13 NON-TUBERCULOUS PELVIC INFLAMMATORY DISEASE AND INFERTILITY

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Introduction

Pelvic inflammatory disease (PID) is a dynamic clinical condition representing upper genital tract infection. Long-term implications of PID include higher rates of infertility, ectopic pregnancy, and chronic pelvic pain. Fertility preservation is a major goal in developing optimal treatment strategies for PID. Tubal disease accounts for 25% - 35% of infertility in women and salpingitis is believed to account for 50% of these cases. Although it is seen occasionally in multiple sites, tubal blockage usually involves the proximal, mid, or distal portion.

Tubal factor infertility has received scant attention since IVF evolved as the primary treatment for occlusive tubal disease and tubal surgery was effectively relegated to the sidelines. The reported observations of paratubal and mesosalpingeal fibrosis in tubal factor infertility have therefore received little investigation. Lower than expected conception rates are observed in these women, whether after assisted conception or reconstructive tubal surgery and attention has recently refocused on the endometrial consequences of tubal disease. Women with tubal factor infertility and delayed endometrial maturation also demonstrated elevated uterine artery impedance and excessive irregularity of endometrial maturation.

Pelvic inflammatory disease (PID) is defined as an ascending infection in the uterus and/or adnexa that could be caused by the sexually transmitted bacteria Chlamydia trachomatis and Neisseria gonorrhoea. Also, Bacterial vaginosis (BV) which involves a relative over-growth of anaerobic vaginal organisms, a depletion of lactobacilli, and an increase in vaginal pH in 10%12% of women and may be responsible for tubal factor infertility. The common organisms causing BV are Gardenerella Vaginalis, Mycoplasma hominis and Ureaplasma Urealyticum.

Chlamydia trachomatis infections:

These are the most prevalent bacterial sexually transmitted infections (STI) of the three mentioned above, recognized throughout the world. In 85% it is non-iatrogenic, occurring in sexually active women of reproductive age, while in the remaining 15% it occurs following uterine instrumentation.

Worldwide, the magnitude of morbidity associated with sexually transmitted chlamydial infections is enormous. C.trachomatis is a common cause of urethritis and cervicitis, and sequelae include pelvic inflammatory disease (PID), ectopic pregnancy, tubal factor infertility, epididymitis, proctitis and reactive arthritis. Although infections with *Chlamydia trachomatis* and bacterial vaginosis (*Mobiluncus* Species) frequently are asymptomatic, both have been implicated in pelvic inflammatory disease and adverse pregnancy outcomes. If recognized, a chlamydial infection in the lower genital tract can be treated effectively and easily by antibiotics.

Studies on the natural course of untreated C. trachomatis genital tract infections in women show spontaneous clearance rates of 30 - 50% in the first 23 years. For tubal tissue damage to occur, prolonged exposure to Chlamydia is considered a major predisposing factor, either by chronic persistent infection or by frequent reinfections. This evokes a chronic low-grade auto-immune response which leads to chronic inflammation and subsequent tissue damage. In young adolescents, re infection rates of 10 - 30% have been found and sexual risk behavior is an important determinant. Host genetic variations have been shown to play a role in the risk of persistence of infection. Besides behavioral factors and host genetics, specific chlamydia strains, called serovars, have also been suggested to affect the course of infection. If pregnancy occurs it can have adverse

pregnancy outcomes which have been associated with uncomplicated chlamydia cervicitis, and include sporadic and recurrent miscarriage, preterm labour, premature rupture of the membranes and low birth weight. In women, ascending cervical infections may cause pelvic inflammatory disease (PID), and ultimely tubal pathology, which increases the risk of ectopic pregnancy, tubal infertility and chronic abdominal pain. As treating PID and tubal infertility is costly both in psychosocial and in financial terms, in order to decrease these costs screening programmes have been introduced. The primary aim of chlamydia screening is to reduce morbidity in individuals by early detection and treatment of uncomplicated lower genital tract infections. The secondary aim is to decrease the overall prevalence of chlamydia infections and subsequently reduce transmission in the population. Screening proves to be overall cost-saving.

N. Gonorrhoea infection is due to a gram negative diplococcus which grows and divides rapidly resulting in an intense inflammatory response by the womans' host defenses, and therefore extensive signs & symptoms are seen and so diagnosed early in the course of the infection.

Clinical Features and diagnosis:

The risk of infertility increases after repeated episodes of salpingitis (Westro m, 1980) due to occlusion of the fal- lopian tubes by fibrous scarring. Such scarring may occur as the result of an immune pathological response after chronic or recurrent infection by C. trachomatis. However, the severity of inflammation observed at laparoscopy during the acute phase of salpingitis also seems directly to influence the long-term fertility prospects.

Criteria for Diagnosis:

Empirical Treatment is to be started in sexually young active women & other women at risk for STD, in the following cases:

1) Pelvic or lower abdominal pain
2) If no cause of illness other than PID identified
3) or in the presence of 1 of the following 3 minimum criteria:
    (i) Cervical motion tenderness
    (ii) Uterine tenderness
    (iii)Adnexal tenderness

Additional criteria:

1) Oral temperature >l01°F(>38.3°C)
2) Abnormal cervical or vaginal mucopurulent discharge
3) Presence of abundant number of WBC on microscopy of vaginal secretion
4) High ESR
5) High C- Reactive protein
6) Laboratory documentation of cervical infection with N. Gonorrhea & C. Trachomatis

Specific Criterion:

1) Endometrial Biopsy with histopathological evidence of endometritis
2) Transvaginal USG or MRI showing thickened, fluid filled tubes with or without free pelvic fluid or Tuboovarian complex or Doppler study pelvic infection (eg. Tubal hyperaemia)

Others

(i) T. Chlamydia - DNA and RNA detection: amplification and non-amplification systems

(ii) T. Chlamydia - Antibody detection in serum

(iii) T. Chlamydia - Heat shock proteins 60 (HSP60) - Several T cell epitopes in C. trachomatis HSP60 and human HSP60 are homologous. Therefore, autoimmunity to human HSP60, resulting from cross-reactivity, has been suggested to be involved in the pathogenesis of TFI following C. trachomatis infection. Association between TFI and antibodies to major outer membrane protein (MOMP) and heat shock protein 60 (HSP60) from C. trachomatis, suggesting antibody testing as a supplement in TFI diagnosis. No connection was observed between TFI and antibodies to human HSP60, pointing to an infectious rather than an autoimmune inflammation as the cause of TFI.

(iv) Bacterial Vaginosis - Wet preparations or Gram's staining (Nugent criteria) showed clue cells and *Mobiluncus* species with positive anaerobic cultures was considered diagnostic of BV

(v) Gonnococal Infection -

- typical gram-negative intracellular diplococci on microscopic examination of a smear of urethral exudate from men or endocervical secretions from women
- growth of a gram-negative, oxidase-positive diplococcus, from the urethra (men) or endocervix (women), on a selective culture medium, and demonstration of typical colonial morphology, positive oxidase reaction, and typical gram- negative morphology;
- detection of *N. gonorrhoeae* by a nonculture laboratory test (Antigen detection test (e.g., Gonozyme [Abbott]), direct specimen nucleic acid probe test (e.g., Pace II [GenProbe]), nucleic acid amplification test (e.g., LCR [Abbott]).
- confirmation of isolates by biochemical, enzymatic, serologic, or nucleic acid testing e.g., carbohydrate utilization, rapid enzyme substrate tests, serologic methods such as coagglutination or fluorescent antibody tests supplemented with additional tests that will ensure accurate identification of isolates, or a DNA probe culture confirmation technique.

(vi) Diagnostic laparoscopy has altered treatment decisions in an unexpectedly high number of patients in cases of idiopathic and tubal factor infertility. Diagnostic laparoscopy may be of considerable value, provided the change of treatment decision is effective.

Risk of developing PID after chlamydia infection

The risk of developing PID after lower genital tract infection varies considerably and is estimated to be between (less than) 1% and 30%. Difference in estimates is largely determined by the characteristics of the tests used (e.g. PCR or culture) & the populations tested (e.g. symptomatic versus asymptomatic, high-risk versus low-risk). Risk of low-load PCR detected infections in low-risk populations will be rather at the lower than at the upper estimate. The risk of developing tubal infertility after PID is estimated at 10 - 20%, approximately 4% develop chronic pelvic pain, 3% infertility, & 2% adverse pregnancy outcome and from this it can be concluded that the risk to test-positive women of developing tubal infertility ranges between 0.1 & 6%. Therefore screening for T. Chlamydia is cost effective & is largely determined by the rates of complications prevented as maximum cases are asymptomatic. They are of paramount importance in the prevention of long-term sequelae.

Chlamydia (C.) trachomatis female genital tract infections usually remain asymptomatic and untreated. Therefore, an adequate immune response, rather than antibiotic treatment, is essential to clear the pathogen.

Most women will effectively clear *C. trachomatis* infections, but some will have persistent *C. trachomatis* infections, which may ascend to the upper genital tract and increase the risk of tubal factor subfertility. Pattern recognition receptors (PRRs) of the toll-like receptor (TLR) and nucleotide-binding oligomerization domain (NOD) families recognize *C. trachomatis* and initiate the immune response. Host immune factors are determinants of the course of *C. trachomatis* infections. Genetic variations in *TLR* and *NOD* genes may affect receptor function, leading to inadequate recognition of *C. trachomatis*, an inadequate immune response, and consequently an increased risk of persistence and late sequelae. For the risk assessment of tubal pathology in subfertile women, *C. trachomatis* immunoglobulin (Ig) G antibody testing (CAT) in serum is widely used. A positive CAT is indicative of a previous infection but not of a persistent infection. Measuring serological markers of persistence, of which C-reactive protein (CRP) seems promising, in CAT-positive women may identify a subgroup of subfertile women with persistent *C. trachomatis* infections and the highest risk of tubal pathology. In predicting tubal pathology, adding markers of the cell-mediated immune system to antibody testing improved the value of measuring markers of the humoral response alone.

A balance, therefore, exists between the protective and deleterious effects of cell-mediated immunity, represented in Figure 1 as a U-shaped curve. An effective immune response that successfully clears infection occurs in the center, lower region of the curve. Each end of the curve indicates either a too weak or too strong cellular immune response, responsible for pathology consequent to chronic chlamydial infection or hyperinflammation, respectively.

Figure 1

Chlamydial infection and the interplay between host immunity, pathology, and infection determine the late sequel. Progression along a particular pathway is determined by particular immune responses, which in turn are determined by a range of host and pathogen factors. At each stage there exists an opportunity for resolution and clearance of organisms, or progression to further serious pathology (Figure 2).

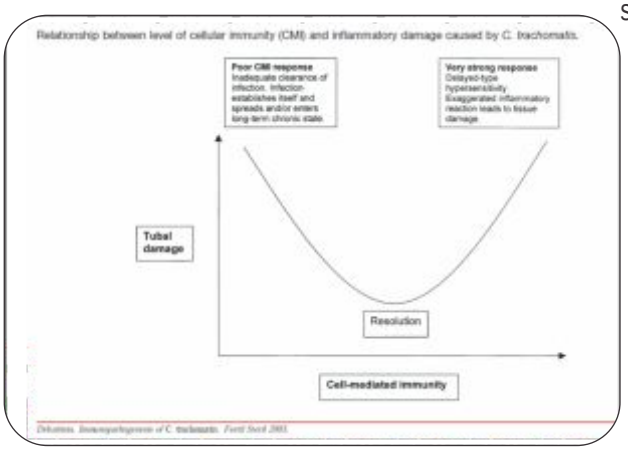
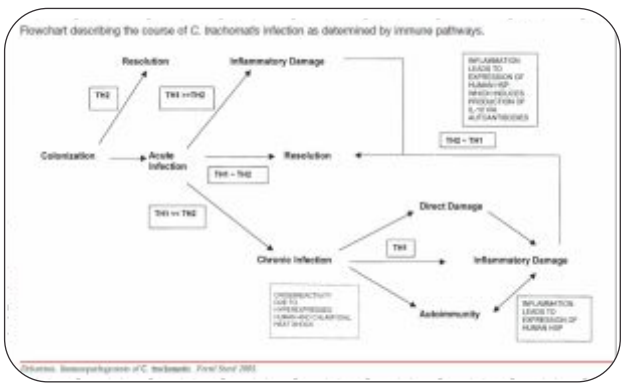


Figure 2

Hydrosalpinx

Chronic inflammation of the human fallopian tubes following chlamydial infection, Neisseria gonorrhea or bacterial vaginosis leads to subsequent hydrosalpinx formation, which has been associated with poor fertility prognosis. IVF/ET is a better alternative to tubal surgery for those patients with severe distal tubal disease, and also more cost effective. However, the presence of hydrosalpinx has a negative effect on IVF/ET by decreasing the pregnancy rates and implantation rates compared with patients undergoing IVF/ET for tubal disease but without hydrosalpinx. Infammatory mediators may act on fallopian tube epithelial cells to directly cause microvascular permeability and via



secondary messengers, leading to abnormal fluid production. Possible links between Chlamydia trachomatis in pelvic infammatory disease and the subsequent Cystic fibrosis transmembrane conductance regulator (CFTR)-mediated events in hydrosalpinx formation leading to infertility in hydrosalpinx are proposed. The interactions between CFTR and other epithelial transporters are important for the balance of secretion/absorption, disruption of which may lead to hydrosalpinx. During infammation, CFTR in oviductal cells may be continually activated, leading to increased fluid secretion and decreased fluid absorption through CFTR inhibition of ENaC. Occlusion of the fimbrial ends prevents the fluid from draining into the pelvic cavity, hence the retrograde spillage of HF into the uterine cavity, which may act as a mechanical barrier between embryo and the endometrium. Decreased glycoprotein production and enhanced CFTR-mediated water permeability may produce a dilution effect on essential embryotrophic substances. A combination of all or some of these factors may explain the low implantation rate following IVF treatment in women with hydrosalpinges. New research focusing on the involvement of CFTR in HF formation may provide crucial information for a better treatment strategy to enhance IVF outcome for patients with hydrosalpinges and tubal infertility.

The hydrosalpingeal fluid has been demonstrated to be embryotoxic to developing embryos, thus leading to increased early pregnancy losses. Poor endometrial receptivity has also been demonstrated in the presence of hydrosalpinges. Removal of the hydrosalpinges leads to improved IVF/ET rates comparable to those patients without hydrosalpinx. Therefore, salpingectomy has been recommended for patients with hydrosalpinx who will be undergoing IVF/ET.

Prevention

Preventative efforts should therefore continue to focus on the detection and eradication of lower genital tract chlamydial infection in high-risk groups.

- Safer sex campaigns, positive attention for sexual health and proper counseling remain a cornerstone in STD prevention.
- Proper case management (diagnosis, counseling and partner treatment) is important
- Early diagnosis and proper treatment will prevent onward transmission and development of sequelae.
- Prophylactic treatment has been shown to be cost-effective in induced abortion, and following uterine instrumentation for other procedures to prevent infection
- If uptake is sufficient, vaccination will decrease the prevalence of chlamydia infections, but it will take several more years before effective vaccines will be available.
- Proper sterilization of instruments before use for uterine instrumentation

<u>Treatment</u>

1. Antibiotics

CDC- RECOMMENDED TREATMENT REGIMENS FOR ORAL THERAPY OF ACUTE PID

- Regimen A

Levofloxacin 500 mg orally once daily for 14 days

OR

Oflaxacin 400 mg orally once daily for 14 days

WITH OR WITHOUT

Metronidazole 500 mg orally twice a day for 14 days

- Regimen B

  Ceftriaxone 250 mg IM in a single dose

  PLUS

  Doxycycline 100 mg orally twice a day for 14 days

  WITH OR WITHOUT

  Metronidazole 500 mg orally twice a day for 14 days

  OR

  Cefoxitin 2 g IM in a single dose and probenecid, 1 g orally administered concurrently in a single dose

  PLUS

  Doxycycline 100 mg orally twice a day for 14 days

  WITH OR WITHOUT

  Metronidazole 500 mg orally twice a day for 14 days

  OR

  Other parenteral third-generation cephalosporin(e.g., ceftizoxime or cefotaxime),

  PLUS

  Doxycycline 100 mg orally twice a day for 14 days

  WITH OR WITHOUT

  Metronidazole 500 mg orally twice a day for 14 days

- Alternative Oral Regimens :

  Amoxicillin / Clavulanic acid plus doxycycline

2. Interventional treatment:

   i. Drainage of Abscess

      (A) POSTERIOR COLPOTOMY can be done in cases of -

      - Midline abscess
      - Abscess adherent to cul de sac & dissecting rectovaginal septum
      - Abscess should be cystic or fluctuant

      (B) Lapraoscopic or Laparotomic

      (C) Treatment of ruptured tuboovarian abscess The operation of choice is removal of free pus together with abscess, the uterus, the tubes and usually ovaries.

      (D) Surgery for chronic PID - Salphingectomy

   ii. Proximal tubal disease

   - Microsurgical tubocornual anastomosis yields a 50% probability of achieving an ongoing pregnancy
   - Macrosurgery has a lower success rate and is indicated only in cases of complete obliteration of the intramural fallopian tube.

- Radiographic therapies for proximal blockage produce live birth rates that are lower (26%) than those obtained with microsurgery. Selective salpingography and transcervical cannulation under fluoroscopic guidance are effective at establishing patency in appropriately selected patients, and are less invasive and costly than the surgical alternatives.

iii. Middle and Distal tubal obstruction

- Microsurgical anastomosis
- Macrosurgery has a lower success rate and is indicated only in cases of frozen pelvis
- Removal, cornual clipping or cauterization of the proximal part with bipolar forceps are indicated in the presence of hydrosalpinx.

3. IVF/ICSI is indicated in women who desire pregnancy and have a tubal factor.

Conclusion

PID can be treated with success if it is diagnosed early. If not treated promptly, the infection may cause permanent, long-term problems, especially in respect to future fertility.

References

1. Akande VA, Hunt LP, Cahill DJ, Caul EO, Ford WCL, Jenkins JM. Tubal damage in infertile women: prediction using chlamydia serology. Hum Reprod 2003;18:18411847.
2. Brunham RC, Rey-Ladino J. Immunology of Chlamydia infection: implications for a Chlamydia trachomatis vaccine. Nat Rev Immunol 2005;5:149161.
3. Bosteels Jan, Bruno Van Herendael, Steven Weyers and Thomas D'Hooghe; The position of diagnostic laparoscopy in current fertility practice; Human Reproduction Update, 2007,Vol.13, No.5 pp. 477485,
4. Debattista Joseph, Peter Timms, John Allan, and Janet Allan; Immunopathogenesis of Chlamydia
5. trachomatis infections in women; FERTILITY AND STERILITY, 2003, VOL. 79, NO. 6 pp 1273 - 1287
6. Hartog J.E.den, S.A.Morré and J.A.Land; Chlamydia trachomatis-associated tubal factor subfertility:
7. Immunogenetic aspects and serological screening; Human Reproduction Update, 2006, Vol.12, No.6 pp. 719730.
8. Land J. A., Van Bergen J.E.A.M. , Morre´ S.A. and Postma M.J.; Epidemiology of Chlamydia trachomatis infection in women and the costeffectiveness of screening; Human Reproduction Update, 2010, Vol.16, No.2 pp. 189204.
9. Macmillan S, Templeton A. Screening for Chlamydia trachomatis in subfertile women. Hum Reprod 1999;14:30093012.
10. Mardh PA. Tubal factor infertility, with special regard to Chlamydia salpingitis. Curr Opin Infect Dis 2004;17:4952.
11. Morre´ SA, Van den Brule AJC, Rozendaal L, Boeke AJP, Voorhorst FJ, De Blok S, Meijer CJLM. The natural course of asymptomatic Chlamydia trachomatis infections: 45% clearance and no development of PID after one-year follow-up. Int J STD AIDS 2002a;13:1218.
12. Paavonen J and W.Eggert Kruse; Chlamydia trachomatis Impact on human reproduction; Human Reproduction Update,1999, Vol.5, No.5 pp. 433437
13. Persson K, Osser S, Birkelund S, Christiansen G and Brade H (1999) Antibodies to *Chlamydia trachomatis* heat shock proteins in women with tubal factor infertility are associated with prior infection by *C. trachomatis* but not by *C. pneumoniae*. Hum Reprod 14,19691973.

14 VIRAL INFECTIONS IN ASSISTED REPRODUCTION

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Introduction

The viral infections of interest in relation to assisted reproduction are the blood borne virsues (BBV). They are HIV, Hepatitis B and Hepatitis C. The prevalence of these infections in reproductive age individuals is estimated as 0.5% - 3%, 2 – 5% and 1 – 3% in various populations, representing a significant disease burden.

A common characteristic in terms of reproductive health is that these infections can spread horizontally (sexual), vertically (mother to child), nosocomially (from one patient to another in hospital settings due to medical procedures) and by occupational exposure (from patient to health care providers). Assisted reproduction therapies should be considered in two settings for people carrying a BBV. Firstly, a couple who is infected may be infertile and need assisted reproduction to conceive. Secondly, a couple who is infected (but otherwise fertile) may consider assisted reproduction as a means to avoid horizontal and vertical transmission. The chapter will review the following areas of interest:

- General health and counseling regarding safe sexual practices
- Screening for BBV in an ART program
- Ethical issues related to providing ART to BBV patients
- Methods to minimize horizontal and (and consequently vertical) transmission
  - o With only male partner infected
  - o With only female partner infected
  - o With both partners infected
- Impact of BBV infections on fertility in men and women
- Laboratory set up
- BBV in relation to third party reproduction programs

General health and safe sexual practices

Couples infected with a BBV are advised to adopt a healthy lifestyle in general and especially in terms of sexual health. They should be immunized for HBV if not already infected. Screening for other sexually transmitted infections (vaginits, chlamydia, gonorrhea, herpes) should be offered. Safe sexual practices promote condom use. This is especially important to couples where one or both partners are infected with HIV. In couples planning a pregnancy, antiretroviral therapy should be modified to maximize fetal safety. Efavirenz should be

avoided. Condom use reduces the chance of transmitting other strains of the virus and consequently reduces the emergence of drug resistant strains. However, in couples seeking fertility, condom use may be abandoned completely or selectively (timed intercourse) by the couple. Couples who are in a monogamous, stable relationship have a much lower risk of transmission than in situations such as sex with a commercial sex worker. In a stable, monogamous relationship in otherwise low risk couples (low viral load, adequately treated with antiretrovirals, no intravenous drug abuse) the risk of transmission from male to female partner is approximately 0.5% per sexual intercourse and from female to male partner is approximately 0.1% per sexual intercourse. This represents a risk of 1 in 200 and 1 in 1000 respectively. In couples where there is a discordance of HBV infection, the uninfected partner can be protected by immunization very effectively. The HBV vaccine provides over 95% seroconversion and risk of sexual transmission is very low. Estimates for spread of HCV by the sexual route are scarce. However, best estimates put this figure at approximately 0.01% where other risk factors are absent. Even though these figures represent very low numerical risk, under no circumstances should couples be counseled that there is no risk of disease transmission.

Screening for BBV in an ART program

There has been some concerns about universal screening for BBV and HIV in particular before a couple is included in an ART program. The arguments against universal screening are that this could lead to discriminatory attitudes and provision of reproductive health services may be affected. However, most national bodies and fertility authorities support screening today on the following basis:

- Patients may be informed about their condition and may modify their lifestyle, sexual practices and reproductive plans.
- They may be offered treatment to control the disease.
- Efforts may be directed to minimize transmission risk horizontally, nosocomially and by occupational exposure.

Screening must be accompanied by adequate pre and post-test counseling.

Ethical issues in providing ART to couples with BBV infections

There are ongoing debates and ideological differences amongst authorities on the ethics of providing couples with BBV infections and in particular those infected with HIV. In the past, a number of authorities have clearly opined that such couples should not be a part of ART programs due to the risk of nosocomial transmission, limited life span and consequently a child raised with no parents or with a single parent. The argument against the first aspect is that effective methods are available to prevent nosocomial transmission. Secondly, HIV infected individuals today face a chronic disease much like diabetes or hypertension rather than an imminently fatal one. Since reproductive therapies are offered to men and women who have advanced cancer, not offering them to HIV infected couples is obviously discriminatory.

Measures to avoid transmission in discordant couples

As discussed earlier, the risk of HBV and HCV by the sexual route is very low. The discussion below mainly pertains to couples who are discordant for HIV.

Only the male partner is infected: Such couples may be offered one of the three following options:

1. Insemination using donor sperm: This effectively removes the risk of viral transmission as sperm donors are screened for HIV and other blood-borne viruses. However, it also removes the option of genetic parenting from the infected man.

2. Adoption : While it is an acceptable route for those wishing to remove the risk of infecting their partners, current adoption practice regards HIV in one or both partners as a significant undesirable factor when assessing the suitability of parents requesting to adopt.
3. Sperm washing : The female partner is inseminated with the infected partner's sperm, centrifuged first to separate spermatozoa from seminal fluid and associated nonsperm cells (NSC). A double centrifugation and suspension method is recommended with 40 to 80% percoll gradient has been described. A 5% risk of the washed semen containing traces of HIV infection still exists. A nucleic acid sequence based amplification (NASBA) can be used to detect this. However, viral load is typically less than 25 copies per ml. At this level, the risk of transmitting infection is less than 1 in 5000. The group from Milan headed by Sempirini has pioneered this technique. It is estimated that approximately 3000 procedures have been performed with no reported infection of the female partner and consequently no child born with parent to child transmission. These results are very encouraging and this has become the standard method adopted in the situation. However, it should be borne in mind that this technique has never been subjected to a randomized trial and from the estimated risks of transmission, to prove that this therapy is efficacious, the number needed to treat would be as high as 1 in 3000 i.e. it would be necessary to treat 3000 couples to prevent one transmission.

Only the female partner is infected:

HIV-positive women planning assisted reproduction techniques should be offered an in-depth preconceptual counselling to discuss in detail the interventions required to reduce vertical transmission risk, their long-term health and the possible effects of antiretroviral medication on the fetus. They are then advised on how to carry out selfinsemination of their partner's sperm at the time of ovulation in order to minimise viral transmission risk through unprotected intercourse.

Both partners are infected:

Such a couple is at risk of cross infecting each other with different strains. They should be offered preconceptional counseling about antiretrovirals and the three options outlined under the scenario of only male partner infection.

Impact of BBV infection on fertility in men and women

Women and men infected with BBV, in particular HIV, may have multiple reproductive health high risk factors compromising fertility. This includes infections of the reproductive tract causing blockages and mechanical issues. Lifestyle factors such as drug use, alcohol abuse, malnutrition and poor hygiene may all contribute to varying degrees to fertility problems. Men with HIV infection have been seen to have worsening semen analysis parameters with progression of the disease. Antiretroviral therapies, especially protease inhibitors, have an adverse impact on androgen levels. This can affect sexual drive and spermatogenesis. Ovarian dysfunction has been documented with HIV and HCV infections. Women with either one of these infections tend to have poor ovarian reserve and are at a risk for cycle cancellation during ART.

Laboratory set up

There are two possibilities when considering laboratory set ups in dealing with biological fluids and gametes from individuals with BBV. The ideal option is to have a completely different laboratory for individuals who are known to carry such infections. The rationale for this is that even with the greatest of precautions, the risk of

nosocomial infection between samples remains a possibility. Cross contamination has been documented in fresh as well as frozen samples. The "infected lab" should be equipped in the same way as the main laboratory. The obvious problem with this approach is that of cost and utilization of the resources. A particular center may not deal with enough infected couples to justify the expense on equipment and resources. The other option is to adopt universal precautions i.e. to treat every sample as potentially infected. This may not allow segregation of samples or patients, but is probably a more practical approach. In either case, it is necessary to institute safe laboratory practices including avoiding mouth pipetting, vertical laminar flow units, etc. to minimize risks.

BBV infection screening in relation to third party reproduction programs

Investigations for BBV infections should routinely be performed for semen donors at the time of recruitment. Semen samples are collected and then cryopreserved. A blood test is done again six months after the date of semen being stored. The sample is released for use only if the second test is negative. Oocyte donors and surrogates are screened at the time of recruitment for BBV. However, it is not feasible to freeze oocytes routinely. Hence most centers do not impose quarantine for oocyte donors.

Conclusions

The subject of blood borne viral infections has a tremendous importance in ART practice from the safety point of view. It has important implications in terms of ethical issues, laboratory practice and impact on fertility outcome and assisted reproduction therapy outcomes as well.

Bibliography

- Englert Y, Lesage B, vanVooren JP, et al. Medically assisted reproduction in the presence of chronic viral diseases. Hum Reprod Update 2004; 10:149 – 162.
- Gilling-Smith C, Nicopoullous JDM, Semprini AE, et al. HIV and reproductive care – a review of current practice. BJOG 2006; 113:869 – 878.
- Sempirini AE, Levi-Setti P, Bozzo M et al. Insemination of HIV-negative with processed semen of HIV-positive partners. Lancet 1992; 340:1317-1319.
- Gilling-Smith C, Emiliani S, Almeida P et al. Laboratory safety during assisted reproduction in patients with blood-borne viruses. Hum Reprod 2006; 20:1433 – 1438.