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Approach and Observation in Clinical Dermatology





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Foreword
Deepika Pandhi

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A Female with Chronic and Recurrent Vaginal Discharge

Neela M Patel, Khushbu R Modi

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INTRODUCTION

"Vaginal discharge" (VD) or "leukorrhea" is the most common health issue for women with reproductive age group, and the term is used traditionally by patients for presenting any genital discomfort with the symptoms of VD, odor, pruritus, and/or discomfort. The complaint must be verified to differentiate physiological discharge from pathological discharge and to determine diagnosis and treatment by physical and laboratory examination. Untreated vaginitis can cause physical, social, and psychological complications.

In premenopausal women, the vagina is rich in glycogen which acts as a substrate for Doderlein's bacilli to glucose into lactic acid. This creates an acidic vaginal environment (pH 4–4.5) which helps in maintaining normal vaginal flora and inhibit growth of pathogenic organisms. The vagina and cervix are susceptible to various pathogens depending on the type of epithelium. *Candida* species and *Trichomonas vaginalis* (TV) can cause infection at squamous epithelium of vagina and ectocervix.

CHRONIC AND RECURRENT VAGINAL DISCHARGE

Chronic VD is defined as women having continuous symptoms despite conventional treatment. Recurrent VD is defined as a woman who is asymptomatic after treatment but subsequently there is recurrence of symptoms, usually three or more episodes within a year.[1]

If it remains untreated for a long period of time, complications like increased risk of sexually transmitted infection (STI) and human immunodeficiency virus (HIV) (associated subsequent infertility), adverse outcomes of pregnancy, miscarriage, preterm delivery, low-birth-weight infants and choriamnionitis can occur, in turn causing a burden on healthcare system.

Chronic and recurrent VD is very frustrating for women, impacting significantly on their self-esteem, sexual relationships, and making them feel ashamed.

There are different causes of chronic and recurrent discharge which are as given here:

- Physiological
- *Pathological*:
  - Infective **(Table 1)**
  - Noninfective **(Table 2)**
- Others **(Box 1)**

Identifying the source of VD is challenging, as it is a distressing and subjective symptom. Though there are multitude of causes for chronic and recurrent VD, majority of them are caused by infection, while less common causes include vaginal atrophy/atrophic vaginitis, cervicitis, foreign body, irritants and allergens, etc. Hence only infective etiology is elaborated in this chapter.

Physiological Vaginal Discharge

The most common cause of VD in reproductive age group is physiological,[2] which tends to change with the menstrual cycle. It increases during high estrogen states such as ovulation, the luteal phase, puberty, pregnancy, with estrogen-based therapies such as combined hormonal contraception as well as hormone replacement therapies and also increased during sexual arousal. Physiological discharge is clear with a stretchable consistency, nonoffensive at the time around ovulation, then may be thicker and slightly yellow during the luteal phase. pH of the physiological

Table 1: Infective causes.[3-6]

	Recurrent BV	***Recurrent CVV***	***Recurrent TV***
Definition	*Recurrent BV*: Defined as three or more episodes in 12 months	*Recurrent CVV*: Four or more symptomatic episodes occur in 1 year or at least three episodes unrelated to antibiotic therapy occur within 1 year	*Recurrent TV*: Infection due to reinfections from untreated sexual partners Persistent infection are concerning for treatment failure due to: • Nitroimidazole resistance • Insufficient long absorption • Lack of adherence • Inadequate treatment
Estimated recurrence rate	50%	5%	12.5–18.5%
Microorganisms responsible	*Gardnerella vaginalis, Alysicarpus vaginalis, Mobiluncus* species, *Bacteroides* species, *Prevotelle* species, *Clostridiales* species, *Leptotrichia, Sneathia species, Lactobacillus, Peptostreptococcus, Fusobacterium*	• Resistance of non-*Candida albicans* species to antifungal agents • *C. albicans* • Non-albicans *Candida* species ○ *Candida tropicalis* ○ *Candida krusei* ○ *Candida parapsolis* ○ *Candida glabrata*	TV

(BV: bacterial vaginosis; CVV: candidal vulvovaginitis; TV: *Trichomonas vaginalis)*

Table 2: Noninfective causes.[7-9]

	Atrophic vulvovaginitis (genitourinary syndrome of menopause)	***DIV***	***GVHD***
Characteristics	Gradual thinning and drying of vaginal walls, mostly occurs in postmenopausal women with less estrogen levels	• It is a diagnosis of exclusion, chronic rare condition in which patient have discharge for more than a year with mean duration of symptoms of 15–31 months • It occurs in 8% women with low-estrogen levels, during breastfeeding or postmenopausal women • Probable etiopathologies are: ○ Bacterial overgrowth, immune-mediated reaction, toxin-induced reaction to *Staphylococcus aureus*	Uncommon cause of chronic vaginal discharge, usually occurs in 25–50% female having allogenic blood transfusion or transplant patients

(DIV: desquamative inflammatory vaginitis; GVHD: graft-versus-host disease)

discharge is between 3.8 and 4.5. Normal healthy discharge should not be associated with itching, redness, or odor. Sometime profuse physiological VD may produce vaginal irritation.

Pathological Vaginal Discharge

Pathological vaginal discharge can be further classified into (1) infective and (2) noninfective.

Chronic infective discharge can be of (1) vaginal origin or (2) cervical origin. Chronic and recurrent vaginal and cervical discharge are due to multiple reasons, most common ones are candidal vulvovaginitis (CVV), bacterial vaginosis (BV), TV, while less common causes are *Neisseria gonorrhea* and *Chlamydia trachomatis*.

Others

Apart from the above listed, there are multiple other causes of chronic and recurrent VD.

APPROACH IN A PATIENT OF CHRONIC AND RECURRENT VAGINAL DISCHARGE

Patients of VD should be evaluated initially by taking history, doing physical examination, microscopy, and cervical

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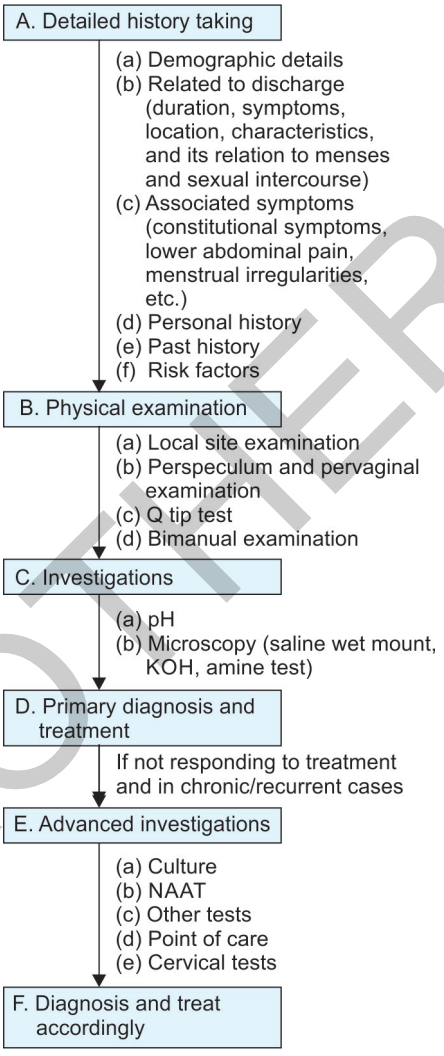
Box 1: Other causes of vaginal discharge.

- *Foreign body* (causes—retained tampon, pessary or condom—mechanical irritation) is often associated with offensive, copious, purulent, sometime blood stained VD, intermittent bleeding, and/or troublesome odor due to inflammation and secondary infection[10]
- *Chemical* (causes—douches, latex condoms, deodorants—chemical irritation, contact dermatitis, or allergy)—soreness is pronounced than discharge[11]
- *Excretions* (causes—contamination with urine or feces—secondary vaginitis) lead to offensive discharge with pruritus[11]
- *Vaginal warts:* Skin/pink colored ranging from smooth flattened papules to verrucous, papilliform lesions. Patients with extensive vaginal warts can present with VD, pruritus, bleeding, burning, tenderness, and pain
- *Presence of granulation tissue or infection at surgical site* can cause VD or bleeding[12]
- *Neoplasia* (fibroid polyps or genital malignancy—necrotic or inflammatory changes associated with malignancy) in the upper or lower genital tract can result in Serosanguinous and often offensive VD, with more common complaint of spotting[12]
- *Disorders like pemphigus, drug reactions* can present with recurrent purulent or Serosanguinous discharge
- *Erosive vulvovaginitis:* The presence of multifocal rounded macular erythematous lesions with purulent discharge and tenderness



FLOWCHART 1: Basic approach in a patient of vaginal discharge.
(KOH: potassium hydroxide; NAAT: nucleic acid amplification test)

tests. Women whose initial evaluation confirms a diagnosis received targeted treatment and those who remain without a diagnosis or whose symptoms recur, go through a more detailed evaluation process.

Detailed History Taking

- *Demographic details*: Related to age, socioeconomic and marital status, education, occupation, etc., helps us in narrowing the diagnosis and easy management of the patients. Age gives us an idea about the etiology of discharge and differentiating physiological from pathological discharge. Early age of marriage and early age of sexual activity makes cervical epithelium more susceptible to ascending infections, in turn increasing the risk of STIs. The chances of recurrence, chronicity, and complications like pelvic inflammatory disease (PID), related to reproductive system are increased in lower socioeconomic status due to lower literacy rate, poor sanitation, nutrition and hygiene practices, ignorance, use of over the counter medications, etc. Similarly, in women with higher economic status the use of spermicides, fancy hygiene products, lubricants, douching, shaving practices, contraceptives, sprays, soaps, detergents increases the chances of chronicity, allergic and irritant dermatitis.
- *Characteristics of discharge* ***(Tables 3 and 4)***: The symptoms and characteristics of discharge can vary from its classical presentation due to a variety of reasons. Specific history of relation to menses and sexual intercourse gives us a general idea about the etiology. Symptoms that develop soon after sexual exposure are suggestive of STI.
- *Associated symptoms* ***(Table 5)***: Provides guide in approaching patient of discharge. Associated systemic symptoms like constitutional symptoms, pelvic pain or tenderness, and menstrual irregularities help in differentiating between vaginal and cervical infections. Dysuria and dyspareunia are suggestive of inflammatory disorders such as allergy, infection, or vulvovaginal atrophy.

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Table 3: Symptoms of infective discharge.[3,4,6,13]

	Recurrent CVV	*Recurrent BV*	*Recurrent TV*
Symptoms	Pruritus, vaginal discharge, soreness, external dysuria, vulvar edema, and superficial dyspareunia	• Vaginal discharge • History of recurrence + • 50% cases are asymptomatic	• Vaginal discharge • Pruritus • Dyspareunia • Dysuria • 50–75% cases are asymptomatic
Relation with menses	Premenses	Postmenses	Postmenses
Relation with sexual intercourse	Aggravation of pruritus	Aggravation of fishy odor	–

(BV: bacterial vaginosis; CVV: candidal vulvovaginitis; TV: *Trichomonas vaginalis*)

Table 4: Symptoms of noninfective discharge.[7-9]

	Atrophic vulvovaginitis (genitourinary syndrome of menopause)	*Desquamative inflammatory vaginitis*	*Graft-versus-host disease*
Symptoms	Vaginal dryness, itching, irritation, dyspareunia, burning micturition	Symptoms like *Trichomonas vaginalis*, itching, burning, redness, dyspareunia, bleeds on touch	Itching, dryness, dyspareunia, burning with irritation, contact bleeding

Table 5: Associated symptoms.

Symptoms	*Condition*
Dysuria	• External dysuria (vulvovaginal irritation results in burning due to micturition): *Candida*, herpes • *Internal dysuria (felt inside the body)*: UTI, gonorrhea, chlamydia
Dyspareunia	Due to inflammatory reaction *(Candida, Trichomonas, Chlamydia trachomatis, Neisseria gonorrhea)*
Pruritus	• Intensely pruritic—*Candida* • Less pruritic—*Trichomonas* • Rarely pruritic—bacterial vaginosis • Allergic dermatoses • Persistent complaint of pruritus in a localized area is suggestive of neoplasia or malignancy
Lower abdominal pain, pelvic pain, pelvic tenderness, fever, tenesmus[14]	• Red flag signs of PID • Inflammatory causes of vaginitis or nonvaginal sources like vulvodynia and pelvic floor myofascial pain
Dysuria, menstrual irregularities, bleeding after intercourse[15]	Cervicitis, erosive causes of vaginitis or a uterine source
Burning, irritation, or other discomfort	Infective conditions like candidal vulvovaginitis and noninfective conditions like vulvodynia

(PID: pelvic inflammatory disease; UTI: urinary tract infection)

- *Personal history* **(Box 2)**
- *Past history*: Similar complaints and history of treatment taken for the same, symptoms in partner, history of urinary tract infection
- *Risk factors*: The risk factors to be kept in mind are risky sexual behavior, history of immunocompromised status, prolonged use of hormonal contraceptives, immunosuppressive drugs, and antibiotics as well as inadequate treatment.[16]

Physical Examination

The physical examination assesses (1) the degree of vulvovaginal inflammation, (2) characteristics of the VD, and (3) presence of lesions or foreign bodies.

- *Cutaneous examination of local sites*: Look for discharge, swelling, erythema, excoriation marks, pustules, papules, satellite lesions, genital ulcers, growth/wart, mass, etc., at following sites. Sites to be examined:

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- Pubis, labia majora and minora, urethral meatus, vaginal opening, and perianal skin
- *Other sites*: Oral mucosa, lips, trunk, palms, and soles
- Abdomen can be examined for lymph node, guarding, tenderness, and abdominal mass

- *Perspeculum and pervaginal examination*: Done after taking patient's consent with patient in dorsal supine lithotomy position after explaining the procedure to the patient. It is performed to evaluate the vagina and cervix for:
  - VD, characteristics and signs of which can suggest the type of infection (**Tables 6 and 7**).
  - Foreign body, growth/warts, malignancy, necrotic/inflammatory changes, signs of allergic and irritant dermatitis

Box 2: Personal history.

- *Hygiene practices*: History of douching, shaving, use of hair removal creams, vaginal washes, etc., can cause mechanical, chemical, or allergic irritation leading to contact dermatitis
- *Sexual history*:
  - Different modes of sexual practices, number of partners, sex of the patient's partner, recent change in partner, complaints in partner, age of starting sexual activity, and sexual behavior have a role to play in aggravating the symptoms
  - Penovaginal sex, vaginal sex after anal sex, females who have sex with females, and females who have sex with both females and males, are at increased risk of BV
  - Sexual activity in extremes of age like early age and postmenopausal women increases chances of STI
- *Medication history*:
  - Antibiotics predispose to CVV by eliminating protective bacterial flora in the vagina, i.e., *Lactobacillus*, thus allowing overgrowth of *Candida*
  - Use of OCP and barrier contraceptives including IUD's increases both physiological and pathological discharge
  - Use of OTC's change the clinical presentation, altering diagnosis
  - Use of lubricants and oils can cause allergic and irritant dermatitis
- *Medical history*: Medical conditions can act as a risk factor for chronic/recurrent VD like:
  - *Diabetes mellitus*: CVV
  - *HIV*: Vaginal infections
  - *Graft-versus-host disease*: Vaginal irritation, discharge, ulceration, and stenosis
  - *Steven–Johnson syndrome/toxic epidermal necrolysis*: Vulvovaginal sequelae
  - *Herpes simplex virus and Behçet syndrome*: Vulvovaginal ulcers
- *Surgical history*: Recent transvaginal surgery, repair of perineal lacerations after childbirth, tubectomy, insertion of IUD, etc. Vaginal symptoms may be related to foreign body, bacterial infection, granulation tissue, or vaginal fistula. Vaginal fistula can develop after surgery like hysterectomy and can present with vaginal discharge

(BV: bacterial vaginosis; CVV: candidal vulvovaginitis; HIV: human immunodeficiency virus; IUD: intrauterine device; OCP: oral contraceptive pills; OTC: over-the-counter; STI; sexually transmitted infection)

Table 6: Infective: Characteristics and signs of discharge (Fig. 1).

	Recurrent CVV	***Recurrent BV***	***Recurrent TV***
Amount	Scanty to moderate	Moderate to profuse	Profuse
Consistency	• Cheesy or curdy (cottage cheese like) • Watery to homogenous thick	Mucoid, thin	Thick, frothy
Color	White	Grayish white	Yellow greenish
Odor	No offensive smell	Fishy (worse at midcycle, after intercourse)	Foul smelling
Signs	*Cervix uteri*: Normal	Discharge coating the vagina	• Blisters developing in one-third cases • *Strawberry cervix*: Punctuate hemorrhagic lesions
Cutaneous examination of vulva	Erythema, edema or fissures, excoriation, satellite lesions	Normal, excoriation marks can be seen	Erythema, edema, or fissures

(BV: bacterial vaginosis; CVV: candidal vulvovaginitis; TV: *Trichomonas vaginalis*)

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Erythematous, friable cervix (cervical inflammation), and mucopurulent discharge with a normal vagina and associated symptoms of cervicitis are suggestive of cervicitis rather than vaginitis.

- *Q tip test*: A cotton swab is applied with pressure at the labia or introitus, if patient complains of pain this is suggestive of candidiasis.[17]
- *Bimanual examination*: It is performed by inserting two fingers into vagina with the other hand over lower part of belly. It helps in assessing the pelvic/cervical motion tenderness in PID or in malignancy.

Symptoms can lead the approach, but alone cannot differentiate between the causes of discharge, office-based test, or laboratory testing must be used with the history and physical examination findings to make the diagnosis in patients of chronic and recurrent VD.

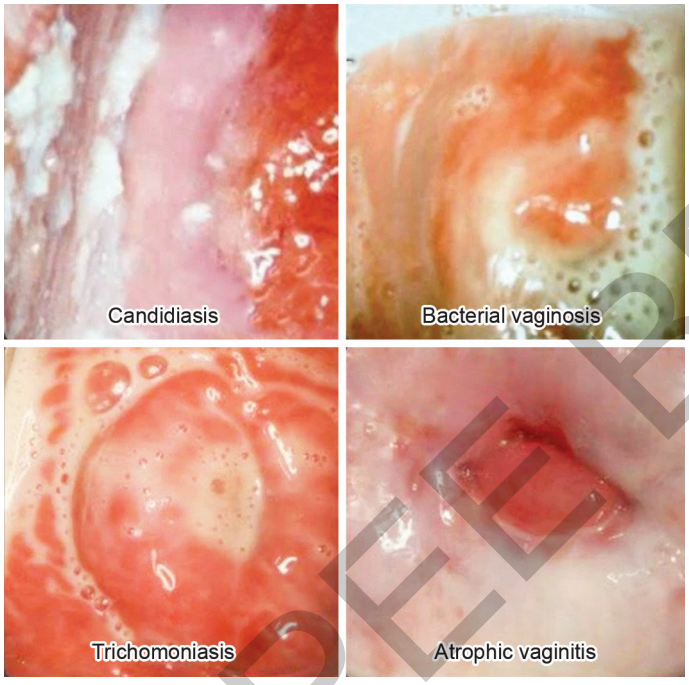

FIG. 1: Infective causes of vaginal discharge

Courtesy: Pillowtalk with Doc Mitch—Dr Michelle Dado; Philippines.

Investigations (Table 8)

Whenever required routine investigations like complete blood count, liver function tests, renal function tests, urine routine microscopy, random blood sugar and in cases of suspected STI's rapid plasma reagin (RPR), HIV, human papillomavirus (HPV), hepatitis B surface antigen (HBsAg), and Pap smear should be considered.

- *pH*: Vaginal pH checking is an outpatient department (OPD)-based procedure and is used for screening purpose, as it has high sensitivity and low specificity. pH strip is applied for few seconds to the middle one-third of vaginal side wall to avoid contamination by blood, semen, or cervical mucus in the posterior fornix. Alternatively, dry swab can be used instead of pH paper strip. For diagnosis of BV, trichomoniasis, or candidiasis, pH measurement is less useful at the extremes of age due to altered pH in these age groups. Vaginal pH may be altered by contamination with lubricating gels, semen, blood, douches, intravaginal medications, and amniotic fluid. ColorpHast pH test strips are commercially available paper strips. The FemExam TestCard pH and amine tests are also available as card tests that contains pH indicators as well as visual evaluation system for amines.[18]
- *Microscopy* ***(Flowchart 2)***: Three samples of patient's VD were obtained with a cotton swab and evaluated under the microscope by saline mount, 10% potassium hydroxide (KOH), and amine test.[15,19]

Additional swab can be taken for gram staining of cervical discharge.

- *Saline wet mount*: Sample mixed with one to two drops of normal saline at room temperature on a glass slide, cover slips are then placed on the slides. Primary goal of the examination is to look for *Trichomonas*, clue cells, and increased no. of polymorphonuclear neutrophils (PMNs). Sample should be examined within 10–20 minutes to reduce the possibility related to loss of motility of *Trichomonas*.
- *10% KOH*: Identifying hyphae and budding yeast for diagnosis of candidiasis becomes easier with addition of 10% KOH, as it destroys cellular elements.

Table 7: Noninfective: Characteristics and signs of discharge.

	Atrophic vulvovaginitis (genitourinary syndrome of menopause)	***Desquamative inflammatory vaginitis***	***Graft-versus-host disease***
Amount	Scanty discharge	Profuse	–
Color	White	Yellow green	White
Signs	Normal/atrophy of vulva and vagina	• Purulent yellowish–green discharge, erythema, vaginal rash (petechial or ecchymotic) • Excoriation marks on vulva and vestibule in severe cases	Purulent discharge, vulvovaginal atrophy, vulval synechiae, vaginal stenosis

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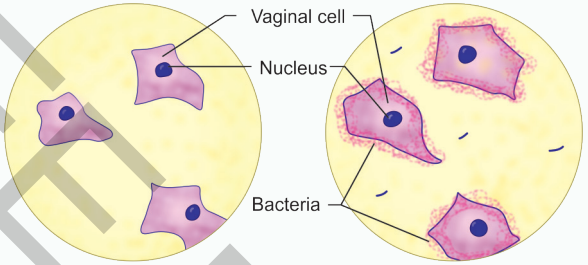
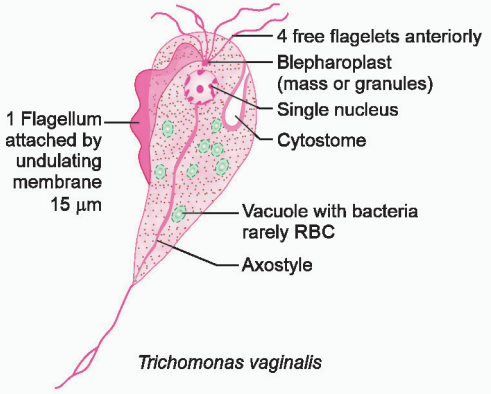
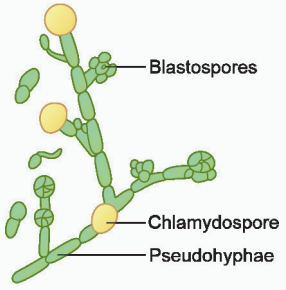
Table 8: Microscopic findings in infective vaginal discharge.

	CVV	*BV*	*TV*
pH test of the vaginal fluid/ discharge from vaginal walls	4–4.5	>4.7	>4.5 Often exceeds 6
Sample collection (preferably from site)	Lateral vaginal wall	Posterior fornix	Posterior fornix
Microscopy *First vaginal swab* • Wet mount	Negative	*Clue cells*: >20% of the total epithelial cells  Normal vaginal cells Clue cells: Vaginal cells with bacteria stuck to them	*Trichomonas* (flagellates with pear-shaped morphology and whip-like processes)  *Trichomonas vaginalis*
• 10% KOH	Yeast cells and mycelia  *Candia albicans*	Negative	Negative
• Whiff test	Negative	Positive	Negative
Second vaginal swab • Gram stain	–	*Nugent score*: Score > 7 indicates BV	–

(BV: bacterial vaginosis; CVV: candidal vulvovaginitis; KOH: potassium hydroxide; TV: *Trichomonas vaginalis*)

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- *Amine test*: Smelling (whiffing) the slide immediately after applying KOH helps in detecting fishy (amine) odor of BV.
- *Gram stain*: Slide is prepared from discharge and gram stained and looked for gram-positive and-negative bacterial score for BV.

Nugent score.[20]

Bacterial morphology	0	1+	2+	3+	4+
Lactobacilli type (gram positive)	4	3	2	1	0
Gardnerella type (gram variable coccobacilli)	0	1	2	3	4
Mobiluncus type (gram negative)	0	1	2	3	4

Calculation of score:
0/oil immersion field: 0
<1/oil immersion field: 1+
1–5/oil immersion field: 2+
6–30/oil immersion field: 3+
>30/oil immersion field: 4+

Score:
0–3: Normal
4–6: Intermediate (test to be repeated later)
7–10: Bacterial vaginosis

Microscopy is negative/not available: If microscopy is negative but *Candida* is suspected and in strongly suspected cases of BV or trichomoniasis, additional testing by culture or nucleic acid amplification test (NAAT) is important.

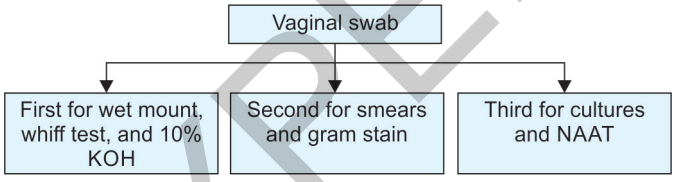
If microscopy is not available, rapid antigen, NAAT, and polymerase chain reaction (PCR) are used for differentiating and confirming clinical diagnosis of CVV, BV, and TV.

Advanced Investigations for Chronic and Recurrent Vaginal Discharge

- *Culture*: Infective vaginal discharge **(Table 9)**. For recurrent TV and recurrent CVV, culture is gold standard. As BV represents a polymicrobial infection, culture is not used for the diagnosis. But, if microscopy is negative in recurrently symptomatic women with normal pH of discharge, then culture of discharge should be done.

  Microscopy requires adequate trained person and is subjective. Recently available test like PCR is objective in nature.
- *NAAT:* It should be conducted after 3 weeks of treatment completion because of possible detection of residual nucleic acid.[23]
  - *PCR*: To identify and amplify specific DNA fragments. Probes and primer are two types of single stranded, oligonucleotides used in various types of PCR. PCR primer method has proven to be the most accurate diagnostic method for TV, BV, and CVV.
  - *DNA probe*: This is an objective test developed to detect directly the presence of *Candida*, *Trichomonas,* and *Gardnerella*. DNA probe test is relatively insensitive to diagnose BV as *Gardnerella vaginitis* is present in vagina as normal flora also. Various kits are available commercially that detects *Gardnerella*, *Trichomonas,* and *Candida* at the same time. For example: The Affirm VPIII (45 minutes).[24]
- *Other tests*:
  - Elevated levels of interleukin (IL)-6, IL-8, ferritin, and granulocyte colony-stimulating factor are some of the secondary predictors that confirm the role of intrauterine infection.[25]
  - In recurrent and persistent VD drug sensitivity testing is indicated.
  - Male partner should also be investigated as in the form of culture from the prepuce, urine routine microscopy, semen culture, and blood sugar.
- *Point of care test*:[18]
  - Proline iminopeptidase (PIP) activity test card (proline aminopeptidase test card)
  - Trimethylamine and high pH
  - *BV blue test*: It detects elevated levels of sialidase in vaginal fluid, which is produced by pathogens that cause BV. It is an office-based objective test that provides result in <1 minute.[26]
  - *Trichomonas* rapid test[27]
  - *Vulvovaginal candidiasis (VVC)*: Savvy check vaginal yeast assay[28]

Advantages of point of care test: Less than 30 minutes result, require minimal training, can be done at any peripheral



FLOWCHART 2: Vaginal swabs for investigations.
(KOH: potassium hydroxide; NAAT: nucleic acid amplification test)

Table 9: Culture: Infective vaginal discharge.

	CVV[21]	*BV*	*TV*[22]
Culture	• SDA • Nickerson's or Microstix-*Candida* • Chromogenic agar *Advantages of chromogenic agar*: It helps in differentiation of different *Candida* species and identification of polyfungal populations *Disadvantage of chromogenic agar*: Costly	BV not cultured as they are normal commensals	Vaginal swab culture *Culture media*: • Inoculate inPouch at bedside/ Amies transport medium • Kupferberg • Diamonds TV medium

(BV: bacterial vaginosis; CVV: candidal vulvovaginitis; SDA: sabourad's dextrose agar; TV: *Trichomonas vaginalis*)

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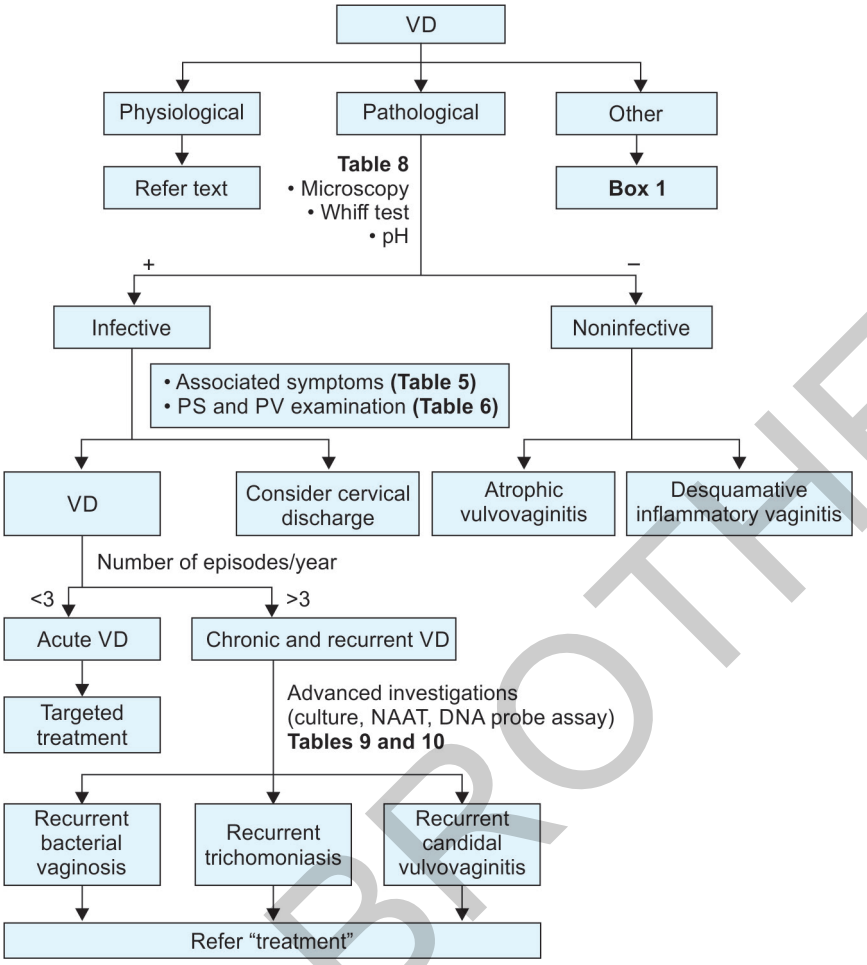

FLOWCHART 3: A practical approach in a female with chronic and recurrent vaginal discharge (VD).

Table 10: Characteristics of detection assays: Sensitivity%/specificity%.[23]

Organism	*Microscopy (wet mount)*	*Culture*	*Antigen detection*	*DNA probe assay*
Candidiasis	35–45%/99%	67%/66%	61–81%/97%	80%/98%
Trichomoniasis	38–82%/100%	98%/100%	86%/100%	88–91%/100%
Bacterial vaginosis	81%/94%	89%/93%	93%/93%	94%/81%

clinic, whole blood-based procedure (no centrifuge/rotator), ingredients can be kept at room temperature, battery dependent

- *Cervical test*: An additional swab taken in suspected cases of cervicitis/cervical discharge is for culture and NAAT.

Diagnostic Criteria

The diagnostic criteria for infective and noninfective vaginitis are given in **Table 11**.

Treatment

Patients with symptoms and history of chronic and recurrent VD: (1) if not responding to empirical treatment, (2) have a risk for STI's, or (3) have symptoms indicative of upper genital tract infection should be investigate thoroughly and treat accordingly.

- *Infective conditions*: As basic management of VD is very well known, we comprise the treatment protocol for chronic and recurrent VD.
- *BV*:[26] For women who have recurrence, different recommended treatment regimens can be considered.
  - Retreatment with the same recommended regimen is an acceptable approach for treating persistent or recurrent BV after the first occurrence.
  - For women with multiple recurrences after completion of a recommended regimen, either 0.75% metronidazole gel or 750 mg metronidazole vaginal suppository twice weekly for >3 months.

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Table 11: Diagnostic criteria.

	Diagnostic criteria
CVV[29]	• Major criteria (≥5) • Discharge, dyspareunia, positive vaginal swab (at present or past), previous response to antifungal medication, exacerbation with antibiotics, cyclicity, swelling, soreness
BV[30,31]	• *Amsel's criteria:* ○ Thin, white, homogenous discharge ○ Clue cells on microscopy of wet mount ○ pH of vaginal fluid >4.5 ○ Release of a fishy odor on adding 10% KOH (At least three of the four criteria are present for the diagnosis to be confirmed) In *Hay/Isoncriteria* gram-stained vaginal smear is evaluated as follows: • *Grade 0*: No bacteria present • *Grade 1 (normal)*: *Lactobacillus* morphotypes predominates • *Grade 2 (intermediate)*: Mixed flora with some Lactobacilli present, but *Gardnerella* or *Mobiluncus* morphotypes also present • *Grade 3 (bacterial vaginosis)*: Predominantly *Gardnerella* and/or *Mobiluncus* morphotypes. Few or absent Lactobacilli • Grade 4 gram-positive cocci predominate
Desquamative inflammatory vaginitis[32]	• At least one symptom (vaginal discharge, dysparunia, pruritus, pain, irritation, or burning) • Evidence of vulvovaginal inflammation • Vaginal pH > 6 • Leukorrhea ± parabasal cells on microscopy
Atrophic vulvovaginitis[24]	• pH > 4.6 • VMI—to assess the relative proportion of parabasal, intermediate, and superficial vaginal epithelial cell types. <5% superficial cells in postmenopausal women points would be suggestive of atrophic vulvovaginitis

(BV: bacterial vaginosis; CVV: candidal vulvovaginitis; KOH: potassium hydroxide; VMI: vaginal maturation index)

- *Other treatment options are*:
  - Oral nitroimidazole (metronidazole or tinidazole 500 mg two times/day for 7 days), followed by intravaginal boric acid 600 mg daily for 21 days, and suppressive 0.75% metronidazole gel twice weekly for 4–6 months.
  - Monthly oral metronidazole 2 g administered with fluconazole 150 mg—as suppressive therapy; this regimen reduced the BV incidence and promoted colonization with normal vaginal microbiota.
  - A dendrimer-based microbicide 1% vaginal gel (astodrimer)—favorable results in prolonging the time to BV recurrence.
  - Lactobacillus crispatus CTV-05 (Lactin-05)-vaginal application for four consecutive days for week 1 then followed by twice daily dose for week 10 - decrease incidence of BV recurrence.
- *Vulvovaginal candidiasis*[28]

Treatment for Candida albicans:

- Most episodes of recurrent VVC caused by *C. albicans* respond well to basic first-line oral or topical azole therapy.
- To maintain clinical and mycological control, a longer duration of initial therapy is needed. Few other options are:
  - *Induction therapy*: Topical azole therapy for 7–14 days or a 100 mg, 150 mg, or 200 mg oral dose of fluconazole every third day for a total of three doses (days 1, 4, and 7)
  - *Maintenance therapy*: Oral fluconazole (i.e., a 100 mg, 150 mg, or 200 mg dose) weekly for 6 months. If this regimen is not feasible, use topical treatments intermittently.

Treatment for non-albicans Candida:

- The optimal treatment of non-albicans *Candida* VVC remains unknown.
- *Options available*:
  - A longer duration of therapy (7–14 days) with a non-fluconazole azole regimen (oral or topical)
  - 600 mg of boric acid in a gelatin capsule administered vaginally once daily for 3 weeks.
- *TV*:[27]
  - *For recurrent infection*:
    - If re-exposed to an untreated partner and/or If treatment failure occurs-metronidazole 500 mg 2 times/day for 7 days.

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- If no re-exposure–metronidazole or tinidazole 2 g once daily for 7 days.

○ For persistent infection: (Drug resistance should be evaluated)
- Treatment for infections demonstrating in vitro resistance–metronidazole or tinidazole 2 g daily for 7 days.
- If a patient has treatment failure after the 7-day regimen of high-dose oral metronidazole or tinidazole, two additional treatment options are:
  - High-dose oral tinidazole 2 g daily plus intravaginal tinidazole 500 mg two times/day for 14 days
  - High-dose oral tinidazole (1 g three times/day) plus intravaginal paromomycin (4 g of 6.25% intravaginal paromomycin cream at night) for 14 days

○ Intravaginal boric acid might be effective but has not been systemically evaluated.

Treatment in pregnancy:

- *BV and TV*: Oral therapy has not been reported to be superior to topical therapy for treating symptomatic BV and TV in effecting cure or preventing adverse outcomes of pregnancy. Pregnant women can be treated with any of the recommended regimens for nonpregnant women, in addition to the alternative regimens of oral clindamycin and clindamycin ovules.
- *VVC*: Topical azole therapy for 7 days.

Treatment in people living with HIV and immunocompromised patients: Same basic treatment regimen has to be followed.

- *Noninfective conditions*:

○ *Desquamated inflammatory vaginitis*:[33]
- Clindamycin 2% vaginal cream, 5 g every night for 3 weeks followed by twice weekly for 2 months.
- Clindamycin 200 mg vaginal pessary, once every night for 2 weeks followed by twice weekly for 2 months.
- Hydrocortisone 300–500 mg vaginal pessary, once a night for 3 weeks followed by twice weekly for 2 months.
- Clobetasol propionate is an ultrapotent steroid that can be used in refractory cases for few weeks to avoid remission before switching to mild potency steroids.
- Women at risk of developing candidiasis (25%) with prolonged clindamycin can be given fluconazole 150 mg weekly suppressive therapy.

○ *Atrophic vaginitis*:[34]
- First-line treatment: Vaginal moisturizer, lubricants, and probiotics
- Second-line treatment: Localized hormone replacement therapy
  - Vaginal cream—estradiol-17b
  - Vaginal tablets—estradiol hemihydrate
  - Vaginal capsules—estradiol-17b softgel capsules
- Third-line treatment: Systemic hormone replacement therapy ospemifene [selective estrogen receptor modulator (SERM)] 60 mg daily

Prevention for Recurrence

These are some hygiene modifications for prevention. Like, wear 100% cotton underpants, and avoid overly tight clothing, sprays, and bubble baths. Keep the vagina clean by washing with a gentle, mild soap, and warm water from the outside. Always wipe from front to back and avoid jet sprays of toilet seats to prevent bacteria from getting into the vagina and causing an infection.

Treatment of every episode of infection with full course of treatment must be done with partner treatment when required.

FUTURE ASPECTS

- *CVV*:[35] A new virulence factor candidalysin secreted by candidal hyphae which is a cytolytic peptide toxin. It triggers protective immune response in form of host cell activation, neutrophil recruitment, type 17 immunity that will help to prevent recurrence. This immune response will also open horizon about targeting new strategies for vaccination. Few are under trial, like NDV-3A (antigen Als-3). Several other antigens to target are virosomal Sap2, Beta-glucan-CRM-conjugate/MF59, HyR-1.
- *BV*:[36] An updated conceptual model on the pathogenesis of BV that centers on the roles of virulent strains of *Gardnerella vaginalis*, as well as *Prevotella bivia* and *Atopobium vaginae* that forms a biofilm which is responsible for the continuance and high-recurrence rates of BV. Absence of inflammation in BV leads to considerable overgrowth of gram-negative and positive anaerobes. Lack of inflammation in BV may be due to majority of vaginal bacteria originates from gut microbiota which leads to immune tolerance acquired through evolution and presence of short-chain fatty acids which modulates the immune response.
- *TV*:[37] Vaccination against *Trichomonads* species infection is already in use for systemic infections in infants. Immune response to *T. vaginalis* infection is heterogenous. Some immunogenic epitopes for *T. vaginalis* are 115 kDa alpha actin protein, 100 kDa protein, and heat shock protein.

TAKE HOME MESSAGE

"Our knowledge of leukorrhea is unsatisfactory and incomplete. The majority of physicians neither appreciate the gross aspects of the condition, nor

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discover the locality from which discharges arise, practically none of us possesses an adequate knowledge of the bacteria involved and most clinicians admit that their curative efforts yield poor results."

–Arthur H Curtis

This comprehensive approach for diagnosis and management in chronic and recurrent VD patients will result in symptom improvement and reduction in recurrence in majority of cases.

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