

The Impacts of *Trichomonas vaginalis* on the Quality of Life in Women

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Abstract

Trichomoniasis is a significant global health concern, particularly affecting women of reproductive age. In many public health settings, diagnosis is commonly based solely on clinical signs and symptoms. However, this approach can lead to misdiagnosis, as trichomoniasis shares similar clinical presentations with other vaginal infections. Caused by the protozoan *Trichomonas vaginalis*, trichomoniasis is one of the most prevalent non-viral sexually transmitted infections (STIs), often linked to reproductive tract infections, infertility, cervical cancer, premature births, and low birth weight in newborns. According to the World Health Organization, approximately 276.4 million cases were reported in 2008, with nearly 90% occurring in resource-limited settings. The global prevalence among women is estimated at 8.1%, making it more common than *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and syphilis combined. Various studies have identified key risk factors associated with *T. vaginalis* infection, particularly among adolescent girls and women attending STI clinics. These include unprotected sexual intercourse, multiple

sexual partners, a longer history of sexual activity, previous STIs, and higher prevalence among Black populations. Beyond its physical health implications, trichomoniasis significantly impacts women's quality of life, affecting sexual function, reproductive outcomes, mental health, and social well-being. The stigma surrounding STIs, coupled with the often asymptomatic nature of trichomoniasis, contributes to delayed diagnosis, untreated infections, and continued community transmission. Effective prevention and control require comprehensive strategies including safe sex practices, regular screening, early diagnosis, partner notification, and timely treatment. Addressing the broader social and psychological dimensions of the disease is essential for improving health outcomes and reducing the burden of trichomoniasis on women's health globally.

Keywords: Impacts; *Trichomonas vaginalis*; Trichomoniasis; Quality of Life; Women's Health

Introduction

Trichomoniasis is a global health problem for women at reproductive age. These infections have detrimental effects on women's quality of life and pose a hazard to their health. Vaginal infections are generally ignored due to their personal nature. In the past, vaginal infections have received little attention and may have been disregarded as a minor issue, even if the symptoms significantly affect the quality of life for the women who experience them. [1].

Seventy percent (70 %) of women cure vaginal infections on their own before getting medical attention, according to the American Social Health Association. They usually think they have a yeast infection, but it's actually bacterial vaginosis or other bacterial diseases that present with similar symptoms. Establish the diagnosis with microbiological testing and a comprehensive sexual health screening to rule out concurrent illness; in addition to that, according to American studies, vaginitis negatively affects women's quality of life; some women experience embarrassment, anxiety, and hygiene issues, particularly if their symptoms are persistent (Chart 1) [2].

Trichomoniasis is one of these sexually transmitted infections, with an estimated 7.4 million cases per year in the United States. In public health services, the diagnosis of vaginal infections is typically based solely on the presence of signs and symptoms; however,

this evaluation may lead to misdiagnosis of certain vaginal infections because clinical manifestations may be similar [3].

Reproductive tract infections, preterm births, low birth weight newborns, infertility, and cervical cancer are frequently linked to trichomoniasis. As one of the most prevalent non-viral sexually transmitted diseases, it is caused by the protozoan *trichomonas vaginalis* [3]. According to Arab-Mazar & Niyati (2015), it is also one of the most prevalent neglected STDs in the world, preferring humans as its host. It has a wide spectrum of symptoms, from asymptomatic infection to severe vaginitis, and is more common in women than men. It is responsible for about half of all treatable infections globally and is commonly observed alongside other sexually transmitted diseases (STDs), including gonorrhoea [4].

According to research done in Brazil, the percentage of women with HIV and pregnant women who are evaluated at primary care facilities across the nation who have *Trichomonas vaginalis* infection varies from 2.6 % to 20 % [3].

According to a World Health Organization analysis, the organization projected that there were about 276.4 million cases in 2008, with about 90% of these infections occurring in settings with minimal resources. Infection with *Trichomonas vaginalis* is more common than syphilis, *Neisseria gonorrhoeae*, and *Chlamydia trachomatis* combined. *Trichomonas vaginalis* has been estimated to affect 8.1% of women worldwide. Since there are no official surveillance systems in place and these numbers are based on research that employed microscopy rather than the more sensitive nucleic acid amplification tests (NAAT), they may be underestimates.

The epidemiology of *Trichomonas vaginalis* is unknown due to the lack of surveillance initiatives. However, it is well recognized to differ significantly by region and population. Two population-based studies in the United States that employed PCR testing discovered rates of 2.3% among teenagers and 3.1% among women aged 14 to 49. In Africa, population-based research reveal noticeably greater rates (Chart 1). Using antibody testing, the rate for both sexes in Zimbabwe was 9.5%. According to NAAT, 11% of Tanzanian men were positive. The prevalence of *Trichomonas vaginalis* in women in Papua New Guinea also seems to be abnormally high, ranging from 42.6% in the general population to 21% in pregnant women.

Trichomonas vaginalis screening rates among women attending antenatal or family-planning clinics are often used as an indicator of the prevalence in the general population; studies at these sites found prevalence rates ranging from 3.2 to 52% in resource-limited settings and 7.6 to 12.6% in the US. Other population-based studies that used NAAT testing among reproductive-aged women in other parts of the world found lower rates (i.e. 1% in rural Vietnam and 0.37 % in Flanders, Belgium, and 2.9 % in Shandong Province, China) [5].

In addition to having a substantial negative influence on a woman's quality of life, health, and general well-being, vaginal infections can also have a detrimental effect on her social, personal, and professional connections. Notably, untreated *Candida* vaginitis causes many women who suffer from recurring yeast infections to miss up to a week of work. More than 50% of women are known to contract bacterial vaginosis on a regular basis, which has a negative influence on their lifestyle, including their sex lives and sense of self. Many women are self-conscious and ashamed of their symptoms, and they frequently don't know why they get vaginitis again. They can also get angry at not being able to regulate their health [5].

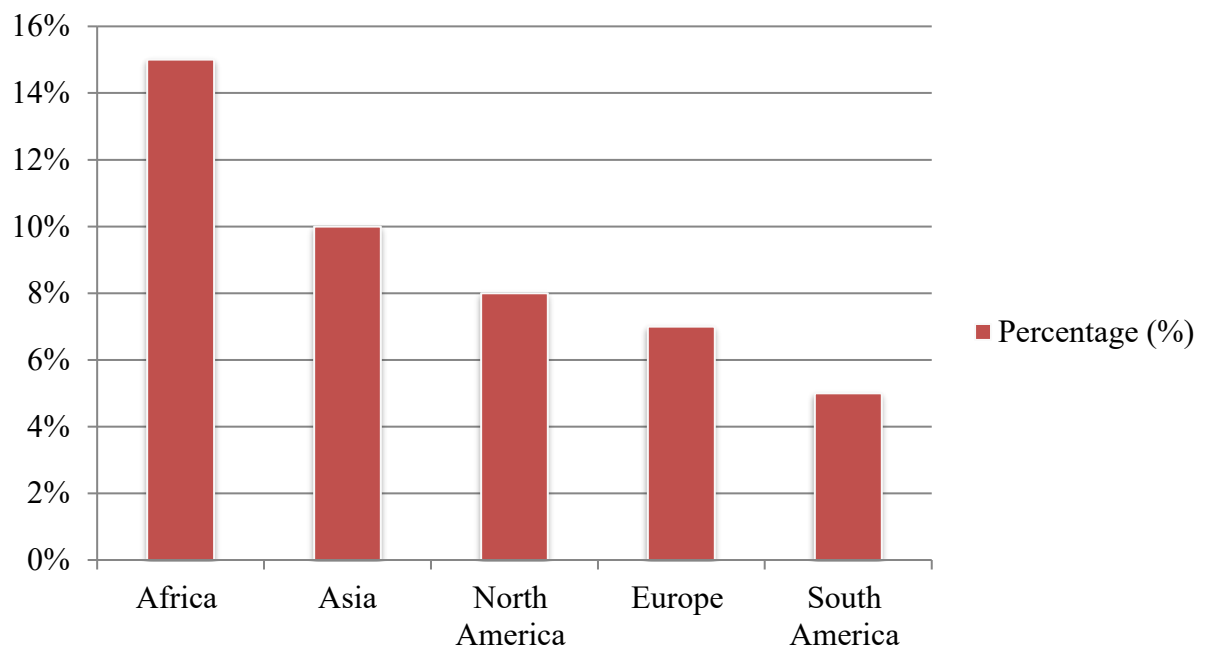


Chart 1: A bar chart can show the global prevalence of *Trichomonas vaginalis* based on regional data from the literature.

Description of *Trichomonas vaginalis*

A protozoan parasite called *Trichomonas vaginalis* is the cause of trichomoniasis, one of the most common STIs in the world. Even though *Trichomonas vaginalis* infections are very common, they frequently get less attention than other STDs, despite the fact that they can have a major negative impact on women's quality of life [6]. *Trichomonas vaginalis* infection is a serious public health problem due to its high incidence worldwide and the frequency of coinfection with other STIs. A higher chance of contracting certain STIs, including as gonorrhea, human papillomavirus (HPV), herpes simplex virus (HSV), and most importantly human immunodeficiency virus (HIV), has been linked to *Trichomonas vaginalis* infection, according to research.

The only known host of *Trichomonas vaginalis* is humans. Sexual contact is the main way that transmission happens. The organism is most frequently isolated from male urethral fluids and female vaginal secretions. Among males who have sex with men (MSM), the rectal prevalence of *Trichomonas vaginalis* seems to be low. Despite the fact that *Trichomonas vaginalis* has not been isolated from oral locations, there is evidence that it can occasionally result in STIs [7].

Due to a number of variables, such as nonspecific symptomatology [8], the low sensitivity of a regularly used diagnostic technique (wet mount microscopy), and a lack of systematic testing, trichomoniasis is believed to be significantly underdiagnosed [9]. Misdiagnosis may also result from self-diagnosis, self-treatment, or diagnosis by professionals without proper laboratory testing. To diagnose trichomoniasis, the Centers for Disease Control and Prevention (CDC) currently advise using a variety of molecular detection techniques, such as an antigen-detection test and multiple validated nucleic acid amplification tests (NAATs) [8].

Trichomonas vaginalis is usually detected in sexually active people since it is mostly transmitted through sexual contact. Despite the fact that *Trichomonas vaginalis* has not been isolated from oral locations, there is evidence that it can occasionally result in an STD [10]. In addition to being vertically transmitted [5], *Trichomonas vaginalis* can go for extended periods of time without showing any symptoms. Almost all infected males and nearly half of infected females do not exhibit any symptoms. Within six months, one-third of asymptomatic women develop symptoms. Therefore, a lack of sexual history should not be used to rule out an infection with *Trichomonas vaginalis*.

Life Cycle of the Parasite

Trichomonas vaginalis is a flagellate that inhabits the urogenital tract's epithelium, where it obtains its energy by anaerobic processes [9]. The male urethra and prostate, as well as the female lower genital tract, are host to this parasite. It causes trichomoniasis in women, which is typically characterized by cervical and vulvar lesions, abdominal pain, or dysuria, along with vaginitis with a thin purulent discharge. It takes five to twenty-eight days to incubate. Men may experience urethritis, epididymitis, or prostatitis symptoms, or the infection may be asymptomatic. *Trichomonas vaginalis* divides its nucleus mitotically and replicates by binary longitudinal fission. The trophozoite form is the only stage visible as a flagellate. No cyst form has been found, and this parasite does not survive well in the external environment. *Trichomonas vaginalis* is commonly spread among humans by sexual intercourse [11].

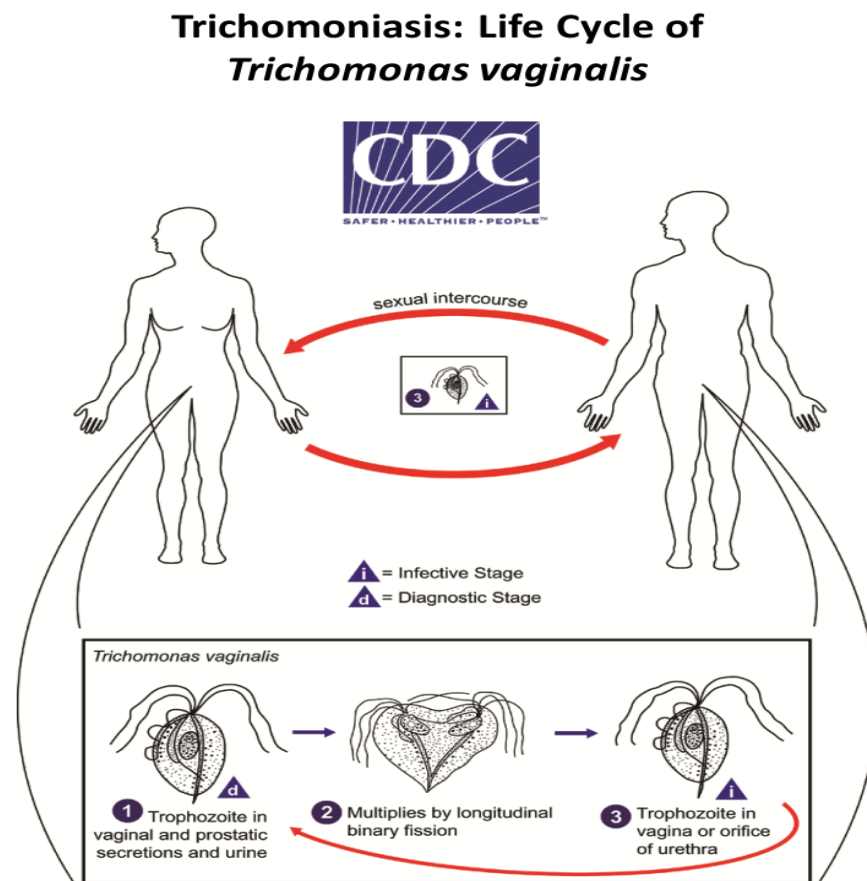


Figure 1: Life Cycle of *Trichomonas vaginalis*

Source: Stephen B: Center for Disease Control 2014

Morphology

Trichomonas vaginalis only exists as a teardrop-shaped trophozoite, with an average length of 10 µm and a width of 7 µm. It does not have a cystic stage in its life cycle. While a single posterior flagellum, which forms the outer edge of the undulating membrane and runs along one side of the cell, aids in motility and the movement of extracellular nutrients towards the cell's cytosome, the parasite's distinctive twitching motility is provided by a total of four anterior flagella. An axostyl, a bundle of microtubules that travels through the cell along its anterior-posterior axis and enters the extracellular environment [12], is another feature of the cell that aids in mitosis and cell attachment. A single distinct nucleus and many hydrogenosomes primitive redox organelles that developed from mitochondria and generate molecular hydrogen and ATP are found in the cytoplasm.

Pathogenesis

Although transmission by fomites has been reported, it is uncommon and contentious. Sexual contact is the primary method of transmission. Due to the parasite's capacity to persist for up to three hours in a moist environment, bathing instruments and shared bathing water are documented as suspected non-sexual transmission pathways [13, 14]. *Trichomonas vaginalis* cells from the infected partner's genital tract are transferred to the uninfected partner during sexual activity and come into touch with the genital epithelia. The normally ovoid *Trichomonas vaginalis* cell undergoes morphological adjustment, taking on an amoeboid shape, when it comes into touch with epithelial cells [14]. AP120, AP65, AP51, AP33, and AP23 are the five main surface adhesins that cause the parasite to adhere to the host epithelia; apart from AP51, the genes encoding these proteins are all transcriptionally upregulated by the presence of iron, which is a crucial mediator of *Trichomonas vaginalis* growth and a major factor in virulence. The parasite's amoeboid morphology allows the parasite to increase the surface area contact, and interaction, with the epithelial cell [15]. Of these surface proteins, AP65 has been hypothesised as the most important; anti AP65 serum IgG antibodies reduce *Trichomonas vaginalis* cytoadherence, which does not occur when the same is carried out on other adhesins. Fascinatingly, it has been revealed that AP65 does not have a covalent anchor motif, and is released extracellularly, where it binds to both the *Trichomonas vaginalis* and epithelial cell surface. The parasite's interaction with vaginal epithelial cells triggers the creation and transport of these adhesins to the outer membrane, along with a morphological change to the amoeboid

form. Large clusters of ameboid cells grow on the epithelial surface as a result of the *Trichomonas vaginalis* cells attracting other parasites to the area after adhesion.

When *Trichomonas vaginalis* infects the urogenital tract, it causes inflammation, destruction to epithelial cells, and changes in immunological responses, among other pathological abnormalities [16]. The virulence and persistence of the parasite are influenced by its capacity to adhere to host cells, elude immune monitoring, and trigger cytokine production. Since sexual interaction is how the organism is spread, a persistent cyst form is not necessary [17]. The bacteria is primarily found in the prostate and vagina. There is no animal reservoir for it; it solely exists in humans.

Surface lipophosphoglycan, the most abundant protein on the *Trichomonas vaginalis* surface membrane, is the other main mediator of cytoadherence to the host epithelia. It attaches itself to the galectin-1 protein found on the surface of human epithelial cells [18]. The significance of this molecule for parasite attachment and virulence has been highlighted by site-directed mutagenesis studies, which have demonstrated that *Trichomonas vaginalis* cells expressing a lipophosphoglycan molecule with modified surface residues have significantly decreased adherence and cytotoxicity to human vaginal epithelial cells. Another protein found on the surface of *Trichomonas vaginalis* that has been linked to cytoadherence is glyceraldehyde-3-phosphate dehydrogenase, or GAPDH [19].

Trichomonas vaginalis's cytotoxic adherence to the surface of epithelial cells is a key component of pathogenesis; it usually causes the host cell to lyse and the epithelial monolayer to erode. Additionally, by releasing chemokines like IL-8 and drawing neutrophils to infected tissues, this mechanism triggers the inflammatory response [20]. Several mechanisms are known to cause damage to the vaginal epithelial monolayer during infection, and phagocytosis is not involved in this contact-dependent death. The junctional complex between individual cells in the epithelial monolayer is weakened when *Trichomonas vaginalis* adheres to epithelial cells. This weakening results from the interaction with the parasite and is caused by a decrease in trans-epithelial electrical resistance, an increase in the distance between adjacent cells, and a change in the distribution of junction complex proteins.

Parasite-mediated death of epithelial cells, which is reliant on the release of CP30 cysteine proteases, also results in damage to the host epithelia. These four cysteine

proteases are crucial components in the pathophysiology of *Trichomonas vaginalis* because they are also connected to adhesion and the parasite's ability to cross the mucosal barrier. Along with commensal bacteria and yeasts of the genital tract, *Trichomonas vaginalis* may also phagocytose vaginal epithelial cells, leukocytes, and erythrocytes in vitro. In vitro experiments using yeasts have revealed two different processes of phagocytosis: a more passive type in which the target cell sinks into the *Trichomonas vaginalis* membrane, and a traditional version in which pseudopodia extend and engulf the target cell. The *Trichomonas vaginalis* cell receives nourishment from phagocytosis, which is followed by intracellular death in lysosomes. The main pathway for horizontal gene transfer between bacteria and *Trichomonas vaginalis* is likewise believed to be phagocytosis, which gives the parasite a crucial mechanism for genetic diversification and adaptation.

Although non-specific mannose receptors on the outer membrane of *Trichomonas vaginalis* have been linked to the internalization of yeast cells, it is unclear exactly how the cells choose target cells suitable for phagocytosis. It has been demonstrated that mannose binding lectins can bind both Gram-positive and Gram-negative bacteria, yeasts, protozoa, and even certain viruses, demonstrating the diverse spectrum of species that can be identified by this ligand. Since leukocytes and epithelial cells also have mannose on their surface [21], *Trichomonas vaginalis* mannose receptors might be involved in identifying these cell types during phagocytosis or lysis.

It is well known that *Trichomonas vaginalis* can identify erythrocytes and lyse them in vitro and in vivo; hemolysis is dependent on the parasite's adherence. It is believed that this gives the parasite access to iron, which is a necessary ingredient for *Trichomonas vaginalis* growth.

Complications

The most prevalent infection-related symptom in women is vaginitis. Cervicitis and infections of the adnexa, endometrium, and Skene and Bartholin glands are additional problems. Additionally possible are tubo-ovarian abscess and pelvic inflammatory illness. The most common symptom of a *Trichomonas vaginalis* infection in men is urethritis. *Trichomonas vaginalis* is responsible for up to 11% of male instances of nongonococcal urethritis. Untreated trichomoniasis in men can lead to infertility, urethral stricture illness, prostatitis, and epididymitis, which may be caused by a decrease in sperm motility and viability [22].

According to research, both men and women are more likely to contract HIV if they have an infection with *Trichomonas vaginalis*. According to estimates by Gaydos and Klausner [23], *Trichomonas vaginalis* facilitates HIV transmission, resulting in 747 new HIV cases annually in women alone. People who have trichomoniasis are often twice as likely as the general population to become infected with HIV [24]. It has been discovered that males with comorbid HIV and *Trichomonas vaginalis* infections had noticeably more HIV RNA particles in their seminal fluid. It has been demonstrated that treating trichomoniasis lowers the rate of viral shedding in HIV-infected patients [8].

Apart from HIV, infection with *Trichomonas vaginalis* also makes one more vulnerable to other viruses, such as Herpesvirus and Papillomavirus, also known as human papillomavirus (HPV). While *Trichomonas vaginalis* may shorten the duration of infection, it may also increase the rate of HPV infection or reactivation [25]. *Trichomonas* has also been linked to the following conditions: Trichomonal peritonitis (rare), cervical intraepithelial neoplasia, and posthysterectomy infections, including cuff cellulitis, cuff abscess, and wound infection [26].

Preterm delivery, low birth weight, and intrauterine infection have all been linked to *Trichomonas vaginalis* infection in pregnant women [27]. There have been reports of neonatal trichomoniasis, which typically manifests as a vaginal infection. *Trichomonas* rarely manifests as a severe respiratory infection.

Clinical Manifestations

About 50% of female *Trichomonas vaginalis* infections result in symptoms, while 30% of asymptomatic cases show some symptoms within six months of infection. Common symptoms include mild to severe vaginitis, a frothy discharge, and itching and pain during sexual activity. Colpitis macularis, also known as "strawberry cervix," is a condition that can cause punctate hemorrhagic patches on the cervical and vaginal mucosa in acute cases [28]. Cervicitis, urethritis, and more severe side effects like pelvic inflammatory disease (PID), cervical cancer, and infertility have all been linked to *Trichomonas vaginalis* infections.

Pregnancy outcomes and the impact of *Trichomonas vaginalis* infection are well-established. Preterm delivery and low birth weight are more likely when *Trichomonas vaginalis* infections occur in the middle of pregnancy. Interestingly, this subsequent preterm delivery is not prevented by successfully treating a *Trichomonas vaginalis* infection in pregnant women at the mid-gestational stage. There have been reports of vaginal and

nasopharyngeal infections in newborns, and it is believed that these illnesses are transmitted during birth.

Although moderate urethritis, epididymitis, and prostatitis can occur, male genitourinary tract infections are typically asymptomatic. The majority of persistent infections in men are believed to be caused by *Trichomonas vaginalis* colonization of the prostate, which can result in chronic infection. Trichomonads have been found in the prostatic urethra as well as in the glandular lumina, submucosa, and stroma, which are the tissues that surround the prostate. Male *Trichomonas vaginalis* infections were regarded as "nuisance infections" until recently, with no real repercussions. The discovery that *Trichomonas vaginalis* colonization of the prostate is a risk factor for prostate cancer development has slightly altered this perspective.

According to a study with 673 prostate cancer patients and an equivalent number of control participants, there is a statistically significant correlation between those with prostate cancer and those who test positive for *Trichomonas vaginalis* antibodies [29]. According to estimates, there is a 23% to 40% increase in the risk of prostate cancer [29]. The host inflammatory response, which includes the increased generation of pro-inflammatory cytokines linked to prostate cancer, is one possible mechanism that explains the higher risk of carcinogenesis observed during *Trichomonas vaginalis* infection [30]. In cultured prostate epithelial cells, *Trichomonas vaginalis* infection has also been demonstrated to upregulate the expression of the proto-oncogene PIM1 [31]. Additionally, it is known that PIM1 can trigger the expression of HMGA1, another proto-oncogene, through the PIM1/c-MYC/HMG1 signaling cascade. Malignant prostate cells commonly overexpress both c-MYC and HMG1, and this overexpression has been connected to enhanced metastasis and proliferation [31]. According to recent research, the pro-inflammatory cytokine Human macrophage migration inhibitory factor (HuMIF) and the new protein *Trichomonas vaginalis* macrophage migration inhibitory factor (TvMIF) have 47% sequence agreement [32]. In addition to generating inflammation and blocking macrophage movement, *Trichomonas vaginalis* macrophage migration inhibitory factor (TvMIF) also phosphorylates ERK, Akt, and Bcl-2-associated death promoters, which prevents apoptosis and promotes cellular proliferation. The same study shows that both normal and malignant prostate cells proliferate and invade when exposed to TvMIF in vitro [32].

Symptoms of Trichomoniasis

Often, trichomoniasis is asymptomatic. According to the CDC, only 30% of individuals with trichomoniasis report experiencing any symptoms at all. Eighty-five percent (85 %) of the afflicted women in one research had no symptoms. When symptoms do appear, they usually start five to twenty-eight days after the illness is contracted. It can take a lot longer for certain folks. Among the most typical symptoms are:

1. Vaginal discharge, typically frothy and odorous, can be white, gray, yellow, or green.
2. Vaginal hemorrhage or spotting
3. Itching or burning in the vaginal area
4. Swelling or redness in the genital area
5. Constant urge to urinate and discomfort when urinating or having sex

After a week, the symptoms should go. The patient should speak with a doctor about getting retested and retreated if the symptoms persist or take longer. At least three months following therapy, the patient should additionally visit a physician for a trichomoniasis follow-up test [33]. In the three months following treatment, the re-acquisition rate for women and those with vaginas can reach up to 17%. Even if partners received the same treatment, reacquisition is still feasible.

Diagnosis

With a higher frequency than the combined infections of *Chlamydia trachomatis* and *Neisseria gonorrhoeae*, trichomoniasis is the most prevalent non-viral STI in the world [8]. However, unlike with *Chlamydia trachomatis*, neither the US nor the UK have a routine screening program outside of pregnancy [34]. The reduced prevalence of asymptomatic infection in female trichomoniasis patients and the increased incidence of PID and tubal infertility brought on by *Chlamydia trachomatis* are partly to blame for this.

Trichomonas vaginalis testing is offered in most GUM clinics for patients with symptoms in the UK. It is rarely possible to diagnose a *Trichomonas vaginalis* infection based solely on clinical presentation because the symptoms of the illness closely resemble those of several other STDs, including *Mycoplasma genitalium* and *Neisseria gonorrhoeae*. Only about 2% of cases have the distinctive inflamed and speckled "strawberry cervix" and frothy discharge, which are particular signs of trichomoniasis and cannot be used as a sole indicator of the infection. Since medications like azithromycin or doxycycline, which are

used to treat general urethritis, are ineffective against trichomoniasis, a precise diagnosis is crucial for the subsequent management of the infection.

A "wet mount" of vaginal or cervical exudates is often examined under a microscope to check for motile parasites in order to diagnose trichomoniasis in female patients. Comparing this procedure to other diagnostic choices, such as culture or molecular methods, reveals that it is relatively easy to do, quick, and economical [35]. Because of its low sensitivity, microscopic examination is not regarded as the best detection tool, despite these benefits. When compared to PCR-based techniques, microscopy has demonstrated a sensitivity of about 60% [36]. Since the organism load in the sample may be less than 10⁴ cells/ml, low level infections are unlikely to be detected by microscopy and may not be included in the fields reviewed on the slide [37]. If there are delays between sample capture and inspection, the sensitivity of this approach rapidly drops; a mere 10-minute delay has been shown to reduce sensitivity by 20% [38]. As a result, it has been recommended that any diagnostic service that is unable to ensure that samples can be tested within an hour of acquisition employ different techniques. Clinics that rely on transporting samples to distant, centralized laboratories for analysis and do not have an on-site microscopy service should be especially concerned about this. The decrease in sensitivity is brought about by a decrease in parasite movement, which makes it more challenging to detect trichomonads. When nonmotile, *Trichomonas vaginalis* cells might be difficult to distinguish from lymphocytes due to their similar shape and size [37].

For many years, the most reliable method for diagnosing *Trichomonas vaginalis* has been to cultivate the organism from clinical samples [35]. Swab samples from female patients' cervixes or vaginal canals, or from male patients' urethral discharge, are usually used to inoculate cultures kept in a broth medium. Although this is not the best sampling technique and results in lower sensitivity, cultures can also be inoculated from urine samples. Although cultures can show growth in as short as 48 hours, they should be incubated for at least 7 days in order to detect low inocula.

Variants of Diamonds (TYM) medium, which initially included trypticase digest, yeast extract, maltose, cysteine, ascorbic acid, and sheep serum, are the most widely used media. Diamonds TYI-S-33 medium, which additionally includes a supply of iron, fetal bovine serum instead of sheep serum, and a vitamin 107-Tween 80 mixture, is perhaps the most often used variation. *Trichomonas vaginalis* depends on nutrients obtained from

secretions or phagocytosed human or bacterial cells in the host genital tract because it is unable to synthesize a variety of macromolecules required for survival and growth, such as purines, pyrimidines, and certain lipids. These components must be present in all culture conditions, but serum in particular is essential for promoting the axenic development of this organism.

When diagnosing a *Trichomonas vaginalis* infection, broth culture has a greater diagnostic sensitivity than wet mount microscopy. According to one study, the sensitivity of microscopy and culture was 52% and 78%, respectively, for 337 samples, including 97 positive samples. There are a few serious drawbacks to using culture to identify trichomonas infections, though. Because it takes a week to incubate, culture is the diagnostic technique that takes the longest between sample capture and outcome. Moreover, molecular techniques like PCR are more sensitive than culture. Although it is rarely utilized in a clinical diagnostic context, the culture of *Trichomonas vaginalis* using solid medium has been documented in the literature. According to one study, a solid modified Columbia agar medium was more sensitive (98.4%) than a *Trichomonas* medium that is sold commercially (92.1%).

The InPouch culture system (Biomed Diagnostics, USA) is one commercially available culture-based diagnostic test. By combining microscopy and culture, this approach offers a diagnostic solution that benefits from both techniques [39]. It comes in a clear plastic pouch with two connected media-filled chambers, one of which is swab-inoculated. The other chamber is thinner and features a narrow viewing glass that allows for microscopic investigation for any trichomonads. In addition to eliminating the requirement for a pre-culture transport media because the pouch is injected straight from the patient, this technique has been demonstrated to be more sensitive than wet-mount microscopy alone [39]. This increases the chances of a successful culture. The ability to evaluate the culture under a microscope without the need for fluid manipulation eliminates the chance of contamination and speeds up the examination process. However, this approach is more costly than conventional techniques based on microscopy or culture.

Although serological techniques for *Trichomonas vaginalis* diagnosis have been established, they are rarely applied in clinical settings. When compared to broth culture, an enzyme-linked immunosorbant assay (ELISA) test based on monoclonal antibodies that is specific to *Trichomonas vaginalis* surface peptides has been demonstrated to have

sensitivity and specificity of 89 % and 98 %, respectively. Another ELISA assay has shown a higher sensitivity than wet mount microscopy, with a detection limit of 100 trichomonads per milliliter. The commercially available ELISA test known as the Trichomonas Direct Enzyme Immunassay (California Integrated Diagnostics, US) is no longer available. It was as sensitive as broth culture and depended on a combination of monoclonal antibodies to various Trichomonas vaginalis proteins that were tagged with peroxidase. As of right now, the OSOM Trichomonas Rapid Test (Sekisui Diagnostics, US) is the only Trichomonas vaginalis immunoassay that has received FDA approval in the United States and is commercially accessible. The test, an immunochromatographic capillary flow dipstick test, can be used at the point of care (POC) because it yields a response in ten minutes. With a sensitivity and specificity of 82% and 97%, respectively [40], the OSOM test is a more sensitive diagnostic test than normal ELISA, wet-mount microscopy, and culture techniques, but it is also faster and easier to perform.

Trichomonas vaginalis can be tested using both commercial and "in house" PCR-based assays, which offer a more sensitive way than the conventional wet-mount microscopy and culture techniques.

Although PCR requires more highly trained staff and more expensive equipment and reagents, than alternative methods, the sizeable increase in sensitivity, coupled with a relatively short turnaround time, makes PCR based assays the optimum diagnostic method in developed countries. A range of genes have been exploited as targets for *Trichomonas vaginalis* specific PCR tests. A standard PCR assay specific to a sequence of the beta-tubulin gene was found to have a sensitivity and specificity of 97% and 98% respectively. The same study found the sensitivities of wet mount microscopy and culture to be 36% and 70% respectively, illustrating the improvement in sensitivity offered by PCR. A study comparing the sensitivity of two real-time fluorescence resonance energy transfer (FRET) hybridisation probe based PCR assays specific to the beta-tubulin gene and 18S rRNA gene found assay sensitivities of 96% and 100% respectively [41]. The *Trichomonas vaginalis* genome harbors a number of conserved repeated DNA sequences, and these are attractive targets for nucleic acid amplification tests (NAATs), as they provide a higher copy number per cell, and improve detection limits and sensitivities [42]. The sequencing of the ~160 Mb *Trichomonas vaginalis* genome identified 59 common repeat families that make up ~39 Mb of the complete sequence [43]. The majority of the repeat sequences have a copy number of >100, with the average being 660 copies. Importantly, these repeats show a high

level of homogeneity, with sequence variation identified between repeats of the same family in only 2.5% of repeats. This provides a stable, high copy number target for molecular assays. Single parasite detection has been demonstrated for PCR assays using these repeated sequences as targets, and the improved sensitivity has enable testing from non-invasive urine samples, which typically contain a lower organism load than the swab samples more frequently used [42].

The overwhelming majority of NAATs available for *Trichomonas vaginalis* identification are PCR based, however novel isothermal diagnostic methods have been applied to the detection of this organism. The commercially available APTIMA *Trichomonas vaginalis* assay (Gen-Probe, US), relies on transcription mediated amplification technology, in combination with a target capture specimen processing system, to provide a highly sensitive assay for *Trichomonas vaginalis* detection [34]. The assay is designed to be used on one of the automation systems available from Gen-Probe, such as the TIGRIS. The assay is approved for use in the US by the Federal Drug Administration (FDA), and is approved for use in the UK. The approval only relates to the use of the assay with a number of sample types from female patients, including urine samples, endocervical swabs, and vaginal swabs.

GenProbe also manufactures AMPTIMA assays for other sexually transmitted pathogens, including *Neisseria gonorrhoeae*, human papillomavirus (HPV), and a combined *Chlamydia trachomatis* and *Neisseria gonorrhoeae* assay (APTIMA COMBO 2 assay). A large scale study of 933 symptomatic and asymptomatic female patients attending an STI clinic found the APTIMA assay to have the following sensitivity and specificity, respectively, in the following samples types; 100% and 99.0% for vaginal swabs, 100% and 99.4% for endocervical swabs, and 95.2% and 98.9% in urine specimens [10].

Another commercially available molecular diagnostic test for *Trichomonas vaginalis* infection is the Affirm VPIII *Trichomonas vaginalis* assay (Becton Dickinson, US), which relies on RNA probe hybridisation to detect target DNA. The test has been shown to be more sensitive than wet mount microscopy [11], but lacks sensitivity compared to NAATs, as the target DNA is not amplified before detection, which results in a higher starting copy number being required in order to generate signal. One study compared the Affirm VPIII assay with the APTIMA assay, and found sensitivities of 63.4% and 100% respectively [44]

(Chapin and Andrea, 2011). The test is fully automated, and takes 45 minutes to run, including 2 minutes “hands on time”, potentially enabling point of care testing.

POC testing for sexually transmitted infections, including trichomoniasis, could be of great benefit in the control of these diseases [45]. Testing at the POC enables consultation, testing, and the provision of appropriate treatment to all be carried out in the same day, at the same site. This removes the risk of patients neglecting to return for results and medication, and also reduces the possibility of transmission by sexual contact during the delay before treatment is instigated [45]. Currently, it is possible to carry out testing via wet mount microscopy at POC, although this is insensitive, low throughput, and effected by the experience and skill of the technician. Also, the immunochromatographic OSOM Trichomonas Rapid Test (Sekisui Diagnostics, US) is able to provide results within 10 minutes, is easy to use and read, and has higher sensitivity than non-molecular methods (82% compared with PCR), making it a very good option for providing a POC diagnostic [40]. The current goal of POC diagnostic research is to provide the sensitivity of NAAT diagnostics, whilst eliminating hands-on processing, and decreasing the time-to-result, enabling maximally sensitive testing at the point of care [46]. The majority of POC NAAT systems in development rely on an automated nucleic acid procedure, rapid target amplification, and detection of reaction products, typically by optical detection of fluorescence [47]. These processes are often carried out in a disposable single use cartridge or chip, preventing contamination of the machine during sample handling [47]. One such system currently in development is the Atlas Io PoC (Atlas Ltd, UK) platform, which is aiming to release a *Trichomonas vaginalis* test in 2014. The test involves automated nucleic acid extraction, followed by amplification of a multi-copy DNA repeat sequence target, and novel electrochemical endpoint detection. A small scale lab evaluation of the test, comparing its performance with that of the APTIMA *Trichomonas vaginalis* test (Hologic Gen-Probe, USA), over 90 clinical samples, found that the sensitivity and specificity of the assay were 95.5% and 97.5% respectively [48]. The most widespread commercially available POC system is the GeneXpert (Cepheid, USA), a platform for processing real-time PCR based assays with fully automated sample preparation, amplification and detection on disposable assay-specific cartridges [49].

Currently there are FDA approved GenExpert assays available for Mycobacterium tuberculosis [50], Clostridium difficile and a combined C. trachomatis and *Neisseria gonorrhoeae* assay [51], all of which have high sensitivities and specificities, and provide

results within 90 minutes. Cepheid has announced that it plans to release a *Trichomonas vaginalis* assay in the 2014-2015 product range, enabling testing for trichomoniasis to be carried out using this platform.

The use of POC testing for trichomoniasis could be of particular benefit in sub-Saharan Africa, where both *Trichomonas vaginalis* and HIV infection are highly prevalent. The improved control of *Trichomonas vaginalis* could potentially reduce HIV transmission, and significantly impact on morbidity and mortality in the region [52]. POC testing has been regarded as being particularly well suited to developing countries, as the automated POC systems reduce the need for skilled technicians, or well-equipped centralized laboratories, which may not be widely available [53]. Additionally, the ease of transport, and lack of additional equipment needed by these systems, enables the testing of remote communities, far removed from traditional hospital based healthcare. However, concerns remain over whether the expense of POC NAAT systems will prevent their widespread use in developing countries, with studies examining the prospective cost of implicating widespread POC NAAT testing in Africa highlighting the increased cost of diagnosis [54]. Field testing of the Cepheid GenExpert *Chlamydia trachomatis* assay in South Africa has given promising results, demonstrating high clinical sensitivity in combination with being well suited for use outside of the traditional laboratory environment, and the GenExpert M. tuberculosis assay is already being widely used in sub-Saharan Africa [55]. As use of the GenExpert system is becoming more widespread in developing countries, especially for detecting *Mycobacterium tuberculosis*, it is possible that healthcare providers may take advantage of the platform to diagnose *Trichomonas vaginalis*, upon the predicted release of the assay in 2015.

Treatment

Metronidazole and tinidazole are the primary treatment options for trichomoniasis, with high cure rates reported [56]. However, emerging drug resistance poses a growing concern, necessitating the exploration of alternative treatment options and antimicrobial stewardship strategies. Without treatment, *Trichomonas vaginalis* can be ongoing [5,56]. With treatment, it's usually cured within a week. You can contract trichomoniasis again after treatment if your partner wasn't treated or if a new partner has contracted it.

METRONIDAZOLE: For women, the standard therapy is 500mg of metronidazole, t.i.d., for ten days. An alternative regimen consisting of one single 2-g dose

can also be employed. Women in the first trimester of pregnancy should not be treated with metronidazole. Infected infants over the age of four months can be treated with metronidazole at a dose of 10 to 30 mg/kg daily for five to eight days.

TINIDAZOLE: Primarily prescribed in cases of metronidazole resistance. The patient is treated with 500mg orally, q.i.d., plus intravaginal 500mg, b.i.d., for 14 days [10].

Reduce your chances of acquiring trichomoniasis again by making sure all of your sexual partners get treatment. Then, wait for the condition to clear before becoming sexually active again. It's recommended that you wait 1 week after taking your medication before having sex again [34].

Table 1: Symptoms, Risk Factors, and Treatments for *Trichomonas vaginalis*

Study	Common Symptoms	Risk Factors	Treatment Used	Treatment Success (%)
Garcia & Clark (2020)	Vaginal discharge, itching, odor	Multiple sexual partners, STIs	Metronidazole	85%
Johnson <i>et al.</i> (2018)	Painful urination, irritation	Low socioeconomic status	Tinidazole	88%
Smith <i>et al.</i> (2017)	Pain during intercourse, discharge	History of STIs	Combination therapy	92%
Nguyen <i>et al.</i> (2021)	Burning sensation, discomfort	Poor access to healthcare	Metronidazole	83%

Sources: Garcia and Clark [570]; Nguyen et al. [58]

This table provides a summary of the symptoms, risk factors, and treatments associated with *Trichomonas vaginalis* infection, highlighting the different approaches used across various studies.

Prevention

Preventive measures, including behavioral interventions, condom use, regular screening, and partner notification, are crucial for reducing the burden of trichomoniasis and its associated sequel. Comprehensive sexual health education, access to affordable healthcare services, and gender-sensitive approaches are essential components of effective prevention strategies.

For improved health, adequate personal hygiene, avoidance of promiscuity, improved education of women on safe sex and the need to know partners' STI status are advocated. It is recommended that routine STIs screening in sexually active patients especially among the young and singles should be incorporated into hospital care. This is

needed to prevent transmission of the parasite, because some infected women and most infected men show no signs of the disease like liquid discharge from the vagina or penis, irritation while urinating and genital itching.

Relationship of *Trichomonas vaginalis* with Other Microorganisms

Trichomonas vaginalis has been linked to the co-occurrence of various other STIs, including *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and human papillomavirus (HPV) (Caron et al., 2012). It also demonstrates a similar epidemiologic connection with herpes simplex virus type 2 (HSV-2). Infection with *Trichomonas vaginalis* can alter the usual vaginal microbiota, making it more susceptible to the development of bacterial vaginosis (BV). Around 40–60% of women with *Trichomonas vaginalis* also experience bacterial vaginosis, and those with BV have an increased risk of contracting *Trichomonas vaginalis* [59].

The presence of *Trichomonas vaginalis* in female patients can cause extensive changes in the vaginal microbiome, and trichomoniasis often occurs in tandem with bacterial vaginosis [60], a condition involving an imbalance in the bacterial flora of the vagina causing vaginal inflammation. This imbalance commonly manifests as a reduction in overall numbers of *Lactobacillus* sp., thought to be crucial for the maintenance of vaginal health, in combination with an increase in other commensal bacteria that are usually only present in lower levels, such as *Gardnerella vaginalis*, *Mobiluncus curtisii*, *Megasphaera* sp., *Atopobium vaginae*, and *Leptotrichia* sp. The lactobacilli, predominant in women with a typical vaginal microbiota, contribute to vaginal health by releasing lactic acid, which maintains optimal vaginal pH. *Trichomonas vaginalis* grows optimally at a pH of 6 to 6.3, whilst the vaginal pH in women with lactobacilli dominated vaginal environment ranges between 2.8 and 4.2 [61]. The disruption of the lactobacilli community seen during trichomoniasis reduces the lactic acid released into the vaginal environment, increasing the pH, and creating more favourable conditions for *Trichomonas vaginalis*.

Lactobacilli also act against pathogenic organisms in the vaginal environment, by out-competing them for nutrients, and also via the release of hydrogen peroxide, which is toxic to a number of potentially Bacterial vaginosis causing organisms such as *Gardnerella vaginalis*. Bacterial vaginosis can have serious health implications, many of which overlap with trichomoniasis; increased risk of HIV transmission, ascending inflammatory infections and preterm birth/low birth weight pregnancy [62]. The combination of *Trichomonas vaginalis* and Bacterial vaginosis associated bacteria have been shown to amplify the host immune response, including an up-regulation of chemokines such as IL-8, and a down

regulation of SLPI, an enzyme which protects epithelial cells from serine [63]. SLPI has virucidal effects, and the down-regulation of this enzyme, in combination with the damage caused to the epithelial monolayer by *Trichomonas vaginalis*, could increase the likelihood of infection with sexually transmitted viral pathogens such as HIV and HPV.

There is a growing body of evidence that suggests *Trichomonas vaginalis* infection increases the chance of the acquisition, and transmission of HIV [64]. This is of particular concern as *Trichomonas vaginalis* is especially prevalent in regions where HIV is considered to be endemic, such as Sub-Saharan Africa, where 32 million *Trichomonas vaginalis* infections occur each year. Epidemiological studies have recorded an increase in the risk of HIV-1 acquisition of between 1.52 and 2.74 fold in *Trichomonas vaginalis* positive women in Sub-Saharan African countries. A similarly sized increase in the risk of transmitting HIV to a serodiscordant partner has also been recorded in *Trichomonas vaginalis* positive women in these regions. The fairly recent realization of the impact that *Trichomonas vaginalis* prevalence has on HIV rates has hastened a greater public health response, and it is now recognized that the control of *Trichomonas vaginalis* could have a sizeable impact on the reduction of HIV transmission in these populations.

The exact mechanism by which *Trichomonas vaginalis* infection acts to increase the risk of contracting HIV is currently undetermined [65], although a number of theories have been suggested and tested. *Trichomonas vaginalis* infection instigates a robust mucosal immune response, involving localized inflammation and the recruitment of lymphocytes and macrophages [63]. This increases the number of potential cells for the virus to invade and proliferate in, and would make transmission more likely in a HIV-negative individual. Additionally, in a HIV-positive individual, the increase in cells infected with the virus localized in the genital tract would aid HIV shedding during sexual contact, exposing any partners to a higher level of viral particles, facilitating transmission. HIV positive men with symptomatic urethritis caused by *Trichomonas vaginalis* have been shown to have a higher seminal viral load than those with either *Trichomonas vaginalis* negative, or with an asymptomatic. Those with symptoms of urethritis will necessarily have the greatest level of inflammation, and the greatest levels of CD4 lymphocytes and macrophages, increasing the targets for HIV invasion. Additionally, *Trichomonas vaginalis* causes damage to the urogenital epithelia, facilitating passage of HIV to deeper layers of the epithelium, and enhancing infection [66].

The relationship with *M. hominis* is not the only symbiotic relationship that occurs involving the *Trichomonas vaginalis*. The majority of *Trichomonas vaginalis* strains encountered in human infections are infected with one or more of a family of four double stranded RNA viruses, from the genus Trichomonasvirus (TVV), family totiviridae. The presence of this virus has been shown to increase the virulence of *Trichomonas vaginalis* in a process hypothesised to involve the modulation of parasite gene expression. *Trichomonas vaginalis* borne TVV is also recognized by the host immune system via its interaction with human toll-like receptor 3 (TLR3), which instigates a pro-inflammatory cytokine cascade; a process previously linked to increased susceptibility to epithelial invasion by HIV. The presence of TVV during trichomoniasis can cause up to 30 fold amplification of the immune response, increasing the severity of the infection, and risk of more serious complications such as PID [63]. It has also been demonstrated that this effect is particularly pronounced during simultaneous bacterial vaginosis [63], highlighting that the interaction between the vaginal microbiome, protozoan parasite, associated endosymbiant TVV and human epithelial cells has a large bearing on the immune response and infection severity.

Cellular and Molecular Basis of *Trichomonas vaginalis* Virulence

A number of recent reviews have discussed various aspects of well-characterised and more speculative virulence factors of *Trichomonas vaginalis* [67,68]. *Trichomonas vaginalis* is a flagellated microbial eukaryote known to exist in several cellular forms. The two best characterized forms are the trophozoite, a free swimming, flagellated, pear-like cell, and an amoeboid form, with a pancake shape characterised by an important increase in surface contact; this is rapidly induced upon trophozoite contact in vivo with epithelial cells from the vagina, cervix, urethra, prostate and extracellular matrix (ECM) proteins [69].

Trophozoites are typically considered as the infective form. A third cellular form called pseudocysts can be induced in vitro upon exposure of trophozoites to cold and other stressors. However, the significance of this form during the infection process is currently unknown. Data for the related bovine parasite Tritrichomonas foetus, which leads to various reproductive complications including abortion and sterility, suggest that pseudocysts are highly relevant corresponding to aggressive forms facilitating transmission to, and the initial colonisation of, a new host [69]. Additionally, aggregates of parasites are also known to form. Very little is known concerning the triggers and cellular signalling that orchestrate *Trichomonas vaginalis* differentiations into these different forms [70,71]. Identifying specific molecular markers for the different *Trichomonas vaginalis* cellular forms

and aggregates will be an essential prerequisite to investigate their relevance during the infection process. The draft genome sequence and its annotation represent an invaluable resource to investigate the molecular cell biology of *Trichomonas vaginalis* by providing specific molecular leads and allowing comparative transcriptomics and proteomics investigations [72]. An initial study of the phospho proteome of *Trichomonas vaginalis* trophozoites, amoeba and pseudocysts grown in vitro suggested differential protein phosphorylation profiles, consistent with specific signalling mechanisms occurring in the different cellular forms of the parasite that are induced upon specific environmental triggers [67,73].

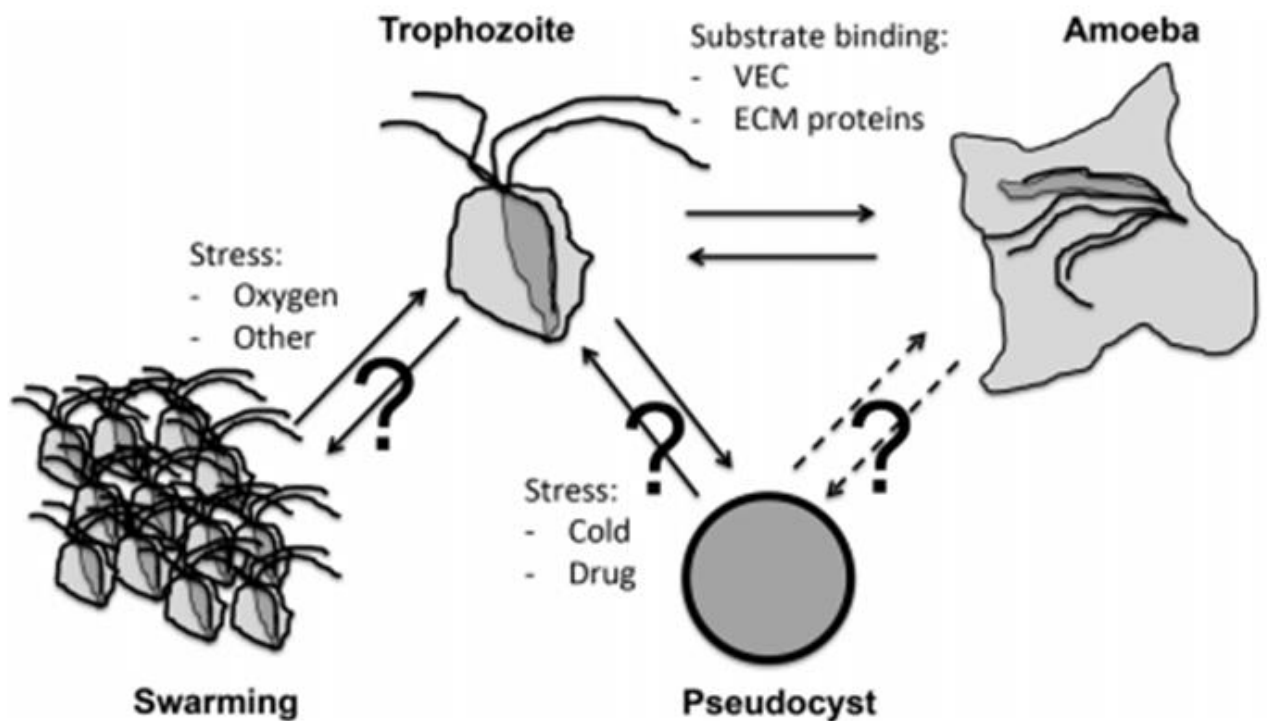


Figure 1: Various Cellular Forms of *Trichomonas vaginalis*.

Source: Hirt, [69]

Clinical isolates of *Trichomonas vaginalis* have been accumulated over the years from many regions of the world. Comparisons of their capacity to bind and kill human (and other species) cell lines in vitro have demonstrated important variations between *Trichomonas vaginalis* isolates [74]. Accordingly, these capacities are considered important virulent traits for *Trichomonas vaginalis*. One of the currently best-characterised adhesins mediating parasite binding to host tissue are *Trichomonas vaginalis* lipoglycans (TvLG), the most abundant surface molecules of the parasite [72,68]. Investigating TvLG also led to the

identification of galectin-1, the only identified human receptor for *Trichomonas vaginalis* so far. TvLGs are also known to modulate inflammatory responses of epithelial cells and macrophages. A proteomics survey of *Trichomonas vaginalis* surface proteins identified a total of 411 proteins, confirming a number of in silico-predicted surface proteins, and also a host of novel and important candidate virulent factors [68]. By contrasting strains with low versus high level of adhesion to vaginal epithelial cells (VECs) in vitro, proteins were shown to be more abundant on the cell surface of the highly adhering strains. These include proteins annotated as hypotheticals—which have no sequence similarity to any other proteins in protein databases. A high level of expression of two of these hypothetical proteins increased the binding to VECs of a poorly binding *Trichomonas vaginalis* strain. Other novel candidate cell surface virulence factors identified in this proteomics survey included three tetraspanins, which are membrane proteins involved in signalling modulating adhesion, motility and tissue invasion in other systems; all these are key processes underlying *Trichomonas vaginalis* pathobiology [75]. The characterisation of one *Trichomonas vaginalis* tetraspanin demonstrated that its expression and cellular localisation was modulated upon TV binding to VEC, and that it plays a role in regulating migration of the parasite through a surrogate ECM gel, strongly supporting tetraspanins as important *Trichomonas vaginalis* virulence factors [68].

Related proteomics studies on *Trichomonas vaginalis* are reviewed elsewhere. During the infection process, *Trichomonas vaginalis* actively phagocytoses human cells, bacteria and fungi to obtain nutrients. Similarly, receptor-mediated endocytosis by *Trichomonas vaginalis* is also considered important in order to internalize nutrients and iron, and to neutralize host defense proteins. However, there are currently no functionally characterized *Trichomonas vaginalis* genes encoding surface proteins mediating the specific binding process underlying phagocytosis or endocytosis. Bioinformatic analyses of candidate trans-membrane proteins have identified a number of cytoplasmic tails possessing classic signals for endocytosis, some of which were supported by proteomics data [69,76]. In silico identification of candidate genes regulating membrane trafficking have also identified a surprisingly large repertoire of proteins, with some gene families unexpectedly larger than those encoding human homologues (eg, ~300 TvRab vs ~70 HsRab GTPases), further suggesting that phagocytosis and endocytosis are important processes for the parasite and represent promising targets for interfering with parasite virulence [76].

Risk Factors Associated with Trichomoniasis

One million new cases of trichomoniasis are estimated each year, according to the American Sexual Health Association (ASHA) and the CDC Trusted Source.

Several studies have identified risk factors for *Trichomonas vaginalis* infection in women. Risk factors for adolescent girls and women attending Sexually Transmitted Infection clinics include having sex without a condom, ethnicity (more prevalent within the black race group), multiple sexual partners, greater years of sexual activity, history of STIs and previous infection with *Trichomonas vaginalis*. Studies conducted by Abbai *et al.* [78] in women from KwaZulu-Natal, South Africa, found that women at the age of 25 years and younger were at a higher risk of acquiring STIs. Reasons related to younger women being more at risk for infection included behavioural and biological factors. Abbai *et al.* [78] also found that women who were previously diagnosed with an STI have a much greater risk for future infection. Other risk factors for acquiring infection included having a lower level of education. A study conducted by Eshete *et al.* [79] in pregnant women from Ethiopia showed that educational status did play a critical role in respect to the increased number of *Trichomonas vaginalis* infections. Mabaso *et al.* [80] found that abnormal vaginal discharge was associated with infection. However, it is important to note that abnormal vaginal discharge would not be considered a risk factor for *Trichomonas vaginalis* infection; rather it is a symptom of infection and is therefore associated with infection. Women with *Trichomonas vaginalis* infections should be counseled on the use of condoms and the risk of new infections as a result of behavioural practices.

Trichomoniasis is more common in women than in men, and 2.3 million Trusted Source women who acquire it are between the ages of 14 and 49 [81]. It's more common among older people and especially in those with vaginas. One study showed that the most positive cases occurred in the over 50 age group.

Impacts of Trichomoniasis on Quality of Life

Trichomonas vaginalis infection can have a profound impact on women's quality of life, affecting physical health, sexual function, reproductive outcomes, mental well-being, and social relationships. The stigma associated with STIs, coupled with the often asymptomatic nature of trichomoniasis, can lead to delayed diagnosis, untreated infection, and ongoing transmission within communities. Psychiatric disorders, also called mental disorders, are defined as clinically significant behavioral or psychological syndromes, with a

high level of individual distress, anxiety and premature mortality [82]. In the USA, the regional disease burden attributable to mental disorders, neurological disorders, substance use disorders and self-harm comprises 19% of total disability-adjusted life-years and 34% of total years lived with disability in 2015. Mental health problems thereby represent important public health challenges worldwide.

Numerous studies have also shown a positive association between *Trichomonas vaginalis* infection and HIV acquisition. *Trichomonas vaginalis* increases the risk of acquiring HIV by an estimated two-fold. As revealed by Davis, *et al.* [83], the biological reasons for *Trichomonas vaginalis* increasing HIV acquisition amongst women could be because of two reasons:

(1) The accumulation of both macrophages and cluster of differentiation 4 (CD4) lymphocytes, which are HIV target cells.

(2) The disruption of the vaginal epithelial barrier enabling the movement of HIV into the laminae propriae.

The high prevalence of *Trichomonas vaginalis* amongst women may be associated with a higher incidence of HIV globally. *Trichomonas vaginalis* infection is also associated with increased HIV transmission. Because *Trichomonas vaginalis* infection is asymptomatic in the majority of cases and often remains untreated, this infection can be easily transmitted [84]. Trichomoniasis has been associated with health complications such as adverse pregnancy outcomes, PID, neoplasia⁵⁸ and co-infection with other infections such as HIV, bacterial vaginosis (BV) and high-risk (HR) human papillomavirus (HPV)-16 genotype [83]. Adverse pregnancy outcomes include preterm delivery, low birth weight, neonatal morbidity and mortality. *Trichomonas vaginalis* infection can be acquired in new-born infants during birth. It has been reported that approximately 25 million pregnant women have trichomoniasis⁶⁶ and 2% – 17% of female infants acquire *Trichomonas vaginalis* infection through direct vulvo-vaginal infection. Africa *Trichomonas vaginalis* has been associated with increased genital shedding of HIV.

A past study found a high prevalence of *Trichomonas vaginalis* amongst HIV sero-discordant African couples [85]. A population-based survey undertaken in rural and peri-urban KwaZulu-Natal, South Africa, reported a co-infection rate of 18.1% for *Trichomonas vaginalis* and HIV in women. A high prevalence of *T. vaginalis* (20%) in a population of HIV-infected pregnant women seeking antenatal care at public health centres in South

Africa was reported. In a cohort of South African women attending primary health care facilities, *Trichomonas vaginalis* was shown to be significantly associated with an HIV-positive status. According to that study, *Trichomonas vaginalis* infection was present in almost 25% of HIV-infected women. In women with trichomoniasis, there is a risk of co-infection with BV (Mabaso & Abbai, 2012). A study conducted by Abbai *et al.* [86] in South African women showed a significant association between baseline BV infections and incident *Trichomonas vaginalis* infections.

Cervical cancer is the most common cause of cancer-related deaths in young women from sub-Saharan Africa. Genital HPV infection, one of the common viral STIs, has been linked to cervical cancer in women. Genital HPV genotypes are classified into either 'HR' or 'low-risk' (LR). It is suggested that *Trichomonas vaginalis* infection might be associated with an increased risk of cervical cancer, and a history of *Trichomonas vaginalis* infection has been shown to be a risk factor for HPV infection. In a population of South African women, *Trichomonas vaginalis* was shown to be prevalent in women diagnosed with cervical intra-epithelial neoplasia (CIN). A study conducted by Lazenby *et al.* [87] in a population of Tanzanian women reported that *Trichomonas vaginalis* was associated with an increased risk of HR HPV. Women with *Trichomonas vaginalis* were 6.5 times more likely to have HPV type 16 when compared with women without *Trichomonas vaginalis*.

Pelvic inflammatory disease is the inflammation of the upper genital tract structures caused by ascension of microbes from the lower genital tract. Approximately half of PID cases are attributable to gonorrhoea and chlamydia, whilst the remainders are of unknown aetiology. A study conducted amongst South African women found a strong association between PID and *Trichomonas vaginalis* infection. In that study, women with trichomoniasis had a significantly higher risk of PID when compared with women without infection. In addition, this association was exacerbated in the presence of HIV infection. Despite the estimated large burden of *Trichomonas vaginalis* infection in the African region, data on clinical outcomes associated with this infection are limited [85].

WHO Responses on Trichomoniasis

The WHO Global health sector strategies on HIV, viral hepatitis and STIs 2022–2030 aims for a 50% reduction in new cases of trichomoniasis by 2030. WHO collaborates with countries and partners to enhance people-centered STI case management methods,

promote suitable treatment recommendations, and implement effective testing and partner services strategies [88].

WHO also supports the development of accessible and affordable high-quality diagnostics and treatment options, as well as advancements in vaccine development. Additionally, WHO focuses on improving country and global-level monitoring of new infections. As part of its efforts, WHO is updating recommendations for the treatment of *Trichomonas vaginalis*. Although antimicrobial resistance in *Trichomonas vaginalis* is not widespread, WHO closely monitors patterns of potential antimicrobial resistance of this pathogen to inform treatment recommendations and national policies.

Sampling Methods on *Trichomonas vaginalis*

1. Simple Random Sampling

Some studies use simple random sampling to ensure each individual in the population has an equal chance of being selected. This is common in large epidemiological studies that aim to assess the prevalence of *Trichomonas vaginalis* across broad populations. For example, Smith *et al.* [89] conducted a population-based study using random sampling to investigate the prevalence of *Trichomonas vaginalis* in urban women attending health clinics in Nigeria.

2. Stratified Sampling

Stratified sampling is often used to ensure that subgroups within a population (such as age or socioeconomic status) are proportionally represented. For example, a study by Garcia and Roberts [90] on the prevalence of *Trichomonas vaginalis* among women in different age groups used stratified sampling to ensure that women aged 18–45 was adequately represented. This method allowed for better understanding of how *Trichomonas vaginalis* prevalence varied across different demographics.

3. Convenience Sampling

In some clinical studies, convenience sampling is commonly used due to ease of access to participants. This method was employed by Johnson *et al.* [91] in a study that focused on patients attending reproductive health clinics. Although this method is cost-effective and practical, it may introduce bias because the sample may not represent the broader population.

4. Purposive Sampling

Purposive sampling is often used when researchers are interested in specific characteristics or outcomes within a population. For example, Nguyen *et al.* [92] selected women with a history of recurrent *Trichomonas vaginalis* infections to assess the effectiveness of new treatment protocols. This method allowed the researchers to focus on a high-risk population.

5. Snowball Sampling

Snowball sampling is typically used for reaching hard-to-access populations, such as sex workers or those with limited access to healthcare services. For example, in a study by Davis *et al.* [93], snowball sampling was used to identify *Trichomonas vaginalis* infections among sex workers in low-resource settings. This method helped reach participants who might otherwise have been missed in more traditional sampling approaches.

According to research conducted as a cross sectional study by Rezaeian *et al.* [94] from May 2008 to March 2009, 500 vaginal discharge samples were obtained from women attended to sexual transmitted disease clinic at Mirzakuchak Khan Hospital in Tehran, Iran. Informed consent and questionnaire from collecting demographic data, sexual history (number of sexual partners) and clinical symptoms were obtained from all participants. Two vaginal specimens were collected with sterile swabs. The first swab was inoculated in liquid phase of Dorse culture medium at the bedside, which was considered as our diagnostic gold standard. The second swab was applied to glass slide with a drop of Ringer solution for microscopic wet mount examination with magnification of $\times 400$ and 50 fields was examined. The culture mediums were transferred to the Parasitological laboratory, School of Public Health, Tehran University of Medical Sciences and incubated at 37°C for 72 hours. The cultures were examined with light microscopy every day until they turned positive. Positive cultures were defined as detection of motile *T. vaginalis*.

Table 2: Prevalence of *Trichomonas vaginalis* in Various Populations

Study	Region	Population	Sample Size	Prevalence (%)	Sampling Method
Miller <i>et al.</i> (2019)	USA (Urban)	Women attending health clinics	600	8.3%	Random Sampling
Roberts <i>et al.</i> (2020)	Nigeria (Rural)	Pregnant women	350	12.5%	Stratified Sampling
Johnson <i>et al.</i> (2018)	South Africa	Women at reproductive health clinics	420	16.7%	Convenience Sampling

Study	Region	Population	Sample Size	Prevalence (%)	Sampling Method
Davis <i>et al.</i> (2021)	Uganda	Sex workers	150	23.2%	Snowball Sampling
Smith <i>et al.</i> (2017)	India	General population female	300	9.4%	Purposive Sampling

Source: (Miller et al. [95]; Roberts et al. [96]; Johnson et al. [91]; Davis et al. [97]; Smith et al. [98])

This table shows the prevalence of *Trichomonas vaginalis* across different populations and regions. The variations in prevalence rates can be attributed to differences in population, geography, and sampling methods.

Importance of Examining *Trichomonas vaginalis* in a Specific Investigated Area

1. Public Health Significance

Trichomonas vaginalis is a sexually transmitted infection (STI) that can lead to significant health issues, including increased susceptibility to HIV and other STIs, pelvic inflammatory disease (PID), adverse pregnancy outcomes, and infertility. By examining its prevalence, public health officials can better understand the scope of the issue in a particular area and develop strategies to reduce transmission. It is also a common sexually transmitted infection (STI) globally, but its impact can vary significantly by region. Understanding its prevalence in a specific area is crucial for determining its burden on public health, especially as it has been associated with adverse pregnancy outcomes, increased risk of acquiring other STIs like HIV, and pelvic inflammatory disease [99]. Examining its prevalence helps in crafting local STI prevention and treatment programs tailored to the needs of the community.

2. Epidemiological Knowledge and Insights

In many regions, *Trichomonas vaginalis* might be underdiagnosed because it is often asymptomatic in men and many women. Investigating its presence helps provide a clearer epidemiological picture, especially in areas where there may be limited awareness or routine screening for this infection. Conducting local investigations into *T. vaginalis* provides valuable epidemiological data about the disease burden in the area. Regions with limited access to routine STI screening might have higher prevalence due to underreporting [100].

Knowing its prevalence allows healthcare providers to assess infection patterns, which are critical for regional health policies and interventions.

3. Targeted Health Interventions

If *T. vaginalis* is common in the investigated area, this data can be used to inform targeted interventions like education campaigns, screenings, and treatments. Without region-specific data, healthcare systems might not prioritize this infection, leaving vulnerable populations untreated. Identifying the presence of *T. vaginalis* in an area helps in developing targeted health interventions. This could include public awareness campaigns, routine screenings in high-risk populations, or preventive education in communities with high infection rates [101]. Targeted interventions reduce the overall burden of STIs by focusing efforts where they are most needed.

4. Impact on Reproductive Health

Since *T. vaginalis* has been linked to adverse reproductive health outcomes such as premature birth, low birth weight, and increased risk of cervical cancer examining the prevalence can help improve overall maternal health care in the region, particularly in settings where access to reproductive health services is limited. In areas where *T. vaginalis* is prevalent, women may experience adverse reproductive health outcomes, such as preterm labor, low birth weight, and increased susceptibility to cervical cancer [102]. Early detection through routine examination helps mitigate these risks, improving maternal and child health outcomes.

5. Monitoring Antibiotic Resistance

There is growing concern about antibiotic resistance in *T. vaginalis*, particularly to drugs like metronidazole. Regular testing and monitoring in an area can help detect potential resistance early, allowing for the adjustment of treatment protocols. There is an increasing concern over metronidazole-resistant strains of *T. vaginalis*. By monitoring infections in different regions, researchers can track the emergence of antibiotic resistance and adjust treatment protocols accordingly [56]. Examining the local population is critical for detecting early signs of treatment failure.

6. Social and Behavioral Insights

Investigating *T. vaginalis* provides a window into local sexual health behaviors and cultural factors that may influence the spread of the infection. This can inform broader behavioral health programs aimed at reducing STI transmission.

IS *Trichomonas vaginalis* a Common Parasite in an Area or Not?

1. Establishing Local Epidemiology and Parasitic Infection Patterns

Determining whether *T. vaginalis* is a common parasite in the area helps establish a baseline for local infection rates and local epidemiology of STIs. This is essential for understanding the overall disease ecology of the region [103]. In some areas, *T. vaginalis* might be the leading STI, while in others it could be outpaced by infections like chlamydia, gonorrhea, syphilis [104] or HIV. Understanding what is prevalent helps allocate resources efficiently.

2. Resource Allocation

If *T. vaginalis* is not common in the area, healthcare providers may prioritize other prevalent infections or parasites, such as malaria, Giardia, or Entamoeba histolytica [105]. Understanding the prevalence of *T. vaginalis* compared to other common parasites helps ensure that healthcare resources are allocated efficiently.

3. Comparison with Other Parasites

If *T. vaginalis* is not commonly found, it may be worthwhile to investigate other common parasites or infections in the area. For example, in some regions, parasitic infections like Giardia or Entamoeba histolytica may be more prevalent and require attention. Knowing whether *T. vaginalis* is a dominant issue can help focus health interventions on the correct pathogens. This is especially important in resource-limited areas where healthcare services may be stretched thin.

3. Detection of Co-Infections with Other STIs

Research into *T. vaginalis* can also reveal the co-infection dynamics in the area. Studies have shown that women with *T. vaginalis* infections are often co-infected with other STIs such as chlamydia or gonorrhea [106]. Testing for *T. vaginalis* can therefore act as a

screening marker for detecting co-infections in the population, providing an opportunity for broader sexual health interventions

4. Environmental, Behavioral and Sociocultural Factors

If *T. vaginalis* is common in the area, this may offer insights into local sexual practices, cultural norms, and healthcare-seeking behaviors. Such findings can help inform educational campaigns and behavioral change strategies aimed at reducing risky sexual behavior and improving STI prevention efforts [107]. Prevalence rates of *T. vaginalis* and other parasitic infections can be influenced by local environmental and social factors, such as sanitation, water quality, healthcare access, and cultural practices. Studying these trends can help improve the general health infrastructure in the area, benefiting a broader spectrum of healthcare needs.

4. Healthcare Prioritization

If *T. vaginalis* is found to be rare, healthcare providers might focus on other health issues that pose a more significant threat. On the other hand, if it is common, it could warrant more screening programs and specialized care in reproductive health clinics.

5. Global Health Comparisons

Investigating whether *T. vaginalis* is a common parasite in an area contributes to global epidemiological databases, which allow for comparisons across regions. This facilitates global health policies aimed at STI control and helps identify regions in need of increased healthcare support [108].

Conclusion

Trichomonas vaginalis has significant negative impacts on women's quality of life, primarily due to its association with various reproductive health issues and broader public health concerns. The infection can lead to serious complications such as increased susceptibility to HIV, pelvic inflammatory disease (PID), and adverse pregnancy outcomes, including premature birth and low birth weight. These conditions can severely affect a woman's reproductive health and overall well-being. The social stigma associated with sexually transmitted infections (STIs) further affects women's emotional and mental health, potentially leading to anxiety, shame, and reluctance to seek treatment. The asymptomatic nature of the infection in many cases complicates early detection and treatment, increasing

the risk of long-term health issues. Moreover, in regions with limited healthcare access, the burden of *T. vaginalis* can be exacerbated by delayed diagnosis, lack of treatment, and the potential for antimicrobial resistance. These factors underscore the importance of targeted health interventions, routine screenings, and effective education programs to reduce the prevalence and improve the quality of life for affected women. Addressing *Trichomonas vaginalis* is crucial for enhancing women's reproductive health and overall quality of life, especially in resource-limited settings.

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