

# 7

## SYNDROMIC APPROACH TO THE MANAGEMENT OF STDs

**STD/HIV**  
Prevention  
Training  
*Center of New England*

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# SYNDROMIC APPROACH TO THE MANAGEMENT OF STDs

## OBJECTIVES

### FOR CERVICITIS AND URETHRITIS

1. State their known etiology.
2. Describe their clinical manifestations and sequelae.
3. State the clinical and laboratory criteria for the presumptive diagnosis of urethritis and cervicitis.
4. Define the recommended diagnostic laboratory tests.
5. Select the appropriate treatment.
6. Discuss the follow-up of the patient and the management of sexual partners.

### FOR GENITAL ULCER DISEASE (GUD)

1. Discuss the epidemiology and etiology of GUD.
2. Describe the clinical manifestations according to the etiologic agent involved.
3. Choose the appropriate diagnostic evaluation.
4. Select the appropriate treatment.
5. Discuss the follow-up of patients and the management of sexual partners.
6. List potential complications.

### FOR PELVIC INFLAMMATORY DISEASE (PID)

1. Define pelvic inflammatory disease and its pathogenesis.
2. Describe the epidemiology and clinical manifestations of PID.
3. List the clinical and laboratory criteria for the diagnosis of PID.
4. Choose the appropriate diagnostic evaluation.

# SYNDROMIC APPROACH TO THE MANAGEMENT OF STDs

## OBJECTIVES

### FOR VAGINAL DISCHARGE

1. List the most frequent vaginal etiologies of discharge
2. Describe the associated clinical signs and symptoms
3. Chose the appropriate diagnostic evaluation
4. State the appropriate treatment
5. Define the management of sexual partners





# MUCOPURULENT CERVICITIS

## 1.0 PATHOPHYSIOLOGY AND DEFINITION

The endocervix is composed of columnar epithelium (CE) and the ectocervix of squamous epithelium (SE). The squamo-columnar junction (SCJ) is the border between CE and SE, and its position varies depending on the degree of squamous metaplasia (SM). SM is a process by which CE is transformed into SE, producing a migration of the SCJ into the endocervix. The SCJ is also described as the transformation zone, because it is an area of intense cellular activity: it is where all CIN/SIL originate. Cervical ectopy (presence of CE on the ectocervix) is most prominent during periods of more intense estrogenic stimulation, such as adolescence, pregnancy and oral contraceptive use.

The cervical mucus may facilitate transport (sperm), particularly during estrogen stimulation, when the mucus is thin and copious (ovulation). It may also act as a barrier (mucous plug), particularly when under the influence of progesterone (OCP).

Mucopurulent cervicitis (MPC) is an **inflammatory process** of the cervical epithelium and/or stroma, which can provide an ascendant pathway to upper genital tract inflammation/infection.

The **clinical importance** of MPC is related primarily to its major complication, **pelvic inflammatory disease (PID)**. The **epidemiological importance** of MPC is related to its **potential as a reservoir for *C. trachomatis* and *N. gonorrhoeae*** in the community.

MPC is characterized by the presence of purulent or **mucopurulent** (green, yellow) **endocervical exudate** visible in the endocervical canal or in an endocervical swab specimen (positive swab test). Some experts also make the diagnosis on the basis of easily induced cervical bleeding.

The presence of PMNs on the gram stain (> 10, > 20, > 30), which has a lower sensitivity, specificity and positive predictive value than the finding of yellow endocervical mucopus by an experienced clinician, is not a required criteria for the diagnosis of MPC syndrome, which remains primarily clinical.

## 1.1 ETIOLOGY

Mucopurulent cervicitis can be caused by *C. trachomatis* or *N. gonorrhoeae*, although in most cases, neither organism can be isolated.

### KEY POINTS:

- Most commonly identified microbial etiologies are CT or GC, but often no etiology is found
- May lead to PID if GC or CT present





- ä Erosa vera: cervical ulceration due to trauma: finger nail, cervical cap, cervical biopsy. Almost always asymptomatic in patients, and rarely associated with mucopurulent d/c
- ä Cervical cancer: usually appears as a fungating lesion. May present as ulcers/ leukoplakia. Larger lesions often associated with intermenstrual, post-menopausal or post-coital bleeding.
- ä Leukoplakia: white plaque on the cervix visible with the naked eye. Most due to HPV infection (condyloma), but may be due to hyperkeratosis, CIN or CIS. Must be evaluated by colposcopy and biopsy, regardless of cytology (Pap smear) results.

## 1.2 CLINICAL MANIFESTATIONS

### SYMPTOMS

Many women may be asymptomatic. The following symptoms may be present, but are not specific to MPC and often overlap with symptoms of vaginitis/vaginosis and PID or other pathology.

- ä Bleeding, especially post-coital and post-examination
- ä Abnormal vaginal discharge (green, yellow, thick) usually not associated with odor, itching or burning

### SIGNS ON CLINICAL EXAMINATION

- ä Mucopurulent (green or yellow) endocervical discharge
- ä Induced endocervical bleeding (“friability”)
- ä Edematous ectopy
- ä General erythema
- ä Discrete lesions (ulcers, erosions)
- ä PMNs on gram stain of endocervical sample (use of this criteria and cut-off for the number of PMNs is controversial)

### PERSISTENT/RECURRENT CERVICITIS

- ä Exposure to new/untreated partner
- ä Incomplete or incorrect therapeutic regimen
- ä Non-infectious etiologies (see above)

**NOTES:**

## 1.3 LABORATORY DIAGNOSIS AND CLINICAL EVALUATION

1. Perform vaginal pH, and vaginal samples for saline and KOH wet preparations. Assess for *Trichomonas vaginalis*, bacterial vaginosis and yeast.
2. Examine the cervix correctly: wipe mucus away from the ectocervix with a large cotton swab. Observe for mucopus, erythema, edema, ulcerations, erosions, ectropion (associated with post coital bleeding, bleeding after pap and leukorrhea most intense at midcycle), leukoplakia, polyps, vegetating lesions (cancer).
3. Assess for friability (bleeding) with Pap smear, swabbing or speculum insertion.
4. Perform swab test: insert a white sterile cotton swab in the endocervix, rotate, and retrieve. If yellow or green mucus is present = positive swab test. If cloudy or clear mucus is present = negative swab test. Use for gram stain (optional).
5. Test for *Neisseria gonorrhoeae* first, then for *Chlamydia trachomatis*. In the presence of mucopus or friability, it may be preferable to defer the performance of the conventional Pap smear until treatment and resolution of the MPC has occurred.
6. Assess for the presence of lesions consistent with HSV.
7. Screen for syphilis with STS.

## 1.4 TREATMENT



### RECOMMENDED APPROACH TO THE MANAGEMENT OF MPC

**The results of sensitive tests for *C. trachomatis* and *N. gonorrhoeae*, such as nucleic acid amplification tests, should determine the need for treatment, unless the likelihood of infection with either organism is high, or the patient is unlikely to return, or will be difficult to locate for treatment.**

- Treat for GC and CT according to recommended treatments described for these organisms in **Sections 3 and 4** of this home study module. Treat for *T. vaginalis*, HSV, *T. pallidum* as appropriate

#### KEY POINTS:

- Laboratory evaluation of MPC should include testing for GC and CT, wet mount for *Trichomonas vaginalis*, and testing for HSV if indicated
- Treatment decisions should be based on preliminary evaluation, prevalence of disease in the geographic area, and patient compliance with follow-up

## 1.5 FOLLOW-UP AND MANAGEMENT OF PARTNERS

Counsel the patient on the etiology, need for testing, treatment. Explain MPC as a syndrome entity as opposed to disease, explain the need to assess and treat partners.

**If symptoms persist, women should be instructed to return for reevaluation and to abstain from sexual intercourse even if they have completed their therapy.** In some cases, MPC persists despite repeated courses of antibiotic therapy. Relapse or reinfection with GC or NG have not been the explanation in the majority of cases. After relapse/reinfection have been ruled out, management of persistent MPC is unclear. In these cases, additional antimicrobial therapy may be of little value.

Follow-up of partners should be as recommended for the STDs identified or suspected. Partners should be notified, examined, and treated for the STD identified or suspected in the index patient. Patients should abstain until therapy is completed.

## 1.6 COMPLICATIONS

The main complications associated with MPC is the development of **pelvic inflammatory disease (PID) and its sequelae if gonorrhea (GC) and/or chlamydia (CT) are present**. The risk of developing asymptomatic or “silent” PID is also present, particularly if CT is present.

Transmission of infectious organisms to partner if present.

Transmission of infectious organisms to newborns if present.

Increased risk of developing post-partum, post-abortal endometritis or puerperal chorioamniotitis if STD related.

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# URETHRITIS

## 2.0 DEFINITION

Urethritis is defined by a urethral inflammation most often manifested by urethral discharge and/or dysuria and/or itching.

The presence of urethritis is confirmed by:

- Visible Discharge
- An increased number of PMNs on the **gram stain of a urethral smear** at 1000 x:  
**>5 PMNs per oil immersion field**
- An increased number of PMNs on the examination of the **sediment** of a first-voided **urine (first 10 to 15 cc)** at 400 x:  
**> 10 PMNs per high dry field**
- **a positive (+1 or more) leukocyte esterase test (LET) on the first 10 to 15 cc of fresh unspun urine.**

## 2.1 ETIOLOGY

Urethritis is classified as gonococcal if caused by *Neisseria gonorrhoeae*, or non-gonococcal if N.G. is not detected.

### GONOCOCCAL URETHRITIS (GU)

*Neisseria gonorrhoeae* (rare reports of *Neisseria meningitidis* urethritis presenting as GU)

### NON-GONOCOCCAL URETHRITIS (NGU)

<i>Chlamydia trachomatis</i> (C.T.)	15% to 40%
<i>Ureaplasma urealyticum</i> (U.U.)	10% to 40%
Neither	20% to 40%
<i>Mycoplasma genitalium</i>	15% to 25%
<i>Trichomonas vaginalis</i> (TV)	< 5% (increasing in USA)
Herpes Simplex Virus (HSV)	< 5% (rare in the absence of skin lesions)
<i>Candida albicans</i>	rare, (some men with balanitis may have associated urethritis)
<i>Haemophilus spp</i>	rare
<i>Adenovirus</i>	rare
Other bacteria	<i>E. Coli</i> may cause some cases of urethritis in MSMs

Adapted from Holmes KK et al. Sexually Transmitted Diseases. 3rd Ed. 1999. Ch. 60, page 834

### NOTES:

- ä E. coli is associated with anal intercourse and is more often seen in men who have sex with men (MSM). Gram stain: WBC + gram negative rods. May be associated with cystitis.
- ä Non-infectious causes of urethritis: trauma, Steven-Johnson syndrome, Reiter's syndrome..

## 2.2 EPIDEMIOLOGY

An estimated incidence of urethritis is difficult to calculate because the syndrome is generally not reportable. Numbers are based on the reporting of gonorrhea and chlamydia in men

**With declining rates of gonorrhea, NGU is more common than GU in the USA and much of the developing world. The ratio of NGU to GU is greater among groups of higher socioeconomic status in the USA.** Men affected by NGU are more likely to be white, of higher socioeconomic status, with higher education and a fewer number of sexual partners. On college campuses, NGU accounts for 85% of cases of urethritis. Although NGU is relatively less prevalent than GU among men who have sex with men (MSMs) compared to men who have sex with women (MSWs), a recent study in San Francisco demonstrated that 65% of MSMs presenting with urethritis had negative tests for gonorrhea (vs 74% of MSWs), that 15.2% of MSMs with gonorrhea were also infected with chlamydia (vs 8.4% for MSWs) and that 18% of MSMs with NGU were infected with chlamydia (vs 20% of MSWs). In some areas of the USA, the proportion of NGU caused by CT has been declining.

For both GU and NGU, the **peak age group affected is 20-24 years**, followed by the 15-19 years, and then 25-29 years.

NGU and GU have an increased incidence during the summer months.

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## 2.3 CLINICAL MANIFESTATIONS

### CLINICAL CHARACTERISTICS OF NGU VS GU

	GU	NGU
<b>Incubation period</b>	1 - 14 days (mean: 3-7)	1 - 5 weeks (peak: 1-3 weeks)
<b>Onset</b>	abrupt	gradual
<b>Dysuria</b>	severe	mild
<b>Asymptomatic</b>	< 3%	up to 25% (>10%)
<b>Discharge</b>	purulent <i>less</i>	mucoid <i>more</i>

Distinguishing on clinical grounds alone GU from NGU is not very reliable (at best, 50% accurate in distinguishing NGU from GU), nor is distinguishing *C. trachomatis* positive NGU from *C. trachomatis* negative NGU. 15-40% of GU also harbor *C. trachomatis*. Therefore treatment for GU should also include treatment for *C. trachomatis*.

Up to  $\frac{1}{3}$  of men presenting at an STD clinic with laboratory confirmed NGU have no signs (discharge) or symptoms (dysuria/itching).

## 2.4 LABORATORY DIAGNOSIS

In the ideal situation, the patient should be examined before the first morning void, or with the first morning void. Ideally, examine 2 or more hours since the last void. Examine the urethra for presence of discharge. If not present, milk/strip the urethra (can be done by the patient). The following tests should be performed for patients presenting with urethritis:

### URETHRAL GRAM STAIN

(See Section 3 for test performance characteristics)

- ä Has the advantage over the LET and the urine sediment testing of detecting GC.
- ä Positive for **GU** : > 1 polymorphonuclear (PMN) cell with intracellular gram-negative diplococci (GNID) of typical morphology. Numerous PMNs are usually seen. Extracellular GND may also be present.
- ä Positive for **NGU**: presence of >5 PMNs per oil immersion field, with no gram negative intracellular diplococci (GNID). Scan the slide at low magnification to identify the areas with the most PMNs, then average the number of PMNs in five

#### KEY POINTS:

- GU typically has an abrupt onset with severe dysuria and discharge
- NGU typically has a gradual onset with mild dysuria and discharge
- Distinguishing GU from NGU on clinical grounds alone is not reliable
- Test all cases of urethritis for both GC and CT

random fields at 1000 X.

## URINE MICROSCOPY/TESTING

### A. Sediment of first voided urine (FVU)

- ä May be more sensitive than the gram stain to detect asymptomatic urethritis
- ä Only the first 10 to 15 cc of urine should be collected, centrifuged, and the sediment examined at 400x
- ä Positive for urethritis: presence of >10 PMNs per 400 x field in first 10 to 15 cc of spun urine.

### B. Leukocyte Esterase Test (LET)

- ä Has been studied mainly in adolescents, and may be useful to screen for urethritis in this population. Less sensitive than the FVU, but easier to perform. Dip stick in fresh urine (do not centrifuge). Wait 2 minutes to read: > 1+ indicative of urethritis.
- ä Sensitivity for CT generally ranges from 72% to 83% with lowest performance when compared to amplified tests. Specificity from 70% to 93%. Because of its low specificity, a positive LET should be confirmed by a test for *N. gonorrhoeae* and *C. trachomatis* to determine adequate treatment and follow-up of the patient and his sexual partners.

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## TEST FOR *NEISSERIA GONORRHOEAE*

(See Section 3 for test performance characteristics)

- ä Thayer Martin medium or if unavailable, an antigen detection test or a DNA hybridization or amplification test (see Section 3).
- ä The urethral exudate is an adequate specimen to culture for GC.
- ä First 10 to 15 cc of urine can also be a specimen if amplified tests are used.

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## TESTING FOR *CHLAMYDIA TRACHOMATIS*

(See Section 3 for test performance characteristics)

- ä Culture, antigen detection test or DNA hybridization or amplification test (see section 3).
- ä If a urethral specimen is used the swab should inserted at least 2-3 cm into the urethra (see Section 1).

### KEY POINTS:

Urethritis confirmed by one of 3 criteria:

- Presence of purulent or mucopurulent discharge
- > 5 WBCs per oil immersion field (1000X) on gram stain of mucopurulent discharge.
- FVU with > 1+ leukocyte esterase or > 10 WBCs per high dry (400X) in sediment of spun urine



- a First 10 to 15 cc of urine can also be a specimen if amplified tests are used.

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## OTHER LABORATORY ASSESSMENTS

### Culture for *Ureaplasma urealyticum*

- a **NOT RECOMMENDED.** Because U.U. is a common colonizer of the urethra (present in up to 59% of men, with a mean of 34%), the clinical significance of its detection in urethritis is unclear.

## OTHER MANAGEMENT CONSIDERATIONS

**All patients with urethritis should be screened for syphilis and offered counseling and testing for HIV.**

## 2.5 TREATMENT

CONSULT THE CDC 1998 GUIDELINES FOR TREATMENT OF STDs FOR COMPLETE INFORMATION.

*See appropriate Sections (3 & 4) for safety profiles of medications.*

**If stat diagnostic tests are not available (gram stain) treat for both GC and CT.**

<b>GU</b>	<p><b>Cefixime</b> 400 mg orally once or <b>Ceftriaxone</b> 125 mg IM once or <b>Ofloxacin</b><sup>2</sup> 400 mg orally once</p> <p><b>Plus</b></p> <p><b>TREAT FOR CONCOMITANT CHLAMYDIAL INFECTIONS</b> <b>Azithromycin</b> 1 g orally single dose or <b>Doxycycline</b> 100 mg orally twice a day x 7 days</p>
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<sup>2</sup>(not effective against incubating syphilis; not approved in children under the age of 18; some resistant strains have been isolated in the USA)

**NGU**

**Azithromycin 1 g orally single dose**

or

**Doxycycline 100 mg orally twice a day for 7 days**

**Alternate regimens**

**Erythromycin 500 mg orally four times a day for 7 days**

**EES 800 mg orally four times a day x 7 days**

**Ofloxacin 300 mg orally twice a day x 7 days**

**Note:** 10% of isolates of U.U. are resistant to tetracyclines.

Ofloxacin is recommended for the treatment of *C. trachomatis*, but has not been fully evaluated for the treatment of NGU.

Doxycycline and azithromycin are 95% to 100% effective against CT NGU, while erythromycin is 85% to 95% against CT NGU. All three are 60% to 80% effective against non CT NGU.

## 2.6 FOLLOW-UP AND MANAGEMENT OF SEXUAL PARTNER(S)

- Ⓐ Patients should be instructed to return if symptoms persist or recur after completion of therapy. Routine test of cure is not recommended.
- Ⓐ **A specific diagnosis facilitates partner referral and management: testing for gonorrhea and chlamydia in the index patient is encouraged.** Partners should be examined and tested if exposed to the index patient within 60 days. Partners of patients testing positive for GC and/or CT by stat (gram stain) or laboratory confirmed tests should also be treated presumptively. Presumptive treatment of partners of patients who test negative is controversial. The last sexual partner should be evaluated and treated (according to test results) if the last sexual contact preceded the time interval described above.
- Ⓐ Avoid sexual contact until both patient and sexual partner(s) have completed therapy and are cured.

## 2.7 RECURRENT OR PERSISTENT URETHRITIS

Persistent or recurrent symptoms occur **within 6 weeks in approximately 20%** of patients who are **chlamydia positive** and **40%** of those who are **chlamydia negative**. Persistent infection may be due to inadequate tissue level of antibiotics (prostate) or a

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resistant pathogen (ureaplasma). Persistent symptoms may also occur because an untreated pathogen is present (*Trichomonas vaginalis*). Chronic “non-bacterial” prostatitis may also be a cause of persistent symptoms (considered a vague entity with scrotal and groin pain). Other possibilities include a Reiter’s variant without conjunctivitis or arthritis, or an autoimmune process.

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#### GUIDELINES FOR THE MANAGEMENT OF RECURRENT OR PERSISTENT URETHRITIS

1. Re-examine and document objective evidence of urethritis by examining urethral secretions for the presence of PMNs. Symptoms alone, without documentation of signs or laboratory evidence of urethral inflammation or of an STD pathogen, are not sufficient basis for treatment.
2. Ask about compliance with medication and potential exposure to untreated sexual partner or new partner.
3. If re-infection/noncompliance is suspected, retreat the patient and his partner(s) with the initial regimen. If resistant GC is suspected (originally treated for GC with a fluoroquinolone, has a smear that is still positive for GC and denies re-exposure), then culture isolate, send it to Public Health Laboratory for antibiotic susceptibility testing, and treat the patient with ceftriaxone.
4. If reinfection and noncompliance unlikely, do testing for *Trichomonas vaginalis* (examination of wet mount of spun FVU or culture of urethral swab or FVU) if available and treat with the following

**Metronidazole 2 g orally single dose**  
Plus  
**Erythromycin base 500 mg orally four times a day x 7 days**  
or  
**EES 800 mg orally four times a day x 7 days**

5. Stress abstinence or condom use while trying to establish whether problem is possible reinfection or true persistent.
6. Urology examinations do not usually reveal a specific etiology.

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## 2.8 COMPLICATIONS

Both local and systemic complication of urethritis are now unusual in developed countries. Symptoms of urethritis will in most cases resolve even if the patient remains untreated.

95% of untreated patients with acute GU will be free of symptoms 6 months after onset. Symptoms of NGU gradually subside over 1 to 3 months in most patients. **Lack of symptoms does not mean eradication of infection.**

Complications associated with gonococcal urethritis: epididymitis (1-2% of cases), seminal vesiculitis, abscess of Tyson gland, penile edema d/t dorsal lymphangitis, periurethral abscess, urethral strictures and regional lymphangitis (all are rare). Systemic complication is DGI, and is rare (see Section 3).

Complications associated with chlamydial urethritis: epididymitis (1-2%), penile edema (rare), Reiter's Syndrome (1-2% of cases of NGU; in > 80% of men with Reiter's syndrome, infection with *C. trachomatis* is concurrent or preceding).

Prostatic involvement may occur (difficult to diagnose in the context of urethritis) in 20 to 30% of men with NGU. Usually asymptomatic and responsive to standard treatment.

Both *N. gonorrhoeae* and *C. trachomatis* can infect the conjunctiva.

NOTES:



# GENITAL ULCERATIVE DISEASE

## 3.0 ETIOLOGY AND EPIDEMIOLOGY

- **In the USA**, the most frequent cause of GUD is **herpes**, followed by syphilis, then chancroid. Demographic and behavioral factors associated with a higher incidence of chancroid include: heterosexual contact, male gender (ratio male:female is 10:1), non-white race, uncircumcised male, contact with a commercial sex worker, cocaine use, and travel to an endemic US city (New York City, New Orleans, Dallas, Jackson) or country. Lymphogranuloma venereum (LGV) is rare in the USA, and granuloma inguinale (donovanosis) is almost never encountered in the US. In the **developing world, chancroid** is the most frequent cause of GUD. Other less common infectious causes include acute HIV infection, candidiasis and scabies.
- No etiology is found in 20% to 50% of cases: most likely related to the sensitivity of the laboratory test (affected by self-medication, duration of lesion, technology of the test).
- **Important to know the epidemiology of disease** in the region, demographic and behavioral characteristics of the patient, including travel abroad or in US regions with high rates of syphilis and chancroid.
- The presence of GUD in an HIV-infected person increases HIV shedding in the genital region (OR = 3.9 - 4.6), thus potentially increasing the risk of transmission. Likewise, the presence of GUD in a person not infected with HIV increases their risk of HIV acquisition with adjusted odds ratios or risk ratios between 2.2 and 11.3.
- Non-infectious causes of GUD include: Behcet's syndrome, fixed drug eruption, Reiter's syndrome, trauma and abrasions.

## 3.1 CLINICAL MANIFESTATIONS

The clinical manifestations of GUD depend on the etiologic agent involved. However, none of these are pathognomonic (overlap, atypical presentations) except perhaps for the presence of vesicles which are generally present only with HSV infections. Relying solely on clinical manifestations to determine the etiology of GUD is neither sensitive nor specific as demonstrated by numerous studies, which is why laboratory confirmation is important. In addition, coinfections can be present in up to 10% of cases of GUD.





## CHARACTERISTICS OF GUD ASSOCIATED WITH THE DIFFERENT ETIOLOGIC AGENTS

<b>Incubation period</b>	<b>Herpes</b>	2 to 28 days
	<b>Syphilis</b>	9 to 90 days (average of 21 days)
	<b>Chancroid</b>	3 to 10 days (average: 4 to 7 days)
	<b>LGV</b>	3 to 21 days
<b>Type of lesion</b>	<b>Herpes</b>	<b>vesicles</b> , then ulcer erythematous borders usually multiple & clustered red, smooth base w/o induration <b>painful</b> superficial
	<b>Syphilis</b>	papule, then ulcer rolled, demarcated borders usually single; multiple lesions can occur <b>indurated</b> , red, smooth, clean base generally <b>painless</b> superficial
	<b>Chancroid</b>	papule, pustule then ulcer ragged, undermined borders usually one; multiple lesions can occur <b>soft base with purulent material</b> <b>painful</b> <b>deep</b>
	<b>LGV</b>	<b>rarely presents as GUD</b> papule, ulcer variable borders usually one base w/o induration <b>painless</b> superficial
<b>Duration of lesions</b>	<b>Herpes</b>	17 to 20 days (primary) 5 to 10 days (recurrent)
	<b>Syphilis</b>	1 to 6 weeks
	<b>Chancroid</b>	2 to 3 weeks or more
	<b>LGV</b>	1 to 2 weeks (heals rapidly, no scar)
<b>Lymph nodes</b>	<b>Syphilis</b>	bilateral, firm, <b>painless</b> , enlarged
	<b>Herpes</b>	bilateral, firm, <b>tender</b>

### KEY POINTS:

While the clinical presentation of GUD differs based on etiology, laboratory confirmation of diagnosis is necessary because:

- Clinical presentations may overlap or be atypical
- Physical diagnosis is neither sensitive nor specific for GUD (inaccurate)
- Coinfections may occur in up to 10% of cases



<p><b>Chancroid</b> <b>LGV</b></p>	<p>often unilateral, <b>enlarged +, suppurative</b> <b>often presenting symptom</b>; multiple, enlarged, matted, tender nodes: may suppurate</p>
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## 3.2 LABORATORY DIAGNOSIS

### SYPHILIS

#### A. DARKFIELD MICROSCOPY (see Section 2)

Ideal, but requires experience and often unavailable in many settings.

#### B. SEROLOGIC TESTING (see Section 2)

##### ä Nontreponemal tests (RPR, VDRL)

May be negative in up to 30% of patients with a chancre of primary syphilis. Less likely to be negative if the lesion has been present for more than 7 days.

Stat qualitative test can be done.

##### ä Treponemal tests

FTA-Abs is more sensitive than the nontreponemal tests early in disease, and turns positive before the RPR and the VDRL.

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### CHANCROID

#### A. GRAM STAIN

ä Requires considerable experience to read with accuracy. Typical appearance include “school of fish,” “railroad tracks,” clumps or whorls.

#### B. CULTURE

ä Gold standard and definite diagnosis

ä 70% to 80% sensitivity at best.

ä Special medium often unavailable (requires hemin for growth “Factor X”). Roll sterile swab across the cleaned ulcer base and near the edges.

ä Growth requirements: 33°C, water saturated atmosphere, CO<sub>2</sub>.

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## HERPES

### A) TZANCK SMEAR (see Section 6)

- ä Less sensitive than culture, but inexpensive and rapid.
- ä Does not differentiate between HSV I & HSV 2; can be positive in CMV and VZV.

### B) CULTURE (see Section 6)

- ä More sensitive in the earlier stages of disease.

### C) TYPE SPECIFIC SEROLOGIES

- ä May be helpful for recurrent lesions.

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## LYMPHOGRANULOMA VENEREUM

### A) SEROLOGY

- ä Complement fixation test: > 1:64 supportive of a diagnosis of LGV, but not diagnostic because cross reaction occurs with non-L serovars of *Chlamydia trachomatis*.
- ä Microimmunofluorescent test (MIF): more type specific and more sensitive, but often unavailable. IgM titer over 1:32 or IgG over 1:1024 or a 4 fold rise to above 1:256 supports a diagnosis of LGV.

### B) CULTURE

- ä Isolation of *Chlamydia trachomatis* L<sub>1</sub>L<sub>2</sub>L<sub>3</sub> from lesion/lymph node

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## GRANULOMA INGUINALE (DONOVANOSIS)

Is almost never encountered in the USA. It is caused by *Calymmatobacterium granulomatis*, a gram negative coccobacillus that cannot be cultured. The diagnosis is made by the identification of intracellular "Donovan bodies" on a biopsy or smear of lesions with a Wright's stain. Lesions are slowly destructive and granulomatous.

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## OTHER LABORATORY METHODS

Amplification techniques for the diagnosis of syphilis, herpes simplex virus and chancroid are currently being assessed, but are not yet commercially available. One such

**NOTES:**



polymerase chain reaction (Multiplex PCR) could be used to test GUD for all three of the above infections. Preliminary data suggests that this test is highly sensitive.

### 3.3 DIAGNOSTIC APPROACH

If vesicles are present, the most likely diagnosis is HSV infection. Perform a Tzanck test and culture if possible. A history of vesicles, recurrent lesions, exposure to HSV, or the presence of painful superficial lesions are also all suggestive of HSV infection. Counsel and treat as appropriate for HSV. Draw RPR.

The presence of large suppurative lymph nodes (bubos) accompanying the ulcer is highly suggestive of chancroid (almost diagnostic). These should be aspirated through intact skin, and the material smeared for gram stain and cultured. Draw RPR.

If no vesicles are present, perform darkfield microscopy and a stat RPR. If stat RPR is not available, perform quantitative RPR (non stat). **Regardless of available tests, all patients with GUD should be screened with a quantitative (non stat) RPR.**

**All patients presenting with GUD should be offered counseling and testing for HIV, and assessed for other STDs.**

<b>DF positive:</b>	<p>Do quantitative RPR and confirm + with TT<sup>1</sup></p> <p>Do HSV and <i>H. ducreyi</i> culture if mixed infection suspected</p> <p>Treat for syphilis</p> <p>Treat for chancroid only if strong suspicion of coinfection</p>
<b>Stat RPR positive:</b>	<p>Do quantitative RPR and confirm + with TT<sup>1</sup></p> <p>Do HSV and <i>H. ducreyi</i> culture if mixed infection suspected</p> <p>Treat for syphilis</p> <p>Treat for chancroid only if strong suspicion of coinfection</p>
<b>Stat RPR negative (or unavailable)</b>	<p>Do quantitative RPR and confirm + with TT<sup>1</sup> and</p> <p>Request FTA-Abs on serum if quantitative RPR negative</p> <p>Do HSV culture</p> <p>Do <i>H. ducreyi</i> culture if chancroid suspected</p> <p>Treat according to clinical manifestations, prevalence of GUD etiologies, risk factors, follow-up compliance, pregnancy (low threshold for syphilis treatment), medication history (fixed drug eruption) and self-medication.</p>

<sup>1</sup> TT = treponemal test (TP-PA or FTA-Abs)

#### NOTES:



## 3.4 TREATMENT

<b>Primary Syphilis:</b>	See Section 2
<b>HSV</b>	See Section 6
<b>Chancroid:<sup>1</sup></b>	Azithromycin 1g orally single dose or Ceftriaxone 250 mg IM single dose or Ciprofloxacin 500 mg orally twice a day x 3 days or Erythromycin 500 mg orally four times a day x 7 days
<b>HSV:</b>	Acyclovir 200 mg orally 5 times a day for 7 to 10 days (See Section 6)
<b>LGV:</b>	Doxycycline 100 mg orally twice a day x 21 days Erythromycin 500 mg orally four times a day x 21 days

1. Healing may take longer in HIV infected patients. In addition, longer courses of therapy may be required. Some experts recommend using the 7 day regimen of erythromycin for treatment of chancroid in HIV infected persons.

## 3.5 FOLLOW-UP AND MANAGEMENT OF PARTNERS

Patients should be reevaluated in **one week**. Check test results and status of lesions. Chancroid lesions generally improve symptomatically after 3 days, and objectively after 7 days of therapy. Treat appropriately any initially untreated infections if tests results return positive.

If all tests were negative (RPR, FTA-Abs, *H. ducreyi* culture, HSV culture), **repeat RPR and evaluate clinical manifestations**. If significant lymphadenopathy, consider LGV. If suppurative lymph nodes, also consider chancroid even if culture is negative. If ulcer(s) is deep, persists or worsens despite therapy for syphilis, chancroid and HSV, consider possibility of resistant *H. ducreyi* or associated HIV infection, malignancy, Behcet's syndrome. If lesions persist, but are superficial, consider fixed drug eruption, circinate or yeast balanitis, scabies.

If initially negative, counseling and testing for HIV, and serologic testing for syphilis should be repeated in three months.

**Partners should be assessed according to the diagnosis of the index patient** and as described in each appropriate section of this module (Section 2 for syphilis, Section 6 for herpes). For **chancroid**, partners who had sexual contact with the index patient within **10 days before the onset of the patients symptoms** should be examined and treated, even in the absence of symptoms. For **LGV**, go back **30 days before the onset of the patients symptoms**.

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## 3.6 COMPLICATIONS

Complications and sequelae of untreated infections have been described for syphilis in Section 2 and for HSV in Section 6. Ulcers can become superinfected.

Complications associated with chancroid include the development of rectovaginal fistulas in women, the destruction of soft tissue/skin and fistula formation secondary to recalcitrant bubos, and scarring with phimosis. If left untreated, lesions can persist for years. Systemic infections with chancroid do not occur. Vertical transmission to the fetus/newborn have not been reported.

LGV in the acute stages can cause proctocolitis. Complications include the formation of fistulas, strictures and pelvic lymphadenitis.

**NOTES:**

# PELVIC INFLAMMATORY DISEASE (PID)

## 4.0 DEFINITION

Ascending infection from the vagina or cervix to the endometrium, fallopian tubes and/or contiguous structures. PID might include endometritis, salpingitis, parametritis, oophoritis, tubo-ovarian or tubal abscess and pelvic peritonitis.

## 4.1 EPIDEMIOLOGY

### INCIDENCE AND PREVALENCE

An estimated **1 million cases occur among US women annually**, affecting 1% of the sexually active population. Annual costs exceed \$4.2 billion. Initial visits to physician offices for PID in 1996 were 300,000. PID affects mainly young women between the ages of **15 to 24**.

**Hospitalizations for PID among women 15-34 years of age have been declining since 1982.** This can be explained by the decrease in the number of severe PID requiring hospitalization, decreases in the rates of gonorrhea (often causing more clinically severe cases of PID than chlamydia), decreases in the rates of chlamydial infections in some areas (Sweden and Europe), general trends towards decreased hospitalization for medical conditions, and increased out-patient management with newer antimicrobials. **Declines in hospitalization for PID were less for the 15 to 19 year old age groups.** This may be explained by the higher rates of STDs in this age group, as well as the more aggressive approach to treatment recommended by professional organizations. In 1994, over 75,000 women were hospitalized for acute PID.

Annual sequelae of PID include infertility (110,000 cases, rate increasing), ectopic pregnancy (26,000 cases, rate increasing) and chronic pain (150,000 cases).

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### DEMOGRAPHIC AND BEHAVIORAL FACTORS ASSOCIATED WITH HIGHER RATES OF PID

- Young age, particularly adolescent (higher rates of GC and CT).
- History of prior PID: damaged fallopian tube mucosa may be more susceptible to recurrent infection.
- History of prior GC and CT: increased risk of recurrent GC or CT

#### KEY POINTS:

- PID mainly affects women aged 15 - 24
- Associated with GC or CT infection, but is often polymicrobial
- Sequelae include chronic pelvic pain, infertility and increased ectopic pregnancy risk
- Risk for sequelae unrelated to severity of the disease, which is often milder for CT

- Male partners with GC, CT or multiple sexual partners
- Current douching, particularly with commercial products: vaginal flora changes or epithelial damage.
- Presence of an IUD
- Bacterial vaginosis
- Lower socioeconomic status, non-white race

## 4.2 PATHOGENESIS AND ETIOLOGY

Pelvic inflammatory disease or PID is generally caused by a contiguous spread of organisms ascending from the cervix via the endometrial cavity to the fallopian tubes and beyond. Indeed, many studies have demonstrated such a continuum (cervicitis/endometritis/salpingitis/oophoritis/tubo-ovarian abscess/peritonitis) by isolation of the organisms at different level of the genital tract and by histopathologic evidence of infection of the cervix, endometrium (PNM infiltration for GC and plasma cell for CT and GC), and salpinx. Such a canalicular spread of organism seems the most common mechanism for the development of PID, and has been documented for *N. gonorrhoeae* and *C. trachomatis*. However, salpingitis has been reported in women who have been sterilized: parametrial infections though lymphatic drainage has been documented, particularly for *M. hominis*.

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### ETIOLOGY

**The most common pathogens associated with PID are STDs: chlamydia and gonorrhea.** These organisms are present alone or in combination in approximately 50% to 60% of cases of PID. The prevalence of each will vary with the setting. *Neisseria gonorrhoeae* recovered from the cervix in **30% to 80%** of women with PID. *Chlamydia trachomatis* is recovered from the cervix in **20% to 40%** of women with PID, and recovered from the endometrium and/or the tubes in a majority of women with cervical chlamydial infections. *C. trachomatis* is especially associated with Fitz-Hugh-Curtis syndrome.

**Most cases of PID are polymicrobial in nature.** Microorganisms that can be part of the normal vaginal flora such as aerobic gram negative rods (*E.coli*), and anaerobes (*Bacteroides fragilis*, an important cause of abscess; peptostreptococcus spp.) can also be associated with PID.

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NOTES:

## FACTORS INFLUENCING THE DEVELOPMENT OF PID

- **Menstruation:** cervico-vaginal bacteria are introduced into the upper genital tract during menses.
- **Antibody status:** specific protection for some organisms or only for some immunotypes (GC). With chlamydial infections, antibody to heat shock protein has been associated with tubal damage.
- **IUD:** increases the risk. Most cases of endogenous PID associated with the insertion of the IUD and occur shortly after insertion..
- **Oral contraceptives:** although the use of OCs had been associated with an increased risk of cervical chlamydial infections, many study results have suggested a decreased risk for chlamydial salpingitis, possibly related to the progesterone content and its effect on the cervical mucus (thickening of the mucus causing a barrier to sperm and possibly bacteria). OC may also cause a down-regulation of immune response to infection.
- **Pregnancy:** PID very unusual. If left untreated, may lead to septic abortion or the transmission of GC and/or CT to the newborn.
- **HIV Infection:** differences in the clinical manifestations of PID between HIV-infected women and noninfected women have not been described clearly. In early observational studies, HIV-infected women with PID were more likely to require surgical intervention. In a subsequent more comprehensive observational study, women with HIV and PID presented with more severe symptoms, but responded equally well to standard parenteral antibiotic regimens. In an other study, the microbiologic findings between HIV infected and non infected women were similar. HIV infected women with immunosuppression, because of theoretical concerns, should be managed aggressively with one of the parenteral antibiotics recommended by the CDC (See later).

## 4.3 CLINICAL MANIFESTATIONS

Clinical findings vary widely, from asymptomatic infection to frank peritonitis. **The occurrence of tubal damage is unrelated to the severity of the clinical presentation. The diagnosis of “silent PID” is difficult. Women can be asymptomatic or present with symptoms such as dyspareunia, irregular bleeding, urinary or GI symptoms.**

It is estimated that only 30 to 50% of PID presents with recognizable clinical manifestations.

NOTES:

In some women, signs and symptoms suggest endometritis: abnormal vaginal bleeding, lower abdominal pain and uterine tenderness on exam. Overall, the clinical diagnosis of PID has a positive predictive value for salpingitis that varies between 65% to 90%, depending on epidemiologic characteristics and the clinical setting.

Salpingitis suggested by lower abdominal pain, adnexal tenderness on exam, cervical motion tenderness. May be associated with fever, nausea, vomiting, tubal mass on exam (tubo-ovarian abscess).

According to some studies, lower abdominal pain for a duration of more than four days was 78% sensitive and 54% specific for the diagnosis of PID. Irregular bleeding was 43% sensitive and 70% specific, a temperature of  $> 38^{\circ}\text{C}$  was 33% sensitive and 82% specific, a palpable mass was 40% sensitive and 76% specific and the presence of vaginal discharge (purulent or unspecified) was 60% sensitive and 61% specific.

**The etiologic agent involved in PID may affect clinical manifestations:**

**gonococcal PID** is more often associated with **fever, a short duration of illness** (3 to 5 days) before consultation **and with menses**. It is also more often associated with urethral symptoms. **Chlamydial PID** is more often characterized by the **absence of fever, longer duration of symptoms** (7 to 9 days) before consultation, **irregular bleeding, milder clinical signs and symptoms**, but **more severe inflammation at laparoscopy**. PID caused by anaerobes is more likely to cause adnexal swelling (abscess) and a more severe clinical presentation. It is also more often associated with bacterial vaginosis.

Perihepatitis (Fitz-Hugh-Curtis syndrome) is more often associated with chlamydial PID, and causes right upper quadrant pain. It can also be associated with nausea, vomiting and fever. Signs and symptoms of PID generally accompany the syndrome. Liver enzymes are generally normal.

## 4.4 DIAGNOSIS

Given the wide range of clinical manifestations, and the overlap with other conditions, **an accurate diagnosis remains difficult**. Because of the sequelae of PID, it is important to maintain a high degree of suspicion.

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### DIAGNOSTIC CRITERIA

- CDC has developed minimum criteria for the diagnosis of PID, and recommends empiric treatment of PID when the following are present in the absence of any other

#### KEY POINTS:

The minimum CDC criteria for initiating empiric treatment of PID are

- **Lower abdominal pain**
- **Cervical motion tenderness**
- **Adnexal tenderness**

Clinical criteria for diagnosis of PID are neither sensitive nor specific, so the patient's risk and the local prevalence of disease should be considered when making treatment decisions



explanation: **lower abdominal pain, cervical motion tenderness and adnexal tenderness. Under some circumstances, a clinician may choose to treat with even less specific findings that may not include all 3 criteria.**

- ä Only about 60% of clinically diagnosed cases of PID according to the minimum criteria are confirmed at laparoscopy. About 15% have other pathology (including appendicitis, ovarian cysts, ectopic pregnancy, endometriosis) and 20% have no discernible pathology.
- ä Additional criteria to increase the specificity of diagnosis (but decrease the sensitivity) include:  $T^{\circ} > 38.3^{\circ} C$ , abnormal cervical or vaginal discharge, elevated C-reactive protein, elevated erythrocyte sedimentation rate, a positive test for GC and/or chlamydia.
- ä When more signs and symptoms are added to the minimum criteria (such as elevated ESR, fever, palpable mass), the positive predictive value of PID diagnosis increases to 95%. However, only 16% of women with salpingitis present with this clinical constellation.
- ä Definite criteria for diagnosing PID, which are warranted in selected cases, include an endometrial biopsy with histopathologic evidence of endometritis, the presence of thickened fluid-filled tubes with or without free pelvic fluid or tubo-ovarian complex as demonstrated by ultrasound or other radiologic tests, and laparoscopic abnormalities consistent with PID.
- ä Laparoscopy is indicated under the following conditions:
  - Severe peritonitis to exclude ruptured tubal abscess or ruptured appendix
  - Patients with mild signs in whom the diagnosis is unclear
  - Patients who fail to respond to antibiotic therapy
  - Percutaneous drainage of abscess

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## DIAGNOSTIC WORKUP

**The following tests should be performed on all women of reproductive age presenting with lower abdominal pain:**

- ä A sensitive urine pregnancy test
- ä A wet mount of vaginal secretions
- ä A sensitive test for *Neisseria gonorrhoeae* and *Chlamydia trachomatis*

Other laboratory tests, depending on the clinical picture, can be performed, such as a CBC, sed rate, C-reactive protein, pelvic ultrasound, endometrial biopsy, etc. The CBC is often normal in mild cases of PID.

**NOTES:**



## 4.5 TREATMENT

Because of the polymicrobial nature of PID, antibiotics chosen should cover *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, anaerobes, gram negative facultative bacteria, and streptococci. All regimens should be effective against gonorrhea and chlamydia, since negative endocervical screening does not preclude upper tract infection. Although many have questioned the need to eradicate anaerobes from women with PID, evidence suggests that this may be important. Anaerobic bacteria have been isolated from the upper genital tract of women with PID and in vitro data clearly show that anaerobes such as *B. fragilis* can cause tubal and epithelial destruction. In addition, many women with PID are also diagnosed with bacterial vaginosis. **Intra uterine devices should be removed after the patient has received at least 24 hours of antibiotherapy.** Treatment should be initiated as soon as the presumptive diagnosis is made, as the prevention of longterm sequelae has been directly linked with immediate administration of appropriate antibiotics.



**RECOMMENDS HOSPITALIZATION UNDER THE FOLLOWING CONDITIONS, BASED ON OBSERVATIONAL DATA AND THEORETICAL CONCERNS**

- Surgical emergencies such as appendicitis cannot be ruled out.
- The patient is pregnant.
- Failure to respond clinically to oral antimicrobial therapy.
- Inability to tolerate or follow an outpatient oral regimen.
- Severe illness, nausea and vomiting, or high fever.
- Tubo-ovarian abscess.
- Current immunodeficiency (HIV infection with low CD4 counts, immunosuppressive therapy, or other disease).

**CONSULT THE CDC 1998 GUIDELINES FOR TREATMENT OF STDs FOR COMPLETE INFORMATION**

**NOTES:**



## RECOMMENDED OUTPATIENT ORAL REGIMENS

### Regimen A

**Ofloxacin** 400 mg orally twice a day x 14 days  
 Plus  
**Metronidazole** 500 mg orally twice a day x 14 days

### Regimen B

**Cefoxitin** 2 gm IM plus probenicid 1 gm orally concurrently  
 or  
**Ceftriaxone** 250 mg IM or other parenteral third generation cephalosporin (ceftizoxime, cefotaxime)  
 Plus  
**Doxycycline** 100 mg orally twice a day x 14 days

- ä Theoretical concerns about the limitation of cefoxitin to cover anaerobes may require the addition of metronidazole, particularly if bacterial vaginosis is present.
- ä Patient should be reexamined within 72 hours after treatment is begun to assess clinical status. Patients should demonstrate clinical improvement after 3 days of therapy. If not, IV therapy, further diagnostic workup, and/or surgical intervention may be required.



## RECOMMENDED PARENTERAL REGIMENS (INPATIENT, OUTPATIENT OR HOME PARENTERAL)

**Cefotetan** 2 g IV q 12 hours or **Cefoxitin** 2 g IV q 6 hours  
 Plus  
**Doxycycline** 100 mg IV or orally twice a day  
 or  
**Clindamycin** 900 mg IV every 8 hours  
 Plus  
**Gentamicin** loading dose 2 mg/kg IV or IM, followed by a maintenance dose of 1.5 mg/kg IV every 8 hours. Single daily dose may be substituted

Most clinicians favor at least 24 hours of direct inpatient observation for patients with tubo-ovarian abscesses, after which home parenteral therapy should be adequate. In

NOTES:

clinical trials, these regimens have been administered for at least 48 hours after clinical improvement, but this is an arbitrary designation, but if no improvement occurs, surgical intervention is required. Clinical experience should guide decisions regarding transition to oral therapy, which may be accomplished within 24 hours of clinical improvement. Complete with doxycycline 100 mg orally twice a day x 14 days. Alternatively, if the second regimen is used, complete with clindamycin 450 mg orally four times a day x 14 days (preferable if abscess is present).

#### ALTERNATE REGIMENS

**Ofloxacin** 400 mg IV every 12 hours  
 Plus  
**Metronidazole** 500 mg IV every 8 hours

or

**Ampicillin/sulbactam** 3 g IV every 6 hours  
 Plus  
**Doxycycline** 100 mg orally or IV every 12 hours

or

**Ciprofloxacin** 200 mg IV every 12 hours  
 Plus  
**Doxycycline** 100 mg orally or IV every 12 hours  
 Plus  
**Metronidazole** 500 mg IV every 8 hours

## 4.6 FOLLOW-UP, SEQUELAE AND PARTNER MANAGEMENT

Reexamine the patients after 48 to 72 hours, then at 7 and 21 days after onset of treatment

**Sexual partner(s) within 60 days prior to onset of symptoms of patients with PID should be treated empirically for GC and CT. This is crucial to prevent reinfection**

Consider rescreening for GC and CT 4 to 6 weeks post therapy

#### KEY POINTS:

- Approximately 25% of women with a single episode of PID will experience sequelae, including ectopic pregnancy, infertility, and chronic pelvic pain.
- The risk of ectopic pregnancy in a subsequent pregnancy is increased 6 to 10 fold.
- Tubal infertility occurs overall in 20% of salpingitis patients.

## 4.7 SEQUELAE OF PID

75 to 85% of women treated for PID have salutary response to antibiotics and both clinical and microbiological cure.

15 to 25% of women have chronic, persistent or recurrent abdominal pain.

Ectopic pregnancy occurs with an incidence of about 10% per salpingitis episode (increased 6-10 fold).

The occurrence of tubal infertility increases with the number of episodes of PID:

One episode of PID	8% infertile
Two episodes	20% infertile
Three episodes	40% infertile

**It is estimated that 40% of all cases of infertility probably due to PID.**

## 4.8 PREVENTION

Patient education regarding primary prevention of STDs that cause PID: condom use, partner selection, use of other barrier methods.

Critical role of diagnosis and treatment of sexual partners.

Secondary prevention: screening women at risk of STDs for GC and CT. At least one study of population based screening for CT within an HMO demonstrated a decreased incidence of PID.

Early recognition of symptoms/signs of PID and prompt treatment.

**NOTES:**

# VAGINITIS

## 5.0 ETIOLOGY AND EPIDEMIOLOGY

### NORMAL VAGINAL ENVIRONMENT

#### A) Histologic Composition of the Vagina

Three layers:

1. Mucous membrane of stratified, non-cornified squamous epithelium bathed in hydrophilic gly.coprotein.
2. Muscular layer.
3. Connective tissue layer.

#### B) Normal Vaginal Fluid

Sources:

1. Transudated serous fluid from vaginal capillary. beds
2. Bartholin's and Skene's gland secretions.
3. Endometrial and fallopian tube secretions.
4. Cervical secretions.

Character:

1. Water, electrolytes, glucose.
2. pH <4.7 favors growth of acidophilic organisms and inhibits growth of non-commensals.

Regulators:

1. Estrogen - directly affects amount of transudation (higher estrogen = increased transudate), gland secretion, epithelium thickness, glycogen deposition and vaginal pH (see below).
2. Vaginal flora (see below).
3. Foreign elements (douching, spermicides, lubricants, antibiotics, see below).
4. Menses: increase vaginal pH due to serum pH contribution.

#### C. Normal vaginal flora

Normal vagina consists of a variety of organisms (usually less than 9 bacterial colony forming units per g of vaginal fluid), with a predominance of acidophilic lactobacillus

**NOTES:**

species (95% of all organisms in flora) important in maintaining a normal vaginal ecology. The ecology and pH of the vagina is dependent on estrogen stimulation: the number of organisms, including lactobacilli, dramatically increases after menarche, and decreases in post-menopausal women. Estrogen also affects the vaginal epithelium. Glycogen is produced and metabolized to become lactic acid. Thus, at menarche, the pH of the vagina decreases from about 7.0 (prepubertal girls) to about 5.0. Lactobacilli are responsible for further decreasing the pH to 3.8 to 4.2 by also producing lactic acid.

The acidic environment inhibits the overgrowth of bacterial and other organisms with pathogenic potential. In addition, certain strains produce hydrogen peroxide, which inhibits the growth of other organisms such as *Gardnerella vaginalis*, *Mycoplasma hominis* and anaerobes, all of which can be part of the normal vaginal ecology. It is hypothesized that the presence of hydrogen peroxide producing lactobacillus protects against the development of bacterial vaginosis, but not against candidiasis or trichomoniasis.

A number of factors other than estrogen stimulation can affect vaginal ecology: certain pathogens (*Trichomonas vaginalis* can reduce the growth of lactobacilli), antibiotic use (effect varies with drug) and douching (reduces the number of lactobacilli).

## MOST FREQUENT ETIOLOGIES

### A) Infectious causes

- Bacterial vaginosis 45%
- Candidiasis 25%
- Trichomoniasis 25%
- Other\* 5%

Prevalence may vary by clinical setting

\*Atrophic vaginitis with secondary bacterial infection; foreign body with secondary infection/xucopurulent cervicitis (GC, CT); Streptococcal vaginitis (Group A)/ulcerative vaginitis associated with *S. aureus* + TSS; vulvar papillomatosis (HPV) (pruritis and dyspareunia).

Bacterial vaginosis is the most frequent cause of vaginal disorders, occurring almost twice as frequently as candidiasis. The prevalence of BV varies by population: 5% to 25% among college students, 12% to 61% among STD patients. Although BV is currently not considered sexually transmitted, it appears related to sexual activity. BV occurs more frequently in sexually active persons, but it can occur in adolescents (10% - 30%) who have never been sexually active and in women who have not had intercourse for many

**NOTES:**

years. It is often coined as a “sexually associated disease”, because it is more often found in sexually active women.

Over 90% of cases of yeast infections are caused by *C. albicans* and the infection is often defined as vulvovaginal candidiasis (VVC). At least 75% of women will experience a symptomatic episode of VVC, with 40-50% experiencing more than one episode. Less than 5% will have recurrent VVC, defined as 4 or more episodes per year. *C. albicans* can be recovered in about 20% (5-55%) of healthy asymptomatic women, and is considered part of the normal flora of the skin and vagina. The presence of *C. Albicans* appears to be closely related to estrogen stimulation, as evidenced by more frequent carriage during pregnancy (30-40%), lower frequency in post menopausal women and rarity in premenarchal girls. Estrogen may enhance adhesion and virulence. Yeast infections are not considered to be sexually transmitted. About 20% of male partners of women with VVC are colonized with *C. Albicans*, more commonly found in the coronal sulcus of uncircumcised males. Treatment of male partners has not been shown to reduce recurrent rates in women.

*Trichomonal vaginalis* (TV) is thought to cause up to 25% of all cases of vaginitis in the USA. Prevalence can vary with settings from 5% (family planning clinic) to nearly 40% (some STD clinics). It is often associated with the presence of *Neisseria gonorrhoeae*. TV is present in 30-40% of sexual partners of infected women, and is responsible for increasing cases of nongonococcal urethritis. It is considered to be almost exclusively sexually transmitted. Transmission appears easier from men to women, and men seem to occasionally clear the infection spontaneously. Although the organism can survive in moist environments, and the potential for fomite transmission exists, no well documented cases of non sexual transmission have been reported.

#### B) Non-infectious causes

- Allergic vaginitis to such products as spermicides/deodorants (burning, pruritis)
- Atrophic vaginitis (post menopausal)
- Vulvar vestibulitis (pain, pruritis and dyspareunia)
- Irritants and allergens (erythema, burning, pruritis)
- Lichen simplex chronicus (pruritis)
- Lichen sclerosis (pruritis)
- Paget’s disease of the vulva (pruritis)

**NOTES:**

## 5.1 PATHOGENESIS

### BACTERIAL VAGINOSIS

A decrease in lactobacilli (particularly H<sub>2</sub>O<sub>2</sub> producing spp.) observed, along with an increase in the number of various anaerobic bacteria, *Gardnerella vaginalis*, *Mycoplasma hominis* and *Mobiluncus curtesii* and *mulieris*. The total number of organisms increases by a factor of 100 to 1000 compared with the normal vaginal flora while the ratio of anaerobes to aerobes increases from 2-5:1 to 100-1000:1. Volatile amines, such as cadaverine, putrescine and trimethylamine, are produced and are responsible for the fishy odor at alkaline pH. No signs of inflammation are present, as evidenced by the lack of polymorphonuclear cells. The underlying factors associated with this change are not clearly understood. As stated previously, it appears to be associated with a decrease in lactobacilli. Douching, the presence of an IUD and having multiple sexual partners appear to increase the risk of BV. Recurrent disease is thought to occur mainly in women who are deficient in hydrogen producing lactobacilli. BV has been linked to premature rupture of membranes, premature deliver and low birth weight deliver. The presence of BV may increase the susceptibility of HIV acquisition.

### VULVOVAGINAL CANDIDIASIS

Most cases of yeast vulvovaginitis (90%) are caused by *Candida albicans*. Over 200 different strains of *C. albicans* have been identified, but none is more virulent than others, nor more frequently associated with recurrent disease. These organisms are dimorphic: the blastophore phenotype form is responsible for transmission and asymptomatic carriage. Germinating yeast with production of mycelia is the invasive form and is associated with symptomatic disease. Other species include *Torulopsis glabrata* and *Candida tropicalis*. Adherence to cells is necessary for carriage and symptomatic disease. *Candida albicans* species seem to better adhere to epithelial cells rather than other species, which may partly explain why they are more frequently encountered. It appears that *Torulopsis glabrata* is more often associated with recurrent disease, and is recovered more frequently in HIV infected women.

### TRICHOMONAS VAGINALIS

*Trichomonas* species are site specific. *Pentatrichomonas hominis* can only be found in the colon, and does not infect the vagina. Similarly, *T. tenax* can be isolated from the mouth, often in association with gingivitis. Trichomoniasis increases susceptibility to HIV acquisition. It occurs among women who have sex with women.

NOTES:

## 5.2 CLINICAL MANIFESTATIONS

Symptoms are not accurate in predicting diagnosis. Women complaining of vaginitis are equally likely to be diagnosed with BV, VVC or no vaginitis; about 40% of women complaining of discharge do not have vaginitis, and over 20% of women without complaints of vaginal symptoms have vaginitis. Laboratory confirmation is important.

### BACTERIAL VAGINOSIS

Women typically complain of malodorous vaginal discharge (50%). The fishy odor is particularly prominent after contact with sperm (“physiological whiff test”, because sperm is alkaline). Women generally do not complain of pruritis or dysuria. Many women are asymptomatic (50%). Upon examination, a thin white, often copious discharge is observed at the introitus; the discharge uniformly coats and adheres to the vaginal walls and there is no inflammation.

### VULVOVAGINAL CANDIDIASIS

Women generally complain of intense vaginal itching and irritation, increased thick, clumpy discharge, and external dysuria (burning when the urine touches the vulva). Some women may be asymptomatic, while others may have a clear discharge. Reliance on clinical signs and symptoms only is poorly correlated with VVC. Upon examination, erythema/edema of the vulva and vagina is often present, along with thick clumpy (“cottage cheese”) adherent white discharge.

### TRICHOMONAS VAGINALIS

Women generally complain of profuse, often malodorous and greenish, bubbly discharge (50-75%). Genital irritation is often present. Up to 50% of patients may be asymptomatic of the disease, although 30% of women initially asymptomatic will develop symptoms within 6 months of acquiring the infection. Upon examination, profuse, often frothy discharge is present. Erythema of the vaginal mucosa and introitus is present. Cervical petechiae are occasionally present (colpitis macularis or “strawberry cervix”), and are more readily observed by colposcopy (45% vs 1-2% with the naked eye). It thrives on squamous, not columnar, epithelium. The urethra is infected in over 90% of cases.

NOTES:



## 5.3 DIAGNOSIS

### DIAGNOSTIC CRITERIA

Assessment of the vaginal discharge, pH determination, and a wet preparation (saline and KOH) of vaginal secretions are the recommended first line clinical/laboratory techniques for guiding a diagnosis in the presence of vaginal complaints. Routine cultures are not recommended.

### BACTERIAL VAGINOSIS

The diagnosis of BV is based on the presence of at least three of the four following findings (Amsel criteria):

1. Characteristic white thin adherent discharge
2. pH of 4.5 or higher
3. Positive whiff test (amine odor released by adding a drop of 10% KOH)
4. Clue cells on the wet mount (at least 20% of all vaginal epithelial cells).

High pH has the highest sensitivity (but lowest specificity as it can also be elevated in mixed infections and trichomoniasis). The whiff test has the lowest sensitivity, as it may not always be present with BV. It can also be positive with trichomoniasis. The presence of clue cells is the finding most closely associated (overall most accurate) with BV diagnosed by gram stain.

Wet mount preparation will show:

**Saline prep** Presence of clue cells. Clue cells are squamous epithelial cells that have lost their distinct contour due to the adhesion of coccobacilli to the cell walls. The border of the cells appears granulated/lacy.

75% of cell wall observed

Few/rare PMNs (ratio PMNs/EC <1)

**KOH prep** Amine odor usually present. Least sensitive diagnostic test for BV  
Clue cells are lysed.

**pH** >4.5

### VULVOVAGINAL CANDIDIASIS

The wet mount is generally positive for yeast when patients are symptomatic. However, some studies have demonstrated a sensitivity as low as 50%, particularly for milder infections and those associated with *Torulepsiss glabrata*.

NOTES:



Wet preparation will show:

**Saline prep** Yeast buds and mycelia may be seen. Buds are oval in shape and in pairs. Pseudohyphae are extensions of buds, and can be identified at 10X. Hyphae appear as long and filamentous  
PMNs may or may not be present, but PNM/EC <1  
Lactobacilli may be seen

**KOH prep** Yeast buds and pseudohyphae can be more clearly seen, because cells are lysed.  
No amine odor

**pH** <4.5

Only *C. albicans* form germinating tubes. *Torulopsis glabrata* does not form hyphae.

### TRICHOMONAS VAGINALIS (TV)

The wet mount can be used to diagnose *T. vaginalis* and sensitivity varies from as low as 42% to over 90%. It is most sensitive when patients are symptomatic, in women, and when the technique is done under optimal conditions (see below). It is important to use a warm slide and saline, and to read promptly. TV is very susceptible to oxygen, cool temperatures and drying. The slide must be read within five minutes. A diagnosis of *T. vaginalis* cannot be made on a wet mount if the organism is not motile (can be confused with PMNs). *T. vaginalis* reproduces by binary fission, so there are no cysts formation as seen with other protozoans. Only the organism will be seen on the wet mount.

**Saline prep** Can be done on both men and women. However, it is difficult to identify *Trichomonas vaginalis* in urethral specimens, and the sensitivity is low (<30%). The first morning urine sediment may be positive in 15% of those with negative wet mounts.  
TV is larger than PMNs (10-20 um), is pear shaped and exhibits definite motility (jerky, rapid and erratic.) Flagella may be seen when the organism is slow moving  
Many PMNs are generally seen (ratio PMN/EC +++++>1)  
Some parabasilar cells may be present, resulting from rapid cell turnover. These are ovoid and about 2/3 the size of squamous epithelial cells

NOTES:



<b>KOH prep</b>	Trichomonads and cells are lysed Amine odor may be present (50%)
<b>pH</b>	>4.5 (usually >5.0 (90%))

## 5.4 LABORATORY DIAGNOSIS

### A) SALINE AND KOH PREPS

The saline wet mount preparations are direct, rapid tests used to identify certain microorganisms (such as *Trichomonas vaginalis*, pseudohyphae and budding yeast cells) and cells (such as white blood cells, red blood cells, clue cells, and epithelial cells) from patient specimens. They are most often used to assist the clinician in making a diagnosis of vaginitis.

Potassium Hydroxide (KOH) 10% wet mount preparations are direct, rapid tests used to better observe fungal structures from patient specimens, because 10% KOH dissolves WBCs and epithelial cells that could hinder the identification of yeast.

KOH also releases the fishy odor (amine or whiff test) characteristic of bacterial vaginosis (BV): organisms present in BV produce amines by converting lysine to cadaverine, arginine to putrescine, and trimethylamine oxide to trimethylamine. These amines are released by the addition of an alkaline product, such as KOH. The whiff test can sometimes also be positive in trichomoniasis.

### B) SPECIMEN COLLECTION AND PROCEDURE (SEE ALSO SECTION 1)

For Saline preparations

Specimens can be collected by using one of the following two methods:

#### METHOD #1

Place a large drop of saline on a slide. Collect a sample from the lateral mid to third inferior vaginal walls with a swab and mix with the saline drop to create a turbid solution. Add a coverslip, being careful not to trap air bubbles. Read immediately under 10X, then 40X objectives.

or

#### METHOD #2

Use a swab to collect a sample from the lateral mid to third inferior vaginal walls. Place the swab in a small test tube containing 0.5 ml of 0.85% sterile saline. The saline must be at room temperature or warmer. Shake the swab to create a turbid solution.

Using the specimen swab in the saline, place a drop of the suspension onto the glass

NOTES:



slide. Add a coverslip, being careful not to trap air bubbles. Examine immediately under the 10X, then 40X objectives.

Note: this method prevents the drying of specimens. It allows for at least 15 minutes in saline before reading.

### **FOR KOH PREPARATIONS**

Use a swab to collect a sample from the lateral mid to third inferior vaginal walls, and then roll the swab in a slide. Add a drop of 10% KOH, and mix with a swab. Bring close to the nose to sniff immediately for amine odor (amines disperse quickly). Add a coverslip. Allow some time (2-5 minutes) for digestion and clearing of cells to occur. Heat may be applied by the flame for a few seconds (do not boil!). Scan for pseudohyphae at low power (10X). Locate yeast buds and confirm pseudohyphae at high dry power (40X).

### **FOR PH DETERMINATION**

Using a sterile swab, collect secretions from the lateral mid to third inferior vaginal walls, and apply to the pH indicator paper strip. Alternatively, the pH strip can be applied directly to the lateral vaginal wall. Determine pH according to manufacturer's instructions and scale. (choose a pH paper with a range of 3 - 7).

Note: pH may be elevated in the presence of sperm, cervical mucus and blood and cannot be used as a diagnostic tool for vaginitis under these circumstances. It is also important to collect specimens from the lateral vaginal wall, as collection from the posterior fornix will include cervical mucus. Finally, it is preferable to collect vaginal specimens first, as cervical sampling may induce bleeding.

## **C) INTERPRETATION**

### **FOR SALINE PREPARATIONS**

Squamous epithelial cells, WBCs, RBCs, sperm, clue cells, motile trichomonads, pseudohyphae, yeast buds can be observed. Other bacteria or cells/material can also be seen.

### **FOR KOH PREPARATIONS**

Only yeast can be seen. Cells and trichomonads have been lysed. Amine odor can also be detected.

**NOTES:**



## NORMAL VAGINAL SECRETIONS

Saline prep	some epithelial cells and WBCs. The ratio of WBCs and epithelial cells should be close to 1:1. Predominance of lactobacillus (5-15 um in length)
KOH prep	negative. No amine odor
pH	3.8 to 4.2 (<4.5)

For bacterial vaginosis, VVC, and *Trichomonas vaginalis*, see “diagnoses”.

## GRAM STAIN

### BACTERIAL VAGINOSIS

A direct Gram stain of vaginal fluid can also be used to diagnose BV. When the *Lactobacillus* morphotype is present only in low numbers (<5 per HPF) and a more mixed flora is present (*Gardnerella* morphotype, small gram-negative/positive and variable rods, fusiforms, gram-positive cocci), the smear is interpreted as consistent with BV (Spiegel). The Nugent scoring system can also be used to grade bacterial flora and evaluate for the presence of BV.

### VVC

A direct Gram stain of vaginal fluid can also be used to detect the presence of vaginal yeast, which are all gram-positive organisms.

### TRICHOMONAS VAGINALIS

Not useful in the diagnosis of *T. vaginalis*.

## CULTURES

### BACTERIAL VAGINOSIS

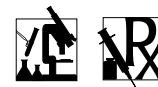
Culture is not recommended for diagnosis or test of cure, since up to 70% of “normal” women may harbor *Gardnerella vaginalis*.

### VVC

Culture (Sabouraud or Nickerson medium) is the most sensitive method to detect yeast, but not useful for routine diagnosis since positive cultures may be detecting clinically insignificant infections which should not be treated. However, it can be used when the identification and isolation of yeast is necessary for further identification/antimycotic susceptibility or when yeast is suspected, but the wet preps (saline and KOH) and Gram stains are negative. 25% to 40% of women with positive cultures are asymptomatic. Therefore, correlation with clinical signs and symptoms is necessary for diagnosis. In general, commensal carriers tend to have less than 10 colonies per plate. Rapid tests for the detection and identification of yeast species are available (InTray Colorex), but may have limited use given the commensal nature of yeast.

It is important to confirm the diagnosis of yeast by a wet prep and culture in women

NOTES:



presenting with chronic vulvar symptoms. The results of the culture will guide therapy pending the species isolated. In addition, many of these women may not have a yeast infection as evidenced by negative cultures, and other conditions need to be investigated.

### TRICHOMONAS VAGINALIS

The culture is the most sensitive method (95%) to detect *T. vaginalis*. A vaginal swab is placed in Diamond's medium and incubated at 35 degrees C. After 24 hours, use a pipette to gather specimen from the precipitate at the bottom of the tube (trichomonads grow in anaerobic conditions). Coverslip and examine for motile *T. vaginalis*. If no organisms are seen, continue to incubate until they are identified, up to a maximum of seven days. Most organisms will be identified after 48-72 hours. The new commercially available InPouch TV can also be used as an alternative to Diamond's medium. It has longer shelf life (1 year) but similar test performance characteristics than the Diamond's medium. Each pouch cost about \$2.50.

### D) PAP SMEARS

In general, Pap smears are not useful for diagnosing the causes of vaginal discharge. Pap smears are 50-70% sensitive to detect TV, but are not specific enough to be used for diagnosis and treatment. They are positive in about only 25% of patients with culture positive symptomatic VVC.

### E) DNA PROBES AND OTHER TECHNOLOGIES

A new probe system (Affirm VP) which detects *T. vaginalis* and *G. vaginalis* has been developed. For the identification of BV, the test has good sensitivity (90%) and specificity (97%) compared to the detection of clue cells on wet mount, but is less sensitive than the culture for the detection of *T. vaginalis* (90% sensitive and 99.8% specific).

## 5.5 TREATMENT

### BACTERIAL VAGINOSIS



Recommended Treatment for Non-pregnant Women:

Metronidazole 500 mg orally twice a day for 7 days (cure rate of over 90-95%)

Intravaginal clindamycin cream 2% daily for 7 days (similar cure rates)

Intravaginal metronidazole 0.75% once or twice a day for 5 days (78-87% cure rate)

NOTES:



## ALTERNATIVE REGIMENS

Oral clindamycin 300 mg bid for 7 days is also effective

Single dose oral metronidazole 2 gm stat (cure rates of 80-85%)

Flagyl ER (750mg) has been approved by the FDA once daily for 7 days for the treatment of BV. However, data concerning clinical equivalency with other regimens have not been published.



**TREATMENT IS GENERALLY RESERVED FOR SYMPTOMATIC WOMEN, AND NOT**

### RECOMMEND FOR SEXUAL PARTNERS, EXCEPT:

asymptomatic women who are to undergo a surgical abortion. BV has been associated with endometritis, PID or vaginal cuff cellulitis in women undergoing ambulatory invasive procedures (endometrial biopsies, hysteroscopy, IUD insertions) and vaginal/abdominal surgery. However, data is insufficient to recommend treatment of asymptomatic patients prior to procedures other than surgical abortions.

Intravaginal lactobacilli formulations are ineffective in preventing relapses because these organisms are not adapted to the vaginal environment, do not adhere to the epithelium, and non contain hydrogen peroxyde producing organisms. In one study, the use of nonoxynol-9 as a contraceptive decreased the incidence of bacterial vaginosis without increasing the incidence of candidiasis or trichomoniasis.



### RECOMMENDED TREATMENT OF PREGNANT WOMEN:

at risk of premature delivery

Recent data supports an association of BV with premature delivery. At least two studies demonstrate that treating high risk (history of a previous premature delivery) pregnant women who have BV (symptomatic or asymptomatic) will reduce their risk of premature delivery. Screening for high risk women should also be conducted early in the second trimester, and women with BV should be treated with the following medications:



### RECOMMENDED REGIMEN FOR BV FOR WOMEN AT HIGH RISK OF

#### PREMATURE DELIVERY

Metronidazole 250 mg orally TID for 7 days

Alternative regimens:

Metronidazole 2 g orally single dose

Clindamycin 300 mg orally BID for 7 days

**NOTES:**



## **CDC** RECOMMENDED REGIMEN FOR BV IN SYMPTOMATIC WOMEN AT LOW RISK

### OF PREMATURE DELIVERY

Metronidazole 250 mg orally three times a day for 7 days

Clindamycin 300 mg orally twice a day for 7 days

### Alternative regimens:

Metronidazole 2 g orally single dose

Metronidazole gel 0.75%, one full applicator intravaginally once or twice a day for 5 days.

Clindamycin cream is NOT recommended during pregnancy because two randomized trials reported an increase in preterm birth after treatment with clindamycin cream. Ampicillin, erythromycin, iodine, dienestrol cream, tetracycline/doxycycline, triple sulfa and ciprofloxacin are NOT effective against BV.

According to one study, BV may recur in up to 80% of women within 7 months. Recurrence may be a result of persistence of BV-associated organisms and failure of lactobacillus flora to recolonize the vagina. There is little data to support yogurt therapy or exogenous lactobacillus treatment. Lactobacillus vaginal suppositories are currently under development by Dr. Sharon Hillier.

## WC

**CDC** TREATMENT IS RESERVED FOR SYMPTOMATIC WOMEN, AND NOT INDICATED FOR SEXUAL PARTNERS, UNLESS THEY ARE SYMPTOMATIC.

The topical azoles are similarly effective in the treatment of VVC (85-90%). Oral fluconazole 150 mg orally in a single dose is similarly effective. Drug interaction with fluconazole includes oral hypoglycemic agents, coumarin-type antioagulants, phenytoin, theophylline, rifampin, terfenadine (seldane) and astemizole (hismanal). Polyenes (nystatin) are less effective (75-80%) than the above regimens. Short term local therapy (<7 days) appears as effective as longer regimens in uncomplicated infections (defined as mild to moderate, sporadic, nonrecurrent disease in a normal host with normally susceptible *C. albicans*). Response appears the same in HIV infected women. Longer treatments (10-14 days) are recommended for complicated infections (severe oral or recurrent VVC in an abnormal host, e.g. an uncontrolled diabetic, or infection caused by a less susceptible pathogen e.g. *C. glabrata*). Pregnant women may also benefit from longer treatment. Fluconazole is contraindicated during pregnancy.

The management of recurrent VVC remains a challenge, and is defined as 4 or more

### NOTES:



episodes per year. The first step is to confirm the diagnosis by culture, as many women with chronic vulvar symptoms may in fact suffer from other conditions. A careful history and management of underlying factors is essential, although most women affected have no predisposing factors, such as HIV infection, repeated courses of antibiotics, corticosteroid therapy or diabetes. Oral ketokenazole 100 mg orally daily for 6 months is effective to reduce recurrence (95%). However, risks and benefits must be carefully weighed as idiosyncratic severe hepatotoxicity can occur in 1/10,000 to 15,000 cases. Other treatments such as weekly fluconazole (100 mg orally) or clotrimazole (500 mg intravaginally) have also been equally effective in reducing recurrences. Treatment of the sexual partner, and use of oral nystatin to reduce intestinal reservoir have not been effective in reducing recurrences. Non *C. albicans* species can be responsible for a significant number of cases of recurrent disease (over 30%). *Torulepsis glabrata*, responsible for some cases of recurrent VVC, is less sensitive to oral fluconazole and topical imidazoles, and seems to respond better to boric acid suppositories (600 mg intravaginally once a day x 14 days).

## TRICHOMONAS VAGINALIS

### RECOMMENDED TREATMENT

Metronidazole is the only treatment available for *T. vaginalis* in the USA. A single dose of 2 g orally is the preferred treatment and achieves a 95% cure rate. Sexual partners should always be treated. Resistance to metronidazole is rare, and response is usually achieved with higher dosages. If the single dose fails, a dose of 500 mg BID orally for 7 days is recommended. (FDA has approved Flagyl 375 mg BID for 7 days, based on pharmacokinetic equivalency, but clinical data lacking).

#### Alternative Regimens

If treatment failure occurs, then a 2 g single dose orally for 2-5 days should be administered. If resistance is suspected, send for MIC studies available at the CDC. Tinidazole is not yet available in the USA. Two recent studies failed to demonstrate any association of teratogenic effects with the use of metronidazole during the first trimester of pregnancy. Intravaginal clotrimazole cream for 6 days has been shown to be effective in reducing symptoms. However, cure rates can be as low as <25% with this regimen. Intravaginal metronidazole is less than 50% effective (most likely about 25%), and is not recommended.

NOTES:

## 5.6 PARTNER MANAGEMENT

*Trichomonas vaginalis* is a sexually transmitted disease and sexual partner(s) should be treated for this infection. Candidiasis is not considered a sexually transmitted disease. Treatment of sexual partner(s) of women with VVC is not recommended unless males have balanitis. It is not been shown to reduce recurrences in women. Similarly, it is not recommended to treat sexual partner(s) of women with BV since this has not been shown to improve cure rates or decrease recurrences.

## 5.7 FOLLOW-UP

Non pregnant patients should be advised to return if symptoms persist or recur. Recurrent VVC is defined as the occurrence of 4 or more episodes per year, and occurs in less than 5% of women having experienced one episode of VVC. Recurrences following treatment for BV are common. Follow-up one month after completion of therapy for BV is recommended for high risk pregnant women to evaluate cure.

NOTES:

## 6.0 REVIEW QUESTIONS

1. A 22 year old patient presents to the family planning clinic complaining of post coital bleeding. She uses oral contraceptives as birth control method. She does not use condoms and has been with the same partner for six months. When you examine her, the cervix is friable, and mucopurulent secretions are visible at the cervical os. How would you manage this patient?

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2. What are the minimum criteria established by the CDC for a presumptive diagnosis of PID and empiric treatment?

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<p><b>NOTES:</b></p>
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3. A 15 year old patient presents at the clinic on a Friday afternoon complaining of lower abdominal pain. She has no nausea or vomiting, no fever, no UTI nor GI symptoms. She uses OCP as a birth control method. She has been with the same sexual partner for three months. The examination reveals lower abdominal tenderness, cervical motion tenderness and moderate adnexal tenderness. The urine pregnancy test is negative. Your presumptive diagnosis is PID. How would you manage this patient?

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4. Answer the question that appears on the video tape for Syndromic Approach to the Management of STDs.

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5. Answer the question that appears on the video tape for Syndromic Approach to the Management of STDs.

A)

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B)

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6. Answer the question that appears on the video tape for Syndromic Approach to the Management of STDs.

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