

Assessing tubal damage

ABSTRACT

The fallopian tube plays an important role in the mechanical transport and physiological sustenance of the gametes and early conceptus. Complex and coordinated neuromuscular activity, ciliary action and endocrine secretions are required for successful tubal function. Compromised tubal damage can occur after external or internal injury, inhibiting the normal transport of gametes. The overall prognosis for fertility depends principally on the insult and the severity of the tissue damage; hence, assessment of tubal damage plays a major role in predicting occurrence of pregnancy and the likelihood of developing ectopic pregnancy.

KEY WORDS: Assessment, damage, fallopian tube, gametes, transport

Madhuri Patil

Dr. Patil's Fertility and Endoscopy Clinic, No 1, Uma Admiralty, Bannerghatta Road, Bangalore - 560 029, Karnataka, India

Address for correspondence:

Dr. Madhuri Patil, Dr. Patil's Fertility and Endoscopy Clinic, No 1, Uma Admiralty, Bannerghatta Road, Bangalore - 560 029, Karnataka, India. E-mail: Drmadhurip@rediffmail.com

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INTRODUCTION

The fallopian tube, far from being a passive channel or conduit for gametes and early embryos, plays an important role in many reproductive functions such as sperm transport and capacitation, ova retrieval and transport, fertilization, embryo storage, nourishment and transport.

Tubal stenocclusive and dilative disease is an important cause of infertility and should be specifically looked for. Tubal disease includes tubal obstruction, narrowing, dilatation, as well as conditions that alter tubal function due to changes in the tubal mucosal lining, muscular wall or any pathology present external to the tube. Tubal disease with blockages can involve the proximal part, the mid part or the distal part. Pelvic adhesions due to infection, inflammation, tuberculosis, endometriosis and previous surgery (tubal or nontubal surgery, appendicitis, others) and ectopic pregnancy (medically or surgically managed) are common factors in tubal subfertility and need to be assessed. Prior abortions, medical termination of pregnancy and myomectomy may predispose to subclinical inflammation or infection with coexistent tubal damage.

Incidence

The tubal factor is reported to account for 25–35% of subfertility in the western medical literature, but the prevalence appears to be higher in India due to the higher rates of unrecognised pelvic inflammatory disease (PID) and tuberculosis.

Proximal (uterotubal) obstruction reportedly

occurs in 10–25% of women with tubal disease.^[1] However, population-based data from India are lacking.

Proximal tubal obstruction may be due to muscular spasm, stromal edema, amorphous debris, mucosal agglutination and viscous secretions. Other factors include cornual polyps, chronic salpingitis, endometriosis, salpingitis isthmica nodosa, intrauterine synechiae and parasite infection.

Proximal tubal obstruction secondary to tubal spasm or intratubal debris may be a reversible condition. Pelvic inflammatory disease is a major clinically unsuspected reason for tubal subfertility. PID may be responsible for more than 50% of the causes of tubal factor infertility. PID can damage the tube at multiple sites and also predispose to ectopic pregnancy. Frequently, unsuspected mild subclinical, mucosal disease may be present on performing investigations. Fimbrial end involvement may lead to hydrosalpinx [Figure 1] and fimbrial agglutination. Midtubal disease causes stenocclusions, typically with bulbous termination from scarring and fibrosis.

Less-severe disease may cause distal tubal stenodilatations, fimbrial adhesions, tubal kinking and fixity from adhesions with preserved tubal patency. Tuberculous involvement of the tube can be mild with damage to the tubal lining or more severe, with tubal scarring, rigidity, fibrosis, stenocclusions, dilatations, hydrosalpinx, peritubal and pelvic adhesions. Other important causes of tubal damage include endometriosis (7–14%), salpingitis isthmica

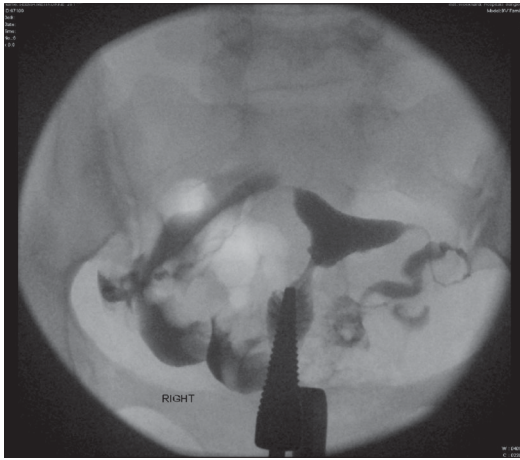


Figure 1: Left hydrosalpinx

nodosa and cornual polypoidal lesions (10%).

Assessment of fallopian tubes

Various methods for the evaluation of tubal factor are complementary and not mutually exclusive. Evaluation of tubal patency and tubal integrity is a key component of the diagnostic work-up in infertile couples.

An ideal (or “gold standard”) test for tubal disease would correctly identify all women with tubal disease. The test should be able to predict pregnancy and also improve pregnancy rates and at the same time, be cost-effective.

Fallopian tube assessment tests

Several tests have been described but only few of them are currently in vogue in clinical practice.

Method of assessment

1. Laparoscopy: Jacobaeus (1910), Palmer (1947).
2. Hysterosalpingogram: Carey (1914).
3. Rubin’s test: Tubal perfusion pressures
 - Oxygen: Rubin (1920).
 - Carbon dioxide: Rubin (1952).
4. Dye injections with culdocentesis: Decker (1952).
5. Injection of radiolabeled xenon solution with gamma-camera screening: Pertynski *et al.* (1977).
6. Selective salpingography and tubal catheterization: Corfman and Taylor (1966).
7. Salpingoscopy: Brosens *et al.* (1987).
8. Falloposcopy: Kerin *et al.* (1990a).
9. Hysterocontrast sonography: Deichert (1993).
10. Fertiloscopy: Watrelot *et al.* (1999).

Accurate diagnosis of tubal integrity and effective treatment of tubal subfertility often require more than one technique.

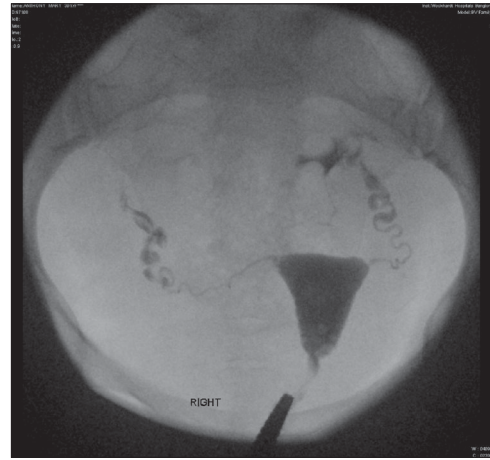


Figure 2: Category 1

Hysterosalpingography (HSG)

Using either a water- or lipid-soluble contrast media is the time-honored method for evaluating tubal patency.

It can document proximal and distal tubal occlusion, demonstrate salpingitis isthmica nodosa, reveal tubal architectural details of potential prognostic value and suggest the presence of fimbrial phimosis or peritubular adhesions when escape of contrast is delayed or becomes loculated, respectively.

Findings suggesting proximal tubal obstruction require further evaluation to exclude transient occlusion resulting from tubal/myometrial contractions.

Tubal cannulation with advanced HSG and tubal assessment categories

(Recent advances in tubal factor - unpublished data, work in progress - Dr. Raghav, Wockhardt Hospitals, Bangalore – personal communication) Improvements in HSG using real time guidance, uterotubal manipulation, tubal cannulation and tubal pressure assessments have yielded the classification of the tubal factor into simple, clinically relevant categories.

The presence or lack of distal tubal disease is an important factor in outcomes in tubal factor subfertility and this classification attempts to address this situation.

By classifying patients to these categories, one can decide the line of treatment and also predict the probability of pregnancy and the likelihood of ectopic pregnancy.

The tubes are categorized into three categories depending on their morphology and patency.

Category 1 - normal [Figure 2]

Characteristics - patency with free spill, preserved distal tubal folds, normal proximal, mid, distal tubal dimensions and appearance, no fimbrial end clumping, no detected peritubal disease, normal tubal pressures with free flow, lack of sharp pain on forceful flushing.

Outcome - good prognosis and outcome for future fertility, very low incidence of ectopic pregnancy on follow-up.

Category 2 - patent tube with tubal disease [Figure 3]

2a - mild tubal disease

2b - moderate tubal disease.

Characteristics - patency with good spill, partly or fully preserved distal tubal folds, normal or slightly altered proximal, mid, distal tubal dimensions and appearance, fimbrial end clumping may or may not be present, peritubal disease may or may not be seen, normal or elevated tubal pressures.

Outcome - moderate prognosis and outcome for future

fertility, highest group incidence of ectopic pregnancy on follow-up.

Category 3 - patent or blocked tubes, severe tubal disease [Figure 4].

Characteristics - patent or blocked tubes, loss of distal tubal folds, altered proximal, mid, distal tubal dimensions and appearance with dilatation/narrowing/scarring/tubal rigidity, fimbrial end dilatation/narrowing with clumping present, peritubal disease may or may not be seen, usually elevated tubal pressures but can be normal.

Outcome - poor prognosis and outcome for nonassisted future fertility, very low group incidence of ectopic pregnancy. *In vitro* fertilization (IVF) is to be considered.

Further long-term study is required to assess whether tubal cannulation [Figure-5] with advanced HSG can be used as a single primary test for tubal factor integrity assessment in the future.

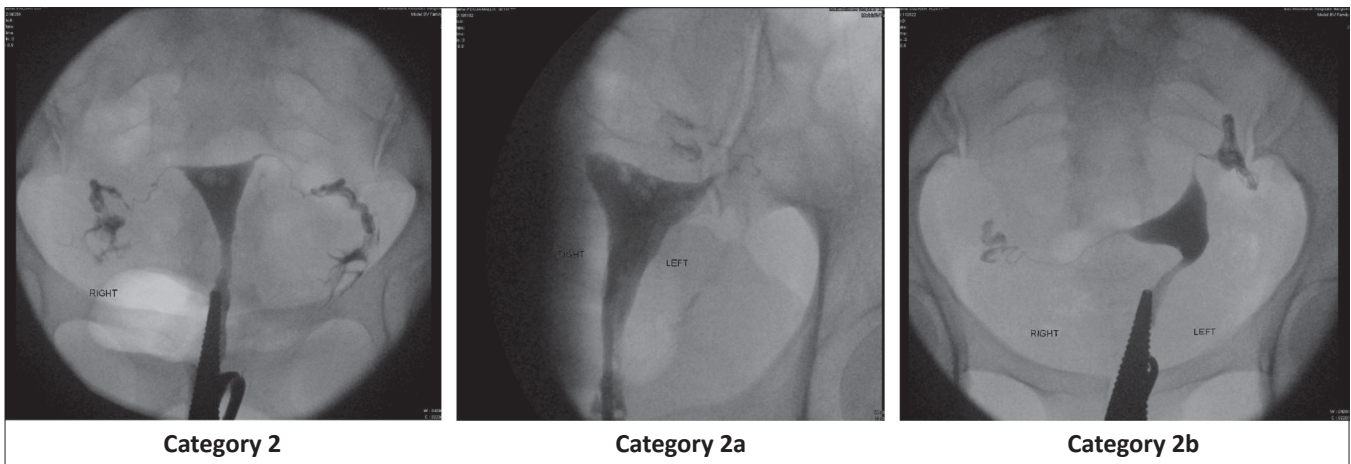


Figure 3: Category 2

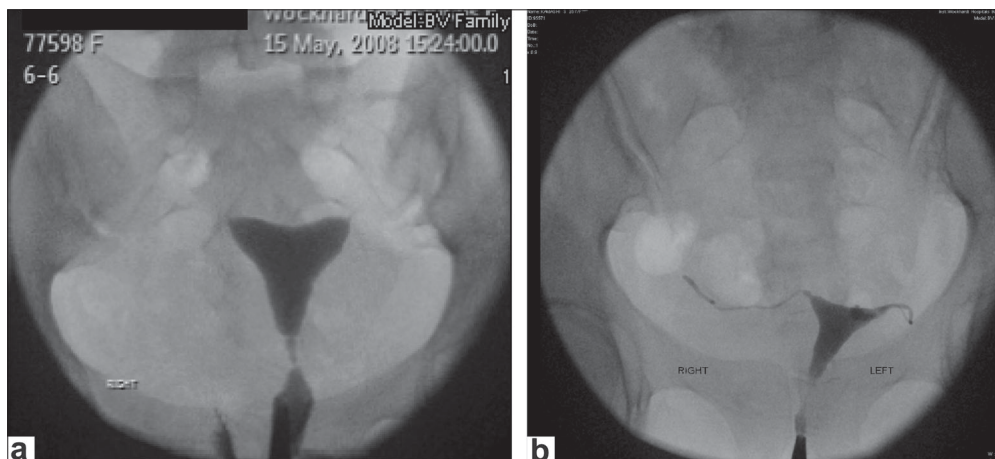


Figure 4 (a and b): Category 3 bilateral tubal block

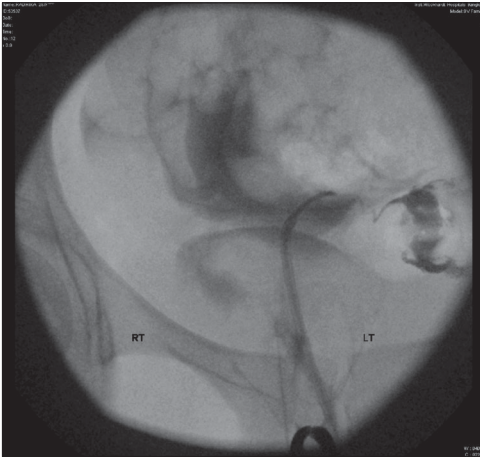


Figure 5: Cannulation

In the presence of patent tubes, intravasation of dye has no significance [Figure 6].

Management implications

Because of its low sensitivity (0.65), simple HSG is of limited use in the assessment of adhesions or endometriosis.^[2] Confirmation by laparoscopy is not necessary if HSG shows no abnormality or tubal obstruction.^[2] (Category 1 by above classification.)

In patients who are going to be treated with intrauterine insemination (IUI), laparoscopy may be performed if HSG shows abnormal results. (Category 2, especially 2b, with more severe disease by above classification.)

In the era of IVF, it is cost-effective to omit laparoscopy, especially in the cases of bilateral tubal abnormalities detected at HSG. (Category 3 by the above classification.) However, some authors report that the predictive value of HSG occurrence of pregnancy is poor and its routine use in the fertility work-up should be reconsidered.^[3,4]

Laparoscopy is of additional value with respect to diagnosis, further treatment decisions after abnormal findings with HSG and before IUI. Laparoscopy provides an external view of the tubes, while HSG provides an internal view and is often complementary.

Tubal cannulation and selective salpingography

The advent of tubal cannulation [Figure 5] and selective salpingography—fluoroscopic and hysteroscopic—has allowed restoration of patency in cases of isolated proximal tubal occlusion due to spasm, tubal plugs and synechiae.^[5] Tubal cannulation enables an indirect assessment of tubal function via measurement of the intratubal pressure as high, suggesting decreased tubal wall compliance.^[6]

Papaioannou *et al.*^[7] found that persistence of elevated

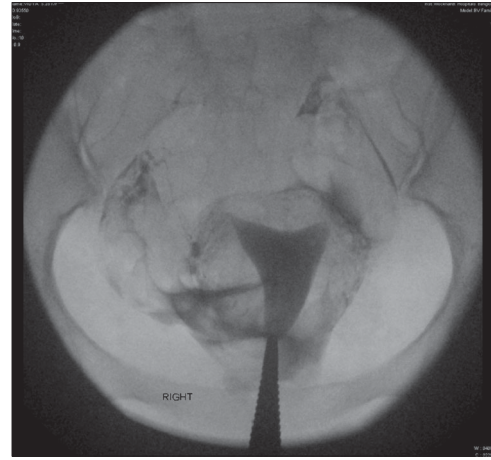


Figure 6: Intravasation of dye

perfusion pressure after cannulation using guide wire was an important determinant in the success rate. The pregnancy rate was significantly lower at 12–14% versus 35% in the low perfusion pressure group. Moreover, in the elevated pressure group, there was a higher ectopic pregnancy rate (25–50% versus 8%).

Several authors have reported case series of radiographic selective salpingography and tubal catheterization. The reported pregnancy rates are between 12 and 44%, with ectopic pregnancy rates ranging from 1.6 to 50%.^[7-10] The pregnancy rates do not differ from those achieved after the hysteroscopic technique.

There is only one meta analysis comparing tubal cannulation radiographic versus hysteroscopic techniques versus microsurgical anastomosis for proximal tubal blockage, which was based on data from cohort and observational studies.^[11] The total pregnancy rate per patient after hysteroscopic tubal cannulation was 48.9% (65/133 patients). The analysis of data showed that microsurgical anastomosis yields an ongoing pregnancy rate of 47.4%, which is higher than that obtained with radiographic cannulation (25.9%).

Laparoscopy and “chromotubation” with a dilute solution of methylene blue introduced via the cervix can demonstrate normal pelvic anatomy [Figure 7] and tubal patency or document proximal or distal tubal occlusive disease. Laparoscopy can also identify subtle tubal factors such as hydrosalpinx [Figure 8], fimbrial phimosis [Figure 9] or peritubular adhesions [Figure 10], endometriosis [Figure 11] that may escape detection with less-invasive methods. It is also beneficial because when abnormalities are encountered during laparoscopy, treatment [Figures 12 and 13] is possible at the same time. Thus, laparoscopy will either confirm or exclude a suspected preoperative diagnosis.

Fluoroscopic/hysteroscopic selective tubal cannulation will

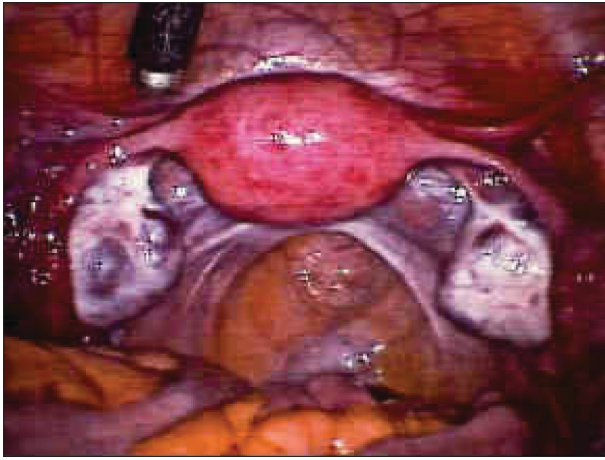


Figure 7: Normal tubes at laparoscopy

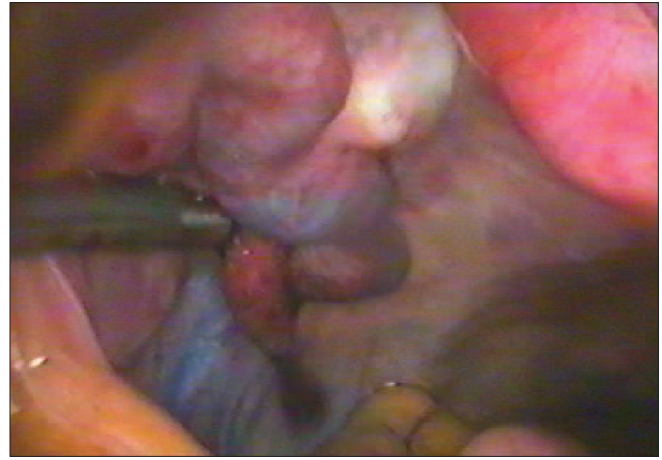


Figure 8: Laparoscopy hydrosalpinx

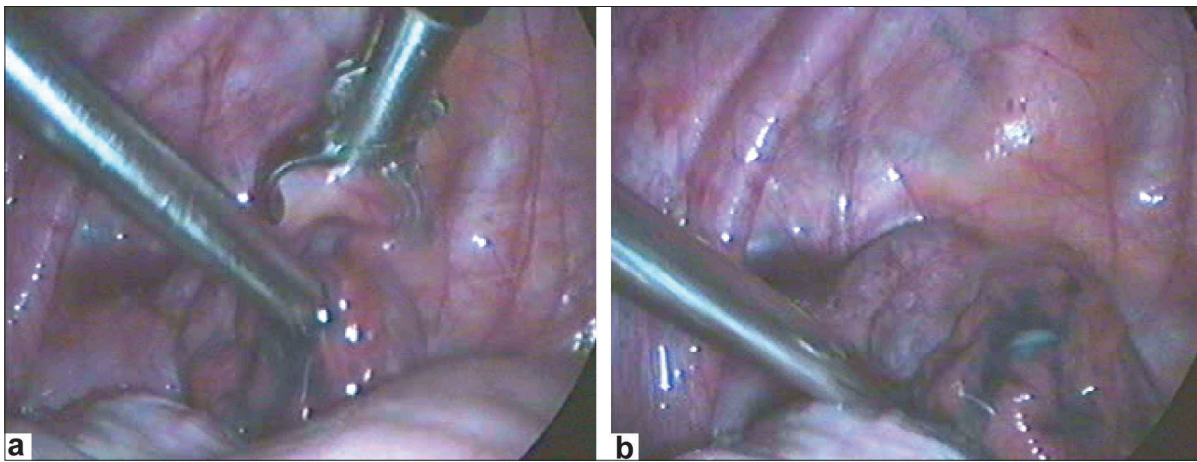


Figure 9 (a and b): Deagglutination of fimbria or broadening of the phimotic tubal opening

confirm or exclude any proximal tubal occlusion suggested by HSG or laparoscopy with chromotubation and provide the means for possible correction via recanalization using specialized catheter systems. Selective salpingography performs well regarding safety and the only complication that can occur is tubal perforation, reported in about 5% of the cases. An ectopic pregnancy has been reported in 5% of the cases and infection is very rare if screening or routine prophylaxis for infection is implemented.

Selective salpingography and tubal catheterization^[12] provides the examiner with the opportunity to measure tubal perfusion pressures, which have been found by life table analysis to be prognostic of future spontaneous fertility.

Hysterosalpingo–contrast–sonography

It is a transvaginal ultrasound technique in which a solution of galactose and 1% palmitic acid (Echovist -Schering-AG, Germany) or a mixture of air and saline is infused into the uterine cavity and observed to flow along the fallopian tubes to assess tubal patency. The bright echoes generated

by the Hysterosalpingo–contrast–sonography (HyCoSy) solution make tubal visualization possible. Results can be further improved by the use of color Doppler imaging or 3D technology.

HyCoSy is a safe outpatient procedure with a relatively low cost and its accuracy has been assessed in a metaanalysis, which compared the results of HyCoSy and laparoscopy and dye tests in 428 infertile women. Sensitivity was 93.3% and specificity was 89.7%.^[13]

Salpingoscopy

Salpingoscopy was originally performed during laparotomy for reconstructive tubal surgery to assess the mucosa of the infundibulum and ampulla. Prediction of fertility outcome by laparoscopy can be improved by the concomitant performance of salpingoscopy.^[14] The two tests probably complement rather than substitute one another. There is no information about accuracy, reliability, prognosis and effectiveness. Special equipment and expertise are required, making salpingoscopy an expensive proposition. It can clearly demonstrate the presence or absence of anatomical

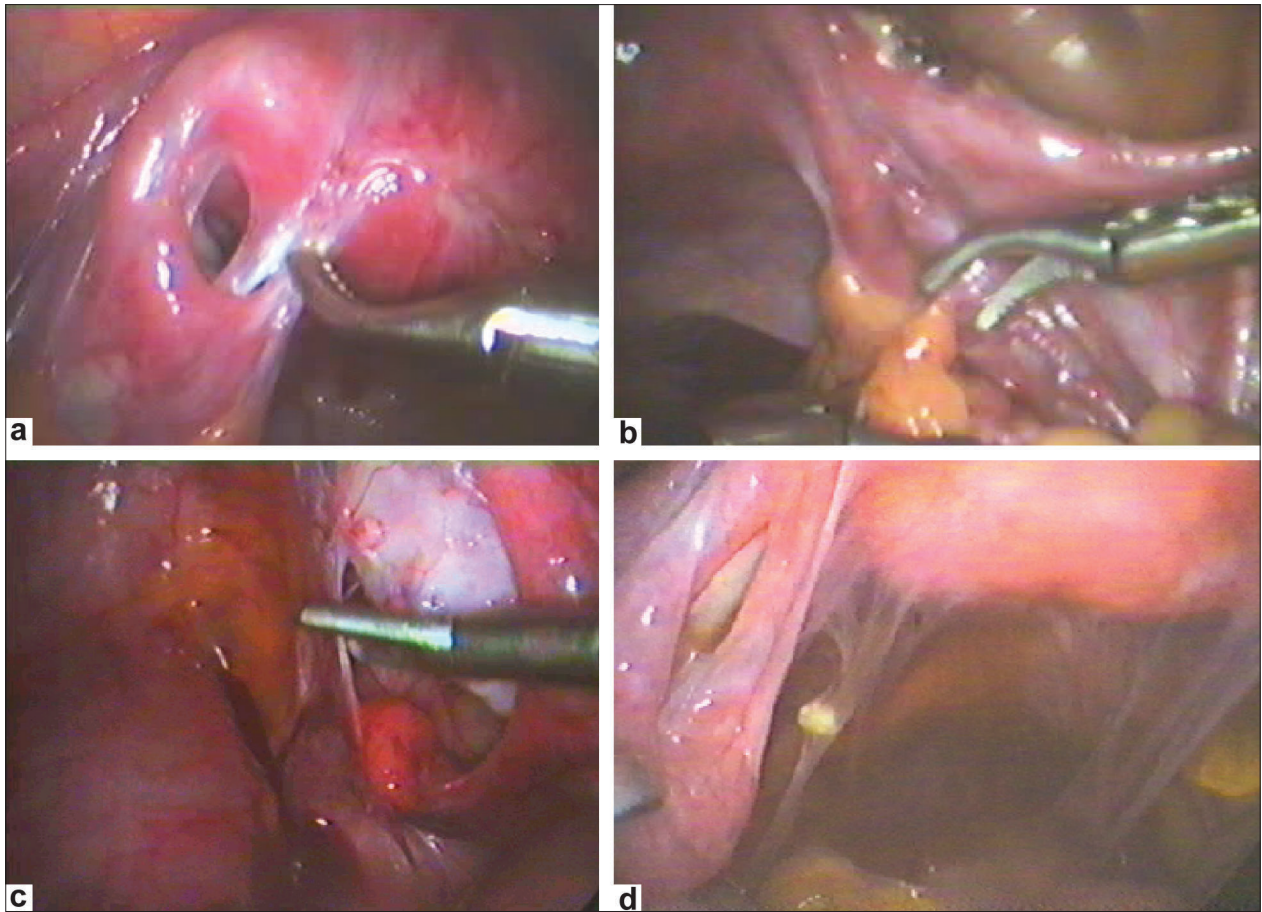


Figure 10 (a–d): Peritubal adhesions

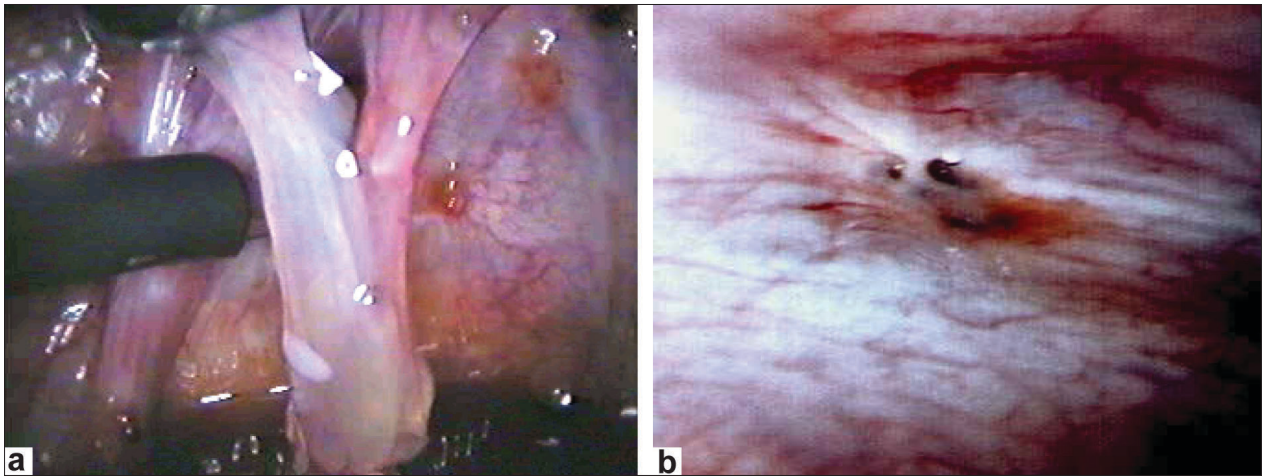


Figure 11 (a and b): Endometriosis

distortions, especially adhesions between and destruction of mucosal folds on a microendoscopic, i.e. mucosal level. Salpingoscopy could direct the infertility investigation and treatment, either toward reconstructive (micro)surgery or toward assisted reproduction technologies. Therefore, not enough is known about these lesions and salpingoscopy remains a research tool. Salpingoscopy can also be performed during transvaginal hydrolaparoscopy as an office procedure.

Fallopscopy

Fallopscopy [Figure 14] is microendoscopy of the oviductal lumen from the uterotubal ostium to the fimbriae by a transcervical approach.^[15] Initially, the technique involved the passage into the tubal lumen, under hysteroscopic vision, of a flexible cannula into which the falloposcope was introduced with the help of continuous fluid irrigation through the flexible cannula (coaxial delivery system).

Today, a miniature tubular balloon system has been used that is rolled out, along the fallopian tube lumen, by the use of hydraulic pressure. This carries the falloposcope forward with it at the same time (linear eversion system).

Transvaginal hydrolaparoscopy (fertiloscopy)

Fertiloscopy, performed under local anesthesia or sedation, is an outpatient assessment of the female reproductive system.

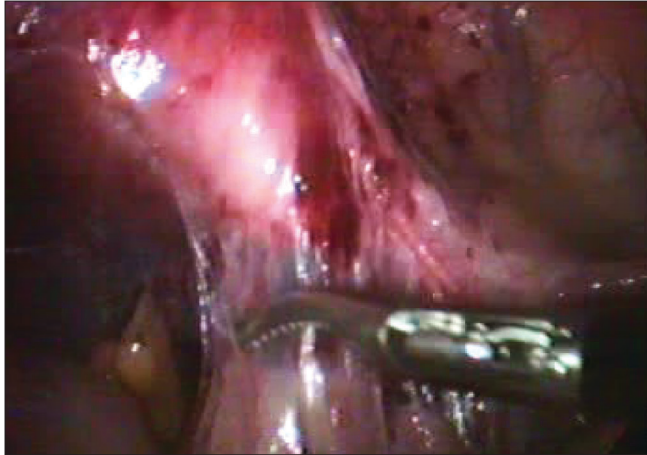


Figure 12: Microscissor cutting adhesions to tube

Microsalpingoscopy is routinely performed, which allows the cells of the tubal mucosa to be examined following the dye test. Staining of the tubal cell nuclei provides a means of assessing the functional capacity of the fallopian tubes: the more colored the nuclei, the less functional is the mucosa.^[16] Although some operative procedures are possible, they are limited due to the absence of a panoramic view.^[17] The sensitivity of fertiloscopy was 86%. In terms of reliability, the interobserver agreement for tuboovarian adhesions at transvaginal hydrolaparoscopy has been reported at 95%, comparable with that of standard laparoscopy.^[17] Complications occurred in 2% of the cases.

Comparing the various modalities of tubal assessment Royal College of Obstetrics and Gynecology^[18]

HSG compared with laparoscopy and dye:
HSG and laparoscopy with dye are the two most widely used methods to test for tubal pathology.^[19]

For tubal evaluation, laparoscopy remains the gold standard. In an era where cost-effectiveness becomes more important, it is debatable whether laparoscopy should always be a mandatory step in the subfertility work-up after HSG.

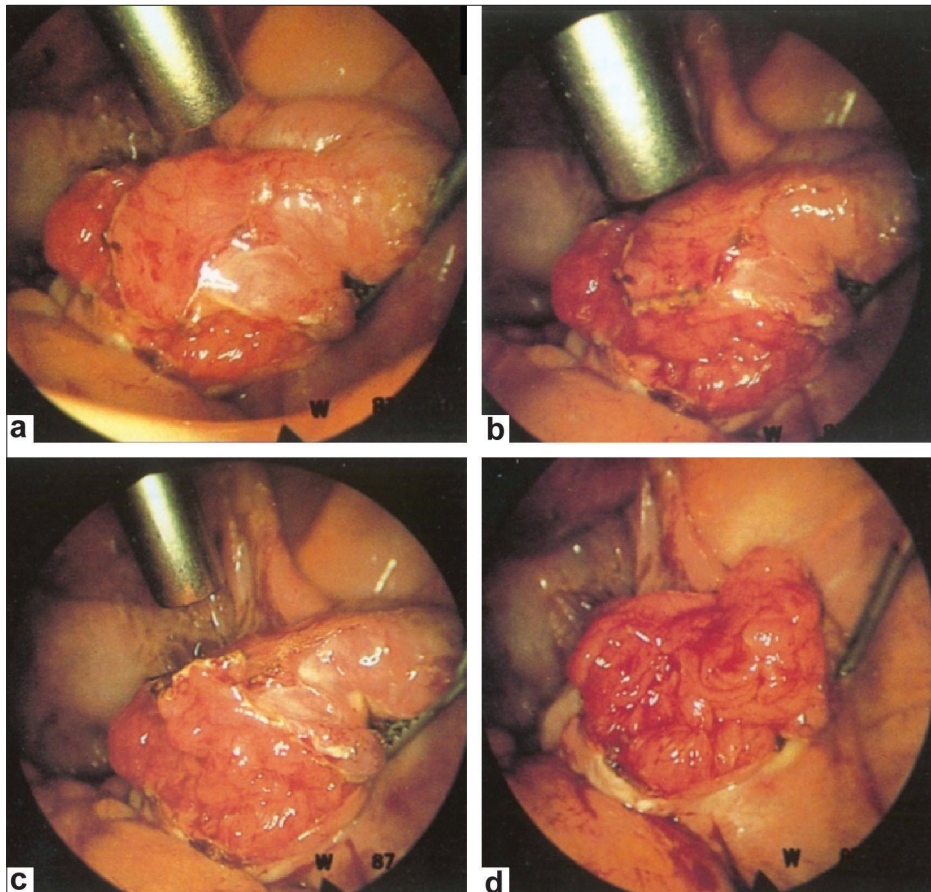


Figure 13 (a-d): Salpingostomy

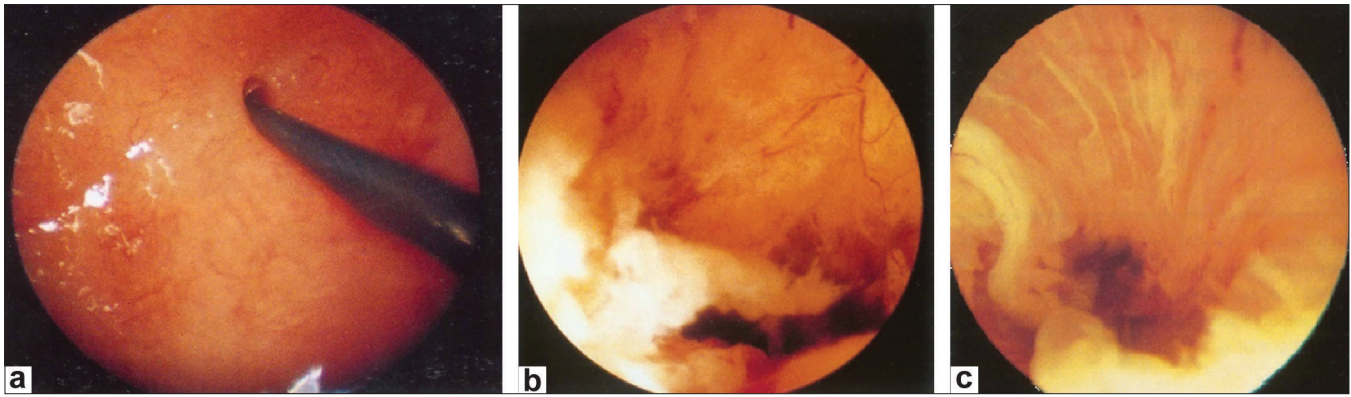


Figure 14 (a–c): Falloposcopy

HSG and laparoscopy are both invasive procedures but HSG is much less. Among women whose tubes were found to be patent using HSG, 18% were found to have tubal obstruction or peritubal adhesions using laparoscopy and a further 34% were found to have endometriosis and/or fibroids.^[20] However, the detection and treatment of pathology missed by HSG did not increase live birth rates. (Evidence level 2b.)

The diagnostic accuracy of HSG has been compared with that of laparoscopy and dye in a systematic review of 20 studies that distinguished between tubal obstruction and peritubal adhesions.^[21] However, only three studies involved judgement of laparoscopy without knowledge of HSG results. Metaanalysis based on these three studies gave pooled estimates of sensitivity and specificity for HSG as a test for tubal obstruction of 0.65 (95% [confidence interval] CI 0.50–0.78) and 0.83 (95% CI 0.77–0.88), respectively.^[21] (Evidence level 2b.) Because of its low sensitivity (0.65), HSG is of limited use for detecting tubal patency and is hardly reliable in the assessment of adhesions or endometriosis. It is estimated that tubal damage accounts for 14% of fertility problems, which suggests that when HSG suggests the presence of tubal obstruction, this will be confirmed by laparoscopy in only 38% of the women.

When HSG suggests that the tubes are patent, this will be confirmed at laparoscopy in 94% of the women and, thus, HSG is a reliable indicator of tubal patency. These findings imply that after abnormal HSG, even in cases of bilateral pathology such as obstruction, it is still worth performing laparoscopy because, in a considerable number of these patients, the laparoscopic diagnosis allows IUI treatment to remain an option.^[22]

Tubal pathology detected at laparoscopy has a stronger effect on future fertility than that detected at HSG.

Bilateral obstruction or hydrosalpinx found by laparoscopy was seen on HSG in 78% of the cases. However, of all bilateral obstructions and hydrosalpinx found by HSG,

only 41% was confirmed by laparoscopy and was scheduled for IVF. Thus, if in these cases laparoscopy was omitted, about 60% were incorrectly treated with IVF. A possible explanation for this discrepancy is that tubal spasm could play a role in some of these cases.^[23] Furthermore, especially in cases of bilateral hydrosalpinx diagnosed by laparoscopy, bilateral salpingectomy before IVF is indicated in order to optimize IVF outcome. In several patients, laparoscopy after abnormal HSG reveals normal findings or abnormalities not requiring IVF treatment, even when the results of HSG suggest bilateral pathology. Thus, laparoscopy is indicated in all patients with abnormal HSG to determine the exact treatment that should be offered to these patients.

HyCoSy compared with laparoscopy and dye or HSG

Evaluative studies of HyCoSy showed good statistical comparability and concordance with HSG and laparoscopy combined with dye.^[24] (Evidence level 1b.) HyCoSy is well tolerated and can be a suitable alternative outpatient procedure.^[25] (Evidence level 1b.) HyCoSy using contrast agent Infuson[®] appears to be more efficient than saline solution in detecting tubal obstruction.^[26] (Evidence level 1b).

Fertiloscopy and falloposcopy

Diagnostic fertiloscopy has also been used to identify tubal pathology as an alternative to laparoscopy. (Evidence level 3.) However, the procedure is not without risk and bowel and rectal injuries following fertiloscopy have been reported. (Evidence level 3.) The diagnostic accuracy of fertiloscopy in comparison with HSG and laparoscopy needs further evaluation.

Falloposcopy may be a more discriminatory test of tubal pathology because women with normal fallopian tubes at falloposcopy achieve higher spontaneous pregnancy rates (27.6%) than those with mild or severe endotubal lesions (11.5–0%). In another study, the management plan was changed in 90% of the women following falloposcopy and 24% conceived naturally.^[27] (Evidence level 3.) Technical

problems with fallopianoscopy limit the use of the procedure in routine clinical practice.^[28,29]

RCOG RECOMMENDATIONS FOR TUBAL ASSESSMENT

Women who are not known to have comorbidities (such as pelvic inflammatory disease, previous ectopic pregnancy or endometriosis) should be offered HSG to screen for tubal occlusion because this is a reliable test for ruling out tubal occlusion and it is less invasive and makes more efficient use of resources than laparoscopy.

Where appropriate expertise is available, screening for tubal occlusion using HyCoSy should be considered because it is an effective alternative to HSG for women who are not known to have comorbidities.

Women who are thought to have comorbidities should be offered laparoscopy and dye so that tubal and other pelvic pathology can be assessed at the same time.

RESEARCH RECOMMENDATIONS BY RCOG

Further research is needed to ascertain the value of fertiloscopy and fallopianoscopy in the investigation of couples who experience problems with fertility.

Further randomized controlled trials are needed to evaluate the potentially therapeutic effects of tubal flushing with water-soluble media.

Good clinical treatment in assisted reproduction: An ESHRE [European Society of Human Reproduction and Embryology] guideline^[30]

Couples who have not conceived after 1 year of regular unprotected sexual intercourse should be offered further clinical investigation, including semen analysis and assessment of ovulation. ESHRE Capri workshop in 2000 published three categories of test: tests that have an established correlation with pregnancy - semen analysis, tubal patency tests by hysteroscopy or laparoscopy and tests to detect ovulation.

Guidelines published in 2008 advocate semen analysis and ovulation assessment before a test of tubal patency is performed. Women thought to have comorbidities should be offered laparoscopy so that any tubal and other pelvic pathology can be investigated and treated at the same time.

Thus, the ESHRE guidelines concluded that if there are no concerns about pelvic or tubal health, it may be appropriate to perform three cycles of ovulation induction before checking tubal patency.

Recommendations by ASRM [American Society of Reproductive Medicine] for tubal factor evaluation^[31]

Evaluation of tubal patency is a key component of the diagnostic work-up in infertile couples. All available methods for evaluation of tubal factors have technical limitations that must be considered when any one technique yields abnormal results. Further evaluation with a second, complementary method is prudent whenever specific diagnosis or the best treatment strategy is uncertain.

CONCLUSION

In assessing the tube by the various tests available, the complexities of tubal function are not completely looked at by a single test. Looking for patency by flushing liquids through the tubes should not be taken into account. Just a simple patency of the tube might give false reassurance for women with tubes that might be open as simple pipes that conduct fluid, but not necessarily functional as far as eggs and sperm are concerned. The tubes may be thickened, which affects the contractility or there may be loss of cilia, which is required for normal transport of the gametes.

There is no single test available today that is an "ideal test" in terms of safety, accuracy, effectiveness and prognostic ability. However, today, the evidence base is good for the older tests, i.e. HSG and laparoscopy with dye test.

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Dr. Raghav, Wockhardt Hospital, Bangalore.

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Forthcoming Events

Biostatistics and Medical Writing for Doctors

Dates : 20th & 21st June, 2009
Venue : Dhanvanthri Hall, Rajiv Gandhi University of Health Sciences, 4th Block, Jayanagar, Bangalore, India.
Organized by : Journal of Human Reproductive Sciences.
Details on : <http://www.jhrsonline.org/>

Workshop on Science & Art of Research & Medical Writing

Dates : 30th and 31st May 2009
Venue : P.D. Hinduja National Hospital & Medical Research Centre, East Building, 4th floor, Conference Hall, V.S. Marg, Mahim, Mumbai 400016, India.
Details on : Dr. Barun Kumar Nayak, Editor – Indian Journal of Ophthalmology
 P.D.Hinduja National Hospital & MRC, Veer Savarkar Marg, Mahim, Mumbai 400016, India.
 Ph. 24447165, 24447405 and 24447131.

National Workshop on Molecular Cytogenetics: Cancer Cytogenetics (solid tissue) by FISH

Dates : August 24-29, 2009
 Department of Reproductive Biology, AIIMS, New Delhi, India
Details on : ashutoshhalder@gmail.com or ahalder@aiims.ac.in or login at www.aiims.ac.in (visit conference/workshop link)