

Part 2

Today is the 18th of April 2020, the number of COVID-19 cases is still growing fast, even in our country the number reached 8,274 patients. I really hope this ends soon and people can go back to their normal lives. I have finished 7 tv series and 11 videogames, soon I will run out of content to entertain me during this pandemic, god I miss my friends, I'm starting to even forget their names, what about their faces you ask? Long forgotten, I don't think I'll recognize any of them if I saw them on the streets, that is if I ever get another chance to see them. What am I saying? I don't even know, the lack of human interaction is driving me insane, writing these notes for no one to read is the only thing keeping me sane, barely that is.

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-A Worried Man.



# Candida infection, trichomonas vaginalis & bacterial vaginosis

## Lecture objectives

- To recognize the different types of infant infections.
- To know major transplacentally transmitted pathogens causing congenital infections .
  - (Toxoplasma , TP ,ParvoV , VZV, Rubella V & CMV.)
- To describe their structures.
- To know their major epidemiology features.
- To describe clinical manifestations of their congenital infections
- To illustrate different laboratory diagnosis of maternal and congenital infections.
- To know their treatment and preventive measures.

● **Important**

● **Color index**

● **Boys' slides**

● **Doctors' note**

● **Extra**

● **Girls' slides**

EDITING FILE



## ● The normal vagina

- Lined with 25 layers of epithelium cells.
- Separation of microbial pathogens from the normal genital microbiota.
- **Characteristic of normal vaginal secretion**
  - Desquamated vaginal epithelial cell
  - **Lactobacilli dominate**
  - PH 3.5 to 4.6 (Acidic)
  - Odorless
  - No itching or irritation
  - Does not soil underclothing



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### ● Normal flora of the vagina:

- **Lactobacilli**
- Streptococcus agalactiae
- Corynebacterium spp.
- Enterococcus spp.
- Gardnerella vaginalis
- Escherichia coli
- coagulase-negative Staphylococci,
- Anaerobes
- Staphylococcus aureus
- Yeasts

## ● Abnormal vaginal secretion

- Normal physiological vaginal secretion **should be colorless and odorless**
- Causes of abnormal vaginal secretion:
  - Vaginal infection
    - Trichomoniasis
    - Vulvovaginitis candidiasis
    - Bacterial vaginosis
  - Desquamative inflammatory vaginitis
  - Cervicitis
    - Infectious
    - Noninfectious
  - Estrogen deficiency

## Types of infections

<b>Females</b>	<ul style="list-style-type: none"> <li>• Cervicitis</li> <li>• Vulvovaginitis</li> <li>• Urethritis</li> <li>• Bacterial vaginosis (BV)</li> <li>• Salpingitis (pelvic inflammatory disease [PID])</li> </ul>	<ul style="list-style-type: none"> <li>• Endometritis</li> <li>• Genital ulcers</li> <li>• <b>Pregnant females:</b> Disease in the neonate.</li> <li>• <b>Children and postmenopausal women</b></li> </ul>
<b>Males</b>	<ul style="list-style-type: none"> <li>• Urethritis</li> <li>• Epididymitis</li> <li>• Prostatitis</li> <li>• Genital ulcers</li> </ul>	

## Vulvovaginitis



(Vaginal disorders in general, not only vulvovaginitis)

### History

### Symptoms

- **General gynecological history** (Age: Neonate, Prepubescent, Adolescent, Adult, Post menopausal (atrophic)).
- Estrogen depletion
- Onset
- Menstrual history
- Pregnancy
- Sexual Hx
- Contraception
- Sexual relationships
- Prior infections
- General medical Hx: Allergies, DM, Malignancies, Immunodeficiency
- Medication: OCP, steroids, douche<sup>1</sup>

- Discharge:
  - quality
  - quantity: scanty
  - Physiological or due to OCP
- Odeur ( BV,FB,EV fistula )
- Vulvar discomfort (HSV)
- Dyspareunia
- Abdominal pain (tricho) PID

### Examination

- Breast for detection of abnormal masses
- Adequate illumination
- Magnification if possible
- Give a patient mirror
- Inspect external genitalia
  - Lesions
  - Erythema
- Vaginal mucosa
  - Erythema
  - Lesion
  - Secretion
- Examination of cervix
  - Ectropion
  - Lesions
  - Erythema
  - Endocervical secretion
- Collect cervical and vaginal specimen
- Bimanual examination

**Footnotes:**

1-Douching is washing or cleaning out the inside of the vagina with water or other mixtures of fluids.

# Vulvovaginitis

## Classification of vulvovaginitis

### Uncomplicated Vulvovaginitis

- Sporadic
- No underlying disease
- By *Candida albicans*
- Not pregnant
- Mild to moderate severity
- Any available topical agent
- Fluconazole 150mg as a single oral dose

### Complicated Vulvovaginitis

- Underlying illness (**HIV, DM**)
- Recurrent infection 4 or more per year
- Non albican candida
- Pregnancy
- Severe infection
- **Culture confirmation mandatory**
- Antifungal suscep. Testing
- Treat for 10-14 days with vaginal or oral agent
- Other: topical
  - Boric acid
  - 5 fluorocytocine
- Consider treatment of the partners
- Long term suppressive treatment for frequently recurrent diseases

Dr. Khalifa skipped most previous content and started here

## Candidal Vulvovaginitis (Vaginal Thrush)

### • Candida infections yeast infection (moniliasis):

- **Candida is a unicellular yeast fungus. That appears on the Microscope as Round Budding yeast and pseudohyphae.**
- **Culture: appears as creamy white colonies on SDA**
- **Candidiasis** or thrush is a fungal infection (mycosis) of any of the *Candida* species (yeasts) of which ***Candida albicans* is the most common.**
- Common superficial infections of skin and mucosal membranes by *Candida* causing local inflammation and discomfort.

### ○ Candidal vulvovaginitis (Vaginal Thrush):

- Infection of the vagina's mucous membranes by ***Candida albicans*.**
- 75% of adult women
- *Candida Albicans* is Found **naturally** in the vagina
- Hormonal changes
- Change in vaginal acidity.
- **Use of Broad-spectrum antibiotics.**
- **Use of corticosteroid medications.**
- **Pregnancy.**
- **Poorly controlled diabetes mellitus.**
- Age: 20-30 years

# Candidal Vulvovaginitis

## Risk factors



**Antibiotics**



**Pregnancy**



**Diabetes (poorly controlled)**



**Immunodeficiency**



**Contraceptives**



**Sexual behaviour**



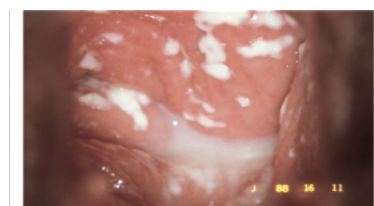
**Tight-fitting clothing**



**Female hygiene**

## Symptoms

- **Vulval itching**
- **Vulval soreness and irritation**
- Superficial dyspareunia.
- Dysuria<sup>1</sup>
- **Odourless** vaginal discharge
  - thin and watery or thick and **white (cheese-like)**<sup>2</sup>
- **Erythema (redness)**
- Fissuring
- satellite lesions.



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## Types of candidal vulvovaginitis

1

### Uncomplicated thrush

- single episode/less than four episodes in a year.
- mild or moderate symptoms
- caused by the *Candida albicans* .

2

### Complicated thrush

- four or more episodes in a year.
- severe symptoms.
- Pregnancy
- poorly controlled diabetes/immune deficiency.
- not caused by the *Candida albicans*

#### Footnotes:

1- if the urethra is infected

2- in all 3 organisms in this lecture , the color of discharge is a hint for the diagnosis

# Candidal Vulvovaginitis

## ● Diagnosis and Treatment

### Diagnosis

- History & symptoms
- physical and pelvic exam
- Gram stain
- Wet mount
- Culture
- Direct Microscopy: Budding yeast cells and pseudohyphae
- Candidiasis can be similar to other diseases:
  - Sexually transmitted diseases
  - Chlamydia
  - Trichomoniasis
  - Bacterial vaginosis
  - Gonorrhea

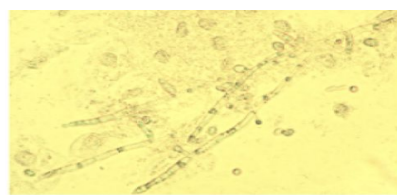


### Treatment

- Butoconazole cream
- Clotrimazole
  - 1% cream
  - vaginal tablet
- Miconazole
  - 2% cream
  - vagina suppository
- Nystatin
  - vaginal tablet
- Oral Agent:
  - **Fluconazole** : oral one tablet in single dose
- Short-course topical formulations
  - single dose and regimens of 1–3 days
  - effectively treat uncomplicated candidal vulvovaginitis
  - Topical azole drugs are more effective than nystatin
  - Azole drugs relief of symptoms in 80%–90% of cases.
- Treatment failure
  - In up to 20% of cases
  - If the symptoms do not clear within 7–14 days



Candida albicans



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#### Footnotes:

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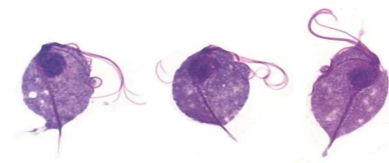
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# Trichomoniasis

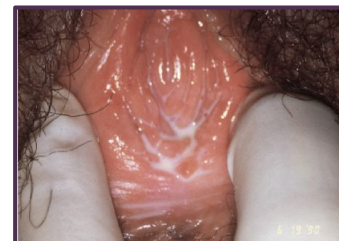
## ● Introduction

- sexually-transmitted infection
- Caused by :
  - Trichomonas vaginalis , a flagellated and motile protozoan parasite
- Transmission:
  - sexual (can't exist outside human because it can't form cysts)



## ● Symptoms

- Purulent vaginal discharge , **yellow or greenish in color**
- **Vulvar irritation (strawberry)**
- Dysuria
- Dyspareunia
- Abnormal vaginal odor



## ● Management

1

### Confirm the diagnosis

- Wet preparation<sup>1</sup> (miss 30%)
- Culture<sup>2</sup>:
  - Culture is considered the gold standard for the diagnosis of trichomoniasis.
  - Its disadvantages include cost and prolonged time before diagnosis , **and it requires a special media**
- Gram Stain

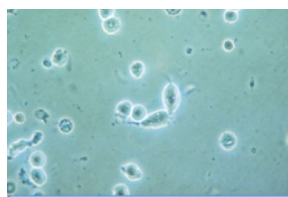
2

Confirm all current sexual partners treated

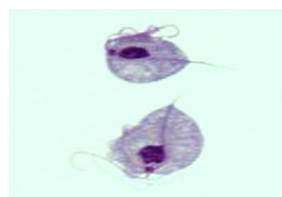
3

### Treatment

- **Oral metronidazole (drug of choice)**
  - 500 mg bid for 7 days
  - 2 g daily for 3-5 days
- **If Rx failure :**
  - Consultation with experts
  - Susceptibility testing
  - Higher dose of metronidazole
  - Alternative Tinidazole



The wet mount's fast results

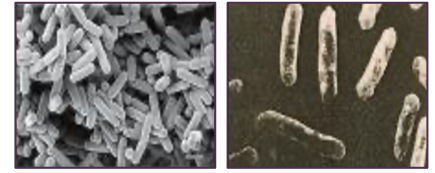


Culture

### Footnotes:

1-placing the specimen of vaginal discharge on a glass slide and mixing with a salt solution to see the motility of the parasite. It should be done immediately or you will lose the motility

2- culture is the gold standard for diagnosis but we don't usually do it because it takes time and clinical diagnosis and wet mount are more than enough



## Bacterial Vaginosis:

- Bacterial Vaginosis is a **floral imbalance**<sup>1</sup>.
- ↓ **Lactobacillus acidophilus** ↑ other normal flora

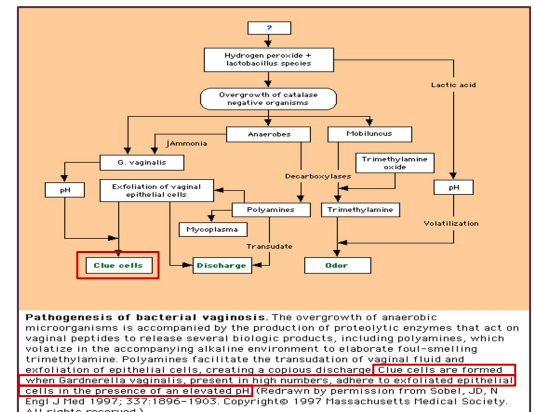
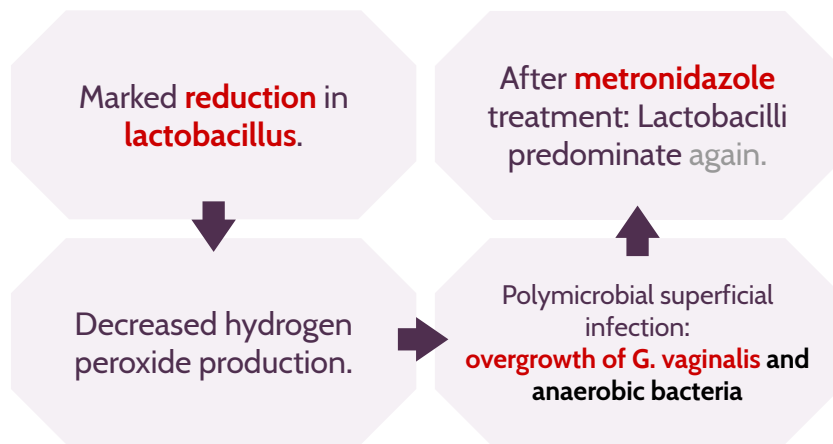
### Vaginal Normal Flora

- Lactobacillus acidophilus**.<sup>3</sup>
- Gardnerella vaginalis.
- Anaerobes:
  - Bacteroides (Porphyromonas).
  - Peptostreptococcus.
- Mycoplasma hominis.
- Mobiluncus species.
  - Prevotella.
  - Fusobacterium.

#### Lactobacilli:

- Compete with other microorganisms for adherence to epithelial cells.
- Produce antimicrobial compounds such as organic acids (which lower the vaginal pH<sup>2</sup>), hydrogen peroxide (**Acidic**), and bacteriocin-like substances.
- Gram positive anaerobic rods

## Pathogenesis



The enzymes released in result to the abnormal balance of the normal flora is responsible for the alkaline PH and the foul smell

## Epidemiology

- Bacterial Vaginosis is the most common vaginal infection in women of childbearing age-29%**
- Risk factors:**
  - Multiple or new sexual partners (sexual activity alteration of vaginal pH).
  - Early age of first sexual intercourse.
  - Douching.
  - Cigarette smoking.
  - Use of IUD.

**Note:** Although sexual activity is a risk factor for the infection, **bacterial vaginosis can occur in women who have never had vaginal intercourse.**

#### Footnotes:

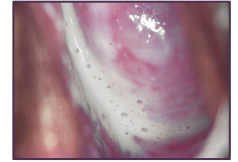
- 1- usually the overgrowth of Gardnerella vaginalis, which is normally found in small amounts
- 2- acidic PH kills bacteria
- 3- is the predominant normal flora



## Clinical Features & Diagnosis of Bacterial Vaginosis

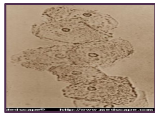
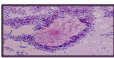

### Clinical Features

- Most cases (50-75%) Homogenous **grey vaginal discharge**.
- Dysuria and dyspareunia rare.
- **Pruritus and inflammation are absent**.
- **Fishy vaginal discharge: (Greyish in color)**
  - During menstruation.
  - After intercourse.
- **Minimal itching or irritation.**



Absence of inflammation is the basis of the term "vaginosis" rather than vaginitis.

### Diagnostic Methods

Clinical/Microscopic Criteria:	-	
<b>Gram Stain "Gold Standard":</b>	<ul style="list-style-type: none"> <li>• <b>Clue cells<sup>1</sup></b> on saline wet mount of vaginal discharge (on &gt;20% cells).</li> <li>• Bacteria adhered to epithelial cells; <b>most reliable single indicator.</b></li> <li>• <b>Vaginal pH &gt; 4.5.</b></li> </ul>	
Elevated pH & increased amine:	<ul style="list-style-type: none"> <li>• Sensitivity: 87%.</li> <li>• Specificity: 92%.</li> </ul>	
<ul style="list-style-type: none"> <li>• Culture has a <b>poor predictive value</b> for G. vaginalis as it is prevalent in healthy asymptomatic women.</li> <li>• DNA probes are expensive, and have a poor predictive value alone.</li> </ul>		

## Treatment Recommendations:

### Oral:

- **Metronidazole (Drug of choice)** 500 mg bid x 7 days (\$5):
  - ▷ 84-96% cure rate.
  - ▷ Single dose therapy (2g) may be less effective.
- **Clindamycin** 300 mg bid x 7 days (\$28):
  - ▷ Less effective.

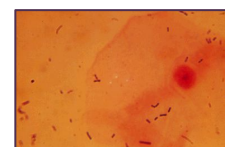
### Topical (higher recurrence rates):

- **Metronidazole gel (0.75%)** 5 g PV qhs x 5 days (\$30);
  - ▷ 70-80% cure rate.
- **Clindamycin cream (2%)** 5 g PV qhs x 7 days (\$31):
  - ▷ Less effective.
  - ▷ May lead to Clindamycin resistant anaerobic bacteria.

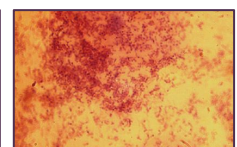
Score	Lactobacillus morphotypes	Gardnerella and Bacteroides morphotypes	Curved gram-variable rods
0	4+	0	0
1	3+	1+	1+ or 2+
2	2+	2+	3+ or 4+
3	1+	3+	
4	0	4+	

The score is determined by the average number of each morphotype seen per oil-immersion field, but varies with the type of bacteria. Excluding lactobacillus morphotypes, a score of 0 means no morphotypes are present; 1, 0 to 1 morphotype present per high power field; 2, 1 to 4 morphotypes present; 3, 5 to 30 morphotypes present; 4, 30 or more morphotypes present. A total score of 7 to 10 is indicative of bacterial vaginosis infection, 4 to 6 is indeterminate, and 0 to 3 is normal. (Total score = lactobacilli score and Gardnerella vaginalis score and Bacteroides species score and curved gram variable rod score).

<sup>1</sup>Adapted from data in Nugent, RP. J Clin Microbiol 1991; 29:291.



**Normal vaginal flora:** Gram stain of vaginal contents (x1000) shows an epithelial cell with well-visualized borders and Gram positive rods similar to lactobacilli. The smear suggests normal vaginal flora, not bacterial vaginosis. Courtesy of Harriet Provine.



**Bacterial vaginosis:** Gram stain of vaginal discharge (x1000) from a patient with bacterial vaginosis shows the borders of an epithelial cell obscured by small, Gram variable coccobacilli. Courtesy of Harriet Provine.

1- epithelial cells covered with adherent Gardnerella vaginalis and other anaerobic bacteria, and is the main diagnostic parameter.

## Microbiology of Gynecological examinations

### Specimens obtained during Gynecological examination

Vaginal secretion	<ul style="list-style-type: none"> <li>• PH.</li> <li>• Saline wet preparation.</li> <li>• KOH wet preparation.</li> </ul>
Cervical cultural and non cultural <sup>1</sup>	<ul style="list-style-type: none"> <li>• GC.</li> <li>• C.trachomatis.</li> </ul>
Vaginal culture	<ul style="list-style-type: none"> <li>• Candida.</li> <li>• Trichomonas vaginalis.</li> </ul>

Cervical cytological examination if not documented within previous 12 months

### Specific Tests

**Routine Bacterial Cultures ARE NOT HELPFUL**

<b>Wet mount</b> (60% sensitive for Trichomoniasis & BV)	<b>Wet mount with yeast &amp; Trichomonas cultures:</b> Recommended tests to diagnose vaginitis.
	<b>Wet mount, without yeast or Trichomonas cultures:</b> 50% of either of these agents of vaginitis will be missed.
(KOH) "Whiff test"	Presence of abnormal or foul odor.
Gram stain (Using the Nugent scoring)	Useful to diagnose BV.
Sensitive DNA probe assay <sup>2</sup>	Combines the detection of yeasts, Trichomonas, and G. vaginalis as a marker for BV.

**Footnotes:**

- 1- we rarely do it , it's usually done in case of resistant candida infection
- 2- easy and rapid way to diagnose yeasts, Trichomonas, and G. vaginalis .

	PH	Sign and symptoms	Whiff test <sup>1</sup>	Gram stain/Wet prep	Culture	Immunologic / Molecular test	Treatment
<b>Candida Vaginitis</b>	< 4.5	<ul style="list-style-type: none"> <li>· Inflammation</li> <li>· Vulval itching and erythema</li> <li>· White discharge</li> <li>· Odorless</li> </ul>	-	Yeast and pseudohyphae	Candida appear as creamy white colonies on SDA	DNA probe <sup>2</sup>	<ul style="list-style-type: none"> <li>· Fluconazole</li> <li>· Nystatin</li> </ul>
<b>Trichomonas vaginalis</b>	> 4.5	<ul style="list-style-type: none"> <li>· Inflammation</li> <li>· Vulvar irritation and erythema</li> <li>· Yellow or greenish in color</li> <li>· Foul smelling discharge</li> </ul>	+-	<ul style="list-style-type: none"> <li>· Trichomonas</li> <li>· culture is the gold standard method for diagnosis but it's not usually used because it takes time and clinical diagnosis and wet mount are more than enough</li> </ul>	Motile trophozoites	<ul style="list-style-type: none"> <li>· DNA probe<sup>2</sup></li> <li>· EIA (enzyme immunoassays)</li> </ul>	Oral metronidazole
<b>Bacterial Vaginosis</b>	> 4.5	<ul style="list-style-type: none"> <li>· No inflammation and pruritus</li> <li>· No or minimal itching or irritation</li> <li>· Grey discharge Fishy odor</li> </ul>	+++	<ul style="list-style-type: none"> <li>· Gram stain: Clue cells</li> <li>· Gram stain is gold standard</li> </ul>	Not helpful	DNA probe <sup>2</sup>	Oral metronidazole

**Footnotes:**

1- Sample of vaginal secretions are placed in a test tube with 10% KOH.

KOH alkalizes amines produced by anaerobic bacteria-results in a sharp "fishy odor"

2- a technique for identifying a segment of DNA, using a known sequence of nucleotide bases from a DNA strand to detect a complementary sequence in the sample by means of base pairing.

## 1- Candidal vulvovaginitis:

- Infection of the vagina's mucous membranes by yeast.
- **Risk factors:**
  - Antibiotics → kill normal flora → yeast overgrowth.
  - Pregnancy
  - Poorly controlled diabetes
  - Immunodeficiency
- **Symptoms:**
  - **White (cheese-like) odourless vaginal discharge.**
- **Types:**
  - Uncomplicated:
    - Single episode or less than 4 episodes in a year.
    - Caused by candida albicans
  - Complicated:
    - 4 or more episodes in a year.
    - Not caused by c.albicans
    - Associated with pregnancy/ poorly controlled diabetes/immune deficiency.
- **Diagnosis:**
  - Gram stain: we will see pseudohyphae yeast
  - Wet mount: we will see pseudohyphae yeast
  - Culture: helpful in cases of recurrent infection
- **Treatment:**
  - Mainly Fluconazole

## 2- Trichomoniasis (vaginitis)

- Sexually transmitted parasitic infection caused by Flagellate protozoa (*T. vaginalis*.)
- **Symptoms:**
  - **Yellow or greenish vaginal discharge**
  - Vulvar irritation (strawberry/reddish)
- **Diagnosis:**
  - Culture (takes time & requires special media): Motile trophozoites
  - Wet mount (quick): We can see corkscrew motility
  - Gram stain
- **Treatment:**
  - Drug of choice: Metronidazole (effective against anaerobes and some parasitic infections)
  - Sexual partner has to be treated as well.

## 3- Bacterial Vaginosis: (not vaginitis)

- A disease caused by floral imbalance: Marked reduction in **lactobacillus** & overgrowth of **G. vaginalis**, Mobiluncus species and anaerobic bacteria. (Normally lactobacillus is the dominant bacterial flora in vagina)
- **Risk factors:** (Although sexual activity is a risk factor for the infection, bacterial vaginosis can occur in women who have never had vaginal intercourse)
  - Multiple or new sexual partners
  - Smoking & Use of IUD
  - Older age
- **Symptoms:**
  - **Fishy vaginal discharge, greyish in color**
  - Pruritus and inflammation are absent
- **Diagnosis:**
  - Gram stain (gold standard): look for **clue cells (bacteria-coated epithelial cells).**
  - Wet mount: look for **clue cells**
  - Vaginal pH >4.5 (will be high in trichomoniasis as well, but unchanged in candida)
- **Treatment:**
  - Drug of choice: oral or topical **Metronidazole**
  - Or clindamycin

# Lecture Quiz

## MCQ:

Answers: Q1:C | Q2:A | Q3:B

**Q1:** A 30-year-old woman presents to her gynecologist with complaints of vaginal itching and a frothy, yellow discharge. She also complains of painful urination. She admits to being sexually active with several men in the past two weeks. Cultures are negative for bacterial growth, but organisms are visible via a wet prep on low power. The most likely causal agent is:

- A- Candida albicans
- B- Trichophyton rubrum
- C- Trichomonas vaginalis
- D- Trichophyton rubrum

**Q2:** A 38-year-old oncology patient comes to the physician complaining of vaginal burning and itching. On physical examination a whitish, curd-like vaginal discharge and inflammation of the walls of the vagina and vulva are observed. Which of the following is a risk factor for this condition?

- A- Immunodeficiency
- B- Cigarette smoking
- C- PPIs
- D- Use of IUD

**Q3:** Which of the following is the most prevalent microorganism in the vagina that may also be protective?

- A-  $\alpha$ -hemolytic streptococci
- B- Lactobacillus
- C- S. epidermidis
- D- E. coli

## SAQs: By Dr. Khalifa

**1- CASE:** A 50 year-old diabetic female presents to family physician complaining of vaginal discharge and itching. The discharge was whitish in consistency (Cheese-like).

**Q1:** What's the most likely diagnosis?

Candidal vulvovaginitis

**Q2:** How to diagnose it?

Wet mount, gram stain, culture.

**Q3:** What are the main risk factors?

Pregnancy, Diabetes, Antibiotics

**Q4:** What's the appropriate treatment?

Mainly fluconazole or nystatin

**2- CASE:** A 60 year-old female presents to family physician complaining of discomfort and vaginal discharge, greyish in color with fishy like odor. The physician took a swab and a sent it to the lab to do gram stain, Clue cells were found.

**Q1:** What's the most likely diagnosis?

Bacterial Vaginosis

**Q2:** What's the appropriate treatment?

Metronidazole (oral or topical)

**3- CASE:** A 30 year-old sexually active female, a new partner recently, and had an unprotected sexual activity. Presents to family physician complaining of Greenish vaginal discharge.

**Q1:** What's the most likely diagnosis?

Trichomoniasis (vaginitis)

**Q2:** What will we see if the physician ordered a wet mount of vaginal discharge?

Motile parasite (Trichomonas)

**Q3:** What's the appropriate treatment?

Metronidazole

# Members Board

- **Team Leaders:**



**Abdulaziz Alshomar**



**Ghada Alsadhan**

- **Team sub-leader:**



**Mohammed Alhumud** (coolest sub leader ever)

- **This lecture was done by:**



**Suhail Basuhail**



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