ΜΕΤΑΠΤΥΧΙΑΚΟ ΠΡΟΓΡΑΜΜΑ
ΛΟΙΜΩΞΙΟΛΟΓΙΑ

Sexually Transmitted Infections

Σ ΤΣΙΟΔΡΑΣ
Καθηγητής Παθολογίας-Λοιμώξεων
Ιατρική Σχολή ΕΚΠΑ

STIs

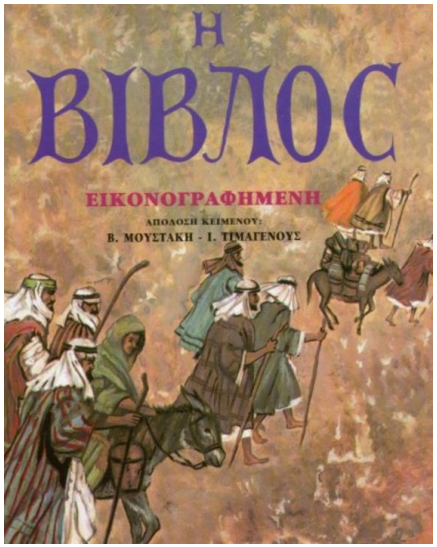
- ✓Transmitted from person to person
  - main mode -> sexual intercourse

- ✓Some w other modes as well eg
  - Infected syringes (AIDS, HBV, HCV)
  - Blood transfusion
  - Mother to infant

STIs

- ✓at least 25 different

- ✓From the time of the Bible & Ancient Egyptians



STIs

- ✓ Important cause
  - ✓ Morbidity
  - ✓ Sterility / infertility
- ✓ Even Mortality!

STIs

- ✓ Annually - 250 million cases globally
- ➢ 1/3 in adolescents

Adolescence & STIs (1)

- Onset of sexual life
- Lack of prevention (ignorance, reaction, spontaneity)
- ↑ risk behaviors (n, choice, drug use, experimentation)

STIs

- ✓ **When to suspect?**
  - **If any Sx from genitalia**
    - Wounds, ulcers, secretions from urethra, vagina, itching, pain or burning during urination, swollen lymph nodes esp inguinal
  - **Rash & fever** may indicate **systemic dz &/or STIs**

STIs

- **When do we suspect?**
  - If a **sexual partner** has a **dx of an STD**
  - very important -> in case of dx w an STD -> have to **inform your partner(s)**

STIs

- ✓ **PROBLEM**
  - They can be **transmitted** even **with no Sxs in one of the partners!!!**
    - eg genital HSV

Important STIs

- ✓ All!!!
- ✓ “Wounds” (ulcers)
  - ✓ Syphilis
  - ✓ Genital HSV (HSV-2, HSV-1)
    - ✓ Other non common
      - ✓ Lymphogranuloma venereum
      - ✓ Chancroid
      - ✓ Granuloma inguinale

Important STIs

- **<u>«Wet» (secretions)</u>**
  - **Gonorrhea (GC)**
  - **Chlamydia, NGU**
  - Trichomonas vaginitis/urethritis
  - Candidiasis (vulvovaginal, ? men)

- Others
  - HIV, AIDS
  - **HPV** (types 16, 18 & others) & cervical Ca

«WET» LESIONS

Case of urethral discharge

- Young sexually promiscuous man comes to the clinic with the following Sxs.

  Possible Dx?

1. **Mycoplasma urethritis**
2. **Gonorrhea**
3. **Chlamydial urethritis**

NGU - etiology

- *C. trachomatis* 20-40%
- Genital mycoplasmas 20-30%
  - *Ureaplasma urealyticum, Mycoplasma genitalium*
  - Occasional *Trichomonas vaginalis*, HSV
  - Unknown in ~50% cases

Chlamydia & Risk factors

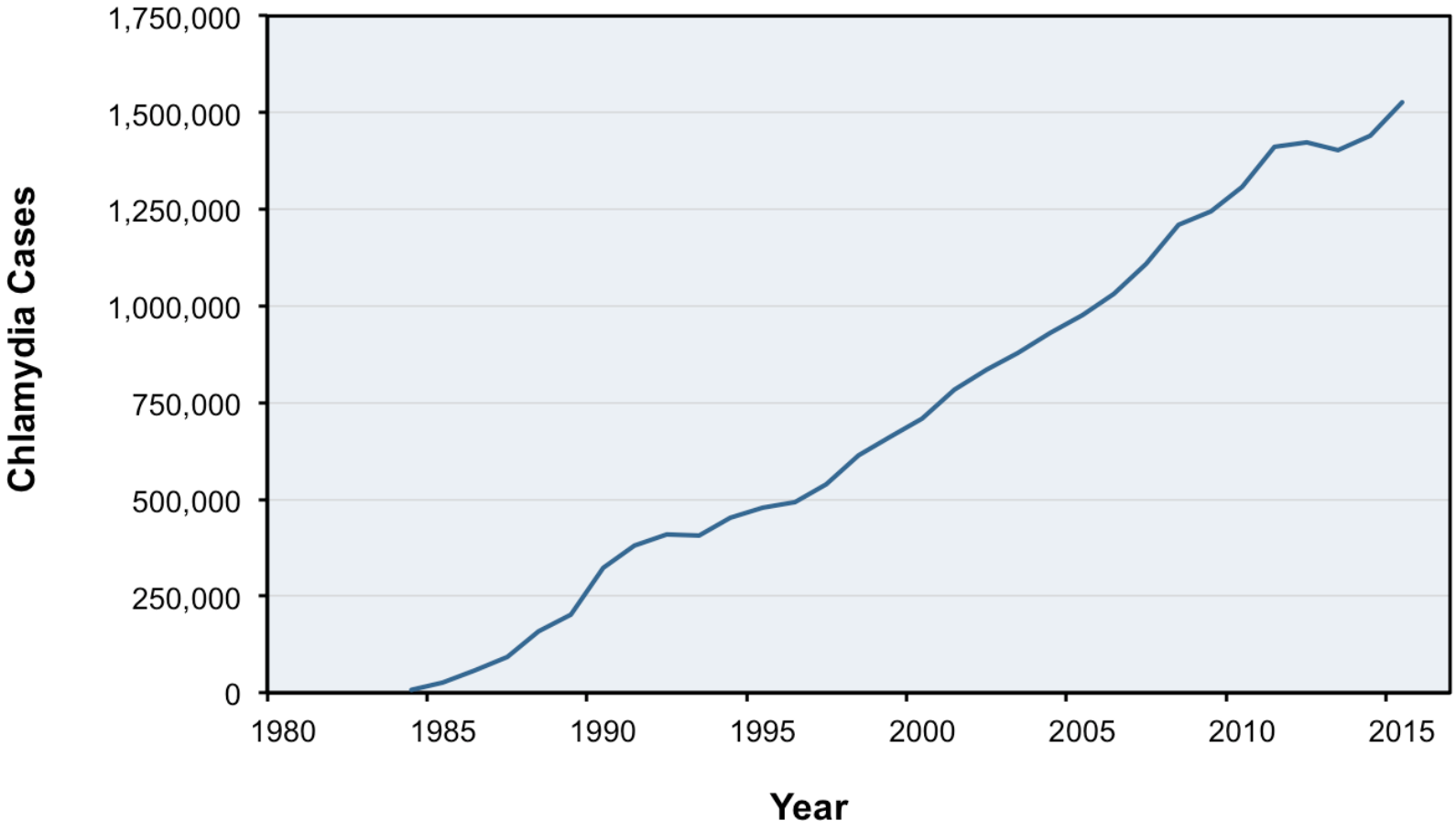
- new or multiple sex partners
- a history of STIs, presence of another STI
- lack of barrier contraception

Ann Intern Med. 2014;161:902-10.

Chlamydia spp

- We can all be affected
  - More common in **adolescence & young adults**

Chlamydia cases per year, USA



Chlamydia

- Chlamydia is the most common reportable bacterial sexually transmitted infection (STI) in the US,
- > 1.5 million cases reported in 2015

Chlamydia spp

- Most people **do not know they have it**
  - **Asymptomatic & spreading !!!**
  - **actual n of infections maybe even higher**

C. trachomatis, transmission

- High rates of Transmission w sex,
  - Between (+) partners -> % infection ~ 55%
  - Per sexual act -> risk of transmission 10%

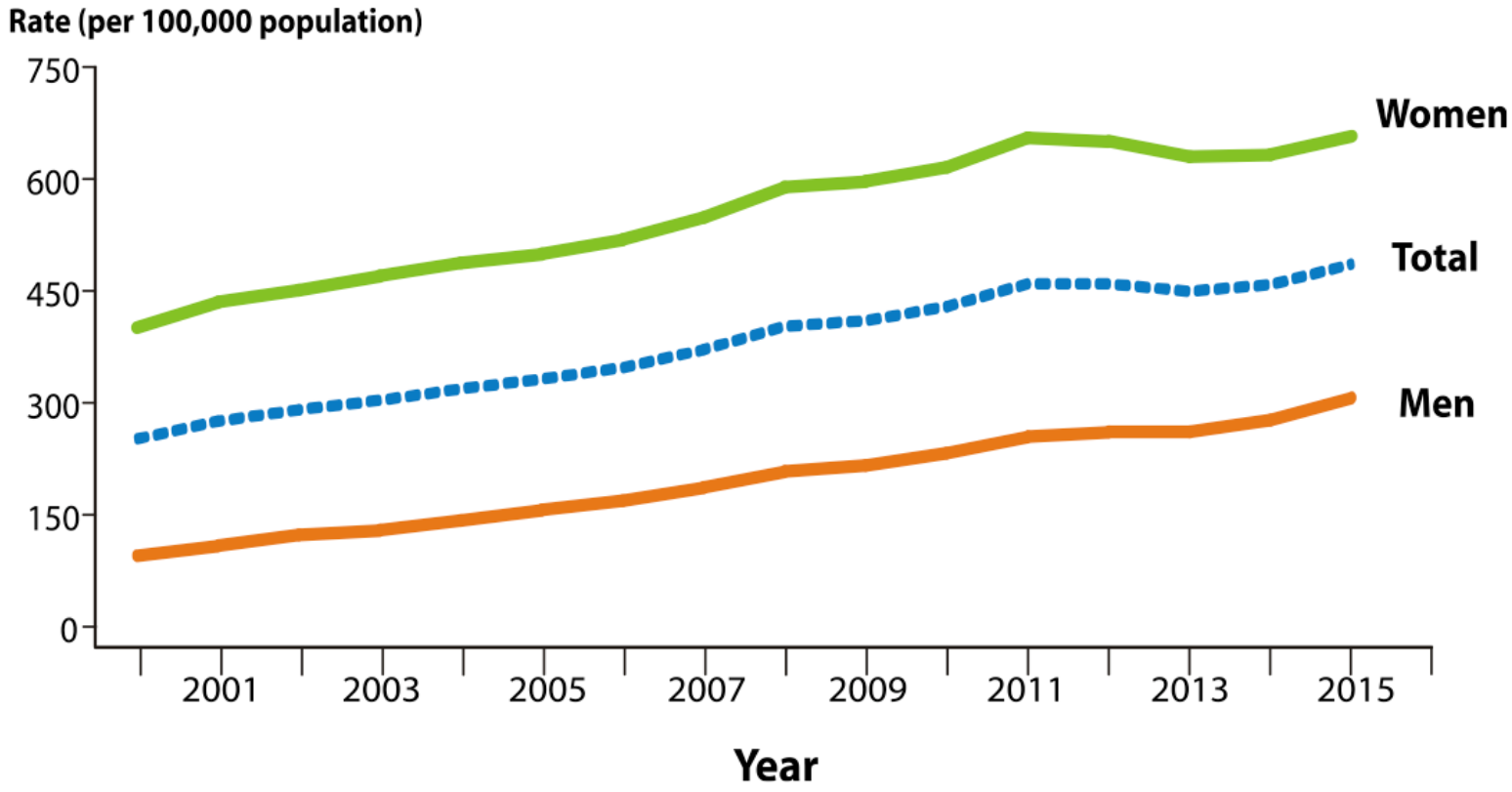
Health Technol Assess. 2014;18:1-100

C. trachomatis, Transmission

- Sexual transmission rates per sex act
  - slightly higher from men-to-women than from women-to-men

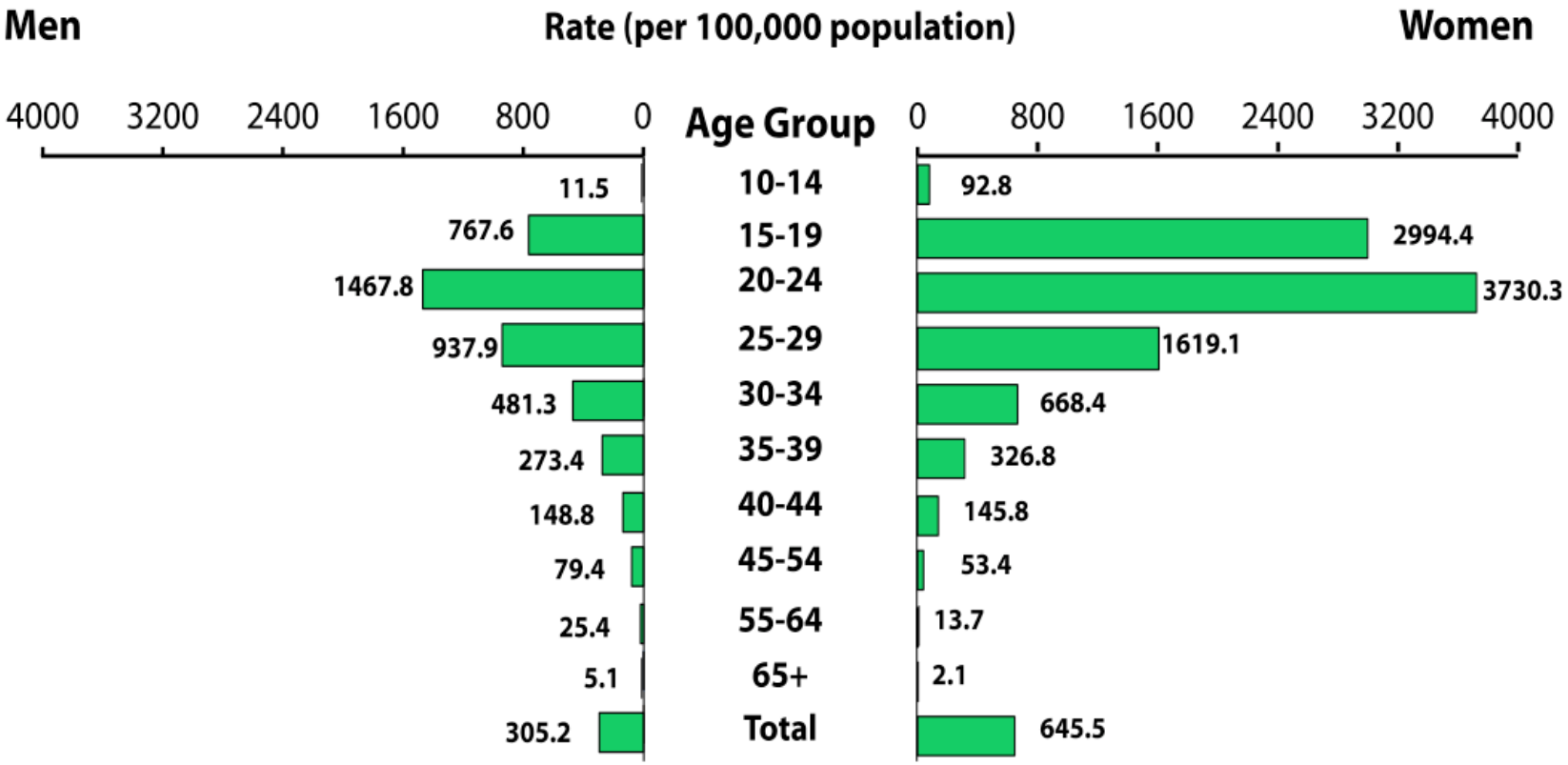
Health Technol Assess. 2014;18:1-100

Chlamydia & young women



Highest rates -> in women 15-24 yrs old

Chlamydia & Ages 15-24 yrs



MMWR Morb Mortal Wkly Rep. 2014 Sep 26;63(38):834-8.

Incubation period

- the incubation period for *C. trachomatis* infection
  - estimated to be 7 to 21 days.

Chlamydia spp

- When Symptoms exist
  - Wet secretions from vagina (women) or urethra (men)
  - Burning in urination (women & men)
  - Burning or itching at the tip of the penis – urethra (men)

Chlamydia in women -> cervicitis
Asymptomatic in 70-80% of cases

- Muco-purulent cervicitis

Seattle STD/HIV center

C. trachomatis
Genital infection in men

- Urethral discharge - non gonococcal urethritis

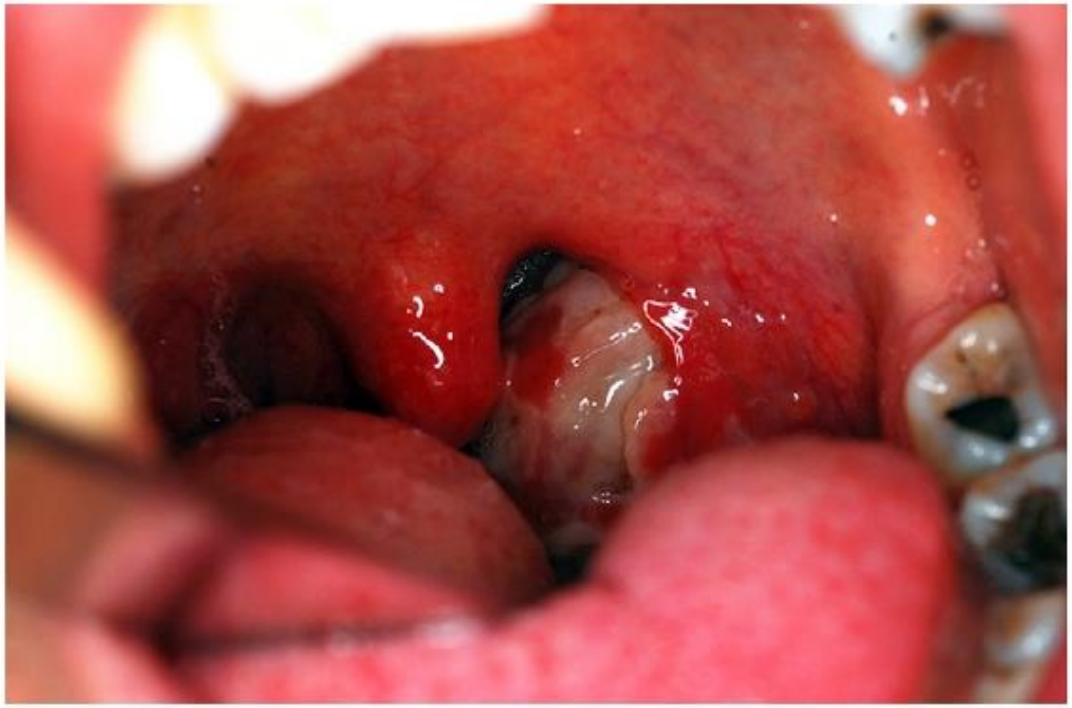
C. trachomatis

Manifestations both in men/women

- **Conjunctivitis**

C. trachomatis
Manifestations both in men/women

- Chlamydial tonsillopharyngitis



Öztürk O et al. Case Rep Otolaryngol 2012

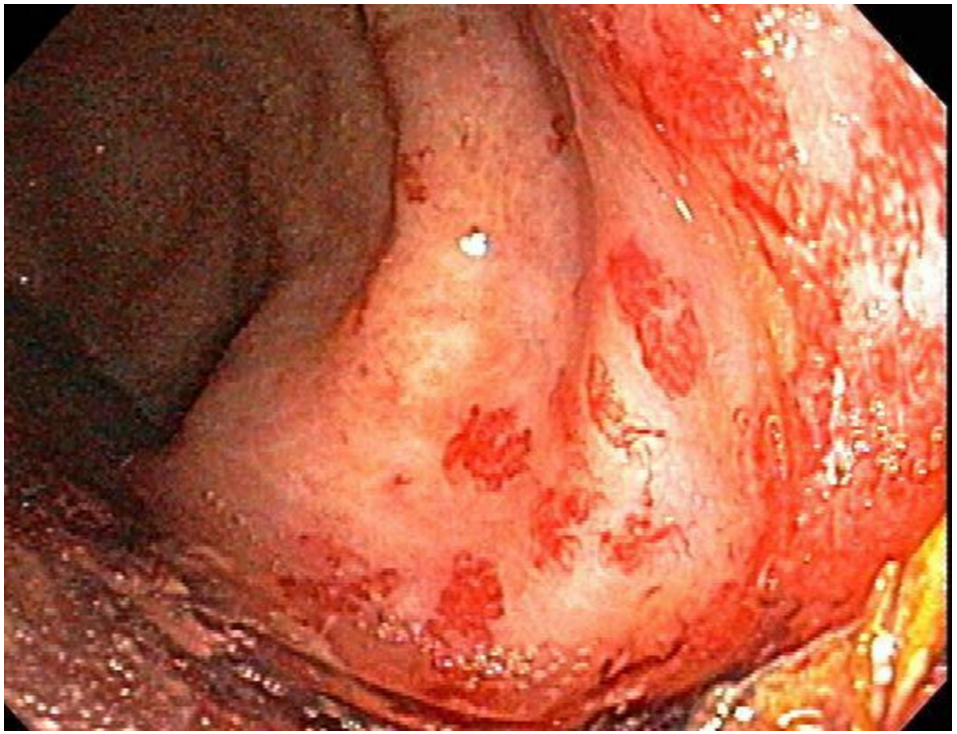
C. trachomatis
Manifestations both in men/women

- Chlamydial proctitis & proctocolitis
  - Asymptomatic usually but may have
    - Rectal pain
    - Mucoid or hemorrhagic discharge
    - Fever &/or Tenesmus

Dig Dis Sci. 2012;57:269-73.

C. trachomatis
Manifestations both in men/women

- Chlamydial proctitis & proctocolitis



Chlamydia & another risk!!!

- rectal chlamydia infection in MSM
- Significantly ↑↑↑ the risk of HIV acquisition

J Acquir Immune Defic Syndr. 2010;53:537-43.

C. trachomatis
Manifestations both in men/women

- Reactive arthritis
  - previously referred to as Reiter's syndrome
  - post-inflammatory autoimmune dz that can result from urogenital chlamydia infection (3-6 wks after)

C. trachomatis
Manifestations both in men/women

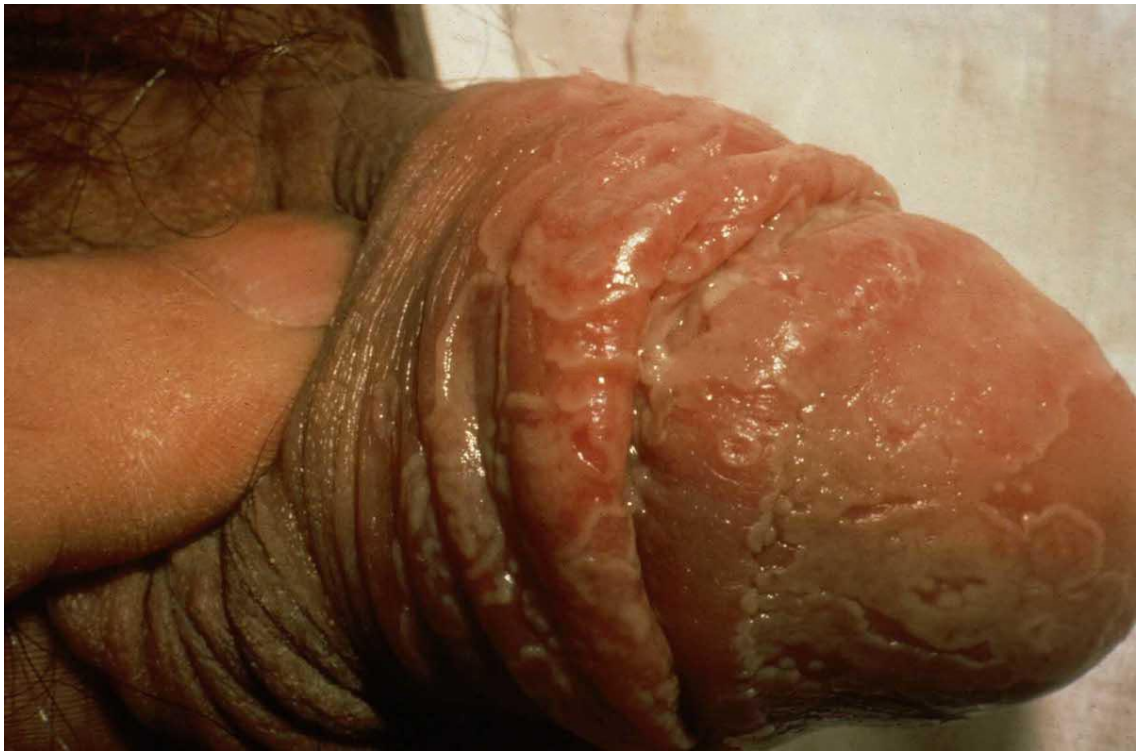
- Reactive arthritis
  - Conjunctivitis
  - Urethritis
  - Oligoarthritis &
  - Skin lesions
    - keratoderma blennorrhagica & circinate balanitis

C. trachomatis
Manifestations both in men/women

- Reactive arthritis & keratoderma blennorrhagica

C. trachomatis
Manifestations both in men/women

- Reactive arthritis & circinate balanitis



C. trachomatis
Manifestations both in men/women

- Reactive arthritis
  - affects predominantly males,
    - Particularly if (+) for HLA-B27
  - usually resolves within 3 to 6 months
    - Responds to NSAIDs

Chlamydia - when to test?

- Young < 25 yrs old & sexually active?
  - Test annually, w pregnancy, more frequent if Hx of recent
- In addition test if
  - > 25 yrs & multiple partners
  - New partner, partner w STD
  - Pregnancy, rescreen in 3rd trimester

C. trachomatis
Laboratory diagnosis

- NAATs, multiple available
  - Urine, urethral/endocervical swabs
    - In men 1st catch urine specimen
    - in women vaginal swab

MMWR Recomm Rep. 2015;64(No. RR-3):1-137.

Chlamydia - Rx

- Need Abx therapy
  - If not serious complications eg
    - PID, ↓ fertility, ectopic pregnancy,chronic pelvic pain
- Can recur or relapse
  - If no Rx in partner

C. trachomatis, Rx

2015 STD Treatment Guidelines: Chlamydial Infections

Table 1. Treatment of Urogenital Chlamydial Infections in Adolescents and Adults

Recommended

Azithromycin
1 g orally in a single dose

or

Doxycycline
100 mg orally twice a day for 7 days

C. trachomatis, Sex partners

- Rx all sex partners -sexual contact
  - in the preceding 60 days
- Abstain from sex x 7 days

Chlamydia & Complications

- major complications for women, including
  - pelvic inflammatory disease
  - chronic pelvic pain
  - fallopian tube scarring
  - infertility

J Infect Dis. 2010;201 Suppl 2:S134-55.
BMJ Clin Evid. 2013;2013.

Pelvic Inflammatory Disease

- General term for uterine, tubo-ovarian infection
- Serious complication of STIs
  - Gonorrhea
  - Chlamydia spp
    - 10-15% if NO Rx
    - Most subclinical infection

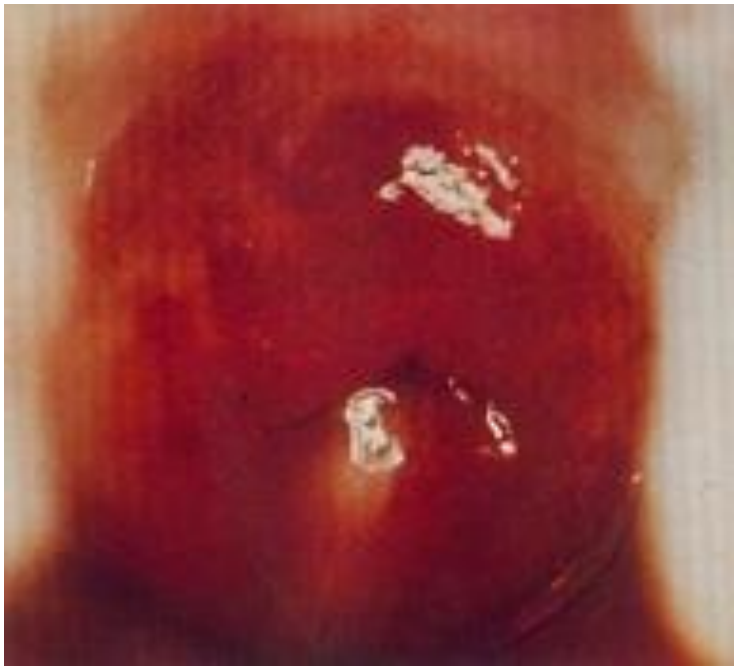
C. trachomatis
Genital infection in women

- Pelvic Inflammatory Disease
  - subclinical to acute clinical syndrome
  - ascending spread of microbes from cervix to
    - endometrium, fallopian tubes, ovaries, and contiguous structures

PID

↑ Cervical motion tenderness, Pain appendages

Cervical sample sent for testing



C. trachomatis
Genital infection in women

- Pelvic Inflammatory Disease
  - can result in tubal scarring that may cause
    - tubal factor infertility &
    - ↑ the risk for ectopic pregnancy

BMJ Clin Evid. 2013;2013
N Engl J Med. 2015;372:2039-48

C. trachomatis
Genital infection in women

- Pelvic Inflammatory Disease
  - 20% of women Rx'ed for PID become infertile,
  - 30% develop chronic pain
  - 1% who conceive have an ectopic pregnancy

Am J Obstet Gynecol. 2002;186:929-37.

Pelvic Inflammatory Disease

- No test for dx – based on Sxs
  - Abdominal pain
  - Fever
  - Vaginal secretion
  - Dyspareunia
  - Blood between menses

  - T, GC/CT dx, CRP/ESR, CMT, mucopurulent secretion

PID-indications for Sx, options

TOA->60-80% resolve w Abx

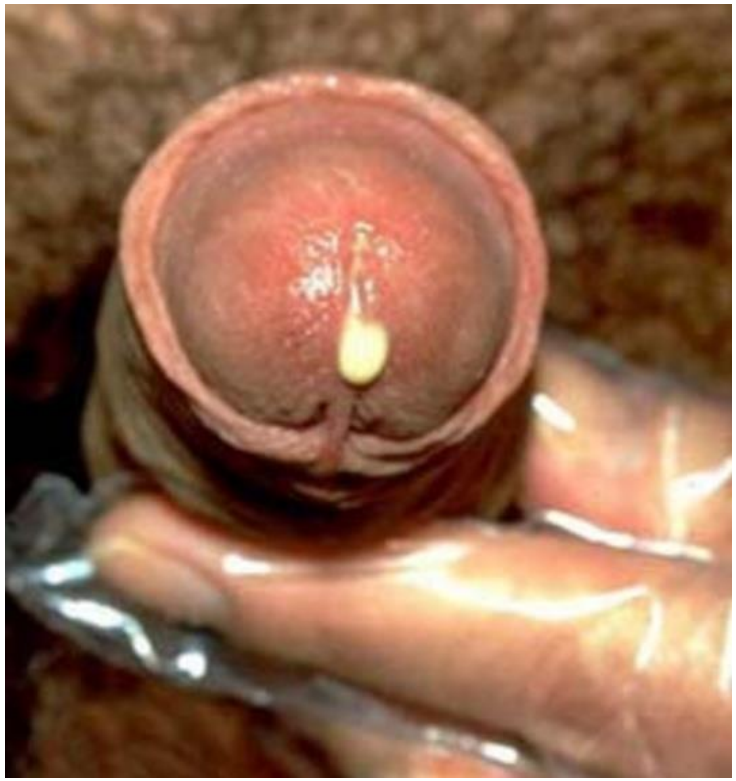
- Ideally after acute infection/inflammation
- no improvement at 72 hrs, ruptured abscess
  - Laparoscopy, ? Other dx
- Difficult in recurrent PID
- Options - may depend on pt's desire for fertility
  - unilateral salpingo-oophorectomy or
  - hysterectomy & b/l salpingo-oophorectomy

Gonococcal urethritis (Gonorrhea)

- Cause: *Neisseria gonorrhoeae*.

Gonorrhea vs. NGU

Gonococcal discharge



Non-Gonococcal discharge

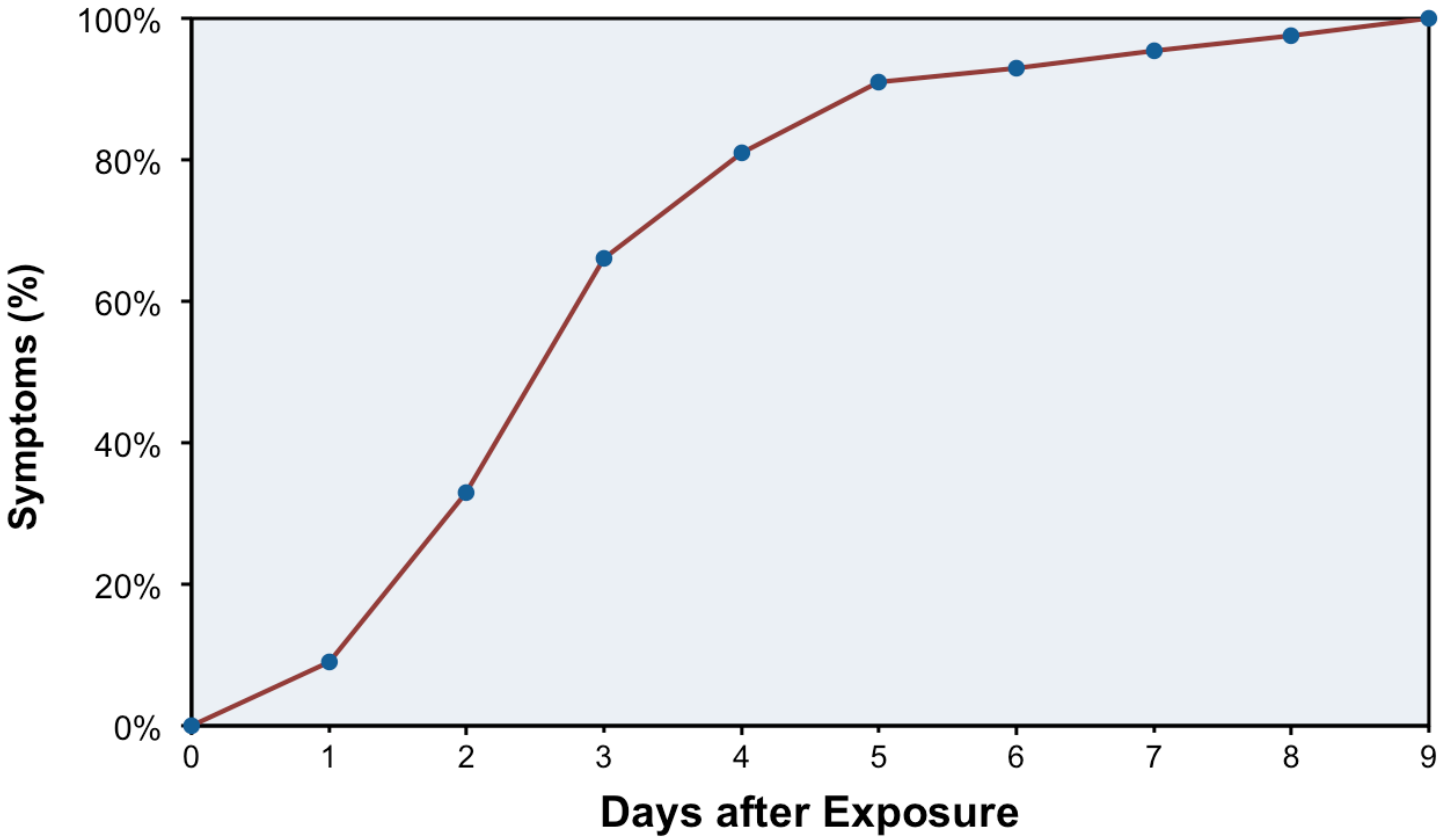
Gonorrhea - male

- ✓ Burning in urination
- ✓ Purulent secretions

Gonorrhea - transmission

- M -> F 50-70%
- F -> M 20%
- F -> M - w >= 4 acts 60-80%
- Oro – genital sex

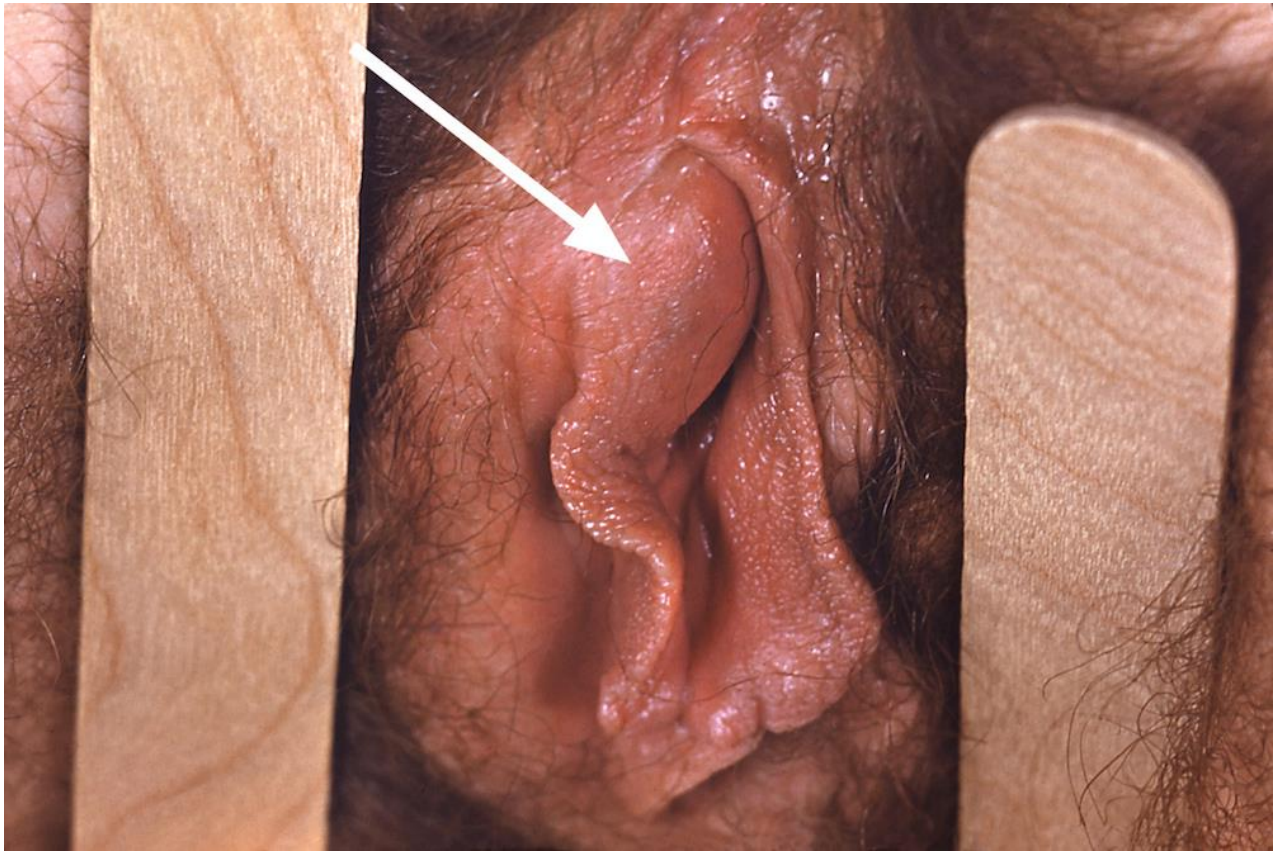
Incubation period



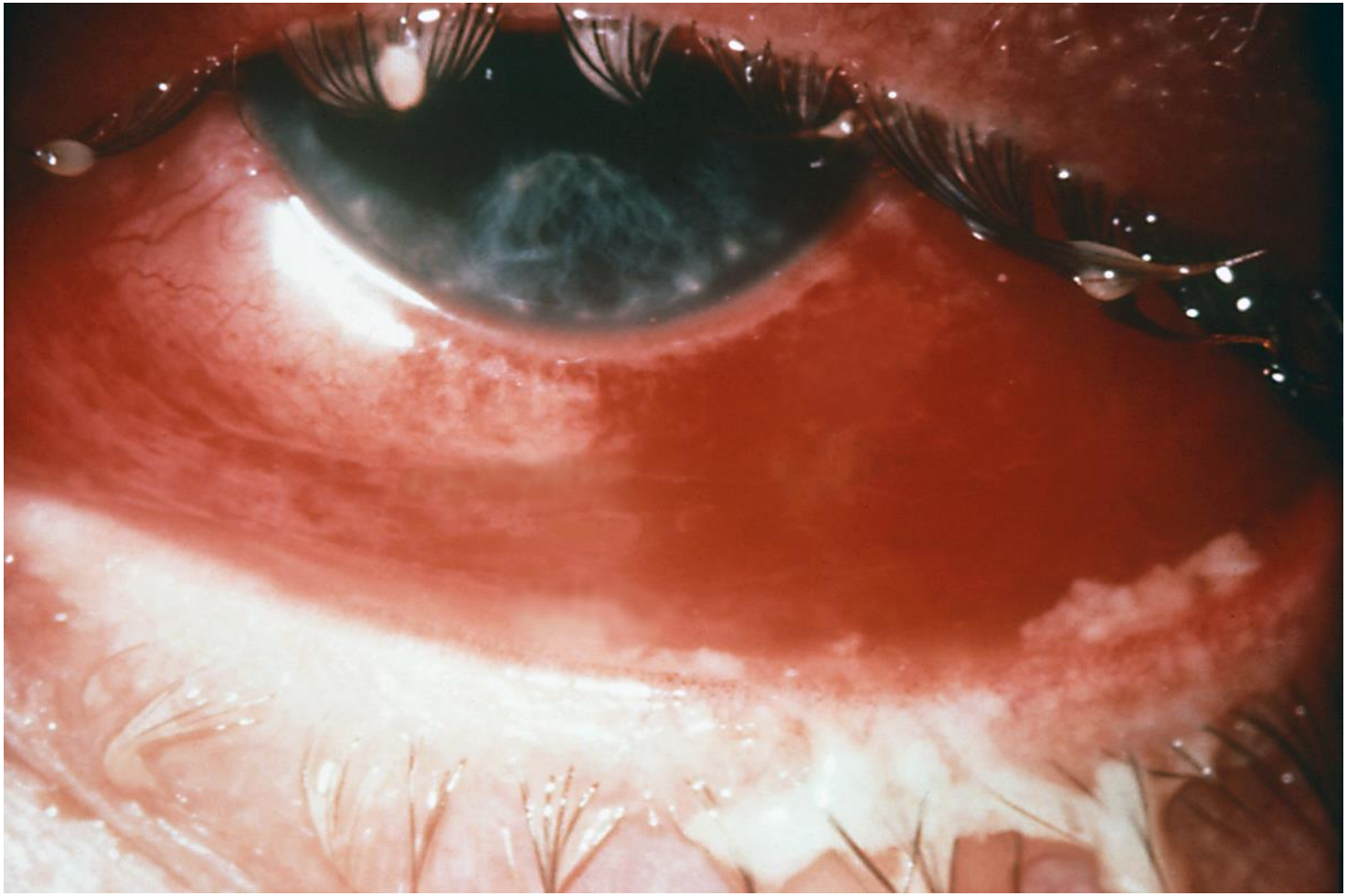
2-7 d after suspicious contact

Gonorrhea - female

- ✓ Cervicitis &/or urethritis – 50% asymptomatic



Gonorrhea - conjunctivitis



Gonorrhea, DGI

- Disseminated gonococcal infection
  - W>M, strains that produce bacteremia w no genital Sxs
  - Complement deficiency
  - Clinical manifestations
    - Skin lesions, arthralgia, tenosynovitis, arthritis, hepatitis, myocarditis, endocarditis, and meningitis.

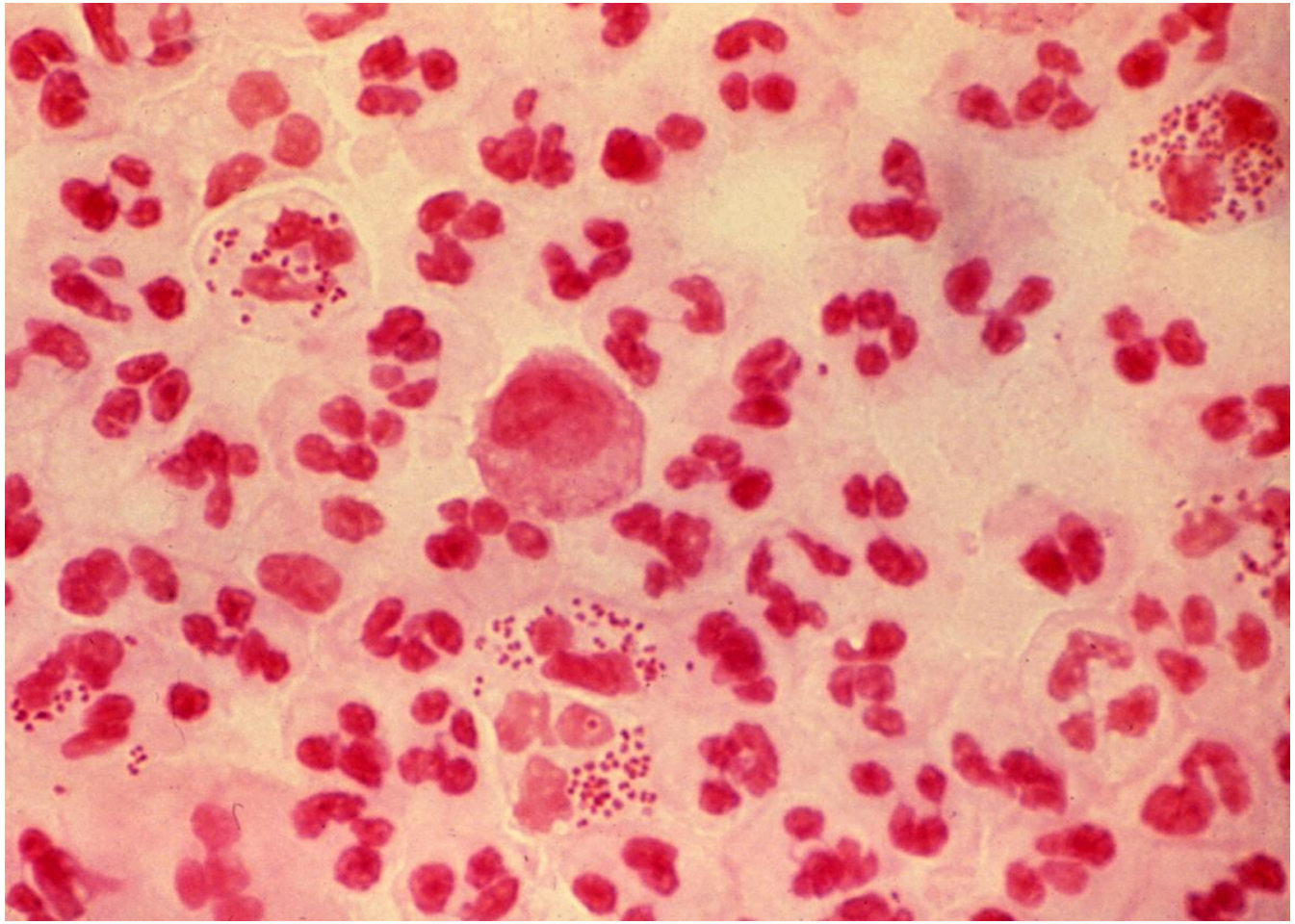
Gonorrhea, arthritis, DGI

Gonorrhea, Laboratory diagnosis

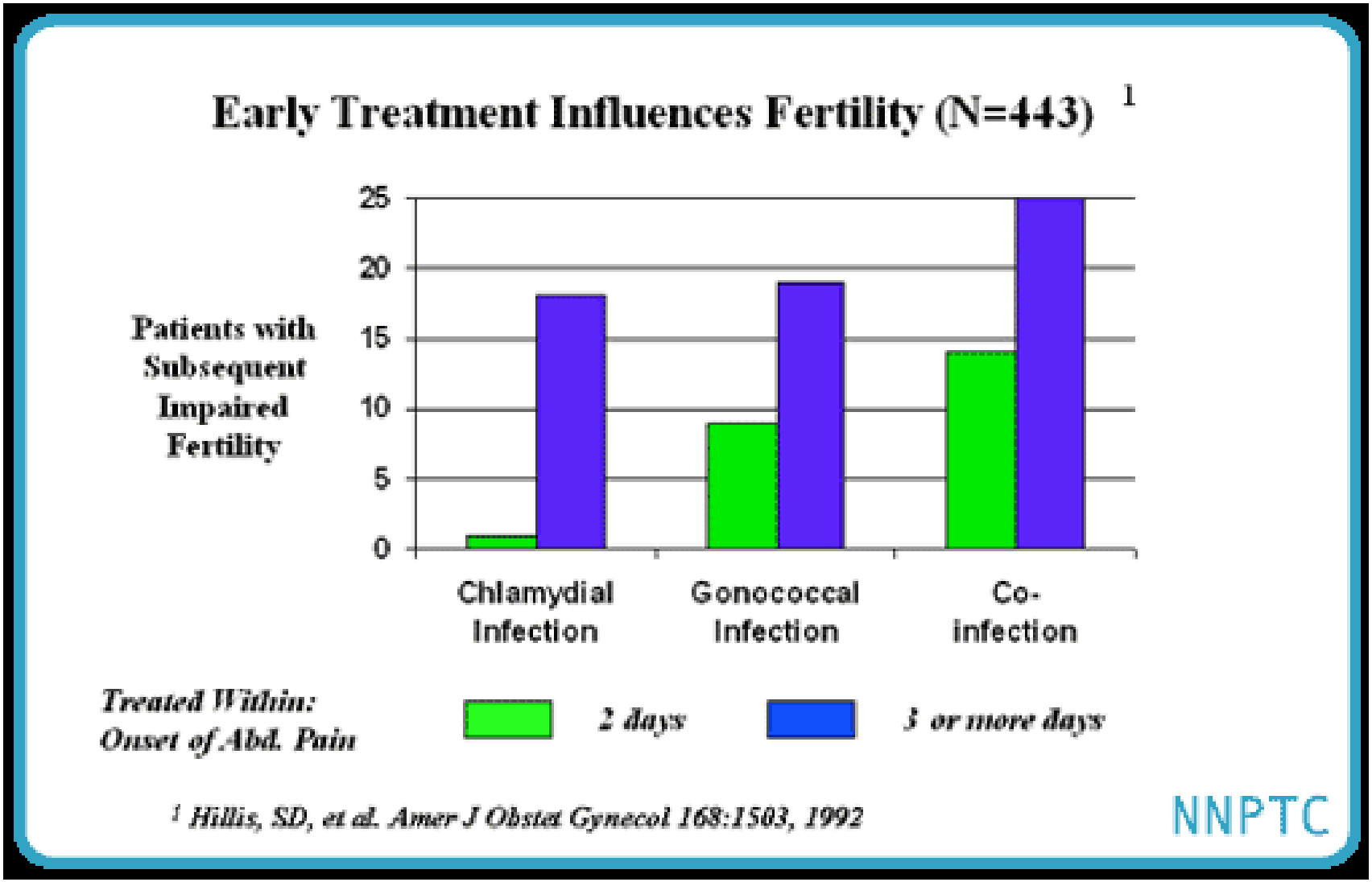
- NAATs
  - Endocervical women, urethral men, urine men/women, vaginal swabs
  - Many of the commercial can test for Chlamydia as well
  - Most sensitive test

Gonorrhea, urethritis in man,

Gram stain



Early Rx & fertility



Gonorrhea-Rx

- Rx'ed w Abx
- Important problem -> ↑ in R, recent XDR cases, UK
- Frequent coinfection w chlamydia
  - Rx for both

XDR Gonorrhea, 2018

R to CFTXN, azithro

RAPID RISK ASSESSMENT

Extensively drug-resistant (XDR) *Neisseria gonorrhoeae* in the United Kingdom and Australia

7 May 2018

XDR Gonorrhea, 2018-2019

R to CFTXN, CFXM, tetra, PCN, cipro, IR to azithro

European Centre for Disease Prevention and Control
An agency of the European Union

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Home > News & events > Extensively drug-resistant gonorrhoea: risk of further dissemination within and across Europe

< News & events

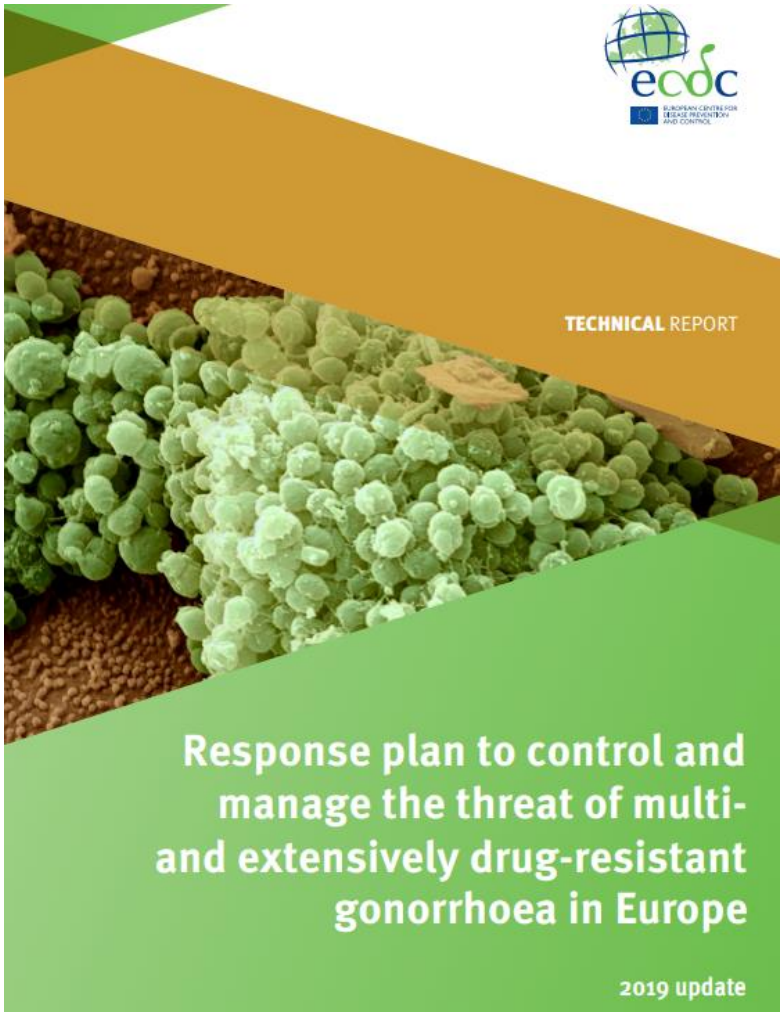
Extensively drug-resistant gonorrhoea: risk of further dissemination within and across Europe

ECDC comment

1 Apr 2019

XDR Gonorrhea, 2018-2019

? Further spread in Europe



Gonorrhea, Rx

2015 STD Treatment Guidelines: Gonococcal Infections

Table 1. Treatment of Uncomplicated Gonococcal Infections of the Cervix, Urethra, and Rectum

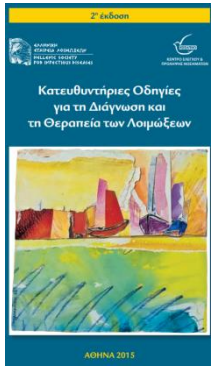
Recommended Treatment of Uncomplicated Gonococcal Infections of the Cervix, Urethra, and Rectum

Ceftriaxone 250 mg IM in a single dose	+	**Azithromycin** 1g orally in a single dose

Note: As **dual** therapy, ceftriaxone and azithromycin should be administered together on the same day, preferably simultaneously and under direct observation.

Alternative if Ceftriaxone is not available:

Cefixime 400 mg orally in a single dose	+	**Azithromycin** 1 g orally in a single dose



Gonorrhea, Rx

Ελληνικές οδηγίες ΚΕΕΛΠΝΟ, 2015

Προτεινόμενο σχήμα	Κεφτριαξόνη 500mg ενδομυϊκώς, εφάπαξ ΜΑΖΙ ΜΕ Αζιθρομυκίνη 2 gr από του στόματος, εφάπαξ
Εάν δεν είναι διαθέσιμη η κεφτριαξόνη ή ο ασθενής αρνείται την παρεντερική θεραπεία	Κεφιξίμη 400 mg από του στόματος, εφάπαξ ΜΑΖΙ ΜΕ Αζιθρομυκίνη 2 gr από του στόματος, εφάπαξ

Vaginitis

- The 3 most common conditions diagnosed among women with vaginal symptoms presenting in the primary care setting are
  - Bacterial vaginosis -> 22-50%
  - Vulvovaginal candidiasis -> 17-39%
  - Trichomoniasis -> 4-35%
  - No etiologic agent identified -> 30%

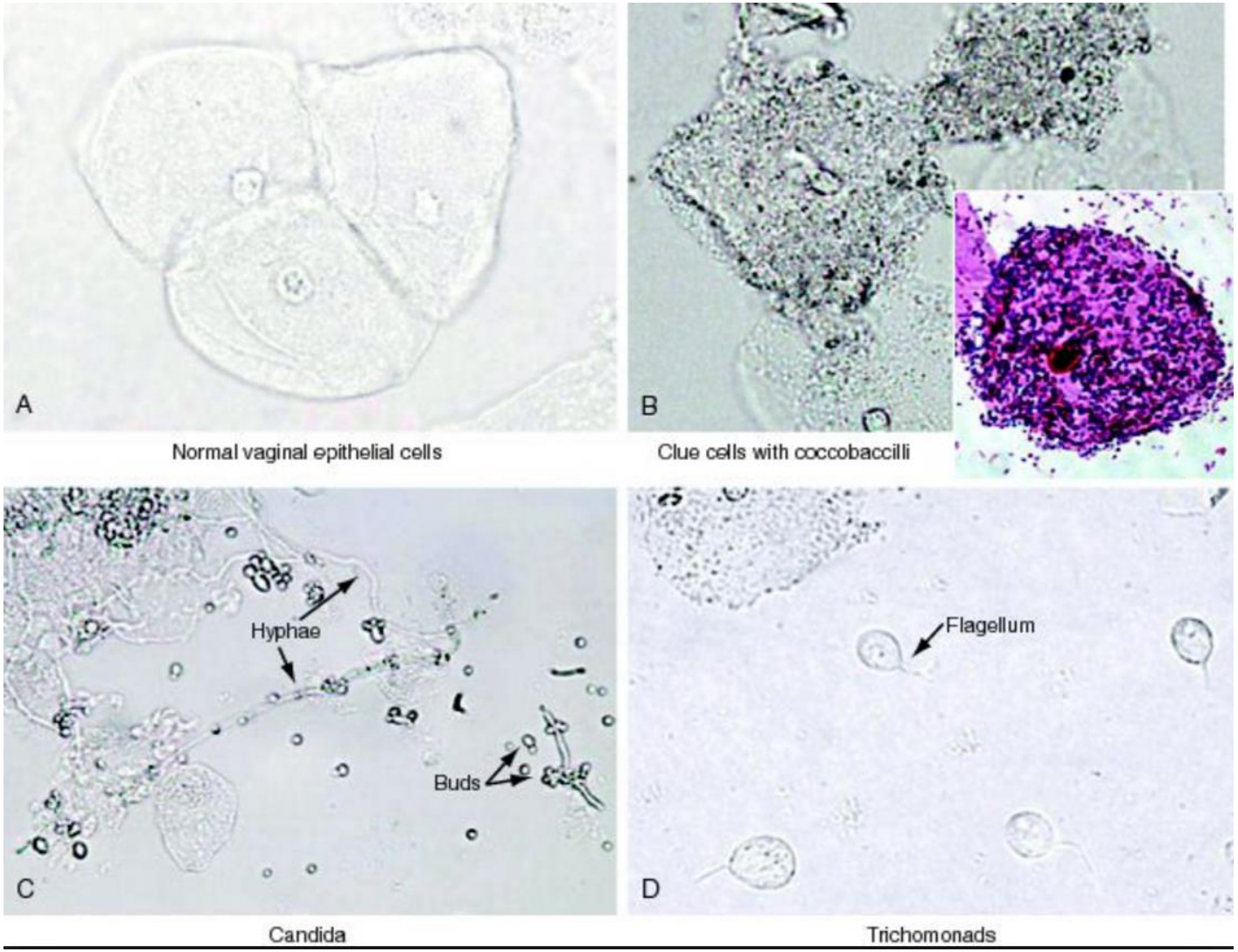
Other causes of vaginal d/c

- Normal physiologic variation
- Allergic reactions (e.g., spermicides, deodorants)
- Genital herpes
- Mucopurulent cervicitis
- Atrophic vaginitis
- Vulvar vestibulitis
- Lichen simplex chronicus, Lichen sclerosis
- Foreign bodies (e.g., retained tampons)
- Desquamative inflammatory vaginitis

Vaginitis, dx...
now POC, NAAT

- Saline wet mount
  - Specimen slide w a drop of warm 0.9% saline and a drop of the vaginal discharge specimen
  - Scanned for clue cells -> BV, motile trichomonad organism
  - No delay > 10 min

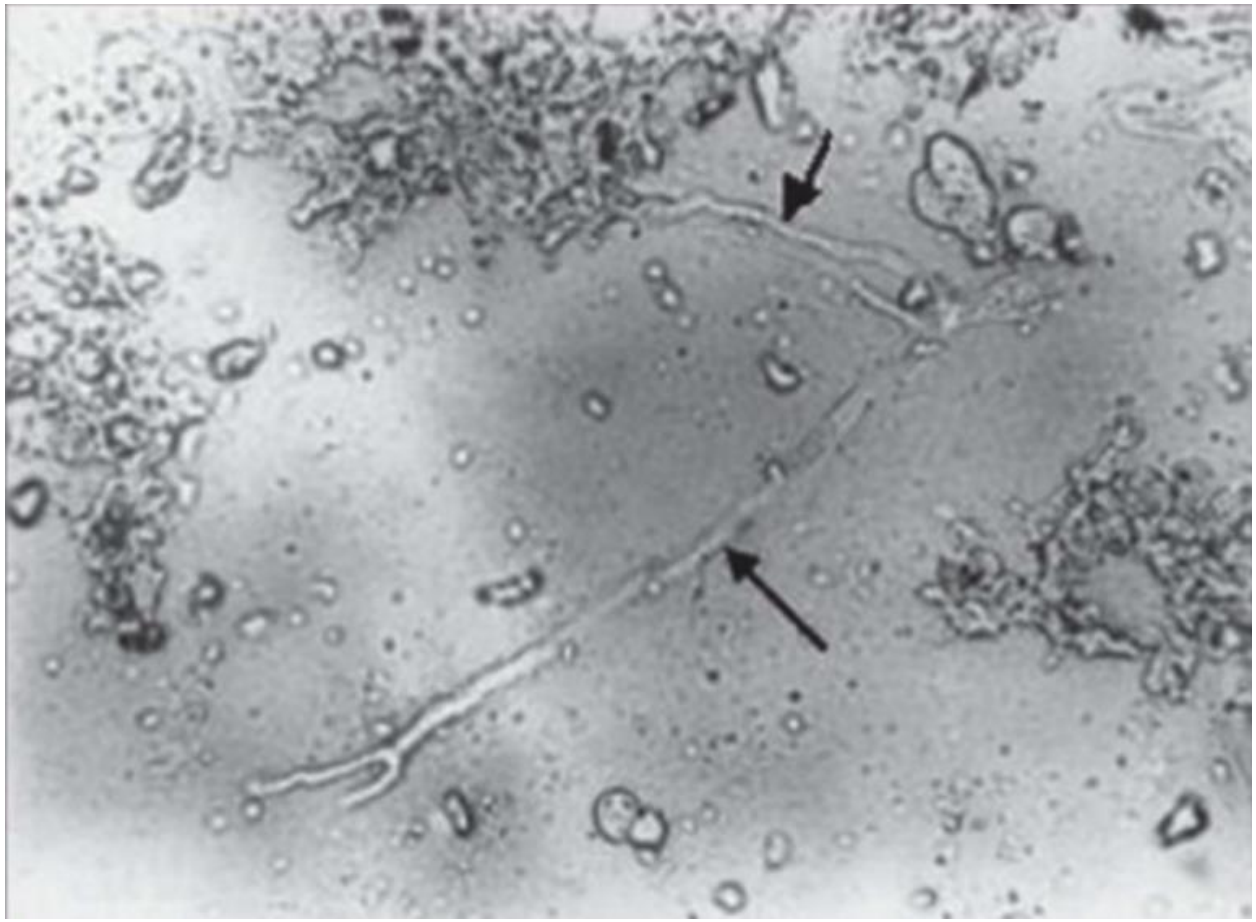
Clue cells, hyphae, Trichomonads



Vaginitis, dx

- Potassium Hydroxide (KOH) Preparation & Whiff Test
  - 2nd Specimen slide w a drop of the vaginal discharge & 10% KOH solution
  - Near nose -> strong amine “fishy” odor -> BV
  - Microscope at 10x, 40x, -> see fungi -> VVC

Wet mount - KOH

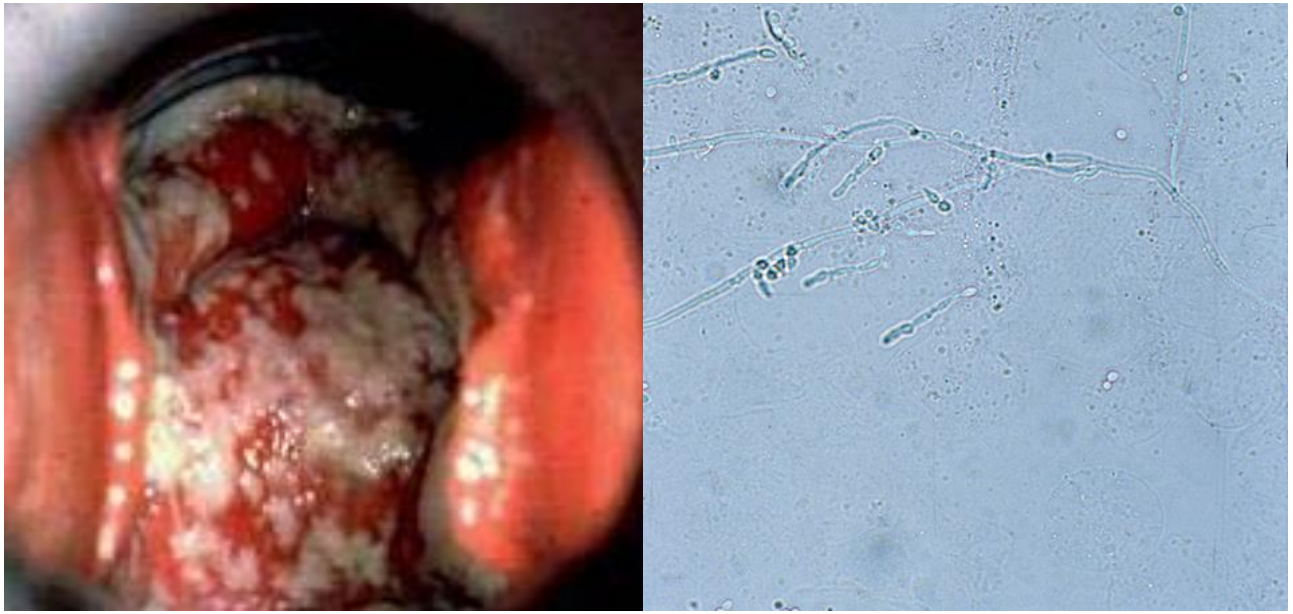


VVC

- *Candida* species may be isolated from the lower genital tract in approximately 20% of asymptomatic women without abnormal discharge

Candida vulvovaginitis

- 16 yo teenager presents with genital itching & white vaginal secretions like cream cheese. Visual below



Candida spp - genital infection

- ↑↑↑ frequency over the last decades
- Symptoms
  - Vaginal secretion & itching
  - Dyspareunia
- Rx - specific antifungals

VVC

- 70-75% will experience ≥ 1 episode of VVC
- 40-50% will experience a 2nd episode
- approximately 5-10% will develop recurrent VVC
  - ≥ 4 episodes of VVC in a single yr

VVC

Uncomplicated VVC

Sporadic or infrequent VVC
AND

Mild-to-moderate VVC
AND

Likely to be *Candida albicans*
AND

Nonimmunocompromised women

Complicated VVC

Recurrent VVC
OR

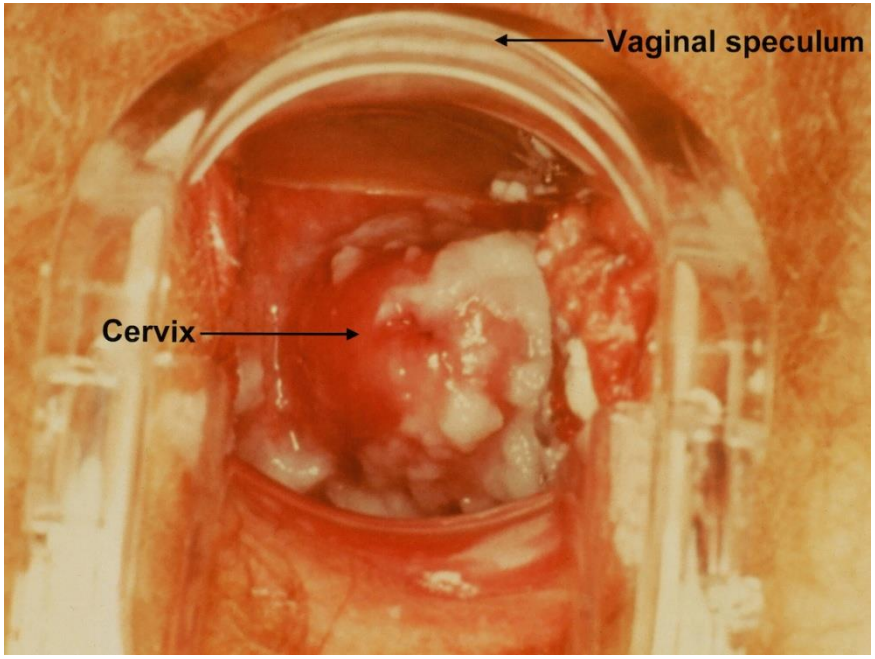
Severe VVC
OR

Nonalbicans candidiasis
OR

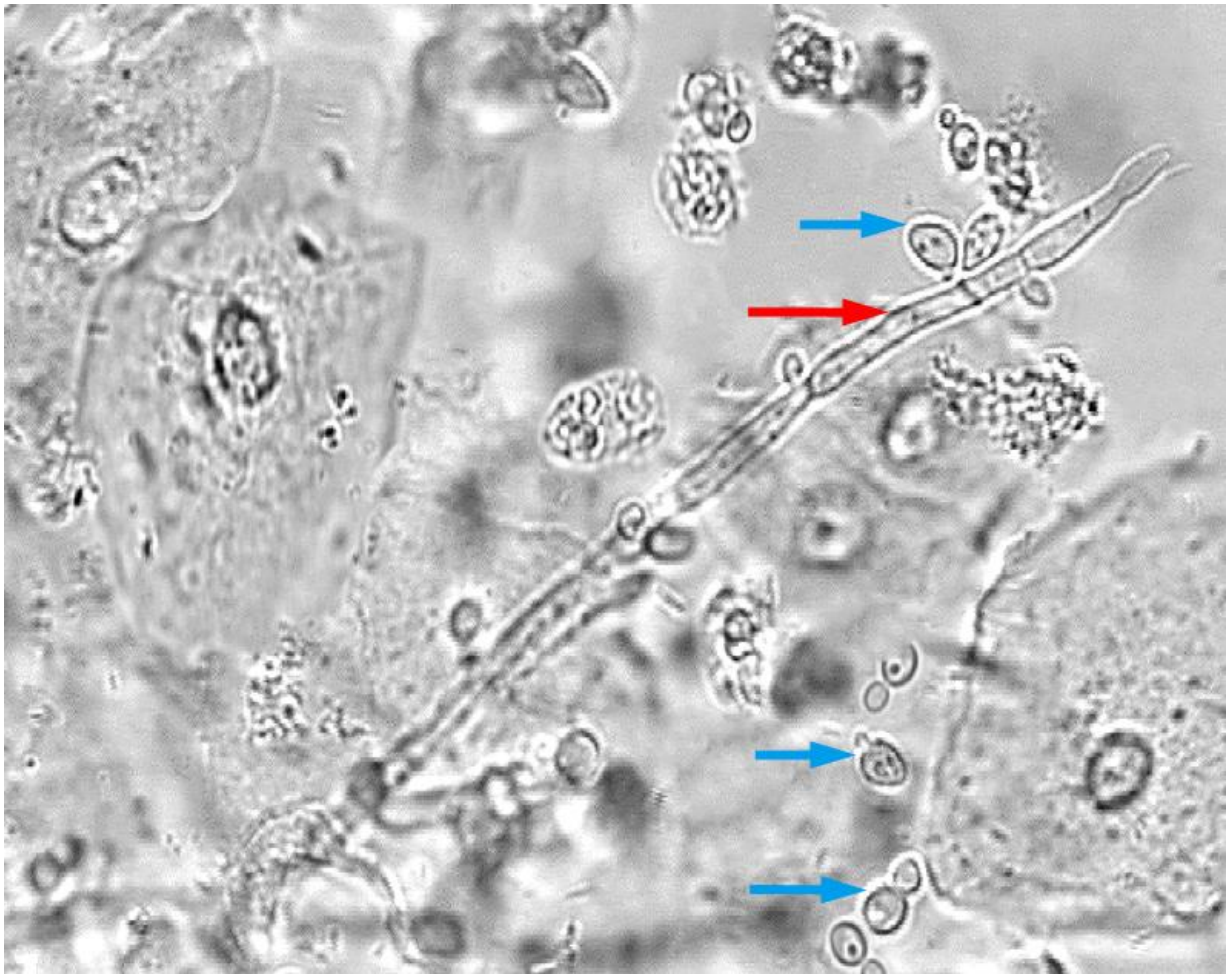
Women with diabetes, immunocompromising conditions (e.g., HIV infection), debilitation, or immunosuppressive therapy (e.g., corticosteroids)

VVC

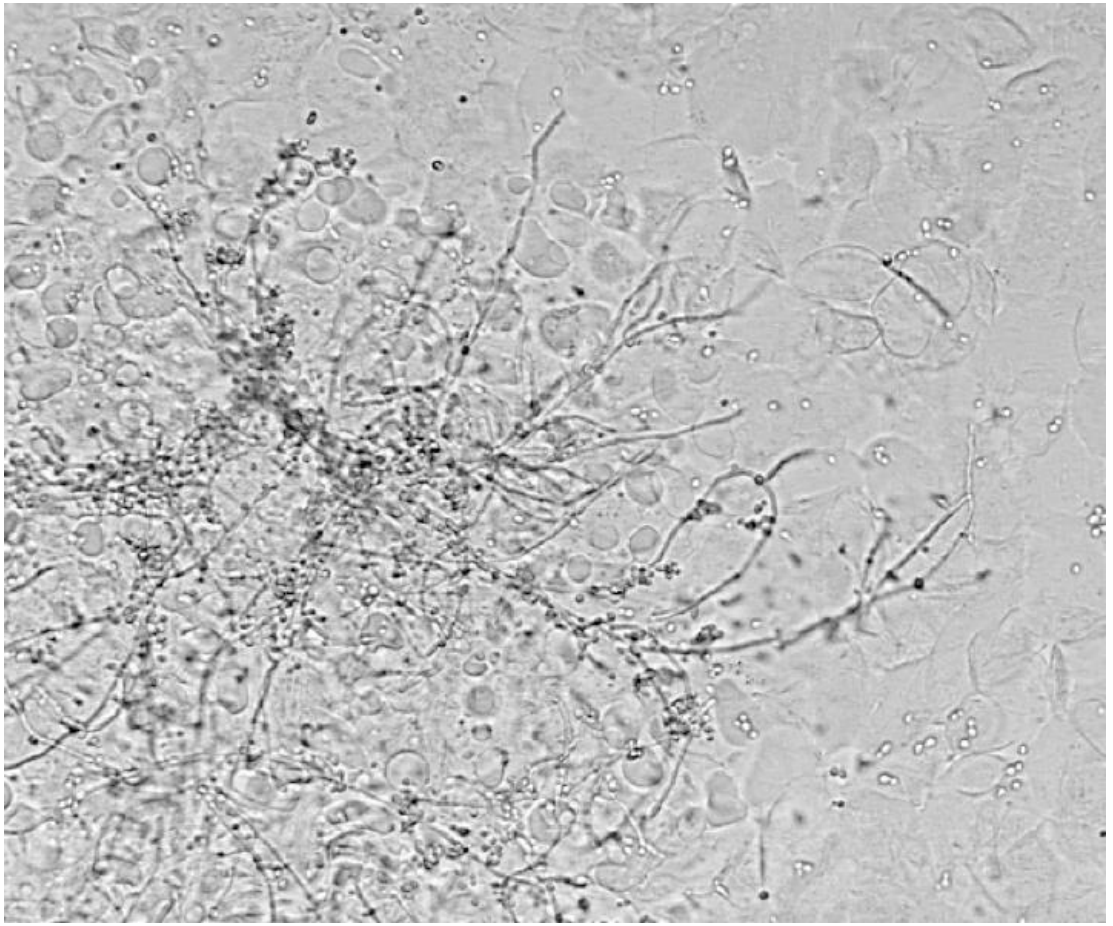
thick, white, and clumpy ("cottage-cheese-like")



VVC, Dx, wet mount



VVC, Dx, 10% KOH prep



Vulvo-vaginal candidiasis, Rx

Recommended : Oral Agent

Fluconazole
150 mg orally in a single dose

Vulvo-vaginal candidiasis, Rx

Recommended Regimens
Over-the-Counter Intravaginal Agents:

Clotrimazole 1% cream 5 g intravaginally daily for 7–14 days
OR

Clotrimazole 2% cream 5 g intravaginally daily for 3 days
OR

Miconazole 2% cream 5 g intravaginally daily for 7 days
OR

Miconazole 4% cream 5 g intravaginally daily for 3 days
OR

Miconazole 100 mg vaginal suppository, one suppository daily for 7 days
OR

Miconazole 200 mg vaginal suppository, one suppository for 3 days
OR

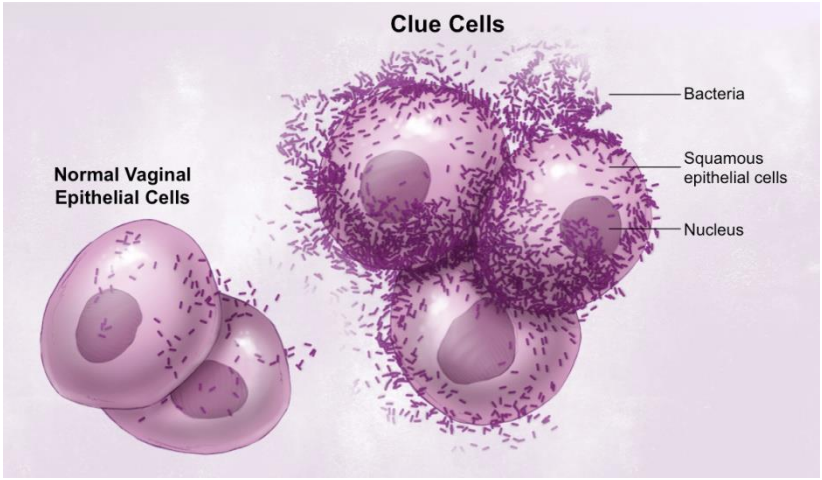
BV, clinical Sxs

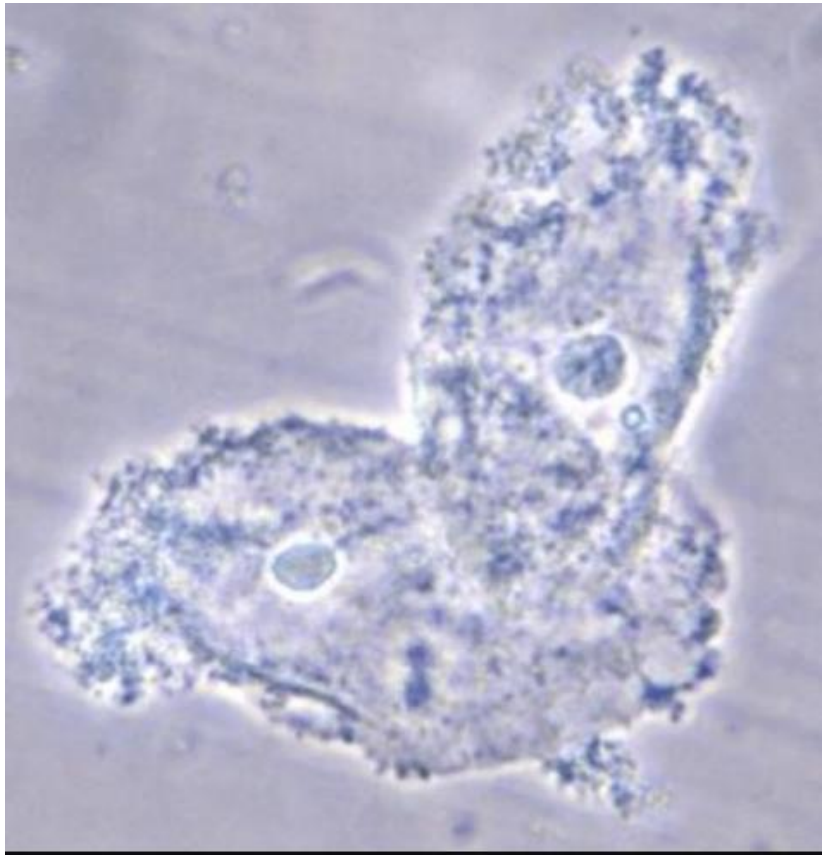
- Up to half of all women with bacterial vaginosis have no symptoms
- Malodorous, “fishy odor”, homogeneous, clear, white or gray vaginal d/c
  - After sex intercourse, completion of menses
  - Sxs may spontaneously remit

BV, Dx, Amsel's criteria

- 3/4 -> sufficient evidence for BV
  - Vaginal pH > 4.5
  - "clue cells" on wet mount -> at least 20% of all Epi's
  - (+) amine, "whiff" or "fishy odor" test w/without KOH
  - Homogeneous, nonviscous, milky-white discharge adherent to the vaginal walls.

Clue cells


Clue Cells
Bacteria
Squamous epithelial cells
Nucleus
Normal Vaginal Epithelial Cells

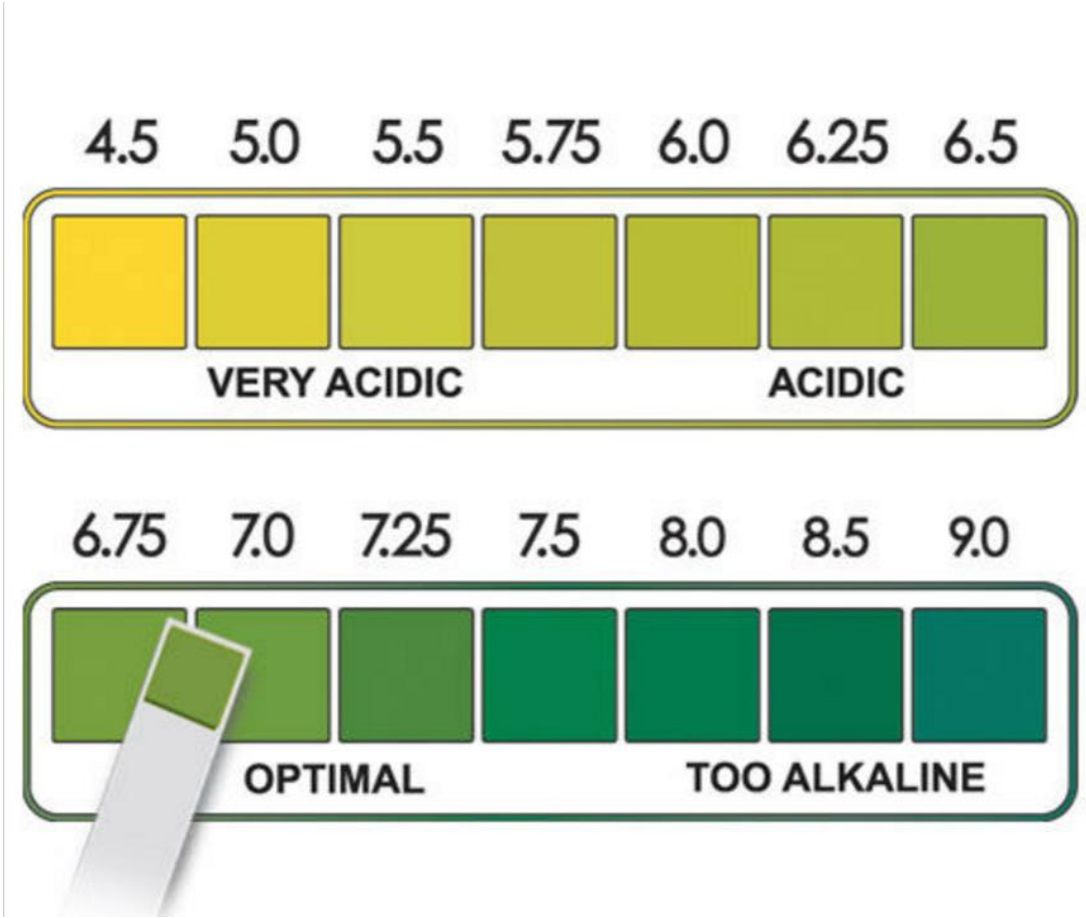


Vaginitis, dx

- Litmus Testing for pH of Vaginal Fluid
  - place a pH litmus paper on the wall of the vagina or directly in pooled vaginal secretions.
  - pH > 4.5 c/w dx of BV

Litmus testing – pH

not recommended by CDC



BV, Dx, other tests

- Affirm VP III
  - a DNA hybridization probe
  - test for high concentrations of *G. vaginalis*
- the OSOM BV Blue test
  - detects vaginal fluid sialidase activity
- acceptable performance characteristics c/w Gram

BV, Rx

Recommended Regimens

Metronidazole 500 mg orally twice a day for 7 days
OR

Metronidazole gel 0.75%, one full applicator (5 g) intravaginally, once a day for 5 days
OR

Clindamycin cream 2%, one full applicator (5 g) intravaginally at bedtime for 7 days

BV, Rx

Alternative Regimens

Tinidazole 2 g orally once daily for 2 days
OR

Tinidazole 1 g orally once daily for 5 days
OR

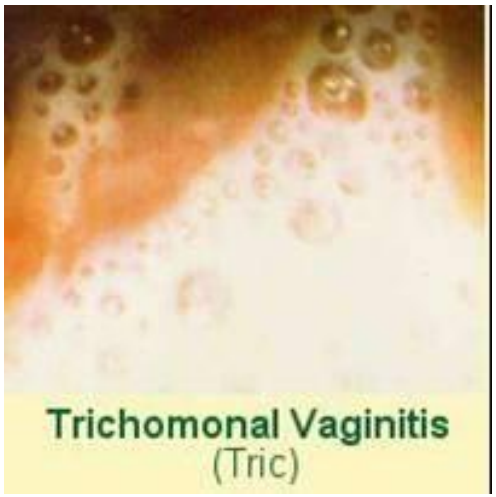
Clindamycin 300 mg orally twice daily for 7 days
OR

Clindamycin ovules 100 mg intravaginally once at bedtime for 3 days*

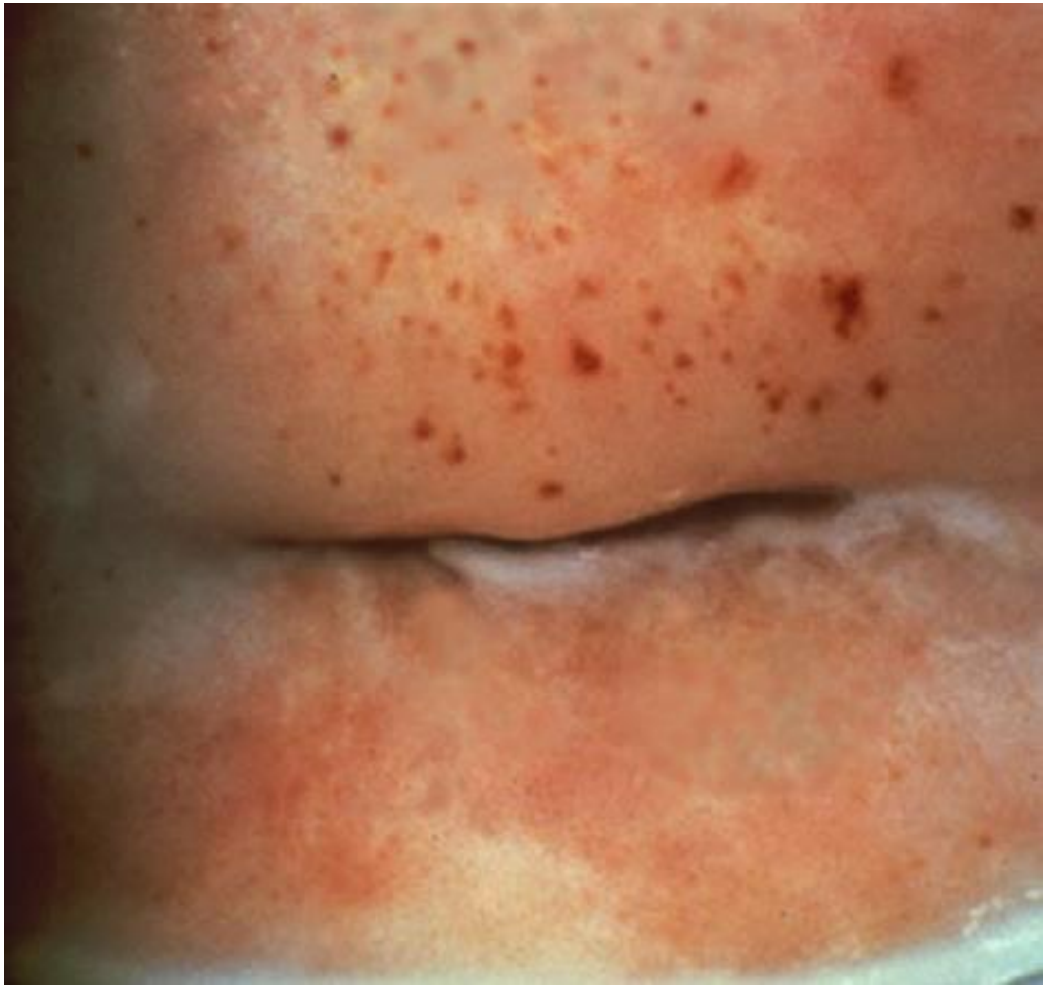
*Clindamycin ovules use an oleaginous base that might weaken latex or rubber products (e.g., condoms and vaginal contraceptive diaphragms). Use of such products within 72 hours following treatment with clindamycin ovules is not recommended.

Trichomonas infection

- Sxs -> similar to NGUs
  - Malodorous secretions, itching, urethritis, pain after sex
  - Asymptomatic in 20% of women
- Men & women
- Rx with ABX - tends to recur

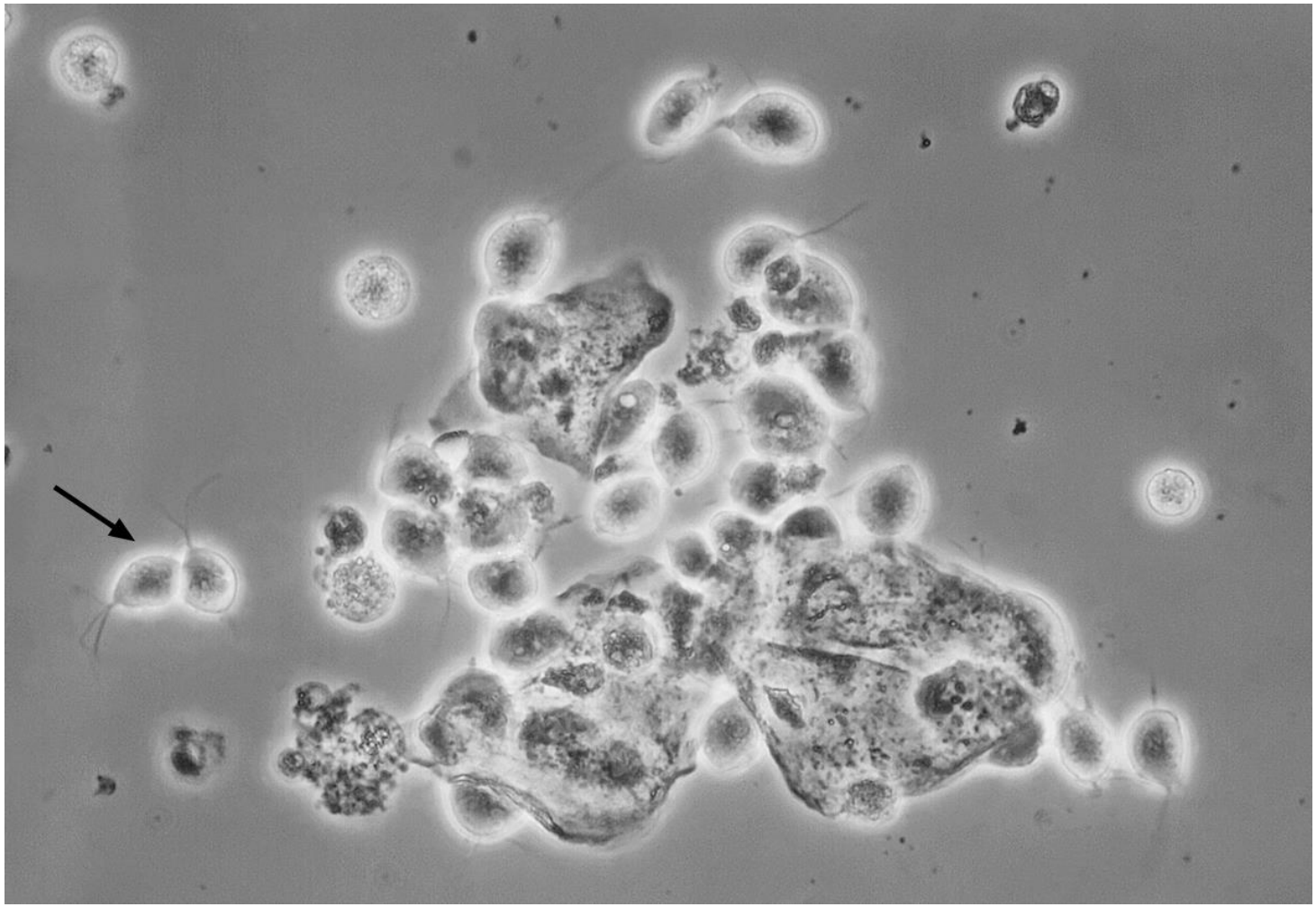


TV, Strawberry cervix



TV, Dx, wet mount

sensitivity (51%–65%)



TV, Dx

- NAAT is highly sensitive, 3-5 more than wet-mount microscopy

- The APTIMA *T. vaginalis* assay (Hologic Gen-Probe, San Diego, CA)
  - FDA-cleared *T. vaginalis* from vaginal, endocervical, or urine specimens
  - RNA by transcription-mediated amplification
  - Clinical sensitivity of 95.3%–100% and specificity of 95.2%–100%
  - vaginal swab and urine have up to 100% concordance

TV, Rx

Recommended Regimen

Metronidazole 2 g orally in a single dose
OR

Tinidazole 2 g orally in a single dose

Alternative Regimen

Metronidazole 500 mg orally twice a day for 7 days

WOUNDS - ULCERS

Case of blisters

- 16 yr old teenager is worried about STIs after sexual contact with unknown individual. Clinical exam discloses the following image.

Case of blisters

- Differential diagnosis includes

1. **HSV 1 (lesions in mouth, lips as well)**
2. **HSV 2**
3. 2ry syphilis
4. Lymphogranuloma venereum

Genital ulcers – painful ?

- **Pain**
  - **Genital HSV**
  - Chancroid (soft chancre)
- **Painless ulcers**
  - **Syphilis**
  - Lymphogranuloma venereum
  - Granuloma inguinale

HSV, transmission

- close contact w a person shedding virus mucosal/epithelial surface, or in genital or oral secretions.
- Sexual transmission of HSV-1 and HSV-2 through
  - genital-to-genital
  - oral-to-genital, or
  - genital-to-oral contact

HSV, clinical manifestations

- Reactivation->viral replication-precipitated by multiple factors
  - trauma, fever, ultraviolet light, physical or emotional stress
  - immunosuppression, fatigue, menses
  - sexual intercourse
  - unknown factors

HSV, 1ry genital episode

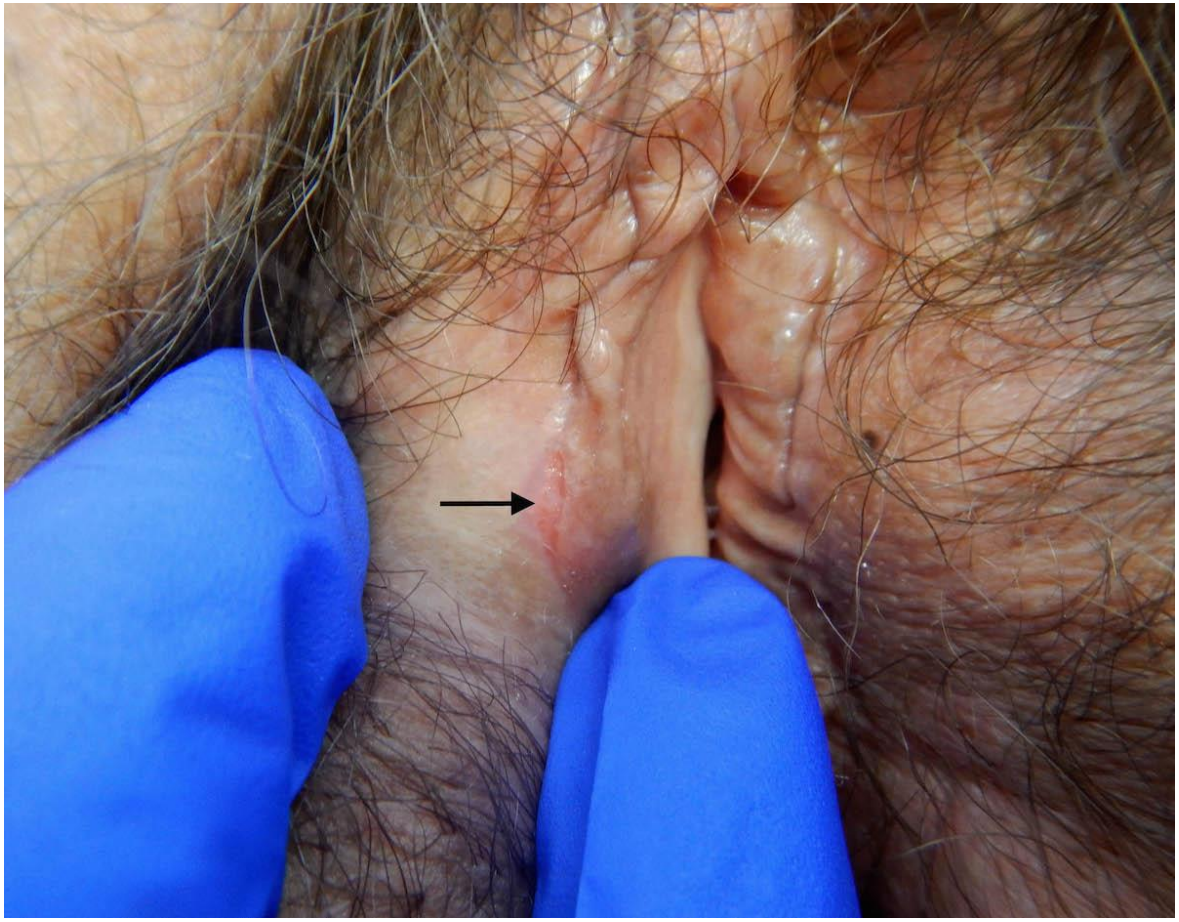
Genital HSV
unrecognized & asymptomatic (?) infection

- Up to two thirds of patients with identified

  "asymptomatic" HSV-2 infection may actually have

- unrecognized symptomatic infection
  - when educated about the myriad of genital herpes symptoms
  - Physicians should educate them

Genital HSV, unrecognized infection



HSV, asymptomatic viral shedding

- Most HSV-2 pts, shorter in duration but viral quantity similar to clinical recurrences
- Highest in 1st yr after infection -> gradually decreases

HSV, asymptomatic viral shedding

- Antiviral suppressive therapy dramatically ↓ HSV-2 shedding by 70 to 80%,
  - but it does not eradicate it

HSV-women-> psychology

Genital HSV

- Rx -> Antivirals
- Long term use for recurrences
- Condoms -> not a 100% protection
- Cesarean section if active lesions present

Genital HSV, Rx-1st clinical episode

2015 STD Treatment Guidelines: Genital Herpes

Table 1. Treatment of First Clinical Episode of Genital Herpes

Recommended
Acyclovir 400 mg orally three times a day for 7–10 days
Note: Treatment can be extended if healing is incomplete after 10 days of therapy.
or
Acyclovir 200 mg orally five times a day for 7–10 days
Note: Treatment can be extended if healing is incomplete after 10 days of therapy.
or
Valacyclovir 1 g orally twice a day for 7–10 days
Note: Treatment can be extended if healing is incomplete after 10 days of therapy.
or
Famciclovir 250 mg orally three times a day for 7–10 days
Note: Treatment can be extended if healing is incomplete after 10 days of therapy.

Genital HSV, Rx-recurrent episodes

2015 STD Treatment Guidelines: Genital Herpes

Table 2. Episodic Therapy for Recurrent Genital Herpes

Recommended
Acyclovir 400 mg orally three times a day for 5 days
or
Acyclovir 800 mg orally twice a day for 2 days
or
Acyclovir 800 mg orally three times a day for 2 days
or
Valacyclovir 500 mg orally twice a day for 3 days
or
Valacyclovir 1 g orally once a day for 5 days
or
Famciclovir 125 mg orally twice daily for 5 days
or
Famciclovir 1 g orally twice daily for 1 day
or
Famciclovir 500 mg once, followed by 250 mg twice daily for 2 days

Genital HSV, Rx-recurrent episodes

2015 STD Treatment Guidelines: Genital Herpes

Table 3. Suppressive Therapy for Recurrent Genital Herpes

The frequency of genital herpes recurrences diminishes over time in many persons, potentially resulting in psychological adjustment to the disease. Therefore, periodically during suppressive treatment (e.g., once a year), providers should discuss the need to continue therapy.

Recommended

Acyclovir
400 mg orally twice a day

or

Valacyclovir
500 mg orally once a day

Note: Valacyclovir 500 mg once a day might be less effective than other valacyclovir or acyclovir dosing regimens in persons who have very frequent recurrences (i.e., ≥10 episodes per year).

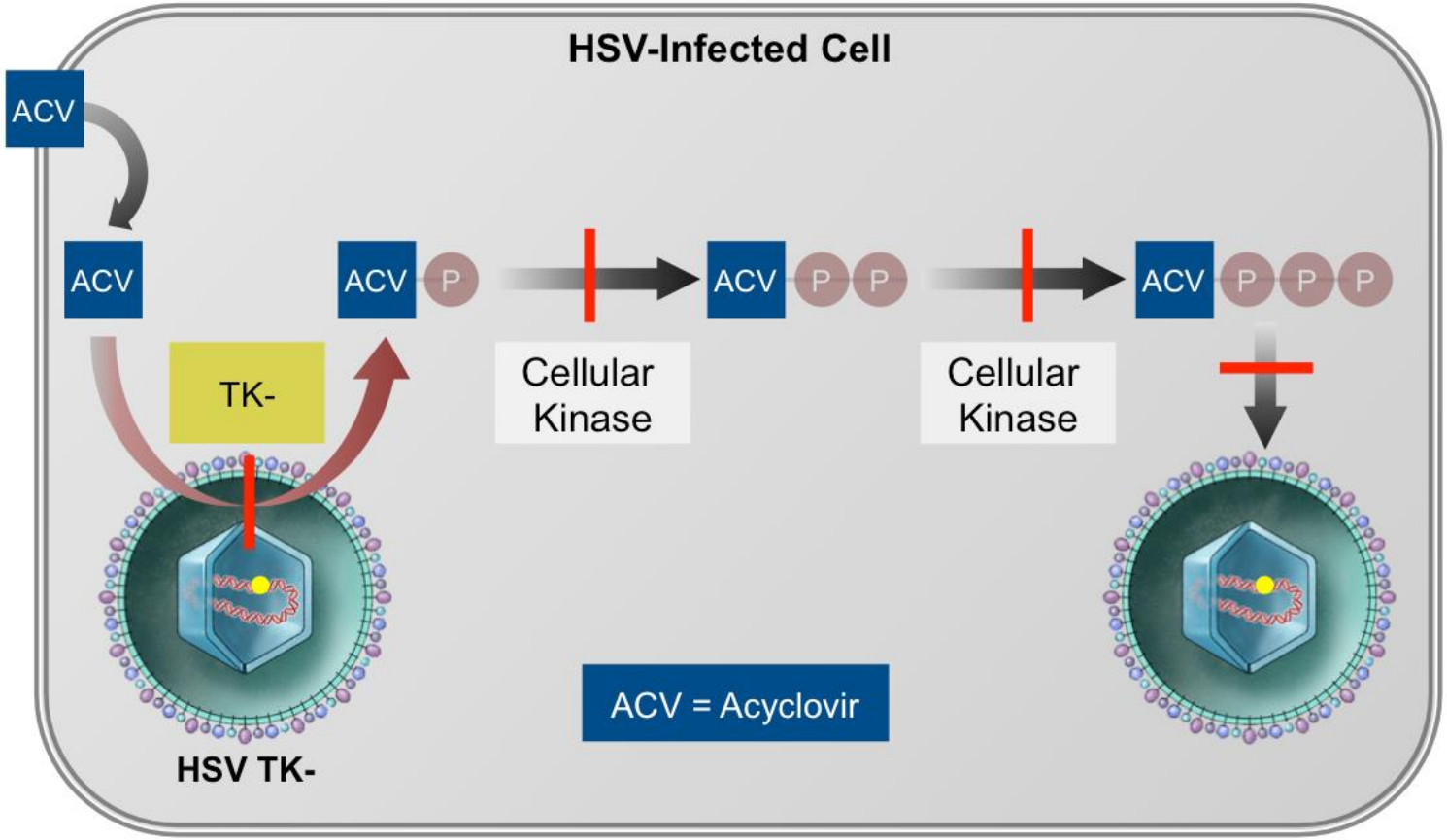
or

Valacyclovir
1 g orally once a day

or

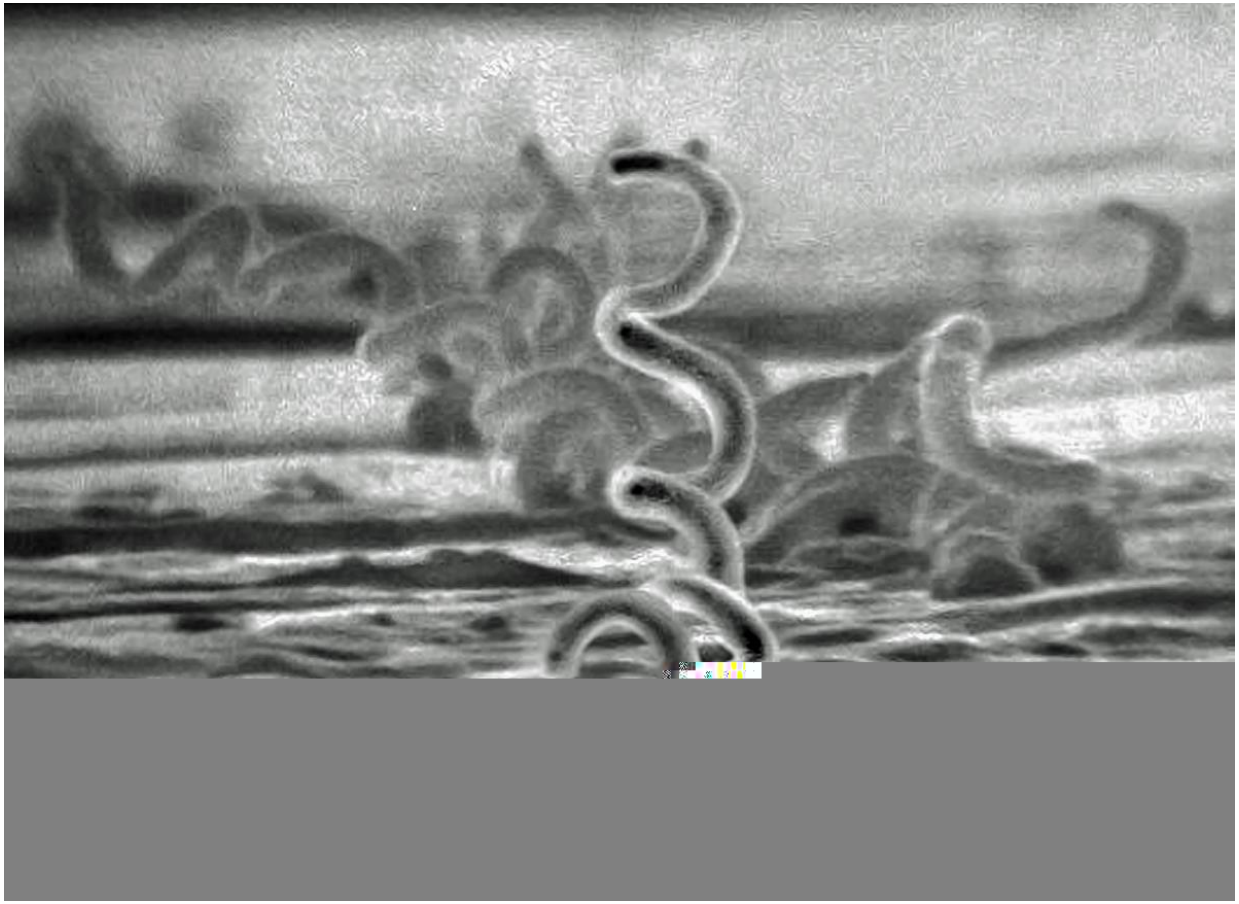
Famciclovir
250 mg orally twice a day

Acyclovir R HSV



Syphilis, incubation t->10-90 d

cause: Treponema pallidum



Syphilis, 1ry, chancre -> painless

Syphilis, 1ry, chancre -> painless

Syphilis, 1ry, chancre -> painless

- Incubation 10-90 d
- 15-30% of pts do not pay attention to chancre
  - Initially papule->erosion->ulcer w smooth border
- Spontaneous resolution in 1-5 wks
- Highly contagious

Syphilis, 1ry, chancre

Syphilis, 2ry

- hematogenous dissemination of T. pallidum
- appear 4 to 8 weeks after onset of 1ry chancre

- Maybe 1st observed!
- 1ry & 2ry stages may overlap
- Relapses occur in 25% of pts if un-Rxed

Syphilis, 2ry

- After interval of 1wk-6m
- various Sxs
  - rash
  - fever, headache
  - Pharyngeal soreness, anorexia, nausea
  - conjunctivitis
  - Hair loss

Syphilis, 2ry, rash

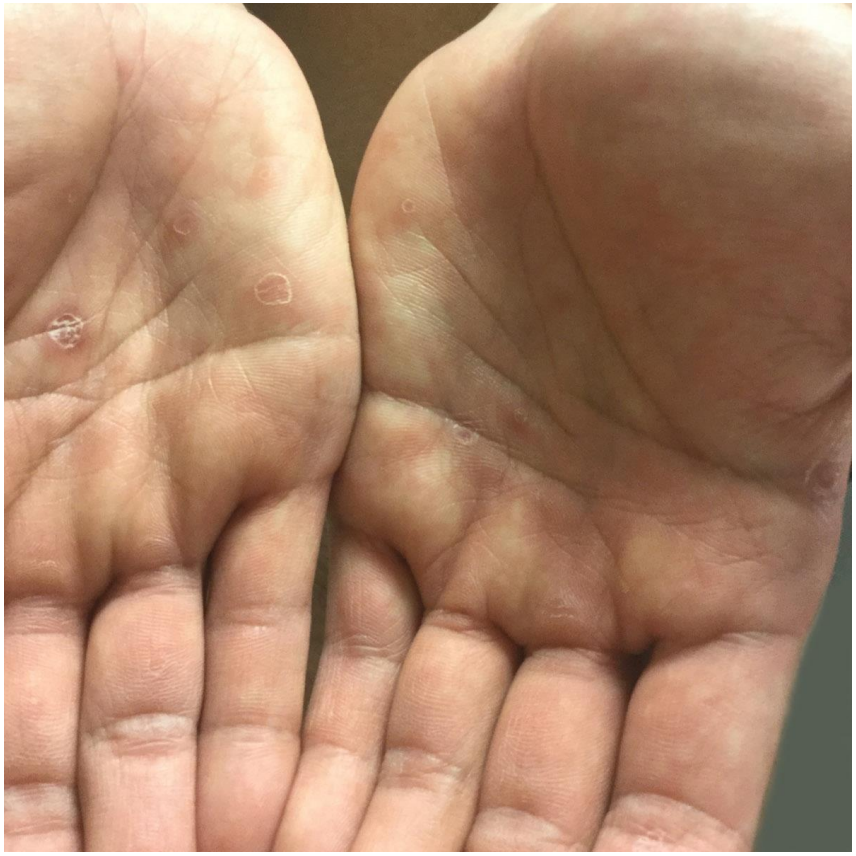
- 75-100% of pts, non-pruritic
- Chest, back, palms & soles

2ry syphilis-generalized rash

- 1wk-6m after acute exposure/infection

Syphilis, 2ry, rash

Syphilis, 2ry, rash



2ry syphilis-rash

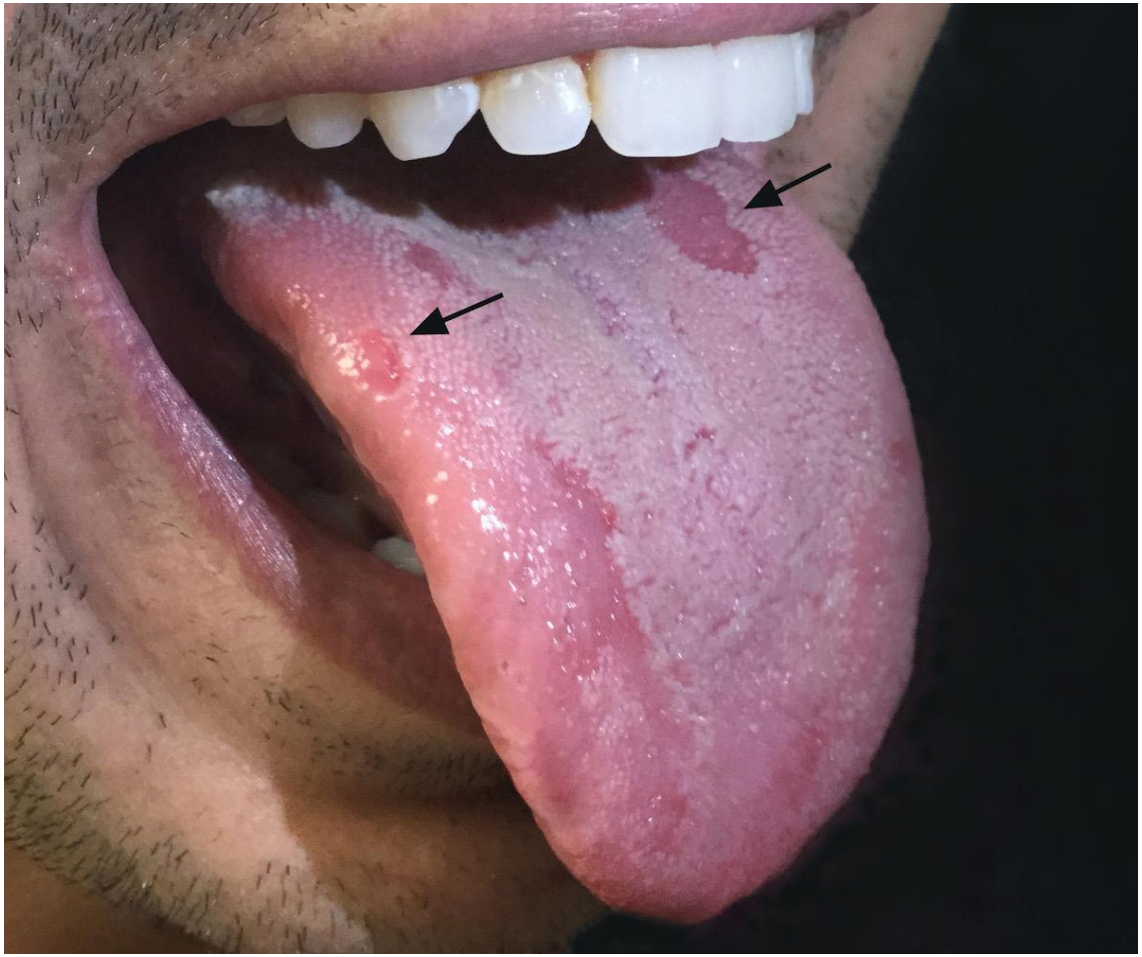
2ry syphilis-rash

Syphilis, 2ry, other

- Lymphadenopathy -> 50-86%, epitrochlear
- Systemic Sxs
- Mucous patches -> 6-30%, flat
- Condylomata lata -> 10-20%, high contagious
- Alopecia -> 5%
- Visceral organ involvement -> liver, kidney, lungs, GI, spleen
- Neurologic Sxs

2ry syphilis-mucosal lesion

Syphilis, 2ry, oral lesions



Syphilis, 2ry, condylomata lata

2ry syphilis-condylomata lata

Syphilis, Latent

- persistence of *T. pallidum* organisms in the body without causing signs or symptoms
- Periods of clinical latency

Syphilis, Latent, Dx

- Sero(+) indicating infection with T. pallidum
  - VDRL, TPPA
- no past diagnosis of syphilis
- no evidence of active 1ry, 2ry, or 3ry syphilis

Syphilis, Latent, Dx

- Early latent
- Late latent
- Latent of unknown duration
- Always test for HIV

Syphilis, Latent

- Early latent
  - Infection of Less than 1 Year in Duration

Syphilis, Latent

- Late latent
  - Infection greater than 1 Year in Duration

Syphilis, Latent

- Latent syphilis of unknown duration
  - Not possible to determine likely duration of infection
  - effectively managed the same as persons with late latent syphilis.

3ry syphilis

- 10-20 later – worst manifestations
- Affects all organs eg
  - Brain, CNS syphilis
  - Heart
  - Eyes - blindness

Syphilis, tertiary

- Late syphilis – rare
- With no Rx -> 30% of pts within 1-20 yrs
  - Average onset 10-15 yrs after infection
- Gummatous lesions
  - Skeletal, spine, mucosal areas, eyes, viscera
  - Can mimic Carcinoma

Neurosyphilis

- Neurosyphilis
  - can occur at any stage of infection

Neurosyphilis

- Invasion of the CNS
  - From paresis & tabes dorsalis to meningeal & meningovascular syndromes
- Can occur at any stage of infection
  - Up to 25% of CSF (+) by PCR in 1ry dz

Tabes dorsalis

- Tabes dorsalis is caused by demyelination secondary to an untreated syphilis infection
  - Slow degeneration (demyelination) of the sensory neurons in the dorsal columns of SC.
  - Syphilitic myelopathy is a complication of untreated syphilis that involves muscle weakness and abnormal sensations.

Tabes dorsalis

- Weakness, Diminished reflexes, hypotonic muscles
- Paresthesias (shooting and burning pains, pricking sensations), Hypoesthesias (abnormally diminished cutaneous, especially tactile)
- Progressive degeneration of the joints
- Loss of coordination, dementia, Personality Δs
- Urinary incontinence
- Visual impairment, Argyll Robertson pupil
- Tabes dorsalgia, Tabetic gait (high stepping)
- Deafness

Argyll Robertson pupil

Caused by neurosyphilis.

They are characterized by bilateral (usually asymmetrical) small, irregular pupils showing a light-near dissociation.

Difficult to dilate.

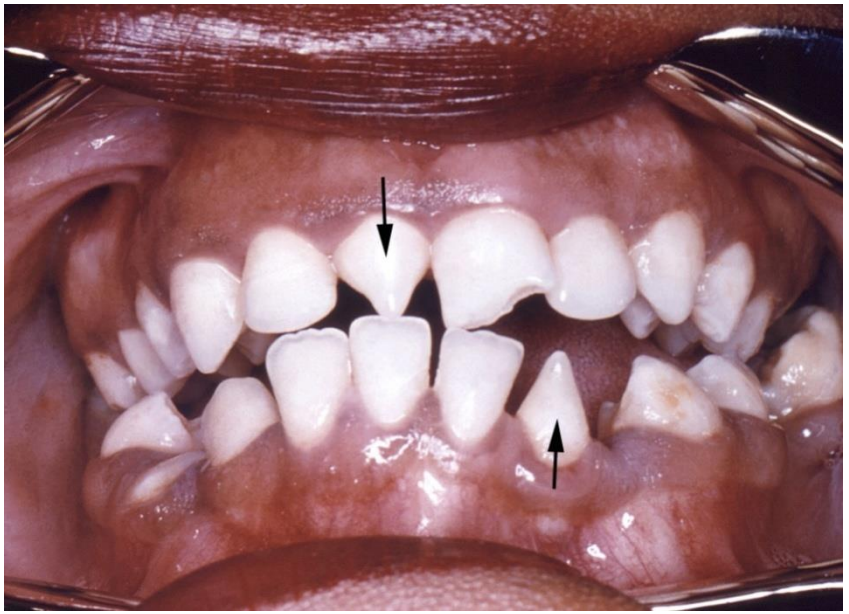
Congenital syphilis

- Can occur at any stage of infection
  - Much higher in 1ry, 2ry
- Can occur at any trimester of pregnancy
  - Mild to severe manifestation

Late Congenital syphilis

Hutchinson's triad

- 8th cranial nerve deafness
- interstitial keratitis
- Hutchinson teeth



Syphilis, Lab Dx

Syphilis, Lab Dx

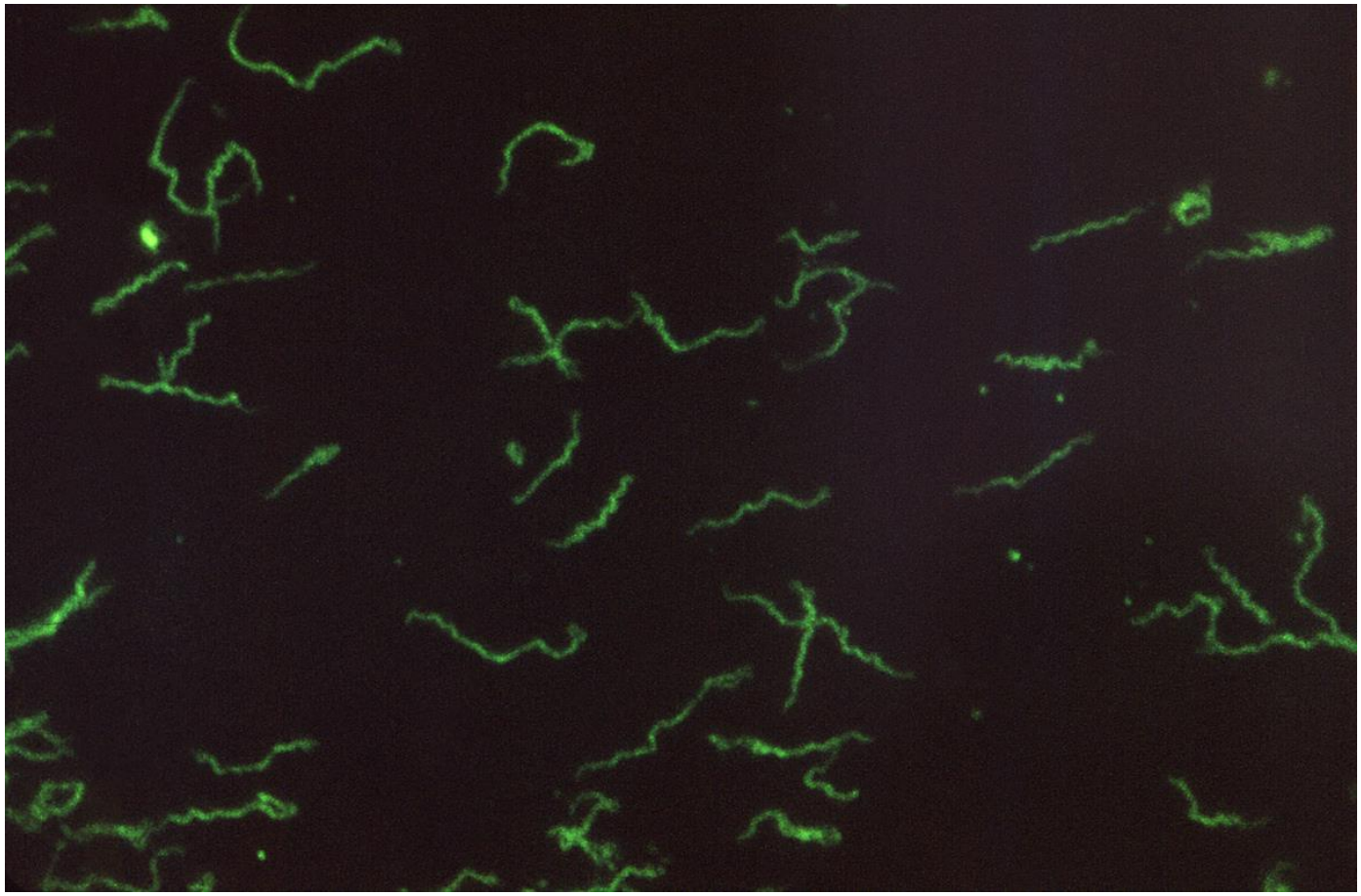
- Non-treponemal serological tests
  - VDRL, RPR, USR, TRUST
- Treponemal serological tests
  - TP-PA, FTA-ABS, EIAs, do not use to assess Rx

- Major limitations
  - False (+)
  - Inability to distinguish recent from past dz

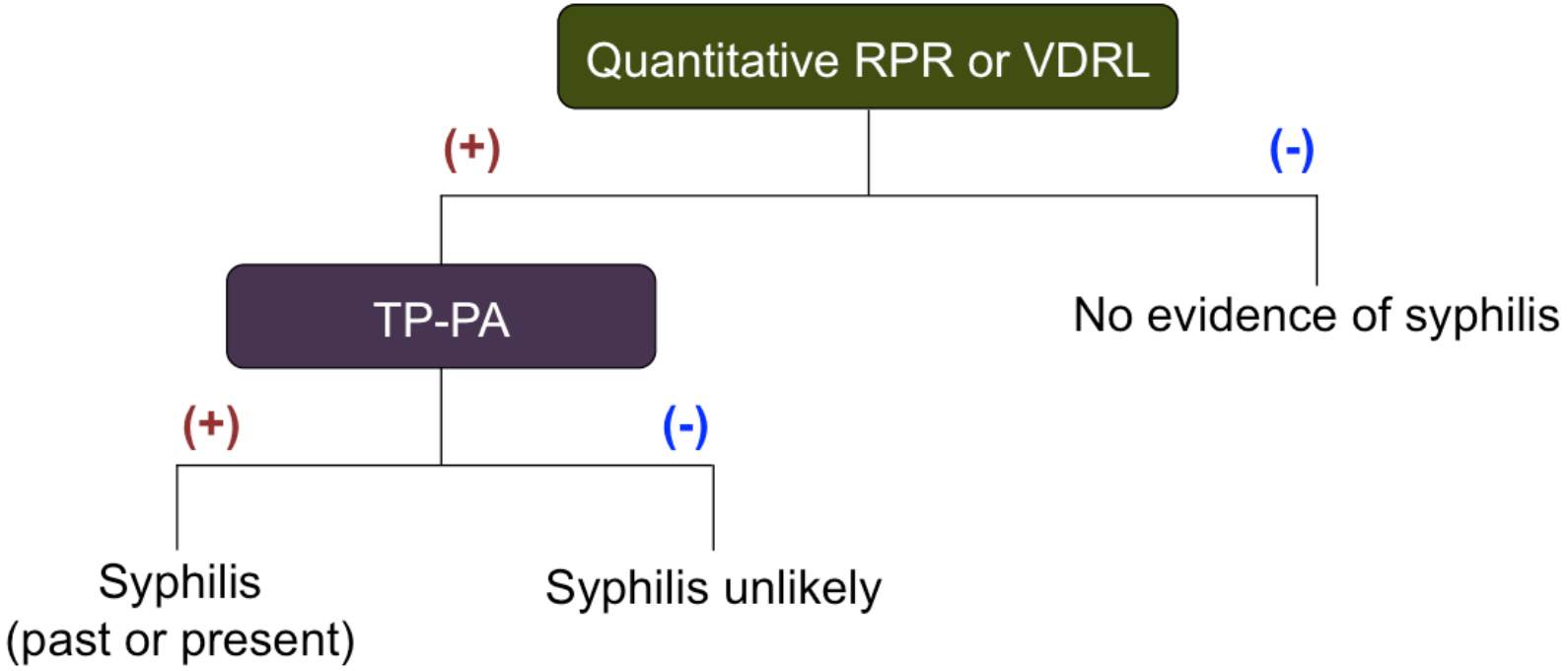
- Both are required for Dx

Syphilis, Dx

treponemal IFA serological test



Standard (Traditional) Screening Algorithm



Syphilis, screening

- Screening for syphilis is recommended in
  - men who have sex with men

Syphilis, Rx

2015 STD Treatment Guidelines: Primary and Secondary Syphilis

Table 3. Treatment of Primary and Secondary Syphilis

Recommended for Adults

Benzathine penicillin G
2.4 million units IM in a single dose

Note: Available data demonstrate that use of additional doses of benzathine penicillin G, amoxicillin, or other antibiotics do not enhance efficacy when used to treat primary and secondary syphilis, regardless of HIV status.

Recommended for Infants and Children

Benzathine penicillin G
50,000 units/kg IM, up to the adult dose of 2.4 million units in a single dose

Note: Infants and children aged ≥1 month with primary or secondary syphilis should be managed by a pediatric infectious disease specialist and evaluated for sexual abuse (e.g., through consultation with child-protection services)

Syphilis, Rx

2015 STD Treatment Guidelines: Latent Syphilis

Table 4. Treatment of Latent Syphilis

Recommended for Adults with Early Latent Syphilis

Benzathine penicillin G
2.4 million units IM in a single dose

Note: Available data demonstrate that additional doses of benzathine penicillin G, amoxicillin, or other antibiotics in early latent syphilis do not enhance efficacy, regardless of HIV infection.

Recommended for Adults with Late Latent Syphilis or Latent Syphilis of Unknown Duration

Benzathine penicillin G
7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals

Syphilis, Rx

- Jarisch-Herxheimer reaction
  - self-limited reaction, usually in early Syphilis Rx
  - associated w initiation of anti-treponemal Rx

- Characterized by
  - fever, malaise, nausea, vomiting
  - less frequently chills, exacerbation of 2ry syphilis rash
  - Occurs within 24hrs -> resolves within 24 hrs

Syphilis
Jarisch-Herxheimer reaction

- Antipyretics can be used
  - to manage symptoms
- They do not prevent it

Syphilis, Rx, f/u

- Extremely important
- 1ry or 2ry
  - Clinically/serologically 6 & 12 months
- Latent
  - Clinically/serologically 6, 12 & 24 months

Syphilis, Rx failure

- persistent or recurring signs or symptoms.
- sustained 4-fold ↑ in nontreponemal titer
- Failure of nontreponemal titers to ↓ 4-fold

  within 12 months p therapy for 1ry or 2ry dz

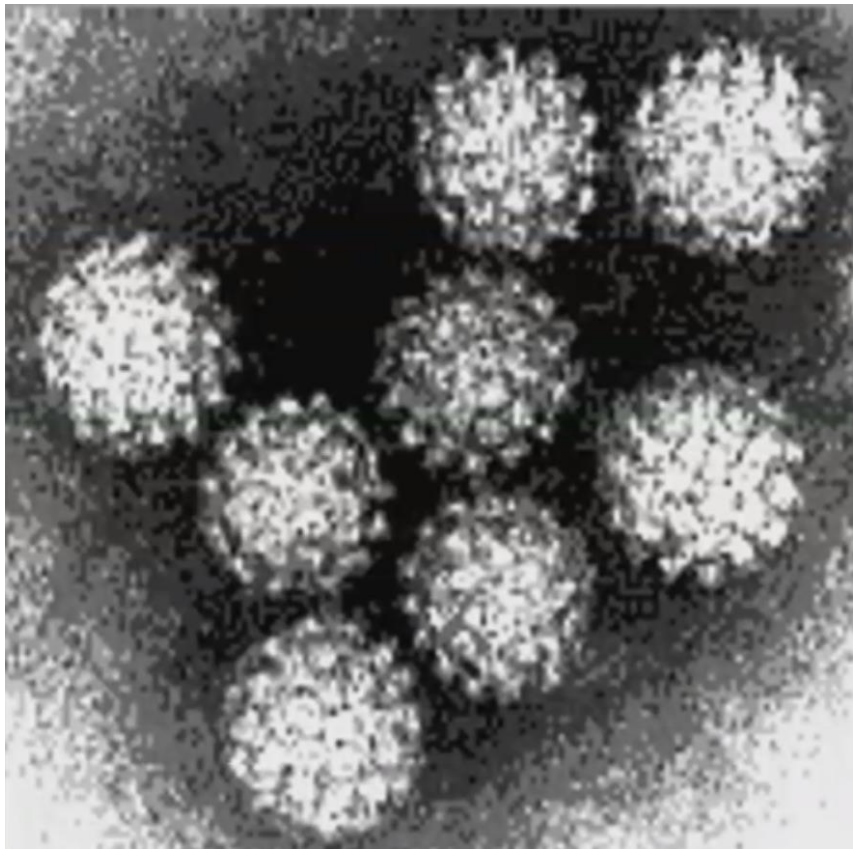
Syphilis, Rx, sexual partners

- Persons who have had sexual contact within 90 days preceding that contact's dx of 1ry, 2ry, or early latent syphilis
  - presumptive Rx for early syphilis even in (-) titers

OTHER STIS

Ιός HPV

- DNA virus
- Infect different areas of epithelium
- Do not circulate in blood
- Over 200 HPV types
- ≥40 genital HPV types



Ιός HPV & Ca

Transmission

- SKIN contact, not blood or bodily fluids
- Sexual

Ιός HPV

high risk vs. low risk types

HPV TYPE	CLINICAL FINDINGS	CANCER POTENTIAL[1]
6, 11	genital warts, low grade lesions, recurrent respiratory papillomatosis (RRP)	Low (negligible)
40, 42, 54, 55/44, 61, 70, 72, 81, CP6108	low grade lesions	Low (negligible)
16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82/IS39	low grade lesions, high grade lesions, cancer	High

Munoz et al Vaccine 2006

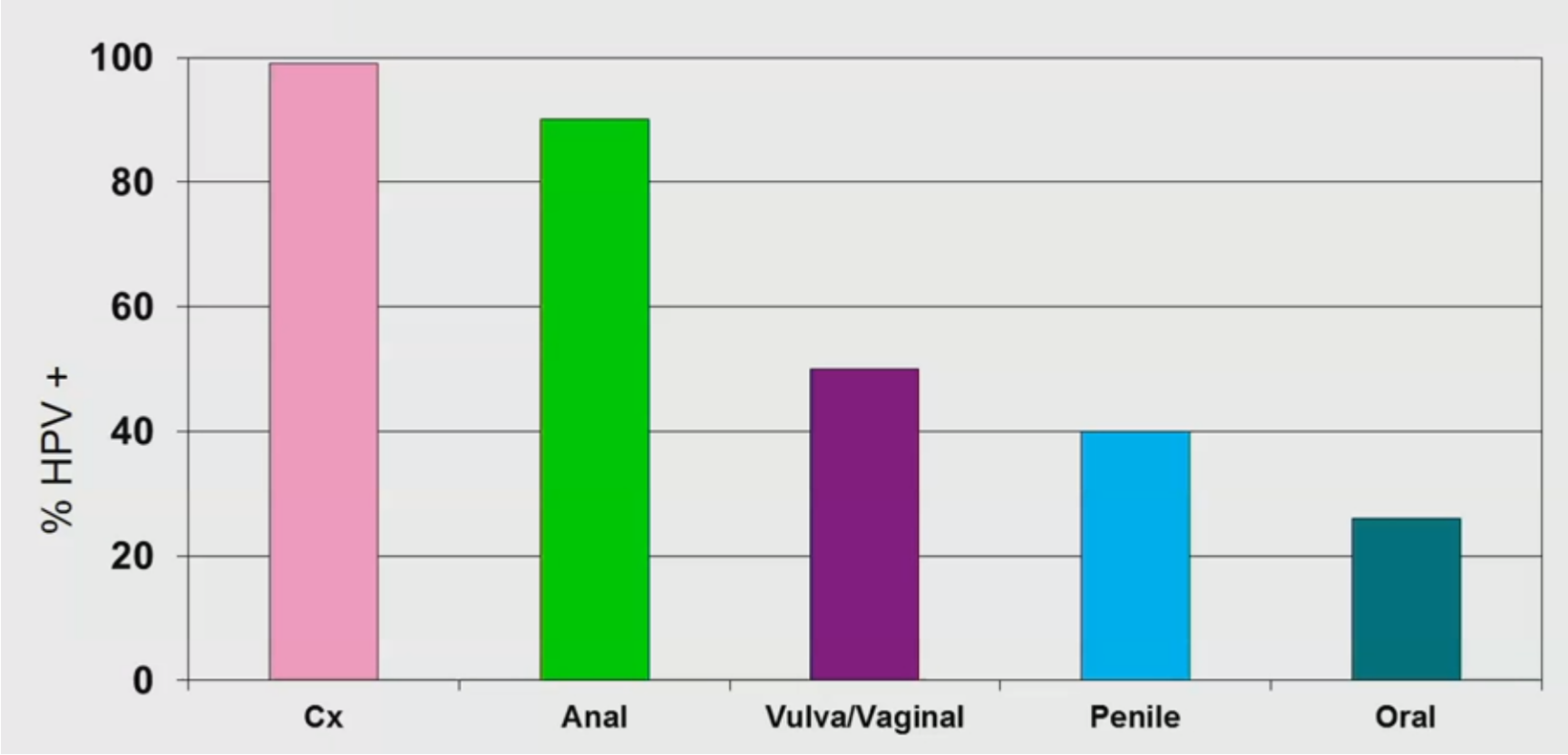
HPV σχετιζόμενοι Ca

Type of Cancer	Papillomavirus types involved	Percentage of cases HPV-positive (%)
Cervical	16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66	>95
Vulval: Basaloid Warty Keratinising	16, 18 16, 18 16	>50 >50 <10
Penile: Basaloid Warty Keratinising	16, 18 16, 18 16	>50 >50 <10
Vaginal	16,18	>50
Anal	16, 18	>70
Oral cavity and tonsils	16, 18, 33	~25
Nail bed	16	~75

DE Vuyst Eur J Cancer 2009; De Vuyst Int J Cancer 2009; Miralles-Guri J Clin Pathol 2009; Kreimer Cancer Epidemiol Biomarkers Prev 2005; von Krogh Eur J Dermatol 2001

Ιός HPV & Ca

strong association,? other Ca as well - larynx, lung, esophagus



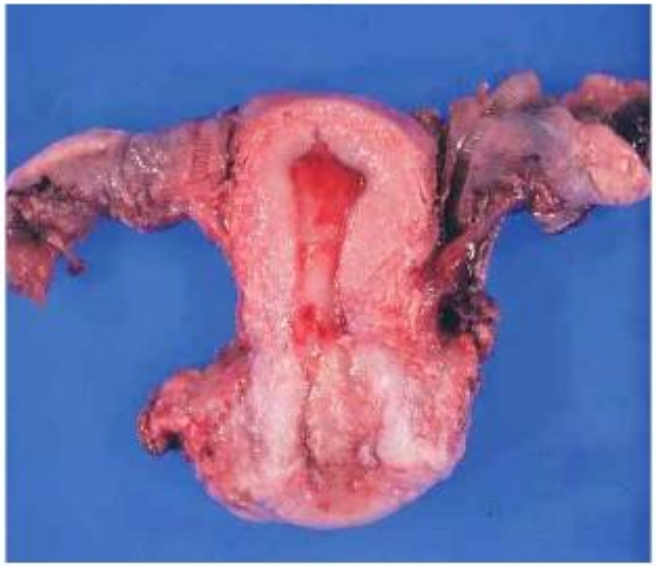
Trottier H et al. Public Health Genomics 2009

HPV-associated diseases

Common warts/plantar warts

Condyloma acuminata

Cervical carcinoma



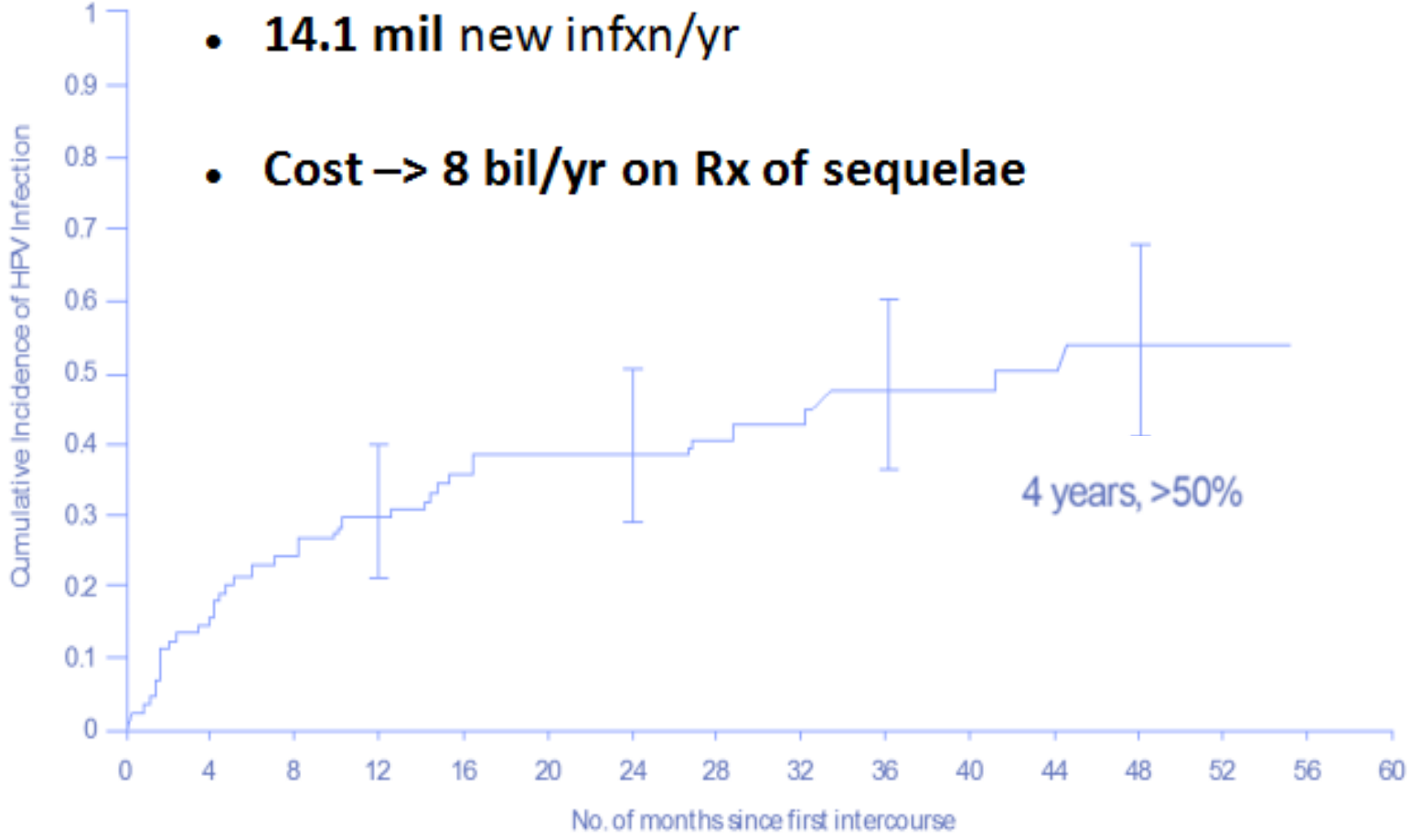
Anal carcinoma

Oral cancer

Επιδημιολογία HPV, post-sex debut

most common STI worldwide, USA->79 mil infected

- **14.1 mil** new infxn/yr
- **Cost –> 8 bil/yr on Rx of sequelae**

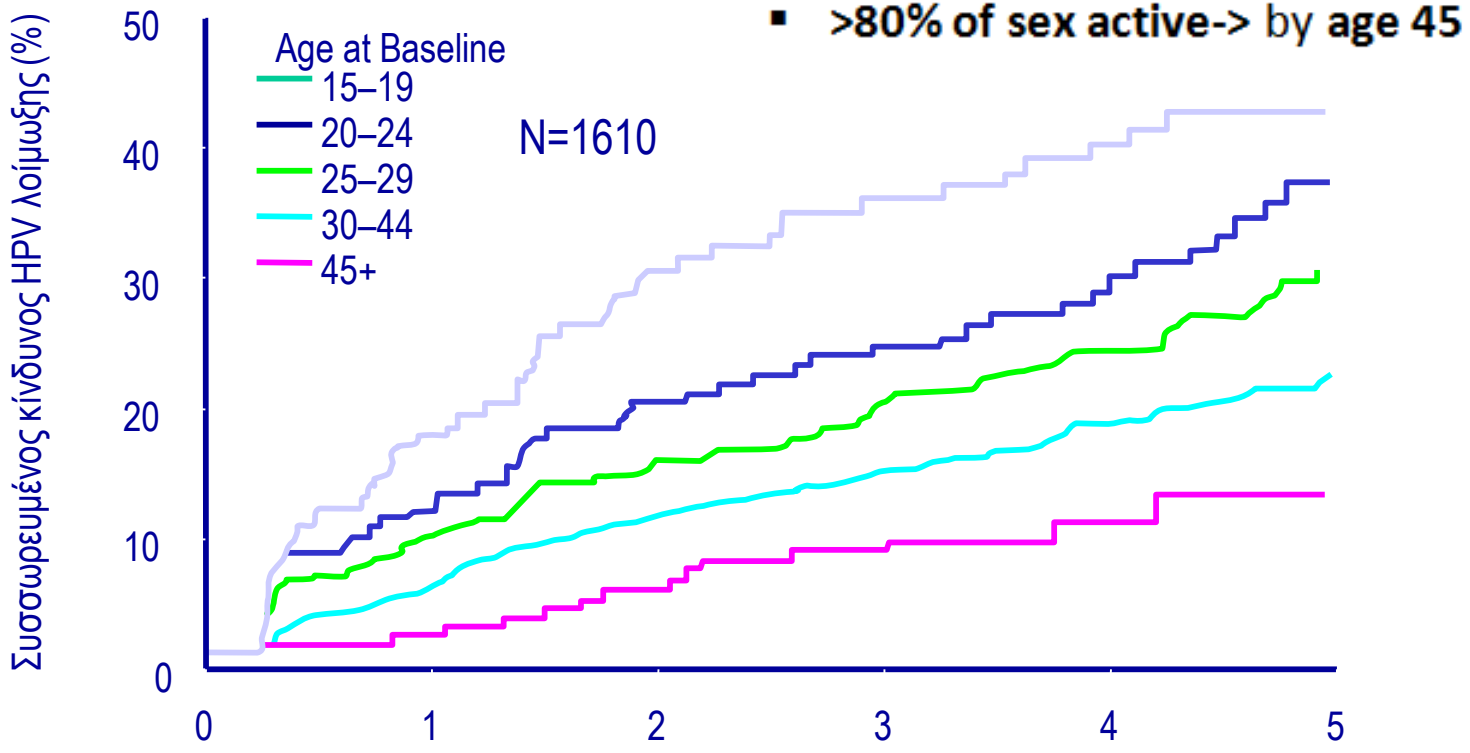


Am J Epidemiol 2003; Chesson et al. Sex Transm Dis 2014; Satterwite et al Sex Transm Dis 2013

Επιδημιολογία HPV, 5yrs post-sex debut

most common STI worldwide, USA->79 mil infected

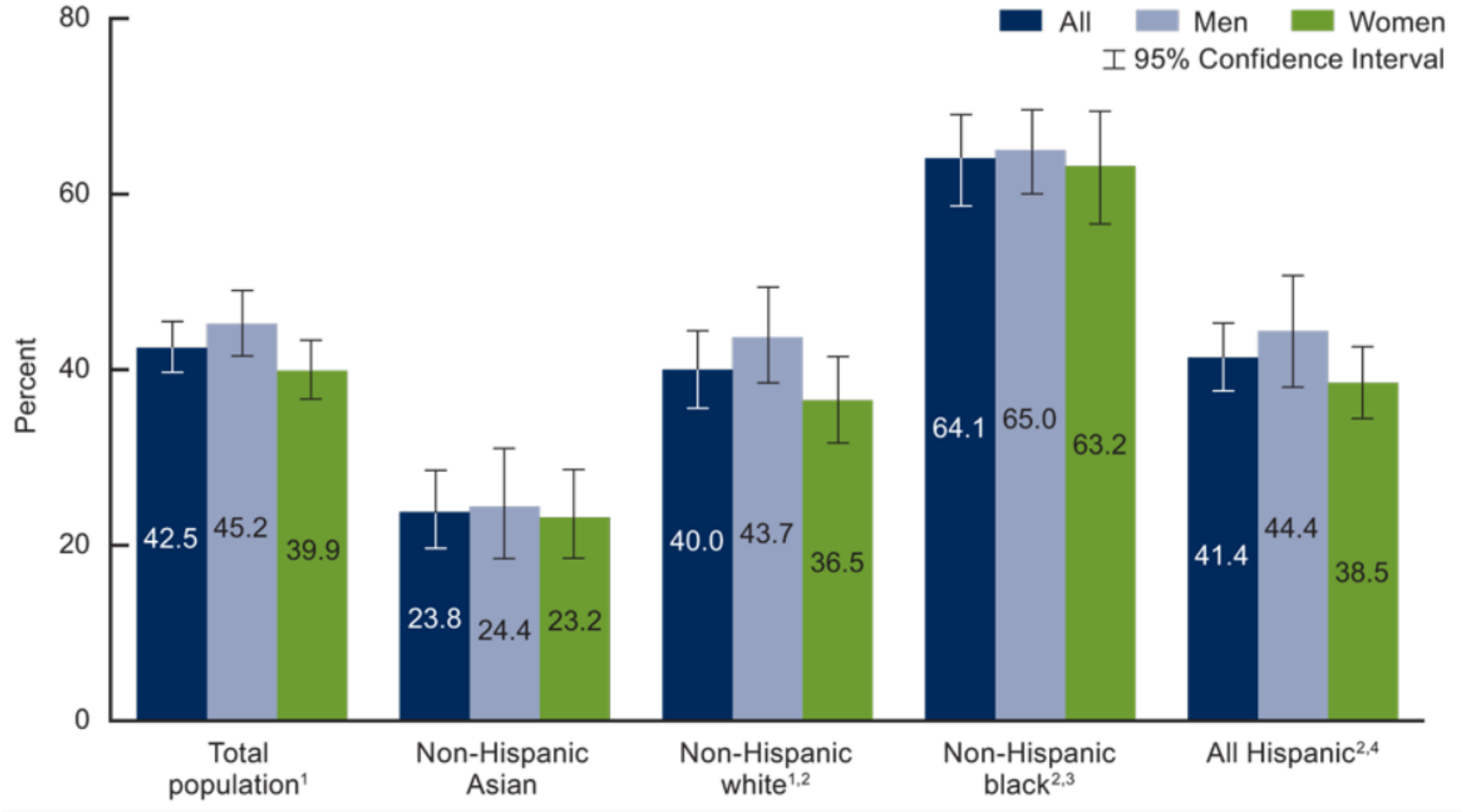
- ~50% in 15-24 yr
- >80% of sex active-> by age 45



Munoz N. 2004 J Infect Dis; Chesson et al 2014 Sex Transm Dis; Satterwite et al 2013 Sex Transm Dis

Ιός HPV

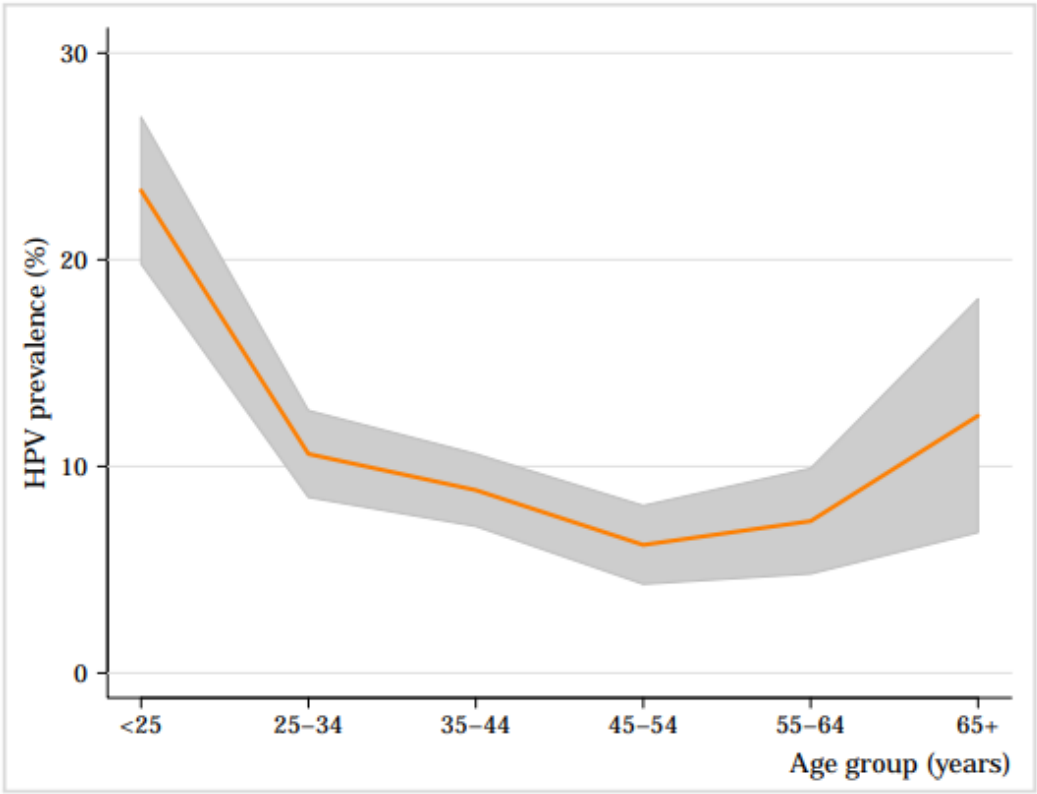
epidemiology genital, USA, NHANES latest data



Επιδημιολογία HPV (+), Ελλάδα

γενικός πληθυσμός γυναίκες, prevalence 5-49% !!!

Crude age-specific HPV prevalence (%) and 95% confidence interval in women with normal cervical cytology in Greece



Tsiodras et al Clin Microbiol Infect. 2011;17(8):1185-8.
Agorastos T, Eur J Cancer Prev 2004; 13: 145

Επιδημιολογία HPV (+), Ελλάδα

γενικός πληθυσμός γυναίκες, prevalence 5-49% !!!

- younger age p<0.001
- younger age of sexual debut p<0.001
- current and total n of sexual partners p<0.001
- short duration of a sexual relationship p<0.001
- marriage / multiparity = protection p<0.001

Tsiodras et al Clin Microbiol Infect. 2011;17(8):1185-8.
Agorastos T, Eur J Cancer Prev 2004; 13: 145

Ca τραχήλου, Ελλάδα

Distribution of new cancer cases in Greece, 2009-13

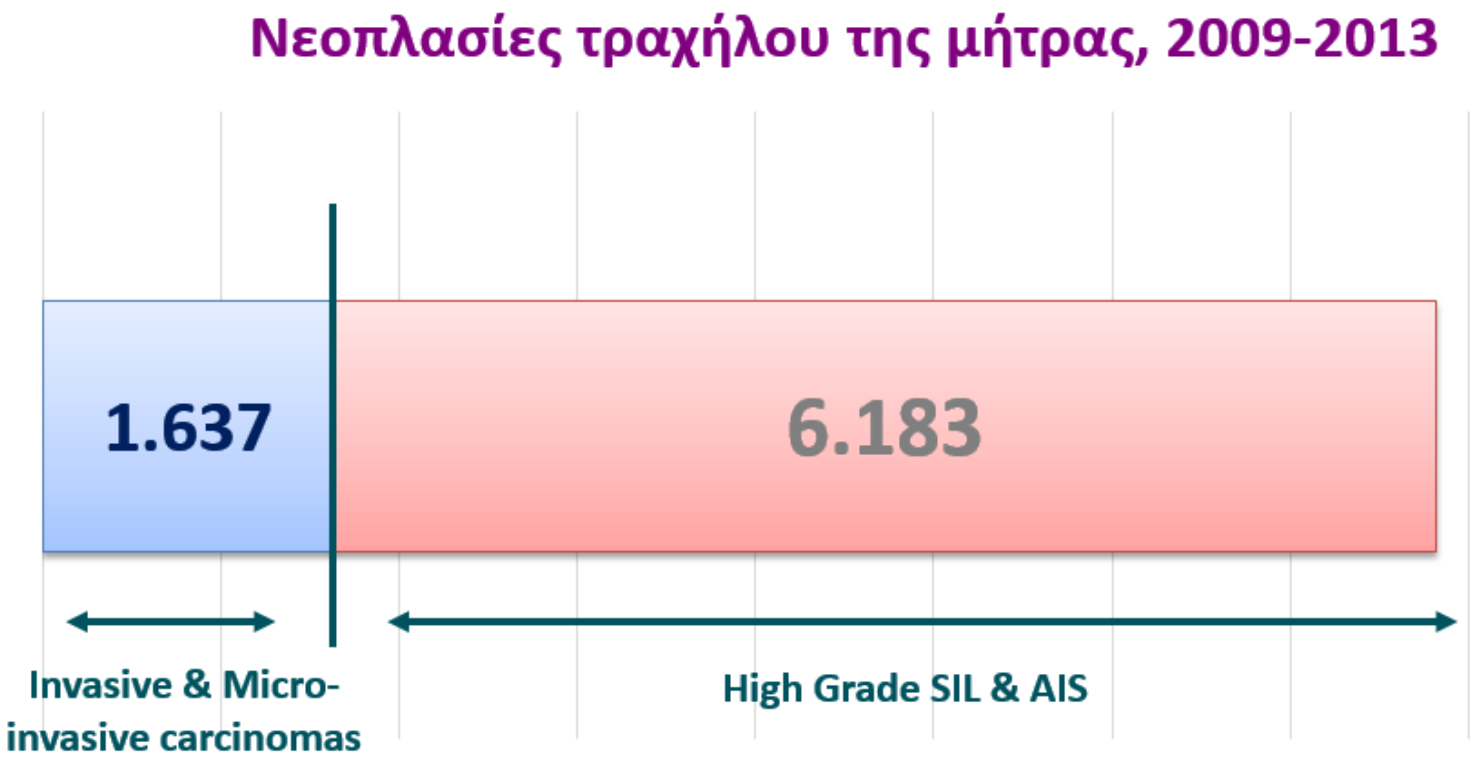
Female

Breast	32.959	18.07%
Colorectum	12.261	6.72%
Thyroid gland	8.865	4.86%
[illegible]	[illegible]	Lung
7.817	4.29%	Cervix uteri
5.910	3.24%	Bone marrow
5.706	3.13%	Lymphomas
3.434	1.88%	Ovaries

Virchows Arch (2018) 472:677–682

Ca τραχήλου, Ελλάδα

Distribution of new cancer cases in Greece, 2009-13

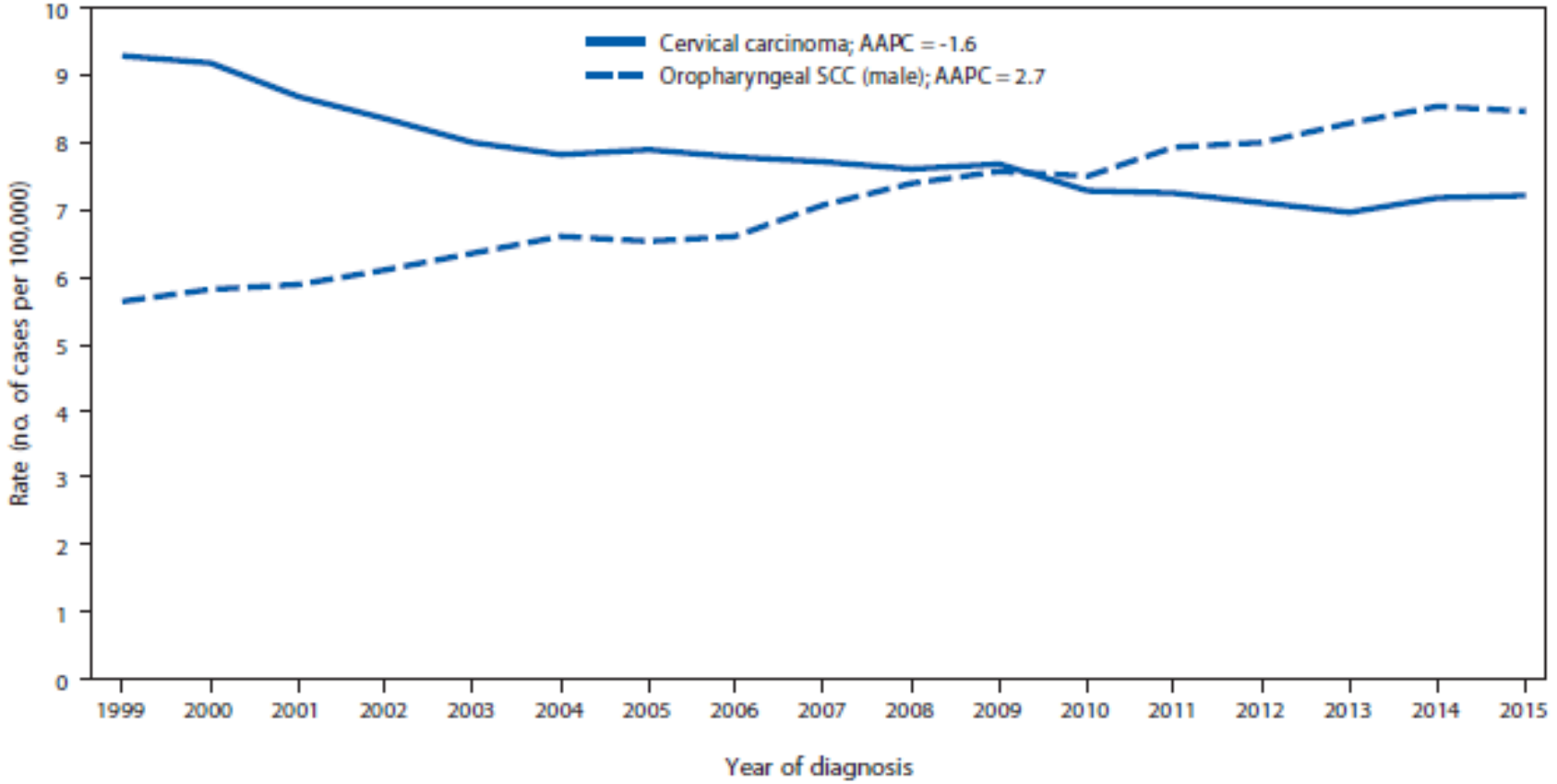


❖***327 νέα περιστατικά Ca / έτος***

Virchows Arch (2018) 472:677–682

Incidence of HPV assoc Ca USA 1999-2015

FIGURE 1. Trends* in age-adjusted incidence of cervical carcinoma among females and oropharyngeal SCC among men,† — United States,§ 1999–2015



Elizabeth A. Van Dyne et al. _ MMRW 67(33): 918-924 201

Oral & oropharynx Ca

- Risk ↑ with
  - ↑ ↑ n of sex partners, Younger sexual debut,
  - Hx of genital warts
- **Odds of tumor being HPV (+)**
  - Hx of orogenital sex, > 6 lifetime partners

Schwartz SM, et al. J Natl Cancer Inst 1998; 90:1626-36
Ritchie JM, et al. Int J Cancer 2003; 104:336-44

The JAMA Network

From: **Prevalence of Oral HPV Infection in the United States, 2009-2010**

JAMA. 2012;307(7):693-703. doi:10.1001/jama.2012.101

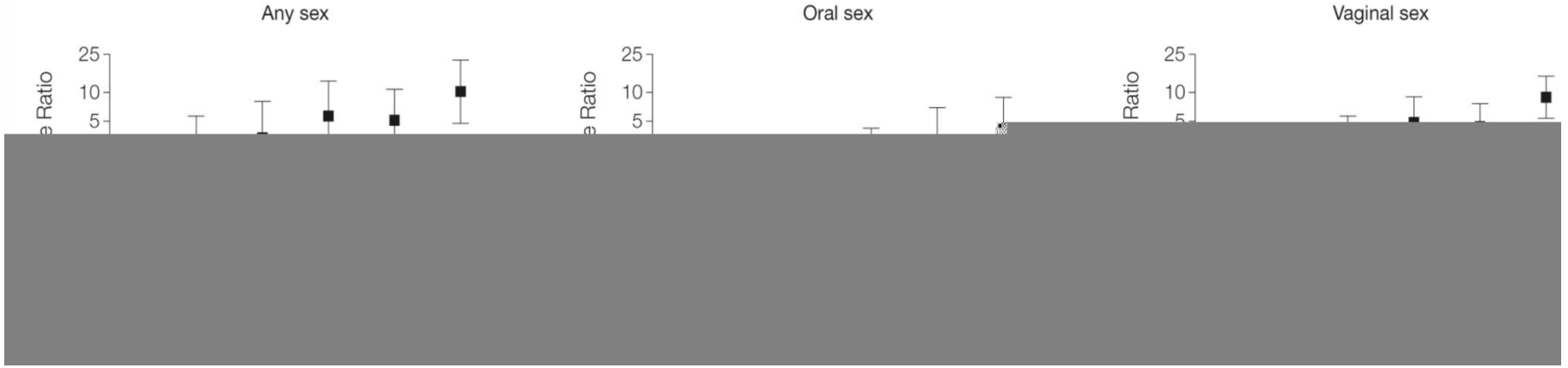


Figure Legend:

Human papillomavirus (HPV) prevalence ratio was adjusted for age (as a linear term), sex, race/ethnicity, marital status, and cigarette use. The analysis was restricted to individuals aged 14 to 59 years, for whom detailed sexual behavior data were available. Given high colinearity across sexual behaviors, each behavior was evaluated in separate models. $P < .001$ for trend in all 3 categories of sexual partner. Lifetime number of partners for performing oral sex included the sum of same- and opposite-sex partners; the reference category was 0 lifetime partners. Error bars indicate 95% CIs.

Date of download: 1/27/2014

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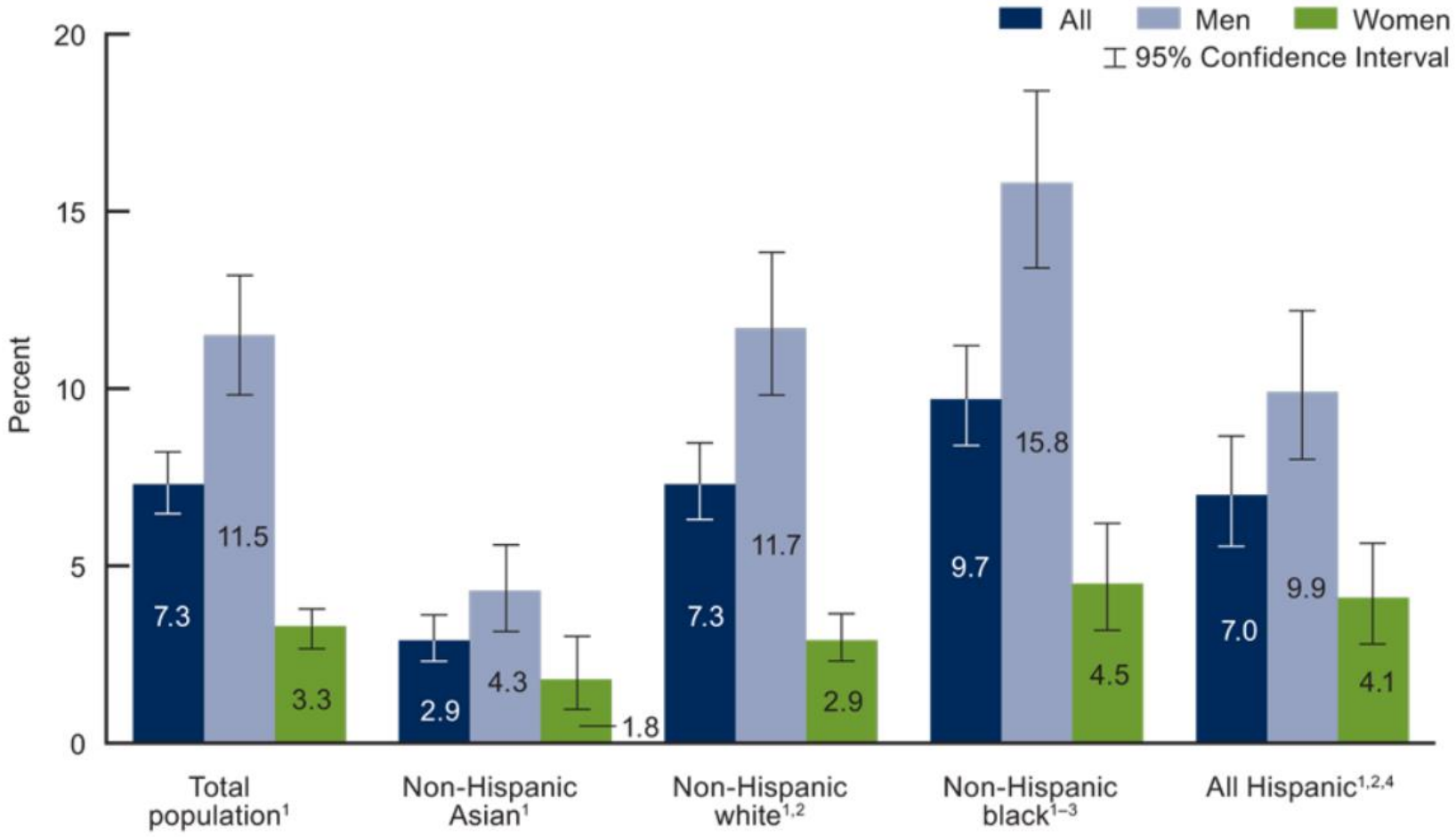
Ιός HPV

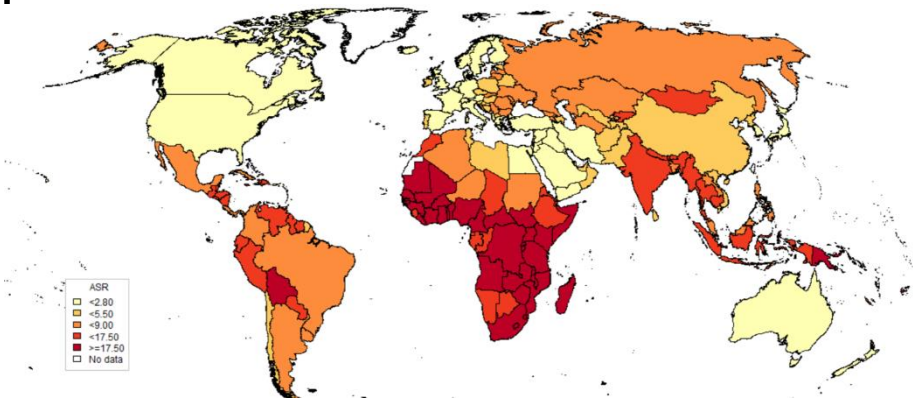
epidemiology oral, USA, NHANES latest data



Ιός HPV & Ca, global burden

cervical vs. non cervical & deaths

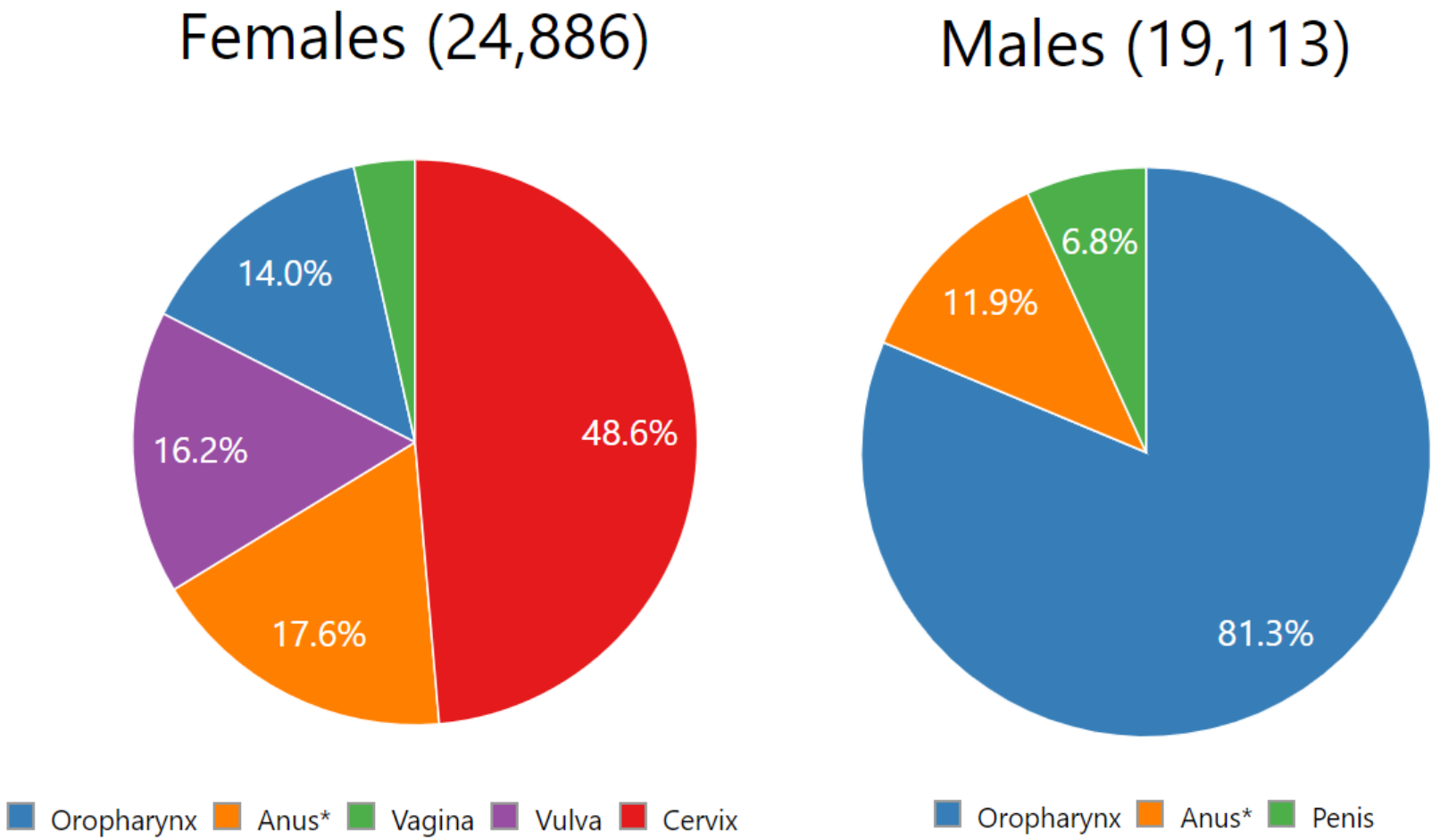
- 570 000 cervical Ca
  - 4th most common Ca in women
  - 311 365 deaths
    - 85% deaths in developing



- 100 000 non cervical Ca

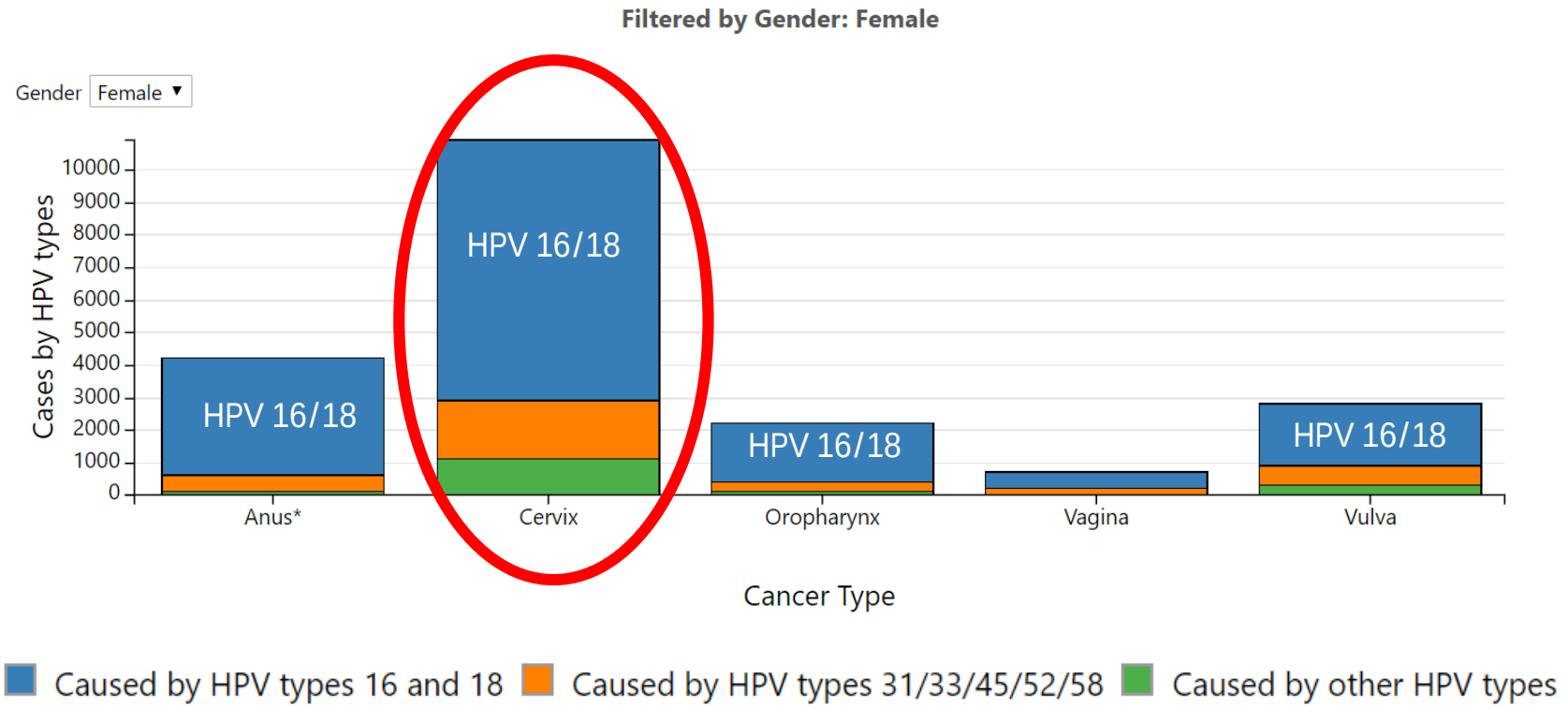
Globocan 2018
De Martel et al Int J Cancer 2017

Ιός HPV & Ca, latest USA data
anatomical site & gender



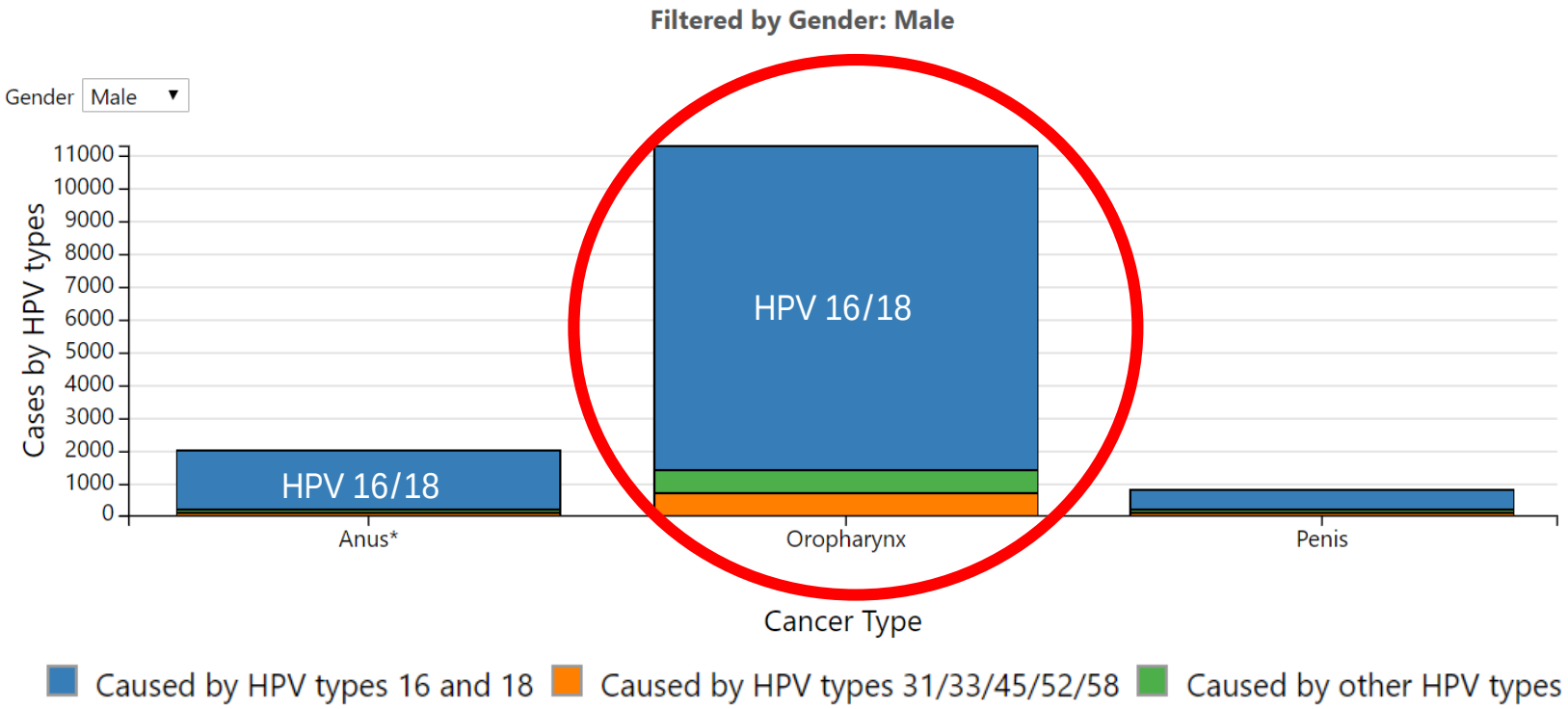
CDC August 2019

Ιός HPV & Ca, latest USA data
female by anatomical site & HPV type



CDC August 2019

Ιός HPV & Ca, latest USA data
male by anatomical site & HPV type



CDC August 2019

Ιός HPV epidemiology gaps in Greece!

Men prevalence , oral prevalence - no data!

Table 26: Studies on HPV prevalence among men in Greece

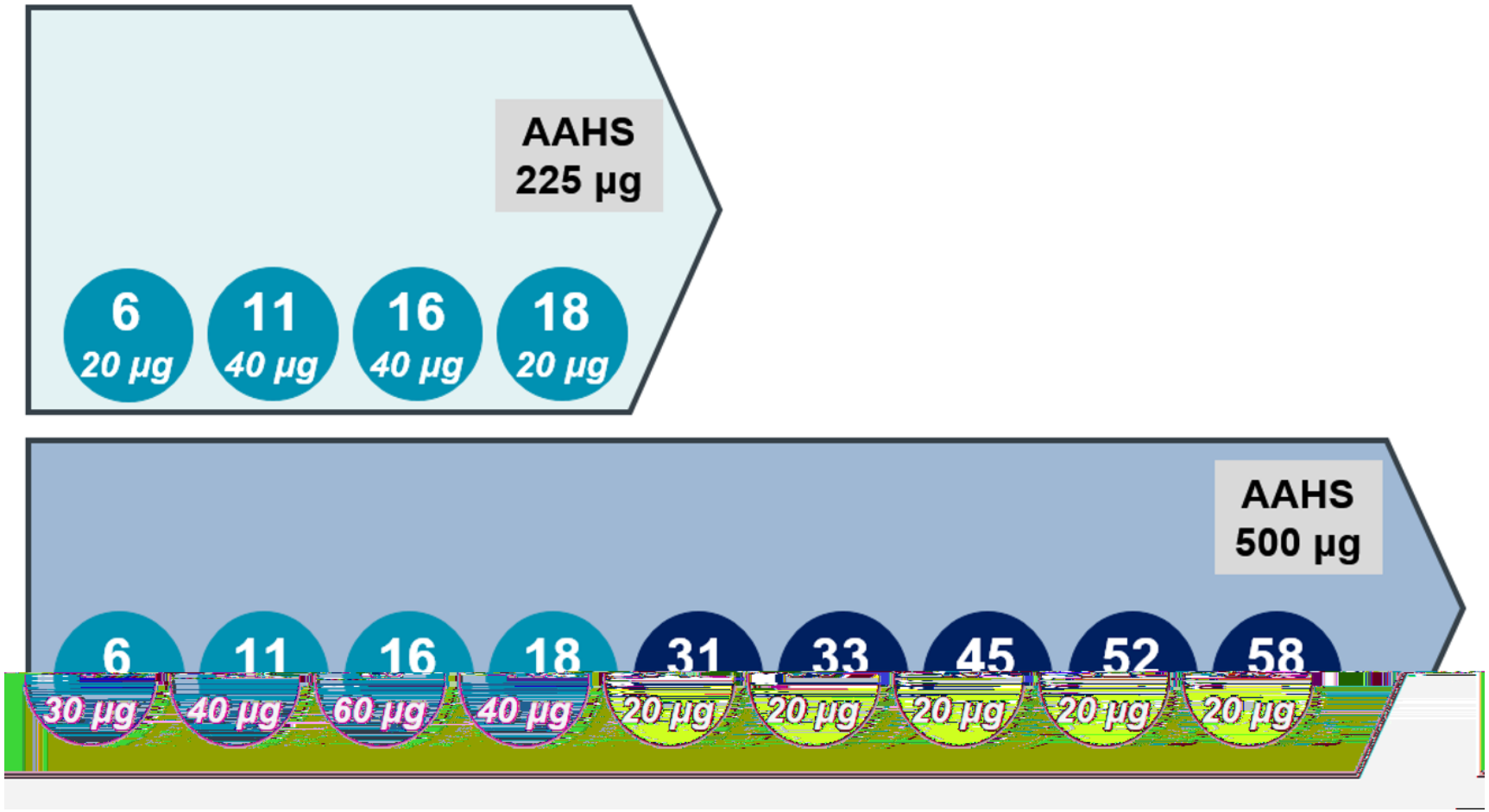
Study	Anatomic sites samples	HPV detection method	Population	Age (years)	HPV prevalence No	%	(95% CI)
No Data Available	-	-	-	-	-	- -	

Table 28: Studies on oral HPV prevalence among healthy in Greece

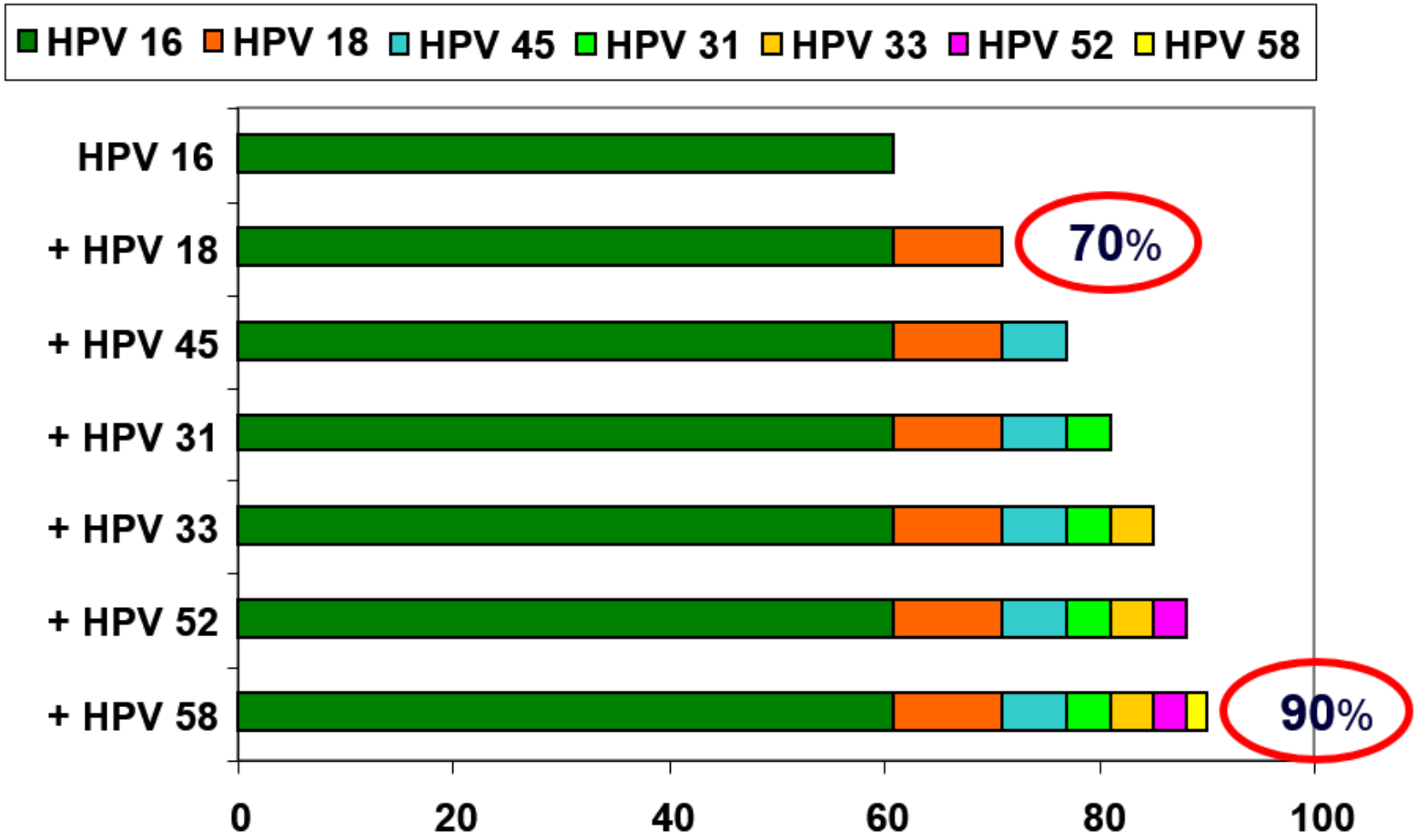
Study	Method specimen collection and anatomic site	HPV detection method and targeted HPV types	Population	Age (years)	No. Tested	HPV prevalence %	(95% CI)	Prev. of 5 most frequent HPVs HPV type (%)
MEN								
No Data Available	-	-	-	-	-	- -		-
WOMEN								
No Data Available	-	-	-	-	-	- -		-
BOTH OR UNSPECIFIED								
Lambropoulos 1997	Cytobrush from the buccal mucosa	PCR-MY09/MY11. Genotyping by SBH with TS probes (6, 11, 16, 18, 33)	Healthy population receiving routine oral examination	14-85	169	9.5 (5.5-14.9)		HPV 6 (3.6%) HPV 16 (2.4%) HPV 11 (0.6%)

HPV INFORMATION CENTRE

4-δύναμο vs. 9-δύναμο εμβόλιο

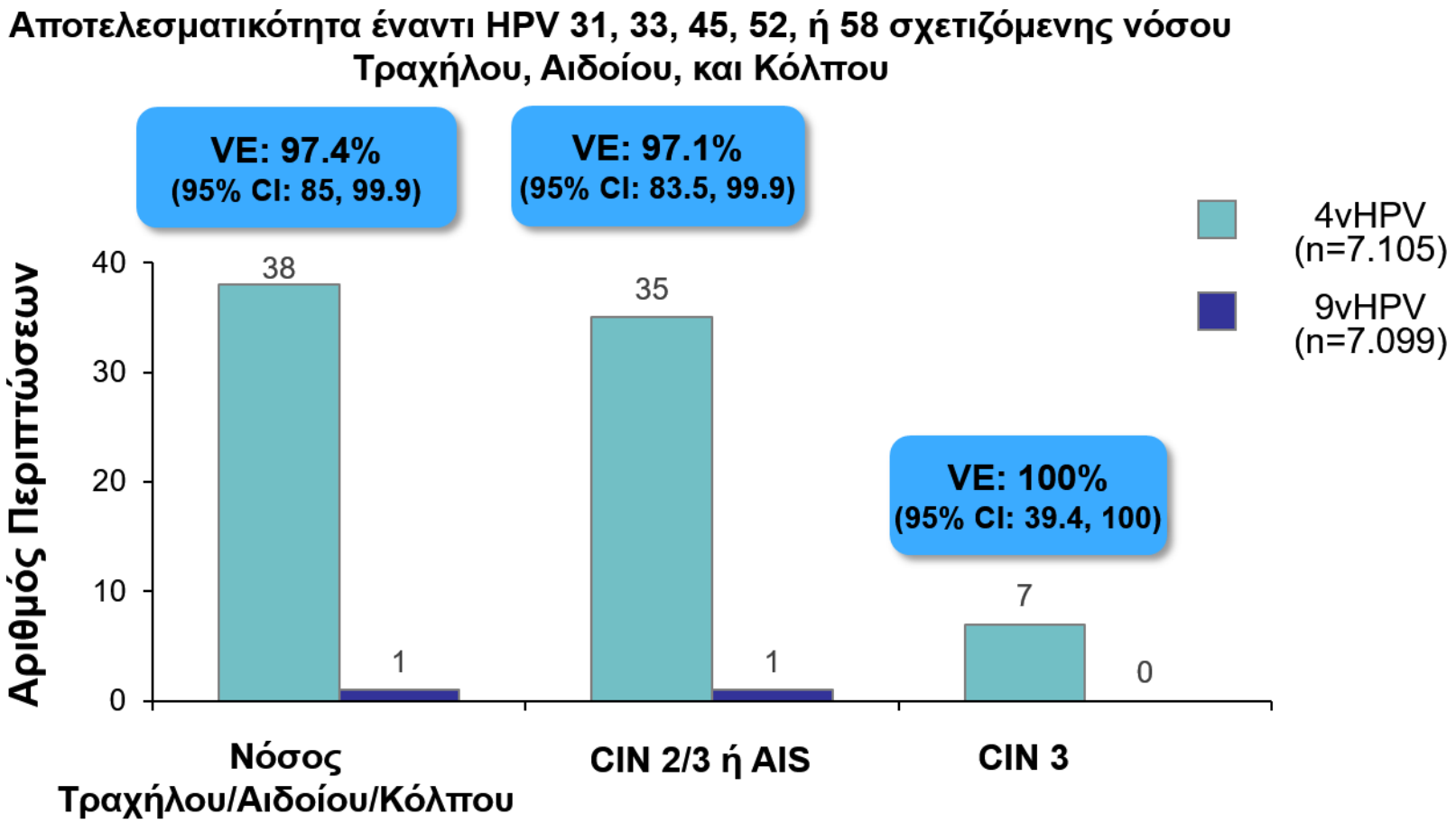


4- vs. 9-δύναμο εμβόλιο, HPV (+) συμβολή σε πρόληψη Cervical Ca



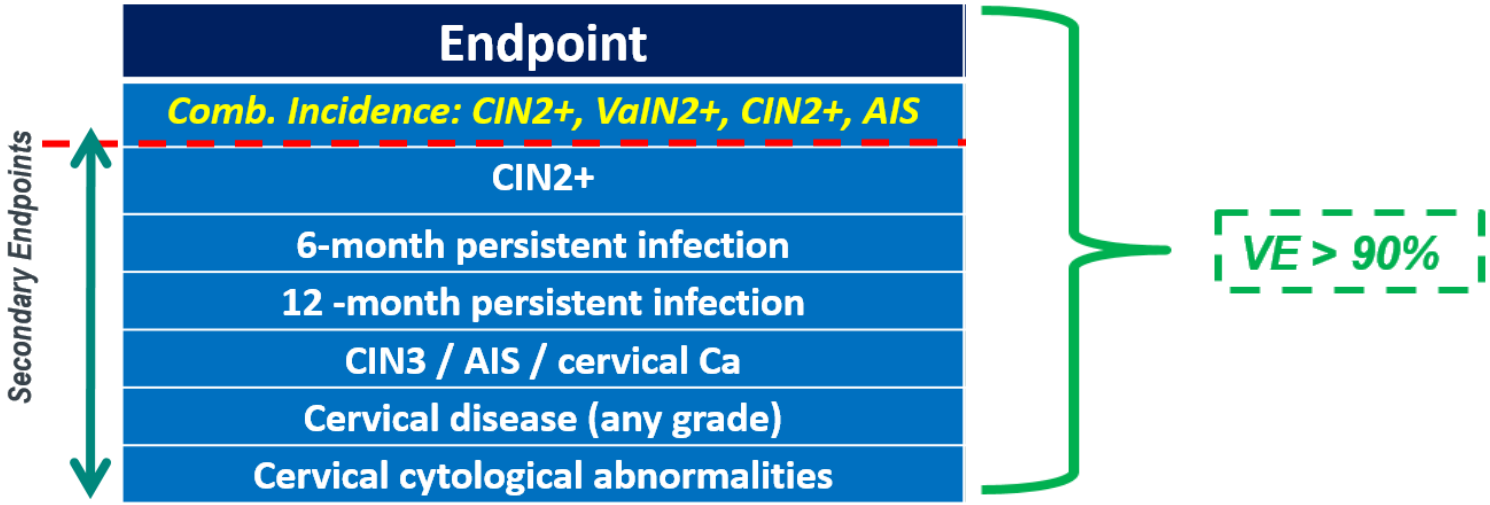
Modified from Serrano B et al. Infect Agent Cancer. 2012;7:38.

Αποτελεσματικότητα, 9vHPV, 97%



Joura EA et al. ***N Engl J Med***. 2015

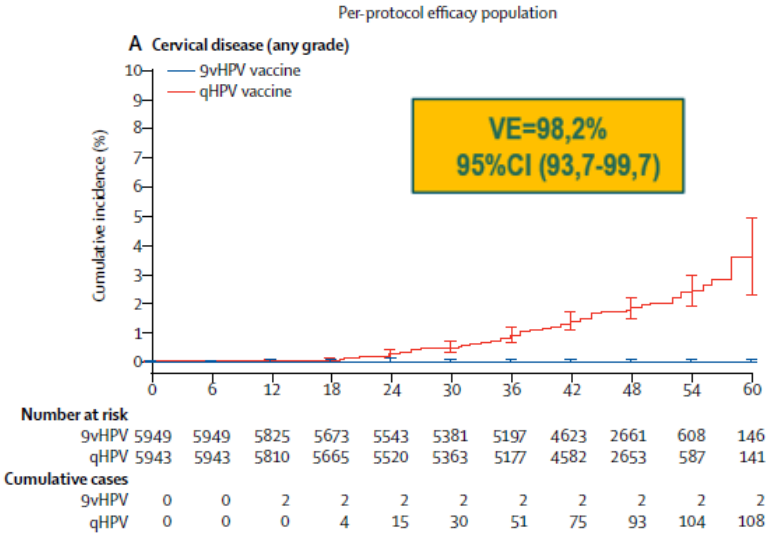
Αποτελεσματικότητα, 9vHPV, εμμένουσα λοίμωξη, 6 yrs f/u

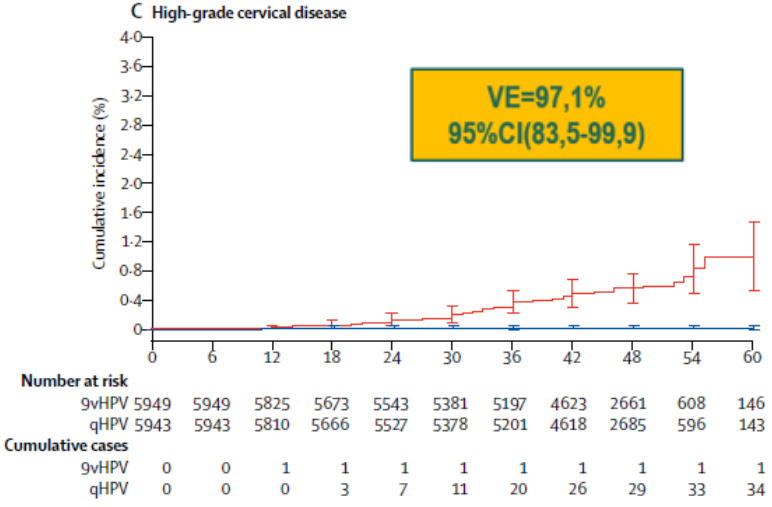


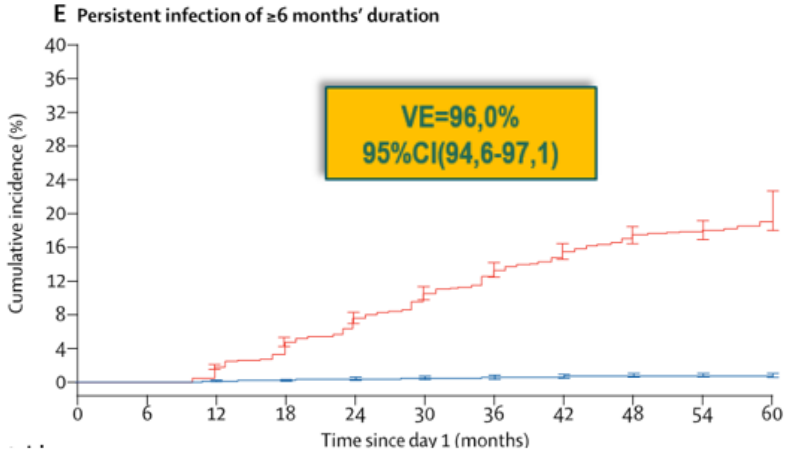
Huh et al. ***Lancet ID***. 2017

Αποτελεσματικότητα, 9vHPV, 6 yrs f/u

...& η σημασία του timely vaccination!



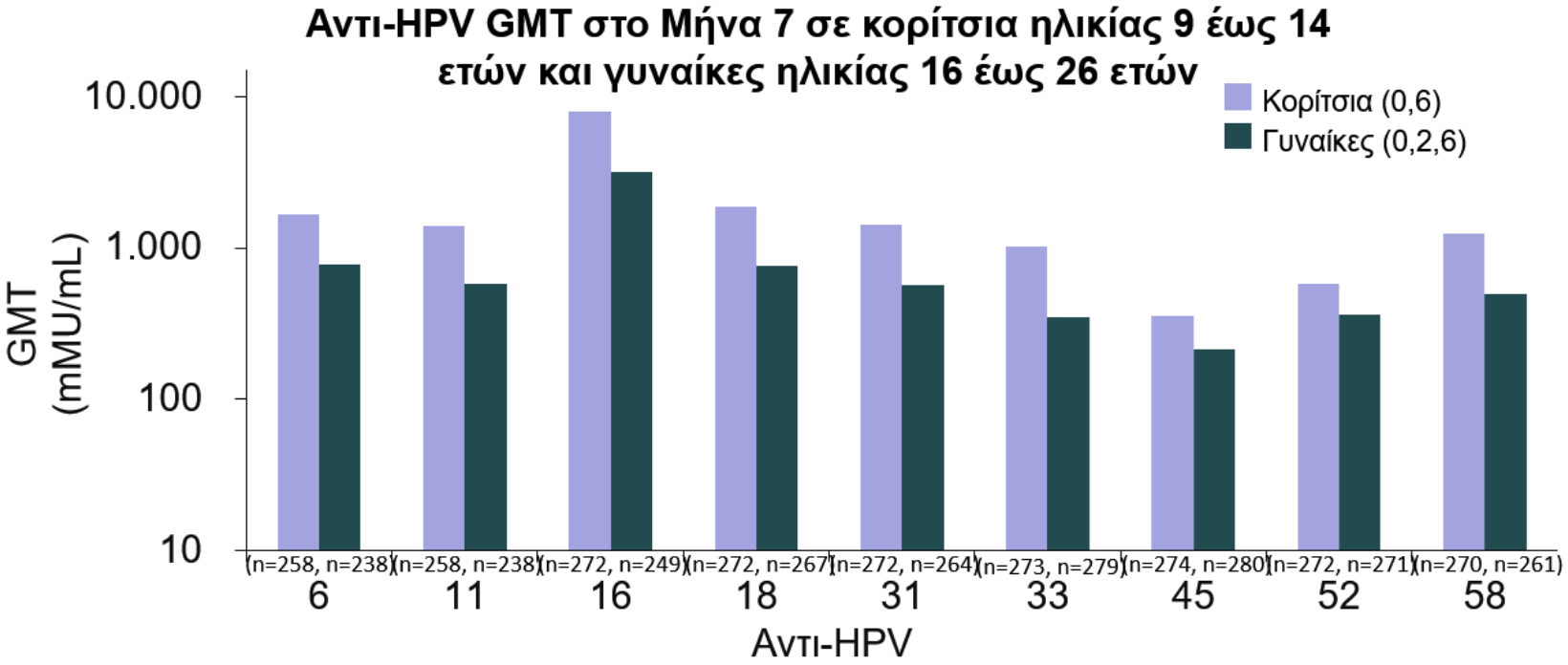




Huh WK, et al. Lancet 2017

2 vs. 3 δόσεις 9vHPV, κορίτσια

...παρόμοια αποτελέσματα σε αγόρια



Iversen OE et al. ***JAMA***. 2016;316:2411-21. Luxembourg A. ACIP 2016

Εθνικό Πρόγραμμα Εμβολιασμών 2018-19
ενήλικες

ΠΑΡΑΡΤΗΜΑ:
ΕΘΝΙΚΟ ΠΡΟΓΡΑΜΜΑ ΕΝΗΛΙΚΩΝ 2018-2019

Εμβόλιο	**19-26 ετών**	**27-59 ετών**	**60-64 ετών**	**≥65 ετών**
Γρίπης	1 δόση ετησίως		1 δόση ετησίως	
Td/Tdap	Υποκαταστήστε μία δόση Td με Tdap ή Tdap-IPV, στη συνέχεια Td κάθε 10 χρόνια			
MMR	1-2 δόσεις ανάλογα με ιστορικό εμβολιασμών*			
VAR	2 δόσεις			
HZV			1 δόση	
HPV	3 δόσεις			
PCV13	1 δόση			1 δόση
PPSV23	1-2 δόσεις ανάλογα με τις ενδείξεις			1 δόση
HepA	2 δόσεις			
HepB	3 δόσεις			
MenACWY	1 ή περισσότερες δόσεις ανάλογα με τις ενδείξεις			
MenB	2-3 δόσεις ανάλογα με το εμβόλιο			
Hib	1-3 δόσεις ανάλογα με τις ενδείξεις			

Συστήνεται για ενήλικες με συνοδές ιατρικές καταστάσεις (ομάδες αυξημένου κινδύνου) ή άλλες ενδείξεις

Δεν συστήνεται

Εθνικό Πρόγραμμα Εμβολιασμών, ομάδες αυξημένου κινδύνου, 2017

Εμβόλιο	Κύηση ή λοχεία	Ανοσοκαταστολή (πλην HIV)	HIV λοίμωξη (CD4+ κύτταρα)		Ασπληνία, μόνιμη έλλειψη τελικών κλασμάτων συμπληρώματος	Νεφρική ανεπάρκεια τελικού σταδίου σε αιμοδύλυση	Χρόνιες καρδιοπάθειες, πνευμονοπάθειες, χρόνιος αλκοολισμός	Χρόνιες παθήσεις του ήπατος	Σακχαρώδης διαβήτης	Υγειονομικό προσωπικό	MSM
			<200	≥200							
Γρίπης	1 δόση ετησίως										
Td/Tdap	1 δόση σε κάθε κύηση	Υποκαταστήστε μία δόσηTd με Tdap ή Tdap-IPV, στη συνέχεια Td κάθε 10 χρόνια									
MMR	Αντενδείκνυται	1-2 δόσεις ανάλογα με την περίπτωση									
VAR	Αντενδείκνυται	2 δόσεις									
HPV - θήλυ		3 δόσεις μέχρι την ηλικία των 26 ετών									
HPV - άρρεν		3 δόσεις μέχρι την ηλικία των 26 ετών									3 δόσεις μέχρι 26
PCV13	1 δόση										
PPSV23	1,2 ή 3 δόσεις ανάλογα με τις ενδείξεις										
HepA	2 δόσεις										
HepB	3 δόσεις							3 δόσεις			
MenACWY	1 ή περισσότερες δόσεις ανάλογα με τις ενδείξεις										
MenB	2-3 δόσεις ανάλογα με το εμβόλιο										
Hib	3 δόσεις στους δέκτες σε μεταμόσχευση μυελού	1 δόση									

Συστήνεται για ενήλικες που πληρούν τα ηλικιακά κριτήρια και δεν έχουν αποδεικτικό προηγούμενου εμβολιασμού ή νόσησης

Συστήνεται για ενήλικες με συνοδές ιατρικές καταστάσεις (ομάδες αυξημένου κινδύνου) ή άλλες ενδείξεις

Εμβόλιο HPV σε ανοσοκαταστολή, 2018

- Το εμβόλιο συνιστάται να γίνεται σε γυναίκες και άνδρες 18-26 ετών εφ’ όσον
  - ανήκουν σε ομάδες υψηλού κινδύνου (π.χ. MSM)
  - παρουσιάζουν ανοσοανεπάρκεια (π.χ. HIV)

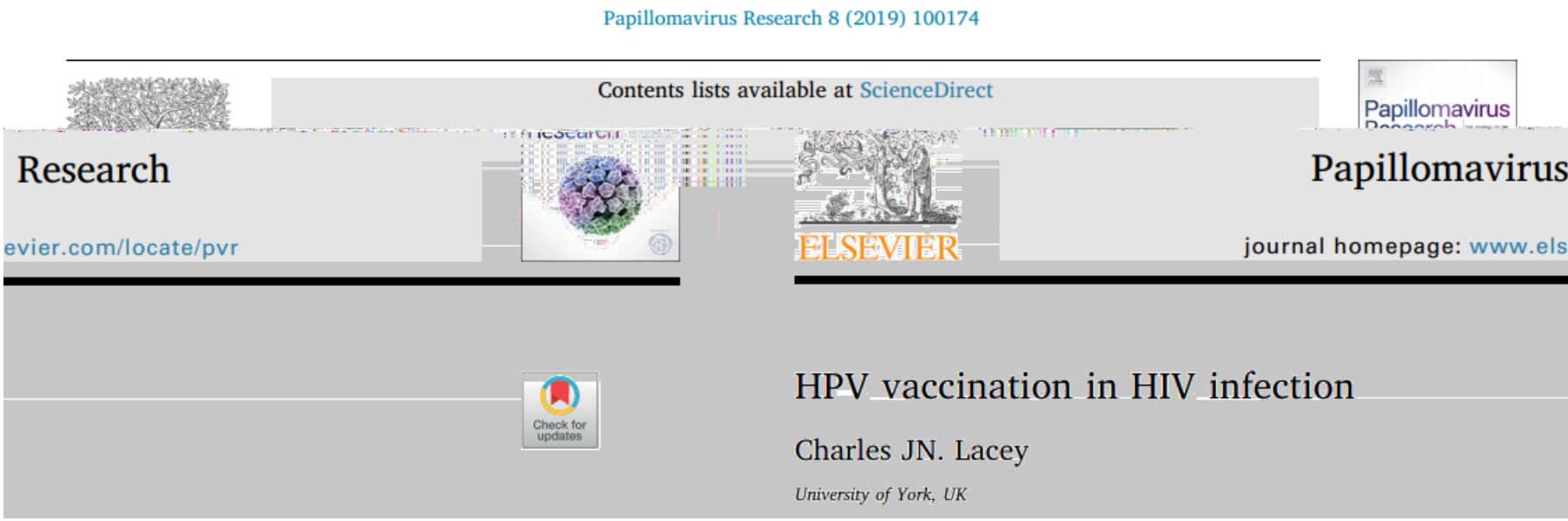
- Συστήνεται η συζήτηση με τον ειδικό κατά περίπτωση

Αποτελεσματικότητα, σε HIV (+)

Limited efficacy data σε HIV πληθυσμό

- HIV may reduce response-effectiveness
- Reported for HepB, PCV

J Infect. Dis. 2013;207:402–410
Clin. Infect. Dis. 2014;59:808–818



Cervical Ca - HPV

- HPV necessary cause for cervical Ca
  - High risk HPV types - oncogenic
    - Globally 16 & 18 cause > 70% of all cervical Ca
- **HPV vaccines -> the new weapon against Cervical Ca**

HPV, screening

- Cervical screening programs should screen women who have received HPV vaccination in the same manner as unvaccinated women.

HPV, Rx of cellular changes

- Complex & requires synthesis of patient age, Pap test results, biopsy pathology, and high-risk HPV DNA testing

- Consult expert!!!

HPV, Rx of warts

Recommended Regimens for External Anogenital Warts (i.e., penis, groin, scrotum, vulva, perineum, external anus, and perianus)*

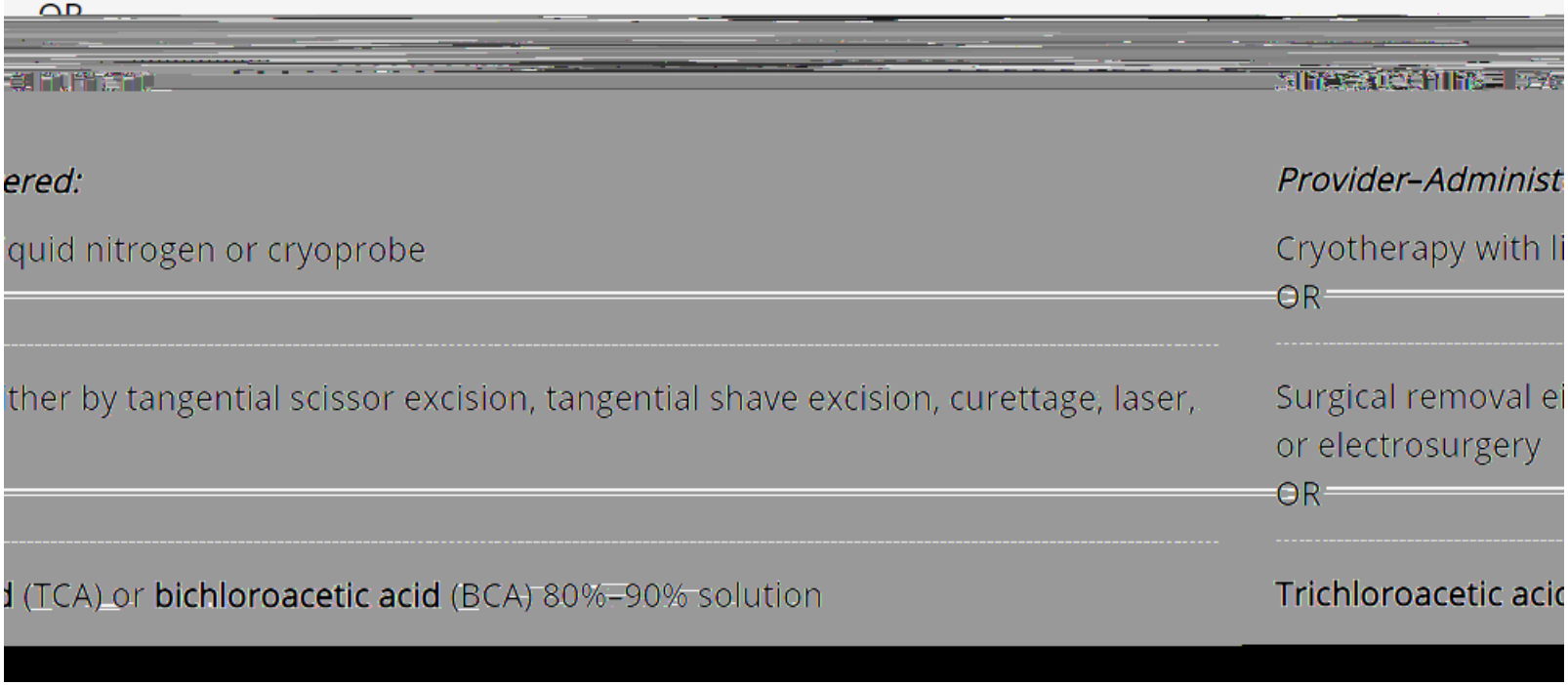
Patient-Applied:

Imiquimod 3.75% or 5% cream†

OR

Podofilox 0.5% solution or gel

OR



HPV, Rx of warts

Recommended Regimens for Cervical Warts

Cryotherapy with liquid nitrogen
OR

Surgical removal
OR

TCA or **BCA** 80%–90% solution

Management of cervical warts should include consultation with a specialist.

For women who have exophytic cervical warts, a biopsy evaluation to exclude high-grade SIL treatment is initiated.

Recommended Regimens for Intra-anal Warts

Cryotherapy with liquid nitrogen
OR

Surgical removal
OR

TCA or **BCA** 80%–90% solution

Sexually Transmitted Diseases (STDs)

Sexually Transmitted Diseases
Diseases & Related Conditions
Prevention
Pregnancy & Infertility
Publications & Products
Program Tools
Projects & Initiatives
Data & Statistics
Training
Treatment
About the Division of STD Prevention

Recommend 33 Tweet 17 Share

Prevention

How You Can Prevent Sexually Transmitted Diseases

This page includes information about STD prevention, testing, and resources.

Get the Facts

Arm yourself with basic information about STDs: How are these diseases spread? How can you protect yourself? What are the treatment options? Learn the answers to these questions by reading the STD Fact Sheets.

Take Control

Centers for Disease Control and Prevention
CDC 24/7: Saving Lives. Protecting People.™

A-Z Index A B C D E F G H I J K L M N O P Q R S T U V W X Y Z #

Sexually Transmitted Diseases (STDs)

Take Control

You have the facts; now protect yourself and your sexual partners. Effective strategies for reducing STD risk include:

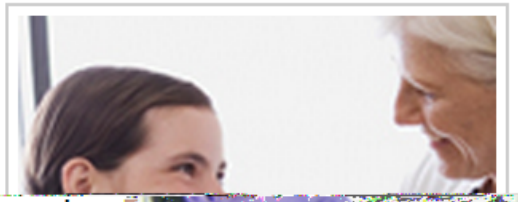
Abstinence:

The most reliable way to avoid infection is to not have sex (i.e., anal, vaginal or oral).

Centers for Disease Control and Prevention
CDC 24/7: Saving Lives. Protecting People.™

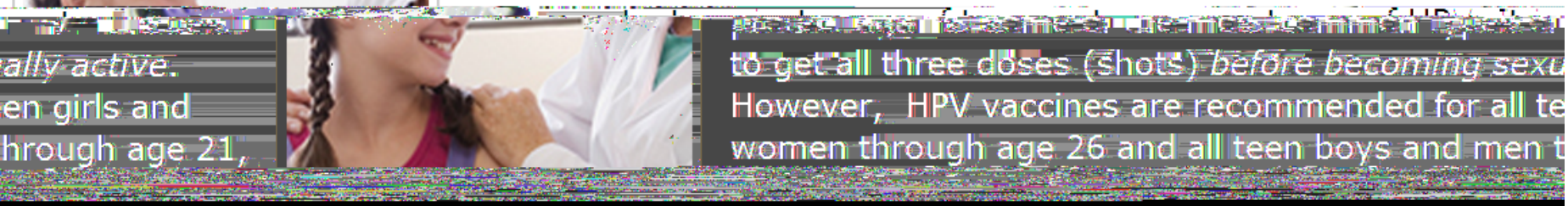
A-Z Index A B C D E F G H I J K L M N O P Q R S T U V W X Y Z #

Sexually Transmitted Diseases (STDs)



Vaccination:

Vaccines are safe, effective, and recommended ways to prevent hepatitis B and HPV. HPV vaccines for males and females can



Centers for Disease Control and Prevention
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A-Z Index A B C D E F G H I J K L M N O P Q R S T U V W X Y Z #

Sexually Transmitted Diseases (STDs)

Mutual monogamy:

Mutual monogamy means that you agree to be sexually active with only one person, who has agreed to be sexually active only with you. Being in a long-term mutually monogamous relationship with an uninfected partner is one of the most reliable ways to avoid STDs. But you must both be certain you are not infected with STDs. It is important to have an open and honest conversation with your partner.

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A-Z Index A B C D E F G H I J K L M N O P Q R S T U V W X Y Z #

Sexually Transmitted Diseases (STDs)

Reduced number of sex partners:

Reducing your number of sex partners can decrease your risk for STDs. It is still important that you and your partner get tested, and that you share your test results with one another.

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A-Z Index A B C D E F G H I J K L M N O P Q R S T U V W X Y Z #

Sexually Transmitted Diseases (STDs)

Condoms:

Correct and consistent use of the male latex condom is highly effective in reducing STD transmission. Use a condom every time you have anal, vaginal, or oral sex.

Use condoms – correct way!

Watch NOT 100% protection

Use condoms – correct way!
Watch NOT 100% protection

- > 80% teenagers used condom
- Only 30% correctly
  - Each contact/act
  - Entire duration of act

THANK YOU!!!