Update on Vulvar Dermatology

Hope K. Haefner, MD
Professor
University of Michigan Health System
August, 2016 Orlando, Florida

Disclosures
Hope K. Haefner, MD

- Previously on the advisory board of Merck Co., Inc.
- Discussing an iphone app, but I have not received and will not receive any income from the app
- Topical steroids that are used for various vulvovaginal conditions are not FDA approved for the vulva and vagina, however, they are the current first line treatment
Learning Objectives

At the conclusion of this presentation, you (participants) should be able to:

• Assess your knowledge of vulvovaginal diseases
• Identify the clinical features of some difficult vulvovaginal conditions
• Familiarize yourself with a variety of treatments for skin diseases

Written Information Available:

University of Michigan Center for Vulvar Diseases

Then, click on Information on Vulvar Diseases

http://obgyn.med.umich.edu/patient-care/womens-health-library/vulvar-diseases
University of Michigan Center for Vulvar Diseases

There are many reasons for seeking a vulvar disease specialist. Many women receive total care, from cutting-edge treatment options to education and counseling to meet every individual’s needs.

The Center for Vulvar Diseases was created in 1993 to better serve and treat women with diseases of the external genitalia. Our center is one of only a handful of clinics that specialize in treating these conditions. We focus on the evidence-based primary approach to help patients improve their health. This team approach allows us to provide a higher intensity of care and expertise to women who have already demonstrated a resilient and chronic illness or an unusual vulvar condition.

Many women experience different forms of vulvar pain, including vulvodynia. Vulvodynia is pain on the lips of the vulva or upon intercourse with a normal appearing vulva. It is a burning, stinging, or painful sensation. Some patients are unable to accept sexual penetration due to intense spasms and tenderness. Other conditions associated with vulvar pain include:

- Lichen sclerosis or lichen planus—chronic inflammatory skin disorders
- Vulvar Streptococcal or Herpes zoster—vulvar herpes zoster, with or without itching, and the human papilloma virus (HPV)
- Molluscum contagiosum—a disease of the anal and vulval, with pain-filled bumps of fluid
- Bartholin’s cysts—fluid-filled cysts at the base of the clitoris

ISSVD Postgraduate Course, July, 2015
- Your Diagnosis Is (PPT PDF)

ACOG District II Annual Meeting, NY, October, 2015
- Vulvar Disorders (PPT PDF)
- Your Diagnosis Is? (PDF)

SOGBA Argentina, NY, December, 2015
- Surgery for Vestibulodynia (PPT PDF)
- References - Surgery for Vestibulodynia (PDF)
- Vulvodynia (PPT PDF)
- Vulvodynia Handout (PDF)
- Clinical Aspects of HPV Infection (PPT PDF)

ASCCP, New Orleans, April, 2016
- Puzzling Cases (PPT PDF)
- Post Test (PPT PDF)
- Comparison of Diagnostic Testing for Trichomonas (PDF)
- Costs/Methods of Detecting T. Vaginalis (PDF)

ACOG, Washington DC, May, 2016
- Your Diagnosis Is (PPT PDF)
- Vulvar Diseases: What Do You Know? (PPT PDF)
- Vulvar Diseases: What Do You Know - Handout (Word PDF)
- Erosive and Ulcerative Diseases of the Vulva - Edwards (PPT PDF)
A 21 y.o. G0 presents with a history of chronic immunosuppression secondary to autoimmune hepatitis. She has noted vulvar changes for one year. She complains of vulvar pain and occasional vulvar bleeding.
The histologic images shown represent which vulvar condition(s)?

A. 1 HSIL of the vulva and 2 condyloma
B. 1 and 2 both condyloma
C. 1 and 2 both molluscum contagiosum
D. 1 condyloma and 2 HSIL of the vulva

Lower Anogenital Squamous Terminology (LAST)
### ISSVD 1986 vs ISSVD 2004

<table>
<thead>
<tr>
<th>ISSVD 1986</th>
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</tr>
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<tbody>
<tr>
<td>VIN 1</td>
<td>Flat condyloma or HPV effect</td>
</tr>
<tr>
<td>VIN 2</td>
<td>VIN, usual type</td>
</tr>
<tr>
<td></td>
<td>a. VIN, warty type</td>
</tr>
<tr>
<td>VIN 3</td>
<td>b. VIN, basaloid type</td>
</tr>
<tr>
<td></td>
<td>c. VIN, mixed (warty/basaloid) type</td>
</tr>
<tr>
<td>Differentiated VIN</td>
<td>VIN, differentiated type</td>
</tr>
</tbody>
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### Treatment for condyloma HSIL in this patient should be:

A. Laser  
B. Wide local excision (WLE)  
C. A combination of laser and WLE  
D. No treatment. Observation only.
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**LAST 2012**

- **Low Grade**
- **High Grade**

???
2015 ISSVD Terminology of Vulvar Squamous Intraepithelial Lesions

- Low grade squamous intraepithelial lesion (Flat condyloma or HPV effect)
- High grade squamous intraepithelial lesion (VIN usual type)
- Intraepithelial neoplasia, differentiated-type

Lichen Sclerosus and VIN Differentiated V-to-Y Flaps
V-to-Y Flaps
Question

I see patients with chronic vaginitis

- Yes
- No

Question

I like to see patients with chronic vaginitis

- Yes
- No
A healthy vagina may contain:

A. Proteus, Klebsiella and E. coli  
B. Candida albicans  
C. Both  
D. Neither

The Normal Vagina

• Complex ecosystem of variable organisms  
• Predominance of Lactobacilli (facultative gram + bacteria) maintain low pH between 3.5-4.5  
• Suppress pathogenic bacteria  
• 60% produce hydrogen peroxide which protects against pathogens  
• Staph, strep, enterococci, E.coli, Proteus, Klebsiella, anaerobes, candida albicans in 20-70% of healthy asymptomatic women
# pH and Wet Mount

<table>
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<tr>
<th></th>
<th>pH (3.0-4.5)</th>
<th>WBC</th>
<th>Para-basals</th>
<th>Features</th>
<th>Discharge</th>
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A 49y.o. G4P2 presents with chronic vulvar pruritus and irritation. Her vaginal pH is 4.0. She has had 3 other identical episodes this year.
Culture Positive for Candida Glabrata

- Low vaginal virulence
- Rarely causes symptoms, even when identified by culture
  - 50% of the time non-albicans yeast is an innocent bystander and is not causing the patient's symptoms
    Nyirjesy 2016
- Exclude other co-existent causes of symptoms and only then treat for C. glabrata

What treatment do you recommend for her symptomatic Candida glabrata?

A. Oral fluconazole
B. Boric acid per vagina
C. Intravaginal metronidazole
D. Terconazole
Other Antifungals
Boric Acid

- Puratronic, 99.99995% (metals basic)
- Formula
  \[ \text{H}_3\text{BO}_3 \]
- Formula Weight
  61.83
- Form
  Crystalline Powder
- Melting Point
  170.9°C
- Merck Number
  11,1336
**Boric Acid Capsule or Suppository PER VAGINA**

Fill 0-gel capsule halfway (600 mg)
For treatment of acute infection; insert *per vagina* qhs x 14 days

For prevention of recurrence; insert *per vagina* twice weekly

**KEEP AWAY FROM CHILDREN**
**CONTRAINDICATED IN PREGNANCY**

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**Before Treatment**

![Image of genital area before treatment]
After Treatment

Does she qualify for the diagnosis of having recurrent Candida infections?

A. Yes
B. No
Yeast/Candida iPhone App

Contributors

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Vulvovaginal Candidiasis

General Information
Simple Candida
Recurrent Infections
Treatment by Type
Pregnancy Considerations
Wet Mount Examples
Clinical Images
Patient Information
About
Treatment by Type

Yeast Culture/Speciation Results

- Candida albicans
- Candida glabrata
- Candida parapsilosis
- Candida tropicalis
- Candida lusitaniae
- Trichosporon
- Saccharomyces cerevisiae
- Candida kefyr
- Candida dubliniensis

There are limited data on some of the treatment regimens. The compounded medications generally are suggestions to consider when other agents are not working. The compounded medications are generally used for resistant strains of Candida.
# Treatment by Type

## Yeast Culture/Speciation Results

- **Candida albicans**
- **Candida glabrata**
- **Candida parapsilosis**
- **Candida tropicalis**
- **Candida lusitaniae**
- **Trichosporon**
- **Saccharomyces cerevisiae**
- **Candida kefyr**
- **Candida dubliniensis**

There are limited data on some of the treatment regimens. The compounded medications generally are suggestions to consider when other agents are not working. The compounded medications are generally used for resistant strains of Candida.

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## Candida lusitaniae

Topical creams can be irritating; vaginal tablets or suppositories may be less irritating. One-day products may be more irritating than longer use products.

Ketoconazole is not included in this list due to the availability of more efficacious and less toxic medications.

Use as directed by package labeling. All pharmacies may not carry all products. The creams and suppositories are often oil-based and might weaken latex condoms and diaphragms.

### Oral

Fluconazole

Additional information on drug interactions with fluconazole can be obtained in the CDC Guidelines [here](http://www.cdc.gov/std/tg2015/candidiasis.htm).

In pregnancy, fluconazole is not to be used, instead use topical creams for treatment.

- Recurrence: 150 mg oral tablet every 3 days for three times, then 150 mg orally weekly for up to six months
- At times, other dosing may be required such as 100 mg oral tablet every 3 days for three times (day 1, 4, and 7), then 100 mg orally weekly for up to six months; or 200 mg oral tablet every 3 days for 3 times (day 1, 4, and 7) then 200 mg orally weekly for up to six months.

- If fluconazole cannot be used, (liver disease, Steven’s-Johnson syndrome, or side effects such as headaches or nausea) consider:
  - Boric acid
  - Maintenance creams for recurrent yeast

### Itraconazole

In pregnancy, itraconazole is not to be used, instead use topical creams for treatment.

- 100mg oral tablet daily for 2 weeks, then twice weekly for up to 6 months.

### Topical

Clotrimazole

- Clotrimazole 1% vaginal cream: 1 applicatorful per vagina nightly for 7 nights
- Clotrimazole 2% vaginal cream: 1 applicatorful per vagina nightly for 3 nights
Miconazole 7 day cream 2% (100 mg per dose)
- One applicatorful per vagina nightly for 7 nights

Miconazole 7 day cream 2% (100 mg per dose) plus miconazole nitrate cream 2%
- One applicatorful per vagina nightly for 7 nights
- Miconazole nitrate 2% cream to the vulva twice a day for up to 14 days

Miconazole 3 day cream, suppository, ovule 4% (200 mg per dose)
- One applicatorful, suppository or ovule per vagina nightly for 3 nights

Miconazole 3 day cream, suppository, ovule 4% (200 mg per dose) plus miconazole nitrate cream 2%
- One applicatorful, suppository or ovule per vagina nightly for 3 nights
- Miconazole nitrate 2% cream to the vulva twice a day for up to 14 days

Miconazole 1 day insert (ovule) (1200 mg per dose) plus miconazole nitrate cream 2%
- One insert (ovule) per vagina for one day or night
- Miconazole nitrate cream 2% cream to the vulva twice a day for up to 14 days

Miconazole nitrate topical 2% cream to the vulva twice a day for up to 14 days

For some recurrent infections, consider using Miconazole 2% vaginal cream: 1 applicatorful per vagina nightly for 14 nights, followed by 1 applicatorful twice weekly for up to six months.

**Compounded**

Boric acid suppositories

In pregnancy, boric acid is not to be used, instead use maintenance creams for recurrent yeast.

Vaginal boric acid suppositories 600 mg per vagina for 14 nights; If recurrent, consider suppression after re-treatment with twice weekly boric acid 600 mg per vagina.

_Boric acid capsules can be FATAL if swallowed/taken orally._
PATIENT INFORMATION
What are the symptoms of Candida (yeast) infection?
These are the symptoms of vaginal candida infection:
- genital itch - this is the most common symptom of thrush. Itching is especially worse before your period;
- soreness or burning inside (in the vagina) during or after sex;
- abnormal discharge – that can be thick and white or sometimes it can seem normal;
- a change in the smell of your vaginal secretions;
- redness and inflammation of the outside (vulva);
- soreness or discomfort on urination (peeing);
- pain – particularly if the infection occurs a number of times or hasn’t been treated properly; and
- small white spots on the vaginal wall or curds in the discharge.

How is it diagnosed?
A diagnosis of vaginal Candida infection is often made based on a number of things including your symptoms, physical examination, examination of vaginal secretions under the microscope and vaginal culture. Moreover, there are many other conditions of the vagina and vulva that have symptoms in common and even associated with Candida, so if there is doubt about the diagnosis, or when it is recurrent, it is essential that your healthcare provider takes a vaginal swab for laboratory testing before treatment is started.

Vulvar Pain Terminology
2015 Consensus Terminology and Classification of Persistent Vulvar Pain and Vulvodynia

A. Vulvar pain caused by a specific disorder*
   • Infectious (e.g., recurrent candidiasis, herpes)
   • Inflammatory (e.g., lichen sclerosus, lichen planus, immunobullous disorders)
   • Neoplastic (e.g., Paget disease, squamous cell carcinoma)
   • Neurologic (e.g., postherpetic neuralgia, nerve compression or injury, neuroma)
   • Trauma (e.g., female genital cutting, obstetric)
   • Iatrogenic (e.g., postoperative, chemotherapy, radiation)
   • Hormonal deficiencies (e.g., genitourinary syndrome of menopause [vulvovaginal atrophy], lactational amenorrhea)

B. Vulvodynia—Vulvar pain of at least 3 months’ duration, without clear identifiable cause, which may have potential associated factors

The following are the descriptors:
   • Localized (e.g., vestibulodynia, clitorodynia) or Generalized or Mixed (Localized and Generalized)
   • Provoked (e.g., insertional, contact) or Spontaneous or Mixed (Provoked and Spontaneous)
   • Onset (primary or secondary)
   • Temporal pattern (intermittent, persistent, constant, immediate, delayed)

* Women may have both
2015 Consensus Terminology and Classification of Persistent Vulvar Pain and Vulvodynia

Appendix:
Potential Factors Associated with Vulvodynia

- Comorbidities and other pain syndromes (e.g., painful bladder syndrome, fibromyalgia, irritable bowel syndrome, temporomandibular disorder; level of evidence 2)
- Genetics (level of evidence 2)
- Hormonal factors (e.g., pharmacologically induced; level of evidence 2)
- Inflammation (level of evidence 2)
- Musculoskeletal (e.g., pelvic muscle overactivity, myofascial, biomechanical; level of evidence 2)
- Neurologic mechanisms
  - Central (spine, brain; level of evidence 2)
  - Peripheral: neuroproliferation (level of evidence 2)
- Psychosocial factors (e.g., mood, interpersonal, coping, role, sexual function; level of evidence 2)
- Structural defects (e.g., perineal descent; level of evidence 3)

a The factors are ranked by alphabetical order.

Skin Abscess

Antibiotic therapy as adjunctive therapy to I and D for
- Abscess greater than or equal to 2 cm
- Extensive surrounding cellulitis
- Multiple lesions
- Signs of comorbidity
- Immunosuppression
- Systemic infection

- Methicillin-resistant Staph
  - Trimethoprim-sulfamethoxazole
Skin Abscess
APPLICATION INSTRUCTIONS:

1. Remove tab labeled "T" (either end) and be careful to unfold flap of Layer "T" back to adhere to drape.

2. Pull back one side of Layer "F" and pull drape-face down over foam by carefully pulling edge down securely and rolling part of foam, making sure to leave at least 12 in drapes around foam (Fig. 2). Be careful to avoid wrinkles, as they may be a source of new pressure marks.

T.R.A.C.™ SYSTEM
Use only with T.R.A.C.™ Therapy Systems
LARGE BLACK FOAM DRESSING
(26.5 x 15 x 3.3 cm)
Re-Order No: M6275053.3 (5 pack)
Re-Order No: M6275053.10 (10 pack)
An Unfortunate Patient

- 55 y.o. female admitted for nausea, vomiting, diarrhea, elevated bili
- Hospitalized for 3 wks bone marrow transplant complications (AML)
- Developed vulvar pain 3 days ago when lesions first developed. No significant change in size of lesions over 3 days. Afebrile.
Your Diagnosis Is?  Part A

A. Rhizopus infection
B. Hematoma secondary to hematologic disorder
C. Malignant melanoma
D. Hidradenitis suppurativa
Your Diagnosis Is? Part B

A. Rhizopus infection
B. Hematoma secondary to hematologic disorder
C. Malignant melanoma
D. Hidradenitis suppurativa

Rhizopus
Rhizopus

- Mucormycosis (sometimes called zygomycosis) is a serious but rare fungal infection caused by a group of molds called mucormycetes
- Fungi live in soil and in association with decaying organic matter, such as leaves, compost piles, or rotten wood
- Examples of the types of fungi that most commonly cause mucormycosis are: *Rhizopus* species, *Mucor* species, *Cunninghamella bertholletiae*, *Apophysomyces* species, and *Lichtheimia* (formerly *Absidia*) species

Rhizopus

- 13/1500 transplant patients developed this infection in study from 1993
- Surgical resection for cure
- Antifungals-liposomal amphotericin B
- Dressing changes/amphotericin B
Desquamative Inflammatory Vaginitis (DIV)

- Occurs in 8% of women presenting to a specialty clinic with chronic vaginitis symptoms
- More frequent in Caucasians
- Peak occurrence in perimenopause
- Diagnosis of exclusion

**Desquamative Inflammatory Vaginitis**

**PH and Wet Mount Findings**

- Vaginal pH greater than 4.5
- Purulent vaginal discharge
  - (PMNs/epith > 1:1 in at least 4 hpfs on wet prep)
- Increase parabasal cells (>10% total)
- Loss of normal vaginal lactobacilli
An important condition to rule out when considering DIV is:

1. Gonorrhea
2. Syphilis
3. Mobiluncus
4. Trichomonas
What other conditions have a similar appearance to DIV?

### Inflammatory Vulvovaginitis

- Atrophic vaginitis
- Erosive lichen planus
- Pemphigus vulgaris
- Behçet’s disease
- Collagen vascular diseases
- Traumatic
  - Foreign body, vesicovaginal fistulae
- Allergic vaginitis
- Chemical vaginitis
- Infection
  - Group A Streptococcus, Trichomonas
  - Cervicitis Degenerating leiomyoma or endometrial polyp
- Idiopathic
## Etiologies

**Proposed etiologies**
- Immune mediated (autoimmune) 
  (response to anti-inflammatory)
- Kallikrein-related peptidase
- Genetic link
- Bacterial infection

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DIV Treatment


Uptodate by Sobel J (slightly different regimen)

DIV

Therapy Options Clindamycin
(Adapted from Reichman and Sobel 2014)

Clindamycin 2% cream 5(g)
one applicator intravaginally qhs x 3 weeks
(consider 2 x per week x 2 months)
   Longer suppression time may be required

Clindamycin 200 mg vaginal suppository qhs x 3 weeks
(consider 2 x per week x 2 months)
   Longer suppression time may be required
DIV
Therapy Options Hydrocortisone
(Adapted from Reichman and Sobel 2014)

Intravaginal hydrocortisone suppositories 25 mg intravaginal bid for 3 weeks (consider 3 x per week x 2 months)
   Longer suppression may be required

Intravaginal hydrocortisone cream 300 to 500 mg intravaginal qhs for 3 weeks (consider 2 x per week x 2 months for maintenance therapy)
   Longer suppression may be required

DIV Other Options

Combine clindamycin cream and hydrocortisone suppositories.
   1 applicatorful of 2% clindamycin cream and 25 mg hydrocortisone nightly x 14 or every other night x 14
DIV Other Options

Compound a high dose intravaginal corticosteroid and 2% clindamycin* (variety of regimens)

Hydrocortisone 100 mg/gram in clindamycin in 2% emollient cream base. Insert 3 to 5 gram (applicator full) (300 to 500 mg active drug) per vagina every other night x 14 doses. Consider taper.

Hydrocortisone 100 mg/gram in clindamycin in 2% emollient cream base. Insert 3 to 5 gram (applicator full) (300 to 500 mg active drug) per vagina every night x 2 weeks, then 3 times per week and taper.

* This needs to be made at a compounding pharmacy.

DIV Other Options

If not working, reconsider the diagnosis! (has estrogen been addressed?)

• May need to add estrogen

Very Early LPErosive Lichen Planus

Lichen Planus (LP)

• Affects the genital skin and mucous membranes producing vaginal scarring
• Can result in complete closure of the vagina
• Can also result in esophageal strictures
Presentation, Diagnosis, and Management of Esophageal Lichen Planus: A Series of Six Cases

- Approximately 80 cases since first report in 1982
- Female to male ratios 5:1

Lichen Planus (LP)

- Surgery for lichen planus (lysis of vulvovaginal adhesions) consists of opening the vagina under anesthesia, followed by long term vaginal dilation and intravaginal steroids

Other Treatments Lichen Planus (and Lichen Sclerosus)

- Hydrodissection with reverse V plasty technique
- Cryosurgery
- Ultrasound therapy
- Use of split thickness skin grafts or full thickness skin grafts
- Release of urethral strictures (oral mucosa grafts)
- Use of acellular human dermal allograft
- Role of adipose derived mesenchymal cells and platelet rich plasma in tissue regeneration
- Stem cell lift
Soft Type Backer Rods

- Ideal for irregular joints, particularly where free flowing and self leveling sealants are employed
- Google
Lysis of Vulvovaginal Adhesions in Lichen Planus

- Surgical lysis of adhesions
  - Goal
    - Improve urine flow, decrease risk of UTI
    - Allow intercourse, reduce dyspareunia
  - Best if disease controlled (koebnerization)
  - Results
    - N=22, 11 patients who underwent surgery for vulvovaginal adhesions and 11 age matched controls
    - 6 months to 6 years post-lysis of adhesions
    - 91% satisfied with procedure
    - 75% of patients with decreased urinary difficulties
    - 55% able to have intercourse
    - 50% continued to fear pain
  - Post op dilator 48-72 hours, long term dilation and steroids

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<th>Timing</th>
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<tr>
<td>Hydrocortisone 100 mg/g in</td>
<td>300 mg (1 g) per</td>
<td>First week postoperatively</td>
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<tr>
<td>ointment cream base</td>
<td>vagina QHS</td>
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<tr>
<td>400 mg (1 g) per vagina QHS</td>
<td>Second week postoperatively</td>
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<tr>
<td>500 mg (1 g) per vagina QHS</td>
<td>Third week postoperatively</td>
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<td>400 mg (1 g) per vagina QHS</td>
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<tr>
<td>100 mg (1 g) per vagina QHS</td>
<td>Starting week 7, indefinitely*</td>
<td></td>
</tr>
</tbody>
</table>

* Depending on disease activity, patients may eventually decrease to 10 mg hydrocortisone ointment nightly per vagina if tolerated and then 25 mg hydrocortisone ointment nightly per vagina. The long-term goal is to utilize hydrocortisone suspension 1-3 times per week. * Any medical-grade dilator set is acceptable.

Medical-Grade Vaginal Dilators
We-Vibe
Lubricants

**Water Based**
- Astroglide
- Astroglide Gel Just Like Me
- Astroglide Silken Secret
- K-Y Liquid Personal
- K-Y SILK-E
- K-Y Ultra Gel
- Liquid Silk
- Me Again
- Pink Water
- Pjur Water Based
- Pre-Seed
- Probe
- Slippery Stuff Gel
- Sliquid H20
- Sweet seduction
- System Jo H20

**Silicone based**
- Astroglide X
- Gun Oil
- ID Millennium
- Jo Premium
- K-Y Intrigue
- Lubrin (Suppository)
- Pink Silicone
- Pjur silicone
- Sliquid Silver
- Wet Platinum Premium Lubricant

**Hypoallergenic**
- Good Clean Love
- Just like Me
Moisturizers

- Extra Virgin Olive Oil
- Vitamin E oil
- Coconut Oil
- Luvena
- Replens
- Moist Again
- KY Silk-E
- K-Y liquibeads

Summary

- Assess your knowledge of vulvovaginal diseases
- Identify the clinical features of some difficult vulvovaginal conditions
- Familiarize yourself with a variety of treatments for skin diseases