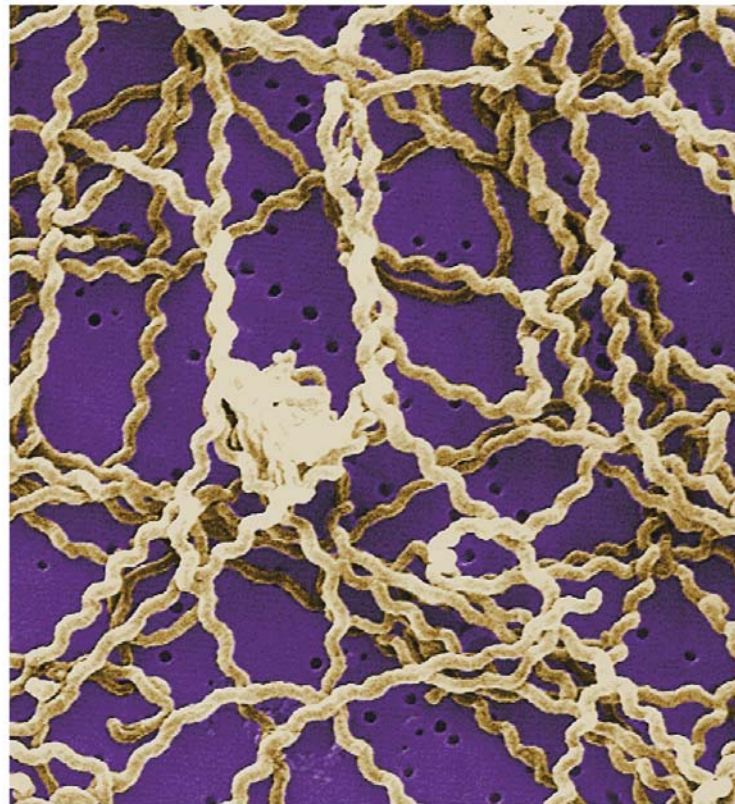


## Chapter 26

# Microbial Diseases of the Urinary and Reproductive Systems



# Structure and Function of the Urinary System

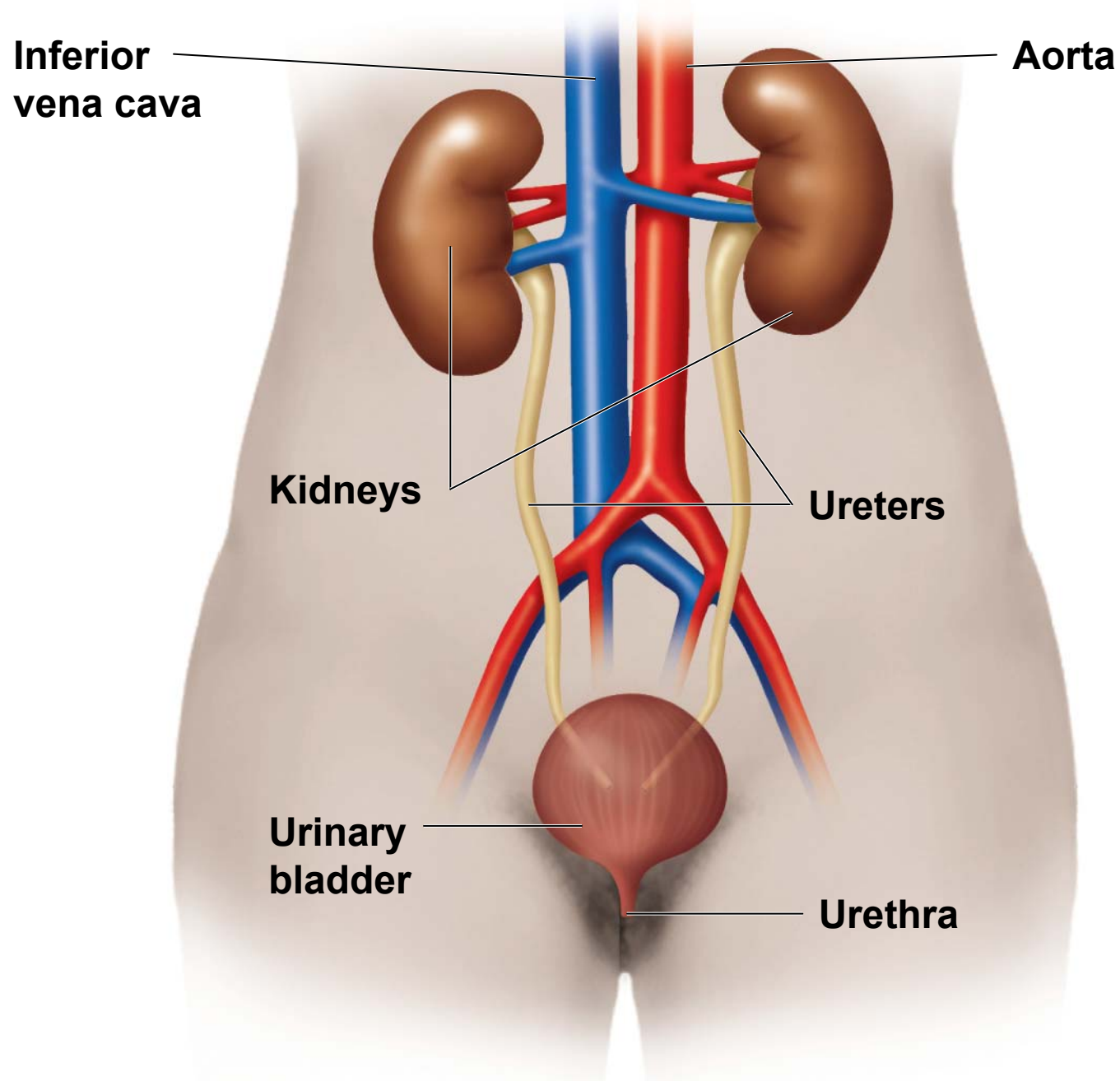
- **Urinary system**

- Two kidneys
- Two ureters
- One urinary bladder
- One urethra

- **Infection prevented by**

- Sphincter muscles (valves) that prevent backflow to kidneys
- Mucous membrane
- Acidity of urine
- Mechanical flushing

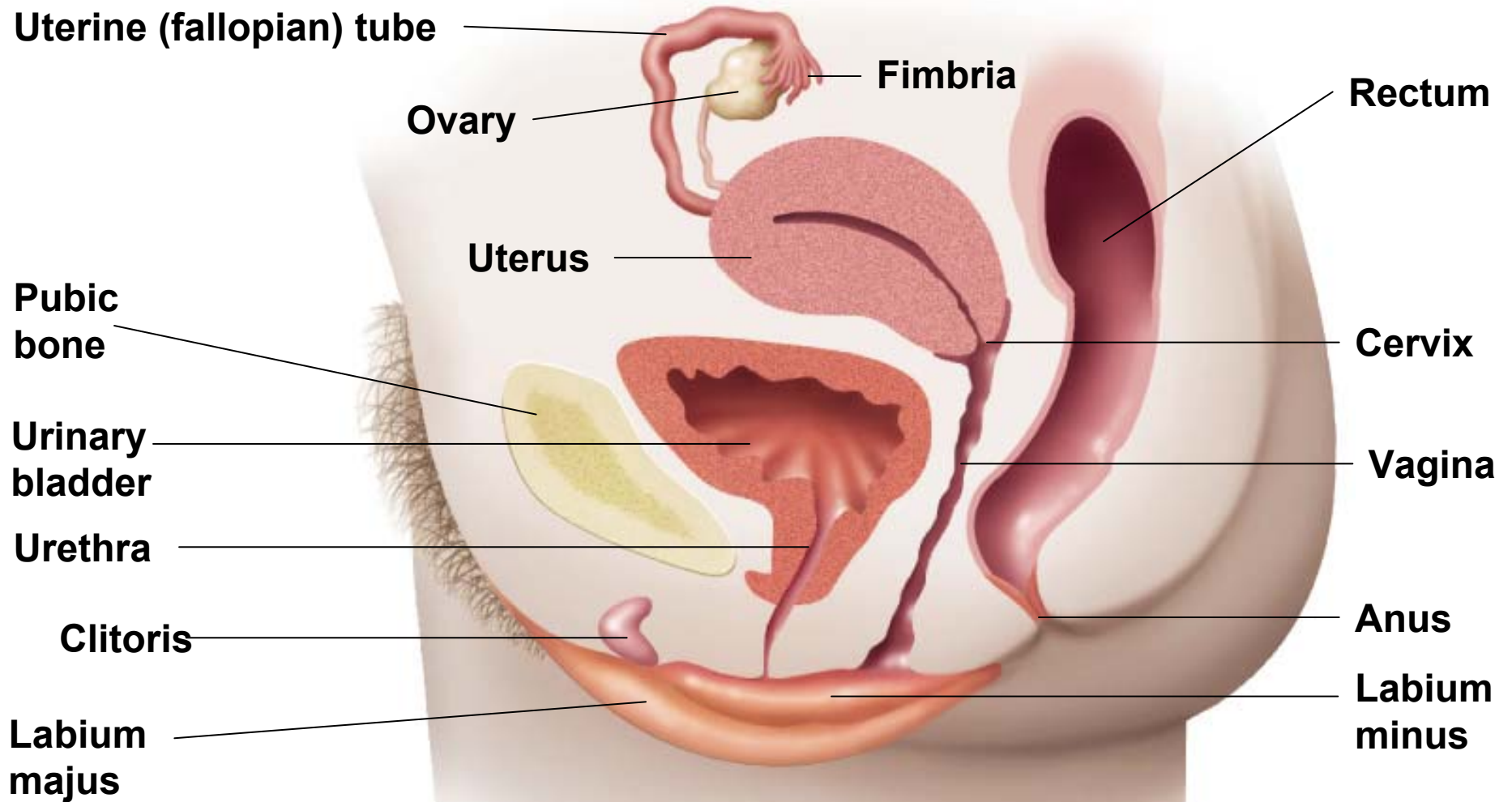
Organs of the human urinary system, shown here in the female.



# The Female Reproductive System

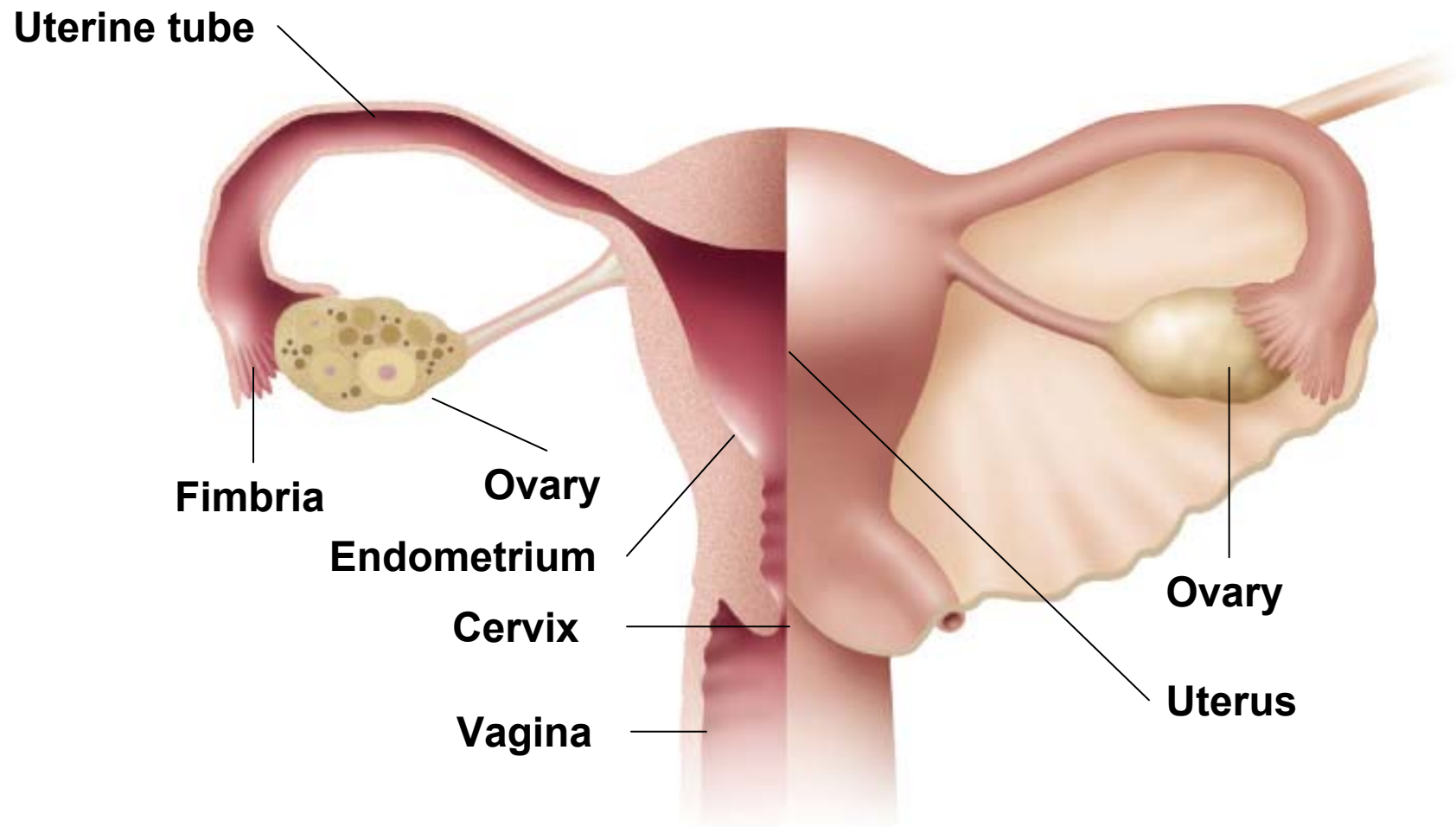
- Female
  - Two ovaries
  - Two uterine (fallopian) tubes
  - The uterus, including cervix;  
vagina
  - External genitals

## Female reproductive organs.



Side view section of female pelvis showing reproductive organs

## Female reproductive organs.



Front view of female reproductive organs, with the uterine tube and ovary to the left in the drawing sectioned.

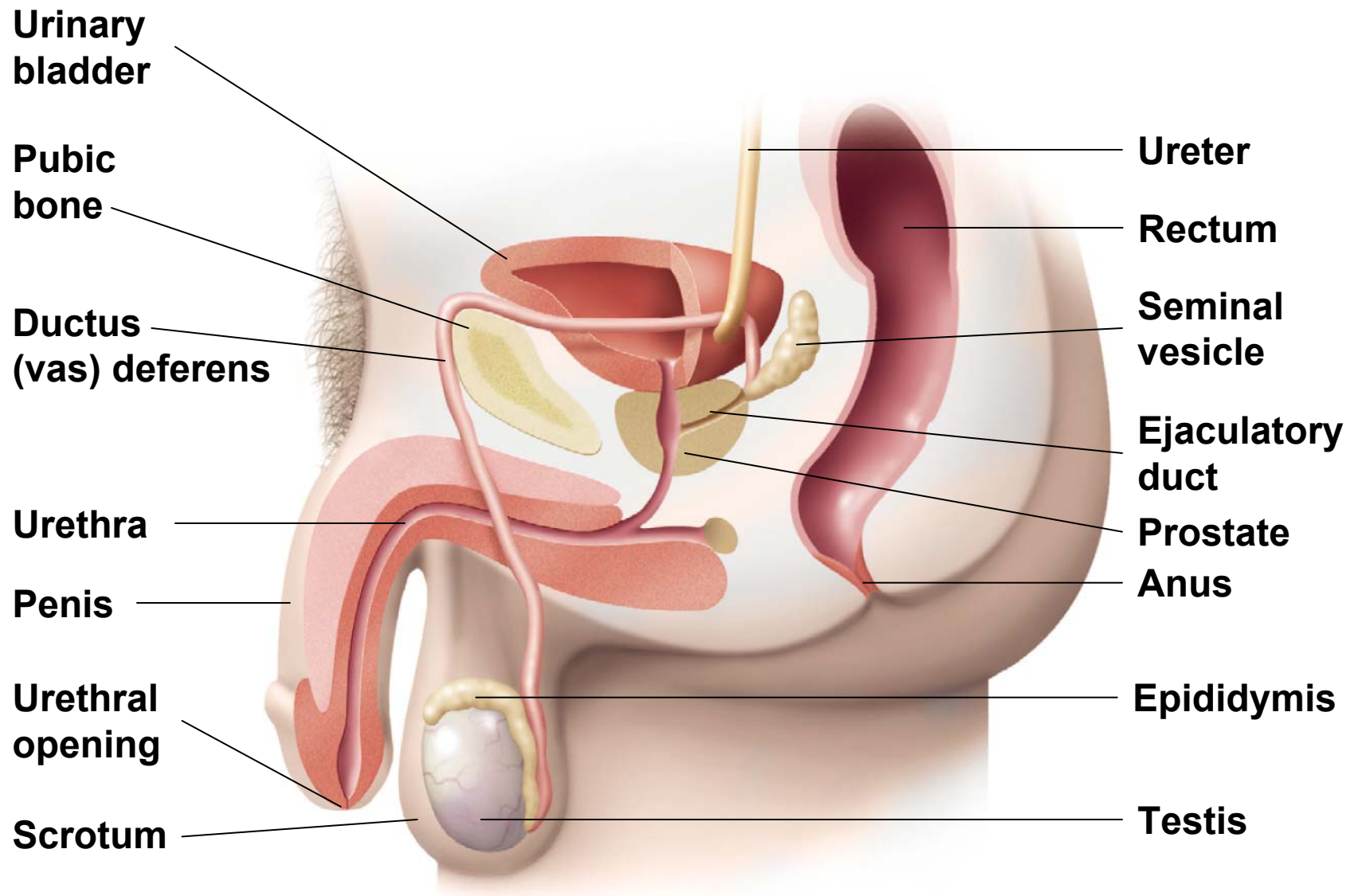
The fimbriae move to create fluid movement that moves the egg into the uterine tube.

# The Male Reproductive System

- Male
  - Two testes
  - Accessory glands
  - Penis
  - Epididymis
  - Ductus (vas) deferens
  - Ejaculatory duct
  - Urethra



**Male reproductive and urinary organs.**



**Side view section of male pelvis**



# Normal Microbiota

- Urinary bladder and upper urinary tract are sterile
- Lactobacilli are predominant in the vagina
  - Grow on glycogen secretions by vagina
  - Metabolize sugars and produce lactic acid
  - Produce  $H_2O_2$
- Infection is indicated by // >10,000 bacteria per ml

# Urinary System Infections

- Urethritis // An inflammation of the urethra
- Cystitis // An inflammation of the urinary bladder
- Salpingitis or Uretitis // An inflammation of the ureters
- Pyelonephritis // An inflammation of one or both kidneys
  - Note: infections commonly progress from urethra's orifice towards kidneys // may also be caused by systemic infections
  - systemic infections (leptospirosis – caused by *Leptospira interrogans*) may infect liver and/or kidney // cause renal failure

# Cystitis

- **Usual causative agents**
  - *E. coli* & *Staphylococcus. saprophyticus*
- **Symptoms**
  - Dysuria (difficult or painful urination)
  - Pyuria (pus in urine)
- **Diagnosis:** >100 CFU/ml of potential pathogens
- **Treatment:** trimethoprim-sulfamethexazole

# Pyelonephritis

- **Causative agent:** usually *E. coli*
- **Symptoms:** fever; back or flank pain
- **Diagnosis:** 10,000 CFU/ml
- **Treatment:** cephalosporin

# Leptospirosis

- Disease of domestic or wild animals which can be transmitted to humans  
// Reservoir: dogs and rats
- Cause damage to kidneys of humans
- Causative agent: *Leptospira interrogans*
- Transmission: skin/mucosal contact from urine-contaminated water



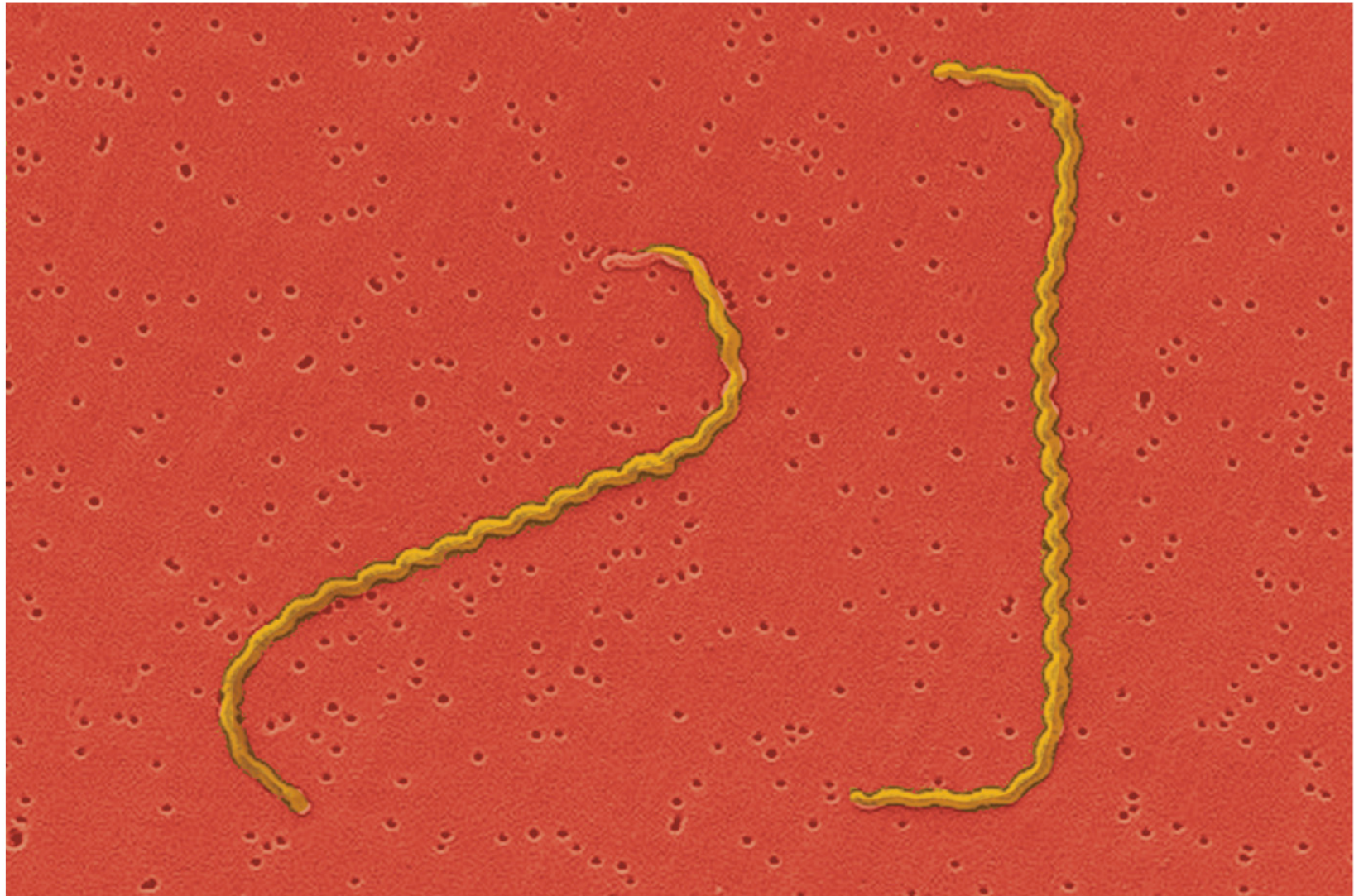
# Leptospirosis

- **Symptoms:** headaches, muscular aches, fever; kidney failure a possible complication
- **Diagnosis:** serological test
- **Treatment:** doxycycline





*Leptospira interrogans*, the cause of leptospirosis.



SEM

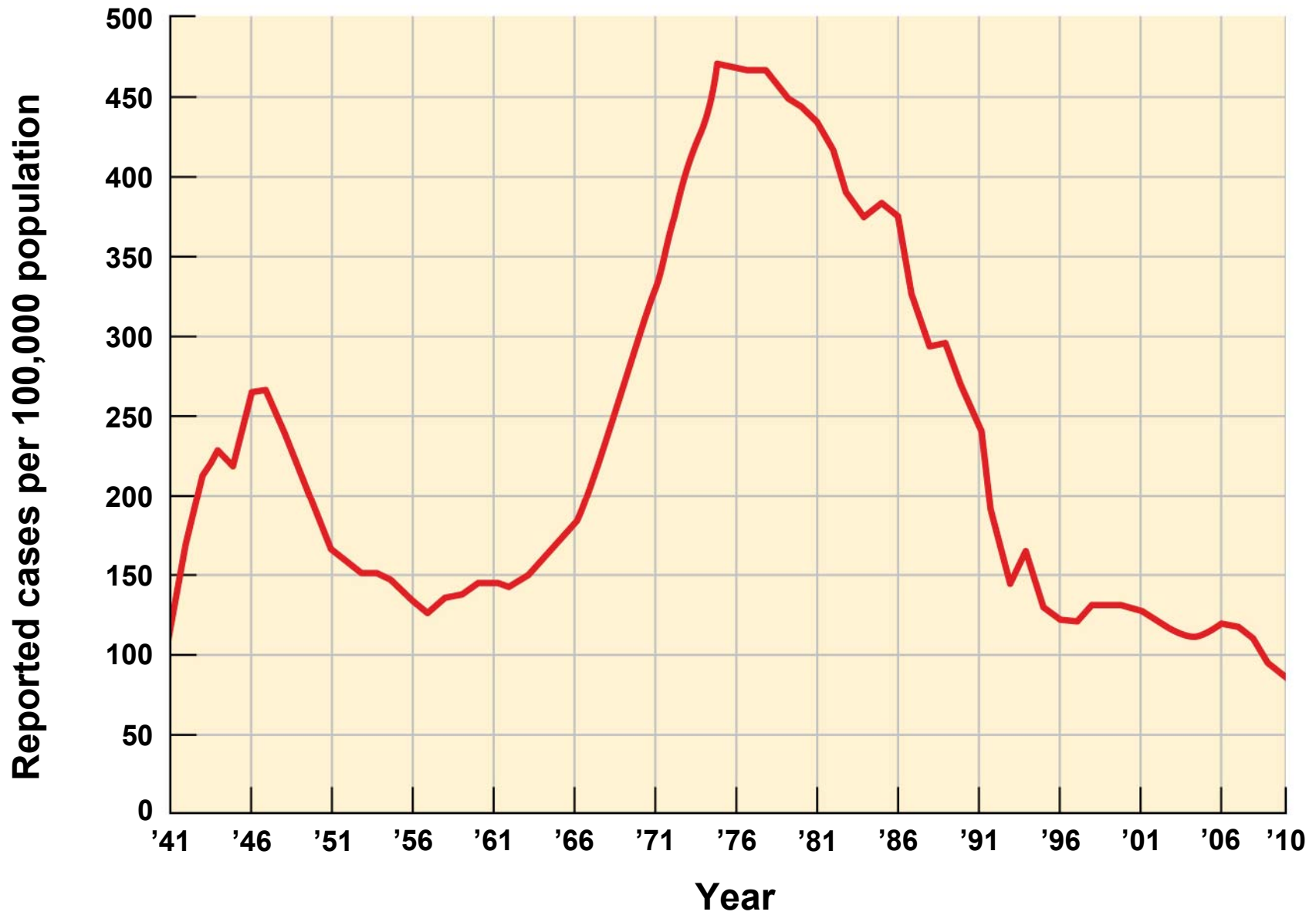
1  $\mu$ m



# Sexually Transmitted Infections (STIs)

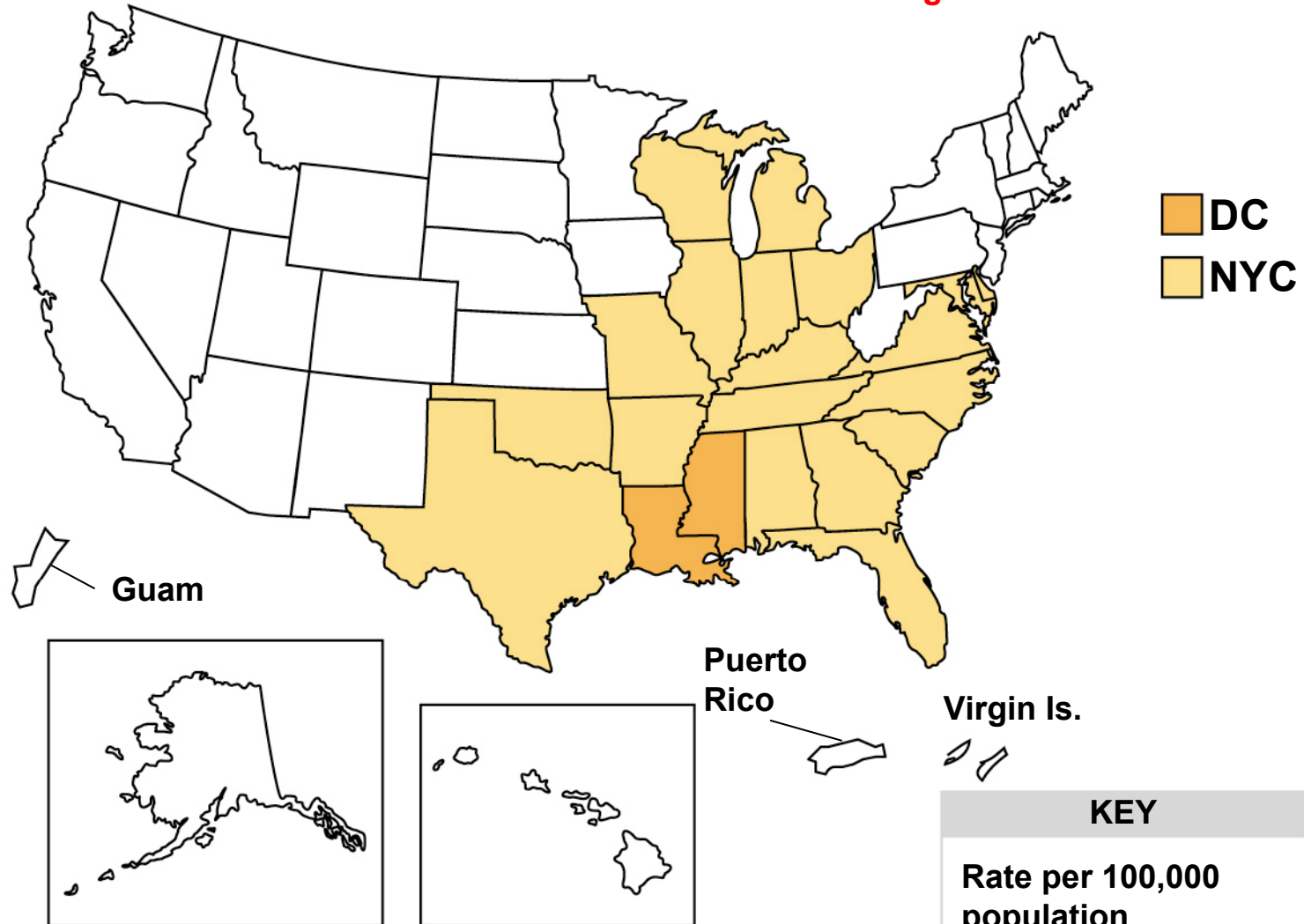
- Transitioning from using sexual transmitted disease to sexual transmitted infections
- Disease implies clear signs and symptoms but STI often do not have clear signs or symptoms
- STI prevented by condoms // female barrier contraceptives with spermicidal cream
- Bacterial infections are treated with antibiotics
- STI are becoming antibiotic resistant // strains of *Neisseria gonorrhoeae* reported untreatable in Asia

**The U.S. incidence and distribution of gonorrhea.**



**Incidence of gonorrhea in the United States, 1941–2010**

## The U.S. incidence and distribution of gonorrhea.

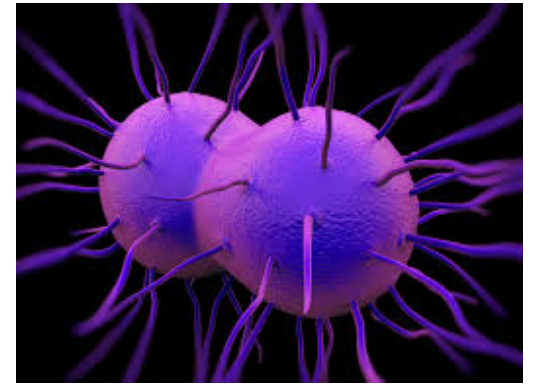


**Note:** The total rate of gonorrhea for the United States and outlying areas (Guam, Puerto Rico, and Virgin Islands) was 97.8 per 100,000 population.

**Geographical distribution of cases in 2009**

# Gonorrhea

- Caused by *Neisseria gonorrhoeae*
- Attaches to oral or urogenital mucosa by fimbriae
- Opa proteins prevent proliferation of CD4<sup>+</sup> T cells
- Also able to infect other tissues // Anal gonorrhea & pharyngeal gonorrhea
- Discharge disease →
- If left untreated, may result in
  - Endocarditis
  - Meningitis
  - Arthritis
  - Ophthalmia neonatorum



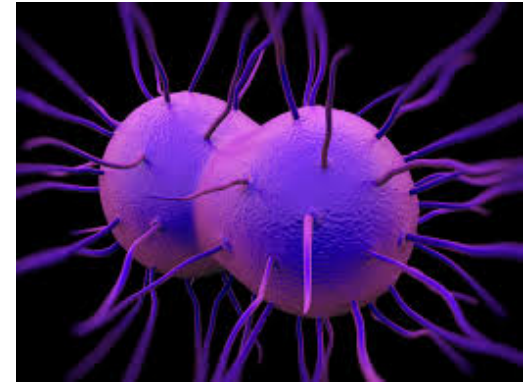
MALE



FEMALE

# Gonorrhea (*Neisseria gonorrhoeae*)

- Bacteria attach to spaces on sides of columnar epithelial cells
- Oral-pharyngeal areas, eyes, rectum, urethra, opening of the cervix, external genitals of prepubertal females
- Infection initiates an inflammatory response
- Migration of leukocytes into area with associated respiratory burst results in formation of puss
- Infection probability per first exposure:
  - *Males = 20-35%    ///    Females = 60-90%*



# Gonorrhea

- **Symptoms**

- Men: painful urination and **discharge of pus**
- Women: few symptoms but possible complications // e.g. Pelvic inflammatory disease (PID)

- **Treatment:**  
cephalosporins



Throat & Oral Gonorrhea

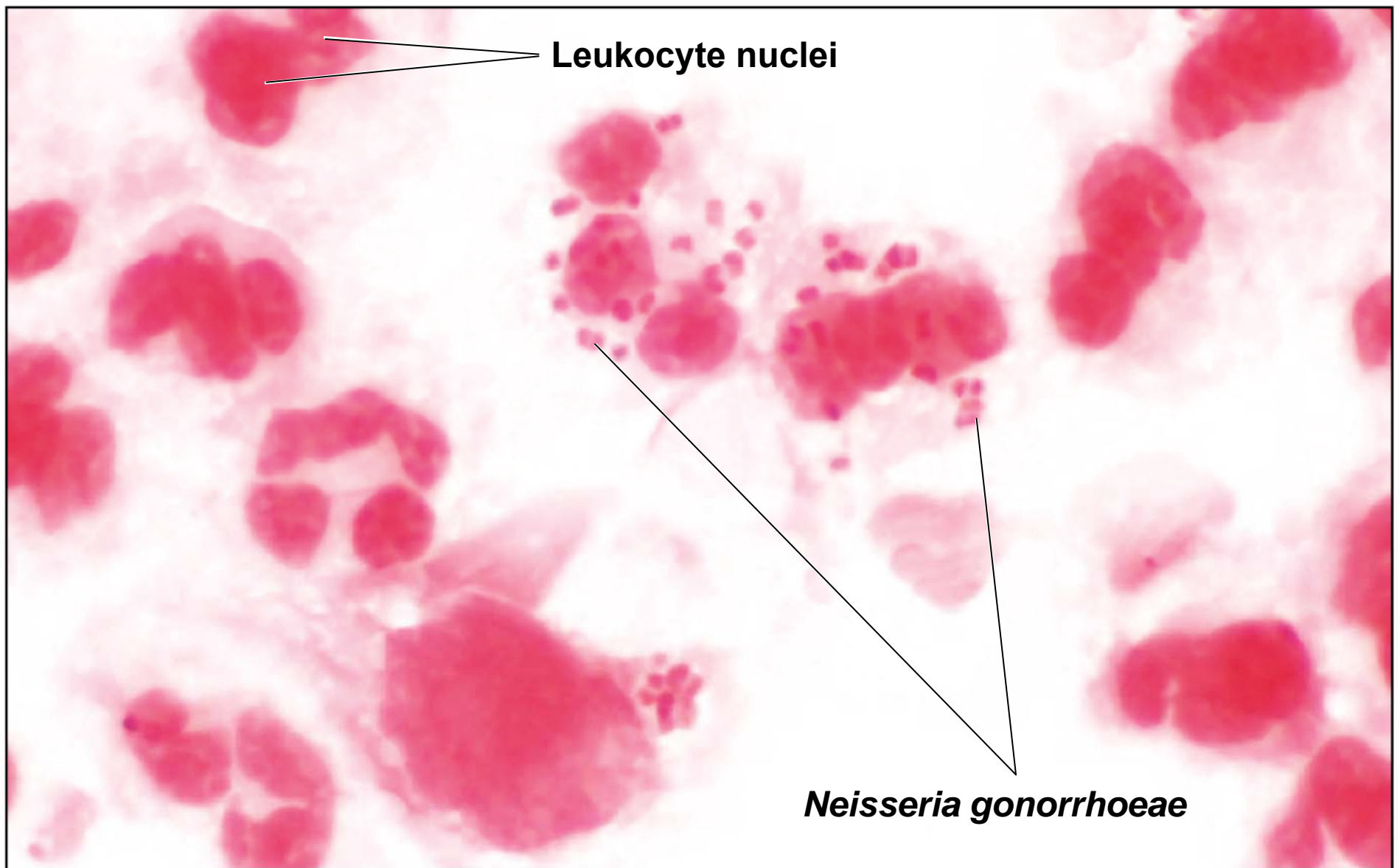


# Bad news of Gonorrhea

- Pregnant women with Gonorrhea can infect their baby during delivery.
- This can cause blindness, joint infection, or life threatening blood infection in the baby.



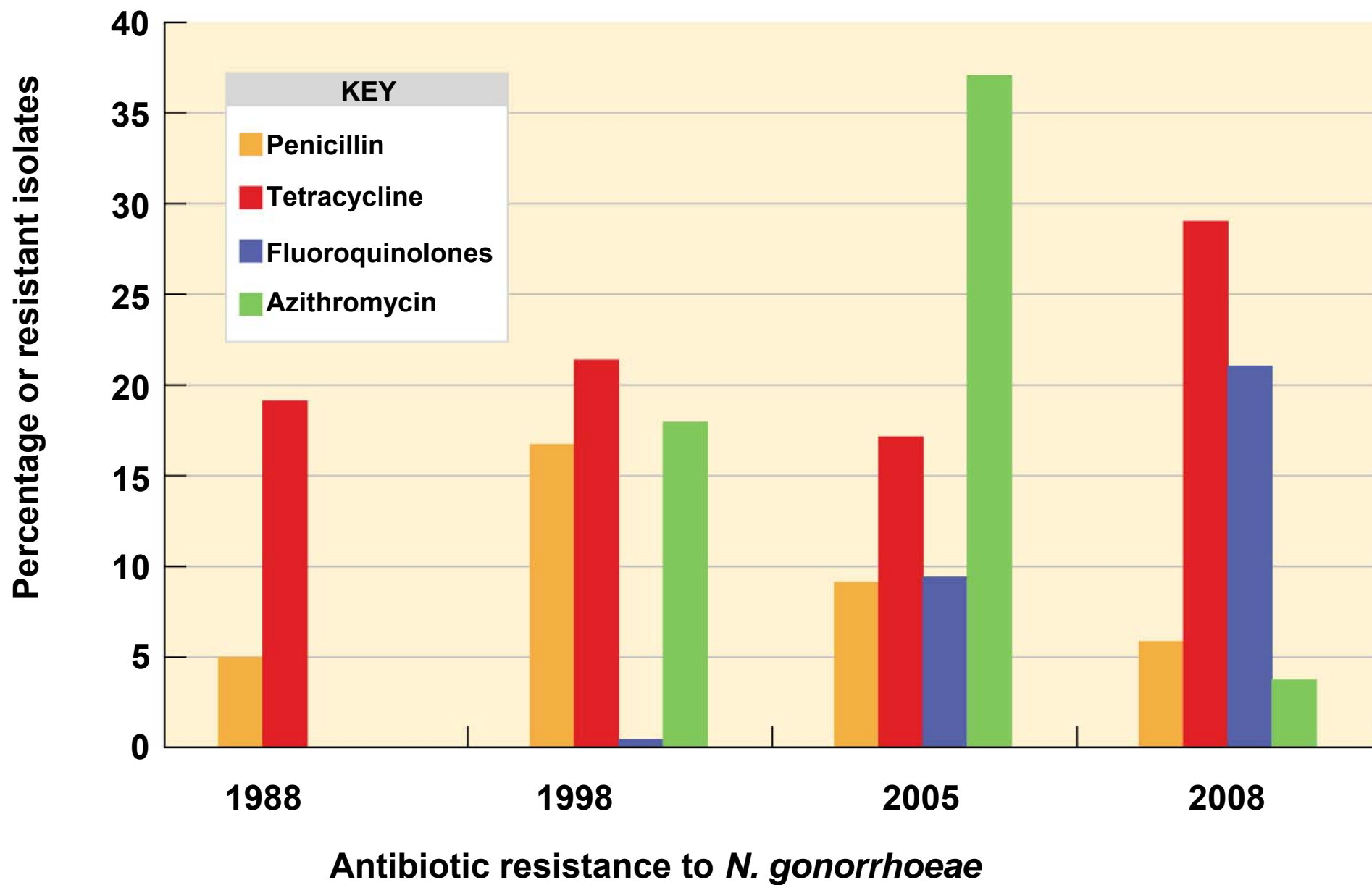




A smear of pus from a patient with gonorrhea.

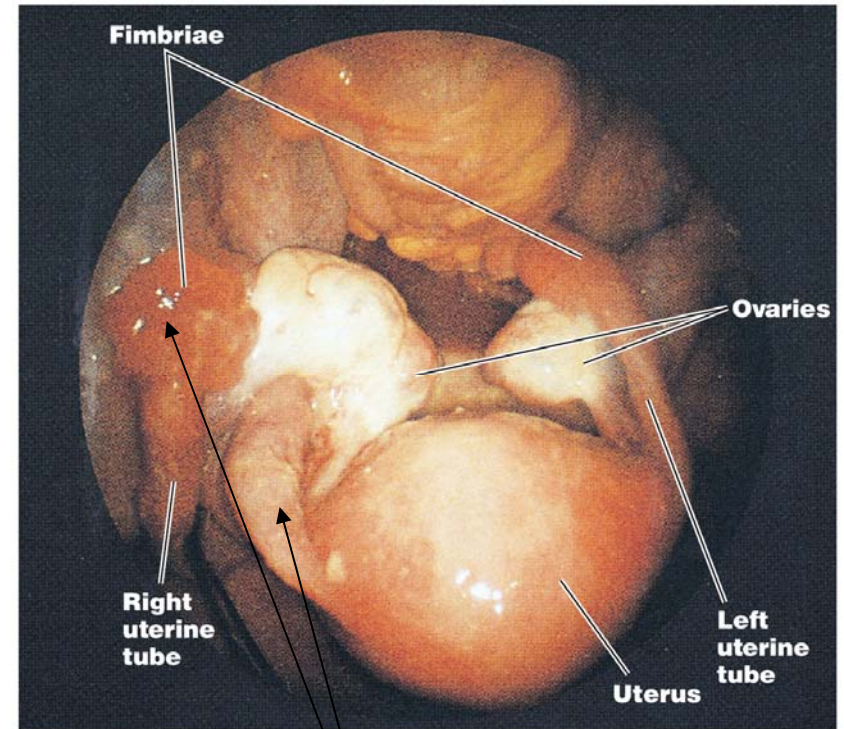
LM

5  $\mu$ m



# Nongonococcal Urethritis (NGU)

- **Nonspecific urethritis**
  - *Chlamydia trachomatis* (most likely)
  - *Mycoplasma hominis* // *Ureaplasma urealyticum*
- **Symptoms:** painful urination and watery discharge; in women, possible complications, such as PID
- **Treatment:** doxycycline, azithromycin



Inflamed right uterine tube  
and fimbriae

# Pelvic Inflammatory Disease (PID)

- Often polymicrobial // usually caused by:
  - *N. gonorrhoeae* & *C. trachomatis*
- Infection of female pelvic organs // uterus, cervix, uterine tubes, or ovaries
- Most serious form = Salpingitis (infection of uterine tubes)
- **Symptoms:** chronic abdominal pain // so painful that walking becomes difficult
- **Treatment:** doxycycline and cefoxitin

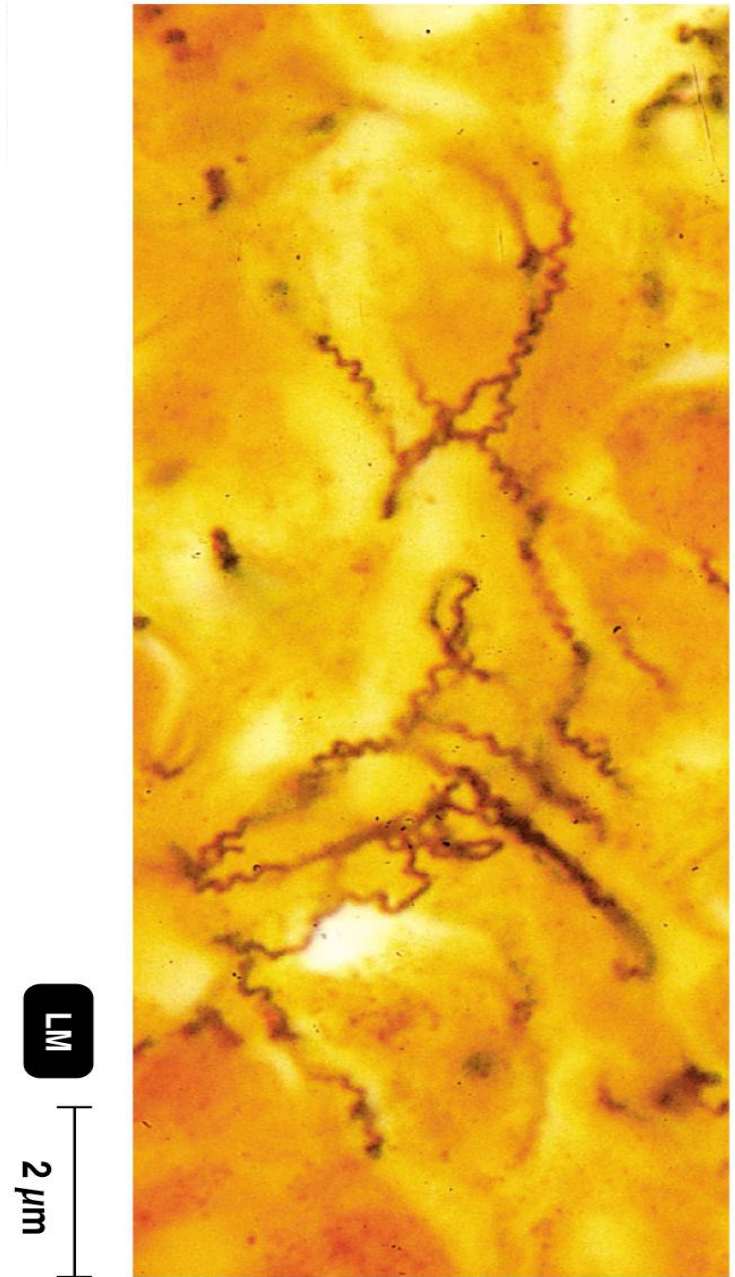
# Pelvic Inflammatory Disease (PID)

- Salpingitis (infection of uterine tubes)
- Resulting scarring of uterine tubes may block passage of ova // ectopic or tubal pregnancy – life threatening – possible rupture and hemorrhage
- Single infection cause infertility in 10-15%
- Three or more infections cause infertility in 50-75%
- Barrier contraceptives with spermicides best way to lower PID risks



# Syphilis

- Caused by *Treponema pallidum* // gram negative spirochete
- Invades mucosa or through skin breaks
- Causes tissue ulcerations
- New syphilis cases relatively stable but *N. gonorrhoeae* cases are increasing // imperfect immunity for syphilis but no immunity for gonorrhea



# Syphilis

- Primary stage: **chancre** at site of infection // average three weeks before it becomes apparent
- Chancre painless but oozes serum with high concentration of bacteria // highly infective
- For many women unaware because chancre most likely on cervix
- bacteria enters lymphatics from chancre then into blood to infect tissues throughout body



# Syphilis

- Secondary stage: skin and mucosal rashes
- Especially apparent on palms and soles
- Tissue damage now due to inflammatory responses (also true of tertiary stage)
- Non-sexual transmission is possible but unlikely from fomites // microbes do not survive long on environmental surfaces

# Syphilis

- Latent stage // symptoms of secondary stage subside after several weeks
- After 2 to 4 years disease no longer infectious except for transmission from mother to fetus
- Majority of cases do not progress to tertiary stage // this is true for untreated cases

# Syphilis

- Tertiary stage // 25% of untreated cases progress to the tertiary stage
- Many years after secondary and latent stages
- *T. pallidum* – outer layer of lipids protects microbe from cell destroying complement response
- However, in tertiary stage it is most likely a cell mediated response which attack surviving spirochetes
- Gummatous syphilis characterized by gummas (rubbery like masses ) formed in tissues // skin, mucous membranes, bones // 15 years later

# Syphilis

- Gummatous syphilis characterized by gummas (rubbery like masses ) formed in tissues // skin, mucous membranes, bones // 15 years later
- Cardiovascular syphilis – weakening of the aorta // post antibiotic era very unlikely
- Neurosyphilis – untreated syphilis affects central nervous system // personality changes and dementia, seizures, loss of coordination of voluntary movement, loss of speech-sight-hearing
- Tertiary stage not considered to be infectious
- Today unlikely to see tertiary syphilis

# Congenital Syphilis

- Most dangerous form of syphilis
- Transmitted across placenta to unborn fetus
- Cause damage to mental development and neurological serious consequences
- Mostly likely to happen when disease in latent stage
- Pregnancy during primary or tertiary stages likely to result in stillbirth

# Diagnosis of Syphilis

- Direct diagnosis // Staining with fluorescent-labeled monoclonal antibodies
- Indirect, rapid screening
- Confirming // tests for anti-treponemal antibodies
- Treatment // benzathine penicillin  
– long acting form // still effective

## Characteristic lesions associated with various stages of syphilis.



**(a)** Chancre of primary stage on a male in genital area



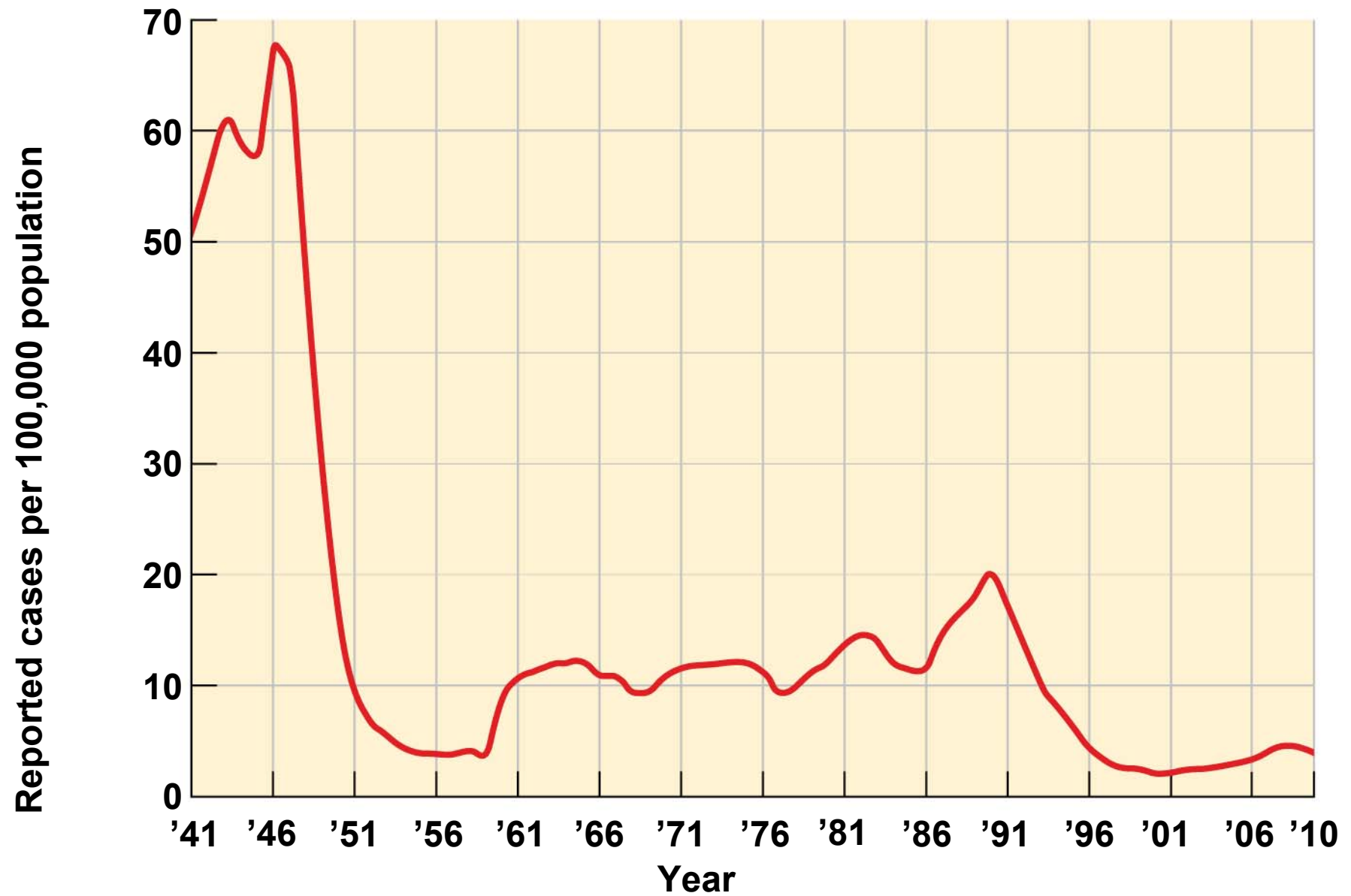
**(b)** Lesions of secondary syphilis rash on a forearm; any surface of the body may be afflicted with such lesions.



**(c)** Gummas of tertiary stage on the back of a forearm; gummas such as these are rarely seen today in the era of antibiotics.

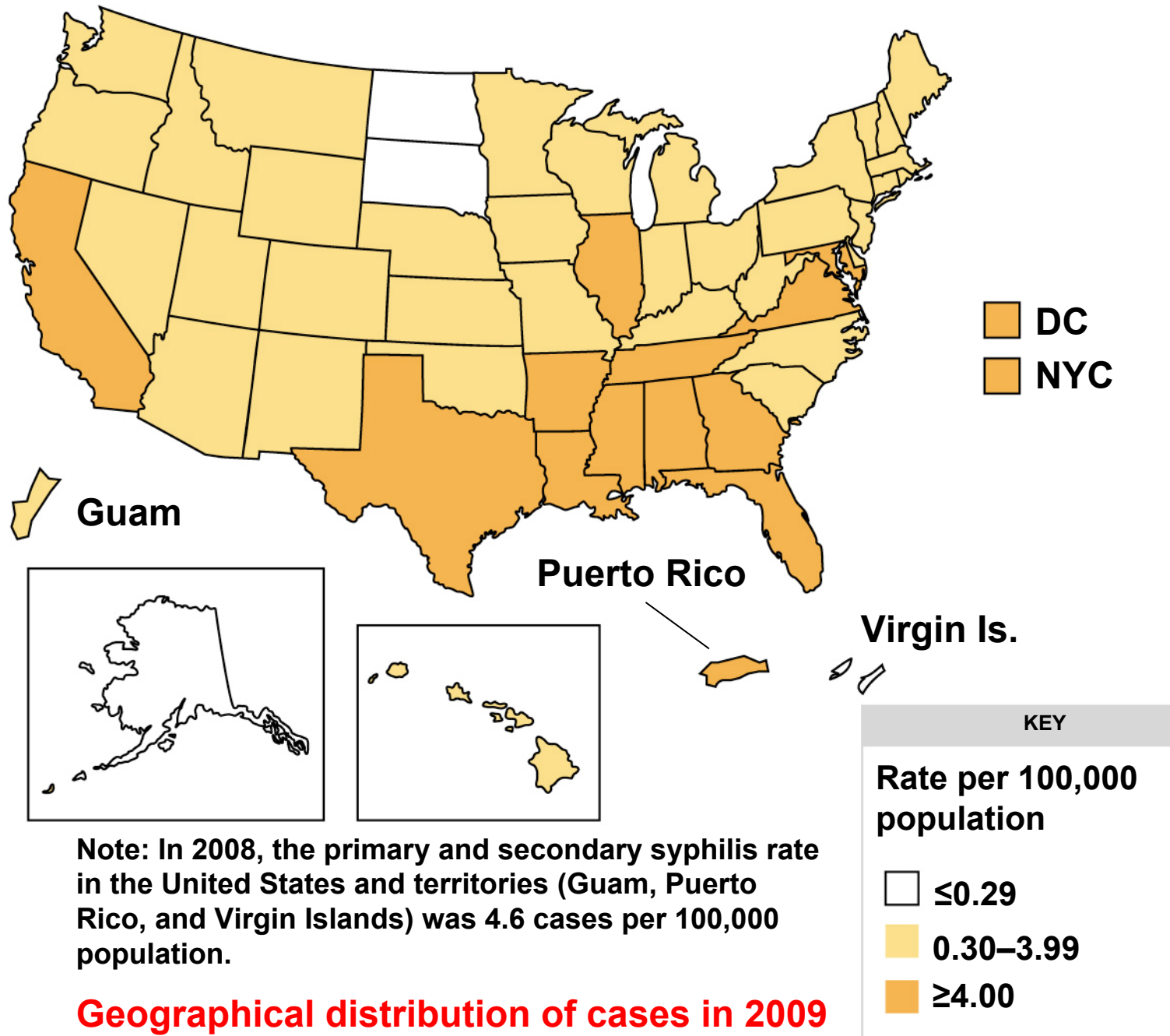


The U.S. incidence and distribution of primary and secondary syphilis.



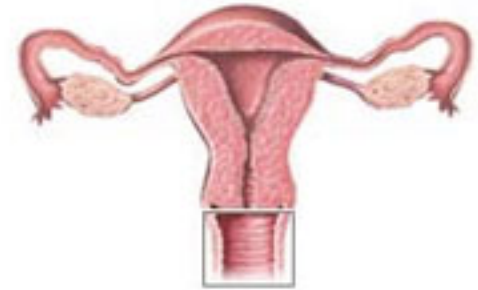
**(a)** Incidence of syphilis in the United States, 1941–2010

The U.S. incidence and distribution of primary and secondary syphilis.



# Bacterial Vaginosis

- Most likely causative agent = *Gardnerella vaginalis* = *bacteria*
- Other causes include *Candida albicans* = *fungu* // *Trichomonas vaginalis* = *protozoa*
- Associated with decrease in normal presence of *Lactobacillus* // characterized by  $\text{pH} > 4.5$
- Symptoms: copious fishy smell, gray-white, thin, frothy discharge // proof is microscopic presence of clue cells = discharged of vaginal epithelial cells covered with biofilm
- Treatment: metronidazole // kills anaerobes which allows colonization of normal *lacobacilli* microbes in vagina



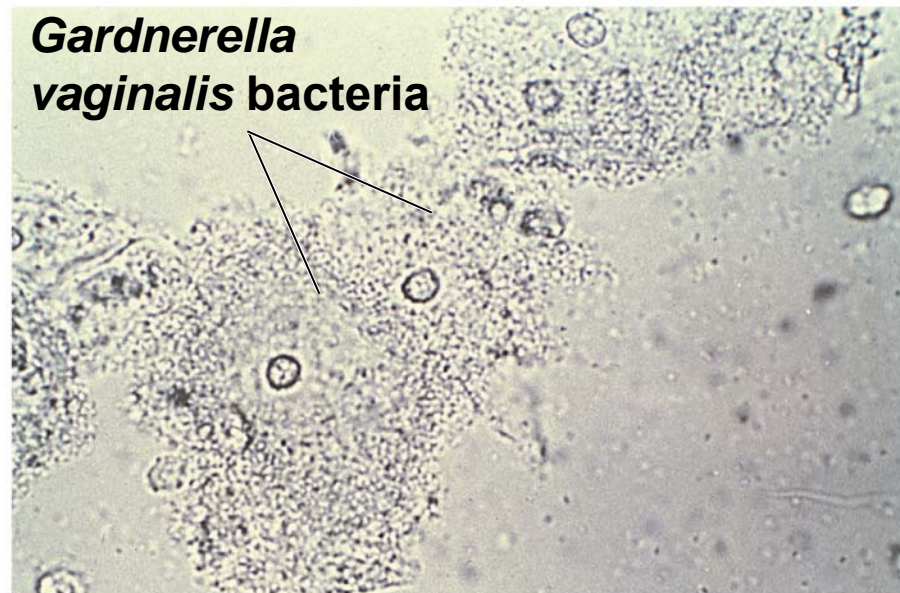
**Bacterial Vaginosis**

Clue cells.



**(a)** Normal vaginal epithelial cell

LM 12.5  $\mu\text{m}$



**(b)** Clue cell

LM 12  $\mu\text{m}$



# Genital Herpes

- Caused by herpes simplex virus 2 (human herpesvirus 2, or HSV-2)
- HSV-1 // associated with cold sores but also able to cause genital herpes
- 25% people above 30 yrs have virus // many unaware
- Incubation period one week
- Painful vesicles on genitals - burning sensation // vesicles disappear in couple weeks
- Vesicles contain infectious fluid

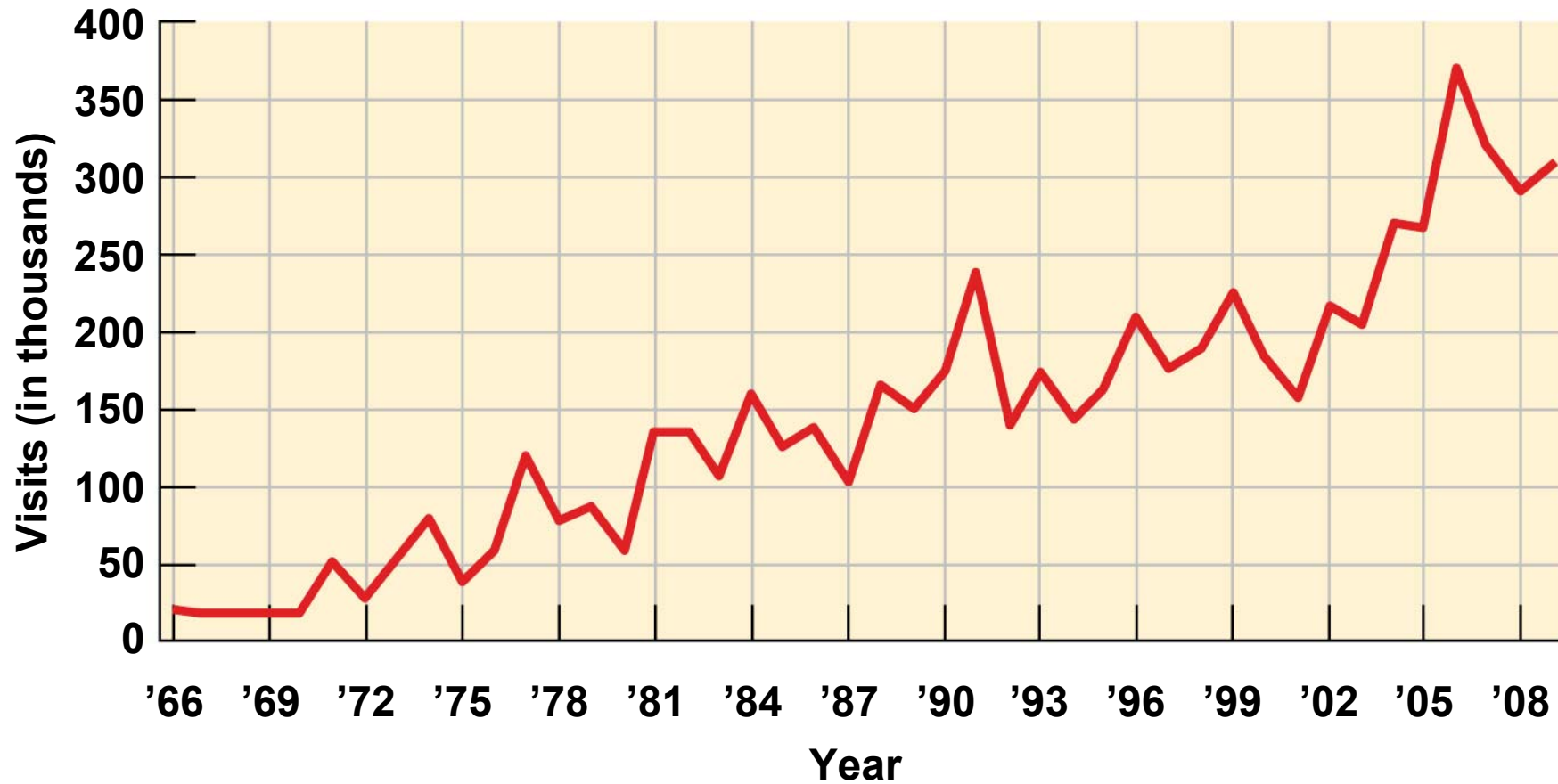


# Genital Herpes

- Possible recurrence // lifelong latent state in nerve cells
- 90% HSV-1 and 50% HSV-2 experience recurrence
- Medical adage: unlike love, herpes is forever
- Triggered by menstruation, emotional stress, illness, perhaps scratching affected area
- Neonatal herpes transmitted to fetus or newborns
- Suppression: (no cure) acyclovir



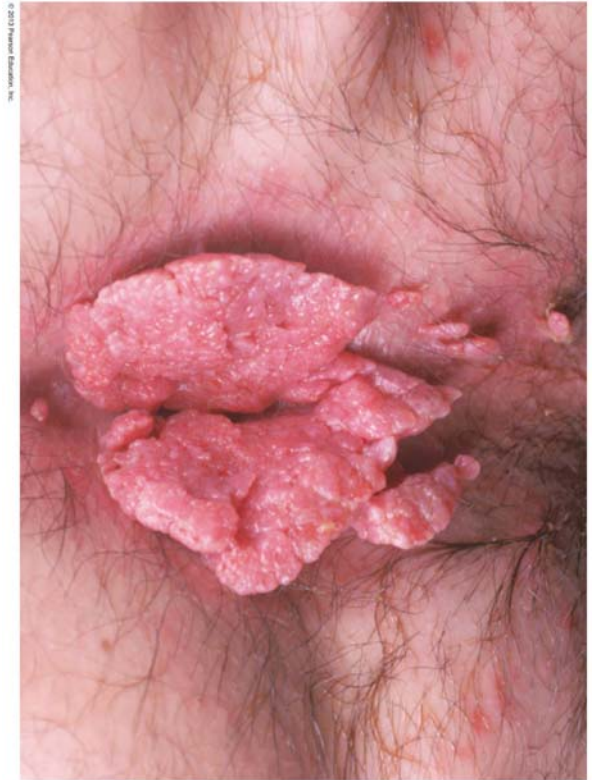
**Genital herpes: initial visits to physicians' offices,  
United States, 1966 to 2009.**





# Genital Warts

- Human papillomaviruses
- Warts in genital area // likely to grow on mucous membranes of respiratory tract, mouth, anus, and genitalia
- Visible warts most likely by serotype 6 and 11
- HPV serotype 16 and 18 most likely to cause cervical cancer and cancer of the penis
- Treatment but no cure // 90% cases clear spontaneously
- Treatment: podofilox; imiquimod
- Prevention: vaccination against HPV strains



# Candidiasis

- Causative agent: *Candida albicans*
- Grows on mucosa of mouth, intestinal tract, and genitourinary tract
- Males // causes NGU
- Females // Vulvovaginal candidiasis - yeasty discharge
- Associated with loss of lactobacilli and pH:  $> 4$  // following broad spectrum antibiotic
- Diagnosis: microscopic and culture
- Treatment: clotrimazole; fluconazole

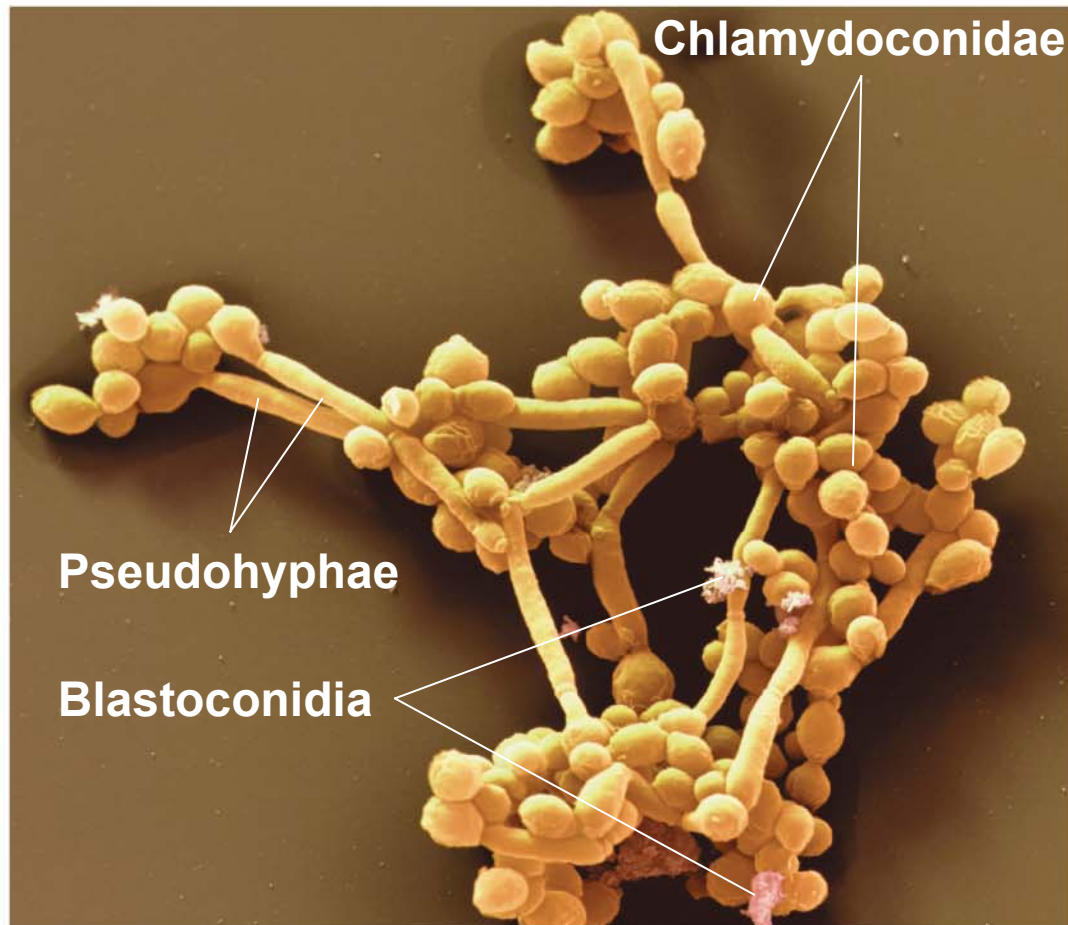


Oral Candidiasis



Vulvovaginal Candidiasis

# Candidiasis.



**(a)** *Candida albicans*

SEM

10  $\mu$ m



**(b)** Oral candidiasis, or thrush

# Trichomoniasis

- Causative agent: *Trichomonas vaginalis* // protozoan disease
- Found in semen or urine of male carriers
- Vaginal infection causes irritation and profuse foul, greenish yellow frothy discharge
- More common than gonorrhea
- Relatively benign // not reportable
- pH: 5–8
- Diagnosis: microscopic identification, DNA probe
- Treatment: metronidazole





# The TORCH Panel of Tests

- Number of different diseases in pregnant women can cause birth defects // screen for antibodies for these diseases
- **T**oxoplasmosis
- **O**ther (such as syphilis, hepatitis B, enterovirus, Epstein-Barr virus, varicella-zoster virus)
- **R**ubella
- **C**ytomegalovirus
- **H**erpes simplex virus