

## Diagnosis and Treatment of Refractory Vulvovaginitis

Ronald S. Gibbs, M.D.

Professor and Chair

E. Stewart Taylor Chair

Department of Obstetrics and Gynecology



## BIDDO Syndrome

- How to diagnose and treat patients with:
  - Burning
  - Itching
  - Discharge
  - Dysparunia
  - Odor

## Diagnosis and Treatment of Refractory Vulvovaginitis

Ronald S. Gibbs, M.D.

### Objectives

1. Name two regimens useful for treating persistent *Trichomonas* vaginitis.
2. State one effective maintenance approach for recurrent candidal vaginitis.
3. Describe desquamative inflammatory vaginitis and state its treatment.

## Diagnosis and Treatment of Refractory Vulvovaginitis

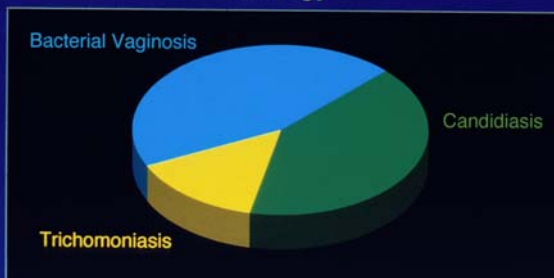
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### Objectives, Cont'd

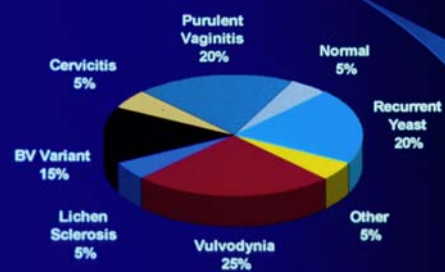
4. Describe non-gonococcal, non-chlamydial cervicitis, and outline a treatment plan.
5. Describe an approach to diagnosis and treatment in a patient with persistent vulvar “burning”.
6. Describe an approach to diagnosis and treatment in a patient with persistent vulvar itching.

## VAGINITIS

### Etiology



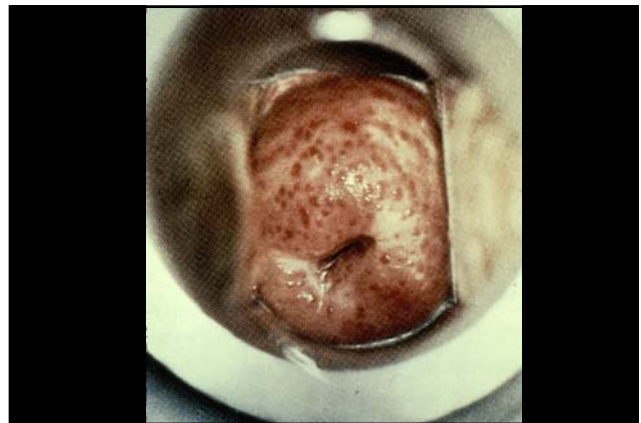
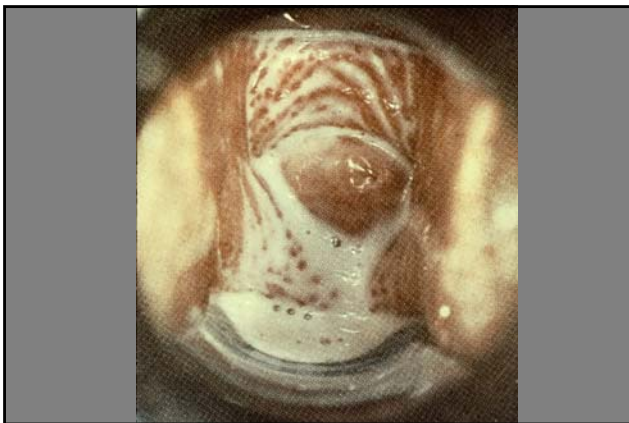
## Vaginitis Etiology in Referral Practice

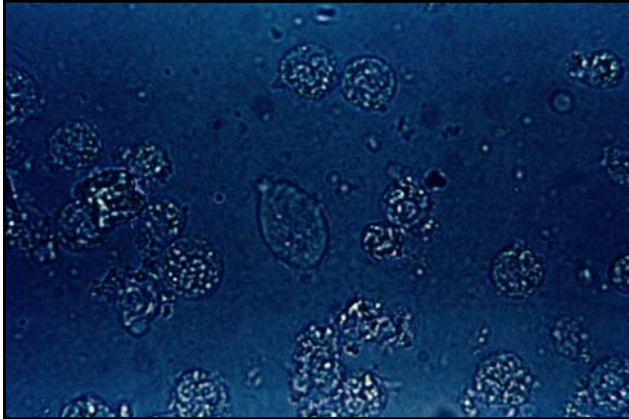


RSG's estimates. Conditions may be mixed.

## Office Evaluation of Patient with "Vaginitis"

pH determination.  
Amine odor test.  
Saline prep for true clue cells, *T. vaginalis*.  
KOH prep for yeasts.  
Culture for yeasts, if above are non-diagnostic, using selective media.





## Diagnosis of Trichomoniasis

- Microscopy – only 60-70% sensitive.
- Culture – most sensitive and specific commercially available method (eg. “In Pouch System”).

2006 STD Guidelines

## Diagnosis of Trichomoniasis

•OSOM Trichomoniasis Rapid Test (Genzyme), immuno chromographic dipstick, takes 10 minutes.

•Affirm VP III (Becton Dickson), nucleic acid probe for T. vaginalis (G. vaginalis and C. albicans) takes 45 minutes.

•Both more sensitive than wet prep. False positives might occur, especially in low prevalence groups.

CDC, 2006 STD Treatment Guidelines

## Treatment of Trichomoniasis with Metronidazole (MTZ)

Dose:	2 gm PO (single dose).
Alternative:	500 mg bid x 7 d.
Efficacy:	90 – 95%.
Partner:	Treat.
Follow-up:	None, if asymptomatic.
Side effects:	Nausea, vomiting, headache, blood dyscrasia. Avoid alcohol for 24 hrs. after completion.

CDC, 2006 STD Treatment Guidelines

## Treatment of Trichomoniasis with Metronidazole, Cont'd

- Pregnancy: 2 gm PO, but asymptomatic women should not be treated.
- Metronidazole gel, approved for treatment of BV, is not recommended for trichomoniasis.\* Efficacy is  $\leq 50\%$ .

\*CDC, 2006 STD Guidelines

## Treatment of Trichomoniasis with Tinidazole

Dose:	2 gm orally, single dose.
Efficacy:	86-100%.
Partner:	Treat.
Follow-up:	None, if asymptomatic.
Side effects:	Similar. Avoid alcohol for 72 hours after completion.
Pregnancy:	Category C, safety in pregnancy “not well evaluated”.

CDC, 2006 STD Treatment Guidelines

## Refractory Trichomoniasis

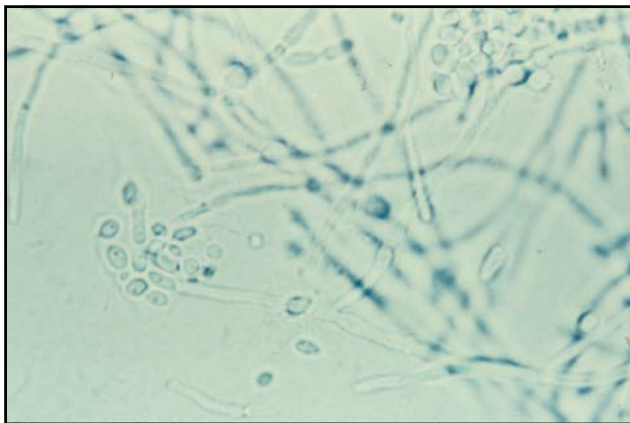
1. Retreat with MTZ 500 mg bid x 7 d. or tinidazole 2 gm.
2. Next, 2 gm MTZ or tinidazole single dose daily x 5 d.
3. Get expert consultation.
4. Culture; e.g., Diamond's medium: susceptibility.
5. Check CBC, LFTs, neurology exam.

CDC, 2006 STD Guidelines

## Refractory Trichomoniasis, Cont'd

6. Tinidazole 1 gm bid (or 500 mg qid) x 10 – 14 d\*  
PLUS Furazolidine in 3% Nonoxonyl 9 cream (100 gm/5 ml), 1 applicator full (5 gm) bid x 14 d.
7. Other regimens such as topical Paromomycin.

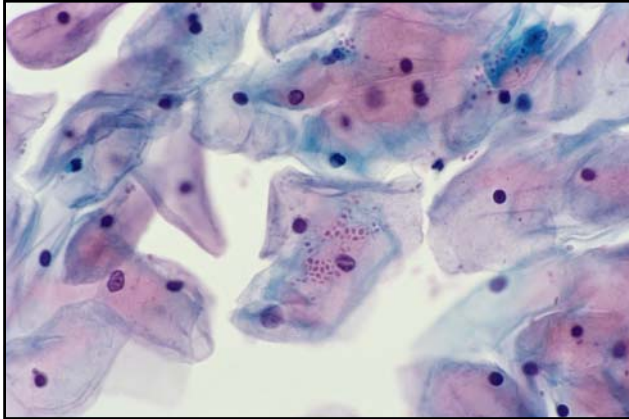
\*Personal Communication, CDC December, 2003



## Species Causing Yeast Vulvovaginitis

- *Candida albicans*
- *Candida glabrata*
- *Candida tropicalis*
- *Candida pseudotropicalis*
- Other *Candida* species\*
- *Saccharomyces cerevisiae* (Baker's yeast)

\**C. parapsilosis*, *C. krusei*, *C. lusitaniae*



## Diagnosis of Candidiasis

- Self diagnosis – inadequate.
  - Microscopy – 75%.
  - Culture – more sensitive.
  - PCR – 2X more sensitive than culture.
- Identification of *Candida* in asymptomatic women is not an indication for treatment.

## Clinical Conditions When A Yeast Culture is Helpful\*

- Suspected yeast infection with negative KOH prep\*\*.
- Recurrent infection\*\*.
- KOH prep shows budding yeast only.
- Failure of therapy.

\*After Sobel, Management of VVC, Wayne State 1997  
 \*\*McCormack AJOG, 1988; Njirjesy AJOG, 1995; Eckert, Ob/Gyn, 1998.

## Getting a Proper Yeast Culture

- Collection with usual swab and transport medium.
- Communicate to lab the need for yeast identification (e.g., Saboraud's media).

## Selection of Therapy for Candidiasis

	<u>Uncomplicated</u>	<u>Complicated</u>
<b>Frequency:</b>	Infrequent	Recurrent ( $\geq 4$ /yr.)
<b>Microscopy:</b>	Pseudohyphae/ Hyphae, likely <i>C. albicans</i>	Budding yeast only, likely non- <i>albicans</i>
<b>Host:</b>	Normal	Immunosuppressed, uncontrolled DM, debilitated, pregnant
<b>Symptoms:</b>	Mild to moderate	Severe

## Selection of Therapy for Candidiasis, Cont'd.

	<u>Uncomplicated</u>	<u>Complicated</u>
<b>Regimen:</b>	Any, including single dose	More intensive ( $\geq 7$ days)

CDC, 2006, STD Guidelines

## Treatment of Uncomplicated Vulvovaginal Candidiasis

### Recommended Regimens

#### *Intravaginal Agents:*

- Butoconazole 2% cream, 5 g intravaginally for 3 d<sup>\*\*\*</sup>, OR
- Butoconazole 2% cream, 5 g (Butoconazole 1-sustained release), single intravaginal application, OR

<sup>\*\*\*</sup> Over the counter (OTC) preparations

## Treatment of Uncomplicated Vulvovaginal Candidiasis, Cont'd

### Recommended Regimens

#### *Intravaginal Agents:*

- Clotrimazole 1% cream, 5 g intravaginally for 7-14 d,<sup>\*\*\*</sup> OR
- Clotrimazole 100 mg vaginal tablet for 7 d, OR
- Clotrimazole 100 mg vaginal tablet, two tablets for 3 d, OR

<sup>\*\*\*</sup> Over-the-counter (OTC) preparations

## Treatment of Uncomplicated Vulvovaginal Candidiasis, Cont'd

### Recommended Regimens

#### *Intravaginal Agents:*

- Miconazole 2% cream, 5 g intravaginally for 7 d\*, OR
- Miconazole 100 mg vaginal suppository, one suppository for 7 d<sup>\*\*\*</sup>, OR
- Miconazole 200 mg vaginal suppository, one suppository for 3 d<sup>\*\*\*</sup>, OR

<sup>\*\*\*</sup> Over-the-counter (OTC) preparations

## Treatment of Uncomplicated Vulvovaginal Candidiasis, Cont'd

### Recommended Regimens

#### *Intravaginal Agents:*

- Miconazole 1200 mg suppository, one suppository for 1 d, OR
- Nystatin 100,000-unit vaginal tablet, one tablet for 14 d, OR
- Tioconazole 6.5% ointment, 5 g intravaginally in a single application<sup>\*\*\*</sup>, OR

<sup>\*\*\*</sup> Over-the-counter (OTC) preparations

## Treatment of Uncomplicated Vulvovaginal Candidiasis, Cont'd

### Recommended Regimens

#### *Intravaginal Agents:*

- Terconazole 0.4% cream, 5 g intravaginally for 7 d, OR
- Terconazole 0.8% cream, 5 g intravaginally for 3 d, OR
- Terconazole 80 mg vaginal suppository, one suppository for 3 d.

#### *Oral Agent:*

Fluconazole 150 mg oral tablet, one tablet in single dose.

## Treatment of Complicated Vulvovaginal Candidiasis

- Culture for species.
- Longer duration of therapy (e.g. 2-3 doses of fluconazole, d.1, d.4, d.8).
- Vaginal boric acid.
- Maintenance regimens.
- Partner treatment "may be considered in women who have recurrent infections."

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## Treatment of Candida Vulvovaginitis

- Topical agents may lead to local burning and irritation.
- Oral agents occasionally cause nausea, abdominal pain and headache and are rarely associated with increased LFTs.
- Clinically important interactions with oral agents and other drugs, including astemizole, calcium channel blockers, tacrolimus, and others.

CDC 2006, STD Guidelines

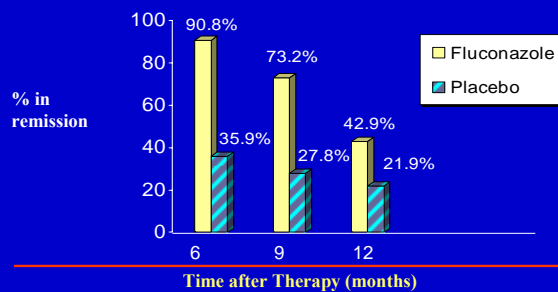
## Maintenance Regimens for Recurrent Vulvovaginal Candidiasis

**First line:** Oral fluconazole 100, 150, or 200 mg weekly for 6 months.

**Other:** Topical clotrimazole 200 mg twice a week or 500 mg vaginal suppository once weekly.

CDC 2006, STD Guidelines

## Maintenance Fluconazole for Recurrent Vulvovaginal Candidiasis (VVC)



Sobel JD, et al. NEJM 2004; 351:876-83

## Boric Acid Treatment of Candidiasis

**Regimen:** 600 mg in size 0 capsule qd or bid x 14 d.

**Mechanism:** Boron toxicity to yeast.

**Side effect:** Watery discharge.

**Warnings:** Do not use in pregnancy. Toxic orally. Keep away from toddlers. No cunnilingus.

## Boric Acid Treatment of Candidiasis, Cont'd

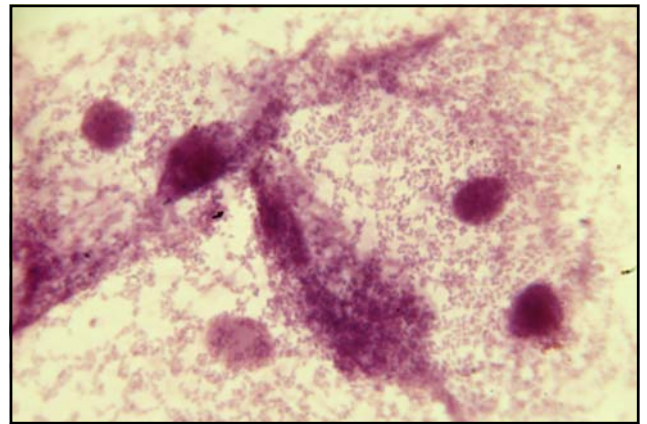
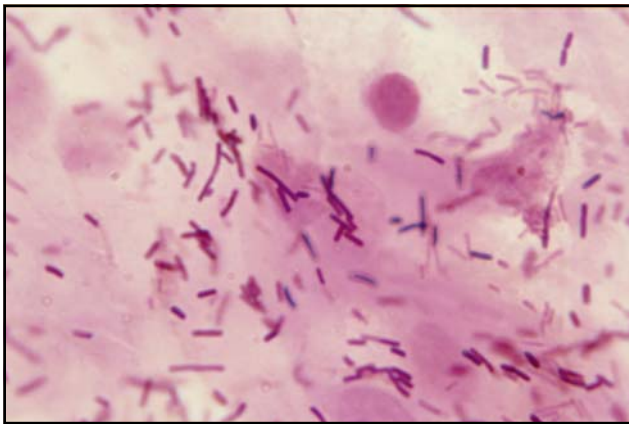
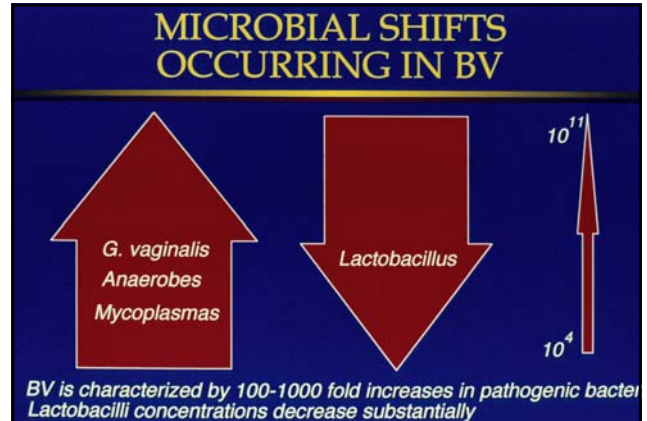
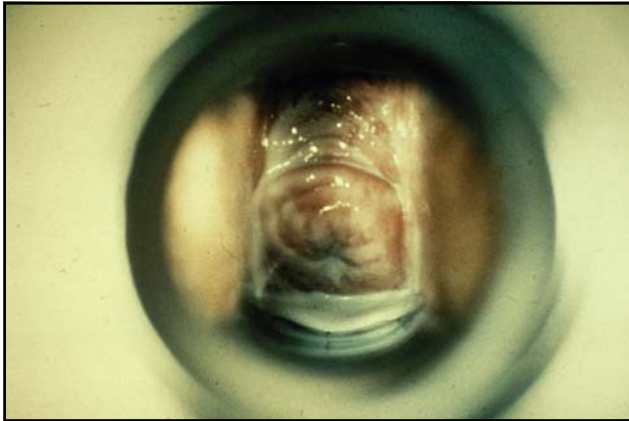
- Uses:**
- Treatment of choice for *C. glabrata* vaginitis.
  - For patients wanting to take an "active" role treatment.
  - Prevention of recurrences.

## Underpants advice leads to small fire

■ WEST JORDAN, Utah

A woman following a newspaper story's advice to yeast infection sufferers tossed her underpants in the microwave and sparked a fire, authorities say.

Firefighters rushed to the woman.....



### Diagnosis of Bacterial Vaginosis (Amsel's criteria)

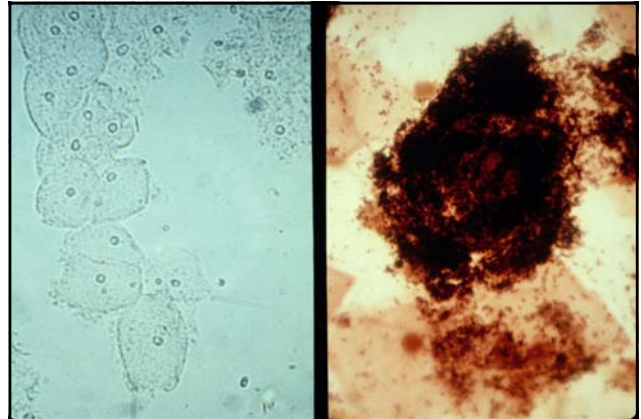
**Three of four criteria:**

- Thin, milky, homogeneous discharge.
- pH > 4.5.
- Amine, fishy odor.
- "Clue cells" (greater than 20%).

### Diagnosis of Bacterial Vaginosis, Cont'd

- Gram stain – acceptable in lab.
- *G. vaginalis* culture – not recommended.
- Pap – "no clinical utility".
- "QuickVue" (pH, amines) \*
- Pip Activity Card (proline-aminopeptidase)\*.
- Affirm VPIII (DNA probe for *G. vaginalis*\*).

\*"May be useful"-CDC 2006, STD Guidelines



## Treatment of Bacterial Vaginosis In Non-pregnant Women

### CDC RECOMMENDATIONS\*

- Metronidazole, 500mg, PO bid x 7 d.
- Metronidazole, 0.75%, vaginal gel 5g qd x 5 d.
- Clindamycin, 2.0%, vaginal cream 5g qhs x 7 d.

2006 STD Guidelines

## Treatment of Bacterial Vaginosis in Non-Pregnant Women' Cont'd

### CDC Alternate Regimens

- Clindamycin 300 mg, PO bid x 7 d,
- OR**
- Clindamycin ovules 100 g, vaginally qhs x 3 d

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## Metrogel for Persistent BV

Regimen: 0.75% gel twice weekly x 4 months.

Efficacy: Significantly reduced recurrences compared with placebo during suppression (25% vs 59%, P=0.001) and at 7 month follow up (51% vs 75%, p=0.02). Candidiasis is more common with metrogel (43% vs 20% in placebo, p=0.02).

Sobel JD, Ferris D, Schwabke J. et al AJOG 2006; 194:1283-9

## Treatment of Bacterial Vaginosis in Pregnant Women

### Rationale:

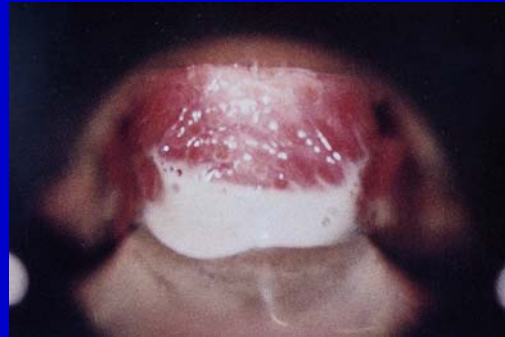
- Relieve symptoms.
- Prevent adverse outcomes, controversial.

## Treatment of Bacterial Vaginosis in Pregnant Women, Cont'd

### Recommended Regimens:

- Metronidazole 500 mg PO bid x 7d.
- OR
- Metronidazole 250 mg, PO tid x 7 d.
- OR
- Clindamycin 300 mg, PO bid x 7 d.

2006 STD Guidelines



## Desquamative Inflammatory Vaginitis (DIV)

**Diagnosis:** Copious homogeneous discharge, may be frothy; pH > 4.4. Wet mount shows WBCs, usually parabasal cells.

**Etiology:** Estrogen deficiency in some cases. Mixed bacterial infection.  
? Variant of lichen planus.

## Desquamative Inflammatory Vaginitis, Cont'd

### Differential Diagnosis:

- Cervicitis
- Trichomoniasis
- Foreign body
- Cancer
- Infected pregnancy
- Pelvic inflammatory disease
- Endometritis

## Desquamative Inflammatory Vaginitis, Cont'd

**Work-up:** R/O *T. vaginalis* and cervicitis. Biopsy if ulcers.

**Treatment:** Clindamycin cream 2% for up to 4 weeks. Vaginal hydrocortisone suppositories.

**Vestibulitis / Vulvodynia /  
Vestibular adenitis**

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**Diagnosis:** Burning vulva, ? Focal redness, positive touch test.

**Etiology:** Probable neuropathic pain; doubt yeast or HPV.

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**Vestibulitis / Vulvodynia/  
Vestibular adenitis, Cont'd**

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**Work-up:**

- Yeast culture.
  - Selective biopsy, rarely needed.
- 

**Vestibulitis / Vulvodynia/  
Vestibular adenitis, Cont'd**

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**Treatment:**

- Reassurance and validation of pain
  - Lidocaine 5% ointment QHS x 6 weeks
  - Soothing applications (e.g. almond oil extract or Domeboro's solution)
  - Topical steroid (e.g. Clobetasol (Temovate), 0.05% bid) if inflammation
- 

**Vestibulitis / Vulvodynia/  
Vestibular adenitis, Cont'd**

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**Treatment:**

- Tricyclics
    - Desipramine (Norpramin)
    - Nortriptylline (Pamellar)
    - Amitriptylline (Elavil, Triavil)
- 

**Vestibulitis / Vulvodynia/  
Vestibular adenitis, Cont'd**

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<u>Drug</u>	<u>Dose</u>	<u>Comment</u>
Desipramine	25mg PO qhs initially, increasing to 75 mg. May need higher dose.	Less sedating
Nortriptylline	Same as Desipramine	More sedating

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### Vestibulitis / Vulvodynia / Vestibular adenitis, Cont'd

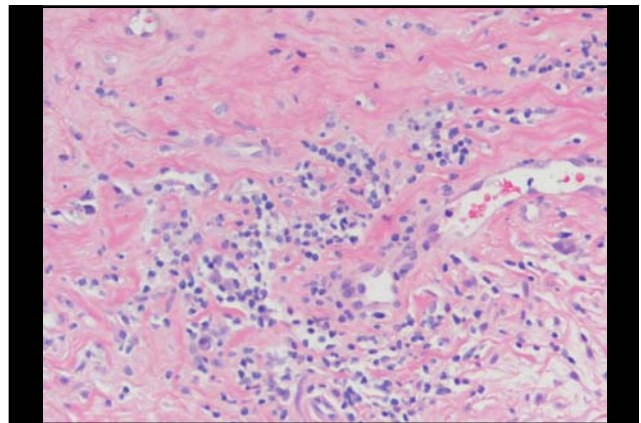
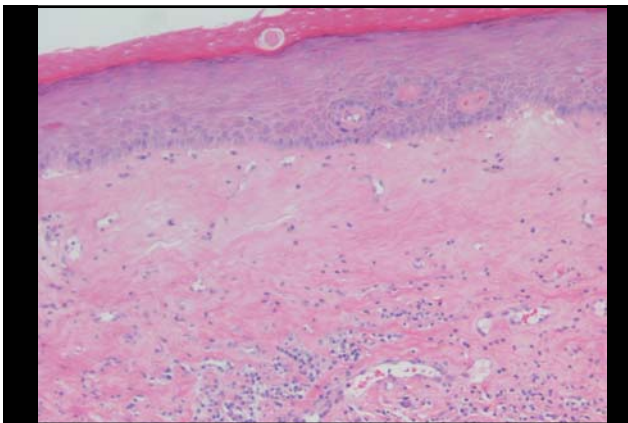
<u>Drug</u>	<u>Dose</u>	<u>Comment</u>
Amitriptylline	10 mg PO qhs initially, increasing to 30-75 mg qhs	More sedating

### Vestibulitis / Vulvodynia / Vestibular adenitis, Cont'd

Neurontin	Used in other neuropathic conditions
Trichloroacetic acid	Rarely used
5 Fluorouracil cream	Rarely used
Interferon injections	Rarely used
Vestibulectomy	"Last resort"

### Vestibulitis / Vulvodynia / Vestibular adenitis, Cont'd

Prophylaxis:	None
Response:	Fair: 50-70% response over time to medical treatment.



## Lichen sclerosus

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**Diagnosis:** Itching; depigmentation; conglutination; contractures

**Etiology:** Unknown

**Work-up:** Selective Biopsy

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## Lichen sclerosus, Cont'd

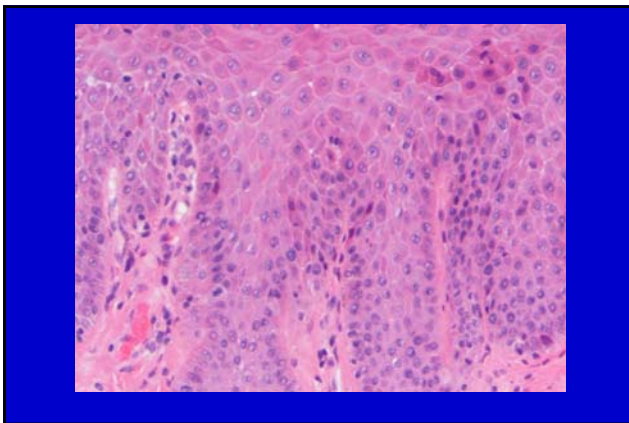
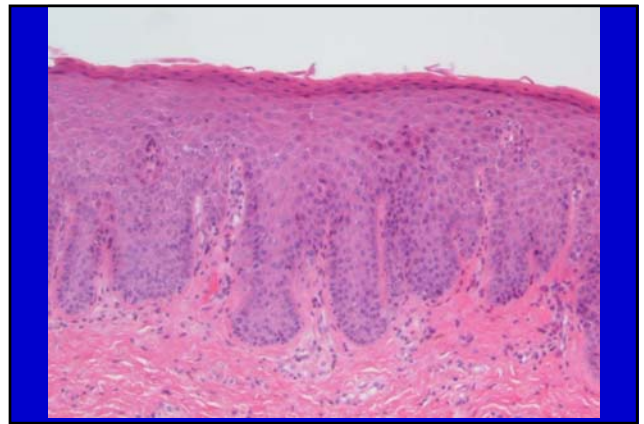
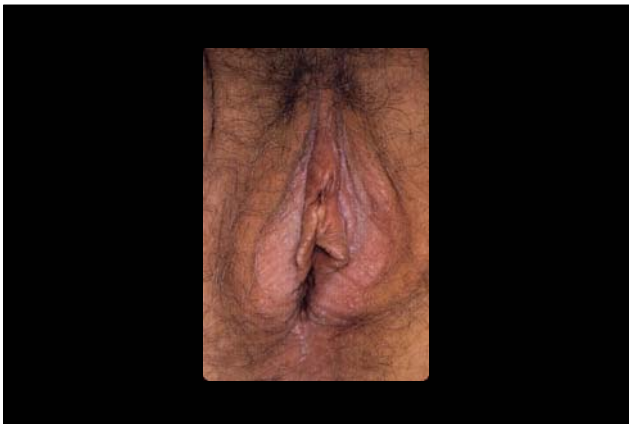
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**Treatment:** Clobetasol, then wean to less-potent steroid;  
Testosterone;  
Progesterone.

**Prophylaxis:** None.

**Response:** Good-excellent.

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## Lichen Simplex Chronicus

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**Diagnosis:** Itching. Skin has leathery appearance with accentuation of normal skin markings.

**Etiology:** Persistent rubbing and scratching.

**Workup:** Biopsy if diagnosis is unclear.

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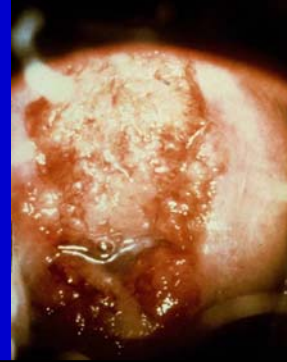
## Lichen Simplex Chronicus

### Treatment:

- Potent to medium strength steroid creams (Clobetasol 0.05% or Triamcinolone 0.1% ointment initially) bid x first month then qd.
- Wean to 1% hydrocortisone 2-3 times/week.
- Antihistamine orally.
- Moisturizing ointments such as A&D or zinc oxide.

**Response:** Good to excellent.

## Chlamydial Cervicitis



## 2006 CDC Regimens for *C. trachomatis*, Non pregnancy\*

- **Recommended:**  
Azithromycin, 1 gm (single dose) **OR**  
Doxycycline, 100 mg bid x 7 d
- **Alternatives:**  
Erythromycin base, 500 mg qid x 7 d **OR**  
Erythromycin ethylsuccinate, 800 mg qid x 7 d **OR**  
Ofloxacin, 300 mg bid x 7 d\*\* **OR**  
Levofloxacin, 500 mg x 7 d\*\*

\* All regimens are oral.

\*\*See 2007 recommendations re: QRNG

## 2006 CDC Regimens for *C. trachomatis* in Pregnancy\*

- **Recommended:**  
Azithromycin 1 gm orally **OR**  
Amoxicillin, 500 mg tid x 7 d
- **Alternatives:**  
Erythromycin base, 500 mg qid x 7d **OR**  
Erythromycin base, 250 mg qid x 14 d **OR**  
Erythromycin ethylsuccinate, 800 mg qid x 7 d **OR**  
Erythromycin ethylsuccinate, 400 mg qid x 14 d **OR**

\*All regimens are oral. Repeat testing 3 weeks after completion of therapy recommended for all pregnant women.

## Gonococcal Cervicitis



## Quinolone Resistant *N. gonorrhoeae* (QRNG)

- CDC had recommended single dose quinolones beginning 1993.
- Resistance noted by 2000 in Asia and Pacific Islands and by 2002 in California
- By 2006, resistance or intermediate resistance had increased to 14% (compared with 2% in 2000) for United States

MMWR 2007;56:332-6.

## Uncomplicated Gonococcal Infections of the Cervix, Urethra, and Rectum\*

### Recommended Regimens

Ceftriaxone 125 mg in a single intramuscular (IM) dose

OR

Cefixime† 400 mg in a single oral dose

PLUS

**TREATMENT FOR CHLAMYDIA IF CHLAMYDIAL INFECTION IS NOT RULED OUT (Azithromycin 1 gm po OR doxycycline 100 mg po BID x 7d.)**

\*For all adult and adolescent patients, regardless of travel history or sexual behavior. Information regarding management of these infections in patients with documented severe allergic reactions to penicillins or cephalosporins is available at <http://www.cdc.gov/std/treatment>.

†Not available in the United States.

## Uncomplicated Gonococcal Infections of the Cervix, Urethra, and Rectum\*

### Alternative Regimens

Spectinomycin† 2 g in a single IM dose

OR

Cephalosporin single-dose regimens§

†Not available in the United States.

§Other single-dose cephalosporin regimens that are considered alternative treatment regimens against uncomplicated urogenital and anorectal gonococcal infections include ceftizoxime 500 mg IM; or cefoxitin 2 g IM, administered with probenecid 1 g orally; or cefotaxime 500 mg IM. Some evidence indicates that cefpodoxime 400 mg and cefuroxime axetil 1 g might be oral alternatives.

## Uncomplicated Gonococcal Infections of the Pharynx\*

### Recommended Regimens

Ceftriaxone 125 mg in a single IM dose

PLUS

**TREATMENT FOR CHLAMYDIA IF CHLAMYDIAL INFECTION IS NOT RULED OUT**

\*For all adult and adolescent patients, regardless of travel history or sexual behavior. Information regarding management of these infections in patients with documented severe allergic reactions to penicillins or cephalosporins is available at <http://www.cdc.gov/std/treatment>.

## Uncomplicated Gonococcal Infections

Azithromycin (2gm) “might be an option for treatment of uncomplicated gonococcal infections (urogenital, anorectal, or pharyngeal) in persons with documented severe allergic reactions to penicillin or cephalosporins.”

MMWR 2007;56:332-6.

### Disseminated Gonococcal Infection

Updated treatment regimens available at <http://www.cdc.gov/std/treatment>.

### Pelvic Inflammatory Disease

Updated treatment regimens available at <http://www.cdc.gov/std/treatment>.

### Epididymitis

Updated treatment regimens available at <http://www.cdc.gov/std/treatment>.

## 2006 CDC Regimens for Uncomplicated *N. gonorrhoeae*, Cervix, Urethra, Rectum in Pregnancy

- Do not use quinolones or tetracyclines.
- Use a recommended or alternate cephalosporin.
- If intolerance, use IM Spectinomycin 2 gm.
- Azithromycin or amoxicillin recommended for *C. trachomatis*.

## **Non-gonococcal, Non-chlamydial Cervicitis (NGNCC) Diagnosis**

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- Mucopurulent cervical discharge, polys on endocervical wet mount, often with ectopy and friability.
- No cervical or pelvic tenderness.

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Thompson, Gibbs. IDSOG 2003

## **Non-gonococcal, Non-chlamydial Cervicitis (NGNCC) Diagnosis**

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- Exclusion of gonorrhea and chlamydia.
- Exclusion of desquamative inflammatory vaginitis, trichomoniasis, and other vaginal infections.

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Thompson, Gibbs. IDSOG 2003

## **Non-gonococcal, Non-chlamydial Cervicitis**

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- Routine bacterial cultures uninformative.
- Oral antibiotic treatments (clindamycin, quinolones, metronidazole, doxycycline, azithromycin) modest effect. Clindamycin vag cream 2% may be helpful.
- Cryotherapy or LOOP if persistent.

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Thompson, Gibbs. IDSOG 2003

## **Vulvovaginitis References**

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1. Sweet RL, Gibbs RG. Infectious Diseases of the Female Genital Tract (4th ed.). Lippincott, Williams & Wilkins. 2002
2. Kaufman RH et al. Benign Diseases of the Vulva and Vagina (5th ed.). Elsevier Mosby. 2005
3. Black MM, McKay M, Braude PR. Color Atlas and Text of Obstetrics and Gynecologic Dermatology (2nd ed.). Mosby. 2002
4. Centers for Disease Control & Prevention. STD Treatment Guidelines 2006. MMWR 2006;55 (No. RR-11):/94
5. Sweet RL, Gibbs RG. Atlas of Infectious Diseases of the Female Genital Tract. Lippincott, Williams & Wilkins. 2005
6. Update to CDC's STD Guidelines 2006: Fluoroquinolones no longer recommended for Treatment of Gonococcal Infections. MMWR 2007;56:332-6

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Mydocs/slides/vaginitis/diagnosis and treatment of refractory vulvovaginitis 8.2.07 91 slides