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FEMALE GENITAL TRACT INFECTIONS (J SOBEL, SECTION EDITOR)

Algorithms for Managing Vulvovaginal Symptoms—a Practical Primer

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Abstract

Purpose of Review To present a comprehensive systematic approach for diagnosing correctly the cause(s) of bothersome genital symptoms.

Recent Findings We searched the PUBMED for practical clinical guidelines, written by a multidisciplinary team of healthcare providers directed for diagnosing bothersome genital symptoms. This search was performed by a professional information specialist using the keywords "vulvovaginal," "vulvar," "multidisciplinary diagnosis," "interdisciplinary consultation," and "vulvology." We found numerous publications defining the criteria for diagnosing specific disorders, but only a few publications presented a multidisciplinary clinical algorithm for diagnosing bothersome vulvovaginal symptoms. The authors, from three different specialities, gathered together (online), in aim to present a comprehensive systematic approach for accurate diagnosing of bothersome vulvovaginal symptoms.

Summary Six principles for accurately diagnosing a woman with bothersome genital symptoms were endorsed: (1) locate the discomfort (vulva, clitoris, vestibule, vagina, cervix, pelvis); (2) consider more than one entity; (3) evaluate each symptom separately (it is common to have more than one entity necessitating treatment for each); (4) use pH and wet mount microscopy; (5) obtain a follow-up visit in 2–4 weeks; (6) perform a biopsy for dermatological conditions that are resistant to treatment.

Keywords Vulvitis · Vaginitis · Genital pruritus · Discharge · Dyspareunia

Introduction

Bothersome genital symptoms (pruritus, irritation, dyspareunia, vaginal discharge, malodour, burning) are a common problem and often are the primary reason for visiting a gynaecologic clinic [1]. Women with such symptoms seek help from a variety of clinical specialties, including gynecology, dermatology, infectious diseases, primary care physicians, physiotherapy, and

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sexology. The main challenge for clinicians is to correctly diagnose the cause of the symptoms as they are nonspecific and often have multiple overlapping etiologies [2–5]. The main limitation in this field of medicine, both in clinical practice and in the literature, is the absence of a comprehensive systematic approach for diagnosing correctly the cause(s) of bothersome genital symptoms. The aim of this review is to present a clinical flow chart algorithm that can help the clinician reason through overlapping symptoms to obtain more accurate diagnoses and institute more appropriate treatments.

Literature Review

We searched the PUBMED for practical clinical guidelines, written by a multidisciplinary team of healthcare providers focused on properly diagnosing bothersome genital symptoms. The search was performed by a professional information specialist using the keywords "vulvovaginal," "vulvar," "multidisciplinary diagnosis," "interdisciplinary consultation," and "vulvology." We found numerous publications defining the criteria for diagnosing specific disorders, but only one publication presented a multidisciplinary clinical algorithm for diagnosing bothersome vulvovaginal symptoms [6]. We also found a comprehensive website addressing vulvovaginal disorders presenting clinical algorithms for accurate diagnosis of vulvovaginal bothersome symptoms [7]. This landmark website was built by a multidisciplinary team of healthcare providers and serves as an online learning program for clinical education of vulvovaginal disorders [7].

Case Scenario

A 27-year-old sexually active woman presents with a 3-month history of intermittent genital pruritus, vaginal discharge, and dyspareunia. This is her third visit in the last 2 months. She was initially diagnosed with a yeast infection, based on symptoms, and was treated with 3 days of antifungal vaginal suppositories. Following a temporary improvement, she was thought to have bacterial vaginosis. It is now 3 weeks after completing treatment with vaginal metronidazole with slight improvement only.

Table 1 Genital diagnoses by anatomical location

Vulva	Vestibule	Vagina	Cervix
Contact dermatitis (irritants or allergens)	Vulvodynia	Candidiasis	Ectropion inflammatory/ non-inflammatory
Lichen sclerosus	Pelvic floor dysfunction—myofascial pain	Trichomonas vaginalis	Cervicitis *non-gonococcal non-chlamydia*
Lichen simplex chronicus	Erosive lichen planus	Bacterial vaginosis	Cervicitis gonococcal/ chlamydia
Lichen planus	Plasma cell vulvitis	Group A Streptococcus	HSIL
Plasma cell vulvitis	Herpes simplex	Lichen planus	Cervical cancer
Psoriasis	Treponema pallidum	Desquamative inflammatory vaginitis	
Herpes simplex	Vulvar aphthae	Vaginal atrophy	
Treponema pallidum	Ulcer	Contact dermatitis (irritant or allergic)	
Candidiasis	Bartholin cyst/abscess	Foreign body	
Tinea cruris	Squamous cell carcinoma	Rectovaginal fistula	
Intertrigo	HSIL	Pelvic floor dysfunction—myofascial pain	
Crohn's disease	dVIN	Graft versus host disease	
Scabies	Graft versus host disease		
Pediculosis	Candidasis		
drug reaction	contact dermatitis (irritant or allergic)		
Ulcer			
Squamous cell carcinoma			
HSIL			
dVIN			
Paget's Disease			

dVIN, differentiated vulvar intraepithelial neoplasia; *HSIL*, high-grade squamous intraepithelial lesion

Table 2 The six principles needed for accurate diagnosing a woman with genital discomfort

I	Locate the discomfort	Vulva, clitoris, vestibule, vagina, cervix, pelvis
II	Consider more than one entity	It is common to diagnose more than one condition
III	Evaluate each symptom separately	Clinical flow chart for each symptom separately
IV	Use pH and wet mount	When symptoms are located in the vagina
V	Follow up visit in 2–4 weeks	Confirm response while on treatment
VI	Vulvovaginal conditions unresponsive to treatment	After excluding other causes perform a biopsy

A Systematic Clinical Flow Chart Approach for Diagnosing Bothersome Vulvovaginal Symptoms

We present a systematic approach aimed at helping healthcare providers in accurate diagnosis in women with bothersome genital discomfort. It is beyond the scope of this clinical guideline to review all genital conditions [8] and we choose to focus on genital conditions listed in Table 1.

We recommend adopting six principles, listed in Table 2. Principle 1 is to locate the discomfort to one or more of five anatomical areas: vulva, clitoris, vestibule, vagina, or cervix.

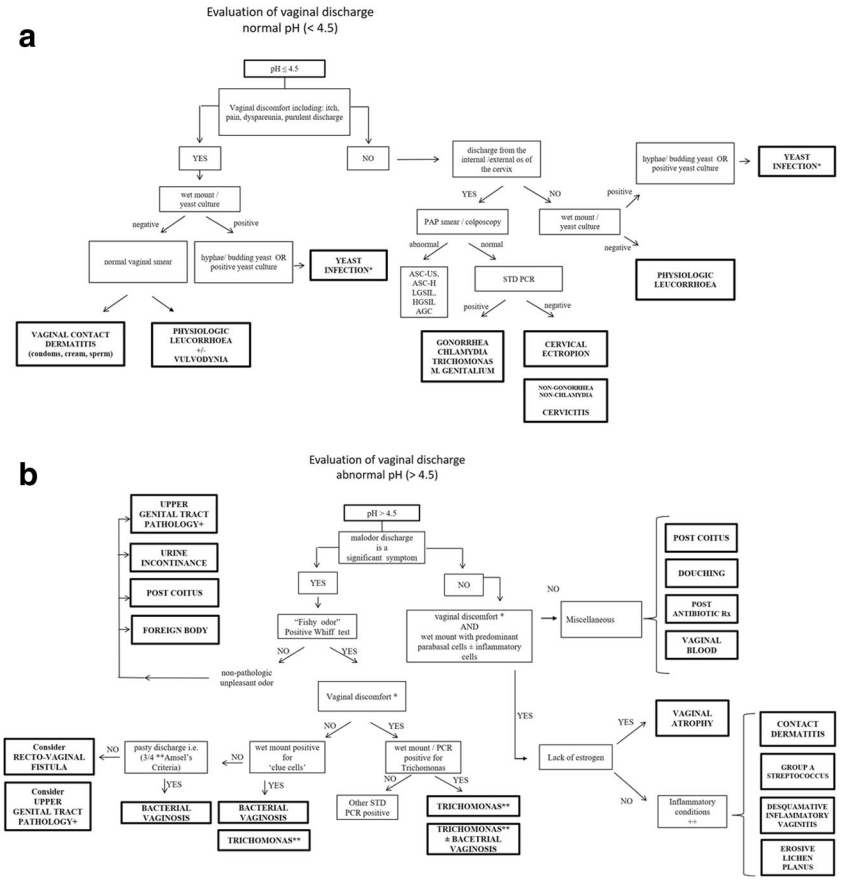

Fig. 1 **a** Vaginal discharge (a normal pH): clinical flow chart. *Yeast infection has a wide clinical presentation. Symptoms can include discharge only or a combination of discharge itch and dyspareunia. Some women are asymptomatic. Pap, Papanicolaou test; ASC-US, atypical squamous cells of undetermined significance; ASC-H, atypical squamous cells cannot exclude HGSIL; HGSIL, high-grade squamous intraepithelial lesion; LGSIL, low-grade squamous intraepithelial lesion; AGC, atypical glandular cells not otherwise specified. **b** Vaginal discharge (an abnormal pH): clinical flow chart. *Vaginal discomfort including at least one of the following: itch, pain, dyspareunia, purulent discharge. ***Trichomonas vaginalis* has a wide clinical presentation; some patients present with acute vaginitis and complain of dyspareunia; malodorous, purulent discharge, and itch; the others (up to 50%) are asymptomatic. If clinically indicated, a PCR for Trichomonas has to be performed. ***Amsel's criteria, at least three of the following: (1) pasty discharge, (2) positive "whiff test" a drop of KOH to vaginal discharge will worsen malodor, (3) positive "clue cells" on wet mount, (4) elevated pH. +Submucosal fibroid, endometrial carcinoma, fallopian carcinoma. ++Any erosive condition of the vagina can cause an inflammatory vaginitis such as pemphigus and pemphigoid and more commonly it is seen with Stevens-Johnson syndrome, toxic epidermal necrolysis, and graft versus host disease

Although adjacent, the histology of the five areas differs [9], and as such they are susceptible to different pathologies that could overlap (Table 1) (vulva: keratinized hair-bearing skin; clitoris: numerous nerves and typical erectile tissue; vestibule: lies exterior to the hymenal ring and within Hart's line and is predominantly nonkeratinized, stratified squamous epithelium; vagina: stratified squamous epithelium; and cervix: the upper cervix (endocervix) is lined by a simple columnar epithelium that contains mucous-secreting cells, the lower cervix (ectocervix) is lined by a stratified squamous epithelium). The difficulty in diagnosing genital complaints is stated in principle 2, "always consider more than one entity." Approximately 20% of women visiting a vulvovaginal clinic will be diagnosed with two different conditions, necessitating combined treatments [4]. In these cases, the symptoms are usually located at two or more of the five anatomical genital areas (see principle 1). The complexity in diagnosis is that symptoms could be located to more than one anatomical area even when there is only one etiology. In addition, it should be emphasized that even after a potential pathogen is identified, it is important to establish causality of identified pathogens, e.g., several Candida species may exist as "innocent bystanders," colonizing the genital tract but not causing symptoms. In such cases, treating non-pathogenic species will not improve symptoms. Principle 3 describes the need to individualize symptoms and adopt a flow chart diagnosis approach oriented for each symptom independently (Figs. 1, 2, and 3), i.e., a woman complaining of discharge, pruritus, and dyspareunia needs to have an independent work-up for discharge (flow chart 1), pruritus (flow chart 2), and dyspareunia (flow chart 3). Eventually, the flow charts could lead to one common causal entity for all presenting symptoms as opposed to two or three different causes. Principle 4, use of pH and wet mount, is based on the understanding that vaginal microbiota are in a delicate equilibrium with reproductive hormones. Adequate levels of estrogen preserve the vaginal barrier function and promote the maintenance of a healthy vaginal biome and acidic vaginal pH $\leq$ 4.5. The acidic environment inhibits growth of anaerobic bacteria. Deficiency of estrogen has several consequences including reversal of this process resulting in decreased titers of lactobacilli with a shift to an abnormal mixed anaerobic flora which could induce a troublesome malodorous discharge [10]. As such, vaginal pH is an excellent screening tool for evaluating the health of the vagina. A normal acidic pH (<4.5) indicates in most cases that there is a mature vaginal epithelium with normal healthy organic acid–producing lactobacilli, whereas an abnormal pH mandates active exclusion of various pathologies that can be diagnosed using the microscope and wet mount (Fig. 1). Principle 5 refers to the time of follow-up visit, which needs to be scheduled in 2–4 weeks from the initial visit. Response to treatment can be divided into three separate groups: no improvement, partial improvement, and good response to treatment, i.e., subjective and objective improvement of 90–100%, Fig. 4. The follow-up visit is essential for confirming diagnosis and educating the patient as what to expect in the future and how to manage with

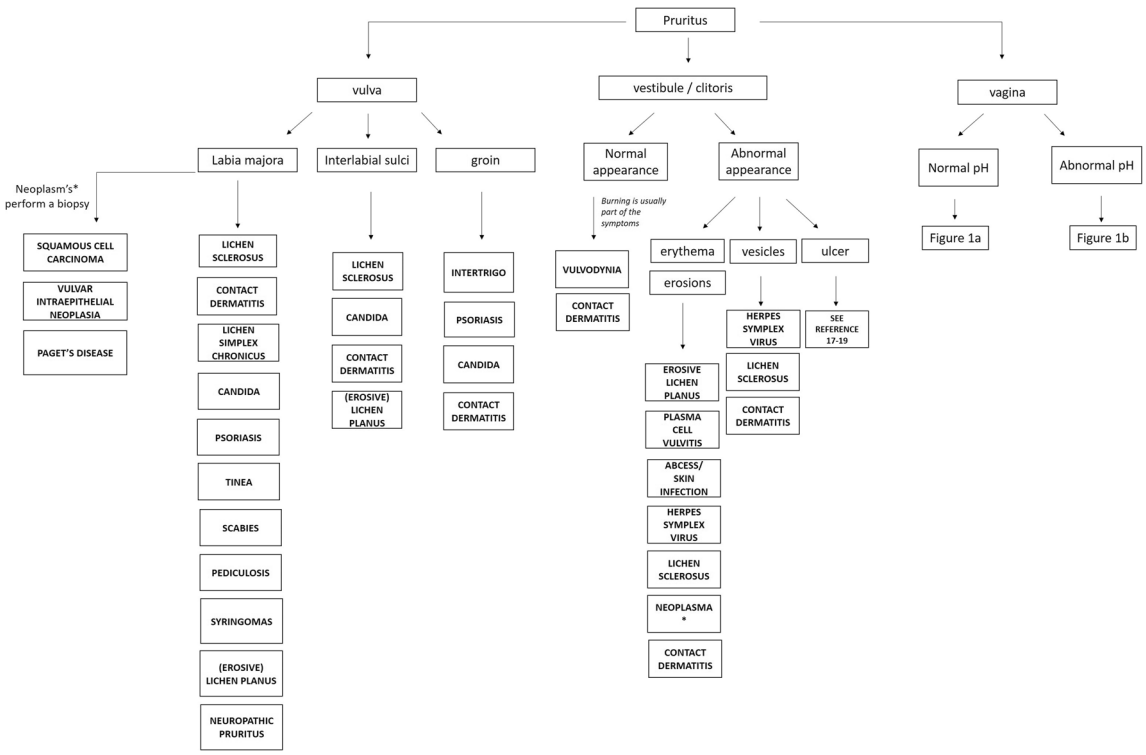

Fig. 2 Genital pruritus: clinical flow chart

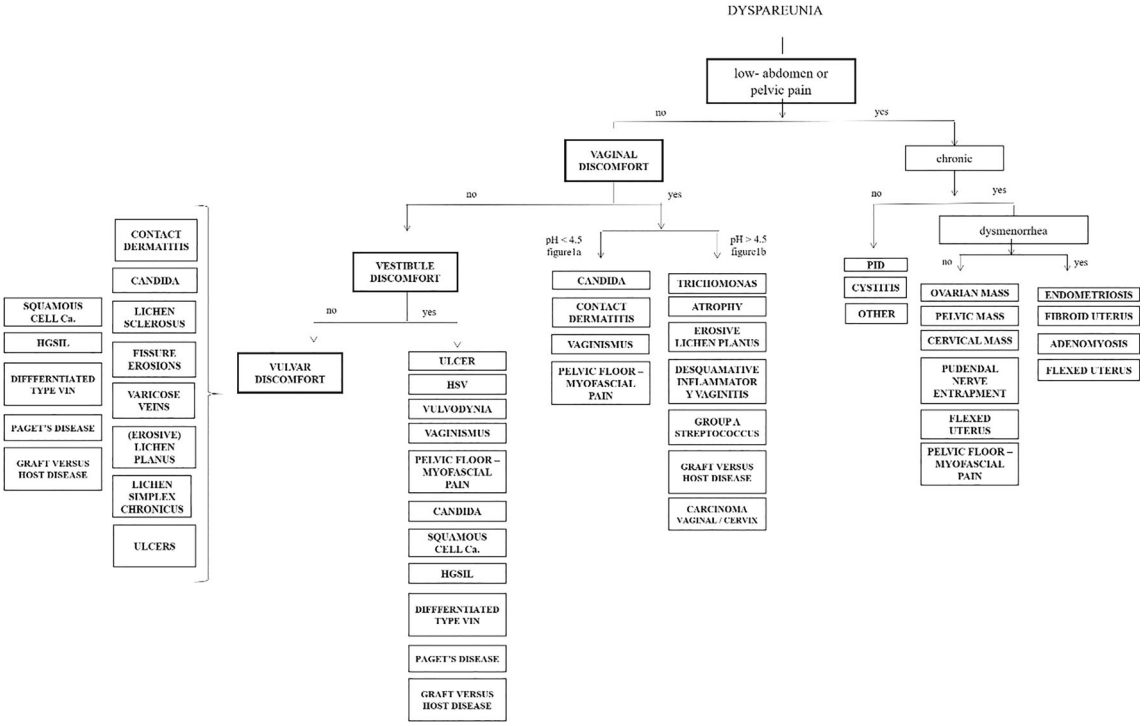

Fig. 3 Dyspareunia: clinical flow chart

maintenance treatment, if needed. Principle 6 recommends performing a biopsy if the patient has a poor response to treatment and other etiologies have been ruled out.

Areas of Uncertainty

Most vulvovaginal conditions listed in Table 1 can be clinically diagnosed and, when needed, confirmed by culture,

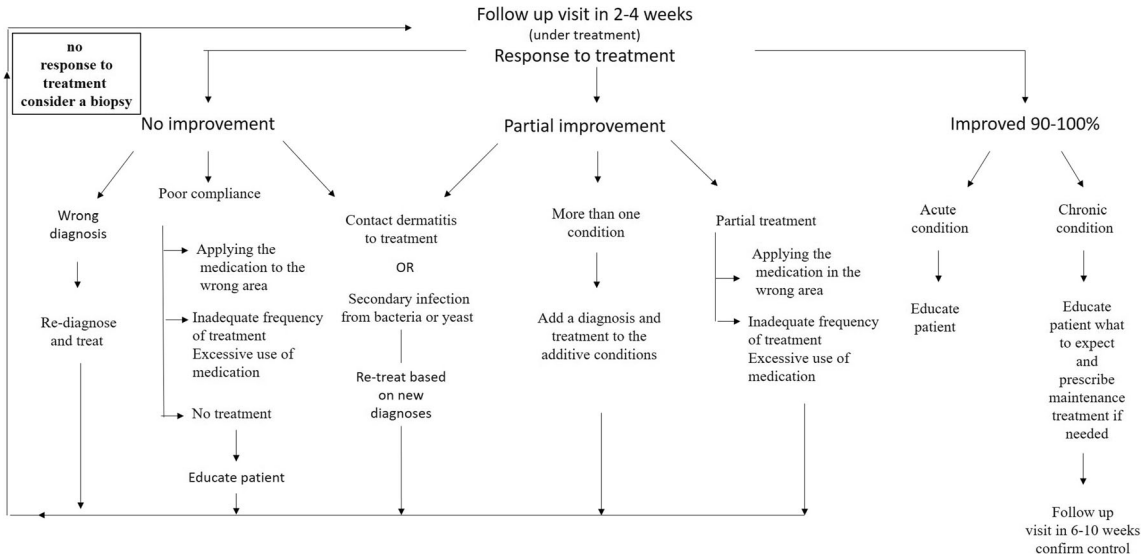

Fig. 4 Follow-up visit in 2–4 weeks from initial visit while on treatment

Table 3 Diagnostic criteria of etiologies that cause vaginal symptoms

	Etiology	Diagnostic criteria
Infectious diseases	Yeast most common *Candida albicans*	(1) Presence of *Candida* blastospores or hyphae on wet mount or 10% KOH (2) Positive yeast culture Vaginal pH is in the normal range
	Trichomonas vaginalis	(1) Elevated vaginal pH (> 4.5) (2) Presence of motile trichomonas on wet mount (poor sensitivity) (3) Elevated inflammatory cells on wet mount ↑ WBC (4) Commercially available nucleic acid amplification test (NAAT)—gold standard (5) Rapid antigen test immunochromatography (OSOM Trichomonas Rapid Test (Genzyme))
	Bacterial vaginosis	Amsel's criteria, at least three of the following: (1) Pasty discharge (2) Positive "whiff test" a drop of 10% KOH to vaginal discharge will produce or worsen fishy malodor (3) positive "clue cells" on wet mount (4) elevated pH > 4.5 Nugent Gram stain score—the score is determined by the average number of one of three morphotypes of bacteria 0–3 normal, 4–6 intermediate, 7–10 bacterial vaginosis
	Neisseria gonorrhea, *Chlamydia trachomatis*	Clinically could present as cervicitis but most patients with *Chlamydia tracomatis* are asymptomatic. Diagnosis is based on commercially available nucleic acid amplification test (NAAT)
	Group A Streptococcus	Positive vaginal culture
Immune induced	Erosive lichen planus (ELP),	Primarily a clinical diagnosis. A biopsy may be obtained to support the clinical diagnosis, but pathology may be nonspecific, and immunofluorescent studies may be helpful for diagnosis
	Desquamative inflammatory vaginitis (DIV)	Clinical syndrome of purulent vaginitis, diagnosis is based on the exclusion of other causes of purulent vaginitis
	Contact dermatitis: irritants/allergens	Suggestive exposure based on history. Confirm diagnosis by clinical response to stopping the irritant/allergen, or an allergy test
Hormonal	Atrophic vaginitis (genitourinary syndrome of the menopause)	The diagnosis of a lack of estrogen is based on the presence of parabasal cells and/or basal cells on wet prep. Vaginal atrophy should be differentiated from atrophic vaginitis. The former refers to a thin vaginal epithelium due to lack of estrogen characterized predominantly by parabasal cells, as opposed to the latter that includes inflammatory cells. Both can be characterized by an elevated pH > 4.5
Miscellaneous	Trauma, post coitus, foreign body, douching, urine incontinence	Suggestive, based on history and physical findings

PCR, or biopsy. These conditions respond well to specific treatment, although maintenance therapy may be necessary to maximize cure and prevent recurrence of symptoms [3, 5, 7, 8, 11]. Only two of the thirty-eight conditions listed in Table 1 are diagnosed by excluding other conditions and cannot be confirmed directly by laboratory evaluations. These include desquamative inflammatory vaginitis (DIV) [12, 13], which is a syndrome of purulent vaginitis responding well to local vaginal anti-inflammatory treatment (steroids or clindamycin), and vulvodynia, which is an idiopathic syndrome of vulvar pain, in which diagnostic confirmation is achieved by exclusion of other known causes listed in Table 1 [14]. Vulvodynia is a most challenging genital condition to both the patient and clinician. It requires the clinician to be an expert in evaluating vulvovaginal diseases, as the diagnosis requires exclusion of all other conditions that can cause pain. There is a need to differentiate between two mechanisms causing dyspareunia that are associated and frequently overlap. One is a pelvic floor muscle dysfunction (PFD, myofascial pain), which is treated by physiotherapy and if needed sexology or cognitive behavioral treatment (CBT). The second is a neuropathic pain disorder, allodynia, frequently characterized by a "burning" sensation rather than pain or pruritus. Treatment of patients with combined allodynia and PFD necessitates a multidisciplinary approach and several weeks of treatment before improvement is seen. The current limited understanding of the pathophysiology of vulvodynia leads healthcare providers to a variety of treatments [15, 16].

Guidelines

As we have emphasized, the challenge for the clinician evaluating women with genital discomfort is to diagnose correctly the cause(s) of symptoms and confirm the diagnosis (Figs. 1, 2, and 3 and Tables 3, 4, and 5). It is beyond the scope of this systematic clinical diagnostic approach to address the various treatments for these etiologies, yet once the condition is properly diagnosed, treatment is usually successful [3, 5, 7, 8, 11, 17, 18].

Case Scenario—Diagnosis

The 27-year-old sexually active woman presented in the case scenario with the 3-month history of genital pruritus, vaginal discharge, and dyspareunia underwent evaluation for each symptom independently. Genital pruritus was localized to both labia majora with no vaginal or vestibular involvement of pruritus. Vulvar anatomy was normal. A slight rash was noticed compatible with the line of the panty liners she was using. Regarding the discharge, the patient complained of a fishy odor that increased with intercourse. Per speculum examination, a pasty discharge was noticed, with normal appearance of vaginal walls and cervix. pH was elevated, whiff test was positive, and clue cells were seen on wet mount without presence of inflammatory cells. Regarding the dyspareunia, she complained of deep penetration pain only located to the

Table 4 Diagnostic criteria of etiologies that cause vestibular symptoms

	Etiology	Diagnostic criteria
Infectious diseases	Ulcerating diseases	References 17, 18
	Herpes simplex virus	Clinical diagnosis of painful vesicle vesicular lesions, confirmation by PCR/culture/serology
	Genital warts Human papillomavirus (HPV)	Clinical diagnosis/biopsy
Immune induced	Lichen sclerosus	Clinical diagnosis/biopsy
	Lichen simplex chronicus	Clinical diagnosis/biopsy
	Contact dermatitis: irritants/allergens	Suggestive exposure based on history. Confirm diagnosis by a clinical response or an allergy test
	Ulcerating diseases	References 17, 18
	Erosive lichen planus (ELP)	Primarily a clinical diagnosis. A biopsy may be obtained to support the clinical diagnosis, but pathology may be nonspecific, and. Immunofluorescence studies may be helpful for diagnosis
	Plasma cell vulvitis	Biopsy
Neuropathy and myofascial pain	Vulvodynia	Diagnosis of exclusion, reference 14
	Pelvic floor dysfunction	Myofascial pain, clinical diagnosis after excluding other conditions
Neoplasms	Squamous cell carcinoma	Biopsy
	HSIL/dVIN	Biopsy
	Paget's disease	Biopsy

Table 5 Diagnostic criteria of etiologies that cause vulvar symptoms

	Etiology	Diagnostic criteria
Infectious diseases	Yeast most common *Candida albicans*	(1) Presence of *Candida* on wet mount or 10% KOH (2) Positive yeast culture Vaginal pH is in the normal range
	Multiple boils caused by *Staphylococcus aureus*	Culture
	Herpes simplex virus	Clinical diagnosis of painful vesicle lesions, confirmation by PCR/culture/serology
Immune induced	Lichen sclerosus	Clinical diagnosis, biopsy
	Lichen simplex chronicus	Clinical diagnosis, biopsy
	Contact dermatitis: irritants/allergens	Suggestive exposure based on history. Confirm diagnosis by a clinical response or Patch testing for specific allergens
	Lichen planus	Clinical diagnosis, biopsy
	Psoriasis	Clinical diagnosis, biopsy
	Hidradenitis suppurativa	Classic appearance of boils in hair-bearing skin
Neuropathy and myofascial pain	Idiopathic post herpetic neuralgia	Vulvodynia—diagnosis based on exclusion Clinical diagnosis: medical history and serology
Neoplasia	Squamous cell carcinoma	Biopsy
	HSIL/dVIN	Biopsy
	Paget's disease	Biopsy

pelvis. Bi-manual examination revealed slight pain with cervical motion with no discomfort located at the vestibule or vagina. She mentioned dysmenorrhea and pelvic ultrasound revealed a right ovarian endometrioma. She was eventually diagnosed with three different conditions: (1) *contact dermatitis* secondary to the panty liners, (2) *bacterial vaginosis* (*BV*), and (3) *endometriosis*. She was treated for the contact dermatitis by discontinuing the use of panty liners and applying a mid-potent steroid ointment. For the BV, she received local treatment with vaginal metronidazole. For the endometriosis, she was educated, and oral contraception was initiated. Three weeks later, first follow-up visit, while on treatment, she reported that the pruritus and odor resolved. There was no vulvar rash, vaginal pH was normal, whiff test was negative, and bacterial rods were seen on wet mount, compatible with normal healthy Lactobacillus species. Unfortunately, as expected, she still had deep penetration dyspareunia. She was educated regarding the condition and referred to an endometriosis specialist for further treatment.

Conclusions and Recommendations

Good clinical practice in all fields of medicine is based on confirming a diagnosis. Six principles for accurate diagnosing a woman with bothersome genital symptoms were endorsed: (1) locate the discomfort (vulva, clitoris, vestibule, vagina, cervix, pelvis); (2) consider more than one entity; (3) evaluate each symptom separately (it is common to have more than one entity necessitating treatment for each); (4) use pH and wet mount; (5) follow up visit in 2–4 weeks; (6) perform a biopsy for dermatological conditions that are resistant to treatment.

We are aware that the complexity of this field cannot be simplified by clinical flow charts alone. However, there should be no guess work in diagnosis, and empiricism is unacceptable. We feel that this multidisciplinary clinical guideline, written by vulvovaginal experts from gynecology, dermatology, and infectious disease, could be of help to the healthcare provider when addressing women with genital discomfort.

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Compliance with Ethical Standards

Conflict of Interest All authors have no conflict of interest to disclose.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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