

Research Article



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Vaginal Microbiota and Bacterial Vaginosis

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Abstract

The vaginal microbiota helps to prevent urogenital diseases and maintain health, through the production of lactic acid. The human body houses microorganisms that inhabit the surfaces and cavities exposed to the external environment. Each part of the body includes groups of microbial species that exist in a symbiotic relationship with the host. The types of organism's present are dependent on the present environmental conditions and host factors, but they vary from site to site and between individuals over time.

Keywords: Vaginal flora; Lactobacilli; Bacterial vaginosis; Culture; Molecular techniques

Abbreviations: HIV: Human Immunodeficiency Virus; DNA: Deoxy Ribonucleic Acid; PCR: Polymerase Chain Reaction; rRNA: Ribosomal Ribonucleic Acid; HPV: Human Papilloma Virus; THM: Terminal Homing Munition; BVAB: Bacterial Vaginosis Associated Bacteria; HSV: Herpes Simplex Virus; NPV: Negative Predictive Value; PPV: Positive Predictive Value; VPP: Value Positive Predictive

Introduction

The human body keeps microorganisms inside that inhabit the surfaces and cavities exposed to the external environment. Each part of the body includes groups of microbial species that exist in a symbiotic relationship with the guest. The types of organisms are dependent coexisting on environmental conditions and host factors and vary from site to site and between individuals in time. The human vaginal microbiota plays a role decisive in disease prevention urogenital diseases (bacterial vaginosis, by fungi, sexually transmitted infections, infections, urinary tract infections, and HIV). For general, lactic acid producing bacteria, the

especially *Lactobacillus sp.* found in the vagina and play a role in protection by reducing the pH the environment through the production of lactic acid, various bacterio static compounds and bactericidal or competitive suppression. Molecular techniques have improved understanding of the vaginal microbiota; they provide information that changes the way it is defines the normal vaginal flora; where flora is dominated by one or two species of lactobacilli [1].

A significant number of women healthy lactobacilli lacks vaginal and bacterial vaginosis is not a disease isolated but consistent in different populations bacterial infections with greater diversity in microbial profiles. It is considered a syndrome of variable composition that gives different symptoms, with different responses to regimens of antibiotics and according to the phenotype [1-3]. The variation functional microbial host can be mediated by the introduction or extinction of certain microbial groups or by changes in the structure of the population. These alterations can, in turn, be induced selection of environmental factors, such as changes in diet or exposure to antibiotics.

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The composition of the microbiota varies according to the anatomical site. The main determinant of the composition of the group is the anatomical location: the variation interpersonal is decisive and superior to the temporal variability seen in the majority of the sites in a single individual. That stability suggests that individuals can be grouped according to the main enteropathy of the vagina, changes in the diet and time. Throughout our lives we humans will form a densely populated microbiome, which is abbreviated in each individual and in each generation. Exposure (or not) to microbe's environment is another important reservoir, but highly variable for the resident microbiota. Antibiotic treatments in the early life lead to major changes in the characteristics of the microbiota. Comprehension of the links between the microbiome and the disease can provide tools prophylactic or therapeutic measures to improve health human. Knowledge of the composition of the flora vaginal microbial is through different techniques [4]. Molecular techniques provide new information about the composition of normal and abnormal vaginal flora in the colonization of the genital tract and help to differentiate the composition and function of the flora normal, microbial diversity, diagnosis and evaluation of the treatment of the abnormal flora of the genital apparatus [5].

Materials and Methods

Microbiota and molecular techniques in the man

The Human Microbiome project on the number of genes in the human genome. Instead of microbiological information have emerged new concepts, such as: "redundancy functional", "structural diversity", "interaction between species", "mutualism", etc, [6-11] which characterize the composition range of the "normal" microbiota of healthy individuals. The main clustering patterns in the but have not been identified by crops. The molecular techniques for the evaluation of microbiota have greater diversity in identification of inopportune organisms. The amplification by PCR of DNA is a reaction competitive enzyme; the 16S templates rRNA in a sample are amplified according to their abundance [12,13].

1.1. Normal vaginal flora

Most of the crops the impression that the vaginal microbial flora is static, without taking into account that communities vaginal microbes experience changes in form, abundance and virulence over

time, and are affected by many factors. The identification of lactobacilli in molecular tests, culture and microscopy of the "normal" vaginal flora typically shows a predominance of Lactobacillus species that promote a healthy vagina, by its dominion with the production of lactic acid to maintain an acidic environment that is inhospitable for many bacteria, and correlates negatively with bacterial vaginosis. Lactobacilli also produce hydrogen (H₂O₂), hydroxyl radicals, bacteriocins antibiotics and probiotics. Before the emergence of molecular techniques, lactobacilli, in general, are only identified by its gender. This was how the bacillus was Döderlein called acidophilic lactobacillus, which demonstrated highly heterogeneous to form a number separated by species within the L. Acidophilus complex [14,15].

Lactobacillus Acidophilus Complex
Lactobacillus acidophilus
Lactobacillus amylolyticus
Lactobacillus amylovorus
Lactobacillus crispatus
Lactobacillus gallinarium
Lactobacillus gasseri
Lactobacillus iners
Lactobacillus jensenii
Lactobacillus johnsoni

Table 1: Homo fermentative Species Bound Between.

Species closely related to L. acidophilus complex are difficult to differentiate by phenotypic methods, which explain the variation in the species of lactobacilli and the culture does not detect annoying organisms and underestimates the diversity of the vaginal microbial flora. Due to the deficiencies in the identification phenotype of the lactobacilli, overestimate the diversity of species of Lactobacillus in the vagina [15,16]. The identification of lactobacilli by Molecular, Lactobacillus iners (L-iners) unknown but now it is known that it plays an important role in the flora of the microbiota vaginal. It is bacteria that produce lactic acid, which is one of the most frequently isolated from the healthy vagina [1-3]. In contrast with Lactobacillus crispatus, which is rare is dominant in bacterial vaginosis. L. iners is detected in the majority of patients with and without bacterial vaginosis. In some the only species of Lactobacillus detected in the bacterial vaginosis. L. iners is better adapted to conditions associated with vaginosis bacterial; that is, the poly microbial state of vaginal flora and high pH, [17] or resistance of L. *iners* leading to the disappearance of other species

of Lactobacillus during initiation of bacterial vaginosis, or lack of antagonism of *L. iners* to the anaerobes associated with bacterial vaginosis that predisposes the person to have bacterial vaginosis [1-3].

Numerical prevalence of lactobacilli

With the help of molecular techniques, identified more than 120 species of lactobacilli and more than 20 species are detected in the vagina. The healthy vaginal microbiota does not contain a number of many different species of lactobacilli; one or two series of lactobacilli three or four species (L. crispatus and L. iners, but also Lactobacillus jensenii and Lactobacilli gasseri) are the dominant, while others species are rare [7,18,19]. In healthy women, isolation vaginal flora is dominated by a only species of lactobacilli, and some women have different species or strains of the same species of lactobacilli. The only species detected have been: L crispatus, L gasseri, L iners and L. jensenii although only one woman was colonized by more than two species of lactobacillus, four were by two different species, and [15] were colonized by a single species. The exclusion of other species is in line with the theory of "competitive exclusion" [7] and the capacity L. iners and L. crispatus to compete with other bacteria or survival strategy known as interference bacterial. Alternatively, the rare coexistence of multiple dominant species of lactobacilli could lead to prevention of colonization by a particular species, or factors of the host that influence in a way very important for species to be able to of colonizing the environment [1-3]. Racial variation and geographical area are important and different racial groups within the same geographic region have differences significant in the dominant organisms in the vagina [1-3,15-18]

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Racial variation and geographical area are important and different racial groups within the same geographic region have differences significant in the dominant organisms in the vagina [1-3,15-18]. In most L populations, crispatus is the dominant commonly isolated and women are more likely to have dominance by L. crispatus and L. jensenii than any other species of lactobacilli. Genetic factors, environmental factors explain at least part of this observation. Alternatively, the diet may to influence the residence of the species of lactobacilli in the genitourinary apparatus and vagina, and lactobacilli of the intestine vary between Eastern and Western women. Production of H₂O₂ by lactobacilli and association with bacterial vaginosis Lactobacilli differ in their ability to producing H₂O₂; the reduction of prevalence and concentration of producing bacteria H_2O_2 is associated with the onset of bacterial vaginosis and vaginal infections. Now, with the techniques it is possible to relate species to or H₂O₂ producing strains there of species of lactobacilli, of the individual instead of gender as a whole.

In Japanese women without bacterial vaginosis found: L. crispatus and L. jensenii in the vagina in 20.8% of the sample. Lactobacillus jensenii no was detected and all strains of L. crispatus were positive for H_2O_2 , whereas 41 and 59% of the strains of L. gasseri were weakly positive for H₂O₂, respectively. It proved that the species of lactobacilli detected in women with and without bacterial vaginosis differ in its ability to produce H₂O₂. The Lactobacilli Crispatus and L. jensenii colonize to 32 and 23% of women, respectively [1-19] 94% of women their strains, respectively, produce H_2O_2 . In contrast, L. gasseri and L. iners colonize 5 and 15% of women, respectively, and only 71 and 9% of their strains, respectively, produce H_2O_2 . It is not surprising that bacterial vaginosis found in 9 and 7% of colonized women by L crispatus and L. jensenii, respectively, and in 43 and 36% of the women colonized by L. gasseri and L iners, respectively. In 16% of women without bacterial vaginosis are not found lactobacilli, and none of the women colonized with L crispatus and L jensenii had bacterial vaginosis; the association between L gasseri and bacterial vaginosis has been confirmed in lesbian women.

The detection of *L gasseri* is associated with 4.2 times greater risk of bacterial vaginosis [20] attributed to rectal colonization, most of them by *L gasseri* and sexual practices that increase the risk of vaginal colonization of the rectum [21]. By culture it

was found that 100% of *L* jensenii produces H_2O_2 . but only 46% produce H₂O₂; with *L* acidophilus the species range which produce H₂O₂ ranged from 43 to 77%. Due to the inability to differentiate species belonging to the complex of *L* acidophilus and the ability of lactobacilli to produce H₂O₂ was associated with the strain origin (either of women with or without bacterial vaginosis) in place of the lactobacilli. In contrast, L gasseri and L iners colonize 5 and 15% of women, respectively, and only 71 and 9% of their strains, respectively, produces H_2O_2 . It is not surprising that bacterial vaginosis found in 9 and 7% of colonized women by L crispatus and L jensenii, respectively, and in 43 and 36% of the women colonized by *L gasseri* and *L* iners, respectively. In 16% of women without bacterial vaginosis are not found lactobacilli, and none of the women colonized with L crispatus and L jensenii had bacterial vaginosis; the association between L gasseri and bacterial vaginosis has been confirmed in lesbian women. The detection of L gasseri is associated with 4.2 times greater risk of bacterial vaginosis [20] attributed to rectal colonization, most of them by *L. gasseri* and sexual practices that increase the risk of vaginal colonization of the rectum. By culture it was found that 100% of L jensenii produces H_2O_2 , but only 46% produces H_2O_2 ; with L. acidophilus the species range which produces H_2O_2 ranged from 43 to 77%. Due to inability to differentiate species belonging to the complex of L acidophilus and the ability of lactobacilli to produce H₂O₂ was associated with the strain origin (either of women with or without bacterial vaginosis) in place of the lactobacilli.

Healthy vaginal flora not subject to lactobacilli It has been shown that a significant proportion (7-33%) of healthy women lacks species of lactobacilli in the vagina, which are replaced by other bacteria producing lactic acid, such as the vaginal species of Megasphaera and Leptotrichia. Atopobium. Although the structure of vaginal flora differs between populations, its maintains the production function of lactic acid [7]; the absence of lactobacilli or existence of certain organisms, such as: Gardnerella vaginalis, species of or Peptostreptococcus, Prevotella, Pseudomonas or Streptococcus, constitute an abnormal state. Some proportions of healthy women is patients in transition from bacterial vaginosis, or has vaginosis bacterial and remain asymptomatic; is to say, they have abnormal flora without symptoms. Even, Gvaginalis is reported to produce dominance transient in healthy women as a result of alterations resulting from pH increase during menstruation [1-3].

Probiotic lactobacilli in the vagina

A culture of *L* acidophilus was demonstrated the eradication of *Neisseria* gonorrhoeae. The exogenous strains of lactobacilli have been suggested as a means of establishing or reestablishing the normal vaginal flora of Lactobacillus fermentum and Lactobacillus rhamnose, probiotic strains used with poor results in infection urogenital, because they do not come from the vagina. In contrast, L crispatus is the best choice because it is common in the healthy vagina; 95% of the strains of lactobacilli produce H₂O₂. L crispatus has a superior ability to persist in vagina. The strains of probiotic *L* crispatus have demonstrated, in vitro, high cell adhesion epithelial cells of the vagina, with vaginal colonization and rectal when colonization is administered through the vagina of lactobacilli producing H₂O₂ which is associated with decreased incidence of bacterial vaginosis. Molecular techniques in non-pregnant women, sexually active, free of infection genital, the capacity of the probiotic L crispatus CTV-05 to vaginal colonization. L crispatus establish established vaginal colonization during follow-up in 69% of women in general, and 90% of those who were not colonized by L crispatus and in women who never were colonized with L crispatus, 85% already were endogenously colonized with L crispatus; self-regulation was seen instead of a probiotic deficiency; it is recommended to investigate lactobacilli that are prevalent in the vagina [1-3].

Abnormal vaginal microbiota

The vaginal macrobiota becomes abnormal as consequence transmission infections of (trichomoniasis) and colonization by a organism that is not part of the normal vaginal flora. Alterations in the vaginal microbiota do not involve disease or symptoms; the illness results from the interaction between microbial virulence, dominance, and the host's immune and adaptive response. The most common is bacterial vaginosis; this condition poly microbial, characterized by decrease in the quality or quantity of lactobacilli and increase of 1000 times in the number of others organisms, in particular anaerobes such as: Mycoplasma hominis, G. vaginalis and species of Mobiluncus. The prevalence of bacterial vaginosis in pregnancy in the United States United States is 1,080,000 per year and is associated miscarriage, recurrent, post abortion sepsis, postpartum endometritis and preterm delivery [1-3].

Bacterial vaginosis is associated with HIV acquisition

The healthy, acid-producing vaginal microbiota lactic acid, acts as a barrier against of HIV and prevents bacterial vaginosis, which acts as a codriver for the acquisition of HIV and their conversion to HIV-positive in HIV. Women with bacterial vaginosis have higher viral load levels in the HIV in genital secretions than women infected with HIV without bacterial vaginosis. Bacterial vaginosis is also associated with increased susceptibility to other infections of sexual transmission, including the herpes virus simple 2 (HSV-2), HPV, gonorrhea, Trichomonas vaginalis and *Chlamydia trachomatis*. The techniques molecules suggest greater diversity in microbiota in HIV positive women with bacterial vaginosis in comparison with who have HIV without bacterial vaginosis. This suggests that HIV infection per se is associated with changes in the diversity of the microbiota

of the genitals [1-3].

Individual bacteria that cause vaginosis bacterial

To show that bacteria work as mono etiological agents it is necessary observe the microenvironment before the episodes infectious. G vaginalis acts synergistically with other organisms to cause vaginosis bacterial. Atopobium vaginal is of the genus Atopobium, part of the family Coriobacteriaceae, and forms a distinct branch within the phylum Actinomycetales, three species of Lactobacilli minutus that formally designate Lactobacilli rimae and Streptococcus parvulus within the group of lactic acid bacteria, reclassified such as Atopobium. Atopobium vaginae is isolated from healthy vaginas although much more frequent in women with bacterial vaginosis than in those of normal flora. In addition to production of lactic acid [7-9] some species of Atopobium exhibit peptidyl peptidase activity and produce significant amounts of ammonia in other settings where sugars are a scarce source of energy. It is the reason why A vaginae is most commonly found in the vagina of postmenopausal women without THM, comparison when they take THM. Prevotella bivia also produces ammonia, which is known to act as a substrate to promote the growth of *G. vaginalis*. Atopobium vaginae is strictly anaerobic and sensitive to lindamycin, but resistant to nitroimidazoles, such as metronidazole and secnidazole.

Greater diversity of bacterial microbiota in bacterial vaginosis compared to healthy microbiota

The use of various molecular techniques and Amsel's clinical criteria, or scoring Nugent to classify the normal flora or have shown a great diversity of organisms in women with bacterial vaginosis compared with normal microbiota. Demonstrate the existence of new species bacterial infections previously unidentified in crops. Many of these specificity for bacterial vaginosis, and the number of filo types is associated with bacterial vaginosis [5,6,17,18]. Many of these micro organisms are unknown to physicians and there is no evidence of their association with disease. Minium atopobium and Atopobium rimae have been associated with dental abscesses and oral infections, tube-ovarian abscesses and abdominal wound infections. This opinion is supported by the fact that these pathogens for the host. Leptotrichia sanguinegens-amnionii is reported in association with postpartum endometritis, adnexal masses and death fetal. It has been detected in amniotic fluid of women with preterm birth, premature rupture of membranes and preeclampsia [22-24] and in women with bacteria closely related philo types with the species Leptotrichia and A vaginae [1-3,23]. Dialister pneumosintes was found to be unique agent in the blood culture of a woman with suppurative postpartum ovarian thrombosis [20-25]. It has been demonstrated that different bacterial vaginosis has different profiles microbial growth, indicating heterogeneity in bacterial composition in women with bacterial vaginosis.

Atopobium vaginae
Bacterial Vaginosis Associated With BVAB1,
BVAB2, and BVAB3
Megasphaera spp
Leptotrichia spp
Dialister spp
Chloro flexi spp
Olsenella spp
Strepto bacillus spp
Shuttleworthia spp
Porphyromonas asaccharolytica

Table 2: Vaginal Organisms Previously UnknownIdentified By Molecular Techniques.

Those who did not have vaginosis bacteria had bacterial communities dominated by Lactobacillus

species, which represent 86% of all sequences. In contrast, women with bacterial vaginosis do not have a single dominant philaids had a different range of bacteria vaginal Bacterial vaginosis is diagnosed clinically, with the use of clinical criteria, microscopic, enzymatic, chromatographic, crops. The reference standard is the score of Nugent, but there is no single ideal test, and all provide false results and negatives. positive Molecular techniques explain why the microscopic diagnosis is inconsistent, one of the three agencies, as part of the Nugent Score, is Mobiluncus and for molecular techniques only rarely identifies. By hybridization fluorescence technique in situ (FISH) has shown that in the bacterial vaginosis associated bacterium 1 (BV-1) to bacterial vaginosis or associated vaginosis with bacterium 1 (BVAB1) has a morphology similar to Mobiluncus morpho types [1]. With the Microscopic examination of vaginal smear of Mobiluncus have been over-represented and confused with BVAB1.

Alternatively, with Specific PCR according to the Nugent score, Mobiluncus often falls below a threshold title where it can be detected. It has also been observed that the urea produced by species Atopobium is associated with halitosis. Two genera associated with metabolites may be smelly and found in the vagina of healthy women, and amines found in women without bacterial vaginosis. The techniques diagnosis of bacterial vaginosis, based on in the production of amine and the formation of odor, make microscopic smears necessary. Atopobium species are gram-positive, coco seliptic as, or of organisms in form of rods that are produced, separately, in pairs or in short chains. The morphology of the cells is variable, the Atopobium hides it among the mix of other species present in the bacterial communities in the that the Nugent Score that ‡. Atopobium vaginae is inopportune, it grows an aerobically and forms small pinhead colonies in crops that are easily lost. Although phylo genetically different from other bacteria producers of lactic acid, which are not phenol typically exceptional, and it is not difficult to see, the importance of this body on the basis of culture, microscopy, and phenotype is passed by high and underestimated. Specific species related to the five incompatible agencies associated with bacterial vaginosis compared with diagnosed bacterial vaginosis by the Amsel criteria and scores of Nugent, or individual clinical criteria for Amsel [1-3,26].

The two biotypes of Urea plasma urealyticum (*Ureaplasma parvum* and Ureaplasma urealyticum (biovar 2)) are associated with vaginal discharge

and pH elevated but not with bacterial vaginosis any of the Amsel or Nugent criteria, or Amsel's individual clinical criteria. By contrast, with Leptotrichia sanguinegens-amnionii, A. vaginas and BVAB1, a pH greater than 4.5 was a universal feature. They were associated with bacterial vaginosis for both Amsel and Nugent, and with the finding of over20% of epithelial cells as key cells characteristics. A positive test for amine odor after of the addition of the 10% hydroxide solution of potassium was significantly more likely in BVAB1 positive women. Vaginal showers are a risk factor recognized for bacterial vaginosis and detection of Leptotrichia and A vaginae was three times, and twice as likely BVAB1, when women reported showers [1-2,26]. Some organisms or combination of organisms had sensitivities high or specificities for diagnosis of bacterial vaginosis using the criteria of Amsel and the Nugent score, using realtime PCR, the association of organisms with bacterial vaginosis diagnosed by the Nugent Score. Lactobacilli and several known organisms are associated with bacterial vaginosis. Lactobacillus species are predictive of the normal flora (sensitivity 44%, specificity100%). BVAB1, BVAB2, and only BVAB3, or incombination, have a high specificity for to diagnose bacterial vaginosis [1-3].

Combination of a Vaginae and g Vaginalis for the Diagnosis of Bacterial Vaginosis

They are detected with the help of molecular techniques in association with bacterial vaginosis [9]. In samples of bacterial vaginosis, they had A vaginae or G vaginal is, or both. The combination of these showed better predictive criteria of the diagnosis of bacterial vaginosis with excellent sensitivity (95%) and specificity (99%). Negative predictive value (NPV) (99%) and value positive predictive value (PPV) (95%). The quality and reproducibility of this combination was applied, prospectively, for the validation of the of Nugent in pregnant women [1-3] and the NPV was 96 and VPP was 99%. Independent farming techniques for evaluate the treatment of recurrence, persistence or resistance of vaginosis bacterial for treatment or reduction of symptoms of bacterial vaginosis is recommended metronidazole or clindamycin with which it may achieve 83-94% effectiveness in 7-21 days of treatment. The response to treatment short term is acceptable, but vaginosis persists or reappears in 11-29% of women in 1 month. Thirty percent of patients fall within the first three months, and recurrence rates are greater than 50% per year. Alone 48% of women are colonized by

lactobacilli producing H_2O_2 70-90 days after treatment with clindamycin or metronidazole by molecular techniques [6,17,27].

Women with positive bacterial vaginosis are almost always colonized by L iners, although many other non-Lactobacillus species coexist [17]. In women with bacterial vaginosis treated properly and followed during months Atopobium vaginae was detected in 75% and G vaginalis in 100% bacterial vaginosis recurrent women and women with higher recurrence of bacterial vaginosis (83%) in compared with women who had G vaginalis alone (38%) (p <0.001). The most important fact is that more than 90% of biofilms identified in the vaginal epithelial cells of women with bacterial vaginosis were from a vaginas and vaginalis [28]. Biofilms interferes with the treatment and it is not determined whether the recurrence is a result of inadequate treatment or low or undetectable levels of organisms after treatment (relapse), re infection of sexual partners, or interruption of normal flora or other exogenous factors. In the atypical form of bacterial vaginosis, several bacterial species are detected, none of which are commonly associated with vaginosis explains why therapy did not work and indicate that another antimicrobial may have been more effective; the PCR, identifies 17 different bacteria associated with bacterial vaginosis; in women with bacterial vaginosis, the vaginal microbiota before treatment and 1 month later for one proof of healing; the treatment was 5 days of intravaginal metronidazole gel, one month later of the treatment, bacterial vaginosis was present in 26% of women. The detection of bacteria associated with bacterial vaginosis or Bacterial vaginosisassociated bacteria (BVAB); VAB 1, BVAB2, and BVAB3 BVAB1, BVAB2, and BVAB3, Lacrimalis Peptoniphilus, or Megasphaera phylotype, are related to persistence of bacterial vaginosis in the test of healing; vaginal microbiology prior to treatment at the time of diagnosis could define the risk of therapeutic failure [1,27]; these correlations will become clearer and meaningful using PCR, instead of simply detecting/incidence [1,28].

Conclusion

Molecular techniques provide new information on the vaginal microbial flora and allows its identification as *L. Iners* and *A. Vaginas*; but will not replace the crop, with its use is best understood the vaginal microbiota. In most circumstances, the microbiota normal vaginal area is dominated by Lactobacillus. In the absence of lactobacilli, normality can be maintained by other lactic acid bacteria, demonstrated that the healthy vagina is colonized usually with one or two species Lactobacillus dominants, mainly *L. Crispatus, L. Iners, L. jensenii*, and *L. gasseri*. The species of Lactobacillus differ racially and geographically. Molecular techniques indicate that there is a greater diversity of microorganism is associated with bacterial vaginosis, we can improve the diagnosis of each subtype of vaginosis bacterial, and give appropriate treatment.

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