# The Role of Hysteroscopic Metroplasty in various uterine anomalies

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## Abstract

OBJECTIVE The aim of this study was to evaluate the impact of hysteroscopic metroplasty (septoplasty in the case of septate uterus and the enlarging hysteroscopic metroplasty in the case of women exposed in utero to Diethylstilbestrol) on the reproductive outcome of women before and after surgery.

*STUDY DESIGN* A web search was performed to identify the relevant publications with no limitations of languages from 1997 till June 2007.

*RESULTS* Following hysteroscopic septum resection, the spontaneous abortion rate decreased from 91% to approximately 15% , the term delivery rates increased from approximately 6% to 57%, and the live birth rates increased tremendously from 11 % to reach 85%. The results of the enlarging hysteroscopic metroplasty were also encouraging; There was a decrease in the rates of abortion from 88% to 12.5%, and the rates of term deliveries increased from 3% to 87.5%.

*CONCLUSION* The enlarging hysteroscopic metroplasty is not innocuous since it may create cervical fragilization thus necessitating the insertion of a cervical cerclage in order to prevent 2$^{nd}$ trimester pregnancy loss. Moreover, the incision on the myometrium weakens the uterus and make it more prone to uterine rupture. So, this type of surgery should be performed only in specific cases such as an advanced age nulligravida (with a dysmorphic or a hypoplastic uterus) willing to enroll in ART programs due to infertility.

The septate uterus is not a primary factor of infertility; by resecting the septum, the normal uterine cavity is restored and the reproductive outcome is ameliorated.

## Keywords

Hysteroscopic metroplasty, Septate uterus, Enlarging hysteroscopic metroplasty, Septoplasty, Uterine hypoplasia.

## I. Introduction

Congenital uterine malformations is a group of miscellaneous anomalies in the uterine cavity that may alter the reproductive outcome of the patient. It is reported in up to 4.3% in the general population and in infertile women. [ 1 ] . Clinically, symptoms may range from being asymptomatic thus remaining undiagnosed, to the development of obstetrical complications such as early and late abortion, preterm delivery, and ectopic pregnancy, to even causing reproductive failure.

So, the basis of hysteroscopic metroplasty treatment is to restore in some of these cases a normal uterine cavity with a good uterine vascularization as much as possible in order to have a better reproductive outcome. A recent study performed by Pace S et al [ 2 ] demonstrated an improvement in uterine perfusion following hysteroscopic metroplasty in arcuate uteri based upon uterine artery Doppler velocimetry indexes.

In fact, hysteroscopic metroplasty comprises the hysteroscopic septoplasty, as well as the enlarging metroplasty which is performed in the case of uterine hypotrophy, or in women exposed in utero to Diethylstilbestrol (DES). [ 3 ]. But the usefulness of hysteroscopic metroplasty in these cases of DES is still to be demonstrated. [ 4 ]

Each type of uterine anomaly has a different impact on pregnancy outcome; Some may benefit from operative hysteroscopy such as septate uterus and arcuate uterus. Whereas, didelphys and unicornuate uterus cannot be corrected surgically. [ 1 ]

Hysteroscopic metroplasty may be performed using Versapoint bipolar needle device, a

resectoscopic knife electrode with cutting current, as well as with Nd:YAG laser. Yang et al

(2006) revealed the effectiveness of Nd:YAG laser in the hysteroscopic treatment of septate uterus.

The main advantage included the need of a less cervical dilation [ 5 ] thus reducing the probability of uterine perforation.. Moreover, the Nd:YAG laser produces no debris, and carries a reduced risk of bleeding [ 6 ]. So, the efficacy of hysteroscopic metroplasty is based upon a short hospitalization stay, low morbidity, and a better reproductive outcome.

## II. Embryology

The uterus is formed from two paramesonephric ducts (Mullerian ducts). The caudal two thirds of these ducts form the uterus, whereas the upper third gives rise to the fallopian tubes.

Failure or arrest of development during any of the following three stages will lead to uterine malformation:

***At 6-9 weeks of gestation***: Müllerian ducts appear and there is a caudal midline fusion and connection with the urogenital sinus. So, failure of development of the Müllerian ducts during this period leads to uterine aplasia;

***At 10-13 weeks of gestation***: There is an upward fusion of the caudal parts of the Müllerian ducts; Any failure of fusion during this period of time leads to uterine duplications (uterus didelphys, bicornuate uterus)

***At 14-18 weeks of gestation***: The normal resorption of the medial septum initially separating the caudal parts of the Müllerian ducts takes place in order to form the utero-vaginal channel which is the origin of the uterine cavity and the superior 2/3 of the vagina. Failure of resorption of the midline septum leads to uterine septation (septate uterus).

Normally, the resorption of the septum occurs caudad to cephalad; It begins at the level of the cervix and continues up to the uterine fundus. Septate uterus is never combined with another anomaly of the genito-urinary tract.

(*Adapted from Dr. Najeeb Layyous [www.layyous.com](http://www.layyous.com)*)

So, based upon a variety of septum resorption anomaly, the defect may range from the completely septate uterus (with two cervices and a vaginal septum too – Figure 1), to a partially septate uterus (Figure 2), or simple fundic spurs.

**UTERINE SEPTUM**

The asymmetric septate uterus is a rare form, which was described in the Musset's classification, but is absent in the AFS classification. In this form, the uterine body is divided into two asymmetric cavities by a septum going from the uterine fundus to the uterine isthmus. One of the two cavities communicates with the cervix, the other is blind with consequent risk of hematometra, endometriosis or ectopic pregnancy (Figure. 3)

**Fig 3**. Assymetric septate uterus (Corporal) *(Adapted from Francois Manson, Frantisek Grochal.10 Uterine malformations 2007-03-27 © Manson www.TheFetus.net)*

Diethylstilbestrol (DES) was prescribed in France from 1950 till 1977. Years later, it was linked to the causation of morphological and structural anomalies in the uterus, cervix and vagina in women who were exposed to it in-utero, thus leading to an increase in their rates of preterm delivery, and second trimester abortions mainly between 19-20 weeks [ 7 ].

**Fig 4. T-shaped uterus in patients exposed in-utero to DES**

(*Adapted from* www.gehealthcare.com)

Myometrial hypertrophy results in a T-shaped uterine cavity and cavity irregularity, which is pathognomonic for the anomaly. Typically, the uteri are hypoplastic.

## III. Classification of congenital uterine anomalies

In France, the classification of Musset is most commonly used (Musset et al, 1967). Elsewhere, the 1988 classification of the American Fertility Society is most widely accepted. The classification is based on the extent of failure of normal development, thus grouping anomalies with similar clinical manifestation and treatment together with prognosis for pregnancy outcome. [ 8 ]

**Table I. Classification system of müllerian duct anomalies developed by the American Fertility Society** [ 9 ]

**Table II. Classification of congenital uterine anomalies according to Musset and the American Fertility Society.**

| Embryological Mechanism | Classification after Musset (1964) | Classification after American Fertility Society "AFS" (1988) |
|---|---|---|

| | | |
|---|---|---|
| **Aplasia or agenesis of the Müllerian ducts** | **Bilateral**<br>• Complete – lethal<br>• Incomplete– Mayer-Rokitansky-Küster-Hauser syndrome | **Type I**<br>Hypoplasia, agenesis |
| | **Unilateral**<br>• Complete – true unicornuate<br>• Incomplete– pseudounicornuate uterus | **Type II**<br>Unicornuate uterus<br>• IIa: with communicating rudimentary horn<br>• IIb: with non-communicating rudimentary horn<br>• IIc: rudimentary horn without cavity<br>• IId: without rudimentary horn |
| | **Dideolphys uterus**<br>complete or partial duplication of:<br>• the vagina<br>• cervix<br>• and uterus | **Type III**<br>Uterus dideolphys |

| | | |
|---|---|---|
| **Anomaly of fusion** | | |
| | **Bicornuate uterus**<br>• Complete (septum from fundus to cervical os)<br>• Partial (septum to body of uterus)<br>• Par (septum confined to the fundus) | **Type IV**<br>Bicornuate uterus<br>● IV a: complete<br>● IV b: partial |
| | **Septate uterus**<br>● Complete<br>● Partial<br>● Corporal (only to the uterine body)<br>● Fundal only confined to the fundus | **Type V**<br>Uterus septate<br>● V a: complete<br>● V b: partial |

| | | |
|---|---|---|
| **Anomaly of resorption** | **Arcuate uterus** | **Type VI**<br>Arcuate uterus according with AFS this form can be considered as a partially septate uterus (fundal) |
| **Hypoplasia** | **Uterine hypoplasia**<br>DES (diethylstilbestrol) syndrome | **Type VII**<br>DES (diethylstilbestrol) uterus (iatrogenic) |

*Adapted from [ 10 ]* Francois Manson, Frantisek Grochal.10 Uterine malformations 2007-03-27© Manson www.TheFetus.net

## VI. Materials and methods

A literature review was performed in order to explore updated informations regarding hysteroscopic metroplasty (septoplasty as well as the enlarging metroplasty), and the reproductive outcome before and after these operations. For this purpose, a web search was performed with no limitations of languages from 1997 till June 2007, and the results will be presented in two different sections accordingly. All study types were reviewed. Randomized controlled trials were considered evidence of the highest quality, followed by cohort studies. Key studies and supporting data for each recommendation were summarized and referenced.

## V. Hysteroscopic Metroplasty

### A. Hysteroscopic Septum Resection

### *Generalities*

Septate uterus is the most common congenital uterine anomaly, comprising approximately 55% of müllerian duct anomalies.[11]. 40% of patients with septate uteri have reproductive problems.[12] which usually manifest as reproductive failure, obstetrical complications, and an increase in the incidence of recurrent miscarriages. The prevalence of septate uterus in patients who have had three or more recurrent spontaneous abortions is estimated to range from 26% to 94% (pooled data, 65%) [ 9 ].

A septate uterus is not a primary factor of infertility [13 ]. But in secondary infertility patients, the incidence of unexplained infertility is significantly higher reaching approximately 40%. Thus, a contribution from the uterine septum in delayed conception of these patients cannot be excluded. [14] .

And even though it is difficult to assess the reproductive outcome definitively, because the majority of studies to date have not been controlled [15 ]. A review of the literature reveals that the septate uterus is associated with a poor obstetrical outcome; Premature birth rates range from 9% to 33% (pooled data, 20%) whereas the fetal survival rates are in between 10% to 75% (pooled data, 30%) [ 9 ]. The length of the septum does not appear to correlate with differences in obstetric outcome [16, 17].

In these malformations the external contours of the uterus are normal. On a coronal section the fundal serosa is rectilinear or with a mild invagination (less than 1cm). The single uterine cavity is divided by a bridge of fibrous myometrium. The septum is in general hypovascularized in comparison to the adjacent myometrium.

**Fig 4**. Power Doppler image showing vascularization of the uterus with hypoechoic poorly vascularized septum. *(Adapted from Francois Manson, Frantisek Grochal.10 Uterine malformations 2007-03-27 © Manson www.TheFetus.net)*

A recent study performed by Duan et al (2005) [18] revealed that:

"* The amount of the endometrium glands on septum was less than that on the uterine wall, or endometrium un-synchronous growth between septum and uterine wall.

* The positive index level of estrogen and progestogen receptors on septum was weaker than that on uterine wall.

* The densities of the smooth muscle cells were thicker, and the collagenous fibers were sparser at the base and the middle of the septum compared with the uterine wall.

* The amount of the small arteries in septum were rarer than in uterine wall. Ultrastructure characters showed glandular epithelium cells distributed irregularly and poor pili on septum in the sterility patients."

So, they concluded that the differences in pathological morphology and the ultra-structure between septum and the uterine wall explain the infertility or sterility cases related to the presence of uterine septum. [18 ]

Color Doppler ultrasound allows visualization of intraseptal vascularity and may help in differentiating the avascular septum from the vascular septum. The presence of a lesser amount of connective tissue in the septum may produce poor decidualization and placentation, while an increased amount of muscle tissue in the septum can cause miscarriage due to the production of local uncoordinated myometrial contractility. [19]

An arcuate uterus has a SINGLE uterine cavity with a convex or flat uterine fundus. the endometrial cavity, which demonstrates a small fundal cleft or impression (>1.5 cm).

The outer contour of the uterus is convex or flat. This form is often considered a normal variant since it is not significantly associated with the increased risks of pregnancy loss and the other complications

found in other subtypes. *This abnormality doesn't need any interference because researchers found that there is no difference in reproductive outcome compared with normal*.

**Fig 5**. Resorption Defects *(Adapted from mar-med.com)* (A) Arcuate Uterus (B) Septate Uterus

## *Indications of hysteroscopy in septate uterus*

Operative hysteroscopy is formally indicated in pregnancy complications such as second-trimester pregnancy loss, or preterm delivery. A possible indication would be the case of recurrent first-trimester spontaneous abortion. But, using hysteroscopy as a preventative treatment before In-Vitro Fertilization is a controversial indication with contradictory results. [20, 21, 22].

However, hysteroscopic metroplasty is contraindicated in the presence of pregnancy, in genitourinary infections, in contraindications to anesthesia, and is also contraindicated in the case of bicornuate uterus due to the possibility of uterine perforation, since in a bicornuate uterus the external uterine contour is concave or heart shaped, and the uterine horns are widely divergent.

The Strassman abdominal metroplasty is the operation of choice destined to treat the bicornuate uterus [ 23 ] or uterus didelphys. [ 24 ]

The MR imaging diagnostic criteria for bicornuate uterus are as follows:

(a) Divergent uterine horns with an inter cornual distance > 4cm

(b) Concavity of the fundal contour

(c) Or, an external fundal cleft >1 cm deep.

**Fig 6**. Bicornuate Uterus (*Adapted from www.geocities.com)*

## *Pre-Operative Period*

The pre-operative work up is important and includes hysterography, diagnostic hysteroscopy, and pelvic sonography. Vaginal sonography with accentuated contrasts may be added.

These exams should confirm that the patient has a septate uterus and not a bicornuate uterus, and check for the presence of other infertility factors such as myomas, endometriosis,….

Nawroth F (2006) [25] reported the presence of a higher incidence of endometriosis reaching 25.8% in patients with septate uteri.

During sonography, it is essential to measure the thickness of the uterine septum, its height and the depth of the healthy myometrium above the septum up to the serosa. If the ultrasound reveals a groove

in the corner facing the posterior surface of the bladder between the two half uteri, the malformation is diagnosed as bicornuate uterus.

**Fig 7** . **Classification criteria for Ultrasound differentiation of septate from bicornuate uteri**:

* **A** When apex (3) of the fundal external contour occurs below a straight line between the Tubal ostia (1, 2) or,

* **B** 5 mm (arrow) above it, the uterus is bicornuate.

* **C** When apex is more than 5 mm (arrow) above the line, uterus is septate.

***Radiology*** *2004; 233:19–34*

**Fig 8** . **MRI differentiation between bicornuate and septate uteri using Axial $T_2$ – weighed image**

Moreover, one month before surgery, a progesterone treatment (with pregnane for example) or the administration of GnRH analogs can be prescribed to prepare the endometrium, so that the absorption of fluid during hysteroscopy may be reduced by 142 to 572 ml, in addition to a reduction in the operating time (between 2 and 25 min) [26].

Triolo et al (2006) [27] conducted a prospective, randomized clinical study on one hundred thirty-five patients in order to compare danazol and gestrinone treatment as a preoperative mean of preparing the endometrium to operative hysteroscopy. Side effects were infrequent in both groups. But the rate of endometrial response was higher for the gestrinone group (97.1% vs. 83.6%), and the operative time (mean +/- SD) was 12 +/- 1.8 and 15.2 +/- 1.9 minutes for the gestrinone and danazol groups, respectively. The gestrinone group showed a lower incidence of moderate bleeding (3% vs. 22.4%) and a lower infusion volume (2,100 +/- 200 mL vs. 2,400 +/- 250 mL).

In studies comparing GnRHa with danazol, no marked differences were observed in mean operating time, but amenorrhea tended to be more frequent 6-12 months after surgery in patients who received GnRH agonists. Odds ratio was 1.9 (95% Confidence Interval,1.0-3.3) [26] In addition, a pre-treatment with MPA (Medroxy Progesterone Acetate) may decrease bleeding intraoperatively, thus allowing a better hysteroscopic visualization. [28 ]

In fact, Donnez J and Nisolle M [6] don't agree on the preoperative hormonal treatment, since they believe that it not only causes endometrial atrophy and decreases intraoperative bleeding, but it reduces also the depth of the myometrium thus leading to uterine perforation!. They usually perform hysteroscopic metroplasty immediately after the end of the menstrual cycle.

## *Surgical Procedure*

A variety of instruments can be used for the resection of septum such as miniature scissors or semi-rigid miniature scissors that are small enough to pass through the resectoscope into the uterine cavity via the cervical canal. The blades can be opened widely so that even a thick septum could be resected, but the use of a high frequency electric current is advisable in this case for a better control of bleeding.

Argon, krypton, KTP 532 and Nd:YAG laser were also successfully used in the resection of uterine septum . But the surgeon should be aware to use only bare fibers and not $CO_2$ conducting fibers since they cause bubbling of the distending medium thus leading to gas embolism, cardiovascular collapse and even death. Moreover, hyskon causes caramelization and may damage the laser fiber. [6]

A thorough visual exploration of the uterine cavity is primordial. The two tubal ostia must be perfectly visualized in order to locate the base of the septum. The resection is performed in a progressive manner by means of a repetitive contact between the electrode and the septum. The resection starts at the apex of the septum in a horizontal manner, halfway between its anterior and posterior surfaces thus causing it to retract to become part of the corresponding surfaces of the uterus and the uterine cavity gradually acquires a normal aspect. Usually, the tissue of the septum is fibrous and does not bleed. The resection ends where a healthy myometrium is visible by the occurrence of minimal bleeding. When this bleeding occurs, the division should be stopped, because it indicates that the septum has been completely divided. Both tubal ostia should be visible under the same hysteroscopic view and it is important to leave a fundic spur of of < 1cm in place in order to avoid weakening the myometrium thus increasing the risk of uterine perforation. [ 29 ]

Concerning the resection of the complete septate uterus, it usually starts with the resection of the vaginal septum (if present) by using CO2 laser or unipolar coagulation (Figure 9B). The cervical septum is then incised with the scissors (Figure 10A) or with a CO2 laser connected to a colposcope, until the lower portion of the uterine septum is seen. The hysteroscope is advanced while maintaining a visual contact on both tubal ostia and the uterine septum is resected as previously described.

**Figure 9**. (A) Vaginal sagittal septum. (B) Resection of the vaginal septum using monopolar coagulation.

*( Adapted from [6] Donnez J and Nisolle M.* ***Endoscopic laser treatment of uterine malformations.*** *Human Reproduction vol.12 no.7 pp.1381–1387, 1997.)*

**Fig 10 (A)** The cervical septum is incised using scissors. (B) The external cervical os is completely normal

**Fig 10**. (**C**) Dilatation of the cervical canal before resection of the the uterine septum resection

## *Post-op management*

An Intrauterine device may not be needed. Estrogen therapy is given for 2 months to facilitate the follow-up of hysteroscopy. But, this is controversial since Nawroth F et al (2002) [30]. conducted a retrospective study infertile patients with septate uteri, and concluded that a post-operative three-months hormone replacement therapy accompanied with the insertion of an intra-uterine device, or the use of hormone replacement therapy alone, are not necessary after hysteroscopic metroplasty since these patients had comparable results to patients who didn't receive any post-operative therapy.[30]

During the immediate post-op period; if the inflow-outflow assessment is > 500 c.c, a chemistry panel must be done.

After 2 months, a follow up diagnostic hysteroscopy is done:

- to check for the presence of possible adhesions, since it is easy to remove these new fine adhesions during the diagnostic procedure with the pointed tip of the hysteroscope. Guida et al (2004)[31] studied the results of intra-uterine application of 10 ml of auto-cross-linked hyaluronic acid gel (ACP Gel) after hysteroscopic surgery in a randomized, double-blind controlled trial on 132 patients. They concluded that ACP Gel has reduced the proportion of women with intrauterine adhesions three months later by 60%. The mean adhesion score and adhesion severity were also significantly lower with the use of ACP gel.
- If the remaining fundic spur is > 1cm, a second procedure is indicated.

The only criterion of success of the hysteroscopic septoplasty is a subsequent pregnancy resulting in a viable birth.

## *Results*

**Table III. Pregnancy outcome in patients with septate uteri before hysteroscopic metroplasty**

| Study | Patients | Pregnancies | Ectopics | Abortions | Preterm Delivery | Term Delivery | Live Birth |
|---|---|---|---|---|---|---|---|
| | N | n | n% | n% | n% | n% | n% |
| Fayez (1986)[a] | 19 | 21 | 0 | 90.5% | 9.5% | 0% | 0% |
| Valle&Sciarra (1986)[a] | 12 | 42 | 0 | 71.4% | 8.6% | 0% | 3% |
| March&Israel (1987)[a] | 91 | 240 | 0 | 88.3% | 8.8% | 2.9% | 12% |
| Perino *et al. (1987)*[a] | 24 | 27 | 0 | 88.9% | 11.1% | 0 % | 3% |
| Daly *et al. (1989)*[a] | 70 | 150 | 0 | 86.7% | 8.7% | 4.7% | 10% |
| Choe& Baggish(1992)[a] | 19 | 41 | 7.3% | 81.6% | 15.8% | 2.6% | 4% |
| Grimbizis *et al. (1998)*[a] | 57 | 78 | 2.6% | 88.4% | 2.6% | 6.4% | NM |
| Heinonen PK (2006)[b] | 49 | 115 | 0 | 27.0% | 12.0% | NM | 72% |

[a] *Adapted from [1] Grimbizis GF, Camus M, Tarlatzis, B.C, Bontis J.N, and Devroey P. C.* ***Clinical implications of uterine malformations and hysteroscopic treatment results****. Hum Reprod Update, 2001; 7 (N0.1): 161-174*

*NM =not mentioned.*

[b] *[13] Heinonen PK.* ***Complete septate uterus with longitudinal vaginal septum****. Fertil Steril. 2006 Mar; 85(3):700-5.*

**Table IV. pregnancy outcome in patients with septate uteri after hysteroscopic metroplasty**

| Study | Patients | Pregnancies (+Ongoing) | Ectopics | Abortions | Preterm Delivery | Term Delivery | Live Birth |
|---|---|---|---|---|---|---|---|
| | N | n | n% | n% | n% | n% | n% |
| DeChemey (1986)[a] | 72 | 67 (+3) | 0 | 11.9% | 1.5% | 85.6% | 85.6% |
| Fayez (1986)[a] | 19 | 16 | 0 | 12.5% | 0% | 87.5% | 87.5% |
| Valle&Sciarra(1986)[a] | 12 | 10 (+3) | 0 | 20.0% | 20.0% | 60.0% | 80.0% |
| March&Israel(1987)[a] | 66 | 56 (+7) | 0 | 14.3% | 7.1% | 78.6% | 85.7% |
| Perino et al(1987)[a] | 24 | 11 (+5) | 0 | 9.1% | 0% | 90.9% | 90.9% |
| Daly et al(1989)[a] | 66 | 84 (+4) | 0 | 20.2% | 6.0% | 73.8% | 77.4% |
| Choe&Baggish(1992) | 14 | 12 (+3) | 0 | 8.3% | 8.3% | 83.4% | 83.4% |
| Fedele et al(1993) | 66 | 66 | 0 | 15.2% | 15.2% | 68.2% | 83.3% |
| Grimbizis et al(1998) | 42 | 44 | 2.3% | 25.0% | 4.5% | 68.8% | NM |
| Ludwin et al(2003)[b] | 31 | 27 | 0 | 44.4% | 11.1% | 44.4% | 55.5% |
| Saygili-Yilmaz(2003)[c] | 361 | 180 | 0 | 16.0% | 18.8% | 57.2% | 75.0% |
| Pabuccu et al (2004)[d] | 61 | 25 | 0 | 28.0% | 20.0% | 52.0% | 72.0% |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Le Ray et al(2006)[e] | 10 | 8 | 12.5% | 50.0% | 12.5% | 25.0% | NM |

[a] *Adapted from [1] Grimbizis GF, Camus M, Tarlatzis, B.C, Bontis J.N, and Devroey .**Clinical implications of uterine malformations and hysteroscopic treatment results**. Hum Reprod Update, 2001; 7 (1): 161-174*

[b] *[32] Ludwin A, Basta A, Pitynski K. **Pregnancy and delivery after hysteroscopic metroplasty**. Ginekol Pol. 2003 Oct;74(10):1180-6*

[c] *[33] Saygili-Yilmaz E, Yildiz S, Erman-Akar M, Akyuz G, Yilmaz Z. **Reproductive outcome of septate uterus after hysteroscopic metroplasty**. Journal Archives of Gynecology and Obstetrics, 2003Oct; 268 (4):289-292*

[d] *[34] Pabuccu R, Gomel V**. Reproductive outcome after hysteroscopic metroplasty in women with septate uterus and otherwise unexplained infertility**. Fertil Steril. 2004 Jun;81(6):1675-8*

[e] *[35] Le Ray C, Donnadieu AC, Gervaise A, Frydman R, Fernandez H. **Management of ten patients with complete septate uterus: hystersocopic section of and obstetrical outcome**. J Gynecol Obstet Biol Reprod (Paris). 2006 Dec;35(8 Pt 1):797-803.*

*NM =not mentioned.*

## B. The enlarging hysteroscopic metroplasty in DES exposed patients and hypoplastic uterus

### *Generalities*

Diethylstilbestrol is a nonsteroidal estrogen that was widely prescribed between 1950 and 1977 as a treatment for threatened abortion and premature deliveries. It was thought that by increasing the production of placental steroid hormones, this may decrease the pregnancy loss. The risks included not only vaginal adenocarcinoma, cervical adenosis, adnexal and uterine malformations, but also early menopause!. Recently Hatch E E et al (2006) [ 36 ] performed a study on 4210 patients who were exposed to DES versus 1829 control women. They found that “DES-exposed women were 50% more

likely to experience natural menopause at **any given age**" especially if they have been exposed to more than 10,000 milligrams of DES.

DES exposure was also related to secondary infertility and even to primary infertility especially if the exposure took place before the 9th weeks of gestation. (table V) [ 37 ]. But Troiano et al (2004) believes that if the exposure took place very early in the first trimester or after 22 weeks of gestation, the presence of structural abnormalities are not likely to occur [ 9 ].

**Table V. Pregnancy and infertility according to timing of diethylstilbestrol exposure, DESAD* and Dieckmann cohorts, mid-1970s-1994**

*Adapted from Palmer JR, Hatch EE, Rao RS, Kaufman RH, Herbst AL, Noller KL, Titus-Ernstoff L, and Hoover RN. Infertility among women exposed prenatally to Diethylstilbestrol. Am J Epidemiol. 2001;154(4):316-21 ).*

## *Classification*

Sixty-nine percent of women exposed to DES have uterine anomalies detected on hysterosalpingographic images. [ 9 ]

Palmer and Meylan (1964) described 3 types of uterine hypoplasias [39]:

1. Simple hypoplasia : The form of the uterus is normal, but it is small scaled.

2. Elongated hypoplasia : The uterus has a normal or elongated length, but it has a narrow fundus.

3. Malformative hypoplasia : Arcuate fundus, T-shaped (seen in 31% of cases), or a Y-shaped uterus (has the worst prognosis). Moreover, strictions in the form of a constriction ring may be seen in the mid uterus (Figure 11) in addition to the coexistence of irregular uterine contours, dilatations, adhesions, rudimentary horns, and diverticulae.

**Fig 11**. The three types of uterine hypoplasias (*Adapted from Troiano R and McCartthy SM**. Müllerian Duct Anomalies: Imaging and Clinical Issues.** Radiology 2004;233:19-34)*

Anomalies of the fallopian tube may also be seen such as foreshortening, presence of sacs, and fimbrial deformities (ex. fimbrial stenosis), in addition to malformations in the cervix leading to cervical incompetence , thus necessitating cervical cerclage in order to avoid second trimester pregnancy loss.

Not all women exposed to DES are infertile, since this depends upon the type of the anomaly present.

**Fig 12. Uterus in DES Exposure .** Coronal oblique fast spin-echo T2 weighted MR images show T configuration of the uterus, constriction bands (long arrows), and cavitary narrowing (short arrows). (*Adapted from Robert N. Troiano, and Shirley M. McCarthy. **Müllerian Duct Anomalies: Imaging and Clinical Issues1.** Radiology 2004; 233:19–34.)*

**Table VI. Selected pregnancy outcomes in any pregnancy exposed versus unexposed**

(Adapted from *Kaufman RH, Adam E, Hatch EE, Noller K, Herbst AL, Palmer JR, et al.* ***Continued follow-up of pregnancy outcomes in diethylstilbestrol-exposed offspring****. Obstet Gynecol 2000;96:483-9.)*

Infertility in patients exposed in-utero to DES is most commonly due to uterine or tubal factors.[37] From the results above we can conclude that some of these patients had normal pregnancies, and they were able to deliver at term in 64.5%. But, there is evidence for an increased risk of first- and second-trimester spontaneous abortion, ectopic pregnancy, and preterm delivery when compared to unexposed control. Consequently, high-risk obstetric care may be indicated for pregnant women who were exposed to DES in utero. [38 ].

In addition, Palmer et al (2001) studied two cohorts: the DESAD (National Cooperative Diethyldtilbestrol Adenosis Study) and the Dieckmann cohorts, and concluded that uterine and tubal factors are the major causes of increased rates of infertility among women exposed to DES in comparison to control group.

(Table VII *is Adapted from Palmer JR, Hatch EE, Rao RS, Kaufman RH, Herbst AL, Noller KL, et al.* ***Infertility among women exposed prenatally to diethylstilbestrol****. Am J Epidemiol 2001;154:316-21).*

**Table VII. Reason for infertility among diethylstilbestrol-exposed women,* DESAD† and Dieckmann cohorts, mid 1970s-1994**

## *Surgical Procedure*

The enlarging hysteroscopic metroplasty is performed early in the follicular phase. The principle is based upon incising with a hook the lateral spurs (including the myometrium) and the arcuate fundus to a depth of 7mm in order to obtain an increase in the size of the uterus and ameliorate its shape while avoiding as much as possible the perforation of the uterus or the fundus. The procedure is ended by placing into the uterine cavity a silastic sheet to a depth of 1mm.

**Fig 13.** Normal Uterus T-Shaped Uterus

The enlarging hysteroscopic metroplasty consists of incising the lateral spurs and an arcuate fundus to obtain an enlargement of uterine size and an improvement in uterine shape. *(Adapted from www.cdc.gov)*

A single dose of antibiotic (Cephalosporin 2$^{nd}$ generation) is usually given intraoperatively, and the patient is discharged on a sequential oestroprogestative treatment (Ovanon®) for 2 months (7 tablets; each 50 µg of ethinylestradiol, 15 tablets of combined 50µg ethinylestradiol associated with 2.5 mg lynestrol.). Afterwards, the silastic strip is removed and a new hysterosalpingogram is performed. [39].

## *Results:*

Garbin et al (1998) [ 39 ] published the reproductive outcome results before and after the enlarging hysteroscopic metroplasty performed on 24 cases. In table VIII we can see a decrease in the rates of abortion from 88% to 12.5%. And the rates of term deliveries were increased from 3% to 87.5%.

Similarly Barranger et al (2002) [ 40 ] evaluated the reproductive outcome on 29 cases; 21 women (72.4%) had 30 pregnancies (follow-up for 13-67 months). Thirteen of them gave birth to 16 live infants. In this study, the rates of delivery increased from 3.8% to 63.2%.

After 18 years of publishing his results in 1998, Garbin O et al (2006) [ 3 ]. believes that the enlarging hysteroscopic metroplasty should not be proposed as a first line treatment in patients exposed in-utero to DES, or those having a dysmorphic uterus except in specific cases such as before enrollement in an Assisted Reproductive Technique Program, in order to decrease the possibility of implantation failure, or in the case of a nulligravida of advanced age.

## VI. Complications

In fact, the enlarging hysteroscopic metroplasty is not innocuous. Since it may **create** cervical fragilization (Garbin 1998) [ 39 ] apart from the cervical incompetency associated with the structural changes due to DES exposure thus necessitating the insertion of a cervical cerclage in order to prevent 2$^{nd}$ trimester pregnancy loss. Moreover, the incision on the myometrium weakens the uterus and make it more prone to uterine rupture. So, pregnancy in such a uterus must be considered a high risk pregnancy.

Of course, complications are not limited to the enlarging hysteroscopic metroplasty alone, since the hysteroscopic septoplasty may be complicated by uterine perforation which occurs either during dilation of cervix, or during the resection of septum. There is also a risk of visceral burns if perforation is not detected. For this reason, some authors recommend a concomitant intra-operative sonography or laparoscopy.

Sentilhes L et al (2006) [ 41 ]. observed that the time interval between hysteroscopic septoplasty and a subsequent pregnancy varied from one month to 5 years with an average delay of 16 months. Uterine rupture occurred in pregnancies between 19 and 41 weeks of gestation, even in the absence of labor (in 12 out of the 18 cases reported). Thus exposing the maternal and fetal prognosis to high risks.

In his study, he denoted that the two most important factors that may increase the likelihood of uterine rupture are: the use of monopolar electrosurgery , and perforating the uterus while resecting the septum. So, instead of using monopolar electrosurgery, he encourages the use of a coaxial bipolar electrode for a safer resection.

In addition to the mechanical complications already mentioned, post- hysteroscopic endometritis occurs in 1% to 5% of cases, thus justifying the systematic use of intra-operative prophylactic antibiotics (Cephalosporins). In order to avoid during hysteroscopy the intravascular passage of a significant quantity of irrigation fluid which can lead to hemodilution, adherence to the procedural protocol is essential with a meticulous monitoring of the inflow and outflow of fluids.

## VII. Conclusion

Hysteroscopic metroplasty has simplified the treatment of women with septate uteri, and those having a uterine hypoplasia since they were treated previously with laparotomy or hysterectomy.

The primary advantage is the avoidance of a laparotomy, and the procedure takes no more than 20 to 60 minutes thus reducing anesthesia time. Pelvic adhesions are minimized, as well as infection and the amount of blood loss. The patient recovers rapidly and she may attempt pregnancy even after one cycle instead of waiting 3 to 9 months as in the case of abdominal procedures. [ 24 ]

Following hysteroscopic septum resection, the spontaneous abortion rate decreased from 91% to approximately 15% , the term delivery rates increased from approximately 6% to 57%, and the live birth rates increased tremendously from 11 % to reach 85%.(Based upon the results of this paper). Moreover, the mean pregnancy rate in previously known infertile women became 47%. [42]

Because of its simplicity, minimal invasiveness, and low morbidity, a more liberal approach to the treatment of some uterine anomalies is advocated.

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