



Scan to know paper details and
author's profile

Strategies for Managing Vaginal Infection

Risav Banerjee & Trisha Bhattacharya

ABSTRACT

Vaginal Infection is the most common problem which almost most girls suffer. It is neglected but it has a serious effect if it is not treated. It is diagnosed if the color of the vaginal discharge changes, has a strong fishy odor, irritation, and burning sensation. The normal microflora of the vagina, act as the first line of defense in preventing the infection from pathogenic fungi, bacteria or protozoa which can cause vaginal infection. Several treatment strategies have been adapted for vaginal infections. Vaginitis trigger UTI (Urinary Tract Infection) in most of the girls. This review, is focused on vaginal infections caused by different types of microorganisms, symptoms and their treatment method.

Keywords: NA

Classification: DDC Code: 616.9 LCC Code: RC111

Language: English



LJP Copyright ID: 392851

London Journal of Medical and Health Research

Volume 22 | Issue 5 | Compilation 1.0



© 2022. Risav Banerjee & Trisha Bhattacharya. This is a research/review paper, distributed under the terms of the Creative Commons Attribution-Noncom-mercial 4.0 Unported License <http://creativecommons.org/licenses/by-nc/4.0/>, permitting all noncommercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Strategies for Managing Vaginal Infection

Risav Banerjee^α & Trisha Bhattacharya^σ

ABSTRACT

Vaginal Infection is the most common problem which almost most girls suffer. It is neglected but it has a serious effect if it is not treated. It is diagnosed if the color of the vaginal discharge changes, has a strong fishy odor, irritation, and burning sensation. The normal microflora of the vagina, act as the first line of defense in preventing the infection from pathogenic fungi, bacteria or protozoa which can cause vaginal infection. Several treatment strategies have been adapted for vaginal infections. Vaginitis trigger UTI (Urinary Tract Infection) in most of the girls. This review, is focused on vaginal infections caused by different types of microorganisms, symptoms and their treatment method.

Author α σ: Department of Genetics, Indian Academy Degree College.

I. INTRODUCTION

A healthy vagina contains some bacteria and a few yeast cells to maintain the natural balance of the vagina, whenever the number of bacteria and yeast cells goes imbalanced it leads to several vaginal infections [1]. Irritation and swelling of the vagina and vulva with unusual vaginal discharge which has a strong odour, and pain with a burning sensation during urination, are common symptoms of vaginal infection [2].

Whenever these symptoms occur, it causes discomfort and distress which lead women to seek medical consultation [3]. In the entire world, 3 out of 4 women suffer from vaginal infections once in their lifetime. The most common vaginal infection seen in women is bacterial vaginosis caused by bacteria, Candidal vaginitis caused by the fungus, and trichomoniasis which is caused by protozoa [4, 5, 6].

II. BACTERIAL VAGINOSIS

Bacterial vaginosis is the most common infection during the reproductive age of women it causes abnormal discharge and inflammation of the vagina [7, 8]. It is the most common infection in women. Bacterial vaginosis is occurred due to the replacement of the regular Lactobacillus bacteria with Prevotella, Mobiluncus, Ureaplasma, Gardnerella vaginitis, Mycoplasma, and many other uncultivated anaerobes [9, 10, 11]. Lactobacillus which is present normally in the vagina produces bacteriocins, lactic acid, and hydrogen peroxide, which help to maintain an acidic pH, and protect against other infections in the vagina [12, 13]. An enzyme produced by the bacteria which causes bacterial vaginosis degrades the gel layer protection of the vaginal epithelium and cervical [14]. They produce inflammatory proteins which associate with complications that occur during pregnancy like preterm labor and birth [14, 15], endometritis, gynecologic surgery, Neisseria gonorrhoeae, Chlamydia trachomatis, pelvic inflammatory disease, increased susceptibility to HIV type 1, and herpes simplex virus type 2 [16, 17, 18].

1. SYMPTOMS

- Burning during urination
- Thin, gray, white, or green vaginal discharge
- Vaginal itching
- Foul-smelling 'fishy' vaginal odor [19, 20]

2. RISK FACTOR

Bacterial vaginosis is not a sexually transmitted infection (STI) [21], but it resembles trichomoniasis, Chlamydia, and gonorrhea which are sexually transmitted infections [22]. Douching, having male partners who have sex with other women, having a new partner, having sex with women, use of an intrauterine device, use of an inconsistent condom, cigarette smoking, and black ethnicity [23, 24]. The use of oral contraceptives has an inverse relation with acquiring bacterial vaginosis [25].

3. DIAGNOSE

Bacterial vaginosis can be diagnosed by the BV test other names are the KOH test, wet mount test, and vaginal pH test [26, 27]. BV tests are done similarly to a Pap smear or pelvic exam. For the BV test Gram stain is the criterion standard to diagnose [28]. The Nugent score which is a Gram stain scoring system for vaginal swabs to diagnose bacterial vaginosis [29], a score of 0 to 3 is considered normal vaginal flora, 3 to 7 are the intermediate which is not identified for any abnormal or normal, and 7 to 10 is over to bacterial vaginosis [30, 31]. Amsel criteria are another method to make a clinical diagnosis of bacterial vaginosis [32]. The following are considered diagnostic for bacterial vaginosis: the fishy odor of discharge, homogenous gray-white vaginal discharge, vaginal pH greater than 4.5, or clue cells on the saline wet mount [33, 34, 35].

Currently, three other tests are being practiced in clinical diagnosis: BVBLUE (Gryphus diagnostics, Knoxville, Tennessee) is a rapid point of care test when mixed with a vaginal swab it will turn blue if there is any elevation of sialidase activity is produced by the bacterial pathogens which are associated with bacterial vaginosis [36, 37].

Pip activity test card (San Diego, Quidel corporation, California) is also a rapid test for confirming bacterial vaginosis by identifying an enzyme produced by *Gardnerella vaginalis* [38].

Affirm VPIII (Becton Dickinson, Maryland, Sparks) is a DNA probe-based test that helps to measure the level of *Gardnerella vaginalis* [39]. All these tests perform similarly to the gram stain. One may feel mild discomfort when the speculum is put inside the vagina to take the sample [40].

There are chances of bacterial vaginosis infection to reoccur after successful treatment [41], if the diagnosed person is pregnant then it is important to treat the infection, it can cause health problems to the unborn baby [42, 43].

4. TREATMENT

For the treatment of bacterial vaginosis, the doctor may prescribe one of the following medications:

Clindamycin (Cleocin, Clindesse): it is available as a cream that is inserted into the vagina [44].

Secnidazole (Solosec): is an antibiotic taken orally in one dose. This medication comes as a packet of granules that is sprinkled onto a soft food, such as pudding or yogurt, and should eat the mixture within 30 minutes, and be careful not to chew or crunch the granules [45, 46].

Metronidazole (Metrogel-vaginal, Flagyl): this medicine is taken orally as a pill, and is also available as a topical gel that can be inserted into the vagina. One can get the risk of abdominal pain, stomach upset, or nausea while using this medication. During treatment, one should avoid alcohol [47].

Tinidazole (Tindamax): even this medication is taken orally. Tinidazole also has the potential to cause stomach upset and nausea same as oral metronidazole, while treatment period one should avoid alcohol for at least three days after completing the treatment [48, 49].

III. CANDIDAL VAGINITIS

Candidal vaginitis is the second most common cause of vaginitis after bacterial vaginosis [50]. The vaginal yeast is caused by the *Candida albicans* strain, and the majority of non-albicans cases are caused by the *Candida glabrata* strain [51, 52]. These organisms may also be present in asymptomatic women [53], the non-albicans fungi are more resistant to the treatment than the Albicans species [54]. The non-albicans candidiasis strain causes severe candidal vaginitis infection, it becomes complicated in women with uncontrolled diabetes, immunosuppression or debilitation, or pregnant women. There are high chances of recurrent candidal vaginitis [55, 56].

The *Albicans candidiasis* strain causes mild to moderate candidal vaginitis, the etiology is likely to be *Candida albicans*, it is non-immunocompromised in women and it is infrequent or sporadic [57].

1. SYMPTOMS

- Vaginal rash
- Watery vaginal discharge

- Vaginal pain and soreness
- thick, white, odor-free vaginal discharge with a cottage cheese appearance
- Irritation and itching in the vagina and vulva
- redness and swelling of the vulva
- a burning sensation, during urinating or while intercourse [58, 59]

2. RISK FACTOR

Recent antibiotic use is a significant risk factor for acquiring candidal vaginitis in women. The other risk factors are to have some type of immuno* suppressive illness, like HIV, AIDs, or diabetes mellitus [60]. Frequent Douching and wearing wet clothes for a long duration of time may also increase the risk [61].

3. DIAGNOSIS

Candidal vaginitis is mostly self-diagnosed. The clinical symptoms are the typical way to diagnose candidal vaginitis. The technical way for diagnosis requires microscopic examination of the vaginal discharge for the identification of yeast buds or yeast hyphae, which is most easily viewed in the wet mount with 10% KOH [62], it depends on the working microscope and the clinical experience of the provider and detects 40% to 70% of cases when compared to culture [63]. Sabouraud agar culture for vaginal discharge is considered the criterion standard for diagnosis, it is an expensive method and requires a long duration of time [64].

Recently the immunochromatographic method has been developed which is rapid screening tests to detect Candida infection within 30 minutes [65].

4. TREATMENT

The treatment depends on the frequency of the infections short-course vaginal therapy: an antifungal medication is taken for three to seven days which usually clears the infection. Antifungal medications are available as creams, ointments, and tablets, which include miconazole and terconazole.

- Single-dose oral medicine: a single dose of fluconazole (Diflucan) is an oral medication prescribed by the doctor, it is not recommended when one is pregnant.

- Long-course vaginal therapy: doctor prescribe an antifungal medication which is taken daily for a few weeks, followed by once a week for six months.
- Multidose oral medication: doctor prescribed two or more doses of an antifungal medication which is an oral medication for vaginal therapy, but is not recommended for pregnant women.
- Azole resistant therapy: boric acid, a capsule is inserted into the vagina. This medication can be fatal if taken orally and is used only to treat candida fungus which is resistant to the usual antifungal agents [66, 67].

IV. TRICHOMONIASIS

Trichomonas vaginalis is the most common, curable, non-viral sexually transmitted infection. It is caused by parasitic, pear-shaped, and motile protozoan, it adheres to the vaginal epithelium and releases cytotoxic substances that cause inflammation and breaks the epithelium [68]. *Trichomonas vaginalis* does not need cervical cells for growth like *Chlamydia trachomatis* and *Neisseria gonorrhoeae*, they are vaginal pathogens, and the whole vagina is at risk of being infected [69].

1. SYMPTOMS

- Pain during urination and intercourse
- Genital redness, burning, and itching
- A large amount of a thin vaginal discharge with a foul smell
- * 🌀 🌀 🌀 ❖ 🌀 🌀 🌀 🌀 🌀 • discharge might be clear, white, gray, yellow, or green
- Discomfort over the lower stomach area [70, 71, 72]

2. RISK FACTOR

Lower education level, ethnicity, socioeconomic status, and douching are the risk factor for acquiring *Trichomonas vaginalis*, multiple sexual partners are also identified as risk factors [72].

3. DIAGNOSIS

The method used most often to diagnose trichomoniasis in the office setting has traditionally been a microscopic examination of saline wet mount for motile *trichomonas*, it has a

sensitivity of 50% to 60% when performed by experienced clinicians [73]. Recently developed methods for diagnosing trichomoniasis are Affirm VPIII (Maryland, Dickson, Sparks), the nucleic acid probe that evaluates for *Trichomonas vaginalis*, and in addition to the *Gardnerella vaginalis*. The sensitivity of these tests is 80% to 90%. OSOM and Trichomonas rapid test (Sekisui Diagnostics, Framingham, Massachusetts) are the rapid antigen test for trichomoniasis. If trichomonads are present then the vaginal collection swab will turn blue when it comes in contact with specific reagents [74]. It has a sensitivity rate of 83% to 90%. The result of Affirm VPIII is available within 45 minutes and OSOM Trichomonas rapid test takes 10 minutes to show the result [75].

4. TREATMENT

The only drug used for treating *Trichomonas vaginalis* are tinidazole and metronidazole [76]. The cure rate of tinidazole is 86% to 100%, whereas the cure rate of metronidazole is 90% to 95% only. Treatment is recommended for all the sex partners of women with trichomoniasis [77].

V. CONCLUSION

Vaginal infection is caused by different types of microorganism i.e. bacteria, fungi, protozoa, mycoplasma etc. Several risk factors are associated with it if not treated on time. Personal hygiene is one of the most crucial factor which girls should follow to avoid vaginal infection. Early signs and symptoms should not be avoided, the treatment should be started as soon as possible.

REFERENCES

1. Bachmann, G. A. & Nevadunsky, N. S. (2000, May 15). Diagnosis and treatment of atrophic vaginitis. *American Family Physician*, 61(10), 3090-3096.
2. <http://www.aafp.org/afp/2000/0515/p3090.html>
3. Nyirjesy, P. (2014, December). Management of persistent vaginitis. *Obstetrics & Gynecology*, 124(6), 1135-1146.
4. https://journals.lww.com/greenjournal/Abstract/2014/12000/Management_of_Persistent_Vaginitis.11.aspx.
5. Lobo RA, et al. Genital tract infections: Vulva, vagina, cervix, toxic shock syndrome, endometritis, and salpingitis. In: *Comprehensive Gynecology*. 7th ed. Philadelphia, Pa.: Elsevier; 2017. <https://www.clinicalkey.com>. Accessed Aug. 26, 2018.
6. Verhelst R, et al. (2004) Cloning of 16S rRNA genes amplified from normal and disturbed vaginal microflora suggests a strong association between *Atopobium vaginae*, *Gardnerella vaginalis*, and bacterial vaginosis. *BMC Microbiol* 4:16.
7. TL Charles, LA Meyn, MA Krohn, JG Lurie, SL Hillier, Association between the acquisition of herpes simplex virus type 2 in women and bacterial vaginosis. *Clin Infect Dis* 37, 319–325 (2003).
8. ER Boskey, RA Cone, KJ Whaley, TR Moench, Origins of vaginal acidity: High D/L lactate ratio is consistent with bacteria being the primary source. *Hum Reprod* 16, 1809–1813 (2001).
9. V Pybus, AB Onderdonk, Evidence for a commensal, symbiotic relationship between *Gardnerella vaginalis* and *Prevotella bivia* involving ammonia: Potential significance for bacterial vaginosis. *J Infect Dis* 175, 406–413 (1997).
10. Goldenberg, R. L., Culhane, J. F., Iams, J. D. & Romero, R. Epidemiology and causes of preterm birth. *Lancet* 371, 75–84 (2008).
11. Koparde, V. N., Parikh, H. I., Bradley, S. P. & Sheth, N. U. MEEPTOOLS: a maximum expected error based FASTQ read filtering and trimming toolkit. *Int. J. Comput. Biol. Drug Des.* 10, 237–247 (2017).
12. Nelson, D. B. et al. Early pregnancy changes in bacterial vaginosis-associated bacteria and preterm delivery. *Paediatr. Perinat. Epidemiol.* 28, 88–96 (2014).
13. Callahan, B. J. et al. Replication and refinement of a vaginal microbial signature of preterm birth in two racially distinct cohorts of US women. *Proc. Natl Acad. Sci. USA* 114, 9966–9971 (2017).

14. Son, K.-A. et al. Prevalence of vaginal microorganisms among pregnant women according to trimester and association with preterm birth. *Obstet. Gynecol. Sci.* 61, 38–47 (2018).
15. Haque, M. M., Merchant, M., Kumar, P. N., Dutta, A. & Mande, S. S. First-trimester vaginal microbiome diversity: a potential indicator of preterm delivery risk. *Sci. Rep.* 7, 16145 (2017).
16. Ban, Y., An, L. & Jiang, H. Investigating microbial co-occurrence patterns based on metagenomic compositional data. *Bioinforma* 31, 3322–3329 (2015).
17. Witkin S.S. Mendes-Soares H. Linhares I.M. et al. Influence of vaginal bacteria and d- and l-lactic acid isomers on vaginal extracellular matrix metalloproteinase inducer: implications for protection against upper genital tract infections. *MBio.* 2013; 4https://doi.org/10.1128/mBio.00460-13vv.
18. O'Hanlon D.E. Moench T.R. Cone R.A. Vaginal pH and microbicidal lactic acid when lactobacilli dominate the microbiota. *PLoS One.* 2013; 8: e80074https://doi.org/10.1371/journal.pone.0080074
19. Fettweis J.M. Brooks J.P. Serrano M.G. et al. Differences in the vaginal microbiome in African American women versus women of European ancestry. *Microbiology.* 2014; https://doi.org/10.1099/mic.0.081034-0.
20. Zárate G. Nader-Macias M.E. Influence of probiotic vaginal lactobacilli on in vitro adhesion of urogenital pathogens to vaginal epithelial cells. *Lett Appl Microbiol.* 2006; 43: 174-180https://doi.org/10.1111/j.1472-765.2006.01934.x
21. Shi Y. Chen L. Tong J. et al. Preliminary characterization of vaginal microbiota in healthy Chinese women using cultivation-independent methods. *J Obstet Gynaecol Res.* 2009; 35: 525-532https://doi.org/10.1111/j.1447-0756.2008.00971.
22. Jaquier A. Stylianopoulos A. Hogg G. et al. Vulvovaginitis: clinical features, aetiology, and microbiology of the genital tract. *Arch Dis Child.* 1999; 81: 64-67 .
23. Pabich W.L. Fihn S.D. Stamm W.E. et al. Prevalence and determinants of vaginal flora alterations in postmenopausal women. *J Infect Dis.* 2003; 188: 1054-1058https://doi.org/10.1086/378203
24. Genc M.R. Onderdonk A. Endogenous bacterial flora in pregnant women and the influence of maternal genetic variation. *BJOG.* 2011; 118: 154-163https://doi.org/10.1111/j.1471-0528.2010.02772.x .
25. Srinivasan S. Fredricks D.N. The human vaginal bacterial biota and bacterial vaginosis. *Interdiscip Perspect Infect Dis.* 2008; 2008: 750479 https://doi.org/10.1155/2008/750479.
26. Altizer, S. M., Nunn, C. L., Thrall, P. H., Gittleman, J. L., Antonovics, J., Cunningham, A. A., et al. (2003). Social organization and parasite risk in mammals: integrating theory and empirical studies. *Annu. Rev. Ecol. Evol. Syst.* 34, 517–547. doi:10.1146/annurev.ecolsys.34.030102.151725.
27. Graver, M. A., and Wade, J. J. (2011). The role of acidification in the inhibition of *Neisseria gonorrhoeae* by vaginal lactobacilli during anaerobic growth. *Ann. Clin. Microbiol. Antimicrob.* 10:8. doi: 10.1186/1476-0711-10-8
28. Thoma, M. E., Gray, R. H., Kiwanuka, N., Aluma, S., Wang, M. C., Sewankambo, N., et al. (2011a). Longitudinal changes in vaginal microbiota composition assessed by gram stain among never sexually active pre- and postmenarcheal adolescents in Rakai, Uganda. *J. Pediatr. Adolesc. Gynecol.* 24, 42–47. doi: 10.1016/j.jpag.2010.07.002
29. Uchihashi, M., Bergin, I. L., Bassis, C. M., Hashway, S. A., Chai, D., and Bell, J. D. (2015). Influence of age, reproductive cycling status, and menstruation on the vaginal microbiome in baboons (*Papio anubis*). *Am. J. Primatol.* 77, 563–578. doi:10.1002/ajp.22378.
30. Leitich, H., Bodner-Adler, B., Brunbauer, M., Kaider, A., Egarter, C., and Husslein, P. (2003). Bacterial vaginosis as a risk factor for preterm delivery: a meta-analysis. *Am. J. Obstet. Gynecol.* 189, 139–147. doi:10.1067/Mob.2003.339.
31. Mirmonsef, P., Hotton, A. L., Gilbert, D., Burgad, D., Landay, A., Weber, K. M., et al. (2014). Free glycogen in vaginal fluids is associated with *Lactobacillus* colonization and

- low vaginal pH. PLoS ONE 9102467: doi: 10.1371/journal.pone.0102467.
32. Nauth, H. F., and Haas, M. (1985). Cytologic and histologic observations on the Sex-Hormone dependence of the Vulva. *J. Reproduct. Med.* 30, 667–674.
 33. Spear, G. T., French, A. L., Gilbert, D., Zariffard, M. R., Mirmonsef, P., Sullivan, T. H., et al. (2014). Human alpha-amylase present in lower genital tract mucosal fluid processes glycogen to support vaginal colonization by *Lactobacillus*. *J. Infect. Dis.* 210, 1019–1028. doi: 10.1093/infdis/jiu231.
 34. Gajer P, Brotman RM, Bai G, Sakamoto J, Schutte UM, et al. (2012) Temporal dynamics of the human vaginal microbiota. *Sci Transl Med* 4: 132ra52.
 35. Zhou X, Brown CJ, Abdo Z, Davis CC, Hansmann MA, et al. (2007) Differences in the composition of vaginal microbial communities found in healthy Caucasian and black women. *The ISME journal* 1: 121–133.
 36. Wilks M, Wiggins R, Whiley A, Hennessy E, Warwick S, et al. (2004) Identification and H₂O₂ production of vaginal lactobacilli from pregnant women at high risk of preterm birth and relation with outcome. *J Clin Microbiol* 42: 713–717.
 37. Aagaard K, Riehle K, Ma J, Segata N, Mistretta TA, et al. (2012) A metagenomic approach to characterization of the vaginal microbiome signature in pregnancy. *PLoS One* 7: e36466.
 38. Relman DA (2012) The human microbiome: ecosystem resilience and health. *Nutr Rev* 70: S2–9.
 39. Hay PE, Lamont RF, Taylor-Robinson D, Morgan DJ, Ison C, Pearson J. Abnormal bacterial colonisation of the genital tract and subsequent preterm delivery and late miscarriage. *BMJ* 1994; 308: 295– 8.
 40. Ralph SG, Rutherford AJ, Wilson JD. Influence of bacterial vaginosis on conception and miscarriage in the first trimester: cohort study. *BMJ* 1999; 319: 220– 3.
 41. Martius J, Eschenbach DA. The role of bacterial vaginosis as a cause of amniotic fluid infection, chorioamnionitis, and prematurity – a review. *Arch Gynecol Obstet* 1990; 247: 1– 13.
 42. Verhelst R, Verstraelen H, Claeys G, Verschraegen G, Delanghe J, Van SL, et al. Cloning of 16S rRNA genes amplified from normal and disturbed vaginal microflora suggests a strong association between *Atopobium vaginae*, *Gardnerella vaginalis* and bacterial vaginosis. *BMC Microbiol* 2004; 4: 16.
 43. Fredricks DN, Fiedler TL, Marrazzo JM. Molecular identification of bacteria associated with bacterial vaginosis. *N Engl J Med* 2005; 353: 1899– 911.
 44. Fredricks DN, Fiedler TL, Thomas KK, Oakley BB, Marrazzo JM. Targeted PCR for detection of vaginal bacteria associated with bacterial vaginosis. *J Clin Microbiol* 2007; 45: 3270– 6.
 45. Collins MD, Wallbanks S. Comparative sequence analyses of the 16S rRNA genes of *Lactobacillus minutus*, *Lactobacillus rimae* and *Streptococcus parvulus*: proposal for the creation of a new genus *Atopobium*. *FEMS Microbiol Lett* 1992; 74: 235– 40.
 46. Hauduroy P, Ehringer G, Urbain A, Guillot G, Magrou J. *Dictionnaire des Bacteries Pathogenes*. Paris: Masson, 1937.
 47. Shukla SK, Meier PR, Mitchell PD, Frank DN, Reed KD. *Leptotrichia amnionii* sp. nov., a novel bacterium isolated from the amniotic fluid of a woman after intrauterine fetal demise. *J Clin Microbiol* 2002; 40: 3346– 9.
 48. Geissdorfer W, Bohmer C, Pelz K, Schoerner C, Frobenius W, Bogdan C. Tuboovarian abscess caused by *Atopobium vaginae* following transvaginal oocyte recovery. *J Clin Microbiol* 2003; 41: 2788– 90.
 49. Thomason JL, Gelbart SM, James JA, Edwards JM, Hamilton PR. Is analysis of vaginal secretions for volatile organic acids to detect bacterial vaginosis of any diagnostic value? *Am J Obstet Gynecol* 1988; 159:1509–11.
 50. Bradshaw CS, Morton AN, Hocking J, Garland SM, Morris MB, Moss LM, et al. months after oral metronidazole therapy and factors associated with recurrence High recurrence rates of bacterial vaginosis over the course of 12. *J Infect Dis* 2006; 193: 1478– 86.
 51. Verstraelen H, Verhelst R, Claeys G, De BE, Temmerman M, Vaneechoutte M. Longitudinal analysis of the vaginal microflora

- in pregnancy suggests that *L. crispatus* promotes the stability of the normal vaginal microflora and that *L. gasseri* and/or *L. iners* are more conducive to the occurrence of abnormal vaginal microflora. *BMC Microbiol* 2009; 9: 116.
52. Wayne LG, Brenner DJ, Colwell RR, Grimont PAD, Kandler O, et al. Report of the ad-hoc-committee on reconciliation of approaches to bacterial systematics. *Int J Syst Bacteriol.* 1987;37:463–4.
 53. Jakobsson T, Forsum U. Changes in the predominant human *Lactobacillus* flora during in vitro fertilisation. *Ann Clin Microbiol Antimicrob.* 2008;7:14–21.
 54. Schloss PD, Handelsman J. Status of the microbial census. *Microbiol Mol Biol Rev.* 2004;68:686–91.
 55. Ravel J, Gajer P, Abdo Z, Schneider GM, Koenig SS, McCulle SL, Karlebach S, Gorle R, Russell J, Tacket CO, Brotman RM, Davis CC, Ault K, Peralta L, Forney LJ. Vaginal microbiome of reproductive-age women. *Proc Natl Acad Sci U S A.* 2011;108 Suppl 1:4680–7.
 56. Bäckhed F, Ley RE, Sonnenburg JL, Peterson DA, Gordon JI. 2005. Host-bacterial mutualism in the human intestine. *Science* 307:1915–1920.
 57. Bäckhed F, Ley RE, Sonnenburg JL, Peterson DA, Gordon JI. 2005. Host-bacterial mutualism in the human intestine. *Science* 307:1915–1920.
 58. Davies TJ, Pedersen AB. 2008. Phylogeny and geography predict pathogen community similarity in wild primates and humans. *Proc R Soc Lond B Biol Sci* 275: 1695– 1701.
 59. Danielsson D, Teigen PK, Moi H. 2011. The genital econiche: focus on microbiota and bacterial vaginosis. *Ann N Y Acad Sci* 1230: 48– 48.
 60. Galhardo CL, Soares JM, Simoes RS, Haidar MA, Rodrigues DLG, Baracat EC. 2006. Estrogen Estrogen effects on the vaginal pH, flora and cytology in late postmenopause after a long period without hormone therapy. *Clin Exp Obstet Gynecol* 33: 85– 89.
 61. Keane FEA, Ison CA, Taylor-Robinson D. 1997. A longitudinal study of the vaginal flora over a menstrual cycle. *Int J STD AIDS* 8: 489– 494.
 62. Kalyoussef S, Nieves E, Dinerman E, Carpenter C, Shankar V, Oh J, Burd B, Angeletti RH, Buckheit KW, Fredricks DN, Madan RP, Keller MJ, Herold BC. 2012. *Lactobacillus* proteins are associated with the bactericidal activity against *E. coli* of female genital tract secretions. *PLoS One* 7, e49506.
 63. Martin HL, Richardson BA, Nyange PM, Lavreys L, Hillier SL, Chohan B, Mandaliya K, Ndinya-Achola JO, Bwayo J, Kreiss J. 1999. Vaginal lactobacilli, microbial flora, and risk of human immunodeficiency virus type 1 and sexually transmitted disease acquisition. *J Infect Dis* 180: 1863– 1868.
 64. Narushima S, Itoh K, Sankai T, Takasaka M, Otani I, Yoshikawa Y. 1997. Changes in normal vaginal flora of African green monkeys (*Cercopithecus aethiops*) during the menstrual cycle. *Exp Anim* 46: 47– 52.
 65. Sewankambo N, Gray RH, Wawer MJ, Paxton L, McNairn D, Wabwire-Mangen F, Serwadda D, Li C, Kiwanuka N, Hillier SL, Rabe L, Gaydos CA, Quinn TC, Konde-Lule J. 1997. HIV-1 infection associated with abnormal vaginal flora morphology and bacterial vaginosis. *Lancet* 350: 546– 550.
 66. Street DA, Taylor-Robinson D, Hetherington CM. 1983. Infection of female squirrel monkeys (*Saimiri sciureus*) with *trichomonas vaginalis* as a model of trichomoniasis in women. *Br J Vener Dis* 59: 249– 254.
 67. Turnbaugh PJ, Ley RE, Hamady M, Fraser-Liggett CM, Knight R, Gordon JI. 2007. The human microbiome project. *Nature* 449: 804– 804– 810.
 68. Weinstein L, Bogin M, Howard JH, Finkelstone BB. 1936. A survey of the vaginal flora at various ages with special reference to the *Doederline bacillus*. *Am J Obstet Gynecol* 32: 211– 218.
 69. Zhou X, Brotman RM, Gajer P, Abdo Z, Schütte U, M S, Ravel J, Forney LJ. 2010a. Recent advances in understanding the microbiology of the female reproductive tract and the causes of premature birth. *Infect Dis Obstet Gynecol* 2010: 737425.
 70. Verstraelen H, Vervaeck C, Remon J: Rationale and safety assessment of a novel intravaginal

- drug-delivery system with sustained DL-lactic acid release, intended for long-term protection of the vaginal microbiome. *PLoS One*. 2016; 11(4):e0153441. 10.1371/journal.pone.0153441
71. Ventegodt S, Clausen B, Omar HA, et al.: Clinical holistic medicine: holistic sexology and acupressure through the vagina (Hippocratic pelvic massage). *Scientific World Journal*. 2006;6(2006):2066–79. 10.1100/tsw.2006.337
 72. McMillan A, Dell M, Zellar MP, et al.: Disruption of urogenital biofilms by lactobacilli. *Colloids Surf B Biointerfaces*. 2011;86(1):58–64. 10.1016/j.colsurfb.2011.03.016
 73. Collins SL, McMillan A, Seney S, et al.: Promising prebiotic candidate established by evaluation of lactitol, lactulose, raffinose, and oligofructose for maintenance of a Lactobacillus-Dominated vaginal microbiota. *Appl Environ Microbiol*. 2018;84(5):pii:e02200-17. 10.1128/AEM.02200-17
 74. Gray RH, Kigozi G, Serwadda D, Makumbi F, Nalugoda F, Watya S, Moulton L, Chen MZ, Sewankambo NK, Kiwanuka N, Sempijja V, Lutalo T, Kagayii J, Wabwire-Mangen F, Ridzon R, Bacon M, Wawer MJ. 2009. The effects of male circumcision on female partners' genital tract symptoms and vaginal infections in a randomized trial in Rakai, Uganda. *Am J Obstet Gynecol* 200:42.e1.
 75. Alcendor DJ. 2016. Evaluation of health disparity in bacterial vaginosis and the implications for HIV-1 acquisition in African American women. *Am J Reprod Immunol* 76:99–107
 76. Turovskiy Y, Sutyak Noll K, Chikindas ML. 2011. The aetiology of bacterial vaginosis. *J Appl Microbiol* 110:1105–1128.
 77. Mackelprang RD, Scoville CW, Cohen CR, Ondondo RO, Bigham AW, Celum C, Campbell MS, Essex M, Wald A, Kiarie J, Ronald A, Gray G, Lingappa JR, Partners in Prevention HSV/HIV Transmission Study Team. 2015. Toll-like receptor gene variants and bacterial vaginosis among HIV-1 infected and uninfected African women. *Genes Immun* 16:362–365.
 78. Mitra A, Macintyre DA, Lee YS, Smith A, Marchesi JR, Lehne B, et al. Cervical intraepithelial neoplasia disease progression is associated with increased vaginal microbiome diversity. *Sci Rep*. 2015;5:16865.
 79. Romero R, Hassan SS, Gajer P, Tarca AL, Fadrosh DW, Nikita L, et al. The composition and stability of the vaginal microbiota of normal pregnant women is different from that of non-pregnant women. *Microbiome*. 2014; 2(1):4.