



**CEPHALOSPORIN - RESISTANT
GONORRHEA**

&

**Some New CDC
Recommendations for
Treatment of STD's**

Disclosure Statement

I have no financial interest in this presentation

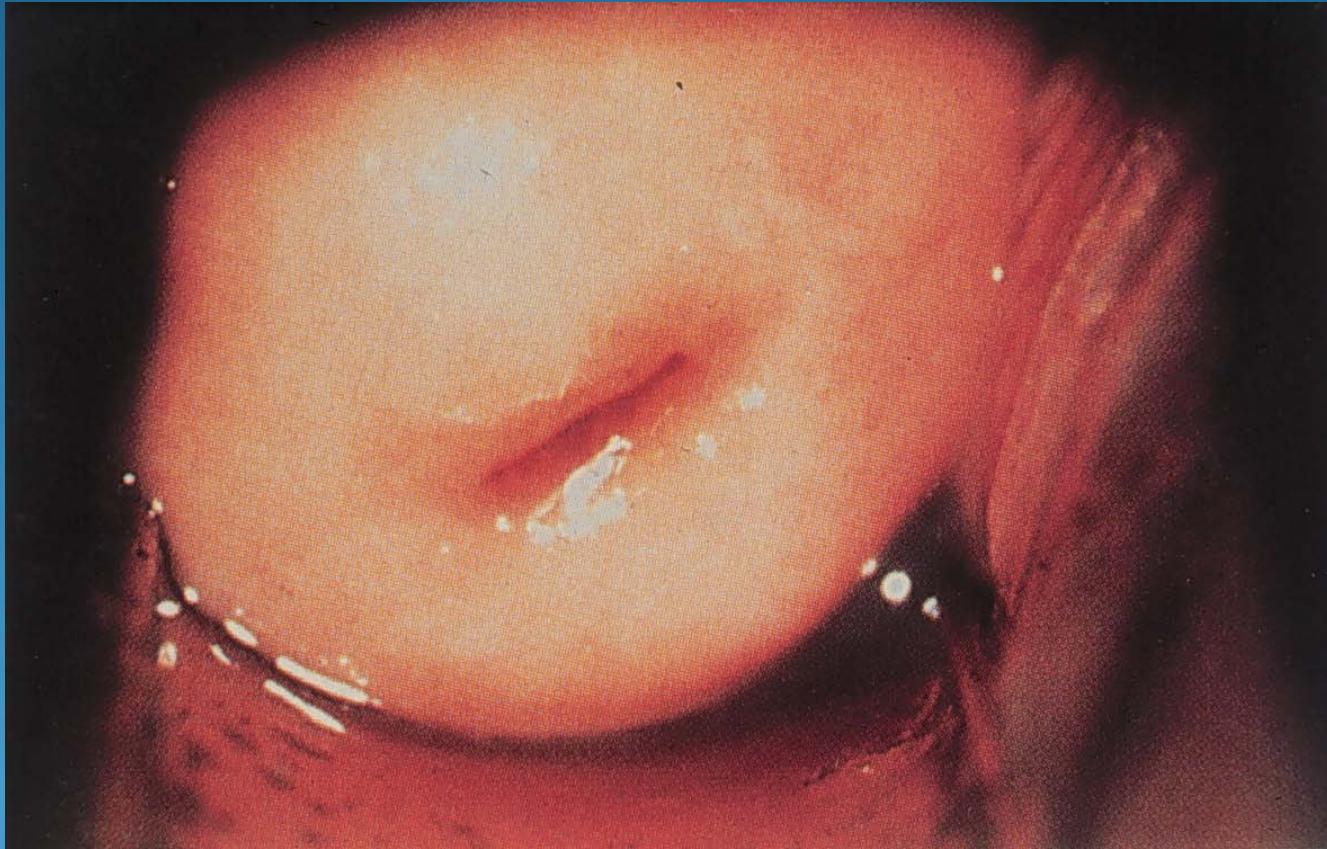
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Gonorrhoea: - Urethral discharge



Normal Cervix



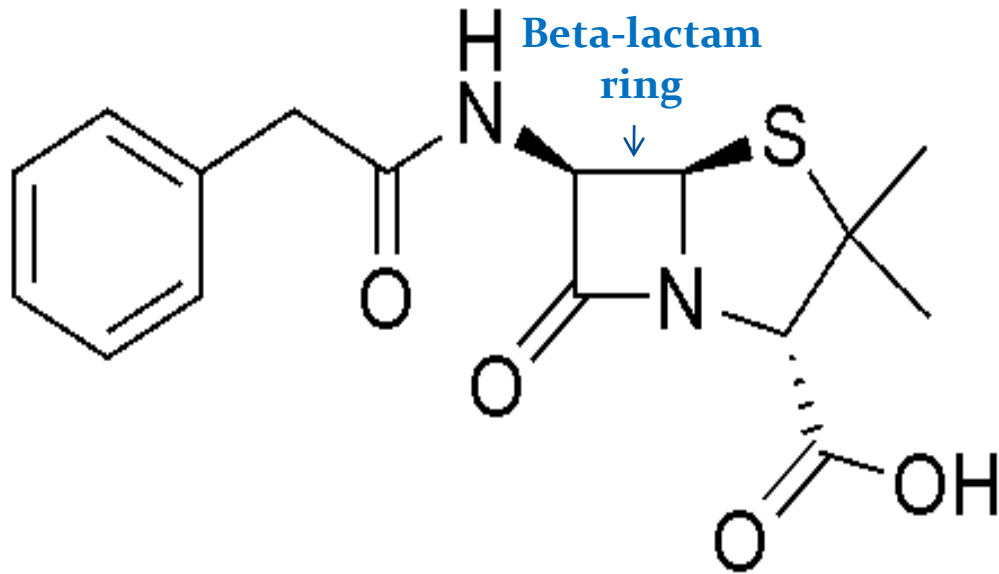
Mucopurulent Cervicitis



Source: Seattle STD/HIV Prevention Training Center

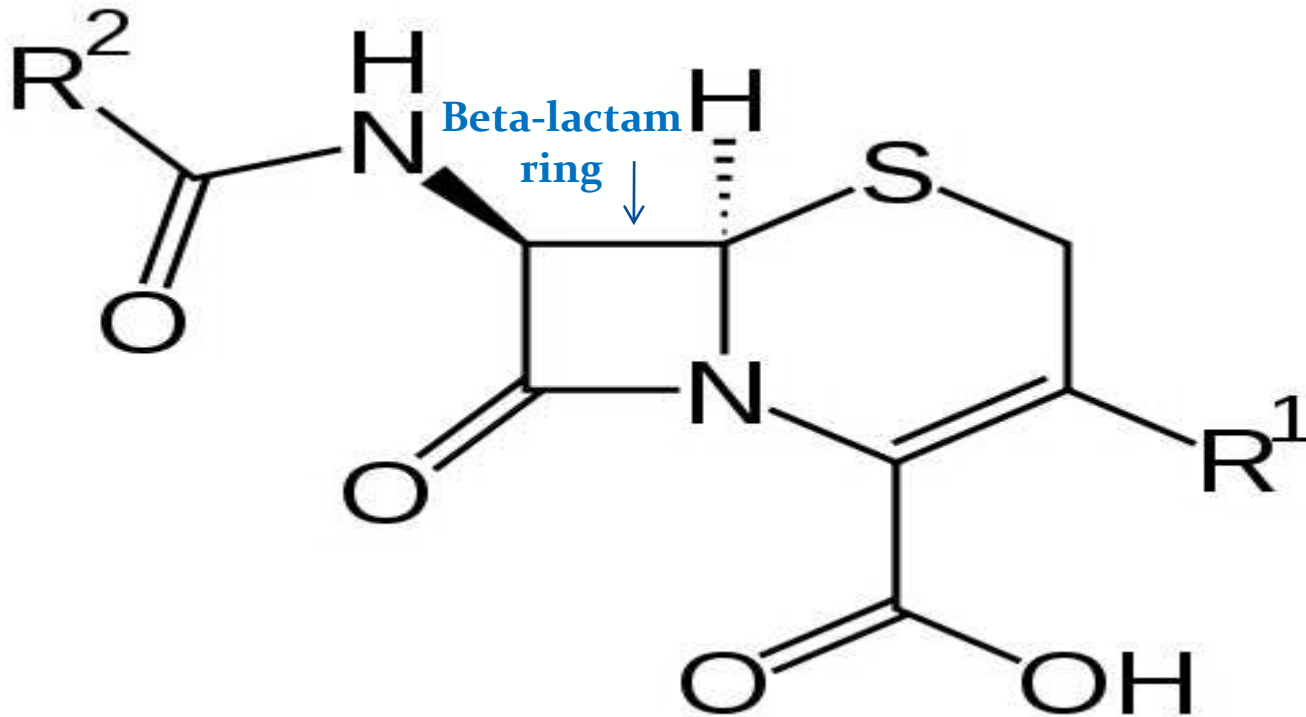
- **1976 - Emergence of *N. gonorrhoeae* with plasmid-mediated β -lactamase (penicillinase) production, which conferred high-level penicillin resistance was first identified**
- **1985 - Plasmid-mediated tetracycline resistance emerged independently in the United States and the Netherland**
- **Mid 1980s - Resistance was already developing with the first fluoroquinolone-resistant isolates described in the mid 1980s**
- **2007 - US CDC recommended that no gonococcal infections in the United States be treated with ciprofloxacin as first-line therapy**

PENICILLIN G



CEPHALOSPORIN ANTIBIOTICS

Core Structure



What makes Penicillin & Cephalosporins Work?

Penicillin-binding proteins (PBPs)

- ❖ Are a normal part of many bacteria
- ❖ Are a group of proteins that have an affinity for and bind to penicillin
- ❖ All beta-lactam antibiotics bind to PBP to prevent cell wall construction by the bacterium

Successful Antibiotic Treatment

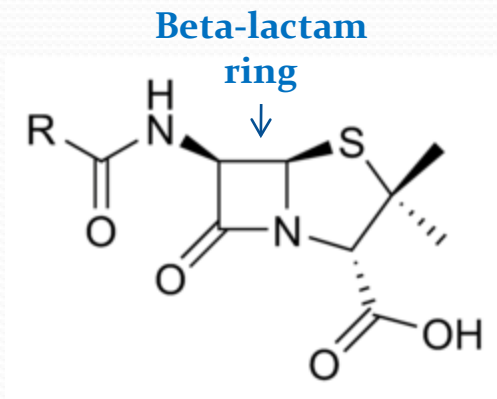
The effectiveness of the beta-lactam antibiotics relies on their ability to reach the Penicillin Binding Protein intact and their ability to bind to that protein

How Resistance Develops

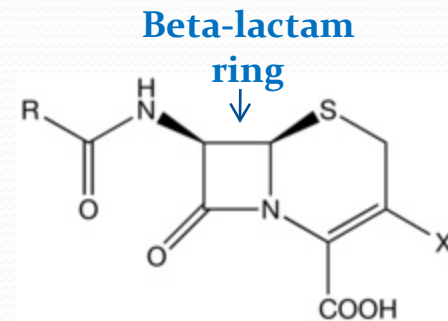
- **Beta-lactamase production**
- **Penicillin binding protein alteration**

Beta-Lactam Antibiotics contain “Beta-Lactam Ring”

“R” represents sites where different chemical side chains attach, depending on the antibiotic

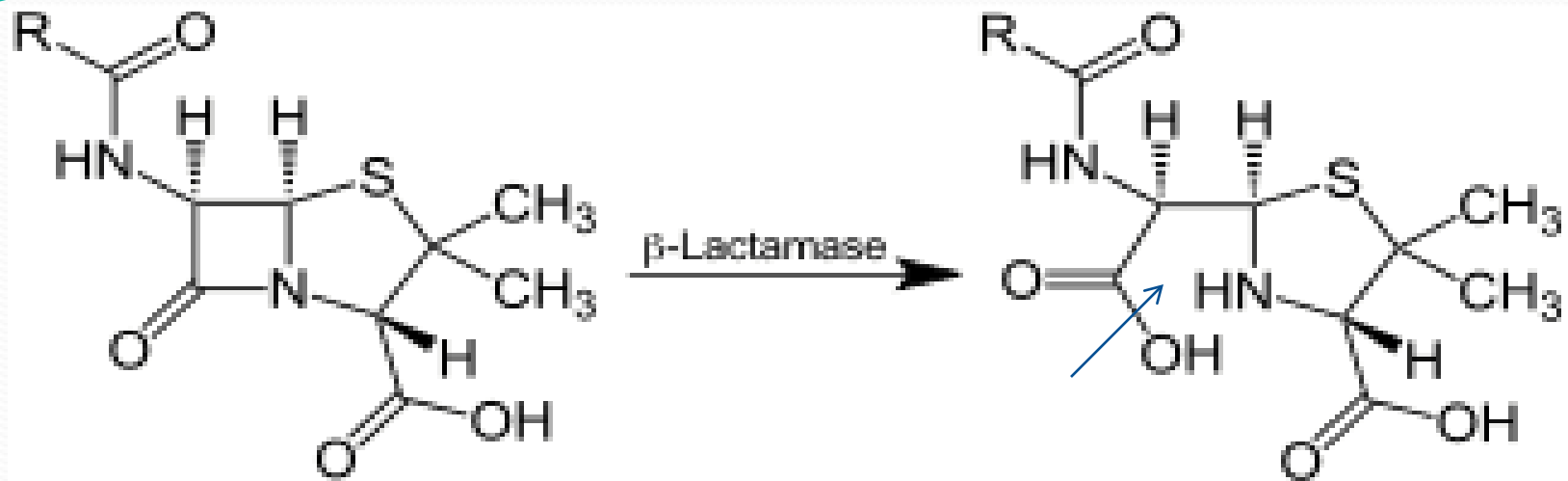


Penicillin



Cephalosporin

Some bacteria produce beta-lactamase enzymes that break the beta-lactam ring & are able to inactivate some forms of these drugs




Penicillinase

- A specific type of Beta-lactamase enzyme showing specificity for penicillins
- If bacteria produce beta-lactamase or penicillinase, the enzyme will break open the β -lactam ring of the antibiotic, rendering the antibiotic ineffective

In Addition...

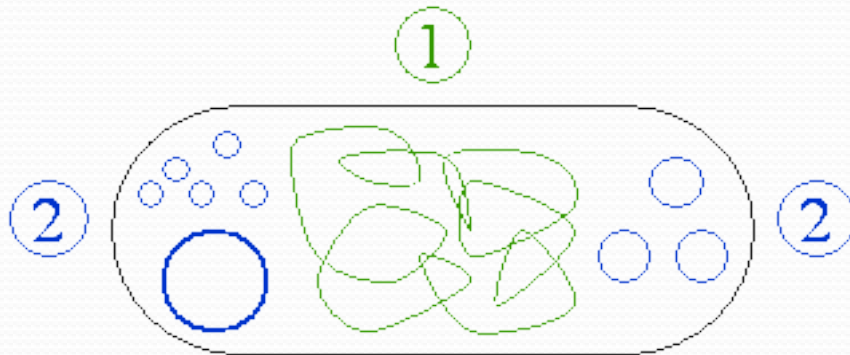
The genes encoding β -lactamase enzymes may be inherently present on the bacterial chromosome or may be acquired via plasmid transfer (plasmid mediated resistance)

β -lactamase gene expression may also be induced by exposure to β -lactam antibiotics



**This probably RESULTS in the BACTERIA
being totally
RESISTANT to that ANTIBIOTIC!!!**

What's a Plasmid?



1 Chromosomal DNA

2 Plasmids

Schematic drawing of a bacterium with plasmids enclosed

A double-stranded or circular DNA present in microorganisms that are capable of replicating independently of the chromosomal DNA

Penicillin Binding Protein Alteration

- Beta-lactam antibiotics cannot bind as effectively to altered PBPs, and, as a result, are less effective at disrupting bacterial cell wall synthesis
- Notable examples of this mode of resistance also include methicillin-resistant *Staphylococcus aureus* and penicillin-resistant *Streptococcus pneumoniae*

“The apple doesn’t fall far from the tree”

**The multiplication of a
cephalosporin resistant bacteria
will invariably result in bacteria
with the same cephalosporin characteristics**



So...to make a long story short...

The mechanism of cephalosporin resistance in gonorrhoea seems to be associated with both an altered Penicillin Binding Protein and other chromosomal mutations which cause β -lactamase production

When Treating Gonorrhoea...

- The production of β -lactamase by a bacterium does not necessarily rule out all treatment options with β -lactam antibiotics
- In all cases where infection with β -lactamase-producing bacteria is suspected, the choice of a suitable β -lactam antibiotic should be carefully considered prior to treatment

What If?

If cephalosporins could not be used...

- **Few good options exist or are in development for treating cephalosporin-resistant gonococci isolates**
- **Preventing the spread of resistant isolates will depend on ambitious antimicrobial management programs, strengthening and expanding surveillance networks, and through effective sexually transmitted disease control and prevention (i.e. public health)**

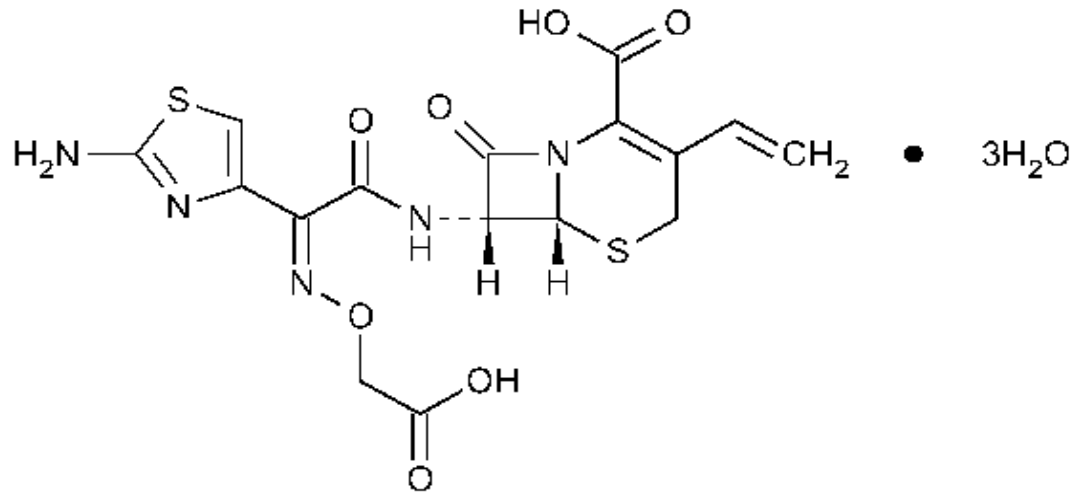
Regardless...

Whether cephalosporin resistance is arising anew or spreading from a few original resistant isolates, or both, surveillance systems are crucial to identify resistant infections for intervention, i.e. public health

From CDC -
**CONSULTATION MEETING ON
CEPHALOSPORIN-RESISTANT GONORRHEA - 2009**

- ✓ *Third generation cephalosporins remain the sole class of antibiotics available which can be used effectively against N.gonorrhoeae*
- ✓ *Recent emergence and spread of gonococcal strains resistant to oral cephalosporins in the Far East is a serious concern*
- ✓ *The emergence of multidrug resistant gonococcal strains which are resistant to both oral and injectable cephalosporin drugs could have a catastrophic effect on gonorrhoea control activities*
- ✓ *The potential emergence and spread of both oral and parenteral cephalosporin-resistance in N. gonorrhoeae (Ceph-R NG) needs to be monitored and appropriate action needs to be taken to avoid a major public health problem*

Cefixime (“Suprax”)



GISP

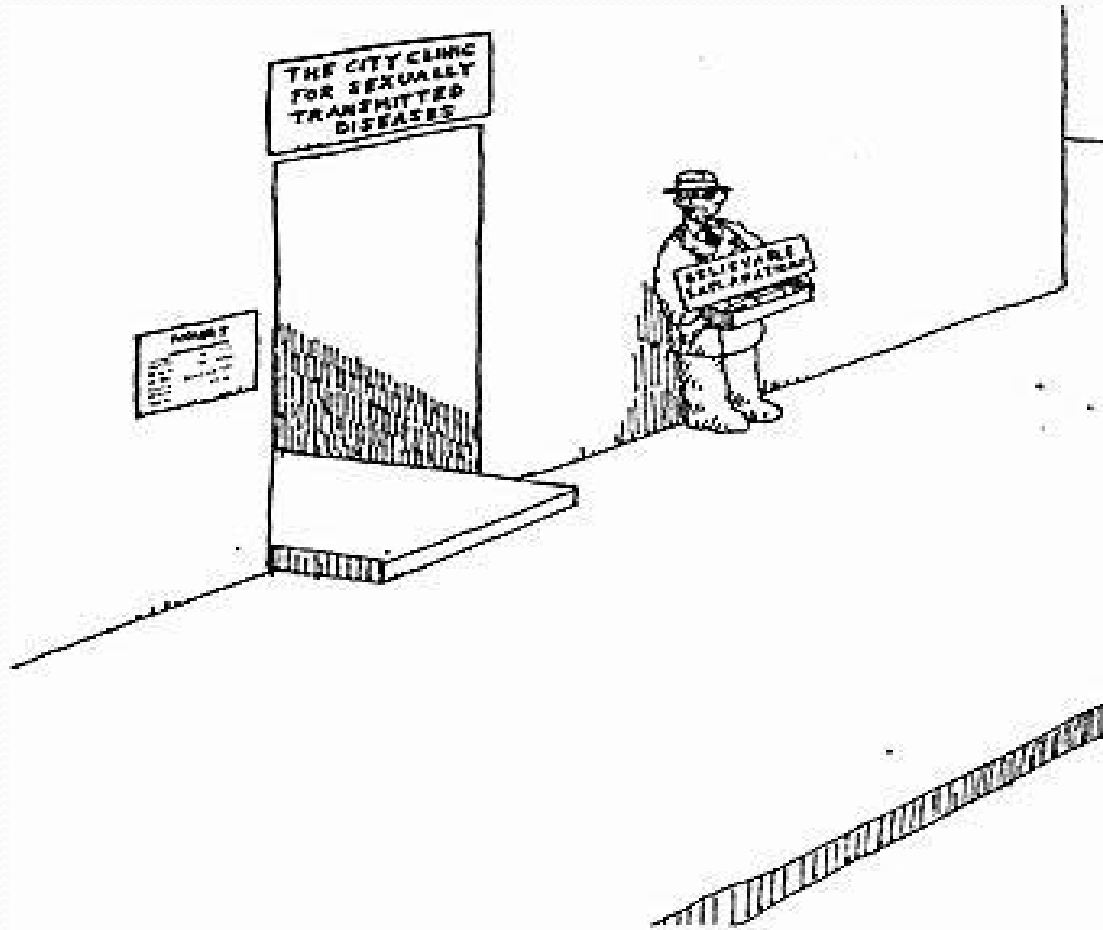
Gonococcal Isolate Surveillance Project

Among GISP isolates, 1990-2008, no isolates with decreased susceptibility to ceftriaxone have been identified in the New Orleans clinic



**....and none as of March 2011,
either!**

**Outside the clinic, an enterprising salesman is selling
“believable explanations...”**



What's new from CDC in the “Guidelines for Treatment?”

Uncomplicated Gonococcal Infections of the Cervix, Urethra, and Rectum

Recommended Regimens

Ceftriaxone 250 mg IM in a single dose

OR, IF NOT AN OPTION

Cefixime 400 mg orally in a single dose

PLUS

Azithromycin 1g orally in a single dose

OR

Doxycycline 100 mg orally twice a day
for 7 days

Uncomplicated Gonococcal Infections of the Pharynx

Recommended Regimens

Ceftriaxone 250 mg IM in a single dose

PLUS

Azithromycin 1g orally in a single dose

OR

Doxycycline 100 mg orally twice a day for 7 days

Remember...

Patients infected with *Neisseria gonorrhoeae* are frequently co-infected with *Chlamydia trachomatis*,

Therefore,

Patients treated for Gonorrhea should routinely be treated for Chlamydia regardless of Chlamydial laboratory results

Note: This dual treatment may also hinder the development of resistant gonorrhea

What about Chlamydial Infection???

Currently...

**No similar recommendation to “dual treat”
if laboratory confirmation is positive
for chlamydia infection
and
negative for gonorrhea**

Chlamydial Infection

During Prenatal Care

**More intensive follow-up is recommended for pregnant women, i.e. re-test 3 weeks after completion of treatment as a test of cure and again 3 months later, if tested + in the 1st trimester; pregnant women <25 years old, women who have a new or more than one sex partner should be re-tested during the 3rd trimester
(In the Office of Public Health we say 30 years old)**

Nongonococcal Urethritis

- *Chlamydia trachomatis* infection most common, but also *Mycoplasma genitalium*
 - Azithromycin treatment best for both micro-organisms

Vulvo-Vaginitis

(Presumptive Trichomoniasis & Candidiasis)

- **TREATMENT:** Metronidazole 2 gm PO STAT *and* Fluconazole 150 mg PO STAT
- Metronidazole is now considered safe for use in a pregnant woman at any time; Fluconazole is not.
- If pregnancy is confirmed or suspected for a patient with vulvo-vaginitis, the patient should be evaluated by a physician and/or an advanced practice registered nurse, so that consideration can be given for prescribing topical treatment of the candidiasis

Trichomoniasis

- “Aptima *Trichomonas vaginalis* Analyte Specific Reagents (ASR)” test now available marketed by Gen-Probe, Inc. – not done in OPH laboratories

Syphilis

- “Azithromycin as a single 2 gram oral dose is effective for treating early syphilis”
- “HOWEVER - *Treponema pallidum* chromosomal mutations associated with azithromycin resistance and treatment failures have been documented in several geographical areas of the United States.”

Genital Warts

Just an item of interest...

a new ointment made from green tea leaves has been added to the list of recommended treatments for genital warts (Rx required) – Sinecatechins 15% Ointment – 16 week treatment, t.i.d., only in those 18 years old and older



Thanks to CDC for continuously updating their recommendations!

Bibliography

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Sexually Transmitted Diseases Treatment Guidelines, 2010;
MMWR December 17, 2010;59 (No. RR-12).

2. Jaber, Parham, MD, MPH **Sexually Transmitted Diseases, A Comprehensive Review of Epidemiology, Pathophysiology, Clinical Management, and Public Health Mitigation Strategies**, Louisiana Office of Public Health Presentation, July 29, 2010 (*Power Point Presentation*)

3. Pennan M. Barry, MD, MPH and Jeffrey D. Klausner, MD, MPH ***The use of cephalosporins for gonorrhea: the impending problem of resistance***, *Expert Opinion on Pharmacotherapy*, March 2009, Vol. 10, No. 4 , Pages 555-577

4. <http://en.wikipedia.org/wiki/Cephalosporin>

5. Many thanks to Mrs. Roma Oliveri, R.N. for her great help in editing this presentation