

# Ectopic Pregnancy Following Reconstructive, Organ-Preserving Microsurgery in Tubal Infertility

Cordula Schippert, Philipp Soergel and Guillermo-José Garcia-Rocha  
*Medical School of Hannover, Department of Gynecology and Obstetrics  
Division of Reproductive Medicine; Carl-Neuberg-Str. 1, 30625 Hannover,  
Germany*

## 1. Introduction

Disease or damage of the fallopian tubes accounts for 25% to 35% of reported cases of infertility (Pandian et al., 2008). Decreased fecundity may be caused by tubal occlusion, fimbrial damage, and/or peritubal adhesions, usually related to previous pelvic inflammatory disease, endometriosis, pelvic surgery, salpingitis isthmica nodosa or otherwise unknown causes. A special group of women affected by tubal infertility are those who have undergone intentional sterilization; 5% to 25% of these women (Neuhaus et al.; 1995; Kim et al.; 1997; Schippert et al., 2004) later regret having undergone this surgery. Some of them desire an operation to restore fertility, the most frequent reason for this is the desire to have a child with a new partner. The diagnosis of "tubal infertility" is a serious and burdensome diagnosis for the affected woman.

In the presence of a functional impairment of the fallopian tubes, the desire to have a child is (if at all) only possible through complicated, risky and cost-intensive therapies: on the one hand through reconstructive surgery or - on the other hand - by means of assisted reproductive technology procedures (ART). The limitations of surgical repair in many cases have been the driving force behind the rising numbers of ART. However, the success of either treatment - even when attempted multiple times - cannot be guaranteed. Outpatient in-vitro fertilization (IVF) can be repeated several times which results in an overall higher success rate. Unfortunately, a large number of couples is not able to afford multiple IVF cycles. An IVF therapy also is not without risks and is associated with physical and mental stresses which not infrequently lead to a discontinuation of therapy.

Problems of IVF therapy in many countries, e.g. in Germany, are found in the low birth rates of at most 21% despite a clinical pregnancy rate of approximately 28-30% per embryo transfer, but it is the large number of multiple pregnancies at approximately 20% with occasionally significant maternal and child morbidity and mortality rates. The overall average pregnancy rate in Germany for all IVF cycles in 2009 was 29.5%, compared with a rate of 28.6% for the ICSI cycles (Bühler et al., 2010). Because of German legal restrictions, no embryo selection is permitted and the German Embryo Protection Act, passed in 1991, permits no more than three embryos to be transferred. Oocyte donation as well as surrogate motherhood is illegal.

Microsurgery of the fallopian tubes to restore functioning in the presence of tubal infertility is a therapeutic standard that has been established for decades. In contrast to IVF therapy, reconstructive surgeries of the fallopian tubes are curative measures. They are performed with the intention of permanently restoring the physiological ability of a woman to have a chance to conceive in every ovulating cycle. After successful surgery, additional spontaneous conceptions are, therefore, possible without renewed therapy. The course of pregnancy and the manner of birth in patients who underwent microsurgery do not differ from childbirth in a normal population. Also with respect to premature births, the rate of cesarean section and multiple births there are no differences versus healthy women who have not undergone surgery.

### 1.1 Ectopic pregnancy

Ectopic pregnancy (EP) is a serious and also nowadays a cause of maternal mortality in early pregnancy. The risk factors for EP in general population are pelvic infection, tubal disease, endometriosis, previous tubal surgery, age >35 years and smoking (Thornburn et al., 1986; Tuomovaara & Kauppila, 1988; Dubuisson et al., 1996; Strandell et al., 1999; Bouyer et al., 2003; Clayton et al., 2006; Practice Committee of American Society for Reproductive Medicine, 2008; Gelbaya, 2010). The incidence of EP in general population is approximately 2% (Strandell et al., 1999).

The first pregnancy conceived after ART and embryo transfer was ectopic (Steptoe & Edwards, 1976). The risk factors for ectopic pregnancy following ART with an incidence of 2.1% to 9.4% (Lesny et al., 1999) in all ART patients and up to 11% in patients with tubal infertility (Dubuisson et al., 1991) are reported to be tubal disease, history of pelvic infection (Marcus & Brinsden, 1995; Strandell et al., 1999) and tubal infertility as it is considered to be the indication for ART (Herman et al., 1990; Dubuisson et al., 1991, Verhulst et al., 1993).

In Germany, the overall rate of EP in women undergoing ART procedures from 1999 to 2009 was 2.0% (95% confidence interval [CI] 1.9-2.1) related to all pregnancies with a maximum of 2.2% in the group of women >39 years of age (95% CI 1.8-2.5). 19.9% of all cycles which lead to a pregnancy are done in couples who had an infertility diagnosis of "tubal factor" or "tubal disease". The incidence of EP according to the presence or absence of tubal pathology ranges from 2.3% to 3.7% in the presence of tubal pathology and from 1.7% to 2.1% in women without documented tubal disease. The highest EP rate was detected to be 4.5% (95% CI: 3.0-6.0) related to all pregnancies in young women <30 years who firstly had a tubal pathology, who secondly had been treated with IVF, and who thirdly smoked (original data from the German IVF-Registry, D.I.R. committee's office, Bismarckallee 8-12, 23795 Bad Segeberg, Germany).

Tubal EP is also a known adverse effect of tubal reconstructive surgery; however the incidence varies widely between 0% and up to 40% depending on the type, location and severity of the tubal disease and the surgical procedure. The success of infertility surgery and the risk for EP depend on the careful selection of appropriate patients.

When compared with the macrosurgical approach, the use of a microsurgical technique has significantly improved the outcome of tubal anastomosis with reduced EP rates (Lavy et al., 1987).

The reconstructive microsurgical techniques should include the following elements (Gauwerky, 1999, Schippert et al., 2010): Atraumatic surgical technique, complete removal of diseased tissue, careful hemostasis, preparation layer by layer and exact adaptation of the tissue structures, complete peritonealization, and continuous irrigation of exposed peritoneal tissue surfaces.

In the presence of only mild or moderate tubal pathology, term pregnancy rates of 65% to 80% for salpingeostomy, adhesiolysis and reversal of sterilization have been reported (Marana et al., 2003, 2008; Practice Committee of American Society for Reproductive Medicine, 2008). The ectopic rate for mild disease is reported to be 1%-10% (Boer-Meisel et al., 1986; Winston & Margara, 1991; Nackley & Muasher, 1998), in contrast, EP rates can increase up to 20% to 40% in the presence of intrinsic tubal damage, salpingitis isthmica nodosa and severe tubal pathology (Posaci et al., 1999; Taylor et al., 2001; Pandian et al., 2008).

## 2. Methods of microsurgical reconstruction of the fallopian tubes

### 2.1 Reversal of sterilization

Microsurgical reversal of sterilization leads to a cumulative pregnancy rate ranging from 40% to 84% and monthly fecundability of 8%-10% (Kim et al., 1997; Land & Evers, 2002), the overall risk of EP appears to be less than 10% (Posaci et al., 1999; Practice Committee of American Society for Reproductive Medicine, 2008). Possible prognostic factors include the type of performed sterilization procedure, the site of anastomosis and the postoperative tubal length (Posaci et al., 1999). Tubal occlusion with rings or clips, isthmic-isthmic anastomosis and a tubal length >5 cm are associated with a greater likelihood of successful pregnancy after re sterilization (Practice Committee of American Society for Reproductive Medicine, 2008).

During a retrospective study time of eleven years, 127 women (median age 35.4 years [26-42]) were refertilized in our clinic after a sterilization was performed before (**Figure 1; Figure 2a and 2b**).

The follow-up data of 89 patients could be collected for analysis. The EP rate following the microsurgical reversal of sterilization was 6.7% (6/89 patients), and the intrauterine pregnancy rate was 73.0% respectively (65/89 patients) (**Table 1**).

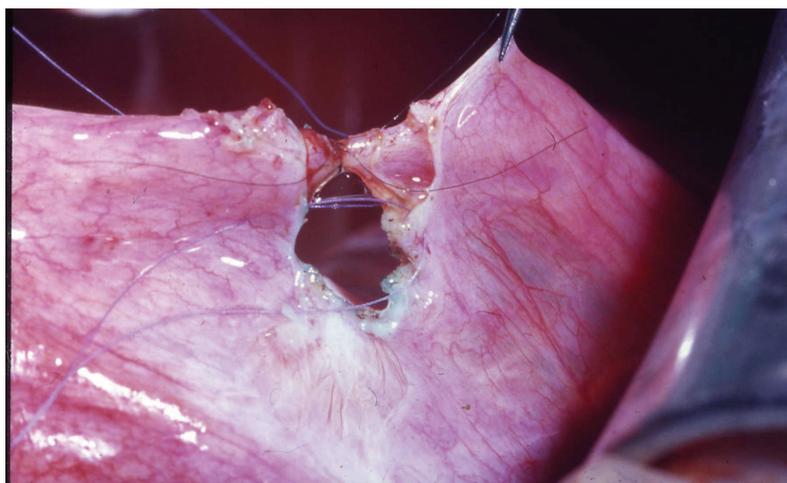


Fig. 1. Isthmic-isthmic reanastomosis of the fallopian tube after sterilization (refertilization) using sutures 8-0 and 6-0 vicryl

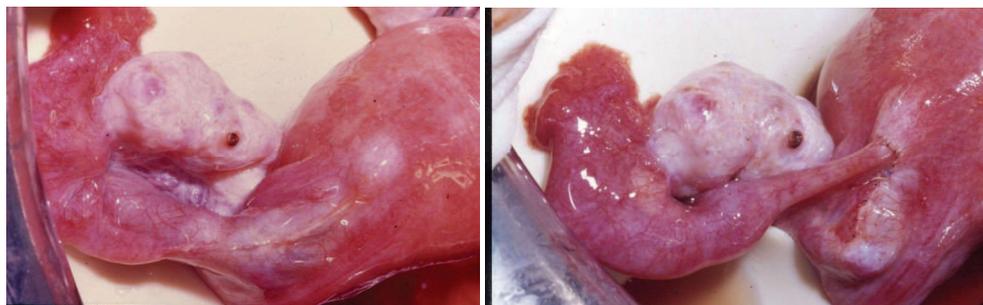


Fig. 2. (a) status after sterilization by bipolar coagulation of the fallopian tube; (b) isthmic-cornual refertilization of the fallopian tube

Method of surgery (microsurgery)	Number of patients (percent)	Pregnancy rate	Ectopic pregnancy rate	Abortion rate	Birth rate
Refertilization after previous sterilization	89 (100%)	65 (73.0%)	6 (6.7%)	14 (15.7%)	45 (50.6%)

Table 1. Results of reversal of sterilization (refertilization): All types of anastomosis and length of fallopian tubes; 127 patients contacted, 89 patients answered; median age 35.4 years (26-42). Medical School of Hannover, Germany, 1990-2001, analysis 2004; percentages are related to all patients. The analysis considered only the first pregnancy that followed the operation, even if an EP or abortion was followed by a normal pregnancy with subsequent childbirth.

## 2.2 Microsurgery due to acquired tubal damages

In our study, 426 women (median age 31 years [21-42]) underwent tubal microsurgery after hysteroscopic and laparoscopic diagnosis of acquired tubal sterility and the prior exclusion of serious ovarian and andrological disorders: Adhesiolysis, anastomosis due to an acquired damage of the fallopian tubes, fimbrioplasty and salpingotomy had been performed. Several of these surgical procedures were occasionally combined in a single procedure, e.g. a fimbrioplasty on one tube and an anastomosis on the other tube. It was finally possible to contact 287 patients and proceed with the analysis (Table 2).

### 2.2.1 Peritubal adhesiolysis

Overall intrauterine pregnancy rates following adhesiolysis by microsurgery vary widely - from 21% to 80% (Feinberg et al., 2008; Lok et al., 2003; Posaci et al.; 1999), mainly because of bias in case selection and the absence of standardized assessment of the extent of tubal damage, especially the mucosal state. In an analysis including nine studies with 456 patients, an EP rate of 0% to 16% following adhesiolysis by microsurgery, and a rate of intrauterine pregnancy (IUP) of 21% to 68% respectively is reported (Posaci et al., 1999). High pregnancy rates of about 60% with EP rates of 6% have been reported in cases of the absence of peritoneal damage of serosa after the surgical procedure and a complete removal of adhesions with a good anatomical reconstruction of ovaries and fallopian tubes. EP rates

increased up to 20% if at least one of these criteria was not fulfilled (Posaci et al., 1999; Lundroff et al., 1991) or if the tubal damage was severe (Lok et al., 2003; Boer-Meisel et al., 1986; Schlaff et al., 1990). For this reason, patients with dense adhesions and a severe tubal pathology are best referred to IVF.

In our study, the rate of EP following microsurgical adhesiolysis was 7.8% (9/116 patients), and the IUP rate was 42.2% (49/116) respectively (**Table 2**).

Method of surgery (microsurgery due to acquired tubal damages)	Number of patients	Pregnancy rate	Ectopic pregnancy rate	Abortion rate	Birth rate
Adhesiolysis 12,8%	116	49 (42.2%)	9 (7.8%)	3 (2.6%)	37 (31.9%)
Fimbrioplasty 17,3%	55	30 (54.6%)	3 (5.5%)	6 (10.9%)	21 (38.2%)
Salpingostomy 49,7%	153	53 (34.6%)	12 (7.8%)	7 (4.6%)	34 (22.2%)
Anastomosis 20,2 %	68	38 (55.9%)	7 (10.3%)	9 (13.2%)	22 (32.4%)
<b>Total 100 %</b>	392 interventions (287 pat.)	170 (43.4%) related to total number of surgery	31 (7.9%)	25 (6.4%)	114 (29.2%) related to total number of surgery

Table 2. Results of reconstructive tubal surgery due to acquired tubal damages: 426 patients contacted, 287 patients answered; median age 31.0 years (21-42), multiple methods of surgeries during one intervention possible, total rates are related to total number of interventions. Medical School of Hannover, Germany, 1990-2001, analysis 2004. The analysis considered only the first pregnancy that followed the operation, even if an EP or abortion was followed by a normal pregnancy with subsequent childbirth.

### 2.2.2 Distal tubal surgery: fimbrioplasty and salpingostomy / salpingotomy

Pregnancy outcome after distal tubal microsurgery has been related to several factors such as preexisting tubal disease, the extent of adnexal or even dense adhesions, the ampullary dilatation, the wall thickness, and the lack of normal mucosa (Posaci et al., 1999). In general, salpingostomy has the lowest success rate among the tubal microsurgeries. Pregnancy rates following fimbrioplasty are higher than those after salpingostomy (60% vs. 31%) (Donnez & Casanas-Roux, 1986). The term pregnancy rates following distal tubal surgery varied from 3% to 59% when patients had only few and non-fixed adhesions, a thin tubal wall, and normal mucosal appearance of the endosalpinx (Boer-Meisel et al., 1986). A meta-analysis including eight studies with 399 patients showed EP rates from 3% to 23% with an IUP rate of 0% to 51% (Posaci et al., 1999) following salpingostomy, salpingoneostomy and fimbrioplasty.

Another analysis with a total of 1,514 patients showed an IUP rate and recurrent EP rate following salpingostomy for the treatment of EP of 61% and 15%, respectively (Yao & Tulandi, 1997). A large review of ten case series in women who underwent salpingoneostomy due to distal tubal occlusion (n=1,128) reported a cumulative EP rate per pregnancy of 23% (Marana & Quagliarello, 1988b) and an EP rate of 8% in women who underwent tubocornual anastomosis for proximal tubal occlusion (n=118) (Marana & Quagliarello 1988a).

In our own patient database (**Table 2**), the EP rates had been 7.8% (12/153 patients) when salpingotomy was performed and 5.5% (3/55 patients) (**Figures 3a and 3b**), respectively, when fimbrioplasty was done (**Figure 4a and 4b**). The pregnancy rates had been 34.6% (53/153 salpingotomy), and 54.6% (30/55 fimbrioplasty) respectively.

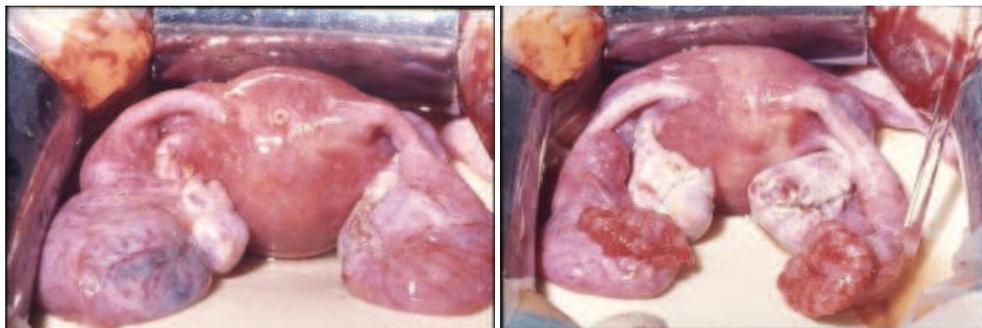


Fig. 3. (a) hydrosalpinges and peritubal adhesions; (b) salpingotomy on both sides and adhesiolysis

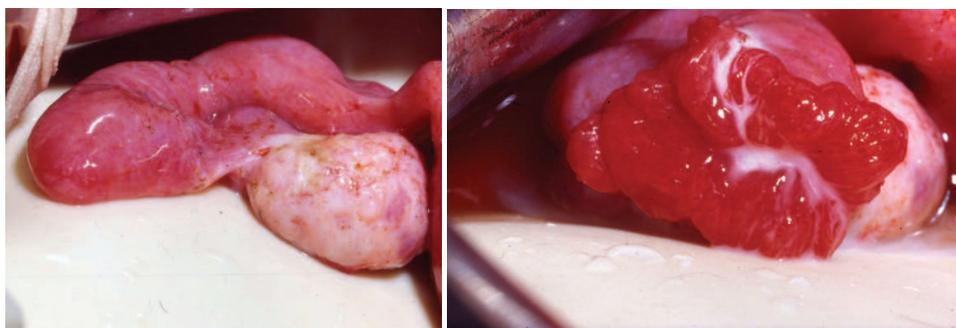


Fig. 4. (a) fimbrial phimosis; (b) fimbrioplasty

### 2.2.3 Proximal tubal disease: tubo-cornual anastomosis

Case series and cohort studies demonstrated high pregnancy rates following microsurgical tubo-cornual anastomosis (Johnson et al., 2010). A review of eleven case series in women who underwent proximal tubal operations by microsurgery ( $n = 490$ ) reported a cumulative EP rate of 0% to 12% and a rate of IUP of 22% to 74% concerning to all patients (Posaci et al., 1999). The largest study from 1997 showed an EP rate of 11% and an IUP rate of 74% after a three year follow-up (Dubiusson et al., 1997). Negative prognostic factors on the pregnancy rate after tubocornual anastomosis are reduced residual length, damaged intramural portion, presence of chronic inflammation and tubal inclusion in the tubal wall, and tubal endometriosis (Posaci et al., 1999).

In our own study with 68 patients, the EP rate was 10.3% (7/68 patients) whereas the IUP rate was 55.9% (38/68 patients) when tubal anastomosis (reversal of sterilization excluded) was performed (Table 2).

## 3. Conclusion

In cases of tubal infertility, it is today possible to fulfill a couple's desire to have a child either by means of a reconstructive operation of the fallopian tubes or by IVF therapy. The success of treatment - even when attempted multiple times - cannot be guaranteed. In

general, microsurgery and IVF therapy are not competing, but complementary therapeutic options for the treatment of tubal infertility. The definitive decision about which therapy to pursue should always be left to the affected couple after the pertinent information has been competently communicated.

The risk for EP and the chances for an intrauterine ongoing pregnancy following tubal reconstructive surgery, respectively, vary widely depending on the type, location and severity of the tubal disease and the performed surgical procedure.

The ectopic rate for mild acquired tubal disease is reported to be 1%-10% (Boer-Meisel et al., 1986; Winston & Margara, 1991; Nackley & Muasher, 1998) and for reversal of sterilization less than 10% (Practice Committee of American Society for Reproductive Medicine, 2008), but in contrast, EP rates increase up to 40% in the presence of intrinsic tubal damage, salpingitis isthmica nodosa and severe tubal pathology (Taylor et al., 2001; Posaci et al., 1999; Pandian et al., 2008; Marana & Quagliarello, 1988a, 1988b; Akande et al., 2004; Mosgaard et al., 1996). For this reason, patients with dense adhesions like frozen pelvis and a severe tubal pathology are best referred to IVF (Schippert et al., 2010).

In our own patient's collective, the EP rate following reversal of sterilization was 6.7%.

In the presence of acquired tubal disease, mainly because of previous pelvic inflammation and salpingitis, the overall EP rate was 7.9% following microsurgical reconstruction using the techniques of adhesiolysis, salpingostomy, salpinxostomy, fimbrioplasty and anastomosis.

The risk factors for developing EP after ART still are inconsistent. The incidence is reported to be between 2.1% and up to 11% in tubal infertility. The data of the German IVF Registry demonstrate a significantly increased incidence of EP in the presence of tubal pathology (original data from the German IVF Registry). The highest EP rate related to all pregnancies was detected to be 4.5% (95% CI: 3.0-6.0) in women <30 years who firstly had a tubal pathology, who secondly had been treated with IVF, and who thirdly smoked. If these women are non-smokers, the EP rate was 4.2% (95% CI: 3.5 - 5.0).

In summary, the risks for EP after ART and microsurgical tubal reconstruction in women with tubal infertility or tubal co-morbidity are significant and approximately comparable. Surgical tubal reconstruction still remains a significant part in the range of modern infertility treatments, however the success and/or failure of infertility surgery depends on a careful selection of appropriate patients. ART is especially recommended in women with severe tubal pathology and in the case of severe male infertility or ovarian dysfunction.

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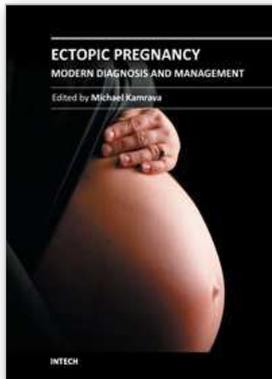
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## **Ectopic Pregnancy - Modern Diagnosis and Management**

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Ectopic pregnancy is the second major cause of maternal mortality in the United States and a leading cause of maternal morbidity and mortality in the world. This book contains the practical methods to early diagnosis of various forms of ectopic pregnancies and their modern management. Ectopic Pregnancy - Modern Diagnosis and Management is a comprehensive book which guides the reader through all features of ectopic pregnancy, both practical and academic, covering all aspects of diagnosis and management of ectopic pregnancy in a clear, concise, and practical fashion. The book is organized so that it can either be read cover to cover for a comprehensive tutorial or be kept desk side as a reference to the ectopic pregnancies. Each chapter introduces a number of related ectopic pregnancy and its diagnosis, treatment and co-morbidities supported by examples. Included chapters bring together valuable materials in the form of extended clinical knowledge from practice to clinic features.

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University Campus STeP Ri  
Slavka Krautzeka 83/A  
51000 Rijeka, Croatia  
Phone: +385 (51) 770 447  
Fax: +385 (51) 686 166  
[www.intechopen.com](http://www.intechopen.com)

### **InTech China**

Unit 405, Office Block, Hotel Equatorial Shanghai  
No.65, Yan An Road (West), Shanghai, 200040, China  
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元  
Phone: +86-21-62489820  
Fax: +86-21-62489821

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