Vulvar Regenerative Medicine

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Disclosures & Conflicts of Interest

• None
• I am not engaged in stem cell research or treatment
• I care for patients in my practice who have undergone the therapy we will discuss today
Educational Objectives

• Understand the basic science behind Regenerative Medicine

• Gain familiarity with the data supporting the use of fat-derived mesenchymal stem cell and platelet rich plasma injections for the treatment of vulvar lichen sclerosus

• Learn how to counsel patients considering regenerative treatments for lichen sclerosus
Emotions Associated with A Diagnosis of Lichen Sclerosus

FEAR
CONFUSION
Loneliness
Shame
“Broken”
Anger
Frustration
Who You Gonna Call? The Internet!!
Sexual Dysfunction

Loss of anatomy
TIME Magazine named fat stem cell extraction one of the 50 Best Inventions of the Year!*

* Fat Stem Cell Extraction was named by TIME Magazine as one of the the 50 Best Inventions of 2011.
You Name It, Stem Cells Will Cure It!

The Premier Stem Cell Institute also serves patients who have Osteoarthritis, Osteoporosis, Rheumatoid Arthritis, Multiple Sclerosis, Fibromyalgia, Parkinson’s Disease & Crohn’s. Click Here

CALL TODAY! 970.613.2030

STEM CELL THERAPY TREATMENTS
The O-Shot: Non-Surgical Procedure Claims To Treat Sexual Dysfunction And Improve Orgasms In Women [VIDEO]

Feb 6, 2014 05:03 PM   By Nadia-Elysse Harris   @NadiaElysse
For-Profit Stem Cell Clinics


• More than 170 stem-cell clinics across the United States.

• Many linked in large, for-profit chains. The largest has 67 locations in 22 states, 100+ doctors. They offer stem cell procedures for more than 30 disease conditions. Co-founder has no formal background in stem cell research.

• A weekend seminar offered by a training company and $25K in cell separating equipment gets newcomers into the field
West Coast Clinic Lichen Sclerosus Treatment Website Claims

• “To date, all patients have had **significant improvement** with [proprietary stem cell treatment]”
• “Most patients are able to **discontinue** the use of topical steroids and hormones”
• “[stem cells] may continue to **improve the tissue** for about one year after the procedure”
• **Reduction** in pain, burning, itching
• Improved **look and feel** of the anatomy
• **Less frequent flares** that are shorter in duration with less intense pain and discomfort
Regenerative Medicine or Reparative Medicine

The potential use of stem cells to replace missing, lost, or damaged tissue
Research on overcoming the effects of radiation injury led to rescuing lethally irradiated animals with bone-marrow derived cells which could replace all the blood elements.

Hematopoietic stem cell transplants are now the standard treatment for leukemia and lymphoma, and to replace bone marrow function lost to radiation and chemotherapy.
Stem Cells 101: 2 Essential Qualities of Stem Cells

What is a stem cell?

A single cell that can...

replicate itself, or...

differentiate into many cell types.

Hierarchy of Stem Cells

- Totipotent cell (capable of dividing and developing to form a complete, mature organism)
- Pluripotent cell (capable of developing into many different cell types)

Self-renewal:

- Blood Stem Cells
  - Red Blood Cells
  - White Blood Cells

Other Stem Cells:
- Muscle
- Nerve
- Bone
- Other Tissues
Stem Cells Hierarchy

- **Totipotent**: can generate all 200 cell types in the human body and placenta and umbilical cord. Exist within a fertilized egg until about 4 days after fertilization.

- **Pluripotent**: can generate all the different types of cells in the human body but not placenta and cord. From the *inner cell mass of the blastocyst*. “Embryonic stem cells” are obtained from blastocysts created by IVF but no longer needed. Use of these cells is ethically controversial but valuable for research since they can grow indefinitely in the lab.
Additional Stem Cell “Potencies”

- **Multipotent**: “adult” or “somatic” stem cells which can produce some or all of the mature cell types found within a specific organ or tissue.

- **Unipotent**: make a single cell type

- **Induced pluripotent stem cells** (iPS cells): tissue specific stem cells *genetically reprogrammed* in the lab to behave like embryonic stem cells and used to generate specific cell types outside their home tissues.
Induced Pluripotent Stem Cells
(a) The coagulation phase
Platelets: First responders
Platelet Growth Factors, Cytokines and Chemokines

- Platelet derived growth factor
- Vascular endothelial growth factor
- Insulin like growth factor
- Transforming growth factor
- Platelet factor 4
- Interleukin 1

- Platelet derived angiogenesis factor
- Epidermal growth factor
- Platelet derived endothelial growth factor
- Osteocalcin, osteonectin
- Fibrinogen, thrombospondin 1
- Vitronectin, fibronectin

FGF (Fibroblast growth factor)  
Tissue repair, cell growth collagen production

EGF (Epidermal growth factor)  
Promotion of epithelial cell growth, angiogenesis, promotion of wound healing

KGF (Keratinocyte growth factor)  
Growth and new generation of keratinocytes

PDGF (Platelet derived growth factor)  
Cell growth, new generation and repair of blood vessels, collagen production

VEGF (Vascular endothelial growth factor)  
Growth and new generation of vascular endothelial cells

TGF – B (Transforming growth factor beta)  
Growth of epithelial cells, endothelial cells, promotion of wound healing
Macrophages
Mesenchymal Stem Cells
Mesenchymal Stem Cells Also Secrete Growth Factors
External Molecular Control:

- Chemicals secreted by other cells
- Physical contact with neighboring cells
- Molecules in the microenvironment
Regenerative Applications in Vulvovaginal Disease

- Injection of autologous fat-derived mesenchymal stem cells and platelet rich plasma into vulvar lichen sclerosus
Sources of Mesenchymal Stem Cells

- Bone marrow
- Umbilical cord blood
- Umbilical cord
- Cord membrane
- Wharton’s Jelly
- Umbilical cord vein
- Adipose tissue
- Breast milk
- Placenta
- Decidua basalis
- Peripheral blood
- Menstrual blood
- Foetal membrane
- Chorionic villi
- Dental pulp
- Amniotic membrane
- Amniotic fluid
- Ligamentum flavum
Fat Derived Stem Cells

A Components of Lipoaspirate

B Components of Adipose Tissue
- Pericytes: CD140b⁺, CD146⁺, NG2⁺, CD31⁺, CD34⁺, CD144⁺, vWF⁺
- Adipocytes
- Adipose Derived Stem Cells: CD13⁺, CD29⁺, CD34⁺, CD44⁺, CD90⁺, CD104a⁺, CD14⁺, CD31⁺, CD45⁺, CD106⁺, CD144⁺
- CD146⁺, αSMA⁺
- Pre-Adipocytes
- Hematopoietic Cells: Monocytes/Macrophages

C Components of SVF Pellet
- Tissue Culture
- Cell-Assisted Lipotransfer

Discard
- Collagenase Digestion & Centrifugation
- Adipose Tissue
- Infranatant Blood & Local Anaesthetic
- Oil
- SVF Pellet

ASCCP 2016
Platelet-rich Plasma 101

A. Blood draw
B. Centrifugation
C. Platelet-rich plasma in a tube
D. Injection
Stem Cell Therapy: Seductive But Challenging

- Will the stem cells differentiate into the desired cell types?
- Will the stem cells survive in their new environment or senesce and die quickly?
- Will stem cells integrate into the surrounding tissue?
- Will they function appropriately for the duration of the patient’s life?
- Will they avoid harming the patient in any way?
The Evidence: Francesco Casabona 2010

- N=15 pts between ages 27 and 62
- All had topical steroids with no improvement
- Peripheral blood for 5 ml of PRP, liposuction for 15 ml of saline washed fat
- Both injected intradermal, intramucosal, subdermal, submucosal. Discharge same day
- No adverse effects, moderate pain X 10 days
Dr. Casabona’s results

• Itching and burning disappeared within 1 month
• Vulvar skin and mucosa appeared more elastic and soft with normal color
• 4 months after procedure total resolution of pain and symptoms, vulvar anatomy normal. All pts regained sexual activity
• Some pts treated 1-2 more times, F/U 6-24 mo

Casabona Pictures
The Evidence: Gayle Fischer May 2014

- Replication of Casabona study, preliminary results
- N=12, ages 18 and older
- Severe biopsy proven lichen sclerosus, no topical steroids for preceding 14 days
- Pre-op photos taken and Dermatology Quality of Life questionnaire (DLQI) completed
- Peripheral blood for PRP obtained & centrifuged
- 5 ml PRP one side of vulva, 5 ml normal saline other side. Treatment side determined by coin toss.
- Return at 2 and 4 weeks for repeat exam, photos, and DQLI
  
The Evidence: Andrew Goldstein June 2015

• N=7 pts with biopsy proven active vulvar lichen sclerosus
• 2 week screening period, 12 week treatment period
• Two injections of 5 ml of PRP injected sub-dermally and intra-dermally 6 weeks apart
• Second biopsy obtained 6 weeks after second injection
• Two blinded dermatopathologists judge change in inflammation between pre and post biopsies
• Secondary endpoint: changes in vulvar pruritus and burning by VAS scales and change of Investigator’s Global Assessment of severity of disease
Goldstein results

- 4 of 7 pts had decreased inflammation on post-treatment biopsies, one pt with no change, 2 pts with minimal increase in inflammation. P=0.016
Stem Cell Therapy: Seductive But Challenging
Stem Cell Therapy: Seductive But Challenging

• **Will the stem cells differentiate into the desired cell types?**
  - Don’t know
  - Not supported by the biology
  - Shouldn’t happen

*We are probably seeing enhanced repair mechanisms mediated by growth factors, cytokines, chemokines and progenitor cells in host tissues*
Stem Cell Therapy: Seductive But Challenging

• Will the stem cells survive in their new environment or senesce and die quickly?
  ➢ Injected stem cells exert a transient effect
  ➢ When injected cells are tagged then looked for later, they are gone
Stem Cell Therapy: Seductive But Challenging

• **Will stem cells integrate into the surrounding tissue?**
  - This does not seem to happen
  - Blood derived stem cells do not engraft
  - They are gone in a few weeks
Stem Cell Therapy: Seductive But Challenging

• Will they function appropriately for the duration of the patient’s life?
  ➢ We are currently seeing only temporary immune modulation
Stem Cell Therapy: Seductive But Challenging

• Will they avoid harming the patient in any way?
  ➢ Can these cells create ectopic growth of tissue: yes.
  ➢ Cancers created by this therapy may not be detected for several years

➢ This is not currently being tracked
Problems with Current Stem Cell Treatment for Vulvar LS

• There is already validated, standard-of-care, effective, non-invasive, less expensive treatment for this potentially premalignant condition (topical steroids)

• Currently lacking validated data supporting the superiority or comparable efficacy of this experimental treatment
  • There is no current standardization for treatment dose, technique or technology
  • Objective endpoints for efficacy have yet to be established
  • Duration of efficacy and potential risks currently unknown
Cost of Stem Cell Treatment Summer 2014

- Single treatment of stem cell injections and PRP injections: $3600.00
- First stem cell and PRP injections with storage of excess stem cells for subsequent injections within 12 months: $7150.00
  - Additional PRP injections $1000.00 each
  - Total for 3 treatments: $9150.00

Average out of pocket expense $10,000

For-profit clinics charge up to $20,000
“Charging patients to participate in medical research is “unauthorized, for-profit human experimentation”.

• Leigh Turner, Bioethics professor, University of Minnesota
Translation: The Missing Link

• Translational research applies findings from basic science to enhance human health and well-being. In a medical research context, it aims to "translate" findings in fundamental research into medical and nursing practice and meaningful health outcomes.
Baer, P. (2011)
Stem Cells and Development

• Adipose derived stem cells are mixed with more differentiated cells like pericytes and endothelial cells.
• What you get depends on where you harvest from
• Cell culture with flow cytometric sorting or immunomagnetic separation can select for various cell types
Initial plating density

Cell culture medium
Glucose concentration
Antibiotics

Method of storage
Coating of culture dishes
Supplements

Method of subculturing
Onesti, M, et al
Stem Cells International 1/10/2016

• **8 patients**: 1 postmenopausal, 2 Graft vs Host Disease, 5 Lichen Sclerosus

• Liposuction, centrifugation, **cell culture with analysis of surface marker expression profile** for 3 weeks

• **Cells suspended in hyaluronic acid**, 4 ml injected in subcutaneous plane of labia minora, \(5 \times 10^5\) cells/ml

• Follow up: 1 wk, 1 mo, 3 mo, 1 yr, 2 yr

• Results: dermal sclerosus reduced, inflammatory infiltrate reduced, pain reduction, improved sexual function
Stem Cells and the Aging Brain

An evening of stem cell science in Stockholm

Guest Blogger Jan Barfoot, EuroStemCell

The evening started with an interactive reception co-ordinated by EuroStemCell, involving a motion controlled 3D brain, a stem cell floor game, the myelination game and great conceptual activity using sweets to explain how cells can return to a naive state! This interactive reception was provided by a collaboration between European Commission-funded research consortia PluriMes, HumEn, ThymiStem and Neurostemcellrepair along with the MRC Centre for Regenerative Medicine, Edinburgh, Karolinska Institutet, Stockholm and the MRC Wellcome Trust Stem Cell Institute, Cambridge. A unique opportunity for these leading European stem cell research consortia and centres to work together on a public event.
The ISSCR Patient Handbook on Stem Cell Therapies

The International Society for Stem Cell Research has created a take-along PDF handbook with information to help you and your family make informed decisions about stem cell treatments.
1. Currently, very few stem cell treatments have been proven safe and effective. *Beware of stem cell treatments offered without regulatory approval or outside the confines of a legitimate and registered clinical trial.*

2. There is something to lose when you try an unproven treatment. *Unproven treatments present serious health, personal and financial considerations. Consider what might be lost and discuss these risks with your family and healthcare providers.*
9 Things To Know About Stem Cell Treatments

3. Different types of stem cells serve different purposes in the body. Be wary of clinics offering treatments with stem cells originating from a part of your body unrelated to your disease or condition.

4. The same stem cell treatment is unlikely to work for different diseases or conditions. View clinics that offer the same cell treatment for a wide variety of conditions or diseases with extreme caution. Be wary of claims that stem cells will somehow just know where to go and what to do to treat a specific condition.
9 Things To Know About Stem Cell Treatments

5. The science behind a disease should match the science behind the treatment. *Your best protection against clinics selling unproven stem cell treatments is an understanding of the science behind your disease, injury, or condition.*

6. Cells from your own body are not automatically safe when used in treatments. *How and where the cells are put back into your body matters, and some clinics inject cells into places where they are not normally present and do not belong.*
9 Things To Know About Stem Cell Treatments

7. Patient testimonials and other marketing provided by clinics may be misleading. *Beware of clinics that use persuasive language, including patient testimonials, on the Internet, Facebook, and newspapers, to market their treatments, instead of science-based evidence.*

8. An experimental treatment offered for sale is not the same as a clinical trial. *Beware of expensive treatments that have not passed successfully through clinical trials.*
9. The process by which science becomes medicine is designed to minimize harm and maximize effectiveness. Beware of clinics that circumvent the accepted process by which science becomes medicine.
New APPs
Vulvovaginal Diseases

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Disclosures & Conflicts of Interest

• Executive Board, American Society for Colposcopy and Cervical Pathology

• Secretary General, International Society for the Study Vulvar Disease - APP
Vulvovaginal Candidiasis: Tips for Diagnosis and Treatment

A Decision-Support Tool & Novel Mobile Application
Background

• Patients with vulvovaginal candida infections regularly seen in healthcare providers’ offices

• Over 13 million cases of vulvovaginal candidiasis infections annually in the United States

• Challenging management of recurrent infections
Objective

• To create a proof-of-concept mobile application and educational tool to assist clinicians with diagnostic and treatment recommendations for vulvovaginal candidiasis, with emphasis on recurrent or resistant candidiasis
App Design

- Keep the design user-friendly
- Maximize clinical efficiency in finding the data the user desires
- Maintain easily updated code in preparation for changes in the recommendations or data for the future
Vulvovaginal Candidiasis

General Information

13 million cases of vulvovaginal candidiasis infections annually in the United States.

Candida albicans is the species, which most often causes these infections.

The second most common species to affect the vulvovaginal area is Candida glabrata.

Rarely is vulvar candidiasis seen without concomitant vaginal candidiasis.

It is a dimorphic fungus that forms both spores and mycelia.

Symptoms/Signs

Symptoms:
Itching
Burning/Irritation

Patient Information
Vulvovaginal Candidiasis

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

Candida Albicans

Wet Mount Examples
Recurrent Infections

Diagnosis Considerations

Cultures

- Cultures for yeast should be obtained when symptoms are not explained on the wet prep or a patient presents with recurrent candidiasis.

Recurrent (Complicated)

Candida glabrata and other nonalbicans Candida species are observed in 10%-20% of women with recurrent vulvovaginal candidiasis.

Include one or more of the following:

- ≥3 episodes/year of culture-verified vulvovaginal candidiasis
Vulvovaginal Candidiasis

Treatment by Type

Yeast Culture/Speciation Results

- Candida albicans
- Candida glabrata
- Candida krusei
- Candida parapsilosis
- Candida tropicalis
- Candida lusitaniae
- Trichosporon
- Saccharomyces cerevisiae
- Candida kefyr
- Candida dubliniensis
Treatment by Type

Yeast Culture/Speciation Results

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

Candida albicans

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
- Itraconazole

Topical
- Clotrimazole
- Miconazole
Candida albicans

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**Oral**
- Fluconazole
- Itraconazole

**Topical**
- Clotrimazole
- Miconazole

---

**Candida albicans**

**Topical**

Miconazole
- Miconazole 7 day cream 2% (100mg per dose)
  - One applicatorful per vagina nightly for 7 nights
  - One applicatorful per vagina nightly for 7 nights, and miconazole nitrate cream 2%, apply externally twice a day for up to 14 days

Miconazole 3 day cream 4% (200 mg per dose)
  - One applicatorful per vagina nightly for 3 nights
  - One applicatorful per vagina nightly for 3 nights, and miconazole nitrate cream 2%, apply externally twice a day for up to 14 days

Miconazole 3 day suppository/insert (200mg/per dose)
  - One suppository/insert per vagina nightly for 3 nights
  - One suppository/insert per vagina nightly
Patient Information

Email directly to your patient

What are the symptoms of Candida (yeast) infection?
These are the symptoms of vaginitis candida infection:
- Itching: 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 or itching (peeing);
- Pain - particularly if the infection occurs a number of times or has not been treated properly; and
- Smell white, yellow or brown 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. However, there are many different 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 smear or laboratory testing before treatment is started.

What can I do to help myself?
Treatment with a cream or ointment in the vagina, or the use of an oral antifungal tablet/capsule, is one of the most effective means of treating the yeast from the vagina. There are many different names for these creams and ointments and usually they come with an applicator that helps to insert them deep in the vagina. Even if your period starts you can still use these medications. The medication is most effective from the first day of your period - that is one that occurs more than a year since the previous episode (see below for treatment of recurrent yeast).

Vaginal candida may also be treated with antifungal tablets or capsules that you take by mouth, and these medications are best administered under the supervision of your medical practitioner.

When should I seek medical advice?
You should see your doctor if:
- You are not sure of the problem you have in Candida;
- This is the second Candida infection you have had in less than a year;
- You are pregnant or breast feeding;
- You have not responded to treatment and there is no improvement;
- If symptoms come back in less than a year, or your response to treatment is unsatisfactory, do not self-medicate or you risk producing a chronic (ongoing) condition. When you see your doctor.

References


ULCER APP

A Decision-Support Tool & Novel Mobile Application
Background

- Broad differential for vulvovaginal ulcers
- Many different types of care providers and settings
  - Provider education difficult
- Potential for confusion with vulvovaginal erosions
App Design

- Keep design user-friendly
- Maximize clinical efficiency in finding useful data
- Maintain easily updated code in preparation for changes in the recommendations or data for the future
The patient has evidence...

Vulvovaginal Ulcers

Vulvovaginal Erosions

Ulcer Algorithm

Please be aware that this algorithm is only applicable to vulvovaginal ulcers, not erosions.

What is an erosion?
What is an ulcer?
Continue to Algorithm
Continue - Do Not Show Again
Ulcers of the Vulva

Ulcers of the vulvar are diagnostically challenging. An ulcer is characterized by loss of both epidermis and dermis. It is often very difficult to differentiate them from erosions. **Erosions** involve loss of the epidermis only, not the dermis, and they appear as deep red, often weeping, patches. Ulcers are deeper, extending into the dermis with a white or yellowish fibrinous base. **Erosions** can be transformed into ulcers by secondary infection, irritant contact dermatitis, rubbing and other.

Erosive diseases of the vulva

Erosive diseases of the vulva consist of a mixture of inflammatory, infectious, and neoplastic processes. A variety of vulvar diseases may be erosive:

- Lichen planus
- Irritant/allergic contact dermatitis
- Fixed drug eruption
- Stevens-Johnson syndrome
- Toxic epidermal necrolysis
- Plasma cell (Zoon) vulvitis
- Bullous pemphigoid
- Cicatricial pemphigoid
- Linear IgA disease
The time course of the ulcer:

Acute

Recurrent

Chronic (> 1 month)

For all patients:

HSV Testing

Additional diagnoses to EBV

Syphilis

Evidence of Trauma

Neuropathy

Positional/Orthopedic

Other considerations

Caustic Materials

Factitial

Diagnosis of exclusion

Aphthous Ulcers
Herpes

There are two types of herpes simplex virus (HSV) that can cause genital herpes: HSV-1 and HSV-2. Most cases of recurrent genital herpes are caused by HSV-2. At least 50 million people in the United States are infected with this type of virus. However, an increasing proportion of anogenital herpetic infections have been attributed to HSV-1 infection. Over 80% of patients do not know they have been infected with the herpes virus. The classical painful multiple vesicular or ulcerative lesions are absent in many infected persons.
The time course of the ulcer

Acute

Recurrent

Chronic (> 1 month)

For all patients:

HSV Testing

Additional diagnoses to... EBV

Syphilis

Evidence of Trauma

Neuropathy

Positional/Orthop...

Other considerations

Caustic Materials

Facticial

Diagnosis of exclusion

Aphthous Ulcers
Aphthae

Aphthous ulcers are canker sores on the vulva. Canker sores are more common on the mouth than the vulva. They can be recurrent or chronic. They can vary in size and can be single or multiple.
The time course of the ulcer

Acute

Recurrent

Chronic (1 month or more)
# Chronic Ulcers

**For all patients:**
- Tissue Biopsies
- HIV Testing
- Syphilis

**Diagnosis of exclusion:**
- Aphthous Ulcers

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**ISSVD Ulcer Algorithm Biopsies**

<table>
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<tr>
<td>Crohn's disease</td>
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2016 new APPs

- Candida
- Ulcer
- Both decision support tools
- I phone
Acknowledgements Candida

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- Rarely is vulvar candidiasis seen without concomitant vaginal candidiasis.

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Symptoms:

- Itching

- Burning/Irritation
Recurrent Infections

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INFORMATION
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- Clinical Images
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Candida albicans

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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
  - Itraconazole

- Topical
  - Clotrimazole
  - Miconazole
Candida albicans

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Oral
Fluconazole
Itraconazole

Topical
Clotrimazole

Miconazole

Candida albicans

Topical

Miconazole
Miconazole 7 day cream 2% (100mg per dose)
- One applicatorful per vagina nightly for 7 nights
- One applicatorful per vagina nightly for 7 nights, and miconazole nitrate cream 2%, apply externally twice a day for up to 14 days

Miconazole 3 day cream 4% (200 mg per dose)
- One applicatorful per vagina nightly for 3 nights
- One applicatorful per vagina nightly for 3 nights, and miconazole nitrate cream 2%, apply externally twice a day for up to 14 days.

Miconazole 3 day suppository/insert (200mg/per dose)
- One suppository/insert per vagina nightly for 3 nights
- One suppository/insert per vagina nightly
Patient Information

Email directly to your patient

What are the symptoms of Candida (yeast) infection?
- Genital itch: this is the most common symptom of thrush. Itching is especially worse before your period.
- Soreness or burning in the vulva during or after sex.
- Abnormal discharge — this can be thick and white or sometimes it can seem normal.
- A change in the color of your vaginal secretions.
- Redness and inflammation of the vulva (vulva).
- Soreness or discomfort or irritation (peeling).
- Pain — particularly if the infection occurs a number of times or hasn't been treated properly; and
- Small white sores on the vulvar skin or in the discharge.

How is it diagnosed?
A diagnosis of vaginal candidiasis is often made based on a number of things including your symptoms. Physical examination, examination of vaginal secretions under the microscope and vaginal culture. However, there are many other conditions of the vagina and ovary that have symptoms in common and are usually associated with Candida. If you forget about the diagnosis, or when it is recurrent, it is essential that your healthcare provider takes a vaginal swab or laboratory testing before treatment is started.

What should I do if I need help?
- Treatment with a cream or pill taken in the vagina is the best way to prevent recurrent candidiasis. There are many different names for these creams and pills and they come with a applicator that helps to insert them deep in the vagina.
- Even if your period starts you can still use these medications. The medication is available in pharmacies and can also be used to treat an isolated episode of yeast infection.
- Vaginal candidiasis may also be treated with anti-fungal tablet or capsules that take by mouth, and these medications are best administered under the supervision of your medical practitioner.

Why should I seek medical advice?
You should see your doctor if:
- You are not aware of the problem you have in candidiasis.
- You have had a Candida infection in the past and had no problem.
- Your candidiasis infection is resistant to treatment.
- If symptoms come back in less than a year, or your response to treatment is unsatisfactory, do not re-treat or you will produce a chronic (ongoing) condition. When you see your doctor.

Adapted from the CDC guide for patient education.

References


ULCER APP

A Decision-Support Tool & Novel Mobile Application
Background

- Broad differential for vulvovaginal ulcers
- Many different types of care providers and settings
  - Provider education difficult
- Potential for confusion with vulvovaginal erosions
App Design

• Keep design user-friendly
• Maximize clinical efficiency in finding useful data
• Maintain easily updated code in preparation for changes in the recommendations or data for the future
The patient has evidence...

Vulvovagina...

Vulvovaginal Ulcers

Vulvovaginal Erosions

Ulcer Algorithm

Please be aware that this algorithm is only applicable to vulvovaginal ulcers, not erosions.

What is an erosion?

What is an ulcer?

Continue to Algorithm

Continue - Do Not Show Again
Ulcers of the Vulva

Ulcers of the vulvar are diagnostically challenging. An ulcer is characterized by loss of both epidermis and dermis. It is often very difficult to differentiate them from erosions. **Erosions** involve loss of the epidermis only, not the dermis, and they appear as deep red, often weeping, patches. Ulcers are deeper, extending into the dermis with a white or yellowish fibrinous base. **Erosions** can be transformed into ulcers by secondary infection, irritant contact dermatitis, rubbing and other.

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Erosive diseases of the vulva

Erosive diseases of the vulva consist of a mixture of inflammatory, infectious, and neoplastic processes. A variety of vulvar diseases may be erosive:

- Lichen planus
- Irritant/allergic contact dermatitis
- Fixed drug eruption
- Stevens-Johnson syndrome
- Toxic epidermal necrolysis
- Plasma cell (Zoon) vulvitis
- Bullous pemphigoid
- Cicatricial pemphigoid
- Linear IgA disease
The time course of the ulcer:

Acute
Recurrent
Chronic (> 1 month)

For all patients:
HSV Testing
Additional diagnoses to EBV
Syphilis
Evidence of Trauma
Neuropathy
Positional/Orthop...
Other considerations
Caustic Materials
Facticial
Diagnosis of exclusion
Aphthous Ulcers
Herpes

There are two types of herpes simplex virus (HSV) that can cause genital herpes: HSV-1 and HSV-2. Most cases of recurrent genital herpes are caused by HSV-2. At least 50 million people in the United States are infected with this type of virus. However, an increasing proportion of anogenital herpetic infections have been attributed to HSV-1 infection. Over 80% of patients do not know they have been infected with the herpes virus. The classical painful multiple vesicular or ulcerative lesions are absent in many infected persons.
The time course of the ulcer

Acute

Recurrent

Chronic (> 1 month)

For all patients:

HSV Testing

Additional diagnoses to ...

EBV

Syphilis

Evidence of Trauma

Neuropathy

Positional/Orthop...

Other considerations

Caustic Materials

Facticial

Diagnosis of exclusion

Aphthous Ulcers
Aphthae

Aphthous ulcers are canker sores on the vulva. Canker sores are more common on the mouth than the vulva. They can be recurrent or chronic. They can vary in size and can be single or multiple.
The time course of the ulcer

Acute

Recurrent

Chronic (1 month or more)
Chronic Ulcers

For all patients:
- Tissue Biopsies
- HIV Testing
- Syphilis
- Diagnosis of exclusion
- Aphthous Ulcers

ISSVD Ulcer Algorithm Biopsies

"Hard" Lesions
- Squamous Cell...
- Melanoma
- Lymphoma
- Adenocarcinoma
- Other malignancies

"Soft" Lesions
- Contact Dermatitis
- Drug reactions
- Crohn's disease
- Lichen planus
- Lupus erythematosus
2016 new APPs

• Candida
• Ulcer

• Both decision support tools
• I phone
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