

## Understanding Intrauterine Adhesions: Hysteroscopic Evaluation

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### Abstract

Intrauterine adhesion (IUA) or Asherman syndrome (AS) also known as uterine atresia, amenorrhea trumatica, endometrial sclerosis is a challenging topic in the field of gynaecology, especially in the field of infertility. It is debatable in many aspects with no clear consensus about classification, management. The causes can vary according to geographical conditions and country to country. This article reviews the epidemiology, pathologic features, classification and management and the problems in all aspects. There are various predisposing, risk factors which can cause intrauterine adhesions. IUA caused by trauma to the basal layer of the endometrium characterized by variable scarring inside the uterine cavity. Trauma can be iatrogenic, infectious origin leading to amenorrhea, hypo menorrhea, infertility and placental abnormalities in pregnancy. Hysteroscopy is the gold standard for both diagnosis and management. Hysteroscopy has revolutionized the scenario of IUA. It is also important to prevent the recurrence of IUA with best available barriers like, hyaluronic acid, platelet rich plasma (PRP), stem cell therapy. Successful treatment of infertility achieved by complete restoration of uterine cavity, prevention of IUA reformation and promotion of healing process. Early diagnosis and treatment plays important role in preservation of infertility.

**Keywords:** Intrauterine Adhesion, Hysteroscopy, Infertility

### Introduction

In 1894, Heinrich Fritsch described first case of intrauterine adhesions in a patient after postpartum curettage who presented with amenorrhoea. Subsequently, in 1948 and 1950, an Israeli scientist Joseph G. Asherman published two reports on the frequency and the aetiology of intrauterine adhesions.<sup>1</sup> He reported a case of severe intrauterine adhesions secondary to trauma to gravid uterus. He identified this pathology in 29 patients. These women presented with amenorrhea with stenosis of internal cervical ostium. Two years later, with the help of hystero-graphy he published another case series of intrauterine adhesions. In this series intrauterine adhesions were involving uterine cavity. The prevalence of Asherman syndrome varies from 1.55 to 20%.<sup>2</sup> It depends upon population, country due to different diagnostic criteria, the number of abortions in the populations, the infectious diseases in that region, choice of management, awareness of clinicians and patients. Intrauterine adhesions (IUAs) are bands of fibrous tissue as a result of trauma to the basal layer of endometrium following pregnancy related curettage such as incomplete abortion, postpartum hemorrhage, and elective abortion<sup>3</sup>. Hysterotomy, myomectomy, caesarean section, hysteroscopic procedures like resection of submucous leiomyomata or septae, mullerian duct malformation, insertion of intrauterine device and endometrial ablation are less common factors which will cause IUA formation. In a country like India, genital tuberculosis is a frequent

cause of intrauterine adhesion<sup>4</sup>. Puerperial sepsis is also common cause in some areas. It has serious clinical sequelae like infertility, recurrent pregnancy loss, menstrual abnormalities and pain. One should remember that, in the literature many cases reported that there were no symptoms even though patient was having IUA. Many times pregnancy after IUAs or after correction may be complicated by abortion, premature labor, placenta previa and placenta accreta. For initial diagnosis the less invasive Sonography, contrast sonohystero-graphy or hysterosalpingo-graphy can be done and very useful. The final diagnosis is based on hysteroscopy. Hysteroscopy is gold standard in the diagnosis and management of IUAs.

### Basic concept

The endometrium in the reproductive age female is an ever-changing structure with remarkable capacity to regenerate. It is divided into three layers-the stratum basalis, stratum spongiosum and stratum compactum. The stratum basalis is the deepest layer, changing little during menstrual cycle and left intact during menstruation but regenerate functional layer due to existence of endometrial stem cells. The endometrial stem cell niche<sup>5</sup> (the microenvironment where stem cell regulation occurs) seems to be located at the endothelium of the spiral arterioles in the basal layer, providing support to both the epithelial and stromal compartments.<sup>6,7,8</sup> This layer is important to the gynaecologist during any intrauterine procedure as well as any infection. As it has capacity of

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regeneration, it maintains the menstrual cycle and fertility. If it is completely destroyed, further endometrial regeneration will not occur. The second and third layers are collectively considered the stratum functionalis. These are the layers that respond to ovarian steroids and are shed at the time of menstruation. The severity of IUA depends upon the damage of these layers.

## Clinical Challenges

IUA is a silent enemy of reproductive women as well as treating gynaecologist. Challenges should cover identification of risk factors, primary prevention of adhesions, proper treatment and secondary prevention of adhesions after surgical treatment. It should also include anticipation of obstetric challenges.

## Risk factors, Epidemiology and what is happening exactly?

Miscarriage accounts for 15% of clinically recognized pregnancies. 5% of women will experience two or more miscarriages during their lifetime.<sup>9</sup> In the era of the medical method of termination like prostaglandins, many miscarriages are still being treated by dilatation and curettage (D&C). Apart from that use of sharp curettage or mechanical suction poses increased risk of IUA<sup>10</sup>. In blind D & C there are more chances of retained trophoblastic tissue and it is more common in cases of Mullerian duct defects such as didelphic uterus or septate uterus.<sup>11</sup> Congenital uterine abnormalities such as septate or bicornuate uterus predispose to adhesion formation (Hooker et al., 2013).<sup>12</sup> Recent studies by Yue Li et al., in 2017 showed that immunological factors are also involved in the etiopathogenesis of missed abortions and miscarriage of karyotypically normal embryos may be caused by abnormal inflammation at the feto-maternal interface.<sup>13</sup> Risk of developing IUA seems to be high in patients with residual trophoblastic tissue as residual tissue causes inflammation as well as stagnation of menstrual debris which provoke inflammation in the uterine cavity. Risk of IUA can be there with uterine compressive sutures for post-partum haemorrhage.<sup>13-1</sup>

Infections represent an important cause of IUA. In the country like India genital tuberculosis by Mycobacterium tuberculosis infection results in severe intrauterine adhesions and important cause of AS and poor prognosis after hysteroscopic surgery<sup>4</sup>. One case reported Schistosomiasis may also cause AS through granulomatous reaction<sup>12</sup>. A recent study concluded that 37.8% of patients affected by IUAs present findings of chronic endometritis (CE) and a higher recurrence of adhesion.<sup>14</sup> Some authors have reported AS with idiopathic origin<sup>15</sup>. So in IUA along with iatrogenic and infectious causes we should also consider anatomical, constitutional predisposition and idiopathic cause.

Inflammation seems to play a pivotal role in the pathogenesis of AS, causing damage to the endometrial niche and the release of factors into the intrauterine environment that stimulate the formation of fibrotic tissue and decrease vascularization following endometrial trauma (Sharma et

al., 2008).<sup>16,4</sup>

Xavi Santamaria et al proposed Hypothesis for development of AS: Infection (endometritis, genital tuberculosis or schistosomiasis) may cause defective endometrial healing as well as inflammation, while miscarriages and Mullerian duct defects, with or without iatrogenic factors such as curettages, may trigger an inflammatory response that can provoke an imbalance in endometrial tissue breakdown, affecting the ECM (extracellular matrix) regeneration and vascularisation and leading to defective endometrial healing and vascularisation<sup>12</sup>. In a study by Shilpa Bhandari et al 60 patients were diagnosed with intrauterine adhesions by hysteroscopy with or without concurrent laparoscopy. In their study regarding aetiology, tuberculosis was the main cause for AS.<sup>17</sup>

Regarding etiology, post-partum curettage has been regarded as the most common cause in previous studies,<sup>19,18</sup> however, in the one of the case series post-partum curettage was seen in only 3.3% of patients<sup>17</sup>. The possible reason for this discrepancy may be due to the fact that their patient profile belongs to the region with a high prevalence of tuberculosis. This finding is comparable to studies from Indian subcontinent wherein a history of tuberculosis was found in 67.8% of women with Asherman's syndrome.<sup>20</sup>

Uterine artery embolization in case of myoma may also cause adhesions in 10% of cases due to necrosis of myoma and healing of the myoma bed when it is expelled after treatment<sup>21</sup>. Literature also mentioned an atypical case of Asherman Syndrome (Fritsch Syndrome) due to prolonged retained fragment of Cu-T in myometrium.<sup>22</sup>

In India the incidence is increasing due to higher number of therapeutic & illegal abortions, higher incidence of genital TB & puerperial infection, lower awareness of this clinical condition.

## Classification

Many classification systems are described, with no universal acceptance of any one system and no validation of any of them. Hysteroscopy is the mainstay of both diagnosis and treatment, with medical treatments having no role in management.<sup>23</sup>

Since Asherman original description, there have been many attempts to find the most accurate classification for IUAs. Toeff and Ballas (1978) were the first authors who tried to classify AS on the basis of hysterosalpingographic findings.<sup>24</sup>

Type 1- Atresia of the internal ostium without concomitant corporal adhesion.

Type 2- Stenosis of internal ostium causing almost complete occlusion without concomitant corporal adhesion.

Type 3- Multiple small adhesions in the internal ostium isthmic region.

Type 4- Supra isthmic diaphragm causing complete separation of the main cavity from its lower segment.

Type 5- Atresia of the internal ostium with concomitant corporeal adhesions.

In the same year March et al<sup>25</sup> classified adhesions as minimal, moderate, or severe based on hysteroscopic assessment of the degree of uterine cavity involvement.

This classification is still used for its simplicity although it is considered insufficiently prognostic

Mild- Filmly adhesion occupying less than one-quarter of uterine cavity. Ostial areas and upper fundus minimally involved or clear.

Moderate- One-fourth or three-fourth of cavity involved. Ostial areas and upper fundus partially involved. No agglutination of uterine walls.

Severe- More than three fourth of cavity is involved. Occlusion of both ostial area and upper fundus. Agglutination of uterine walls.

Hamou et al<sup>26</sup> –Adhesions classified as isthmic, marginal, central, or severe according to hysteroscopic assessment.

Valle and Sciarra<sup>27</sup> used a classification based on uterine involvement observed in HSG, the extension and the type of adhesions seen on hysteroscopy and are described as follows:

- Mild: Fine adhesions, composed of basal endometrium
- Moderate: Fibromuscular, dense and endometrium covered adhesions that bleed when ruptured
- Severe: Composed of fibrous tissue, adhesions do not bleed when sectioned.

Wamsteker- The European Society of Hysteroscopy (ESH)<sup>28</sup> proposed a classification of IUA as grade one to four with several subtypes based on HSG and hysteroscopy findings with clinical symptoms while the American Society for Reproductive Medicine (ASRM)<sup>29</sup> also considered the menstrual pattern based on extent of endometrial cavity obliteration, appearance of adhesions and patient menstrual pattern.

## Evaluation

There are various modalities to evaluate the IUA. IUA can be visualized by hysterosalpingography (HSG), ultrasonography including contrast sonohysterography (SHG), 3D ultrasonography, hysteroscopy and magnetic resonance imaging (MRI).

Transvaginal 2D ultrasonography is the first-line diagnostic tool for the assessment of uterine and endometrial morphology. It assesses endometrial thickness, disruptions to the endometrial–myometrial junction. We can appreciate typical irregular endometrial line or at places it is absent. Sometimes hyperechogenic bridges can be seen. The typical ultrasound finding is the presence of hypoechoic areas with interruptions of the endometrial layer (skip lesions representing entrapped menstrual blood or secretions from preserved functioning endometrium).<sup>32</sup> Adhesions on ultrasound are seen as bands of myometrial tissue traversing the endometrial cavity and adjoining the opposing uterine walls. The bands may vary in thickness, but their echogenicity is usually the same as that of the adjacent myometrium<sup>33</sup>. It has been observed, in a study of 16 women with AS and 50 controls that, transvaginal ultrasonography in women with AS showed substantially thinner endometrium compared to normal menstruating women<sup>34</sup>. In cases of severe IUAs, the uterine cavity may appear irregular with a loss of endometrial echo.<sup>35</sup>

HSG can be used for diagnosis of AS. Advantage of HSG is that it will give graphical picture of uterine cavity as well as

### The American Fertility Society Classification for IUA-1988

Extent of cavity involved	<1/3 1	1/3-2/3 2	>2/3 4
Type of Adhesions	Filmy 1	Filmy & Dense 2	Dense 4
Type of Adhesions	Normal 0	Hypomenorrhoea 2	Amenorrhoea 4

Accordingly to score Mild(1-4), Moderate(5-8), Severe(9-12) [Fertil Steril 1988;49;944-55]

The Donnez and Nisolle<sup>30</sup> classified in six grades and consider the location to be one of the most important factors in determining the pregnancy rate after surgery. It includes:

- Grade I: Central; fine (IA) or fibrous or fibromuscular (IB) adhesions
- Grade II: Marginal adhesions; compact pillars (IIA) or obliterating one of the ostia (IIB)
- Grade III: Absence of cavity on HSG; occlusion only of the internal orifice (IIIA, pseudo-Asherman's) or complete synechia of uterine walls (IIIB, true Asherman's)

Nasr et al<sup>31</sup> suggested a complex system creating a prognostic score by incorporating menstrual and obstetric history with IUA findings at hysteroscopic assessment with HSG.

fallopian tube. Positive predictive value of HSG was only about 50% and false positive rate as high as 74%.<sup>36</sup> Using hysteroscopy as the reference standard for the diagnosis of IUAs, HSG had a sensitivity of 75–81%, specificity of 80% and positive predictive value of 50%.<sup>37,38</sup> The high rate of false-positive diagnoses, coupled with radiation exposure and invasiveness, are the main disadvantages of HSG. But considering cornual and fimbrial block, tubes showing dilatation, sacculations or multiple constrictions along the length with agglutinated fimbria, HSG is very helpful to diagnose it. These can be a sign of tuberculosis which is common in developing countries.

3D-TVUS provides useful information on the location and extent of the IUAs. It gives fair idea about the areas of functional endometrium. So it helps in managing the complex intrauterine adhesiolysis, so decreasing

complications, improving surgical outcomes and improving potential future fertility. Preoperative 3D-TVUS plays an important role in intra-operative judgment during hysteroscopic adhesiolysis.<sup>39</sup>

Magnetic resonance imaging has been used to investigate IUAs, especially when cervical obstruction is suspected, but experience with this technique is limited<sup>40,32</sup>. Uterine synechiae can be visualized as thick or thin bands of soft tissue (signal intensity similar to myometrium on T1W and T2W imaging) that stretch from one wall to another.<sup>41</sup>

## Preoperative preparations

Misopristol has been considered as a simple and effective method for cervical priming prior to hysteroscopy in IUA with dose 200 or 400 µg vaginally prior to operative hysteroscopy. Twenty-five randomized controlled trials involving 2,203 females were systematically analyzed<sup>42</sup>. As compared to placebo or no medication the use of misopristol prior to hysteroscopy led to significant relief in cervical dilatation, fewer hysteroscopy complications with mild and insignificant side effects.

## Treatment-

IUAs are commonly treated with hysteroscopic resection followed by mechanical or hormonal treatments. Clinical challenges include primary prevention of adhesions, surgical removal, and prevention of recurrent disease. So the complete management can be divided into four main categories.

1. Surgical treatment- By hysteroscopy
2. Preventing recurrence of adhesions
3. Restoring normal endometrium
4. Second look Hysteroscopy-Postoperative assessment

## Surgical treatment

It is always by hysteroscopy. Hysteroscopy is a wonderful technology giving clear access to diagnose the synechiae, to judge the extent of it, confirming location as well as type of adhesions (soft, muscular, fibrous). And in the same sitting treatment can be done. But we have to follow the principles to achieve the goals.

1. Restoration of the triangular cavity,
2. Visualization & confirmation of permeability of the ostiums
3. Avoid destruction to normal endometrium
4. Minimal manipulation
5. Avoid Perforation.

Importance to be stressed on proper indication and careful performance of intrauterine surgical procedures.<sup>43</sup> Primary prevention as well as timely diagnosis and treatment seems to be crucial in the management of this pathology.

To start with it is necessary to analyze the causative factors of Asherman's syndrome, history of curettage (post-partum or for miscarriage) and any uterine surgery to be noted. Consider history of genital or extra genital

tuberculosis diagnosed by acid fast bacilli (AFB) culture and/or histopathology especially in India. Difficulties can be encountered since beginning i.e. from the entry of hysteroscope through the external orifice till the negotiation through cervical canal, internal os to the uterine cavity. We can negotiate through the external cervical orifice with the help of 2.9mm hysteroscope and semirigid 5 Fr. scissors and forceps. The revolution in hysteroscopic instruments, optics and technology in last few years made hysteroscopy as the first choice.<sup>44,45</sup> Filmy adhesions alone can be divided by using the tip of the hysteroscope without any energy source or scissors.<sup>45</sup> Sometimes even with distension and pressure, but with patience, the filmy adhesions can be released. Thus, in favourable cases the restoration of cavity can be obtained through "no touch" hysteroscopy in out-patient setting without general anaesthesia.<sup>45</sup> According to many experts, the removal of the adhesions should start from the lower part of the uterus and progress toward the upper part.<sup>46,32</sup> Routinely the division of adhesions begins in the central and moves laterally and toward the fundus. So the central and filmy adhesions should be separated initially in order to allow adequate distension of the uterine cavity. Dense and lateral adhesions should be treated at the end, bearing in mind the greater risk of uterine perforation and bleeding<sup>47</sup>. An effective way to recognize the margins of the original uterine cavity is to detect the myometrial vasculature by using the lowest intrauterine pressure and distension that allows visualization.<sup>49,50,51</sup>

A wide range of mechanical or electric equipment has been used for hysteroscopic adhesiolysis. Different hysteroscopic instruments are used like, 16-gauge, 80-mm Touhy needle (Portex Ltd., Hythe Kent, England) introduced alongside a 5-mm hysteroscope under fluoroscopic guidance<sup>52</sup>, biopsy forceps, sharp or blunt scissors<sup>53,54</sup> and division of strings with energy like monopolar diathermia<sup>55</sup>, bipolar diathermia<sup>56,49</sup> or laser<sup>57</sup>. Nowadays we are commonly using 2.9mm office hysteroscopes with 5 Fr.scissors and forceps. (Fig.1 to 6) Use of mechanical instruments like cold-knife is supposed to prevent thermal damage of the residual endometrium and reduce the rate of perforation during the procedure. Though the use of powered instruments (electric surgery or laser) has also proven efficient for hysteroscopic adhesiolysis,<sup>58,59,60,61</sup> the use of electric surgery is associated with potential damage to the residual endometrium.<sup>62,63</sup>

High frequency electrical surgical instruments ( such as monopolar or bipolar electrocautery electrodes, resectoscopic electrocautery needles or loops) should be avoided for adhesiolysis in Asherman patients, in order to prevent deep local damage to the endometrium, though these methods for adhesive band vaporization have also been described. Bipolar surgery appears to be better than monopolar as tissue effect is more focal and the electrolyte containing distension media is safer concerning to fluid overload. So even monopolar surgery has provided results as satisfactory as bipolar one, the latter is more preferred.<sup>64</sup> If thermal energy is used, the minimum amount of energy must be applied to minimize endometrial damage.<sup>65,66</sup> A pilot study suggested the use of mini-resectoscope for hysteroscopic adhesiolysis is associated with reduced operative morbidity. Use of the mini-resectoscope is an effective and safe alternative to the conventional system.<sup>68</sup>

The treatment with laser vaporization using an Nd-YAG (neodymium-doped yttrium aluminium garnet) and KTP (potassium-titanyl-phosphate) laser has also been applied in the treatment of AS.<sup>62,67</sup> But considering costs and increased uterine damages, it does not offer significant advantages over other electric equipment. Therefore its use in hysteroscopic adhesions has been increasingly abandoned<sup>63</sup>.

The treatment of the severe and dense adhesion is the real challenge as in these cases; the cavity may be completely

occluded or too narrow to allow the insertion of hysteroscopic sheath inside the cervix. Moreover, multiple procedures may be required because of post-surgical recurrence of the adhesions.<sup>40,69,70</sup> Routinely mechanical methods are used widely. Mc Comb and Wagner in 1997 treated six cases with severe IUA under laparoscopic control: their technique was based on separation of uterine wall into two hemicavities by inserting a 13 French Pratt cervical dilator. Subsequently, the residual fibrotic “septum” was cut up to the fundus with hysteroscopic scissors.<sup>71</sup> “Myometrial scoring”<sup>72</sup>, an innovative technique, consists cutting six to eight incisions from the fundus of the uterus to the isthmus using a knife electrode with the aim of enlarging the uterine cavity and potentially uncovering functional endometrium. A transcervical resectoscopy after the dilatation of cervix with laminaria tent was also suggested in the treatment of severe AS.<sup>73</sup>

In patients with suspected tuberculosis, one has to be very careful in adhesiolysis. Jai Bhagwan Sharma et al demonstrated the association between genital endometrial tuberculosis and Asherman’s syndrome. In a study of 28 women diagnosed as genital tuberculosis by endometrial biopsy, they did hysteroscopy. And they found, there were

various grades of adhesions in all women, with grade I in 17.8%, grade II in 28.5%, grade III in 28.5% and grade IV in 17.5% women. Only four women (14.3%) had open ostia, while others had bilateral (28.5%) or unilateral (21.3%) blocked ostia or inability to see ostia (28.5%).<sup>4</sup>

In 70% infertile patients with GTB, cavity is normal with bilateral open ostia and normal looking endometrium. Classical hysteroscopic findings of endometrial TB is a rough dirty looking bizarre pale endometrium (Fig 13) with gland openings not seen and with overlying whitish deposits.<sup>74</sup> After adhesiolysis many times cavity appears shrunken. (Fig 14). Sometimes there can be total corporal synechiae due to tuberculosis which carries a very poor prognosis.<sup>75</sup> Adhesion dissection can be technically difficult and must be performed with care in order to not create new scars and further exacerbate the condition. In more severe cases, adjunctive measures such as laparoscopy are used in conjunction with hysteroscopy as a protective measure against uterine perforation. Microscissors are used to dissect as well as to judge and dilate to proceed forward smoothly. There are chances of uterine perforation following hysteroscopic lysis of synechiae due to tuberculosis.<sup>76</sup>

**Fig 1: Circular Fibrosis at Internal Ostium**



**Fig 2: Central adhesions just above internal os**



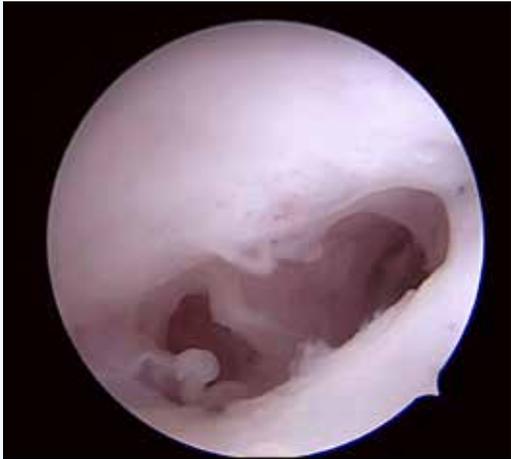
**Fig 3: Judging with scissors**



**Fig 4: Central Thick adhesions in the cavity**



**Fig 5: After cutting the band**  
(note the whitish endometrium)



**Fig 6: Cavity after complete adhesiolysis**



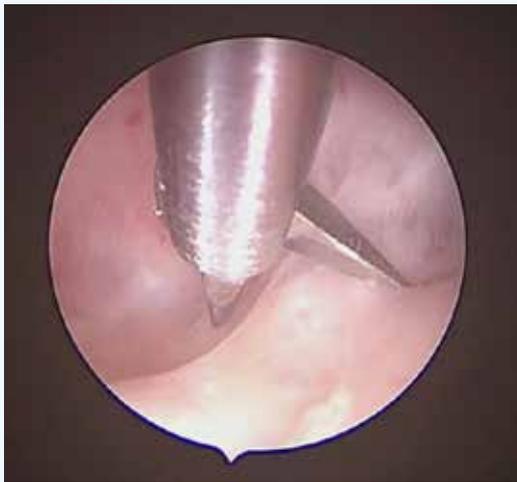
**Fig 7: Second look after 3 months-same patient**  
( Note pink colour of the endometrium)



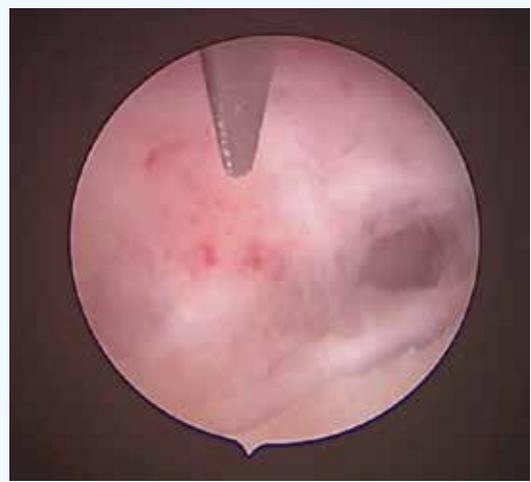
**Fig 8: Second look- left lateral wall adhesions**



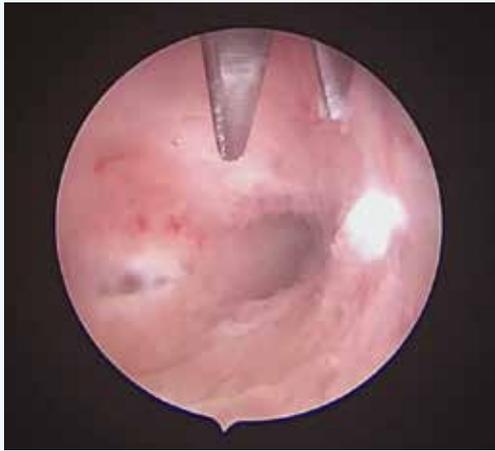
**Fig 9: Adhesiolysis with 5 French scissors**



**Fig 10: Releasing left lateral wall adhesions**



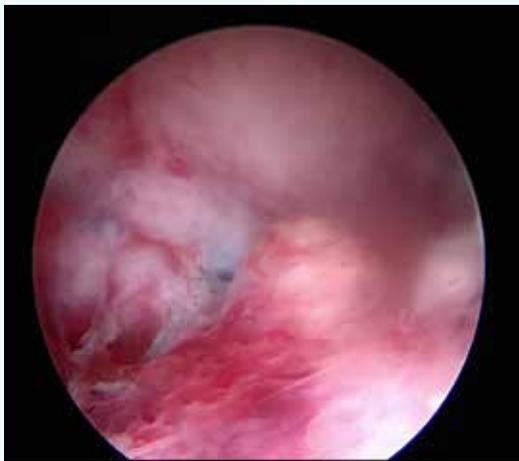
**Fig 11: Synechiae at fundus and left lat wall released**



**Fig 12: left ostium adter adhesiolysis**



**Fig 13: Rough dirty Bizzare endometrium with whitish deposit**



**Fig 14: view of uterine cavity from intorifice -Shrunken small cavity**



## Preventing recurrence of adhesions- Secondary Prevention

Any intrauterine surgery including adhesiolysis for IUA needs very careful approach to avoid reappearance of adhesions. Hysteroscopic adhesiolysis is necessary for restoring menstrual function and fertility.<sup>77</sup> Apart from that future obstetric complications can be minimized with proper precautions. Since surgical wounds are prone to re-adhesion, the postoperative recurrence rate is as high as 3.1–62.5%.<sup>77,78</sup> Especially in case of tuberculosis the chances are high hampering reproductive potential.<sup>79,80</sup> The mechanisms by which the endometrium is repaired, are not entirely understood. The duration of endometrial healing also depends upon the pathology. A recent prospective study stated that the time needed for the endometrium to heal completely ranges from 1-3 months.<sup>81</sup> Five RCTs are currently evaluating outcomes for secondary prevention strategies like an IUD, amnion graft, or stent, typically comprising an intrauterine catheter with an inflatable balloon tip, the use of gels such as hyaluronic acid and polyethylene oxide-sodium carboxymethylcellulose.

### A-Intrauterine Device-

It was one of the first described method in literature<sup>82</sup> it has been widely recommended in many studies. But few studies and AAGL practice report stated that there was no reported difference in rate of postoperative de novo adhesion formation assessed hysteroscopically, and there were no differences in pregnancy outcomes.<sup>83</sup> Adding on, the uses of IUD with different shapes were also described as a possible treatment option. However, copper-containing uterine-shape and T-shape IUD can induce inflammation and are thus not recommended because of their insufficient surface area.<sup>84,85,86</sup>

### B-Foley's Catheter-

It is also one of the first described in the literature. Eight observational studies report it as an alternative for this purpose. A pilot study done by Sahana Gupta et al shows no intrauterine adhesions with use of Foley's catheter balloon (FB) for prevention of intrauterine adhesions following breach of uterine cavity in complex myoma surgery.<sup>87</sup> At the time of follow-up hysteroscopy 6 months after the myomectomy, they found no intrauterine adhesions in 16 consecutive women treated with balloon, compared to 3 out of 10 (30 %) historical controls where the balloon was not used.

But a definite defect is noted in the FB. The shape of the balloon does not match that of the uterine cavity, and hence it cannot isolate the two sides of the uterine cavity and uterine horn accurately. The local pressure might affect the blood supply of the endometrium.<sup>88</sup>

Recently Christine Shan et al used Malecot catheter to prevent IUA. They found it is an inexpensive, easy-to-operate, and effective physical barrier method for preventing IUA in infertile patients undergoing hysteroscopic myomectomy with high live birth rate and no obvious visible post-operative adhesions.<sup>89,90</sup>

The intrauterine suitable balloon (ISB) is better than the Foley balloon (FB) in preventing the adhesion reformation and reducing the AFS (American Fertility Society) score after hysteroscopic adhesiolysis in severe IUAs. Also, it can effectively prevent the adhesion reformation in severe IUAs with a similar effect on moderate IUAs.<sup>91</sup>

#### **C-Intrauterine Balloon Stent-**

March et al described intrauterine stent as a mechanical method to prevent adhesions recurrence. The author reported among 1240 patients treated using intrauterine stent, pregnancy rate of 61.6% and spontaneous miscarriage rate of 15.6%.<sup>92</sup> Ru Zhu and Hua et al designed an intrauterine balloon stent and compared with foley's balloon.<sup>93</sup> The device can effectively isolate the two sides of the uterine cavity and bilateral uterine horn, and it also consists of a drainage channel and an injection channel. The channels can sufficiently drain the exudate from the uterine cavity and inject the antiadhesion drugs into the uterus or promote the growth of the endometrium. Recently Huan Huang et al designed a novel intrauterine stent for prevention of intrauterine adhesions.<sup>94</sup> In this design, the uterine stent fits into the normal shape of the uterine cavity and keeps the normal uterine cavity shape after surgery. Another RCT by X shi et al has demonstrated that following hysteroscopic adhesiolysis, the use of intermittent dilatation balloon therapy can significantly reduce adhesion reformation rates, while improving menstruation flow.<sup>95</sup> Cook Medical (Cook Medical Inc., Bloomington, USA) introduced an intrauterine balloon, specially designed in a triangular-shaped form to simulate the uterine cavity. Most studies recommend that this balloon to be kept in the uterine cavity not more than a week due to risk of infection.<sup>96</sup> In a comparative study Lin et al found that the insertion of an intrauterine balloon or intrauterine device is more effective than the use of hyaluronic acid gel in the prevention of intra-uterine adhesion reformation.<sup>97</sup> But in 2015 Lin et al stated that the heart-shaped intrauterine balloon and IUD are of similar efficacy in the prevention of adhesion reformation after hysteroscopic adhesiolysis for Asherman syndrome.<sup>98</sup>

#### **D-Word's Catheter-**

The Word catheter is a 5.5cm length, 3ml balloon catheter of silicone with 15 French canal manufactured by Cook medical Inc. Bloomington USA. Jaimi Ferro et al proposed the usages of this catheter.<sup>96</sup> It acts as a foreign body preventing uterine walls to collapse as well as creates re-epithelization in the uterine cavity. It is placed in the uterine cavity with distal end slightly outside the cervical

canal or at its border and inflated with 3-4ml of saline. The catheter can remain in position for at least 21 days and for up to two menstrual cycles. So the endometrium heals properly preventing the adhesions. There is no discomfort to the patient due to short tubing and the risk of ascending infection is less.

#### **E-Anti-adhesion Barrier Gels-**

Hyaluronic acid is one of the most widespread components in human tissue and it is involved in many biological functions such as mechanical support, cell migration and proliferation. It is a water soluble polysaccharide with known viscoelastic properties and works as a mechanical barrier between the uterine walls and prevents the development of adhesions. Autocross-linked hyaluronic acid (Hyalobarrier©) is a new anti-adhesion barrier capable of preventing adhesion formation after gynaecological surgery (Fidia Advanced Biopolymers SRL, Padova, Italy).<sup>96,99,100</sup> Barriers methods are the most widely used and, among these, gel barriers have been proven to have a significant clinical effect on IUA prevention, because of higher adhesiveness and prolonged residence time on the injured surface (Level of evidence: 1b).<sup>101</sup>

Another modified hyaluronic acid (sodium hyaluronate) and carboxymethylcellulose (Septrafilm©) (Genzyme Corporation, Cambridge, MA, USA). In a randomized controlled blind study involving 150 patients who underwent surgical evacuation or curettage after missed or incomplete abortion, the rate of IUA in the treated group was low compared with the control group.<sup>102</sup> In a prospective randomized trial including 187 cases alginate carboxymethylcellulose hyaluronic acid was used and it was more effective than carboxymethylcellulose hyaluronic acid.<sup>103</sup>

Bosteels J et al<sup>101,105</sup> conducted 11 randomised studies on use of an inserted device versus no treatment in 2015 and 16 RCTs in 2017 comparing a device versus no treatment. They concluded that, the effectiveness of anti-adhesion treatment for improving key reproductive outcomes or for decreasing IUAs following operative hysteroscopy in subfertile women remain uncertain. Another innovative study by Gretchen Garbe Collins et al suggested that amnion graft may provide an alternative treatment option for patients with Asherman syndrome who desire future menses and pregnancy.<sup>104</sup>

## **Restoring the Normal Endometrium**

#### **A- Hormonal Treatment-**

One of the most common therapies recommended is hormonal treatment. But there is no consensus about its usage as a sole treatment or in combination with other modalities; pre or post-operatively; combination of estradiol with progesterone and the duration of therapy.<sup>106</sup> Yuqing Chen et al in their findings also revealed that, after TCRE and artificial menstrual cycle therapy for 3 months, the VEGF (vascular endothelial growth factor) expression and MVD(micro vessel density) increased significantly when compared with the IUA patients before therapy and the controls. These findings indicate that estrogen may promote

the angiogenesis in the endometrium, which is helpful for the endometrial repair.<sup>107</sup> Most of the studies recommended estrogen and progesterone after hysteroscopic adhesiolysis.<sup>108</sup> Jolinda Johary et al reviewed and twenty-six studies were identified that reported use of hormone therapy as ancillary treatment after adhesiolysis. There was a wide range of reported menstrual and fertility outcomes. At present, hormone therapy, in particular estrogen therapy, is beneficial in patients with IUA, regardless of stage of adhesions.<sup>109</sup>

#### **B-Platelet-rich plasma (PRP)**

PRP is the plasma fraction of autologous blood with platelet numbers that are enhanced four- to six-fold compared with that of whole blood. Intrauterine infusion of PRP tried in many study trials. Jintao peg et al evaluated efficacy of an intrauterine infusion of platelet-rich plasma (PRP) in patients with intrauterine adhesions (IUAs).<sup>110</sup> The mixture of PRP and PRP activator (with a ratio of 1:1) would be infused into the uterine cavity with a catheter for intrauterine insemination. There were no significant differences between the intrauterine infusion of PRP and the intrauterine balloon. However more RCT are needed. Meenu Agarwal et al<sup>111</sup> tried the injection of platelet-rich plasma (PRP) guided by hysteroscopy into the endomyometrial junction on 32 patients of thin endometrium. They found it improves endometrial thickness and vascularity. After PRP instillation, the endometrium was 7 mm or thicker in 24 of 32 patients, and all 24 patients underwent frozen embryo transfer. Moreover, 12 of 24 patients who underwent embryo transfer conceived, whereas 10 had a clinical pregnancy with visualization of cardiac activity at 6 weeks and two had a biochemical pregnancy.

#### **C- Stem Cells Therapy-**

Autologous stem cell implantation is an innovative therapy for endometrial regeneration in patients with AS. Endometrial regeneration from the basal layer, postulated to have stem cells or progenitor cells, contributes to the replacement of the functional layer.<sup>112</sup> There is ample evidence that adult stem cell populations exist in human endometrium, and hence it might be possible to activate endogenous endometrial stem/progenitor cells in cases of atrophic or thin endometrium or to transplant bone marrow (BM) derived stem cells in the uterine cavity for endometrial regeneration in AS or severe cases of IUAs.<sup>113</sup> In a study by Neetu Singh et al<sup>112</sup> total of six women were included in the study and all of them had secondary amenorrhea with primary infertility. All of them had undergone hysteroscopic adhesiolysis (2-3 times) and received oral estrogens (2-3 cycles) in the past, but had failed to respond. Five out of six patients resumed menstruation after 3 months. The maximum ET achieved by any patient was 6.7 mm. Majority of the patients had a past history of treated genital tuberculosis ( $n = 5$ ) and only one had a history of D and C. Santamaria X et al published a prospective study in 16 women and found improvement after two months with autologous cell therapy with CD 133+. Improvements were seen in endometrial thickness, increased mature vessel density and menses. This study also some promising

pregnancy rates.<sup>114</sup>

## **Second look Hysteroscopy- Postoperative assessment-**

In the management of intrauterine adhesions, it is very important to analyze the prevalence of IUA in women undergoing intrauterine surgeries for intrauterine synechiae, polyp, submucous myoma. So evaluation of uterine cavity to diagnose and treat post-surgical adhesions with second look hysteroscopy is an essential part. Lauren Sebbag et al<sup>115</sup> observed that IUA occurred most commonly after hysteroscopic lysis of adhesion (26.9%) and myomectomy (20.5%), polypectomy (10.9%). They found that in 55.2% of cases, IUA could be treated by second-look hysteroscopy. If initial stage of AS is more severe, then it is more difficult for the endometrial cavity to recover. So it is imperative to detect and treat adherence recurrence promptly to improve patient's reproductive potential.<sup>116</sup> In our case studies in last two years, six cases were with severe IUA (AFS score severe) presented with secondary amenorrhoea. Three of them had tuberculosis. We have achieved regular menstrual cycles in all cases and pregnancy in one case. One patient of 25 years was having amenorrhoea for three years after D & C for missed abortion. She had good improvement in endometrium from white to pink. (See Fig 7-12)

Post-adhesiolysis-. A significant improvement in the endometrial thickness was observed on day 2 ( $p < 0.0001$ ) and day 21 ( $p < 0.0001$ ) 3 months post-adhesiolysis. The spiral artery RI was statistically significant ( $p < 0.04$ ) on day 2 pre-adhesiolysis compared to post-adhesiolysis.<sup>80</sup>

Reproductive outcome following hysteroscopic adhesiolysis by K K Roy et al reported that in the majority (64%) of patients, the possible cause of Asherman's syndrome was previous curettage on gravid uterus. The overall conception rate was 40.4% after hysteroscopic adhesiolysis.<sup>117</sup>

Outcome of hysteroscopic adhesiolysis in women who had Asherman's syndrome after uterine artery embolization (UAE) was worse than women who had Asherman's syndrome caused by surgical trauma.<sup>21</sup> Reproductive outcome in patients with tuberculosis is always guarded because by the time its diagnosis is done, major destruction already occurred.

#### **AAGL Guidelines for primary prevention of intrauterine adhesions<sup>83</sup>**

1. The risk for de novo adhesions during hysteroscopic surgery is impacted by the type of procedure performed with those confined to the endometrium (polypectomy) having the lowest risk and those entering the myometrium or involving opposing surfaces a higher risk. Level B
2. The method of pathology removal may impact the risk of de novo adhesions. The risk appears to be greater when electrosurgery is used in the non-gravid uterus and for blind versus vision-guided removal in the gravid uterus. Level C
3. The application of an adhesion barrier following surgery that may lead to endometrial damage significantly reduces the development of IUAs in the short term, although limited fertility data are available following this intervention. Level

A

## Post-Adhesiolysis Obstetric problems-

In dealing with patients of IUA, the clinician has to be alert when patient conceives after adhesiolysis. There was increased incidence (43.8%) of cesarean section. Four (12.5%) patients had postpartum hemorrhage for adherent placenta.<sup>2</sup> There was no conception in patients who needed repeat adhesiolysis.<sup>2</sup> Placenta accreta: adherent placenta due to Asherman syndrome.<sup>118</sup> It is important to be aware of the risk of a placenta accreta if the patient is having previous history of Asherman syndrome and uterine scarring. And antenatal diagnosis is necessary so that counselling and mode of delivery can be planned. In the study of Limei Chen et al 7.9% had postpartum hemorrhage, including 4.3% due to adherent placenta and 2.1% due to placenta accreta.<sup>119</sup>

## Conclusion

As such, medical awareness seems to be important in minimizing the risk of IUA. Medical method for termination of pregnancy should be followed. The leading cause for Asherman's is D and C done for abortion or RPOC.<sup>120</sup> If at all D & C is needed then sharp curettage to be avoided. Hysteroscopy is the most accurate method for diagnosis of IUAs and should be the investigation of choice when available. In developing countries like India Genital tuberculosis is an important cause of Asherman's syndrome causing significant pelvic morbidity due to uterine adhesions and infertility. Primary prevention is very important and the operating surgeon should always consider the risk of adhesions according to type of endometrial pathology, avoidance of electrosurgery. To reduce the recurrence of adhesions after adhesiolysis, secondary prevention is necessary. According to availability clinician has to select judiciously. Stem cell treatment may ultimately provide an effective adjuvant approach. Follow up assessment is required after two to three months. If the woman conceives after AS treatment, there should be vigilant surveillance and early diagnosis for placental abnormalities to avoid obstetric complications.

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## References

1. Asherman JG. Amenorrhoea traumatica (atretica). *J Obstet Gynaecol Br Emp*. 1948; 55 (1): 23– 30. [PubMed] [Google Scholar]
2. *Journal of Minimally Invasive Gynecology*, Volume 17, Issue 5, September–October 2010, Pages 555-569; Review Article, Review of Intrauterine Adhesions Panel Rebecca Deans MBBS,

3. MRANZCOG Jason AbbottB MED (Hons), MR-COG, FRANZCOG, PhD  
Prevalence of uterine synechia after abortion evacuation curettage; October 2007, *Sao Paulo Medical Journal* 125(5):261-4; Source-PubMed; Adriana Salzani, Daniela Yela, José Roberto, Erbolato Gabiatti, Ilza Monteiro
4. *Arch Gynecol Obste*. . 2008 Jan;277(1):37-41. doi: 10.1007/s00404-007-0419-0. Epub 2007 Jul 25. Genital tuberculosis: an important cause of Asherman's syndrome in India. Jai Bhagwan Sharma 1, Kallol K Roy, M Pushparaj, Nupur Gupta, Sunesh Kumar Jain, Neena Malhotra, Suneeta Mittal
5. Schofield; The relationship between the spleen colony-forming cell and the haemopoietic stem cell *Blood Cells* 1978;4:7-25 Google Scholar, PubMed
6. Co-expression of two perivascular cell markers isolates mesenchymal stem like cells from human endometrium, *Hum Reprod* 2007;22:2903-2911 Google Scholar Crossref PubMed Schwab KE Gargett CE
7. Endometrial stem/progenitor cells: the first 10 years; Caroline E. Gargett, Kjjiana E.Schwab, James A. Deane: *Human Reproduction Update*, Volume 22, Issue 2, March/April 2016, Pages 137–163, <https://doi.org/10.1093/humupd/dmv051>, Published:09 November 2015
8. Uterine stem cells: from basic research to advanced cell therapies. Xavier Santamaria, Aymara Mas, Irene Cervelló, Hugh Taylor, Carlos Simon; *Human Reproduction Update*, Volume 24, Issue 6, November-December 2018, Pages 673–693, <https://doi.org/10.1093/humupd/dmy028> Published:15 September 2018
9. *Lancet*.; 2006 Aug 12;368(9535):601-11. doi: 10.1016/S0140-6736(06)69204-0.Recurrent miscarriage: Raj Rai 1, Lesley Regan
10. Review Article, Published: 27 August 2008; Intrauterine adhesions(IUA): has there been progress in understanding and treatment over the last 20 years?, Costas Panayotidis, Steven Weyers, Jan Bosteels & Bruno van Herendael ,*Gynecological Surgery* volume 6, pages197–211(2009)
11. *Journal of Minimally Invasive Gynecology*, Volume 16, Issue 4, July–August 2009, Pages 487-490, Instruments and Techniques, Hysteroscopic Management of Residual Trophoblastic Tissue and Reproductive Outcome: A Pilot Study, panel Erika Mrazguia MD, Amelie Gervaise MD, Aurelia Chauveaud-Lambling MD, Rene Frydman MD, PhD, Heeve Fernandez MD PhD.
12. Hooker et al., 2013, Krolikowski et al., 1995 , cited in Asherman's Syndrome: it may not be all our fault. Xavi Santamaria, Keith Isaacson, Carlos Simón, *Human Reproduction*, Volume 33, Issue 8, August 2018, Pages 1374–1380, <https://doi.org/10.1093/humrep/dey232>, Published: 25 July 2018
13. Original Article, Published: 30 December 2017, The Expression of PDCD4 in patients with missed

- Abortion and its Clinical Significance: Yue Li MS, Xihong Li MS, Xihong Liu BS, Yingshun Sun MS, Yanping Liu MS, Lu Wan MS, Lining Zhang MD, Zhenghui Fang BS, Zengtao Wei MD & Xiaoyan Wang MD 13-1 Ibrahim MI, Raafat TA, Ellaihy MI, Aly RT. Risk of postpartum uterine synechiae following uterine compression suturing during postpartum haemorrhage. *Aust N Z J Obstet*
14. *Journal of Minimally Invasive Gynecology*, Volume 24, Issue 1, 1 January 2017, Pages 74-79, Original Article; Prevalence and Impact of Chronic Endometritis in Patients With Intrauterine Adhesions: A Prospective Cohort Study panel YuqingChenMDLixiangLiuMDYuannaLuoMD-MinghuiChenPhDYangHuanMDRuiliFangMD
  15. Polishuk et al. (1975), Fernandez et al., 2012, 2006, Dawood et al., 2010, Santamaria et al., cited in 2016 Asherman's Syndrome: it may not be all our fault, Xavi Santamaria, Keith Isaacson, Carlos Simón. *Human Reproduction*, Volume 33, Issue 8, August 2018, Pages 1374–1380, <https://doi.org/10.1093/humrep/dey232>, Published: 25 July 2018
  16. *International Journal of Gynecology and Obstetrics* 104 (2009) 49–52, CLINICAL ARTICLE Hysteroscopic findings in women with primary and secondary infertility due to genital tuberculosis Jai Bhagwan Sharma, Kallol K. Roy, Mohanraj Pushparaj, Sunesh Kumar Department of Obstetrics and Gynecology, All India Institute of Medical Sciences, New Delhi, India
  17. *J Reprod Infertil.* 2015 Oct-Dec; 16(4): 229–235. Reproductive Outcome of Patients with Asherman's Syndrome: A SAIMS Experience, Shilpa Bhandari,\* Priya Bhave, Ishita Ganguly, Asha Baxi, and Pallavi Agarwal
  18. Conforti A, Alviggi C, Mollo A, De Placido G, Magos A. The management of Asherman syndrome: a review of literature. *Reprod Biol Endocrinol.* 2013; 11: 118. [PMC free article] [PubMed] [Google Scholar]
  19. *BJOG-an international journal of obstetrics and gynaecology*, TRAUMATIC INTRA UTERINE ADHESIONS; Joseph G. Asherman, First published: December 1950
  20. Roy KK, Baruah J, Sharma JB, Kumar S, Kachawa G, Singh N. Reproductive outcome following hysteroscopic adhesiolysis in patients with infertility due to Asherman's syndrome. *Arch Gynecol Obstet.* 2010; 281 (2): 355– 61. [PubMed] [Google Scholar]
  21. *J Minim Invasive Gynecol.*; Nov-Dec 2014; 21(6):1022-8. doi: 10.1016/j.jmig.2014.04.015. Epub 2014 May 16. A matched cohort study comparing the outcome of intrauterine adhesiolysis for Asherman's syndrome after uterine artery embolization or surgical trauma Dongmei Song 1, Yuhuan Liu 2, Yu Xiao 2, Tin-Chiu Li 3, Fengqiong Zhou 2, Enlan Xia 4 Affiliations expand
  22. *SM Journal of case Report*, Feb 22 2017; Atypical case of Asherman Syndrome (Fritch Syndrome) due to prolonged Retained Fragment of Cu-T in Myometrium: Amera Anjum and Tabassum K Elsevier-*Journal of Minimally Invasive Gynecology*, Volume 17, Issue 5, September–October 2010, Pages 555-569, Review of Intrauterine Adhesions, panel Rebecca Deans MBBS, MRANZCOG Jason Abbott B MED (Hons), MRCOG, FRANZCOG, PhD
  23. Toaff R, Ballas S. Traumatic hypomenorrhea-amenorrhea (Asherman' syndrome) *Fertil Steril.* 1978;11:379–387. [PubMed] [Google Scholar]
  24. March C, Israel R, March A. Hysteroscopic management of intrauterine adhesions. *Am J Obstet Gynecol.* 1978;11:653–657. [PubMed] [Google Scholar]
  25. Hamou J, Salat-Baroux J, Siegler A. Diagnosis and treatment of intrauterine adhesions by microhysteroscopy. *Fertil Steril.* 1983;39: 321–326. (Class II-3).
  26. Valle RF, Sciarra JJ. Intrauterine adhesions: hysteroscopic diagnosis, classification, treatment, and reproductive outcome. *Am J Obstet Gynecol.* 1988;158:1459–1470. (Class III).
  27. Wamsteker K. European Society for Hysteroscopy (ESH) classification of IUA. 1989. (Class III)
  28. American Fertility Society classifications of adnexal adhesions, distal tubal occlusion, tubal occlusion secondary to tubal ligation, tubal pregnancies, mullerian anomalies and intrauterine adhesions. *Fertil Steril.* 1988;49:944–955. (Class III).
  29. Donnez J, Nisolle M. Hysteroscopic Adhesiolysis of Intrauterine Adhesions (Asherman Syndrome). In: Donnez J, editor. London, England: Parthenon Publishing Group; 1994. (Class III).
  30. Nasr A, Al-Inany H, Thabet S, Aboulghar M. A clinicohysteroscopic scoring system of intrauterine adhesions. *Gynecol Obstet Invest.* 2000; 50:178–181. (Class III).
  31. Yu D, Wong YM, Cheong Y, Xia E, Li TC. Asherman syndrome – one century later. *Fertil Steril* 2008; 89: 759– 779. Crossref PubMed Web of Science@Google Scholar
  32. Leone FP, Timmerman D, Bourne T, Valentin L, Epstein E, Goldstein SR, Marret H, Parsons AK, Gull B, Istre O, Sepulveda W, Ferrazzi E, Van den Bosch T. Terms, definitions and measurements to describe the sonographic features of the endometrium and intrauterine lesions: a consensus opinion from the International Endometrial Tumor Analysis (IETA) group. *Ultrasound Obstet Gynecol* 2010; 35: 103– 112. Wiley Online Library CAS PubMed Web of Science@Google Scholar
  33. St L, Ramsay P, Pierson R, et al. Endometrial thickness measured by ultrasound in women with uterine outlet obstruction due to intrauterine or upper cervical adhesions. *Human Reprod.* 2008;23(2):306–309. [PubMed] [Google Scholar]
  34. Naftalin J, Jurkovic D. The endometrial–myome-

- trial junction: a fresh look at a busy crossing. *Ultrasound Obstet Gynecol* 2009; 34: 1– 11. Wiley Online Library CAS PubMed Web of Science®-Google Scholar
36. Acholonu UC, Silberzweig J, Stein DE, et al. Hysterosalpingography versus sonohysterography for intrauterine abnormalities. *JSLs*. 2011;15(4):471-474.
  37. Soares SR, Barbosa dos Reis MM, Camargos AF. Diagnostic accuracy of sonohysterography, transvaginal sonography, and hysterosalpingography in patients with uterine cavity diseases. *Fertil Steril* 2000; 73: 406– 411, Crossref CAS PubMed Web of Science®Google Scholar
  38. Roma Dalfó A, Ubeda B, Ubeda A, Monzón M, Rotger R, Ramos R, Palacio A. Diagnostic value of hysterosalpingography in the detection of intrauterine abnormalities: a comparison with hysteroscopy. *AJR Am J Roentgenol* 2004; 183: 1405– 1409. Crossref PubMed Web of Science®Google Scholar
  39. ATM ANNALS OF TRANSLATIONAL MEDICINE, Vol 8, no.14(July 2020); Use of 3D ultrasound in the hysteroscopic management of Asherman syndrome; Jose Carugno1, Antonio Simone Laganà2, Salvatore Giovanni Vitale3
  40. AJUM, Published online 2015 Dec 31. doi: 10.1002/j.2205-0140.2011.tb00118.x The role of imaging in the investigation of Asherman's syndrome: I Ferne Tan, MBBS DRANZCOG 1 and Meiri Robertson, MB ChB, Bsc, Med-ScHon 2
  41. Levine D. obstetric MRI. *J Magn Reson Imaging*. 2006;24(1):1-15.
  42. Dovepress Journals Volume 10. The use of misoprostol for cervical priming prior to hysteroscopy: a systematic review and analysis; Authors Hua Y, Zhang W, Hu X, Yang A, Zhu X, Received 28 April 2016, Accepted for publication 11 June 2016, Published 6 September 2016 Volume 2016:10 Pages 2789—2801
  43. Ashermans syndrome: the description of two case reports. Miklošová M, Mára M *Ceska Gynekologie*, 01 Jan 2018, 83(6):440-444. PMID: 30848149
  44. Valle RF, Sciarra JJ. Intrauterine adhesions: hysteroscopic diagnosis, classification, treatment, and reproductive outcome. *Am J Obstet Gynecol*. 1988;158(6 Pt 1):1459–1470. [PubMed] [Google Scholar]
  45. Sugimoto O. Diagnostic and therapeutic hysteroscopy for traumatic intrauterine adhesions. *Am J Obstet Gynecol*. 1978;131(5):539–547. [PubMed] [Google Scholar Scoccia, H, Glob. libr. woman's med., (ISSN:1756-2228); DOI 10.3843/GLOWM.10298, Intrauterine Adhesion: Asherman's syndrome;
  46. Deans R, Abbott J. Review of intrauterine adhesions. *J Minim Invasive Gynecol*. 2010;11:555–569. doi: 10.1016/j.jmig.2010.04.016. [PubMed] [CrossRef] [Google Scholar]
  47. Al-Inany H. Intrauterine adhesions: an update. *Acta Obstet Gynecol Scand*. 2001;11:986–993. [PubMed] [Google Scholar]
  48. Fernandez H, Gervaise A, de Tayrac R Hum Reprod. Operative hysteroscopy for infertility using normal saline solution and a coaxial bipolar electrode: a pilot study. 2000;15(8):1773.
  49. Betjes HE, Hanstede MM, Emanuel MH, Stewart EA. Hysteroscopic myomectomy and case volume hysteroscopic myomectomy performed by high- and low-volume surgeons. *J Reprod Med*. 2009;54:425–458.
  50. Emanuel MH. New developments in hysteroscopy. *Best Pract Res Clin Obstet Gynaecol*. 2013;27:421–429.
  51. T Broome JD, Vancaille TG. Fluoroscopically guided hysteroscopic division of adhesions in severe Asherman syndrome. *Obstet Gynecol*. 1999;11:1041–1043. doi: 10.1016/S0029-7844(99)00245-8. [PubMed] [CrossRef] [Google Scholar]
  52. Hanstede MMF, van der Meij E, Goedemans L, Emanuel MH. Results of centralized Asherman surgery, 2003–2013. *Fertil Steril*. 2015;104(6):1561–1568. [PubMed] [Google ScholarAA
  53. Ann Transl Med. 2020 Feb; 8(4): 50. doi: 10.21037/atm.2019.11.136. PMID: 32175344; Cold scissors ploughing technique in hysteroscopic adhesiolysis: a comparative study, Xingping Zhao, Aiqian Zhang, Bingsi Gao, Arvind Burjoo, Huan Huang, and Dabao Xu Pabuçcu R, Atay V, Orhon E, Urman B, Ergün A. Hysteroscopic treatment of intrauterine adhesions is safe and effective in the restoration of normal menstruation and fertility. *Fertil Steril*. 1997;68(6):1141–1143. [PubMed] [Google Scholar]
  55. Fernandez H, Gervaise A, de Tayrac R. Operative hysteroscopy for infertility using normal Saline solution and a coaxial bipolar electrode: a pilot study. *Hum Reprod*. 2000;15(8):1773–1775. [PubMed] [Google Scholar]
  56. Newton JR, Mackenzie WE, Emens MJ, Jordan JA. Division of uterine adhesions (Asherman's syndrome) with the Nd-YAG laser. *Br J Obs Gyn*. 1989;96(1):102–104. [PubMed] [Google Scholar]
  57. Valle RF, Sciarra JJ. Intrauterine adhesions: hysteroscopic diagnosis classification, treatment, and reproductive outcome. *Am J Obstet Gynecol*. 1988;11:1459–1470. doi: 10.1016/0002-9378(88)90382-1. [PubMed] [CrossRef] [Google Scholar]
  58. Chervenak FA, Neuwirth RS. Hysteroscopic resection of the uterine septum. *Am J Obstet Gynecol*. 1981;11:351–353. [PubMed] [Google Scholar]
  59. DeCherney A, Polan ML. Hysteroscopic management of intrauterine lesions and intractable uterine bleeding. *Obstet Gynecol*. 1983;11:392–397. [PubMed] [Google Scholar]

60. Capella-Allouc S, Morsad F, Rongieres-Bertrand C, Taylor S, Fernandez H. Hysteroscopic treatment of severe Asherman's syndrome and subsequent fertility. *Hum Reprod.* 1999;11:1230–1233. doi: 10.1093/humrep/14.5.1230. [PubMed] [CrossRef] [Google Scholar]
61. Chapman R, Chapman K. The value of two stage laser treatment for severe Asherman's syndrome. *Br J Obstet Gynaecol.* 1996;11:1256–1258. doi: 10.1111/j.1471-0528.1996.tb09641.x. [PubMed] [CrossRef] [Google Scholar]
62. Emanuel MH. New developments in hysteroscopy. *Best Pract Res Clin Obstet Gynaecol.* 2013;11:421–429. doi: 10.1016/j.bpobgyn.2012.11.005. [PubMed] [CrossRef] [Google Scholar]
63. Zikopoulos KA, Kolibianakis EM, Platteau P, de Munck L, Tournaye H, Devroey P, Camus M. Live delivery rates in subfertile women with Asherman's syndrome after hysteroscopic adhesiolysis using the resectoscope or the Versapoint system. *Reprod Biomed Online.* 2004;11:720–725. doi: 10.1016/S1472-6483(10)61654-9. [PubMed] [CrossRef] [Google Scholar]
64. Cararach M, Penella J, Ubeda A, Labastida R. Hysteroscopic incision of the septate uterus: scissors versus resectoscope. *Hum Reprod.* 1994;9(1):87–89.
65. Te Linde RW, Rock JA, Thompson JD. *The Linde's operative gynecology*, 8th edn. Lippincott-Raven, Philadelphia. 1997
66. 47Newton JR, MacKenzie WE, Emens MJ, Jordan JA. Division of uterine adhesions (Asherman's syndrome) with the Nd-YAG laser. *Br J Obstet Gynaecol.* 1989;11:102–104. doi: 10.1111/j.1471-0528.1989.tb01584.x. [PubMed] [CrossRef] [Google Scholar]
67. Oman Med j. 2017 Nov; 32(6): 492-498. A pilot Study Compressing Hysteroscopic Adhesiolysis by Conventional Resectoscope Versus Mini-resectoscope; Kallol Kumar Roy, Archana Lingampally, Yamini Kansal, Juhi Bharti, Sunesh Kumar, Perumal Vanamail, Seema Singhal, and Jyoti Meena
68. Deans R, Abbott J. Review of intrauterine adhesions. *J Minim Invasive Gynecol.* 2010;11:555–569. doi: 10.1016/j.jmig.2010.04.016. [PubMed] [CrossRef] [Google Scholar]
69. Al-Inany H. Intrauterine adhesions: an update. *Acta Obstet Gynecol Scand.* 2001;11:986–993. [PubMed] [Google Scholar]
70. McComb PF, Wagner BL. Simplified therapy for Asherman's syndrome. *Fertil Steril.* 1997;11:1047–1050. doi: 10.1016/S0015-0282(97)00413-5. [PubMed] [CrossRef] [Google Scholar]
71. Protopapas A, Shushan A, Magos A. Myometrial scoring: a new technique for the management of severe Asherman's syndrome. *Fertil Steril.* 1998;11:860–864. doi: 10.1016/S0015-0282(98)00036-3. [PubMed] [CrossRef] [Google Scholar]
72. Chen FP, Soong YK, Hui YL. Successful treatment of severe uterine synechiae with transcervical resectoscopy combined with laminaria tent. *Hum Reprod.* 1997;11:943–947. doi: 10.1093/humrep/12.5.943. [PubMed] [CrossRef] [Google Scholar]
73. Kumar A, Kumar A. Hysteroscopic findings of starry sky appearance and impregnated cobwebs in the endometrial tuberculosis. *Int J Gynecol Obstet.* 2014;126:280-1
74. Total corporal synechiae due to tuberculosis carry a very poor prognosis following hysteroscopic synechialysis; Orhan Bukulmez1, Hakan Yarali and Timur Gurgan+Author Affiliations Hacettepe University, Faculty of Medicine, Department of Obstetrics and Gynaecology, Ankara 06100, Turkey ,Received September 24,1998.Accepted April 15, 1999
75. Uterine rupture following hysteroscopic lysis of synechiae due to tuberculosis and uterine perforation; Timur Gürkan1, Hakan Yarali, Biilent Urman, Vural Dagli and Levent Dogan+Author Affiliations ;Division of Reproductive Endocrinology and Infertility, Faculty of Medicine, Department of Obstetrics and Gynecology, University of Hacettepe Ankara, Turkey; Received July 17, 1995. Accepted November 8, 1995
76. *Arch Gynecol Obstet.* 2010 Feb;281(2):355-61. doi: 10.1007/s00404-009-1117-x. Epub 2009 May 20. Reproductive outcome following hysteroscopic adhesiolysis in patients with infertility due to Asherman's syndrome. K K Roy 1, Jinee Baruah, Jai Bhagwan Sharma, Sunesh Kumar, Garima Kachawa, Neeta Singh.
77. Yu D, Li TC, Xia E, et al. Factors affecting reproductive outcome of hysteroscopic adhesiolysis for Asherman's syndrome. *Fertil Steril* 2008;89:715-22. 10.1016/j.fertnstert.2007.03.070 [PubMed] [CrossRef] [Google Scholar]
78. *BMC Res Notes.* 2017; 10:683. Published online 2017 Dec 4. Doi: 10.1186/s13104-017-3057-zFemale genital tuberculosis and infertility: series cases report in Bandung, Indonesia; Tono Djuwanton, Wiryawan Permadi, Leri Septiani, Ahmad, Danny Halim and Ida Parwati
79. 2012 Aug;286(2):525-30. doi: 10.1007/s00404-012-2336-0. Epub 2012 Apr 26. Changes in endometrial receptivity in women with Asherman's syndrome undergoing hysteroscopic adhesiolysis, Neena Malhotra 1, Anupama Bahadur, Mani Kalaivani, Suneeta Mittal
80. Yang JH, Chen MJ, Chen CD, Chen SU, Ho HN, Yang YS, Optimal waiting period for subsequent fertility treatment after various hysteroscopic surgeries, *Fertil Steril* 2013;99(7):2092-6
81. Polishuk WZ, Kohane S. Intrauterine adhesions: diagnosis and therapy. *Obstet Gynecol Digest.* 1966;8:41
82. AAGL Practice Report: Practice Guidelines on Intrauterine Adhesions Developed in Collaboration With the European Society of Gynaecological En-

- doscopy (ESGE) March 2017 *Gynecological Surgery* 14(1):6
83. Vesce F, Jorizzo G, Bianciotto A, et al. Use of the copper intrauterine device in the management of secondary amenorrhea. *Fertil Steril* 2000;73:162-5. 10.1016/S0015-0282(99)00475-6 [PubMed] [CrossRef] [Google Scholar]
  84. March CM, Israel R. Gestational outcome following hysteroscopic lysis of adhesions. *Fertil Steril* 1981;36:455-9. 10.1016/S0015-0282(16)45792-4 [PubMed] [CrossRef] [Google Scholar]
  85. Salma U, Xue M, Md Sayed AS, et al. Efficacy of intrauterine device in the treatment of intrauterine adhesions. *Biomed Res Int* 2014;2014:589296. 10.1155/2014/589296 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
  86. *Arch Gynecol Obstet.* 2013 Oct;288(4):829-32. doi: 10.1007/s00404-013-2838-4. Epub 2013 Apr 12. A pilot study of Foley's catheter balloon for prevention of intrauterine adhesions following breach of uterine cavity in complex myoma surgery; Sahana Gupta 1, Vikram Sinai Talaulikar, Joseph Onwude, Isaac Manyonda
  87. M. W. Healy, B. Schexnayder, M. T. Connell et al., "Intrauterine adhesion prevention after hysteroscopy: a systematic review and meta-analysis," *American Journal of Obstetrics & Gynecology*, vol. 215, no. 3, pp. 267–275.e7, 2016. View at: Publisher Site | Google Scholar
  88. *Taiwanese Journal of Obstetrics and Gynecology*, Volume 59, Issue 1, January 2020, Pages 56-60; Intrauterine adhesion prevention with Malecot catheter after hysteroscopic myomectomy: A novel approach; Christine Shan-ChiChiuYuh-MingHwuabcdRobert Kuo-KuangLeeabeMing-HueiLinabcd
  89. Kachhawa, N. Malik, A. Kriplani, R. Mahey; Pregnancy with Malecot catheter in situ following cervical and vaginal reconstruction of a cicatrized vagina and cervix: a rare case; *J Obstet Gynaecol India*, 66 (2016), pp. 583-586. CrossRefView Record in ScopusGoogle Scholar
  90. 205 Lin XN, Zhou F, Wei ML, Yang Y, Li Y, Li TC, et al. Randomized, controlled trial comparing the efficacy of intrauterine balloon and intrauterine contraceptive device in the prevention of adhesion reformation after hysteroscopic adhesiolysis. *Fertil Steril.* 2015;104(1):235-40.
  91. March CM: Management of Asherman syndrome. *Reprod Biomed Online.* 2011, 23: 63-76.
  92. Biomed Research international Clinical Study | Open Access, Volume 2018 | Article ,Comparison of Intrauterine Suitable Balloon and Foley Balloon in the Prevention of Adhesion after Hysteroscopic Adhesiolysis; Ru Zhu,1,2 Hua Duan,1 Lu Gan,1 and Sha Wang1, Academic Editor: Alessandro Favilli
  93. *Ann Transl Med.* 2020 Feb; 8(4): 61. doi: 10.21037/atm.2019.12.82, PMID: 32175355; A novel intrauterine stent for prevention of intrauterine adhesions; Huan Huang,1 Bin Xu,2 Chunxia Cheng, and Dabao Xu *BJOG An International Journal of Obstetrics and Gynaecology*, Gynaecological surgery ; Prevention of postoperative adhesion reformation by intermittent intrauterine balloon therapy: a randomised controlled trial, X Shi , SH Saravelos , Q Zhou , X Huang , E Xia, TC Li, First published: 17 June 2019
  94. Innovative Alternatives in the Postoperative Management of Asherman Syndrome; 42,438-445, Jaime Ferro, Pedro Montoya; Mastering techniques in hysteroscopy-Ref.book
  95. 204 Eur J Obstet Gynecol Reprod Biol . 2013 Oct;170(2):512-6. doi: 10.1016/j.ejogrb.2013.07.018. Epub 2013 Aug 7. A comparison of intrauterine balloon, intrauterine contraceptive device and hyaluronic acid gel in the prevention of adhesion reformation following hysteroscopic surgery for Asherman syndrome: a cohort study ;Xiaona Lin 1, Minling Wei, T C Li, Qiongxiao Huang, Dong Huang, Feng Zhou, Songying Zhang
  96. 205 Lin XN, Zhou F, Wei ML, Yang Y, Li Y, Li TC, et al. Randomized, controlled trial comparing the efficacy of intrauterine balloon and intrauterine contraceptive device in the prevention of adhesion reformation after hysteroscopic adhesiolysis. *Fertil Steril.* 2015;104(1):235-40.
  97. Mais V, Cirronis MG, Peiretti M, Ferrucci G, Cossu E, Melis GB: Efficacy of auto-crosslinked hyaluronan gel for adhesion prevention in laparoscopy and hysteroscopy: a systematic review and meta-analysis of randomized controlled trials. *Eur J Obstet Gynecol Reprod Biol.* 2012, 160: 1-5. 10.1016/j.ejogrb.2011.08.002.
  98. Eur J Obstet Gynecol Reprod Biol, . 2016 Aug;203:182-92. doi: 10.1016/j.ejogrb.2016.05.050. Epub 2016 Jun 10. Prevention of intrauterine post-surgical adhesions in hysteroscopy. A systematic review;Attilio Di Spiezio Sardo 1, Gloria Calagna 2, Marianna Scognamiglio 3, Peter O'Donovan 4, Rudi Campo 5, Rudy L De Wilde 6
  99. Bosteels J, Weyers S, Kasius J, Broekmans FJ, Mol BW, D'Hooghe TM. Anti-adhesion therapy following operative hysteroscopy for treatment of female subfertility. *Cochrane Database Syst Rev.* 2015;11:Cd011110.
  100. Tsapanos VS, Stathopoulou LP, Papathanassopoulou VS, Tzingounis VA: The role of Seprafilm bioresorbable membrane in the prevention and therapy of endometrial synechiae. *J Biomed Mater Res.* 2002, 63: 10-14. 10.1002/jbm.10040.
  101. Kim T, Ahn KH, Choi DS, Hwang KJ, Lee BI, Jung MH, Kim JW, Kim JH, Cha SH, Lee KH, et al: A randomized, multi-center, clinical trial to assess the efficacy and safety of alginate carboxymethylcellulose hyaluronic acid compared to carboxymethylcellulose hyaluronic acid to prevent postoperative intrauterine adhesion. *J Minim Invasive Gynecol.* 2012, 19: 731-736. 10.1016/j.jmig.2012.08.003.

103. Glob J Fertil Res, 30 Dec.2016: An Innovative New treatment for Asherman Syndrome with an Intrauterine Aminograft: A case series; Gretchen Garbe Collins, Suruchi Thakore, Bansari Patel and James Liu
104. Cochrane Database Syst Rev. 2017 Nov 27;11(11):CD011110. doi: 10.1002/14651858.CD011110.pub3. Anti-adhesion therapy following operative hysteroscopy for treatment of female subfertility; Jan Bosteels 1, Steven Weyers, Thomas M D'Hooghe, Helen Torrance, Frank J Broekmans, Su Jen Chua, Ben Willem J Mol
105. Conforti A, Alviggi C, Mollo A, De Placido G, Magos A. The management of Asherman syndrome: a review of literature. *Reproductive Biology and Endocrinology*. 2013;11(1): 1-11.
106. *Int J Clin Exp Pathol*, v.6(7); 2013, PMC3693199, *Int J Clin Exp Pathol*. 2013; 6(7): 1343–1350. Published online 2013 Jun 15. Role of angiogenesis in endometrial repair of patients with severe intrauterine adhesion; Yuqing Chen, 1 Yajie Chang, 2 Shuzhong Yao 1
107. Deans R, Abbott J. Review of intrauterine adhesions. *J Minim Invasive Gynecol*. 2010;17(5):555-69.
108. Johary J, Xue M, Zhu X, Xu D, Velu PP. Efficacy of estrogen therapy in patients with intrauterine adhesions: systematic review. *J Minim Invasive Gynecol*. 2014;21(1):44-54.
109. *International Journal of Gynecology & Obstetrics*; Clinical Article :Intrauterine infusion of platelet rich plasma is a treatment method for patients with intrauterine adhesions after hysteroscopy: Jintao Peng, Manzhao Li, Haitao Zeng, Zhi Zeng, Jiana Huang, Xiaoyan Liang, First published: 20 August 2020
110. Management of a Thin Endometrium by Hysteroscopic Instillation of Platelet-Rich Plasma Into The Endomyometrial Junction: A Pilot Study; - by Meenu Agarwal 1, Liselotte Mettler 2, Smita Jain 1, Sandhya Meshram 1, Veronika Günther 2 and Ibrahim Alkatout 2,\* *J. Clin. Med*. 2020, 9(9), 2795; <https://doi.org/10.3390/jcm9092795>
111. *J Hum Reprod Sci*. 2014 Apr-Jun; 7(2): 93–98. Autologous stem cell transplantation in refractory Asherman's syndrome: A novel cell based therapy; Neeta Singh, Sujata Mohanty, Tulika Seth, Meenakshi Shankar, Sruthi Bhasaran, and Sona Dharmendra
112. Gargett CE, Ye L. Endometrial reconstruction from stem cells. *Fertil Steril*. 2012;98:11–20. [PubMed] [Google Scholar]
113. Santamaria X, Cabanillas S, Cervelló I, Arbona C, Raga F, Ferro J, et al. Autologous cell therapy with CD133+ bone marrow-derived stem cells for refractory Asherman's syndrome and endometrial atrophy: a pilot cohort study. 2016;31(5):1087-96.
114. *Front Surg*. 2019; 6: 50. Published online 2019 Aug 16. doi: 10.3389/fsurg.2019.00050 PMID: PMC6706867, PMID: 31475154, Early Second-Look Hysteroscopy: Prevention and Treatment of Intrauterine Post-surgical Adhesions; Lauren Sebbag,\* Marc Even, Stéphanie Fay, Iptissem Naoura, Aurélie Revaux, Marie Carbonnel, Paul Pirtea, Dominique de Ziegler, and Jean-Marc Ayoubi
115. Innovative Alternatives in the Postoperative Management of Asherman Syndrome; 42,438-445, Jaime Ferro, Pedro Montoya; Mastering techniques in hysteroscopy-Rfe.book
116. *Arch Gynecol Obstet* 2010 Feb;281(2):355-61. Reproductive outcome following hysteroscopic adhesiolysis in patients with infertility due to Asherman's syndrome, K K Roy 1, Jinee Baruah, Jai Bhagwan Sharma, Sunesh Kumar, Garima Kachawa, Neeta Singh, Affiliations expand PMID: 19455349 DOI: 10.1007/s00404-009-1117-x
117. Placenta accreta: adherent placenta due to Asherman syndrome; Line Engelbrechtsen, Jens Langhoff-Roos, Jens Joergen Kjer, Olav Istre; First published: 22 January 2015
118. *J Minim Invasive Gynecol*. 2017 Feb;24(2):299-304. doi: 10.1016/j.jmig.2016.10.018. Epub 2016 Nov 14.
119. Reproductive Outcomes in Patients With Intrauterine Adhesions Following Hysteroscopic Adhesiolysis: Experience From the Largest Women's Hospital in China: Limei Chen 1, Hongwei Zhang 1, Qing Wang 1, Feng Xie 1, Shujun Gao 1, Yu Song 1, Jing Dong 1, Hua Feng 1, Kangyun Xie 2, Long Sui 3
120. *International Journal of Current Research Vol. 10, Issue, 08, pp.72429-72434, August, 2018*; Research Article Revisiting Diagnostic and Therapeutic Challenges in Asherman's Syndrome: A Retrospective Analysis of 5 years. Richa Sharma, 2Rahul Manchanda and 3Nidhi Chandil