Saline infusion sonohysterography

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Saline infusion sonohysterography (SIS) is the term for ultrasound imaging of the uterine cavity, using sterile saline solution as a negative contrast medium. It imitates the clarity and exquisite definition of the uterine cavity afforded by amniotic fluid during pregnancy. In principle, any clear liquid could be used to define surfaces. However, sterile saline is inexpensive, easily available and safe to infuse into the peritoneal cavity through the reproductive lumen.

SIS is a low-tech, low-cost, painless enhancement of transvaginal sonography which obviates the need for diagnostic hysteroscopy in cases of abnormal uterine bleeding, reproductive failure or abnormal endometrial images obtained with any modality. The same idea had occurred sporadically to imagers around the world for the past 20 years, but widespread use has come about only recently.

EVOLUTION OF THE TECHNIQUE

Independent efforts were reported from Italy in 1981 [1] and Israel in 1982 [2]. Initially, rigid uterine cannulas and abdominal scanning were used. Nevertheless, the techniques allowed very accurate assessment of the uterine cavity. In 1984, Richman et al. [3] distended the uterine cavities with 70% dextran through a rigid uterine cannula while performing transabdominal ultrasound in 34 patients, and then compared the results with those of conventional hysterosalpingography (HSG). They observed that tubal obstruction produced sustained expansion of the uterine cavity, and that the accumulation of peritoneal fluid in 25 out of 34 patients indicated at least unilateral tubal patency with an accuracy of 97%.

In 1986, Randolph et al. [4], using a similar approach but with sterile saline as the medium, sought to predict surgical findings in anesthetized women about to undergo laparoscopy or hysteroscopy. 53 of 54 uteri were accurately described. Abnormalities, including unicornuate uteri, septae, polyps and intracavitary or submucous myomas, were detected with 98% sensitivity and 100% specificity. The only error was a unicornuate uterus with a non-communicating horn, which was mistaken for a small normal uterus. They also found that identification of fluid accumulation in the posterior cul-de-sac reliably indicated at least unilateral patency with a sensitivity of 100% and specificity of 91%. Fimbria were seen in the posterior cul de sac after instillation of at least 100 ml of fluid, and they noted isolated accumulation of fluid above the fundus in cases where dense adhesions or a mass obliterated the cul-de-sac. They also correctly identified tubal obstruction when hydrosalpinges occurred.

Sterile saline solution provides exquisite definition of the uterine cavity.

Other small series [5, 6] also described pelvic pooling of transcervically infused fluid as a simple screening technique for at least unilateral tubal patency, but made little comment on the uterine cavity.

Van Roessel et al. [7] scanned 30 Belgian women transabdominally during hysteroscopy using dilute dextran 70, and compared the ultrasonic and endoscopic diagnoses. Only one 2 mm polyp was missed; eight normal cavities were accurately assessed as normal. Intra- and extracavitary myomas, septae, synechiae and six polypoid lesions were predicted. Irregular 'ragged' endometrium turned out to be cancer with hyperplasia in seven cases, and normal proliferative endometrium in three cases. Precise location of two intrauterine devices (IUDs) was also possible. One of these was extracavitary and unseen by the hysteroscopist. Resection was successfully monitored by ultrasound rather than laparoscopy in two of the three septae found.

Saline infusion sono-hysterography can obviate the need for diagnostic hysteroscopy.

As high-frequency vaginal sonography spread in the late 1980's, detailed imaging of the pelvic organs produced more accurate diagnoses of both hormonal and structural causes of abnormal bleeding [8, 9], as well as amenorrhea [10, 11, 12] and infertility [13]. Even so, all series describing endometrial pathology included cases with indecipherable images. Fedele et al. [14] found transvaginal ultrasound comparable to hysteroscopy in detecting intracavitary and extracavitary lesions, but ultimately had difficulty distinguishing between myomas and polyps, and the extent of the intramural component of myomas; critical to surgical planning.

Dodson [9] evaluated 45 women with abnormal bleeding, and imaged structural abnormalities in one third of them. He used the ovarian and endometrial

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INTERMEZZO

Sonohysterography Tips

The catheter can be inserted through the side of a standard speculum, rather than down the channel, for easier removal of the speculum.

Deflexion of the uterus to make cannulation easier can be effected by suprapubic pressure on the fundus, or manipulation of the cervix with the toe of the speculum.

Use a gyne chair or table for better perineal exposure and in order to have a basin in which to place instruments and collect expelled fluid.

Press the probe gently against the internal os during sagittal scanning in order to distend the cavity more efficiently.

Videotape the images so that the cavity can be studied in detail while the examination remains brief. Here, too, 3D acquisition improves archiving and image analysis by saving the complete data set efficiently.

If biopsy is anticipated, 1% xylocaine can be used instead of saline to verify the location, number and nature of lesions while affording excellent local anesthesia. It should be maintained in the cavity for at least 3 minutes for optimal effect.

Platt et al. [54] reported the use of a chorionic villus biopsy catheter with a stylet to enter difficult or obstructed cervical canals.

The advent of vaginal transducers produced even clearer images.

appearance to confirm functional ovulatory abnormalities in the rest of the patient sample. Three thick hyperechoic endometria had intermenstrual bleeding that eluded diagnosis, suggesting they might have had polyps obscured by secretory endometrium.

Narayan and Goswamy [13] recommended midcycle transvaginal ultrasound for screening infertility patients, having correctly diagnosed abnormalities in 182 of 193 women (94%). After weekly sonographic evaluation of 200 patients throughout their cycles, followed by hysteroscopy, they found that periovulatory multilayered endometrium best revealed intracavitary lesions and the uterotubal junctions. However, fourteen patients had nonspecific irregularities on ultrasound that required diagnostic hysteroscopy for definition. These were found to be two normal cavities, four polyps, two synechiae, and one septum. The remaining three had polycystic ovaries and murky looking endometrium which yielded endometritis on biopsy, probably due to chronic incomplete shedding of functionalis. 14 % of 51 submucosal myomas defined by ultrasound were not visible on hysteroscopy. Five of 76 synechiae, three of 46 polyps and one of six septae were not diagnosed with TVU, and there was a 5.5% false-positive rate. These are the type of cases which can benefit from saline infusion.

SIS has high sensitivity and specificity.

The advent of vaginal transducers brought reports of even clearer images obtained with infusion of sterile clear media through rigid cannulas, beginning with that of Deichert in Germany in 1988 [15]. He sought to explain constant bleeding attributed to a 'perpetual gestational sac' which did not grow for months. Infusion of saline showed that it was not a sac of fluid, but a hypoechoic intracavitary myoma.

In 1991, Mitri et al. in South Africa, using an 8 F Foley catheter in the cervix, demonstrated that SIS was more informative than conventional HSG [16]. Fifty normal cavities were demonstrated by both methods, but nine women had otherwise undetectable extracavitary myomas visible by ultrasound. All 4 submucous myomas were seen by both methods. Four bifid uterine cavities were tentatively diagnosed as septate by HSG, and definitively diagnosed as harboring three septae and one intramural myoma by ultrasound. All four submucous myomas were seen by both methods. The two methods agreed in one case of intrauterine synechiae. One HSG failed due to intravasation of contrast, whereas SIS and laparoscopy demonstrated a normal uterus and bilateral hydrosalpinges.

A report from Bonilla-Musoles et al. from Spain followed in 1992 [17]. They found that SIS, using a balloon catheter, had a sensitivity of 96%, a specificity of 97%, positive predictive value (PPV) of 96% and negative predictive value (NPV) of 97%. Twenty-two normal women, 16 women with menometrorrhagia and 16 infertile women were

studied. In 74 patients, only two cases of focal hyperplasia were missed, and one normal endometrium was incorrectly diagnosed as hyperplastic. Two cervices were not cannulated, due to pain and stenosis respectively. Submucosal myomas, hyperplasia, synechiae, and a septum were correctly diagnosed, and the group considered SIS to be equal to hysteroscopy, with the exception of the detection of tiny focal hyperplasia. They suggested that SIS should be used for preoperative and posttreatment evaluation and monitoring.

In 1992 Syrop and Sahakian [18] diagnosed polyps in 10% of over 100 infertility patients with abnormal sonographic screening before in-vitro fertilization, using a rigid Rubin's cannula and Ringer's lactate or human tubal fluid.

At the American Fertility Society Meeting in Washington DC, in October 1990, we reported the evaluation of intrauterine synechiae in infertility patients using a flexible 5 F HS balloon catheter (Ackrad Laboratories, Cranford NJ, U.S.A.) for infusion of sterile saline The same technique, with either the balloon catheter or a 2 mm intrauterine insemination Soules catheter (Cook Co., Spencer Ind, U.S.A.) was used for evaluation of a variety of intracavitary abnormalities, and reported at the American Institute of Ultrasound in Medicine meeting in Atlanta the following year. The report was published in 1993 at the American Fertility Society Meeting in Washington DC.

Using 2 mm intrauterine insemination catheters, in most cases without balloons, we achieved 100% detection of intracavitary abnormalities in 39 patients with abnormal bleeding and abnormal endometrial images. The abnormalities were confirmed by hysteroscopy or hysterectomy. Polyps, myomas, synechiae, and abnormal irregular thickening that proved to be hyperplasia or cancer were accurately identified. In addition, two women had small polypoid islands of what proved to be normal proliferative endometrium, which we termed 'wrinkles'. These had both persisted through two cycles and were removed hysteroscopically. The wrinkles were thought to be due to luteal insufficiency, one in a patient with habitual abortion, and one in a perimenopausal woman with abnormal bleeding. We could not distinguish stage I cancer from hyperplasia, because both produced irregularly thickened endometrial surfaces. Twenty infertile patients judged to have normal cavities by SIS were shown to have normal cavities with hysteroscopy, HSG, or both.

Author	Year	n	Sensitivity %	Specificity %
Bonilla-Musoles [17]	1992	76	96	97
Syrop [18]	1993	14	100	100
Parsons [52]	1993	59	100	94
Widrich [41]	1995	130	96	100
Wolman [47]	1996	47	86	100
Keltz [31]	1997	34	100	100
Bernard [50]	1997	109	99	76
Schwarzler [39]	1998	104	87	91
Williams [51]	1998	39	100	85
Dijkhuizen [53]	2000	50	100	85

Table 1. Comparison of SIS with surgery. A sampling of studies in which findings on SIS were compared with surgical findings by hysteroscopy or hysterectomy. Histology was used as the gold standard, and it can be seen that although the nature of the lesion may be in question, abnormalities in the cavity are almost always identified. The two series with lowest sensitivity used an intrauterine 8 F Foley catheter (Wolman) or an air-filled intracavitary balloon (Schwarzler), both of which cause obtrusive artifacts in the region of interest.

Reports of the use of this technique, performed in conscious patients using a flexible 2 mm catheter with or without a balloon, increased exponentially over the rest of the decade in both radiologic and gynecologic publications. The results of SIS compared with visualization of the cavity by either hysteroscopy or hysterectomy have shown 95 % to 100% sensitivity for intracavitary lesions (Table I), and a negative predictive value of essentially 100%.

The specificity has been reported to be poor in premenopausal women because of cyclic proliferation. An understanding of uterine physiology is essential for optimal use of SIS, because of the complex geography of the secretory phase endometrial surface, which is a natural result of normal proliferation and secretory maturation. As in the rest of life, timing is everything.

Performance of SIS after induced or natural menses minimizes confusion, because at that time functionalis should be entirely shed, leaving only the basalis layer: a 4 mm double-layered endometrium. Goldstein [19] recommended SIS following menses after studying 21 perimenopausal women with abnormal bleeding. An algorithm was then tested in 433 women with menorrhagia or menometrorrhagia [20]: TVS was performed following withdrawal bleeding, when a thickness of <5 mm is expected. SIS was done in those with endometrium greater than 5 mm. 79% of women did shed the functionalis, and had a symmetrical

Familiarity with uterine physiology is essential for optimal use in pre-menopausal women.

Figure 1. A marker on the catheter at about 7cm is useful for gauging the location of the catheter tip. Gentle insertion to just touch the fundus is important, in order to avoid acute pain from a sharp impact.

postmenstrual endometrium of ≤ 5 mm. They were diagnosed with true dysfunctional uterine bleeding ascribed to erratic ovarian function, and were managed with progestins. 18 % had focal masses such as polyps (n =58) or myomas (n = 22) and were treated by operative hysteroscopy. Ten had global thickening, which was sampled immediately by Pipelle, which demonstrated abnormal proliferation in half of the group and hyperplasia in the other half; all of these were treated hormonally. SIS failed in two cases which were investigated with hysteroscopy. Appropriate hormonal treatment with no further evaluation was thus instituted in over 80%, with biopsy required in only 21%. Wolman et al. [21] compared women with abnormal bleeding who underwent SIS during the first 10 days of the cycle, with those evaluated later in the cycle. They found no false positive abnormalities in the former group, while 27% of the latter had false positive tests.

The baseline study for orientation is performed in the midsagittal plane.

TECHNIQUE

The baseline ultrasound study is performed first. The uterus is imaged in the midsagittal plane, which includes the entire length of the cervical canal, as a landmark for orientation. For best resolution of the endometrium, the probe must be in contact with the uterus through the vaginal wall, perpendicular to the long axis of the uterus. The maximum thickness (measured from basalis to basalis) of the dual-layered endometrium is measured as the entire cavity is scanned from cornu to cornu. The current convention is to measure both walls of the endometrium together, unless there is fluid in the cavity, in which case they are measured individually and added together. The sum of the two walls in an expanded cavity will be slightly greater than the apposed wall dual thickness. Symmetry of both the cavity and of the endometrium are noted. Next, the following questions are answered:

The thickness of the endometrium is measured as the cavity is scanned from cornu to cornu.

- Is there a focal thickening or absence of the endometrium?
- Is there an anomalous cavity?
- Is the cavity distorted by either a myometrial or intracavitary lesion?
- Is the appearance of the endometrium appropriate for the woman's history, treatment, and her ovarian activity?

We expect the thickness to be uniform and no more than a total of 4 mm in untreated postmenopausal women, in women who are within seven days following the onset of menses, or those whose treatment is designed to suppress functionalis growth. We expect a layered appearance in those women with incremental exposure to no more than two to three weeks of estrogen: (the normal proliferative phase), and a dominant follicle of more than 10 mm. In women who have a corpus luteum present in one ovary (secretory phase) we expect a hyperechoic endometrium of 6 mm or more.

The transducer is turned 90°, and the uterus is scanned in the transverse view from cervix to fundus, enabling the examiner to construct a mental three-dimensional image of the cavity. The use of 3D ultrasound machines enables more rapid and precise understanding of the uterine cavity, with the ability to dissect it electronically from any angle, after the patient is gone.

The cervix is visualized and the external os cleansed through a speculum. A speculum with its own light source is very helpful, as is an open-sided speculum. A 2 mm (outer diameter) by at least 20 cm long flexible catheter is inserted gently into the cavity to the fundus. Many intrauterine insemination and SIS catheters have a mark at about 7 cm which alerts the operator to approach the fundus very gently in order to avoid the pain of sudden impact. The catheter can be primed with fluid before insertion in order to minimize air artifacts (Figure 1).

Balloon catheters are only required if the internal os is patulous, the uterus is very large, intrauterine synechiae are suspected, or if tubal patency is being tested. The balloon should be lodged in the cervix, and filled with water in order to minimize the risk of image artifacts in the cavity.

The speculum is removed, holding the catheter in

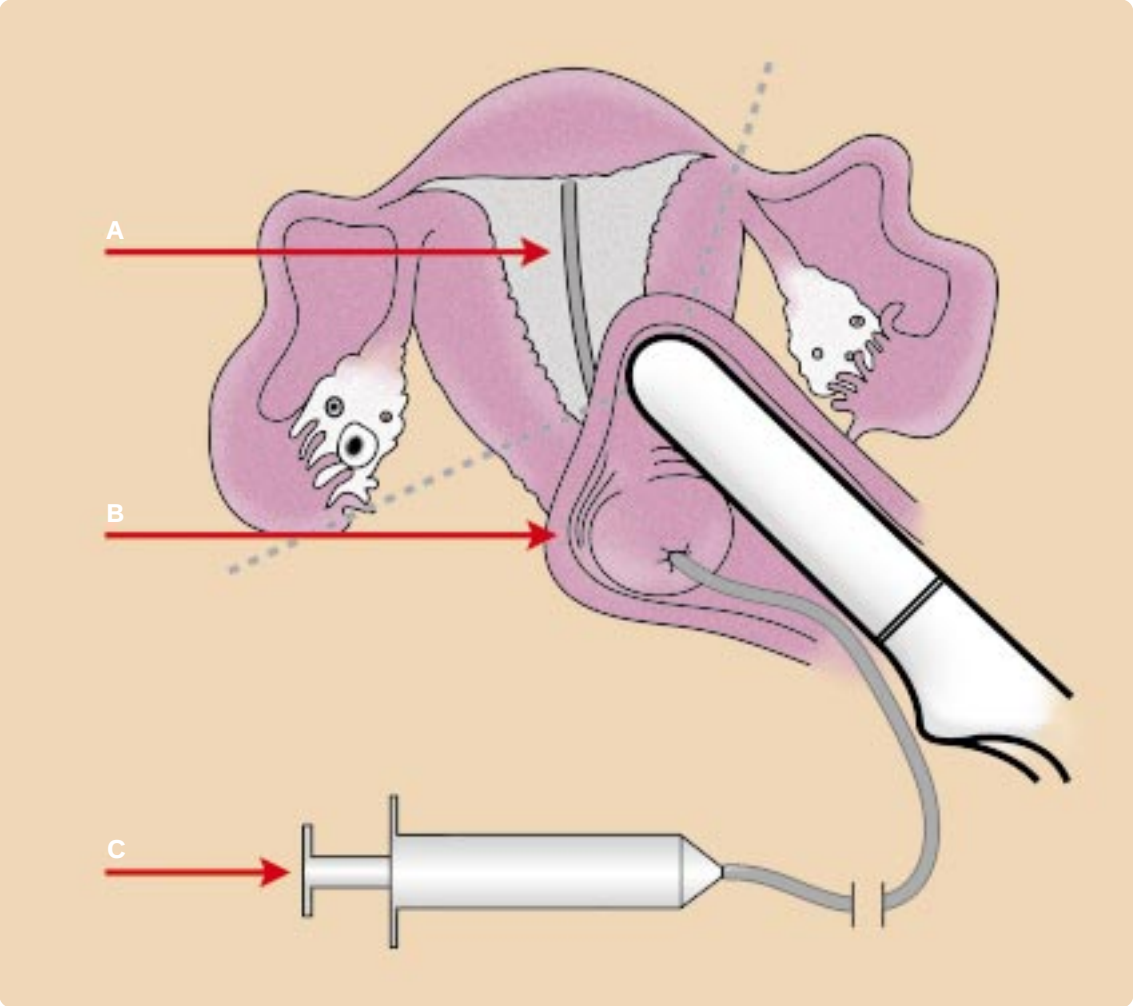


Figure 2. Saline infusion sonohysterography.

A. The straight catheter is inserted to the fundus.

B. In the case of an anteverted uterus (shown here) the ultrasound wand touches the uterus through the anterior vaginal wall. In the case of a retroverted uterus it would be inserted against the posterior vaginal wall (below the catheter).

C. A 10 ml syringe of normal saline (or 1% lidocaine when local anesthesia is required and there is no allergy) is attached to the catheter after removal of the speculum.

place, and the saline-filled syringe is attached to the catheter (Figure 2).

The vaginal probe, with plenty of lubricant over the protective sheath, is re-inserted above the catheter in anteverted uteri, and below the catheter in retroverted uteri, to avoid dislodgement.

The same sagittal and transverse maneuvers are performed to study the entire uterine cavity surface while slowly infusing saline until the walls are adequately expanded or the patient complains of pain. This amounts to about 2 cc of saline in a postmenopausal woman, and 5 to 10 cc in a premenopausal woman.

INDICATIONS

Evaluation of abnormal bleeding

As for hysteroscopy, the most common reason to perform SIS is evaluation of abnormal bleeding at any age. Standard TVU will provide a diagnosis of abnormal proliferation in postmenopausal or postmenstrual women in most cases, but SIS is useful to distinguish between focal and global lesions, in order to determine the best method of biopsy or resection. Small focal lesions off the midline may be missed by an office biopsy, which samples less than 5% of the cavity [22], as will many polyps and all myomas.

Clarification of the anatomy

SIS will clarify the anatomy when the endometrium is asymmetrical, unexpectedly thickened or obscure by any imaging method, including hysteroscopy. SIS provides an interpretable image despite uterine bleeding, although clots may have to be evacuated.

The most common indication for SIS is abnormal bleeding.

The accurate diagnosis of endometrial abnormality obviously requires histologic examination, but SIS allows one to make the distinction between global and focal processes in order to decide the most fruitful approach for a representative biopsy. The popular Pipelle office biopsy instrument samples less than 5% of the endometrial surface in the midline [22] and is thus suitable for midline or global processes, while ultrasound directed biopsy

Figure 3. Myoma.

Figure 3a. TVU showing a submucous myoma. However, it is not clear how much of the myoma is intracavitary.

Figure 3b. SIS of the myoma shows that half of the myoma protrudes into the cavity, forming an acute angle with the myometrium, and that the distance from the intramural edge of the myoma to the serosal surface is almost 2 cm, making this lesion a candidate for hysteroscopic resection

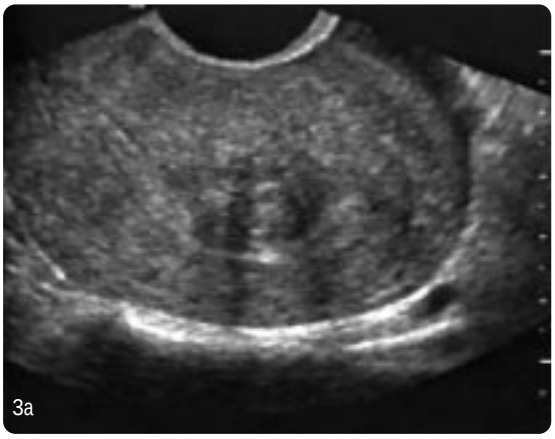


Figure 4. Tamoxifen-treated atrophic uterus with apparent thickening and subendometrial cysts.

Figure 4a. TVU showing indeterminate endometrium and cysts.

Figure 4b. SIS shows a very thin endometrium setoff by subbasalis cysts. These myometrial changes explain the impression of thickness. The endometrial cavity itself is atrophic. There is an air artifact at the internal os in this retroverted uterus. With a little patience, this air escapes around the straight catheter. In anteverted uteri, bubbles collect at the fundus and escape out of the tubes if they are patent. Priming the catheter with saline before insertion can avoid this artifact

or operative hysteroscopy is indicated for removal and diagnosis of focal lesions [23, 24, 25]. An inexplicably abnormal endometrial image (CT, MRI, hysterosalpingography or TVS) with thickness or distortion can be conveniently and atraumatically assessed to plan further intervention where it is warranted.

Secondary amenorrhea, hypomenorrhea, infertility or recurrent abortion

Secondary amenorrhea, hypomenorrhea, infertility or recurrent abortion are infrequently caused by endometrial synechiae due to trauma or infection in a poorly estrogenized endometrium. These are easily demonstrated by SIS, enabling hysteroscopic resection if pregnancy is desired, or observation if it is not.

Evaluation of the endometrial cavity is a standard part of the workup for infertility, usually by hysterosalpingography (HSG). The use of hysteroscopy has increased in the past 25 years as it has become clear that there is a high incidence of intracavitary abnormalities in infertile patients [26, 27]. HSG, however, produces a high rate of false-positive uterine findings, reported to be as high as 30% by Valle [28], prompting many unnecessary procedures. Sonographic screening with SIS before undertaking in-vitro fertilization is increasingly practiced [18, 29, 30], and it has also been found to be superior to HSG in diagnosis of intracavitary abnormalities in women with recurrent abortion [31].

Preoperative planning

Pre-operative planning for myomectomy and post operative evaluation of the results are facilitated by SIS [32] after myomas are diagnosed in women with menorrhagia or infertility (Figure 3).

Monitoring effects of drugs on the endometrium TVU and SIS provides an acceptable and informative means of monitoring treatment effects, particularly in evaluation of novel treatments such as raloxifene, a SERM (selective estrogen receptor modulator) used for prevention and treatment of osteoporosis in postmenopausal women, on postmenopausal endometrium [33]. Serial evaluation of endometrial thickness using TVU and SIS in double-blinded randomized trials confirmed that raloxifene's effects on the endometrium were no different from those of placebo, i.e. atrophy was maintained in women of normal weight. The use of SIS and TVU in addition to biopsy also marked the first study of postmenopausal treatment in completely characterized endometrial cavities, allowing assessment of uterine drug effects separate from those of unknown pathology. Much confusion

would have been avoided had this approach been used before tamoxifen came into widespread use.

Intact postmenopausal women undergoing treatment with tamoxifen, a SERM widely used for the treatment and prevention of breast cancer, have a fourfold increased risk of endometrial cancer [34]. Tamoxifen's unpredictably agonistic effects stimulate endometrial proliferation, hyperplasia, polyp formation and cancer in 20% [35] to 70% [36] of asymptomatic users in various controlled series, and the effects are not apparent until treatment is under-way. Most postmenopausal uteri, however, seem to remain atrophic and asymptomatic but may develop non-proliferative distension of basalis glands into cysts, from submillimeter to a centimeter in size, in the basalis layer (Figure 4). These protrude into the myometrium, creating an impression of endometrial thickening due to abnormal functionalis proliferation, leading to unnecessary repetitive biopsies, hysteroscopy and other invasive testing. Goldstein [37] used SIS to demonstrate a smooth atrophic endometrial surface, despite the peculiar but innocuous 'pseudo-polypoid glandulocystic endometrial atrophy' [38]. Schwarzler et al. [39] used SIS to elucidate apparently thickened or obscure endometrium in 44 tamoxifen treated women, ending the investigation in about half of them.

The landmark study by Berliere et al [40] in 264 women who were studied with ultrasound and hysteroscopy before beginning tamoxifen treatment, then yearly for three years of treatment, demonstrated that 17% had asymptomatic abnormal proliferation before treatment, including hyperplasia and polyps, all of which were removed. The women with atypical hyperplasia underwent hysterectomy. 20% of those with original lesions and 23% of originally normal women developed polyps or hyperplasia. However, only one of the 51 new lesions contained atypia, while three of the nine recurrent lesions did.

Despite the dictum by the American College of Obstetricians and Gynecologists that women taking tamoxifen should not be evaluated until they bleed [41], it seems prudent to screen women before treatment in order to detect and remove the pre-existing lesions in the one out of five who are at very high risk for uterine complications. Evaluation after six months of treatment will help determine which women will respond to tamoxifen as though

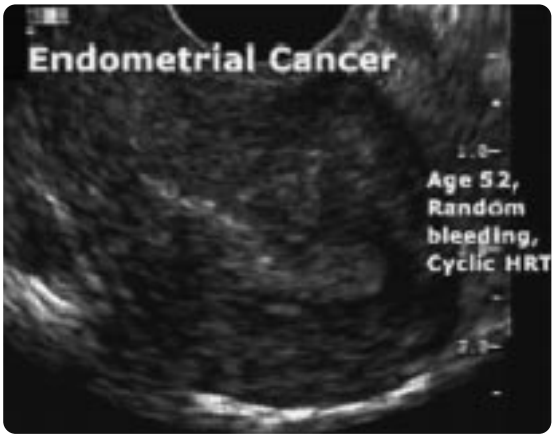


Figure 5. Endometrial cancer: This is a woman with cyclic sequential estrogen/progestin hormone replacement for 1 year who had random spotting and erratic withdrawal bleeding, every other month.

Figure 5a. TVU shows an endometrial thickness of 7 mm, 5 days after the last progestin pill, when the functionalis should have been completely shed and the endometrium should have measured no more than 4 mm.

Figure 5b. SIS shows that the posterior endometrium in this retroverted uterus was 2 mm thicker than the anterior wall, and a biopsy revealed well-differentiated adenocarcinoma. The inappropriate thickness and asymmetry prompted biopsy, which was done with a pipelle because the lesion was global.

it were estrogen, since endometrial proliferation is reliably detected with TVU and SIS. Those who do not grow polyps or have thickening of the endometrium within a year of initiating treatment may then avoid further scrutiny unless they bleed.

Typical lesions

The purpose of SIS is to delineate masses or defects in the uterine cavity which indicate that biopsy is necessary, and to direct the best approach for biopsy. It can be difficult to predict the histology of lush, proliferating endometrium based only on its appearance. Late or disorderly proliferative, secretory, hyperplastic and cancerous endometrium can all appear polypoid.

SIS delineates masses or defects in the uterine cavity.

Widrich, in an independent comparison between diagnostic hysteroscopy and SIS [42], found the latter to be more accurate in predicting hyperplasia, but inaccuracies occurred with both techniques. Hyperplasia and subcentimeter myomas have been confused with polyps in various series, and may occur together. Cancers are not reliably distinguishable from atypical or typical hyperplasia, or even some cases of secretory endometrium, because any endometrium with large ectatic glands looks hyperechoic and may have surface elevations (Figure 5).

Figure 6. Polyp.

Figure 6a. An ill-defined thickening in the uterus of a 42 year old nullipara who seeks a second opinion for hysterectomy for menometrorrhagia. It is day 5 of her cycle, and the inappropriately thickened endometrium prompts SIS.

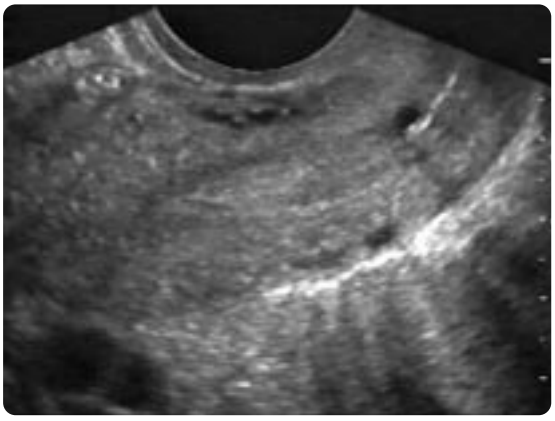
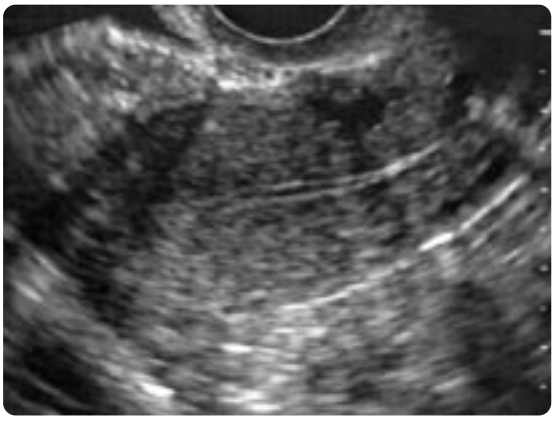


Figure 6b. SIS demonstrates a fundal polyp, as well as a nabothian or cervical inclusion cyst at the anterior internal os, and an otherwise normal postmenstrual cavity.

Figure 6c. the polyp was removed under ultrasound guidance in the office, and the patient has returned 1 month later following menses. TVU confirms complete removal of the polyp, and her symptoms have resolved.



Having said this, a smooth isolated uniformly textured mass with a single vessel leading to it, surrounded by an unstimulated regular cavity is highly likely to be a benign polyp (Figure 6), and a relatively hypoechoic well-defined mass crossing the basalis layer from the myometrium is reliably an intracavitary myoma. Intracavitary myomas tend to make the cavity conform to their shape, while polyps tend to conform to the shape of the cavity.

SIS distinguishes between focal lesions and global thickening.

Endometrial polyps are true benign tumors, the cause, behavior and incidence of which are incompletely understood. The incidence of cancer in, or associated with, true polyps is reportedly < 0.5%. The true denominator was not approximated until recent noninvasive sonographic observation of polyps in asymptomatic women became possible. It is probably even less, although neither clinicians nor pathologist always make a distinction between polyps and polypoid tumors.

Saline infusion is more accurate than TVU at demonstrating small polyps, diminishing the false positive and false negative rates of TVU by at least 66% in one comparison [43]. We have found that polypoid masses, most of which are not sampled by office biopsy, were demonstrated with SIS in about 8% of asymptomatic untreated postmenopausal women undergoing screening for participation in a study of the effects of raloxifene on the endometrium (unpublished data) [32]. Polyps were present in 10% of asymptomatic premenopausal women v. an incidence of 33% in women with abnormal bleeding, diagnosed with SIS [44]. The asymptomatic polyps tended to be smaller, suggesting that over time, with growth, they may become symptomatic. We have found that immediate removal of polyps in symptomatic women relieved the abnormal bleeding in 88% of cases [45] (Figure 6c). Similar results have been found by others [46], confirming the utility of inspecting the cavity of abnormally bleeding women as the first step in evaluation.

Intrauterine synechiae may appear with TVU as endometrium which is inappropriately thin for the patient's history, for instance measuring 4 mm at midcycle when she also has a 23 mm preovulatory follicle. They may demonstrate irregular focal hyperechoic surfaces due to a film of mucus along one of their flat surfaces, or pockets of hypoechoic fluid when there is more mucus distending the small spaces between scars. A partial hematometra may form with cervical outlet obstruction due to synechiae. Saline infusion demonstrates these fibrous scars which tether the anterior and posterior walls, but a cervical balloon may be required in order to generate adequate opening pressure. Very slow infusion is used in order to minimize pain, especially if the tubes are obstructed.

Unextractable IUD

The location of an unextractable IUD among myomas or embedded in the uterine wall can be verified by SIS, and operative hysteroscopy can be planned if necessary. However, once their location is confirmed within the uterus, they can also be extracted under abdominal ultrasound guidance using an instrument such as a pediatric bronchoscopy alligator forceps.

Failures, false positives and complications

A clear understanding of uterine physiology and anatomy is essential in order to optimize interpretation of SIS.

Pseudomasses or irregular thickening may produce false positive results with both TVU and SIS when they are performed during a normal secretory phase. On the other hand, a thickened endometrium with no evidence of imminent or recent ovulation more than three weeks from the onset of bleeding suggests an ovulatory cycle. This is a positive finding, even if the endometrial biopsy retrieves 'normal proliferative' endometrium. An 8 mm proliferative endometrium is not normal in a post-menopausal woman on continuous combined hormonal treatment, which should provide enough progesterone to suppress the growth of functionalis. Rather than performing a biopsy for every finding in women who are perimenopausal, however, timing SIS to the postmenstrual window is both therapeutic and diagnostic. As Goldstein demonstrated [20], identifying residual functionalis (>5 mm thickness on TVU) within five days of the onset of bleeding is likely to yield advanced proliferative abnormalities such as hyperplasia or polyps: lesions which do not shed promptly with medical treatment. The use of SIS distinguishes between focal lesions, which require a directed biopsy for diagnosis and removal, and global thickening, which can reliably be sampled with an office biopsy approach. It also distinguishes between an atrophic endometrium with sub-basalis benign cysts caused by tamoxifen, and true endometrial proliferation and lesions in tamoxifen treated women. Both can have apparently thickened endometrium on TVU, but only the woman with actual proliferation seems to be at increased risk for endometrial cancer.

Complete cervical stenosis will prevent cannulation of the cervix, even with a 5 F straight catheter with a 2 mm outer diameter. However, in our experience, real cervical obstruction is rare. Failure to pass the cannula is much more likely to be due to sharp cervical flexion. This can be appreciated by bimanual examination or by sonography. It is relieved by deflexing the uterus with gentle suprapubic pressure on the fundus through the abdominal wall, and/or cervical manipulation with the toe of the speculum, or in extreme cases, with traction on a tenaculum attached to the anterior or posterior cervical lip.

A completely effaced cervix following a cone biopsy or prolonged vaginal atrophy can sometimes only be identified sonographically, oriented on the vaginal canal. Digital palpation of the cervix allows one to identify the dimple of the external os and gently abrade the surface. This is then identified through a speculum, and an os finder or cytobrush can be introduced into it to delineate the canal, followed by cannulation with the catheter.

Artifacts can interfere with diagnosis: air, when introduced into the canal, will obscure the endometrium. Observation of its movement through the tubes can be used to ascertain tubal patency. However in the anteverted uterus with ligated tubes, it can be difficult to remove the air. Extensive synechiae in the cavity can also trap the air and obscure the cavity, however this typical appearance allows one to make the diagnosis of synechiae, if not to fully evaluate the endometrial cavity.

There is no contraindication to SIS in non-pregnant, non-infected women who are bleeding, but one should be wary of intracavitary 'masses' with web-like connections to the endometrium at several sites. These may be clots, and they can often be expelled through the cervix with continued gentle infusion and manipulation of the catheter.

Placement of a balloon in the cavity, particularly one with air in it, can obscure the cavity. One series with a relatively low sensitivity of 86% used an 8F pediatric Foley: a relatively bulky catheter and a balloon [47]. Cervical mucus and small divots of endometrium can also be dislodged by the movement of the balloon, particularly in lush midcycle endometrium, and this can create apparent irregularities in the endometrial surface. Straight 5F catheters are atraumatic and effective in the majority of cases.

The axial uterus is hard to evaluate by conventional 2D ultrasound, because of poor resolution of the endometrium when scanning down the barrel in line with the long axis of the uterus. This can be remedied by manipulation of the uterus with the abdominal hand, for instance pushing the uterus into retroversion with direct suprapubic pressure, or gently increasing its anteversion by pushing the colon against the posterior uterine wall from above.

One must pay attention to the rest of the anatomy. The baseline study before instrumenting the cavity is therefore essential, and videotaping the study

Videotaping the baseline study enables later review of details.

There is no contraindication to SIS in non-pregnant, non-infected women who are bleeding.

Steps should be taken to avoid uterine lavage propelling cancer cells into the peritoneal cavity.

3D provides a faster and less manipulative procedure, with an interactive image record.

enables later review of details which might have been missed. Masses in the ovary, which may be incidental or instrumental in the bleeding, may occur more often in women with bleeding. Cervical polyps can be missed unless the cervical canal is scrutinized along with the uterine cavity. The baseline study also enables one to detect adnexal pain which may indicate infection, and we treat the patient and her partner with antibiotics before doing even minimally invasive procedures.

Vasovagal reactions have been reported with SIS; they may occur after the procedure is completed. The avoidance of pain is obviously of utmost importance. Gentle manipulation, controlled introduction of the catheter to avoid poking the fundus with its tip, and the liberal use of local anesthesia, reward the practitioner and the patient by minimizing pain-related complications. One per cent plain lidocaine can be used as the medium, in place of saline, for both distension and for local anesthesia. Most women have had dental work, and therefore know if they are allergic to this amide-type local anesthetic. A few milliliters (up to ten), held in the uterine cavity for at least three minutes, provides enough anesthesia to perform almost any intracavitary biopsy without pain. Injection around the external os likewise allows dilation of the cervical canal without distress. Vasovagal reactions are a nuisance in younger women, but in women with atherosclerosis they can drop the blood pressure enough to provoke an MI. Responding to patient's pain with cessation of the procedure is the key to avoiding complications of pain.

SIS clearly delineates the inner landscape of the endometrial cavity.

The concern that uterine lavage will propel cancer cells into the peritoneal cavity is a real one, since retrograde bleeding through patent tubes is a physiological certainty. One study recorded fimbrial spill during saline infusion with 10 to 20 ml in 5 of 14 women with stage I endometrial cancer at laparotomy. Peritoneal carcinoma cells were recovered after this in one patient [48]. Understanding that natural bleeding, and any manipulation of the endometrium which causes bleeding, will produce flow into the peritoneal cavity, we can take steps to minimize the phenomenon, such as using sterile water in order to lyse free cells, and using low-pressure infusion by avoiding the use of balloons in women at risk for cancer. A previous study using hysterosalpingography for cancer staging failed to demonstrate any difference in outcome, stage for stage, in women with tubal spill v. those without [49]. While this circumstantial evidence suggests that SIS should not increase women's risk for developing metastases, continued study of the question is in order.

Fewer women need be subjected to biopsy, hysteroscopy or even hysterectomy.

The advantages of using 3D ultrasound machines to perform SIS include: a rapid acquisition time, leading to a shorter duration of uterine distension, less use of saline, a shorter, less manipulative procedure, and very inexpensive archiving of an interactive electronic image record, with no diminution of diagnostic accuracy.

CONCLUSION

Saline infusion sonohysterography (SIS), or saline infusion into the uterine cavity under vaginal sonographic observation, clearly delineates the inner landscape of the endometrial cavity. The women are awake and responsive, and require no preparation except an empty bladder.

Ultrasound is widely available and relatively inexpensive, as is the other equipment required.

This technique is now the subject of over 100 reports, most of them generated in the past four years, and the evidence is coherent and unanimous that it is a reliable method of identifying the presence of an intrauterine lesion when TVU is unclear or nonspecific.

Specificity and positive predictive value are improved by performing SIS after complete shedding of the functionalis, whether this is induced or menstrual, since only true lesions will remain. Diagnosis still depends on examination of endometrial histology, but fewer women need be subjected to biopsy, not to mention hysteroscopy and even hysterectomy.

With TVU and SIS available, we also have a method of evaluating the results of treatment , as well as of safely observing natural processes in great detail without disturbing them.

REFERENCES

[1] Chelo E, Branconi F, Tantini C, Scarselli GF. *Dynamic Echohysteroscopy: A New Diagnostic Technique in the Study of Female Infertility.* Acta Eur Fertil 1981; 12: 167-71.

[2] Beyth Y, Beller U, Yarkoni S. *A Simple Technique for Visualization of the Uterine Cavity and its Pathology during Ultrasound Scanning.* Isr J Med Sci 1982; 18: 817.

[3] Richman TS, Viscomi GN, Decherney A et al. *Fallopian Tubal Patency assessed by Ultrasound following Fluid Injection.* Radiology 1984; 152: 507-11.

[4] Randolph JR, Ying YK, Maier DB et al. *Comparison of Real-Time Ultrasonography, Hysterosalpingography and Laparoscopy/ Hysteroscopy in the Evaluation of Uterine Abnormalities and Tubal Patency.* Fertil Steril 1986; 46: 828-832.

[5] Rasmussen R, Larsen C, Justesen P. *Fallopian Tube Patency Demonstrated at Ultrasonography.* Acta Radiol Diagn 1986; 27: 61-63.

[6] Sharma RP. *Fallopian Tube Patency by Ultrasound Scan*. Obstet Gynaecol India. 1989; 39: 700.

[7] Van Roessel J, Wamsteker K, Exalto N. *Sonographic Investigation of the Uterus during Artificial Uterine Cavity Distension.* J Clin Ultrasound 1987; 15: 439-450.

[8] Goldstein SR, Nachtigall M, Beller U et al. *Endometrial Assessment by Vaginal Ultrasound Prior to Endometrial Sampling in Patients with Postmenopausal Bleeding.* Am J Obstet Gynecol 1990; 153: 119-123.

[9] Dodson MG. *Use of Transvaginal Ultrasound in Diagnosing the Etiology of Menometrorrhagia.* J Reprod. Med. 994; 39: 362-372.

[10] Morcos RN, Leonard MD, Smith M. *Vaginosonographic Measurement of Endometrial Thickness in the Evaluation of Amenorrhea.* Fertil Steril 1991; 55: 543-546.

[11] Mehta AE, Matwijiw I, Lyons EA, et al. *Noninvasive Diagnosis of Resistant Ovary Syndrome by Ultrasonography.* Fertil Steril 1992; 57: 56-61.

[12] Shulman A, Shulman N, Weissenglass L et al. *Ultrasonic Assessment of the Endometrium as a Predictor of Estrogen Status in Amenorrheic Patients.* Hum Reprod1989; 4: 616-619.

[13] Narayan R, Goswamy RK. *Transvaginal Sonography of the Uterine Cavity with Hysteroscopic Correlation in the Investigation of Infertility.* Ultrasound Obstet Gynecol 1993; 3: 129-133.

[14] Fedele L, Bianchi S, Dorta M et al. *Transvaginal Ultrasonography versus Hysteroscopy in the Diagnosis of Uterine Submucous Myomas.* Obstet Gynecol. 1991; 77: 745-748.

[15] Deichert U, Van De Sandt M, Lauth G, Daume E. *Transvaginal Contrast Hysterosonography. A New Diagnostic Procedure for the Differentiation of Intrauterine and Myometrial Findings.* Geburtshilfe und Frauenheilkunde 1988; 48: 835-44.

[16] Mitri F, Andronikou AD, Perpinyal S, Hofmeyer GJ, Sonnendecker EW. *A Clinical Comparison of Sonographic Hydrotubation and Hysterosalpingography.* Br J Obstet Gynecol 1991; 98: 1031-1036.

[17] Bonilla-Musoles F, Simon C, Serra V, Sampaio M, Pellicer A. *An Assessment of Hysterosalpingosonography (HSSG) as a Diagnostic Tool for Uterine Cavity Defects and Tubal Patency*. J Clin Ultrasound 1992; 20,3: 175-81.

[18] Syrop CH, Sahakian V. *Transvaginal Sonographic Detection of Endometrial Polyps with Fluid Contrast Augmentation.* Obstetrics & Gynecology 1992. 79,6: 1041-3.

[19] Goldstein SR. *Use of Ultrasonohysterography for Triage of Perimenopausal Patients with Unexplained Uterine Bleeding*. Am J Obstet Gynecol 1994; 170: 565-70.

[20] Goldstein SR, Zeltser I, Horan CK, et al. *Ultrasonography-Based Triage For Perimenopausal Patients with Abnormal Uterine Bleeding.* Am J Obstet Gyneco. 1997; 177: 102-8.

[21] Wolman I, Groutz A, Gordon D, Kupfermic MJ, Lessing JB, Jaffe AJ, *Timing of SHG in Menstruating Women.* Gynecol Obstet Invest 1999; 48: 254-8.

[22] Rodriguez GC, Yaqub N, King ME. *A Comparison of the Pipelle Device and the Vabra Aspirator as Measured by Endometrial Denudation In Hysterectomy Specimens: The Pipelle Device Samples Significantly Less of the Endometrial Surface than the Vabra Aspirator.* Am J Obstet Gynecol 1993; 168: 55-59.

[23] Scott R. *The Elusive Endometrial Polyp.* Obstet Gynecol 1953; 1: 212-218.

[24] Word B. *Pitfalls of Uterine Curettage.* South Med J 1954; 47: 38-47.

[25] Karlsson B, Granberg S, Hellberg P, Wikland M. *Comparative Study of Transvaginal Sonography and Hysteroscopy for the Detection of Pathologic Endometrial Lesions in Women with Postmenopausal Bleeding.* J Ultrasound Med 1994; 13: 757-762.

[26] Seinera P, Maccario S, Visentin C et al. *Hysteroscopy in an IVF-ET Program.* Acta Obstet Gynecol Scand. 1988; 67; 135-7.

[27] Mohr J, Lindemann HJ. *Hysteroscopy in the Infertile Patient.* J Reprod Med. 1977; 19: 161-2.

[28] Valle RF. *Hysteroscopy in the Evaluation of Female Infertility*. Am J Obstet Gynecol. 1980; 137; 425-31.

[29] Ayida G. Chamberlain P. Barlow D. Kennedy S. *Uterine Cavity Assessment prior to In Vitro Fertilization: Comparison of Transvaginal Scanning, Saline Contrast Hysterosonography and Hysteroscopy.* Ultrasound in Obstetrics & Gynecology 1997; 10,1: 59-62.

[30] Hamilton JA, Larson AJ, Lower AM, Hasnain S, Grudzinskas JG. *Routine use of Saline Hysterosonography in 500 Consecutive, Unselected, Infertile Women.* Human Reproduction 1998; 13,9: 2463-73.

[31] Keltz MD, Olive DL, Kim AH, Arici A. *Sonohysterography for Screening in Recurrent Pregnancy Loss*. Fertility &Sterility 1997; 67(4): 670-4.

[32] Cohen LS, Valle RF. *Role of Vaginal Sonography and Hysterosonography in the Endoscopic Treatment of Uterine Myomas.* Fertil Steril 2000; 73: 197-204.

[33] Goldstein S, Scheele W, Rajogopalan S,Wilkie JL, Walsh BW, Parsons AK. *A 12-Month Comparative Study of Raloxifene, Estrogen and Placebo on the Postmenopausal Endometrium.* Obstetrics & Gynecology 2000; 95: 95-103.

[34] Fisher B, Constantino JP, Wickerham DK et al. *Tamoxifen for Prevention of Breast Cancer: Report of the National Surgical Adjuvant Breast and Bowel Project P-1 Study*. J Natl Cancer Inst 1998; 90: 1371-88.

[35] Cohen I, Rosen DJ, Shapira J, Cordoba M et al. *Endometrial Changes with Tamoxifen: Comparison between Tamoxifen-Treated and Nontreated Asymptomatic Postmenopausal Breast Cancer Patients.* Gynecol Oncol 1994; 52: 185-190.

[36] Lahti E, Blanco G, Kauppila A et al. *Endometrial Changes in Postmenopausal Breast Cancer Patients Receiving Tamoxifen.* Obstet Gyneocl 1993; 81: 660-664.

[37] Goldstein SR. *Unusual Ultrasonographic Appearance of the Uterus in Patients Receiving Tamoxifen.* Am J Obstet Gynecol 1994; 170: 447-51.

[38] Neven P, Van Belle Y, De Muylder X, Campo R, Vanderick G. *The Hysteroscopic Assessment of Women taking Tamoxifen.* Acta Obstetricia Et Gynecologica Scandinavica 1997; 76 (167 Suppl 1): 13.

[39] Schwarzler P, Concin H, Bosch H et al. *An Evaluation of SHG and Diagnostic Hysterscopy for the Assessment of Intrauterine Pathology.* Ultrasound in Obst and Gyne 1998; 11: 337-42.

[40] Berliere M, Charles A, Galant C, Donnez J. *Uterine Side Effects of Tamoxifen: A Need for Systematic Pretreatment Screening.* Obstet Gynecol 1998; 91: 40-44.

[41] *Tamoxifen and Endometrial Cancer.* ACOG Committee Opinion, 1996, No. 169.

[42] Widrich T, Bradley LD, Mitchinson AR, Collins RL. *Comparison of Saline Infusion Sonography with Office Hysteroscopy for the Evaluation of the Endometrium.* Am J Obstet Gynecol 1996; 174: 1327-34.

[43] Kamel HS, Darwish AM, Mohamed SA. *Comparison of TVU and SIS For Polyps.* Acta Obstet. Gynecol Scand 2000; 79: 60-4.

[44] Clevenger-Hoeft M, Syrop CH, Stovall DW, Van Voorhis BJ. *SHG in Premenopausal Women with and without Abnormal Bleeding.* Obstet Gynecol 1999, 94: 516-20.

[45] Londono J, Parsons A. Abstract: *Ultrasound Directed Endometrial Biopsy.* 8th Annual World Congress of Ultrasound in Obstetrics and Gynecology, Edinburgh, Scotland, Nov. 9, 1998.

[46] Tjarks M, Van Voorhuis BJ. *Treatment of Endometrial Polyps.* Obstet & Gynecol 2000; 96: 886-89.

[47] Wolman I, Jaffa A, Hartoov J, Bar-Am A, David M. *Sensitivity and Specificity of Sonohysterography for the Evaluation of the Cavity in Perimenopausal Patients.* Journal Ultrasound Med 1996; 15: 285-8.

[48] Alcazar JL, Errasti T, Zornoza A. *Saline Infusion Sonohysterography in Endometrial Cancer: Assessment of Malignant Cells' Dissemination Risk.* Acta Obstetricia et Gynec Scand 2000; 79: 321-2.

[49] Devore GR, Hysterography: *A 5 Year Followup in Patients with Endometrial Carcinoma.* Obstet Gynec 1972; 60: 369-72.

[50] Bernard JP, Lecuru F, Darles C, Robin F, Depierre P et al. *Saline Contrast Sonohysterography as First Line Investigation for Women with Uterine Bleeding.* Ultrasound in Obstet Gynec 1997; 10: 121-5.

[51] Williams CD, Marshburn PB. *A Prospective Study of Transvaginal Hydrosonography in the Evaluation of AUB.* Am J Obstet Gynecol 1998; 179: 292-8.

[52] Parsons AK, Lenz JJ. *Sonohysterography for Endometrial Abnormalities: Preliminary Results.* Journal of Clinical Ultrasound 1993; 21: 87-95.

[53] Dijkhuizen FPHLJ, DeVries LD, Mol BWJ et al. *Comparison of Transvaginal Ultrasonography and Saline Infusion Sonography for the Detection of Intracavitary Abnormalities in Premenopausal Women.* Ultrasound Obstet Gynecol 2000; 15: 372-376.

[54] Platt LD, Agarwal SK, Greene N. *The use of Chorionic Villus Biopsy Catheters for Saline Infusion Sonohysterography.* Ultrasound Obstet Gynecol 2000; 15: 83-4.