

PATHOLOGY OF THE UTERINE TUBAL JUNCTION *

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SUMMARY

First the Author reviews briefly the anatomy and the physiology of the Uterine-Tubal Junction (UTJ) with a main concern for the muscular pattern and the secretory activity of this part of the tube, in relation with the hormonal and nervous control. Speaking about the pathology of the UTJ that can impair fertility, different are the causes: chronic infections and their sequelae, salpingitis isthmica nodosa, polyps, iatrogenic lesions (mainly following sterilization procedures), congenital malformations. Other pathologies might be: ectopic pregnancies - 2.5% of all tubal pregnancies - and neoplasmas even if not related to infertility. The therapy in most cases for restoring the continuity and hopefully the function of the tube is surgery through a microsurgical approach.

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The Fallopian tube is unique as it is the only segment of the female genital tract that must be capable of effecting sequentially transport of sperms and egg in opposite directions.

First, I'll review briefly the anatomy and physiology of this part of the tube. Here it is possible to recognize three muscular layers (fig. 1):

- 1) External spiral shaped
- 2) Intermediate circular
- 3) Inner longitudinal⁽¹⁾.

The last one increases in thickness toward the uterus and diminishes gradually toward the ampulla where it can not be demonstrated.

The tubal lumen, of course, is narrowing and reaches a diameter of 0.5 and 1.5 mm.

According to this muscular pattern it was possible to demonstrate its function in relation to different adrenergic stimulations that have their target in the "alpha" and "beta" adrenoreceptors.

Each of them mediates a response that for the « alpha » ones is excitatory in the outer spiral-shaped layer and inhibitory for the beta neurotransmitters in the two other layers⁽²⁾.

Beside this nervous control, the activity of the isthmus is function, as well, of the different hormonal conditions that we have through the phases of the menstrual cycle⁽⁵⁾.

In other words, it was shown the lowest contraction frequency in the latter part of the luteal phase, while an increase of frequency was recorded in both the late follicular and early luteal phase⁽³⁾.

This offers support for the concept that production and secretion of estrogen and progesterone is an essential regulatory mechanism for oviductal motility in synchronisation with the sperm and subsequent fertilized egg transit through the Uterine-Tubal Junction (UTJ).

The activity of this tubal segment is under the influence of Prostaglandins, as well (PGE₂, PGF_{2α}, PGI₂)⁽¹⁾.

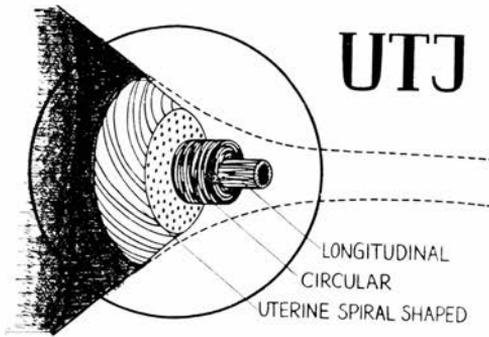


Fig. 1. — Schematic muscular arrangement of the human utero-tubal junction: the external, spiral shaped uterine layer, the intermediate circular and the internal longitudinal tubal layers. (By: B. Lindblom, Goteborg, Sweden).

They probably contribute to determine the effective closure of isthmic lumen at ovulation, preventing premature ovum transport.

A scanning electron microscopy study of the UTJ has demonstrated the presence of secretory and a high number of ciliated cells, plus endometrial glands (⁴).

Under the influence of varying concentrations of estrogen and progesterone during the cycle, their activity and morphology changes.

In the late follicular phase we have an overwhelming activity of the secretory cells with persistence of isthmic secretion through ovulation that decreases at the early secretory changes starting in the endometrium.

The above mentioned isthmic secretion contains the constituents of acid mucus glycoprotein and it seems reasonable to be called "mucus". In this way, this tubal segment, according to the sperm filtration and selection might be compared to the uterine cervix and, on the other side, the isthmic secretion allows the sperms to migrate in a direction opposite to that of ciliary beating and fluid flow (⁶).

It is clear that isthmic mucus with its thickness may constitute a barrier also

to ascending organisms. As a matter of fact, salpingitis is more likely to complicate gonorrhoea around the time of menstruation than at midcycle when the activity of the secretory cells is more prominent. However, an essential role of the interstitial oviduct can not be demonstrated because a significant degree of fertility is preserved both in the humans and in the rabbit after surgical bypassing the cornual region (up to 50% fertility rate in the rabbit, similar to that obtained in women).

PATHOLOGY

Tubal pathology is one of the most important causes of infertility and pathologic occlusions of the proximal part of the oviduct rarely affect the intramural segment, while the proximal isthmus and the distal interstitial oviduct are usually the regions affected.

Many diverse diseases damage the proximal oviduct; the most frequent are the infections such as endometritis or salpingitis.

The bacterial agents responsible of the flogosis are mainly the gonococci, while enterobacteria, anaerobic streptococci, tuberculosis, viruses, chlamydia and mycoplasma are more responsible for the chronic forms of salpingitis (⁷). As a matter of fact, chronic salpingitis in its different aspects such as chronic endosalpingitis or chronic interstitial salpingitis is the one that can impare most frequently the anatomy and the physiology of the isthmus, causing infertility. In these diseases the infiltrate usually penetrates the thickened tubal musculature with predominant perivascular concentrations that together with a hypertrophy of the adjacent muscles give: *salpingitis isthmica nodosa*.

Novak confirms that salpingitis isthmica nodosa is a lesion resulting from the residue of a chronic interstitial salpingitis even if some investigators have suggested an endometriotic etiology (⁸).

Although it is not uncommon to find endometrium at this level of the tube, the presence in the wall near the cornua or in the serosa of endometrial stroma is the key diagnostic feature and this is generally absent in salpingitis isthmica nodosa. Often the distal part of the tube may seem essentially normal, while the isth-

The incidence of this pathology was reported from different Authors to vary between 0.6%-6.0% with lower incidence in the Caucasian women⁽¹⁰⁾.

The diagnosis of salpingitis isthmica nodosa is done mainly in women seeking medical advice for sterility problems. It is asymptomatic and sterility is the main

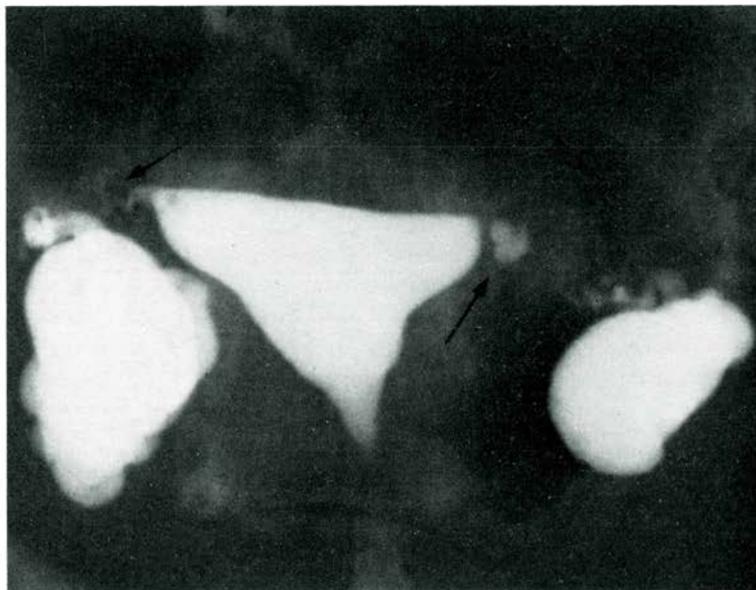


Fig. 2. — Hysterosalpingogram showing filling by the opaque medium of the diverticula in the isthmus portion of the tube (arrow). The tubes are dilated by bilateral hydrosalpinx.

mic portion is characterized by the presence of one or more nodules that can involve the superior surface of the uterine cornua.

Microscopically the tubal lumen has been spilt up into numerous small canals lined by epithelium; they are scattered throughout the muscularis which presents itself hypertrofied around them. At the hysterosalpingographic examination this may reveal a typical honeycombed appearance, caused by retention of opaque medium in the diverticula (fig. 2) or the tubes may present cornual block⁽⁹⁾.

complain that allows the diagnosis or it can be shown after an ectopic pregnancy.

In a study of more than 900 hystero-grams the diverticula when seen were present in almost 70% of the cases in the UTJ that confirms the typical location of the diseases at this level⁽¹⁰⁾.

Salpingitis isthmica nodosa can be missed at hysterosalpingography while at laparoscopy careful observation, palpation and manipulation plus tubal dye injection that in this case often gives no-tubal filling with an increasing resistance, are essential.

Another controversial utero-tubal pathology in causing infertility is the presence of *intramural polyps* (fig. 3).

They are less frequently recognized cause of damage other than inflammatory diseases. The reported frequency of cornual polyps varies from 1.2% to 2.7% regarding those lesions large enough to be seen on hysterosalpingography, while careful histologic studies have shown that endo-

the size of the polyps or on some of their characteristics. In this way they can be speculated as an adjoining factor of infertility. In these patients the treatment should take care first of the other possible causes of infertility and when all of them are detected and eventually corrected, if the patient still remains infertile, she should be reevaluated according to a possible role of polyps in determining

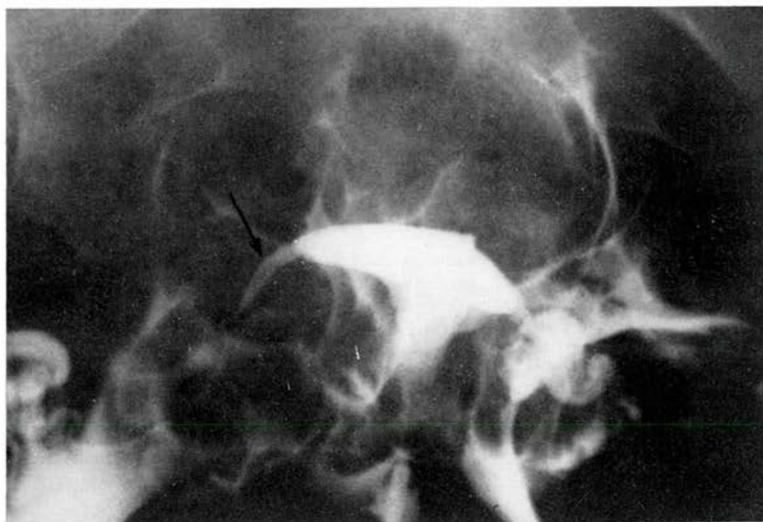


Fig. 3. — Hysterosalpingogram showing a large filling defect within the intramural and isthmic portion of the tube (arrow), characteristic of a tubal polyp. Such polyps are often multiple and can block the tube completely.

metrial polyps occur in the intramural portion of the tube in 11% of examined specimens⁽¹⁾. They are composed of endometrial or fibrous tissue. The associated infertility in these patients is between 20% to 60%. It was also reported that polyps are present thirty times more frequently in infertile rather than fertile women. However it is important to note that patients who have these radiologic findings are not infertile and many women who do not conceive have reasonable functional disturbances such as oligo-anovulation that in the long run may act on

infertility. Thus, they have to be considered as a cause of "relative sub-fertility" and be treated medically first and afterwards with a microsurgical approach. This could be done through a tubo-cornual anastomosis. Somebody suggests also the excision by anti-mesosalpingeal salpingotomy and resection of the polyps themselves.

As I told before, even bypassing the proximal portion of the oviduct, fertility still remains, but at the same time somebody has shown a higher abortion rate. In a recent report, Gomel has reported

on 38 tubo-cornual anastomosis 53% of pregnancies and 8% abortion rate and 5% of ectopic (12).

Among the causes of cornual lesions we can remember those having a *iathrogenic ethiology*, in other words those following sterilization procedures. Sometimes a too extended laparoscopic cauterization may determine destruction or damage of this tubal segment impairing the future pregnancy rate after the eventual microsurgical reparation of the tube. Beside the direct injury of the cornual region that can be done by electron coagulation it has been shown by scanning electron microscopy that secondary lesions such as micropolyps arising from the top of mucosal folds or endometriosis and fistulas can develop also in the interstitial and isthmic part of the tube (13). According to their dimensions it is not surprising that these polyps were not diagnosed by preoperative hysterosalpingograms.

They consist of stroma covered by essentially normal epithelium that in some cases presented features of endometrial metaplasia. These lesions were most common in those women that had been sterilized for more than 5 years. As a matter of fact it seems that at least 3 years are necessary to develop such structures that might derive from aberrant regenerative process after the occlusive damage of the tubes or from foci of acquired endometriosis.

The pregnancy rate after reversal was shown to be higher (around 60%) in the patients sterilized for less than 5 years while it dropped to 30% in women that sought reversal after a period longer than 5 years. It may be that the cornual-tubal lesions subsequent to chronic-tubal blockage interferes with the normal transport of gametes hence reducing fertility.

A similar study was done on the UTJ after sterilization comparing the pathologic outcomes with the different procedures that were used. It turned out

that after laparoscopic cautery the incidence of fistulas and endometriosis were definitely higher (46% and 63% respectively) than other methods such as Pomeroy or the use of silastic rings. Furthermore the percentage of this pathology was also a matter of time lasted since sterilization was done and a matter of length of the remaining proximal tube. The incidence of fistulas and endometriosis for a segment of less than 4 cm was respectively of 45% and 74%.

Lastly, we can remember briefly other possible cornual pathologies that can be related directly or indirectly with sterility and infertility.

The interstitial portion of the tube might be the site of implantation of an *ectopic pregnancy* that is often discovered after its rupture. Even rare, its incidence is of 2.5% of all tubal pregnancies and may be secondary to a previous chronic salpingitis.

The *congenital malformations* of the tube at the UTJ may be found in association with other congenital anomalies of the uterus as a sequence of a deficient development of the Mullerian tract. However there are also reported few cases of segmental absence of the isthmus with a distal fimbria and a normal ovary (14). Among these rare cases we can remember also cases of congenital cornual block and congenital cornual diverticula.

Even not related to infertility, we can remember also the *neoplasms* of the Fallopian tube that have the lowest incidence among the malignancy of the female genital tract (0.3%). The proliferation of an adenocarcinoma is rarely primitive at this level and is generally due to a diffusion from an endometrial adenocarcinoma.

THERAPY

The therapy suggested for restoring the continuity and hopefully the function of the tube impaired by one of the different

pathologies mentioned is the tubo-cornual anastomosis. Through the use of the microscope is possible to avoid damages of the major vessels and maintain the anatomy at the UTJ and to achieve a good percentage of successful pregnancies.

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