The female genitourinary tract is home to a wide range of microbial life. The microorganisms in the vagina (known collectively as the vaginal microbiome) play an important role in vaginal and cervical health, and in the development of additional comorbidities [1]. Vaginal dysbiosis refers to an abnormality of the vaginal microbiome, either due to increased microbial diversity, low levels of lactobacilli, or increased levels of anaerobes such as Gardnerella vaginalis [2].

The vaginal microbiome is dynamic [3] and appears to be influenced by many factors: ethnicity, smoking, douching, menstrual cycles, hormonal contraceptives, progesterone and estrogen levels, and sexual intercourse [4]. Variations in the vaginal microbiome are associated with a range of conditions, including sexually transmitted infections (STIs), pelvic inflammatory disease (PID), delayed clearance of human papillomavirus (HPV), bacterial vaginosis, urinary tract infections (UTIs) [2], and even cervical cancer [5].

**INTRODUCTION**

Patients with vaginal dysbiosis may present with a variety of signs or symptoms, though many patients may have no active clinical indications present in their history or examination.

Presenting signs and symptoms may include:

- Change in urinary frequency
- Dysuria
- Dyspareunia
- Vaginal pruritis or pain
- Vulvovaginal irritation
- Vaginal discharge
- Vaginal odor
- Vaginal erythema or edema
- Abnormal vaginal bleeding
- Abdominal or lower back pain
- Cervical pain
- Cervical discharge
Clinical approach and recommendations

- Sexually transmitted infections
- Idiopathic infertility
- Pelvic inflammatory disease
- High-risk HPV infection
- Low-risk HPV infection
- Bacterial vaginosis
- Urinary tract infections
- Urogenital, anal, or oral carcinoma
- Cervical cancer

Related diagnoses may include:

- Sexually transmitted infections
- Idiopathic infertility
- Pelvic inflammatory disease
- High-risk HPV infection
- Low-risk HPV infection
- Bacterial vaginosis
- Urinary tract infections
- Urogenital, anal, or oral carcinoma
- Cervical cancer

TESTING

The SmartJane clinical test extracts microbial DNA from an at-home vaginal swab sample and identifies microorganisms that may be associated with health conditions. The test yields information about overall microbial diversity, high-risk human papillomavirus (HPV) strains, and the presence of individual microorganisms associated with certain health conditions. SmartJane results also include a Significance Index (SI): a measure of how your vaginal microbiome’s composition departs from that of healthy individuals for species known to be associated with a particular health condition, based on published research.

INDIVIDUALS SUITABLE FOR TESTING

- Asymptomatic patients who seek to learn more about their vaginal microbiome in collaboration with their physician (screening test)
- History of sexually transmitted infection (including HPV)
- History of high-risk HPV infection
- History of low-risk HPV infection
- Active symptoms of vaginitis or cervicitis
- Recurrent urinary tract infections
- Idiopathic infertility
- Vaginal dryness or dyspareunia
- History of genitoanal cancer
- History of HIV+ or immunosuppression
- History of tobacco smoking
- Family history of cervical cancer
TEST RESULTS

SmartJane results enable a better understanding of:

- Specific pathogens present that might be causing illness
- Specific microorganisms that may potentially influence disease

REPORT INFORMATION

PATHOGENIC MICROORGANISMS

The SmartJane clinical test currently detects 14 high-risk HPV types (16/18/31/33/35/39/45/51/52/56/58/59/66/68), five low-risk HPV types (6/11/42/43/44) as well as four additional etiologic agents of sexually transmitted infections (STIs): *Treponema pallidum, Chlamydia trachomatis, Mycoplasma genitalium* and *Neisseria gonorrhoeae*. Presence of one or more of these types of organisms may indicate the need for clinical screening and/or treatment. Note that carriers of those microorganisms causing STIs are often asymptomatic.

Presence of pathogenic microorganisms and high-risk HPV types are associated with:

- Cervical, vulvar, vaginal, anal and oral cancer (high-risk HPV) [5]
- Anogenital warts (low-risk HPV) [6]
- Pelvic inflammatory disease (*N. gonorrhoeae, C. trachomatis* and *Mycoplasma genitalium*) [7]
- Infertility (*N. gonorrhoeae, M. genitalium* and *C. trachomatis*) [8,9]

POTENTIALLY HARMFUL MICROORGANISMS

The SmartJane clinical test provides information about individual microorganisms that have been associated with vaginal dysbiosis. An increased abundance of anaerobic organisms such as *Atopobium vaginae* and *Gardnerella vaginalis*, both part of biofilms, as well as members of *Prevotella*, were associated with the abnormal microbiota observed in bacterial vaginosis [10-12]. Presence of these microorganisms may be indicative of increased risk for certain health conditions. See the table below for specific correlations and the condition treatment guides for additional treatment options.

POTENTIALLY BENEFICIAL MICROORGANISMS

The SmartJane clinical test provides information about individual microorganisms that appear to be inversely associated with certain health conditions (e.g. *Lactobacillus* species, key members of the healthy vaginal microbiota [10]). Lowered levels of these microorganisms may be indicative of increased risk for certain health conditions. See the chart below for specific correlations and the SmartJane Physician Treatment Guides for additional treatment options.
TREATMENT APPROACH

The composition of the vaginal microbiome can be modified using interventions such as diet [13,14], antibiotics [15], or oral and vaginal probiotics [16-18], as well as by the practice of vaginal hygiene techniques such as douching [19]. Regular monitoring of vaginal microbes can encourage patient compliance, and can assist physicians in formulating a treatment plan to prevent active and future disease.

Clinical applications for SmartJane include:

• Monitoring of high-risk HPV infection and clearance
• Carcinoma risk assessment
• Identification of sexually transmitted disease
• Risk assessment for pelvic inflammatory disease
• Diagnosis and monitoring of bacterial vaginosis
• Assessment of Significance Index between vaginal microbiota and HPV infection, bacterial vaginosis, aerobic vaginitis, pelvic inflammatory disease, idiopathic infertility and cervicitis

Please refer to our SmartJane Physician Treatment Guides for more treatment guidance on the following categories of conditions:

Human Papillomavirus Treatment Guide
Sexually Transmitted Infections Treatment Guide
Vaginal Dysbiosis Treatment Guide
## HEALTH ASSOCIATIONS FOR SMARTJANE TARGETS

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<th>Microorganism</th>
<th>Human Trichomonas Infection</th>
<th>Cervical Cancer</th>
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<th>Genital Warts</th>
<th>Genital Herpes Infection</th>
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METHOD

- Patient-friendly, at-home sampling process following standardized procedures [20,21].
- Sampling takes under 2 minutes, simplifying patient responsibility and burden.
- Microorganisms in samples are lysed and the DNA is stabilized in a buffer solution before patient mails to uBiome laboratory.
- Microbial DNA is extracted, then marker genes are amplified by polymerase chain reaction (PCR) and sequenced using the Illumina® NextSeq 500 sequencer.
- Samples are analyzed using high-throughput bioinformatics, which incorporate phylogenetic algorithms and custom databases specifically developed for microbiome data.
- On average, the sensitivity, specificity, precision, and negative prediction value for the microorganisms on our target list are 99.4%, 100.0%, 98.2%, 100.0% for the species, and 97.1%, 100.0%, 99.9% and 100.0% for the genera, respectively.

SUMMARY

- The genitourinary tract is home to a diverse microbial population, which appears to play a vital role in human health, and in the development and progression of certain symptoms and diseases.
- Disruptions to the vaginal microbiota can lead to vaginal dysbiosis, which is asymptomatic in many patients.
- Vaginal dysbiosis is associated with certain disease conditions: chronic HPV infection, cervical cancer, sexually transmitted infections, pelvic inflammatory disease, and bacterial vaginosis.
- The presence or absence of certain microorganisms appear to contribute to vaginal dysbiosis. Certain microorganisms appear to be associated with poor health and increased morbidity.
- The vaginal microbiome can be optimized through interventions such as dietary changes, prudent use of antibiotics, and certain probiotics and prebiotics.
- Monitoring the vaginal microbiome at regular intervals can assist with patient adherence, provide information about the effectiveness of interventions, and help monitor overall health and disease progression.
References

5. A. Mitra, D.A. MacIntyre, J.R. Marchesi, Y.S. Lee, P.R. Bennett, M. Kyrgiou, Microbiome 4 (2016) 58