Vaginitis

Dr Evelyn Yeo

21st June 2015
Vaginitis

• Vaginitis is the most common reason why women attend gynaecological or STD clinics.

• **Bacterial vaginosis, vulvovaginal candidiasis & trichomoniasis** are the 3 most frequent vaginitis worldwide.
Epidemiology

Bacterial Vaginosis

- Reported prevalence vary based on the population studied
- Bacterial vaginosis has been found in
  - 15–19% of ambulatory gynaecology patients
  - 10–30% of pregnant women
  - 24–40% of patients with sexually transmitted disease

Candidiasis

- An estimated 75% of women have vulvovaginal candidiasis at some time in life, and approximately 5% of women have recurrent episodes

Trichomoniasis

- The third most common cause of vaginitis
- Currently accounts for 10–25% of vaginal infections
- Transmitted sexually and may be identified in 30–80% of male sexual partners of infected women

Vaginitis

• Although anti-infective Rx is available & usually highly efficient in eradicating the pathogenic microorganisms, the long term efficiency is hampered by relapses.
Recurrent vaginitis

• To understand the Rx failures frequently occurring in vaginal infections, we must look at the **vaginal ecosystem** in healthy state and in disease state.
(Risk factors for vaginitis)

Complex interactions between host and microbes as well as among microbial species

<table>
<thead>
<tr>
<th>Endogenous factors</th>
<th>Exogenous factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hormone level variations</td>
<td>Anti-infective therapy</td>
</tr>
<tr>
<td>Menstruation</td>
<td>Incorrect personal hygiene</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Synthetic underwear</td>
</tr>
<tr>
<td>Lactation</td>
<td>Stress, anxiety</td>
</tr>
<tr>
<td>Glycogen deposition</td>
<td>Chlorine water</td>
</tr>
<tr>
<td>Competition among microorganisms</td>
<td>Unprotected sex (sperm)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>Contraception</td>
</tr>
<tr>
<td>Other serious systemic disorders</td>
<td>Immunosuppression</td>
</tr>
<tr>
<td></td>
<td>Surgery / Radiation therapy</td>
</tr>
</tbody>
</table>
Vaginal Epithelium

- Stratified squamous epithelium consisting of basal, parabasal, intermediate and superficial cells
- Proliferation, maturation and desquamation depending on hormone levels
Vaginal ecosystem

- Superficial cells
- Intermediate cells
- Parabasal cells
- Basal cells

Mucosa

pH < 4.5
Estrogen

• Estriol (E3)
  – short-acting estrogen
  – fully vaginotrophic response
  – no uterotrophic effects

• Estradiol, Estrone
  – long-acting estrogen
  – fully vaginotrophic and uterotrophic response

⇒ Proliferation and maturation of the vaginal epithelium
⇒ Deposition of glycogen in the vaginal epithelium
Vaginal ecosystem and estrogen

A well-balanced hormonal status provides sufficient estrogen levels to:

- Ensure the *proliferation & maturation* of the vaginal *epithelium*.

- Provide an adequate supply of *glycogen* as nourishment for the lactobacilli.
Age Dependent Effects
Vaginal Microflora

• Complex array of bacterial species
• The normal microflora is dominated by lactobacilli
• Predominant species: *L. acidophilus, L. jensenii, L. crispatus*
• $10^7$ to $10^8$ cfu/g of vaginal fluid
Lactobacilli

- Production of lactic acid from glycogen
  ➜ acidification of the vaginal milieu, low pH
- Production of hydrogen peroxide and bacteriocins
  ➜ antimicrobial activity
- Adherence to vaginal epithelial cells
  ➜ inhibition of pathogen adherence
Vaginitis

Vaginal infections are usually accompanied with:

- **Diminished** number of lactobacilli,
- **Overgrowth** of pathogens, &
- A more or less **damaged vaginal epithelium**
Recurrent vaginitis

• **Anti-infective Rx** further lowers the number of **lactobacilli** dependent on the type & duration of the Rx used.

• Even the antifungal agent **clotrimazole** has been shown to **alter the vaginal microflora** & was reported as **bactericidal** against lactobacilli & streptococci in vitro.
Disturbed vaginal epithelium: Infections

- Bacterial vaginosis
- Candidiasis
- Trichomoniasis
Disturbed Vaginal Ecosystem

- Intermediate cells
- Parabasal cells
- Basal cells
- Pathogens

Bacterial vaginosis

Aerobic vaginitis
Atrophic vaginitis

pH > 4.5

pH > 5.0
Recurrent infections

- Restoration of a **protective healthy microflora** & parallel restitution of a **well-proliferated vaginal epithelium** is necessary to avoid recurrent or re-infections
Vaginal Infection
Normal Vaginal Milieu

• In normal, healthy women with a **Lactobacillus-dominated flora**, the vaginal milieu is more **aerobic**.

• These **lactobacilli** are able to **inhibit** the growth of facultative **pathogenic microorganisms**, including Gardnerella, Chlamydia, Gonococcus, Gram –ves (e.g. E. Coli), Gram +ves (e.g. Group A Strep) by producing **lactic acid, hydrogen peroxide & bacteriocins**
Bacterial vaginosis

• In BV, the normal microflora of the vagina is replaced by *Gardnerella vaginalis* (anaerobic bacteria), other anaerobic microorganisms, or *mycoplasma* hominis.

• *Gardnerella vaginalis* is the most common pathogen, isolated from 92% women affected with BV (which actually cause the bad odor & discharge)

• This pathogen is reported to be present in 96% males sexually involved with BV affected females.

• The most important condition predisposing a woman to BV is the lack of proteolytic vaginal lactobacilli.
Bacterial vaginosis

- "Vaginosis" stresses the fact that, in contrast to a vaginitis, BV generally does not involve acute inflammatory processes.

- No polymorphonuclear leukocytes in the vaginal flora.

- Reduction or absence of lactobacilli in vaginal flora
Microbial Shifts Occurring in BV

- BV is characterized by a 100- to 1,000-fold increase in pathogenic bacteria. Lactobacilli concentrations decrease substantially.

- Ecological disorder
  - G. Vaginalis
  - Anaerobes
  - Mycoplasmas

- 10^{11}
- 10^4

- No Leucocytes
- No pain, no itch, no dyspareunia
- No redness nor edema of the vagina

---

- NO INFLAMMATION in BV!!

---

- BV is characterized by 100- to 1,000-fold increase in pathogenic bacteria. Lactobacilli concentrations decrease substantially. = **Ecological disorder**
Bacterial vaginosis

Microscopic analysis:

• **BV +ve**: < 6 lactobacilli per field of view, 1000x magnification

• **Intermediate cases**: 6-30 lactobacilli per field of view, 1000x magnification

• **BV –ve**: > 30 lactobacilli per field of view, 1000x magnification
Bacterial vaginosis

Diagnosis

Clinical criteria according to Amsel: 3 out of 4

<table>
<thead>
<tr>
<th></th>
<th>Homogenous grey watery discharge</th>
<th>Fishy smell (10%KOH)</th>
<th>pH &gt; 4.5</th>
<th>Clue cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Bacteria Vaginosis Discharge
Bacterial vaginosis

The objectives of the Rx of BV are:

- To **eliminate** the vast numbers of overgrown *BV-associated* microorganisms

- To **re-establish** a normal, healthy vaginal flora which is dominated by *lactobacilli*. 
Bacterial vaginosis

• Rx of BV with first line medication (metronidazole, clindamycin) achieves high clinical cure rate of 85-90 %

• However, persistent abnormalities in the vaginal flora & late recurrences, despite apparently successful initial Rx, are common problems
Candida Vaginitis

• Vuvlovaginal candidiasis is second most common cause of vaginitis, after bacterial vaginosis.¹

• Often caused by *Candida albicans*, other species may also be involved.¹

• About 50% of asymptomatic women have candidal organisms as part of their endogenous vaginal flora.²

Recently, the frequency of non-albicans species (e.g., *Candida glabrata*) has increased, possibly secondary to greater use of over-the-counter antifungal products.²

Candida Vaginitis

• When the ecosystem of the vagina is disturbed, *C. albicans* becomes an *opportunistic* pathogen.

• *Lactobacilli inhibit* the growth of fungi in the vagina.

• When the relative concentration of lactobacilli declines, rapid overgrowth of *Candida* species occurs.

• Following the traditional 10-14 days of PO *broad-spectrum antibiotics*, the % of women who have vaginal colonization with *Candida* ↑3-fold.
Candida Vaginitis

• **Hormonal factors** (pregnancy & menstruation), **depressed immunity** (exogenous steroids, AIDS, DM), & **antibiotic use** (broad spectrum, esp those destroy lactobacilli: penicillin, tetracycline, cepharosporins) are the 3 most important factors that **enhance growth of candida**

• Presently, with low-dose estrogen OCP, there is no ↑ in the incidence of fungal vaginitis
Candida Vaginitis

• Vaginal candidiasis often becomes symptomatic following successful Rx of Trichomonas or bacterial vaginosis

• No direct relationship between the number of organisms & the patient’s signs & symptoms.
Incidence of Vulvovaginal Candidosis

Candida Vaginitis

• The **filamentous** forms of *C. albicans* have the ability to **penetrate the mucosal surface** & become intertwined with the host cells. This results in secondary **hyperemia** & limited **lysis of tissue** near the site of infection.
Candidiasis

Diagnosis:
Typical signs & symptoms:

• white non-watery, curdy discharge,
• pruritus,
• vulvar burning +/- external dysuria,
• dyspareunia,
• redness of the vulva/vagina, vulvar edema, excoriation +/- pustules
**Candida Vaginitis**

- **Speculum examination:** cottage cheese-type discharge is often visualized with adherent white or yellow clumps & plaques (thrush patches) attached to the vaginal walls

- **Vaginal pH < 4.5**

- Presence of Candida species in the *wet smears* & the growth of microbial *culture*

- A negative smear does not exclude Candida vulvovaginitis
Candida Vaginitis

• The Rx of choice is the **topical** (suppositories or creams) application of one of the synthetic **imidazoles** or one of the **triazoles** or **oral fluconazole** (single oral tablet of 150mg stat – CDC recommends that fluconazole Rx should be reserved for refractory or resistant cases)

• They exert their action by **changing the permeability** of the surface membrane of the fungus
Candida Vaginitis

• The newer 3-day or 1-day Rx is less expansive & provides improved patient compliance

• Symptoms **cure rates** are >90%

• Before the introduction of synthetic **imidazoles**, nystatin were the standard Rx (10-14 days, clinical cure rates of ~80%)
Candida Vaginitis

- Is not considered a STD
- 10% of male partners have concomitant symptomatic penile infection
- Rx of the male partners & elimination of Candida species from the gastrointestinal tract do not reduce the recurrence rate
- Recurrence rate after an apparent cure varying from 20% to 80%
Recurrent Candida Vaginitis

- Often difficult to distinguish a relapse from a reinfection

- It is important first to confirm that the woman’s symptoms are not the result of drug sensitivity

- Should screen for DM

- Vaginal discharge should be cultured & the identity of the fungus species determined (2-fold rate of recurrence with *C. tropicalis* because it is not as susceptible to the imidazoles as *C. albicans*, Similarly *C. glabrata* infections are often resistant to imidazoles)
Recurrent Candida Vaginitis

- Seen multiple specialists
  - Family doctor
  - Several gynecologists
  - Dermatologist
  - Infectious disease specialists

- Self medication: over the counter

- Alternative medicine, internet advice

- Incurable, lost self esteem, poor sex life
Recurrent Candida Vaginitis

- is a **chronic illness**

- **Treatment** = **suppressive therapy**
  - long term
  - prophylactic (even without symptoms)
  - under strict medical guidance
  - individualised

- Different education of Patient / change attitude of Physician
Recurrent Candida Vaginitis

• Provide patient with enough medication to self Rx at the first suggestion of recurrent symptoms or signs

• Prophylactic Rx either immediately before or after menses or at the first sign of recurrence is often beneficial
Trichomoniasis

- **Trichomonas vaginalis** is an anaerobic, flagellated unicellular protozoon that inhabits the vagina & lower urinary tract (resides in the paraurethral glands of both the male and female)

- = the most prevalent nonviral, nonchlamydial STD of women

- Can survive for up to 24hrs on a wet towel & up to 6 hrs on a surface
Trichomoniasis

- Studies have established that successful vaginal infection depends on the deposition of an inoculum of several thousands organisms.

- Thus it is unlikely that infection may be related to exposure from infected towels or swimming pools.

- Trichomonas vaginitis is a disease primarily of women in the reproductive years.
Trichomoniasis

Diagnosis:

- Many are asymptomatic. 50% c/o profuse malodorous, yellowish grey vaginal discharge, 25% c/o vulvar pruritus, 20% c/o dysuria.

- The classic “frothy” (w bubbles) discharge is only present in 10-25% of cases. This discharge is not diagnostic!
Trichomoniasis

• The vulva and vagina have erythema & oedema

• The classic sign of strawberry appearance of the upper vagina & cervix is rare (noted in <10% of cases)

• Vulvar skin involvement is limited to the vestibule & labia minora
Trichomoniasis

• When lactobacilli predominate in the vaginal fluid, a woman will not develop symptoms

• However, menstrual blood, semen or other vaginal pathogens that transform the vaginal pH to a more basic level favor the growth of Trichomonas organisms

• The **vaginal pH** associated with *T. vaginalis* is between **5.0 & 7.0**
Trichomoniasis

- Diagnosis confirmed by detection of Trichomonas vaginalis in the vaginal secretion at the microscopic examination
Trichomoniasis

Treatment:

- **Metronidazole** is the Rx of choice
- 99% cure rate
- Single-day Rx: 1g B.D. PO (incidence of nausea is higher)
- 7-days Rx: 200 mg tds
- S.E.: nausea, vomiting, metallic taste, secondary candida infections
- Contraindicated in 1st trimester of pregnancy
Trichomoniasis

• Asymptomatic female should be treated
• 1/3 of asymptomatic females will become symptomatic within 3 months
• Might be a vector for viral or bacterial pelvic infections
Trichomoniasis

• Metronidazole gel is inferior to oral Rx for the Rx of Trichomonas

• May be identified in 30 to 80 % of the male sexual partners of infected women.

• Male is frequently asymptomatic but must be treated.

• There is a > 2.5-fold reinfection rate when the sexual partner was not treated.
Recurrent Trichomoniasis

- Either been reinfected or poor Rx compliance
- A few resistant strains (a wet smear obtained 3 to 5 days after Rx showed the Trichomonas organisms are larger & plumper than normal)
- Resistant cases usually respond to daily doses of 1 or 2 g of metronidazole PO for 7 days, if not successful, try a combination of oral & topical Rx or high-dose IV Rx
<table>
<thead>
<tr>
<th>Type</th>
<th>Etiology</th>
<th>Discharge</th>
<th>Pain</th>
<th>Pruritus</th>
<th>Clinical signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial vaginosis</td>
<td><em>Gardnerella vaginalis,</em> <em>Mycoplasm hominis,</em> Anaerobic bacteria: <em>Prevotella species,</em> <em>Mobiluncus species</em></td>
<td>Malodorous; homogenous; clear, white or grey; fishy odor</td>
<td>Not primary symptom</td>
<td>Not primary symptom</td>
<td>No signs of inflammation</td>
</tr>
<tr>
<td>Trichomoniasis</td>
<td><em>Trichomonas vaginalis</em></td>
<td>Green-yellow, frothy</td>
<td>Pain with sexual intercourse, vaginal soreness, dysuria</td>
<td>Not primary symptom</td>
<td>Signs of inflammation, ‘strawberry Cx’</td>
</tr>
<tr>
<td>Vulvovaginal candida</td>
<td><em>Candida albicans,</em> <em>Candida krusei,</em> <em>Candida glabrata</em></td>
<td>White, thick, lack of odour</td>
<td>Burning, dysuria, dyspareunia</td>
<td>Frequent</td>
<td>Signs of inflammation, oedema</td>
</tr>
</tbody>
</table>

Antifungals in Vaginosis

**Rising frequency of non-albicans species:**
- Recently, the frequency of non-albicans species (e.g., *Candida glabrata*) has increased, possibly secondary to greater use of over-the-counter antifungal products.¹

**Overuse of antifungals based on self-diagnosis**
- Self-diagnosis of yeast vaginitis is unreliable.
- Incorrect diagnosis results in the overuse of topical antifungal agents, with subsequent risk of contact and irritant vulvar dermatitis.²

Resistance to Antifungals is Observed in Patients with Recurrent Vaginitis

Almost 90% of isolates from patients with recurrent vaginitis were resistant to ketoconazole and more than 40% cross-resistant to clotrimazole & ketoconazole.¹

Antifungal treatment with either fluconazole (single 150 mg oral dose) or clotrimoxazole (200 mg intravaginally for 3 days) does not appear to adequately treat recurrent disease.²

Optimal treatment of recurrent vaginal infections remains a challenge.

BETADINE® — A Broad-Spectrum Fungicidal Antiseptic

• PVP-I 10% vaginal pessaries were prescribed (once-a-day) for 7 days to patients suffering from vaginitis with vaginal discharge and irritation.

• Inflammation quickly subsided during the course of treatment.

• PVP-I was highly effective — 73.3% completely cured symptomatically & 16.7% had good improvement in symptoms (both have microbiological cures).

• No complications or apparent side-effects were reported during treatment.
Added advantage of the Dual Action of Povidone-Iodine

Povidone-Iodine is advantageous over other single-purpose treatments due to its dual action against candidal and trichomonal infections.

- Conditions conducive to flare-up of candidiasis is observed with single agents targeting trichomonal infection.
- Similar effect is not reported with Povidone-Iodine due to its dual action against both the causative organisms.

The authors recommend that the 28-day course of povidone-iodine pessaries is used in those cases where trichomoniasis or candidosis has been a therapeutic problem in the past, particularly if the patient is currently on the oral contraceptive pill.

Effective Treatment of Bacterial Vaginosis

Allowing native lactobacilli to rapidly re-colonize

- An **optimal therapeutic agent** for vaginitis.
- Keeps the normal vaginal **inhabitants intact** while reducing infections to a minimum.

---

**Total scores in acute bacterial vaginosis**

<table>
<thead>
<tr>
<th>Day</th>
<th>Score</th>
<th>BETADINE® (povidone iodine) vaginal suppositories</th>
<th>Lactobacilli vaginal capsules</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>9</td>
<td><img src="image.png" alt="Graph" /></td>
<td><img src="image.png" alt="Graph" /></td>
</tr>
<tr>
<td>7</td>
<td>6</td>
<td><img src="image.png" alt="Graph" /></td>
<td><img src="image.png" alt="Graph" /></td>
</tr>
<tr>
<td>14</td>
<td>3</td>
<td><img src="image.png" alt="Graph" /></td>
<td><img src="image.png" alt="Graph" /></td>
</tr>
</tbody>
</table>

- **p = 0.074**
- **p = 0.008**

Source: BETADINE® Doctor Detail Aid
Proper Procedure to Use Vaginal Suppository

• The applicator is cleaned by pushing the plunger out of the tube and washing in hot water. After washing the plunger is replaced in the tube.

• For minor vaginal irritation, itching and soreness, the treatment should be continued for 7 days. For infectious vaginitis, irrespective of intervening menstruation the treatment should be continued for at least 2 weeks.

Source: BETADINE® Vaginal Suppository Product Information Leaflet. For detailed information please refer to the product information leaflet in your country.
Gynoflor

- 0.03 mg estriol, $10^8$ L. acidophilus, lactose

**Dose**: 1 vaginal tablet daily for 6 days (2 tablets: pregnant women with more abundant leukorrhea)
Indication

• Restoration of the Lactobacillus flora after local and/or systemic treatment with anti-infective

• Atrophic vaginitis

• Mild to intermediate cases of bacterial vaginosis
Dosage

• Restoration therapy, mild to intermediate Bacterial vaginosis
  ➢ 1-2 vaginal tablets daily for 6-12 days

• Atrophic vaginitis
  ➢ 1 - 2 vaginal tablets / day for 1 – 2 weeks, followed by a maintenance dose of 1 – 2 vaginal tablet / week
Gynoflor use in BV

- **BV** is not an inflammatory condition, but an ecological disorder.

- Its ecological peculiarities, harbouring millions of bacteria, are caused by **disappearance of lactobacilli**, and are sustained by existence of a therapy resistant biofilm.

- Hence **recurrences are frequent**.

- For recurrent BV patients may want to use natural drugs like **probiotics**, rather than repetitive courses of antibiotics (side effects and resistance induction).
Gynoflor use in BV

- **Probiotics** like Gynoflor have an interesting potential to improve or cure different conditions of AVF (Abnormal Vaginal Flora)

- For treatment of full blown BV, *single treatment* comparable to metronidazole after one week

- For *long term cure* (≥ 1 month) single course therapy with probiotics is suboptimal: *repetitive courses or interval treatment* may be necessary
Lactobacillus acidophilus, informally known as "Doderlein's bacillus" colonizes the vagina because glycogen is produced which provides the bacteria with a source of sugar that they ferment to lactic acid.

- Fermentation of lactose $\rightarrow$ pH normalization of the vaginal milieu
- Production of hydrogen peroxide
- Competitive Adherence to vaginal epithelial cells
Conclusion : Probiotics as adjuvant therapy

- If given together with antibiotics, *cure rate of BV* is better

- Also after antibiotic treatment for *other infections* better cure rates if probiotics are used
Advice to patients with recurrent vaginitis

- Don’t have unprotected sex, but also beware of condoms
- And if you still want to have sex, certainly don’t start young, and don’t do it orally, anally, nor during menses and never with casual or multiple partners
Evidence based risk factors???

- Individual patient may have a particular risk factor
- Don’t ruin peoples lifes with unnecessary and exagerated bans
- Test one risk factor at a time and imply change in life habit only if successful
In conclusion: how to optimize management of vaginitis in 3 lines?

1. Confirm diagnosis
2. Consider maintenance treatment for chronic illness
3. Don’t accumulate ‘don’t do’s’ for no reason
Conclusion

• Manage a woman with a recurrent vaginitis as a patient with a chronic illness: give attention and consider individualized maintenance therapy.
Thank You