

TUBAL DISEASE

The incidence of tubal disease in an infertile population varies worldwide. In the UK it is estimated at 15%, in Singapore 11.7% while in Cameroon 88% (Hull M.R. et al, 1985).

In the UK there are about 8,500 new cases of tubal disease per year.

The common causes are:

- Gonorrhoea
- Tb
- Bacteroides
- Other bacteria
- Chlamydia: 50% tubal disease in Europe (Westran L., Mardh P.A. 1983)
- Mycoplasma
- Post-pregnancy: puerperal sepsis
- IUCD
- Post surgical

The association of IUCD with infertility is good enough reason to make it a contraindication to use it in nulliparous patients.

The incidence of PID in multiples who use an IUCD as compared to the pill is 1.8:1. The incidence is five times higher in similar groups of nullips; i.e. the incidence of PID in nullips who use the IUCD as compared to those who use the pill is 5:1.

About 78% of patients with tubal disease will have had previous surgery – In 16% of these, it is an appendicectomy. Other procedures are salpingectomy for ectopic pregnancy, curettage and ERPC's.

20% of patients undergoing wedge resection will develop tubal problems. Ventrone suspension performed for retroversion, which is associated with infertility may itself cause tubal disease.

INVESTIGATION OF TUBAL DISEASE

Tubal patency may be assessed by either hysterosalpingography or laparoscopy and dye. Air insufflation (Rubin's Test) is no longer performed since it can cause air embolism.

75% of HSG reports will be correct while 25% will be either false-positive or false-negative. The test is of tubal patency but will say nothing about tubal motility.

Laparoscopy is best performed as the motility of the tube, especially of the fimbrial end, over the ovary, can be assessed.

Endometriosis can further be diagnosed and if a corpus luteum is seen the punctum indicating that our egg has been released, should be identified.

TREATMENT

Primary PID, should be accurately diagnosed by laparoscopy (Pearce M.J. 1990) and treated vigorously with antibiotics to prevent residual disease as much as possible.

The place of tubal surgery has been re-evaluated with many opting for IVF as a first option, this being possibly an overall more cost effective approach besides patient discomfort and anxiety (Lilford R.J., Watson J., 1990).

However until IVF is more widely available, tubal surgery will continue to be practised especially for reversal of sterilisation. The results will depend much upon patient selection.

Overall results of tubal surgery (Winston R.)

Salpingolysis	25 - 35%
Salpingostomy	20 - 25%
Tubal reimplantation	40 - 15%
Tubal re-anastomosis	30 - 70%
Cornual block	30%
Reversal of sterilisation	
Microscopic	90%
Macroscopic	70%

CERVICAL FACTORS

The investigation of cervical factors as a cause of infertility is by the following tests:

1. Postcoital test
2. Crossed Hostility test
3. Antisperm antibodies

The W.H.O. definition of a positive PCT is when 15 or more active sperm per highpower field are present. It is negative if there are five or less.

If there are no sperm at all, not even dead ones, one should suspect that no intercourse took place or no normal sexual intercourse.

A Crossed Hostility test or formal sperm penetration test (Kremer, 1968) should be performed in the event of a negative PCT.

Method: The couple are advised to avoid sexual intercourse for 3 days and after that a separate sample of husband's semen and wife's mucous are obtained.

These are tested separately in the following combinations:

1. Husband vs wife
2. Husband vs fertile donor (mucous)
3. Male fertile donor sperm vs wife's mucous
4. Fertile male donor sperm vs fertile female donor mucous

In a local hospital setting a husband sperm / wife mucous challenge is enough. The preparation is observed over a 20 minute period and the formation of a Phalinx as the sperm ascends through the mucous.

Where the Kremer test is abnormal anti-sperm antibodies should be sought in both serum and semen samples. Cervical factors are responsible for about 3% of cases of infertility (Hull M.R. et al, 1985).

ENDOMETRIOSIS

Endometriosis is present in 10 - 15% of premenopausal women undergoing gynaecological surgery and about 25% of premenopausal women will have evidence of endometriosis if this is looked for. The discrepancy is because the behaviour of endometriosis is highly variable. The diagnosis of endometriosis depends on direct inspection of the peritoneum, not on history and examination and laparoscopy is therefore mandatory.

Endometriosis is found to be the cause in 6% of infertile couples.

Using a weighted point system, the American Fertility Society (1985) has proposed a classification system which distinguished a minimal, mild-moderate and severe stage of the disease.

The association between infertility and endometriosis is not straightforward except in cases where there is anatomical distortions of the pelvic organs.

The management of endometriosis may be either medical, by hormone therapy or surgical.

Hormone therapy aims at suppressing ovarian activity and therefore withdrawing the stimulus for the endometriotic tissue i.e. a pseudo pregnancy or pseudo-menopause.

A pseudo-pregnancy state can be created by either oral contraceptive or progestins (most of the experience being with medroxy-progesterone acetate) while a pseudo-menopause is induced by danazol, gestrinone or LHRH agonists.

Withdrawal of the hormone therapy may however be associated with re-activation of the disease. Furthermore fertility is postponed while on treatment. Surgical treatment is therefore to be considered more definitive treatment but this must be meticulous and excision of all dressed tissue is necessary. For infertile patients laparoscopic surgery is better than laparotomy as it is less likely to cause post-operative pelvic adhesions and tubal occlusion than laparotomy (Sutton C., 1990).

Simple endometriotic spots visualised at laparoscopy may be easily and definitely treated by simple diathermy or better still by laser vaporisation.

UNEXPLAINED INFERTILITY

10-15% of couples attending a clinic will be labelled as suffering from unexplained infertility. The possible underlying pathology in these cases include:

1. Anatomical Causes

(a) a combination of uterine retroversion and low sperm count may lead to difficulty to conception. The treatment is not ventro-suspension but A.I.H.

(b) kinking-tube syndrome: the incidence of pregnancy in this group is small. It is suggested that it may be due to old PID. The tube is either S or snake shaped.

(c) abnormalities in physiological oocyte pick

up e.g. a non-mobile fimbrial end.

2. Abnormalities of Follicular Growth
3. Abnormalities of the oocyte
4. Luteinised unruptured follicle: even in the presence of a punctum, the ovary could still be trapped inside
5. Abnormalities of the Luteal Phase: a short luteal phase is one that is 7 - 9 days long. The serum progesterone rises in normal patients
6. Immunological causes
7. Psychological factors

RESULTS OF TREATMENT

As a result of treatment about 18% of infertile couples can be expected to conceive (Lifford R.J. and Daltur M.E., 1987). Half the couples presenting with one year infertility can expect to become pregnant spontaneously in the following year.

Table II shows the two year conception rates (Hull Mr et al, 1985).

Causes

Failure of ovulation:

Amenorrhoea	96%
Oligomenorrhoea	78%
Tubal damage	19%
Sperm defects	0.27 %
Unexplained	72%

The cumulative success rates of treatment if only one abnormal factor is present is 65% and by 4 years the maximum rate is achieved.

With two factors, the success rate falls to 50% and with 3 factors, if correctable, the success rate is only a little lower by 4 years

ASSISTED REPRODUCTION

In-Vitro Fertilisation

IVF was originally developed for the treatment of patients with tubal disease but has since found an ever increasing application especially in cases of male infertility (Hewith et al, 1987).

A number of factors are generally considered when selecting patients for IVF, though many may be further discussed in individual cases.

The main selection criteria include

- Age - not generally suitable for patients over 40 years
- Pathology - failed surgery/ idiopathic infertility/ suspected male infertility
- Parity - proven gametes
- Religion
- General Health
- Weight - especially overweight
- Frozen pelvis on pelvic examination

Now that most units perform ovum pick-up by trans-vaginal ultrasound, the presence of contra-indications to laparoscopy (eg abdominal scars) are no longer relevant.

Cases not considered suitable for IVF methods:

- Anovulation
- Uterine fibroids, hypoplastic uterus, cervical stenosis
- Azospermia, successful fertilisation can occur in cases of extreme oligoasthebospermia (<0.5 x 10 motile spermatozoa/ml).

Procedure:

In order to obtain a large number of ova the ovaries are stimulated with clomiphene and Pergonal or Metrodine (FSH).

Follicular development is followed up on ultrasound in combination with serial serum oestradiol estimation.

32 hours after the HCG/LH ovulation dose, ovum retrieval is undertaken. This is usually by transvaginal ultrasound. Prior to insemination the semen sample is prepared by the swim-up technique selecting the most mobile portion. In cases of male infertility the use of split-ejaculates produce a relatively spermatozoa rich first fraction.

If fertilisation occurs, embryo transfer is performed 4.8 hours after insemination, usually at the 4-cell stage, by the trans-cervical route.

Up to 3 embryos may be replaced per cycle (R.C.O.G., 1990). The luteal phase may be supported either by HCG or progesterone. With the introduction of LHRH agonists (eg Buselerin) used to down regulate the pituitary-ovarian axis, subsequent stimulation is more synchronous with more better quality one.

In cases of male infertility the pregnancy rates ranges from 11 to 23% the lowest fertilisation rate being obtained in cases of oligoasthenospermia. IVF has been shown to be superior to intra uterine AIH.

Micro-manipulation of spermatozoa and oocytes may make it possible to treat patients who do not at present benefit from conventional IVF.

The report of the last Interim Licensing Authority (1988) showed the overall pregnancy rate to be 12.9% per treatment cycle and the take-home baby rate 9.1% (Interim Licensing Authority, 1990).

The introduction of IVF in 1975 opened the way for other methods of assisted reproduction and 6 years later Asch et al reported the first pregnancy following translaparoscopic gamete intrafallopian transfer i.e. GIFT.

As another method of assisted reproduction GIFT requires the same ovarian stimulation and ovulation induction as IVF as well as semen preparation. Laparoscopy remains essential in this procedure unlike IVF where oocyte retrieval is now largely by transvaginal ultrasound.

The main steps in a GIFT programme are:

- Induction of multiple follicular developments: clomiphene, HMG, FSH and LHRH agonists.
- Monitoring of follicular developments, ultrasound and oestradiol levels.
- Ovulation induction, HCG is given 24-30 hours after the last dose of HMG to stimulate an LH surge.
- Oocyte recovery: 34-326 after HCG
- Semen preparation: 2-2 1/2 hours before oocyte recovery

GIFT selected eggs together with the sperm preparation are loaded into a catheter into the fimbrial ostium and expelled into the ampulla.

Luteal phase support.

Outcome - menses - biochemical pregnancy (+ve β -HCG only) or pregnancy confirmed by ultrasound.

GIFT was originally developed for patients suffering from unexplained infertility when one or more aspects of the reproductive process may be defective (Wang P.C. and Asch R.H., 1989). The process of fertilisation in GIFT is left undisturbed and therefore provides an alternative for patients with normal tubes.

- Indications for GIFT (Wang P.C. and Asch R.H., 1989)
- Unexplained infertility
- Endometriosis
- Male factor
- Cervical or Immunological Factor

Failed AID
Premature ovarian failure
(oocyte donation)
Periadnexal adhesion

Patients with previous failed AID achieve high success rates with GIFT; this may be due to the fact that the defect in these patients is either one of sperm transport or of oocyte expulsion or pick-up.

As with IVF the most important complication of GIFT is multiple pregnancy. With the improvement in quality achieved using LHRH agonists high-order multiple pregnancy is a greater problem with its consequent increased incidence of fetal wastage (abortion and prematurity). Except in special cases oocytes (GIFT) and embryo (IVF) replacement should be limited to 3 (Interim Licencing Authority, 1990).

Another important complication resulting from ovarian stimulation is ovarian hyperstimulation which in its severe form is associated with large ovarian cysts, ascites and pulmonary effusions, electrolyte imbalance and coagulation defects.

GIFTS has been proposed as a diagnostic procedure for infertility i.e. at the first laparoscopy for infertility (Abdilla H. et al, 1990) perform also a GIFT cycle thereby minimising the number of procedures and maximising on the possible benefits.

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