Intra Uterin Sineşilerde Histeroskopik Cerrahi

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Risk factors, diagnosis and clinical relevance of intrauterine adhesions versus true Asherman's syndrome

Intrauterine

adhesions

+/- Symptoms

menstrual abnormalities, pelvic pain, infertility, recurrent miscarriage, and abnormal placentation

Asherman JG. Amenorrhoea traumatica (atretica)

ETIOLOGY&RISK FACTORS

Inflamation

Hypoestrogenemia

Opposite walls

Table 1 Occurrence of intrauterine adhesions following surgery for various conditions and in those with various symptoms.

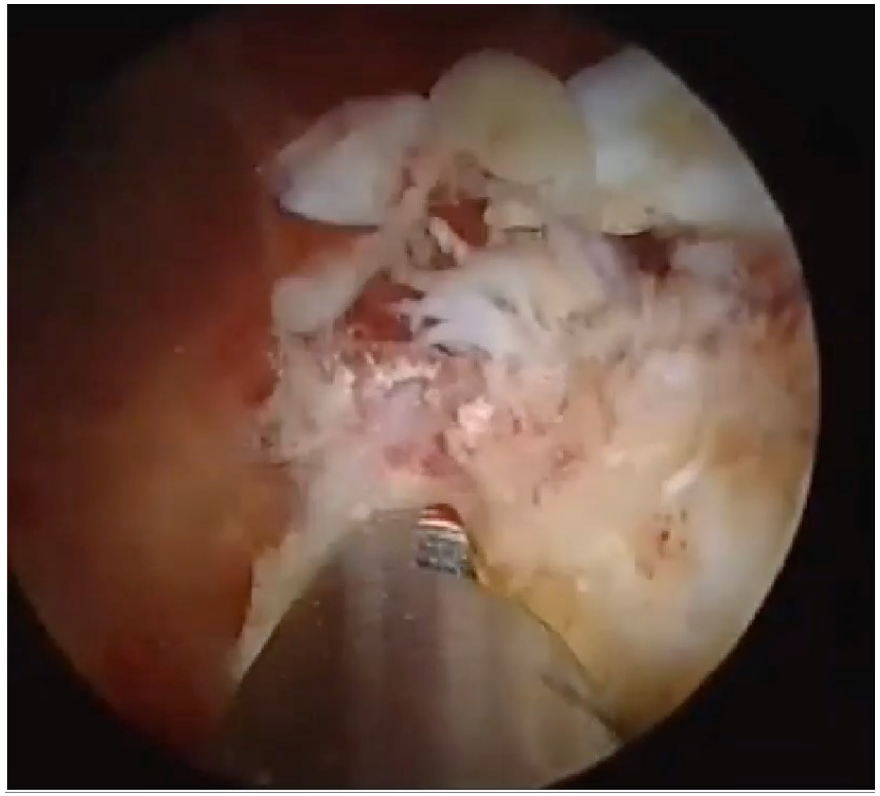
Condition/procedure	*Prevalence (%)*	*Reference*
Secondary amenorrhoea	1.7	Jones (1964)
Infertility	6.9	Nawroth et al. (2003)
Post-Caesarean section	2.8	Rochet et al. (1979)
Post-partum D and C (any time)	3.7	Bergman (1961)
Post-partum D and C (2–4 weeks)	23.4	Eriksen and Kaestel (1960)
Early spontaneous abortion D and C	6.4	Adoni et al. (1982)
Late spontaneous abortion D and C	30.9	Adoni et al. (1982)
Missed abortion	35	Schenker and Margalioth (1982)
Elective abortion D and C	13	Kralj and Lavric (1974)
Recurrent abortion	39	Toaff and Ballas (1978)
Retained products of conception	40	Westendorp et al. (1998)
Spontaneous abortion		
One	16.3	Friedler et al. (1993)
Two	14	
Three or more	32	
Hysteroscopic myomectomy		
Single	31.3	Taskin et al. (2000)
Multiple	45.5	
Hysteroscopic metroplasty	6.7	

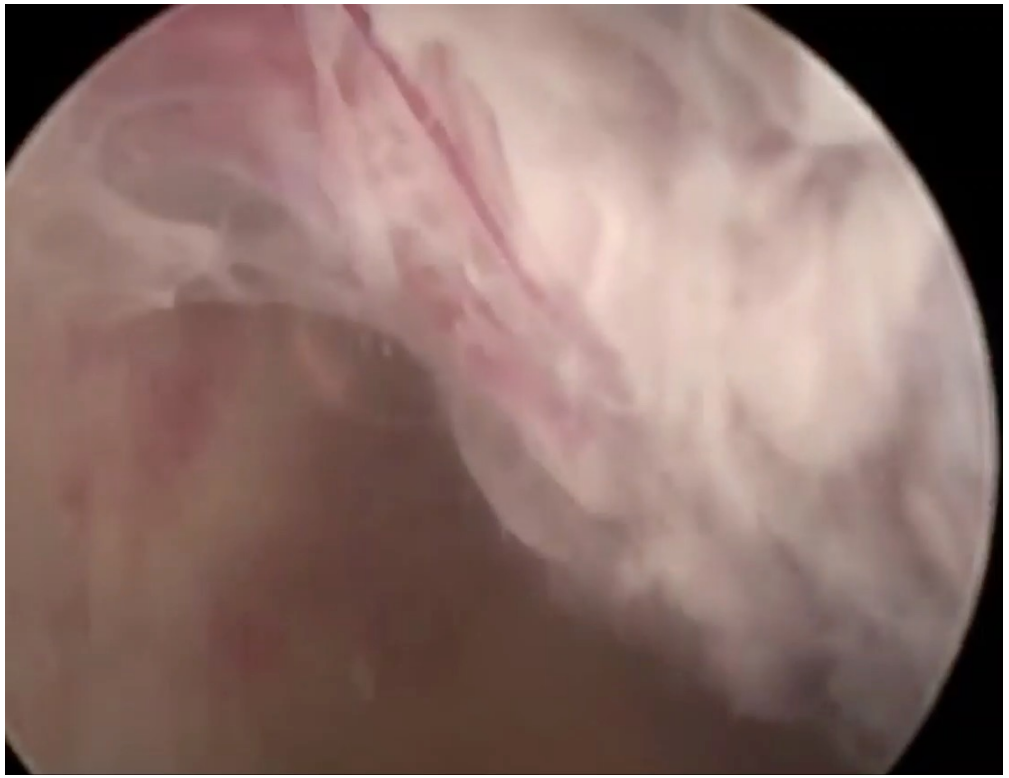
D and C = dilation and curettage.

Charles M March Reproductive BioMedicine Online (2011) **23**, 63–76

Focus on the Primary Prevention of Intrauterine Adhesions

Prevention of IUA after hysteroscopic procedures





Human Reproduction, Vol.33, No.8 pp. 1374–1380, 2018
Advanced Access publication on July 31, 2018 doi:10.1093/humrep/dey232

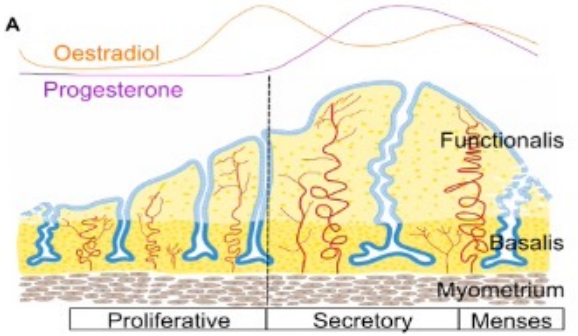
human reproduction OPINION

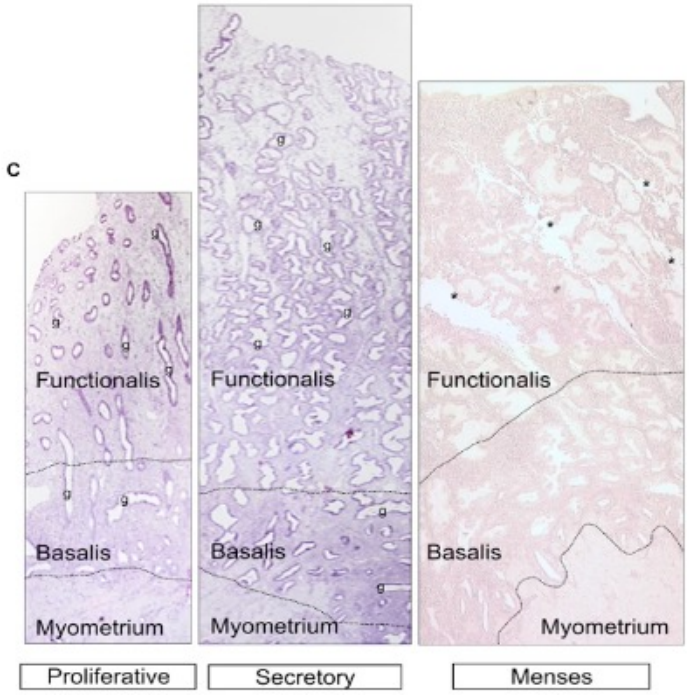
Asherman's Syndrome: it may not be all our fault

Xavier Santamaria[1,2,*], Keith Isaacson[3], and Carlos Simón[1,4,5]

The endometrium has a remarkable capacity to regenerate the functional layer from its basalis under the influence of oestrogen due to the existence of endometrial stem cells in its 'niche' which is thought to be located at the endothelium of the spiral arterioles in the basal layer (Cervello 2007, Murakami 2014).

In the normal menstrual cycle, endometrial breakdown and repair occur simultaneously, side by side, under a carefully regulated balance that have been termed 'orderly inflammation' (Evans 2012, Nathan 2010).





Hypoxia, infection and inflammation*

Table 1: European Society of Hysteroscopy (ESH).

Grade	Description
1	Thin or filmy adhesions
2	Singular dense adhesion, patent tubal ostia
	Grade 2A – with occluding adhesions of interal cervical os
3	Multiple dense adhesions, unilateral obliteration of ostia
4	Extensive dense adhesions, partial occlusion of uterine cavity, both ostia occluded (partial)
5	Extensive endometrial scarring and fibrosis
	Grade 5A – with Gr1/Gr2 adhesions
	Grade 5B – with Gr3/Gr4 adhesions + amenorrhoea

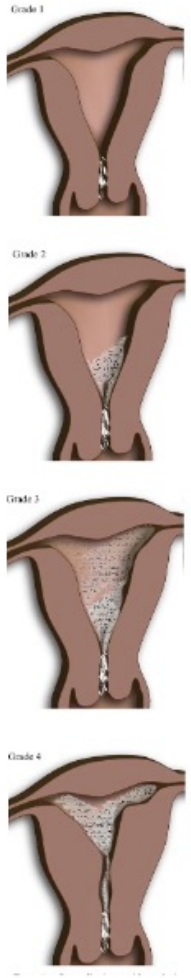


Table 2: American Society for Reproductive Medicine (ASRM) classification of intrauterine adhesions.

Extent of cavity involved	< 1/3	1/3 – 2/3	> 2/3
	1	2	4
Type of adhesions	Filmy	Filmy-dense	Dense
	1	2	4
Menstrual pattern	Normal	Hypomenorrhoea	Amenorrhoea
	0	2	4

* There are no data from any comparative analysis of these classification systems

* Adhesions should be classified as prognosis is correlated with severity of adhesions

Table I Defined clinical categories to describe the extent and degree of intrauterine adhesions (IUAs) after miscarriage.

Clinical category	Classification systems: American Fertility Society (AFS), 1988	European Society of Hysteroscopy (ESH), 1989[a]	European Society of Gynecological Endoscopy (ESGE), 1995	March, 1978
Mild	Stage I	Stage I	Stage I	Mild
Moderate	Stage II	Stage II, IIa or III	Stage II, IIa or III	Moderate
Severe	Stage III	Stage IIIa, IIIb or IV	Stage IV, Va or Vb	Severe

[a]The European Society of Hysteroscopy (ESH) was adopted by the European Society of Gynecological Endoscopy (ESGE) in 1995.

- Extent of cavity involved
- Type of adhesions
- Menstrual pattern

Poor prognosis

*Amenorrhea

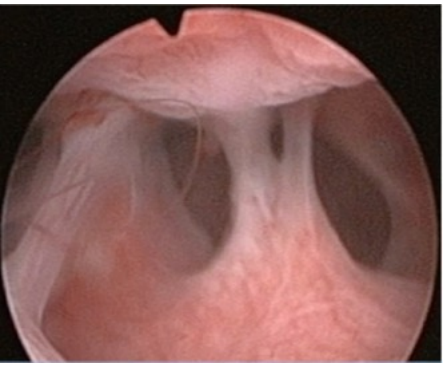
*Inability visualiation of the upper uterine cavity and ostia

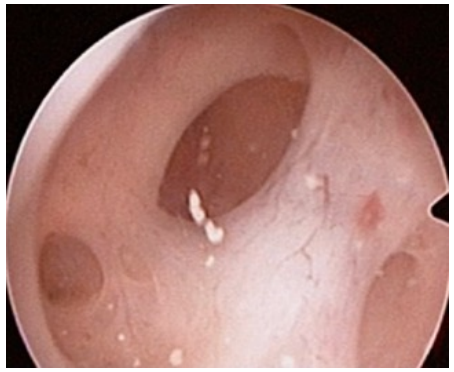
*Presence of tuberculosis

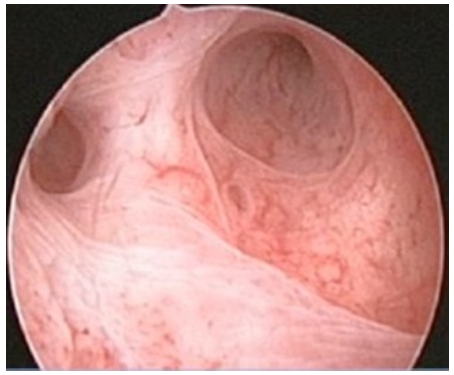
*Developed secondary to surgery

Guidelines for Classification of Intrauterine Adhesions

1. Intrauterine adhesions should be classified as prognosis is correlated with severity of adhesions. Level B.
2. The various classification systems make comparison between studies difficult to interpret. This may reflect inherent deficiencies in each of the classification systems. Consequently, it is currently not possible to endorse any specific system. Level C.







Classification according to the location and the aspect of the adhesions.

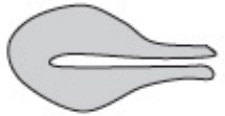
Degree	Location
I	Central adhesions (bridge-like adhesions) (a) thin or filmy adhesions (endometrial adhesions) (b) myofibrous or connective adhesions
II	Marginal adhesions (always myofibrous or connective) (a) ledge-like projections (b) obliteration of one horn
III	Uterine cavity absent on hysterosalpingography (a) occlusion of the internal os (upper cavity normal) (pseudo-Asherman's syndrome) (b) extensive coaptation of the uterine walls (absence of uterine cavity;true Asherman's syndrome)

Santamaria. Fertile Battle. Fertil Steril 2020.

Clinical pathology correlation of Asherman syndrome.

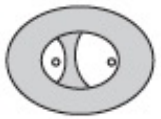
Location of the pathology of Asherman`s syndrome

1. Intrauterine fibrosis without visible adhesion or obliteration of cavity

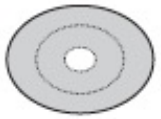


2. Cervical canal adhesion (Atretic amenorrhea)

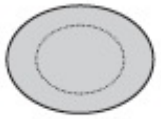
3. Uterine cavity adhesion
   1) Central adhesion without obliteration of cavity



   2) Partial obliterate and constriction of cavity

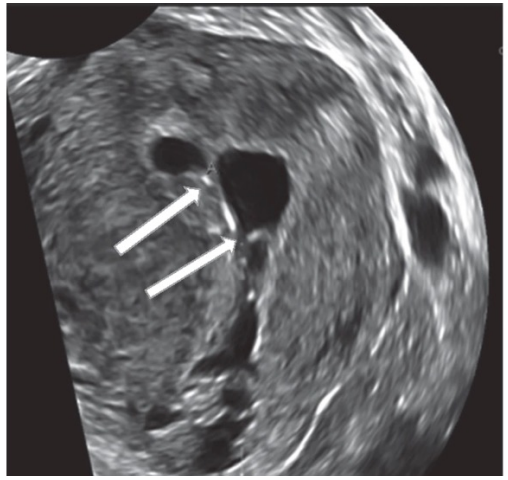


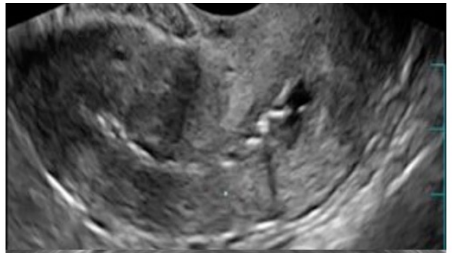
   3) Complete obliterate of whole uterus cavity

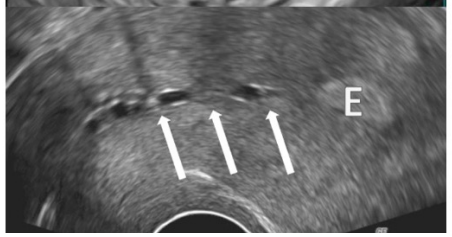


4. Uterine cavity combined with cervical canal adhesion

Yu. Asherman syndrome. Fertil Steril 2008.







Transvaginal Ultrasound Diagnostic Ability
(compared to hysteroscopy)
2D-Ultrasound Alone[30]
Sensitivity= 52%
Specificity= 11%
Saline Sonohysterogram (SIS)[27, 30]
As effective as HSG
Sensitivity= 75%
Specificity= 75%
Positive predictive value= 43%
3-D SIS[32]
Sensitivity= 70%
Specificity= 87%

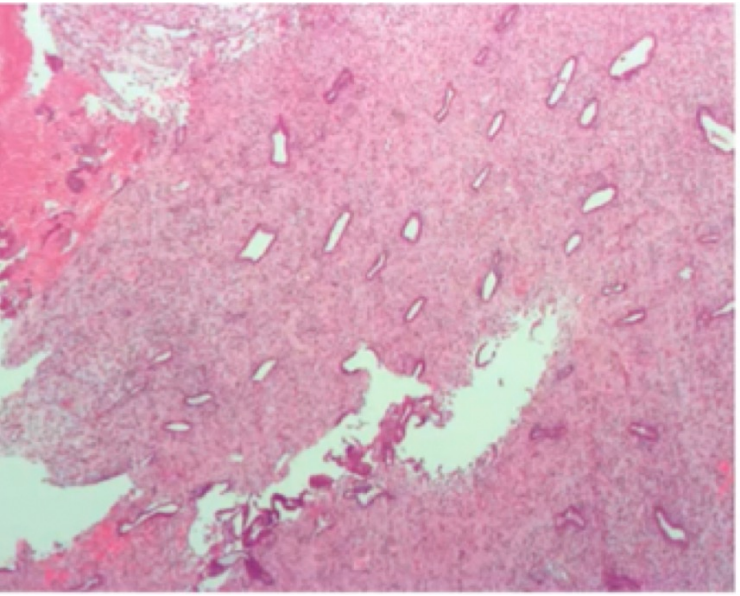
3D Ultrasound compared to 3D SIS[31]
Sensitivity= 87%
Specificity= 45%

Guidelines for diagnosis of intrauterine adhesions

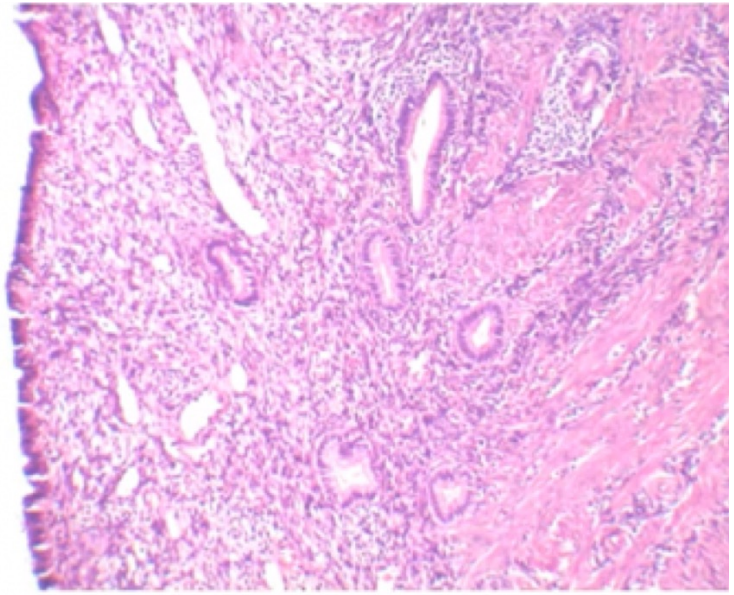
1. Hysteroscopy is the most accurate method for diagnosis of IUAs and should be the investigation of choice when available. Level B.
2. If hysteroscopy is not available, HSG and SHG are reasonable alternatives. Level B.
3. Magnetic resonance imaging should not be used for diagnosis of IUAs outside of clinical research studies. Level C.

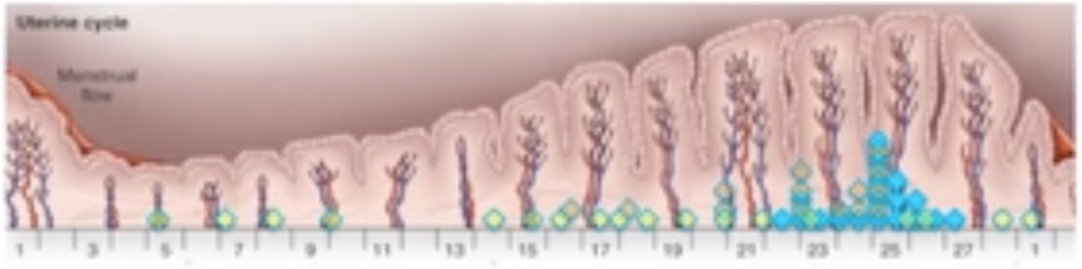
ENDOMETRIAL INACTIVITY*

ATROPHY



ASHERMAN





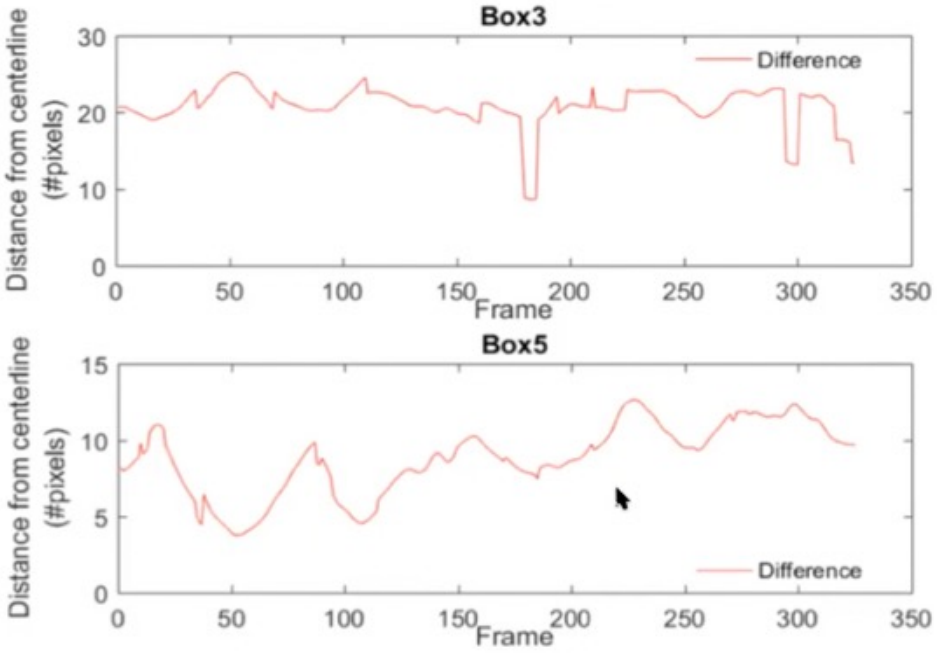
*Decidualized stroma
*Simple glands

Disparity between stroma and glands

Non physiologic combination?

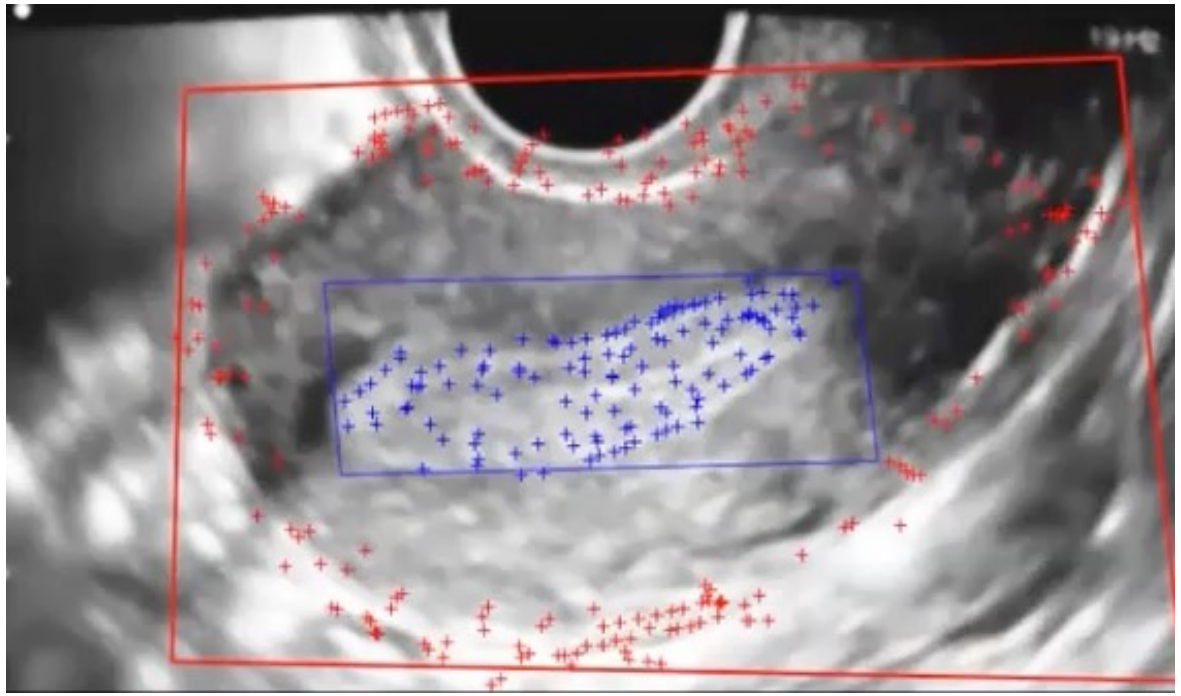
Secretorial arrest

MYOMETRIAL ARREST



AS

Control



Biological pathway ?

Management of Asherman's syndrome

SYMPOSIUM: REPRODUCTIVE SURGERY REVIEW

Charles M March

Reproductive BioMedicine Online (2011) 23, 63–76

Principles critical to a successful approach to Asherman Syndrome are encompassed in the acronym '**PRACTICE**':

PRevention, **A**nticipation, **C**omprehensive therapy, **T**imely surveillance of subsequent pregnancies, **I**nvestigation, **C**ontinuing **E**ducation

Treatment Targets

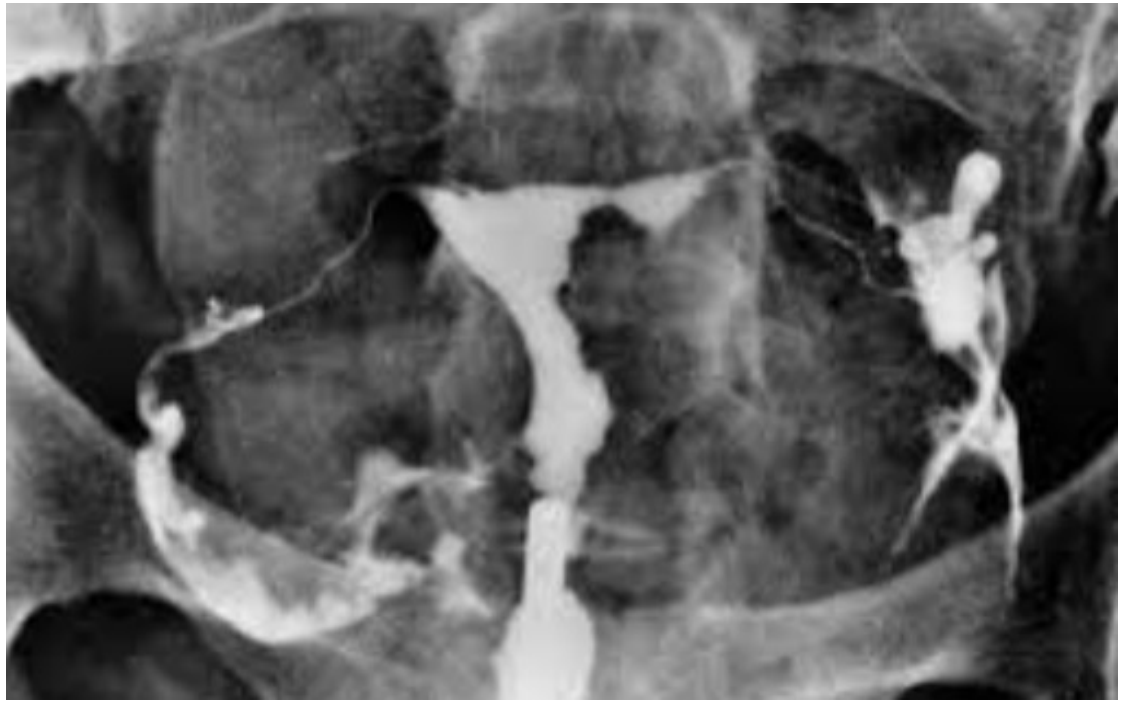
*Restoration of normal cavity

*Enhancement of wound healing

*Restoration of endometrial function

*Prevention of recurrences (30-60%)

HYSTEROSALPINGOGRAPHY (HSG)



Hysterosalpingography Before the invention of the hysteroscope, HSG was the first-line investigation to visualize the uterine cavity. Today, many gynecologists still consider it to

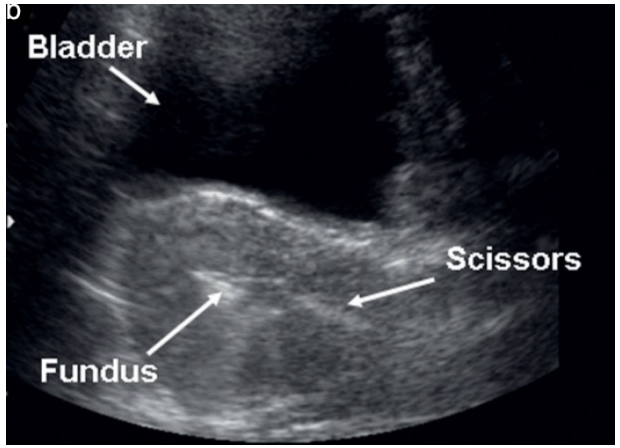
H/S ADHESIOLYSIS

Methods of guidance

Ultrasound is the optimal choice for guidance in difficult hysteroscopy

J. D. KRESOWIK, C. H. SYROP, B. J. VAN VOORHIS and G. L. RYAN

Division of Reproductive Endocrinology & Infertility, Department of Obstetrics & Gynecology, University of Iowa Carver College of Medicine, Iowa City, IA, USA



Perforation

- L/S → 8.7%
- Usg → 1.9%
- No guidance→ 5.3%

Ultrasound Obstet Gynecol 2012;


16:41:25
GE


16:38:20
Tis 0.4
Abdomen
GE

The effectiveness of hysteroscopy in improving pregnancy rates in subfertile women without other gynaecological symptoms: a systematic review

- RCT?
- Heterogenity of the patients (different classification systems)
- Comparison of surgical techniques?

Human Reproduction Update, Vol.16, No.1 pp. 1–11, 2010

Hysteroscopic Management of Asherman's Syndrome

JMIG The Journal of Minimally Invasive Gynecology

Zaraq Khan, MBBS, and Jeffrey M. Goldberg, MD

From the Divisions of Reproductive Endocrinology & Infertility and Minimally Invasive Gynecologic Surgery, Mayo Clinic, Rochester, Minnesota (Dr. Khan), and Division of Reproductive Endocrinology & Infertility, Cleveland Clinic Foundation, Cleveland, Ohio (Dr. Goldberg).

- Mechanical division of adhesions by scissors

  No additoinal thermal damage*

- Monopolar and bipolar electrosurgical instruments

  Precise cutting and good hemostasis

  Further endometrial damage **/ Energy may destroy otherwise healthy endometrium**

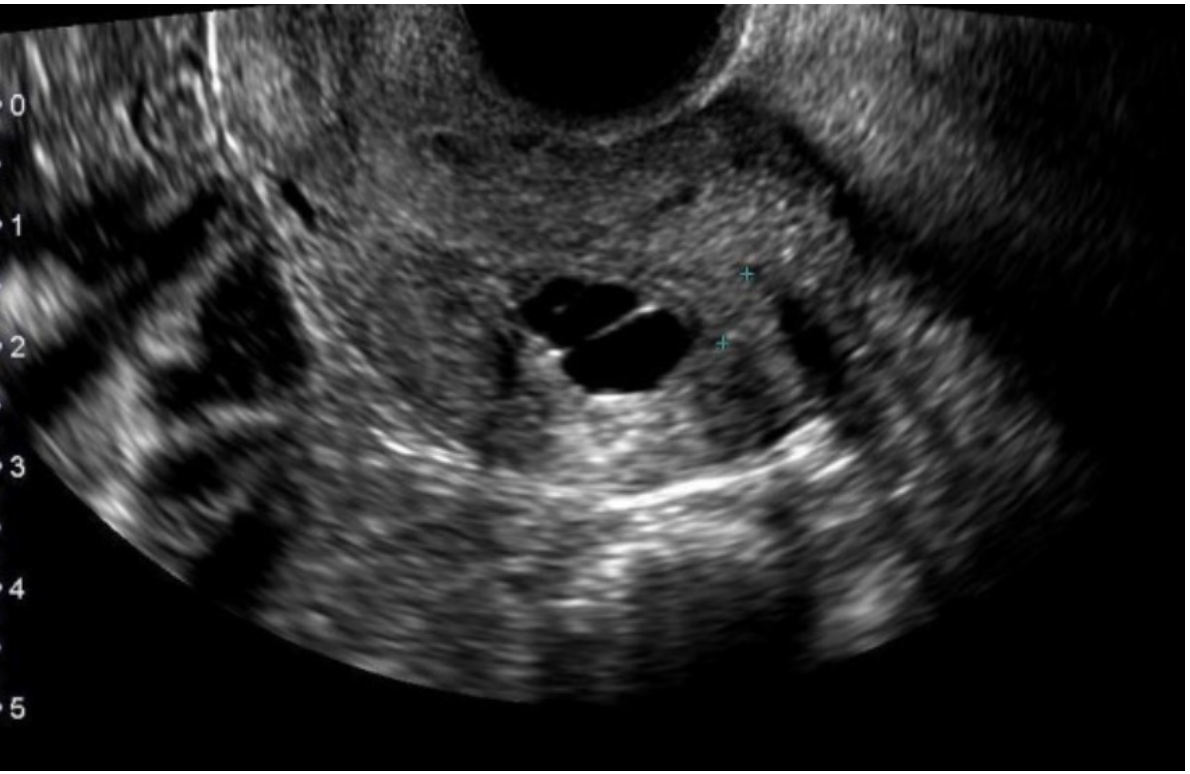
- Nd-YAG laser

* None of these techniques has been compared with any other

- The basic principle involves beginning adhesiolysis in a **caudad to cephalad** manner.

- The **filmy and central cavity adhesions** are taken down first to enable cavity distension.

* The more **lateral the adhesions and the greater their density**, the more difficult the dissection and the greater the risk of complications such as uterine perforation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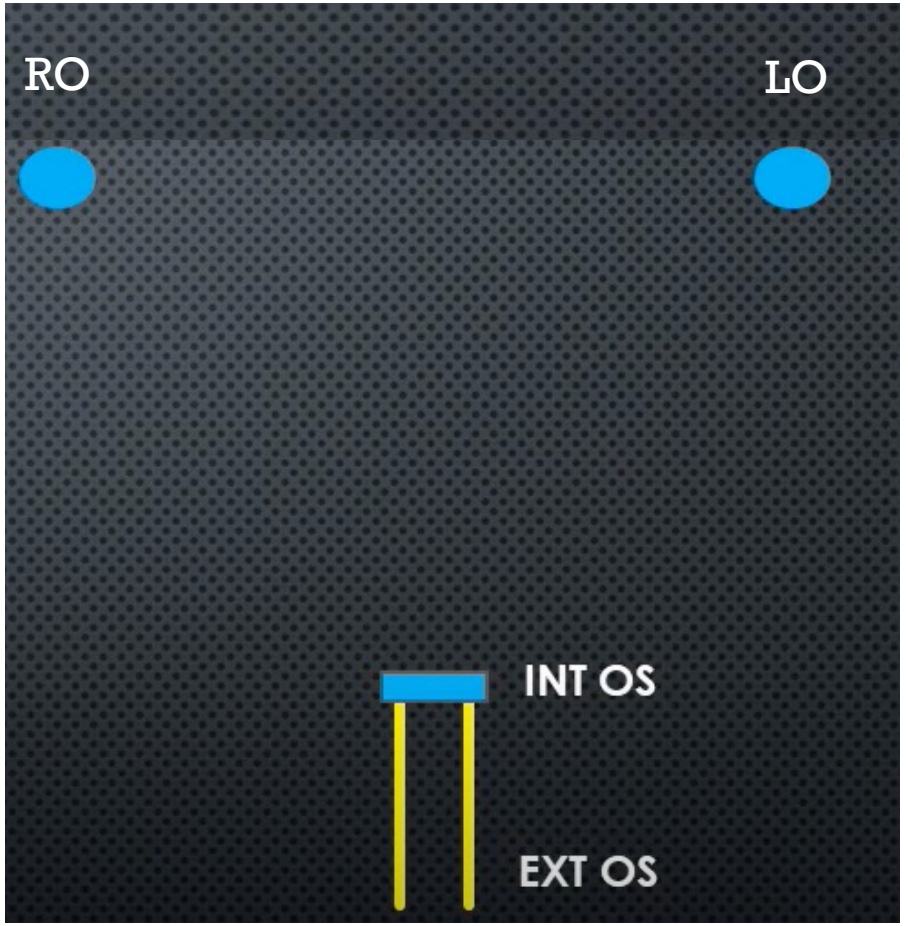
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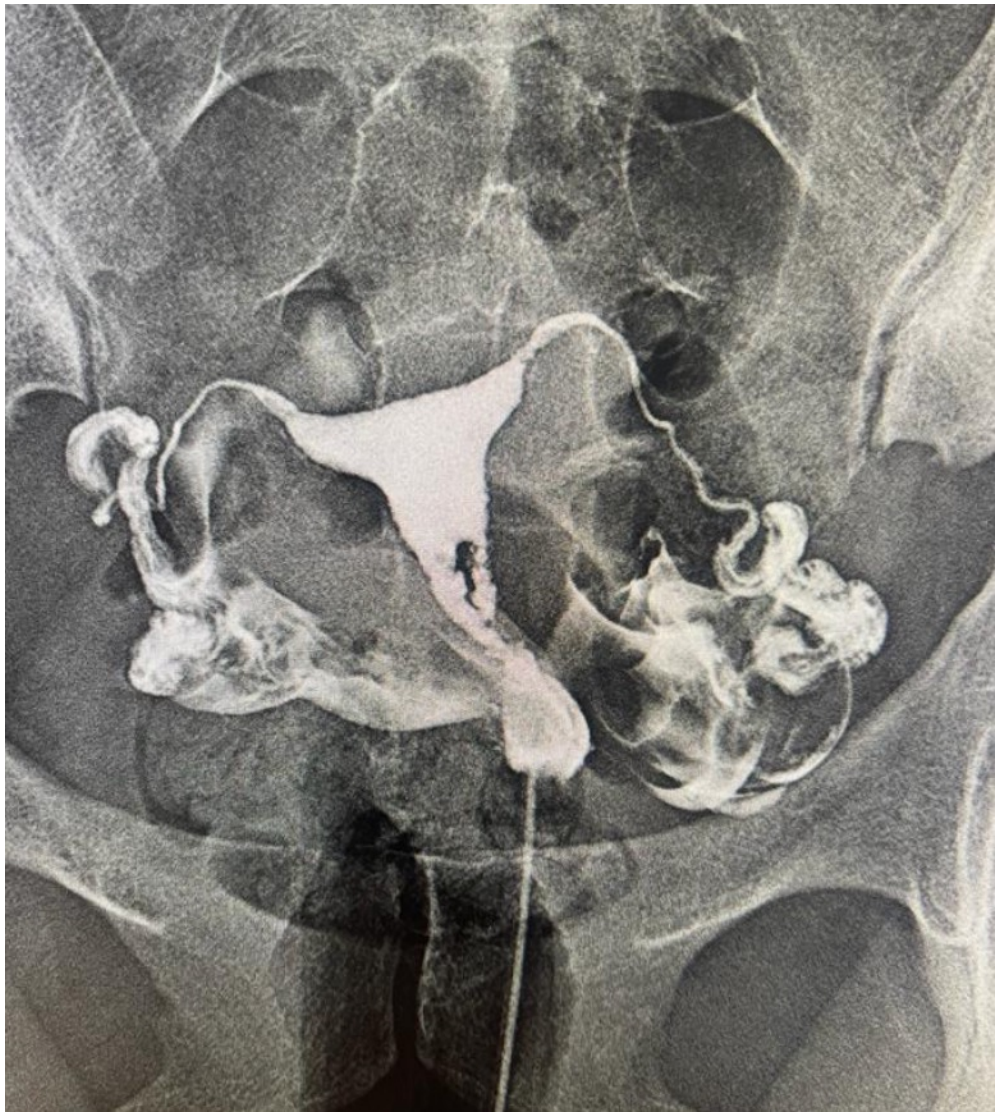

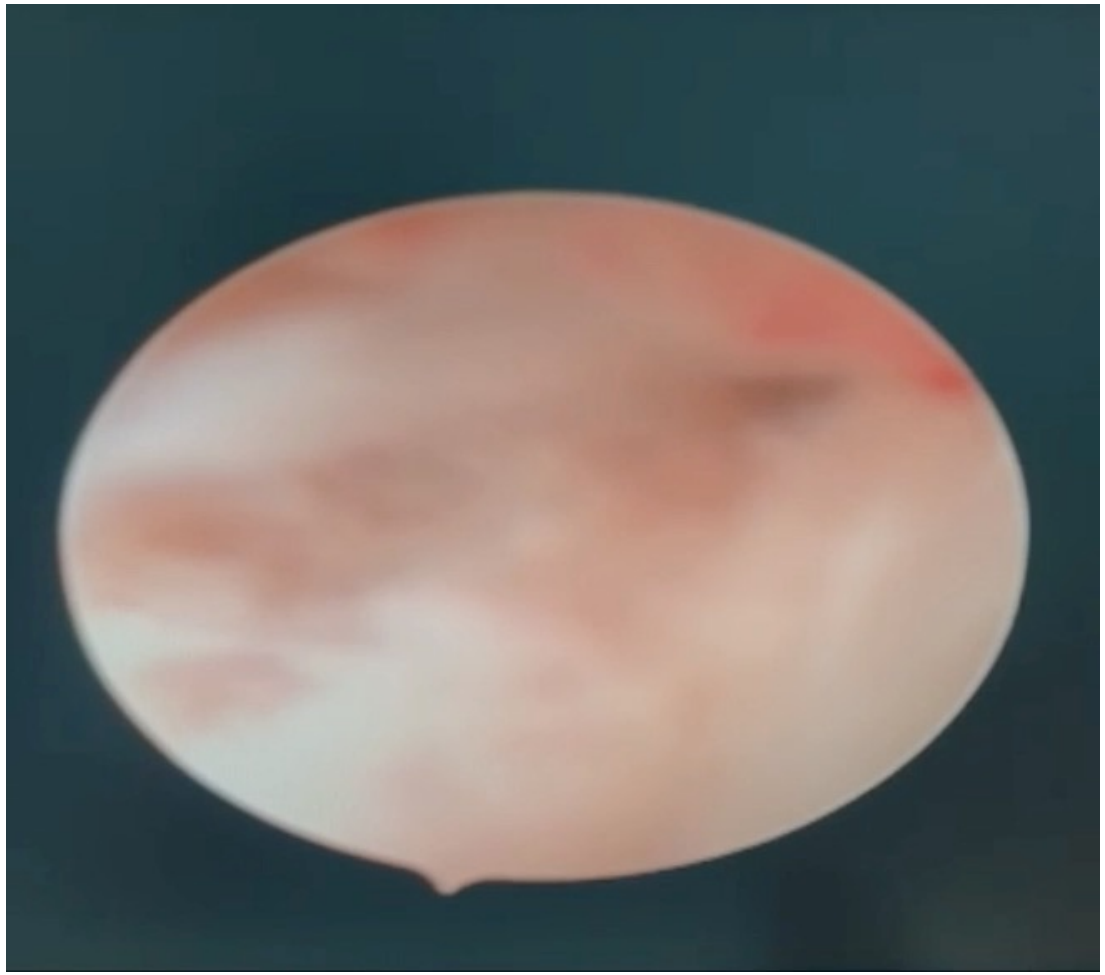

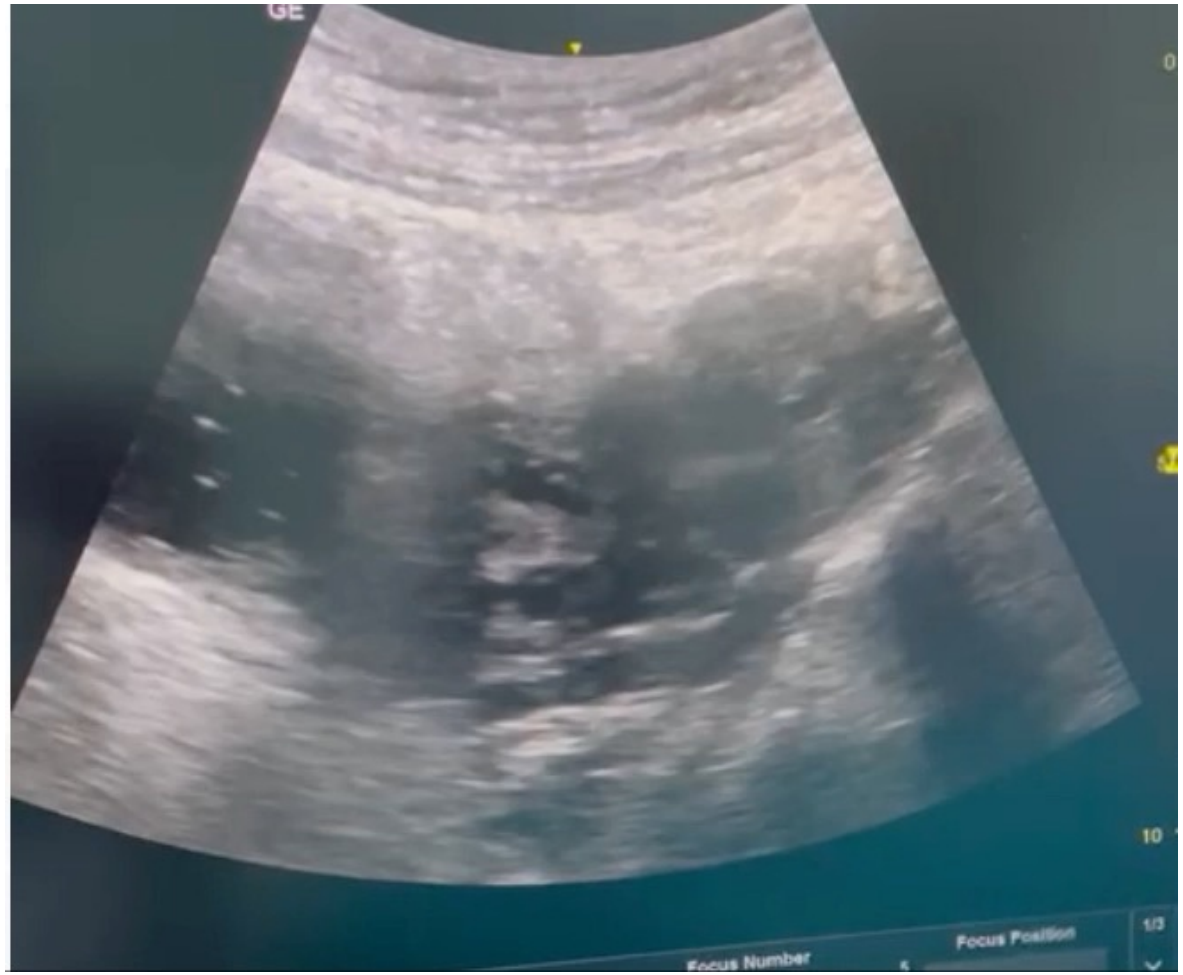
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Focus Position
Focus Number

Secondary prevention

* Recurrence rate following hysteroscopic lysis varies based on the initial adhesion burden

A comparison of two adjunctive treatments for intrauterine adhesions following lysis

A.A.E. Orhue, M.E. Aziken, J.O. Igbefoh

- Catheter vs IUD
- Atrophia due to pressure !
- Risk of infection (%8)
- Pain

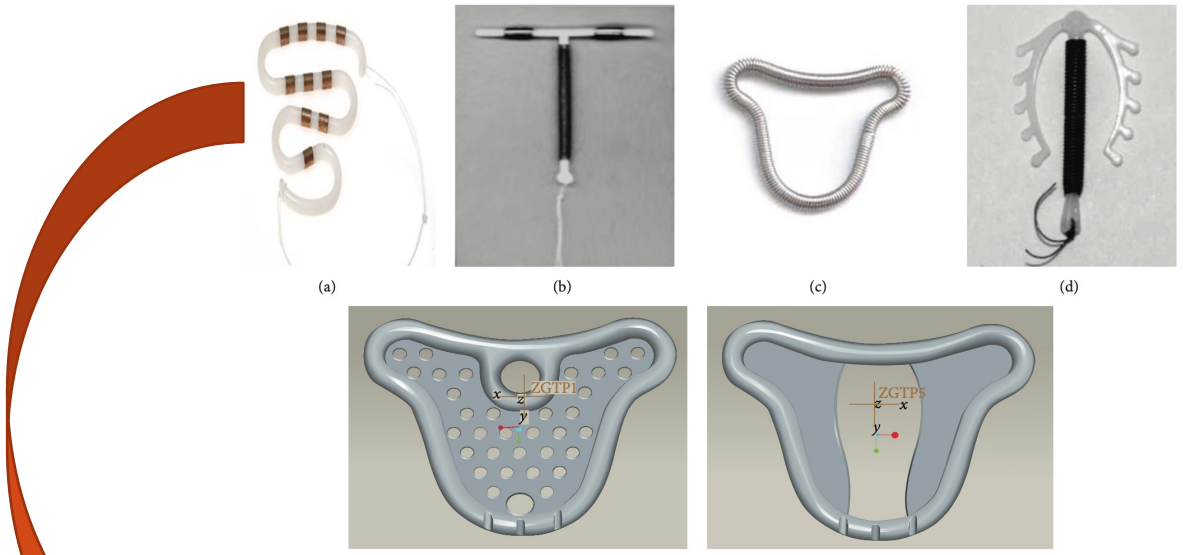
*The use of an IUD or catheter appears to reduce the rate of reformation

*There are limited data regarding subsequent fertility outcomes

Efficacy of Intrauterine Device in the Treatment of Intrauterine Adhesions

Umme Salma,[1] Min Xue,[1] Ali Sheikh Md Sayed,[2] and Dabao Xu[1]

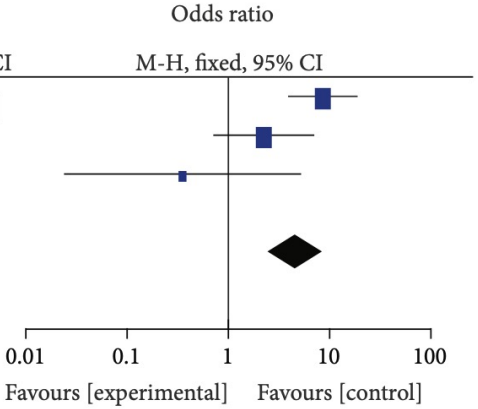
3 cycles

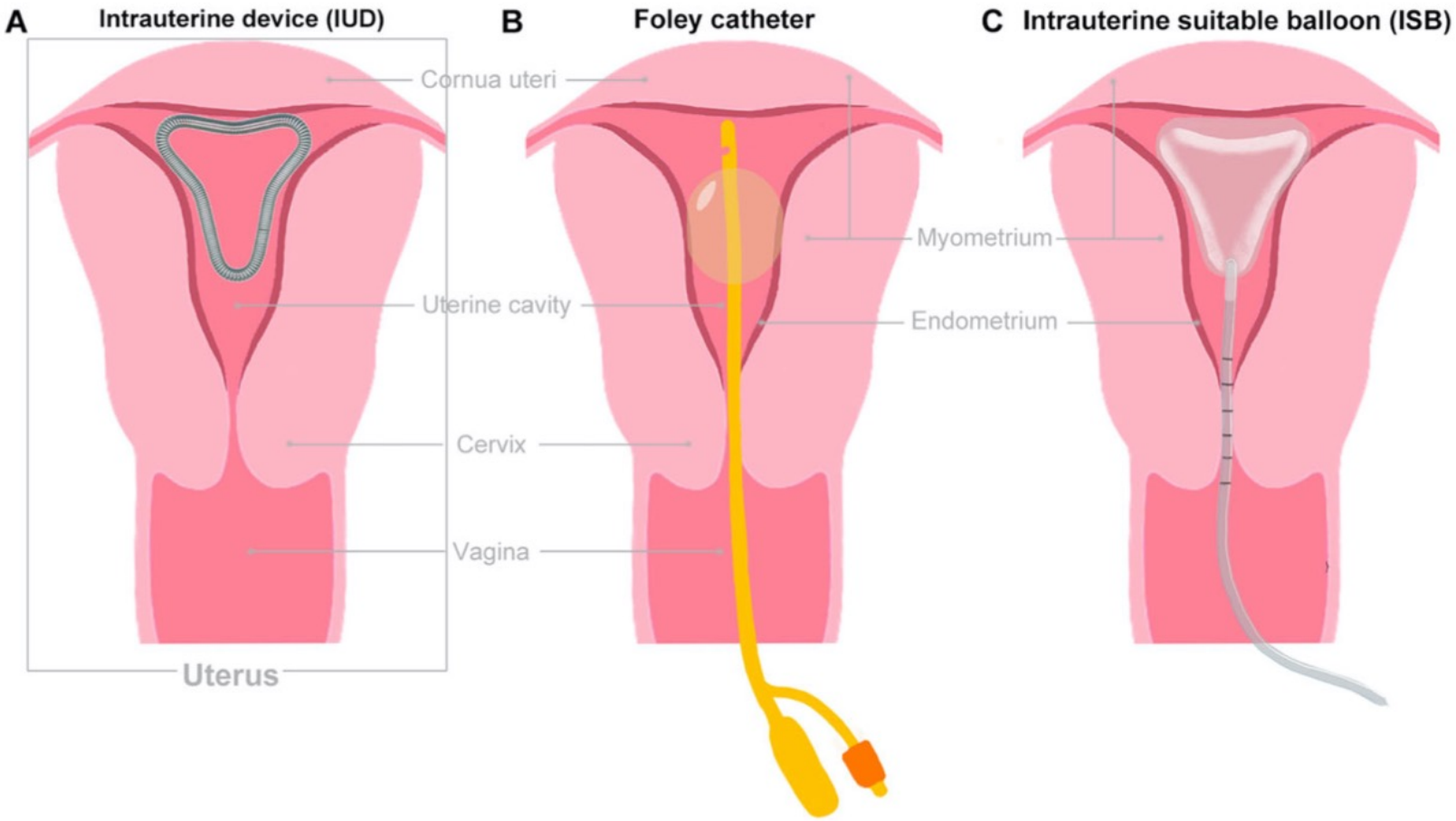


or subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds ratio M-H, fixed, 95% CI
Caspi 1	60	74	20	60	42.5%	8.57 [3.88, 18.92]
Orhue 2003	21	51	5	21	42.4%	2.24 [0.71, 7.06]
Yasmin 2007	3	20	1	3	15.0%	0.35 [0.02, 5.23]
Total (95% CI)		**145**		**84**	**100.0%**	**4.65 [2.48, 8.72]**
Total events	84		26			

Heterogeneity: $\chi^2 = 7.36$, df = 2 ($P = 0.03$); $I^2 = 73\%$

Test for overall effect: $Z = 4.79$ ($P < 0.00001$)




A
Intrauterine device (IUD)
Cornua uteri
Uterine cavity
Cervix
Vagina
Uterus
B
Foley catheter
Myometrium
Endometrium
C
Intrauterine suitable balloon (ISB)

Hormonal Support after Adhesiolysis in Women with Asherman's

A prospective, randomized, controlled trial comparing two doses of oestrogen therapy after hysteroscopic adhesiolysis to prevent intrauterine adhesion recurrence

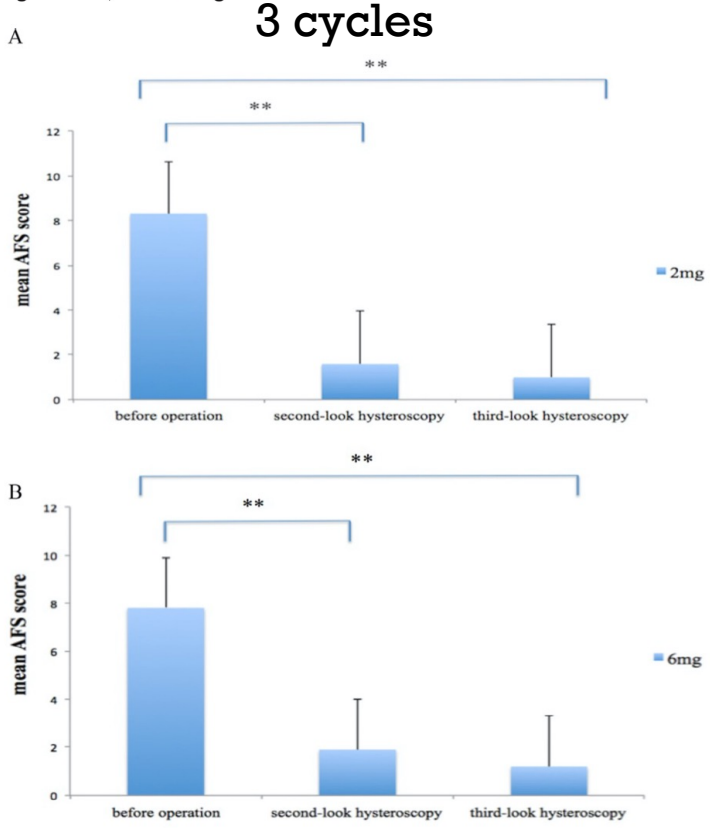
Jun Guo [a], TC Li [a,b], YuHuan Liu [a,], EnLan Xia [a], Yu Xiao [a], FengQiong Zhou [a], Xue Yang [a]*

Table 2 – A comparison of demographic and clinical details between subjects receiving 2 mg or 6 mg oestradiol after hysteroscopic adhesiolysis.

	2 mg oestradiol *n* = 59	6 mg oestradi *n* = 62
Age (years)[a]	31.9 ± 5.0	32.3 ± 4.1
BMI (kg/m^2)[a]	21.2 ± 2.2	21.0 ± 2.3
Parity[a]	0.2 ± 0.4	0.2 ± 0.4
Number of miscarriages[a]	2.3 ± 1.2	2.1 ± 1.2
Number of prior uterine curettage relating to pregnancy[b]		
None (%)	3 (5.1%)	7 (11.3)
One (%)	14 (23.7)	11 (17.7)
Two (%)	18 (30.5)	23 (37.1)
Three or more (%)	24 (40.6)	21 (33.9)
Menstrual pattern before operation[b]		
Amenorrhoea (%)	4 (6.8)	1 (1.6)
Scant spotting (%)	26 (44.1)	35 (56.5)
Light period (%)	26 (44.1)	25 (40.3)
Normal period (%)	3 (5.1)	1 (1.6)
AFS score[a]		
Before operation	8.3 ± 1.6	7.8 ± 1.8
At second-look	1.6 ± 1.4	1.9 ± 1.6
At third-look	1.0 ± 1.1	1.2 ± 1.4
Menstrual pattern at 3 month follow-up[b]		
Amenorrhoea (%)	0 (0%)	0 (0)
Scant spotting (%)	1 (1.7)	3 (4.8)
Light period (%)	31 (52.5)	25 (40.3)
Normal period (%)	27 (45.8)	34 (54.8)

AFS = American Fertility Society; BMI = body mass index.

3 cycles



Induction of endometrial growth

*Varying regimes

Dose?

Route?

Timing?

No superior effect of the high dosage was demonstrated

Intrauterine adhesion prevention after hysteroscopy: a systematic review and meta-analysis

Mae Wu Healy, DO; Brian Schexnayder, MD; Matthew T. Connell, DO; Nancy Terry; Alan H. DeCherney, MD; John M. Csokmay, MD; Belinda J. Yauger, MD; Micah J. Hill, DO

Summary of postoperative adhesion formation rates in control and treatment groups of the included studies

Study	Therapy type	Control, n, % adhesions		Treatment, n, % adhesions		*P* value
Acunzo et al, 2003[11]	Hyaluronic acid	41	31.7%	43	13.95%	< .05
Amer et al, 2010[29]	Intrauterine balloon vs plus fresh amnion graft vs plus dry amnion graft	15	14.0%	Fresh amnion, 15 dry amnion, 5	10.7% 13.3%	.27
Dabirashrafi et al, 1995[25]	Conjugated estrogen	23	0%	23	0%	NS
Fuchs et al, 2014[10]	Oxiplex/AP gel	26	14.0%	26	4%	.30
Guida et al, 2004[12]	Hyaluronic acid	69	26.15%	69	10.44%	< .05
De Iaco et al, 2003[24]	Hyaluronic acid	22	21.8%	18	17.8%	.78
Kim et al, 2012[30]	Carboxymethylcellulose hyaluronic acid gel	95	17.9%	92	9.1	.18
Pabuccu et al, 1997[16]	Intrauterine device	35	82.8%	36	8.3%	< .05
Roy et al, 2014[26]	Estradiol valerate	45	6.9%	45	0%	.24
Sardo et al, 2011[7]	Oxiplex/AP gel	55	22.0%	55	6%	< .05
Tonguc et al, 2010[27]	Estrogen therapy intrauterine device	25	5.3%	Estrogen, 16 IUD, 19 Estrogen plus IUD, 25	0% 10.5% 12%	.50
Vercellini et al, 1989[28]	Estrogen and intrauterine device	10	0%	10	0%	1.0

CONCLUSION: There was a lack of definitive evidence to conclude that any treatment is effective in preventing posthysteroscopy uterine adhesion formation. The available literature has significant heterogeneity and a high risk of bias, making any definitive conclusions difficult.

Semi solid barriers such as hyaluronic acid and autocross-linked hyaluronic acid gel reduce adhesion reformation

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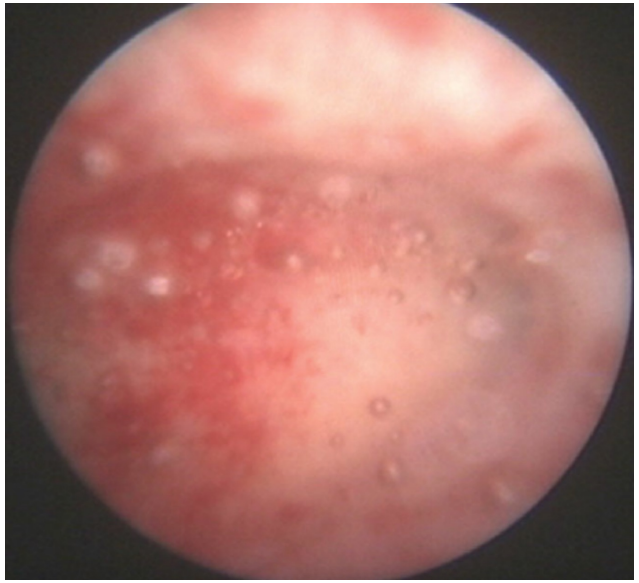

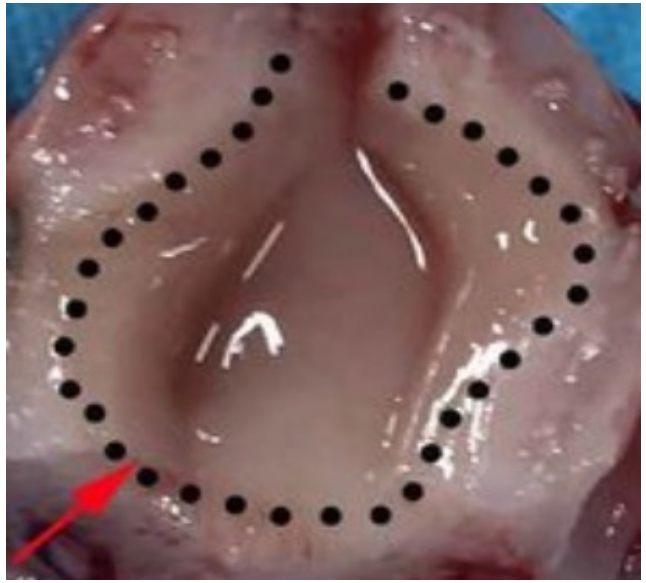

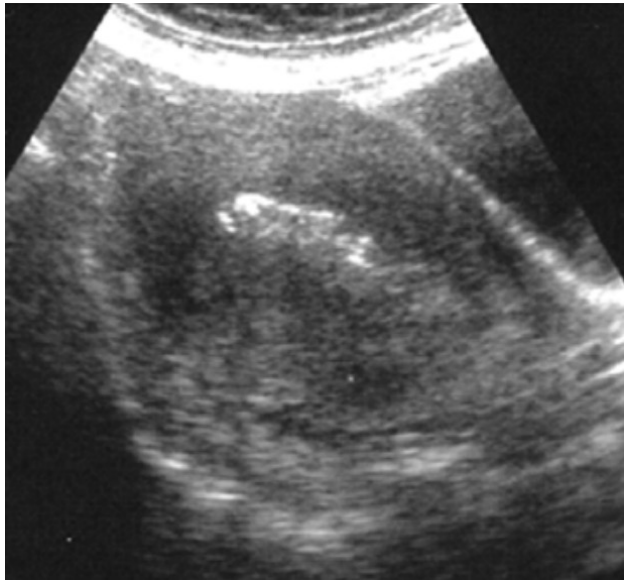

PRO: Alternative therapies should be considered for the treatment of Asherman syndrome

CON: Operative hysteroscopy should be repeated as many times as necessary for the treatment of Asherman syndrome

Should we consider alternative therapies to operative hysteroscopy for the treatment of Asherman syndrome?

PRO: Alternative therapies should be considered for the treatment of Asherman syndrome

Pro 1. Xavier Santamaria M.D., Ph.D.

CON: Operative hysteroscopy should be repeated as many times as necessary for the treatment of Asherman syndrome

Con 1. Keith Isaacson, M.D.

Pro 2. James H Liu, M.D.

During the menstrual cycle, the uterine endometrium has enormous regenerative capacity and over a 12 to 14-day follicular phase can regenerate up to a 10-14 mm endometrial thickness. AS results

Peter Movilla, M.D.

The term refractory AS loosely refers to a subset of patients that have persistent intrauterine adhesions despite repeat hysteroscopic procedures or persistent clinical symptomatology following treat-

Pro 3. Aghajanova Lusine, M.D., Ph.D.

Con 2. Hervé Fernandez, M.D.

Perrine Capmas, M.D.

There is no unanimous definiti of refractory AS but it exclu women with a normal cavity af a first operative surgery. The ma issue is recurrence of adhesio after the first procedure. If

Con 3. Jacques D M.D., Ph.D.

Since it was first desc Fritsch [83] in 1894 Asherman in 1950 [84] classification systems h proposed to characte

Refractory AS should consist in patients with **no clinical improvement** (infertility) after the diagnosis and complete treatment with the gold standard procedure (hysteroscopy)

*Bone marrow derived stem cell

*Amniotic membrane (Amniograft)

*PRP

TAKE TO WORK

- Recognize true AS
- Specialized centers/Surgical approach***
- More focus on prevention
- Secretorial Arrest/Spontaneus Endometrial reactivation after adhesiolysis*
- We need basic science to understand the local regulation of endometrium


EĞİTİM FAKÜLTESİ