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62.1 Introduction

Intrauterine adhesions or synechiae refer to situations where scar tissue develops within the uterine cavity. It was first described and published by Heinrich Fritsch in 1894 [1]. In 1948, an Israeli gynecologist Joseph Asherman identified intrauterine adhesions in 29 women presenting with amenorrhea and associated stenosis of the internal cervical os. Two years later, he also documented a series of cases with intrauterine cavity involvement following hystero-graphy [2]. It became known as Asherman syndrome when there are associated symptoms such as menstrual irregularities and infertility. The terms Asherman syndrome and intrauterine adhesions are often used interchangeably. Sometimes the symptoms of Asherman syndrome are present in a woman in whom the cause of the intrauterine adhesion was not pregnancy related; in such scenarios, the term Asherman syndrome can still be used [3].

62.1.1 Definition of Abortion

The definition of abortion is sometimes riddled with controversies. For this reason abortion has numerous definitions. What is generally agreed upon is that abortion is the termination of a pregnancy before the period of viability [4]. The issue is what constitutes viability? The Centre for Disease Control (CDC) and the World Health Organization (WHO) define abortion as pregnancy termination prior to 20 weeks gestation or a fetus born weighing less than 500 g [5]. In Nigeria and most third world countries for example, abortion is defined as the spontaneous or induced termination of pregnancy before the age of fetal viability which is taken as 28 weeks gestation [6].

The different types of abortions include: Spontaneous/induced, Threatened/inevitable, Incomplete/complete, and Septic abortions.

62.1.2 Epidemiology of Abortion

Reliable data on the incidence of abortion and its complications are difficult to ascertain especially in areas with restrictive abortion laws [7]. Estimates show that worldwide, 26–53 million induced abortions are carried out each year [8]. In Nigeria, it is estimated that about 610,000 induced abortions are performed annually [9]. The Centre for Disease Control reports that the rate of termination of pregnancy in the United States of America in 2008 was 16 per 1000 women aged 15–44 years, with a 4% decrease in the rate from 1999 [10]. Worldwide estimates for that same year put the induced abortion rate at 28 per 1000 women aged 15–44 years [11]. Western Europe recorded the lowest rate while Eastern Europe had the highest figure of 43 per 1000 in women aged 15–44 years in 2008 [11]. Approximately 42% of all induced abortions in the United States were repeated pregnancy terminations [10].

Unsafe abortion is a significant problem in countries, with restrictive abortion laws. In most developing countries such as Nigeria, abortion services might either be restricted or unaffordable. This therefore limits the access of women to abortion services [12]. For this reason, over 90% of the estimated 70,000 maternal deaths from unsafe abortions worldwide occur in developing countries [8]. In Nigeria for example, an estimated 1.25 million induced abortions occurred in 2012 alone equivalent to a rate of 33 abortions per women aged between 15 and 49 years [13]. Each year about 20,000 deaths occur from unsafe abortions in Nigeria [14].

Methods of procuring an abortion include both the medical and surgical methods. While the medical methods involve the use of medications, the surgical methods consist of either a dilatation and curettage or the use of vacuum aspiration. Medical and surgical abortions are both considered safe and

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effective methods of termination of pregnancy, albeit, the choice is based upon availability, gestational age of the pregnancy, and patient preference [15]. Medical abortion however takes a much longer time to expel the fetus compared with the surgical method. The two commonly used medications, used alone or in combination for medical abortions are Mifepristone, an anti-progestogen, and misoprostol, a prostaglandin. They are approved for use in combination for abortions up to 70 days of gestation [16]. The evidence-based regimen involves administering mifepristone 200 mg orally and following this up with misoprostol 800 µg within the buccal cavity (the cheek pouch) 14–48 h later and consulting a physician for follow-up 1–2 weeks after first ingesting the mifepristone [17].

While vaginal route of administration of misoprostol is as effective as the buccal or oral routes, rare cases of clostridial sepsis and even death have been reported in women who used this route [18, 19].

Methotrexate followed by vaginal misoprostol is another alternative, as it successfully terminates pregnancy in 88–96% of cases [20]. The main disadvantage is the prolonged interval it takes before complete abortion is accomplished. In a study by Pazol and his colleagues, they found that for gestational ages ≤ 13 weeks of gestation, 76% of the abortions were performed by vacuum aspiration while 15% had medical abortions [10]. In another study in Benin City, Nigeria, over 70% of the abortions were done by dilatation and curettage, with over 70% of the patients reporting having at least one previous termination of pregnancy [21]. Suction evacuation can conveniently be used for pregnancy termination up to 14 weeks of gestation. Postabortal endometritis occurs in 5–20% of women who were not placed on antibiotics following aspiration abortion but the figure is reduced by half if prophylactic antibiotics are administered [22]. For this reason, antibiotic prophylaxis was recommended following this method of abortion [23, 24]. The use of prophylactic antibiotics following a medical induced abortion, however, is controversial [25]. In several prospective studies, the rate of infection following medical abortions was found to be low at approximately 0.3% [26–28].

Unfortunately, no randomized controlled trials exist on the use of prophylactic antibiotics for first trimester medical abortions. The Planned Parenthood Federation conducted an observational study which looked at over 227,000 women at gestational ages up to 63 days who used mifepristone/misoprostol to procure an abortion: the rate of serious infections decreased from 0.93 to 0.06 per 1000 women following the use of prophylactic doxycycline [18]. The Society for Family Planning currently does not recommend universal antibiotic use following a medical abortion, albeit, they do recognize the individual practitioner's preferences.

A systematic review comparing manual vacuum aspirator with electric vacuum aspirator for pregnancy termination at less than 10 weeks reported no significant differences between the two methods for complete rate or patient satisfaction [29].

Second trimester termination of pregnancy is associated with more morbidities and mortalities. They can also be performed by either dilatation and evacuation or with the use of medical agents for inducing abortion. However, because of the many complications associated with second trimester dilatation and evacuation, including the possibility of retained fetal bones, its role should probably be limited in modern gynecological practice [30]. About 10% of women who have a medically induced second trimester abortion further require procedures to remove a retained placenta [31].

62.1.3 Epidemiology of Intrauterine Adhesions

The true prevalence of intrauterine adhesions is unknown as the condition is rare in the general population while many patients are largely asymptomatic. Hooker et al. in a recent meta-analysis evaluated 912 women hysteroscopically, within 12 months of a spontaneous miscarriage or medical/surgical expulsion [32]. About 86% of the patients had uterine curettage. The prevalence of intrauterine adhesions was 19.1%. The most common predisposing factors to intrauterine adhesions seem to be curettage of a pregnant or recently pregnant uterus such as a miscarriage, termination of pregnancy, causing damage to the basal layer of the endometrium [33]. Intrauterine adhesions can however occur following a Caesarean section, myomectomy (both open and hysteroscopic/laparoscopic myomectomies), use of the B-lynch compression sutures, use of intrauterine devices, infections such as schistosomiasis and tuberculosis of the genital tract, and surgeries for Mullerian abnormalities [34, 35].

Schenker and Margalioth studied 1856 cases of Asherman syndrome and found that 90.8% of the patients had a preceding curettage for a miscarriage [36]. While 66.7% had undergone curettage on account of induced or spontaneous abortions, 21.5% had curettage for postpartum hemorrhage, 2.0% followed a Caesarean section and 0.6% after evacuation for a hydatidiform mole. A missed abortion once detected is usually evacuated by the most appropriate means. However, a delay in evacuation can become a harbinger for future occurrence of Asherman syndrome. The time interval between the death of the fetus and dilatation and curettage may increase the chances of

adhesion formation as a result of the fibroblastic activity of the retained tissues; therefore the longer the period between fetal demise and dilatation and curettage, the greater the risk of Asherman syndrome [37]. In the same vein, the number of procedures increases the risk of Asherman syndrome, with an estimated 16% risk after one dilatation and curettage and 32% after three or more attempts [38].

A randomized controlled trial which analyzed 82 women using three different approaches: conservative management, medical evacuation or surgical evacuation of retained products of conception, concluded that both the conservative management and medical evacuation were acceptable alternatives to standard surgical evacuation [39]. However, intrauterine adhesions were only found to be established in the group of patients that underwent surgical treatment following a second look hysteroscopy 6 months after treatment [39]. Following manual vacuum aspiration of 191 patients with early pregnancy losses, none of the patients developed Asherman syndrome, making this a better alternative to sharp dilatation and curettage [40].

Unsafe abortions, which connotes abortion carried out by an unskilled individual and/or in an environment that does not meet the minimum medical standards, is a common cause of Asherman syndrome [6, 41]. In countries with restrictive abortion laws, women tend to self-induce abortions or patronize quacks. Objects and substances that have been reported as being used to procure such abortions include: bicycle spoke, straws, sticks, herbal preparations, vigorous abdominal massage, salt water solution, ampiclox capsules, lime and potash [42, 43]. Most of these have the potential of causing significant trauma to the endometrium and therefore become harbingers for future Asherman syndrome.

In Brazil where abortion is also illegal, there are reports of women using misoprostol to initiate the abortion process before seeking treatment for incomplete abortion (which in itself is legal) [44]. As a result of the abdominal pains the women experience after ingesting the drug, most are forced to go to hospital [45]. Interestingly, hospital staff evaluated in a study considered this type of induced abortion more acceptable than other methods as it reduces abortion complications, including infections and Asherman syndrome [45]. The contribution of infection to Asherman syndrome is unclear [46, 47]. It has been proposed that infection may be a primary cause of intrauterine adhesions [48]. The role for infection was also supported by a study which showed the presence of peritubal adhesions, endometritis, and the isolation of bacteria in cases diagnosed with Asherman syndrome [49]. In direct contrast, another

study suggested that bacteria were rarely isolated and that inflammatory cells, degenerative products, and tissue edema at histologic analysis of endometrial cells in patients with intrauterine adhesions were similar in patients without intrauterine adhesions [50]. The American Fertility Society suggests that dilatation and curettage in the settings of endometritis has a nonsignificant effect on adhesion formation [51]. However, it is logical to believe that postinfectious inflammatory processes could worsen or exacerbate a traumatic endometrial damage [48].

Following damage to the basal layer of the endometrium, granulation tissue on the opposing surfaces of the uterine cavity can coalesce, giving rise to adhesions which can partially or totally obliterate the uterine cavity. Electric microscopic evaluation of endometrial glandular cells of women affected by severe Asherman syndrome revealed significant subcellular modifications such as ribosome loss, mitochondrial swelling, vascular closure, and hypoxic cellular modifications [52]. Malhotra and colleagues in a prospective study observed a high impedance of spiral arteries in 40 patients with Asherman syndrome [53]. It was hypothesized that this high impedance could be responsible for the reduced endometrial receptivity and regeneration observed in these women. Endometrial insufficiency may prevent the implantation of the blastocyst [54]. Poor vascularization could also have a detrimental effect on implantation leading to early fetal losses [55]. Recurrent miscarriage is often associated with intrauterine adhesions with 5–39% of women with recurrent miscarriages said to have intrauterine adhesions [46, 49, 56–58].

62.2 Diagnosis

The diagnosis of intrauterine adhesion and hence Asherman syndrome can sometimes be missed. Patients with Asherman syndrome could present with symptoms which include menstrual irregularities such as hypomenorrhea and amenorrhea; cyclical lower abdominal/pelvic pain; recurrent pregnancy loss; and infertility. All these are consequences of the intrauterine adhesions. Following the above history, other investigative modalities can be performed to establish a diagnosis of Asherman syndrome.

62.2.1 Hysteroscopy

The gold standard for establishing a diagnosis is hysteroscopy. During hysteroscopy, the intrauterine adhesions can be visualized and the severity of the condition assessed as

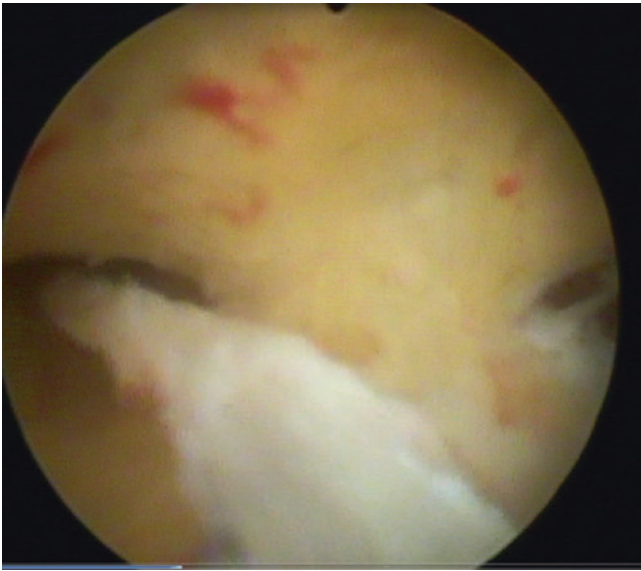


Fig. 62.1 Intrauterine adhesions. Copyright Gynoscope Specialist Hospital

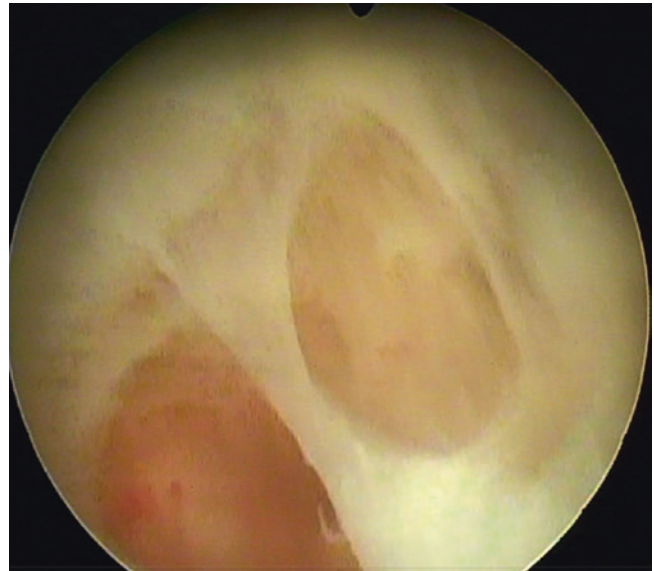


Fig. 62.3 Mild intrauterine adhesions. Copyright Gynoscope Specialist Hospital

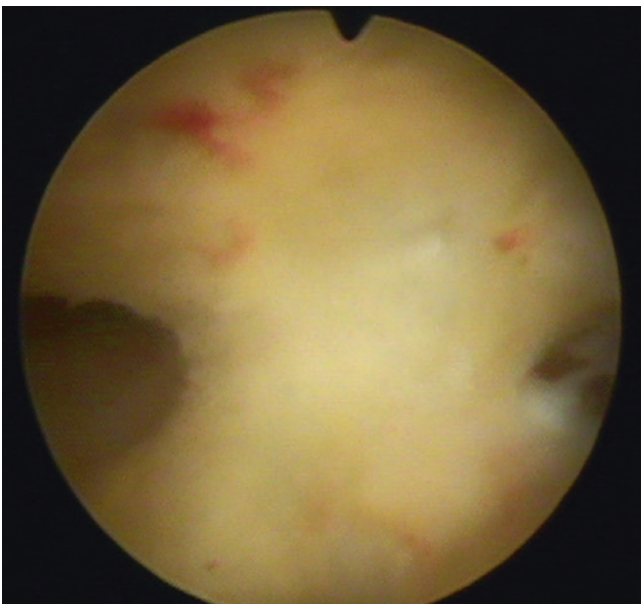


Fig. 62.2 Intrauterine adhesions. Copyright Gynoscope Specialist Hospital Nigeria

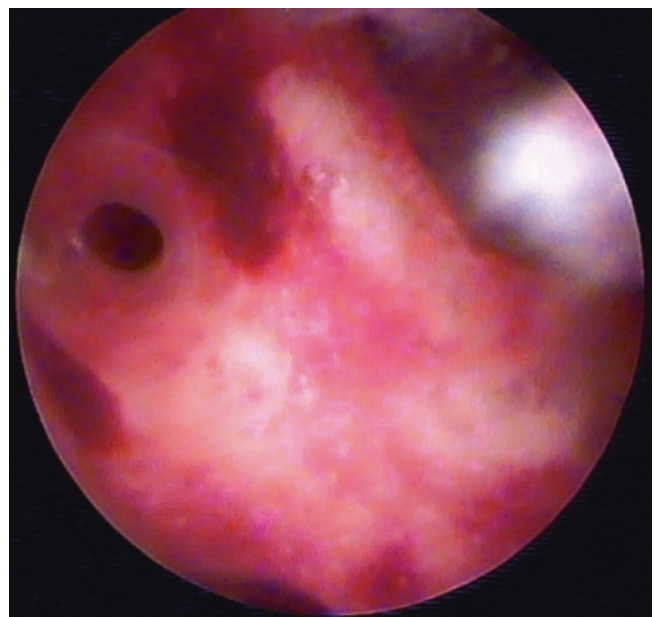


Fig. 62.4 Intrauterine adhesions. Copyright Gynoscope Specialist Hospital

shown in Figs. 62.1, 62.2, 62.3, 62.4, 62.5, 62.6, 62.7, and 62.8. It is also possible to estimate the proportion of healthy endometrial tissue, which may help in prognosticating the condition.

62.2.2 Hysterosalpingography

Hysterosalpingography is an imaging technique, which also helps in establishing a diagnosis. It will often show filling defects within the endometrial cavity (Figs. 62.9

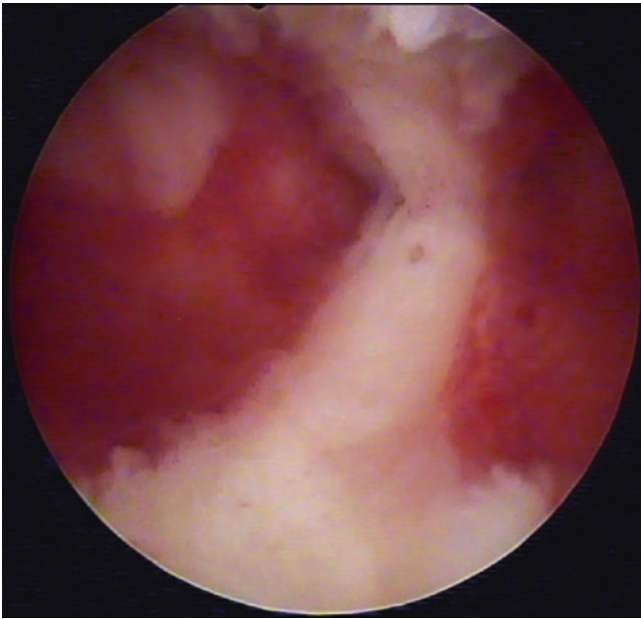


Fig. 62.5 Intrauterine adhesions during excision



Fig. 62.7 Intrauterine adhesions. Copyright Gynscope Specialist Hospital

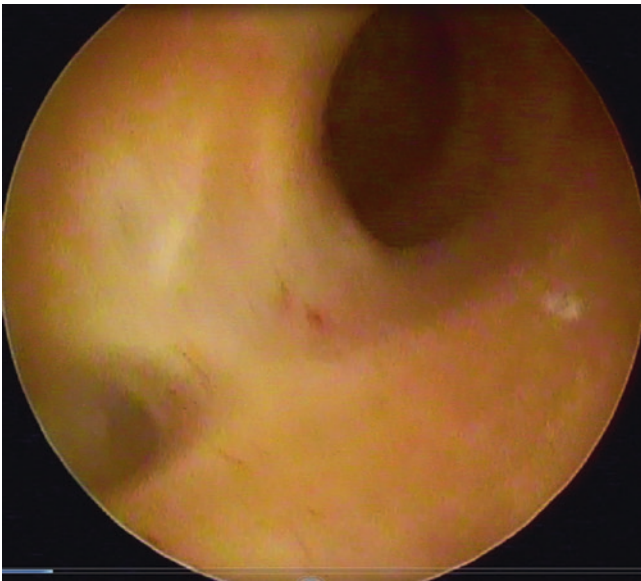


Fig. 62.6 Intrauterine adhesions. Copyright Gynscope Specialist Hospital



Fig. 62.8 Severe intrauterine adhesions. Copyright Gynscope Specialist Hospital

and 62.10). Unfortunately, it might not reliably decipher the full extent of the condition. In severe cases however, there will usually be severe narrowing and complete distortion of the uterine cavity.

62.2.3 Saline Infusion Sonography (SIS)

This can quite easily be performed in the office setting just like office hysteroscopy; it also helps in the diagnosis of intrauterine adhesions. Hysterosalpingography and SIS are



Fig. 62.9 HSG findings of intrauterine adhesion



Fig. 62.10 HSG findings of intrauterine adhesions

both equally sensitive for diagnosing intrauterine adhesions with a sensitivity of 75% [59].

62.2.4 Transvaginal Ultrasound Scan (TVS)

This is not a reliable method of diagnosing Asherman syndrome although very versatile sonologists might be able to delineate intrauterine adhesions with the use of this investigative tool [60]. Also, just like hysteroscopy, albeit, to a

lesser extent, transvaginal ultrasound scan can help in the determination of the prognosis.

62.2.5 Magnetic Resonance Imaging (MRI)

This is a less commonly used diagnostic modality. The cost of the procedure can be exorbitant, limiting its use in the diagnosis of Asherman syndrome. Three-dimensional ultrasonography may also be helpful in establishing a diagnosis of Asherman syndrome.

62.3 Classification

Intrauterine adhesions should be classified as this can serve as a guide to the prognosis following treatment, which in itself is related to the severity of the disease [61].

A number of classification systems exist. Unfortunately, no comparative analysis has been performed for the classification systems as comparisons between studies are difficult to interpret.

Two of the available classification systems include: The European Society for Hysteroscopy classification of intrauterine adhesions which is shown in Table 62.1 and the American Society for Reproductive medicine classification of intrauterine adhesions shown in Table 62.2.

62.4 Treatment

Historically, intrauterine adhesions were managed by blind adhesiolysis, which did not allow for proper visualization of the adhesions. Unfortunately, there are no randomized controlled trials of any treatment modality compared with

Table 62.1 European Society for Hysteroscopy classification of intrauterine adhesions

Grade	Extent of intrauterine adhesions
I	Thin or filmy adhesions easily ruptured by hysteroscope sheath alone, cornual areas normal
II	Singular filmy adhesions connecting separate parts of the uterine cavity, visualization of both tubal ostia possible, cannot be ruptured by hysteroscope sheath alone
IIA	Occluding adhesions only in the region of the internal cervical os. Upper uterine cavity normal
III	Multiple firm adhesions connecting separate parts of the uterine cavity, unilateral obliteration of ostial areas of the tubes
IIIA	Extensive scarring of the uterine cavity wall with amenorrhea or hypomenorrhea
IIIB	Combination of III and IIIA
IV	Extensive firm adhesions with agglutination of the uterine walls. Both tubal ostial areas occluded

Table 62.2 American Society for reproductive medicine classification of intrauterine adhesions

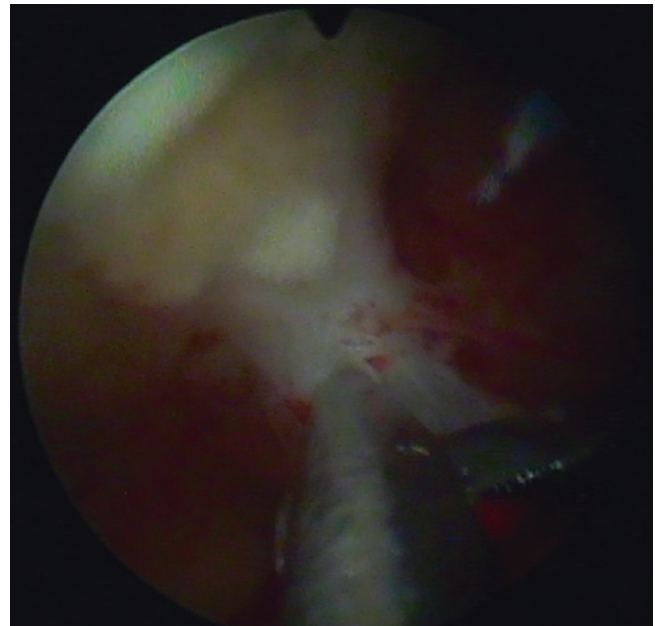
Patient's name _____		Date _____		Chart _____		Chart _____	
Age _____	G _____	P _____	Sp Ab _____	VTP _____	Ectopic _____	Infertile yes _____	No _____
Other significant history (i.e., surgery, infection, etc.) _____							
HSG _____		Sonography _____		Photography _____		Laparoscopy _____	Laparotomy _____
Extent of cavity involved	<1/3 1	1/3–2/3 2	>2/3 4				
Type of adhesions	Filmy 1	Filmy and dense 2	Dense 4				
Menstrual pattern	Normal 0	Hypomenorrhea 2	Amenorrhea 4				
Prognostic classification		HSG Score	Hysteroscopy Score	Additional findings			
Stage I (mild)	1–4	_____	_____	_____			
Stage II (moderate)	5–8	_____	_____	_____			
Stage III (severe)	9–12	_____	_____	_____			

expectant management, or a treatment modality, compared with another treatment modality. Treatment therefore is based to a large extent on the personal experience of the gynecologist, case series, and reported cases, and is also structured to meet the individual needs of the patient.

Patients with intrauterine adhesions but without signs and symptoms and not trying for conception might be left alone. Spontaneous resumption of menstruation in as many as 78% of patients within seven years had previously been reported [36]. Those with presentations already enumerated should be considered for hysteroscopic resection of the adhesion as there is significant improvement in menstrual pattern with improved pregnancy rates [62]. Intrauterine adhesions remain one of the most common indications for hysteroscopy [63].

The aim of treatment is to restore the normal anatomy of the uterine cavity while taking steps to prevent a recurrence of the adhesions. In cases with severe, dense adhesions, there is a risk of creating a false passage and such cases are best done under ultrasonographic guidance. Some authors had advocated a concurrent laparoscopy or fluoroscopy guidance when faced with such difficult cases [64, 65]. Patients with cervical stenosis might benefit from the use of intravaginal misoprostol insertion the evening before hysteroscopy, ensuring the cervical canal is easier to dilate [66, 67].

Mild adhesions might be separated during hysteroscopy, due to the effect of the distension medium; the tip of the hysteroscope can also be used to bluntly separate the adhesions [68]. While some gynecologists would prefer to use hysteroscopic scissors for adhesiolysis as it is associated with less injury to the endometrium (Figs. 62.11, 62.12, 62.13, and 62.14), others advocate the use of an energy

**Fig. 62.11** Hysteroscopic adhesiolysis with scissors

source, either monopolar or bipolar; although there is a higher risk of damage to the residual endometrium with this energy sources [3, 46].

Other treatment modalities that have been reported include the use of NdYAG (neodymium-doped yttrium aluminum garnet) and KTP (potassium-titanyl-phosphate) LASER, which have been largely abandoned on account of cost and damage to the endometrium [69]. Case reports also abound of ways gynecologists have tried to manage severe cases of Asherman syndrome. McComb and Wagner reported a rather interesting way they managed six cases, five with

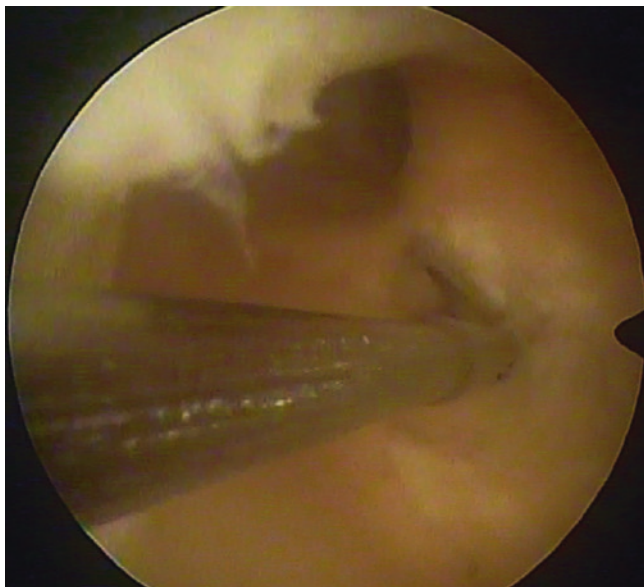


Fig. 62.12 Hysteroscopic adhesiolysis with scissors

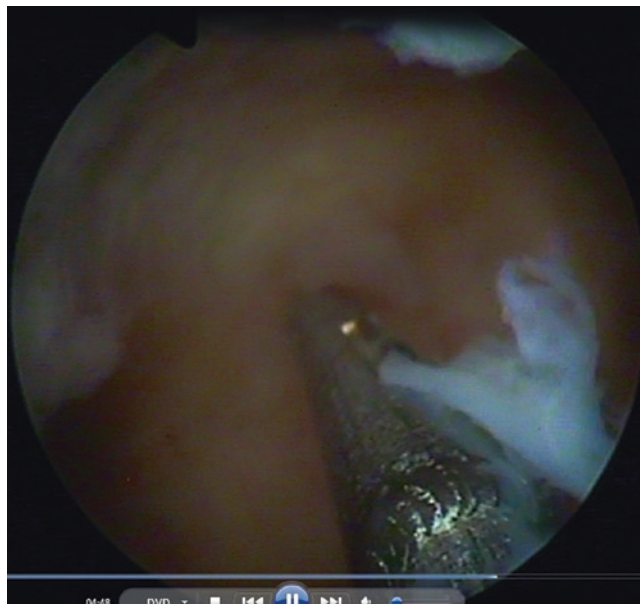


Fig. 62.14 Hysteroscopic adhesiolysis with scissors

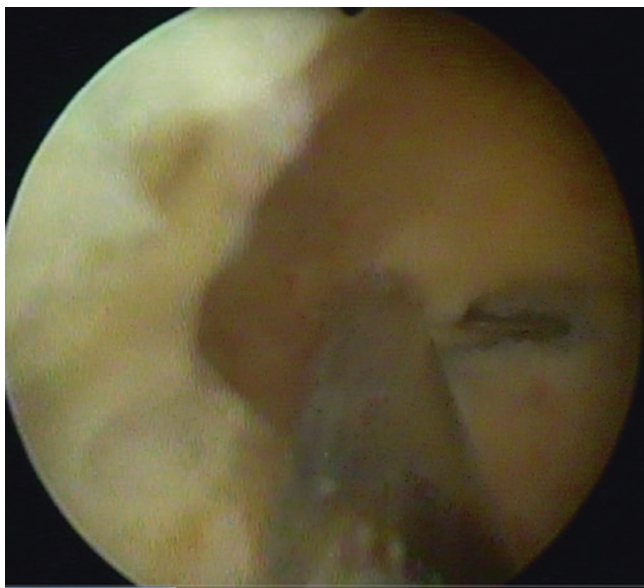


Fig. 62.13 Hysteroscopic adhesiolysis with scissors

complete and one with incomplete obliteration of the uterine cavity, at their facility [70].

Under laparoscopic control, they separated the uterine wall into two hemi-cavities by inserting a 13 French Pratt cervical dilator. The fibrotic septum that was subsequently formed was cut up to the fundus with hysteroscopic scissors. This technique is however not recommended because of the high morbidity associated with it [71].

In a prospective observational study, Protopapas and colleagues described a hysteroscopic technique that involved making 6–8, 4 mm longitudinal incisions into the myometrium extending from the uterine fundus to the isthmus with

a resectoscope fitted with a Collins knife electrode [72]. The aim was to enlarge the uterine cavity hoping to uncover functional endometrium. The amount of menstrual bleeding increased in all cases including two women who were amenorrheic before the procedure. Three to four months after surgery, hysteroscopy showed a normal sized uterine cavity in five cases with three women conceiving four pregnancies including a missed abortion, a tubal abortion, a seven week ongoing pregnancy, and a delivery at 36 weeks following prelabor spontaneous rupture of membranes. Abdominal laparotomy and hysterotomy with direct adhesiolysis were traditional treatments for severe intrauterine adhesions but are rarely done these days, reserved only for severe cases in which other techniques cannot be performed [47].

62.5 Prevention of Adhesion Reformation

It is important to institute measures that would reduce or totally eliminate the chances of adhesion recurrence as this can have deleterious effects on reproductive outcome.

62.5.1 The Intrauterine device (IUD)

This is a physical barrier that separates the walls of the endometrium following adhesiolysis. The IUD of choice was the Lippes loop, whose manufacture was stopped by the pharmaceutical company citing economic reasons [73]. The Copper T IUD has inflammatory properties on the endometrium on account of the copper [74]. It also has the disadvantage of a small surface area [75].

In my practice, some severe cases where it becomes impossible for the uterus to retain a Foley catheter, we still make do with the Copper T IUD after detaching the copper from the arms and stem of the device (the benefit of this however has not been tested).

62.5.2 Intrauterine Foley Catheter

This also acts as a physical barrier and in a non-randomized study comparing its use for 10 days following adhesiolysis compared with IUD insertion for 3 months, there were fewer infections in the Foley group and a lower recurrence rate of intrauterine adhesions following HSG assessment [76]. Amenorrhea following treatment was 19% in the Foley catheter group and 38% in the IUD group. There are limited data supporting a benefit for using a Foley catheter or an IUD after lysis [71].

62.5.3 Intrauterine Balloon Stent

This acts in a similar fashion as the Foley catheter but has the added advantage of being triangular in shape in conformity with the shape of the endometrial cavity. In a recent study of 107 women with Asherman syndrome, the use of the stent compared with either an IUD or hyaluronic acid gel resulted in a significant reduction of adhesions recurrence rate [77].

62.5.4 Intrauterine Gel

Hyaluronic acid is a naturally occurring component of peritoneal fluid that aids in tissue lubrication and structural integrity. A randomized trial comprising 92 women compared postoperative hyaluronic acid gel with polyethylene oxide-sodium carboxymethyl cellulose in preventing the reoccurrence of intrauterine adhesions, with no treatment after hysteroscopic adhesiolysis. A lower rate of adhesions was observed after 3 months in the intrauterine gel group compared to the no treatment group (14% versus 32%) [78]. A recent systematic review and meta-analysis concluded that the intrauterine gels were effective in preventing post-hysteroscopy uterine adhesion formation [79].

62.5.5 Endometrial Regeneration

The aim is to stimulate residual growth of the endometrium after hysteroscopic adhesiolysis. Different estrogen preparations, dosages and duration of treatment have been proposed, with or without a progestogen. No comparative studies have

been performed investigating dosage administration or combination of hormones [71].

Schenker and Margalioth administered estrogen to their patients with placement of an intrauterine device following a D and C for missed abortion, with favorable results [36]. March et al. advocated the use of micronized estradiol 2 mg twice daily for 30–60 days and medroxyprogesterone acetate 10 mg daily for the last 5 days on estradiol [34].

Medications that increase blood flow have been investigated in the postoperative management of intrauterine synechiae. Such medications include aspirin, nitroglycerine, and sildenafil citrate. They are believed to increase blood flow to the endometrium [80–83]. The number of women treated using these therapies is however small.

The American college of Obstetricians and Gynecologists guidelines for antibiotic use in gynecological procedures do not recommend their use for diagnostic or therapeutic hysteroscopy [71].

62.6 Recent Development

This involves work on stem cells. In a woman with severe Asherman syndrome, curettage followed by placement of an IUD and hormonal therapy was tried for 6 months but failed. Autologous stem cells were tried as an alternative therapy, isolated from the patient's bone marrow. Endometrial angiogenic stem cells were separated using immunomagnetic isolation. These cells were placed in the endometrial cavity under ultrasound scan guidance after first carrying out an endometrial curettage. The patient was then placed on cyclical hormonal therapy. Following the development of endometrial thickness up to 8 mm with good vascularity, a clinical pregnancy ensued after IVF treatment [84].

62.7 Follow-Up of Patients and Outcome of Treatment

Follow-up of patients is important in order to detect a recurrence and manage appropriately.

Assessment can be via the following:

- Office hysteroscopy
- Saline infusion sonography
- Hysterosalpingography

Recurrence rate of 33% for mild to moderate and 66% for severe adhesions have been reported [71] and patients therefore need to be properly counseled about the sequelae which includes intrauterine growth restriction, cervical incompetence, preterm births, and morbidly adherent placentation.

62.8 Conclusion and Recommendation

Abortion, whether induced or spontaneous, is an important cause of Asherman syndrome. An effective health education for women, especially teenage and adolescent groups will go a long way in reducing the abortion and hence Asherman syndrome statistics. The highly restrictive abortion laws obtainable in many developing countries have accentuated a rather clandestine approach towards abortion procurement thereby worsening the Asherman syndrome debacle with its attendant sequelae. More liberal abortion laws have been confirmed to stem the tide and are recommended. Finally, proper training and continuous medical education of health personnel, especially on the use of vacuum aspiration, will go a long way in further curbing the menace of Asherman syndrome.

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