VAGINITIS

IT'S NOT JUST YEAST

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LEARNING OBJECTIVES

- Become familiar with EVALUATION & MANAGEMENT of the 3 most common vaginal infections
- Understand the pathogenesis, differential diagnosis, and treatment of Bacterial Vaginosis, Vulvovaginal Candidiasis, & Trichomonas
- Understand the appropriate use of wet preps in diagnosis.
- To individualize therapy to the women's choice & to ensure the most efficacious outcome.
- Understand the diagnosis and treatment for less common forms of vaginitis

QUESTION # 1

- What % of women with vaginal symptoms have some type of vaginitis?
  A. 10%
  B. 25%
  C. 40%
  D. 60%
  E. 80%

QUESTION #2

Which is the most common form of "vaginitis"?

A. Bacterial Vaginosis
B. Monilia Vaginitis (yeast)
C. Trichomonas Vaginitis
D. Atrophic vaginitis
E. Desquamative inflammatory vaginitis (DIV)

Vaginitis

- Usually characterized by:
  - Vaginal discharge
  - Vulvar itching
  - Irritation
  - Odor

SCOPE OF THE PROBLEM

- VAGINAL DISCHARGE: frequent reason for office visit
- Vaginal Discharge is normal physiologically
- VAGINITIS: most frequent complaint in gyn clinic
- 40% with vaginal symptoms have some type of vaginitis
- 90% of Vaginitis = one of 3 common infections:
  - Bacterial Vaginosis 40-50%
  - Vulvovaginal Candidiasis (vaginitis) 20-25%
  - Trichomonas Vaginitis 20-25%
- Accurate Diagnosis: key to effective therapy
- S/S are unreliable in diagnosis
**CAUSES OF VAGINITIS IN ADULT WOMEN**

- **Bacterial Vaginosis (40-50%)**
- **Vulvovaginal Candidiasis (20-25%)**
- **Trichomonas vaginitis (15-20%)**
- **Miscellaneous**
  - Atrophic Vaginitis
  - Postpureperal Vaginitis
  - Foreign body
  - Ulcerative Vaginitis (staph., toxic shock)
  - Desquamative Inflammatory Vaginitis
  - Cytolytic Vaginitis
  - Strep Vaginitis (B hemolytic)
  - Collagen Vascular Disease
  - Idiopathic causes

**Diagnosis of Vaginitis**

- Patient history
- Visual inspection of internal/external genitalia
- Appearance of discharge
- Collection of specimen
- Preparation and examination of specimen slide

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**In-Office Evaluation of women with Vaginal Symptoms**

**HISTORY**
- Type & extent of symptoms (itching, swelling, odor, & pelvic pain)
- Duration or change in symptoms over time
- Changes in sexual partners or sexual activities
- Contraceptive method (and recent changes in contraception)
- Changes in diet, exercises, or medications
- History of genital infections, either patient or partner(s)
- Current pregnancy risk
- Patient's concern & opinion about diagnosis.

**In-Office Evaluation of women with Vaginal Symptoms**

**PHYSICAL EXAM**
- Erythema, swelling or lesions on perineum, vulva, vagina and cervix
- Tenderness at introitus
- Color, texture and odor of vaginal and cervical discharges
- Size and tenderness of uterus, adnexae
- Evidence of other infections (e.g. cervicitis, herpes, syphilis, HPV)

**In-Office Evaluation of women with Vaginal Symptoms**

**STI'S: GONORRHEA, CHLYMADIA**

- In Office Laboratory Assessment: **WET PREP AND PH**
  - pH of vaginal secretions
  - **Amine test** (fishy odor after KOH added to vag. Secretions)
  - Normal saline preparation (in fluid form) for micro evaluation: presence of white blood cells, motile trichomonads, background flora (Normal: long rods suggestive of lactobacilli; Abnormal: predominance of short rods, cocci, and curved motile rods). **Clue cells** (epithelial cells studded with bacteria, with obscured borders), WBCs.
  - **KOH prep** for microscopic evaluation: presence of hyphae or budding yeast forms
In-Office Evaluation of women with Vaginal Symptoms

- As indicated:
  - In-office culture for Trichomonas Vaginalis & Candida species, using modified Diamond media (T.V), plus Sabouraud's or Nickerson's agar (for Candida species)
  - Gram stain of vaginal or cervical secretions
  - Urinalysis, indicated by symptoms or signs
  - Pregnancy testing
  - Serum testing for concomitant sexually transmitted diseases, such as syphilis or HIV infection

Wet Prep: Common Characteristics

Wet Prep: Lactobacilli and Epithelial Cells

Question #3
The normal pH of vaginal secretions of reproductive aged women is:
A. 3.5-4.5
B. 5.0-6.0
C. 6.5-7.5
D. 8.0-9.0

Question #4
What percent of sexual partners of women with trichomonas infections also have the infection?
A. 10%
B. 20-30%
C. 40-50%
D. >60%

TRICHOMONAS VAGINALIS

- MOTILE OVOID FLAGELLATED ANEROBIC Protozoan
- GROWS BEST IN ANAEROBIC CONDITIONS
- ATTACHES TO MUCUS MEMBRANES
- MOST PREVALENT NON-VIRAL STI
  (what is most prevalent viral STI?)
**Trichomonas vaginalis**

**Pathogenesis**

Source: CDC, National Center for Infectious Diseases, Division of Parasitic Diseases

**TRICHOMONAS: CLINICAL PRESENTATION**

- Asymptomatic in 50% males/females
- 80% symptomatic in pregnancy
- 1/3 to 1/2 will become symptomatic in 3-6 months
- Incubation: 3-28 days
- Vag discharge and V-V irritation in women
- Excess Vag discharge: Frothy, bubbly yellow-green (25%)
- Strawberry cervix: Colposcopy
- Diagnosis: Wet prep: Increased pH, WBCs, motile trich., +/- clue cells
- Culture: Diamond’s media:
  - Vaginitis with increased pH, PMN’s, absent motile trichomonads, & clue cells absent.

**Vaginitis Curriculum**

**Vaginitis Differentiation**

<table>
<thead>
<tr>
<th>Normal</th>
<th>Bacterial Vaginosis</th>
<th>Candidiasis</th>
<th>Trichomoniasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom presentation</td>
<td>Odor, discharge, itch</td>
<td>Itch, discomfort, dysuria, thick discharge</td>
<td>Itch, discharge, 50% asymptomatic</td>
</tr>
<tr>
<td>Vaginal discharge</td>
<td>Clear to white</td>
<td>Homogenous, adherent, thin, milky white, malodorous “neut fishy”</td>
<td>Thick, clumpy, white “cottage cheese”</td>
</tr>
<tr>
<td>Clinical findings</td>
<td>Inflammation and erythema</td>
<td>Cervical petechiae “strawberry cervix”</td>
<td></td>
</tr>
<tr>
<td>Vaginal pH</td>
<td>3.8-4.2</td>
<td>&gt;4.5</td>
<td>Usually &lt;4.5</td>
</tr>
<tr>
<td>KOH “whiff” test</td>
<td>Negative</td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>NaCl wet mount</td>
<td>Lacto-bacilli</td>
<td>Clue cells (&gt;20%), no/few WBCs</td>
<td>Few WBCs</td>
</tr>
<tr>
<td>KOH wet mount</td>
<td>Pseudohyphae or spores if non-albicans species</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**TRICHOMONAS VAGINALIS**

- Bubbly discharge of vaginal fluid

**Purulent bubbly C-V fluid/trich**

Microscopic view of Cervix

Caused by parasite, there may be either no symptoms or a smell, green yellow discharge and lower abdominal pain. The infection is most often acquired through intercourse, but can also be transmitted by sharing damp towels or bathing suits with an infected person.
"Strawberry cervix" due to *T. vaginalis*

Source: Claire E. Stevens/Seattle STD/HIV Prevention Training Center at the University of Washington

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**TRICHOMONIASIS**

- Microscopic View of Trichomonad in Saline Wet Mount Prep. Organisms are Motile.

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**Diagnosis--Trichomoniasis--Females**

- **Motile** trichomonads seen on saline wet mount
- Vaginal pH >4.5 often present
- Culture is the “gold standard”
- Pap smear has limited sensitivity and low specificity
- DNA probe
- Rapid test

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**Wet Prep: Trichomoniasis**

Saline: 40X objective

*Trichomonas shown for size reference only: must be motile for identification*

Source: Seattle STD/HIV Prevention Training Center at the University of Washington

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**Treatment**

- CDC-recommended regimen: (90% efficacy)
  - Metronidazole 2 g orally in a single dose OR
  - Tinidazole 2 g orally in a single dose

- CDC-recommended alternative regimen
  - Metronidazole 500 mg twice a day for 7 days

**Side Effects**

- Metronidazole: Nausea, metallic taste, interactions with ETOH.
- Tinidazole: Similar side effects, but reduced incidence

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**TREATMENT: TRICHOMONAS**

- **TX. ASYMPOTOMATIC FEMALE**
  - 1/3 WILL BECOME SYMPTOMATIC IN 3 MONTHS

- **TX. MALE PARTNER**
  - This is a STI

- **CHECK FOR BACTERIAL VAGINOSIS**
  - TRICH IS FREQUENTLY A MIXED INFECTION
**T. vaginalis in Men**

- May cause up to 11%-13% of nongonococcal urethritis in males
- Urethral trichomoniasis has been associated with increased shedding of HIV in HIV-infected men

**Diagnosis- Males**

- First void urine concentrated
  - Examine for motile trichomonads
  - Culture
- Urethral swab
  - Culture

**TRICHOMONIASIS: Prevention**

**Partner Management Trichomoniasis**

- Sex partners should be treated
- Patients should be instructed to avoid sex until they and their sex partners are cured (when therapy has been completed and patient and partner(s) are asymptomatic)

**Patient Counseling and Education**

- **Nature of the disease**
  - May be symptomatic or asymptomatic, douching may worsen vaginal discharge, untreated trichomoniasis associated with adverse pregnancy outcomes
- **Transmission issues**
  - Almost always sexually transmitted, fomite transmission rare, may persist for months to years, associated with increased susceptibility to HIV acquisition

**Risk Reduction**

The clinician should:

- Assess patient’s potential for behavior change
- Discuss individualized risk-reduction plans with the patient
- Discuss prevention strategies such as abstinence, monogamy, use of condoms, and limiting the number of sex partners
- Latex condoms, when used consistently and correctly, can reduce the risk of transmission of T. vaginalis
Question #5
Which of the following is characteristic of bacterial vaginosis?
A. Vaginal ph of < 4.5
B. Curdy consistency
C. Greenish tinge
D. Fishy odor

QUESTION # 6
The most common symptom associated with a vaginal infection is
• Fever
• Pain
• Pruritus
• Discharge

QUESTION # 7
The most common cause of increased vaginal discharge is
A. Candidiasis
B. Trichomoniasis
C. Bacterial vaginosis
D. Human papillomavirus

Epidemiology
• Most common cause of vaginitis
• Prevalence varies by population:
  - 5%-25% among college students
  - 12%-61% among STD patients
• Widely distributed
Epidemiology (continued)

- Linked to:
  - premature rupture of membranes,
  - premature delivery and low birth-weight delivery,
  - acquisition of HIV,
  - development of PID, and
  - post-operative infections after gynecological procedures

Risk Factors

- African Americans
- Two or more sex partners in previous six months/new sex partner
- Douching
- Lack of barrier protection
- Absence of or decrease in lactobacilli
- Lack of $H_2O_2$-producing lactobacilli

Transmission

- Currently not considered a sexually transmitted disease, but acquisition appears to be related to sexual activity

BV: Diagnosis

Wet Prep: Bacterial Vaginosis

- Saline: 40X objective

BV Diagnosis: Amsel Criteria

- Vaginal pH > 4.5
- Presence of >20% per HPF of "clue cells" on wet mount examination
- Positive amine or "whiff" test
- Homogeneous, non-viscous, milky-white discharge adherent to the vaginal walls

Amsel Criteria:
Must have at least three of the following findings:
Other Diagnostic Tools

- Vaginal Gram stain (Nugent or Speigel criteria)
- Culture
- DNA probe
- Newer diagnostic modalities include:
  - PIP activity
  - Sialidase tests

**BACTERIAL VAGINOSIS**

- The characteristic milky or creamy vaginal discharge of BV assoc with high vag Ph & Fishy Odor

- Microscopic view of Clue Cells in a wet-mount preparation. Note irregular or serrated cell walls.

- Note absence of WBC's & stippling of epithelial cells.
BV: Patient Management

Treatment: BV

CDC-recommended regimens:
- Metronidazole 500 mg orally twice a day for 7 days, OR
- Metronidazole gel 0.75%, one full applicator (5 grams) intravaginally, once a day for 5 days, OR
- Clindamycin cream 2%, one full applicator (5 grams) intravaginally at bedtime for 7 days

Alternative regimens:
- Clindamycin 300 mg orally twice a day for 7 days, OR
- Clindamycin ovules 100 g intravaginally once at bedtime for 3 days

Multiple recurrences:
- Twice weekly metronidazole gel for 6 months may reduce recurrences

ORAL TINIDAZOLE FOR BV

- 2ND GENERATION NITROIMIDAZOLE
- LONGER HALF LIFE THAN METRONIDAZOLE & Fewer Side Effects
- 1 gm daily for 5 days (single daily dose)
  OR
- 2 gm. once daily for 2 days (single daily dose)

Treatment in Pregnancy

- Pregnant women with symptomatic disease should be treated with
  - Metronidazole 500 mg twice a day for 7 days, OR
  - Metronidazole 250 mg orally 3 times a day for 7 days, OR
  - Clindamycin 300 mg orally twice a day for 7 days

- Asymptomatic high-risk women (those who have previously delivered a premature infant)
  - Some experts recommend screening and treatment at first prenatal visit; and
  - A follow-up evaluation at 1 month after completion of therapy
**Intravaginal Clindamycin Therapy for BV**

- May be less effective than Metronidazole
- 2% Cream, intravaginal x 7 days
- Single day dose (Clindesse), may have lower efficacy than metronidazole
- Pseudomembranous colitis has been reported with both oral and topical clindamycin

**Screening and Treatment in Asymptomatic Patients**

- Therapy is not recommended for male partners of women with BV
- Female partners of women with BV should be examined and treated if BV is present
- Screen and treat women prior to surgical abortion or hysterectomy

**Recurrence**

- Recurrence rate is 20-40% 1 month after therapy
- Recurrence may be a result of persistence of BV-associated organisms and failure of lactobacillus flora to colonize
- Data do not support yogurt therapy or exogenous oral lactobacillus treatment
- Under study: vaginal suppositories containing human lactobacillus strains
- Twice weekly metronidazole gel for 6 months may reduce recurrences

**BV: Prevention ??**

**Vaginitis**

**Vulvovaginal Candidiasis** *(VVC)*

**QUESTION #8**

VAGINAL CANDIDIASIS IS CHARACTERIZED BY

A. WHITE CELLS
B. FOUL ODOR
C. THIN, HOMOGENEOUS CONSISTENCY
D. INTENSE ITCHING
QUESTION #9

Approximately 90% of vaginal “yeast” infections are caused by
A. Candida albicans
B. Candida tropicalis
C. Candida glabrata
D. Torulopsis glabrata

CANDIDA VAGINITIS

- 2ND MOST COMMON CAUSE OF VAGINITIS
- 75% OF WOMEN WILL HAVE AT LEAST ONE EPISODE IN LIFE
- 40-50% HAVE 2 OR MORE INFECTIONS IN LIFE
- 5% HAVE CHRONIC RECURRENT C. VAGINITIS

- 75-85% CANDIDA ABLICANS
- 5-25% C. GLABRATA or C. TROPICALIS
- HYphae associated with tissue invasion
- Candida Virulence: Adheres to vaginal epithelial cell
  Estrogen enhances vag epithelial cell avidity for Candida adherence

CLINICALLY IMPORTANT CANDIDA PATHOGENS IN HUMANS

- C. albicans
- C. guilliermondii
- C. krusei
- C. parapsilosis
- C. tropicalis
- C. pseudotropicalis
- C. lusitaniae
- C. rugosa
- C. glabrata (also classified as Torulopsis glabrata)

RISK FACTORS FOR VULVOVAGINAL CANDIDIASIS

- **Predisposing conditions**
  - Pregnancy, especially 3rd trimester
  - Diabetes mellitus (poorly controlled)
  - Cushing's disease
  - Addison's disease
  - Hypo- or hyperthyroidism
  - Debilitating disease
  - AIDS or HIV infection
  - Vaginal trauma

- **Predisposing Practices**
  - High-estrogen medical usage
  - Antibiotic usage
  - Hormone usage
  - Radiotherapy or chemotherapy
  - Immunosuppressive drug usage
  - Cytotoxic drug usage
  - Frequent, traumatic sexual intercourse
  - Wearing of tight clothing or nylon underwear
  - Use of certain contraceptive devices (IUD or diaphragm/contr. Jelly
  - Ingestion of large amounts of candy
Clinical Presentation and Symptoms
- Vulvar pruritis is most common symptom
- Thick, white, curdy vaginal discharge ("cottage cheese-like")
- Erythema, irritation, occasional erythematous "satellite" lesion
- External dysuria and dyspareunia

Vulvovaginal Candidiasis

Candidiasis Diagnosis
- History, signs and symptoms
- Visualization of pseudohyphae (mycelia) and/or budding yeast (conidia) on KOH or saline wet prep
- pH normal (4.0 to 4.5)
  - If pH > 4.5, consider concurrent BV or trichomoniasis infection
- Cultures not useful for routine diagnosis

PMNs and Yeast Pseudohyphae
- Saline: 40X objective
- Yeast pseudohyphae
- Yeast buds
- Squamous epithelial cells

Yeast Pseudohyphae
- 10% KOH: 10X objective
- Lysed squamous epithelial cell
- Masses of yeast pseudohyphae
PMNs and Yeast Buds

Saline: 40X objective

Folded squamous epithelial cells

PMNs

Yeast buds

Source: Seattle STD/HIV Prevention Training Center at the University of Washington

VULVOVAGINAL CANDIDIASIS

• Cottage cheese ("curd like") appearance of vaginal discharge is typical of vulvovaginitis due to yeast.

VULVOVAGINAL CANDIDIASIS

• Mycelial tangles of yeast pseudohyphae in KOH wet mount preparation.

Candidiasis:
Patient Management
THERAPY: V.V. CANDIDIASIS

• TOPICAL
  - NYSTATIN (POLYENE)
  - AZOLES

• SYSTEMIC
  - FLUCONAZOLE (Diflucan)
  - KETOCONAZOLE

Classification of VVC

Uncomplicated VVC
- Sporadic or infrequent vulvovaginal candidiasis
  Or
- Mild-to-moderate vulvovaginal candidiasis
  Or
- Likely to be C. albicans
  Or
- Non-immunocompromised women

Complicated VVC
- Recurrent vulvovaginal candidiasis (RVVC)
  Or
- Severe vulvovaginal candidiasis
  Or
- Non-albicans candidiasis
  Or
- Women with uncontrolled diabetes, debilitation, or immunosuppression or those who are pregnant

Uncomplicated VVC
- Mild to moderate signs and symptoms
- Non-recurrent
- 75% of women have at least one episode
- Responds to short course regimen

CDC-Recommended Treatment Regimens

• Intravaginal agents:
  - Butoconazole 2% cream, 5 g intravaginally for 3 days†
  - Butoconazole 2% sustained release cream, 5 g single intravaginally application
  - Clotrimazole 1% cream 5 g intravaginally for 7--14 days†
  - Clotrimazole 100 mg vaginal tablet for 7 days
  - Clotrimazole 100 mg vaginal tablet, 2 tablets for 3 days
  - Miconazole 2% cream 5 g intravaginally for 7 days
  - Miconazole 100 mg vaginal suppository, 1 suppository for 7 days
  - Miconazole 200 mg vaginal suppository, 1 suppository for 3 days
  - Miconazole 1,200 mg vaginal suppository, single suppository for 1 day
  - Nystatin 100,000 unit vaginal tablet, 1 tablet for 14 days†
  - Tioconazole 6.5% ointment 5 g intravaginally in a single application†
  - Terconazole 0.4% cream 5 g intravaginally for 7 days
  - Terconazole 80 mg vaginal suppository, 1 suppository for 3 days
  - Fluconazole 150 mg oral tablet, 1 tablet in a single dose

Note: The creams and suppositories in these regimens are oil-based and may weaken latex condoms and diaphragms. Refer to condom product labeling for further information.
† Over-the-counter (OTC) preparations.

Complicated VVC
- Recurrent (RVVC)
  - Four or more episodes in one year
  - Severe
    - Edema
    - Excoriation/fissure formation
  - Non-albicans candidiasis
  - Compromised host
  - Pregnancy

Complicated VVC Treatment

• Recurrent VVC (RVVC)
  - 7-14 days of topical therapy, or
  - 100mg,150 mg , or 200mg oral dose of fluconazole repeated 3 days later
  - Maintenance regimens (see CDC STD treatment guidelines)

• Severe VVC
  - 7-14 days of topical therapy, or
  - 150 mg oral dose of fluconazole repeated in 72 hours
Complicated VVC Treatment (continued)

- Non-albicans
  - Optimal treatment unknown
  - 7-14 days non-fluconazole therapy
  - 600 mg boric acid in gelatin capsule vaginally once a day for 14 days for recurrences
- Compromised host
  - 7-14 days of topical therapy
- Pregnancy
  - Fluconazole is contraindicated
  - 7-day topical agents are recommended

CANDIDIASIS: Prevention

Over the Counter Treatment for Candidiasis
An opportunity to educate

VULVOVAGINAL CANDIDIASIS
Failure of Traditional therapy Suggests the Following Possibilities

1. Candidiasis is not the true cause of the patient's symptoms
2. A resistant non albicans strain may be present
3. The patient's persisting symptoms (and susceptibility to Candida) may be due to an irritant reaction to the topical agent
4. The patient may have truly recurrent candidiasis due to immunocompromise
**RECURRENT VULVOVAGINAL CANDIDIASIS**

- Recurrent vulvovaginal candidiasis is defined as four or more mycologically confirmed episodes of symptomatic VVC within 1 year.
- RVVC occurs in approximately 5% of patients.
- **Treatment:**
  - Weekly suppressive dose of topical imidazoles
  - Weekly oral fluconazole (150 mg)
  - Boric acid (600 mg vaginal gelatin capsules) three times daily for 1 week

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**VAGINITIS**

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**THE END**

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**Case Study: VAGINITIS**

**History**

**Tanya Walters**

- 24-year-old single female
- Presents with complaints of a smelly, yellow vaginal discharge and slight dysuria for 1 week
- Denies vulvar itching, pelvic pain, or fever
- No history of sexually transmitted diseases, except for trichomoniasis 1 year ago
- Last check up 1 year ago

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**Physical Exam**

- Vital signs: blood pressure 112/78, pulse 72, respiration 15, temperature 37.3°C
- Cooperative, good historian
- Chest, heart, breast, musculoskeletal, and abdominal exams within normal limits
- No flank pain on percussion
- Normal external genitalia with a few excoriations near the introitus, but no other lesions
- Speculum exam reveals a moderate amount of frothy, yellowish, malodorous discharge, without visible cervical mucopus or easily induced cervical bleeding
- Bimanual examination was normal without uterine or adnexal tenderness

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**Questions**

1. What is your differential diagnosis based on history and physical examination?
2. Based on the differential diagnosis of vaginitis, what is the etiology?
3. Which laboratory tests should be offered or performed?
Laboratory Results

- Vaginal pH -- 6.0
- Saline wet mount of vaginal secretions -- numerous motile trichomonads and no clue cells
- KOH wet mount -- negative for budding yeast and hyphae

4. What may one reasonably conclude about Tanya's diagnosis?
5. What is the appropriate CDC-recommended treatment for this patient?

Partner Management

Jamie
- Last sexual contact: 2 days ago
- First sexual contact: 2 months ago
- Twice a week, vaginal sex

Calvin
- Last sexual contact: 6 months ago
- First sexual contact: 7 months ago
- 3 times a week, vaginal and oral sex

6. How should Jamie and Calvin be managed?

Follow-Up

- Tanya was prescribed metronidazole 2 g orally, and was instructed to abstain from sexual intercourse until her partner was treated.
- She returned two weeks later. She reported taking her medication, but had persistent vaginal discharge that had not subsided with treatment. She reported abstinence since her clinic visit, and her partner had moved out of the area. Her tests for chlamydia and gonorrhea were negative.
- The vaginal wet mount again revealed motile trichomonads.

7. What is the appropriate therapy for Tanya now?
8. What are appropriate prevention recommendations for Tanya?

Desquamative inflammatory vaginitis (DIV)

- An uncommon clinical syndrome,
- Features
  - a purulent vaginal discharge,
  - vulvovaginal burning or irritation, and
  - dyspareunia

DIV: CLINICAL PRESENTATION

- Diffuse vulvovaginal erythema is apparent in most patients.
- The vaginal pH is elevated and
- Microscopy reveals leukorrhea and parabasal epithelial cells.
- The whiff test is negative.
- DIV is clinically indistinguishable from atrophic vaginitis with resulting bacterial infection, except that it fails to respond to topical estrogen therapy.
DIV

• SYMPTOMS:
  - Discharge,
  - Vulvar burning, irritation,
  - Dysparunia.

• EXAM:
  - Normal vulva (mucosa and skin),
  - dripping thin yellowish discharge at introitus
  - petechial redness on vaginal walls.

Clinically, the diagnosis of DIV is rendered in patients who complain of increased vaginal discharge and pain with intercourse when no identifiable cause of vaginitis can be identified. Because postmenopausal atrophic vaginitis may have similar presentation.

DIV

• Examination of the vulva is often normal,
• discharge of variable consistency may be present.
• Speculum examination may reveal
  • synechiae,
  • vaginal stenosis,
  • and most commonly, erythema.
• Stroking the vaginal walls with a cotton swab is commonly associated with an intense burning sensation.
• Generally, histology shows nonspecific inflammation.
• Because DIV patients present with nonspecific symptoms of burning and pain, and because cursory examinations reveal limited clinical findings, it is important to conduct a detailed assessment of the vaginal wall and to specifically look for erythema and mechanical allodynia (burning sensation on stroking of the vaginal wall with a q-tip).

DIV: TREATMENT

• Topical clindamycin (2% vaginal cream, one applicator per vagina before bedtime for 14 days) has been successful,
• However, topical estrogen can prevent relapse.
• Retreatment is common in up to 30% of women with DIV.

VAGINITIS: Noninfectious causes

• Normal vaginal secretions are characterized by a vaginal pH <4.5, epithelial cells with crisp cell borders, and a lactobacilli–predominant vaginal flora. Given that most patients seek out a physician to garner a prescription, a clinician must have considerable confidence in his or her microscopy skills to forgo empiric therapy without lab testing confirming the diagnosis.
• However, no infectious cause of lower genital tract symptoms is found in up to 30% of cases.
• Empiric therapy in these cases is neither cost effective nor prudent.

Vaginitis:
2010
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(electronic version available on request)
Genital and Perirectal Herpes Simplex Virus Infection

Herpes Simplex Virus (HSV) Type 2

Background and Burden of Disease

• Genital herpes is a chronic, lifelong viral infection
• Two HSV serotypes – HSV-1 & HSV-2
• HSV-2 causes the majority of cases of recurrent genital herpes in the U.S.
• Approximately 1 million new cases occur each year

Background and Burden of Disease (continued)

• In the U.S., 17% of adults aged 14-49 years have HSV-2 antibodies
• HSV-2 antibodies are not routinely detected until puberty
• HSV-2 seroprevalence is higher in women than men in all age groups and varies by race/ethnicity

Transmission

• HSV-2 is transmitted sexually and perinatally
• Majority of genital herpes infections are transmitted by persons who are
  – unaware they are infected with HSV-2 or
  – asymptomatic when transmission occurs
• Efficiency of sexual transmission is greater from men to women than from women to men

Transmission (continued)

• Likelihood of transmission declines with increased duration of infection
• Incubation period after acquisition is 2-12 days (average is 4 days)
• Drying and soap and water readily inactivate HSV; fomite transmission unlikely

HSV-2 and HIV Infection

• HSV-2 infection increases the risk of acquiring HIV infection at least 2 fold
• HSV-2 infection is also likely to facilitate transmission of HIV infection from persons co-infected with both viruses
Virology

• HSV-1 and HSV-2 are members of the human herpes viruses (herpetoviridae)
• All members of this species establish latent infection in specific target cells
• Infection persists despite the host immune response, often with recurrent disease

Pathology

• The virus remains latent indefinitely
• Reactivation is precipitated by multiple known and unknown factors and induces viral replication
• The re-activated virus may cause a cutaneous outbreak of herpetic lesions or subclinical viral shedding
• Up to 90% of persons seropositive for HSV-2 antibody have not been diagnosed with genital herpes

Definitions of Infection Types

First Clinical Episode
• **Primary infection**
  – First infection ever with either HSV-1 or HSV-2
  – No antibody present when symptoms appear
  – Disease is more severe than recurrent disease
• **Non-primary infection**
  – Newly acquired HSV-1 or HSV-2 infection in an individual previously seropositive to the other virus
  – Symptoms usually milder than primary infection
  – Antibody to new infection may take several weeks to a few months to appear

<table>
<thead>
<tr>
<th>Infection Type</th>
<th>Lesions/ Symptoms</th>
<th>Type-specific antibody at time of presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>HSV-1</td>
<td>HSV-2</td>
<td></td>
</tr>
<tr>
<td>First episode, Primary (Type 1 or 2)</td>
<td>+/Severe, bilateral</td>
<td>-</td>
</tr>
<tr>
<td>First episode, Non-primary Type 2</td>
<td>+/Moderate</td>
<td>+</td>
</tr>
<tr>
<td>First episode, Recurrence Type 2</td>
<td>+/Mild</td>
<td>+/-</td>
</tr>
<tr>
<td>Symptomatic, Recurrence Type 2</td>
<td>+/Mild, unilateral</td>
<td>+/-</td>
</tr>
<tr>
<td>Asymptomatic, Infection Type 2</td>
<td>-</td>
<td>+/-</td>
</tr>
</tbody>
</table>
First Episode Primary Infection without Treatment

- Characterized by multiple lesions that are more severe, last longer, and have higher titers of virus than recurrent infections
- Typical lesion progression:
  - papules → vesicles → pustules → ulcers → crusts → healed
- Often associated with systemic symptoms including fever, headache, malaise, and myalgia
- Illness lasts 2-4 weeks

Clinical Manifestations

1. Typical lesion progression:
   - papules → vesicles → pustules → ulcers → crusts → healed

2. Often associated with systemic symptoms including fever, headache, malaise, and myalgia

3. Illness lasts 2-4 weeks

Asymptomatic Viral Shedding

1. Most common sites of asymptomatic shedding are vulva and perianal areas in women and penile skin and perianal area in men
2. Antiviral suppressive therapy dramatically reduces, but does not eradicate shedding

Complications of Genital Infection

1. Aseptic meningitis
   - More common in primary than recurrent infection
   - Generally no neurological sequelae
2. Rare complications include:
   - Stomatitis and pharyngitis
   - Radicular pain, sacral parathesias
   - Transverse myelitis
   - Autonomic dysfunction
HSV Diagnosis

- **Clinical diagnosis** is insensitive and nonspecific
- Clinical diagnosis should be confirmed by **laboratory testing**:
  - Virologic tests
  - Type-specific serologic tests

Virologic Tests

- **Viral culture** (gold standard)
  - Preferred test if genital ulcers or other mucocutaneous lesions are present
  - Highly specific (>99%) for HSV-1
  - Sensitivity depends on stage of lesion; declines rapidly as lesions begin to heal
  - Positive more often in primary infection (80%-90%) than with recurrences (30%)
  - Cultures should be typed
- **Polymerase Chain Reaction (PCR)**
  - More sensitive than viral culture; has been used instead of culture in some settings; however PCR tests are not FDA-cleared or widely available
  - Preferred test for detecting HSV in spinal fluid

Virologic Tests (continued)

- **Antigen detection** (DFA or EIA)
  - Fairly sensitive (>85%) in symptomatic shedders
  - Rapid (2-12 hours)
  - May be better than culture for detecting HSV in healing lesions
- **Cytology** (Tzanck or Pap)
  - Insensitive and nonspecific and should not be relied on for HSV diagnosis

Type-specific Serologic Tests

- Type-specific and nonspecific antibodies to HSV develop during the first several weeks to few months following infection and persist indefinitely
- Presence of HSV-2 antibody indicates anogenital infection
- Presence of HSV-1 does not distinguish anogenital from orolabial infection

Uses of Type-specific Serologic Tests

- Type-specific serologic assays might be useful in the following scenarios:
  - Recurrent or atypical genital symptoms with negative HSV cultures
  - A clinical diagnosis of genital herpes without laboratory confirmation
  - A sex partner with herpes
  - As part of a comprehensive evaluation for STDs among persons with multiple sex partners, HIV infection, and among MSM at increased risk for HIV acquisition

Evaluation of Genital Ulcer

- All patients with genital ulcers should be evaluated with a serologic test for syphilis and a diagnostic evaluation for genital herpes
- In settings where chancroid is prevalent, a test for *Haemophilus ducreyi* should also be performed
Principles of Management of Genital Herpes

• Counseling should include natural history, sexual and perinatal transmission, and methods to reduce transmission
• Antiviral chemotherapy
  – Partially controls symptoms of herpes
  – Does not eradicate latent virus
  – Does not affect risk, frequency or severity of recurrences after drug is discontinued

Antiviral Medications

• Systemic antiviral chemotherapy includes 3 oral medications:
  – Acyclovir
  – Valacyclovir
  – Famciclovir
• Topical antiviral treatment is not recommended

Management of First Clinical Episode of Genital Herpes

• Manifestations of first clinical episode may become severe or prolonged
• Antiviral therapy should be used
  – Dramatic effect, especially if symptoms <7 days and primary infection (no prior HSV-1)

CDC-Recommended Regimens for First Clinical Episode

• Acyclovir 400 mg orally 3 times a day for 7-10 days, or
• Acyclovir 200 mg orally 5 times a day for 7-10 days, or
• Famciclovir 250 mg orally 3 times a day for 7-10 days, or
• Valacyclovir 1 g orally twice a day for 7-10 days

Suppressive Therapy for Recurrent Genital Herpes

• Reduces frequency of recurrences
  – By 70%-80% in patients with > 6 recurrences per year
  – Also effective in those with less frequent recurrences
• Reduces but does not eliminate subclinical viral shedding
• Periodically (e.g., once a year), reassess need for continued suppressive therapy

Recurrent Episodes of Genital Herpes

• Most patients with symptomatic, first-episode genital HSV-2 experience recurrent outbreaks
• Episodic and suppressive treatment regimens are available
• Treatment options should be discussed with ALL patients
CDC-Recommended Regimens

### For Suppressive Therapy
- Acyclovir 400 mg orally twice a day, or
- Famciclovir 250 mg orally twice a day, or
- Valacyclovir 500 mg orally once a day, or
- Valacyclovir 1 g orally once a day

### Episodic Treatment for Recurrent Genital Herpes
- Ameliorates or shortens duration of lesions
- Requires initiation of therapy within 1 day of lesion onset
- Provide patient with a supply of drug or a prescription and instructions to self-initiate treatment immediately when symptoms begin

### For Episodic Therapy
- Acyclovir 400 mg orally 3 times a day for 5 days, or
- Acyclovir 800 mg orally twice a day for 5 days, or
- Acyclovir 800 mg orally 3 times a day for 2 days, or
- Famciclovir 125 mg orally twice a day for 5 days, or
- Famciclovir 1000 mg orally twice a day for 1 day, or
- Valacyclovir 500 mg orally twice a day for 3 days, or
- Valacyclovir 1 g orally once a day for 5 days

### Severe Disease
- IV acyclovir should be provided for patients with severe disease or complications requiring hospitalization
- CDC-Recommended Regimen:
  - Acyclovir 5-10 mg/kg IV every 8 hours for 2-7 days or until clinical improvement
  - Follow with oral antiviral therapy to complete at least 10 days total therapy

### Herpes in HIV-Infected Persons
- HIV-infected persons may have prolonged, severe, or atypical episodes of genital, perianal, or oral herpes
- HSV shedding is increased in HIV-infected persons

### Allergy, Intolerance, and Adverse Reactions
- Allergic and other adverse reactions to acyclovir, valacyclovir, and famciclovir are rare
- Desensitization to acyclovir is described by Henry RE, et al., Successful oral acyclovir desensitization. Ann Allergy 1993; 70:386-8
CDC-Recommended Regimens for Daily Suppressive Therapy in HIV-Infected Persons

- Acyclovir 400-800 mg orally twice a day or three times a day, or
- Famciclovir 500 mg orally twice a day, or
- Valacyclovir 500 mg orally twice a day

Genital Herpes in Pregnancy

- Majority of mothers of infants who acquire neonatal herpes lack histories of clinically evident genital herpes
- Risk for transmission to neonate is high (30%-50%) among women who acquire genital herpes near the time of delivery
- Risk is low (<1%) in women with histories of recurrent herpes at term or who acquire genital HSV during the first half of pregnancy

Genital Herpes in Pregnancy (continued)

- At the onset of labor:
  - All women should be questioned carefully about symptoms of genital herpes, including prodromal
  - All women should be examined carefully for herpetic lesions
  - Women without symptoms or signs of genital herpes or its prodrome can deliver vaginally

CDC-Recommended Regimens for Episodic Infection in HIV-Infected Persons

- Acyclovir 400 mg orally 3 times a day for 5-10 days, or
- Famciclovir 500 mg orally twice a day for 5-10 days, or
- Valacyclovir 1 g orally twice a day for 5-10 days

Genital Herpes in Pregnancy (continued)

- Prevention of neonatal herpes depends on:
  ✓ avoiding acquisition of HSV during late pregnancy
  ✓ avoiding exposure of the infant to herpetic lesions during delivery
  ✓ All pregnant women should be asked whether they have a history of genital herpes

Genital Herpes in Pregnancy (continued)

- Safety of acyclovir, valacyclovir, famciclovir in pregnancy not definitively established, but no clear evidence for increased birth defects
- Oral acyclovir may be given for first-episode or severe recurrent herpes; IV acyclovir should be used for severe infection
- Suppressive acyclovir late in pregnancy reduces frequency of cesarean sections in women with recurrent genital herpes; many specialists recommend it
Patient Counseling and Education

- Goals
  - Help patients cope with the infection
  - Prevent sexual and perinatal transmission
- Counsel initially at first visit
- Education on chronic aspects may be beneficial after acute illness subsides
- HSV-infected persons may express anxiety about genital herpes that does not reflect the actual clinical severity of their disease

Counseling: Natural History

- Recurrent episodes likely following a first episode; with HSV-2 more than HSV-1
  - Frequency of outbreaks may decrease over time
  - Stressful events may trigger recurrences
  - Prodromal symptoms may precede outbreaks
- Asymptomatic viral shedding is common and HSV transmission can occur during asymptomatic periods

Counseling: Transmission and Prevention

- Inform current and future sex partners about genital herpes diagnosis
- Abstain from sexual activity with uninfected partners when lesions or prodrome present
- Correct and consistent use of latex condoms might reduce the risk of HSV transmission
- Valacyclovir suppressive therapy decreases HSV-2 transmission in heterosexual couples in which source partner has recurrent herpes
Counseling: Neonatal Herpes Prevention

- Risk of neonatal HSV infection should be explained to all patients, including men
- Pregnant women should inform their prenatal/perinatal providers that they have genital herpes
- Pregnant women without HSV-2 infection should avoid intercourse during third trimester with men who have genital herpes
- Pregnant women without HSV-1 infection should avoid oral sex from a partner with oral herpes

Counseling for Asymptomatic Persons

- Give asymptomatic persons diagnosed with HSV-2 infection the same counseling messages as symptomatic persons
- Teach the common manifestations of genital herpes, as many patients will become aware of them with time

Partner Management

- Symptomatic sex partners
  - Evaluate and treat in the same manner as patients who have genital lesions
- Asymptomatic sex partners
  - Ask about history of genital lesions
  - Educate to recognize symptoms of herpes
  - Offer type-specific serologic testing

Questions

8. What questions should be asked of ALL women beginning labor?
9. If Roberta has genital herpetic lesions at the onset of labor, should she deliver vaginally or abdominally? What is the risk to the infant?

Questions

10. Roberta is asymptomatic at the time of delivery. Is it medically appropriate for her to deliver vaginally?
11. If Roberta had acquired genital herpes around the time of delivery, would she be more or less likely to transmit genital herpes to her baby during a vaginal delivery than if she had a history of recurrent genital herpes?

HSV: 2010

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