



子宮外孕的診斷與治療之最新趨勢

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Ectopic pregnancies after infertility treatment: modern diagnosis and therapeutic strategy.

Ectopic pregnancy (EP) is a major event in a woman's reproductive life. It complicates infertility treatment and must be recognized early to simplify the treatment strategy, which must always be directed towards optimizing subsequent fertility. Epidemiological findings indicate that tubal history and smoking are the principal risk factors of those EP that are considered reproductive (rather than contraceptive) failures. Adding together the attributable risks for EP allows the construction of a risk scale to determine its probability for any given patient. This risk calculation makes it easier to establish a diagnostic strategy that uses abdominal and transvaginal ultrasound and hCG assays. Progesterone assays are useful only for determining the activity of the pregnancy but do not help to identify its site. Conservative treatment is to be preferred unless the EP occurs on a known hydrosalpinx. All the treatment trials and the Cochrane database meta-analysis show that medical treatment with methotrexate, preferably multidose, is equivalent in efficacy to conservative treatment with laparoscopy in the populations studied. Heterotopic pregnancies, which occur most often after assisted reproduction technology (1–3%), should preferably be treated by salpingectomy except in interstitial sites. There is no consensus that IVF is indicated after EP. The patient's age is probably the determining factor: fertility treatment should not be delayed to an age where the results would be altered, especially with the risk of a recurrent EP.

Epidemiology

Ectopic pregnancy

- ❖ Accounts for 80% of first trimester maternal deaths
- ❖ 11.1 per 1000 pregnancies in 1997–99 in UK
- ❖ Increasing use of outpatient therapy for ectopic pregnancy has been shown to make incidence data increasingly unreliable

Reproductive failure vs Contraceptive failure

- ❖ EP differ in almost every respect: incidence, site, risk factors and subsequent fertility
- ❖ Increased risk of EP has been repeatedly noted among **infertile** women and whose pregnancies result from ovulation induction especially **CC**, from all **IVF**(2.2%) and from **ICSI** (1.9%)



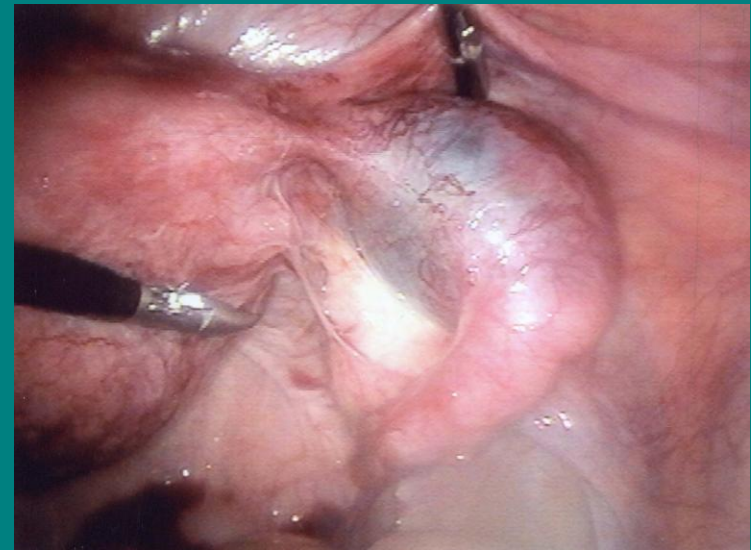
Diagnosis

- ❖ Assessment: **TVU** vs **LSC**
- ❖ 3D USG
- ❖ Serum markers
- ❖ Progesterone
- ❖ Strategies
- ❖ Risk factors and risk scale
- ❖ Screening

Diagnosis with or without laparoscopic approach

Laparoscopic approaches:

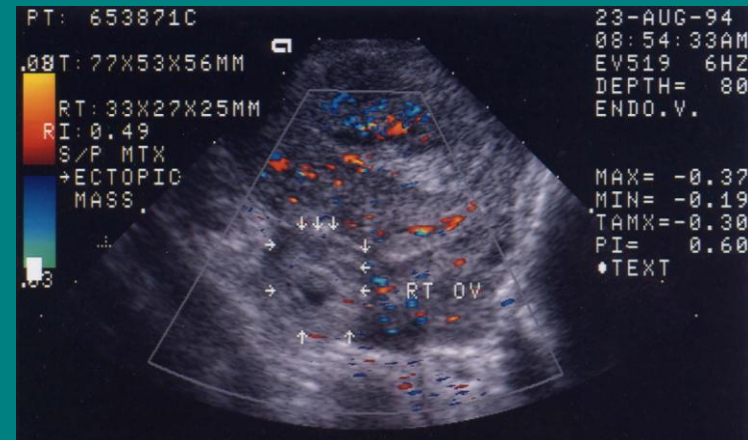
- ❖ Although laparoscopy is still widely accepted as the “**gold standard**” in the diagnosis of ectopic pregnancy, it has been reported to have a **false negative** rate of 3–4% and a **false positive** rate of up to 5%.
- ❖ Disadvantage: **complication** rate 1/1000 ~ 3.9/1000 and more **expensive**



Diagnosis with or without laparoscopic approach

Non-laparoscopic approaches:

- ❖ **trans-vaginal ultrasound** and the quantitative measurement of **serum β -hCG** (discriminatory zone) and (in some algorithms) the measurement of **serum progesterone** concentration
- ❖ Condition: **high quality TVU** and **same day** serum β -hCG assay; FU clinic with **on-call medical staff** (every 48 hours and prn)



Advantages:

Many women with a pregnancy of unknown site will have trophoblast in regression which does not require any therapy, Some women can be managed medically.



Diagnosis

- ❖ Transvaginal ultrasound had a sensitivity of 89.9% and a specificity of 99.8%. Positive and negative predictive values of 92.5% and 99.8% (Condous UOG 2003).
- ❖ Transvaginal ultrasound has largely replaced laparoscopy in the diagnosis of ectopic pregnancy,
- ❖ The **role of laparoscopy** as a **diagnostic** tool is limited to a small number of women **with symptoms and normal ultrasonography** (Atri JCU 2003).
- ❖ However, for most women with a suspected ectopic pregnancy, laparoscopy should be regarded as a **therapeutic tool** rather than a diagnostic one.

Diagnosis

- ❖ Three-dimensional ultrasound seems unlikely to ever play a major role
- ❖ One possible role is in the determination of the **exact location** of **unusually sited** ectopic pregnancies (Luis 2003, Wang 2004).
- ❖ Color Doppler imaging (CDI) technique (3-D VOCAL imaging system): the geometric shape of the gestational mass was extracted virtually with a simultaneous display of the **volume of a lesion** and the surrounding spatial vascular network architectural pattern and **indices of blood flow** (Chou 2004).

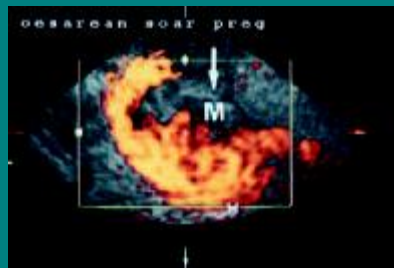


FIG. 2. Reconstructed 3-dimensional oblique coronal sonogram demonstrating a gestational sac (arrow) and interstitial portion of the fallopian tube.

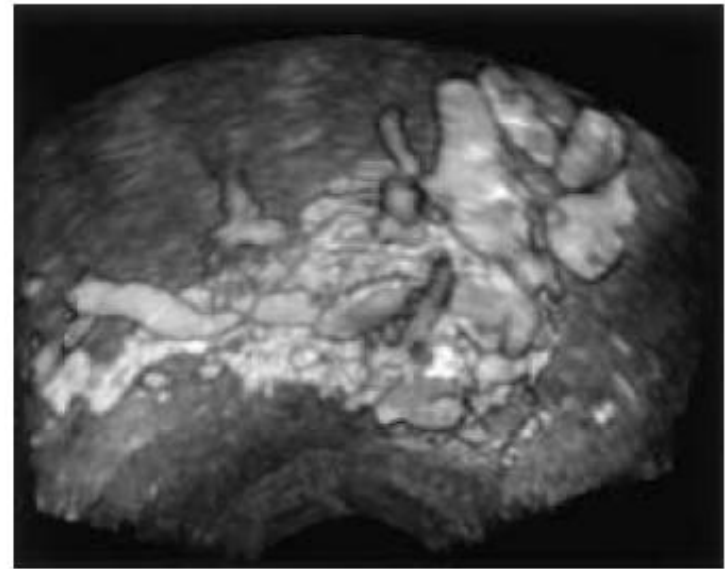


FIG. 2. Three-dimensional power Doppler ultrasound demonstrating a viable pregnancy with irregular course and branching peritrophoblastic vascularity in the myometrium of the anterior uterine wall.

Diagnosing Ectopic Pregnancy: Decision Analysis Comparing Six Strategies

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Results: Ultrasound followed by serum hCG in women with nondiagnostic scans yielded the most favorable outcomes; no ectopic pregnancy was missed, only 1% of all potential intrauterine pregnancies were interrupted, and time to diagnosis averaged 1.46 days. Quantitative hCG measurement followed by ultrasound only in women with hCG levels above the discriminatory zone was optimal if sensitivity of ultrasound to diagnose intrauterine pregnancy was less than 93%. Serum progesterone measurement was not favored because it was associated with missed ectopic pregnancies (2.6%).

Conclusion: Given the current accuracy of tests for diagnosing ectopic pregnancy, algorithms using a combination of ultrasound and hCG resulted in the best outcomes. Ultrasound as the first step was the most efficient and accurate method of diagnosing ectopic pregnancies. (Obstet Gynecol 2001;97:464–70. © 2001 by The American College of Obstetrics and Gynecology)

Table II. Odds ratios for ectopic pregnancy (EP) (compared with women with recent successful pregnancies) and the attributable risks associated with different risk factors

	Odds ratio	Attributable risk ^a
History of genital infection		0.18 ^b
Probable salpingitis	2	
Confirmed salpingitis	3.5	
History of tubal surgery	3.5	0.18 ^b
Smoking		0.35
Ex-smoker	1.5	
1–9 cigarettes per day	2	
10–19 cigarettes per day	3	
≥20 cigarettes per day	4	
Age (years)		0.14
30–39	1.5	
≥40	3	
Obstetric history		
Spontaneous abortion	3	0.07
Elective abortion	2	0.03
IUD history	1.5	0.05
Previous infertility	2.5	0.18
All factors, taken together		0.76



Surgical treatment

- ❖ A large proportion of women with an ectopic pregnancy will require surgical treatment.
- ❖ Laparoscopic approach will be preferred for most of these women
- ❖ Choice of salpingectomy or salpingotomy is controversial.
- ❖ Reviews suggest that there is **no definite increase** in the likelihood of subsequent intrauterine pregnancy after salpingotomy compared with salpingectomy.



Treatment by laparoscopy vs. laparotomy

- ❖ Data from controlled studies show that a laparoscopic approach offers significant advantages when compared to laparotomy
- ❖ Of concern is that when a salpingo(s)tomy was performed, the persistent trophoblast rate in these controlled trials was significantly **higher following laparoscopy** (12.2% versus 1.7%)
- ❖ Reproductive outcome: 145 women subsequently desired future fertility and the intra-uterine pregnancy rate was **61%** after laparoscopic surgery and **52%** after laparotomy. The recurrent ectopic pregnancy rate was **7%** after laparoscopy and **14%** after laparotomy (**no statistical significance**).

Treatment by laparoscopic salpingo(s)tomy vs. salpingectomy

- ❖ A **laparoscopic salpingectomy** can be performed using pre-tied ligatures; coagulation of the mesosalpinx with bipolar or monopolar diathermy forceps and cutting with scissors; thermocoagulation with CO2 KTP or argon laser, or the use of endoscopic staplers.
- ❖ **Laparoscopic salpingo(s)tomy** can be performed by making an incision over the anti-mesenteric border of the fallopian tube with either a needle diathermy probe, scissors or laser.
- ❖ **Bleeding** from the salpingo(s)tomy site can be troublesome. **Dilute vasopressin** solution (**5 IU vasopressin in 100 ml** normal saline) can be injected into the mesosalpinx prior to performing.
- ❖ **Primary closure** of the incision site at ampullary salpingo(s)tomy has **not** been shown to be of benefit.

Laparoscopic salpingo(s)tomy

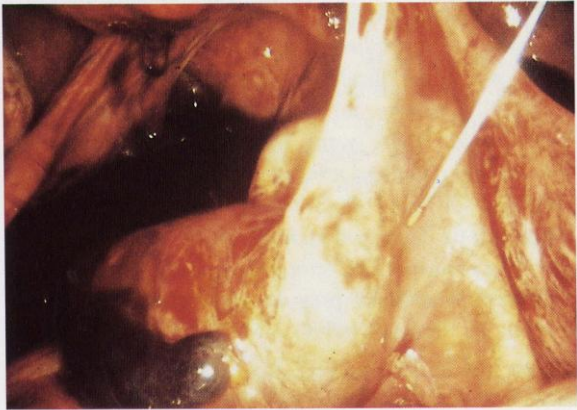


Figure 1 Injection of vasopressin into the mesosalpinx

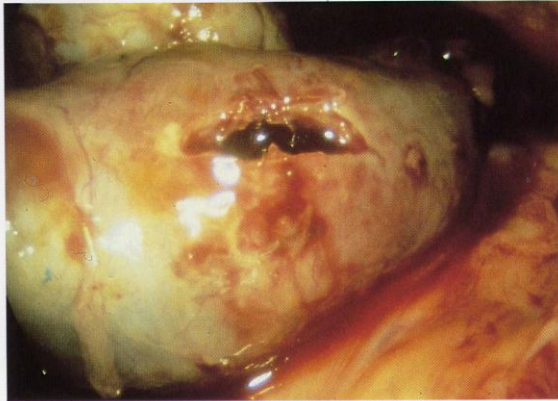


Figure 3 The incision

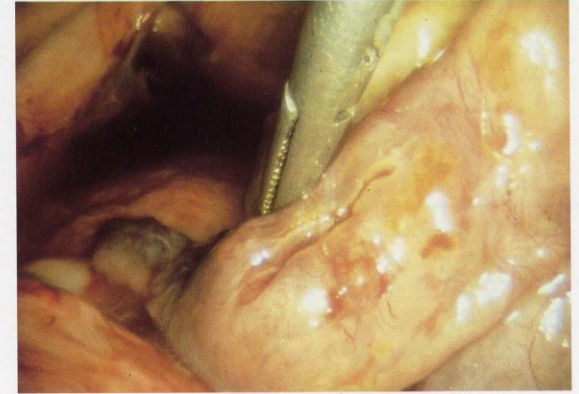


Figure 5 At the end of the procedure, the salpingotomy is left open

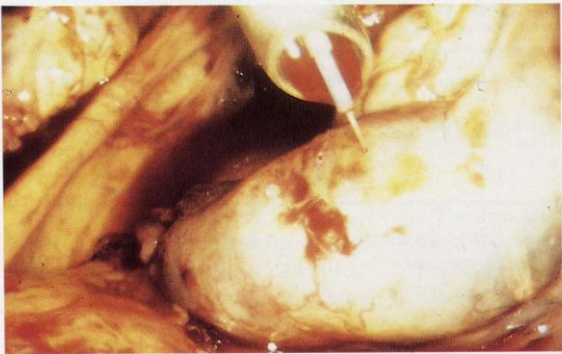


Figure 2 Salpingotomy in the antimesenteric proximal portion of the hematosalpinx with the needle electrode of the triton



Figure 4 Aspiration of the trophoblast with the triton

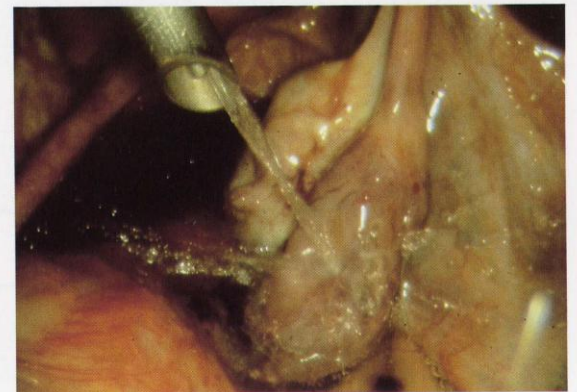
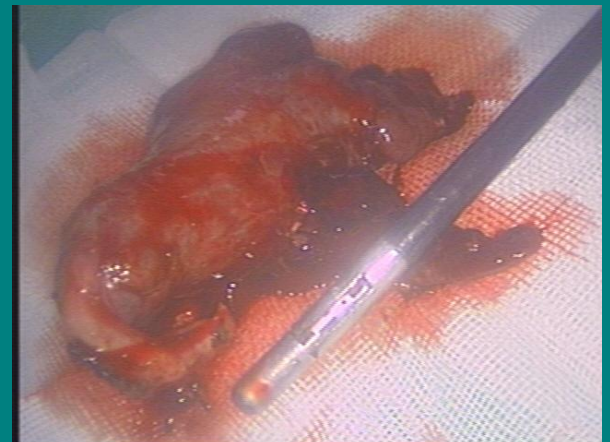
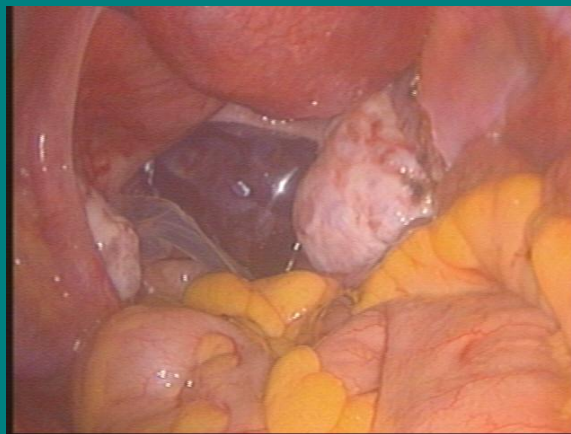
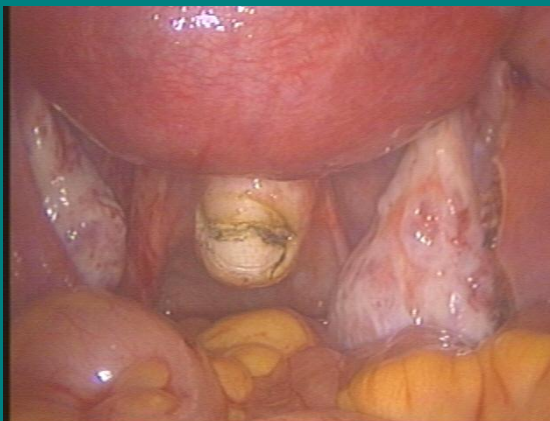
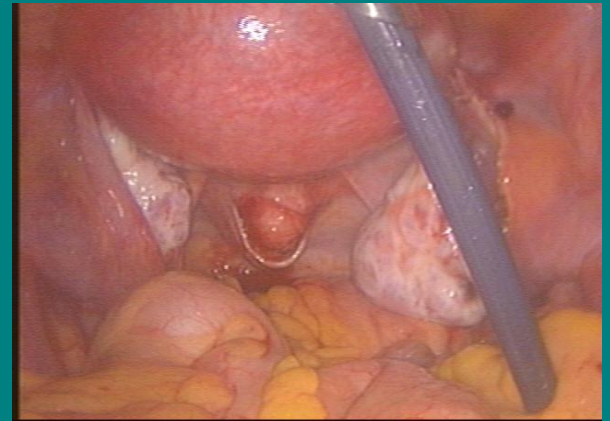
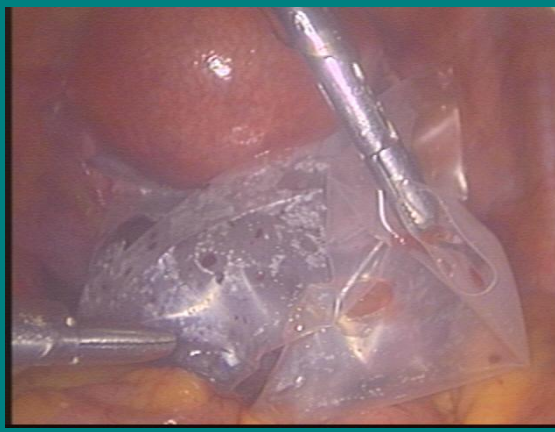
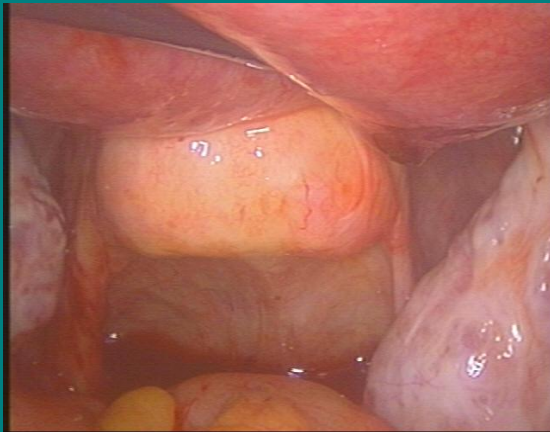


Figure 6 Washing of the pelvis

Laparoscopic ectopic surgery

- ❖ Checking tubal patency
- ❖ Specimen removal





Treatment by laparoscopic salpingo(s)tomy

- ❖ If **persistent trophoblast** is suspected then most women can be successfully treated with a **single dose** of intra-muscular **methotrexate** at a dose of 50 mg/m² or 1 mg/kg.
- ❖ Treating women if serum β -hCG concentrations remain above 10% of their pre-operative levels on day 12 after surgery, or are above 1000 IU/l on post-operative day 7, or have **failed to fall to below 65% of pre-operative levels within 48 h.**

Ruptured isthmal pregnancy following laparoscopic salpingostomy in the ipsilateral tube

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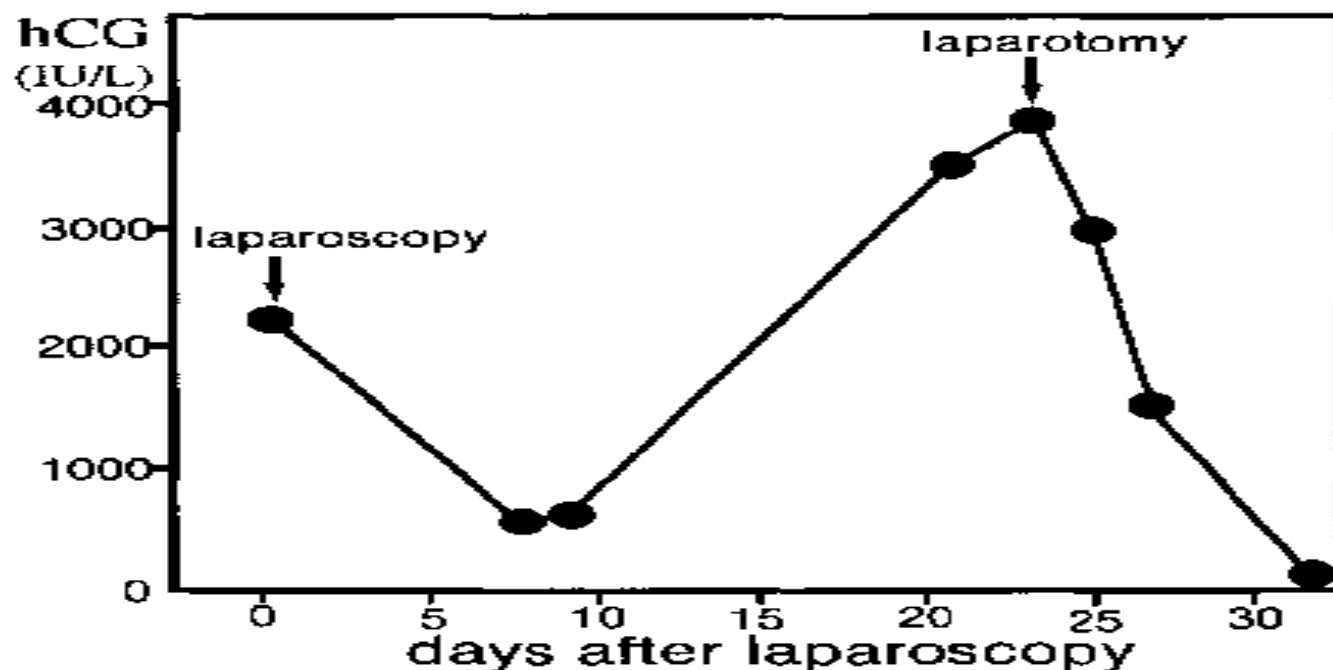


Fig. 1. Urinary concentrations of hCG in a patient with ectopic pregnancy. The day of laparoscopic surgery was arbitrarily set at 0. Laparotomy was performed on the 24th day following linear salpingostomy.

Outcome of treatment by laparoscopic salpingo(s)tomy vs. salpingectomy

- ❖ In analyses of factors affecting reproductive outcome after ectopic pregnancy, the presence of **pre-existing tubal disease**, the **status of the contra-lateral tube**, and a **history of infertility** all appear to have a greater deleterious effect on reproductive outcomes than the **type of surgery** performed.

Fertility prognosis factors after laparoscopic treatment of EP

Factors without influence on the prognosis	Factors which influence the prognosis
— Size of EP	— Homolateral adhesions
— Amount of hemo-peritoneum	— State of contralateral tube
— Site of EP	— Antecedents +++
— Tubal rupture	* EP
	* Salpingitis
	* Solitary tube
	* Tubal microsurgery
	* Laparoscopic adhesiolysis

From: Pouly JL, Chapron C, Manhes H et al. Fertil Steril 1991;56:453-460.

Probability of IUP

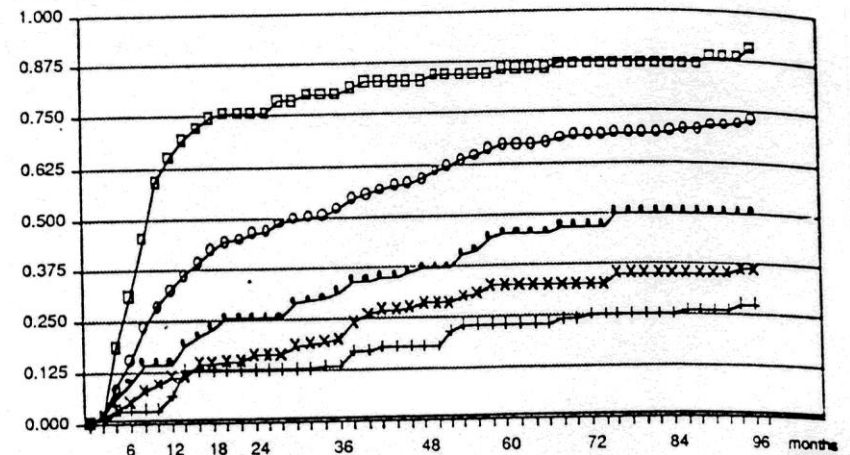


Figure 1 Cumulative PR according to the patients' history. O, Total group; □, group D (no significant history); +, history of ectopic; ●, history of salpingitis; x, history of tubal infertility.



Cohort studies of laparoscopic salpingo(s)tomy vs. salpingectomy

- ❖ **Silva 1993** examined reproductive outcomes prospectively in **143** women. The intrauterine pregnancy rates were similar 60% after salpingotomy versus 54% after salpingectomy; relative risk **1.11** (95% CI 0.74–1.68)
- ❖ **Job-Spira 1996** reported subsequent intrauterine pregnancy rates of **155** women with salpingotomy that were comparable to those following salpingectomy (hazard ratio **1.22**, 95% CI 0.68–2.20). The cumulative pregnancy rates at 1 year were 72.4% after salpingotomy and 56.3% after salpingectomy surgery

Salpingectomy or Salpingotomy?

- ❖ Mol 1998, in a cohort of 135 women, the fecundity rate ratio when comparing laparoscopic salpingotomy with salpingectomy during the 18-month follow-up period was 1.4 (95% CI 0.68–2.7) for women with a healthy contra-lateral tube and 3.1 (95% CI 0.76–12) for women with contra-lateral tubal disease. The 3-year cumulative pregnancy rate was 62% after salpingotomy and 38% after salpingectomy
- ❖ Bangsgaard 2003 reviewing a cohort of 276 women undergoing salpingotomy or salpingectomy, the subsequent cumulative pregnancy rate at 7 years was 89% following salpingotomy and 66% following salpingectomy. The hazard ratio for intrauterine pregnancy following salpingectomy was 0.63 (95% CI 0.42–0.94) when compared with salpingotomy.

Analysis of economic impact by laparoscopic salpingo(s)tomy vs. salpingectomy

Rulin, 1995

- ❖ If half of the 109,000 ectopic pregnancies treated annually in the USA were treated by salpingotomy, add US\$ 16,000,000 a year to their treatment costs, with no clearly improvement in subsequent reproductive outcomes

Mol, 1997

- ❖ concluded that although the short-term costs of salpingectomy are less, if the need for subsequent assisted conception is taken into account, an increase in intra-uterine pregnancy rate after salpingo(s)tomy of only 3%, would make it more cost-effective than salpingectomy.

Laparoscopic treatment of severely damaged tubes: remove or not remove

Therapeutic scoring system for ectopic pregnancy

Factors significantly affecting fertility after EP	Statistical weighting	Coefficient
Antecedent: one EP	0.434	2
For each further EP	0.261	1
Antecedent: laparoscopic adhesiolysis ^a	0.258	1
Antecedent: tubal microsurgery	0.351	2
Solitary tube	0.472	2
Antecedent: salpingitis	0.242	1
Homolateral adhesions	0.207	1
Contralateral adhesions ^b	0.198	1

^aCount only one occasion.

^bIf the contralateral tube is missing or obstructed, count as solitary tube.

Score 1 to 4: Conservative laparoscopic treatment This choice is motivated by three factors:

- The likelihood of IUP is greater after conservative treatment.
- Radical treatment does not eliminate the risk of recurrence.
- For this type of patient, whose past history is relatively clear, recurrence affects both tubes with the same frequency.

Score 5: Radical laparoscopic treatment

These patients stand an equal chance of IUP or recurrence after conservative laparoscopic treatment [20]. Their tubal antecedents are considerable so salpingectomy will avoid the 80% risk of homolateral recurrence, thus giving them a higher chance of IUP than recurrence.

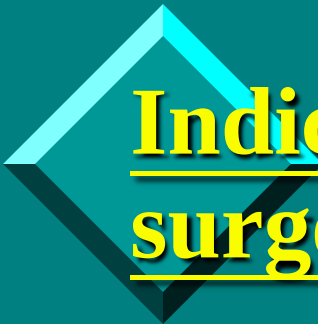
Score 6 and over: Radical laparoscopic treatment and contralateral sterilization

The chance these patients have for IUP is not only very low but considerably below that of recurrence [20]. IVF will offer them far more likelihood of becoming pregnant with a risk of EP of about 4–5% [31].



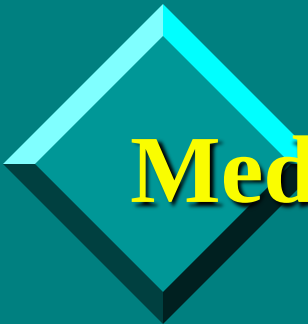
Treatment by laparoscopic salpingo(s)tomy vs. salpingectomy

- ❖ Salpingo(s)tomy may offer **little advantage** over salpingectomy **if the contra-lateral tube is normal**. As long as assisted conception techniques remain beyond the means of most women with tubal infertility, even a small increase in post-ectopic fertility would justify the additional short-term morbidity associated with salpingo(s)tomy.



Indications for non-conservative surgery

- ❖ No desire for fertility
- ❖ Ipsilateral recurrence
- ❖ Uncontrollable bleeding
- ❖ Extensive tubal damage
- ❖ History of previous tuboplasty
- ❖ Heterotopic pregnancy



Medical treatment

- ❖ Comparing medical and surgical therapy
- ❖ Improving the efficacy of medical therapy
 - Single dose vs multiple dose
 - addition of mifepristone
 - route of administration
- ❖ Predicting methotrexate failure

Comparing medical and surgical therapy

- ❖ Saraj (1998 O&G) found a 78% success rate (30 of 38 women) for one dose of methotrexate compared with 92% (34 of 37 women) for laparoscopic surgery (difference not significant). In the methotrexate group 16% (six women) required additional methotrexate and 5% (two women) required surgery during follow-up. 8% (three women) of the laparoscopic surgery group had persistent trophoblast.

Table 2. Mean Number of Days Required to Achieve Ectopic Pregnancy Resolution (Serum hCG Level <15 mIU/mL and Serum Progesterone Level <1.5 ng/mL) and Success, Tubal Patency, and Pregnancy Rates

	Methotrexate (n = 38)	Laparoscopic salpingostomy (n = 36)	P
Serum hCG (d)	27.2 ± 2.3	20.2 ± 2.7	.03
Serum progesterone (d)	17.6 ± 2.2	7.8 ± 1.7	.001
P	.004	.0001	
Success rate	94.7% (36/38)	91.4% (32/36)	NS
Tubal patency rate	72.8% (16/22)	76.2% (16/21)	NS
Pregnancy rate	27.7% (5/18)	28.6% (4/14)	NS

NS = not significant.

Data are presented as mean ± standard deviation or %.

P < .05 was considered statistically significant.

9Ms

- ❖ Medical therapy has an established place in the treatment of ectopic pregnancy, and in selected patients it appears to be as effective as surgery. However, many women with an ectopic pregnancy are not suitable for medical therapy.
- ❖ Medical treatment associated with reduced direct and indirect costs, although at hCG levels above 1500 IU/l these benefits were lost due to the need for prolonged follow-up and surgical intervention.

Table 4. A sensitivity analysis showing the effect of initial serum β -hCG concentrations on total direct and total indirect costs. Figures are in \$NZ. Women have been divided into those with an initial serum β -hCG concentration below 1000 IU/l, below 1500 IU/l, and above 1500 IU/l.

Initial β -hCG level (IU/l)	Methotrexate			Laparoscopy			Mean difference (95% CI)	
	Mean	Median	(Range)	Mean	Median	(Range)		
Direct costs								
< 1000 ($n = 34$)	1106	937	(634 to 2191)	3037	2911	(1717 to 530)	-1931	(-2402 to -1459)
< 1500 ($n = 44$)	1258	1040	(634 to 3196)	3017	2888	(1717 to 4530)	-1759	(-2215 to -1302)
> 1500 ($n = 18$)	1977	1424	(707 to 4976)	3248	3171	(2655 to 3918)	-1271	(-2358 to -184)
All women	1470	1206	(634 to 4976)	3083	2953	(1717 to 4530)	-1613	(-2061 to -1166)
Indirect costs								
< 1000 ($n = 31$)	896	692	(97 to 2393)	2134	1931	(294 to 4267)	-1238	(-1860 to -577)
< 1500 ($n = 40$)	940	911	(97 to 2393)	2039	1931	(294 to 4267)	-1099	(-1621 to -577)
> 1500 ($n = 18$)	1582	1306	(241 to 3963)	1584	1499	(661 to 3325)	-2	(-1052 to 1050)
All women	1141	1039	(97 to 3963)	1899	1788	(294 to 4267)	-758	(-1240 to -277)

Medical treatment : who is the candidate?

- ❖ Women most suitable for methotrexate therapy are those with a serum β -hCG **below 5000 IU/l**, an ectopic pregnancy **without fetal cardiac activity** and with **minimal symptoms**

TABLE 2. ANALYSIS OF FACTORS RELATED TO THE EFFICACY OF METHOTREXATE THERAPY IN WOMEN WITH ECTOPIC PREGNANCIES.*

FACTOR	SUCCESS	FAILURE	P VALUE
Age — yr	26±6	26±5	0.76
Parity — no.	1±1	1±1	0.15
Serum chorionic gonadotropin — mIU/ml	4019±6362	12,420±16,500	<0.001
Serum progesterone — ng/ml†	6.9±6.7	10.2±5.5	0.02
Size of mass — cm	2.0±0.8	2.1±0.8	0.89
Volume of mass — cm ³	5.4±6.1	5.6±6.8	0.88
Total mass volume — cm ³	9.3±16.0	6.4±6.8	0.34
Presence of free peritoneal fluid — no. (%)	102 (32)	12 (40)	0.48
Presence of fetal cardiac activity — no. (%)	37 (12)	9 (30)	0.01

*Plus-minus values are means ±SD. Treatment was successful in 320 women and failed in 30.

†To convert values for progesterone to nanomoles per liter, multiply by 3.18.

TABLE 3. SUCCESS RATES OF METHOTREXATE TREATMENT IN WOMEN WITH ECTOPIC PREGNANCIES AS A FUNCTION OF THEIR INITIAL SERUM CHORIONIC GONADOTROPIN CONCENTRATIONS.

SERUM CHORIONIC GONADOTROPIN CONCENTRATION (mIU/ml)	SUCCESS	FAILURE	SUCCESS RATE (95% CI)*
	no.	no.	percent
<1000	118	2	98 (96–100)
1000–1999	40	3	93 (85–100)
2000–4999	90	8	92 (86–97)
5000–9999	39	6	87 (79–98)
10,000–14,999	18	4	82 (65–98)
≥15,000	15	7	68 (49–88)

*CI denotes confidence interval. Treatment was successful in 320 women and failed in 30.

Improving the efficacy of medical therapy

- Single dose vs multiple dose

- ❖ **Metaanalysis** of 26 studies included **267** women receiving a multiple-dose treatment and **1067** treated with single-dose therapy.
- ❖ The **success rates** (defined as not requiring surgery) were **88.1%** (940 of 1067) for single-dose therapy and **92.7%** (241 of 260) for multiple-dose therapy,
- ❖ the chances of **failure** were **greater with single-dose therapy** (odds ratio 1.71; 95% CI 1.04–2.82). This difference was much more marked when results were adjusted for serum hCG values and the presence of fetal cardiac activity (odds ratio 4.74; 95% CI 1.77–12.62).
- ❖ **Side effects** were **lower with single-dose** therapy (odds ratio 0.44; 95% CI 0.31–0.63). Amongst women who were due to receive a single dose, **13.6%** required two or more doses.

- addition or not of mifepristone;
- route of administration

- ❖ 212 women were treated with either methotrexate and placebo or methotrexate and mifepristone (600 mg orally) and success rates of 79.6% (90/133) and 74.2% (72/97) were found in the two groups. However, in a sub-group of women with progesterone levels greater than 10 ng/ml, the mifepristone–methotrexate group had a success rate of 83.3% (15/18) versus 38.5% (5/13) in the methotrexate only group.
- ❖ 137 women treated by either intramuscular (50 mg/m²) or local ultrasound guided administration (1 mg/kg). The overall success rate was 67.1% and 92.5% in the two groups. Multivariate analysis confirmed a higher success rate with locally administered methotrexate (odds ratio 9.7; 95% CI 3.1–30).



Predicting MTX success/ failure

- ❖ The serum **hCG** level at presentation is the most important factor in the failure of medical treatment.
- ❖ Gamzu 2002: a success rate of **97%** was found at an hCG level below **2000 IU/l**, falling to **74%** at levels above 2000 IU/l.
- ❖ Tawfiq 2000: on 60 patients treated with a single-dose methotrexate regimen and found a **92.5%** success rate in women with a serum hCG level below **4000 IU/l**, falling to 35% at serum levels above 4000 IU/l (odds ratio 52; 95% CI 4.88–556).
- ❖ Potter 2003: on 81 women similarly treated and found success rates of **98%** in women with hCG levels of less than **1000 IU/l**, falling to **80%** at levels between 1000 and 4999 IU/l and **38%** at levels above **5000 IU/l**.

Characterizing ectopic pregnancies that rupture despite treatment with methotrexate

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Result(s): The hCG incremental rate before as well as after MTX administration was positively associated with tubal rupture. HCG values prior to ectopic diagnosis that increased at least 66% over 48 hours and rising hCG values after treatment with methotrexate were independent predictors of tubal rupture. A disproportionate number (47%) of ectopic pregnancies that ruptured were located in the tubal isthmus.

Conclusion(s): The hCG incremental rate both before and after MTX represents an independent risk factor for subsequent tubal rupture. Concentrations of hCG before ectopic diagnosis that increased at least 66% over 48 hours, or persistently rising hCG concentrations after treatment with MTX, may lower the threshold for surgical intervention. Implantation site may represent an unidentifiable risk factor for tubal rupture. (Fertil Steril® 2004;82:1374–8. ©2004 by American Society for Reproductive Medicine.)

Autotransfusion for ruptured ectopic pregnancy

Table 1
Studies and methods of salvage autotransfusion

Author	Year	Country	No. of patients	No. of deaths due to autotransfusion
<i>A: simple autotransfusion</i>				
Pathak et al. [3]	1970	Jamaica	168	0
Carty et al. [4]	1972	Kenya	12	0
Mati et al. [5]	1973	Kenya	5	0
Carty et al. [6]	1973	Kenya	10	0
Maleki et al. [7]	1975	Iran	20	0
Price et al. [8]	1985	Sierra Leone	1	0
Malik [9]	1987	Pakistan	1	0
de Boer [10]	1989	Liberia	1	0
Twycross [11]	1989	Kenya	40	0
Laskey et al. [12]	1991	Liberia	58	1
Poeschl [13]	1992	Malawi	25	0
Ansaloni et al. [14]	1996	Uganda	16	0
Jongen [15]	1997	Tanzania	48	-
Selo-Ojeme et al. [16]	1997	Nigeria	33	-
Obiechina et al. [17]	2001	Nigeria	64	-
Awojobi et al. [18]	2001	Nigeria	107	-
<i>B: device-based autotransfusion</i>				
Bonfils-Roberts [19]	1977	USA	2	-
Merrill et al. [20]	1980	USA	17	-
Curtis [21]	1983	USA	1	-
Silva et al. [22]	1989	USA	1	-
Yamada et al. [23]	2000	Japan	2	-

Table 4
Mean volume of blood autotransfused

	Volume, ml
<i>Simple salvage method</i>	
Pathak et al. [3]	915* (250–3000)
Maleki et al. [7]	1800* (1500–2500)
Price et al. [8]	2000
de Boer [10]	1000
Ansaloni et al. [14]	1014 ^b (348)
Jongen et al. [15]	1239* (500–1500)
Selo-Ojeme et al. [16]	1420*
Awojobi et al. [18]	1252* (500–3000)
<i>Device-based method</i>	
Merrill et al. [20]	1300* (450–8500)
Curtis [21]	600
Silva et al. [22]	1500
Yamada et al. [23]	1325

Case report

Laparoscopic surgery for heterotopic pregnancies: a case report and a brief review

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because of its rarity and difficulty. We report a case of a woman with a viable intrauterine pregnancy who had a complication of ovarian hyper-stimulation syndrome secondary to ovulation induction following in vitro fertilization and embryo transfer, but who, during hospitalization, presented with clinically progressive abdominal pain. An unruptured ectopic pregnancy of the right fallopian tube was diagnosed accidentally by laparoscopy and laparoscopic salpingectomy was immediately performed. Post-operative follow-up revealed that the intrauterine pregnancy continued normally. She delivered a normal female baby at 38 weeks of gestation. The promising neonatal outcome might suggest that laparoscopy might be safely performed to aid differential diagnosis in an uncertain condition during pregnancy; therefore, laparoscopic surgery might be an appropriate method to manage some carefully selected patients with HP. A brief

Heterotopic pregnancy in a spontaneous cycle: do not forget about it!

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Abstract

Heterotopic pregnancies are estimated to be less frequent than 1:30 000 if no assisted reproduction technologies (ART) are performed. After ART this entity is more frequent and in the range of 1:100. In the case reported here an ectopic pregnancy was detected in the right fallopian tube at 7+1 weeks of gestation. It was misdiagnosed as an ectopic singleton, and treated by laparoscopic salpingectomy, because of a previous ectopic in the same tube. Rising hCG after laparoscopy during the subsequent days followed by ultrasound evaluation revealed a viable intrauterine pregnancy. The pregnancy continued uneventfully and a healthy child was delivered at term. The problems, which lead to the misdiagnosis are discussed. The problem of rare cases in medicine, and the problems of a 'modern' medicine are discussed. © 1999 Elsevier Science Ireland Ltd. All rights reserved.

Case report

Heterotopic pregnancy in a natural conception cycle presenting with tubal rupture: a case report and review of the literature

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Accepted 17 April 2002

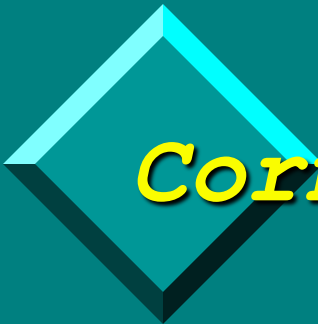


Live birth of healthy twins after a heterotopic tubal and intrauterine twin pregnancy in a woman who was stimulated with clomiphene citrate

N. Cenk Sayin, M.D., and Turgut Yardim, M.D.

Trakya University, Faculty of Medicine, Edirne, Turkey

Objective: To report a heterotopic pregnancy with successful delivery of monochorionic–diamniotic twins after rupture of the tubal ectopic gestation.



Cornual Pregnancy

- ❖ Cornual ectopic pregnancy refers to an ectopic pregnancy that has implanted in the uterine cornu. It accounts for 1% of all ectopic pregnancies and one in every 2500– 5000 live births, with a mortality rate of 2–2.5%.
- ❖ The diagnosis can be made with transabdominal or transvaginal ultrasound, using three criteria: (1) empty uterus, (2) a gestational sac seen separately and <1 cm from the most lateral edge of the uterine cavity and (3) a thin myometrial layer surrounding the sac
- ❖ Traditionally, treatment has been cornual resection by laparotomy or hysterectomy.
- ❖ The use of systemic methotrexate has been described in several case reports and some larger series. Local injection of methotrexate, potassium chloride or prostaglandin has also been described,
- ❖ Various operative laparoscopic techniques have been used, including cornual resection and cornuostomy.

Hysteroscopic Management of Cornual Ectopic Pregnancy

Luis E. Sanz, MD, and Jessica Verosko

Department of Obstetrics and Gynecology, Georgetown University Hospital, and Georgetown University School of Medicine, Washington, DC

CONCLUSION: Hysteroscopic removal under sonographic guidance after methotrexate treatment is a conservative option for the treatment of cornual ectopic pregnancy in some patients. (Obstet Gynecol 2002;99:941-4. © 2002

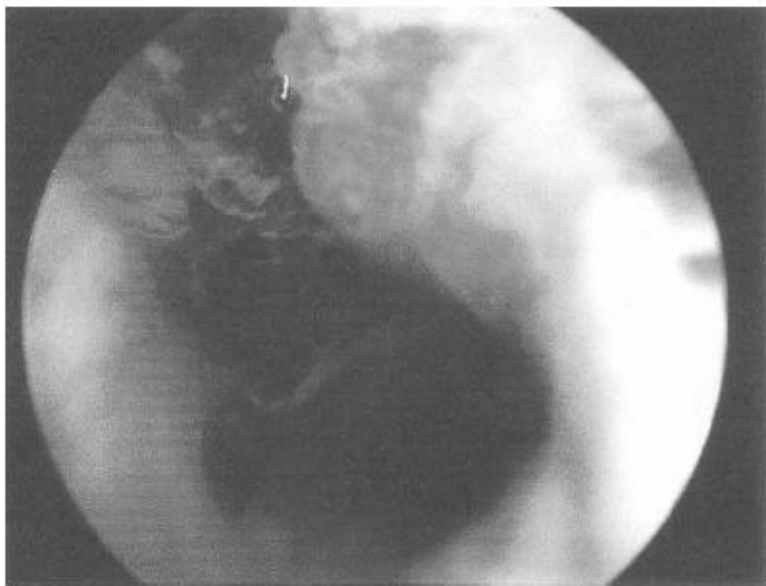


Figure 1. Hysteroscopic view of interior of patient's uterus during removal of the left cornual ectopic gestation under sonographic guidance.

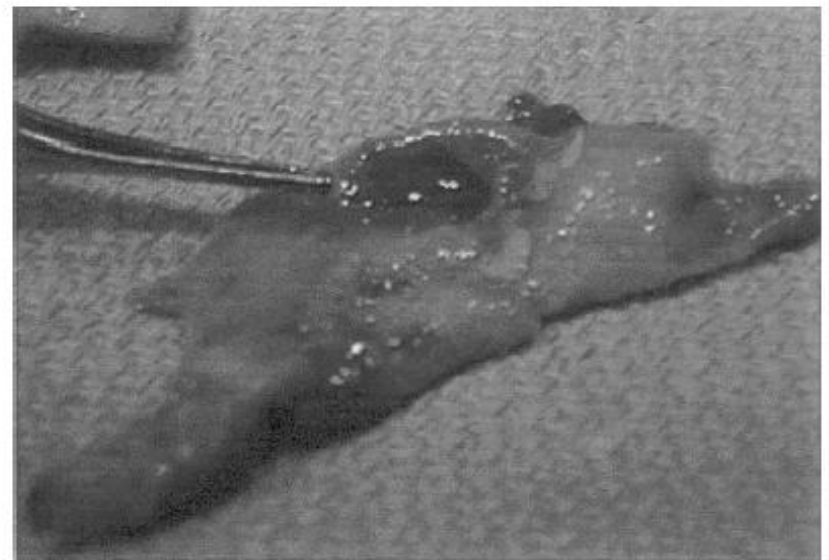


Figure 2. The intact, tube-shaped placental tissue, gestational sac, and partially resorbed embryo after hysteroscopic removal from the left cornu.

Sanz. New Treatment of Cornual Ectopics. Obstet Gynecol 2002.

**Uterine artery ligation for the management of ruptured
cornual ectopic pregnancy**

active bleeding and
uterus. Numerous

- ❖ Uterine artery ligation for the management of **ruptured** cornual ectopic pregnancy

Naveed Khawaja* T. Walsh

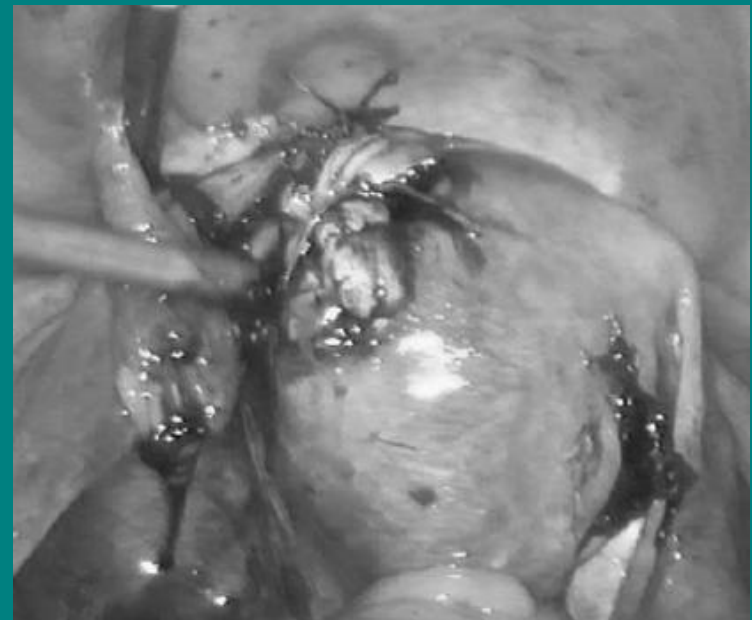
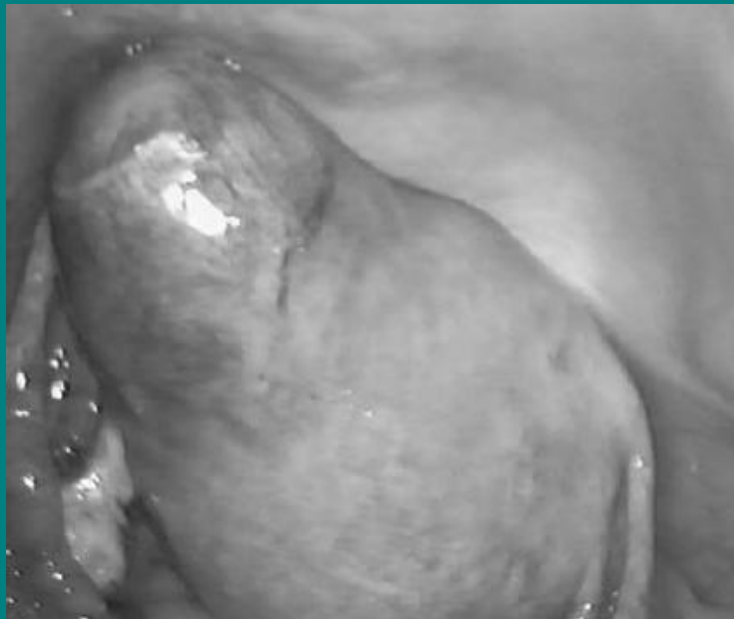
Rotunda Hospital Parnell Street, Dublin, Ireland

- ❖ We suggest uterine artery ligation should be performed first before attempting to repair ruptured cornu of uterus. This will decrease the morbidity associated with this rare but fatal condition in a young patient where you would like to conserve the uterus and preserve fertility. It helps to achieve haemostasis and allows time to repair the ruptured cornu of uterus.

CASE REPORT

Mario Ćorić · Dubravko Barišić · Mihajlo Strelec

Laparoscopic approach to interstitial pregnancy



Brief communication

Single-dose methotrexate for the management of interstitial ectopic pregnancy

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Departments of Obstetrics and Gynecology, Jackson Memorial Hospital/University of Miami School of Medicine, Miami, FL,

Over the period of 4 years, 14 patients were diagnosed with IP. Seven of them received medical management with single-dose MTX. Their characteristics are shown in Table 1. The mean initial hCG level, and the mean size of the ectopic mass was 18098 mIU/ml and 1.96 cm, respectively. The overall success rate was 100%. However, one patient required a second dose of MTX. None of the patients experienced MTX-related side effects. The average time for the resolution of the ectopic pregnancy (hCG < 5 mIU/ml) was 55 days.

Table 1
Characteristics of patients with interstitial ectopic pregnancy treated with single-dose methotrexate (MTX)

Age	Gravidity	Parity	GA by LMP ^a	hCG ^b	GS size ^c	FHT ^d	Previous EP ^e	F/U days ^f	MTX doses
25	4	2	10w3d	5876	3.3	No	No	59	1
26	2	0	10w6d	5583	0.55	No	No	35	1
32	6	4	7w6d	1592	1.6	No	Yes	14	1
34	2	1	11w5d	14157	1.8	No	No	57	1
29	1	0	3w2d	75 868	2.8	No	No	108	2
30	2	1	3w4d	4309	0.8	No	No	70	1
34	5	1	5w1d	19 304	2.9	No	No	56	1



Cervical Pregnancy

- ❖ Cervical pregnancy is a serious complication of pregnancy with a rare incidence of **one per 1,000~2,400** to 18,000 pregnancies
- ❖ **Conservative surgical techniques** are performed in an effort to avoid hysterectomy and preserve fertility: include intra-cervical **balloon tamponade** after cervical curettage, cervical cerclage, **angio-embolization** of feeding uterine arteries, curettage and **local prostaglandin injection**, hysteroscopic resection, and bilateral **ligation of uterine or hypogastric arteries**

Conservative treatment of cervical ectopic pregnancy with transvaginal ultrasound-guided aspiration and single-dose methotrexate

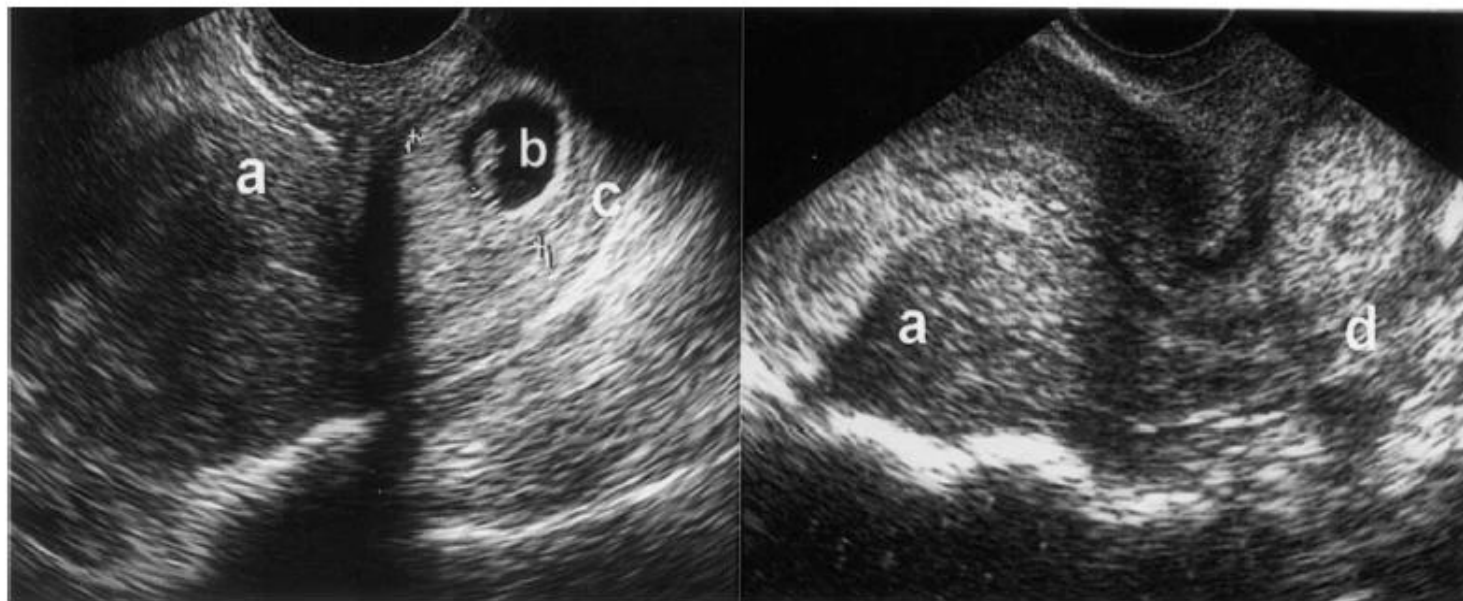
Ismail Cepni, M.D., Pelin Ocal, M.D., Sanli Erkan, M.D., and Burcak Erzik, M.D.

Department of Obstetrics and Gynecology, Cerrahpasa Medical Faculty, Istanbul University, Istanbul, Turkey

Result(s): The cervical ectopic pregnancy was successfully aborted, and the reproductive capability of the patient was preserved.

Conclusion(s): Transvaginal ultrasound-guided aspiration in combination with single-dose methotrexate administered systemically can be safely used to treat cervical ectopic pregnancies. (Fertil Steril® 2004;81: 1130–2. ©2004 by American Society for Reproductive Medicine.)

Transvaginal ultrasonography shows cervical ectopic pregnancy. (a) Empty uterine cavity. (b) Gestational sac and embryo. (c) Trophoblastic activity in the cervical canal. (d) Gestational sac and its contents are emptied with transvaginal ultrasound-guided aspiration. However, trophoblastic activity still persists in the cervical canal.



Clinical Outcomes of Patients treated for Cervical Pregnancy with or without Methotrexate

- ❖ The objective of this study is to describe the clinical outcomes of patients treated for cervical pregnancy **with or without methotrexate** (MTX) Between January 1993 and February 2000, 31 patients were diagnosed with cervical pregnancy. **Twenty-two** patients were treated **with** MTX chemotherapy and **nine** patients were treated with surgical procedures **without** MTX treatment.
- ❖ In the **non-MTX** treatment group, **three** (33.3%) **patients underwent total abdominal hysterectomy**, five required adjuvant procedures to control the bleeding during dilatation and curettage (D&C) and only one patient was treated with a simple D&C.
- ❖ In the **MTX treatment** group, fourteen (63.6%) patients were treated with **only MTX** and eight (36.4%) cases underwent concomitant procedures (simple curettage, curettage and Foley catheter tamponade, cervical cerclage, ligation of the descending branches of uterine arteries, or ligation of hypogastric arteries). **The uterus was preserved in all cases** and three women delivered healthy babies in their subsequent pregnancy.

Consecutive cervical pregnancies

Christopher J. Radpour, M.D.,^{a,c} and Jeffrey A. Keenan, M.D.^b

University of Tennessee Medical Center, Knoxville, Tennessee

Objective: Report of a rare case of consecutive spontaneous cervical pregnancies.

Design: Case study.

Setting: Teaching hospital.

Patient(s): One healthy nulliparous woman in the early years of her fourth decade.

Intervention(s): The first of two cervical pregnancies was treated with two doses of methotrexate and subsequent uterine artery embolization. The second was treated with methotrexate, intracervical Foley catheter placement, hysteroscopic ablation of the bleeding cervical bed, and replacement of the Foley catheter with gradual deflation of balloon.

Cervico-isthmic pregnancy: a case report, critical reappraisal of the diagnostic criteria, and reassessment of the outcome

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Acta Obstet Gynecol Scand 2001; 80: 586–588. © Acta Obstet Gynecol
Scand 2001

During the first trimester, ultrasonography **cannot distinguish** the transition between isthmus and cervical canal, but only between isthmus and uterine corpus. From the 12th week onward, the **isthmus progressively unfolds into the uterine cavity**, becomes occupied by the gestational sac, and takes the name of lower uterine segment

Table I. Cervical or cervico-isthmic pregnancies managed conservatively at ≥ 20 weeks of gestational age. Summary of the reports

Authors	Year	No. of cases	Delivery GA	Treatment	Fetal outcome	Definition*
David et al. (4)	1980	1	40 weeks	CS, Hysterectomy	3700 g, alive	C-I
Parente et al. (8)	1983	2	20 weeks	D&C, Hysterectomy	Not viable	C
			20 weeks	D&C, Hysterectomy	Not viable	C
Kalakoutis & Lilford (9)	1985	1	28 weeks	VD, Hysterectomy	1100 g, alive	C
Hofmann et al. (10)	1987	2	21 weeks	D&C, Hysterectomy	Not viable	C
			32 weeks	CS, Hysterectomy	1930 g, alive	C
Cohen et al. (11)	1985	1	27 weeks	CS, Hysterectomy	1050 g, alive	C-I
Weyerman et al. (12)	1989	1	26 weeks	CS, Hysterectomy	830 g, neonatal death	C
Jelsema & Zuidema (7)	1992	1	38 weeks	CS, Hysterectomy	3100 g, alive	C-I
Iloabachie et al. (13)	1993	1 (twins)	37 weeks	CS	2500 g, alive	C-I
					2200 g, alive	
Present case	1999	1	30 weeks	CS, Hysterectomy	1450 g, alive	C-I

GA=Gestational age; CS=Cesarean section; D&C=Dilatation and curettage; VD=Vaginal delivery; C=Cervical; C-I Cervico-isthmic; *The implantation site is reported as described in the original publication.

Case report

Heterotopic cervical and intrauterine pregnancy
in a spontaneous cycle

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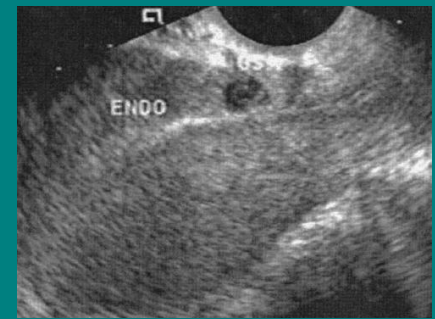
Received 20 December 2002; received in revised form 15 April 2003; accepted 9 June 2003

Review of literature

Reference	Year	Risk factor	Method of conception	GA at diagnosis (weeks)	Treatment	Follow-up
Bayati et al. [4]	1989	One abortion IUD use Cervical stenosis Uterine synechie	IVF-ET	8	D&E, ligation of bilateral cervical arteries, hemostatic sutures on cervix and vaginal packing	Resumed regular menstrual cycles after 2 months
Davies et al. [5]	1990	Previous CP	IVF-ET	10	Digital evacuation of CP + application of cervical cerclage with preservation of IUP	D&E done at 13 weeks due to intrauterine fetal demise
Ginsburg et al. [7]	1994	None	IVF-ET	5–6	Embolisation of uterine and internal iliac arteries and D&E	Resumed normal menstrual cycles and underwent IVF 6 months later and conceived
Peleg et al. [11]	1994	None	IVF-ET	7	Intraarterial MTX	Not mentioned
Frates et al. [1]	1994	None	Induced ovulation + IUI	7	KCl	Delivery of healthy neonate 7 months later
Bratta et al. [12]	1996	None	Not reported	7	Systemic MTX	Normal menstrual cycles after 30 days
Monteagudo et al. [15]	1996	Previous CP	–	–	KCl	Delivery of healthy baby at 34 weeks by cesarean section
Honey et al. [6]	1999	Previous one abortion and two ectopic pregnancies	IVF-ET	7 + 4	KCl + uterine artery embolisation	Underwent hysterectomy 1 week later due to heavy bleeding and sepsis
Seow et al. [8]	1999	Previous two ectopic pregnancies	IVF-ET	5	Transvaginal manual forceps evacuation	Delivery of healthy twin babies at 37 weeks by a cesarean section
Carreno et al. [16]	2000	None	IVF-ET	7	KCl	Delivery of a healthy baby at 36 weeks
Mashiach et al. [10]	2002	Pre H/o EP	IVF-ET	8 + 3	Application of Shirodker cervical cerclage	Normal vaginal delivery at 39 weeks
Jozwik et al. [9]	2003	None	ICSI-ET	5–6	Hysteroscopic resection	Delivery of healthy baby at 38 weeks by cesarean section
Present case	2003	Previous cesarean section	Spontaneous	7 + 4	KCl	Delivery of a healthy baby at 35 weeks by cesarean section, bilateral ligation of hypogastric arteries and application of local hemostatic sutures to control severe bleeding

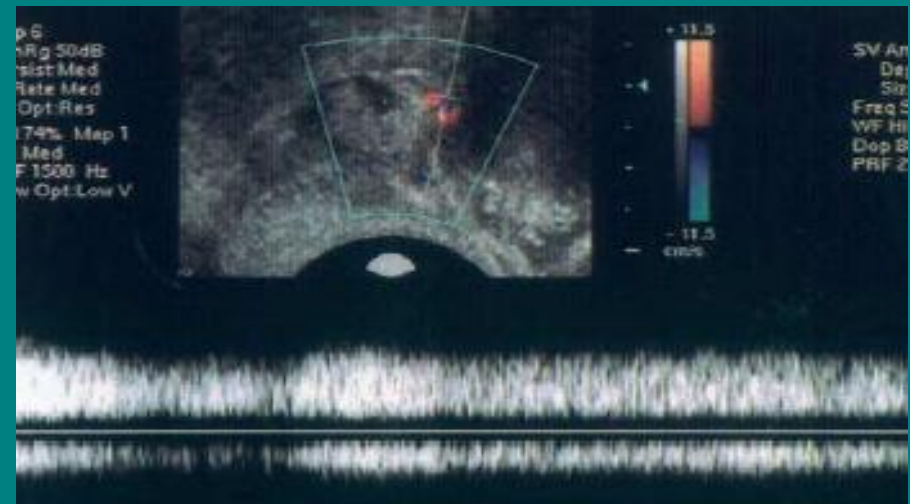
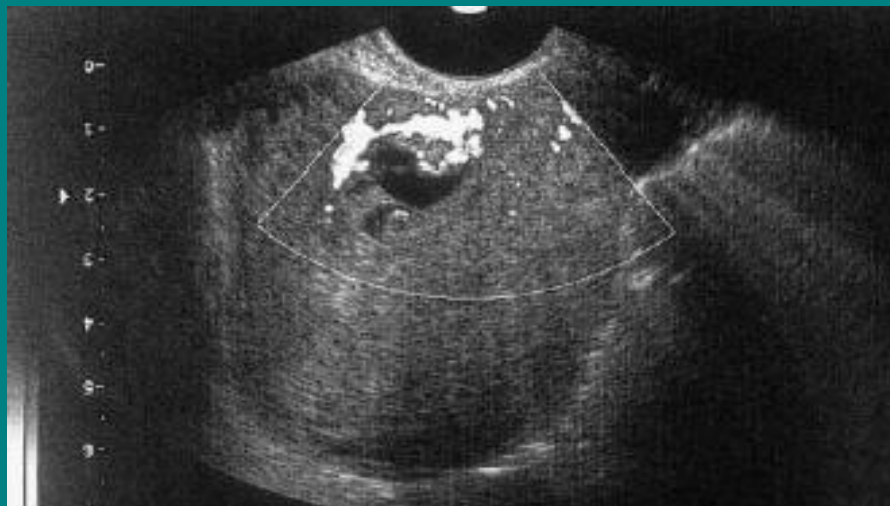
CP: cervical pregnancy; GA: gestational age; MTX: methotrexate; KCl: potassium chloride; EP: ectopic pregnancy.

Caesarean Scar Pregnancy



- ❖ The first case was reported in **1990** by Rempen and Albert; The second case was reported by Herman et al. in 1995
- ❖ 1966~1999: 9 cases; 2000~2001: 9 cases; 2002~2004: 38 cases
- ❖ **0.13%** (10/7980 pregnancies) previous caesarean section; **5%** (10/198) of ectopic pregnancies in women with at least one previous caesarean section (Jurkovic UOG 2003)
- ❖ DDx of two different types: **on** a scar and **in** a scar defect
- ❖ Diagnostic **criteria** included (1) the trophoblast must be mainly located between the bladder and the anterior uterine wall; (2) no fetal parts must be visible within the uterine cavity; (3) on a sagittal view, a discontinuity in the anterior wall of the uterus should be identified.
(an empty uterine cavity, an empty cervical canal, development of the gestational sac in the anterior part of the uterine isthmus, and an absence of healthy myometrium between the bladder and sac)

Those at risk for pregnancy in a Caesarean scar appear to have a history of **multiple Caesareans**, **dilatation and curettage**, **placental pathology**, **ectopic pregnancy**, and **IVF**. Twenty-one out of 39 for which this information was available (54%) had undergone multiple (≥ 2) Caesareans and 13 had previous dilatation and curettage



Unsuccessful medical treatment of cesarean scar ectopic pregnancy with systemic methotrexate: a report of two cases

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Key words: methotrexate; ectopic pregnancy; cesarean section scar

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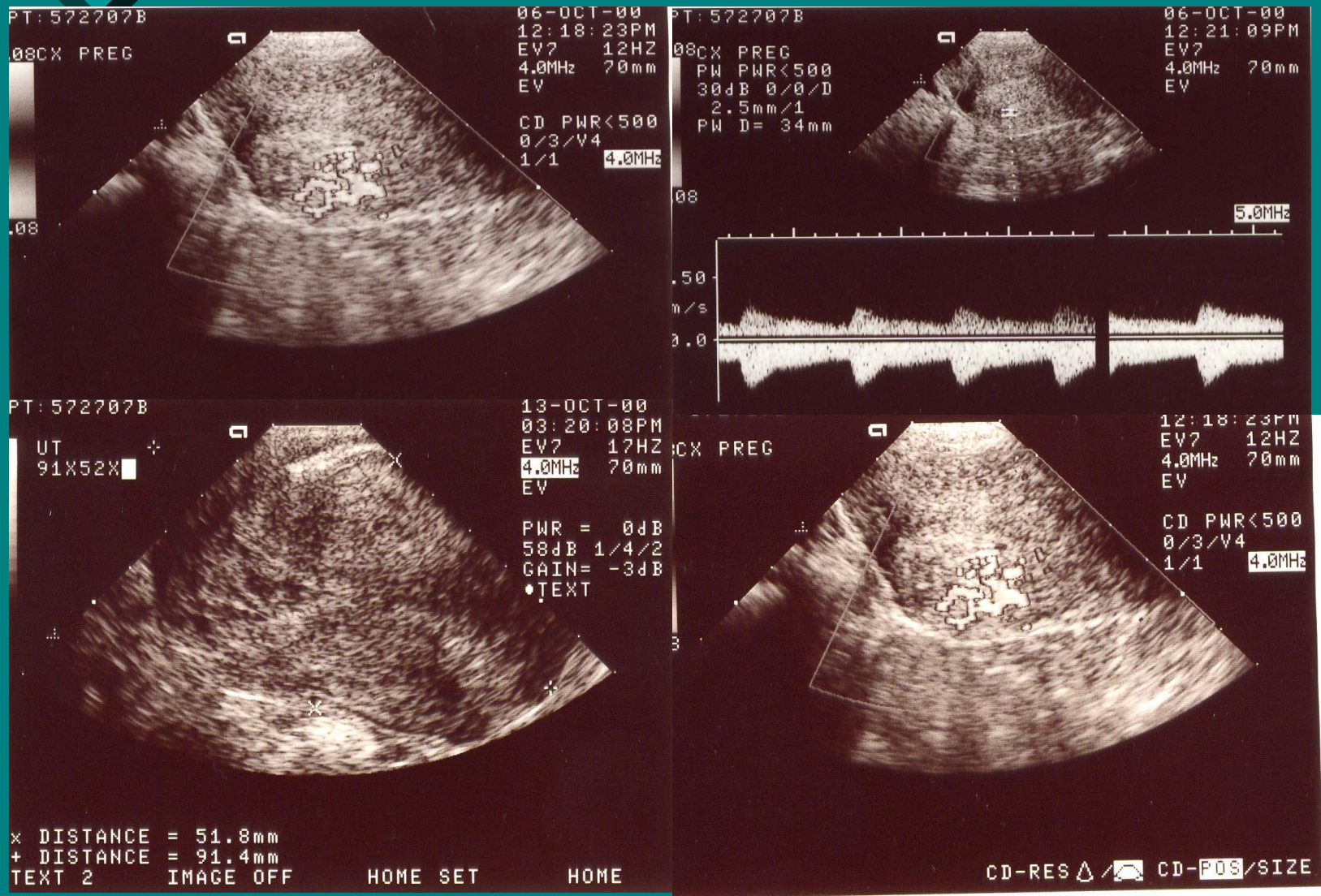
Cesarean Scar Pregnancy

- ❖ Uterine scar dehiscence will accompany cesarean scar implantation, only surgical resection offers the opportunity to **simultaneously repair** the defect.
- ❖ Primary surgical treatment by **laparotomy and hysterotomy** as soon as the diagnosis is confirmed may be the best treatment option.
(OGS CME Review 2002 by Donald L. Fylstra)

- ❖ Case in Oct 16, 2000 in TC-VGH Mrs 畢XX, MTX Oct 06, 2000
- ❖ **Laparoscopic hysterotomy**



Cesarean Scar Pregnancy



Case Report

Three-Dimensional Power Doppler Ultrasound Diagnosis and Laparoscopic Management of a Pregnancy in a Previous Cesarean Scar

**CHIN-JUNG WANG, MD, LEUNG-TO YUEN, MD, CHIH-FENG YEN, MD,
CHYI-LONG LEE, MD, and YUNG-KUEI SOONG, MD**

branching vessels. The diagnosis of pregnancy in a previous Cesarean scar was made. Laparoscopic ligation of bilateral uterine arteries followed by excision of the ectopic pregnant mass was undertaken, and the patient's uterus was successfully preserved. Conservative management with the laparoscopic approach may be a safe and effective alternative to hysterectomy in patients with a pregnancy in a previous Cesarean scar.

Case report

Conservative treatment by chemotherapy and uterine arteries embolization of a cesarean scar pregnancy

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Carlo Fugazzola, Pierfrancesco Bolis

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Received 9 October 2001; accepted 21 December 2001

Abstract

We report a case of a viable cesarean scar pregnancy diagnosed at 7 weeks of gestation. The patient was conservatively managed by chemotherapy, intra-amniotic instillation of potassium chloride, and bilateral uterine artery embolization. The gestational sac was not sonographically visible 44 days after the treatment. No surgical treatment was necessary. © 2002 Elsevier Science Ireland Ltd. All rights reserved.

Cesarean scar pregnancy: Quantitative assessment of uterine neovascularization with 3-dimensional color power Doppler imaging and successful treatment with uterine artery embolization

Min M. Chou, MD, Jen I. Hwang, MD, Jenn J. Tseng, MD, Ying F. Huang, MD,
Esther Shih C. Ho, MD

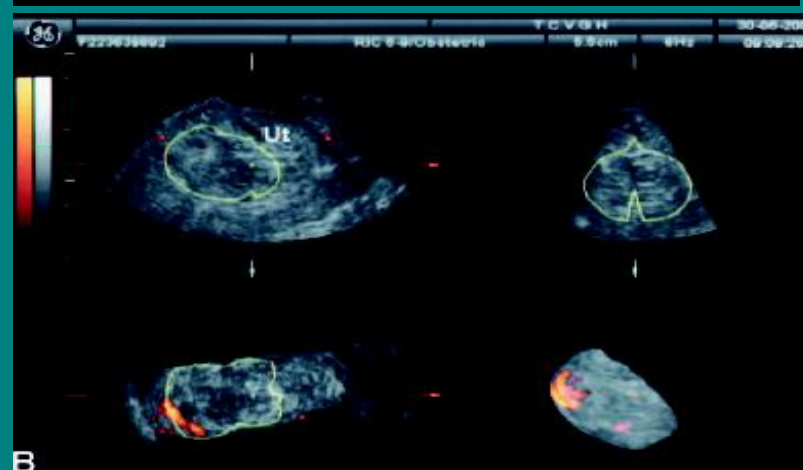
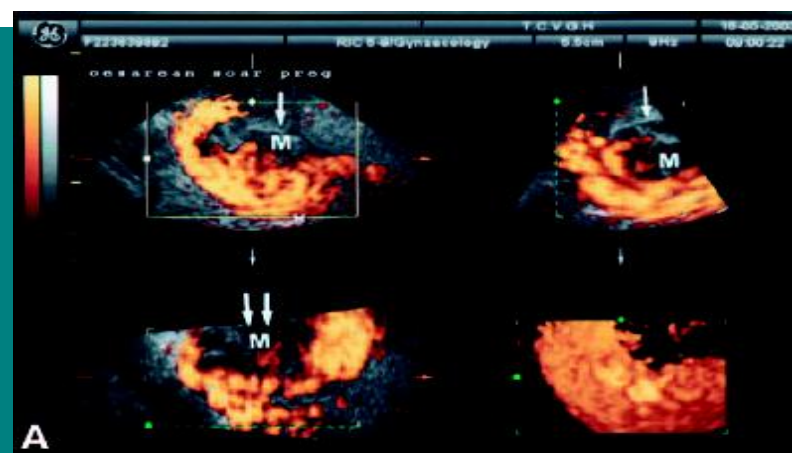
Departments of Obstetrics and Gynecology and Radiology, Taichung Veterans General Hospital, Chung Shan Medical University and Huang Kung University, Taichung, Taiwan

Received for publication September 25, 2003; revised October 21, 2003; accepted November 19, 2003

Objective: The purpose of this study was to investigate the use of a 3-dimensional virtual organ computer-aided analysis imaging system for the monitoring of the quantification of changes of uterine neovascularization before and after successful treatment with uterine artery embolization in cesarean scar pregnancy.

Study design: A case of cesarean scar pregnancy that was associated with extensive uterine neovascularization was diagnosed at 8 weeks of gestation with the 3-dimensional virtual organ computer-aided analysis imaging system. After appropriate counseling, a bilateral uterine arteries embolization procedure was performed with nonresorbable microspheres by interventional radiologists.

Results: The gestational cystic mass at the site of previous cesarean scar completely disappeared at the follow-up examination 3 months later.



Cesarean scar pregnancy: issues in management

Ultrasound Obstet Gynecol. 2004 Mar;23(3):247

Seow KM, Huang LW, Lin YH, Lin MY, Tsai YL, Hwang JL.

Department of Obstetrics and Gynecology, Shin Kong Wu Ho-Su Memorial Hospital, and School of Medicine, Fu-Jen Catholic University, Taipei, Taiwan.

During a **6-year** period, **12 cases** of Cesarean scar pregnancy were diagnosed using transvaginal color Doppler sonography and treated conservatively to preserve fertility.

- The incidence of Cesarean scar pregnancy was 1:2216 and its rate was 6.1% in women with an ectopic pregnancy and at least one previous Cesarean section. Gestational age at diagnosis ranged from 5 + 0 to 12 + 4 weeks. The time interval from the last Cesarean section to the diagnosis of Cesarean scar pregnancy ranged from 6 months to 12 years.
- Eleven of the 12 patients preserved their reproductive capacity; the remaining patient, treated by dilatation and curettage, underwent a hysterectomy because of profuse vaginal bleeding.

- 
- Patients were treated as follows: **transvaginal** ultrasound-guided **injection of methotrexate** into the embryo or gestational sac (n = 3), **transabdominal** ultrasound-guided **injection of methotrexate** (n = 2), transabdominal ultrasound-guided injection of methotrexate followed by **systemic methotrexate** administration (n = 2), systemic methotrexate administration alone (n = 2), dilatation and curettage (n = 2), or **local resection** of the gestation mass (n = 1).
 - The Cesarean scar mass **regressed from 2 months to as long as 1 year** after treatment. Uterine rupture occurred in one patient during the following pregnancy at 38 + 3 weeks' gestational age.
 - **CONCLUSION: Ultrasound-guided methotrexate injection** emerges as the **treatment of choice** to terminate Cesarean scar pregnancy. **Surgical** or invasive techniques, including dilatation and curettage are **not recommended** for Cesarean scar pregnancy due to high morbidity and poor prognosis.

Ovarian pregnancy resulting from cornual fistulae in a woman who had undergone bilateral salpingectomy

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Departments of ^aObstetrics and Gynecology, and ^bPathology, China Medical University and Hospital, Taichung, Taiwan

Objective: To report a case of ovarian pregnancy following in vitro fertilization-embryo transfer (IVF-ET) treatment for which the cornual fistulae was the most probable explanation of the cause.

Design: Case report.

Setting: University department and assisted reproduction unit.

Patient(s): A 29-year-old woman with primary infertility.

Intervention(s): Hydrosalpinx of the bilateral fallopian tubes has been noted in patients who have decreased pregnancy rates in the IVF-ET treatment cycles. Salpingectomy before IVF cycles has been suggested to increase the pregnancy rate. We report a patient who presented with bilateral hydrosalpinx for whom bilateral salpingectomy was performed before IVF treatment.

Main Outcome Measure(s): Clinical pregnancy.

Result(s): The treatment cycle resulted in a primary ovarian pregnancy and required laparoscopic operation. A cornual fistulae was found that have might led to ectopic implantation of the embryos.

Conclusion(s): Ovarian pregnancy may be an unexpected complication of those receiving bilateral salpingectomy before IVF treatment. The presence of cornual fistulae after salpingectomy was probably the cause of the ectopic pregnancy. (Fertil Steril® 2005;83:205–7. ©2005 by American Society for Reproductive Medicine.)

Key Words: Ovarian pregnancy, cornual fistulae, bilateral salpingectomy