

## Review Article

# Hysterosalpingography in the assessment of uterine cavity: A wide spectrum of acquired structural pathology

Firoozeh Ahmadi, Fatemeh Zafarani, Gholam Shahrzad

Department of Reproductive Imaging at Reproductive Biomedicine Research Center, Royan Institute for Reproductive Biomedicine, ACECR, Tehran, Iran

Kuwait Medical Journal 2019; 51 (1): 3 - 15

## ABSTRACT

Hysterosalpingography (HSG) has been used for various indications in clinical gynecology for many years. Despite recent developments in reproductive imaging and various diagnostic options such as magnetic resonance imaging, ultrasonography, laparoscopy and hysteroscopy, HSG is still a quick and minimally invasive method in the early evaluation of infertility. This method provides valuable diagnostic information about the inner surface of the uterine cavity, fallopian tubes and endocervical canal. The technical quality of the HSG is important to avoid misinterpretations.

The teamwork between the gynecologist and radiologist should be presented at HSG for appropriate evaluation and diagnostic workup of infertile couple. This review describes the normal variants and a spectrum of acquired structural pathology involving uterus along with their imaging features on HSG. The radiographic appearances of technical artifacts, normal variants, benign and malignant endometrial neoplasm, intrauterine synechiae, retained products of conception and foreign bodies within the uterine cavity will be discussed.

**KEY WORDS:** acquired uterine abnormalities, hysterosalpingography

## INTRODUCTION

Uterine abnormalities account for about 10 - 15% of the cases of infertility and abnormal uterine findings are reported in approximately in 50% of women with infertility<sup>[1]</sup>. Abnormalities of the uterus can be described as either congenital or acquired. Acquired uterine abnormalities may interfere with uterine structure or function and affect endometrial receptivity that leads to subinfertility, recurrent implantation failures or preterm delivery. As a result, investigation of the uterine cavity is one of the initial steps in female infertility workup. Clinical imaging is essential in stratification of the different abnormalities of the uterus. Despite recent developments in reproductive imaging and various diagnostic options such as magnetic resonance imaging (MRI), ultrasound, laparoscopy and hysteroscopy, hysterosalpingography (HSG) is still a fast and minimally invasive method in the early evaluation of infertility. This method is the radiographic study of the uterine cavity and fallopian tubes after introduction of a radio-opaque contrast through the cervical canal. Although HSG is limited

to evaluate the external uterine contour adequately<sup>[2]</sup>, it provides valuable diagnostic information about the uterine cavity and allows clinicians to observe any filling defects or irregularities, and define the general configuration of the cavity<sup>[3,4]</sup>. In comparison with hysteroscopy, HSG has been reported to have high sensitivity (79 - 81%) and specificity (80 - 82%) in the detection of intrauterine abnormalities<sup>[3,4]</sup>.

We retrospectively reviewed 41,407 HSGs performed over a 31-year period (January 1985 – December 2015) by one author (GS). The indications for HSG were infertility, abnormal uterine bleeding, lost IUD and symptoms related to uterine fibroids.

## LITERATURE REVIEW

The present article intends to review the normal variants and pathological conditions involving uterus along with their imaging features on HSG. These findings should be considered by all radiologists and gynecologists for precise diagnosis and optimal management.

The cases with structural lesions, such as

### Address correspondence to:

Fatemeh Zafarani, Department of Reproductive Imaging at Reproductive Biomedicine Research Center, Royan Institute for Reproductive Biomedicine, ACECR, P.O.Box: 16635-148-Tehran, Iran. Tel: +98 21 235 621 42; Fax: +98 21 235 621 72; Email: fzafarani@royaninstitute.org, fzafarani1391@gmail.com

endometrial polyp, leiomyoma, endometrial hyperplasia and carcinoma, adenomyosis, intrauterine synechiae, early pregnancy, and retained products of conception were confirmed by other diagnostic tools such as hysteroscopy with directed biopsy, ultrasound and/or cytological results.

### Embryology of female genital tract

Around the 6<sup>th</sup> week of development, the female embryo's reproductive system begins growth from the paired Müllerian (paramesonephric) ducts, fusing to create the uterus, cervix, and upper two-thirds of the vagina. The process involves three main stages including the development of both Mullerian ducts, fusion, and septal absorption that form the fallopian tube, uterus, cervix and upper two thirds of the vagina. At week 12, the uterus presents its triangular configuration. Mesonephric or Wolffian ducts play an important role as inductors for development of Müllerian ducts. There is controversy over formation of the vagina. The results of most studies have demonstrated that the vagina forms from both mesonephric ducts and Mullerian tubercle<sup>[5]</sup>.

By week 20, the vagina is completely canalized and the process of development is completed.

### Radiographic anatomy of the uterus

The uterine cavity is variable in shape and size. In the normally anteflexed uterus, the uterine cavity is observed as inverted triangular. The contour of the fundus may be straight, convex or slightly concave. Mild fundic concavity is normal and differentiated from a malformed arcuate uterus. An arcuate uterus should be characterized when the ratio between the height of the fundal indentation and the distance between the lateral apices of the horns is less than 10%<sup>[6]</sup>.

The convexity of the fundal outline is moderate unless the whole uterine cavity is overestimated by a large amount of contrast material introduced under high pressure or extreme antero-posterior flexion is present. The lateral margins of the uterine cavity may be straight, concave or (rarely) convex.

The normal radiographic appearance of the cornual lumen is pear-shaped and may be separated from the uterine cavity by a short lucent line. This linear lucency is owing to the localized muscular contraction corresponding to the tubal sphincter.

Lateral displacement of the uterus is considered a common normal variant, unless the other evidence of a pathologic process causes uterine displacement.

The uterine isthmus is the transition between the cervix and the uterine body. Its length and width are approximately 1.5 cm and 0.05 cm respectively<sup>[6]</sup>. Some patients show a well-defined, narrow internal os and

others show virtually no definition of the internal os, having a gradual, funnel-shaped internal os. The diameter of internal os ranges from 1 - 10 mm. The diameter of the internal os varies in the same patient during different phases of the menstrual cycle.

### Patient preparation

Specific patient preparation is not required for HSG. The patient should be instructed to abstain from sexual intercourse from the time menstrual bleeding ends until the day of the study to avoid a potential pregnancy. Most patients can tolerate the procedure with minimal discomfort.

However, in cases suspicious for tubal occlusion, the patients may have more pelvic pain, thus requiring a slower medium injection. Prior to the procedure, a patient may be given a mild sedative or a pain relief medication to minimize any potential discomfort. Administration of one of the prostaglandin synthesizer inhibitors 30 minutes before the procedure reduces the patient's discomfort and diminishes errors associated with HSG<sup>[7]</sup>. Some physicians prescribe an antibiotic prior to and/or after the procedure. The choice antibiotic is doxycycline, 100 mg twice daily, starting the day before HSG and continuing for 3 to 5 days<sup>[7]</sup>.

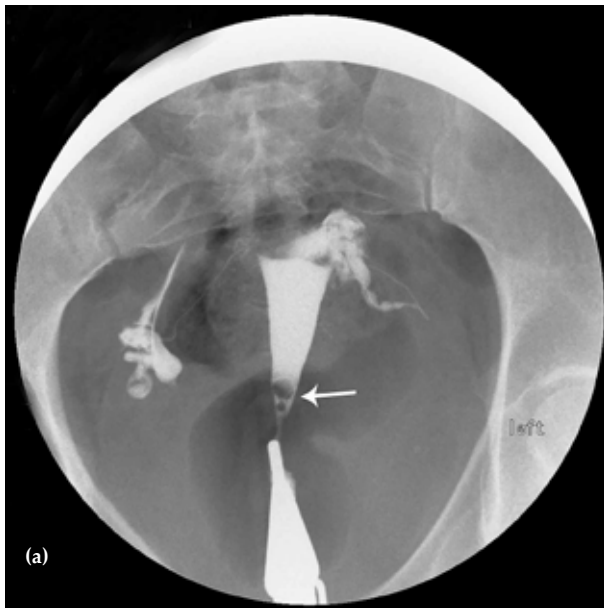
### Indications and contraindications

HSG is recommended for any condition that requires morphological demonstration of the endocervical canal, uterine cavity and uterine tubes for clinical decisions. It is indicated in early evaluation of the infertile couple. Potentially serious causes contributing to infertility, such as tubal occlusion, intrauterine synechiae or uterine anomalies are diagnosed readily<sup>[7]</sup>. The procedure is often used to examine the reasons that may be associated with repeated miscarriages<sup>[8]</sup>. Recently, HSG has become important prior to using assisted reproductive methods, such as gamete and zygote intrafallopian transfer and in vitro fertilization and is an integral part of transcervical tubal recanalization techniques<sup>[9]</sup>. The other advantage of HSG for infertile couples is the therapeutic effect of the procedure. It has been recognized that, after a normal HSG finding, the infertile patient has a 30% chance to conceive spontaneously within the first 3 months<sup>[9]</sup>.

Contraindications for HSG are acute pelvic inflammatory disease with abdominal tenderness or palpable mass, recent uterine and tubal surgery, active uterine bleeding, pregnancy and allergic reaction to the contrast medium<sup>[7]</sup>.

### Normal variants and non pathological findings

The radiographic appearance of the uterine cavity and tubes is affected by various factors such



**Fig 1a:** Large filling defect in the lower segment of the uterus (arrow) owing to introduction of an air bubble into the uterine cavity during HSG. The air bubble was removed by the additional injection of contrast into the uterine cavity.

as technique of HSG, type of contrast medium used, and the amount and pressure of the contrast material injected. The technical quality of the HSG is important to provide sufficient information for proper interpretation. Variation in the position of the normal uterus or cyclic changes in the endometrium may cause a different normal appearance.

### Technical artifact

#### Air bubble

Air bubbles may be inadvertently injected into the uterine cavity during HSG and sometimes mistaken for other intrauterine filling defects such as polyps, submucosal myomas, or endometrial hyperplasia. Air bubbles manifest as transient solitary or multiple rounds, well-circumscribed lucencies which are usually identified by their mobility (Fig 1a)<sup>[10,11]</sup>. Another indication to prove its true nature is that they collect in the non-dependent portion of the uterus when the patient turns.

Introduction of air bubbles can be prevented by introducing the instrument into contrast medium prior to initiation of the procedure. Air bubble is usually removed by additional injection of contrast material to the uterine cavity.

#### Cervical mucus and blood clots

Sometimes cervical mucus is retrogradely pushed through the uterine cavity and produces an unusual filling defect. On HSG, an amorphous mass often appears in linear shape without obvious rounded



**Fig 1b:** Mucus plugging pushed through the uterine cavity produced a linear-shaped filling defect without a rounded contour (arrow). Following image shows vanishing of this mobile filling defect.

contour (Fig 1b). The subsequent image represents disappearing of this mobile filling defect.

Blood clots owing to either pre-existing bleeding or trauma of the instrumentation are another cause of such mobile filling artifacts, which should be differentiated from a polyp or submucosal myoma. Usually, blood clots are mobile and displaced by more injection of contrast into the uterine cavity. Transvaginal ultrasound is useful in the assessment of blood clots. A thin endometrial lining with echogenic material within the endometrial cavity separating from uterine is suggestive of adherent blood clots.

#### Venous or lymphatic intravasation

Intravasation of contrast media into the venous plexus or lymphatic system can occur in up to 6% of patients undergoing HSG<sup>[12]</sup>. The contrast transits from the uterine cavity directly to myometrial vessels, subsequently entering the pelvic veins.

The most common causative factor is excessive pressure within the uterine cavity during injection<sup>[12]</sup>. Other predisposing factors are recent endometrial instrumentation (surgery, biopsy, endometritis, dilatation and curettage), acute endometritis, tubal occlusion and synechiae; especially when intrauterine pressure is markedly elevated.

Intravasation of contrast is diagnosed by HSG. The radiographic appearance of early intravasation is represented as filling of multiple thin beaded channels following an ascendant course (Fig 2). When vascular channels are outlined by contrast, their appearances are transitory and become clear in seconds as a reflection of normal blood flow. Contrast in thin delicate lymphatics is differentiated from blood vessels by their thinner caliber and slower emptying.



Fig 2: Intravasation of contrast medium into the venous and lymphatic channels (arrows) secondary to bilateral tubal occlusion.

### Tubal spasm

Fallopian tube spasm is a temporary tubal muscle contraction which mimics a true proximal tubal obstruction. At radiography, tubal spasm cannot be distinguished from a tubal occlusion. Tubal spasm usually occurs in patients with high levels of stress and anxiety<sup>[13]</sup>. Cornual spasm should be differentiated from true organic obstruction of the proximal fallopian tube. Many drugs such as analgesia and antispasmodic agents have been administered to reduce lower abdominal pain and to prevent tubal muscular spasms.

Rotation of the patient toward the non-filling side or placing her prone while introducing more contrast often reveals previously non-visualized tubes.

### Normal variants

#### Myometrial folds

Normal myometrial folds are multiple longitudinal linear filling defects parallel to the long axis of the uterine cavity and appear in 0.6% of HSGs<sup>[14]</sup>. They are usually observed at 5 - 10 mm linear defects in early stages of HSG (Fig 3). Although the exact etiology is unknown, it is probably the result of undulations on the inner surface of the myometrium or the remnants of mullerian duct fusion during fetal development. These folds are not associated with endometrial abnormalities and are diagnosed by HSG.



Fig 3: Longitudinal myometrial uterine folds parallel to the long axis of the uterine cavity (arrows) owing to undulation of the inner surface of the myometrium.

#### Double-outlined uterine cavity

HSG should be scheduled during the proliferative phase, 2 - 5 days after cessation of menstrual flow. The procedure should be avoided during an early pregnancy. If HSG is performed during the late secretory phase or if it is accidentally done on an early pregnancy patient, a double uterine contour may be seen as a thin line of contrast that surrounds the uterine cavity (Fig 4). This rare normal variation



Fig 4: Double outlined uterine cavity (DOUC). Hystero-graphic double outline uterine cavity following contrast penetrating endometrial gland in secretory phase (arrow).

occurs in about 1% of HSGs and is not associated with infertility or obstetric complications<sup>[15]</sup>.

### Spiculated uterine cavity

Fine spiculation of the uterine cavity is occasionally visible on HSGs by using water-soluble contrast material. The cause of these spiculations is not clear. This spiculation may be associated with a thin, inactive endometrial and atrophic uterus, caused by lack of hormonal stimulation (both pre-and postmenopausal), exogenous hormonal suppression and sometimes other pathologic conditions such as tuberculosis<sup>[16]</sup>. Occasionally, the contrast medium may have entered mucosal glands, possibly due to pressure of the injection and the impairing of endometrial surface, and produce spiculated uterine appearance (Fig 5). Available method for its diagnosis is HSG<sup>[3]</sup>. HSG shows uterus with diffuse irregularities and spiculated aspects.

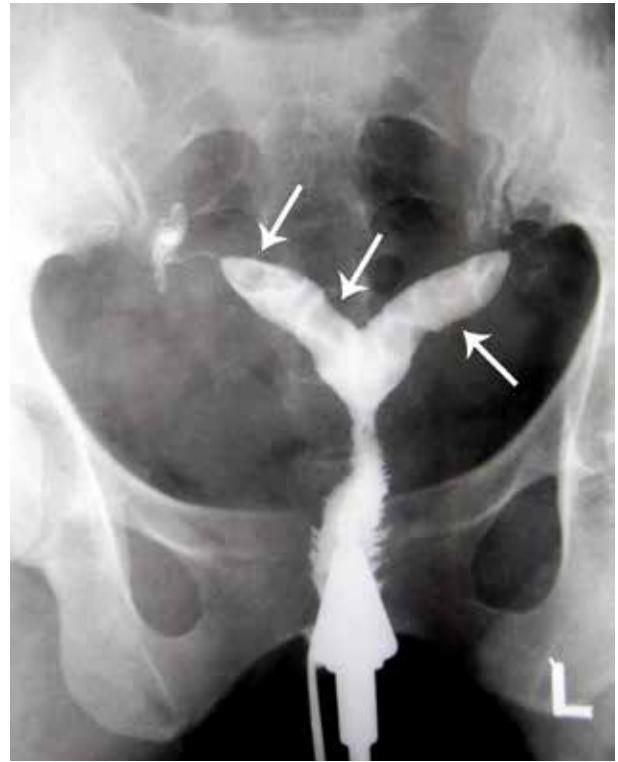
### Polypoid defects in uterine cavity

Sometimes, normal endometrium shows polypoid filling defects ranging from 5 mm to 10 mm in diameter without any clinical importance<sup>[17]</sup>.



**Fig 5:** Fine spiculation in a pre-menopausal uterine cavity (long arrow). Hysterosalpingography of a woman with a history of abnormal uterine bleeding showed entrance of contrast into the mucosal glands. The biopsy showed atrophic endometrium. Note the filling defect observed in cervical canal was owing to rapid evacuation of contrast medium. It is not pathologically significant (short arrow).

This normal variation should not be confused with endometrial hyperplasia producing a shaggy and irregular contour in the contrast medium, found in patients with a history of amenorrhea and menstrual irregularities. Hysterosalpingographic features of the polypoid filling defects are similar to small submucous leiomyomas or endometrial polyps (Fig 6).



**Fig 6:** Multiple filling defects in a septate uterus (arrows). The patient had a history of oligomenorrhea. Note the normal contour and size of the uterine cavity. This normal variation should not be confused with endometrial hyperplasia which produces a shaggy and irregular contour.

On transvaginal sonography, the endometrium is asymmetrically thickened and irregular. In doppler evaluation, the presence of color flow within the lesion, excludes polypoid defects from a blood clot.

Moreover, further hysteroscopic investigation provides a more precise analysis of this normal endometrial variation from submucous leiomyomas and polyps.

### Acquired structural abnormalities of the uterus

The uterine cavity shows various imaging manifestations in addition to the normal manifestation such as reactive, inflammatory, benign and malignant neoplasm. Intrauterine abnormalities can be found only if they are of sufficient size, distort the uterine cavity or present as a mass with displacement of the contrast medium. Acquired uterine abnormalities are an important cause of infertility. Intrauterine

abnormalities often present as filling defects, outpouchings or uterine wall irregularities. Abnormalities of the uterine cavity which can be diagnosed by HSG are endometrial lesions such as benign/malignant endometrial neoplasms, intrauterine synechiae; abnormalities of the myometrium include submucous and intramural leiomyomas as well as foreign bodies in the uterine cavity.

## Uterine neoplasms

### Endometrial polyp

Endometrial polyps are common benign localized endometrial tumors, which are usually found in women between 40 and 50 years of age<sup>[18]</sup>.

The prevalence of endometrial polyps ranges from 10%<sup>[18]</sup> in symptomatic women to 33%<sup>[19]</sup> in symptomatic patients, but polyps is much higher in postmenopausal women<sup>[20]</sup>. Clinically endometrial polyp can cause abnormal uterine bleeding, infertility, recurrent abortion, infection endometritis or pain.

Abnormal bleeding mostly results from vascular fragility, chronic inflammatory changes and surface erosions. Endometrial polyps may occur in the setting of endometrial hyperplasia or less commonly, carcinoma<sup>[21]</sup>. Hormonal factors in patients taking hormone replacement therapy<sup>[22]</sup> or tamoxifen treated women<sup>[23]</sup> may be associated with endometrial abnormalities such as polyp.

Endometrial polyps can be single or multiple, small or large, pedunculated or sessile. Recognition of endometrial polyps is very important to avoid unnecessary operation.

On HSG, the endometrial polyp appears as a persistent round filling defect which is regular and sharply outlined (Fig 7). The uterine cavity has normal size and shape. The lateral borders of the uterine cavity may represent some irregularities produced by the attachment of the sessile type of polyps. Endometrial polyps are better visualized when small amounts of contrast medium is introduced into the uterine cavity, since large amounts of medium may obscure the defect. The polyps must be distinguished from air bubbles, submucosal leiomyomas, synechiae, adenomyosis and normal functional variants by their fixed position, oval shape and more rounded and regular appearance.

Polyps may appear as a thickened area of endometrium with a transvaginal sonography. Although polyps can be seen by ultrasound in the follicular phase, they are more accurately visualized by hysterosonography during the periovulatory phase, when surrounded by anechoic fluid. On HSG, they look like an echogenic mass with smooth edges. Polyps are infrequently illustrated as an irregular marginated echogenic endometrial mass.

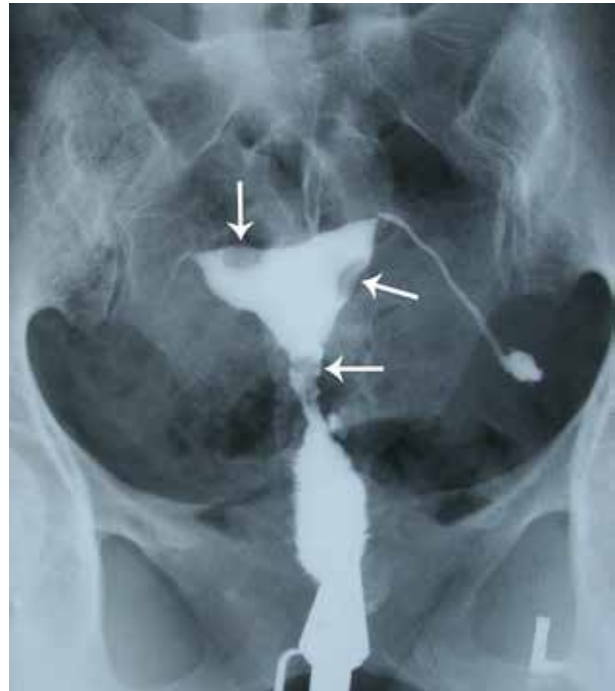


Fig 7: Multiple oval-shaped filling defects which are distributed in the uterine cavity (arrows). This feature is distinguished from air bubbles by the fixed position after injection of additional medium.

### Leiomyoma

Leiomyomas or fibroids are the most common benign uterine tumor that may occur in more than 30% of women of reproductive age<sup>[24]</sup>. This monoclonal tumor consists of uterine smooth muscle and large amounts of extracellular matrix including collagen, fibronectin, and proteoglycan. The target risk factors include obesity, nulliparity, diabetes, polycystic ovary, familial history, black race and hypertension<sup>[2]</sup>. Cytogenetic abnormalities, particularly deletions of chromosome 7 have been identified in up to 50% of leiomyoma specimens<sup>[25]</sup>.

Uterine leiomyoma are often asymptomatic, but they may be associated with abnormal uterine bleeding, urinary incontinence or retention, pelvic pain and reproductive dysfunction such as infertility, recurrent miscarriage and premature labor<sup>[26]</sup>. As a neoplasm, small percentages of leiomyomas undergo malignant transformation<sup>[27]</sup>.

They vary in size from buds to massive uterine tumors. They may be single or multiple, and are classified into three types depending on the location: submucosal (least common), intramural (most common), and subserosal. Most leiomyomas are hybrids and have more than one anatomical location.

Leiomyomas show a broad spectrum of radiographic appearances, depending on their number, size and location relative to the uterine cavity<sup>[28]</sup>.



**Fig 8:** Spectrum of radiographic findings of leiomyoma, depending on the number, size, and location of tumor. **(a)** Smooth fundal submucosal leiomyoma giving a concavity in the central area (arrow). The uterus simulates an arcuate uterus. **(b)** Multiple submucosal leiomyoma produce a bizarre radiographic appearance (arrows). Note the marked stretching, deformity and enlargement of the cavity requiring large amounts of contrast material. **(c)** Asymmetric enlargement of the uterus due to intramural/ submucosal leiomyoma of the right uterine wall. Elongation, distortion and compression of the uterine cavity giving the crescent sign (arrows). The right tube is stretched over the surface of the tumor. **(d)** Large calcified subserosal leiomyoma with elongation of left uterine wall. **(e)** Pedunculated subserosal leiomyomas which is attached to the uterus by a narrow stalk.

Hysteroscopy is considered the gold standard for identification of a submucosal leiomyoma<sup>[29]</sup>. A submucosal leiomyoma must be differentiated from air bubbles, endometrial polyps, blood clots, and retained products of conception. Large masses may cause generalized enlargement of the uterine cavity. Submucosal leiomyoma usually distort the uterine contour and size (Fig 8 a and b). Polyps are smaller and more sharply outlined than submucosal fibroids, while blood clots and retained placenta have more angular outlines. Intramural leiomyomas may enlarge, distort, displace and rotate the uterine cavity. Asymmetric enlargement of the uterus produced by large intramural or subserosal myoma gives the uterus a crescenting appearance (Fig 8c).

Smooth and symmetric fundal myomas may simulate a subseptate or bicornuate uterus (Fig 8a).

Subserosal myomas will not be apparent on hystero-grams unless they are large enough to cause obvious displacement of the uterus. Subserosal leiomyomas may also be pedunculated and they are attached to the uterus by a narrow stalk (Figs 8 d and e). Subserosal leiomyomas should be differentiated from solid ovarian and pelvic tumors. Since leiomyomas are responsive to estrogen, they tend to regress after menopause.

#### Endometrial hyperplasia

Endometrial hyperplasia is characterized by a proliferation of endometrial glands of irregular size

and shape with an increase in gland/stroma ratio compared to normal proliferative endometrium<sup>[30]</sup>. It is caused by endometrial stimulation by unopposed estrogen and is a common cause of dysfunctional bleeding in pre- and postmenopausal women<sup>[31]</sup>.

The World Health Organization classifies endometrial hyperplasia into two broad categories: hyperplasia without cytologic atypia and hyperplasia with cytologic atypia<sup>[32]</sup>. These two main categories are further subdivided into simple or complex, based on the extent of glandular texture<sup>[32]</sup>.

Several imaging tools including HSG, ultrasound, hysterosonography, and MRI can be applied to evaluate suspected endometrial hyperplasia, but hysteroscopy with directed biopsy is considered the gold standard in the differential diagnosis of hyperplasia and different subtypes<sup>[33]</sup>.

Radiographic feature of endometrial hyperplasia depends on the gross appearance of endometrial hyperplasia and is variable. In cases with normal endometrial thickness, the outline of the uterine cavity is regular and smooth; however, in patients with moderately thickened hyperplastic endometrium, some irregularity in the inner surface of the uterine wall is present (Fig 9 a). When the endometrium is polypoid, the uterine shadow shows variations in density and projections of lesions may be seen as well (Figs 9 b and c). In such cases, the border of defects is usually smoother than in cases of carcinoma, but a certain diagnosis is made after histological examination.

Hysterograms performed during the secretory phase of the menstrual cycle demonstrate a very prominent mucosal pattern, which should not be confused with endometrial hyperplasia. Other sources of misinterpretation include mucus secretions

and blood clots within the uterine cavity and endometrial polyps. Endometrial hyperplasia should be differentiated from tuberculosis endometritis. In endometrial tuberculosis, uterine tubes are often involved and irregularity in the uterine borders which mimic heterogeneous thickening are observed.

### Endometrial carcinoma

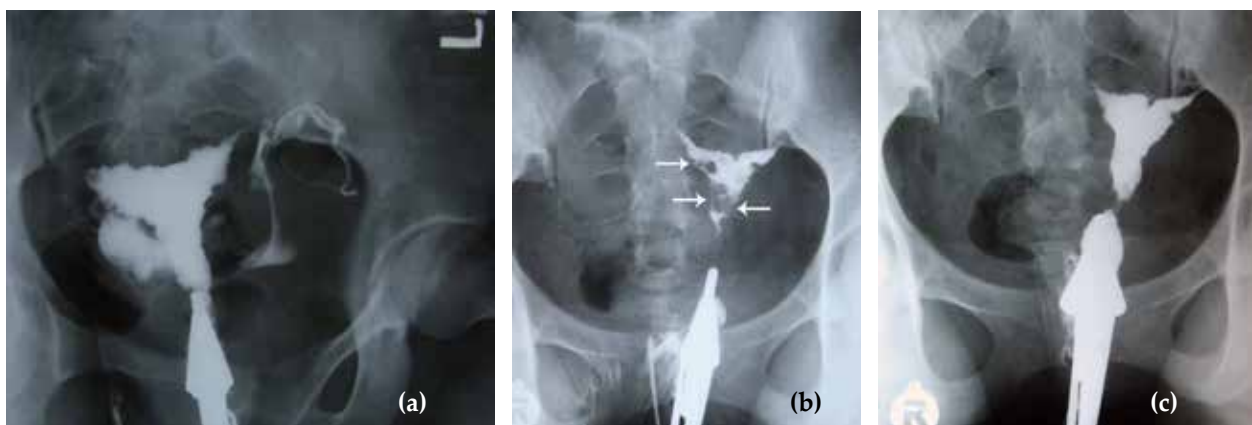
Uterine cancer is the fourth most common malignancy in women and most commonly affects postmenopausal women, particularly in the sixth and seventh decades, while less than 5% occurs in women under 40 years of age<sup>[34]</sup>.

Several risk factors have been identified for the development of endometrial cancer. Nulliparity, unopposed estrogen replacement therapy, adenomatous endometrial hyperplasia, polycystic ovary syndrome, diabetes mellitus, hypertension and obesity are associated with an increased risk of developing endometrial cancer<sup>[35]</sup>.

The presenting symptom in 75 - 90% of patients is postmenopausal or intermenstrual bleeding or spotting, which often has been investigated by endometrial biopsy or dilation and curettage<sup>[35]</sup>.

HSG is not routinely used for the investigation of uterine malignancy, but it may occasionally reveal an endometrial carcinoma. In the past, HSG has been used in patients with suspected endometrial carcinoma and the technique was useful to predict the volume and distribution of the tumor, to differentiate between benign and malignant lesions, and to diagnose the point of maximum invasion of tumor to modify patient management<sup>[36,37]</sup>.

Radiographic findings of endometrial carcinoma vary from case to case<sup>[36]</sup>. The malignancy may be detected as a solitary growth, often in the uterine



**Fig 9:** Spectrum of radiographic finding of endometrial hyperplasia depending on the gross appearance of lesion in two different patients. (a) Thickened endometrial mucosa with a diffusely irregular outline. The endometrial biopsy confirmed endometrial hyperplasia. (b) Early filling view of uterine cavity shows polypoid filling defect secondary to endometrial hyperplasia (arrows). (c) This pattern was hidden completely with further filling. The diagnosis was confirmed by biopsy.



fundus, as a multiple circumscribed tumor, a diffuse spreading lesion, or as a process filling defect in the uterine cavity. In cases with well-defined extensive tumor, HSG represents a smooth and localized filling defect, whereas in patients with slightly exophytic, ill-defined and widely extensive lesion, an irregularity in the outline of uterine contour is present (Fig 10).



**Fig 10:** Extensive involvement of the uterine cavity by endometrial carcinoma. Hysterosalpingogram shows irregular shaggy outline of the cavity. The diagnosis was confirmed after surgery.

The differential diagnosis includes large polyps for the smooth masses and severe endometrial hyperplasia for infiltrate tumors. Both polyps and hyperplasia usually have a less aggressive appearance than that of carcinoma.

### Adenomyosis

Adenomyosis is a benign condition of the uterus characterized by the infiltration of endometrial stroma and glands into the myometrium.

The etiology is unclear, but it is generally accepted that adenomyosis occurs when the normal boundary between the basal layer of endometrium and the myometrium is damaged and the endometrium is exposed to direct contact with the myometrium. Adenomyosis has been found in 10 - 50% of uteri examined at autopsy and in 5.6% to 61.5% of surgical specimens<sup>[38]</sup>.

Adenomyosis is characterized by the ingrowing of the endometrial tissue into the myometrium with adjacent smooth muscle hyperplasia. The degree of invasion is variable and can involve the whole uterine wall up to the serosa.

Adenomyosis is usually asymptomatic, but it may be presented by uterine bleeding, dysmenorrhea, dyspareunia, metrorrhagia, and infertility<sup>[33]</sup>. These symptoms are non-specific and can occur as part of many other gynecological disorders.

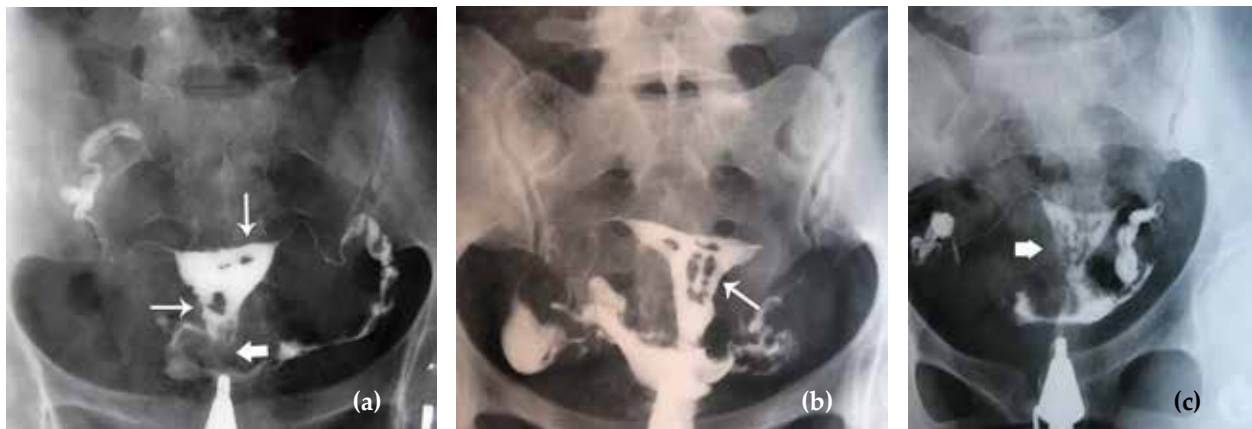
HSG was the first imaging tool utilized for the diagnosis of adenomyosis. The characteristic findings on HSG are mild to moderate enlargement of the uterine cavity and the presence of small rounded or oval diverticulum-like structures (1 - 2mm) that extend from the border of the uterine cavity into the walls of the uterus presenting a honeycomb appearance<sup>[39]</sup>. The diverticuli may be localized to one area or involve the uterine wall diffusely (Fig 11).



**Fig 11:** Uterine adenomyosis. Multiple, generalized and variable-sized diverticula extending perpendicularly from the endometrium into the uterine wall (arrows).

The ultrasound features of adenomyosis are often subtle and extremely variable. The most common findings on transvaginal sonography in the patient with adenomyosis are poorly marginated hypoechogenic and heterogeneous areas (Swiss cheese appearance). In about 50% of the cases, small (1 - 6 mm) myometrial cysts are present<sup>[40]</sup>.

The differential diagnosis includes localized intravasation of contrast into myometrial vascular channels and endometrial hyperplasia. Intravasated contrast medium is rapidly vanished from the veins,



**Fig 12:** The categories of intrauterine adhesion classified by both hysterosalpingographic and hysteroscopic criteria and menstrual pattern, which is diagnosed by HSG (a) Mild intrauterine adhesion; if adhesions involve one-fourth of the uterine cavity (arrows). Large filling defect in the lower segment of the uterus (open arrow) is owing to introduction of an air bubble into the uterine cavity during hysterosalpingography, (b) Moderate intrauterine adhesion, if adhesions involve one-half of the uterine cavity (arrow), (c) Severe intrauterine adhesion, if adhesions involve three-fourths of the uterine cavity (open arrow).

whereas it persists within adenomyotic diverticula or sinuses. Endometrial hyperplasia is characterized on HSG by irregularities of the contours of the uterine cavity and variations in density of the uterine shadow.

When adenomyosis and endometrial hyperplasia coexist, precise diagnosis may be difficult. Confusion may sometimes occur with the diverticula seen in HSGs after cesarean sections, which are different in character from those of adenomyosis. They are large and usually single in comparison to the small and usually multiple sinuses found in adenomyosis.

### Intrauterine adhesion

Intrauterine adhesion, known as an acquired uterine condition, is characterized by the destruction of endometrium which may produce subsequent scar in endometrium and expansion of scar tissue band within the uterine cavity. Asherman described the association of intrauterine adhesions both with menstrual dysfunction, especially hypomenorrhea, and with infertility<sup>[41]</sup>. Uterine synechiae is caused by trauma to the basal layer of the endometrium, generally following curettage<sup>[41]</sup>. However, any uterine surgery (myomectomy, cesarean section, or repair of Müllerian anomalies) or endometrial infection owing to schistosomiasis, genital tuberculosis and intrauterine devices may lead to intrauterine synechiae<sup>[41]</sup>. The main symptoms are infertility (43%) and menstrual disorders (62%), followed by amenorrhea<sup>[41]</sup>.

Scarring may range from minor filmy synechiae that affects a small area of the uterine wall with no reproductive consequences to severe diffuse involvement of the uterine cavity that affects menstrual function and fertility due to extensive obliteration and destruction of the endometrial cavity.

According to severity stages of synechiae diagnosed by both hysterosalpingographic and hysteroscopic criteria and menstrual pattern, intrauterine adhesion is classified into three categories: mild (involvement of 1/4), moderate (involvement of 1/2), and severe (involvement of 3/4 or more)<sup>[41]</sup> (Figs 12 a-c).

HSG can show both extent and the location of the synechiae. The radiographic feature of intrauterine adhesions varies with the sites and the degree of involvement. Synechiae appear as filling defects that distort the contour of the uterine cavity; they typically have an irregular, angulated shape and are immobile. They are readily defined because the uterine walls are adhered and contrast material does not completely surround the filling defects. Occasionally, synechiae may obliterate the whole endometrial cavity or obstruct the lower uterine segment and allow contrast opacification of only a short segment of the blunt-ending to cervical canal giving Glove's finger appearance (Netter syndrome)<sup>[42]</sup> (Fig 13).

In cases with extensive symmetrical obliteration of the uterine cavity, sometimes the cavity is smaller than its normal size and gives the appearance of an infantile uterus. A history of previous endometrial trauma or disease, as well as clinical and sonographic signs can be useful in this particular situation. On ultrasound, adhesions are observed as endometrial irregularities or hypoechoic bridges within the endometrial cavity. Intrauterine synechiae do not present with increased vascularity on color Doppler examination<sup>[43]</sup>. Three-dimensional ultrasound demonstrates a significant reduction of the endometrial cavity volume in all reformed sections<sup>[44]</sup>.



**Fig 13:** Netter syndrome. Total obliteration of the uterine cavity following endometrial tuberculosis allows contrast opacification of only a short segment of the blunt-ending cervical canal, and gives Glove's finger appearance (arrow).

### Retained products of conception

Inadvertently, retained products of conception following spontaneous pregnancy loss may be detected within the endometrial cavity on HSG. The symptoms include irregular bleeding, dysmenorrhea, dyspareunia, chronic pelvic pain and a high risk of secondary infertility<sup>[45]</sup>.

It may be completely asymptomatic and found only during a preliminary pelvic ultrasound as part of a routine infertility workup. Although HSG is useful in outlining the endometrial cavity and in determination the state of fallopian tubes; its utility in the diagnosis of retained fetal products is limited. Hysterosalpingographic features are asymmetrical enlargement, irregularity in the border of the uterus and filling defects (Fig 14).

### Intrauterine device

Intrauterine device (IUD) as a contraceptive device was firstly introduced by Richard Richter in 1909 and now it is a common form of birth control<sup>[46]</sup>. These small devices fit into the uterus and provide long-term contraception. In rare cases, the IUD can be pushed through the wall of the uterus and uterine perforation



**Fig 14:** Hysterosalpingography in a patient with a history of recent pregnancy loss; asymmetrical enlargement, irregularity in the border of the uterus and filling defects in the cornua containing retained conception products are seen. Intravasation of contrast material is also present (arrow).



**Fig 15:** Radiographic image verified a Copper T IUD was completely outside of the uterine cavity (arrow).

into the peritoneal cavity or uterine musculature, but both perforations are usually asymptomatic<sup>[47]</sup>. HSG should be performed to check the relationship between the uterus and the site of the IUD (Fig 15). Lost IUDs may tear into or through uterine wall or through cervix into the vagina.

## CONCLUSION

Morphological evaluation of the intrauterine cavity and tubal patency is indicated for many clinical conditions in gynecology clinic and infertility workup. Although HSG is limited to evaluate the external uterine contour adequately, it potentially allows clinicians to diagnose any filling defects or irregularities contributing to infertility.

Modern radiographic equipment by using a fluoroscopic control system provides an ability to observe sequential filling of the uterine cavity and fallopian tubes. An accurate interpretation of the HSG is essential to prevent unnecessary and aggressive treatment.

## ACKNOWLEDGMENTS

This study was supported by the Department of Reproductive Imaging of Royan Institute. There was no conflict of interest in this pictorial review.

## REFERENCES

- Brown SE, Coddington CC, Schnorr J, Toner JP, Gibbons W, Oehninger S. Evaluation of outpatient hysteroscopy, saline infusion hysterosonography, and hysterosalpingography in infertile women: a prospective, randomized study. *Fertil Steril* 2000; 74(5):1029-1034.
- Braun P, Grau FV, Pons RM, Enguix DP. Is hysterosalpingography able to diagnose all uterine malformations correctly? A retrospective study. *Eur J Radiol* 2005; 53(2):274-279.
- Roma Dalfó A, Ubeda B, Ubeda A, Monzon M, Rotger R, Ramos R, *et al.* Diagnostic value of hysterosalpingography in the detection of intrauterine abnormalities: a comparison with hysteroscopy. *AJR Am J Roentgenol* 2004; 183(5):1405-1409.
- Gaglione R, Valentini AL, Pistilli E, Nuzzi NP. A comparison of hysteroscopy and hysterosalpingography. *Int J Gynaecol Obstet* 1996; 52(2):151-153.
- Ación P, Ación MI. The history of female genital tract malformation classifications and proposal of an updated system. *Hum Reprod Update* 2011; 17(5):693-705.
- Chen MYM, Zagoria RJ. Normal radiographic anatomy. In: Ott DJ, Fayeze JA, Zagoria RJ, eds. *Hysterosalpingography: a text and atlas*. 2<sup>nd</sup> edn. Baltimore, MD: Lippincott Williams & Wilkins; 1998; p. 29-39.
- Yao MWM, Schust DJ. Infertility. In: Berek JS, Adashi EY, Hillard PJA, editors. *Novak's gynecology*. 13th ed. Philadelphia: Lippincott, Williams & Wilkins; 2002; p. 973-1066.
- Proctor JA, Haney AF. Recurrent first trimester pregnancy loss is associated with uterine septum but not with bicornuate uterus. *Fertil Steril* 2003; 80(5):1212-1215.
- Dhaliwal LK, Gupta KR, Aggarwal N. Is hysterosalpingography an important tool in modern gynecological practice? *Int J Fertil Womens Med* 1999; 44(4):212-215.
- Simpson WL Jr, Beitia LG, Mester J. Hysterosalpingography: a reemerging study. *Radiographics* 2006; 26(2):419-431.
- Eng CW, Tang PH, Ong CL. Hysterosalpingography: current applications. *Singapore Med J* 2007; 48(4):368-373.
- Yoder IC. Hysterosalpingography and pelvic ultrasound: imaging in infertility and gynecology. Boston: Little, Brown. 1983; 23-28, 133-193.
- Yoder IC (ed). Disease of the fallopian tube. In: *Hysterosalpingography and pelvic ultrasound*. Little brown, Boston, 1988; pp37-82.
- Slezak P, Tillinger KG. The occurrence and significance of broad longitudinal folds in the uterine cavity at hystero-graphy. *Radiology* 1973; 106(1):87-90.
- Slezak P, Tillinger KG. The occurrence and significance of a double-outlined uterine cavity (DOUC) in the hystero-graphic picture. *Radiology* 1968; 90(4):756-760.
- Slezak P, Tillinger KG. The significance of the spiculated outline of the uterine cavity on hystero-graphy. *Radiology* 1973; 107(3):527-531.
- Slezak P, Tillinger KG. Hystero-graphic evidence of polypoid filling defects in the uterine cavity. *Radiology* 1975; 115(1):79-83.
- Pereira N, Petrini AC, Lekovich JP, Elias RT, Spandorfer SD. Surgical management of endometrial polyps in infertile women: a comprehensive review. *Surg Res Pract* 2015; 2015:914390.
- Clevenger-Hoeft M, Syrop CH, Stovall DW, Van Voorhis BJ. Sonohystero-graphy in premenopausal women with and without abnormal bleeding. *Obstet Gynecol* 1999; 94(4):516-520.
- Salim S, Won H, Nesbitt-Hawes E, Campbell N, Abbott J. Diagnosis and management of endometrial polyps: a critical review of the literature. *J Minim Invasive Gynecol* 2011; 18(5):569-581.
- Antunes A Jr, Costa-Paiva L, Arthuso M, Costa JV, Pinto-Neto AM. Endometrial polyps in pre- and postmenopausal women: factors associated with malignancy. *Maturitas* 2007; 57(4):415-421.
- Orvieto R, Bar-Hava I, Dicker D, Bar J, Ben-Rafael Z, Neri A. Endometrial polyps during menopause: characterization and significance. *Acta Obstet Gynecol Scand* 1999; 78(10):883-886.
- McGurgan P, Taylor LJ, Duffy SR, O'Donovan PJ. Does tamoxifen therapy affect the hormone receptor expression and cell proliferation indices of endometrial polyps? An immunohistochemical comparison of

- endometrial polyps from postmenopausal women exposed and not exposed to tamoxifen. *Maturitas* 2006; 54(3):252-259.
24. Evans P, Brunsell S. Uterine fibroid tumors: diagnosis and treatment. *Am Fam Physician* 2007; 75(10):1503-1508.
  25. Okolo S. Incidence, aetiology and epidemiology of uterine fibroids. *Best Pract Res Clin Obstet Gynaecol* 2008; 22(4):571-588.
  26. Khan AT, Shehmar M, Gupta JK. Uterine fibroids: current perspectives. *Int J Womens Health* 2014; 6:95-114.
  27. Schwartz PE, Kelly MG. Malignant transformation of myomas: myth or reality? *Obstet Gynecol Clin North Am* 2006; 33(1):183-198.
  28. Karasick S, Lev-Toaff AS, Toaff ME. Imaging of uterine leiomyomas. *AJR Am J Roentgenol* 1992; 158(4):799-805.
  29. Bingol B, Gunenc Z, Gedikbasi A, Guner H, Tasdemir S, Tiras B. Comparison of diagnostic accuracy of saline infusion sonohysterography, transvaginal sonography and hysteroscopy. *J Obstet Gynaecol* 2011; 31(1):54-58.
  30. Hannemann MM, Alexander HM, Cope NJ, Acheson N, Phillips A. Endometrial hyperplasia: a clinician's review. *Obstet Gynaecol Reprod Med* 2010; 20(4):116-120.
  31. Montgomery BE, Daum GS, Dunton CJ. Endometrial hyperplasia: a review. *Obstet Gynecol Surv* 2004; 59(5):368-378.
  32. Baak JP, Mutter GL, Robboy S, van Diest PJ, Uytterlinde AM, Orbo A, *et al.* The molecular genetics and morphometry-based endometrial intraepithelial neoplasia classification system predicts disease progression in endometrial hyperplasia more accurately than the 1994 World Health Organization classification system. *Cancer* 2005; 103(11):2304-2312.
  33. Nalaboff KM, Pellerito JS, Ben-Levi E. Imaging the endometrium: disease and normal variants. *Radiographics* 2001; 21(6):1409-1424.
  34. American College of Obstetricians and Gynecologists. ACOG Committee Opinion No. 440: The role of transvaginal ultrasonography in the evaluation of postmenopausal bleeding. *Obstet Gynecol* 2009; 114(2 Pt 1):409-411.
  35. Denschlag D, Ulrich U, Emons G. The diagnosis and treatment of endometrial cancer: progress and controversies. *Dtsch Arztebl Int* 2010; 108(34-35):571-577.
  36. Stock RJ, Gallup DG. Hystero-graphy in patients with suspected uterine cancer: radiographic and histologic correlations and clinical implications. *Obstet Gynecol* 1987; 69(6):872-878.
  37. Norman O. Hystero-graphy in cancer of the corpus of the uterus. *Acta Radiol Suppl* 1950; 79:1-156.
  38. Peric H, Fraser IS. The symptomatology of adenomyosis. *Best Pract Res Clin Obstet Gynaecol* 2006; 20(4):547-555.
  39. Gompel C, Silverberg SG. The corpus uteri. In Gompel C, Silverberg SG, editors. *Pathology in gynecology and obstetrics*. 4<sup>th</sup> ed. Philadelphia: Lippincott Williams & Wilkins; 1994;163-284 .
  40. Reinhold C, Atri M, Mehio A, Zakarian R, Aldis AE, Bret PM. Diffuse uterine adenomyosis: morphologic criteria and diagnostic accuracy of endovaginal sonography. *Radiology* 1995; 197(3):609-614.
  41. Asherman JG. Traumatic intra-uterine adhesions. *J Obstet Gynaecol Br Emp* 1950; 57(6):892-896.
  42. Schenker JG. Etiology of and therapeutic approach to synechia uteri. *Eur J Obstet Gynecol Reprod Biol* 1996; 65(1):109-113.
  43. Netter A, Musset R, Lambert A, Salomon Y, Montbazet G. [Tuberculous endo-uterine symphysis; an anatomo-clinical and radiologically characteristic syndrome]. *Gynecol Obstet (Paris)* 1955; 54(1):19-36. [Article in French]
  44. Kupesic S. [Three-dimensional ultrasonographic uterine vascularization and embryo implantation]. *J Gynecol Obstet Biol Reprod (Paris)* 2004; 33(1 Pt. 2):S18-20. [Article in French]
  45. Dawood MY, Jarrett JC 2<sup>nd</sup>. Prolonged intrauterine retention of fetal bones after abortion causing infertility. *Am J Obstet Gynecol* 1982; 143(6):715-717.
  46. Thiery M. Pioneers of the intrauterine device. *Eur J Contracept Reprod Health Care* 1997; 2(1):15-23.
  47. Knudsen HJ, Rasmussen K. The "forgotten" intrauterine device: a cause of infertility. *Arch Gynecol Obstet* 1993; 253(3):143-144.