Trichomonas vaginalis: an irritating protozoan or an important viral co-factor.

Pamela Greenwell
Sanjiv Rughooputh
School of Biosciences

This is an electronic version of an article published in The Biomedical Scientist, 48(1), pp. 40-41, January 2004.

ARTICLE

For many years, *Trichomonas vaginalis* has been regarded simply as an irritating but easily treatable protozoan; however, recent research implicates it in a range of problems from pre-term delivery to human immunodeficiency virus infection and cervical cancer. Here, Sangiv Rughooputh and Pamela Greenwell review the evidence.

Trichomonas vaginalis: an irritating protozoan or an important viral co-factor?

Trichomonas vaginalis **(TV) is one of the most successful protozoan pathogens and the most common non-viral sexually transmitted disease, responsible for around 180 million new infections worldwide every year.[1] Presentation in females is usually profuse, purulent, malodorous vaginal discharge and vaginal irritation, although infection can be subclinical or asymptomatic.[2] TV may also be associated with inflammation of the cervix (strawberry cervix) that may mimic the cervical tenderness associated with pelvic inflammatory disease (PID).[3] Changes in the cervical cells in women with TV have been likened to the changes seen in early cervical intraepithelial neoplasia (CIN), while in men the infection often presents as urethritis[4] and prostatitis.[5]**

For many years, TV infection has been seen simply as an irritating protozoan that was relatively easy to treat. Recently, however, there has been evidence to implicate TV in pre-term delivery, low birthweight, infant mortality and predisposition to human immunodeficiency virus (HIV) infection and cervical cancer.[6] Although all these areas are interesting, this article will only review the links between TV and HIV.

'Studies from Africa have shown that the rate of HIV transmission is increased two-fold in women with TV'

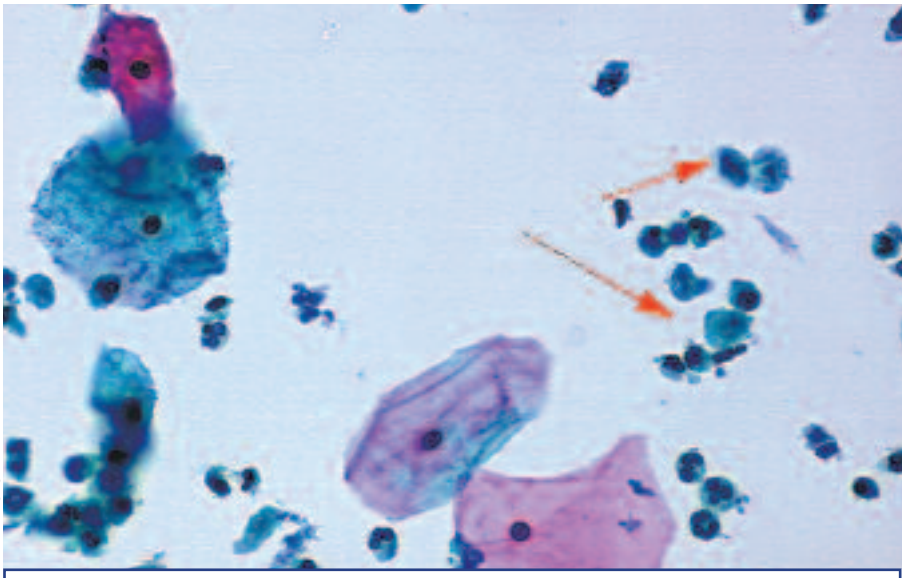
Classical study

T. vaginalis is a classical parasite that harvests almost all its nutrients and needs from its host. To accomplish such a task, TV produces hydrolases to break down host proteins, oligosaccharides, DNA and lipids to obtain the building blocks with which to reconstruct its own macromolecules.[7-10]

In its quest for these building blocks, TV produces a range of highly active enzymes that also destroy the protective mucin of the host's urogenital tract, allowing the TV to attach to the underlying cells and cause lesions. These then provide a portal of entry for HIV, which, under normal circumstances, does not easily infect females. Indeed, heterosexual intercourse with a man infected with HIV only carries a 1% risk of HIV transmission.

Draper *et al.*[11] studied the effect of TV on secretory leucocyte protease inhibitor (SLPI), which protects against viral infection, and found that the inhibitor was non-functional in vaginal secretions due to the action of cysteine proteinases secreted by the trichomonads.

Studies from Africa have shown that the rate of HIV transmission is increased two-fold in women with TV. In a study in four cities in sub-Saharan Africa, Buve *et al.*[12] found a correlation between the prevalence of TV and HIV. The prevalence of trichomoniasis was higher in cities where there were a higher number of HIV-positive individuals (31.8%) compared to cities where HIV incidence was lower (TV prevalence 10.4%). Sorvillo *et al.*[13] calculated that, if TV infection amplifies transmission of HIV by a factor of



TriPath Imaging

Characteristic forms of *Trichomonas vaginalis* (arrowed) in a liquid-based cytology preparation from the cervix.

> ‘Treatment of TV infection is cheap and readily available, whereas treatment for HIV is outside the reach of poor communities’

two in a country where the prevalence of TV is 25% (a level common in parts of Africa), then 20% HIV transmission could be attributed its presence.

Taboo subject

From an economic standpoint, treatment of TV infection is cheap and readily available, whereas treatment for HIV is outside the reach of poor communities; thus, diagnosis and therapy for TV are vital. With reports of emerging strains resistant to metronidazole – the drug of choice for the treatment of TV infection – fewer patients clear infections and thus are susceptible to the formation of lesions, making the penetration of other sexually transmitted infections (STIs) easier. Clearly, an understanding of the pathogenicity of sexually transmitted organisms and their interactions should allow development of new diagnostic and treatment regimes.

Sadly, discussion about STIs remains taboo; there is a stigma attached to their acquisition, and reluctance, both by governments and individuals, to discuss the scale of the problem. Nonetheless, it may be possible to reduce levels of infection through education and the development of new treatments. In the UK, however, where there is access to education, confidential counselling and screening, and free medication, there has been an upsurge in the numbers of cases of STIs reported.

Continuing quest

In the quest to eradicate sexually transmitted diseases, including HIV, the UK Medical Research Council (MRC) will benefit from funding of some £16 million from the Department for International Development over the next five years. In a move likely to provide a breakthrough in the treatment and prevention of STIs, government agencies in the USA allocated $60 million in 2001 for the development of microbicides and, in the UK, ML Laboratories is to start an MRC-funded trial of a product that disrupts organism binding.[14]

Such microbicides could provide a safe and undetectable barrier to infection for women who currently cannot persuade their partners to use a condom. An alternative in the form of the female condom has been singularly unacceptable and very costly. Thus, the use of microbicides could bring about a change in responsibility for protection and result in women having the responsibility to safeguard their sexual health.

> ‘TV can be categorised as an important co-factor in the pathogenesis of cervical cancer’

More than just an irritation?

If TV infection predisposes to HIV, does it also permit access of other viruses to the urogenital tract? Recent work by Sayed el-Ahl *et al*.[15] showed that in 48 patients with invasive cervical cancer and 100 random age-matched controls, 19% and 5%, respectively, had antibodies to TV, suggesting that, at some stage, the cancer patients had contact with TV. Patients with TV infection had a three-fold increased likelihood of contracting cervical cancer, hence TV can be categorised as an important co-factor in the pathogenesis of cervical cancer. Since there is a strong proven link between cervical cancer and human papillomavirus, is TV a co-factor in the acquisition of this virus?

In conclusion, one thing is crystal clear; TV is not just an irritating protozoan!

REFERENCES

1 Chavalitshewinkoon-Petmitr P, Ramdja M, Kajorndechakiat S, Ralph RK, Denny WA, Wilairat P. *In vitro* susceptibility of *Trichomonas vaginalis* to AT-specific minor groove binding drugs. *J Antimicrob Chemother* 2003; **52**: 287–9.

2 Burja IT, Shurbaji MS. Clinical impact of identifying *Trichomonas vaginalis* on cervicovaginal (Papanicolaou) smears. *Diagn Cytopathol* 2001; **4**: 195–9.

3 Moodley P, Wilkinson D, Connolly C, Moodley J, Sturm AW. *Trichomonas vaginalis* is associated with pelvic inflammatory disease in women infected with human immunodeficiency virus. *CID* 2002; **34**: 519–22.

4 Krieger JN, Verdon M, Siegel N, Holmes KK.. Natural history of urogenital trichomoniasis in men. *J Urol* 1993; **149**: 1455–8.

5 Ohkawa M, Yamaguchi K, Tokunaga S, Nakashima T, Shinichi F. The incidence of *Trichomonas vaginalis* in chronic prostatitis patients determined by culture using a new modified liquid medium. *J Infect Dis* 1992; **166**: 1205–6.

6 Dunne RL, Dunn LA, Upcroft P, O’Donoghue PJ, Upcroft JA. Drug resistance in the sexually transmitted protozoan *Trichomonas vaginalis*. *Cell Res* 2003; **13**: 239–49.

7 Lockwood BC, North MJ, Scott KI. The use of a highly sensitive electrophoretic method to compare the proteinases of trichomonads. *Mol Biochem Parasitol* 1987; **24**: 89–95.

8 Alderete JF, Newton E, Dennis C, Neala KA. The vagina of women infected with *Trichomonas vaginalis* has numerous proteinases and antibody to trichomonad proteinases. *Genitourin Med* 1991; **67**: 331–4.

9 Connaris S, Greenwell P.. Glycosidases in mucin-dwelling protozoans. *Glycoconj J* 1997; **14**: 879–82.

10 Das S, Stevens T, Castillo C, VillasenÇ’r A, Arredondo H, Reddy K. Lipid metabolism in mucus-dwelling amitochondriate protozoa. *Int J Parasitol* 2002; **32**: 655–75.

11 Draper D, Donohoe W, Mortimer L, Heine RP. Cysteine proteases of *Trichomonas vaginalis* degrade secretory leucocytes protease inhibitor. *J Infect Dis* 1998; **178**: 815–9.

12 Buve A, Weiss HA, Laga M *et al*. The epidemiology of trichomoniasis in women in four African cities. *AIDS* 2001; **15** (Suppl 4): S89–96.

13 Sorvillo F, Smith L, Kerndt P, Ash L. *Trichomonas vaginalis*, HIV and African-Americans. *Emerg Infect Dis* 2001; **7**: 927–32.

14 Stone A. Protect and survive. *New Scientist* 2003; **177** (2381); 42–4.

15 Sayed el-Ahl SA, el-Wakil HS, Kamel NM, Mahmoud MS. A preliminary study on the relationship between *Trichomonas vaginalis* and cervical cancer in Egyptian women. *J Egypt Soc Parasitol* 2002; 32: 167–78.

Sangiv Rughooputh and Pamela Greenwell are members of the molecular and medical microbiology research group in the School of Biosciences, University of Westminster, London.