We are IntechOpen, the world's leading publisher of Open Access books
Built by scientists, for scientists

6,900
Open access books available

185,000
International authors and editors

200M
Downloads

154
Countries delivered to

Our authors are among the

TOP 1%
most cited scientists

12.2%
Contributors from top 500 universities

CLARIVATE ANALYTICS
BOOK CITATION INDEX
INDEXED

WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com

Human Trichomoniasis due to
Trichomonas vaginalis – Current Perspectives

Nancy Malla
Department of Parasitology, Postgraduate Institute
of Medical Education and Research, Chandigarh
India

1. Introduction

Human trichomoniasis caused by protozoan parasite, *Trichomonas vaginalis* is one of the most prevalent non-viral sexually transmitted urogenital disease with more than 180 million cases annually worldwide. Annual incidence varies between 0-65 percent depending upon different geographical locations, age groups and population studied. In North America and Canada, more than 8 million new cases are reported annually, with an estimated rate of asymptomatic cases as high as 50 percent (Sobel, 2005). The number may be underestimated as symptomatic patients may be underdiagnosed because of insensitive wet mount procedure and most of the infected subjects remain asymptomatic, thus are not being reported (Petrin et al, 1998). Recent review on Global epidemiology in high risk populations and control of T.vaginalis has highlighted that the burden of infection is found in resource-limited settings and high risk groups in industrialized settings. The World Health Organization estimated global prevalence figures are based on a wet mount microscopy (sensitivity range of 60-80%), however recent data, using PCR suggests sensitivity may be lower (35-60%), thus underestimating global prevalence (Johnston and Mabey, 2008) In India, hospital based studies reveal 4-10 percent positivity in symptomatic women attending gynaecology clinics and almost similar percentage in asymptomatic women attending infertility, post-natal and family planning clinics (Sharma et al, 1988; Malla et al, 1989; Divekar et al, 2000; Vishwanath et al, 2000;Valadkhani et al, 2003; Chakraborty et al, 2005; Yadav et al, 2006). The significantly higher percentage has been observed amongst contraceptive users (7.31%), antenatal patients (7.59%) and women with gynaecological disorders (9.21%) compared to postnatal (3.62%) and infertile woman (2.83%) (Sharma et al, 1988). The association of infection with contraceptive practices indicates controversial figures. Lazer (1970) found an increase, McLellan et al (1982) found no such correlation while Krieger et al (1985) found prevalence to be less amongst women using oral contraceptive and Sharma et al (1988) found barrier contraceptive to be protective. This observation and the tendency for symptomatic disease to occur during menstrual periods, suggests a hormonal component to the susceptibility. In contrast, Demes et al (1988) reported fewer parasites in vaginas of infected women during menstruation, suggesting trichomonacidal effect of menstrual blood complement in-vivo and survival of parasites during menstrual bleeding has been explained by the existence of subpopulations of

trichomonads that are resistant to complement lysis. The infection is low in women in higher socio-economic groups and high (55%) in the developing countries and in minority groups of industrialized populations (Tapsall et al, 1979). Based on family income, we have observed that 90% infected women belonged to middle and lower socio economic status, while only 10% were from upper socio-economic status, thereby indicating that socio-economic factors seem to play role in this infection (Kaur et al, 2008).

The infected men are usually asymptomatic, acting as carriers of infection. In men with non-gonococcal urethritis (NGU), although a median prevalence of 11 percent is suggested (Krieger, 1990), yet it varies from 10% to 21% in adolescents at high risk and 45% in those who have been in contact with infected women (Sobel, 2005). Report from India revealed that one (2.5%) out of 40 NGU male patients harboured *T.vaginalis* (Dawn et al, 1995). The rate of transmission from men to women appears to be higher (67-100%) than the other way round (14-80%) suggesting that in men, the disease is self limiting (Rein and Muller, 1990) and parasites are spontaneously cleared, possibly by the trichomonacidal action of prostatic secretions (Langley et al, 1987) or due to mechanical elimination of protozoa during micturition (Rein, 1990).

T.vaginalis and HIV infections are both sexually transmitted, yet there are controversial reports of the association of presence of T.vaginalis and HIV. No significant differences were observed between the presence of parasite and status of HIV infection from studies conducted in different geographical locations (Minkoff et al, 1999; Frankel and Monif, 2000; Susan et al, 2002; Klinger et al, 2006). It is concluded that HIV infection does not make a woman more likely to have prevalent, incident, persistent or recurrent trichomoniasis (Susan et al, 2002). No association of prevalence of *T.vaginalis* in HIV infected women and CD4+ cell count has been found (Sorvillo et al 1998). In support of this, in our study, none of the 100 HIV seropositive patients including 30% patients with <200/μl CD4+ cell count was found to harbour *T.vaginalis* (Kaur et al, 2008). The reason for absence of *T.vaginalis* in the study may be because most of the females (71%) were sexually inactive and 25% were using different contraceptive devices. In contrast, two cross-sectional studies in Africa (Ter Muelen et al, 1992; Ghys et al, 1995) and in Mexico (Bersoff-Matcha et al, 1998) have demonstrated an association between *T.vaginalis* and HIV infection in women. T.vaginalis was found in 18.6% HIV positive and 10.2% HIV negative pregnant women (Sutton et. al, 1999). *T.vaginalis* infected HIV women had 4.2 fold reduction in the quantity of cell-free HIV-I virus in vaginal secretions following metronidazole therapy (Wang et al, 2001). Study from Tanzania showed that treatment of trichomoniasis in HIV-infected women decreased vaginal HIV RNA levels. It is concluded that control of *T.vaginalis* infection may be single, most cost effective strategy for reducing the incidence of HIV transmission (Gosskurth et al,1995). It is postulated that although *T.vaginalis* infection may not be significantly high in HIV infected women, yet the Trichomonas infected subjects may be more susceptible and at higher risk of acquiring the HIV infection.

Although, sexual mode of transmission is the only documented route of acquisition of infection, yet, 2-17 percent female offspring of mothers infected with *T.vaginalis* acquired urinary tract trichomoniasis or vaginal infection (Rein and Muller, 1990) and 2 infants suffering from respiratory tract infection were delivered vaginally by infected mothers indicating respiratory route of infection (McLaren et al, 1983). The parasites have been

reported from toilet seat towels and allied objects, but, so far, no case of fomite transmission has been documented (Heine and McGregor, 1993).

2. The parasite

Honigber and King (1964) have detailed out initially the morphological characteristics of this urogenital pathogen and further detailed morphological, parasitological, biochemical and clinical aspects of the parasite have been amply reviewed earlier (Petrin et al, 1998; Schwebke and Burgess, 2004). Recently with the cracking of the genome of the parasite, and identification of 26,000 confirmed genes, the new ways of diagnosing and treating the disease may come to light (Carlton et al, 2007). It is postulated that an additional 34,000 unconfirmed genes are on the way for identification.

3. Pathogenesis

The exact mechanism of pathogenesis is still under elucidation. Reports have revealed multifaceted interplay of parasite and host factors leading to different clinical spectrum. Initial events invariably have been focused on parasite factors revealing cell-to cell adhesion, haemolytic activity, pore-forming proteins, excretion of extracellular proteinases and cell detaching factors playing significant role in pathogenesis (Fiori et al, 1999). Host factors include role of Lactobacilii, local pH, hormonal components, humoral and cytokine responses and free radical generation (oxidative stress and No radicals).

3.1 Adherence and adhesions

Cytoadherence, one of the early steps in the infection process is essential for colonization. Initially, following cytoadherence, parasite changes its morphology from pear shape to amoeboid form with numerous cytoplasmic projections interdigetating with the microvilli of the host cell plasma membrane (Arroya et al, 1993) and allowing the formation of isolated intracelllular spaces (Gonzalez et al, 1995). The adherence is specifically mediated by four adhesion proteins (AP 65, 51, 33 and 23) which act in a specific receptor-ligand interaction and is time, temperature and pH dependent. The adhesions are concentrated on the side opposite the undulating membrane while laminin binding proteins are ubiquitous on the entire surface of the parasite (Costa et al, 1988). Parasite binds to numerous host macromolecules which may serve a nutritive purpose while few may protect the parasite by modifying their host defences, thereby helping in evasion of the host immunity (Honigberg, 1990). In Vitro studies have indicated time dependent significant difference in the percentage of vaginal epithelial cells (VEC) attached by trichomonads as well as number of parasites attached per VEC in *T.vaginalis* isolates from symptomatic and asymptomatic women. Significant difference in attachment of VEC's was observed only during first 15 minutes while maximum number of VEC's attached by parasite was significantly different at initial 20 to 25 minutes following incubation of VEC's and parasites (Valadkhani et al 2003). These observations suggest that adhesion proteins and / or other virulence markers may be playing significant role in the initial stages of attachment. Experimental studies revealed that sustained infection in mice could only be induced in presence of *Lactobacillus acidophilus* (McGrory and Garber, 1992). *L.acidophilus* may be playing role in sustaining

trichomoniasis by providing low pH (4-4.5) in the environment. *In vitro* study demonstrated that in presence of *L.acidophilus* more number of VEC's were found attached by *T.vaginalis* as compared to controls and significant reduction was observed in presence of excretory secretory products of *L.acidophilus* (Valadkhani et al, 2003), thereby suggesting that adhesion of parasite to target cells is pH dependent.

T.vaginalis alpha-actinin is diffusely present throughout the parasite before interaction with target cell and gets localized in the peripheral regions of the amoeboid cell which is accompanied by an enhanced expression of the genes coding for some cytoskeletal components (Fiori et al, 1999). *T.vaginalis* cysteine proteinase 30 (CP30) has been found to bind to host cell surface and shown to play a role in cytoadherence (Menduza-Lopez et al, 2000). CP30 was detected in 40 fresh *T.vaginalis* isolates from both symptomatic and asymptomatic women, while intensity of CP30 band was significantly higher in isolates from symptomatic as compared to asymptomatic women. In long term culture maintained isolates, the band was detected in all the 20 (100%) isolates from symptomatic women and only in 14 (70%) isolates from asymptomatic women, thereby suggesting that CP30 expression of isolates leading to symptomatic infection appears to be more stable characteristic (Yadav et al, 2007). Further, CP30 was detected in serum and vaginal washes of 100% *T.vaginalis* infected women and in 65% serum and 80% vaginal wash samples from 15 asymptomatic infected women. Antibody to CP30 was detected in 100% serum samples of both symptomatic and asymptomatic women, in 54.5% vaginal washes of symptomatic and 35% asymptomatic women and also in 3/20 (15%) serum samples from uninfected women, thereby suggesting that besides CP30, other factors may also be playing role in leading to symptomatic infection (Yadav et al, 2007a).

3.2 Haemolysis

T.vaginalis is capable of producing haemolysis and utilizing haemoglobin as a source of iron. Experimental studies have indicated that virulence of parasite is reduced under iron depleted conditions (Ryu et al, 2001). The parasite possibly causes lysis of red blood cells both by contact dependent (Krieger et al, 1985; Fiori et al, 1999; Valadkhani et al, 2003) and contact independent mechanisms (Pindak et al, 1993). The contact of parasite with RBC's is thought to derive lipids and iron. This is suggested mechanism to exacerbate the symptoms during and following menstruation. The temperature and Ca^{2+} dependent mechanisms of haemolysis suggest the role of pore-forming proteins, which are able to insert themselves in the lipid bilayer of the target cell, forming transmembrane channels that lead to cell death, by osmotic lysis. The size of the pores formed on the target cell membrane is between 1.14 and 1.34 nm and alteration of membrane permeability eventually leads to cell lysis and loss of haemoglobin. The pore-forming proteins are active at pH lower than 6.5 and at 37°C. Electron microscopic studies have revealed that following parasite and target cell interaction, the change in shape of the target cell is due to loss of spectrin, the predominant protein of the RBC cytoskeleton and acid intact, metabolically active parasites can disrupt the target cell spectrin which is contact dependent (Fiori et al, 1999). The parasite has a haemolytic Phospholipase A (pore forming proteins) which is rich in membranes, hydrogenosomes, vesicles and vacuoles. The three pathogenic isolates showed maximum hemolytic activity at pH 6.0 and 8.0, indicating that the parasite have both acidic and

alkaline hemolysins and activity was also related to type of RBC's from different sources, rat and human (Vargas – Villarreal et al, 2003).

3.3 Free radical generation

It is apparent that free radicals play a critical role in a variety of normal regulatory pathways and oxidant-antioxidant balance is important for immune cell function. Trichomonads are equipped with several oxygen scavenging systems localized in both cytoplasm and hydrogenosomes. The main systems operating in the cytoplasm consists of NADH and NADPH oxidases, (Linstead & Bradley, 1988) which reduce O_2 to H_2O and H_2O_2 respectively. Polymorphs recruited at the site of infection and when activated, initiate oxidative stress by releasing toxic oxidants such as superoxide anion and H_2O_2, which lead to cell damage surrounding VEC's. Shaio et al (1991) observed that neutrophil could kill *T.vaginalis* only in presence of normal human serum, indicating that trichomonicidal activity is complement dependent. However, low concentration of $C\overset{1}{\circ}$ in vagina may explain survival of the parasite in presence of significant number of PMN's. Davis and Lushbaugh (1993) observed inter-strain heterogenity in the oxidative stress response of *T.vaginalis*. The parasite has developed mechanisms to deal with oxidative stress and upon exposure to H_2O_2, it upregulates the production of various heat shock proteins (Bozner,1997). Experimental study showed that vaginal tissue (VT) of mice infected with isolates from symptomatic women generated significantly higher superoxide radicals (SOD) while vaginal washes (VW) and blood samples generated less SOD as compared to mice infected with isolates from asymptomatic women(Valadkhani et al, 2006). It is suggested that different responses by VT, VW and blood may be due to functional differences in different tissue and circulating PMN's.

Nitric oxide appears to play an important function as a cytotoxic effector molecule for several parasites. Significant increase in reactive nitrogen intermediates (RNI) levels in mice infected with *T.vaginalis* isolates from infected women as compared to uninfected controls has been reported (Malla et al, 2004). The inducible nitric oxide synthase (iNOS) protein and RNI was detected in leucocytes (stimulated with *T.vaginalis* in vitro) and VW of all the *T.vaginalis* infected 22 symptomatic and 20 asymptomatic women studied. The mean iNOS protein band intensity was significantly higher in leucocytes of asymptomatic as compared to symptomatic women, while no significant difference was observed in VW between symptomatic and asymptomatic women. The study suggested that reactive nitrogen radicals may be playing role in limiting *T.vaginalis* infection (Yadav et al, 2006).

3.4 Other mechanisms

Host humoral immune responses to the parasite seem to be important determinants of virulence. High concentrations of IgG, IgM and IgA antibody to trichomonads have been observed in serum from experimental infected animals and infected subjects. Specific IgG and IgA are present in vaginal washes from women with trichomoniasis and significantly higher IgA levels have been found in vaginal secretions in asymptomatic than symptomatic women suggesting its role in preventing the establishment of infection (Ackers et al, 1975; Sharma et al, 1991). Significant increase in specific IgG and particularly IgG_1 was observed

in experimental study (Yadav et al, 2005) and in infected human subjects (Kaur et al 2008). It is suggested that the IgG and IgM may be playing significant role in establishing symptomatic infection. *T.vaginalis* can coat itself with host plasma proteins, thus hosts immune system does not recognize the parasite as foreign (Peterson and Alderete, 1982) and continuous release of antigens may neutralize antibody or cytotoxic T lymphocytes, thus short-circulating specific anti-*T.vaginalis* defense mechanisms (Alderete and Garza, 1984). Numerous CP's secreted by the parasite degrade IgG, IgM and IgA, allowing the parasite to survive the antibody response (Provenzano and Alderete, 1995). It is proposed that the balance between different IgG subclasses influences the clinical outcome of infection in various parasitic diseases.

Cytokines and chemokines provide a mechanism for initiation, amplification or containment of inflammation during disease status. Experimental studies have revealed that the Th-I cytokine (IL2 and IFN-γ) responses might play a role in the elimination of *T.vaginalis* (Paintlia et al, 2002; Malla et al, 2007) and thus might be maintaining low levels of infection in asymptomatic infected subjects.

It is observed that the parasite induces cell death in host cells via apoptosis. The study indicated that p38 MAPK signaling cascade is requisite to apoptosis of *T.vaginalis* infected macrophage, and apoptotic process occurs via the phosphorylation of p38 MAPK, which is located downstream of mitochondria-dependent caspase activation, conferring insight into the plausible molecular mechanism of *T.vaginalis*- immune evasion from macrophage attack (Chang et al, 2006).

Recently, the influence of *T.vaginalis* lysate and excretory-secretory products (ESP) on the fate of neutrophils has been reported. The study revealed that *T.vaginalis* lysate inhibits apoptosis of human neutrophils. It is suggested that an intrinsic mitochondrial pathway of apoptosis was involved in *T.vaginalis* lysate-induced delayed neutrophil apoptosis and this phenomenon may contribute to local inflammation in trichomoniasis (Song et al, 2010).

3.5 Molecular mechanisms

Molecular analysis of the membrane molecules and virulence factors have begun. The recent sequencing of the T.vaginalis genome has allowed comprehensive computational analysis of the general transcription machinery and the identification of novel eukaryotic DNA involved in directing gene expression in this parasite. Identification of Genes, particularly, required for synthesis of an unusual nucleotide sugar found in *T.vaginalis* lipophosphoglycan, the monosaccharide rhamnose, which is absent in the human host, may make it a potential drug target. Genes involved in sialic acid biosynthesis consistent with the reported presence of this sugar on the parasite surface were identified. It is suggested that the discovery of previously unknown metabolic pathways, the elucidation of pathogenic mechanisms, and the identification of candidate surface proteins likely involved in facilitating invasion of human mucosal surfaces may provide potential leads for the development of new therapies and novel methods for diagnosis (Carlton et al, 2007).

Control of gene expression is essential to the survival of an organism and with the available genome data, additional analyses have been made possible. The wealth of data present in the *T.vaginalis* genome has been utilized to identify aspects of an array of

biological processes, including small nuclear RNAs involved in splicing of introns, components of transcriptional complexes and the presence of discrete DNA elements that direct basal transcription. It is suggested that both evolutionarily conserved and novel features of T.vaginalis serve to inspire further questions specifically concerning this parasite, as well as the molecular mechanisms shared with other eukaryotic groups (Smith and Johnson, 2011).

4. Clinical spectrum

The clinical spectrum in women ranges from asymptomatic carrier state in approximately 50 percent infected women while symptomatic patients may complain of vaginal discharge in 50-75 percent, with pruritus in 25-50 percent and dysuria in 30-50 pertcent and dyspareunia in 10-50 percent (Heine and McGregor, 1993; Valadkhani et al, 2003; Kaul et al, 2004). Infection during pregnancy may be associated with premature rupture of membranes, preterm delivery, low birth weight babies and also respiratory infection in infants. The disease may be associated with endometritis and cervical erosion with predisposition to malignant transformation. There are contrasting reports of association of cervical carcinoma and presence of *T.vaginalis*. Kharsany et al (1993) in the study conducted in Durban have found no association while reports from other areas (Boyle et al, 1989; Zhang & Begg, 1994; Zhang et al, 1995; Vikki et al, 2000) indicated significant association. *T.vaginalis* could not be isolated in any of the 100 cervical cancer patients in our earlier study (Kaur et al, 2008).

In infected females, perspeculum examination usually reveals copious loose discharge that pools in the posterior vaginal formix and bubbles may be seen in about 10 to 33 percent. The vaginal epithelium is inflamed in 15 percent with small punctate haemnorrhagic spots on vaginal and cervical mucosa in 2 percent (Rein, 1990).

In men, the clinical spectrum varies from asymptomatic carrier state to acute state characterized by profuse purulent urethritis and mild symptomatic infection including scanty clear to mucopurulent discharge, dysuria and mild pruritus or burning sensation immediately after sexual intercourse (Krieger, 1990; Schwebke and Burgess, 2004).

5. Laboratory diagnosis

Laboratory diagnosis is established by examination of wet mount preparation of vaginal discharge and / or urine specimen. This method is least cost-effective but has low sensitivity (38% - 82%) (Petrin et al, 1998). Best results are obtained, if wet smear preparation is examined in bed side laboratory, within half an hour, as parasites thereafter loose motility. Low sensitivity is attributed to the loss of motility after the parasite has been removed from body temperature. The broth culture method is the gold standard, has been found most sensitive for routine diagnosis and requires 300 to 500 trichomonads/ml of inoculum (Sharma et al, 1991a; Petrin et al, 1998). "In Pouch™ culture has been found with added advantages and can be conveniently transported from the site of collection to the laboratory (Sood and Kapil,2008).The main limitation for its routine use is the high cost involved. Cell culture technique is reported superior to broth culture, since it is able to detect *T.vaginalis* at a concentration as low as 3 parasites/ml (Garber et al, 1987). However, it is not routinely performed because it is expensive and not convenient for rapid diagnosis (Petrin et al, 1998). Although, antigen in vaginal secretions and specific circulating and local antibody

response have been demonstrated in infected subjects (Ackers et al, 1975; Alderete, 1984; Sharma et al, 1991), yet it has limited value in diagnosis due to lower sensitivity than culture technique. Anti-trichomonad, IgA antibodies decreased significantly post treatment and appear to be specific to the presence of parasite in the urogenital tract (Sharma et al, 1991). Review of reports indicates that DNA detection in clinical samples by PCR yielded higher sensitivity than wet mount and culture (Schwebke and Burgess, 2004). It requires expertise and availability. Further research is required to develop cheap, point of care diagnostic tests which will allow a greater understanding of *T.vaginalis* epidemiology (Johnston and Mabey, 2008).

6. Strain variation

The reasons for different clinical spectrum ranging from asymptomatic to acute and chronic symptomatic state and complications are still unclear, although, data supports that in addition to host factors, differences in parasite intrinsic virulence play role in such phenomenon. The differences in virulence in different strains by In-Vivo (Honigberg et al, 1966) and In-Vitro (Honigberg, 1990) assays have been reported. The In-Vivo virulence assays in experimental mouse model have shown that intraperitoneal infection of trichomonads produces visceral (pancreatic and hepatic) necrosis and extent of necrosis is proportional to the level of virulence of the inoculated strain, which can result in death. The effect of two strains, one highly virulent and other very mild strain on chick embryo fibroblast cultures was quite different. The pathogenic changes caused by the virulent parasites appeared much sooner and were far more extensive than those observed with mild-strain. A correlation between the length of time *In Vitro* of *T.vaginalis* strains and the attenuation of their virulence for cell cultures was observed. Although, the extrapolation of data from In Vitro experiments and In-Vivo animal models to human situation needs to be interpreted with caution, few recent molecular studies support these earlier observations. Antigenic heterogenicity (Krieger et al, 1985a) has differentiated *T.vaginalis* isolates and has been correlated with pathogenicity (Mason and Gwanzura, 1988). Isoenzyme analysis (Soliman et al, 1982;Vohra et al, 1991) and restriction digestion patterns (Sapru et al, 1994) could not differentiate clinical isolates from symptomatic and asymptomatic women. Phenotypic (Alderete et al, 1986, 1987) and genotypic variation by RAPD analysis (Vanacova et al, 1997) have demonstrated the presence of different strains, We have reported that dendogram based on RAPD data obtained from fresh 30 (15 each from symptomatic and asymptomatic women) *T.vaginalis* isolates showed upper branch representing 7 out of 15 isolates, from symptomatic women and other eight isolates constituted another cluster, whereas all the isolates from 15 asymptomatic women were represented in lower branch of the tree. The study indicated that the RAPD traits can be of utmost importance in differentiating isolates from symptomatic and asymptomatic women (Kaul et al, 2004).

Further, the same 30 isolates were maintained in culture for long term (6 months to 2 yrs) and were subjected to RAPD analysis. Following long term cultivation changes in RAPD patterns were observed. The phylogenetic tree of same 30 long term (up to 2 years) culture maintained isolates divided the isolates into two distinct branches. The upper half of tree represented all 15 isolates from symptomatic women, while the lower half of the tree represented all 15 isolates from asymptomatic women (Fig. 1.) (Kaul 2004a).
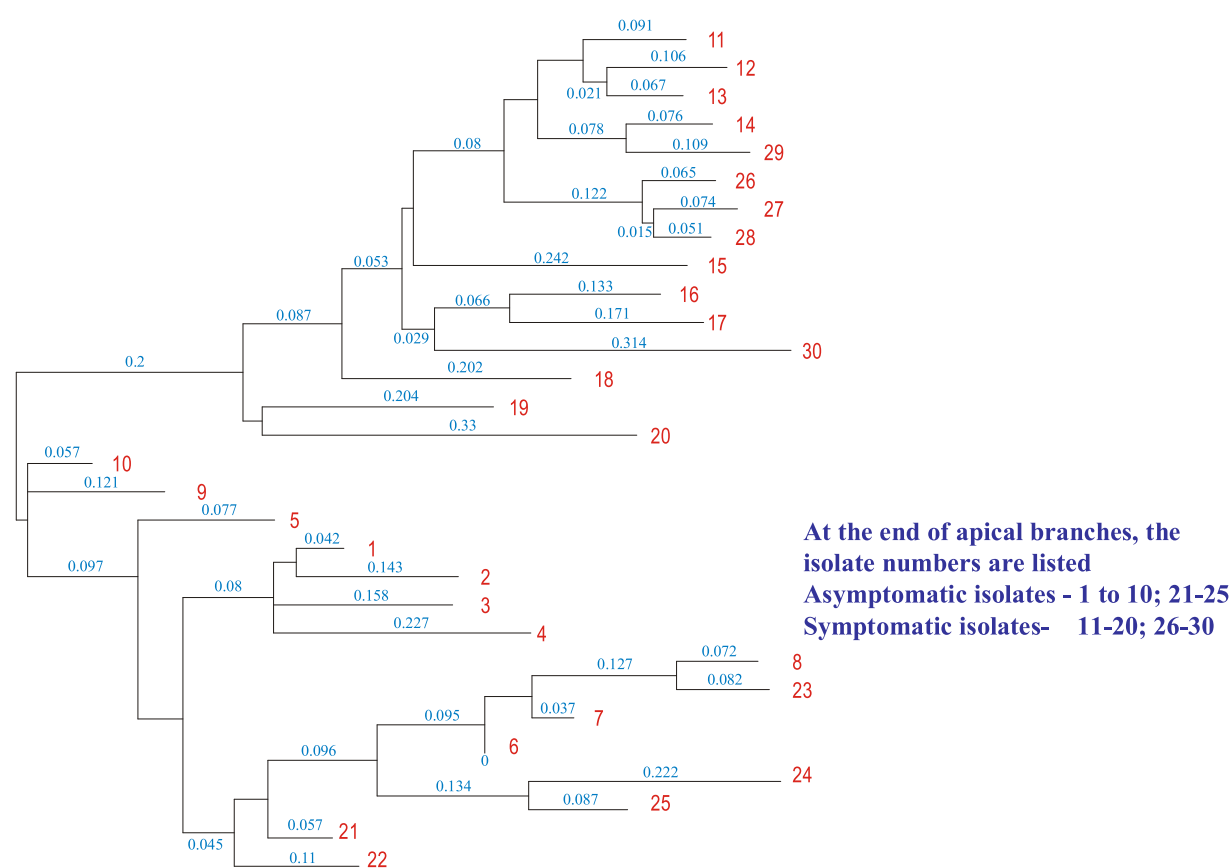
Fig. 1. Dendrogram constructed by RAPDistance programme for 30 long term culture isolates of *T.vaginalis*. The integers represent branch lengths, which reflect the genetic distance between the isolates.

7. Trichomonas Vaginalis Virus (TVV)

Double stranded RNA virus has been identified in *T.vaginalis* (Wang and Wang, 1985) and was found in about 50% clinical isolates. It was thought that most probably this virus is transferred from parent to progeny. Presence of TVV correlated with 270 kDa surface protein (P270) positive isolates and on long term culture loss of TVV was associated with absence of P270 (Wang et al, 1987). The loss of viral dsRNA and concomitant absence of the surface disposition of specific immunogens strengthens the likelihood of involvement of virus in the sequestration of immunogens into trichomonal membranes. All virus harbouring trichomonads contained at least three dsRNA segments (5.5, 4.8 to 4.3 kb) and the study suggested segmented nature of the TVV (Khoshnan and Alderete, 1993). Different studies from different geographical locations indicated different sizes of the segments of TVV (Tai et al, 1993; Shaio et al, 1993). It is suggested that *T.vaginalis* may be reservoir for several different dsRNA viruses simultaneously (Benchmol et al, 2002). Older women patients, infected with *T.vaginalis* were found with virus positive isolates as compared to younger patients and men. We analysed presence of dsRNA virus in *T.vaginalis* same 30 Indian isolates (15 each from symptomatic and asymptomatic women) in whom RAPD analysis was carried earlier (Kaul et al, 2004) and presence of three bands (5.5, 2.5 and 1.5 kb) were observed in all the 30 fresh isolates, while following long term cultivation (up to 2

years) TVV was observed only in 7 isolates, (3 from symptomatic and 4 asymptomatic women isolates) (Malla et al, 2011). The study suggests that genetic changes might be taking place during *in vitro* cultivation of parasites and this might be related to phenotypic variation and loss of dsRNA virus. No significant association was found between isolates from symptomatic and asymptomatic women and presence of TVV (P >0.05), which is in agreement with an earlier report (Wendel et. al, 2002). The same fresh isolates were also subjected to *in vitro* metronidazole drug resistance assay. The study suggests that the presence of TVV alone may not be a virulence marker and loss of TVV on long term cultivation of *T.vaginalis* isolates appear to be related to drug resistance. Correlation of absence of TVV and drug resistance (p<0.05) in our study supports the earlier studies (Wang and Wang, 1985; Snipes et al, 2000). However, on retrospective analysis of presence of TVV and drug sensitivity with RAPD analysis of isolates, no significant correlation was found, which is in agreement to the earlier report (Stiles et al, 2000), whereby no significant correlation between metronidazole resistance and RFLP subtypes was reported. In contrast, Vanacova et al. (1997) have reported that all the 5 isolates refractory to metronidazole constituted single branch of tree by RAPD analysis. Out of these 5 isolates, 4 were metronidazole resistant while fifth was susceptible to metronidazole by *in vitro* assay. Metronidazole resistance existing in a closely related group of isolates indicated that only one or few mutations have occurred which resulted in resistance. It is suggested that some genealogical line of *T.vaginalis* may be genetically predisposed for the development of metronidazole resistance and same may be true for the capability of strains to cause disease in patients. The contrasting correlations in different reports from different geographical locations may be due to phenotypic and genotypic variations.

8. Treatment and drug resistance

Nitromidazole derivatives are drugs of choice for the treatment of trichomoniasis. The standard treatment is metronidazole 250 mg thrice a day given orally for 7 days or in a single 2 gm dose. The infected patient and sexual partner, both should be treated irrespective of symptomatology, to prevent reinfection. The drug does cross placental barrier, therefore is not prescribed during first trimester of pregnancy (Lossick and Kent, 1991).

Drug resistant cases have been reported (Sobel, 1999). It can be due to several mutational changes and can affect both aerobic and anaerobic mechanisms of metabolism (Upcroft and Upcroft, 2001). In the parasites resistant by aerobic mechanisms, the transcription of ferridoxin (Fd) gene is reduced, thereby decreasing the ability of cell to activate the drug. However, gene knock out mice were not found resistant to the drug under aerobic or anaerobic conditions and it is postulated that Fd gene product eliminated in knock out cells is neither necessary for hydrogen production nor metronidazole production (Land et al, 2004). Metronidazole has to be first reduced by certain mechanism(s) in *T.vaginalis* at the relatively low redox potential, before it exerts the antitrichomonad action (Muller et al, 1983). It is suggested that reductase(s) responsible for reducing metronidazole or its precursor, could be transitional product of dsRNA in *T.vaginalis.* The studies suggest that it might be possible to identify a marker for resistance that could lead to improved treatment strategies.

Many alternative drugs and treatments have been tested in vivo in cases of refractory trichomoniasis, as well as in vitro with some successes including the broad spectrum anti-parasitic drug nitazoxanide. Drug resistance incidence of *T.vaginalis* appears to be on the increase and improved surveillance of treatment failures is urged (Dunne et al, 2003).

9. Prevention and control

The main focus to prevent and control the disease should be on the identification of infected women and treatment of both the sexual partners. High rates of asymptomatic infection in male partners of infected females and subsequent re-infection have significant implications for control programmes. HIV-infected women are at increased risk of trichomoniasis and local HIV prevention strategies should target such women for intervention efforts. In addition, the effect of treatment on outcome of pregnancy and HIV acquisition requires further study. This will, in turn, facilitate operational studies evaluating optimal control strategies and their impact on the complications of *T.vaginalis* (Johnston and Mabey, 2008).

Vaccine

The Solco Trichovac Vaccine prepared from inactive Lactobacilli was thought to induce protection, however, further reports indicated its inconclusive efficacy. Experimental studies revealed that the mice which were inoculated whole, live trichomonads with adjuvant/s subcutaneously and then infected intravaginally, had significantly less intravaginal infection than control groups (Abraham et al, 1996). High levels of proteolytic activity found in T.vaginalis and involvement of some of these proteases in the colonization of the host suggest that proteases may have protective role. Intranasal immunization of T.vaginalis 62 kDa protease in a murine model induced significant IgG and IgA response against this antigen in the vaginal washes and suggests that the 62kDa protease is a potential vaccine candidate against trichomoniasis (Hernandez et al, 2006). The reports provides hope for the goal of vaccine development in future.

10. References

Abraham, M.C., Desjardins, M., Fillon, L.G. And Garber, G.E. (1996). Inducible immunity to *Trichomonas vaginalis* in a mouse model of vaginal infection. Infect Immun. 64, 3571-3575.

Ackers, J.P., Lumsden, W.H.R., Catterall, R.D., Coyle, R. (1975). Antitrichomonal antibodies in the vaginal secretions of women infected with *T.vaginalis*. Br. J. Vener. Dis. 51, 319-23.

Alderete, J.F. (1984). Enzyme linked immunosorbent assay for detecting antibody to *T.vaginalis*. Br. J. Vener. Dis. 60, 164-70.

Alderete, J.F. and Garza, G.E.(1984). Soluble *Trichomonas vaginalis* antigens in cell-free culture supernatants. Mol. Biochem. Parasitol. 13, 147-158.

Alderete, J.F., Kasmala, L., Metcalfe, E., Garza, G.E. (1986). Phenotypic variation and diversity among *Trichomonas vaginalis* isolates and correlation of phenotype with trichomonal virulence determinants. Infect. Immun. 53, 285-293.

Alderete, J.F., Demes, P., Gombosova, A., Valent, M., Yanoska, A., Fabusova, H., Kasmala, L., Garza, G.E., Metcalfe, E.C. (1987). Phenotypes and protein epitope phenotypic variation among fresh isolates of *Trichomonas vaginalis*. Infect. Immun. 55(5), 1037-1041.

Arroya R., Gonzalez-Robles, A., Martinex Palomo, A., Alderete, J.F. (1993). Signaling of *Trichomonas vaginalis* for amoeboid transformation and adhesion synthesis followed cyto-adherence. Mol. Microbiol. 7,299-309.

Benchmol, M., Chang, T.H., Alderete, J.F. (2002). *Trichomonas vaginalis* observation of coexistence of multiple viruses in the same isolate. FEMS Microbiol. Let. 215,197-201.

Bersoff-Matcha, S.J., Horgan, M.M., Fraser, V.J., Mundy, L.M., Stoner, B.P. (1998). Sexually transmitted disease acquisition among women infected with human immunodeficiency virus type 1. Journal of Infectious Diseases,178, 174-7.

Boyle, C.A., Lowell, D.M., Kelsey, J.L., Livolsi, V.A., Boyle, K.E. (1989). Cervical intraepithelial neoplasia among women with *Papillomavirus* infection compared to women with *T.vaginalis* infection. Cancer. 64, 168-72.

Bozner, P. (1997). Immunological detection and subcellular localization of Hsp70 and Hsp60 homologs in *Trichomonas vaginali.* J. Parasitol. 83, 224-229.

Carlton, J.M., Hirt, R.P., Silva, J.C., Delcher, A.L., Schatz, M., Zhao, Q., Wortman, J.R., et al. (2007). Draft genome sequence of the sexually transmitted pathogen *Trichomonas vaginalis.* Sci. 315, 207-211.

Chakraborty, T., Mulla, S.A., Kosambiya, J.K., Desai, V.K. (2005). Prevalence of *T.vaginalis* infection in and around Surat. Ind. J. Pathol. Microbiol. 48, 542-45.

Costa e Silva Filko, F., Souza W de and Lopex, J.D. (1988). Presence of Laminibinding proteins in Trichomonads and their role in adhesion. Proc. Natl. Acad. Sci.85, 8042-8046.

Chang, J.H., Kim, S.K., Choi, I.H., Leed, S.K., Morio (2006). Apoptosis of macrophages induced by *Trichomonas vaginalis* through the phosphorylation of p38 mitogen activate protein kinase that locates at downstream of mitochondria-dependent caspase activation. Int. J. Biochem. Cell Biol. 38, 638-647.

Davis, S. and Lushbaugh, W.B. (1993). Oxidative stress and *Trichomonas vaginalis*: The effect of hydrogen peroxide in vitro. Am. J. Trop. Med. Hyg. 48(4), 480-7.

Dawn, G., Sharma, M., Kumar, B., Malla, N. (1995). Prevalence of microorganisms in patients with non-gonococcal urethritis from North India. Ind. J. Sex. Trans. Dis. 16, 9-14.

Demes, P., Gombosova, A., Valent, M., Fabusova, H., Janoska, A. (1988). Fewer *Trichomonas vaginalis* organisms in vaginas of infected women during menstruation. Gen. Med. 64, 22-24.

Divekar, A.A., Gotate, A.S., Shivkar, L.K., Gotate, S., Badhwar, V.R. (2000). Disease prevalence in women attending STD clinic in Mumbai, India. Int. J. STD & AIDS 11, 45-48.

Fiori, P.L., Paola, R., Maria, F.A., 1999. The flagellated parasite *Trichomonas vaginalis*: new insights into cytopathogenicity mechanisms. Micro. Inf. 2,149-156.

Frankel, T.L., Monif, G.R. (2000). *T.vaginalis* and bacterial vaginosis: coexistence in vaginal wet mount preparations from pregnant women. J. Rep. Med. 45, 131-4.

Garber, G.E., Sibou, L., Ma, R., Proctor, E.M., Shaw, C.E., Bowis, W.R. (1987). Cell culture compared with broth for detection of *Trichomonas vaginalis*. J. Clin. Microbiol. 25,1275-1279.

Ghys, P.D., Diallo, M.O., Ettiegne-Traore, V., Yeboue, K.M., Gnaore, E., Lorougnon, F. et al. (1995). Genital ulcers associated with HIV related immunosupression in female sex workers in Abidjan, Ivary Coast. J. Infect. Dis. 172, 1371-4.

Gosskurth, H., Mosha, F., Todd, J. (1995). Impact of improved treatment of STDs on HIV infection in rural Tanzania: demised controlled trail. Lancet 346, 530-6.

Gonzalez-Robles, A., Lazaro-Haller, A., Espinosa-Castellano, M., Anaya-velazques, F., Martinez-alomo, A. (1995). *Trichomonas vaginalis*: Ultrastructural basis of the cytopathic effect. J. Euk. Microbil. 42, 641-51.

Heine, P. and McGregor, J.A. (1993). *Trichomonas vaginalis*: a reemerging pathogen. Clin. Obst. Gyncol. 36, 137-144.

Hernandez, H., Figueredo, M., Garrido, N., Sariego, I., Sarracent, J. (2006). Protective effect of a protease against *Trichomonas vaginalis* infection of the murine gential tract. Biotecnologia Aplicada, 23(3). 248-250.

Honigberg, B.M. and King, V.M. (1964). Structure of *Trichomonas vaginalis* (Donne). J. Parasitol. 50, 345-364.

Honigberg, B.M., Livingston, M.C., Frost, J.K. (1966). Pathogenecity of fresh isolates of *Trichomonas vaginalis*: "The moust assay" versus clinical and pathologic findings. Acta Cytol. 10, 353-361.

Honigberg, B.M. (1990). Host cell trichomonad interactions and virulence assays using in vitro systems. In: Trichomonads parasitic in humans. Springer-Verlag, New York, pp 155-212.

Johnston, V.J. and David, CM. (2008). Global epidemiology and control of *Trichomonas vaginalis.* Current Opinion in Infectious Diseases, 21, 56-64.

Kaul, P., Gupta, I., Sehgal, R., Malla, N. (2004). *Trichomonas vaginalis*: random amplified polymorphic DNA analysis of isolates from symptomatic and asymptomatic women in India. Parasitol. Int. 53,255-262.

Kaul, P. (2004a). Molecular and biochemical characterization of *Trichomonas vaginalis* isolated from symptomatic and asymptomatic women. Ph.D. Theses submitted to Postgraduate Institute of Medical Education & Research, Chandigarh, India.

Kaur, S., Khurana, S., Bagga, R., Wanchu, A., Malla, N. (2008). Trichomoniasis among women in North India: A hospital based study. Ind.Jl. Of Sexually Transm. Dis., 29, 76-81.

Kaur, S., Khurana, S., Bagga, R., Wanchu, A. and Malla, N. (2008). Kinetics of immunoglobulins G, M, A and IgG subclass responses in human intravaginal trichomoniasis. Parasit. Res., 103 (2), 305-312.

Kharsany, A.B.M., Hoosen, A.A., Moodley, J., Bagaratee, J., Gouws, E. (1993). The association between sexually transmitted pathogens and cervical intra epithelial neoplasia in a developing community. Gen. Med. 69, 357-360.

Khoshnan, A. and Alderete, J.F. (1993). Multiple double stranded RNA segments are associated with virus particles infecting *Trichomonas vaginalis*. J. Viro. 67(12), 6950-6955.

Klinger, E.V., Kapiquasn, Sam, N.E., Aboud, S., Chen, C.Y., Ballard, R.C. et al. (2006). A community based study of risk factors of *T.vaginalis* infection among women and their male partners in Moshi Urban Districts, North Tanzania. STD 33, 712-18.

Krieger, J.N., Ravdin, J.I., Rein, M.F. (1985). Contact-dependent cytopathogenic mechanisms of *Trichomonas vaginalis*. 50, 778-786.

Krieger, J.N., Holmes, K.K., Spence, M.R., Rein, M.F., McCormack, W.M. and Tam, M.R. (1985a). Geographic variation among isolates of *Trichomonas vaginalis*. Demonstration of antigenic heterogeneity by using monoclonal antibodies and the indirect immunofluorescence techniques. J. Inf. Dis. 152, 979-984.

Krieger, J.N. (1990). Epidemiology and clinical manifestations of urogenital trichomoniasis in men. In: BM Honigberg Ed, *Trichomonads parasitic in humans*, Springer-Verlag, New York, N.Y.

Land, K.M., Delgadillo-correa, M.G., Tachezy, J., Vanacova, S., Hsieh, C.L., Sutak, R., Johnson, P.J. (2004). Targeted gene replacement of a ferredoxin gene in *Trichomonas vaginalis* does not lead to metronidazole resistance. Mol. Microbiol. 51(1), 115-122.

Langly, J.G., Goldsmith, J.M., Davies, N. (1987). Venereal trichomoniasis: Role of men. Genito. Med.63, 264-267.

Lazar, A. (1970). *Trichomonas vaginalis* infection: Incidence with use of various contraceptive methods. J. Med. Soc. 67,225-227.

Linstead, D.J. And Bradley, S. (1988). The purification and properties of two soluble reduced nicotinamide: acceptor oxidoreductases from *Trichomonas vaginalis.* Mol. Biotech. Parasit. 27, 125-133.

Lossick, J.G. and Kent, H.L. (1991). Trichomoniasis: trends in diagnosis and management. Am. J. Obst. Gynae. 165, 1217-1222.

Malla, N., Wattal, C., Khan, I.A., Kaul, R., Raina, V. (1989). Study of trichomoniasis in Kashmir (North India). Ind. J. Med. Microbiol. 7,121-126.

Malla, N., Valadkhani, A., Harjai, K., Sharma, S., Gupta, I. (2004). Reactive nitrogen intermediates in experimental trichomoniasis induced with isolates from symptomatic and asymptomatic women. Parasitol. Res. 94, 101-105.

Malla, N., Yadav, M., Gupta, I. (2007). Kinetics of serum and local cytokine profile in experimental intravaginal trichomoniasis induced with *Trichomonas vaginalis* isolated from symptomatic and asymptomatic women. Parasit. Immunol. 29, 101-105.

Malla, N., Kaul, P., Sehgal, R and Gupta, I. (2011). The presence of DsRNA virus in *Trichomonas vaginalis* isolates from symptomatic and asymptomatic Indian women and its correlation with *in vitro* metronidazole sensitivity. Ind. Jl. Of Med. Microbiology, 29(2), 152-157.

Mason, P.R. and Gwanzura, L. (1988). Mouse spleen cell responses to trichomonal antigens in experimental *Trichomonas vaginalis* infection. J. Parasitol. 74(1), 93-97.

McGrory, T. and Garber, G.E. (1992). Mouse intravaginal infection with *Trichomonas vaginalis* and role of *Lactobacillus acidophilus* in sustaining infection. Infect. Immun. 60, 2375-2379.

Mc Laren, L.C., Davis, L.E., Healy, G.R., James, C.G. (1983). Isolation of *Trichomonas vaginalis* from the respiratory tract of infants with respiratory disease. Paediatr. 71, 888-90.

McLellan, R., Spence, M.R., Brockman, M., Raffel, L., Smith, J.L. (1982). The clinical diagnosis of trichomoniasis. Obst. Gynae. 60, 30-34.

Menduza-Lopez, M.R., Garcia, C.B., Fattel-Facenda, L.V., Avila-Gonzales, L., Ruiz-Tachiquin, M., Oriego Lopez, J., Aproyo, R. (2000). CP30-a cysteinase involved in *Trichomonas vaginalis* cytoadherence. Infect. Immun. 4907-12.

Minkoff, H.L., Eisenberger-Matityahu, D., Feldman, J., Burk, R., Clarke, L. (1999). Prevalence and incidence of gynaecological disorders among women infected with HIV. Am. J. Obst. Gynae. 180, 824-36.

Muller, M. (1983). *Trichomonas vaginalis* and other sexually transmitted protozoan infections. In: International perspectives of neglected STDs. Holmes, K.K. And Mardh, P. Eds. Hemisphere Publishing Corporation, New York, pp 113-124.

Paintlia, M.K., Kaur, S., Gupta, I., Ganguly, N.K., Mahajan, R.C., Malla, N. (2002). Specific IgA response, T-cell subtype and cytokine profile in experimental intravaginal trichomoniasis. Parasit. Res. 88, 338-343.

Peterson, K.M. and Alderete, J.F., 1982. Host plasma proteins on the surface of pathogenic *Trichomonas vaginalis*. Infect. Immun. 37, 755-762.

Petrin, D., Delgaty, K., Bhatt, R., Garber, G. (1998). Clinical and Microbiological aspects of *Trichomonas vaginalis*. Clin. Microbiol. Rev. 11(2), 300-317.

Pindak, F.F., Mora de Pindak, M., W.A Gardner, Jr. (1993). Contact- independent cytotoxity of *Trichomonas vaginalis*. Genito. Med. 69, 35-40.

Provenzano, D. and Alderete, J.F. (1995). Analysis of human immunoglobulin degrading cysteine proteinases of *Trichomonas vaginalis*. Infect. Immun. 63, 3388-3395.

Rein, M.F. (1990). Clinical manifestations of urogenital trichomoniasis in women. In: Trichomonads parasitic in humans. Honigberg BM Ed. Springer-Verlag, New York, pp225-234.

Rein, M.F. and Muller, M. (1990). *Trichomonas vaginalis* and trichomoniasis. In: Sexually transmitted diseases. 2nd ed. Holmes, K.K., Mardh, P.A., Sparling, P.F., Wiesner, P.J., Cates, W. Jr., Lemon, S.M. and Stamm, W.E. Eds. McGraw-Hill, New York.

Ryu, J.S., Choi, H.K., Min, D.Y., Ha, S.E., Ahn, M.H. (2001). Effect of iron on the virulence of Trichomonas vaginalis. J. Parasit. 87(2), 457-60.

Sapru, P., Mohan, K., Gupta, I., Ganguly, N.K., Mahajan, R.C., Malla, N. (1994). DNA banding patterns of *Trichomonas vaginalis* strains isolated from symptomatic and asymptomatic subjects. J. Protozo. Res. 4, 40-47.

Shaio, M.F., Chang, F.Y., Hou, S.C., Lee, C.S., Lin, P.R. (1991). The role of immunoglobulin and complement in enhancing the respiratory burst of neutrophils against *Trichomonas vaginalis*. Parasit. Immun. 13, 241-50.

Shaio, M.F., Lin, P.R., Lee, C.S. (1993). Killing of *Trichomonas vaginalis* by complement mediated lysis is not associated with the presence of *Trichomonas vaginalis* virus. Intern. J. Parasitol. 23, 675-680.

Sharma, P., Malla, N., Gupta, I., Ganguly, N.K., Mahajan, R.C. (1988). Prevalence of trichomoniasis in symptomatic and asymptomatic subjects using different contraceptive devices. Ind. J. Med. Microbiol. 6,315-322.

Sharma, P., Malla, N., Ganguly, N.K., Mahajan, R.C. (1991). Anti-trichomonad IgA antibodies in Trichomoniasis before and after treatment. Folia Microbiol. 36(3),302-304.

Sharma, P., Malla, N., Gupta, I., Ganguly, N.K., Mahajan, R.C. (1991a). A comparison of wet mount, culture and enzyme linked immunosorbent assay for the diagnosis of Trichomoniasis in women. Trop. Geog. Med. 43, 257-260.

Schwebke, J.R. and Burgess, D. (2004). Trichomoniasis. Clin. Microbiol. Rev. Oct, 794-803.

Smith, A., Johnson, P. (2011). Gene expression in the unicellular eukaryote *Trichomonas vaginalis.* Research in Microbiology, 162, 646-654.

Sobel, J.D. (1999). Metronidazole resistance vaginal trichomoniasis – an emerging problem. N. Eng. J. Med. July, 292.

Sobel, J.D. (2005). What's new in bacterial vaginosis and trichomoniasis? Infect. Dis. Clin. N. Am. 19, 387-406.

Soliman, M.A., Ackers, J.P., Catterall, R.D. (1982). Isoenzyme characterization of *Trichomonas vaginalis.* Bri. J. Venerol. Dis. 58,250-253.

Song, Hyun-Ouk, Young-Su Lim, Sun-Joo Moon, Myoung-Hee Ahn and Jae-Sook Ryu. (2010). Delayed human neutrophil apoptosis by *Trichomonas vaginalis* lysate. Korean Parasitol., 48 (1), 1-7.

Sood, S., Kapil, A. (2008). An update on *Trichomonas vaginalis.* Indian J. Sex Transm. Dis., 29(1), 7-14.

Sorvillo, F., Kovacs, A., Kerndet, P., Stek, A., Muderspach, L., Sanchez-Keeland, L. (1998). Risk factors for trichomoniasis among women with human immunodeficiency virus (HIV) infection at a public clinic in Los Angeles county, California implications for HIV prevention. Am. J. Trop. Med. Hyg. 58(4), 495-500.

Snipes, L.J., Gamard, P.M., Narcisi, E.M., Beard, C.B., Lehmann, T., Secor, W.E.(2000). Molecular epidemiology of Metronidazole resistance in a population of *Trichomonas vaginalis* clinical isolates. J. Clin. Microbiol. 38, 3004-3009.

Stiles, J.K., Shah, P.H., Xue, L., Meake, J.c., Lushbaugh, W.B., Cleary, J.D., Finely, W. (2000). Molecular typing of *Trichomonas vaginalis* isolates by HSP70 and restriction fragment length polymorphism. Am. J. Trop. Med. Hyg. 62(4), 441-445.

Susan, C.U., Hyejin, K., Denise, J.J., Joseph, W.H., Paula, S., Jean, A. et al. (2002). Prevalence, incidence and persistence or recurrence of trichomoniasis among Human Immunodeficiency Virus (HIV) - positive women and among HIV negative women at high risk for HIV infection. Clin. Infect. Dis. 34, 1406-11.

Sutton, M.Y., Stenberg, M., Nsuami, M., Behets, F., Nelson, A.M., St Louis, M.E. (1999). Trichomoniasis in pregnant HIV infected and HIV uninfected Congolese women: prevalence, risk factors and association with low birth weight. Am. J. Obstet. Gynae. 181, 656-62.

Tai, J.H., Su, H.M., Tsai, J., Shaio, M.F., Wang, C.C. (1993). The divergence of *Trichomonas vaginalis* virus RNAs among various isolates of *Trichomonas vaginalis*. Exp. Parasitol. 76, 278-286.

Tapsall, J.W., Puglisi, J., Smith, D.D. (1979). *Trichomonas vaginalis* infections in Sydney: Laboratory diagnosis and prevalence. Med. J. Aus. 1, 193-4.

Ter Muelen, J., Mgaya, H.N., Chang-Claude, J., Luande, J., Mtiro, H., Mhina, M. et al., 1992. Risk factors for HIV infection in gynaecological inpatients in Dar Es Salaam, Tanzania, 1988-90. East Afr. Med. J. 69, 688-92.

Upcroft, J.A. and Upcroft, P. (2001). Drug susceptibility testing of anaerobic protozoa. Antimicrob Ag. Chemother. June 45, 1810-1814.

Valadkhani, Z., Sharma, S., Harjai, K., Gupta, I., Malla, N. (2003). In vitro comparative kinetics of adhesive and haemolytic potential of *T.vaginalis* isolates from symptomatic and asymptomatic females. Ind. J. Pathol. Microbiol. 46(4), 693-699.

Valadkhani, Z., Sharma, S., Harjai, K., Gupta, I., Malla, N. (2004). Evaluation of *Trichomonas vaginalis* isolates from symptomatic and asymptomatic patients in mouse model. Ira. J. Pub. Hlth. 33,60-66.

Valadkhani, Z., Sharma, S., Harjai, K., Gupta, I., Malla, N. (2006). Superoxide radical formation in isolated PMN from experimental vaginal trichomoniasis. Ira. J. Pub. Hlth. 35,76-82.

Vanacova, S., Tachezy, J., Kulda, J., Flegr, J. (1997). Characterization of trichomonad species and strains by PCR Fingerprinting. J. Euk. Microbiol. 44(6), 545-52.

Vargas – Villarreal, J., Mata-Cardenas, B.D., Gonzalez-Salazar, F., Lozano-Garz, H.G., Cortes-Gutierrez, E.I., Palacios-Corona, R., Martinez-Rodriguez, H.G., Ramirez-Bun, E., Said Fernandez, S. (2003). *Trichomonas vaginalis*: identification of a phospholipase A dependent haemolytic activity in a vesicular subcellular fraction. J. Parasitol. 89(1), 105-112.

Vikki, M., Pukkala, E., Nieminen, P., Hakama, M. (2000). Gynaecological infections as risk determinants of subsequent cervical neoplasia. Acta Oncol. 39, 71-5.

Vishwanath, S., Talwar, V., Prasad, R., Coyaji, K., Elias, C.J., De Zoysa, I. (2000). Syndromic management of vaginal discharge among women in reproductive health clinic in India. Sex. Trans. Infect. 76, 303-306.

Vohra, H., Sharma, P., Sofi, B.A., Gupta, I., Ganguly, N.K., Mahajan, R.C., Malla, N. (1991). Correlation of zymodeme patterns, virulence and drug sensitivity of *Trichomonas vaginalis* isolates from women. Ind. J. Med. Res. 93, 37-39.

Wang, A.L. and Wang, C.C. (1985). A linear double stranded RNA in *Trichomonas vaginalis*. J. Biol. Chem. 260, 3697-702.

Wang, A., Wang, C.C. and Alderete, J.F. (1987). *Trichomonas vaginalis* phenotypic variation occurs only among trichomonads with the double stranded RNA virus. J. Exp. Med. 166, 142–150.

Wang, C., McClelland, S., Reilly, M., Overbaugh, J., Emery, S.L., Mandaliya, K. et al. (2001). The effect of treatment of vaginal infections on shedding of HIV-type 1. J. Infect. Dis. 183, 1017-22.

Wendel, K.A., Rampalo, A.M., Erbelding, E.J., Chang, T.H., Alderete, J.F. (2002). Double stranded RNA viral infection of *T.vaginalis* infected patients attending a STD clinic. J. Infect. Dis. 186, 558-61.

Yadav, M., Gupta, I., Malla, N. (2005). Kinetics of immunoglobulin G, M, A and IgG subclass responses in experimental intravaginal trichomoniasis: prominence of IgG_1 response. Parasit. Immunol. 27,461-467.

Yadav, M., Dubey, M.L., Gupta, I., Malla, N. (2006). Nitric oxide radicals in leucocytes and vaginal washes of *Trichomonas vaginalis* – infected symptomatic and asymptomatic women. Parasitol. 132,339-43.

Yadav, M., Dubey, M.L., Gupta, I., Bhatti, G., Malla, N. (2007). Cysteine proteinase 30 in clinical isolates of *T.vaginalis* from symptomatic and asymptomatic infected women. Exp. Parasitol. 116(4), 399-406.

Yadav, M., Dubey, M.L., Gupta, I., Malla, N. (2007a). Cysteine proteinase 30 (CP30) and antibody response to CP30 in serum and vaginal washes of symptomatic and asymptomatic *Trichomonas vaginalis* infected women. Parasit. Immunol. 29, 359-365.

Zhang, Z.F. and Begg, C.B. (1994). Is *T.vaginalis* a cause of cervical neoplasia? Results from combined analysis of 24 studies. Internat. J. Epidemiol. 23, 682-90.

Zhang, Z.F., Graham, S., Yu, S.Z., Marshall, J., Zielezny, M., Chen, Y.X. et al. (1995). *Trichomonas vaginalis* and cervical cancer. A prospective study in China. Ann. Epidemiol. 5, 325-32.

Sexually Transmitted Infections

Edited by Prof. Nancy Malla

ISBN 978-953-51-0258-8

Hard cover, 244 pages

Publisher InTech

Published online 21, March, 2012

Published in print edition March, 2012

Sexually transmitted infections (STIs) are infections that are spread primarily through person to person sexual contact. There are more than 30 different sexually transmissible bacteria, viruses and parasites. STIs lead to high morbidity and complications. This book entitled as Sexually Transmitted Infections is not a text book but provides useful information for general reference work for physicians, researchers and students interested in the subject. Each chapter is abundant in tips useful to general readers as well. It also includes the Introductory chapter providing an overview with special emphasis on syndromic approach to the management of STIs in clinical setting.

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Nancy Malla (2012). Human Trichomoniasis due to Trichomonas vaginalis - Current Perspectives, Sexually Transmitted Infections, Prof. Nancy Malla (Ed.), ISBN: 978-953-51-0258-8, InTech, Available from: http://www.intechopen.com/books/sexually-transmitted-infections/human-trichomoniasis-due-to-trichomonas-vaginalis-current-perspectives

INTECH
open science | open minds