Routine use of saline hysterosonography in 500 consecutive, unselected, infertile women

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Saline hysterosonography was attempted as a routine, first-line screening test of uterine structure in 500 consecutive, unselected, infertile women. The procedure was completed in 96.8% (484/500) women and the observations were interpretable in 483 of these women. Intrauterine pathology was suspected in 67/499 (13.4%) women on plain ultrasound scan and 58/484 (12%) women with saline hysterosonography. Ultrasound alone had a superior specificity (96.3%) to sensitivity (81.8%) and better negative (97.6%) than positive (73.8%) predictive value for the detection of any intrauterine abnormality, using saline hysterosonography as the reference procedure. Suspected pathology at saline hysterosonography led to hysteroscopy in 20 women, after a median of 5.7 months (range, 1–14). The overall concordance rate between the two procedures was 65% with lesions suspicious of intrauterine polyps not present at subsequent hysteroscopy on six occasions. Criteria were established to help identify women with potentially self-limiting lesions, in whom a re-scan should be considered before resorting to hysteroscopy. The procedure was well tolerated with no significant complications. Saline hysterosonography appeared to be an acceptable first-line screening procedure for uterine structure which enhanced the predictive power of ultrasound alone for uterine anomalies and provided additional information which was potentially of value when planning operative hysteroscopy.

Key words: endometrium/hysterosonography/infertility/saline infusion/transvaginal ultrasonography

Introduction

Almost one quarter of women with congenital or acquired structural uterine abnormalities experience difficulty with conception, accounting for up to 10% of infertility cases (Collins and Woodward, 1995). Anatomical distortion of the endometrial cavity can predispose, in certain cases, to implantation failure (Nickerson, 1977; De Cherney, 1990; Fedele et al., 1996a; Stovall et al., 1998) and to difficult embryo transfer at in-vitro fertilization (IVF) treatment. Other anomalies increase the risk of miscarriage and later pregnancy complications (Buttram and Reiter, 1981; Rock and Schlaff, 1985; Valle and Sciarra, 1988; Bardeguez, 1990; Marcus et al., 1996; Raga et al., 1997). Surgical correction of these disorders can improve treatment-dependent and treatment-independent pregnancy rates (Valle, 1989; Narayan and Goswamy, 1994) and live birth rates (Verkauf, 1992; Fedele et al., 1993a; Dubuisson et al., 1996; Jacobsen and De Cherney, 1997). Assessment of uterine structure is particularly relevant to the large number of women who present for assisted reproductive technologies at an advanced age, when the risk of pregnancy complications (Berkowitz et al., 1990) and the prevalence of acquired uterine anomalies have increased (Schenker and Margalioth, 1982; Van Bogaert, 1988; Verkauf, 1993), and who do so against a background of increasingly restricted funding and cost-effectiveness analysis of such interventions (van Voorhis et al., 1997).

The traditional screening test for uterine anomalies, the hysterosalpingogram (HSG) (Rubin, 1914) is now recognized to have a false-positive rate as high as 38–54% and a false-negative rate of 10–28%, when compared with hysteroscopy (Mencaglia et al., 1988; Raziel et al., 1994). Information is not provided on the external uterine surface and, therefore, bicornuate uteri can only be distinguished from septate uteri in 53% cases (Reuter et al., 1989). Septate uteri have been associated consistently with a poor reproductive outcome relative to that of other Mullerian duct abnormalities (Buttram and Gibbons, 1979) and can be surgically corrected transcervically, unlike bicornuate uterus and, thus, accurate pre-operative diagnosis is important. Magnetic resonance imaging (MRI) and three-dimensional ultrasonography are both methods which visualize the internal and external uterine contours simultaneously (Woodward et al., 1993; Jurkovic et al., 1997) but neither of these procedures is routinely available in fertility centres. Hysteroscopy remains the ‘gold standard’ but it is felt that general anaesthesia is not justifiable in a first-line screening test for uterine anomalies. Office hysteroscopy still requires specialized equipment and sterilization facilities and is not widely available; only 28% of American gynaecologists actually offer this service (Hulka et al., 1995).

Expertise in transvaginal ultrasonography is readily accessible in all fertility centres and the ability of ultrasound to detect uterine abnormalities (Narayan and Goswamy, 1993) is now known to be enhanced significantly after the transcervical instillation of sterile saline solution – saline hysterosonography (Balen et al., 1993; Parsons and Lense, 1993; Goldstein 1996). Use of this technique has been described previously in women with abnormal uterine bleeding (n = 220) (Rudigoz et al., 1995), in whom it has been shown to have a detection rate not significantly different from that of office hysteroscopy.
(Widrich et al., 1996); in those on adjuvant tamoxifen therapy after treatment for carcinoma of the breast \( n = 68 \) (Tepper et al., 1997); in sufferers of recurrent miscarriage \( n = 34 \) (Keltz et al., 1997); in women in whom either a septate uterus \( n = 14 \) (Salle et al., 1996) or any uterine abnormality \( n = 40 \) (Goldberg et al., 1997) was suspected at HSG; during infertility investigations \( n = 62 \) (Alatas et al., 1997) and prior to IVF treatment \( n = 148 \) (Syrop and Sahakian, 1992).

This study has examined for the first time the performance of saline hysterosonography as a routine, first-line, out-patient investigation of uterine structure in 500 consecutive women presenting for investigation of infertility. Any suspected pathology thought to be relevant to the delay in conception was compared, prospectively, with the findings at operative hysteroscopy, which was performed after a median interval of 5.7 months (range, 1–14).

Materials and methods

Patients

Examination of 500 consecutive women attending a teaching hospital tertiary referral centre for the investigation of infertility was undertaken from February 1996 to July 1997. The women had a median age of 31.0 years (range, 20–44), body mass index (BMI) of 23.0 kg/m\(^2\) (range, 16–45) and their median length of infertility was 3.5 years (range, 1–18). Primary infertility was the complaint in 62.6% (313/500) of the women and 86.8% (434/500) were nulliparous. Investigations were preferably performed throughout the proliferative phase of the menstrual cycle on a median cycle day of 8, with a range from day 1 to day 35. Exclusion criteria were symptoms or signs of active pelvic infection and risk of conception in the menstrual cycle during which the procedure was undertaken. All patients received 1 g mefenamic acid, orally, 30 min prior to the examination but prophylactic antibiotics were not routinely administered.

Investigation

The first two authors (J.A.H. and A.J.L.) performed 85% (425/500) of the saline hysterosonography procedures together. If either of these authors was absent, which occurred in 7% (35/500) and 8% (40/500) cases, respectively, the other was always present. Initially, a conventional B-mode, precontrast (plain) transvaginal ultrasound scan was performed, with the patient in the dorsal lithotomy position, using a Toshiba ‘SSA-220A’ ultrasound scanning machine (Tokyo, Japan) with a 6 MHz transvaginal probe. Sector images of the uterus, ovaries and any adnexal pathology identified were obtained, in longitudinal and transverse sections, and copies made on to heat-sensitive paper. The method of insertion of the 5-French intrauterine balloon catheter (Schering AG, Berlin, Germany) is detailed in the separate report on assessment of Fallopian tubal patency (Hamilton et al., 1998). Sterile 0.154 M sodium chloride solution was drawn up into a 10-ml syringe and slowly injected via the catheter side arm in 1–2 ml boluses, under sonographic control. Injecting the saline too rapidly introduced air into the cavity which was highly echogenic and made interpretation of the normally hyperechoic endometrium more difficult. Any saline which contained air was, thus, allowed to pass along the Fallopian tubes before slowly injecting more unagitated saline. Once the endometrial cavity contained approximately 2 ml of saline the catheter balloon was deflated, to avoid confusion with any intrauterine lesions and to permit assessment of the supracervical region.

Detailed examination of the uterus and in particular the endometrial cavity was performed by slowly scanning from the cervix through to the fundus, in longitudinal and transverse planes in an attempt to achieve a three-dimensional impression of its structure and to minimize the chance of overlooking any focal pathology. The dimensions of any suspected lesions were noted, including the width and length of any septae visualized, and copies made on to both heat-sensitive paper and videotape. The details of tubal assessment with a galactose microbubble contrast agent (Echovist\textsuperscript{®}, 200; Schering AG Berlin), which immediately followed this examination with saline are reported elsewhere (Hamilton et al., 1998).

All women investigated were requested to remain under observation, in a reclining armchair, until they felt sufficiently comfortable to leave the department. Women in whom suspected pathology was identified at saline hysterosonography which was thought to be relevant to their infertility were scheduled for operative hysteroscopy at a future date, dictated by our National Health Service waiting list. The third author (A.M.L.) performed or supervised all of these hysteroscopies, undertaken using saline distension medium and a rigid 4-mm, 30\(^0\) hystroscope (Olympus Optical, Hamburg, Germany).

Statistical analysis

Non-parametric analysis (Mann–Whitney U test) was applied to the characteristics of lesions suspected at hysterosonography which were still present at hysteroscopy and to those which did not persist, because the data were not normally distributed. The level of statistical significance was chosen as \( P < 0.05 \).

Results

Procedures completed

Saline hysterosonography (SHS) was not completed in 16 out of the 500 women (3.2%) in whom the procedure was attempted. One patient who suffered from severe vaginismus, secondary to previous sexual abuse, could not tolerate insertion of the transvaginal ultrasound probe. Catheterization and saline injection were not undertaken in seven women who attended the assessment consultation when the precontrast scan appearances were suspicious of ovulation already having occurred in that menstrual cycle. Problems relating to insertion of the intrauterine catheter caused a further eight procedures to be abandoned: three of these because of severe vasovagal reactions on passing the catheter or inflating its balloon, whilst the presence of a tight nulliparous cervical os led to an additional five procedures not being completed. Inadequate visualization of the uterine cavity occurred in only one woman in whom even plain transvaginal sonography was technically extremely difficult due to her increased BMI and an oblique uterine position. In all other cases it was possible to instil an adequate volume of saline, typically only 2–5 ml, to visualize the endometrial cavity, including the three women in whom an insufficient cervical seal prevented subsequent adequate assessment of Fallopian tubal patency with Echovist.

Suspected pathology

Uterine lesions were suspected in 67/499 (13.4%) women on plain ultrasound scan, 58/484 (12%) with saline hysterosonography and 14/20 (70%) women referred for hysteroscopy as a result of positive findings, of potential relevance to infertility in the latter procedure (Table 1). These figures only include those leiomyomata suspected to be submucosal. The overall
Hysterosonography in 500 consecutive, infertile women

Table I.

<table>
<thead>
<tr>
<th>Suspected lesion</th>
<th>No. on plain USa (n = 499)</th>
<th>No. on SHSb (n = 484)</th>
<th>No. at hysteroscopyc (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical polyps</td>
<td>0</td>
<td>1d</td>
<td>1/1</td>
</tr>
<tr>
<td>Endometrial polyps</td>
<td>16</td>
<td>11</td>
<td>5/7</td>
</tr>
<tr>
<td>Submucosal leiomyomata</td>
<td>10</td>
<td>3</td>
<td>2/3</td>
</tr>
<tr>
<td>Polyp?/leiomyoma?</td>
<td>4</td>
<td>4</td>
<td>2/4</td>
</tr>
<tr>
<td>Menstrual debris?</td>
<td>0</td>
<td>5</td>
<td>0/0</td>
</tr>
<tr>
<td>Thick, irreg. endo – ?pathol.</td>
<td>2</td>
<td>0</td>
<td>0/0</td>
</tr>
<tr>
<td>Intrauterine synchieae</td>
<td>1</td>
<td>1</td>
<td>1/1</td>
</tr>
<tr>
<td>Arcuate/subseptate</td>
<td>20</td>
<td>21</td>
<td>1/0c</td>
</tr>
<tr>
<td>Bicornuate</td>
<td>2</td>
<td>2</td>
<td>0/0</td>
</tr>
<tr>
<td>Unicornuate</td>
<td>0</td>
<td>1</td>
<td>0/0</td>
</tr>
<tr>
<td>Cystic glandular hyperplasia</td>
<td>1</td>
<td>1</td>
<td>0/0</td>
</tr>
<tr>
<td>Adenomyosis</td>
<td>3</td>
<td>3</td>
<td>1/18</td>
</tr>
<tr>
<td>Cystic degeneration of fibroid</td>
<td>1</td>
<td>1</td>
<td>1/1</td>
</tr>
<tr>
<td>Intravasation?</td>
<td>0</td>
<td>1</td>
<td>0/0</td>
</tr>
<tr>
<td>Endometrial ‘wrinkles’/‘folds’</td>
<td>0</td>
<td>1</td>
<td>0/0</td>
</tr>
<tr>
<td>Not assessable</td>
<td>7</td>
<td>1</td>
<td>0/1</td>
</tr>
<tr>
<td>Unclassifiabled</td>
<td>0</td>
<td>1</td>
<td>1/1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>67 (13.4%)</strong></td>
<td><strong>58 (12.0%)</strong></td>
<td><strong>14/20 (70%)</strong></td>
</tr>
</tbody>
</table>

a U/S = ultrasound; b SHS = saline hysterosonography; c x/y = number confirmed at hysteroscopy/number suspected at SHS who underwent hysteroscopy; d detected on direct vision, not sonographically; e one of these cases diagnosed on histology; f thickened, irregular endometrium – ? of pathological significance; g same woman, counted once as ‘not in agreement’ in concordance statistics; h patient referred for operation but did not attend; i see text for details.

The concordance rate of plain sonography with hysterosonography for the detection of any intrauterine lesion was 94.6%. This gave ultrasonography a sensitivity of 81.8%, a specificity of 96.3%, positive predictive value (PPV) of 73.8% and a negative predictive value (NPV) of 97.6%, with SHS as the reference procedure. Only women with suspected pathology on SHS were referred for hysteroscopy, performed after a median interval of 5.7 months (range, 1–14). The concordance rates of each of precontrast ultrasonography and SHS with hysteroscopy for the subgroup of women referred for this procedure were 52.6% and 65%, respectively.

**Polyps and leiomyomata uteri**

A cervical polyp was identified on attempting catheterization in one woman which protruded beyond the external cervical os and, thus, lay too close to the transvaginal probe to be detected sonographically. This has since been removed at hysteroscopy. An isolated, hyperechoic lesion, apparently within the endometrial cavity and seen on precontrast scan (Figure 1a) was suggestive of the presence of an intrauterine polyp after saline injection on 10/16 (62.5%) occasions (Figure 1b). The six ‘false positives’ with plain sonography were investigated on a median cycle day of 12 (range, 8–15), since last menstrual period. Table II provides details of the women in whom intrauterine polyps were suspected at SHS. Six women were referred for a re-scan (see later): in three of these cases the echogenic area was no longer visible, a fourth woman decided against any further investigations and, of the two women in whom the potential polyps persisted, subsequent hysteroscopy confirmed the presence of both lesions. Hysteroscopy was performed in a further five women, at a median of 5.5 months (range, 2–8) after the initial SHS.

A sonographic appearance compatible with the presence of leiomyomata uteri was seen on precontrast scan in 44 women, although in 34 of these the fibroids appeared not to impinge upon the endometrial cavity, an impression which was subsequently endorsed after saline instillation. Despite uncertainty with plain sonography, saline provided evidence of an unaffected endometrial cavity in seven of the remaining 10 of these women (70%), whilst both procedures suggested the presence of submucosal leiomyomata in the other three women (Figure 2a, b and c). In another four women, two of whom appeared to have co-existing intramural and subserosal fibroids, it was not possible to differentiate between the presence of a broad-based sessile polyp or a pedunculated leiomyoma. Table III provides details of these seven, further women with sus-
A single case of acquired intrauterine synechiae was suspected, along with 21 minor and three more major congenital uterine anomalies (Table I). Despite 60 of the women (12%) demonstrating an ultrasound appearance which fulfilled the classic sonographic criteria of polycystic ovarian disease (Adams et al., 1985) only one case of possible cystic glandular hyperplasia was identified which had been suspected on plain scan (Figure 3a) but saline infusion provided additional evidence that these cystic areas were within the endometrium. In contrast, similar sonoluent areas were present but appeared to lie within the myometrium (Figure 3b and c) in three women in whom adenomyosis was, therefore, suspected (Walsh et al., 1979). One woman who had previously undergone unilateral salpingectomy and in whom proximal blockage of the remaining Fallopian tube had been demonstrated at laparoscopy and dye chromopertubation had unremarkable findings on plain sonography but intravasation of saline was seen at SHS. One case of cystic/haemorrhagic degeneration of a leiomyoma was suspected with plain ultrasound, hysterosonography and a subsequent MRI scan and this lesion has since been resected hysteroscopically and the provisional diagnosis confirmed by histopathological examination (Figure 4).

The ‘unclassifiable’ lesion in Table I refers to a woman in whom saline infusion, on cycle day 10, revealed a narrow echogenic band apparently attached to the two lateral uterine walls, below the level of the cornual portions of each Fallopian

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**Table II. Details of women in whom polyps were suspected at hysterosonography and their follow-up**

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Type infert.</th>
<th>Years infert.</th>
<th>Menst. sympt.</th>
<th>SHS K Day^a</th>
<th>Suspected plain US^b</th>
<th>SHS findings</th>
<th>Months to hyst./re-scan</th>
<th>Histology findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>32</td>
<td>1°</td>
<td>8</td>
<td>Dysmen.</td>
<td>8</td>
<td>Yes</td>
<td>12×5 mm, fundal</td>
<td>6</td>
<td>Hyst. – profuse, proliferative endometrium</td>
</tr>
<tr>
<td>41</td>
<td>2°NP^c</td>
<td>8</td>
<td>None</td>
<td>7</td>
<td>Yes</td>
<td>9.5×4.2 mm, fundal</td>
<td>1.5</td>
<td>Re-scan – polyp gone</td>
</tr>
<tr>
<td>34</td>
<td>2°NP</td>
<td>2.5</td>
<td>OA</td>
<td>16</td>
<td>Yes</td>
<td>10 mm, R^d cornum</td>
<td>2</td>
<td>Re-scan – Polyp gone</td>
</tr>
<tr>
<td>43</td>
<td>2°NP</td>
<td>6</td>
<td>None</td>
<td>7</td>
<td>Yes</td>
<td>8.1×5.5 mm, fundal</td>
<td>0^e</td>
<td>Not available</td>
</tr>
<tr>
<td>29</td>
<td>1°</td>
<td>3</td>
<td>None</td>
<td>6</td>
<td>Yes</td>
<td>12.1×7.1 mm, ?debris</td>
<td>8</td>
<td>Hyst. – Normal cavity</td>
</tr>
<tr>
<td>31</td>
<td>1°</td>
<td>2</td>
<td>None</td>
<td>9</td>
<td>No</td>
<td>11.3 mm, fundal</td>
<td>8</td>
<td>Hyst. – 1cm fundal polyp</td>
</tr>
<tr>
<td>32</td>
<td>1°</td>
<td>6</td>
<td>Dysmen.</td>
<td>9</td>
<td>Yes</td>
<td>14 mm, fundal</td>
<td>2</td>
<td>Hyst. – L^f sided polyp</td>
</tr>
<tr>
<td>33</td>
<td>1°</td>
<td>12</td>
<td>Dysmen., menorr.</td>
<td>10</td>
<td>Yes</td>
<td>10.7×9.4 mm, R. fundal</td>
<td>5</td>
<td>Hyst. – 0.75 mm polyp R. cornual orifice</td>
</tr>
<tr>
<td>33</td>
<td>1°</td>
<td>2</td>
<td>Dysmen.</td>
<td>8</td>
<td>Yes</td>
<td>5×8 mm, fundal</td>
<td>14</td>
<td>Re-scan – polyp gone</td>
</tr>
<tr>
<td>31</td>
<td>2°NP</td>
<td>3</td>
<td>None</td>
<td>7</td>
<td>Yes</td>
<td>7.9×6.5 mm, fundal</td>
<td>7^i</td>
<td>Re-scan – polyp present, Hyst. – 1 cm fundal</td>
</tr>
<tr>
<td>36</td>
<td>2°</td>
<td>3</td>
<td>Dysmen.</td>
<td>3</td>
<td>Yes</td>
<td>9.1×4.8 mm, R. cornuum</td>
<td>5^j</td>
<td>Re-scan – polyp present, ?fibroid polyp</td>
</tr>
<tr>
<td>31</td>
<td>1°</td>
<td>1.5</td>
<td>None</td>
<td>8</td>
<td>No</td>
<td>? Cervical polyp</td>
<td>2</td>
<td>Hyst. – broad-based polyp</td>
</tr>
</tbody>
</table>

^aInfert. = infertility; ^bMenst. sympt. = usual menstrual symptoms (menorr. = menorrhagia; OA = oligoamenorrhea; dysmen. = dysmenorrhea); ^cSHS K Day = cycle day on which hysterosonography (SHS) performed; ^dUS = ultrasound; ^eHyst. = hysteroscopy; ^fNP = nulliparous; ^gR = right; ^hreferred for re-scan but declined further investigations; ^il = left; ^mtime to hysteroscopy (months).
Figure 2. (a) Longitudinal section through the uterus, prior to fluid injection showing a 19.9 × 17.0 mm area of altered echogenicity supracervically (see calipers) and a 15.1 × 18.0 mm suspected lesion at the fundus (see arrowheads), obscuring the ultrasonographic view of the endometrium; (b) longitudinal section after saline instillation, confirming positions of submucosal leiomyomata (M) and (c) transverse section through (i) supracervical region showing submucosal leiomyoma and (ii) fundal region demonstrating a pedunculated myoma.

Saline could pass anterior and posterior to this band to reach the tubes (Figure 5a). A hysteroscopy, performed 5 months later, reported fronds of endometrium arising from the lateral uterine walls. A single case consistent sonographically with characteristics previously reported as ‘endometrial wrinkles’ was noted (Figure 5b) (Parsons and Lense, 1993) but no further investigation was scheduled since such lesions were associated with normal hysteroscopies in that study.

Procedure acceptability
There were no significant post-procedure complications and, in particular, no cases suspicious of pelvic infection. Further details of this and the pain perceived by the women after plain sonography and injection of both saline and Echovist are provided in the separate report on assessment of Fallopian tubal patency (Hamilton et al., 1998).

Discussion
This study describes observations in the largest series of consecutive, unselected, infertile women to undergo saline hysterosonography as part of their routine infertility assessment and the subsequent hysteroscopic findings in those in whom the appearances at this procedure were suspicions of the presence of pathology which was considered to potentially be of relevance to their difficulty in conception.

Saline hysterosonography was technically uncomplicated, with only 1.6% (8/500) of the procedures not being completed because of severe vasovagal reactions or difficulty in the catheterization process and in one further woman in whom the sonographic findings were not interpretable, with or without saline enhancement. Use of the intrauterine balloon catheter ensures a good cervical seal, necessary in our study for subsequent assessment of Fallopian tubal patency, but can increase patient discomfort and the risk of vasovagal reactions. An intrauterine insemination type catheter is, therefore, probably preferable if only uterine assessment is required. Our findings agree with those previously published (Goldstein, 1996) in that only a small volume of sonolucent fluid needs to be retained within the uterine cavity to permit adequate visualization of the endometrium. This is particularly relevant to those women with bilateral Fallopian tubal patency in whom the saline tends to pass rapidly out of the uterine cavity and in whom continual, slow infusion under minimal pressure is, therefore, necessary. The degree of distension necessary to accommodate this small volume of fluid is less than that required for adequate visualization at hysteroscopy. This may partially explain why saline hysterosonography has been noted to be significantly less uncomfortable than office hysteroscopy (Widrich et al., 1996).

In the current study, SHS suspected the presence of uterine cavity pathology in 9.7% (47/484) women (excluding the presumed cases of menstrual debris and intravasation). This figure increased to 19.2% (93/484) of these asymptomatic, infertile women if all pathologies, including leiomyomata in all sites and the cervical polyp, are counted. Endometrial polyps have previously been demonstrated in 9.5% (14/148) patients prior to an IVF cycle (Syrop and Sahakian, 1992) and
any intra-cavity pathology was found in 16.1% (10/62) infertile women (Alatas et al., 1997); both studies used SHS. Intrauterine polyps and leiomyomata have been noted at 12.7–21.3% of hysteroscopies performed as a routine infertility investigation (van der Leij and Lammes, 1997). The data from this study, therefore, support previous findings that the prevalence of uterine pathology in asymptomatic, infertile women justifies routine evaluation of the uterus as a first-line infertility investigation (Gaucherand et al., 1995; Alatas et al., 1997). A oblique uterine position can also render adequate assessment of the endometrium difficult with plain sonography, as occurred in six women, but in all these cases saline instillation was able to demarcate the endometrial cavity.

Precontrast ultrasonography tended to overdiagnose lesions which would be compatible with intrauterine polyps or submucosal leiomyomata, compared with our findings at SHS. Hyperechoic areas suspicious of the presence of an intrauterine polyp on plain scan were seen, after saline injection to represent normal late proliferative phase thickening of the endometrium which, although not desirable, is possible. The views obtained are, perhaps, less influenced by the presence of heavy bleeding than those obtained at hysteroscopy. Menstrual debris is usually obvious at SHS as a less discrete lesion, arising from a generally more irregular endometrium and which can often be displaced by continuous injection of the contrast agent (Figure 6). Menses, therefore, was not considered to be an absolute contraindication to the procedure, provided that a high degree of suspicion was maintained about the possible transitory nature of any apparent lesions viewed and a re-scan scheduled in the small number of cases where doubt persisted.

### Table III. Details of women with suspected leiomyomata/sessile polyps at hysterosonography and their follow-up

<table>
<thead>
<tr>
<th>Age</th>
<th>Type infert.*</th>
<th>Years infert.</th>
<th>Menstr. symp.</th>
<th>SHS K Day</th>
<th>SHS findings</th>
<th>Months to hyst.</th>
<th>Hyst. findings</th>
<th>Histology</th>
</tr>
</thead>
<tbody>
<tr>
<td>?Leiomyomata uteri</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>27</td>
<td>1°</td>
<td>3</td>
<td>Menorr., dysmen.</td>
<td>13</td>
<td>Yes</td>
<td>19.9×17 mm S/M, supracervically and 17.7 mm S/M, pedunculated, fundally</td>
<td>7</td>
<td>2 cm supracervical, 2 cm pedunculated at fundus</td>
</tr>
<tr>
<td>36</td>
<td>1°</td>
<td>4</td>
<td>Menorr., dysmen.</td>
<td>8</td>
<td>Yes</td>
<td>31×13.6×15 mm S/M, posterior uterine wall at fundus</td>
<td>1</td>
<td>2 cm posterior wall with 1.5 cm base</td>
</tr>
<tr>
<td>36</td>
<td>1°</td>
<td>5</td>
<td>None</td>
<td>9</td>
<td>Yes</td>
<td>Multiple intramural, largest 20×16 mm, 12×11×8 mm S/M supracervically</td>
<td>3</td>
<td>Regular uterine cavity</td>
</tr>
</tbody>
</table>

| ?Sessile polyp/?pedunculated leiomyoma |
| 33  | 1°           | 3.5          | Menorr.       | 12       | Yes | 8×15×24 mm S/M, fundal and subserosal, anterior wall | 12 | ? Fibroid polyp R.³ cornum | Benign adenomatous polyp |
| 33  | 1°           | 5            | Menorr.       | 12       | Yes | 9.5×6.9×6.3 mm, fundal | 2 | Regular uterine cavity | None available |
| 31  | 1°           | 8            | None          | 12       | Yes | 6.8 mm S/M, fundal and 41×35 mm, subserosal ×3 S/M, all only 5–6 mm | 6 | Regular uterine cavity | None available |
| 39  | 2°           | 3            | None          | 13       | Yes | 17 mm S/M f , 7 2 cm supracervical, Benign dysmen. and subserosal, anterior wall | 8 | Regular uterine cavity | Hyperplastic endometrial polyp |

*See Table II. S/M = submucosal.

### Table IV. Criteria for recommending re-scan after at least one further menstrual bleed, prior to scheduling hysteroscopy for suspected intrauterine lesions

(i) Greatest diameter < 10 mm
(ii) Patient currently menstruating
(iii) No other abnormalities, especially myometrial
(iv) Lesion not well defined (should have regular external contour and be well circumscribed by saline)
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Saline hysterosonography also appeared to overdiagnose the number of intrauterine polyps actually found at subsequent hysteroscopy, leading to the low concordance rate between the two procedures. The potentially transitory nature of such lesions is, however, well recognized, especially in pre-menopausal women (Van Bogaert, 1988). It is possible that a proportion of these polyps had actually been shed by the time hysteroscopy was subsequently undertaken, after a median delay of just under 6 months. The concordance rate for these findings may, therefore, have been greater had hysteroscopy been undertaken immediately after SHS or within the next cycle, as previous studies have described (Widrich et al., 1996; Alatas et al., 1997). Repeating the ultrasound scan after at least one further menstrual bleed, in women whose suspected lesion fulfils any of the criteria in Table IV may also reduce the number of unnecessary hysteroscopies performed by selecting out pathology which is more likely to be self-limiting. The clinical history should be taken into consideration, in addition to these criteria, although in our series only the woman with the cervical polyp was symptomatic of irregular vaginal bleeding. This may, however, have been because the polyps identified were of only small-to-moderate size. Whether intrauterine polyps actually influence patients’ ability to conceive is a source of debate (Taylor and Cumming, 1979; Cooper et al., 1983, Glazener et al., 1987) but most clinicians would opt to remove those which were persistent prior to commencing treatment which is often expensive and/or invasive and because some evidence exists that they may predispose to endometrial hyperplasia and even carcinoma, in later life (Pettersson et al., 1985).

It was not always possible to distinguish a sessile polyp from a pedunculated, submucosal leiomyoma, especially if there were coexisting subserosal and intramural leiomyomata. The ability of precontrast ultrasonography to detect concurrently leiomyomata in these latter sites and to assess the degree
of any overall enlargement in uterine size has previously been cited as an advantage of the procedure over the HSG (Khastgir et al., 1993). The extent of endometrial cavity distortion is often difficult to assess, however, as occurred in 10 women in our series. Injection of the negative-contrast agent saline helped clarify these cases and also provided an indication of the depth of myometrial invasion of those leiomyomata which were apparently submucosal, which is important if planning hysteroscopic resection. Assessment of the myometrium and its relationship to the endometrium is one of the key reasons why saline and not the galactose microbubble contrast agent, Echovist, was chosen for uterine assessment. Echovist is highly echogenic which makes demarcation of the normally hyperechoic endometrium more difficult and also tends to generate acoustic shadows which can obscure the myometrium, particularly on the posterior uterine wall. Saline infusion has previously been used to help distinguish between sonoluent areas in the endometrium and those in the adjacent proximal myometrium, in studies of women on adjuvant tamoxifen therapy for carcinoma of the breast (Perrot et al., 1994). In this study, saline has proven most useful in distinguishing areas of possible adenomyosis from those of cystic glandular hyperplasia. Conservative surgery for adenomyosis is not commonly practised (Fedele et al., 1993b); therefore, in a woman wishing to preserve her fertility, no definitive method of confirming this diagnosis exists but MRI is currently considered to be the most reliable radiological test (Arnold et al., 1995). Owing to differing referral patterns of the clinicians who subsequently reviewed the three women with suspected adenomyosis, only one subsequently underwent an MRI scan which provided supportive evidence for the diagnosis at SHS. This woman also underwent laparoscopy and hysteroscopy, as a result of the co-existing finding of a suspected ovarian endometrioma, and was found at hysteroscopy to have a mildly subseptate uterus which had not been commented upon at SHS.

Saline instillation did indicate the presence of an arcuate or very mildly subseptate uterus in 21 other women who were not referred for hysteroscopy, since these appearances are probably not of any relevance to reproduction per se (Fedele et al., 1996b; Raga et al., 1997). Although we did not identify any septae of significant length (Buttram and Gibbons, 1979; American Fertility Society, 1988), the arcuate/mildly subseptate cases accustomed us to the smooth external uterine appearance found with septate or subseptate anomalies (Figure 7a), which was useful for comparison with the less common, notched, fundal indentation seen in cases of bicornuate uteri (Figure 7b). Both cases of bicornuate uteri were suspected with plain ultrasonography but instilling saline helped clarify whether both horns communicated and which side was dominant. Saline hysterosonography indicated the presence of a unicornuate uterus with only a right horn present, as is most commonly the case because of the embryological tendency for a dominance of the right side (Heinonen, 1997). The precontrast ultrasound picture for this woman had been difficult to interpret because of the apparently oblique position of the uterus. Unfortunately, she has not yet attended for hysteroscopy and laparoscopy and we await confirmation of this finding. One case of acquired...
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Figure 7. (a) Transverse section through the uterine fundus after saline instillation showing an arcuate-shaped cavity. Note the smooth external uterine contour (arrowheads); and (b) bicornuate uterus, in transverse section, on precontrast scan. Calipers highlight the two endometrial cavities. Note the indentation of the serosal surface (arrowheads) at the fundus.

Figure 8. (a) Longitudinal section on precontrast scan demonstrating an apparent constriction within the endometrial cavity (arrowhead) (b) saline instillation revealed incomplete adherence of the anterior and posterior uterine walls at multiple levels, in different planes (arrowheads). Intrauterine synechiae were later resected at hysteroscopy.

intrauterine synechiae was suspected on plain sonography (Figure 8a), more specifically delineated with SHS (Figure 8b), and has since been confirmed and resected hysteroscopically. This woman gave a history of severe endometritis following a first trimester miscarriage but was experiencing apparently normal, monthly menses. Single cases of isolated lesions which are less easy to define are probably consistent with any relatively new procedure being performed in a large number of women. Previously described 'endometrial wrinkles' may represent what hysteroscopists refer to as 'endometrial folds', although why these do not 'straighten' under the continuous pressure of saline injection is not known. It is difficult to envisage how these miscellaneous lesions could compromise fertility, but they remain as deviations from the most commonly observed contour of the endometrial cavity which may eventually be encountered if a sufficient number of procedures are undertaken.

This study has confirmed that the use of transvaginal ultrasonography in consecutive, infertile women can suggest the presence of a range of uterine anomalies. However, it tends to overdiagnose the presence of lesions and often cannot clearly differentiate between particular types of pathology or, indeed, the site of this pathology within the uterus. SHS was undertaken comfortably as an out-patient procedure and helped exclude some false-positive findings on precontrast scan whilst providing important, additional details on those specific lesions which appeared to persist. A considerable amount of information of potential relevance to these women’s infertility was highlighted which would not have been obtainable at HSG. Despite a moderate concordance rate with hysteroscopy, only one operative finding, of questionable relevance to the woman’s infertility, was not obviously explicable when the original SHS images were reviewed and the natural history of the suspected lesions was taken into consideration. We therefore consider saline hysterosonography to be the most useful first-line screening test for uterine pathology which selects out those women in whom hysteroscopy is most likely to reveal pathology. We advocate its routine use in infertility investigations but caution that attention must be paid to the possible transitory nature of certain of the lesions identified and the fact that,
occasionally, incidental findings will be observed which are sufficiently different from normal to justify individual comment but are probably not of any relevance to the long-term fecundity of these patients.

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