

Management of hydrosalpinx

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- INTRODUCTION

- In the beginning of the in vitro fertilization (IVF) era, **tubal factor infertility was the sole indication** for the treatment. Today, other indications constitute the majority of treatments and tubal disease may account for as little as 20% in some centers.
- It is notable that tubal factor infertility is often reported to yield worse results than other causes of infertility.

DEFINITIONS

- Hydrosalpinx is a commonly used term to describe a heterogeneous spectrum of pathology of distal tubal occlusion.
- A strict definition is a collection of watery fluid in the uterine tube, occurring as the end stage of pyosalpinx.
- However, hydrosalpinx is used **for any distal tubal occlusion** regardless of the cause, implying that a non-tubal infection such as an adjacent appendicitis can also cause hydrosalpinx.

METHODS OF DIAGNOSIS

- The diagnosis of hydrosalpinx can be suspected and, in many cases, also confirmed by transvaginal ultrasound, if the tube is fluid filled.
- Ultrasound has the obvious **advantage** over hysterosalpingography of detecting the condition without the instillation of fluid, which carries a high risk of subsequent infection .
- instillation of contrast, can be used to diagnose a distally occluded tube without any fluid prior to instillation. **Antibiotic prophylaxis is mandatory.**
- Laparoscopy is obviously the ultimate method for diagnosis of hydrosalpinx and associated pathology of pelvic adhesions. However, the method is highly invasive, and the opportunity **should be taken to perform all diagnostic and therapeutic procedures at the same time.**

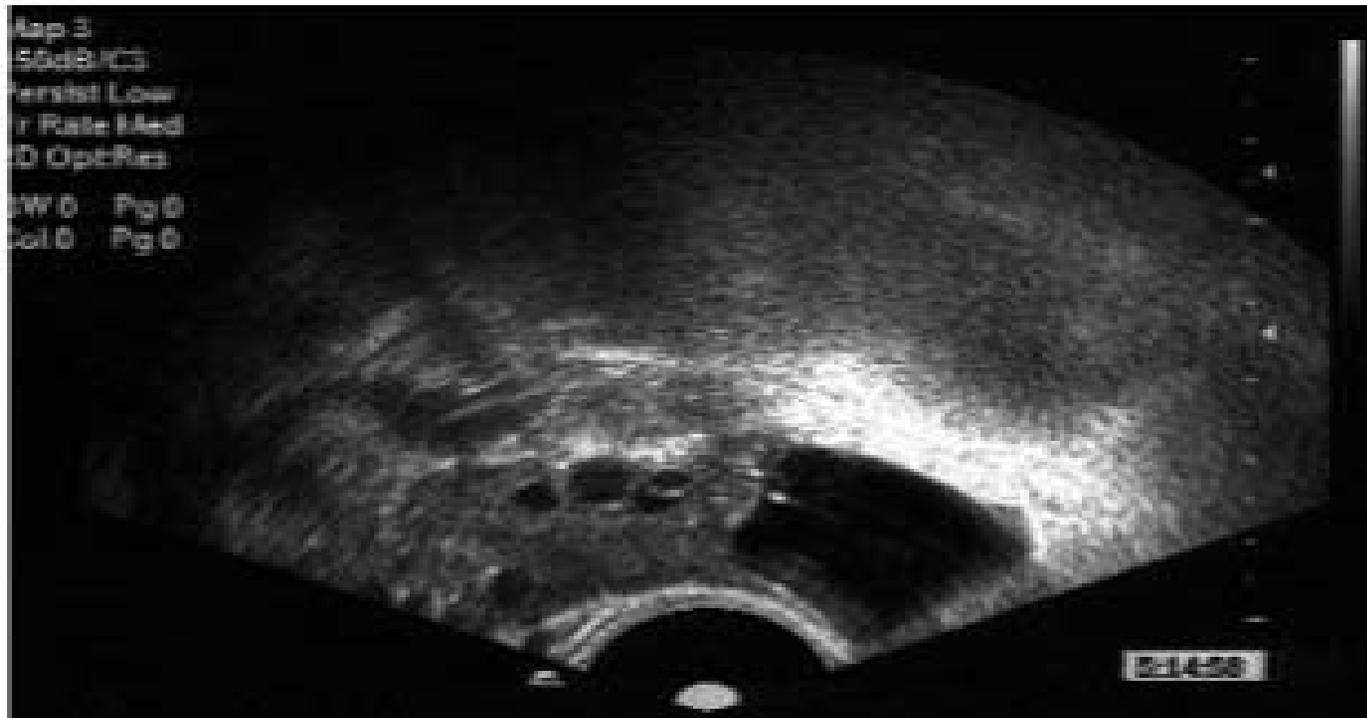


Figure 61.1 Typical appearance of a hydrosalpinx beside the ovary at transvaginal ultrasound investigation.

HYDROSALPINX: A SIGN OF POOR PROGNOSIS

Patients with hydrosalpinges have been identified as having **significantly lower implantation and pregnancy rates** than patients suffering from other types of tubal damage.

There is a consistency in the results, showing a reduction by **half in clinical pregnancy and delivery rates** and a **doubled rate of spontaneous abortion** in women with hydrosalpinx.

The rate of ectopic pregnancy was non-significantly increased in hydrosalpinx patients (odds ratio [OR] 1.3, 95% confidence interval [CI] 0.7–2.6). Patients with tubal infertility have an increased risk of ectopic pregnancy after IVF compared with patients with other indications, **but it has not been possible to establish that patients with hydrosalpinges have an increased risk of ectopic pregnancy** compared with patients suffering from other types of tubal infertility.

- Some of the retrospective studies have attempted to characterize further and subdivide the different features of hydrosalpinx.
- deWit et al. also demonstrated the importance of size by using ultrasound, and allocated hydrosalpinges according to **size depending on whether they were visible or not** .
- Pregnancy rates were significantly lower (15%) in patients with **visible** hydrosalpinges compared with patients in whom the hydrosalpinges were not visible (31%).
- Wainer et al. demonstrated that the presence of **bilateral** as opposed to unilateral hydrosalpinx was associated with significantly lower pregnancy (12% vs. 24%) and implantation rates (5% vs. 11%) .
- These findings suggest that the total amount of fluid in the hydrosalpinges is negatively correlated to the chance of achieving a pregnancy.

WHAT IS THE MECHANISM OF HYDROSALPINX IMPAIRING IMPLANTATION?

- The hydrosalpinx fluid may act on two different target systems: directly on the **transferred embryos** or on the **endometrium** and its receptivity for implantation, **or both**.

Is hydrosalpinx fluid toxic in individual cases?

- Even though there may not be a common toxic factor in all fluids, the presence of factors inhibitory to embryo development in fluids from certain individuals cannot be excluded.
- No pathogenic microorganisms have been detected in any of the published studies, but slightly elevated concentrations of endotoxin have been demonstrated in individual fluids as a sign of previous infection .

Endometrial receptivity

The cross-talk between the embryo and the endometrium, which is essential for allowing the embryo to implant, and mediated by the secretion and expression of certain cytokines and other substances during the implantation window, may be disturbed under the presence of hydrosalpinx fluid.

Cytokines like interleukin-1 (IL-1), leukemia inhibitory factor (LIF), colony stimulating factor-1 (CSF-1), and the integrin $\alpha\beta3$ are all factors that have been shown to be of importance to implantation. These molecular markers and some of their receptors are secreted or expressed by either the embryo or the endometrium in an increased manner during the implantation window. **By contrast, in hydrosalpinx patients, their expression is reduced.**

- Chlamydia trachomatis is the most common pathogen, and **antibodies to chlamydial heat shock proteins** were found to be more prevalent in patients with hydrosalpinx compared with women in couples of male infertility. Heat shock proteins elicit intense immune and inflammatory reactions and are thought to be responsible for a local immune response, leading to inflammatory reactions, impaired implantation, and immune rejection after embryo transfer.

- Ultrasonographic parameters have been investigated in search of effects on endometrial receptivity. Results have been **contradictory when measuring the sub-endometrial blood flow among hydrosalpinx patients** .
- However, **the triple-line endometrial pattern was less common among hydrosalpinx** patients compared with controls , supporting the theory of hydrosalpinx being involved in the regulation of endometrial receptivity and possibly causing simultaneous damage to the endometrium as the original infection.

Mechanical explanations

- **Leakage of hydrosalpingeal fluid through the uterine cavity**, resulting in embryo disposal, has been suggested as a mechanism by several authors .
- Retrospective studies have demonstrated an association between endometrial cavity fluid and increased cancellation rates and lower clinical pregnancy rates in ART cycles, but without any association with hydrosalpinges visible on ultrasound .It has also been suggested that hydrosalpinx fluid **may cause an increase in endometrial peristalsis**.
- The authors described, **a reflux phenomenon (opposing the cervix-to-fundus intrauterine peristalsis)** generated by a pressure gradient from tubal fluid accumulation. It was suggested that this reflux phenomenon could explain the reduced implantation rate associated with hydrosalpinx.

INTERVENTIONS AGAINST HYDROSALPINX IN CONJUNCTION WITH IVF

- According to the theory that the hydrosalpingeal fluid plays a causative role in impairing implantation and/or embryo development, any surgical intervention interrupting the communication to the uterus would remove the leakage of the hydrosalpingeal fluid and restore pregnancy rates.
- Treatment with **salpingectomy** prior to IVF is the only surgical method that has been evaluated in a sufficiently large randomized controlled trial (RCT).
- Other suggested treatments for hydrosalpinx prior to IVF, such as tubal ligation and transvaginal aspiration, may also be considered, but they need further evaluation in large prospective trials.

Salpingectomy

- Salpingectomy is the only method of prophylactic surgery in patients with hydrosalpinx that has been properly evaluated in a large randomized trial .
- A multicenter study in Scandinavia compared laparoscopic salpingectomy to no intervention prior to the first IVF cycle. The study demonstrated a **significant improvement in pregnancy and birth rates** after salpingectomy in patients with hydrosalpinges that were large enough to be visible on ultrasound. Clinical pregnancy rates were 46% versus 22%, and birth rates were 40% versus 17% in salpingectomized patients versus patients without any surgical intervention .

- The difference in outcome was not statistically significant in the total study population of 204 patients, which included patients with hydrosalpinges that **were not visible on ultrasound** , **demonstrating that the benefit of salpingectomy is only evident if the tube is fluid filled.**
- Within the group of hydrosalpinges visible on ultrasound, there can still be tubes that are suitable for reconstructive surgery, and the main rule must be that tubes with healthy-looking mucosa should not be removed.
- The psychological aspect of removing the tubes in an infertile patient is very important and has to be considered.

- This result, as well as the compiled data from the Cochrane review, suggests that all patients with hydrosalpinx, **regardless of size or fluid accumulation**, should undergo salpingectomy. However, the cumulative data from the Scandinavian study revealed that the **benefit of salpingectomy mainly affected patients with hydrosalpinges visible on ultrasound, and consequently, those are the only patients to be recommended prophylactic salpingectomy prior to IVF.**

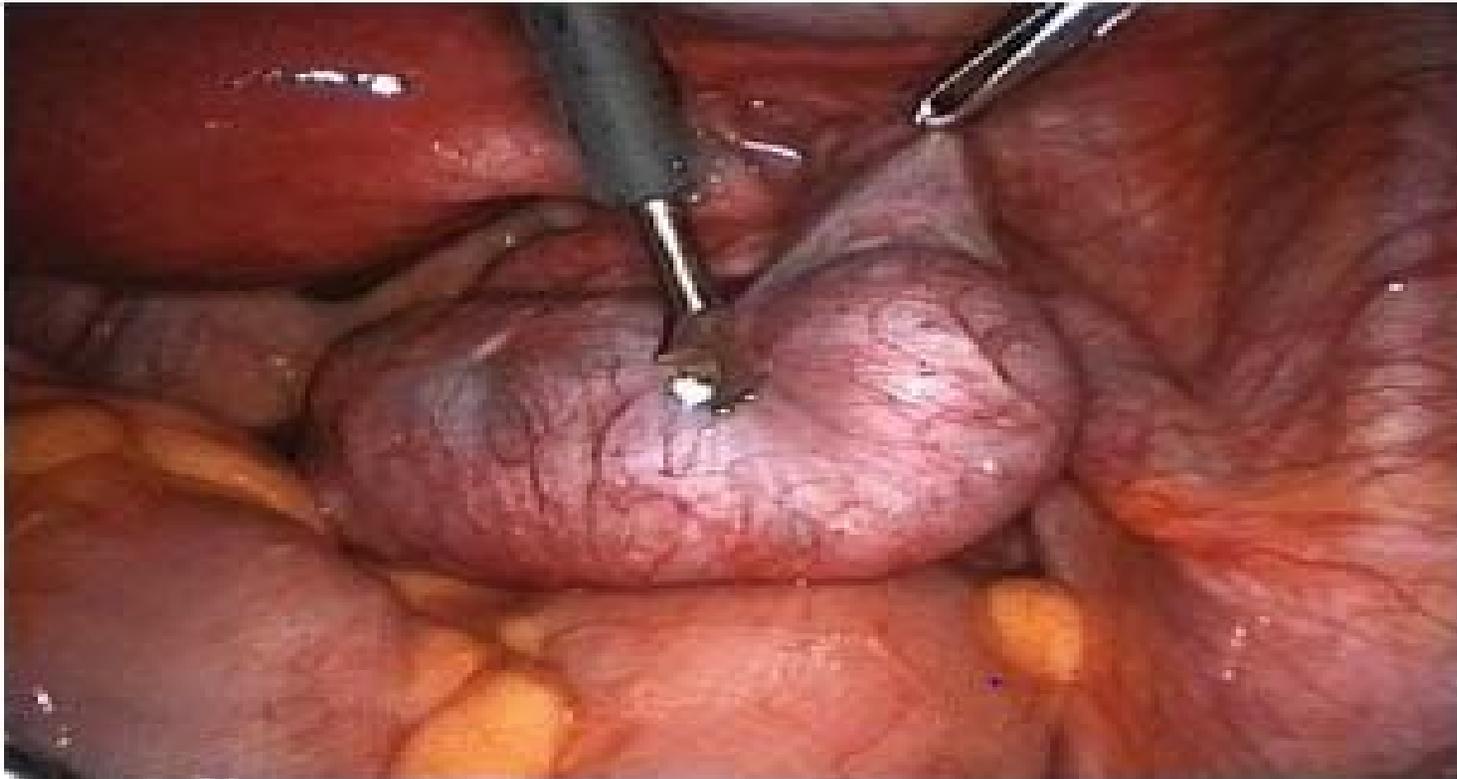


Figure 61.5 A hydrosalpinx without adjacent adhesions is easy to assess at laparoscopy.



Figure 61.6 Assessment of mucosal status through a distal opening of the hydrosalpinx is recommended before the final decision of salpingectomy or distal tuboplasty is taken.

Effect on ovarian function after salpingectomy

- The effect of salpingectomy on ovarian function has been debated, and the results of hitherto published studies are not entirely in consensus .
- The close anatomical association of the vascular and nervous supply to the tube and ovary constitute the theoretical rationale for the risk of impaired ovarian function after surgery.
- From the results, we cannot conclude that patients with a low ovarian reserve are at greater risk of suffering from poor response after salpingectomy. However, theoretically, it seems important to be very careful not to damage the vascular and nervous supply when performing a salpingectomy. **A laparoscopic salpingectomy should be performed with cautious use of electrocautery, with no unnecessary excision of the mesosalpinx, but resection very close to the actual tube to avoid damage to the medial tubal artery.**
- It is preferable to leave a portion of **an adherent tube on the ovary rather than to perform an excessively radical salpingectomy.** The risk of dehiscence in the uterine wall and subsequent protrusion of the fetus has been described, suggesting that resection not too close to the uterus is to be recommended.

Tubal occlusion by laparoscopy

- There was no significant difference in clinical pregnancy rate when salpingectomy was compared with proximal tubal occlusion (OR 1.3, 95% CI 0.8–2.1).
- According to the theory of the hydrosalpingeal fluid affecting the endometrium negatively, the procedure of tubal ligation is likely to be effective at improving pregnancy results. The procedure is currently recommended when **pelvic adhesions** are too extensive to perform a salpingectomy.

Tubal occlusion by hysteroscopy

- Tubal occlusion through hysteroscopy has been suggested **when laparoscopy is contraindicated**, like in cases with **severe obesity or frozen pelvis**.
- The first case report describing the **use of the microinsert sterilization device (Essure™)** has been followed by several case series . The obvious advantage is that the method can be performed under local anesthesia and thus avoids complications related to laparoscopy and general anesthesia.
- The use of electrocoagulation with a monopolar roller ball electrode for closing the internal tubal orifice has been reported as an alternative method in a small case series.

Salpingostomy

- Salpingostomy is naturally the method of choice if the tube is suitable for reconstructive surgery.
- The selection of patients suitable for surgical repair has to be based on the evaluation of the tubal mucosa through an endoscopic technique, and tubes with more than half of the mucosa in a good condition may have a fair chance of spontaneous conception .
- These patients should be given sufficient time to await spontaneous conception, although the woman's age may hasten the need for IVF.

Transvaginal aspiration

- There is a rapid re-occurrence of fluid that is already noticeable at the time of transfer in many cases, which most likely compromises any beneficial effect of drainage .
- The majority of studies have examined the effect of aspiration if conducted at the time of oocyte retrieval.
- It has been clearly shown that aspiration before ovarian stimulation has started is not effective, possibly due to high recurrence rate .
- The RCT comparing aspiration at the time of oocyte retrieval with salpingectomy clearly demonstrated the importance of re-accumulation of fluid . In the aspiration group, 34% had rapid re-accumulation of hydrosalpinx fluid, and the clinical pregnancy rate reached 19% compared with 34% in the group without re- accumulation of fluid after aspiration ($p = 0.28$).
- To overcome the problem of the high recurrence rate after transvaginal aspiration of hydrosalpinx fluid, **ethanol sclerotherapy has been introduced** . The proposed mechanism of ethanol is to coagulate the endothelial cells lining the hydrosalpinx to harden the salpingeal wall and reduce secretion. There are, however, reported risks of possible harm to the ovarian reserve mediated by the development of fibrosis and severe adhesions.

- The occurrence of infections in association with puncture of a hydrosalpinx seems to be rare when antibiotics have been given, according to the published reports.
- It can be concluded that **transvaginal aspiration** of hydrosalpingeal fluid **at the time of oocyte collection** is a treatment option, particularly if there is a contraindication to or non-acceptance of surgery, or if a hydrosalpinx develops during ovarian stimulation.
- In case of rapid re-accumulation of fluid after aspiration, the chance to conceive with a fresh embryo transfer is further reduced. Cryopreservation of embryos and surgical correction of the hydrosalpinx before a frozen–thawed transfer is a better option.

Repeated implantation failure in patients with tubal factor infertility

- Indeed, the Scandinavian multicenter study demonstrated that salpingectomy in comparison with no surgery did not increase pregnancy rates among patients **with distally occluded tubes without fluid accumulation** (OR 1.6, 95% CI 0.6–4.8).

INTERVENTIONS AGAINST HYDROSALPINX WITHOUT IVF

- As IVF developed and the results improved, the importance of using surgical methods for treating tubal infertility declined. It is well known that the success rate was closely related to the status of the tubal mucosa; the less damage to the tubes, the better chance of a subsequent intrauterine pregnancy.
- Today, IVF is often also offered as a first-line treatment to patients with mild tubal damage.
- The work-up of the subfertile couple has also changed over time, so that laparoscopy is no longer a compulsory investigation.
- This new mode implies that fewer patients will be evaluated laparoscopically during the work-up, unless a hydrosalpinx is detected.

- Even if a patient is scheduled for a laparoscopic salpingectomy, it is necessary to open the distally occluded tube for evaluation of the mucosa before a final decision of salpingectomy is taken. If it is appropriate to perform a salpingostomy, time for spontaneous conception should be given instead of immediate IVF.
- Salpingectomy of a unilateral hydrosalpinx may imply an increased chance of spontaneous conception.

- The negative effect of a unilateral hydrosalpinx has also been recognized among patients with recurrent abortion.
- Obviously, it is also important to diagnose and treat a unilateral hydrosalpinx in patients who suffer from recurrent miscarriages.

SUMMARY AND CONCLUSIONS

- In patients with severe tubal disease presented as a hydrosalpinx on ultrasound and with a destroyed mucosa upon endoscopic inspection, **IVF is the method of choice.**
- In cases of extensive adhesions, rendering the salpingectomy difficult and bearing a risk of complications, **proximal tubal occlusion is the preferred method.**
- If the laparoscopic route is contraindicated, **hysteroscopic tubal occlusion can be achieved by the placement of sterilization devices.** The psychological aspects of removing or interrupting the tubes are very important and always have to be considered.

- If no surgical intervention is performed prior to IVF, **transvaginal aspiration** of the fluid can be performed in conjunction with oocyte retrieval under antibiotic cover. If there is a re-accumulation of hydrosalpinx fluid before the time of transfer, cryopreservation of embryos would allow time for a surgical intervention to improve the chance of conception at a subsequent freeze transfer.
- Patients with a preserved mucosa in the hydrosalpinx may have a good chance of spontaneous conception if salpingostomy is performed.
- In the presence of a **unilateral hydrosalpinx** and a contralateral healthy tube, a unilateral salpingectomy can be recommended, followed by sufficient time to await spontaneous conception, before proceeding to IVF. Also, patients with recurrent abortion and a unilateral hydrosalpinx may benefit from unilateral salpingectomy or proximal tubal occlusion.

Tanks for your attention