VOLUME - XV
ISSUE - LXXXV
JAN/FEB 2018

The Crux

BIMONTHLY FORUM FOR THE LABORATORIANS

CONTENTS

Editorial

Trichomoniasis (**trich**) is an infectious disease caused by the parasite *Trichomonas vaginalis*. About 70% of women and men do not have symptoms when infected. When symptoms do occur they typically begin 5 to 28 days after exposure. Symptoms can include itching in the genital area, a bad smelling thin vaginal discharge, burning with urination, and pain with sex. Having trichomoniasis increases the risk of getting HIV/AIDS. It may also cause complications during pregnancy.

Trichomoniasis is a sexually transmitted infection (STI) which is most often spread through vaginal, oral, or anal sex. It can also spread through genital touching. People who are infected may spread the disease even when symptoms are not present. Diagnosis is by finding the parasite in the vaginal fluid using a microscope, culturing the vagina or urine, or testing for the parasite's DNA. If present other sexually transmitted infections should be tested for.

Methods of prevention include not having sex, using condoms, not douching, and being tested for STIs before having sex with a new partner. Trichomoniasis can be cured with antibiotics, either metronidazole or tinidazole. Sexual partners should also be treated. About 20% of people get infected again within three months of treatment.

There were about 122 million new cases of trichomoniasis in 2015. It occurs more often in women than men. *Trichomonas vaginalis* was first identified in 1836 by Alfred Donné. It was first recognized as causing this disease in 1916. The **"DISEASE DIAGNOSIS"** segment delves deep into clinic-diagnostic aspects of this very entity.

Papanicolaou stain (also **Papanicolaou's stain** and **Pap stain**) is a multichromatic staining cytological technique developed by George Papanikolaou, the father of cytopathology.

Pap staining is used to differentiate cells in smear preparations of various bodily secretions; the specimens can be gynecological smears (Pap smears), sputum, brushings, washings, urine, cerebrospinal fluid, abdominal fluid, pleural fluid, synovial fluid, seminal fluid, fine needle aspiration material, tumor touch samples, or other materials containing cells.[1]

Pap staining is a very reliable technique. As such, it is used for cervical cancer screening in gynecology. The entire procedure is known as Pap smear. **"INTERPRETATION"** and **"TROUBLE SHOOTING"** have been combined in this issue to keep continuity in sequence.

Fun and flare is all there. Flip over please!

DISEASE DIAGNOSIS

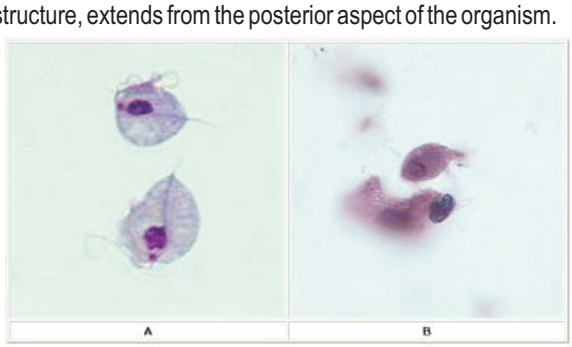
TRICHMONIASIS

Background

Trichomoniasis is a sexually transmitted infection (STI) caused by the motile parasitic protozoan *Trichomonas vaginalis*. It is one of the most common STIs, both in the Western and developing world. The high prevalence of *T vaginalis* infection worldwide and the frequency of coinfection with other STIs make trichomoniasis a compelling public health concern. Notably, research has shown that infection with *T vaginalis* increases the risk of HIV transmission in both men and women. Trichomoniasis is also associated with adverse pregnancy outcomes, infertility, postoperative infections, and cervical neoplasia. Humans are the only known host of *T vaginalis*. Transmission occurs predominantly via sexual intercourse. The organism is most commonly isolated from vaginal secretions in women and urethral secretions in men. It has not been isolated from oral sites, and rectal prevalence appears to be low in men who have sex with men. Women with trichomoniasis may be asymptomatic or may experience various symptoms, including a frothy yellow-green vaginal discharge and vulvar irritation. Men with trichomoniasis may experience nongonococcal urethritis but are frequently asymptomatic. Trichomoniasis is thought to be widely underdiagnosed due to a variety of factors, including a lack of routine testing, the low sensitivity of a commonly used diagnostic technique (wet mount microscopy), and nonspecific symptomatology. Self-diagnosis and self-treatment or diagnosis by practitioners without adequate laboratory testing may also contribute to misdiagnosis. Testing is recommended for *T vaginalis* in all women seeking care for vaginal discharge and screening for *T vaginalis* in women at high risk of STI. Sex partners of infected women should also be treated. Both patient and partner should abstain from sex until pharmacological treatment has been completed and they have no symptoms. Infected women who are sexually active have a high rate of reinfection; thus, rescreening at 3 months post treatment should be considered. Currently, no data are available on rescreening men. Oral metronidazole (Flagyl) remains the treatment of choice for trichomoniasis. In cases in which the first-line agent is ineffective, other nitroimidazoles or high doses of metronidazole may be used. Topical metronidazole and other antimicrobials are not efficacious and should not be used to treat trichomoniasis.

Pathophysiology

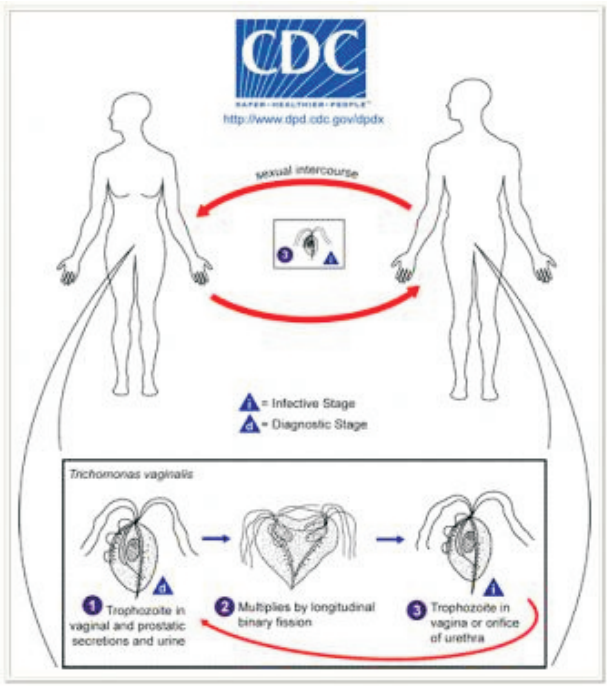
T vaginalis is approximately the size of a white blood cell (WBC)—about 10-20 µm long and 2-14 µm wide—though its size may vary with physical conditions (see the image below). It has 4 flagella projecting from the anterior portion of the cell and 1 flagellum extending backward to the middle of the organism, forming an undulating membrane. An axostyle, a rigid structure, extends from the posterior aspect of the organism.



Trichomonas vaginalis. (A) Two trophozoites of T vaginalis obtained from in vitro culture, stained with Giemsa. (B) Trophozoite of T vaginalis in vaginal smear, stained with Giemsa.

View Media Gallery

In women, *T vaginalis* is isolated from the vagina, cervix, urethra, bladder, and Bartholin and Skene glands. In men, the organism is found in the anterior urethra, external genitalia, prostate, epididymis, and semen (see the image below). It resides both in the lumen and on the mucosal surfaces of the urogenital tract. The flagella allow the trophozoite to move around vaginal and urethral tissues.



Life cycle of Trichomonas vaginalis. T vaginalis trophozoite resides in female lower genital tract and in male urethra and prostate (1), where it replicates by binary fission (2). The parasite does not appear to have a cyst form and does not survive well in the external environment. T vaginalis is transmitted among humans, the only known host, primarily via sexual intercourse.

During infection with *T vaginalis,* jerky motile trichomonads may be observed on wet mount microscopy. *T vaginalis* destroys epithelial cells by direct cell contact and by release of cytotoxic substances. It also binds to host plasma proteins, thereby preventing recognition by the alternative complement pathway and by host proteinases. During infection, the vaginal pH increases, as does the number of polymorphonuclear leukocytes (PMNs). PMNs, a type of white blood cell, are the predominant host defense mechanism. These cells respond to chemotactic substances released by trichomonads. There is also evidence that lymphocyte priming occurs, as shown by the presence of antigen-specific peripheral blood mononuclear cells. An antibody response has been detected both locally and in serum. However, infection produces an immunity that is only partially protective, at best. Despite the interaction the human immune system has with *T vaginalis,* there is little evidence that a healthy immune system prevents infection. One study showed no association between trichomoniasis and the use of protease inhibitors or immune status in HIV-infected women. Another study showed that HIV seropositivity did not alter the rate of infection in males. Symptoms of trichomoniasis typically occur after an incubation

period of 4-28 days. Infection may persist for long periods in women but generally persists for fewer than 10 days in males. Anecdotal evidence suggests that asymptomatic infection may persist for months or even years in women.

Etiology

The risk of acquiring *T vaginalis* infection is based on the type of sexual activity. Women who engage in higher-risk sexual activity are at a greater risk of infection. Risk factors for *T vaginalis* infection include:

- New or multiple partners
- A history of STIs
- Current STIs
- Sexual contact with an infected partner
- Exchanging sex for money or drugs
- Using injection drugs
- Not using barrier contraception (eg, because of oral contraceptives)

In a study that considered risk factors for prevalent trichomoniasis, drug use in the preceding 30 days was the one most strongly associated with infection and with incident infection (new infection observed during the study). The most significant risk factor was sexual activity in the preceding 30 days (with 1 or more partners). Women with 1 or more sexual partners in the preceding 30 days were 4 times more likely to have *T vaginalis* infection.

Epidemiology

Western World

Trichomoniasis is one of the most common STIs in the USA, with a prevalence estimated at 8 million cases annually. Exact numbers are difficult to obtain because the infection is not nationally reportable and many infections are asymptomatic. Prevalence is also thought to be underestimated due to the low sensitivity of diagnostic tests, particularly the commonly used wet mount technique. Research done among high-risk populations shows that the prevalence varies widely. The prevalence of *T vaginalis* infection at STI clinics ranges from 15% to 54%. The reported prevalence from a different study done among inner-city STI clinics approached 25%. In 2 samples of female prison inmates, the prevalence was 31.2-46.9%. In men, trichomoniasis accounts for 10-21% of urethritis cases not attributable to gonorrheal or chlamydial infection. Multiple studies have found that *T vaginalis* infection is less prevalent in men than in women.

International statistics

Estimates of the worldwide prevalence of trichomoniasis range from 170-180 million cases annually. The World Health Organization estimates the worldwide incidence of trichomonas infection at over 170 million cases annually. The incidence of trichomoniasis in Europe is similar to that in the United States. In Africa, the prevalence of trichomoniasis may be much higher. The prevalence of vaginal *T vaginalis* infection was estimated to be 11-25% among African study populations.

Age-related demographics

Trichomoniasis is an STI. As such, it is typically found in sexually active adolescents and adults. In female adolescents, trichomoniasis is more common than gonorrhea; this is particularly disconcerting in that it increases susceptibility to other infections. Vertical transmission of *T vaginalis* during birth is possible and may persist up to 1 year. From 2-17% of female offspring of infected women acquire infection. Unlike other STIs, trichomoniasis generally becomes more common with age and lifetime number of sexual partners. The National Longitudinal Study of Adolescent Health Study found a prevalence of 2.3% among adolescents aged 18-24 years and 4% among adults 25 years and older. A prevalence of 3.1% in females aged 14-49 years was observed based on a nationally representative sample of women in the National Health and Nutrition Examination Survey (NHANES) 2001-2004 study. In a study of men attending an STI clinic in Denver, the prevalence of trichomonal infection was 0.8% in men younger than 30 years and 5.1% in men 30 years and older. The increase in prevalence was thought to be due to age-related enlargement of the prostate gland.

Sex-related demographics

Symptomatic trichomoniasis is more common in women than in men. Trichomoniasis infection in men tends to be less clinically apparent. However, women can also frequently be asymptomatic carriers. The NHANES 2001-2004 study conducted on a nationally representative sample of women aged 14-49 years found that 85% of women found to have trichomoniasis reported no symptoms. The reported incidence of trichomoniasis among men in various populations has ranged from 2.8-17%. This incidence may be underestimated, depending on the method of detection and the site of specimen collection. The use of multiple sites in the genitourinary tract (urine, urethral swab, and semen) in male patients has been shown to increase sensitivity. In one study, *T vaginalis* was detected in 72% of male sexual partners of women with trichomoniasis. Of these, 77% patients were asymptomatic.

Race-related demographics

In the National Longitudinal Study of Adolescent Health Study, significant differences in the prevalence of trichomoniasis among adolescents were noted by race: white, 1.2%; Asian, 1.8%; Latino, 2.1%; Native American, 4.1%; and African American, 6.9%. Considerable differences were also observed in the national NHANES 2001-2004 study conducted among women ages 14-49: non-Hispanic whites, 1.2%; Mexican Americans, 1.5%; and non-Hispanic blacks, 13.5%. Evidence suggests that *T vaginalis* infection likely increases HIV transmission. Thus, the observed higher prevalence of *T vaginalis* infection among African American women is cause for great concern. Control of *T vaginalis* may represent an important means of slowing HIV transmission, particularly among African Americans.

Prognosis

Recommended metronidazole therapy regimens have produced a 90-95% cure rate in randomized clinical trials. The recommended tinidazole regimens have produced cure rates of 86-100%. Cure rates may be even higher with concurrent treatment of a patient's sexual partners. Recurrent infections are common in sexually active patients. One study found that 17% of sexually active patients with *T vaginalis* infection were reinfected at 3-month follow-up. *T vaginalis* infection is strongly associated with the presence of other STIs, including gonorrhea, chlamydia, and sexually transmitted viruses. *T vaginalis* infection increases the susceptibility to other viruses, including herpes, human papillomavirus (HPV), and HIV. Persons with trichomoniasis are twice as likely to develop HIV infection as the general population. There are 2 explanations for the association between *T vaginalis* and HIV, as follows:

- Disruption of the epithelial monolayer leads to increased passage of the HIV virus
- *T vaginalis* induces immune activation, specifically lymphocyte activation and replication and cytokine production, leading to increased viral replication in HIV-infected cells

Pregnant women with *T vaginalis* infection are more likely than uninfected women to deliver preterm or to have other adverse pregnancy outcomes, including low birth weight, premature rupture of membranes, and intrauterine infection. Respiratory or genital infection in the newborn may also occur. *T vaginalis* infection may also increase the vertical transmission of HIV due to a disruption of the vaginal mucosa. One study reported a higher risk of pelvic inflammatory disease

(PID) in women with trichomoniasis. Other studies have reported a 1.9-fold risk of tubal infertility in women with trichomoniasis. Trichomoniasis may also play a role in cervical neoplasia and postoperative infections.

Patient Education

Education concerning STI treatment and prevention is vital (see Prevention). Because *T vaginalis* infection is strongly associated with the presence of other STIs (gonorrhea, chlamydia, and sexually transmitted viruses such as HIV), providers should provide appropriate counseling, testing, and treatment. Upon diagnosis of trichomoniasis, healthcare providers should discuss treatment, including the adverse effects and interactions encountered with metronidazole and other nitroimidazole drugs, and should address the treatment of sexual partners. Persons with trichomoniasis who notify partners of their infection help disrupt the transmission of trichomoniasis and other STIs. Providers should also discuss methods of preventing *T vaginalis* reinfection. It may be important to explain that the infection may have been longstanding and not due to a recent sexual encounter. Lastly, the US Centers for Disease Control and Prevention (CDC) advises providers to consider rescreening sexually active women at 3 months after the completion of treatment.

History

Trichomoniasis is typically found in sexually active patients. Transmission occurs predominantly via sexual intercourse. The organism is most commonly isolated from vaginal secretions in women and urethral secretions in men. It has not been isolated from oral sites, and rectal prevalence appears to be low in men who have sex with men. While it is possible to contract trichomoniasis without engaging in sexual intercourse, it is less common. Nearly half of infected females and nearly all infected males are asymptomatic. One third of asymptomatic women become symptomatic within 6 months.

Women

Trichomoniasis symptoms in women range from none to severe pelvic inflammatory disease (PID). Women with trichomoniasis frequently report an abnormal vaginal discharge, which may be purulent, frothy, or bloody. Frothy vaginal discharge, which is thought to be the classic presentation of trichomoniasis, may be observed in only 12% of patients with this infection. Women with trichomoniasis also commonly report abnormal vaginal odor (often described as musty); vulvovaginal itching, burning, or soreness; dyspareunia (pain during sexual intercourse), which is often the major complaint; and dysuria (pain during urination). Patients may also complain of postcoital bleeding and lower abdominal pain. Cervicitis due to trichomoniasis is characterized by 2 major signs: purulent discharge in the endocervical canal and easily induced endocervical bleeding. However, it may also be asymptomatic. *T vaginalis* infection is one of the top 3 causes of vaginitis. Vaginitis is usually characterized by vaginal discharge, which may be accompanied by vulvar itching, irritation, and odor. The two other most common causes of vaginal discharge are anaerobic bacterial overgrowth of normal flora and candidiasis (infection with *Candida albicans*).

Men

Men with trichomoniasis may be divided into the following 3 groups on the basis of their symptoms :

- Asymptomatic carrier state (comprising the majority of patients)
- Mild symptomatic disease
- Acute trichomoniasis

Trichomoniasis symptoms in men range from none to urethritis complicated by prostatitis. Nongonococcal nonchlamydial urethritis is the most common symptom reported by men with trichomoniasis. Symptoms of urethritis include discharge (purulent to mucoid in character), dysuria, and urethral pruritus. Some patients report pain in the urethra, testicular pain, or lower abdominal pain. Most symptomatic infections are intermittent and self-limiting.

Physical Examination

Women

Vaginal discharge is found in 42% of infected women. The discharge is classically described as thin and frothy; however, this is only seen in about 10% of patients. The discharge is often yellow and sometimes is thick enough to be confused with that seen in candidiasis. Abnormal vaginal odor was found in 50% of infected women, and edema or erythema was found in 22-37%. Vaginal pH is often elevated (>4.5). Colpitis macularis, or strawberry cervix, describes a diffuse or patchy macular erythematous lesion of the cervix. This is a specific sign for trichomoniasis but is visible in only 1-2% of cases without the aid of colposcopy; with colposcopy, colpitis macularis is detected in up to 45% of cases. Together, colpitis macularis and frothy vaginal discharge have a specificity of 99%; individually, they have positive predictive values of 90% and 62%, respectively. Lower-abdominal tenderness may be present; however, this is described in fewer than 10% of patients. If this occurs, coexisting salpingitis or an intra-abdominal pathology is possible. Coexisting *Neisseria gonorrhoeae* infection, candidiasis, and bacterial vaginosis are common and may produce a mixed clinical picture. Most of the symptoms described above are not specific for trichomoniasis and can occur in other vaginal or cervical infections. In one study, the clinician's ability to accurately diagnose *Tvaginalis* infection on the basis of physical findings alone had a positive predictive value of only 47%. Relying on physical examination findings alone misses the diagnosis of most patients with trichomoniasis. Definitive diagnosis requires appropriate laboratory testing.

Men

Most men with trichomoniasis have no physical findings. Infrequently, infected men have abnormal penile discharge. However, the discharge usually is only scant and thin. Trichomoniasis in men may be associated with local inflammatory states, including balanitis and balanoposthitis. Physical findings of epididymitis and prostatitis may also occur.

Children

In female newborns, *T vaginalis* acquired during birth may cause vaginal discharge during the first week of life. Respiratory infection of the newborn is also possible. An infected infant may present with fever. Prepubertal children with trichomoniasis may present with symptoms similar to those seen in the adolescent and adult patient. *T vaginalis* infection in prepubertal children is suggestive of sexual abuse.

Complications

In women, vaginitis is the most common manifestation of infection. Other complications include infection of the adnexa, endometrium, and Skene and Bartholin glands. Pelvic inflammatory disease and tubo-ovarian abscess may also occur. Research has shown that infection with *T vaginalis* increases the risk of HIV transmission in both men and women. It is estimated that in women alone, 747 new HIV cases per year are a result of the facilitative effects of *T vaginalis* on the transmission of HIV. Overall, persons with trichomoniasis are twice as likely to develop HIV infection as the general population. Treatment of trichomoniasis has been shown to decrease the rate of viral shedding in HIV patients. In addition to HIV, *T vaginalis* infection also increases the susceptibility to other viruses, including herpes and human papillomavirus (HPV). *T vaginalis* may increase the rate of infection or reactivation of HPV, although it may shorten the duration of infection. An association with cervical intraepithelial neoplasia has also been demonstrated. Trichomoniasis has also been associated with postoperative infections.

An increased risk of posthysterectomy infection, including cuff cellulitis, cuff abscess, and wound infection, has been documented. Rare cases of trichomonal peritonitis have been reported. In pregnant women, *T vaginalis* infection has been associated with an increased risk of low birth weight, preterm delivery, and intrauterine infection. Systemic immune response has been demonstrated in pregnant women infected with *T vaginalis*; a significant increase in granulocyte-macrophage colony-stimulating factor (GM-CSF) and C-reactive protein (CRP) was noted. Neonatal trichomoniasis has been described. Respiratory or genital infection in the newborn may also occur. In men, when symptoms occur, *T vaginalis* infection usually manifests as urethritis. As many as 11% of nongonococcal urethritis cases in men are caused by *T vaginalis*. Complications of untreated trichomoniasis in men include prostatitis, epididymitis, urethral stricture disease, and infertility, potentially resulting from decreased sperm motility and viability. Symptomatic men with comorbid *T vaginalis* and HIV infections have been found to have significantly higher numbers of HIV RNA particles in their seminal fluid.

Diagnostic Considerations

Prompt trichomoniasis diagnosis is important for eliminating infection in the patient and sexual partners and avoiding complications (see Complications).

Differential Diagnoses

- Appendicitis
- Bacterial Vaginosis
- Balantidiasis
- Candidiasis
- Cervicitis
- Chlamydial Genitourinary Infections
- Cystitis, Nonbacterial
- Epididymitis Imaging
- Gonorrhea
- Nonbacterial Prostatitis
- Pelvic Inflammatory Disease
- Urethritis
- Vaginitis

Trichomoniasis Workup

Approach Considerations

Given the poor reliability of history and physical findings, diagnosis of trichomoniasis depends on laboratory testing. According to the CDC, providers should obtain laboratory tests in all women seeking care for vaginal discharge and women at high risk of sexually transmitted infection. Tests for trichomoniasis are quick and can be performed in the medical office. Self-testing has also been proposed but is not currently approved by the US Food and Drug Administration (FDA). The basic office evaluation includes tests to exclude other possible causes of the patient's complaints. Because *T vaginalis* infection is strongly associated with the presence of other STIs, providers should test for other STIs, including gonorrhea, chlamydia, syphilis, HIV infection, hepatitis B, and hepatitis C. In multiple studies, the majority of women with *T vaginalis* infections were also found to have bacterial vaginosis.

Standard Laboratory Studies

Saline wet mount evaluation

In women, vaginal trichomoniasis has historically been diagnosed by wet mount microscopy. Saline wet mount evaluation is performed by placing a small amount of vaginal discharge on a microscope slide and mixing with a few drops of saline solution. The slide is then examined under a microscope at low or medium power (see the video below). The presence of flagellated pyriform protozoa, or trichomonads, indicates a positive test result. These ovoid-shaped parasites are slightly larger than polymorphonuclear leukocytes (PMNs), a type of white blood cell, and may be identified by their ameboid mobility. Trichomonads cause an inflammatory reaction; therefore, a large number of PMNs are usually present and correlate with the severity of infection. Slides must be read immediately after collection. Kingston et al looked at samples that were positive for trichomonads on initial reading and then reevaluated them every 10 minutes. At 10 minutes, 20% of samples became negative; by 30 minutes, 35% were negative; and by 2 hours, 78% had become negative. It is important to note that microscopy has a low sensitivity (estimated at 50-70%) in the detection of *T vaginalis* in vaginal secretions and is not the criterion standard technique for trichomoniasis diagnosis. Because they involve the direct visualization of the trichomonads, wet mounts are more likely to be positive in women with high organism loads. The absence of trichomonads on microscopy does not rule out a diagnosis of vaginal trichomoniasis. Despite their limitations, wet mounts are frequently used, because they are quick, cheap, and easy to perform. The relatively poor sensitivity of saline wet mount evaluation may be increased somewhat by using cervical vaginal lavage. In one study, sensitivity was increased to 74.4% using the cervical vaginal lavage technique versus 54.7% vaginal swab alone. Wet mount microscopy is not an effective test for the diagnosis of trichomoniasis in men. A short downloadable video illustrating this test is available from the Seattle STD/HIV Prevention Training Center.

Standard culture

Culture is the current criterion standard for trichomoniasis diagnosis. Providers should perform *T vaginalis* cultures when the suspicion of trichomoniasis is high but saline wet mount evaluation does not reveal the protozoan. Culture may also be useful as diagnostic screening for high-risk populations. Culture is more sensitive and specific than microscopy. In a study by Wolner-Hanssen et al, 35.6% of trichomoniasis cases were detected by culture and not by wet mount or Papanicolaou (Pap) smear. A swab is put in broth and incubated anaerobically at 37°C. Growth is usually detected within 48 hours, and samples without growth after 7 days are considered negative for trichomoniasis. In addition to improved diagnostic value, an advantage of culture is delayed inoculation. Swab specimens may sit for some time prior to inoculation, allowing for the reading of a wet mount prior to pouch inoculation. Another advantage of culture is that swab specimens may be obtained by the patient (self-obtained specimens), a technique useful with adolescents and in resource-poor settings. Culture has also been demonstrated to be useful in individuals with suspected resistant trichomoniasis. Physicians can determine whether trichomonads are the cause of the vaginitis and can obtain the susceptibility of the strain. Culture is especially important for diagnosing trichomoniasis in men, in whom wet mount preparations are particularly unreliable. Urethral swab, urine, and semen cultures are used to maximize sensitivity. The CDC does not recommend oral and rectal testing, as infection rates at these sites appear to be low. Disadvantages of the culture method include testing time and availability.

InPouch TV Culture System

The InPouch TV Culture System (Biomed, White City, Ore), a combined wet mount and culture kit, is commonly used and readily available. This test kit has a sensitivity of 81-100%. It may detect as little as 1 parasite in the sample. Samples taken during menses are not adversely affected. The clinician inoculates the upper chamber of the pouch with a cotton swab. The pouch can be kept at room temperature for up to 18 hours without significant alteration of sensitivity. In the laboratory, a viewing clamp is placed across the upper chamber and examined under a microscope at a magnification of 100. If no trichomonads are viewed, the

bottom chamber is inoculated by using the medium from the upper chamber. The InPouch is incubated at 37°C and viewed at regular intervals.

Papanicolaou smear

Trichomonads may be viewed on Pap smear, but this test yields low sensitivity and should not be relied on for diagnosis of *T vaginalis* infection. The sensitivity of Pap smear for detecting trichomonads is 40-60%. Specificity approaches 95% in the hands of trained technicians. False-positive results are also common with this technique.

pH testing

Vaginal pH may be determined by touching a swab containing vaginal secretions to pH indicator paper. A normal pH practically excludes the diagnosis of trichomoniasis. A pH greater than 4.5 is usually found with trichomoniasis. However, an elevation in pH is not specific for trichomoniasis. Bacterial vaginosis frequently also elevates vaginal pH.

Whiff test (amine odor test)

Perform the whiff test (amine odor test) by adding several drops of 10% potassium hydroxide to a sample of vaginal discharge. A strong fishy odor is indicative of a positive test result. Such a result may suggest either trichomoniasis or bacterial vaginosis. Thus, the whiff test should not be considered an accurate means of diagnosing trichomoniasis. It is 1 of the 4 parts of the Amsel criteria used to diagnose bacterial vaginosis. The whiff test is now combined with vaginal pH on a single card, the FemExam pH and Amines TestCard. On this card, the pH paper color change and the odor test are replaced with plus or minus signs.

Molecular Techniques for Detecting Antigen, DNA, or RNA

Use System as approved by authorities in your country of usage. The OSOM Trichomonas Rapid Test uses color immunochromatographic "dipstick" technology with murine monoclonal antibodies. Results are read within 10 minutes. Freezing and transportation of specimens do not appreciably alter the test results. In a comparison with a composite reference standard of wet mount microscopy and culture, Huppert et al found the sensitivity of the OSOM test to be 83.3% and the specificity 98.8%. A second study by Huppert et al found a sensitivity of 82% in comparison with a composite reference standard of wet mount, culture, rapid antigen testing, and polymerase chain reaction (PCR). A third study compared the OSOM test to a composite reference standard for which a positive sample was defined as one that was positive by any combination of wet mount, Aptima ATV assay, or OSOM test. The prevalence of infection in the population tested was low, at 2%. The sensitivity was 94.7%, and the specificity was 100%. The Affirm VPIII Microbial Identification Test detects the presence of *Trichomonas, Gardnerella,* and *Candida* species by using direct hybridization technology. Its sensitivity is 90-100%,and the detection threshold is reported to be 5000 trichomonads/mL. Results from the Affirm VPIII test take about 45 minutes. A bulletin on proper preparation and testing of specimens is available from the manufacturer. Specimens for which testing is expected to be delayed for more than 1 hour at ambient temperature or 4 hours with refrigeration should be stored in the Affirm VPIII Ambient Temperature Transport System (ATTS) for up to 72 hours. In a study by Hollman et al, no difference was noted in detection of *T vaginalis* in urine samples compared with vaginal swabs. The APTIMA *Trichomonas vaginalis* ATV Assay (Gen-Probe, San Diego, Calif) uses nucleic acid hybridization technology to detects the presence of *T vaginalis*. Sensitivity is 74-98% and specificity is 87-98%. One study reported decreased sensitivity for tests performed on first-void urine specimens in male patients. The sample is run on a proprietary processing system capable of running about 1000 samples per day. Expected turnaround time is about 1-2 days. Currently, the APTIMA Combo2 assay is FDA-approved for the diagnosis of chlamydia and gonorrhea, so laboratories using this technology may wish to add the *T vaginalis* assay to their existing technology. PCR methods yield a high sensitivity (84%) and specificity (94%). PCR is based on DNA amplification and detection using known primers to *TV* genes. Because no approved PCR tests are available for general use, this approach is limited to research studies. Sensitivities of PCR tests for *T vaginalis* have been reported at 85-100%. Amplicor, an FDA-approved PCR assay for gonorrhea and chlamydia modified to detect *T vaginalis,* was found to have a sensitivity of 88-97% and specificity of 98-99%. Some researchers have suggested that PCR has great diagnostic potential, particularly in men, while others maintain it offers little advantage over culture. In men, performing PCR on urine sediment rather than urethral swabs may improve detection rates. Direct fluorescent antibody (DFA) staining is more sensitive than saline wet mount but less sensitive than culture. DFA allows rapid diagnosis but requires a trained microscopist and a fluorescent microscope.

Histologic Findings

Trichomonads may be observed in a saline wet mount of a vaginal swab or secretion in approximately 60-70% of women with trichomoniasis. Trichomonads are ovoid in shape and approximately the size of a white blood cell (WBC)—about 10-20 µm long and 2-14 µm wide. They are identifiable by their ameboid mobility. A trichomonad has 4 flagella projecting from the anterior portion of the cell and 1 flagellum extending backward to the middle of the organism, forming an undulating membrane. An axostyle, a rigid structure, extends from the posterior aspect of the organism. Because trichomonads cause an inflammatory reaction, a large number of white blood cells are usually present, correlating with the severity of the infection.

Trichomoniasis Treatment & Management

Approach Considerations

Trichomoniasis is not a nationally mandated reported sexually transmitted disease, although other sexually transmitted disease reporting requirements vary by state. Evaluation is typically conducted in the outpatient setting. Treatment should be instituted immediately and, whenever possible, in conjunction with all sexual partners. Patient-delivered partner therapy is a safe and effective means of treating the sexual partners of patients diagnosed with trichomoniasis. Both patient and partner should abstain from sex until pharmacological treatment has been completed and they have no symptoms. Patients undergoing pharmacotherapy should be advised to avoid alcohol consumption during the course of treatment and for an appropriate amount of time after the completion of their medication. Because trichomoniasis is an infection of multiple sites (eg, vaginal epithelium, Skene glands, Bartholin glands, and urethra), systemic treatment is needed. Because of the high rate of coinfection with other sexually transmitted infections (STIs), the healthcare provider should consider empiric treatment of gonorrhea and chlamydia. Patients should also be offered counseling and testing for HIV. In clinical practice, repeat testing is rarely performed unless symptoms do not improve with drug treatment. However, the CDC recommends rescreening at 3 months post therapy for sexually active women, as they have a high rate of reinfection. Currently, no data are available on rescreening men. Inpatient therapy is usually not required but may be indicated when resistance is present and intravenous (IV) therapy is indicated. For patients in whom treatment fails and in whom reinfection is ruled out, consultation with experts from the CDC may be advisable (770-488-4115). Consultation with an infectious diseases specialist, a gynecologist, or both may be helpful.

HIV

Patients who are HIV positive should generally receive the same treatment as those who are HIV negative. The notable exception is that the multiday treatment drug regimen (metronidazole 500 mg twice daily for 7 days) was recently shown to be more effective in treating *T vaginalis* in HIV-positive women than a single-dose treatment (metronidazole 2 g single dose). Thus, the CDC recommends considering the multidose treatment in HIV-positive women with trichomoniasis. The CDC recommends rescreening at 3 months after the completion of therapy for HIV-positive women due to the likelihood of recurrent or persistent infection and the increased risk of HIV transmission with comorbid trichomonal infection.

Pregnancy

Failure to treat trichomoniasis during pregnancy may result in preterm birth, low birth weight, and other adverse fetal outcomes. Accordingly, pregnant women should seek prompt treatment during pregnancy. Routine screening for trichomoniasis in asymptomatic pregnant women is not currently recommended. The CDC recommends that infected symptomatic pregnant women be considered for treatment, as metronidazole has not been definitively shown to be harmful during pregnancy and may prevent transmission to the newborn. Infected asymptomatic pregnant women may wish to defer treatment to after 37 weeks' gestation. Pregnant women should be treated with 2 g metronidazole in a single dose, according to the CDC. The safety of tinidazole in pregnancy is not known. Transmission of trichomoniasis from an infected mother during delivery is rare, but respiratory or genital infection of the newborn is possible. An infected infant may present with fever. In breastfeeding women, the CDC recommends stopping breastfeeding during the course of metronidazole treatment and for 12-24 hours after the last day. For treatment with tinidazole, the CDC recommends stopping breastfeeding for the course of treatment and for 3 days after the last dose.

Pediatric populations

T vaginalis infection in a pediatric patient may suggest child abuse. Young girls may present with vaginal discharge.

Pharmacologic Therapy

5-Nitroimidazole drugs are used for the treatment of trichomoniasis. In the United States, metronidazole and tinidazole are FDA-approved. In a Cochrane review, metronidazole and other nitroimidazoles had comparable efficacy in treating trichomoniasis. Randomized clinical trials comparing single 2-g doses have also shown metronidazole and tinidazole to be equally effective. With recommended dosages, the expected cure rate of trichomoniasis is 95%. Treating the patient's sexual partners to prevent reinfection further improves the cure rate. The mechanism of action is not well understood. Target organisms preferentially reduce the 5-nitro group, and active metabolites likely disrupt the helical structure of the DNA within them, preventing nucleic acid synthesis and eventually leading to cell death. The advantages of single-dose therapy of metronidazole or tinidazole for trichomoniasis are better patient compliance, lower total dose, and, possibly, decreased subsequent candidal vaginitis. For both metronidazole and tinidazole, patients should not consume alcohol during the course of treatment. For those on metronidazole therapy, abstinence should continue for 24 hours after the last dose. For those on tinidazole therapy, abstinence should continue for 72 hours after completion of the medication. Despite the widespread use of nitroimidazoles in the treatment of trichomoniasis, resistance to these drugs is rare and is typically solved by increasing the dose or switching to another nitroimidazole. The CDC has reported incidents of trichomoniasis resistant to metronidazole that were susceptible to tinidazole. When standard treatment regimens fail, a regimen of 2 g of oral metronidazole or tinidazole for 5 days may be considered. Inpatient intravenous (IV) therapy may be indicated when resistance is present. Because trichomoniasis is an infection of multiple sites, systemic (oral) treatment is needed. Topical medications should are not recommended by the CDC, as they are unlikely to reach therapeutic levels. Topical metronidazole and other antimicrobials yield low cure rates (under 50%). Patients allergic to this class of drug should be referred to an allergist for desensitization.

Diet and Activity

Patients should be instructed to avoid alcohol while taking metronidazole, tinidazole, or other nitroimidazole drugs. The interaction of these drugs with alcohol may cause a disulfiramlike reaction. Modifying sexual behavior helps reduce the incidence of infection. Patients should avoid sex until drug therapy is completed and all symptoms have disappeared. Treatment of the patient's partner is crucial for minimizing reinfection. Thereafter, consistent use of condoms and other barrier contraceptives reduces the chance of infection.

Prevention

Abstinence from sexual intercourse prevents trichomoniasis. Limiting the number of sexual partners decreases the risk of trichomoniasis. Male condoms can protect against the transmission of trichomoniasis. Although the efficacy of female condoms is undefined, they may also provide some protection. Diaphragms have been shown to protect against trichomoniasis but should not be used as the primary source of protection against HIV. Spermicides that contain nonoxynol-9 are not recommended for the prevention of sexually transmitted diseases. Frequent use is associated with disruption of the genital epithelium, which may be associated with an increased risk of HIV infection and other sexually transmissible agents.

Long-Term Monitoring

Infected women who are sexually active have a high rate of reinfection and, thus, rescreening at 3 months post treatment should be considered. Because trichomoniasis has a high rate of comorbidity with other STIs, providers should consider empiric treatment of infections that frequently coexist with trichomoniasis. Patients should be advised to follow up on results of other studies performed. If symptoms persist despite pharmacotherapy, patients should follow up with their primary care providers. Persistent treatment failures may require metronidazole susceptibility testing through the CDC. Sexual partners of patients infected with trichomoniasis must be treated to prevent reinfection. Patient and sexual partners should abstain from sexual intercourse until they have both completed therapy and are asymptomatic.

Medication Summary

Oral metronidazole is the treatment of choice and may be administered as either a single 2-g dose or as prolonged therapy with 500 mg twice daily for 7 days. Tinidazole (single 2-g dose) is an FDA-approved alternative to metronidazole that has been shown to be equally effective in clinical trials. opical treatments are not recommended due to inadequate therapeutic levels. Treatment with oral metronidazole has not been shown to have teratogenic effects and may prevent transmission to the infant. The CDC currently recommends that infected symptomatic pregnant females be treated with 2 g metronidazole in a single dose. Infected asymptomatic pregnant women may wish to defer treatment to after 37 weeks' gestation. Drug resistance is rare, despite the prevalent use of nitroimidazole drugs in the treatment of trichomoniasis. Treatment failures may require a higher-dose metronidazole regimen or the use of a different nitroimidazole (eg, tinidazole).

INTERPRETATION ✡ TROUBLESHOOTING

1

•Cytodiagnosis is the diagnosis of disease through the microscopic examination of cells (of human, animal or plant origin) collected by various means.

•In the case of human cytodiagnosis, there are two areas of cytology – gynecological and non-gynecological – in which specimen material is examined for the presence of malignant and premalignant cells, which, through certain procedures, may be classified as:

- •Normal
- •Inflammatory
- •Suspect / Uncertain
- •Malignant

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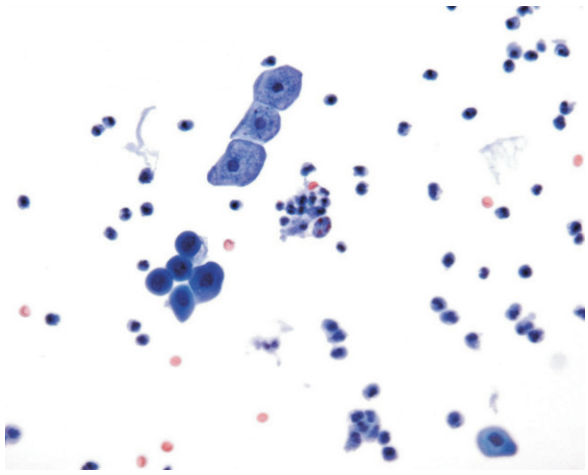

2

WHAT IS "PAP TEST"?

- Pap test is a method of examining with a microscope a sample of superficial cells that line the inner wall of the uterine cervix to detect any abnormal cell for early diagnosis of uterine cancer.
- It was developed in 1928 by the Greek doctor George Nicholas Papanicolaou (1883-1962) at the Cornell Medical College of New York. He also developed the particular polychrome staining reaction designed to demonstrate variations of cellular maturity and metabolic activity.
- The name "Pap test" derives from the first letters of his surname.

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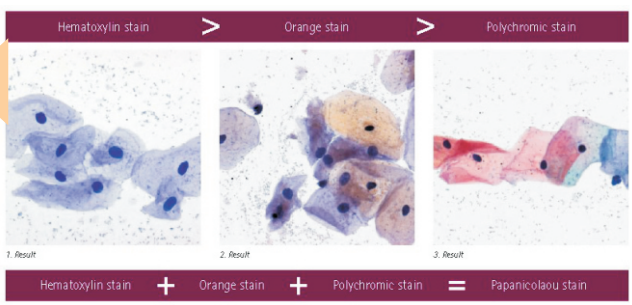
Papanicolaou stain



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The Papanicolaou stain is also used for non-gynecological (clinical) material. For instance, specimens of sputum or urine, containing squamous epithelial or similar cells, demonstrate excellent results when stained according to the Papanicolaou technique.

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Papanicolaou stain

The three main advantages of this staining procedure are:

(1) Good definition of nuclear detail.
(2) Cytoplasmic transparency.
(3) Indication of cellular differentiation of squamous epithelium.

It is a polychrome staining method which depends on degree of cell maturity and cellular metabolic activity. Cytoplasmic transparency is a function of high ethanol concentration of the stain. This is important in order to view multilayered cell agregates.

PRINCIPLES OF PAP STAIN

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- HAEMATOXILYN (violet): a basic stain with chemical affinity for acid substances (i.e. nuclei of cells, filled with DNA).
- EA50 (light blue): an acid stain that reacts with the cytoplasm of less mature squamous (exocervical) cell (basal, parabasal and intermediate cell) and with glandular (endocervical) cell.
- OG6 (orange): an acid stain that reacts with superficial squamous cell, filled with keratin.

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- The haematoxylin nuclear stain demonstrates chromatinic patterns of normal and abnormal cells.
- The counterstains, Orange-G and E.A. (eosin-azure) have a high alcoholic concentration which provides cytoplasmic transparency. This enables clear visualization through areas of overlapping cells, mucus and debris.
- There are four main steps in the staining procedure:
  (1) Fixation.
  (2) Nuclear staining.
  (3) Cytoplasmic staining.
  (4) Clearing.

Staining steps

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1) Ethanol 95° (Fixation)	2 minutes
2) Distilled water	2 minutes
3) Harris Hematoxylin	1 minute
4) Tap water	5 minutes
5) Ethanol 95°	15 seconds
6) OG 6	2 minutes
7) Ethanol 95°	15 seconds (twice)
8) EA 50	5 minutes
9) Ethanol 95°	15 seconds
10) Absolute Ethanol	30 seconds (twice)
11) Xilene or Bio Clear	2 minutes (twice)

Fixation

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- ***Specimens must be fixed immediately after being taken and while still moist!!!!***
  - To prevent drying out and shrinking of cells
  - To maintain specimen's structural features
  - To permit clear staining and differentiation
- If specimens are fixed too late, so-called artifacts can be found in Papanicolaou-stained smears on single cells or cell clusters.
- The classic method of fixing is to immerse the microscope slides in 96% ethanol for 30 min.
- A more efficient and quicker way is to fix them with a spray fixative. Spray fixatives are aqueous-alcoholic solutions containing polyethylene glycol (PEG, Carbowax), and are suitable for all types of cytological material due to be stained by the Papanicolaou method.

Air drying artifacts

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Air drying is a physiochemical process where there is more or less complete loss of water from the cells (especially from the nuclei) connected with structural alterations of the cell, as spreading of the nucleus or reduction of the staining reaction after application of the PAP stain.

Alterations caused by airdrying:
1. Spreading of cells on the slide surface with a change of nuclear area. 3D cell nuclei become flat,
2. Condensation of chromatin. This cannot be fully restored after reimmersion in water,
3. Favouring/preventing staining reactions.

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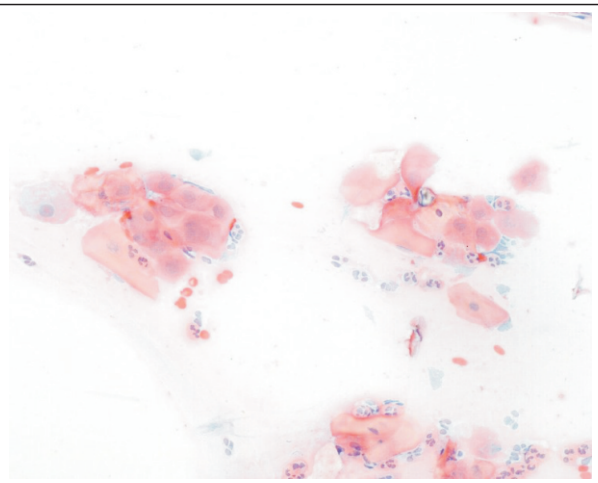

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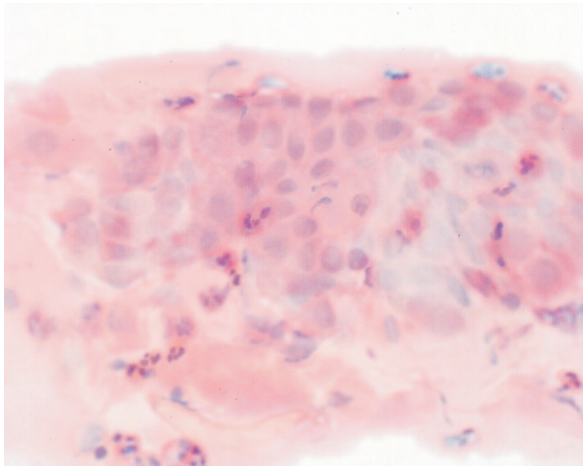

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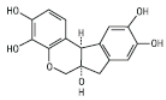
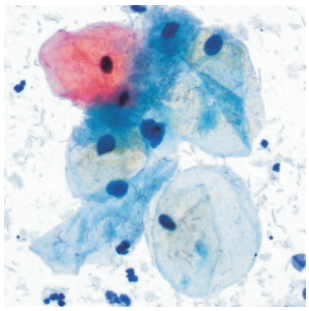
Hematoxylin



- The haematoxylin nuclear stain is a natural stain which has been used for over 100 years in histology.
- It has affinity for chromatin, attaching to sulphate groups on the DNA. molecule.
- Rinse under tap water to remove excess dye



14

Staining steps

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7) Ethanol 95°	15 seconds (twice)
8) EA 50	5 minutes
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11) Xilene or Bio Clear	2 minutes (twice)

17

Staining steps

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- From fixative (95% alcohol) the cells are hydrated through a graded series of alcohols to water preparatory to haematoxylin immersion (the haematoxylin is an aqueous solution).
- The cells are then dehydrated prior to immersion in the alcohol based cytoplasmic counterstains.
- Grading the alcoholic solutions in a stepwise manner is thought to minimise cellular distortion and reduce cell loss from the glass slide, due to convection currents in the solutions.

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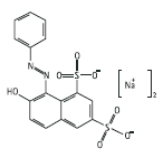
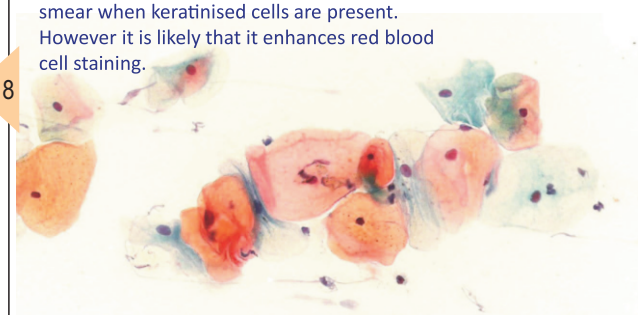
Orange G



- A monochromatic stain which colours keratin a brilliant orange.
- The effects of Orange G are only evident in smear when keratinised cells are present. However it is likely that it enhances red blood cell staining.



19

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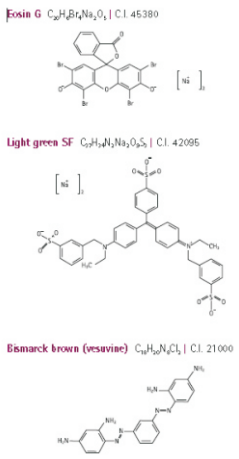
20

EA-50 (Eosin – Azure)

- a polychromatic mixture of:
  1. Eosin G
  2. Light Green SF
  3. Bismarck Brown
- Various EA modifications are known. They differ simply through the various concentrations of the individual dyes.
- Staining solutions commonly used in cytology are EA 31 and EA 50, while EA 65 is preferred for mucous material such as sputum, bronchial secretions and other non-gynecological material.
- Bismarck Brown reportedly does not have a staining effect but rather contributes to stabilizing the staining solution.



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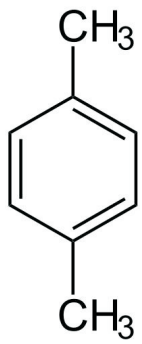
Clearing

- Clearing in xylol results in cellular transparency and precedes mounting.
- Xylol is the commonest clearing agent and is miscible with alcohol (absolute only).
- Xylol is colorless, chemically non-reactive and has almost the same refractive index as glass which is important to give the best possible transparency of the image.
- The presence of water in xylol causes cloudiness due to water droplets. Water and xylol are immiscible.



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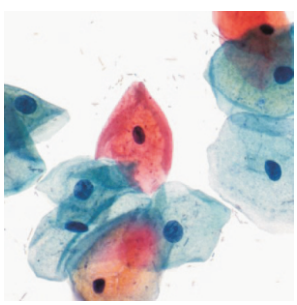
- The two dyes Eosin G and Light Green SF compete for the same target structures and cause the cells to be differently stained at various cyclic stages.
- Mature squamous epithelial cells, nucleoli and ciliae, for instance, have a stronger affinity for Eosin G, while parabasal and intermediate cells appear green, blue-green or blue after being stained with Light Green SF.



Omission of Orange G did not affect the accuracy of diagnosis (since keratin and red blood cell are also stained by eosin).

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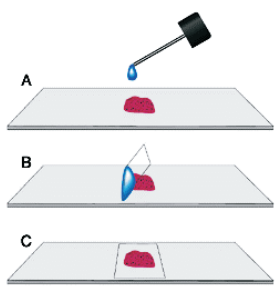
Mounting



The mountant:

(a) acts as a permanent bond between slide and coverslip

(b) protects cell material from air drying and shrinkage

(c) acts as a seal against oxidation and fading of the stain.

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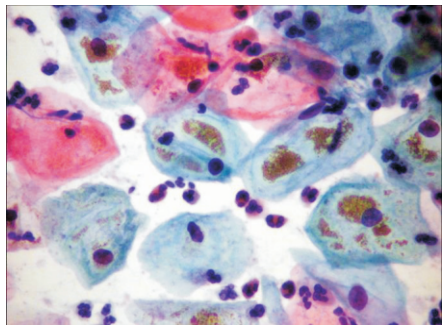
Causes of inconsistent staining

1.varying thickness of material on slide
2. type of fixative used
3. inadequate filtering of stain solutions
4. age of staining solution
5. degree of usage of staining solutions
6. use of chlorinated tap water
7. pH of water can effect nuclear staining
8. temperature of water
9. insufficient rinsing after acid
10.air drying of slides between solutions
11.improper draining of slides during staining.

26

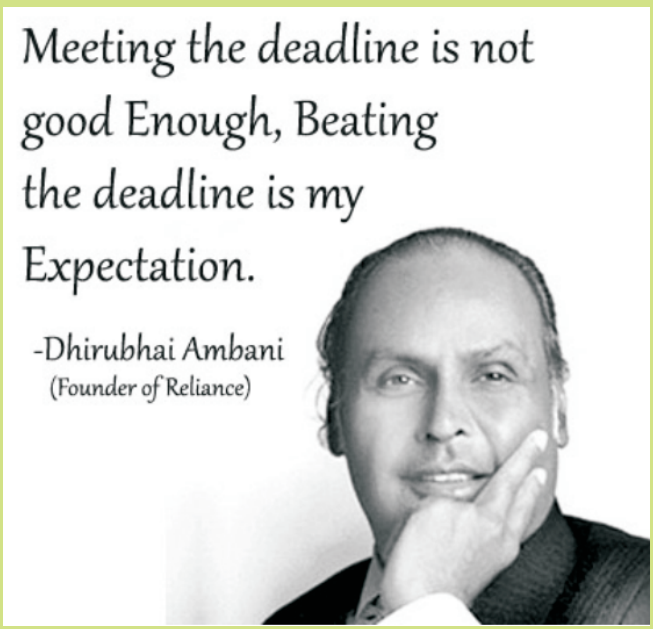
CORNFLAKE ARTIFACT

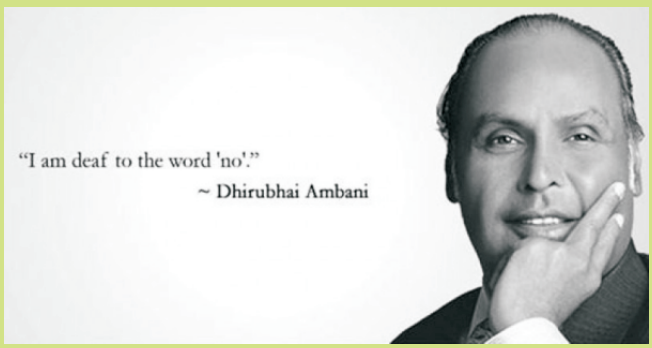


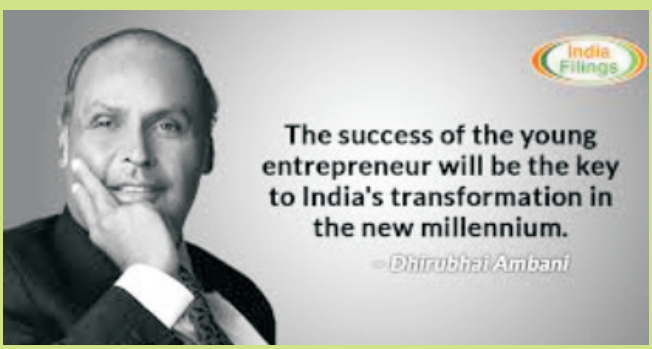
This common brown artifact is said to be caused by air bubbles formed when xylol dries before the slide is mounted. It can sometimes Be so extensive as to render the slide unsuitable for evaluation. Remounting the slide can sometimes improve the appearance of the smear.

BOUQUET

Wisdom Whispers







BOUQUET

In Lighter Vein

Dad: I want u 2 marry a girl of my choice.
Son: No
Dad: The girl is Bill Gates' daughter.
Son: Then ok
Dad goes 2 Bill Gates
Dad: I want ur daughter 2 marry my son.
Bill Gates: No
Dad: My son is d CEO of the World Bank.
Bill Gates: Then ok
Dad goes 2 the President of the World Bank..
Dad: Apoint my son as the CEO of ur bank.
President:No!
Dad: He is the son-in-law of Bill Gates.
President:Then ok!
This is BUSINESS.

Wife: Look at that drunk guy. Husband; who is he?
Wife: 10 yrs back he proposed to me & I rejected him.
Husband: Oh My God He's still celebrating...

One of Ajit's servants had twins. Appreciation (of a possible future raise) in his heart, he asked Ajit to give the two girls some English names.
"Call the first one Kate."
"And the second?"
"Duplicate."

Murder of English

1. Pick up the paper and fall in the dustbin.
2. Both of you stand together separately.
3. Why are you looking at the monkeys outside when I am inside.
4. Will you hang the calendar or else I will hang myself.
5. I have 2 daughters both are girls.
6. Give me a blue pen of any color.
7. The principal is revolving in the corridor.
8. all of u stand in a straight circle
9. Open the Window - Let the AIRFORCE come in.

Brain Teasers

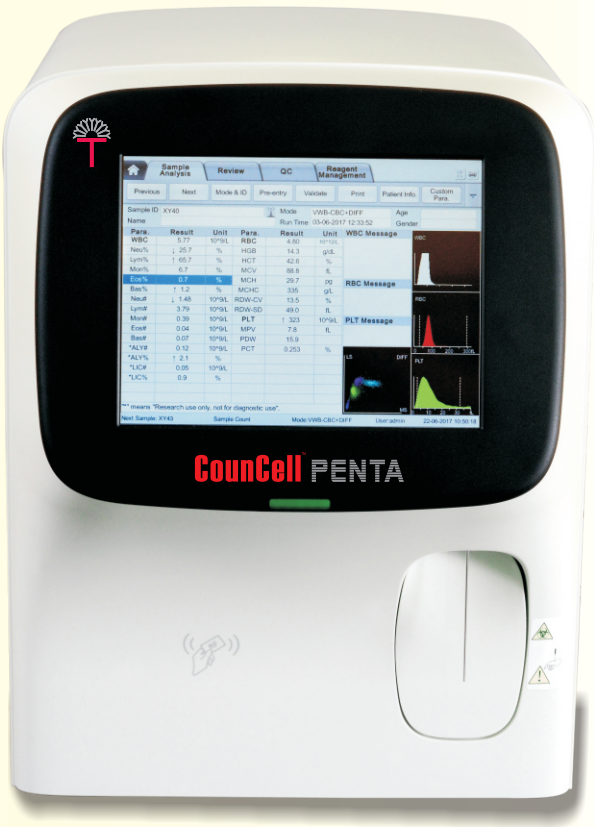
1. **In relation to nucleic acid technologies (NAT), what does P stand for in PCR methods?**
   A. Peroxide
   B. Polymerase
   C. Photon
   D. Polymorphic.
2. **What steps does one PCR cycle consist of?**
   A. Denaturation
   B. Annealing
   C. Extension
   D. All of the above.
3. **What kinds of PCRs exist in clinical practice?**
   A. Reverse transcriptase
   B. Real time
   C. Nested and differential
   D. All of the above.
4. **In relation to immunoassays what does R stand for in RIA?**
   A. Rapid
   B. Radio
   C. Resonance
   D. Real.

ANSWER: 1. B, 2. D, 3. D, 4. B

CounCell™ PENTA

5-Differential Automated Hematology Analyzer

Coral | Clinical Systems

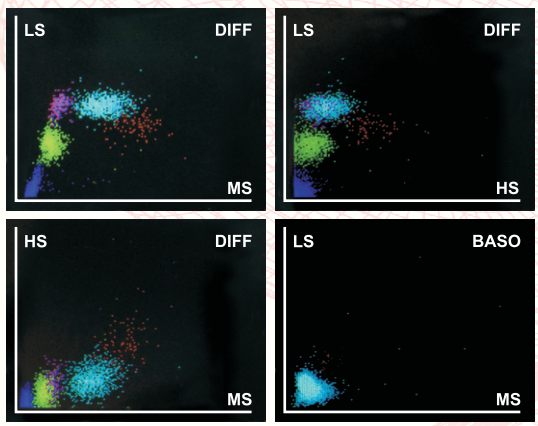


Principle:

Flow Cytometry (FCM) + Tri-angle Laser scatter method

Electrical Impedance method

Cyanide free Colorimetric method for HGB.



Four scattergram useful for better understanding of Blood Cells

Features

- **Parameters:**
  - 27 Parameters, consisting four RUO parameters
  - 3 Histograms for WBC, RBC AND PLT.
  - 3 LMNE-Differential Scattergram and 1 BASO Scattergram.
- Independent channel for Basophil measurement.
- Powerful capability of flagging abnormal cell.
- 3 routine use reagent for cell counting.
- Through put of 60 sample per hour.
- Large storage capability of 50,000 test including histograms and scattergrams.
- Large colour touch screen display of 10.4 inches.
- Software for user friendly and hassle free operation.
- Good repeatability and High Precision.
- Maintenance free Syringe.
- One button error resolving capability.

15 µL ultralow sample requirement, more suitable for paediatric & geriatic patients.

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