and the catheter is then withdrawn.

Figure 2.5. Surrounding tissue grows into the matrix over the next few weeks, resulting in tubal occlusion.
2.10. Chemical methods of intrauterine sterilisation

For many years the goal of permanent contraception has been attempted by trying to sterilise the female partner by the intrauterine instillation of chemical agents. In 1849 Friorep infused silver nitrate into the uterine cavity towards the cornua via a cannula to attempt occlude the uterotubal junction. In the early 20th century other caustic substances such as phenol and iodine were infused into the uterine cavity with the aim of causing endometrial and cornual obliteration (Zipper et al., 1970). Zipper et al. used even more aggressive chemicals in 1968. The substances that were tested on rats were; cadmium, the antimitotic agents podophyllin and colchicine, alkylating agents and 100% alcohol and the results were successful at preventing implantation. The success of these experiments led the team to perform intrauterine instillation of 100% ethanol and formalin on volunteers. To achieve complete occlusion up to six applications were required. Silver nitrate was again used by Neuwirth et al. (1971), as was zinc chloride in experiments on pigtailed monkeys, which was successful in causing tubal closure. This led the group to perform the procedure in women via the culdoscopic approach; drawing the distal end of the fallopian tube into the vagina and cannulating the fallopian tube and instilling 10% silver nitrate solution. Half the patients subsequently became febrile and all complained of abdominal pain for up to five days and tubal occlusion was demonstrated in all patients. Ringrose in 1973 also reported on the use of silver nitrate, applied via an endometrial biopsy curette to the uterine cornu. The use of 15mls of 15% silver nitrate solution produced
bilateral tubal blockage in 70% of cases.

In 1970 the first report of the use of quinacrine intrauterine instillation to effect sterilisation was reported (Zipper et al., 1970, Zipper et al., 1972). In this report three consecutive monthly applications produced a tubal closure rate of 88.2% and a pregnancy rate of 1.2 per 100 women. Alvarado et al. (1974) adapted the blind intrauterine instillation of quinacrine of Zipper et al. to perform it via the hysteroscopic approach, however their results were poor with a 28.5% bilateral closure rate.

The same group felt that the hysteroscopic distension medium might be washing out the concentrated quinacrine solution. Hence they then placed the solution 6mm into the intramural portion of the fallopian tube after devising a way of instilling the solution simultaneously to both tubal ostias (Quinones et al., 1976b). This was still unsuccessful and led them to double the strength of the quinacrine solution but this again led to poor results. Ng et al. in Singapore also found difficulty of maintaining the quinacrine solution in place in the presence of an irrigating solution. To avoid this they favoured the use of hysteroscopic tubal electrocoagulation, although this only provided bilateral closure at the initial attempt in 41% (Ng et al., 1976).

To overcome the problem of dispersal of the quinacrine prior to it producing the desired effect in the intramural portion of the fallopian tube Zipper et al.
(1980) developed the use of quinacrine pellets for intrauterine installation. They believed this would also lead to a slower systemic absorption as there had been reports of severe psychiatric disturbances after hysteroscopic installation (Zipper et al., 1980). The 4mm pellets contained 10mg of quinacrine, which were placed at the uterine fundus via a plastic tube and push rod; this procedure was repeated twice (Zipper et al., 1980). The results demonstrated a 3.1% pregnancy rate at up to twelve months post treatment. Post instillation histological assessment of the fallopian tubes demonstrated that the quinacrine pellets had caused tubal obliteration and fibrosis. However the results were unpredictable with one side potentially showing fibrosis and obliteration but the opposite side could remain patent (Bhatt et al., 1980). Hence this led to the requirement for three separate instillations, after which all intramural fallopian tubes should be occluded by fibrosis (Merchant et al., 1995).

The use of quinacrine pellets appeared to eliminate the problem of the transient psychosis, which occurred in 2% of women undergoing the hysteroscopic approach (Zipper et al., 1982). Further centres also studied the use of quinacrine pellet application and reported high success rates with few side-effects (Guzman-Serani, 1983; El-Kady et al., 1993). The effectiveness of quinacrine to cause tubal closure led investigators to look at different methods of introducing the quinacrine pellets into the uterine cavity (Wheeler, 1983). Techniques that have been postulated have been to apply the quinacrine as a gel or a paste, or to apply the quinacrine pellet directly into
the tubal ostia hysteroscopically or the use of quinacrine intrauterine contraceptive devices (Wheeler, 1983).

The safety and efficacy of quinacrine pellet application was reported in 1985 (Kessel et al., 1985). There was no increased risk of ectopic pregnancy and the overall failure rate at 3 years post 3 applications was 5%. To reduce the need for multiple applications of the quinacrine pellets Zipper et al. (1987) devised a pellet that required only two applications with a longer duration of absorption. This method was similarly effective but there were still a substantial number of side-effects (12.6%), with haematometra occurring in 3% of women (Zipper et al., 1987). The largest series reporting the use of quinacrine pellet application to effect tubal sterilisation was by Hieu et al. in Vietnam. Two years after treating 31,781 women, the post procedure pregnancy rate was 4.31%, with a significantly higher failure rate in those women only undergoing one application (Hieu et al., 1993). Amenorrhoea occurred up to three months post procedure in 0.3% of women, lower abdominal pain (15.3%), vaginal puritis (23.2%) and headache (20.2%), were all reported for several days after the insertions. There were no deaths caused by this technique, consequently as these women would otherwise have undergone surgical sterilisation the authors postulated that the quinacrine method of sterilisation saved between 6 and 31 women's lives.

The quinacrine method of sterilisation has been studied in India where the three-year life-table failure rate was 8.5%. This group also looked at the
effectiveness of intrauterine instillation of three doses of 200mg of tetracycline, however there were 32 failures among the 55 cases producing a failure rate of 58% at two years post treatment (Mullick et al., 1987).

As quinacrine is a rapid, cheap and effective way to provide sterilisation it is a very valuable tool with which to prevent unwanted pregnancies and hence also maternal mortality in large populations, particularly the third world. However this technique has run in to substantial of opposition from a group of feminists who believe that this technique is unethical, which has unfortunately hindered its development and introduction in the third world. Kessel, Mumford and Zipper have been the leading proponents of the use of quinacrine as a method of sterilisation particularly in the third world. Unfortunately due to concerns raised during animal studies by the WHO of the potential for malignant transformation of cells they issued an advisory warning against its use in 1991 and the Federal Drug Administration advised against its use. Due to political pressure in India its use as a method of sterilisation was banned in 1998. However its use continues in other parts of the world with two reports in 2001 with pregnancy rates of up to 3.9% after up to 10 years of follow-up (Bhuiyan and Begum, 2001; Thakur, 2001).

Another chemical agent that has been employed with the aim of effecting tubal closure is phenol, either as a mucilage (Zheng and Chen, 1983) or as a phenol-atabrine paste (PAP) (Wu et al., 1983) both instilled by a blind application procedure. The use of the radio-opaque mucilage was effective at
causing tubal closure on post procedure X-ray examination (85.2%), with a pregnancy rate of 2.6% in the 2,487 women who had successful injection, although after refinement the authors achieved successful application in 97.8% of the 448 women treated (Zheng and Chen, 1983). The PAP solution was also effective, with X-ray demonstration of formation of a satisfactory plug in the fallopian tubes in 93.0% of the 1837 women treated, although there was a substantial incidence of severe systemic upset for the patient (Wu et al., 1983). These side effects consisted of fever in 20-50% of patients depending on the concentration of atabrine used and two uterine perforations were caused by the procedure. Other side effects that were reported but were not detailed in terms of their frequency of occurrence were; a bearing down sensation in the anal area associated with backache and lower abdominal distension, dizziness, paleness, nausea and sweating were also reported (Wu et al., 1983).

2.11. Conclusion

There have been a large number of methods by which fallopian tube closure has been attempted over time. Unfortunately the majority have been unsuccessful due to the problems associated with poor tubal closure at the time of the procedure or extrusion of the plug or polymer after instillation at the uterine cornu with the exception of the ESSURE™ pbc device, which appears very promising.
If a hysteroscopically applied tubal plug could be correctly and firmly placed at the uterotubal junction with a negligible chance of being extruded over time then it would represent a simple, safe and rapid method of sterilisation which would become the gold-standard of procedures. To this aim we set out to assess the feasibility of a hysteroscopically applied novel tubal screw.
Chapter 3

Review of the anatomy of the uterotubal junction, studies of uterine morphology and review of the safety of insertion of a PTFE tubal screw
3.1. Introduction

The development of a hysteroscopic sterilisation technique relies on an accurate and detailed knowledge of uterine anatomy particularly the uterotubal junction, where the uterus is contiguous with the intramural part of the fallopian tube. Of particular importance is the angle of deflection that is required from the hysteroscope to approach the uterotubal junction for the purpose of sterilisation (see Figure 3.1). This angle is in part a function of the length of the uterine cavity, and the transfundal width of the uterine cavity but also the angle at which the fallopian tube enters the uterus.

This chapter is divided into three parts:

A  Embryology, anatomy and physiology of the uterotubal junction.
B  Three experiments to determine the angle of deflection required to place the tubal screw at the tubal ostia.
C  Medical uses of PTFE and potential consequences of the insertion of the PTFE screw
3A. Anatomy and physiology of the fallopian tube

3A.1. Embryology of the fallopian tubes

Gabriele Fallopius in 'Observationes Anatomicae', first described the fallopian tubes (oviducts, uterine tubes or salpinx) in 1561 (cited by Beck and Boots in 1974). In a woman in her reproductive years, the fallopian tubes are highly specialised structures derived from the Müllerian (paramesonephric) ducts. Johannes Müller discovered the paramesonephric ducts in 1830, and noted that they remained in females but regressed in the male of several mammals. This observation was recorded in Müller's handbook of physiology in 1834 (Müller, 1834). In males, it is the Wolffian (mesonephric) duct that remains under the influence of a hormone secreted from the testes (Price et al., 1969); in contrast, retention of the Müllerian ducts in the female beyond the ambisexual stage is hormonally independent.

The Müllerian ducts are not detectable until early in the sixth week of development when they are seen as a linear invagination of the coelomic epithelium, with a smooth muscle muscularis derived from the underlying mesenchyme and an internal mucosa derived from an invaginated tube of coelomic epithelium. The caudal tips of the Müllerian ducts migrate alongside the mesonephric system towards the urogenital sinus. As they grow they move
medially passing over the mesonephric ducts entering the genital cord. They then bend caudally in close proximity to the contralateral duct reaching the dorsal wall of the urogenital sinus during the third month (Price et al., 1969; Gray's Anatomy 1989). Subsequently in the first half of gestation, the fallopian tubes coil, develop folds and fimbriae. Cilia and secretory cells start to develop in the epithelium in the latter half of gestation (Price et al., 1969).

3A.2. Anatomy of the uterus and fallopian tube

Fallopius and subsequently Henle in 1873 gave some more detail in describing the fallopian tube, and Williams gave an even more detailed description in 1891. In all mammals the degree of convolution of the fallopian tubes varies from being completely straight in rabbits to the extreme convolution found in mares (Nalbandov 1969). The tubes are suspended between the peritoneal layers of the mesosalpinx derived from the broad ligament. The fimbriae embrace the ovary to enable oocyte uptake. Proximal to the fimbriae is the dilated ampulla of the fallopian tube where fertilisation occurs. The ampulla is continuous with the isthmus of the tube. This then leads to the intramural portion of the fallopian tube to join the endometrial cavity. The body of the uterus lies in the mid-plane of the pelvic cavity with its horns diverging laterally to the left and right. The uterotubal junction is the area of transition between the uterus and the fallopian tube (Beck and Boots, 1974) (Figures 3.1-2).
Figure 3.1  Diagrammatic representation of the uterus demonstrating the angle of approach required to cannulate the tubal ostia.
Figure 3.2 Position of uterus, fallopian tube and ovary. Gray's Anatomy (37th Edition, 1989).
3A.2.1. Anatomy of the uterotubal junction and intramural fallopian tube

The uterotubal junction is the part of the fallopian tube which blends with the uterine cavity. In mammals Beck described ten morphological variants (Beck and Boots 1974). The uterotubal junction of humans is distinguished by the lack of mucosal projections present throughout the rest of the fallopian tube as high, multibranched, longitudinal folds. Humans have a simple uterus with a long intramural part of the fallopian tube traversing the thick myometrium of the supero-lateral aspect of the uterus. The fallopian tubes enter the uterine cavity at an oblique angle via a funnel shaped orifice.

The intramural fallopian tube was initially described to have a straight course (Rubin, 1928), but this was subsequently disputed (Sweeney, 1962; Pauerstein, 1974). The intramural fallopian tube is narrow at the uterotubal junction being 0.1mm to 4mm in diameter (Rubin, 1928; Sweeney, 1962; Hafez and Black, 1969; Nilsson and Reinius, 1969). Dickinson in 1916, who cited reports by Testut from 1895, and Poirer and Charpy from 1907 remarked upon this narrow diameter:

Testut (1895):

"the inner opening of the tube scarce permits the introduction of a boar's bristle".
Poirer and Charpy (1907):

"the ostium uterinum measures about 1 millimeter and is impossible to catheterize in the living...and even difficult to see in the dead."

Hafez and Black (1969) reported that an oviductal papilla surrounding the mouth of the oviduct was a frequent finding, and that distal to this within the intramural fallopian tube there were one or two vascular rings accompanied by muscle bundles which may act as a sphincter.

Sweeney performed the largest study of the intramural portion of the fallopian tube in 1962. He felt that it was a part of the oviduct that had previously received scant attention. He described the findings of previous authors. For instance, Hermstein and Neustadt (1924) and Geist and Goldberger (1925) had found at the time of hysterosalpingography on extirpated uteri that the intramural fallopian tube was often curved but more commonly convoluted (cited by Sweeney 1962).

Rubin refuted this description in 1928, finding by *in-vivo* hysterosalpingography that the intramural portion of the fallopian tube was straight in almost all cases (Rubin 1928). To explore this further, Sweeney dissected out the interstitial portion of 100 fallopian tubes and found that 8 had a curved course, 23 had a straight course, and 69 had a tortuous course. The length of this portion of the
fallopian tube ranged from 1 to 3.5cm, and from 2 to 4mm in diameter (Sweeney 1962).

3A.2.1.1. Light microscopy of the intramural fallopian tube

Hafez and Black in 1969 described the diameter of the intramural fallopian tube as 2 to 4mm with usually a constriction to 0.1mm. The mucosa had primitive folds shaped from a star to a ‘H’ shape. The histology of the mucosa was described as transitional, between that of the endometrium and the columnar epithelium of the fallopian tube. They also found that endometrial epithelium may persist in the intramural fallopian tube.

Eddy and Pauerstein in 1983 described the mucosal lining of the tubal lumen as consisting of an epithelial layer lying on the lamina propria, surrounded by 3 muscular layers, with a diameter down to a minimum of 0.1mm. The lamina propria consisted of loose connective tissue, interspersed with numerous blood vessels and lymphatic channels within a collagen matrix. The epithelium of the intramural portion of the fallopian tube was made up of predominantly ciliated and some secretory cells. Other cells consisted of ‘peg’ cells, depleted secretory or ciliary cells, and basal cells, which may be the precursors of epithelial cells. These authors also described the epithelium here as transitional in nature. With regard to potential tubal sterilisation they stated that to deliver a chemical
substance to cause tubal occlusion a very high distension pressure would be
required to overcome the narrow diameter of the fallopian tube. Indeed Rubin in
1925 had reported that a distension pressure of 180-200mm Hg was required to
force gas through the uterotubal junction before or at menses whereas the figure
was 80-100mm Hg after menses. Eddy and Pauerstein (1983) described a
physiological sphincter at the uterotubal junction as a circle of blood vessels
around the narrow lumen, which either due to congestion or contraction of the
perivasular muscle fibres resulted in constriction of the tubal lumen. Another
mechanism of lumen closure is contraction of the inner longitudinal muscle fibres
resulting in acute angulation.

Merchant et al. in 1983 examined the uteri of 75 women who had undergone
hysteroscopy and hysterosalpingography prior to hysterectomy for dysfunctional
uterine bleeding. The extirpated uteri were examined by naked eye inspection of
the uterotubal junction and subsequently by light microscopic examination. The
course of the intramural portion of the fallopian tube was straight, arched or
convoluted and ranged from 5 to 14mm in length (mean 8mm). The diameter of
the 'pit' at the entrance to the fallopian tube was 0.5 to 1.5mm. Light microscopic
examination demonstrated that the endometrial funnel of the uterine cornu was
surrounded by decreasing thickness of uterine musculature on all sides. At the
uterotubal junction the mucosa abruptly changed to a tall columnar epithelium
with or without cilia in 67% of cases, and a transitional epithelium in 28% or
remained endometrial in 5%. This part of the fallopian tube is unique in that there is an inner longitudinal layer of muscle (David and Czernobilsky, 1968; Nilsson and Reinius, 1969; Pauerstein et al., 1970; Blaundau 1978), without an intervening lamina propria, surrounded by an outer circular muscle layer (Merchant et al., 1983).

Rocca et al. in 1989 examined the anatomical course of the intramural segment of the fallopian tube by injection of latex into ten uterine specimens as well as histological examination of a further ten specimens. The intramural segment of the fallopian tube was S-shaped but not in same plane. The length of the intramural portion of the fallopian tube was calculated to be 9 to 17mm (mean 10mm). The authors also described a transitional epithelial layer at the uterotubal junction and reported that the mucosal folds were 'star' shaped.

Crow et al. reported that the fallopian tube undergoes cyclical changes in the epithelium with the menstrual cycle analogous to that in the uterus, although there was no specific mention of the uterotubal junction (Crow et al., 1994).

3A.2.1.2. Vascular supply and lymphatic drainage of the fallopian tube

The arterial blood supply of the fallopian tube is derived from the uterine and ovarian arteries. Normally the uterine artery supplies the medial two-thirds of the
fallopian tube and the interstitial portion of the fallopian tube, the remainder being supplied by the ovarian artery. Although there is great anatomical variation the uterine artery and its branches anastomose with the ovarian artery in the mesosalpinx to supply the cornu of the uterus and fallopian tube (Figure 3.3). Commonly at the cornu of the uterus, the uterine artery branches to supply the cornu and interstitial portion of the fallopian tube.

The uterine artery then divides again into the isthmic branch, supplying the medial portion of the fallopian tube and the ovarian branch to anastomose with the ovarian artery (Hafez and Black, 1969; Beck and Boots 1974; Pauerstein 1974). Previous reports in the literature have given different accounts of the fallopian tube blood supply; for instance, Sweeney in 1962 described the interstitial portion of the tube as being supplied by the ovarian artery.

Of relevance to methods of tubal ligation is the fact that one report stated that some women only have one artery supplying the entire fallopian tube (Borell and Fernstrom, 1953). The venous drainage of the fallopian tube is generally stated to follow the arterial blood supply, draining into the internal iliac veins (Woodruff and Pauerstein 1969) (Figure 3.4).

The lymphatic drainage of the fallopian tube is into three lymphatic networks draining the mucosa, muscularis and serosa respectively. After emerging from
this system within the fallopian tube these vessels combine, entering the mesosalpinx and ultimately draining into the para-aortic nodes (Beck and Boots 1974) (Figure 3.5).
Figure 3.3  Blood supply to uterus and fallopian tube. Gray's Anatomy (37th Edition, 1989).
Figure 3.4 Venous drainage of the fallopian tube via uterine veins to the internal iliac vein. Gray's Anatomy (37th Edition, 1989).
Figure 3.5 Lymphatic drainage of the pelvis. Gray’s Anatomy (37th Edition, 1989).
3A.2.1.3. Nervous innervation of the fallopian tube

The nervous innervation of the fallopian tube is from both the sympathetic and parasymathetic systems. The sympathetic nervous supply is derived from T10 to L2 with some pre-ganglionic fibres terminating in the inferior mesenteric ganglion and others in the hypogastric plexus. These then synapse with post-ganglionic fibres that are conveyed through the uterovaginal plexi to supply the proximal portion of the fallopian tube. Other pre-ganglionic fibres synapse in the renal, aortic and coeliac plexi sending post-ganglionic fibres through the ovarian plexus to supply the ampulla of the fallopian tube. Afferent visceral fibres run with sympathetic nerves to T11-L2. Parasympathetic nervous innervation of the proximal tube is derived from S2-4 by short post-ganglionic fibres from the pelvic plexi, whereas the distal portion of the tube is innervated by from the vagus nerve via the ovarian plexus. The circular musculature of the isthmic portion of the fallopian tube is richly innervated with adrenergic nerve terminals (Pauerstein 1974, Beck and Boots 1974).

3A.3. Physiology of the intramural portion of the fallopian tube

Due to the arrangement of muscle fibres, the fallopian tube is capable of peristaltic, antiperistaltic and segmental contractions, which propagate in opposite directions over short distances (Eddy and Pauerstein 1983). The peak
of contractility occurs at around the time of ovulation when the oestrogen level is maximal, and at the time of menstruation. At both of these times the progesterone levels are at a minimum, progesterone having an inhibitory effect on smooth muscle contractility (Nakanishi and Wood, 1968).

3A.4. Effects on uterotubal junction of various drugs

It has been known for a long time that up to 20% of patients with uterotubal occlusion seen at hysterosalpingography may have functional as opposed to actual anatomical blockage of the fallopian tube, a fact Rubin described as early as 1928. Nakanishi and Wood in 1968 demonstrated that the isthmus of the fallopian tube might act as a physiological sphincter. Adrenergic stimulation of the fallopian tube causes contraction and β receptor stimulation causes muscular relaxation. The profound contractile response to nervous and autonomic stimulation, together with the abundance of adrenergic nerve terminals in the isthmus led the authors to conclude that this area of the fallopian tube may act as a physiological sphincter (Nakanishi and Wood, 1968). They also reported decreased activity in the pregnant uterus, probably secondary to a progesterone effect, and minimal activity in the postmenopausal uterus. It has been postulated that local prostaglandin release may act as regulators of adrenergic neural activity (Marshall 1973).
3A.5. Trauma and healing of the intramural portion of the fallopian tube

Healing of the epithelium of the intramural portion of the fallopian tube in response to minimal trauma, such as caused by mild chemical or physical injury of a brief duration, is by epithelialisation (healing by first intention). In the case of extensive trauma healing is by secondary intention involving the formation of granulation tissue with resultant defects in the anatomical architecture and poor epithelialisation. This type of trauma is characteristic of the damage caused by corrosive substances or high power electrosurgical injury.

Thermal injury is difficult to induce in view of the very vascular nature of the intramural portion of the fallopian tube, which causes a buffering of the thermal insult (Eddy and Pauerstein, 1983). These authors suggested that intraluminal plugs offer the hope of a reversible method of tubal sterilisation without the need for surgical repair, as very limited damage to the intramural fallopian tube is caused. However, this only applies to plugs that do not generate a fibrotic reaction, such as our tubal screw.

In contrast, intraluminal devices such as the Essure™ pbc, which rely on the ingrowth of fibroblasts, will not ultimately be reversible. Such devices provoke marked disruption of the fallopian tube epithelium and the surrounding smooth muscle, with healing by secondary intention generating granulation tissue and
ultimately fibrosis. If plugs that require the generation of this chronic inflammatory and fibrotic response are removed the cornu will be extensively damaged, with a substantial risk of a subsequent cornual ectopic pregnancy and its attendant high morbidity (Hart and Magos, 1998).

3A.6. Hysteroscopically detected uterine abnormalities

Of particular relevance in the women about to undergo a method of hysteroscopic tubal occlusion is the incidence of uterine abnormalities, as this has the potential to prevent the correct application of tubal plugs. For instance Cooper et al. in 1983 reported an incidence of 13% of uterine abnormalities in women seeking hysteroscopic sterilisation, as opposed to the much higher incidences reported at hysteroscopy for symptomatic indications. In this series of 323 cases 41 abnormalities were detected, which prevented successful plug application in 18 instances (5.6%) (Cooper et al., 1983).
3B. Studies performed to derive the deflection required to cannulate the tubal ostia

3B.1. Introduction

To effectively perform hysteroscopic tubal sterilisation by occlusion of the uterotubal junction it was initially important to derive the degree of deflection required from our operating hysteroscope in the longitudinal axis of the uterus, to direct the tubal plug towards the laterally sited tubal ostia. To this aim we used hysterosalpingography, which is a recognised technique to assess the shape of the uterine cavity and fallopian tubes by contrast radiography (Williams 1891). The first study was a review of the hysterosalpingograms of 25 patients to derive the deflection required for hysteroscopic tubal screw application. The second study involved performing hysterosalpingograms on extirpated uteri, to see if these results could be validated in the in-vitro setting. The third study was to perform ultrasound scans on 25 women, without uterine abnormalities, to describe the normal uterine anatomy in parous women, and to see if the angle of approach to the uterotubal junction could be derived.
3B.2. Methods

3B.2.1 Study 1. Review of normal hysterosalpingograms

100 consecutive hysterosalpingogram reports were sought using the hospital X-ray reporting system. The first 25 hysterosalpingograms that were reported as normal by a consultant radiologist were studied. A normal hysterosalpingogram was defined as the absence of any uterine or tubal filling defect and the presence of bilateral spill of dye through the distal ends of the fallopian tubes.

Each patient had several sequential X-ray films taken during hysterosalpingography screening process. The two films that had the best definition of uterine shape and demonstrated bilateral fill and spill of contrast were used. The angle of insertion of each fallopian tube to the cornu of the uterus was calculated, as described in Figure 3.6, and this was repeated for the second hysterosalpingogram so as to give two readings for each side. A line was drawn along the main axis of the uterus and a line was drawn from the cornu of the uterus (along the axis of the proximal fallopian tube) so as to bisect this line. This provided the angle of deflection required to cannulate the fallopian tube.

The four readings for each patient were averaged to give a mean figure for each patient. This was performed in order to reduce any influence of the uterus being deviated to one side and an incorrectly drawn uterine axis (Figures 3.7-8).
Figure 3.6  Schematic representation of measurements performed on hysterosalpingogram to gauge required deflection for uterine cornual access.
Figure 3.7 Uterus deviated to right.
Figure 3.8 Uterus deviated to right with incorrect uterine axis drawn.
3B.2.2. Study 2. Hysterosalpingograms performed on extirpated uteri

Seven uteri were pinned to a dissecting board after hysterectomy. The X-ray table was tilted $30^\circ$ to simulate uterine ante- or retroversion of $-30^\circ$ or $+30^\circ$. The radiological contrast media was instilled into the uterine cavity using a Leech-Wilkinson catheter. Two X-ray projections were performed, and the length and transfundal width of each uterus was measured, as was the angle of approach to the uterine cornu along the axis of the fallopian tube, as previously described (Figure 3.9).
Figure 3.9  Hysterosalpingogram on extirpated uterus. (Poor projection as background is radiolucent and uterus has many fibroids)

Consecutive parous women referred for pelvic ultrasound examination to investigate dysfunctional uterine bleeding were assessed for the presence of uterine pathology. Recruitment continued until 25 normal pelvic sonograms were available for assessment. These pelvic sonograms were examined to determine mean cavity dimensions for these anatomically normal parous uteri (Figure 3.10).
3.10 The uterine cavity ultrasound measurements.
3B.3. Results

3B.3.1. Study 1. Review of normal hysterosalpingograms

The hysterosalpingograms of the first 25 patients reviewed were all adequate for assessment. One hundred readings were performed and the results recorded. The mean angle of deflection required to cannulate the tubal ostia was calculated to be $67.6^\circ$ with 95% confidence intervals $60.8^\circ$ to $74.4^\circ$ (Table 3.1-2 and Figures 3.11-12).
Table 3.1 The angle of deflection required for perpendicular approach to the uterine cornu derived from reviewing old hysterosalpingograms.

<table>
<thead>
<tr>
<th>Case Number</th>
<th>Right cornual angle 1st reading (°)</th>
<th>Right cornual angle 2nd reading (°)</th>
<th>Mean of right cornual reading (°)</th>
<th>Left cornual angle 1st reading (°)</th>
<th>Left cornual angle 2nd reading (°)</th>
<th>Mean of left cornual reading (°)</th>
<th>Mean of cornual readings (°)</th>
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<td>79.8</td>
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Table 3.2  Statistics for the angle deflection required for access to the uterine cornu.

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<th>Value</th>
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<td>25% Percentile</td>
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<td>95% confidence intervals</td>
<td>60.8 - 74.4°</td>
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<td>Kolmogorov-Smirnov Normality Test</td>
<td>P &gt; 0.10 (Distribution is Gaussian)</td>
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</table>
Figure 3.11 Plot representing the angle of deflection required to approach uterine cornu.

- Right cornu
- Left cornu
Figure 3.12 Scatter of cornual angles as measured by reviewing old hysterosalpingograms.
3B.3.2. Study 2. Hysterosalpingograms performed on extirpated uteri.

Seven uterine specimens underwent hysterosalpingography immediately after hysterectomy; only seven were performed, as the results were so markedly different from the *in-vivo* analysis (Tables 3.3-5 and Figure 3.13). The mean length of the uterine cavity was 8.4cm and the width was 7cm, with a mean weight of 213.9g. The mean angle of deflection required to cannulate the tubal ostia was calculated to be 33.9°, with 95% confidence intervals 28.8° to 39.1°. This difference was significantly different to that derived from the *in-vivo* hysterosalpingograms (p<0.0001) (Figure 3.14).
Table 3.3 Table of uterine specimens used for extirpated hysterosalpingogram assessment.

<table>
<thead>
<tr>
<th></th>
<th>Age of patient (years)</th>
<th>Parity</th>
<th>Day of cycle on day of hysterectomy</th>
<th>Indication for surgery</th>
<th>Current drugs</th>
<th>Uterine length (cm)</th>
<th>Uterine width (cm)</th>
<th>Presence of fibroids</th>
<th>Uterine weight (g)</th>
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<td>-</td>
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<td>-</td>
<td>-</td>
<td>diffuse</td>
<td>143</td>
</tr>
<tr>
<td>5</td>
<td>48</td>
<td>2</td>
<td>2</td>
<td>menorrhagia</td>
<td>NET</td>
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<td>-</td>
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<td>nil</td>
<td>8.5</td>
<td>8</td>
<td>no</td>
<td>125</td>
</tr>
<tr>
<td>mean</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>8.4</td>
<td>7.0</td>
<td></td>
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NET norithesterone
TA tranexamic acid
Table 3.4  The angle of deflection required in extirpated hysterosalpingogram assessment.

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<tr>
<th>Case Number</th>
<th>Right cornual angle 1&lt;sup&gt;st&lt;/sup&gt; reading (°)</th>
<th>Right cornual angle 2&lt;sup&gt;nd&lt;/sup&gt; reading (°)</th>
<th>Mean of right cornual readings (°)</th>
<th>Left cornual angle 1&lt;sup&gt;st&lt;/sup&gt; reading (°)</th>
<th>Left cornual angle 2&lt;sup&gt;nd&lt;/sup&gt; reading (°)</th>
<th>Mean of left cornual reading (°)</th>
<th>Mean of right and left cornual readings (°)</th>
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<td>27</td>
<td>27.5</td>
<td>30.5</td>
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<td>27.0</td>
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<td></td>
<td>37.6&lt;sup&gt;†&lt;/sup&gt;</td>
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<sup>†</sup>Difference non-significant using paired T-test.
Table 3.5  Statistics for the angle deflection required for access to the uterine cornu performed on extirpated uteri.

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<td>75% Percentile</td>
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<tr>
<td>95% confidence intervals</td>
<td>28.8 -39.1°</td>
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</table>

Kolmogorov-Smirnov Normality Test  \( p > 0.10 \) (Distribution is Gaussian)

Difference from in-vivo Hysterosalpingograms  \( p=0.0007 \) (up-paired Student T-Test)
Figure 3.13  Graph showing the distribution of the angle of deflections required to approach the uterine cornu as demonstrated by hysterosalpingography on uterine specimens immediately after hysterectomy.
Figure 3.14. The difference in angle of deflection required comparing *in-vivo* hysterosalpingograms of subfertile women and hysterosalpingograms performed on extirpated uteri.

Difference from *in-vivo* hysterosalpingograms \( p < 0.0001 \) (up-paired Student T-Test)

The mean length of the uterine cavity from the 25 examinations was 5.0cm (95% confidence intervals 4.6 to 5.4cm) and the mean width of the uterine cavity was 2.8cm (95% confidence intervals 2.4 to 3.1cm) (Table 3.6 and Figure 3.15).

From our ultrasound measurements, the angle of deflection that would be required to approach the uterotubal junction from within the uterine cavity was 16°. This is markedly different from the previous readings derived from the hysterosalpingogram studies. The reason for this discrepancy is that the ultrasound derived reading is the angle required to reach the uterine cornu only, not the angle required for perpendicular cannulation of the tubal ostia and fallopian tube as in the X-ray studies (defined by an arrow in Figure 3.6). This ultrasound-derived figure infers that deflection towards the fallopian tube can commence at the internal os. This reading is useful assuming that the tubal screw and applicator are very plastic in nature, to bend sharply along the path of the fallopian tube. Whereas in practice, the important angle to be derived is that angle which would provide for perpendicular cannulation of the fallopian tube to enable the tubal screw to be inserted along the intramural fallopian tube without the risk of uterine perforation. In view of the firm nature of the tubal screw and application cannula described in Chapter 4 these readings were therefore not thought to be clinically useful for the purposes of our study and were discounted.
Table 3.6  Morphological measurements of uteri as made by ultrasound assessment, in parous women with dysfunctional uterine bleeding.

<table>
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</table>
Figure 3.15  Plot of uterine morphological measurements.

- Cavity length
- Cavity width

Mean cavity length 5.0cm
Median length 5.0cm
95% confidence intervals 4.6 - 5.4cm

Mean cavity width 2.8cm
Median cavity width 2.8cm
95% confidence intervals 2.4 - 3.1cm
3B.4. Discussion

The ideal way to assess the angle of insertion of the fallopian tube into the uterine cornu, without dissection and distortion of the uterine anatomy, would be external cannulation of the intramural part of the fallopian tube. However the intramural portion of the fallopian tube is tortuous in up to 69% of cases (Sweeney, 1958; Sweeney, 1962; Merchant et al., 1983; Rocca et al., 1989) and consequently a false passage would be created on insertion of a firm sound. The use of a viscous polymer injected under pressure to form a cast of the uterus was also felt to likely to cause distortion of the cornu of the uterus and consequently hysterosalpingography was used as it is dynamic process which was felt to be the most reliable technique.

The results derived from the in-vivo and in-vitro hysterosalpingograms were markedly different (67.6° and 33.9°). The explanation for this difference could be the fact that the uteri were different in morphology, in that the in-vivo uteri were normal whereas the hysterectomy specimens were by definition abnormal. For instance it is known that a normal premenopausal parous uterus weighs on average 104.1g (Langlois, 1970), whereas the mean weight of the extirpated uterine specimens was 213.9g. Current gynaecological practice has led to a move away from hysterectomy as a first line treatment for menorrhagia. Medical management is tried first then less invasive solutions to excessive menstrual loss
exist, such as the levonogestrel releasing intrauterine contraceptive device, endometrial resection and other methods of endometrial destruction (Hart and Magos, 1997). Another explanation of the differences in the readings between the in-vivo and in-vitro studies could be that the myometrium of the extirpated uteri contracts as soon as it is removed from the patient distorting the uterine anatomy, leading to a false reading in the in-vitro setting.

An error in the measurement in the in-vivo study may have been introduced due to rotation around the long axis of the uterus. Such rotation would artificially reduce the angle of deflection required to cannulate the tubal ostia (see Figure 3.16). However, it is usually evident from the appearance of the fallopian tubes if there is a major degree of uterine rotation, in which case most radiologists would tilt the X-ray table to minimise this effect and optimise the view. Marked uterine anteversion or retroversion would also introduce an artefactual alteration in the angle of deflection required to approach the tubal ostia (see Figure 3.17), however this also is usually corrected by the radiologist by gentle traction on the cervix during hysterosalpingography. Consequently the figure derived from the in-vivo study of hysterosalpingograms, 67.6° C, was thought to be reliable and a more useful result than the in-vitro derived reading.

As discussed previously, the important angle to be derived is that angle which would provide for perpendicular cannulation of the fallopian tube hence we felt it
reasonable to discount the data obtained after ultrasound examination (Figure 3.18). Hence based on our clinical experience, we believe that a deflection angle of 60° to 70° off the midline is the more realistic. Logically, the appropriate angled hysteroscope for a sterilisation procedure should therefore be a 70° endoscope. However, as is discussed in the following chapter, due to the natural human instinct to point the instrument at the intended target, as well as difficulties with visualising the endocervical canal during insertion of the hysteroscope, use of a 30° endoscope was preferred for inserting the tubal plugs.

Previous measurements of the uterine dimensions have been performed. Langlois (1970) reported on 1348 hysterectomy specimens. Only 468 specimens met the criteria for analysis, of which 30 were nulliparous and 53 were over 50 years of age. Of the 173 women who had delivered 2 or 3 children, the mean uterine weight was 104.1g (standard deviation 36.0g). The external uterine dimensions of women aged 30 to 39 years (parity not mentioned), were 9.4 cm by 5.7 cm for length and width respectively. This uterine length measurement was similar to our findings at the time of hysterosalpingogram on the extirpated uteri (8.4cm). However the transfundal width of the uteri was much greater in our patients, presumably due to the much greater size of the uteri removed in our group (214g vs 104g), which is a reflection of changing gynaecological surgical practice.
If uterus is rotated along its long axis angles ‘a’ and ‘b’ become ‘a’ and ‘b’ respectively.

Figure 3.16 The effect of rotation of the uterus reducing the apparent deflection required to cannulate the tubal ostia by artefact.
Figure 3.17 Demonstration of the projection of the hysterosalpingogram. The cornual angles subtended from the mid-line are dependant on the degree of uterine anteversion.
Figure 3.18 Using the ultrasound study the angle of deflection that would be required to approach the uterine cornu is $16^\circ$. 
Platt et al in 1990 also reported uterine ultrasound measurements of 52 parous women pre-hysterectomy. The readings taken were of 8.9cm for mean uterine length and 5.8cm for width. To confirm that these were normal uteri they were subjected to histopathological analysis. Another study reported these respective measurements to be 8.9cm by 5.6cm with a mean weight of 100g (Flickinger et al. 1986). However in both these studies measurements were taken from the uterine fundus to the external os of the cervix and across the uterus at the widest diameter, whereas our measurements were of the endometrial cavity, which we felt to be the most important dimensions when considering hysteroscopic sterilisation. Of relevance to all these studies is the fact that uterine size is significantly greater in the secretory phase than the proliferative phase (Piironen and Kaihola, 1975) and that uterine size also increases significantly with increasing parity. One study measured the length of the uterine body excluding the cervix in the proliferative phase of the menstrual cycle and derived a value of 4.9cm in 50 women who had delivered 1 child and 5.6cm in 53 women who had delivered 2 or more children. The respective measurements for the width of the uterine body were 4.6cm and 5.1cm (Merz et al. 1996).
3C. Review of the safety of insertion of a PTFE screw

3C.1. Manufacture of PTFE

PTFE (polytetrafluoroethylene) was discovered in 1938 by Dr. Roy Plunkett at the DuPont research laboratories and was first marketed under the DuPont Teflon® trademark in the late 1940s (Tetrafluoroethylene Polymers Patent No. 2,230,654). Dr. Plunkett was working with gases related to refrigerants and upon checking a frozen, compressed sample of tetrafluoroethylene, he discovered that the sample had polymerised spontaneously into a white, waxy solid to form polytetrafluoroethylene (Encyclopaedia Britannica 2000). PTFE is an extremely stable plastic material that is waxy and soft. It is an organic polymer with a molecular weight between 500,000 and 2,000,000 Daltons. It has the lowest coefficient of friction of all the plastics, and is highly crystalline (>94%). The polymer has a low tensile strength (17-28 MPa) and a low surface tension (18.5 ergs/cm²). It is formed upon treating tetrafluoroethylene with oxygen (see Figure 3.19). The monomer is made by heating chlorodifluoromethane at about 600°-750° C. Teflon is inert to all solvents and chemicals reagents and is only attacked by molten alkali metals and by fluorine at high temperatures. It is capable of withstanding continuous exposure to extremely low temperatures and it begins to depolymerise above 600°C. These extreme thermal properties allow it to be used to act as a heat shield for spacecraft entering the earth’s atmosphere from
space. Due to the very strong carbon-fluorine covalent bonds, it is resistant to chemical attack and it is even used to store sulphuric acid (Dewan, 1992). As PTFE is a tough, non-flammable material, it is also widely used for electrical insulation. As its coefficient of friction is extremely low and it shows the effect of self-lubrication, PTFE is widely utilised in gaskets, bearings, linings for containers and pipes, and parts for valves and pumps that must operate in corrosive environments and for protective coatings on cooking utensils, saw blades, and other articles. It may be shaped by compression and sintering (heating to a temperature sufficient to cause the particles to adhere to each other without actually melting) into bottles and beakers where its chemical stability and non-wettability make it suitable for use in extreme circumstances (see Figure 3.20). Medical uses are diverse, ranging from arteriovenous grafts to mandibular prostheses.
Figure 3.19 Creation of polymer polytetrafluoroethylene (PTFE) from tetrafluoroethylene.
The fluorine atoms of PTFE prefer their own kind, drawing to each other, while repelling any other kind of molecule, like this water molecule, for example.

Figure 3.20 Demonstration of the non-stick and non-wettability properties of PTFE which is used in medicine as an inert implant.
3C.2. Medical applications of PTFE

The uses of PTFE in medicine are diverse. It is commonly used in radiology as a vascular stent (de Giovanni, 2001; Cartes-Zumelzu et al., 2002) and in cardiovascular surgery both as a vascular graft (Umana and Mitchell, 2002; Strozzi et al., 2002) and as a heart valve, where it can be used for infants with pulmonary atresia (Sahoo et al, 2001) as well as in adults (Turrentine et al., 2002). PTFE prosthesis can even be used to occlude the left atrium in patients with atrial fibrillation who are suffering with recurrent pulmonary emboli (Sievert et al, 2002). The material is also used for long-term venous access for patients undergoing dialysis and in palliative care (Ross et al., 2002).

PTFE is used in gynaecology as an injection for female stress incontinence (Yamada et al., 2001) and to reduce postoperative adhesions after laparoscopic myomectomy (Myomectomy Adhesion Study Group, 1995). In urology, PTFE can be injected to treat vesico-ureteric reflux (O'Donnell and Puri, 2002) and as a prosthetic penile implant (Herschorn and Ordonez, 1995). It is used in maxillo-facial surgery as an orbital implant (Kao, 2000), in nasal surgery (Robertson and Dyer, 1999), and as prosthesis in the temporomandibular joint (Raphael et al., 1999). PTFE is licensed in the USA by the Food and Drug Administration as a dental prosthetic agent (FDA1987).
PTFE is used in head and neck surgery as a middle ear implant, as a prosthetic stapes (Kwok et al., 2001), and as an implant in laryngeal surgery (Herman, 2002). In plastic surgery of the face, PTFE can be used to augment the lips (Linder, 1992) and is a protective cover for the skin after a burn (Martin et al., 1990).

PTFE is used in orthopaedics as a joint replacement (Kurtz et al., 2000) and it has been used as an artificial ligament (Fukubayashi and Ikeda, 2000).

3C.3. Toxicology of PTFE

3C.3.1. Acute inflammatory response to PTFE exposure

Generic PTFE is listed as product classifications number 872.3680 (Polytetrafluoroethylene, PTFE, vitreous carbon material). With regard to the toxicology of PTFE, the U.S. Department of Health and Human Services, part of The United States Food and Drug Administration, studied the toxicological effect of particulate matter produced by mechanical trauma to PTFE implants (1998). The scientists developed an in vitro assay using established murine macrophages. This assay system was incorporated into an ASTM (American Society for Testing and Materials) standard on the Biological Responses to Particles (F04.16.01). In the in vitro studies, murine macrophage cells were
exposed to particles of PTFE with and without bacterial lipopolysaccharide, which is a component of bacterial cell walls that mimics bacterial infections. The cells were then evaluated for cytotoxicity, production of nitric oxide, tumour necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), both of which are inflammatory cytokines. Nitric oxide is induced by lipopolysaccharide and is critically important in eradicating micro-organisms associated with infections, but it can also be harmful by causing tissue injury and vascular collapse. The in vitro studies showed that TNF-α was induced by PTFE but did not stimulate IL-6 or nitric oxide production. Also for licensing in The United States, all implants are tested for the presence of endotoxin by the Limulus Amebocyte Lysate test as endotoxin is a pyrogen and can stimulate fever in a host. The particulate PTFE studied in these tests was free of endotoxin. In conclusion PTFE was shown to have a limited ability to provoke an acute inflammatory response.

3C.3.2. Chronic inflammatory response to PTFE exposure

The risk of a chronic inflammatory process developing with the use of PTFE is low as PTFE is biologically and chemically inert and was reported as producing no acute or chronic inflammatory response when left in the peritoneal cavity of dogs for up to six months, as far back as 1949 (LeVeen and Barberio, 1949), although at six months a mild fibroblastic reaction was reported around the implant. A further report in 1957 of various plastic materials reported that a very
mild acute and chronic inflammatory reaction was provoked around implants of PTFE left in the subcutaneous tissue of dogs for six months, but that the reaction was less than that provoked by Dacron, Ivalon, Nylon or Orlon and that after being implanted for ten months the strength of the PTFE was not reduced (Harrison, et al., 1957). However, there are rare reported cases of the development of chronic inflammatory granulomas. A lesion peculiar to PTFE after vocal cord injection is the ‘Teflonoma’, which is caused by extravasation of the Teflon and infiltration into the soft tissues of the neck and larynx. This produces a mass that clinically simulates a malignant lesion. Dedo and Carlsoo reported the association of Teflon injections with the later development of a granulomas in 1982. Subsequently Wenig et al., reported eight cases of “Teflonomas” of the larynx in 1990. The authors made their diagnosis by fine needle aspiration or by excision of the suspicious mass and subsequent identification of a foreign body granulomatous reaction. Infrared absorption spectrophotometry identified the foreign material as a fluorocarbon, which was further, substantiated by scanning electron microscopy and energy dispersive X-ray analysis. Surgical removal of the mass alleviated all symptoms.

It has also been reported that PTFE can migrate from the original site of implantation. Claes et al., reported a case of clinically significant migration of PTFE paste particles to the lungs after periurethral injection to treat urinary incontinence. These particles were confirmed and identified as PTFE by
polarised light microscopy. These authors were so concerned about this case that they counselled against using this paste in children or young adults with a normal life expectancy (Claes et al., 1989). Solid PTFE (cf. paste) can also migrate, and there have been reports of a small piece of the PTFE from an artificial heart valve becoming detached and embolising to the lungs (Weingarten and Kauffman, 1997).

However, these are rare reports. Plastic surgeons, for instance, perceive the risk of an inflammatory reaction and subsequent fibrous reaction to be exceedingly low, and they widely employ both expanded solid PTFE, Teflon, (as used in our tubal screw) and the microporous form of PTFE, Gore-Tex, for facial surgery. They believe PTFE to be 'the most bioinert material available' (Ellis and Cousin, 2000). In support of this, PTFE is used as an anti-adhesion barrier as prevents fibrous tissue forming (Myomectomy Adhesion Study Group, 1995).

3C.3.3. Allergic response to PTFE exposure

No case of an allergy to PTFE has ever been reported despite its wide use throughout medicine and indeed PTFE is used in the creation of allergen barriers to cover bedding and is marketed along with titanium as the ideal body-piercing material for someone with multiple allergies. The International Agency for Research on Cancer report that the polymer has not been found to produce skin
irritation or act as an allergic agent. (1972a).

3C.3.4. Carcinogenecity in humans after PTFE exposure

Despite the wide application of PTFE in medical practice over many years, for instance PTFE has been used for over fifty years in the field of urology with no documented risk of malignant transformation (Dewan, 1995), there are only rare case reports linking PTFE with malignancy (Lewy, 1976; Montgomery, 1982; Hakky et al., 1989). Montgomery described a fibrosarcoma adjacent to a aortic graft implanted 10 years previously (Montgomery, 1982), Hakky et al., described a patient who developed a chondrosarcoma of the larynx secondary to a PTFE implant six years previously (Hakky et al., 1989), and similarly Lewy described a single case of development of carcinoma adjacent to the site of laryngeal injection for vocal cord paralysis in a series of 1139 patients (Lewy, 1976). In contrast, other authors reported no malignancies detected in their series of 100 patients followed-up for ten years (Arnold and Stephens, 1980). The International Agency for Research on Cancer report a 31-year-old man who developed a fibrosarcoma 10.5 years after implantation of a Dacron - PTFE graft. (1972b).

With regard to PTFE injections at other sites and the risk of malignant transformation, Politano (1991) in the United States reported no malignant transformation in 10,000 patients treated for urinary incontinence by PTFE
injections since 1964. An argument that may be used to counter this claim is that some of the PTFE implants are put inside patients who are either seriously ill or have a relatively short life expectancy such as patients requiring vascular grafts, hip replacements or treatment for urinary incontinence. In these patients, a long-term risk of developing a malignancy may never manifest. However, PTFE implants have also been used for over thirty years in children with vesico-ureteric reflux, and a recent review of the world literature found that PTFE 'has not been found to cause any malignancies in humans' (Puri, 2000). However some surgeons have counselled against this use until clear evidence of its safety has been established (Dewan, 1992). However the evidence of risk of malignant transformation is less clear with relation to the use of PTFE where there is expected to be a degree of mechanical movement, such as in an articulating joint (Dewan, 1992).

3C.3.5. Carcinogenicity in animals after PTFE exposure

Animal studies of relevance to the carcinogenic risks of PTFE have involved development of fibrosarcomas in 12.5% of Swiss mice after incubation with a sheet of PTFE for 54.5 weeks, similar to control mice treated with a glass cover slip (The International Agency for Research on Cancer, 1972c). In similarly treated Wistar rats, intraperitoneal PTFE produced no local tumours over their
lifetime, although two of the 17 rats treated with intraperitoneal PTFE powder developed sarcomas. The International Agency for Research on Cancer has performed a further five studies of subcutaneous implants of PTFE in mice of different species and reported the risk of developing a sarcoma as high as 94% in some mice. Their conclusion for evidence of carcinogenicity in humans is that there is no adequate data available for a clear conclusion and they believe the agent is not classifiable as to its carcinogenicity risk in humans as there is inadequate evidence as to its effect in animals (The International Agency for Research on Cancer, 1987). The conclusion of this group was that they recommend follow-up over the long term of patients with PTFE implants.

3C.3.6. Environmental exposure to PTFE

With regard to ingestion of PTFE, rats fed a diet of 25% PTFE for 90 days demonstrated no signs of toxicity (International Agency for Research on Cancer, 1979b). PTFE does react to elevated temperatures and indeed if heated to around 400°C will release toxic chemicals as it starts to break down. These toxic chemicals are also released during its manufacture and consist of difluorophosgene, perfluoroisobutylene and hydrofluoric acid (Bischoff, 1972). Consequently rodents housed in a room with PTFE died from haemorrhagic lung disease caused by these toxic products (Harris, 1951; Truffett, 1958 cited by Dewan). A similar effect toxic has also been reported in human as 'polymer fume
fever’ (Harris, 1951; Robins and Ware, 1969; Williams et al., 1974; Brubaker, 1977; Haugtomt and Haerem, 1989). There have been a few instances of pulmonary oedema in patients who smoked cigarettes contaminated with PTFE particles (American Conference of Governmental Industrial Hygienists, 1980). It is believed that these harmful breakdown products of PTFE are present in very small quantities within the finished PTFE product at the time of manufacture and it is these products that are released upon heating to cause the lung disease, which can present with ‘flu-like’ symptoms. It has been suggested that these particles present within polymers may have a carcinogenic effect on cells (Bischoff, 1972). However it is thought more likely that it is the mechanical irritation caused by the implant rather than the substance per se that is the cause of potential malignant transformation (Oppenheimer et al., 1958).

3C.4. Potential complications related to tubal screw insertion

3C.4.1. Short-term complications

The short-term risks of the insertion of the PTFE implant include the risk of uterine perforation, haemorrhage and infection. The risk of uterine perforation was thought to be low as the insertion of the tubal screw was to be under direct view, although we knew from other techniques of hysteroscopic sterilisation that uterine perforation can occur. For instance, Essure™ pbc has been shown to be
associated with a uterine perforation rate of 1.5%, although as with other
techniques of hysteroscopic sterilisation such patients are managed
conservatively (Valle et al., 2001; Kerin et al., 2001). The risk of haemorrhage
was thought to be exceedingly rare as there are no reports of this complication
from other techniques of fallopian tube cannulation (Risquez and Confino, 1993).
The short-term risk of infection was thought to be remote, similar to the case with
women undergoing hysteroscopic surgery; as an additional precaution, all our
patients were to be treated with a prophylactic broad spectrum antibiotic such as
Co-amoxiclav 1.2g (amoxycillin trihydrate and clavulinic acid) intravenously at the
time of induction of anaesthesia, providing the patient had no sensitivity to
penicillin (Hart and Magos, 1997). The risk of an allergic reaction to the PTFE
was thought to be very rare, as previously discussed.

3C.4.2. Long-term complications

An inflammatory response to PTFE is rare, as mentioned previously, and indeed
PTFE is an ideal material for a screw that could potentially be removed thus
reversing the sterilisation. To facilitate re-canalisation of the fallopian tube after
screw removal, the amount of fibrous tissue and granulomatous material at the
uterine cornu must be minimal. It is also important with regard to tubal screw
retention that the inflammatory process is minimised. The greater the degree of
chronic inflammation causing disruption of the local tissue architecture, the less
likely is the tubal screw to remain at the uterotubal junction through traction on the surrounding muscle fibres. This would be manifest in early and late tubal screw expulsion and potentially tubal screw migration into the myometrium or peritoneal cavity. There also exists the potential to develop a ‘Teflonoma’ (Dedo and Carlsoo, 1990) at the site of screw insertion although almost certainly the development of such a degree of chronic inflammation would lead to early plug expulsion prior to the development of such a granuloma. Evidence from the urological injection of PTFE suggests that the risk of any long-term complication is remote. For instance Puri and Grenata (1998) reported on the treatment of 8332 children treated with up to 13 years of follow-up and stated that there were ‘No clinically untoward effects as a result of the use of PTFE as an injectable material were reported in any patient.’

The possibility of tubal screw migration exists as it does with other methods of sterilisation such as the Filshie clip. There are various reports of migration of Filshie clips, and they have been found in a femoral hernia (Garner et al., 1998), the urinary bladder (Kesby and Korda, 1997), the vagina after a vaginal hysterectomy (Buckett et al., 1998), and in an inguinal abscess (Scheel-Hincke and Berendtsen, 1994). Migration is however not synonymous with the restoration of fertility as the sterilisation itself usually remains effective because of damage and fibrosis to the fallopian tubes. In contrast, it is likely that with our inert tubal plug effecting sterilisation by the mechanical occlusion of the fallopian
tube with minimal fibrosis, screw migration would result in loss of efficacy. This is unlike with the Essure™ pbc where the chance of plug migration is low as the method of sterilisation is by obliteration of the fallopian tube by the in growth of fibroblasts, a process which may take up to 6 months in some cases (Valle et al., 2001; Kerin et al., 2001).

Another potential side effect of tubal screw insertion, particularly at the time of concurrent Filshie clip application, is the development of a hydrosalpinx. There are reported cases of the development of hydrosalpinges between two occlusive clips placed to ensure complete occlusion of a fallopian tube (Frishman and Brest, 1992; Shinde et al., 1976). However, a recent article appears to refute this suggestion (Chi, 1994). Chi analysed a multi-centre database of women undergoing Hulka and Filshie clip application and could find no increased risk of pelvic pain or complications in those women who had two clips applied to ensure effective occlusion of a fallopian tube, although follow-up was only for one month after the procedure. Another possible complication in women undergoing concurrent Filshie clip application at the time of tubal screw insertion is the development of a haematosalpinx. This complication could arise as endometrial tissue has been reported to exist in the intramural portion of the fallopian tube (Hafez and Black, 1969; Eddy and Pauerstein, 1983; Merchant et al., 1983). This could result in cyclical shedding of endometrium and the development of a haematosalpinx, which could cause discomfort. An analogous situation is the
occurrence of haematosalpinx in women who have been sterilised and subsequently undergo endometrial resection. In such circumstances the incidence of cyclical pelvic pain and haematosalpinx has been reported as high as 8.4% (Bae et al., 1996; Webb et al., 1996). If this complication arose in patients after combined Filshie clip plus tubal screw sterilisation, then it should be possible to remove the tubal screw hysteroscopically in most cases (although as described in Chapter 7 we were unable to remove the plugs in one patient). Ultrasound examination is a potential way to monitor for the development of either a haematosalpinx or a hydrosalpinx. Although no such collections were observed at the time of interval ultrasonography in our patients, this complication had not been envisaged, and consequently was not sought at the time of ultrasound examination, and unfortunately our patients were not counselled regarding this risk pre-operatively.

The risk of infection caused by the insertion of the PTFE implant was expected to be very low in view of its record in medicine without any reports of infection. It was also felt likely that if infection did occur the tubal screw would inevitably become dislodged from the uterotubal junction and be expelled vaginally.

3C.5. Teratology of PTFE

There are no reports in the literature as to the teratology of PTFE despite its wide use in medicine and its use to prevent adhesions in women trying to conceive. It is recognised that no other PTFE prosthesis would be in such close proximity to the developing fetus as the tubal screw. Patients who conceived after screw insertion should be warned of the lack of evidence as to the safety of PTFE.
Figure 3.21  The medical uses of PTFE.
In conclusion, there is expected to be an exceedingly low risk of allergic reaction related to the insertion of the PTFE tubal screw, and the risk of infection is predicted to be low. The potential for developing an inflammatory reaction exists, however PTFE is reported to be the most inert polymer implant. The risk of developing a malignancy is expected to be exceedingly low as there are no documented malignancies in humans attributed solely to PTFE, although the International Agency for Research on Cancer advise that more long term follow-up studies are performed (1987). There are no studies as to the teratogenecity of PTFE.

3C.6. Toxicology of titanium

The titanium bayonet through the base of the PTFE tubal screw is inert and will not provoke an allergic reaction, an inflammatory response or be a potential carcinogen as it extensively used in medicine and indeed is the base metal used in the Filshie clip. Studies on experimental animals as well as human clinical studies have shown that titanium in implants and prostheses is non-toxic and extremely well tolerated by osseous and soft tissues. This is shown by lack of irritation, normal wound healing, and encapsulation of the metal by fibrous tissues (Browning, 1969; WHO Working Group, 1982; Friberg et al., 1986; Flood and Hobar, 1995; Bianco et al., 1996).
3.2. Conclusion

This chapter described the anatomy of the uterotubal junction and derived the angle required for cannulation of the tubal orifice with the PTFE tubal screw. It also addressed the past and current uses of PTFE and its toxicology in humans. The literature review suggests that the use of PTFE as an implant is safe, although it does conclude that despite its use in medicine for over 50 years there have been very few long-term studies to confirm this safety.

The studies to derive the angle of approach to the uterine cornu demonstrated that in the in-vivo setting the angle of approach required to cannulate the uterotubal junction was between 60.8° to 74.4°, which was statistically different from that derived in the in-vitro setting. Consequently the use of extirpated uteri would be a poor model for the testing of application process of the hysteroscopically applied tubal screw. The development of the tubal screw application system must consequently be able achieve substantial deflection from the uterine axis to place the screw at the tubal ostia. The screw applied must also have an effective method of remaining in situ.
Chapter 4

Developmental changes in the design of the tubal screw and insertion system.
4.1. Introduction

As described for over 100 years gynaecologists have been attempting to develop a transuterine approach to achieve sterilisation using chemicals, glues, sclerosants, thermal energy, cryocautery, electrocoagulation, laser energy and several different tubal plugs. Despite over a century of innovation and refinements to many techniques the final success rates have been unsatisfactory. As described in Chapter 2 various plugs have been developed but have not usually been retained with time, either due to relaxation of the circular smooth muscle at the uterotubal junction or due to the body's innate ability to expel foreign bodies. This is despite various ingenious techniques employed to overcome the poor retention rate. Unfortunately none have been consistently successful which has led to the persistence of laparoscopic approaches as the optimal route to achieve sterilisation (Sokal et al 2000).

Consequently it was expected that the first choice of plug and application system would not become immediately successful at occluding the uterotubal junction and that further refinements would be required, indeed the Femcept system was altered 14 times (Bolduc et al., 1983).

4.2. Development of the instrumentation and equipment

To facilitate hysteroscopic tubal sterilisation the insertion of a mechanical device into the uterotubal junction presented several practical design problems; these were addressed and refined during the development process:
1. The device (tubal screw)
2. The hysteroscope/cystoscope
3. Hysteroscopic applicator for the screw
4. Mounting of the tubal screw on applicator
5. Adequate uterine distension
6. Sufficient deflection to position the screw by the tubal ostia
7. Application of screw into tubal ostia
8. Disimpaction of applicator from tubal screw following insertion

4.2.1. The tubal screw

The diameter of the intramural portion of the fallopian tube is very narrow and tortuous, with a maximum diameter 4mm (Rubin, 1928; Sweeney, 1962; Hafez and Black, 1969; Nilsson and Reinius, 1969). Potentially only 0.1mm at the uterotubal junction (Nilsson and Reinius, 1969) but more recently the diameter of the ‘pit’ at the entrance to the fallopian tube was reported to be 0.5 to 1.5mm (Merchant et al., 1983). The intramural portion of the fallopian tube is between 10 to 35mm in length (Sweeney 1962; Risquez and Confino, 1993) with a convoluted course with up to 69% being tortuous (Sweeney, 1962; Rocca et al., 1989). Eddy and Pauerstein (1983) suggested that intraluminal plugs offer the hope of a reversible method of tubal sterilisation without the need for surgical repair. They believed that they cause very limited damage to the intramural fallopian tube, although this is an incorrect assumption for tubal plugs that cause fibrosis such as Essure, as previously discussed.

Previous plugs of pertinence to the development of the tubal screw were
designed by Sugimoto in Japan (1974), Craft (1976), Hosseinian et al. (1976), (Brueschke et al., 1977), Droegemueller et al. (1978). As these authors used a tubal plug with varying degrees of success, with diameters varying from 1.2mm to 2.2mm and from 7mm to 12mm in length, and with different methods of securing the plug in place. Sugimoto (1974) developed a device 10mm long and 1.2mm in diameter with notches every 1.5mm to prevent expulsion and the plug had to be grasped for removal. To insert the plug it was mounted in a Teflon tube and was dislodged by a wire plunger. The results of this technique as reported in chapter 2 were reasonably successful and had some similar features to our tubal screw.

From the fallopian tube measurements above we decided that the maximum diameter of the tubal screw should be approximately 3mm to ensure that this would guarantee occlusion of almost all uterotubal junctions. The method by which the screw was designed to effect tubal sterilisation was for the screw to block the fallopian tube at the uterotubal junction and be retained in position by traction on surrounding muscle fibres. As the screw is 15mm long (only 10mm is actively used) then any fallopian tubes that were not completely blocked at the uterotubal junction would be occluded more distally.

4.2.1.1. The original tubal screw

Adam Magos developed the hysteroscopically applied tubal screw (British Patent Application no.980634.7) in 1996 (Figure 4.1). Its design was based on a 'self-tapping' screw with a backward pointing thread enabling it to grip
the surrounding tissue preventing it from being pulled out. The prototype, made out of polytetrafluoroethylene (PTFE), was 15mm long and 3mm in diameter at the broadest point (Figure 4.2). The tubal screw was made of polytetrafluoroethylene (PTFE), a strong, tough, waxy, non-flammable resin, which has a remarkable chemical resistance and has been used extensively in medicine for over 50 years.

The initial prototype tubal screw (Figure 4.1) had a hole at its proximal end in its base for insertion of a suture to facilitate the in-vivo weight study described in Chapter 6.

Over the duration of the study period the tubal screw underwent some minor changes, however these were not always intended as there were occasional quality control problems in the manufacture of the tubal screw. For instance, case number 2 (Chapter 6, table 4) in the weight study to assess strength of application of in-vivo applied tubal screws, where the screws were both very blunt. Consequently when they were applied to the tubal ostia, which as previously described is usually much smaller than the diameter of the tubal device, they were very difficult to screw into place.

As will be described later the disimpaction of the tubal screw was a difficult problem to address, and hence to facilitate delivery of the hysteroscopic screw to the tubal ostia further alterations were required.
Initial design of tubal screw

Figure 2: Screw-in device

Figure 4.1 The original tubal screw developed by Adam Magos (British Patent Application no.980634.7)
Figure 4.2  The hysteroscopic tubal screw British Patent Application no.980634.7.
4.2.1.2. Change of base of tubal screw to a cylindrical structure

The initial tubal screw base was square in cross-section to provide for screw removal if required. It was felt that the easiest and fastest method to remove the screws would be to use hysteroscopic-grasping forceps and to ‘un-screw’ the device. This technique was required for case number 3 (Chapter 6, table 6.2) in the weight study, to assess strength of application of in-vivo applied screws, as the patient declined to have the screws retained until the end of her hysterectomy. The tubal screw removal by this technique was technically very difficult due to the requirement for precise positioning of the forceps around the screw base. Then the plug was ‘un-screwed’ which was difficult as the PTFE has excellent properties to prevent a firm grip.

With the forced alteration in the applicator cannula to a circular coil (as will be described later in the chapter) the base of the tubal screw was changed to a cylindrical structure so as to fit within its coils. This led to concerns regarding the potential difficulty of tubal screw removal if necessary, which therefore required a further change.

4.2.1.3. A reverse screw thread in the base of the tubal screw

As the tubal screw base was changed to a cylindrical shape it was essential that a potential method of screw removal be developed. Therefore a nozzle was placed on the applicator cannula (see Figure 4.3). It was also evident
that the tubal screw should be mounted on the applicator loosely and a means to hold it in place for easy plug disimpaction was required.

To this end a reverse screw thread was scored into the cylindrical base of the plug and mounting on the applicator (Figure 4.3). Hence as the tubal screw is screwed into place at the uterotubal junction it should be held fast in the mounting. To disimpact the tubal screw a reverse screw action was performed to release the plug. Despite very successful practice in-vitro (not reported) it was unsuccessful in-vivo (this design of screw was used in cases 18-21 in the simultaneous laparoscopic and hysteroscopic plug application as described in Chapter 7).
Figure 4.3  A reverse screw thread scored into base of the tubal screw which is mounted on the applicator with a screw thread.
4.2.1.4. The use of a PTFE ‘finger-like’ projection on applicator mounting

To prevent the difficulty encountered with a reverse screw thread of disimpacting the tubal screw, a prototype screw and mounting were developed with a 'male-female' connection system. To hold the screw loosely it was felt that a finger projection on the mounting would allow for easy disimpaction of the plug. To facilitate a rotational torque being applied to the tubal screw the PTFE was scored in a hexagonal shape in cross-section with a corresponding area cutout of the base of the screw (Figure 4.4).

When this prototype system was developed it was tested with the entire application system but the screw was too loosely mounted and would consequently become dislodged in the application process. Hence it could not be applied correctly at the uterotubal junction and this system was not therefore tested in the in-vivo setting.
Cross-section of base of tubal screw. This area cut-out

Coiled applicator → Base of tubal screw

'finger-like' projection into base of screw

Figure 4.4 Hexagonal PTFE mounting on applicator and corresponding recessed area in base of tubal screw.
4.2.1.5. The use of a titanium rod, through the base of the screw, as a locking-pin.

The final innovation of the tubal screw was developed due to the difficulty in disimpacting the tubal screw employing the reverse screw thread. A fine titanium rod was passed through the PTFE plug which then rested very loosely in the applicator mounting (Figure 4.5). It was prevented from becoming dislodged by a locking mechanism in the mounting on the applicator. During the insertion of the plug to the uterotubal junction the screwing action held it fast in place in the mounting. To disimpact the screw a twist of the mounting enabled the mounted plug to become easily detached (Figure 4.6).
Figure 4.5 Tubal screw with titanium bayonet mounted on coil applicator.
Figure 4.6 Diagrammatic representation of plug in applicator showing bayonet pin locking mechanism.
4.2.2. The hysteroscope / cystoscope

4.2.2.1. Modified single channel 7mm operating hysteroscope (Rimmer Brothers, London)

The initial system we employed to deliver the tubal screw to the uterotubal junction was by using a modified single channel 7mm operating hysteroscope (Rimmer Brothers, London) using saline as the distension medium. The hysteroscope employed was a 4mm 30° telescope (Karl Storz, Tuttlingen, Germany). The indication for the use of a 4mm scope was to provide a good panoramic view of the fundus and the cornua of the uterus. To place the device at the uterotubal junction lateral deflection away from the midline was required; consequently it was felt appropriate to use a 30° optic. To minimise the dilatation of the cervix that would be required but to maximise fluid delivery only a single channel was used in the manufacture of the hysteroscope. To improve uterine distension a 2.9mm hysteroscope was tested although the view was in fact not as good. To improve visualisation of the tubal ostia 15° and 70° endoscopes were tested. As was evident from the extirpated uterine hysterosalpingograms, performed in Chapter 3, the angle of deflection from the axis of the operating hysteroscope required to approach the tubal ostia was approximately 60°. Both 15° and 70° endoscopes were initially tried along with the frequently used 30° hysteroscope. The view from the 15° hysteroscope was unsatisfactory as would be expected. The 70° hysteroscope would be expected to provide the best view of the tubal ostia,
however due to the natural tendency to ‘point’ the hysteroscope towards the tubal ostia the $30^\circ$ endoscope provided for the best view (Figure 4.7). Consequently the hysteroscope that was employed for initial tubal plug applications in both the in-vivo weight (case 1) and the histology studies (cases 1-4) was the modified single channel 7mm operating hysteroscope with a $30^\circ$ optic (Rimmer Brothers, London) (Figure 4.8). It was also used in the study involving concurrent laparoscopic sterilisation cases 7 and 9-13.
Figure 4.7 Demonstration of the field of view with the $15^\circ$ and $70^\circ$ lens optical hysteroscopes, however with the natural tendency to 'point' towards the area being treated the $30^\circ$ hysteroscope was favoured.
Figure 4.8  The original Rimmer Brothers modified single channel hysteroscope.
The benefit of this operating hysteroscope was that it was a single channel hysteroscope. This allows the maximal amount of space to be used for fluid irrigation to provide for maximal uterine distension, however there were three problems with this system.

1. *Excessive fluid leakage*

The first problem that was encountered with the Rimmer operating hysteroscope was that there was no effective seal or valve to prevent leakage of the distension fluid prior to the loading of the applicator cannula. Due to the lack of this valve there was also continual fluid leakage during the entire procedure, leading to poor uterine distension and consequently a poor view of the tubal ostia was obtained. Therefore a conventional cystoscope was used due to the presence of a valve to control the operating channel preventing excessive fluid leakage.

2. *Inability to alter the required deflection of the applicator cannula*

As it can be seen from Figures 4.9 and 4.10 the deflecting bridge at the distal end of the operating hysteroscope is fixed. In the design of the system it was felt that this would not be a problem as from Chapter 3 it was demonstrated that the deflection for tubal occlusion is relatively consistent. However it was evident during the experiments that a greater deflection than was possible by Rimmer Brothers' operating hysteroscope was required.
Figure 4.9 The fixed deflector at the distal end of the Rimmer hysteroscope.
Figure 4.10 Distal end of the Rimmer hysteroscope with PTFE cannula and tubal screw demonstrating the fixed deflector.
Despite the modifications to this hysteroscope that were employed below (see; sufficient deflection to position the plug by the tubal ostia) the results of tubal screw application were poor and consequently a method by which the angle of deflection could be varied was sought. The conventional cystoscope has a built in variable deflection bridge and was therefore used for further experiments.

3. Requirement for repeated repair of attachment of operating channel with hysteroscope

As the operating hysteroscope described was made of a single channel the joint of the accessory channel and the sheath for the hysteroscope was a point of weakness. This joint was re-welded on several occasions, which eventually led to distortion of the hysteroscope and it was therefore superseded by a cystoscope.

4.2.2.2 Urological cystoscope

Due to the difficulties encountered as described with fluid leakage and the inability to alter the angle of deflection to approach the tubal ostia, a 25 French gauge operating urological cystoscope was used. It was used for cases 1-8 and 14-35 in the concurrent laparoscopic sterilisation study (Chapter 7) and cases 2-5 and 5-10 in the in-vivo histological assessment and weight study respectively (Chapter 6).
The operating urological cystoscope was very effective as it had a variable deflector to alter the path of the cannula as it approached the tubal ostia. The drawback with this system was that it did not allow for good cornual distension as it has two operating channels which hence limited the flow rate of the saline. At times the deflecting bridge was inadequate at achieving the required deflection and an extra deflector was employed (see below). There was also the practical problem in that the operating channel of the urological cystoscope was narrower than that of the original Rimmer hysteroscope, which was noted, in case 2 of the in-vivo weights study (Chapter 6). Hence the application cannula was altered to fit down the operating channel (see below).

4.2.3. Hysteroscopic applicator for the tubal screw

4.2.3.1. PTFE cannula

Initially, the tubal screw was mounted on a tight-fitting PTFE cannula through which a flexible metal push-rod could be passed; to displace the screw once in situ as described in Chapter 4. To prevent sudden loss of fluid via this cannula, after the screw had been disimpacted, the proximal end of the cannula was plugged. To screw the device into place, the cannula on which the tubal screw was mounted was rotated through $360^\circ$ seven times until the screw thread was completely buried in the target tissue (Figures 4.11 - 4.12).
Figure 4.11 Tubal screw mounted on distal end of PTFE cannula with push-rod for disimpaction.

Figure 4.12 Original green PTFE cannula demonstrating water tight seal of push-rod at proximal end to enable disimpaction.
4.2.3.2. Portex tubing © SIMS Portex Limited

With time it became evident that although the PTFE cannula was very flexible allowing adequate deflection, it was very fragile. Therefore an alternative flexible tubing was sought. Portex tubing, (© SIMS Portex Limited, Hythe, United Kingdom), a strong, flexible, latex based tubing, was thought to be suitable. It is used widely in medicine for respiratory tubing, internal transducers and epidural catheters. This tubing was used for cases 1-4 in the weight study and 5-7 in the histological assessment study (Chapter 6) (Figure 4.13). Unfortunately this tubing was relatively inflexible and hence directing the cannula to the tubal ostia was difficult. It also lacked the friction free properties of the PTFE cannula hence rotation of the tubing was difficult. Although the results achieved with this tubing were relatively successful, a different technique was felt to be required.
Figure 4.13 Rotation of the Portex tubing by seven $360^\circ$ rotations (© SIMS Portex Limited) after placement of the screw at the tubal ostia.
As we had now developed a precise way to provide adequate and accurate placement of the tubal screw at the uterotubal junction, it became evident that a further problem existed. The problem was that although the cannula carrying the screw could be bent to the requisite angle to apply the plug to the uterotubal junction, if it was then subsequently rotated to screw it into position, then the application cannula described an arc. That is a small proximal rotational torque applied proximally at the hysteroscope/cystoscope is amplified distally to describe a large arc (Figure 4.14).

The concern with this effect is that the large distal arc would cause marked disruption of the uterotubal junction, and consequently disruption of the screw thread in the myometrium, leading to poor plug retention. A method to limit this large arc was sought.
Figure 4.14  Demonstrating that a proximal small rotational torque when applied to a curved cannula is amplified distally to describe a large arc.
4.2.3.3. Altering operating channel of hysteroscope to limit rotation

A channel was scored in the outer sheath of the hysteroscope, at the point where the delivery system exits the sheath, to prevent the cannula describing an arc (Figure 4.15). This was unsuccessful in limiting the arc distally and it also decreased the deflection of the cannula and was therefore discontinued. This scored operating channel was only used for case 10 of the concurrent laparoscopic sterilisation study (Chapter 7).
Figure 4.15 Scoring in outer sheath of hysteroscope.
4.2.3.4. Coiled applicator

After several bench tests it became evident that the way to circumvent this obstacle was to use a coiled applicator cannula to apply the tubal screw (as is seen in Figure 4.3). If a coil is deflected and then rotated it does not describe a large arc but a tight circle. This method of tubal screw application appeared both to provide for an easier screw application at the time of attempted sterilisation, and improved results with regard to screw retention as would be expected with less cornual disruption (Chapter 7).

A rubber outer sheath was applied to the coil to minimise loss of distension fluid (Figure 4.16). But in a subsequent applicator a tighter coil obviated the need for a rubber seal on the outside to prevent fluid leakage.
Figure 4.16 The coil with rubber casing to prevent fluid leakage.
4.2.4. Mounting of the tubal screw on applicator

As has been previously described there were several forced changes in both the tubal screw and the application cannula. In summary the screw mounting changed from a square base on the PTFE and subsequently Portex tubing, to a cylindrical based screw. The cylindrical base tubal screw was initially placed in the end of the coiled applicator (cases 14-17 in Chapter 7), then mounted with a 'male-female' connector manner, then with a reverse screw thread and finally with an un-locking mechanism. The main reason for these changes was due to the difficulty in displacing the tubal screw from the end of the cannula.

When the tubal screw was placed at the end of the cannula (irrespective of the method) it was always loose but when the device was screwed into the tubal ostia it was inevitably held firmly. This was a further result of deflecting the cannula from its axis (see Figure 4.17).

When the screw had been screwed into place the natural elasticity of the cannula led to the cannula pressing very firmly on the lateral aspect of the tubal screw base as it attempted to return to its original axis prior to deflection. This pressure on the tubal plug equated to a frictional force preventing the plug and cannula from separating. This force was minimised by the use of a very loose fitting 'un-locking' mechanism as described.
Figure 4.17 Demonstration of the lateral frictional force generated by the natural elasticity of the application cannula.
When the coiled cannula was first employed this frictional force was at its greatest as this method required a push-rod to displace the tubal screw from the distal end. As the push-rod pressed on the base of the screw to disimpact it this caused elongation of the applicator coil. This led to a reduction in the diameter of the coil causing the screw to be held with an increasing frictional force (see Figure 4.18).
Tubal screw resting in spring

Spring applicator in resting position

Push-rod

Spring applicator now stretched by push-rod

Before attempted disimpaction

After attempted disimpaction with elongated spring and narrower diameter coils

Figure 4.18 Demonstrating the effect of using a coil mounting to hold the tubal screw.
4.2.5. Adequate uterine distension

4.2.5.1. Standard hysteromat pump

As in any hysteroscopic surgery there was a requirement for uterine distension to enable visualisation of the endometrial cavity and particularly to ensure adequate distension of the uterine cornu. There was no requirement for electrosurgery; hence an electrolyte solution could be used. 0.9% saline is physiological, cheap and frequently used in diagnostic hysteroscopy and was thought to be the most appropriate choice. The first method of delivery of the solution was via a standard hysteromat pump (Hamou Hysteromat, Karl Storz) (cases 1-3 of the concurrent laparoscopic sterilisation study, Chapter 7) (Figure 4.19). This pump, which typically has a setting of 300 mls/min at an intrauterine pressure of 120 mmHg (O'Connor and Magos, 1996) for hysteroscopic surgery, was not able to maintain adequate uterine distension due to the large amount of fluid escaping from the system notably around the cervix. The points of fluid leakage were, as in any hysteroscopic surgery, around the cervix and through the operating channel of the hysteroscope. However the leakage around the cervix was greater using our modified operating hysteroscope than in conventional surgery as in cross-section it was intentionally made oval in shape. This was to minimise the need for cervical dilatation required for the procedure. As the external cervical os of most multiparous women appear oval in shape, it was felt that this shape was the most appropriate (Figure 4.20).
4.19 Standard Hamou Hystromat.
Figure 4.20 Leakage of distending fluid around the oval diameter of the hysteroscope as compared to the conventional hysteroscope.
But in practice all patients needed cervical dilatation, which was performed by Hegar dilators, which are circular in cross-section which left a large potential space for fluid leakage. There was further fluid leakage around the seals of the operating channel of the hysteroscope and application cannula due to the high uterine distension pressure required to visualise the tubal ostia (Figure 4.21). This was exacerbated after tubal screw disimpaction, as a jet of saline would pass up the application cannula (Figure 4.22).
Fluid escaping around the seals

Figure 4.21 Leakage of distending fluid around rubber seal to the operating channel of the hysteroscope.

As the screw is disimpacted the distending fluid pours into the application cannula

Tubal screw

The push-rod

Figure 4.22 Distension fluid pours into the application cannula after the screw is disimpacted and out of the operating channel of the hysteroscope.
4.2.4.2. Continuous pressure variable flow hysterosmat pump

To improve uterine distension by overcoming the multiple points of fluid leakage a continuous pressure variable flow pump was used, infusing saline at a distending pressure of 200mmHg (Litechnica Statflo Liquid infusion system) (Figure 4.23). This pump was used in cases 4-15 in the concurrent laparoscopic sterilisation study.

This system was more satisfactory as the pump worked rapidly to overcome the multiple points of fluid leakage to sustain an adequate intra-uterine pressure. Although this was better, we were concerned about this very high intra-uterine pressure and consequently the risk of fluid over-load.
Figure 4.23 Litechnica Statflo Liquid infusion system.
4.2.5.3. Three litre pressure-bag

In view of the concern of fluid overload due to the high distension pressure, the system was simplified to use a 3-litre bag of 0.9% saline and a 3-litre pressure cuff (VBM Medizintechnik GMBH, Germany) (Figure 4.24). This irrigation system had larger diameter tubing than was possible to use with the previous pump; hence a greater flow rate of saline was possible. As this was also in effect a constant pressure, variable flow system, it gave better control over uterine distension and produced adequate distension of the cornu of the uterus for insertion of the device and remained our preferred method of irrigation. This system was used in cases 16-18 and 20-35 in the concurrent laparoscopic sterilisation study.
Figure 4.24 The 3 litre pressure bag - the preferred method of uterine distension. VBM Medizintechnik GMBH, Germany.
4.2.5.4. Carbon dioxide hystroflator

Carbon dioxide, CO$_2$, does not enable endometrial debris to be displaced from the field of view as effectively as the flushing effect of a liquid distension medium. It is an excellent modality for diagnostic hysteroscopy but is seldom used in operative hysteroscopy. Therefore CO$_2$ was only used for cases 19 and 20 in the concurrent laparoscopic sterilisation study (Chapter 7) as it provided inadequate uterine distension due to the multiple points of gas leakage.

4.2.6. Methods to deflect the plug towards the tubal ostia

4.2.6.1. Built in deflecting bridge on original operating hysteroscope

The original hysteroscope had a fixed deflecting bridge (Figure 4.9) but as described this was not always adequate to gain the requisite deflection.

4.2.6.2. Use of two separate systems.

This technique relied on the use of a separate deflector and the tubal screw introducer; the operating hysteroscope and application cannula, to effect the required deflection (Figures 4.25 and 4.26). This technique was attempted in case 11.
Figure 4.25 The use of two separate systems to effect deflection towards the tubal ostia. Operating hysteroscope not shown for clarity.

Figure 4.26 The separate deflector used for case 11 in Chapter 7.
Unfortunately this technique was unsuccessful, as it was very difficult to manoeuvre two separate instruments in the limited space of the cervical canal.

4.2.6.3. ‘Trombone outer sheath’ for varying angle of deflection

The aim of this technique was to develop a ‘trombone like-system’ whereby an outer metal sheath was placed around the operating hysteroscope. The extension or withdrawal of the sheath altered the angle of deflection of the application cannula (Figures 4.27, 4.28 and 4.29). Unfortunately the outer sheath led to trauma on the cervix on introduction, spreading debris in the uterine cavity. The tubal screw exacerbated this, as it was now unable to rest inside the sheath of the operating hysteroscope with this system. It was therefore left partially protruding from the hysteroscope causing further cervical trauma on instrumentation. This cervical trauma produced debris in the endometrial cavity leading to poor visualisation of the uterine cornu and this technique was therefore abandoned after being used for case 13 in Chapter 7.
Applicator cannula deflection controlled by 'trombone'

Moveable 'trombone outer sheath' around operating hysteroscope

Pulling the outer sheath back bends the cannula

Fixed deflecting bridge in original single channel operating hysteroscope

Figure 4.27 The technique of altering the angle of deflection with the 'trombone outer sheath'.
Figure 4.28 The 'trombone' outer sheath.

Figure 4.29 The 'trombone' outer sheath overlying the hysteroscope.
4.2.6.4. Techniques that were not tested in the *in-vivo* setting

After the unsuccessful attempt to alter deflection by using the ‘trombone technique’ several other ideas were piloted, although none were tested in the *in-vivo* setting.

4.2.6.4.1. Use of an introducer with 'elastic memory'

Elastic memory is the ability to build into an object a fixed angle of deflection that only becomes evident when it is released from a restraining force. It is a technique used in several specialties in medicine particularly angiography.

The design of this method consisted of the tubal screw mounted on the hollow cannula. The push-rod used to disimpact the plug from the distal end of the cannula had an elastic memory which was held straight whilst inside the operating channel of the hysteroscope. On extrusion of the cannula and push-rod out of the hysteroscope the push-rod would immediately cause the requisite deflection (Figure 4.30). The problem of this technique was that there existed no ability to vary the deflection required. It was also noted that when a push-rod with elastic memory is rotated it also describes a large arc making application of the device difficult.
Figure 4.30 Tubal screw mounted on cannula which adopts a predetermined angle of deflection once extruded from the hysteroscope.
4.2.6.4.2. Use of a 'joy-stick'

This system relied on a lever at the proximal end of the operating hysteroscope, which via a fixed metal rod would act on the deflecting bridge at the distal end of the hysteroscope to alter its angle via a fulcrum (Figure 4.31 and 4.32).

In designing these 'joy-stick' controlled operating hysteroscopes we were essentially describing a cystoscope with an in-built variable deflecting bridge. Therefore rather than build these instruments we used a cystoscope with an added extra deflector to vary the angle of deflection achievable.
Figure 4.31  An active method to alter deflection with a proximal ‘joy-stick’.

Figure 4.32  A passive method to alter deflection with a proximal ‘joy-stick’.
4.2.6.5. Cystoscope with extra deflector

The urological cystoscope has a variable deflecting bridge at the distal end of the operating channel. However it was evident that this deflection achieved was seldom adequate even when using the flexible coil application cannula. Therefore an extra bridge was manufactured that could be placed onto this variable deflector to extend it and hence increase the angle of deflection achieved (Figure 4.33). This extra deflector was used in cases 14-35 in the concurrent laparoscopic sterilisation study in Chapter 7.
Figure 4.33 The extra deflecting bridge attachment on the cystoscope with tubal screw mounted on coiled applicator with rubber outer coating.
4.2.7. Application of screw into tubal ostia

As previously described the screw was carried towards the tubal ostia during these experiments via a PTFE or Portex cannula, a coil with an unlocking mechanism. To effect obstruction of the uterotubal junction for all these techniques the plug was screwed into place by a seven $360^\circ$ clockwise rotations of the application cannula (Figure 4.34, 4.35 and 4.36).
Figure 4.34 Application of the tubal screw to the tubal ostia.
Figure 4.35 The bayonet mounted tubal screw prior to disimpaction after being screwed into place at the tubal ostia.
Figure 4.36 Bilaterally placed tubal screws demonstrating the bayonet mounting of the tubal screws.
The initial method used to disimpact the tubal screw was the push-rod (Figure 4.11), however as described, a consequence of using a coil delivery system to disimpact the screw led only to lengthening of the coil and hence tightening of the grip on the screw (Figure 4.18). Therefore alternative methods to disimpact the screw were tested. These consisted of the 'male-female' connector, the reverse threaded screw and finally the 'un-locking' mechanism of the bayonet mounted tubal screw as described. This final method was rapid, easy to perform for both screw application and removal (4.37).
Figure 4.37 The tubal screw with bayonet mounting enabling easy insertion and disimpaction.
4.3 Discussion

This chapter details the difficulty of developing an effective application system for a hysteroscopically applied tubal screw. As with previous authors we had to alter our method of uterine distension, application system and tubal screw many times to derive our favoured equipment. For instance the Femcept system was altered 14 times during development (Bolduc et al., 1983). The progression of the development of the hysteroscopic tubal screw sterilisation equipment that was tested *in-vivo* is described in Figure 4.38 and figure 4.39.

4.4 Conclusion

In our experience, the system which appeared to be the most efficient for the safe delivery of the plugs into the uterotubal junction consisted of; a pressure bag for uterine distension with saline, a 25 French cystoscope with deflecting bridge, a 4mm 30 degree endoscope and unsealed spring applicator with bayonet mounted screw.
Figure 4.38 Developmental changes in equipment in chronological order

- **Endoscope**
  - Rimmer hysteroscope
  - Cystoscope

- **Distension**
  - Hamou hysteromat
  - Litechnica infusion system

- **Plug**
  - Original plug
  - Circular base of plug

- **Applicator**
  - PTFE cannula
  - Portex cannula
  - Coil applicator

- **Deflection**
  - In-built deflector
  - In-built variable deflector
  - Altered hysteroscope to limit rotation

- **Release**
  - Push-rod disimpaction
  - Plug loosely placed at end of applicator
  - Un-screwing of reverse thread
  - Titanium bayonet in plug base

- **Components**
  - 3 litre pressure bag
  - CO₂ distension
  - 'Male-female' connection
  - Titanium bayonet in plug base

- **Other Notes**
  - Use of separate deflector
  - 'Trombone outer sheath'
  - Detachable bridge on cystoscope
  - Altered hysteroscope to limit rotation
  - Push-rod disimpaction
Figure 4.39 The development of the hysteroscopic plug sterilisation equipment that was tested in vivo.

Key: Indications for changes

- Improve distension
- Improve deflection
- Aid disimpaction

Original modified operating hysteroscope with Hamou Hysteroflator

Cystoscope with added extra deflecting bridge and spring applicator

Same but reverse threaded plug to improve disimpaction

Same but attempt at better uterine distension with CO₂

Use of original hysteroscope with spring applicator cannula with plug resting in distal end

Same with Portex applicator tubing and cut away end replaced

Use of original hysteroscope with hand-held separate deflector

Same with cut away end of operating sheath

Same with high flow hysteroflator

Same with 'trombone system' for deflection

Same but 3L pressure bag for distension and spring wrapped in rubber to decrease fluid leakage and 'bayonet' un-locking mechanism
Chapter 5

\textit{In-vitro} studies of a new tubal screw sterilisation device
5.1 Introduction

As reported in Chapters 1 and 2 there exists a great need for a simple, rapid and effective method of sterilisation. We designed the tubal screw (British Patent Application no.980634.7) 3mm in diameter and 10mm long based on a 'self-tapping' screw. As described in the preceding chapter the diameter of the fallopian tube is 0.1mm-4mm (Hafez and Black, 1969; Nilsson and Reinius, 1969) and is usually tortuous in course (Sweeney, 1962). We believed that a tubal screw of the above dimensions would guarantee occlusion of the fallopian tube.

Prior to embarking on testing the tubal screw in-vivo we aimed to test the 'screw' in-vitro to see if it would remain in-situ at the utero-tubal junction. These experiments were designed to test the strength of the tubal screw when 'screwed' into the uterine cornu.

5.2 Materials and methods

The tubal screw that was developed (Figure 4.2) was modelled on the 'self-tapping' screw. It had a backward inclined thread to ensure that it would dig into the mucosa of the intramural portion of the fallopian tube once it had been screwed into place and hence prevent it becoming dislodged with time. The uteri of 17 patients undergoing hysterectomy for benign pathology were
removed from the operating theatre immediately after surgery. The uteri were weighed, and their length and transfundal width were measured between the two fallopian tubes, they were then incised from the fundus to internal cervical os over the anterior aspect.

The uteri were then placed on a dissecting board and transfixied by several needles (Figure 5.1). They were positioned so as to have the cavity of the uterus and the cornu facing the pulley system.
Figure 5.1  The uterus fixed on board and suture attached to plug.
A 2/0 Prolene suture was passed through the 'eye' of the screw and the screw was screwed in, by means of an applicator (Figures 5.2 and 5.3), into the cornu of the uterus, by rotating the cannula seven times through \(360^0\). The Prolene suture was passed over the pulley and incremental weights were attached to the dependant portion of the pulley (Figures 5.4 and 5.5).
Figure 5.2 The applicator to screw tubal screw in place.

Figure 5.3 The applicator with tubal screw mounted prior to performing in-vitro study.
Figure 5.4 The dissecting board and jig system used in the *in-vitro* weights study
Figure 5.5  Weights attached to the plug suspended by the jig.
After each weight was applied to the pulley five seconds elapsed prior to placing another weight upon the pulley. The weight, which caused the tubal screw to be dislodged from the uterus, was recorded. If the maximum weight was applied and the screw did not become dislodged, then the cornu of the uterus was dissected to ensure that the screw had been correctly placed at the cornu and the weight recorded. After the experiment the uterine specimen was sent for histological analysis, as is normal practice after hysterectomy.

5.3. Results

17 uteri were used for the in-vitro experiment, (Table 5.1) menorrhagia was the most common indication for hysterectomy. Of the women undergoing hysterectomy 16 were parous, seven were in the proliferative phase, six were in the secretory phase and three women were mid-cycle. The mean gestational size equivalent of the uteri was 8 weeks, with a mean weight of 261.6g. Thirty of a possible 34 plug applications were performed, and 28 applications were tested by applying weights (Table 5.2, Figure 5.6). Twenty-one were performed successfully, with nine being applications performed without a clear view of the cornu. In four instances no application of the screw was attempted as the cornu had been damaged at the time of hysterectomy. It was felt that in the majority of cases that the fit of the screw at the cornu was satisfactory, in that it appeared to fit tightly at the cornu.
Table 5.1 Description of uterine specimens used in the in-vitro application study.

<table>
<thead>
<tr>
<th>Case number</th>
<th>Parity</th>
<th>Day of cycle</th>
<th>Indication for hysterecmy</th>
<th>Uterine size (gestation equivalent in weeks)</th>
<th>Uterine length (cm)</th>
<th>Uterine width (cm)</th>
<th>Uterine weight (g)</th>
<th>Presence of fibroids</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4</td>
<td>14</td>
<td>pain + menorrhagia</td>
<td>6</td>
<td>10.50</td>
<td>6.00</td>
<td>188</td>
<td>no</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>16</td>
<td>menorrhagia</td>
<td>6</td>
<td>9.50</td>
<td>5.00</td>
<td>243</td>
<td>no</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>8</td>
<td>menorrhagia + dysmenorrhoea</td>
<td>6</td>
<td>11.00</td>
<td>5.00</td>
<td>150</td>
<td>no</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>8</td>
<td>menorrhagia + fibroids</td>
<td>16</td>
<td>15.50</td>
<td>11.50</td>
<td>602</td>
<td>large fundal fibroid</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>1</td>
<td>endometriosis</td>
<td>10</td>
<td>8.00</td>
<td></td>
<td>270</td>
<td>multiple intramural</td>
</tr>
<tr>
<td>6</td>
<td>2</td>
<td>7</td>
<td>menorrhagia</td>
<td>14</td>
<td>11.50</td>
<td>7.50</td>
<td>250</td>
<td>no</td>
</tr>
<tr>
<td>7</td>
<td>0</td>
<td>21</td>
<td>severe endometriosis</td>
<td>4</td>
<td>8.50</td>
<td>7.50</td>
<td>108</td>
<td>no</td>
</tr>
<tr>
<td>8</td>
<td>1</td>
<td>9</td>
<td>endometriosis</td>
<td>4</td>
<td>8.00</td>
<td>4.00</td>
<td>78</td>
<td>no</td>
</tr>
<tr>
<td>9</td>
<td>4</td>
<td>8</td>
<td>menorrhagia post TCRE</td>
<td>6</td>
<td>11.50</td>
<td>7.50</td>
<td>232</td>
<td>no</td>
</tr>
<tr>
<td>10</td>
<td>2</td>
<td>-</td>
<td>postmenopausal + prolapse</td>
<td>-</td>
<td>5.00</td>
<td>4.50</td>
<td>56</td>
<td>small intramural</td>
</tr>
<tr>
<td>11</td>
<td>0</td>
<td>20</td>
<td>menorrhagia + fibroids++</td>
<td>16</td>
<td>14.50</td>
<td>9.50</td>
<td>1200</td>
<td>throughout</td>
</tr>
<tr>
<td>12</td>
<td>3</td>
<td>21</td>
<td>menorrhagia + fibroids++</td>
<td>10</td>
<td>9.00</td>
<td>7.50</td>
<td>180</td>
<td>sub + intramural</td>
</tr>
<tr>
<td>13</td>
<td>2</td>
<td>4</td>
<td>endometriosis</td>
<td>6</td>
<td>7.50</td>
<td>6.00</td>
<td>110</td>
<td>no</td>
</tr>
<tr>
<td>14</td>
<td>2</td>
<td>26</td>
<td>menorrhagia + dysmenorrhoea</td>
<td>6</td>
<td>9.50</td>
<td>7.00</td>
<td>190</td>
<td>intramural</td>
</tr>
<tr>
<td>15</td>
<td>2</td>
<td>26</td>
<td>menorrhagia</td>
<td>14</td>
<td>12.50</td>
<td>7.50</td>
<td>350</td>
<td>intramural</td>
</tr>
<tr>
<td>16</td>
<td>2</td>
<td>15</td>
<td>menorrhagia</td>
<td>6</td>
<td>9.00</td>
<td></td>
<td>120</td>
<td>submucosal</td>
</tr>
<tr>
<td>17</td>
<td>4</td>
<td>13</td>
<td>prolapse</td>
<td>6</td>
<td>8.00</td>
<td>7.00</td>
<td>120</td>
<td>intramural</td>
</tr>
</tbody>
</table>

**mean (sd)**
- 8 (4.6)
- 9.9 (2.6)
- 6.9 (1.9)
- 261.6 (273.6)

**95%CI**
- (5.6-10.4)
- (8.6-11.3)
- (5.8-7.9)
- (120.9-402.3)

**TCRE** transcervical endometrial resection
**++** multiple numbers of fibroids
Table 5.2 In-vitro application of tubal screw experimental data

<table>
<thead>
<tr>
<th>Case number</th>
<th>Correct application of screw L</th>
<th>Correct application of screw R</th>
<th>Fit of screw L</th>
<th>Fit of screw R</th>
<th>Force required to remove screw L (Newton) *</th>
<th>Force required to remove screw R (Newton) *</th>
<th>Path of screw L</th>
<th>Path of screw R</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>+</td>
<td>-</td>
<td>Good</td>
<td>Good</td>
<td>1.50</td>
<td>2.10</td>
<td>Good</td>
<td>Cut out</td>
</tr>
<tr>
<td>2</td>
<td>+</td>
<td>+</td>
<td>Good</td>
<td>Good</td>
<td>2.00</td>
<td>&gt;5.50</td>
<td>Good</td>
<td>Cut out</td>
</tr>
<tr>
<td>3</td>
<td>+</td>
<td>+</td>
<td>Good</td>
<td>Good</td>
<td>4.00</td>
<td>4.00</td>
<td>Good</td>
<td>Good</td>
</tr>
<tr>
<td>4</td>
<td>+</td>
<td>-</td>
<td>Good</td>
<td>Good</td>
<td>5.00</td>
<td>&gt;5.50</td>
<td>Good</td>
<td>Cut Out</td>
</tr>
<tr>
<td>5</td>
<td>+</td>
<td>+</td>
<td>Good</td>
<td>Good</td>
<td>&gt;6.50</td>
<td>&gt;5.50</td>
<td>Good</td>
<td>Good</td>
</tr>
<tr>
<td>6</td>
<td>-</td>
<td>-/+</td>
<td>Good</td>
<td>-</td>
<td>4.50</td>
<td>- ‡</td>
<td>Cut out</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>+</td>
<td>+</td>
<td>Good</td>
<td>Poor</td>
<td>&gt;6.50</td>
<td>2.00 ‡</td>
<td>Good</td>
<td>Good</td>
</tr>
<tr>
<td>8</td>
<td>-</td>
<td>+</td>
<td>Good</td>
<td>Good</td>
<td>&gt;6.50</td>
<td>6.00</td>
<td>Cut out</td>
<td>Good</td>
</tr>
<tr>
<td>9</td>
<td>-</td>
<td>-/+</td>
<td>Good</td>
<td>-</td>
<td>&gt;6.00</td>
<td>- ‡</td>
<td>Cut out</td>
<td>-</td>
</tr>
<tr>
<td>10</td>
<td>+</td>
<td>-</td>
<td>Good</td>
<td>Good</td>
<td>4.50</td>
<td>&gt;6.50</td>
<td>Good</td>
<td>Cut out</td>
</tr>
<tr>
<td>11</td>
<td>-/+</td>
<td>-</td>
<td>Good</td>
<td>-</td>
<td>- ‡</td>
<td>&gt;4.50 †</td>
<td>-</td>
<td>Cut out</td>
</tr>
<tr>
<td>12</td>
<td>+</td>
<td>+</td>
<td>Good</td>
<td>Good</td>
<td>5.00</td>
<td>3.50</td>
<td>Cut Out</td>
<td>Cut out</td>
</tr>
<tr>
<td>13</td>
<td>+</td>
<td>+</td>
<td>Good</td>
<td>Good</td>
<td>3.50</td>
<td>3.50</td>
<td>Good</td>
<td>Cut Out</td>
</tr>
<tr>
<td>14</td>
<td>+</td>
<td>+</td>
<td>Good</td>
<td>Good</td>
<td>&gt;5.50†</td>
<td>&gt;5.50</td>
<td>Good</td>
<td>Cut Out</td>
</tr>
<tr>
<td>15</td>
<td>-</td>
<td>-</td>
<td>Poor</td>
<td>Poor</td>
<td>#</td>
<td>- #</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>16</td>
<td>+</td>
<td>+</td>
<td>Poor</td>
<td>Good</td>
<td>1.50</td>
<td>3.50</td>
<td>Good</td>
<td>Good</td>
</tr>
<tr>
<td>17</td>
<td>-/+</td>
<td>+</td>
<td>Good</td>
<td>-</td>
<td>- ‡</td>
<td>2.50</td>
<td>Good</td>
<td>Good</td>
</tr>
</tbody>
</table>

(+): Good application of screw as cornua visualised, (-): Blind application of screw, (-/+): Impossible to apply screw
†: At this point the Prolene suture snapped
‡: Cornua of uterus damaged during the hysterectomy
#: Cornua obscured by fibroids

* The gravitational force acting upon the weights applied to the screw is assumed to be 10 m/s² downward force
Figure 5.6  The weight required to dislodge the tubal screw from the uterine cornu after in-vitro application.
In four cases the uterus was too damaged by the hysterectomy and one uterus had too many fibroids for the test to be performed. In 9 cases the force required to dislodge the screw from the uterine cornu exceeded the weights at our disposal and in two instances the force exceeded the tensile strength of the suture, which consequently snapped. Consequently a median figure of the force required to dislodge the tubal screw was impossible to derive, but if the last recorded weight applied was used the median maximum weight applied to the screw was 475g on the left and 425g on the right, overall 450g with inter-quartile range 350-550g (25% percentile to 75% percentile). This overall figure produced a downward force of 4.50 Newton (Figure 5.7)
Figure 5.7 The force required to dislodge the tubal screw from the uterine cornu after in-vitro application. (The gravitational force acting upon the weights applied to the screw is assumed to be $10 \text{ m/s}^2$ downward force).
After the procedure the track left by the tubal screw was explored, or in instances where the screw remained the screw was dissected out. In 16 cases it was felt that the screw passed along the path of the intramural portion of the fallopian tube and in 12 cases after initially passing through the uterotubal junction the screw passed straight into the muscle of myometrium.

5.4 Discussion

This study demonstrated that if it is possible to apply this tubal screw to the cornu of the uterus it could be firmly held in place. It is fixed in place due to the fact that the intramural fallopian tube is very narrow and tortuous; consequently the screw occludes the lumen proximally at the uterotubal junction and is firmly held in place by the nature of the screw gripping the muscle fibres of the myometrium. The main problem encountered with previous methods of hysteroscopic tubal occlusion was that the plugs became dislodged over time. We believe that this device if correctly applied will have a high likelihood of remaining in place.

As these uteri were hysterectomy specimens it was to be expected that there were to be some potential problems with application of the screws to an enlarged and potentially distorted specimen. The mean size of the uteri was 8 weeks gestation equivalent and 53% of specimens had fibroids. One uterus (case 15) had fundal submucosal fibroids making it impossible to see the
cornu, and five cornu were damaged at the time of the hysterectomy rendering them unsuitable for the experiment. However it was still possible to apply the tubal screws to the right uterotubal junction of a uterus weighing 1.2Kg (case 11) and the weight to dislodge it exceeded the tensile strength of the suture. Screws were even applied to a uterus after a transcervical endometrial resection had been performed two years previously.

Several cases were reported to have 'poor fit of the screw'. These poor applications were due to the fact that the cornu was either damaged at hysterectomy (case 7), due to the presence of fibroids blocking the cornua (case 15) or due to a poor application technique (case 16). A correctly positioned screw is lodged in place by a gentle screwing action; the use of excessive pressure will overcome the screw thread generated in the surrounding muscle fibres and effectively push the screw into place. A similar analogy is using a hammer to drive in a screw. As the screw thread in the surrounding muscle is now lost the plug will have a loose fit. Consequently those screws with a 'poor' fit were dislodged easily, as their thread was not gripping muscle fibres, whereas those tubal screws applied in a correct manner were held firmly in place.

This in-vitro experiment demonstrated that the screw if applied correctly in the in-vitro setting is held firmly by the myometrial fibres and that if replicated in-vivo would mean that these screws are unlikely to become dislodged in the
short term. No assumption of long-term retention can be inferred as this depends on in-vivo mechanisms that were not addressed in this study.

5.5 Conclusion

This in-vitro experiment demonstrated that the tubal screw if screwed in place carefully, as opposed to being ‘pushed’ in as in previous sterilisation techniques, is held very firmly in place. However it remains to be seen whether the application of the plugs into the tubal ostia in the in-vivo setting is different, as the myometrial fibres around the intramural part of the fallopian tube may act differently, reducing the screw retention.

The in-vivo technique would also be expected to be very different in the method of application of the screws, as in this current study we were able to screw the tubal device directly into the cornu. In the in-vivo setting we would be applying the screw from the mid-line position of the uterus requiring a substantial degree of deflection.
Chapter 6

*In-vivo* hysterectomy studies of the tubal screw sterilisation device
6.1. Introduction

As we demonstrated in the preceding chapter the tubal screw, in the in-vitro setting, the tubal screw is held very firmly in place if applied correctly. Although the tubal screw appears to perform well on extirpated uteri, the strength of retention may not be repeated in-vivo, as the method of application of the tubal screw is different and the myometrial fibres around the intramural portion of the fallopian tube may react in a different manner in-vivo.

Consequently we aimed to test the tubal screw at the time of hysterectomy and perform either of two experiments:

a) test the strength of the tubal device when 'screwed' into the uterine cornu.

b) test by histological analysis whether the screws were placed in the correct position.

6.2. Materials and methods

Ethical permission was sought and granted for the study from our local ethical practice sub-committee (reference no. 62-96). The patients were fully counselled prior to undergoing the procedure and their consent sought. Two studies were to be performed, the first was to insert the tubal screws
hysteroscopically and then send the uterine specimen for histological assessment to ensure correct placement. The second was to insert the tubal screws hysteroscopically, with a loop of a suture attached, to enable weights to be applied to test for the strength of placement, as performed in Chapter 5.

After anaesthesia and prior to hysterectomy, the cervix was grasped with a volsellum, and then dilated to Hegar 10 and the specially modified operating hysteroscope (Karl Storz, Tuttlingen Germany) inserted (Figure 4.8). The initial equipment used for uterine distension was a continuous pressure, variable flow hysteromat pump, Litechnica Statflo Liquid infusion system, infusing saline at a distending pressure of 200mmHg (Figure 4.23).

With our initial system when the fallopian tube ostium was clearly seen the tubal screw, mounted on the introducing cannula was advanced and screwed into the ostium under direct vision (Figure 6.1).

When the screw thread was buried by the endometrium at the cornua of the uterus, the screw was disimpacted and the hysteroscope withdrawn. The tubal screw was displaced from the end of the introducing cannula by the means of the push-rod (Figure 6.2 and 6.3).
Figure 6.1 A prototype pointed tubal screw approximated to the tubal ostia prior to insertion.
Figure 6.2  The push-rod to disimpact the tubal plug.

Figure 6.3  The push-rod to disimpact the tubal plug close-up.
With time it became evident that changes in the design of the equipment were required, see Chapter 4, and hence the initial equipment described was not used in all the procedures (see Table 6.1).

If the intended procedure was to be either a laparoscopic or abdominal hysterectomy the abdominal cavity was initially visualised via the respective approach prior to commencing the hysteroscopy. A Spackmann cannula was inserted into the cervix and tubal dye hydrotubation was performed with methylene blue. Then the screw insertion was observed from an intrabdominal perspective. After the screws were inserted fallopian tube dye hydrotubation was again performed to assess whether tubal blockage had been achieved. The hysteroscope was then withdrawn and the hysterectomy completed.

After the hysterectomy was completed the uterus either underwent histological assessment to ensure that the tubal screw passed into the intramural fallopian tube or underwent the weight study.
Table 6.1 The histological assessment study to assess correct placement of in-vivo applied screws.

<table>
<thead>
<tr>
<th>Application technique</th>
<th>No. of screws</th>
<th>Histological analysis</th>
<th>Successful application</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Fluid leakage + Push-rod used to disimpact the screw. Insertion visualised laparoscopically, initial fill &amp; spill of dye, post application no fill or spill of dye. Original application system. No uterine perforation.</td>
<td>2</td>
<td>'Uterine weight 95g secretory endometrium, both cornu stripped of endometrium by plugs.'</td>
<td>+ +</td>
</tr>
<tr>
<td>2 Original application system. Excessive leakage around seals, impossible to maintain view and distension.</td>
<td>0</td>
<td></td>
<td>- -</td>
</tr>
<tr>
<td>3 Original application system. New seals used, still large amount of fluid leakage.</td>
<td>2</td>
<td>'Weight 83g proliferative endometrium, tubal devices in lumen of fallopian tube'</td>
<td>+ +</td>
</tr>
<tr>
<td>4 Original application system used on left and conventional cystoscope used on the right.</td>
<td>2</td>
<td>'Weight 78g proliferative endometrium stripped by the plugs which appear at the utero-tubal junction.'</td>
<td>+ +</td>
</tr>
<tr>
<td>5 Use of Portex tubing via conventional cystoscope.</td>
<td>2</td>
<td>'Weight 108g proliferative endometrium, device in lumen at utero-tubal junction sections around the device shows endometrial tissue suggesting neither device reached the fallopian tube.'</td>
<td>(+/-) (+/-)</td>
</tr>
<tr>
<td>6 Use of Portex tubing via conventional cystoscope.</td>
<td>2</td>
<td>'Weight 96g proliferative endometrium, small sub-mucous fibroids, both contraceptive devices were penetrating the myometrium'</td>
<td>- -</td>
</tr>
<tr>
<td>7 Use of Portex tubing via conventional cystoscope.</td>
<td>1</td>
<td>Weight 287g, multiple fibroids, normal endometrium-No comment made on presence or position of plugs</td>
<td>(+/-) -</td>
</tr>
<tr>
<td>8 Use of cystoscope, with coil mounted screw with un-locking mechanism.</td>
<td>2</td>
<td>'Weight 248g, endometrium normal, tissue from around the plugs shows on in the uterine cornu and one in a false cavity by the isthmic portion of the fallopian tube'</td>
<td>+ -</td>
</tr>
<tr>
<td>9 Use of cystoscope, coil mounted screw with un-locking mechanism. Visualised via laparotomy initial fill &amp; spill of dye, post application no fill or spill of dye.</td>
<td>2</td>
<td>'In-situ are 2 plugs running from the uterine cornu to the ostia of the fallopian tubes on both sides, histology demonstrated adenomyosis.'</td>
<td>+ +</td>
</tr>
<tr>
<td>10 Use of cystoscope, with coil mounted screw with un-locking mechanism.</td>
<td>2</td>
<td>'Two plastic plugs in position in the region of the fallopian tube cornu, endometrium normal, endometrium lines part of cavity left by the plugs and the remainder is denuded.'</td>
<td>+ +</td>
</tr>
</tbody>
</table>

+ Successful application
6.2.1. The histological assessment study

After fixing in formalin the uterine cornu were incised around the tubal screw by a histopathologist (see Figures 6.4 - 6.9). The tubal screw was then removed and slices of tissue in this area were inspected under the microscope to assess whether the device was positioned at the utero-tubal junction.
Figure 6.4 Tubal screw in-situ at the uterotubal junction. Note presence of methylene blue around screw suggesting correct placement. Patient 1 in the histological assessment study.
Figure 6.5 Tubal screw at uterine cornu after serial sections have been performed. Patient 1 in the histological assessment study.
Figure 6.6 Uterine cornu incised and tubal screw transected to confirm correct placement by the methylene blue dye and subsequently by histology (with 1cm scale).
Figure 6.7 Patient 2 in the histological assessment study with uterine cornu bisected after screw placement.
Figure 6.8  Patient 2 with close up of uterine cornu.
Figure 6.9  Patient 3 in histological assessment study after bisection of the uterus showing tubal screw at uterine cornu.
6.2.2. The testing of strength of tubal screw application by weights study

The tubal screws that were to be inserted into the uteri intended for the weight test were threaded with a 2/0 Prolene suture before the hysteroscopy to enable weights to be applied via the jig system (Figures 6.10 and 6.11). The uteri of these patients were opened after hysterectomy to perform the weight study as described in Chapter 5.
Figure 6.10 Preparing to perform the weights study on an in-vivo applied tubal screw in the operating theatre.

Figure 6.11 The purpose built weights and their support for the in-vitro and in-vivo weights studies.
6.3. Results

Fifteen patients agreed to undergo the procedure, ten in the histological assessment group (Table 6.1) and five in the weight study group (Table 6.2).

6.3.1. The histological assessment study

At the time of hysterectomy six patients were in the proliferative phase of their menstrual cycle, one patient was in the secretory phase (patient 1), one patient was taking a gonadotrophin releasing hormone agonist (patient 4) and one patient was receiving depot injections of medroxyprogesterone acetate (patient 8). No other patients were using a hormonal method of contraception prior to their admission for hysterectomy.

During the screw application performed on patient 2 there was excessive fluid leakage around all seals in the equipment leading to the cancellation of the procedure and new seals had to be developed. Histological assessment of the remaining nine patients who had tubal screws inserted demonstrated that five had confirmation that they were correctly sited bilaterally. Patient 6 had misplaced screws, patient 7 only had one screw applied due to an obstructing submucosal fibroid (and the location of this tubal screw was unfortunately not commented on by the histopathologist). Patient 8 had one correctly positioned screw and one incorrectly positioned. Patient 5 is marked equivocally in the
results table, although both devices are reportedly at the utero-tubal junction, the pathologist did not feel that the screws went to the fallopian tube due to the presence of endometrial tissue around the tubal screw. As patient 7 is not commented on the success rate of screw application is 11/16 (68.8%). If patient 5 is included the success rate is 13/16 (81.3%).

At the time of hysterectomy in two patients it was possible to view the peritoneal cavity during the hysteroscopic sterilisation to ensure that tubal occlusion had occurred (one laparoscopically assisted vaginal hysterectomy and one abdominal hysterectomy, patients 1 and 9 respectively). In both instances bilateral tubal occlusion was effected by the hysteroscopic tubal screw application, as there was an absence of peritoneal spill of methylene blue dye after hydrotubation.

The screw and applicator system underwent several changes in design during both the histological assessment study and the study to assess the strength of application. The initial applicator system described previously had problems related to fluid leakage and hence different seals were introduced from patient 3, and from patient 4 onwards a conventional cystoscope was used. From patient 5 onwards the cannula for the tubal screw was changed and a replacement tube of Portex was used. Due to difficulties in achieving adequate deflection of the plug towards the ostia and disimpacting the screw from patient 7 onwards a coil-mounted screw with an un-locking mechanism
was employed.

6.3.2. The testing of strength of plug application by weights study

At the time of hysterectomy three patients were in the proliferative phase of the menstrual cycle, one patient was in the secretory phase of her menstrual cycle (patient 2) and one patient was postmenopausal (patient 4). No patients were using a hormonal method of contraception prior to their admission for hysterectomy.

The results of the weights tests are detailed in Table 6.2. and Figure 6.12. As in the histological assessment study the equipment evolved during the study and consequently different techniques and instruments were being tested. Patient number 3 insisted that her uterus was to be removed without the screws in place and hence we were unable to test the strength of application of the tubal screws, however we were able to apply the screws and remove them hysteroscopically with hysteroscopic forceps. Case 2, on the right side, there was noted to be a small uterine perforation when the hysterectomy specimen was inspected prior to the weight testing. Case 4 was complicated by a fault in the applicator, which occurred after application of the right screw. Hence the left screw could not be properly applied. The median force required to remove the tubal screws from the uterotubal junction of the uteri was 2.95N, significantly different to that required in the in-vitro study 4.50N, p<0.0001, however the power of this study was only 65%.
As in the histological assessment study the equipment evolved during these experiments. Only patient 5 underwent the test with the final prototype tubal screw and applicator system.
### Table 6.2 The weight study to assess strength of application of in-vivo applied screws.

<table>
<thead>
<tr>
<th>Application technique</th>
<th>No. of plugs</th>
<th>Force required to dislodge screw (Newton) *</th>
<th>Mean force to dislodge screws (Newton) *</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Portex tubing with PTFE screw to decrease fluid leakage, original hysteroscope,</td>
<td>2</td>
<td>L 3.50</td>
<td>4.00</td>
</tr>
<tr>
<td>push-rod disimpaction</td>
<td></td>
<td>R 4.50</td>
<td></td>
</tr>
<tr>
<td>2 Tubing as above with conventional cystoscope. Excessive friction between tubing and</td>
<td>2</td>
<td>L 1.00</td>
<td>1.25</td>
</tr>
<tr>
<td>operating channel (making screwing in tubal screw very difficult)</td>
<td></td>
<td>R 1.50 †</td>
<td></td>
</tr>
<tr>
<td>3 Application as above but testing of new screws: blunt.</td>
<td>N/A</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>(Patient declined to have screws put in place therefore just screwed in and out)</td>
<td></td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>4 Application as above (L side difficult disimpaction)</td>
<td>2</td>
<td>L 0.50</td>
<td>2.00</td>
</tr>
<tr>
<td></td>
<td></td>
<td>R 3.50</td>
<td></td>
</tr>
<tr>
<td>5 Application as above with coil mounted screw with bayonet un-locking mechanism.</td>
<td>2</td>
<td>L 3.50</td>
<td>2.95</td>
</tr>
<tr>
<td></td>
<td></td>
<td>R 2.40</td>
<td></td>
</tr>
</tbody>
</table>

Mean 2.55N  
Median 2.95 N

L Left  
R Right  
† Uterine perforation noted on uterine specimen

* The gravitational force acting upon the weights applied to the tubal screw is assumed to be 10 m/s² downward force
Figure 6.12 Graph demonstrating the force required to dislodge the *in-vivo* hysteroscopically applied tubal screws.
6.4. Discussion

In the histological assessment study the success rate of correct tubal screw application to the fallopian tubes was potentially 13 of 16 applications (81.3%). Patient 5 was reported to have 'device in lumen at utero-tubal junction sections around the device shows endometrial tissue suggesting neither device reached the fallopian tube'. However the finding of endometrium in the interstitial portion of the fallopian tube is not an uncommon occurrence. Hafez and Black in 1969 reported that the uterotubal junction of the fallopian tube has a transitional layer of endometrium in 28% of uteri and an endometrial lining in 5% (Merchant et al, 1983). It is therefore possible that the tubal screws were indeed correctly sited. The method of tubal occlusion desired was to block the uterotubal junction. It was not expected that the tubal screw would remain in the lumen of the fallopian tube along its length, as it is known that its course is convoluted and often tortuous (Sweeney, 1962; Rocca et al., 1989), although this is disputed in-vivo (Rubin, 1928; Risquez and Confino, 1993). Consequently, without using a very flexible screw, it would not be possible for the occlusive device to remain in the lumen of the intramural fallopian tube throughout its length. This is not essential, as what is required is for the tubal screw to completely obstruct the uterotubal junction and maintain traction in the surrounding muscle fibres to remain in-situ. We believe this was achieved in this preliminary study in 81.3% of cases.
This experiment was a learning process and was being performed concurrently with an in-vivo study of tubal screw application at the time of laparoscopic sterilisation. Hence the equipment changed over the duration of the period of the study. Our final equipment was only used on patients 8-10 and in these patients the success of tubal screw application was 5 out of 6 applications. We therefore feel that the equipment is able to perform the required task of adequate uterine distension, approximation of the plug towards the cornu of the uterus and application of a rotational torque to screw the device into place at the uterotubal junction.

In the weight study the median force that was required to dislodge the hysteroscopically applied screws at the time of hysterectomy was 2.95N (inter-quartile range 1.25-3.50N). This is significantly less than the median weight required to dislodge the screws in the in-vitro study in Chapter 5 (4.50N), p<0.0001. The explanation for this discrepancy is that in the in-vitro study a rotational force perpendicular to the ostia of the fallopian tube directly inserted the tubal plugs. Conversely, in the in-vivo study, the rotational force was applied after deflection from the midline of the uterus. This caused the distal end of the applicator to describe an arc (see Chapter 4) rather than being screwed directly into the tissue and hence there was a looser ‘fit’ of the device. This is partly overcome by the use of an applicator based on a coil, used in patient 5.
Case 2 had a poor result due to the difficulty in applying the screws as the applicator tubing was of too large a diameter for the cystoscope and consequently could not be manipulated in a controlled fashion due to the friction within the cystoscope. Case 4 was complicated by the fact that the connection of the tubal screw mounting to the applicator weakened on one side. As a result the applicator bent and hence correct approximation of the plug to the tubal ostia was not possible. If cases 2 and 4 (left screw) are excluded, due to the marked difficulty in screw application, then the median weight applied that dislodged the tubal screws was 350g (producing a traction force of 3.50N) which is closer to that achieved in the in-vitro setting.

In this study one uterine perforation occurred, in patient number 2, at a time when we had exhausted our supply of original plastic tubing and were using a less pliable cannula made of Portex. Consequently to achieve the desired deflection excessive pressure may have been applied to the tubal screw. Also in this case the applicator tubing was very difficult to manipulate within the cystoscope. This would potentially have the effect of ‘pushing’ the screw into place rather than ‘screwing’, overcoming the thread of the screw, this is reflected in the small magnitude of the force required to dislodge the device.
6.5. Conclusion

These two experiments demonstrate that in four of five applications the tubal screws appeared to have been correctly applied to the uterotubal junction. If applied correctly, these screws require a significant force to overcome the thread generated in the surrounding myometrium for the device to become dislodged.

Consequently 20% of the tubal screws were not positioned correctly at the uterotubal junction. Therefore the application system requires modification to overcome the difficulties encountered that may have contributed to this poor success rate. In fact only patients 8-10 (histological assessment) and patient 5 (the weight study) had the procedure performed with our final apparatus. The main difficulties thought to have contributed towards this 20% failure rate in plug placement were;
1. inadequate uterine distension

2. poor deflection of the application cannula to approximate the screw to the uterotubal junction

3. difficulty in effecting a rotational force to the screw 'around a corner'

4. difficulty in disimpacting a screw without destroying the thread generated in the surrounding tissue.

In conclusion these studies demonstrate that this hysteroscopic method of sterilisation, with improvements in application, can be successful at firmly placing the tubal screw at the uterotubal junction. Although it remains to be seen how a firm grip of the surrounding myometrium correlates to the length of time the plug remains in place.
Chapter 7

The retention of tubal screws in patients undergoing simultaneous laparoscopic sterilisation
7.1. Introduction

Laparoscopic tubal sterilisation is the current gold standard method of permanent contraception against which any new procedure should be judged. It relatively simple to perform for an operator trained in laparoscopy, with a failure rate of 1.7 per 1000 for tubal ring and Filshie clip application when performed by experienced operators at 12 months (Sokal et al 2000). However the largest study of the failure rate of sterilisation was the US Collaborative Review (CREST study). This study prospectively followed-up 10,685 patients from several US centres who had undergone sterilisation. After exclusion of luteal phase conceptions 143 women conceived despite sterilisation. None of the patients in this study were sterilised using the Filshie clip as it was not available in the United States at this time. The 10-year cumulative life-table probability of failure was 18.5 per 1000 procedures, when pregnancies ending in spontaneous abortion based on self-reports were included and 16.6 per 1000 procedures, when those pregnancies were excluded. The 10-year life-table method-specific probabilities of failure indicated a substantial difference in effectiveness among the methods used. The most effective methods were postpartum partial salpingectomy and laparoscopic monopolar coagulation (7.5 pregnancies per 1000 procedures). Laparoscopic spring clip application (analogous to the Hulka clip) had the highest probability of failure (36.5 pregnancies per 1000 procedures). The probability of failure for women sterilised when less than 28 years of age was
greater than that for women sterilised at ages greater or equal to 34 years of age for all methods of sterilisation other than interval partial salpingectomy. After adjustment for sterilisation method, race-ethnicity, and study site, women sterilised at ages greater or equal to 34 years were at significantly less risk for sterilisation failure than were women sterilised at age 28 to 33 years of age.

After adjustment for sterilisation method, age, and study site; black, non-Hispanic women were at significantly greater risk for sterilisation failure than were white, non-Hispanic women. There were also noted to be significant differences in sterilisation failure between centres, suggesting that the success of a procedure is operator dependent. As the Filshie clip was not included in the CREST study, but is the commonest method used in the UK, the best available evidence suggests that this technique has a failure rate of 2-3 per 1,000 at two years (personal communication, Professor John Guillebaud). The RCOG guidelines extrapolate this figure using the CREST model to derive a lifetime risk of sterilisation failure of 1 in 200 for Filshie clip application.

The Crest group analysed their data further to assess the risk of ectopic gestation after sterilisation (Peterson et al., 1997). They reported that the ten-year cumulative probability of an ectopic pregnancy for all methods of sterilisation was 7.3 per 1,000 procedures. Bipolar tubal coagulation had the
highest risk of an ectopic pregnancy (17.1 per 1,000 procedures) and the risk was lowest after post-partum salpingectomy (1.5 per 1,000 procedures). Interestingly, the overall risk of an ectopic pregnancy is the same in each year after sterilisation and does not decrease with time (rate between 0.7-0.8 per 1,000 woman-years) (Peterson et al., 1997). The CREST group subsequently reported that women who have undergone tubal sterilisation are no more likely than other women to have menstrual abnormalities than women who had not undergone sterilisation (Peterson et al., 2000).

A study to assess the success rate of our hysteroscopic method of sterilisation cannot be performed until it is known the length of time that the tubal screws are retained at the utero-tubal junction. Previous methods of hysteroscopic tubal sterilisation have been unsuccessful, as the plugs have become dislodged with time. Unfortunately none have been consistently successful which has led to the persistence of the laparoscopic approach as the optimal route to achieve sterilisation (Risquez and Confino, 1993). However the authors believed that a tubal device based on a 'self-tapping' screw would be less likely to become dislodged with time due to the multiple screw threads preventing it from being displaced.

To address the duration of screw retention a study involving the long-term follow-up of patients who had the hysteroscopic screws applied was performed. As the success of the hysteroscopic route at preventing
conception is unknown, these patients underwent the hysteroscopic procedure at the time of laparoscopic sterilisation.

Patients recruited to this study were sterilised at the time of publication of the CREST study of 1996 (Peterson et al., 1996), but prior to the RCOG guidelines on sterilisation were issued (RGOG, 1999), and consequently the counselling of our patients reflected this. Our patients were informed that the failure rate of laparoscopic sterilisation was approximately one in 100 procedures, but could potentially be higher.

7.2. Method

Ethical approval of this study of concurrent hysteroscopic sterilisation at the time of laparoscopic Filshie clip sterilisation was granted from our local ethical practice sub-committee (reference no. 62-96). All patients referred for sterilisation to The Royal Free Hospital during the study period were seen in a special sterilisation clinic where they were assessed for their suitability for sterilisation and referral for family planning advice or their partner for vasectomy was arranged if appropriate.

Detailed obstetric and gynaecological histories were taken, an abdominal and pelvic examination was performed, with note taken of any scars from previous surgery. Alternative contraceptive choices were discussed, as was the method of sterilisation to be performed and the risks of laparoscopy.
Patients suitable for laparoscopic tubal sterilisation were counselled, as was our normal practice for this procedure;

1. the patient must understand that the procedure is irreversible
2. the patient must continue contraceptive precautions throughout the cycle in which the sterilisation is performed
3. the operation has a risk of a laparotomy either due to the inability to complete the procedure or due to intraoperative visceral injury
4. the procedure has a failure rate of approximately 1 in 100 (pre-report of Working Party of RCOG and Guidelines for sterilisation, 1999)
5. if the woman subsequently conceives she has an increased risk of a tubal pregnancy.

A patient information leaflet produced by the Family Planning Association was offered to the patient for her to read later and discuss with her partner. When the woman agreed to undergo sterilisation the outline of the study was described to her and if she expressed an interest in being involved detailed counselling and consent was performed (see information sheet and consent form in appendix). The laparoscopic sterilisation was scheduled irrespective of whether the patient agreed or declined to be involved in the study.

On the day of the procedure the woman was asked for confirmation of her last menstrual period. If there was any concern as to the possibility of pregnancy then a pregnancy test was performed. Confirmation of the woman's decision to be sterilised and involved in the study was sought. In women agreeing to
be involved in the study after administration of the general anaesthetic, generation of a pneumoperitoneum and insertion of a laparoscope, the patency of the fallopian tubes was assessed by conventional dye hydrotubation with methylene blue dye. After noting the status of the fallopian tubes the hysteroscopic sterilisation was attempted by deflecting the tubal screw towards the tubal ostia. A gentle rotational force was applied to the application cannula under direct vision and the ‘screwing’ action was continued until the thread of the screw was no longer visible. The method by which uterine distension was achieved, the hysteroscope or cystoscope, the cannula used to deliver the tubal screw and the design of the tubal screw was changed as the study developed. The reasons for the alterations in the instrumentation are described in Chapter 4. The description of the equipment used in each individual case is reported in Table 7.1 and the changes are summarised in Figure 7.1.

The patients were observed postoperatively as for any woman undergoing tubal sterilisation and were discharged the same day when they were eating and drinking, mobilising unaided, after passing urine and when not in undue discomfort. Each patient received a telephone call the following day to ensure that they were well. Follow-up ultrasound scans were arranged for approximately 3, 6 and 9 months after the sterilisation (Figure 7.2 to 7.7)
Table 7.1 Method of hysteroscopic tubal screw application, follow-up ultrasound reports and interval screw removal.

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Contraception used</th>
<th>Type of distension system, applicator system, screw inserted and comments</th>
<th>Tubal patency prior to sterilisation</th>
<th>Tubal patency post hysteroscopic sterilisation</th>
<th>Number of screws applied</th>
<th>1st U/S (approximately 3 months post insertion)</th>
<th>2nd U/S (approximately 6 months post insertion)</th>
<th>3rd U/S (approximately 9 months post insertion)</th>
<th>Tubal screw removal (Duration until screw removal / months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Abstinence</td>
<td>Cystoscope Hamou hysteromat Push-rod disimpaction</td>
<td>Y Y</td>
<td>N N</td>
<td>1</td>
<td>L screw in place</td>
<td>L screw in place</td>
<td>L screw in place</td>
<td>Screw not seen hysteroscopically despite U/S (15)</td>
</tr>
<tr>
<td>2</td>
<td>IUCD Proliferative phase</td>
<td>Unchanged</td>
<td>N Y</td>
<td>N N</td>
<td>2</td>
<td>L screw only in place</td>
<td>Declined further U/S</td>
<td>Easy with polyp forceps (15)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Condom Proliferative phase</td>
<td>Unchanged</td>
<td>Y N</td>
<td>Y N</td>
<td>0</td>
<td>Deflection required too acute</td>
<td>Not applicable</td>
<td>Not applicable</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Condom Proliferative phase</td>
<td>Unchanged</td>
<td>Y Y</td>
<td>N N</td>
<td>2</td>
<td>L screw only in place</td>
<td>No screws seen</td>
<td>Hysteroscopy no screws seen</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>OCP</td>
<td>Unchanged</td>
<td>Y Y</td>
<td>Not tested</td>
<td>0</td>
<td>Inadequate deflection achieved</td>
<td>Not applicable</td>
<td>Not applicable</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>IUCD Secretory phase</td>
<td>Unchanged</td>
<td>N N</td>
<td>Not tested</td>
<td>0</td>
<td>Asherman's</td>
<td>Not applicable</td>
<td>Not applicable</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Condom Proliferative phase</td>
<td>Original Rimmer hysteroscope Same distension &amp; disimpaction</td>
<td>Y Y</td>
<td>N N</td>
<td>2</td>
<td>Both screws seen</td>
<td>Both screws seen</td>
<td>Both screws removed with polyp forceps (15)</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Condom Proliferative phase</td>
<td>Cystoscope Same distension &amp; disimpaction</td>
<td>Y Y</td>
<td>As uterus perforated</td>
<td>0</td>
<td>Not applicable</td>
<td>Not applicable</td>
<td>Not applicable</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Condom Proliferative phase</td>
<td>Original Rimmer hysteroscope Same distension &amp; disimpaction</td>
<td>N N</td>
<td>N N</td>
<td>2</td>
<td>Both screws seen</td>
<td>Patient did not attend</td>
<td>L screw only seen</td>
<td>L screw removed with polyp forceps (14)</td>
</tr>
<tr>
<td>10</td>
<td>OCP</td>
<td>Unchanged but cut away sheath to ensure no rubbing of application cannula, but then poor deflection.</td>
<td>Y Y</td>
<td>N Y</td>
<td>1</td>
<td>L screw perforated retrieved</td>
<td>Patient did not attend</td>
<td>Patient did not attend</td>
<td>Screw seen</td>
</tr>
<tr>
<td>11</td>
<td>OCP</td>
<td>Separate deflector used Same distension &amp; hysteroscope</td>
<td>N Y</td>
<td>Not tested</td>
<td>0</td>
<td>Too difficult to manipulate</td>
<td>Not applicable</td>
<td>Not applicable</td>
<td>Not applicable</td>
</tr>
<tr>
<td>12</td>
<td>OCP</td>
<td>1st use of coil with screw resting in end Same distension &amp; hysteroscope</td>
<td>Y Y</td>
<td>Not tested</td>
<td>0</td>
<td>Impossible to disimpact screws</td>
<td>Not applicable</td>
<td>Not applicable</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Patient Number</td>
<td>Contraception used</td>
<td>Phase of menstrual cycle</td>
<td>Type of distension system, applicator system, screw inserted and comments</td>
<td>Tubal patency prior to sterilisation</td>
<td>Tubal patency post hysteroscopic sterilisation</td>
<td>Number of screws applied</td>
<td>1st U/S (approximately 3 months post insertion)</td>
<td>2nd U/S (approximately 6 months post insertion)</td>
<td>3rd U/S (approximately 9 months post insertion)</td>
</tr>
<tr>
<td>----------------</td>
<td>-------------------</td>
<td>--------------------------</td>
<td>--------------------------------------------------------------------------</td>
<td>------------------------------------</td>
<td>---------------------------------------------</td>
<td>--------------------------</td>
<td>----------------------------------------------</td>
<td>-----------------------------------------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>13</td>
<td>OCP</td>
<td></td>
<td>Trombone technique</td>
<td>Y Y</td>
<td>Not tested (Trauma to cervix led to poor view)</td>
<td>0</td>
<td>L screw seen</td>
<td>No screw seen</td>
<td>Hysteroscopy no screw seen</td>
</tr>
<tr>
<td>14</td>
<td>IUCD</td>
<td>Proliferative phase</td>
<td>Cystoscope with detachable bridge and screws applied by a coil. Same distension system</td>
<td>Not tested</td>
<td>Not tested</td>
<td>1</td>
<td>L screw seen</td>
<td>No screw seen</td>
<td>Hysteroscopy no screw seen</td>
</tr>
<tr>
<td>15</td>
<td>Depot – Provera</td>
<td></td>
<td>Unchanged</td>
<td>Not tested</td>
<td>Not tested</td>
<td>0</td>
<td>L screw seen</td>
<td>No screw seen</td>
<td>Hysteroscopy no screw seen</td>
</tr>
<tr>
<td>16</td>
<td>OCP</td>
<td></td>
<td>1st Use of 3 litre pressure bag</td>
<td>Y Y</td>
<td>Not tested</td>
<td>2</td>
<td>No screws seen</td>
<td>Hysteroscopy no screws seen</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>Abstinence</td>
<td>Secretory phase</td>
<td>Unchanged</td>
<td>Y Y</td>
<td>Not tested</td>
<td>0</td>
<td>Impossible to disimpact screw</td>
<td>Not applicable</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>Condom</td>
<td>Proliferative phase</td>
<td>Use of coil mounted threaded screw to enable disimpaction</td>
<td>Y Y</td>
<td>Not tested</td>
<td>0</td>
<td>Would not disimpact</td>
<td>Not applicable</td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>IUCD</td>
<td>Proliferative phase</td>
<td>CO\textsubscript{2} insufflator</td>
<td>Y Y</td>
<td>Not tested</td>
<td>2</td>
<td>R screw seen</td>
<td>No screws seen</td>
<td>No screws seen</td>
</tr>
<tr>
<td>20</td>
<td>Mini-pill</td>
<td></td>
<td>Unchanged</td>
<td>Y Y</td>
<td>Not tested</td>
<td>0</td>
<td>Would not disimpact</td>
<td>Not applicable</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>OCP</td>
<td></td>
<td>3 litre pressure bag and 1st use of strong coiled introducer with plastic surround to minimise leakage and screw with titanium rod for disimpaction</td>
<td>Y Y</td>
<td>Not tested</td>
<td>2</td>
<td>Both screws seen</td>
<td>Both screws seen</td>
<td>Both screws removed (12)</td>
</tr>
<tr>
<td>22</td>
<td>Mini-pill</td>
<td></td>
<td>Unchanged</td>
<td>Y Y</td>
<td>Not tested</td>
<td>2</td>
<td>Both screws seen</td>
<td>Both screws seen</td>
<td>Both screws removed (12)</td>
</tr>
<tr>
<td>23</td>
<td>Mini-pill</td>
<td></td>
<td>Unchanged</td>
<td>N N</td>
<td>Not tested</td>
<td>2</td>
<td>R screw only seen</td>
<td>Both screws seen</td>
<td>Both screws seen</td>
</tr>
<tr>
<td>24</td>
<td>OCP</td>
<td></td>
<td>Unchanged</td>
<td>N N</td>
<td>Not tested</td>
<td>2</td>
<td>Both screws seen</td>
<td>Both screws seen</td>
<td>Both screws seen</td>
</tr>
<tr>
<td>25</td>
<td>OCP</td>
<td></td>
<td>Unchanged</td>
<td>N N</td>
<td>Not tested</td>
<td>2</td>
<td>Both screws seen</td>
<td>Both screws seen</td>
<td>Both screws removed (13)</td>
</tr>
<tr>
<td>Patient Number</td>
<td>Contraception used</td>
<td>Phase of menstrual cycle</td>
<td>Type of distension system, applicator system, screw inserted and comments</td>
<td>Tubal patency prior to sterilisation R L</td>
<td>Tubal patency post hysteroscopic sterilisation R L</td>
<td>Number of screws applied</td>
<td>1st U/S (approximately 3 months post insertion)</td>
<td>2nd U/S (approximately 6 months post insertion)</td>
<td>3rd U/S (approximately 9 months post insertion)</td>
</tr>
<tr>
<td>----------------</td>
<td>--------------------</td>
<td>--------------------------</td>
<td>--------------------------------------------------------------------------------</td>
<td>------------------------------------------</td>
<td>-----------------------------------------------</td>
<td>--------------------------</td>
<td>-----------------------------------------------</td>
<td>-----------------------------------------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>26</td>
<td>Mini-pill</td>
<td>Unchanged</td>
<td>Y Y</td>
<td>Not tested</td>
<td>R L screw dropped</td>
<td>1</td>
<td>R screw seen</td>
<td>R screw seen</td>
<td>R screw seen</td>
</tr>
<tr>
<td>27</td>
<td>Mini-pill</td>
<td>Unchanged</td>
<td>Y Y</td>
<td>N N</td>
<td>2</td>
<td>Both screws seen</td>
<td>Both screws seen</td>
<td>Both screws seen</td>
<td>Hysterectomy both screws removed (13)</td>
</tr>
<tr>
<td>28</td>
<td>Mini-pill</td>
<td>Unchanged</td>
<td>Y Y</td>
<td>N N</td>
<td>2</td>
<td>R screw seen</td>
<td>L screw seen</td>
<td>Both screws seen</td>
<td>At hysterectomy no screws found</td>
</tr>
<tr>
<td>29</td>
<td>OCP</td>
<td>Unchanged</td>
<td>Salpingectomy</td>
<td>Y</td>
<td>1</td>
<td>L screw seen</td>
<td>No screw seen</td>
<td>Not applicable</td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>Condom</td>
<td>Secretory phase</td>
<td>Y Y</td>
<td>N N</td>
<td>2</td>
<td>Both screws seen</td>
<td>Patient did not attend</td>
<td>No screws seen</td>
<td>At hysterectomy no screw found</td>
</tr>
<tr>
<td>31</td>
<td>IUCD</td>
<td>Proliferative phase</td>
<td>Y Y</td>
<td>N N</td>
<td>2</td>
<td>Both screws seen</td>
<td>Patient did not attend</td>
<td>Patient did not attend</td>
<td>Hysterectomy both screws removed (21)</td>
</tr>
<tr>
<td>32</td>
<td>OCP</td>
<td>Unchanged</td>
<td>Y Y</td>
<td>N N</td>
<td>2</td>
<td>Both screws seen</td>
<td>Patient did not attend</td>
<td>Patient did not attend</td>
<td></td>
</tr>
<tr>
<td>33</td>
<td>Depot-Provera</td>
<td>Unchanged</td>
<td>Y Y</td>
<td>Not tested</td>
<td>0</td>
<td>Outer coat too inflexible led to uterine perforation</td>
<td>Not applicable</td>
<td>Not applicable</td>
<td></td>
</tr>
<tr>
<td>34</td>
<td>OCP</td>
<td>Unchanged</td>
<td>Y Y</td>
<td>N N</td>
<td>2</td>
<td>Both screws seen</td>
<td>Patient did not attend</td>
<td>Patient did not attend</td>
<td>At hysterectomy only L present-removed (13)</td>
</tr>
<tr>
<td>35</td>
<td>Condom</td>
<td>Proliferative phase</td>
<td>Y Y</td>
<td>N N</td>
<td>2</td>
<td>Patient did not attend</td>
<td>Patient did not attend</td>
<td>L screw seen</td>
<td>At hysterectomy L screw removed (13)</td>
</tr>
</tbody>
</table>

**Key**

- **R**: Right
- **L**: Left
- **Y**: Yes
- **N**: No
- **DNA**: Did not attend
- **†**: Phase of cycle reported only in women using non-hormonal method of contraception
- **IUCD**: Intrauterine contraception device
- **OCP**: Oral contraceptive pill

291
Figure 7.1 Flow chart showing the changes in the equipment and technique of hysteroscopic tubal screw sterilisation.

Cases 1 - 6, 8
Cystoscope
Hamou hysteromat
Push-rod disimpaction

Cases 7 & 9
Original Rimmer hysteroscope
Same distension & disimpaction

Case 10
Unchanged but cut away sheath to ensure no rubbing

Case 11
Separate deflector
Same distension & hysteroscope

Case 12
Coiled applicator with screw resting in end
Same distension & hysteroscope

Case 13
Trombone technique
Same distension & hysteroscope

Case 14 & 15
Cystoscope with detachable bridge and screws applied by a coil. Same distension system

Case 16 & 17
Pressure bag
Same cystoscope & applicator

Case 18
Coil mounted threaded screw
Same cystoscope & distension

Cases 19 & 20
CO₂ insufflator
Same cystoscope & applicator

Cases 21 - 35
Pressure bag, strong coil applicator with plastic surround, screw with titanium rod for disimpaction
Same cystoscope

Key: Indications for changes

Improve distension
Improve deflection
Aid disimpaction
Figure 7.2  Ultrasound appearance of a hysteroscopically placed tubal screw viewed on ultrasound scan 3 months post insertion.
Figure 7.3  Ultrasound appearance of a hysteroscopically placed tubal screw viewed on ultrasound scan 3 months post insertion. (patient number 4)
Figure 7.4  Further ultrasound scan demonstrating a single tubal screw. (patient number 14)
Figure 7.5  Further ultrasound scan demonstrating bilaterally placed tubal screws. (patient number 22)
Figure 7.6 3-D ultrasonography demonstrating the presence of a tubal screw at the uterine cornu. (patient number 1).
Figure 7.7 3-D ultrasound scan demonstrating bilateral placement of tubal screws.
Between 12 and 20 months after hysteroscopic sterilisation the tubal screws were removed via the hysteroscopic approach, further ultrasound scans were arranged during this interval to confirm the presence of the tubal screws prior to surgical removal. Plug removal was initially performed under a general anaesthetic using grasping forceps to ‘unscrew’ the screws from the uterotubal junction. With the evolution of the disimpaction process to use the titanium rod through the proximal end of the screw (cases 21-35) the disimpaction was effected by reinserting the applicator system onto the end of the screw and ‘unscrewing’ it from the uterotubal junction under local anaesthetic. Although ultrasound scans may have been unable to determine the presence of the tubal screws in some volunteers these patients were encouraged to have an outpatient hysteroscopy to ensure that a screw had not been missed.

7.3. Results

The mean age of the patients in whom hysteroscopic sterilisation was attempted was 36.3 years (range 28-45 years, standard deviation 4.86) with a median number of two previous deliveries (range 0-4). Ten women were in the proliferative phase of their menstrual cycle, five in the secretory phase, twelve were taking the combined oral contraceptive pill, six the mini-pill and two patients had received injections of medroxyprogesterone acetate prior to their sterilisation. The mean uterine size was 4.7 weeks size, 3 women had uteri of at least 8 weeks gestation equivalent or more, with an overall mean uterine length of 7.6 cm.
All patients in whom hysteroscopic sterilisation was attempted are reported in Table 7.1, along with the complications of insertion which consisted of 4 small uterine perforations (two of which involved tubal screw disimpaction and required laparoscopic retrieval), and cervical trauma using the ‘trombone technique’ which did not require any action. In the first 20 cases 25 tubal screws could not be applied at all, due to an inability to disimpact the screw from the cannula (11), inability to achieve the required deflection (6), uterine perforation (4), poor view (2) and Asherman’s syndrome (2). In cases 21-35 there were only 4 tubal screws that could not be applied due to previous salpingectomy (1), uterine perforation with an inflexible new rubber sheath for the coiled spring cannula (2) and 1 tubal screw was dropped prior to attempted insertion.

Of the 24 tubal screws recorded as being inserted in the proliferative phase of the menstrual cycle, 13 were still present after 12 months after being inserted (54.2%). Six of the 13 screws reported as being applied in the secretory phase of the menstrual cycle were still present 12 months after insertion (46.2%), P=1.00 for the difference.

As has been previously described the equipment evolved during the study however from patient 21 the equipment and tubal screw remained the same and consequently patients in the development phase, cases 1-20 (Table 7.2), were analysed separately to the subsequent cases 21-35 (Table 7.3).
Table 7.2  Duration of screw retention or until removal at the time of hysteroscopy (cases 1-20).

<table>
<thead>
<tr>
<th>Time / months</th>
<th>Right screw retention / %</th>
<th>Left screw retention / %</th>
<th>Total screw retention / %</th>
<th>No. cornu censored by ultrasound at each time interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>15</td>
</tr>
<tr>
<td>3</td>
<td>57.1</td>
<td>75.0</td>
<td>66.7</td>
<td>15</td>
</tr>
<tr>
<td>6</td>
<td>42.9</td>
<td>50.0</td>
<td>46.7</td>
<td>12</td>
</tr>
<tr>
<td>9</td>
<td>28.6</td>
<td>50.0</td>
<td>40.0</td>
<td>7</td>
</tr>
<tr>
<td>11</td>
<td>14.0</td>
<td>50.0</td>
<td>33.0</td>
<td>6</td>
</tr>
<tr>
<td>14</td>
<td>14.0</td>
<td>50.0</td>
<td>33.0</td>
<td>5</td>
</tr>
<tr>
<td>16</td>
<td>14.0</td>
<td>50.0</td>
<td>33.0</td>
<td>4</td>
</tr>
<tr>
<td>18</td>
<td>50.0</td>
<td>33.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 7.3  Duration of screw retention or until removal at the time of hysteroscopy (cases 21-35).

<table>
<thead>
<tr>
<th>Time / months</th>
<th>Right screw retention / %</th>
<th>Left screw retention / %</th>
<th>Total screw retention / %</th>
<th>No. cornu censored by ultrasound at each time interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>26</td>
</tr>
<tr>
<td>3</td>
<td>92.3</td>
<td>100</td>
<td>96.2</td>
<td>26</td>
</tr>
<tr>
<td>6</td>
<td>76.9</td>
<td>78.6</td>
<td>77.7</td>
<td>26</td>
</tr>
<tr>
<td>6.5</td>
<td>69.2</td>
<td>71.4</td>
<td>70.3</td>
<td>20</td>
</tr>
<tr>
<td>9</td>
<td>69.2</td>
<td>71.4</td>
<td>70.3</td>
<td>18</td>
</tr>
<tr>
<td>11</td>
<td>69.2</td>
<td>71.4</td>
<td>70.3</td>
<td>18</td>
</tr>
<tr>
<td>12</td>
<td>61.5</td>
<td>64.2</td>
<td>62.3</td>
<td>15</td>
</tr>
<tr>
<td>13</td>
<td>61.5</td>
<td>64.2</td>
<td>62.3</td>
<td>8</td>
</tr>
<tr>
<td>20</td>
<td>61.5</td>
<td>64.2</td>
<td>62.3</td>
<td>2</td>
</tr>
</tbody>
</table>
In total 23 patients had 41 tubal screws inserted at the time of concurrent laparoscopic sterilisation and the duration of their retention is demonstrated by life-table analysis in Tables 7.2 and 7.3 and Figures 7.8 - 7.13. 21 tubal screws were removed from 13 patients between 9 and 20 months after insertion. In the early cases when there were problems with poor visualisation of the uterine cornu, the mean time taken to achieve bilateral screw placement was approximately 25 minutes but in the latter cases this was 15 minutes.

In those patients in whom tubal patency was checked pre and post tubal screw insertion 29 of 30 fallopian tubes were occluded (96.7%). The life table analysis plots demonstrate a non-significant difference in the duration of screw retention between the equipment in the development phase (cases 1-20) when compared to the later attempts (cases 21-35), $P=0.132$ using the log rank test (Figure 7.14). Overall tubal screw retention being 33% for cases 1-20, up to 18 months, as compared to 62.3% of screws retained for cases 21-35. There was no significant difference between the tubal screw retention at 6 and 12 months using the earlier and later equipment; 46.7% vs 77.7% ($P=0.077$) and 33% vs 62.3% ($P=0.096$) for 6 and 12 months respectively. Although due to the low numbers involved this study only a 60% power to detect a significant difference between cases 1-20 and cases 21-35.

Tubal screws that were removed hysteroscopically were sent for microbiological assessment and all were free from bacteriological contamination.
Figure 7.8  Life table plot of right tubal screw retention (cases 1-20).

Figure 7.9  Life table plot of left tubal screw retention (cases 1-20).

Figure 7.10  Life table plot of retention of all tubal screws (cases 1-20).
Figure 7.11  Life table plot of right tubal screw retention (cases 1-20).

Figure 7.12  Life table plot of left tubal screw retention (cases 1-20).

Figure 7.13  Life table plot of retention of all tubal screws (cases 21-35)
Figure 7.14 Log rank test to compare the life table plots between the initial and latter cases.

p = 0.132 for difference between survival plots
7.4. Discussion

This follow-up of hysteroscopic tubal screw retention demonstrated that after refinement of our equipment, technique and potentially overcoming a ‘learning curve’ then tubal screw retention rates of the order of 60% may be achieved, with the majority of failures occurring in the initial 6 months. Consequently as with previous techniques there was a high incidence of early plug expulsion. The causes of tubal expulsion are thought to be; relaxation of the circular smooth muscle at the utero-tubal junction, or the body’s innate ability to expel foreign bodies (Craft, 1976; Hosseinian et al, 1976; Brueschke et al, 1977; Erb and Reed, 1979; Hamou et al, 1984; Loffer, 1984; Brundin 1991). The rate of tubal screw expulsion was even higher in the early phase of the development of this technique, with less than 50% of screws still present at 6 months post insertion. Indeed in the first 20 cases 25 screws could not be applied at the time of hysteroscopy, which demonstrates the great difficulty involved in accurate placement of the tubal screw at the uterotubal junction. This compares with the subsequent 15 cases (20-35) where there were only 4 screws that could not be applied. Consequently the rate of failed sterilisation due to equipment factors, in the first 20 cases, was 23 of a potential 38 applications (60.5%), case 6 excluded due to Asherman’s syndrome. This compares to 2 failed applications of a potential 28 (7.1%) for cases 21-35, one screw not attempted due to previous salpingectomy and one screw was dropped.
There was no difference in screw retention according to the phase of the menstrual cycle, although this may in part be a function of the small number of patients who had the tubal screws applied.

From the life table analysis there is a non-significant difference in the duration of screw retention between the equipment in the development phase (cases 1-20) when compared to the later attempts (cases 21-35). Overall tubal screw retention being 33% for cases 1-20, at up to 18 months, as compared to 62.3% of screws retained for cases 21-35, with the majority of failures in both groups occurring by 6 months. Although these differences were not significant, p=0.077 and p=0.096 for screw retention at 6 and 12 months respectively (due to low numbers, this study only had 60% power to detect a significant difference).

These results highlight marked differences in the effectiveness of the equipment to provide for; good cornual distension, adequate deflection towards the uterotubal junction, an effective means to apply a rotational torque to the tubal screw and a simple method of disimpaction. The introduction of the 3 litre pressure bag provided excellent cornual visualisation for screw application. The earlier equipment with their multiple points of fluid leakage, as documented in Chapter 4, could not sustain sufficient uterine distension with pump distension systems, as the required fluid flow rate was excessive. The operating urological cystoscope was the preferred method of introducing the hysteroscopic screw as it had a variable deflector to alter the path of the application cannula as it
approached the tubal ostia. An initial drawback with this system was that it did not provide good cornual distension, as it has two operating channels limiting the flow rate of the saline, the introduction of the pressure bag circumvented this problem. Also at times the deflecting bridge was inadequate at achieving the required deflection therefore an extra deflector was devised. There was also the practical problem in that the operating channel of the urological cystoscope was narrower than that of the original Rimmer hysteroscope requiring the applicator cannula to be altered to fit down the operating channel. As reported in Chapter 4 the vector for the tubal screw was changed several times but after bench tests it became evident that the most effective way to apply a rotational torque at an angle was to use a coil applicator cannula.

However this system will require further refinement as the rate of tubal screw displacement even in the later stages of the study was still excessive. This suggests that there is still some lateral movement around the intended direction of the screw which leads to disruption of the muscle fibres in the myometrium in the intramural portion of the fallopian tube and hence a 'loose fit' of the screw thread. Another problem maybe that although the screw is 'screwed' into place, a force is applied along the axis of the tubal screw to drive it into the uterotubal junction. There is consequently potential for this forward force to be excessive. This will disrupt the path of the screw thread generated in the surrounding circular muscle in the intramural portion of the fallopian tube and therefore
a loosely held tubal screw. With regard to tubal screw disimpaction the adoption of the titanium bayonet with the 'locking' and 'unlocking' mechanism enabled easy screw application and removal.

Of importance from the Table 7.1 it can be seen that there were four instances of uterine perforation, with only one of these being in the latter stages of the study. The initial uterine perforations can be attributed to the combined problems of a 'learning curve' of the technique, with the difficulties of encountered with poor uterine distension, combined with the push-rod disimpaction technique. The cause of the uterine perforation in case 33 was due to the replacement of the cover of the coil applicator with a very firm rubber. This led to an inability to deflect the screw correctly and consequently the uterus was perforated. All of the procedures were monitored laparoscopically and none of the perforations led to significant bleeding where the screw had been disimpacted, the cause of uterine perforation in the other cases was the push-rod disimpaction technique (cases 1, 8 and 10). All screws were retrieved laparoscopically.

As discussed in Chapter 3 an important omission in taking the consent of the patient for this study was that if a segment of fallopian tube was blocked proximally and distally this may have led to the development of either a hydrosalpinx, or a haematosalpinx. This would be expected to cause profound discomfort. Fortunately none of our patients did complain of pain
whilst having the tubal screws in place.

To ensure that the ultrasonographer did not overlook any of the tubal screws at the time of sonographic review, hysteroscopy was still performed in the majority of volunteers. The need for this was highlighted in patients 23 and 28 in whom a tubal screw was missed at the time of an early ultrasound. It is felt that with time and experience and by using a more up to date ultrasound machine that in future no tubal screws will be missed. In contrast in case 1 there was clear ultrasound documentation of the presence of a tubal screw. However at hysteroscopy the screw was not seen despite its presence being confirmed on 3-D ultrasonography (Figure 7.6). The patient was informed that the screw was placed deeply, and as PTFE is a safe substance widely used in medicine, it was unlikely to cause problems in the future. The longest any tubal screw was left in place was 20 months in patient 32 who did not attend two ultrasound appointments and was lost to follow-up for several months. This was a frequent problem, as understandably, many patients were reluctant to come to the hospital for vaginal ultrasound scans with busy lives, with young children to care for, and many were working mothers. Consequently although the aim was initially to perform ultrasound scans at 3, 6 and 9 months with hysteroscopic removal after approximately 12 months this was seldom achieved.

An important fact requiring clarification is that even if the tubal screw retention
was 100% at up to 20 months this does not correlate with uterotubal occlusion at this time. However tubal patency was tested before and after attempted tubal occlusion with a 97% success rate at occluding the uterotubal junction, with only 1 fallopian tube remaining patent after attempted occlusion (case 16). In this patient both screws that were inserted were absent by the time of the 3 month ultrasound scan, suggesting that insertion was poor from the outset or that there exists in some patients an efficient process to extrude the tubal plugs from their uterine cornu which other patients may not posses.

In the future to ensure the efficacy of the tubal screw at occluding the uterotubal junction a simple test of tubal patency will be required, for instance hysterosalpingography or by using an ultrasound contrast agent. This would be performed several days after the concurrent hysteroscopic and laparoscopic sterilisation study to determine whether any tubal spasm had settled, allowing contrast around the screw, or if any plugs had become dislodged. However the tests may be difficult to evaluate in the presence of Filshie clips as they will limit proximal tubal fill around a poorly fitted tubal screw, potentially leading to misleading results.

7.5. Conclusion

This study of the retention of tubal screws placed hysteroscopically at the time of concurrent laparoscopic sterilisation demonstrated an improvement
with experience and refinement of the equipment with time. Despite being very effective at blocking fallopian tubes at the time of sterilisation screw retention even in the later stages of development was poor. Consequently further refinements to the tubal screw and the application system must be made to improve retention rates. A further study must be commenced to ensure that screw retention correlates with tubal occlusion.
Chapter 8

The future of the hysteroscopic tubal screw to effect sterilisation
8.1 Introduction

These studies describing the development of a novel method of hysteroscopic sterilisation demonstrate that the tubal screw when inserted correctly requires a substantial force to dislodge it. The results were better in the *in-vitro* study as the tubal screw was held firmly as it was screwed directly along the path of the proximal tube. In contrast in the *in-vivo* study the tubal screw was applied by deflection from the midline axis of uterus. However despite many changes in the equipment to apply the screws to the tubal ostia they have a high expulsion rate when followed-up over time. As mentioned previously many authors have alluded to the body's innate ability to expel foreign bodies (Craft, 1976; Hosseinian *et al*, 1976; Brueschke *et al*, 1977; Erb and Reed, 1979; Hamou *et al*, 1984; Loffer, 1984; Brundin 1991). The reason for this maybe due to fallopian tube spasm which is frequently reported during uterine distension (Novy *et al*, 1988). This may resolve after the procedure leading to displacement of the screw. There may also be a reduction in the grip of the screw in the surrounding musculature due to the development of an area of foreign body induced chronic inflammation, as described by authors using PTFE at other sites in the body (Dedo and Carlsoo, 1982). There may also a large inter-patient variation in the anatomy of the uterotubal junction or ability to expel intraluminal plugs, making identification of patients suitable for this method of sterilisation difficult.
The tubal screw retention study demonstrated marked but non-significant improvements in screw retention as the equipment used evolved. Tubal screw retention being only 33% for cases 1-20 up to 18 months, as compared to 62.3% of screws retained for cases 21-35. This was achieved by using a cystoscope with an added deflector, improving uterine distension by using a 3 litre pressure bag and using a coiled applicator with an 'un-locking' mechanism to apply the tubal screw at the ostia. However despite these major improvements tubal screw retention at 12 months was only 62.3%. Consequently major improvements in the technique and design of the equipment must be made to achieve an acceptable screw retention rate.

8.2. Further improvements required

8.2.1. The tubal screw

The diameter of the fallopian tube can vary considerably in size so it may be wise to have a selection of different size screws to apply. However in our studies it was felt that this was not a cause of screw failure, the main reason for their dislodgement was thought to be disruption of the screw thread. Potentially having a narrower screw but a deeper thread may enable the screw to 'seek' the ostia with greater ease and be held firmer, or by increasing the number of threads on the screw. A further improvement may lie in the development of a
plug with a degree of plasticity so the tubal screw may follow the path of the tubal ostia more effectively. If none of these refinements result in an improved retention rate then a substance may have to be added to the screw to provoke a fibrotic reaction to improve retention. This is a similar approach to that employed by the ESSURE™ device. This would now consequently make the method of sterilisation irreversible.

8.2.2. Cystoscope / hysteroscope

Unfortunately the purpose built Rimmer Brothers operating hysteroscope was not adequate for the procedure of hysteroscopic sterilisation, however the cystoscope proved to be an effective vector for the applicator cannula. An improvement to this would be to permanently fix the deflecting bridge onto the cystoscope.

8.2.3. Hysteroscopic application cannula for the tubal screw

The use of the coiled applicator to bend towards the tubal ostia to apply the screw was a major improvement in the equipment. Potentially the coil can be improved so as to ensure there is no lateral rotation as it is screwed into place at the tubal ostia. As has been previously described this lateral rotation along the axis of the applicator cannula potentially will generate a wider diameter path
through the myometrium around the tubal ostia, leading to a poor grip in the surrounding tissues. Consequently further studies using different coils may improve tubal screw retention rates.

8.2.4. Mounting of the tubal screw on application cannula

The current tubal screw base has a titanium bayonet enabling screw disimpaction by an ‘un-locking’ mechanism. This technique works very effectively, and as it is held loosely in the applicator it does not lead to unwanted movement at the ostia during disimpaction, which can disrupt the thread generated in the surrounding muscle leading to poor screw retention. It also enables easy screw retrieval, so if they are incorrectly applied or if the patient desires the screws to be removed at a later date, then this can be readily achieved.

8.2.5. Distension

The current method of uterine distension using a 3 litre pressure bag appears to be highly effective in distending the uterine cornu and hence no improvements would appear to be required.
8.2.6. Methods to deflect the tubal screw towards the tubal ostia

As described the next step to improve the cystoscope is to permanently fix the deflecting bridge onto the cystoscope.

8.2.7. Application of tubal screw into tubal ostia

Current application of the screw into the tubal ostia consists of a seven 360° clockwise rotations of the application cannula. To improve screw retention the aim must be to limit the potential for disruption of the thread generated in the surrounding tissue. Altering the screw to increase the number of threads on the screw will necessarily lead to an increase in the number of rotations performed. Any force applied along the axis of the screw can potentially disrupt the screw thread (analogy; using a hammer to insert a screw). This can only be minimised by extreme caution in the application process and limiting the number of screw threads, this is therefore in conflict with improving plug retention.

8.2.8. Disimpaction of application cannula from screw following insertion

The current disimpaction process using the ‘un-locking’ mechanism appears highly effective. To minimise disruption of the thread generated in the
surrounding tissue the operator must be careful not to apply any force along the axis of the screw leading to a 'loose' fit of the screw. To minimise this the operator must use extreme caution to un-lock and release the screw.

**8.2.3. Conclusion**

Undeniably the current equipment used to attempt to effect tubal sterilisation is ineffective. Major changes must be made in either the technique or the equipment to improve tubal screw retention rates. These changes will continually be made to improve the efficacy of this method of hysteroscopic sterilisation in the future. It is also essential that any patient undergoing long-term PTFE tubal screw application be monitored, to ensure that this substance is medically safe over many years of use.
Chapter 9

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Appendix
Appendix 1

Publications


Appendix 2

Presentations


   **Gynaecology Poster Prize:**

   "The development of a new hysteroscopic method of female sterilisation."

   Roger Hart, Adam Magos  *Poster Presentation*

2. British Society of Gynaecological Endoscopy, Plymouth 1999

   "A new method of hysteroscopic sterilisation its development and results."

   Roger Hart, Meir Ruach, Adam Magos  *Oral Presentation*
Appendix 3

Protocol For New Contraceptive Device

Studies A and B (In-vivo studies of device insertion)

**Study A:** The device will be inserted immediately prior to laparoscopic or abdominal hysterectomy after establishing an external view of the uterus and providing the utero-tubal junction is clear of adhesions. The fallopian tubes will be hydrotubated with a dilute solution of methylene blue to ensure tubal patency. The uterus will be distended with CO₂ or Saline for hysteroscopy. Any intra-uterine abnormalities will be noted. Inability to adequately visualise the tubal ostia or insert the device, degree of difficulty and time taken will be recorded. Insertion will be monitored externally throughout to observe signs of imminent perforation of the uterus or fallopian tube. Once the device is in place a repeat hydrotubation will be performed to ensure complete tubal occlusion.

The hysterectomy will then be carried out by the intended route ensuring that at least 2cm of the proximal fallopian tube remains part of the operative specimen. Once the uterus has been excised it will be prepared by bisection in the midline. The pulling force required to remove the device will be measured on both sides. The contralateral device will be carefully removed to minimise tissue damage and its path and the extent of any uterine/tubal damage determined histologically. The age of the patient, phase of the menstrual cycle, obstetric history, current medication, size and weight of the uterus, and the presence of any fibroids or any other abnormalities will be recorded.

Adjustments to the size, shape of the device and to the insertion system will be made on the basis of these results. Approximately 10-20 patients will be required.

**Study B:** In this study the device will be inserted as in study A. The uterus will be examined by a histopathologist. The device carefully removed to minimise tissue damage and its path and the extent of any uterine/tubal damage determined histologically. The age of the patient, phase of the menstrual cycle, obstetric history, current medication, size and weight of the uterus, and the presence of any fibroids or any other abnormalities will be recorded.

Adjustments to the size, shape of the device and to the insertion system will be made on the basis of these results. Approximately 10 patients will be required in total.
Appendix 4

PATIENT INFORMATION SHEET

A NEW CONTRACEPTIVE DEVICE: PILOT STUDIES

Background to the studies Currently, sterilisation of the woman is one of the most popular and effective means of preventing unwanted pregnancies. It is usually performed as an in-patient procedure under general anaesthesia, and involves inserting a telescope (laparoscope) into the abdomen and placing clips or rings around the fallopian tubes via another cut in the skin. Once inserted, it is impossible to remove the clips or rings without a major abdominal operation.

Our new device A sterilisation technique which can be performed as a single out-patient procedure, is based on vaginal insertion without any external scars, is immediately effective, and does not require any invasive post-application investigations to prove correct positioning seems the ideal method. We would like to test out a new device designed at the Royal Free Hospital which we believe fulfills these criteria. It is made of an inert plastic material of the type, which is already widely used in medicine for prostheses.

What would be involved if you decide to take part? We have planned two pilot studies to test the efficacy of the new device before larger studies involving several hospitals. Only women having or who plan to have a hysterectomy are suitable to take part.

Study A: The device would be inserted once you have been anaesthetised and immediately before the hysterectomy. The position of the device would be checked by injecting some dye into the cavity of the womb (same as when we test for infertility). Insertion and checking of the device will add approximately 5 minutes to the total operating time. After the hysterectomy, the device would be checked once more and removed, and the womb (uterus) would be returned to the pathology department for testing as is usual. The device will have no effect on the hysterectomy and will not affect the examination of the uterus afterwards.

Study B: Women undergoing diagnostic hysteroscopy (a routine investigation for abnormal periods) and who plan to have a hysterectomy afterwards will have the device inserted at the time of the hysteroscopy. Even if the hysteroscopy is performed as an out-patient under local anaesthesia, insertion of the device is not expected to cause any additional discomfort and should take less than five minutes. The usual contraceptive methods must be continued until the hysterectomy. At the hysterectomy, the position of the device will be checked as already described. After the hysterectomy, the device would be checked once more and removed, and the womb (uterus) would be returned to the pathology department for testing as is usual. As before, the device will have no effect on the hysterectomy and will not affect the examination of the uterus afterwards.

Further information If you would like any further details about the studies, please do not hesitate to contact Dr. Roger Hart, Clinical Research Fellow, University Department of Obstetrics and Gynaecology at the Royal Free Hospital, London (Tel: 0171 794 0500 and ask for bleep 859).

Remember You are under no obligation to take part in these studies. If you do not wish to participate, your planned hysterectomy will not be affected in any way.

These studies have been approved by the RFH Ethical Practices Sub-Committee (Ref No. 62-96).
Appendix 5

PATIENT CONSENT FORM

A NEW CONTRACEPTIVE DEVICE: STUDY TO ASSESS CORRECT INSERTION

Name
Date of Birth
Hospital Number

I confirm that I understand the information which has been given to me regarding the purpose of the study and that I agree to hysteroscopy and insertion of the contraceptive device at the time of my hysterectomy.

Signature
Date

Name

I confirm that I have explained the purpose of the study and the procedures involved.

Signature
Date
Appendix 6

Protocol For New Contraceptive Device

Device insertion at the time of laparoscopic sterilisation

Study: The device will be inserted immediately prior to laparoscopic sterilisation after establishing an external view of the uterus and providing the utero-tubal junction is clear of adhesions. The fallopian tubes will be hydrotubated with a dilute solution of methylene blue to ensure tubal patency. The uterus will be distended with CO$_2$ or Saline for hysteroscopy. Any intra-uterine abnormalities will be noted. Inability to adequately visualise the tubal ostia or insert the device, degree of difficulty and time taken will be recorded. Insertion will be monitored externally throughout to observe signs of imminent perforation of the uterus or fallopian tube. Once the device is in place a repeat hydrotubation will be performed to ensure complete tubal occlusion.

The laparoscopic sterilisation will be performed as usual. The age of the patient, phase of the menstrual cycle, obstetric history, current medication, size and weight of the uterus, and the presence of any fibroids or any other abnormalities will be recorded.

Follow-up: The patient will be discharged later the same day if well. A telephone call will be made to the patient the following day to ensure the patient is well and to answer any questions. Ultrasound scans will be performed every 3 months and the device will be removed during the first 12 months. Removal will be performed under local anaesthetic in the out-patient hysteroscopy suite.

Adjustments to the size, shape of the device and to the insertion system will be made on the basis of these results. Approximately 20 patients will be required.
Appendix 7

PATIENT INFORMATION SHEET
A NEW CONTRACEPTIVE DEVICE: STUDY AT THE TIME OF LAPAROSCOPIC STERILISATION

Background to the study Currently, sterilisation of the woman is one of the most popular and effective means of preventing unwanted pregnancies. As you are aware it is usually performed as an in-patient procedure under general anaesthesia by inserting a telescope (laparoscope) into the abdomen and placing clips or rings around the fallopian tubes via another cut in the skin. (The procedure that you are due to have performed). Once inserted, it is impossible to remove these clips or rings without a major operation.

Our new device A sterilisation technique that could be performed as a single out-patient procedure through the vagina and cervix without any external scars, is immediately effective, and did not require any invasive post-application tests to prove correct positioning would be the ideal method. We would like to test out a new device designed at the Royal Free Hospital which we believe fulfils these criteria. It is made of an inert plastic material of the type that is already widely used in medicine for prostheses.

What would be involved if you decide to take part? Only women having or who plan to undergo a laparoscopic sterilisation are suitable to take part.

At the time of your operation, once you are anaesthetised before the laparoscopic sterilisation, a test will be performed to check that your fallopian tubes are open (this is a routine test performed in women undergoing infertility investigation). A small telescope will be passed into the womb through the cervix to help place our new plug device into your fallopian tubes. The position of the device will then be checked by repeating the previous test. Insertion and checking of the device will add approximately 5 minutes to the total operating time. Then the planned laparoscopic sterilisation will be performed. After the sterilisation you will return to the ward prior to discharge home later that day.

The following day a doctor will contact you to ensure that all is well, although we do not believe that you should suffer any discomfort due to the device insertion, other than the usual post laparoscopic sterilisation discomfort. You will be required to attend follow-up appointments to ensure that the devices are still in place. This will involve undergoing a vaginal ultrasound scan at three monthly intervals up to 1 year and to undergo a hysteroscopy to have the contraceptive device removed. There is a possibility that the device cannot be removed but it is made of a safe substance, which is widely used in medicine, and hence we believe it to be safe if left in place.

Further information If you would like any further details about the studies, please do not hesitate to contact Dr. Roger Hart, Clinical Research Fellow, University Department of Obstetrics and Gynaecology at the Royal Free Hospital, London (Tel: 0171 794 0500 and ask for bleep 859).

Remember You are under no obligation to take part in these studies. If you do not wish to participate, your planned hysterectomy will not be affected in any way.

This study has been approved by the RFH Ethical Practices Sub-Committee (Ref No. 62-96).
Appendix 8

PATIENT CONSENT FORM

A NEW CONTRACEPTIVE DEVICE: STUDY TO TEST TUBAL OCCLUSION

Name
Date of Birth
Hospital Number

I confirm that I understand the information which has been given to me regarding the purpose of the study and that I agree to hysteroscopy and insertion of the contraceptive device at the time of my laparoscopic sterilisation. I understand that I will be required to attend the hospital for vaginal ultrasound scans every 3 months for up to 1 year and to undergo a hysteroscopy to have the contraceptive device removed. I understand there is a possibility that the device cannot be removed but I understand that it is made of a safe substance, which is widely used in medicine.

Signature
Date

Name

I confirm that I have explained the purpose of the study and the procedures involved.

Signature
Date
Appendix 9

To run CD-ROM open PowerPoint Presentation