

# Vulvovaginal Candidosis

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# EPIDEMIOLOGY



## REAL STATISTICS IS UNKNOWN

- Epidemiologic data is not real because VVC is not reported
- It is mostly diagnosed only by examination (no microscopy or culture) –
- 50% has wrong diagnose
- Candidosis is, with bacterial, the most common form of vaginitis (30%)

## VVC is not an STD

- NOT AN STR
- PROVEN IN WOMEN IN CELIBACY

### STILL

- IT IS MORE COMMON IN WOMEN DURING SEXARCHAE, AND SEX PARTNERS OF INFECTED WOMEN ARE 4X MORE COLONIZED
- INCIDENCE IS NOT RELATED TO THE NUMBER OF SEXUAL INTERCOURSES OR PARTNERS
- ORO-GENITAL AND LESS ANO-GENITAL SEX IS A PREDISPOSING FACTOR

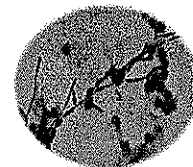
## PREVALENCE




- *Candida spec.* – normal part of vaginal flora in 20 – 50 % of healthy, asymptomatic women
- 75% of women will have at least one episode of VVC
- 45 % of women will have two or more episodes
- 50% students will have VVC diagnosed at least once
- 75 % of premenopausal women will be diagnosed at least once
- 45% of women will have  $\geq 2$  episodes of VVC
- 3-4 % prepubertal girls have vaginal colonisation with Candida



ODOR PC. *Candida* and *Candidosis*: A Review and Bibliography. London, Philadelphia, Toronto, Sydney, Tokyo, Baltimore, Toronto: 1986.  
ODONOVIC M, WATT F, LAMDON N, RAJESKI L, IGURAN J, VESSEY M. Vaginal microbial flora in normal young women. Br Med J 1992;31:154-6.  
FORNARI E. The epidemiology of vulvovaginal candidosis: Risk factors. Am J Public Health 1990;80:229-31.  
BERG AD, WEIDENICH PE, FRIN ED I sur. Establishing the cause of genital/ovary symptoms in women in a family practice. Comparison of clinical reactions and

# MICROBIOLOGY





**Candida includes around 200 species**


- *Candida albicans* 80 - 92% VVC
- *Candida glabrata* 1 
- *Candida tropicalis* 
- *Candida parapsilosis*

- **Blastoconidia**- the fungal cell - transmission
- **Hyphae**- forms from blastoconidia by germination
- Invasive form, most commonly present in symptomatic vaginitis - able to invade the vaginal epithelium and pass through intact epithelial cells
- *C. glabrata*, low virulent type-it cant form hyphaenema
  - Growing and branching of the hyphae forms micellium
- **Chlamidospore** are *in vitro* form of the fungus which is formed in harsh conditions: low temperature of incubation, in the atmosphere with low oxygen content and bad nutritional conditions.
- *C. albicans* is the only yeast form with the ability of germination.
- **germ-tube test** is used for the fast laoratory diagnosis of yeast infection in gynecology and dermatovenerology
- The cells from 24-hour culture are incubated in human or animal serum on 37°C and after 1-3 hours, hyphae are visualized microscopically

## PATHOPHYSIOLOGY


- ***Candida spec.* IN VAGINA – COME FROM RECTUM THROUGH THE PERINEUM**
- **Cultures from GI tract and vagina often show identical strain**


## ETIOLOGY










## *Candida albicans*

**Oportunistic pathogen**




**Predisposing factors:** 

- Elevated glucose levels (NR DM) 
- Antibiotic therapy (1/4-1/3) 
- Elevated estrogen levels (contraceptives with high E2 dose) 
- Pregnancy 
- IUD 
- Corticosteroid treatment 
- Imunosuppressives
- AIDS
- Supressed immun system due to disease
- Hereditary immune diseases
- Radiotherapy 

**E B M**  
**Not predisposing**

- Bad hygiene
- Synthetic underwear
- Multiple sexual intercourses

**SIGNS AND SYMPTOMS**



**MEDICAL HISTORY**



- Vulvar pruritus is the most common symptom
- Abnormal vaginal discharge: Thick, white, cottage cheese-like discharge
- Erythema (redness), irritation, occasional erythematous "satellite" lesion
- Dyspareunia
- Dysuria

*none of these symptoms are specific*

**PHYSICAL EXAM**

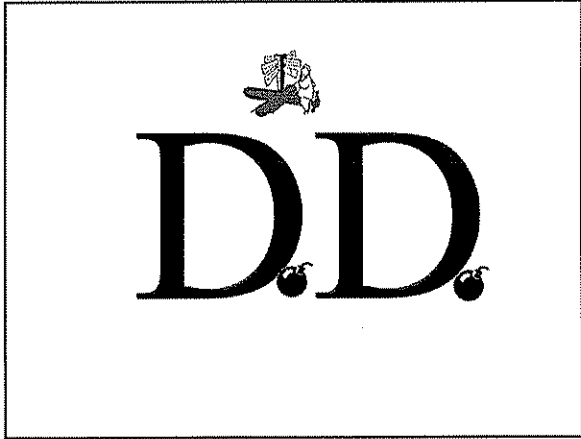
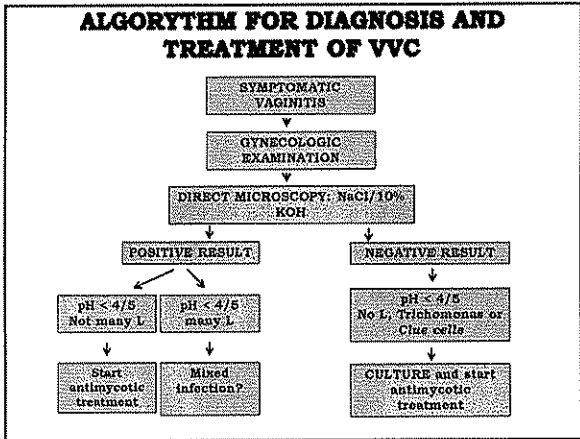
- Increased amount of vaginal discharge
- The color of vaginal discharge: white
- Consistency of vaginal discharge: thick, curdy, cottage-cheese like
- vaginal discharge "cottage cheese-like")
- The smell: not unpleasant
- Swelling, redness, irritation of vulva and/or vagina
- Normal vaginal pH (4,0 - 4,5)

**Diagnosis**

- Anamnesis
- Physical Exam
- *saline wet prep*: ↓lactobacilli, micellium
- Wet preparation with the addition of 10-20% KOH (destroys cellular elements: E, L), enables easier visualisation of hyphae and pseudohyphae
- Normal vaginal pH (4,0 - 4,5)
  - if pH > 4,5 BV or VVT
- Microscopy is false negative in 50% cases

- Culture is not mandatory:
    - price,
    - time,
    - It is positive in asymptomatic colonisation
  - Cultures only in recurrent candidosis (often not *C. albicans*): Sabouraud agar, Nickerson medium and Microstix candida medium – all equally good
- The smears are cultivated in the Sabouraud broth (liquid medium) and incubated for 48 hrs at 37°C and then moved to Sabouraud medium and incubated for 48 hrs at 37°C



- Differential diagnosis**
- Other vaginitis
  - Allergy, chemical and contact dermatitis
  - Physical irritation, intercourse with poor lubrication

- Physiologic discharge**
- Cervical mucus
  - Endometrial fluid
  - Fluid from Skene's and Bartholin's glands
  - Exfoliated squamous cells
  - Normal pH: 3.5 – 4.5 during reproductive years; 6 – 8 after menopause

Differential Diagnosis of Vaginal Infections Source: ZPCO Educational Series on Women's Health Issues				
Diagnostic	Syndrome			
Criteria	Normal	Bacterial Vaginosis	Trichomonas Vaginitis	Candida Vulvovaginitis
Vaginal pH	3.8-4.2	>4.5	>4.5	≤4.5 (usually)
Discharge	White, clear, flocculent	Thin, homogeneous, white-grey, adherent when increased	Yellow-green, frothy, adherent, increased	White, curdy, cottage cheese-like, sometimes increased
Amine odor (KOH) whiff test	Absent	Present (fishy)	May be present (fishy)	Absent
Main patient complaints	None	Discharge, bad odor (possibly worse after intercourse), possible itching	Frothy discharge, bad odor, vaginal pruritus, dysuria	Itching/burning, discharge
Microscopic				
	1. Lactobacilli 2. Epithelial cells	3. Clue Cell	4. Trichomonads 5. White blood cells	6. Budding yeast 7. Pseudohyphae

## Citolytic or lactobacillar vaginitis

- Rare
- Often not recognised and thus mistreated
- White vaginal discharge, with low acidity (pH 3,5 - 4,5)
- Gramm staining: plenty lactobacilli, few leucocytes and signs of citolysis
- Pruritus, dyspareunia and dysuria with more intensive symptoms during luteal phase of menstrual cycle
- It is treated by irrigating vagina with an alkaline solution (one teaspoon of baking soda (sodium bicarbonate) in 600 ml of saline solution) once a day, during 7-14 days

## CLASSIFICATION

- Colonisation - 20-50% of healthy, asymptomatic women
- Uncomplicated
- Complicated
  - recurrent

## UNCOMPLICATED

- RARE
- MILD TO MEDIUM SYMPTOMS
- HEALTHY WOMEN
- NOT PREGNANT

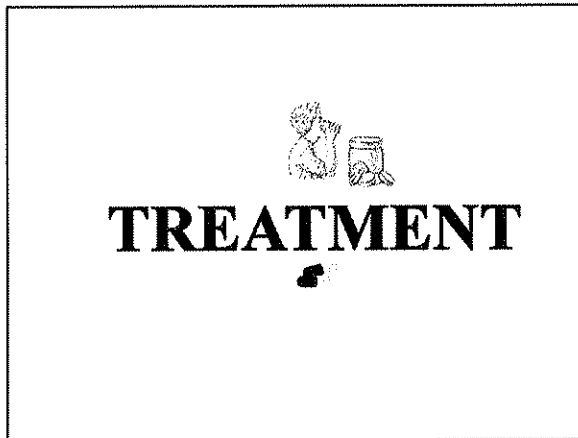
## COMPLICATED

- Badly regulated DM
- Immunosuppressive th.
- Intensive signs and symptoms
- Often *C. glabrata*
- Pregnancy
- ≥4 epizode / year in medical history = recurrent

## COMPLICATED RECURRENT



- ≥ 4 episodes / year
- 5-8 % of healthy women
- Culture is necessary
- Look for DM (OGTT)
- Genetic predisposition (Lewis BT antigenes): ↓ *mannose binding lectin* and ↑ conc. of Interleukine 4



**ASYMPTOMATIC COLONIZATION**  
Parasite and pathogen

- DO NOT TREAT
- *Candida spec.* – normal part of vaginal flora in 20-50% of healthy asymptomatic women

**TREATMENT OF SEX PARTNERS**

- Seks partners do not require any treatment
- In recurrent VVC - controversial

**VVC IN PREGNANCY**

- Does not affect the pregnancy outcome
- Oral treatment with azoles is not indicated
  - High doses → embriopathy
- Local treatment (vag., ung.):
  - Clotrimazole 7 d
  - Myconazole 7 d
  - Nistatine 14 d

**EMPIRICAL TREATMENT**

**YES:**

- Medical history
- Physical exam
- Normal vaginal pH
- It does not have to be proven microscopically, but there aren't any other pathogens

**NO:**

- Culture

**ORAL / LOC.  
(vag./ung.)**

- Same effect
- Side effects
  - Loc: irritation, burning
  - Oralno: abdominal pain, diarrea, flatulence, headache, rash, transitory liver disfunction
- Women prefer oral treatment

### \*CDC guidelines for VVC treatment

- For oral use:
  - Fluconazole caps. a 150 mg - once a day 1 caps.
- Za intravaginainu primjenu:
  - Butoconazole 2% cream, 5 g intravag., 3 days
  - Butoconazole 2% slow-release cream, 5 g intravaginally, once
  - Clotrimazole 1% cream 5 g intravaginal 1x1, 7-14 days
  - Clotrimazole 100 mg vaginal tbl, 1x1, 7 days
  - Clotrimazole 100 mg vaginal tbl 2x1, 3 days
  - Clotrimazole 500 mg vaginal tbl, 1 one time
  - Miconazole 2% krema 5 g intravaginal 7 days
  - Miconazole 100 mg vaginal tbl, 1x1, 7 days
  - Miconazole 200 mg vaginal tbl, 1x1, 3 days
  - Nistatine 100,000 ij vaginal tbl 1x1, 14 days
  - Tioconazole 6,5% cream 5 g intravaginal single dose
  - Terconazole 0,4% cream 5 g intravaginal 7 days
  - Terconazole 0,8% cream 5 g intravaginal, 3 days
  - Terconazole 80 mg vaginal tbl, 1x1, 3 days

\*Centers for Disease Control and Prevention of United States of America and World Health Organization, WHO

# CURE

- Itraconazole (200 mg 2x day)

## • Fluconazole Zenafluk® (PLIVA)

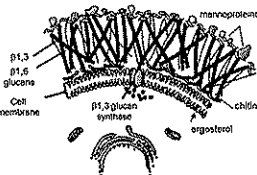
– caps. a 150 mg single dose

C13H12F2N6O



### The mechanism of action

Cell wall  
It inhibits the fungal cytochrome P450 enzyme 14 $\alpha$ -demethylase. And this inhibition prevents the conversion of lanosterol in ergosterol = necessary substance of cytoplasmatic membrane and causes the accumulation of 14 $\alpha$ -metil steroles



INHIBITION OF REPLICATION  
INHIBITION OF HYPHAE TRANSFORMATION = PATHOGEN FORM

### NONCOMPLICATED

- Vag. 1-3 days
  - RARE
  - MILD TO MEDIUM SYMPTOMS
  - HEALTHY WOMEN
  - NOT PREGNANT
- Fluconazole (Zenafluk® PLIVA) single dose
  - Cheaper than local treatment (generics)
  - As effective as local
  - Women prefer oral treatment – more pleasant
  - the only oral medication for candidosis recommended by WHO and CDC
  - It can be taken anytime, with or without food
  - In therapeutic concentration in vaginal discharge for 72h (3d)
- Itraconazole (200 mg 2x day)

World Health Organization. Candidiasis. Guidelines for the management of sexually transmitted infections. 2003;58-60.  
Centers for Disease Control and Prevention. Vulvovaginal Candidiasis. MMWR 2010;59 (No. RR 12):61-3.

## COMPLICATED

- Vag. 7-14 days (azoles)
  - Badly regulated DM
  - Immunosuppressive th.
  - Intensive signs and symptoms
  - Often C. glabrata
- Fluconazole
  - caps. a 150 mg x1 / 1. i 4. day
  - For particularly severe cases, some recommend the topical corticosteroid treatment for 2 d
  - C. glabrata is resistant to azoles in 50% of cases
    - 600 mg vag acidi borici 1x1/ 14d – success 65-70%
    - Flucytosin ung. Intravag > 90% success – to us

Centers for Disease Control and Prevention. Vulvovaginal Candidiasis. MMWR 2010;59 (No. RR 12):61-3.

## COMPLICATED RECURRENT

Medical history  $\geq 4$  epizodes/ year

- Eliminate the predisposing factors
  - Glycaemia
  - OC with ↓conc. E2
  - (Avoid tight) ?
  - (Drink black currant juice) ?
- Diflucan caps. a 150 mg Zenafluk® (PLIVA)
- 1x1 / 1. - 4. - 7. day – then 1x week 6 months (or continue with vaginal clotrimazol a 500 mg 1x week – 6 months)
- Fluconazole dependent recurrent VVC – therapy for years

SOBEL JD, WIESENFELD HC, yearsMARTENS M i sur. Maintenance fluconazole therapy for recurrent vulvovaginal candidiasis. N Engl J Med 2004;351:876-83.

**Rp.**

**Dg. Vulvovaginitis mycotica rec.**

**Th. Zenafluk caps. a 150 mg every 3. day one capsule (1. - 4. - 7. day), followed by one capsule every week for 6 months**

## **PREVENTION**

### **Nistatine PO does not prevent recurrent symptomatic VVC**

- ***Candida spec.* Of vagina comes from rectum through preineum**
- **Cultures of GI tract and vagina often show identical strains**
- **Still, Nistatine treatment does not prevent recurrent symptomatic VVC**

## **PREVENTION WITH LAKTOBACILLI**

**Treatment with Lactobacilli orally or vaginally does not prevent post-antibiotic treatment VVC**

DONDERS GG, BABULA O, BELLEN G, LINHARES IM, WITKIN SS. Mannose-binding lectin gene polymorphism and resistance to therapy in women with recurrent vulvovaginal candidiasis. *BJOQ* 2008;115:1225-31.

## **Postantibiotic VVC**

- **Fluconazole caps a 150 mg at the start and finish of antibiotic treatment is proved to prevent post-antibiotic VVC**
- **Educatin – unnecessary antibiotic treatment (viral infections)**

SOBEL JD. Vulvovaginal candidosis. *Lancet* 2007;369 :1961-71.