

A FOGSI President's Initiative



Infection Practice Points
By Dr. Nandita Palshetkar



INFECTION PRACTICE POINTS VAGINITIS EVALUATION AND MANAGEMENT



Presenting

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- Vaginal Candidiasis

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Hyaluronic acid releases water molecules to the tissues,
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- After 10 Applications significant improvement in
- Dryness by 84.44%
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 - Burning by 85.83%

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Dear FOGSIANS,

The theme of FOGSI this year is "We for Stree". I would like to thank every FOGSIAN who has helped making every woman Safer, Stronger and Smarter. Through various academic and social programs FOGSI aims to uplift the quality of care that is given to every woman who comes to us.

TOG IPP (Infection Practice Points) is one such conclave that brings to light some of challenging health issues like Vaginitis, Pelvic inflammatory disease (PID) and Urogenital infections.

I would like to thank Zuventus for their contributions towards the TOG IPP Conclave.

We, as clinical practitioners are always busy, therefore the TOG IPP that is released has been a quick and easy way to update you with the latest evidence in the field of Infections. This year we ask all FOGSIANS to focus on the Stree and help make them safer, smarter and stronger.

Select FOGSIANS across India came together to deliberate and create these practice points. I am sure that you will appreciate the efforts which has gone into preparing the Infection Practice Points and find them useful in your day to day practice.

Best wishes!

Nandita P. Palshetkar

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VAGINITIS

Evaluation & Management

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From left to right: Dr. Meeta Nakhare, Dr. Suvarna Khadilkar, Dr. Vidya Pancholia, Dr. B.S. Jodha, Dr. Jiteeka Thakkar, Dr. Sunita Arora, Dr. Parag Biniwale, Dr. Sunil Jindal, Dr. Nandita Palshetkar, Dr. Hrishikesh Pai, Dr. Monika Doshi, Dr. Milind Shah, Dr. Reena Wani, Dr. Brajbala Tiwari, Dr. Usha Shekhawat, Dr. Oby Nagar

VAGINITIS

Evaluation & Management

Introduction

Vaginitis is indicative of a condition with symptoms of abnormal vaginal discharge, odor and irritation, itching, or burning. The most common causes of vaginitis are vulvovaginal candidiasis, bacterial vaginosis and trichomoniasis. Bacterial vaginosis affects about 40% to 50% of women, which includes vulvovaginal candidiasis accounting for 20% to 25% and trichomoniasis for about 15% to 20% of cases. Noninfectious causes such as atrophic, irritant, allergic and inflammatory vaginitis are less common, accounting for about 5% to 10% of all cases of vaginitis.¹

Diagnosis of vaginitis involves the use of a combination of symptoms, physical examination findings and office-based or laboratory testing. Bacterial vaginosis is conventionally diagnosed using Amsel criteria, but the diagnostic standard is Gram staining. Advances in the laboratory tests has enabled to detect ion of *Gardnerella vaginalis* DNA or vaginal fluid sialidase activity. These tests have sensitivity and specificity similar to Gram stain. Bacterial vaginosis is treated with oral metronidazole, intravaginal metronidazole, or intravaginal clindamycin.¹ However, treatment of bacterial vaginosis with clindamycin is associated with marked evidence of antimicrobial resistance among vaginal anaerobic bacteria, which increases the vaginal reservoir of macrolide-resistant bacteria.² In a study, researchers have shown that all tested strains, except one, were sensitive to clindamycin and amoxicillin/clavulanic acid. The susceptibility test results

also showed that 68.7% strains were resistant to metronidazole and all strains were sensitive to both clindamycin and amoxicillin/clavulanic acid.³

Bacterial Vaginitis is characterized by an overgrowth of predominantly anaerobic organisms (e.g. *Gardnerella vaginalis*, *Prevotella* spp., *Mycoplasma hominis*, *Mobiluncus* spp.) in the vagina leading to a replacement of lactobacilli and an increase in vaginal pH. Other commonly seen are vaginal candidiasis and trichomoniasis.

In cases of vulvovaginal candidiasis, diagnosis is made using a combination of clinical signs and symptoms with potassium hydroxide microscopy. However, DNA probe testing is also available. The culture is useful for the diagnosis of complicated vulvovaginal candidiasis by identifying nonalbicans strains of *Candida*. Treatment of vulvovaginal candidiasis involves oral fluconazole or topical azoles, although only topical azoles are recommended during pregnancy. Trichomoniasis is treated with oral metronidazole or tinidazole and patients' sex partners should be also be treated. Treatment of non-infectious vaginitis should be directed at the underlying cause. Atrophic vaginitis is treated with hormonal and non-hormonal therapies. Probiotics positively effects on vaginal microflora composition by promoting the proliferation of beneficial microorganisms, alters the intravaginal microbiota composition, prevents vaginal infections in postmenopausal women.¹

First-line non-hormonal treatment recommendations include vaginal lubricants and moisturizers; continued sexual activity should be encouraged.⁴ Probiotics reduce the symptoms of vaginal infections (e.g., vaginal discharge, odor, etc.) and are useful in the treatment and prevention of bacterial vaginosis and vulvovaginal candidiasis.⁵ Inflammatory vaginitis may improve with topical clindamycin as well as steroid application.

RECURRENT VAGINITIS⁶

- Vaginitis recurring within 3 to 4 months and within 3-4 years.
- Investigation of female partner: PAP smear, HPV screening, vaginal swab
- Investigation of male partner: Culture from the prepuce, urine routine & microscopy, semen culture, blood sugars

Signs and symptoms of vaginitis

Table 1. Signs and symptoms of vaginitis¹

Diagnosis	Etiology	Symptoms	Signs	Other risks
Bacterial vaginosis	Anaerobic bacteria (Prevotella, Mobiluncus, Gardnerella vaginalis, Ureaplasma, Mycoplasma)	Fishy odor; thin, off-white homogenous discharge that may worsen after intercourse; pelvic discomfort may be present	No inflammation	Increased risk of HIV, gonorrhoeae, chlamydia and herpes infections
Vulvovaginal candidiasis	<i>Candida albicans</i> , can have other <i>Candida</i> species	White, thick, cheesy, or curdy discharge; vulvar itching or burning; no odor (pruritis dysuria)	Vulvar erythema and edema	-
Trichomoniasis	<i>Trichomonas vaginalis</i>	Green or yellow, frothy discharge; foul odor; vaginal pain or soreness copious, malodorous, yellow-green (or discolored) discharge Pruritus Vaginal irritation No symptoms in 20% to 50% of the affected women	Inflammation; strawberry cervix	Increased risk of HIV infection Increased risk of preterm labor Should be screened for other sexually transmitted infections
Atrophic vaginitis	Estrogen deficiency	Thin, clear discharge; vaginal dryness; dyspareunia; itching	Inflammation; thin, friable vaginal mucosa	-
Irritant/allergic vaginitis	Contact irritation or allergic reaction	Burning, soreness	Vulvar erythema	-
Inflammatory vaginitis	Possibly autoimmune	Purulent vaginal discharge, burning, dyspareunia	Vaginal atrophy and inflammation	Associated with low estrogen levels

HIV = human immunodeficiency virus.

Risk factors contributing to vaginitis⁷

Bacterial vaginosis	Low socioeconomic status, vaginal douching, smoking, use of an intrauterine contraceptive device, new/multiple sex partners, unprotected sexual intercourse, homosexual relationships, frequent use of higher doses of spermicide nonoxynol-9
Trichomoniasis	Low socioeconomic status, multiple sex partners, lifetime frequency of sexual activity, other sexually transmitted infections, lack of barrier contraceptive use, illicit drug use, smoking
Vulvovaginal candidiasis	Vaginal or systemic antibiotic use, diet high in refined sugars, uncontrolled diabetes mellitus, HIV
Atrophic vaginitis	Menopause, other conditions associated with estrogen deficiency, oophorectomy, radiation therapy, chemotherapy, immunologic disorders, premature ovarian failure, endocrine disorders, antiestrogen medication , HIV, Baleno prostatitis, infected male partners
Irritant contact dermatitis	Soaps, tampons, contraceptive devices, sex toys, pessary, topical products, douching, fastidious cleansing, medications, clothing, HIV
Allergic contact dermatitis	Sperm, douching, latex condoms or diaphragms, tampons, topical products, medications, clothing, atopic history

HIV: human immunodeficiency virus.

Complications of vaginitis

Bacterial vaginosis is associated with⁸

- Post-hysterectomy vaginal cuff infection
- Post-abortion endometritis
- Increased risk of spontaneous miscarriage ranging from 13 to 24 gestational weeks and preterm birth
- Increased risk of acquiring sexually transmitted infections (STI), especially genital herpes and HIV

Vaginal trichomoniasis is associated with⁸

- Adverse pregnancy outcomes
- Premature rupture of membranes and preterm delivery
- Low birth weight

There is evidence that trichomoniasis may enhance HIV transmission⁸

Risk factors leading to vaginitis should be looked for.

Diagnosis⁹

Table 2. Diagnosis of bacterial vaginosis, vulvovaginal candidiasis and trichomoniasis

Basis of diagnosis	Bacterial vaginosis	Vulvovaginal candidiasis	Trichomoniasis
Physical examination (clinical signs)	Usually, normal appearance of tissue; discolored discharge with abnormal odor, homogeneous discharge that adheres to vaginal walls	Vulvar and vaginal erythema, edema and fissures Thick, white discharge that adheres to vaginal walls	Vulvar and vaginal edema and erythema 'Strawberry' cervix in up to 25% of affected women Frothy, purulent discharge
Laboratory tests			
Vaginal pH (normal ≤ 4.5)	Elevated (> 4.5)	Normal	Elevated (> 4.5)
Microscopic examination of wet-mount and KOH preparations of vaginal discharge	'Clue cells' (vaginal epithelial cells coated with coccobacilli) Few lactobacilli, occasional motile, curved rods (Mobiluncus species)	Pseudohyphae, mycelial tangles or budding yeast cells	Motile trichomonads Many polymorphonuclear cells
'Whiff' test (normal = no odor)	Positive	Negative	Can be positive
Additional tests	Amsel's criteria (three of four criteria must be met): provides correct diagnosis in 90% of affected women	KOH microscopy Gram stain Culture	DNA probe tests: sensitivity of 90% and specificity of 99.8%
	Criteria of Nugent or Spiegel for Gram stain to diagnose bacterial vaginosis Other tests are controversial.		Culture: sensitivity of 98% and specificity of 100%

KOH = potassium hydroxide.

Nugent's diagnostic criteria for bacterial vaginosis⁹

Scoring system (zero to 7+)* is a weighted combination of the following bacterial morphotypes:

- A. *Lactobacillus acidophilus* (large Gram-positive rods)
- B. *Gardnerella vaginalis* and Bacteroides species (small Gram-variable or Gram-negative rods)
- C. Mobiluncus species (curved Gram-variable rods)

The total score is the sum of the weighted quantity of the three bacterial morphotypes.

Scoring for each of the above bacterial morphotypes:

Zero = No morphotypes per oil-immersion field

- 1+ = Less than one morphotype per oil-immersion field
- 2+ = One to four morphotypes per oil-immersion field
- 3+ = Five to 30 morphotypes per oil-immersion field
- 4+ = More than 30 morphotypes per oil-immersion field

Amsel diagnostic criteria for bacterial vaginosis⁹

- Thin, homogenous discharge
- Positive whiff test (i.e., the amine odor produced by mixing 10% potassium

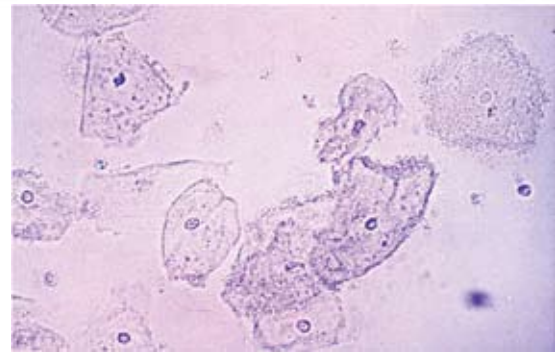
hydroxide solution with vaginal discharge sample)

- Clue cells present on microscopy† (Figure 1)
- Vaginal pH > 4.5

Recurrent vaginitis⁶

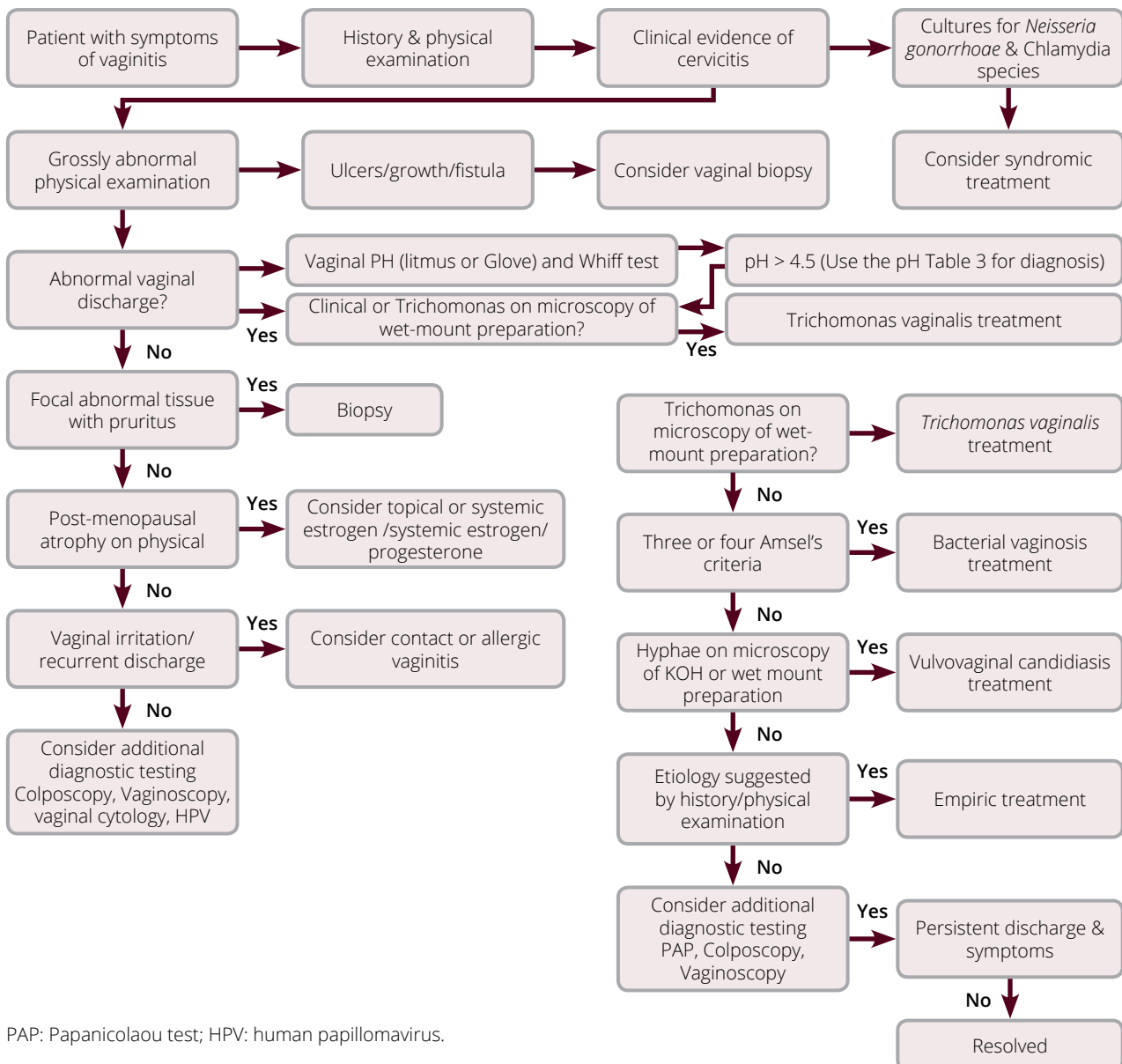
- Vaginitis recurring within 3 to 4 months
- Investigation of female partner: PAP smear, HPV screening, vaginal swab
- Male partner: Culture from the prepuce, urine routine and microscopy, semen culture and blood sugars

Figure 1. Clue cells (400 ×). Vaginal epithelial cells with borders obscured by adherent coccobacilli visible on saline wet-mount preparation



*Three out of four criteria must be met; establishes accurate diagnosis of bacterial vaginosis in 90% of affected women.
†Highly significant criterion.

Algorithm for the diagnosis of vaginitis⁹



PAP: Papanicolaou test; HPV: human papillomavirus.

Use of vaginal pH in diagnosis

Simple tools like pH test and Whiff test can be done without high expertise, microscope and even speculum. This can improve diagnostic value of syndromic approach of abnormal vaginal discharge. As per Amsel diagnostic criteria for bacterial vaginosis, the presence of three out of four factors are necessary for diagnosis of bacterial vaginosis. In presence of abnormal vaginal discharge, both vaginal PH and Whiff test has 100% sensitivity.¹⁰ A number of studies have shown that trichomoniasis grows when there is pH more than 4.5 and candidiasis when pH is less than 4.5.¹¹

Elevated vaginal pH is associated with adverse pregnancy outcomes, such as increased risk of preterm labor, low birth weight delivery and premature rupture of membranes (ROMs). Hence, it is recommended to screen for increased vaginal pH during pregnancy. The studies have shown its usefulness in lowering preterm birth rates.¹²

It is recommended to screen for increased vaginal pH during pregnancy, as it may be useful in reducing preterm birth rates.

Table 3. Use of vaginal pH in diagnosis¹³

	3.5	4.0	4.5	5.0	5.5	6.0
The normal vaginal pH is between 3.8 and 4.5. An altered vaginal pH is indicative of vaginal infection						
pH		≤ 4.5	< 4.5	> 4.5		≥ 5.0
Vaginal discharge		+/-	+ (white, thick, clumpy discharge)	+ (white/grey, thin, clumpy discharge)		+ (greenish-yellow, frothy discharge)
Malodour		-	-	+		+
Itching		-	+	-		+
Burning		-	+	-		+
		Normal	Candidiasis	Bacterial vaginosis		Trichomoniasis

Methods for diagnosis of vaginal pH

1. Litmus paper
2. Gloves¹³

Differential diagnosis⁹

- Vaginal infection
- Bacterial vaginosis
- Candidiasis
- Trichomoniasis

Table 4. Clinical recommendation¹

	Evidence rating	References
Symptoms alone cannot differentiate between the causes of vaginitis. Office-based or laboratory testing should be used with the history and physical examination findings to make the diagnosis.	C	a-c
Do not obtain culture for the diagnosis of bacterial vaginosis because it represents a polymicrobial infection.	C	d
Nucleic acid amplification testing is recommended for the diagnosis of trichomoniasis in symptomatic or high-risk women.	C	d
Treatment of bacterial vaginosis during pregnancy improves symptoms but does not reduce the risk of preterm birth.	A	e,f
In nonpregnant women, oral and vaginal treatment options for uncomplicated vulvovaginal candidiasis have similar clinical cure rates.	B	g

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to <http://www.aafp.org/afpsort>.

a. Anderson MR, Klink K, Cohn A. Evaluation of vaginal complaints. *JAMA*. 2004; 291(11): 1368–79. b. Schaaf VM, Perez-Stable EJ, Borchardt K. The limited value of symptoms and signs in the diagnosis of vaginal infections. *Arch Intern Med*. 1990; 150(9): 1929–33. c. Bornstein J, Lakovsky Y, Lavi I et al. The classic approach to diagnosis of vulvovaginitis: A critical analysis. *Infect Dis Obstet Gynecol*. 2001; 9(2): 105–11. d. Workowski KA, Bolan GA; Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. 2015; 64(RR-03): 1–137. e. Koss CA, Baras DC, Lane SD, et al. Investigation of metronidazole use during pregnancy and adverse birth outcomes. *Antimicrob Agents Chemother*. 2012; 56(9): 4800–05. f. Brocklehurst P, Gordon A, Heatley E, Milan SJ. Antibiotics for treating bacterial vaginosis in pregnancy. *Cochrane Database Syst Rev*. 2013; (1): CD000262. g. Sobel JD, Brooker D, Stein GE, et al. Single oral dose fluconazole compared with conventional clotrimazole topical therapy of *Candida* vaginitis. Fluconazole Vaginitis Study Group. *Am J Obstet Gynecol*. 1995; 172(4 pt 1): 1263–68.

Hypoestrogenemia induced atrophic vaginitis

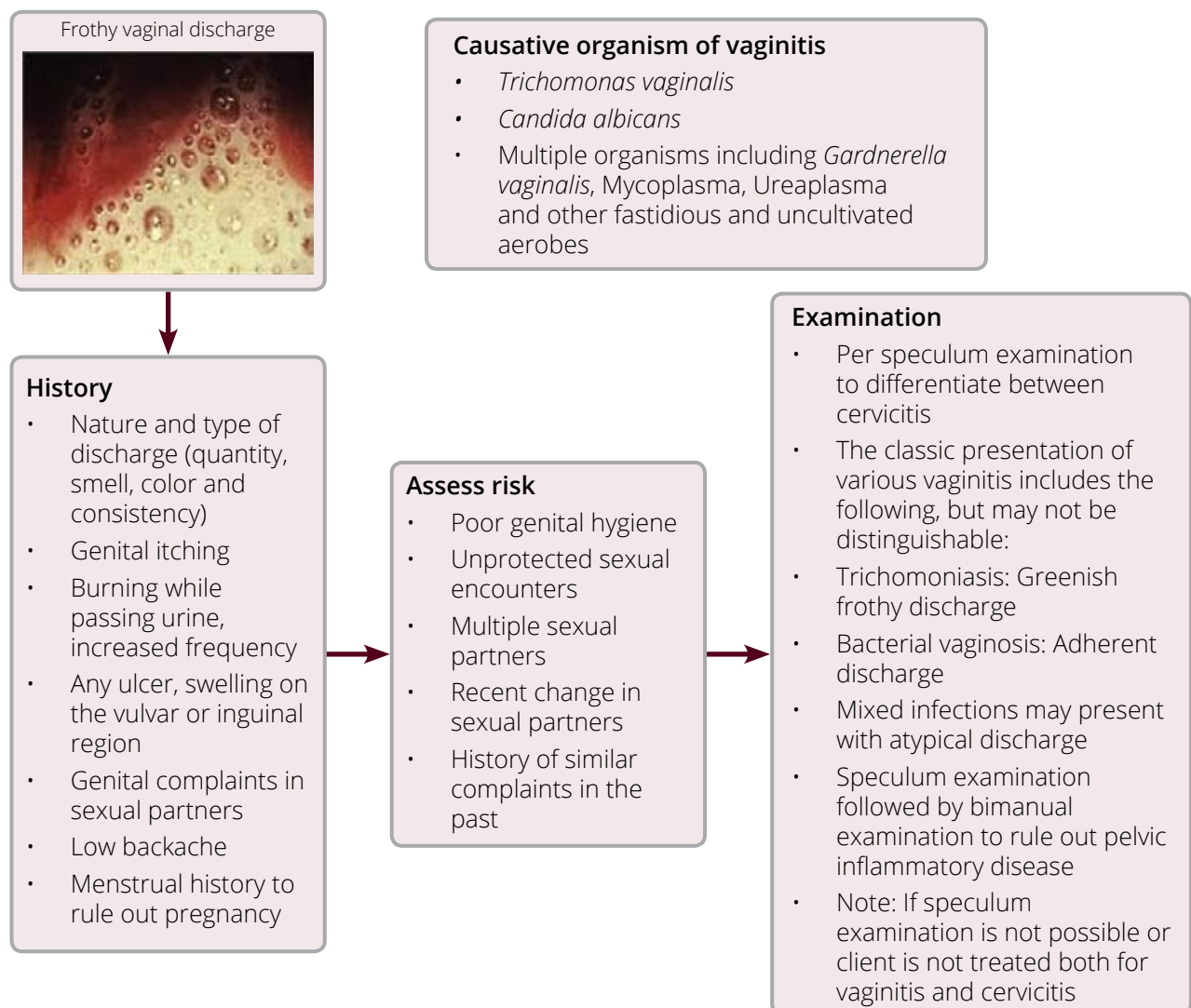
During reproductive age, estradiol levels typically range from 30–40 pg/mL in the early follicular phase to more than 200 pg/mL at ovulation. In menopause or due to other medical reason, estradiol levels fall to less than 20 pg/mL. Because the mucosal health of the vulva, vagina, urethra and bladder trigone is dependent on estrogen support, these women are at risk of developing symptomatic atrophic vaginitis.¹⁴

Bacterial vaginosis and complicated vulvovaginal candidiasis are frequent vaginal infections caused by an imbalance in vaginal microflora.

A normal, healthy vaginal microflora mainly comprises *Lactobacillus species* (spp.), which act beneficially as a bacterial barrier in the vagina, interfering with uropathogens. During premenopausal period, estrogen promotes vaginal colonization by lactobacilli that metabolizing glycogen and producing lactic acid and maintains intravaginal health by lowering the intravaginal pH level. A lower vaginal pH inhibits uropathogen growth, preventing vaginal infections. Decreased estrogen secretion in postmenopausal women depletes lactobacilli and increases intravaginal pH, resulting in increased vaginal colonization by harmful microorganisms (e.g., *Enterobacter*, *Escherichia coli*, *Candida* and *Gardnerella*).⁵

- Vaginally administered probiotics positively affects vaginal microflora composition by promoting the proliferation of beneficial microorganisms, alters the intravaginal microbiota composition and prevents vaginal infections. Probiotics also reduce the symptoms of vaginal infections such as vaginal discharge, odor, etc. and are helpful for the treatment and prevention of bacterial vaginosis and complicated vulvovaginal candidiasis⁵
- Hyaluronic acid vaginal gel and estriol cream can significantly improve the clinical symptoms of vaginal dryness¹⁵
- Researchers have shown the effectiveness of a topical vaginal preparation containing hyaluronic acid in controlling signs and symptoms correlated with postmenopausal vulvovaginal atrophy¹⁶
- Moisturizers help maintain natural secretions and coital comfort. The length of effectiveness is generally less than 24 hours¹⁷

Assessment of vaginal discharge¹⁸



Vaginal dryness

The hypoestrogenic symptoms of atrophic vaginitis includes vaginal dryness, dyspareunia and certain urinary problems.

Hyaluronic acid is found to be effective in relieving the symptoms of vaginal dryness. A multicenter, randomized, controlled, open-label, parallel-group clinical trial was conducted to evaluate the efficacy and safety of hyaluronic acid vaginal gel to treat vaginal dryness compared with estriol cream in postmenopausal women. The study included 140 individuals, 72 were randomized to the test group treated with hyaluronic acid vaginal gel and 72 to the control group treated with estriol cream. Treatment in both groups was applied by means of a device once every 3 days for a total of 10 applications over 30 days. Both hyaluronic acid vaginal gel and estriol cream are effective in the treatment of vaginal dryness. Hyaluronic acid vaginal gel may be considered as a valid alternative to estrogen-based treatments in relieving the symptoms of vaginal dryness.¹⁵

Isoflavone containing vaginal gel has been shown to be effective for relief of vaginal dryness and dyspareunia symptoms and an

increase in the intermediate and superficial cells. According to the researchers, the results were similar to the effects with use of conjugated equine estrogens and superior to placebo gel. Isoflavones proved good treatment options for relief of vulvovaginal symptoms especially in women who do not wish to use hormonal therapy or have contraindications for this treatment.¹⁹

Management of vaginitis Indications for treatment of bacterial vaginosis⁸

- Symptoms
- Positive direct microscopy with/without symptoms in some pregnant women (those with a history of prior idiopathic preterm birth or second trimester loss)
- Women undergoing some surgical procedures
- Optional: Positive direct microscopy in women without symptoms. They may report a beneficial change in their discharge following treatment
- Male partners do not require treatment

TREATMENT RECOMMENDATIONS FOR VAGINAL DRYNESS

- Topical estrogen therapies reverse these mucosal changes and are effective treatments for the symptoms of atrophic vaginitis¹⁴
- Vaginal moisturizers and lubricants also provide symptomatic relief for vaginal dryness and dyspareunia, respectively¹⁴
- Probiotics help reduce vaginal discharge, odor and prevent bacterial vaginosis and complicated vulvovaginal candidiasis¹⁶
- Topical vaginal preparation containing hyaluronic acid may improve symptoms of vaginal dryness in vulvovaginal atrophy¹⁵
- Isoflavone containing vaginal gel may provide relief of vaginal dryness and dyspareunia²⁰

Treatment

The primary regimen for the treatment of bacterial vaginosis is oral metronidazole 400 mg given thrice a day for 7 days.²¹

The cure rate immediately after treatment with metronidazole is up to 95%, but after 4 weeks this declines to 80% in open-label studies and less than 70% in blinded studies.²⁰

- A single 2.0 g dose of metronidazole in treating trichomoniasis is less effective and is not recommended²²
- Vaginal preparations containing 0.75% metronidazole gel or 2% clindamycin cream or ovules containing 100 mg OD clindamycin are effective and have few systemic effects²²

Treatment failure occurs fairly commonly, presumably because normal Lactobacillus-dominated flora fails to become established after anaerobes and other components of bacterial vaginosis flora have been reduced in number with use of antimicrobial agents. Also, persistence of *G. vaginalis* in biofilms on the vaginal wall may be associated with treatment failure.²³

Although some pathologic conditions causing vaginitis are well defined like bacterial vaginosis, vulvovaginal candidiasis and trichomoniasis. However, 7%–72% of women with vaginitis may remain undiagnosed and such forms of abnormal vaginal flora is called 'intermediate flora' and its management probably differ from that of bacterial vaginosis. It is of crucial importance in pregnant women at risk of preterm delivery.²⁴

Indications for therapy of candida⁸

- Symptomatic women found to have candida on either microscopy or culture
- Asymptomatic women do not require treatment.
- Asymptomatic male partners do not require treatment –

Indications for therapy of *Trichomonas vaginalis*⁸

- Positive test for trichomoniasis regardless of symptoms
- Epidemiological treatment of sexual partners

Treatment of vulvovaginal candidiasis

- Treatment of uncomplicated vulvovaginal candidiasis involves a short course of antifungals; oral and topical preparations are similarly effective (Table 5)^{25,26}
- Treatment of complicated vulvovaginal candidiasis involves an intensive, longer course of antifungals (Table 5)
- Vaginal tablets containing lactobacilli can cure bacterial vaginosis and reduce vaginal inflammatory response²⁷
- Lactobacilli vaginal pessaries successfully establish normal vaginal flora and the non-responders may need vaginal antifungal and antibiotic therapy so that clinical signs of the inflammation of the vagina could disappear²¹

Table 5. Treatment regimens for the most common causes of vaginitis^{21,25, 26}

Initial regimens	Alternative regimens	Pregnancy	Recurrence	Treatment of sex partners
Bacterial vaginosis				
Metronidazole 400 mg orally thrice daily for seven days* or Metronidazole 0.75% gel one full applicator (5 g) intravaginally daily for 5 days or Clindamycin 2% cream, one full applicator (5 g) intravaginally at bedtime for 7 days†	Tinidazole 2 g orally once daily for 2 days or Tinidazole, 1 g orally once daily for 5 days or Clindamycin, 300 mg orally twice daily for 7 days or Clindamycin, 100 mg intravaginally at bedtime for 3 days	Metronidazole, 400 mg orally thrice daily for 7 days	First recurrence: Retrial of same regimen or Trial of alternative initial regimen Multiple recurrences: Metronidazole 0.75% gel, intravaginally twice weekly for 4 to 6 months	Routine treatment of sex partners is not recommended
Vulvovaginal candidiasis				
Topical azole therapy‡ or Fluconazole 150 mg orally, single dose	-	Topical azole therapy applied intravaginally for 7 days	To achieve mycologic cure§: Topical azole therapy for seven to 14 days or Fluconazole 150 mg orally every third day for three doses For maintenance: Oral fluconazole (100 mg, 150 mg, or 200 mg) weekly for 6 months; consider topical treatment if oral is not feasible	Routine treatment of sex partners is not recommended unless the partner is symptomatic
Trichomoniasis				
Metronidazole 2g orally, single or divided dose on the same day or Tinidazole, 2 g orally, single dose	Metronidazole, 400 mg orally thrice daily for 7 days	Metronidazole 2 g orally, single dose in any stage of pregnancy	Differentiate persistent or recurrent infection from reinfection If metronidazole, 2 g single dose fails: Trial of metronidazole 400 mg thrice daily for 7 days If metronidazole 400 mg thrice daily for 7 days fails: Trial of metronidazole 2 g daily for 7 days If above regimens fail: Consider susceptibility testing	Concurrent treatment of sex partners is recommended Advise refraining from intercourse until partners are treated and symptom-free

*—Because of disulfiram-like reaction, alcohol should be avoided for at least 24 hours after completing oral regimen.

†—Clindamycin cream is oil-based and can weaken latex condoms and diaphragms for at least five days after use.

‡—Topical azole creams and suppositories may be oil-based and can weaken latex condoms and diaphragms.

§—For *Candida albicans* infection. Consider culture to exclude nonalbicans infection. If nonalbicans infection is present, consider first-line therapy with seven to 14 days of a nonfluconazole azole agent. If infection recurs, prescribe 600 mg of boric acid in a gelatin capsule intravaginally once daily for two weeks. Boric acid may also be used with initial induction therapy followed by monthly maintenance therapy for recurrent albicans infection per the Society of Obstetricians and Gynaecologists of Canada recommendations.

||—Follow-up with retesting as early as two weeks but within three months is recommended because rates of reinfection are high.

Table 6. Recommended topical treatment regimens for vulvovaginal candidiasis^{25,26}

Over-the-counter intravaginal agents
Clotrimazole 1% cream, 5 g intravaginally daily for seven to 14 days
Clotrimazole 2% cream, 5 g intravaginally daily for 3 days
Miconazole 2% cream, 5 g intravaginally daily for 7 days
Miconazole 4% cream, 5 g intravaginally daily for 7 days
Miconazole 100 mg vaginal suppository, one suppository daily for 7 days
Miconazole 200 mg vaginal suppository, one suppository daily for 3 days
Miconazole 1,200 mg vaginal suppository, one suppository for 1 day
Tioconazole 6.5% ointment, 5 g intravaginally in a single application
Prescription intravaginal agents
Butoconazole 2% cream 5 g intravaginally in a single application
Terconazole 0.4% cream, 5 g intravaginally daily for 7 days
Terconazole 0.8% cream, 5 g intravaginally daily for 3 days
Terconazole 80 mg vaginal suppository, one suppository daily for 3 days
Fenticonazole 600 mg single dose vaginally; 300 mg vaginally on day 1 and day 3
Itraconazole 200 mg orally twice a day for 1 day

Non-infectious vaginitis

- Non-infectious vaginitis affects 10% to 40% of women who have conditions associated with estrogen deficiency⁷
- Irritant contact dermatitis and allergic contact dermatitis are two non-infectious causes of vaginitis that may be associated with use of woman's hygiene products or contraceptive materials⁷
- Diagnosis is based on history and physical findings, supplemented by vaginal pH levels, vaginal wet-mount preparation (to exclude superimposed infection) and, rarely, culture or cytology. Both systemic and topical estrogen treatments are effective in relieving symptoms⁷
- Estrogen therapy: Topical vaginal estrogen is preferred because of the low systemic absorption and reduced risk of adverse effects compared with oral therapy. Estrogen-containing creams, pessaries, intravaginal tablets and the estradiol vaginal ring appear equally effective for the symptoms of atrophic vaginitis⁷
- First-line nonhormonal treatment recommendations include vaginal lubricants and moisturizers; continued sexual activity should be encouraged⁴

Table 7. Percentage of sensitivity of aerobic vaginal isolates to various antibiotics²⁴

Antibiotics	<i>E. coli</i>	<i>K. pneumoniae</i>	<i>P. aeruginosa</i>	<i>S. aureus</i>	β -hemolytic Streptococci	Enterococci
Amoxicillin	25	9.52		32.8	81.3	
Amoxicillin/ clavulanic acid	46.8	60.29	30	67.1		85.7
Cefoperazone/ sulbactam	100					

Role of probiotics

Antimicrobial therapy is generally effective, there is still a high incidence of recurrence and increase of microbial resistance due to the repetitive use of antimicrobials. Thus, it has been suggested that administration of probiotics incorporating selected *Lactobacillus* strains may be an effective strategy for preventing vaginal infections.²⁸

Probiotics have positive effects on vaginal microflora composition by promoting the proliferation of beneficial microorganisms, alters the intravaginal microbiota composition, prevents vaginal infections in postmenopausal. Probiotics also reduce the symptoms of vaginal infections and are useful in treating and preventing vaginitis. The use of *Lactobacillus acidophilus*, *Lactobacillus rhamnosus* GR-1 and *Lactobacillus fermentum* RC-14 at a dose of at least 10 CFU/day for 2 months is found to be effective.²⁹

Vaginal probiotics significant in maintaining the vaginal flora

The presence of *Lactobacillus* spp is a major determinant of normal vaginal microbial flora. Hence, lactobacilli are usually used as probiotics to treat bacterial vaginosis, which would presumably maintain or restore the vaginal microecology through competition for nutrients, inhibition of epithelial and mucosal adherence of pathogens or stimulation of host immunity. The domination of lactobacilli in healthy vaginal microbiota and its reduction in bacterial vaginosis has given rise to the concept of oral or vaginal use of probiotic *Lactobacillus* strains for the treatment and prevention of bacterial vaginosis.³⁰

The ability of lactobacilli to colonize vaginal epithelial cells depends on the route of delivery. Vaginally inserting tablets may be an effective way to regenerate the local lactobacilli of

Post antibiotics administration of vaginally administered probiotics for the treatment of bacterial vaginosis is an effective treatment for bacterial vaginosis and vaginitis.

women. In a Cochrane analyse the efficacy and safety of probiotics administered intravaginally combined with antibiotic therapy for the treatment of bacterial vaginosis. In theory, antibiotics can break down the overgrowth of vaginal anaerobes and formation of biofilm. Hence, probiotics administered intravaginally will adhere to and colonize vaginal epithelial cell surfaces.³⁰

Administration of probiotics incorporating selected *Lactobacillus* strains may be an effective strategy for preventing vaginal infections.²⁸ A Cochrane analysis suggests beneficial outcome of microbiological cure with the oral metronidazole/probiotic regimen and the probiotic/estriol preparation. For the probiotic/estriol preparation, the OR and 95% CI for physician-reported resolution of symptoms was OR 0.04.³¹

Probiotic prophylaxis with vaginal capsules containing *L. rhamnosus*, *L. acidophilus* and *Streptococcus thermophilus* resulted in lower recurrence rates for bacterial vaginosis in women with a history of recurrent bacterial vaginosis.³²

Clinical trials showed that intra-vaginal administration of *Lactobacillus acidophilus* for 6–12 days, or oral administration of *L. acidophilus* or *Lactobacillus rhamnosus* GR-1 and *Lactobacillus fermentum* RC-14 for 2 months, resulted in the cure of bacterial vaginosis (defined as a 0–1 positive score according to Amsel's criteria) and/or reduced the recurrences of bacterial vaginosis and/or caused an increase in vaginal lactobacilli and

restoration of a normal vaginal microbiota, significantly more frequently than did a placebo, acetic acid or no treatment.³³

Vaginitis and its impact on reproductive outcomes and in treatment: Role of vaginally administered probiotics to improve reproductive outcomes in female host

Chorioamnionitis which results due to subclinical ascend of infection is a common pathway to the induction of preterm labor, which in turn leads to preterm delivery. In most cases, the lactobacilli-dominated microbiota is overgrown by potentially pathogenic rods that ascend from the gut, as observed in bacterial vaginosis, which is an independent risk factor for preterm delivery.³⁴

Bacterial vaginosis is associated with complications, such as chorioamnionitis and preterm delivery, as well as with urinary tract infections and sexually transmitted infections. Bacterial vaginosis can affect women's reproductive health at all phases, from conception to childbirth. Bacterial vaginosis have been shown to directly affect fertility, since an ascending dissemination of the involved species may lead to tubal factor infertility. It increases the risk of acquiring sexually transmitted diseases contributes to damage to reproductive health.³⁴

The exogenous strains of lactobacilli have been suggested as a means of re-establishing a normal healthy vaginal flora. Select probiotic strains can eliminate bacterial vaginosis and also exert an antiviral effect, thus reducing viral load and preventing fetal and neonatal infection. The administration of probiotics can aid recovery from infection and restore and maintain a healthy vaginal ecosystem, thus improving female health also in relation to reproductive health.³⁵

The use of vaginally administered probiotics treat vaginitis during pregnancy is effective alternative option to antibiotics. Several recent studies have indicated that the use of probiotics during pregnancy is safe. According to meta-analysis and systematic review of randomized controlled trials of probiotic use in more than 1500 pregnant women did not report an increase in adverse fetal outcomes. There were no increase in the incidence of miscarriages or malformations and no significant difference in birth weight, gestational age, or the incidence of cesarean section.³⁶ In meta-analysis of randomized control trials of more than 2000 pregnant women reported that oral administration of multistrain probiotics improves pregnancy outcomes, with some success in terms of modulating immune parameters and the vaginal microbiota.³⁷ The use of selected probiotic strains can eliminate bacterial vaginosis and also exert an antiviral effect, thus reducing viral load and preventing fetal and neonatal infection.

Researchers conducted a study to determine the effect of lactobacilli on vaginal health and proinflammatory cytokines.²⁷ The study included 67 women with bacterial vaginosis, 50 with intermediate flora and 42 with normal vaginal flora. In this double-blind study, patients were randomized to receive probiotic lactobacilli vaginal tablets (*L. brevis* CD2, *L. salivarius* subsp. *salicinius*, *L. plantarum*) or the vaginal pH tablet (active comparator). The researchers reported that:

- A cure rate of $\approx 80\%$ was observed
- 32% of the women could restore normal vaginal flora and 47 % had improved Nugent score
- The pH tablet containing pH lowering compounds induced resolution of bacterial

and restoration of normal vaginal flora in 74 % and 26 %, respectively

- Vaginal probiotic tablet was well tolerated and no side effects

A significant reduction in IL-1 β and IL-6 vaginal cytokines was observed after the treatment with lactobacilli.

Vaginally administered probiotic tablets containing *L. brevis* CD2, *L. salivarius* subsp. *salicinius* and *L. plantarum* can cure bacterial vaginosis and reduce vaginal inflammatory response.

Krpina D et al, evaluated vaginal Lactobacillus probiotics in pregnant women (n=137) of different age, parity, trimester or week of pregnancy for its impact on the recovery of microflora in the reproductive tract of pregnant women. After assessing the vaginal discharge, the study participants were divided into three groups, Group 1 [102 pregnant women (74. 45%) who had a mass of lactobacilli and no clinical signs of inflammation; received no therapy]; Group 2 [20 pregnant women (14. 59%) who had vaginal imbalance (vaginosis) with a reduced

number of lactobacilli without clinical signs of inflammation and with subjective difficulties, received vaginal probiotics for 10 days]; Group 3 [13 women (9.48%) who had clinical signs of inflammation of vagina and discomfort with low lactobacilli, received vaginal probiotics with antifungal agent).⁶

- Pregnant women receiving vaginal probiotics only, 100% of them had established normal vaginal flora
- Pregnant women treated with vaginal probiotics and an antifungal agent, the normal vaginal flora was established after the therapy which was confirmed by vaginal smear control 10 days later

Vaginally administered probiotics containing lactobacilli enables to establish normal vaginal flora. Women who were given vaginally administered probiotics post antifungal and antibiotic therapy also had established normal vaginal flora. Also Vaginal inflammation had disappeared 10 days after treatment.

SUMMARY

Definition

Vaginitis is characterized by an overgrowth of predominantly anaerobic organisms (e.g. *Gardnerella vaginalis*, *Prevotella* spp., *Mycoplasma hominis*, *Mobiluncus* spp.) in the vagina leading to a replacement of lactobacilli and an increase in vaginal pH.

Signs and symptoms

Signs and symptoms to look out for in patient include for bacterial vaginosis are fishy odor; thin, off-white homogenous

discharge that may worsen after intercourse; pelvic discomfort without inflammation. For vulvovaginal candidiasis, the signs and symptoms to look out for are white, thick, cheesy, or curdy discharge; vulvar itching or burning; no odor (pruritis dysuria), vulvar erythema and edema. For trichomoniasis, the signs and symptoms include Green or yellow, frothy discharge; foul odor; vaginal pain or soreness copious, malodorous, yellow-green (or discolored) discharge, pruritus vaginal irritation. No symptoms in

SUMMARY

20% to 50% of the affected women along with inflammation and strawberry cervix.

- Symptoms alone cannot differentiate between the causes of vaginitis. Office-based or laboratory testing should be used with the history and physical examination findings to make the diagnosis
- The complication of vaginitis includes vaginal infections, endometriosis and increased risk of spontaneous miscarriage, adverse pregnancy outcomes, premature rupture of membranes (PROM) or preterm delivery, low birth weight

Screening and diagnosis

- Screening of asymptomatic individuals for trichomoniasis is not recommended
- Do not obtain culture for the diagnosis of bacterial vaginosis because it represents a polymicrobial infection
- Nucleic acid amplification testing is recommended for the diagnosis of trichomoniasis in symptomatic or high-risk women
- Elevated vaginal pH in the absence of current vaginal infection is a risk for adverse pregnancy outcome that is mediated by systemic inflammatory response

Treatment

- It is recommended to screening for increased vaginal pH during pregnancy, as it may be useful in reducing preterm birth rates
- Vaginally administered probiotics positively affects vaginal microflora

composition by promoting the proliferation of beneficial microorganisms, alters the intravaginal microbiota composition and prevents vaginal infections. Probiotics also reduce the symptoms of vaginal infections such as vaginal discharge, odor, etc. and are helpful for the treatment and prevention of bacterial vaginosis and complicated vulvovaginal candidiasis

- Hyaluronic acid vaginal gel and estriol cream can significantly improve the clinical symptoms of vaginal dryness
- Moisturizers help maintain natural secretions and coital comfort. The length of effectiveness is generally less than 24 hours
- Vaginal dryness
 - » Topical estrogen replacement therapies reverse these mucosal changes and are effective treatments for the symptoms of atrophic vaginitis
 - » Vaginal moisturizers and lubricants also provide symptomatic relief for vaginal dryness and dyspareunia, respectively
 - » Vaginally administered probiotics help reduce vaginal discharge, odor etc and prevent bacterial vaginosis and complicated vulvovaginal candidiasis
 - » Topical vaginal preparation containing hyaluronic acid improves vaginal dryness in vulvovaginal atrophy
 - » Isoflavone containing vaginal gel provides relief of vaginal dryness and dyspareunia symptoms

SUMMARY

- Treatment of uncomplicated vulvovaginal candidiasis involves a short course of antifungals; oral and topical preparations are similarly effective
- Treatment of complicated vulvovaginal candidiasis involves an intensive, longer course of antifungals
- Vaginally administered probiotics containing *L. brevis* CD2, *L. salivarius* subsp. *salicinius*, *L. plantarum* can cure bacterial and reduce vaginal inflammatory response
- For non-infectious vaginitis topical vaginal estrogen is preferred because of the low systemic absorption and reduced risk of adverse effects compared with oral therapy. Estrogen-containing creams, pessaries, intravaginal tablets and the estradiol vaginal ring appear equally effective for the symptoms of atrophic vaginitis
- First-line nonhormonal treatment recommendations include vaginal lubricants and moisturizers; continued sexual activity should be encouraged
- Antibiotics such as amoxicillin/clavulanic acid are shown to be effective in women with anaerobic vaginal isolates
- Post infection vaginal probiotic pessaries for the treatment of bacterial vaginosis is an effective treatment for treating vaginitis
- The exogenous strains of lactobacilli have been suggested as a means of re-establishing a normal healthy vaginal flora
- In women with manifest clinical signs of bacterial vaginosis or yeast vaginitis, vaginal probiotics given in combination with antibiotic or antimycotic therapy, lowered clinical symptoms and led to lower Nugent scores compared with a treatment with antibiotics/antimycotics alone
- Vaginal probiotics containing Lactobacilli enables successfully establish normal vaginal flora in pregnant women with imbalance in vaginal flora
- In pregnant women requiring vaginal probiotics along with antifungal or antibiotic therapy, attain normal vaginal flora and reduces inflammation after 10 days of therapy
- Vaginal lactobacilli tablet containing at least 1 billion viable lactobacilli (*L. brevis* CD2, *L. salivarius* subsp., *salicinius* and *L. plantarum*) is effective, safe and well-tolerated in reducing the symptoms of vaginal infections and restoring the vaginal flora to normal

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