

# STD Update 2: Genital Ulcer Disease

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# Genital Ulcer Disease: The Big Three

Genital herpes

Syphilis

Chancroid

# Classic Signs of Genital Ulcer Disease

## Syphilis

- Induration
- Painless lesion
- Clean based lesion

# Classic Signs of Genital Ulcer Disease

## Chancroid

- Undermined lesion border
- Painful lesion
- Purulent exudate

# Classic Signs of Genital Ulcer Disease

## Genital Herpes

- Multiple ulcers
- Shallow lesions
- Painful lesions

# Utility of “Classic” GUD Signs for the Diagnosis of Genital Ulcer Disease

	<u>Sensitivity</u>	<u>Specificity</u>
Syphilis	31%	98%
Chancroid	34%	94%
Genital herpes	35%	94%

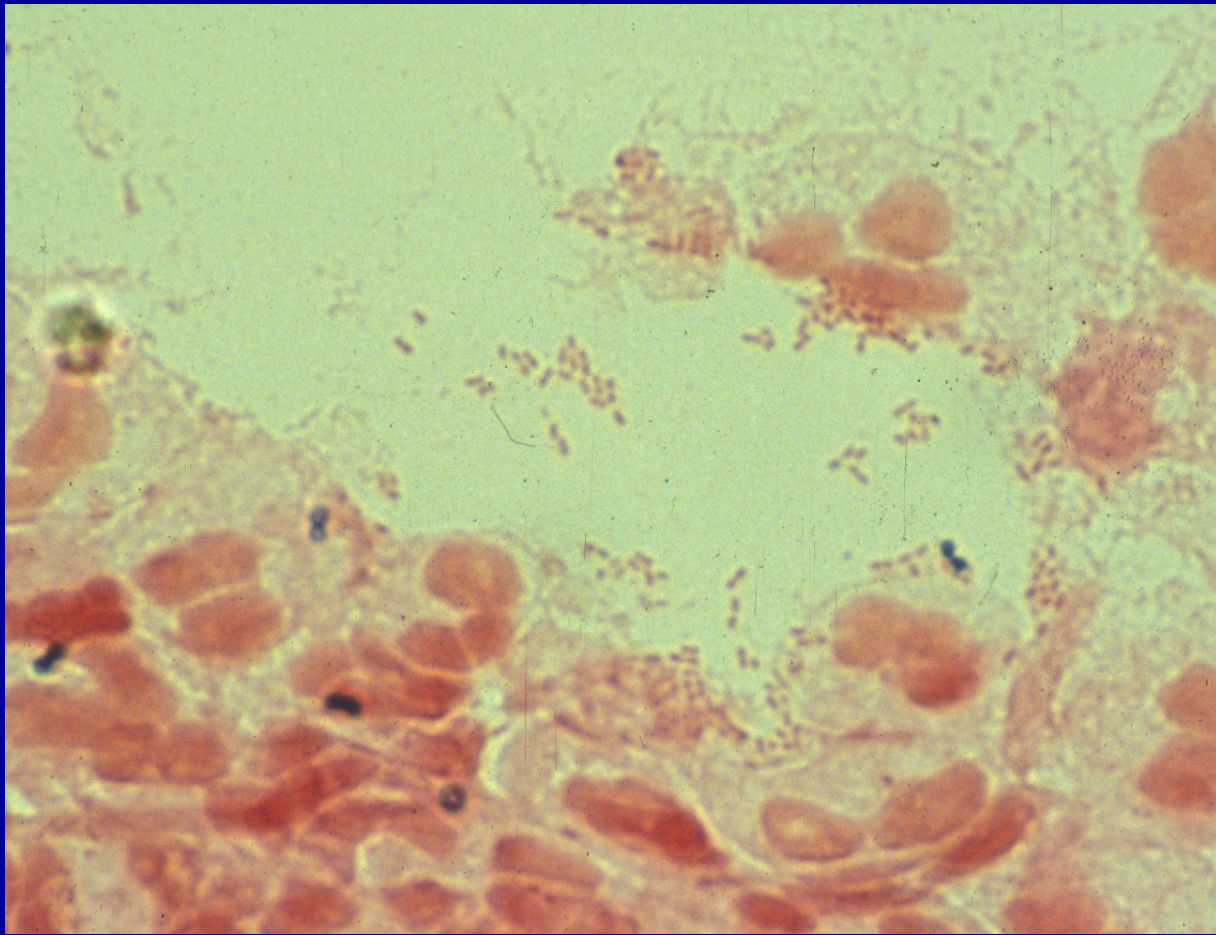
DiCarlo RP and Martin DH, Clin Infect Dis 1997;25:292-8.

# Diagnosis





Lesion Swab Gram Stain Showing  
*Haemophilus ducreyi*



# Syphilis Serologic Assays

## Reagin tests

- Venereal Disease Research Lab (VDRL)
- Rapid Plasma Reagin (RPR)
- Automated Reagin Test (ART)

## Treponemal tests

- Fluorescent Treponemal Antibody – Absorbed (FTA-ABS)
- Micro Hemagglutination Antibody – *T. pallidum* (MHA-TP)
- Automated *T. pallidum* Enzyme Immunoassay



The RPR in this patient is negative.  
Therefore, primary syphilis is ruled-out  
leaving genital herpes and chancroid as  
the likely diagnoses.

1. True
2. False

# Expected Results of Serologic Testing in Patients With Untreated Syphilis

## % Positive at Disease Stage

### Primary

Reagin test  
(e.g. RPR, VDRL)

70

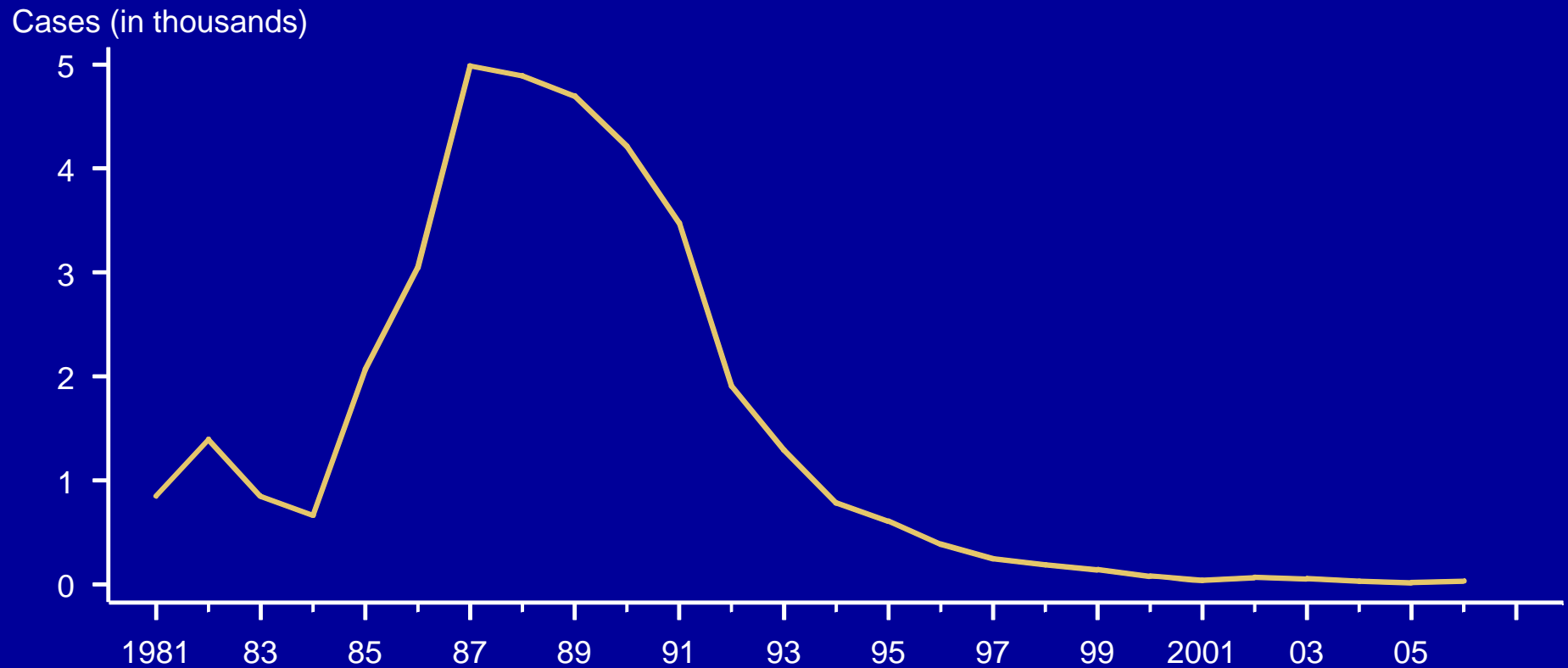
Treponemal test (e.g.  
MHA-TP, new EIA  
automated assays)

85

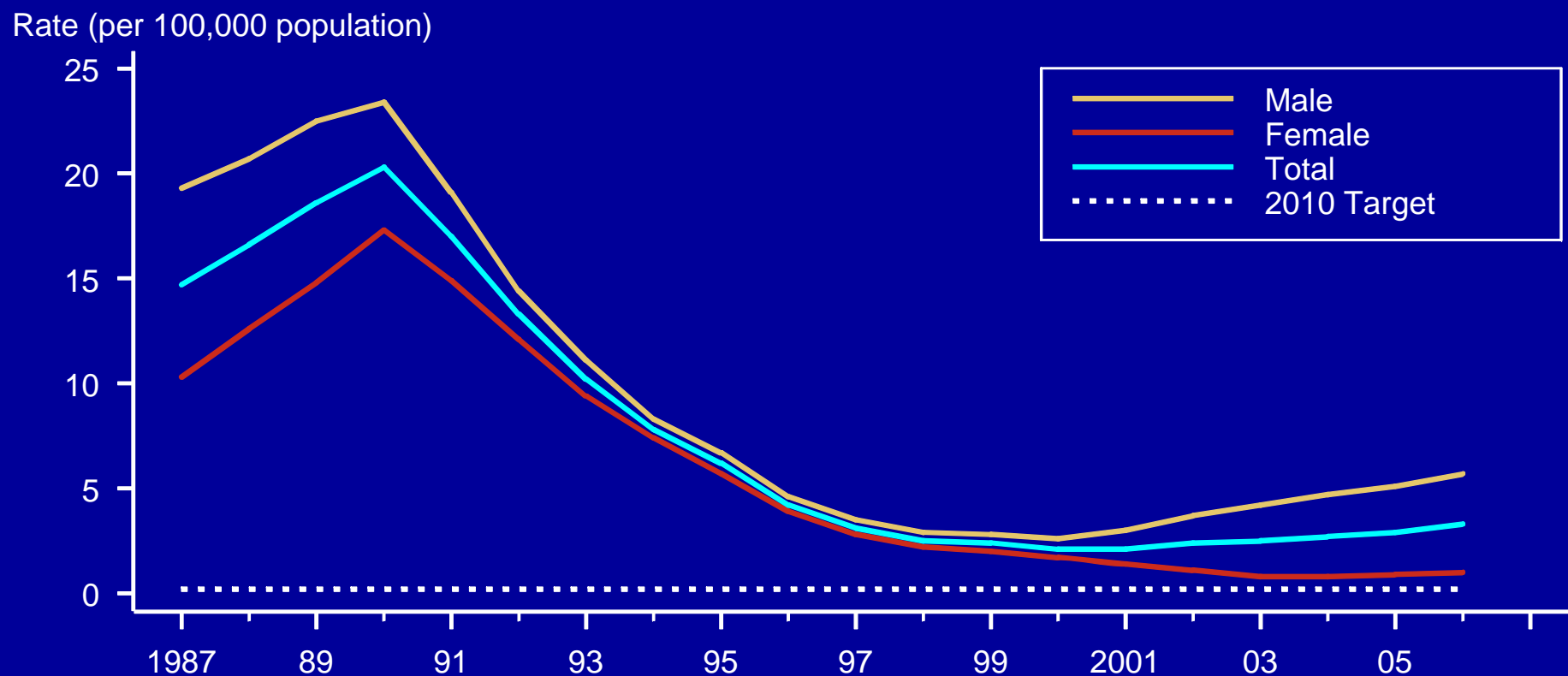
# Epidemiology



# Chancroid Cases Reported to CDC Through 2005

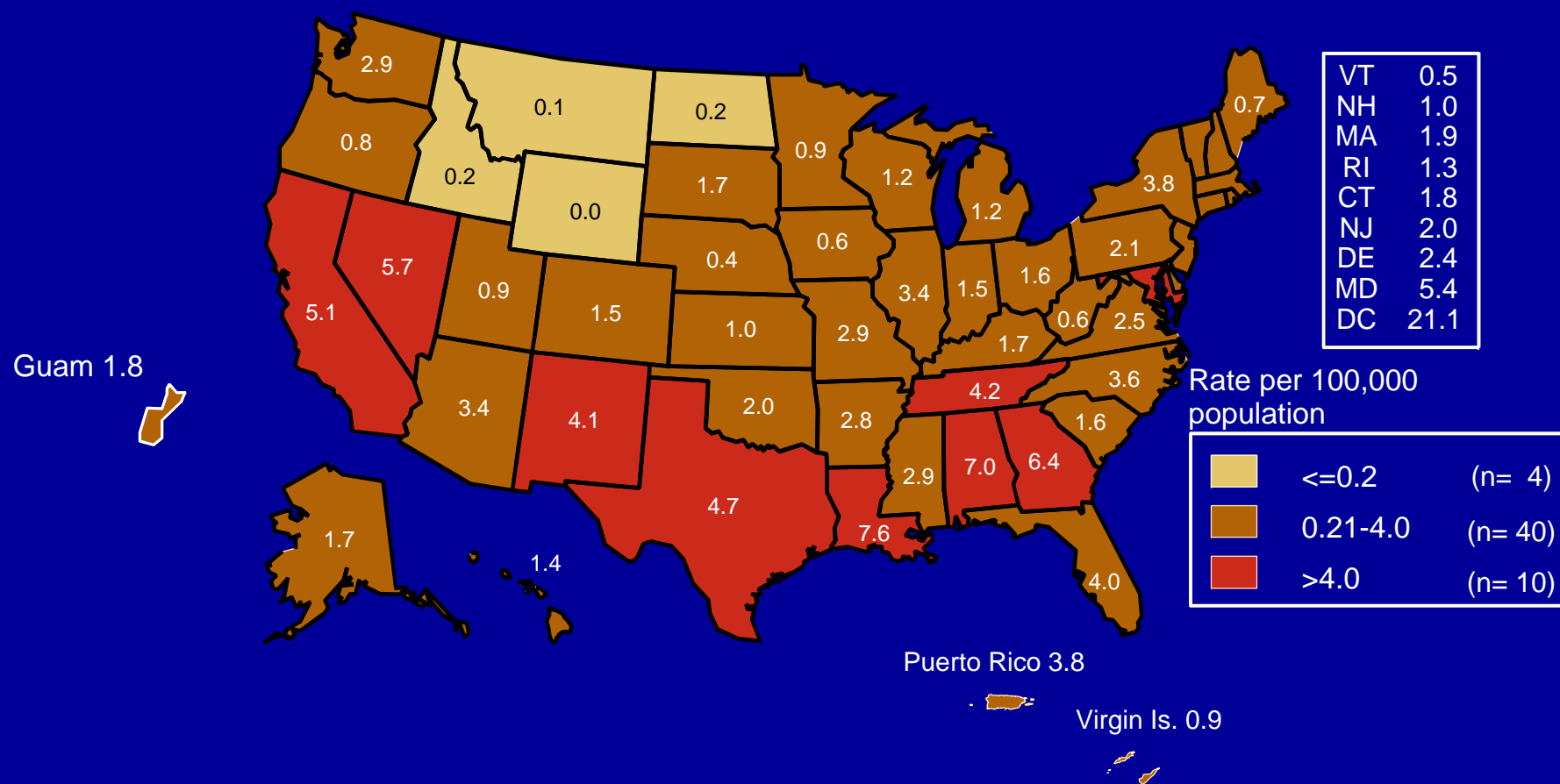


# U.S. Primary and Secondary Syphilis Rates: Total and by sex:

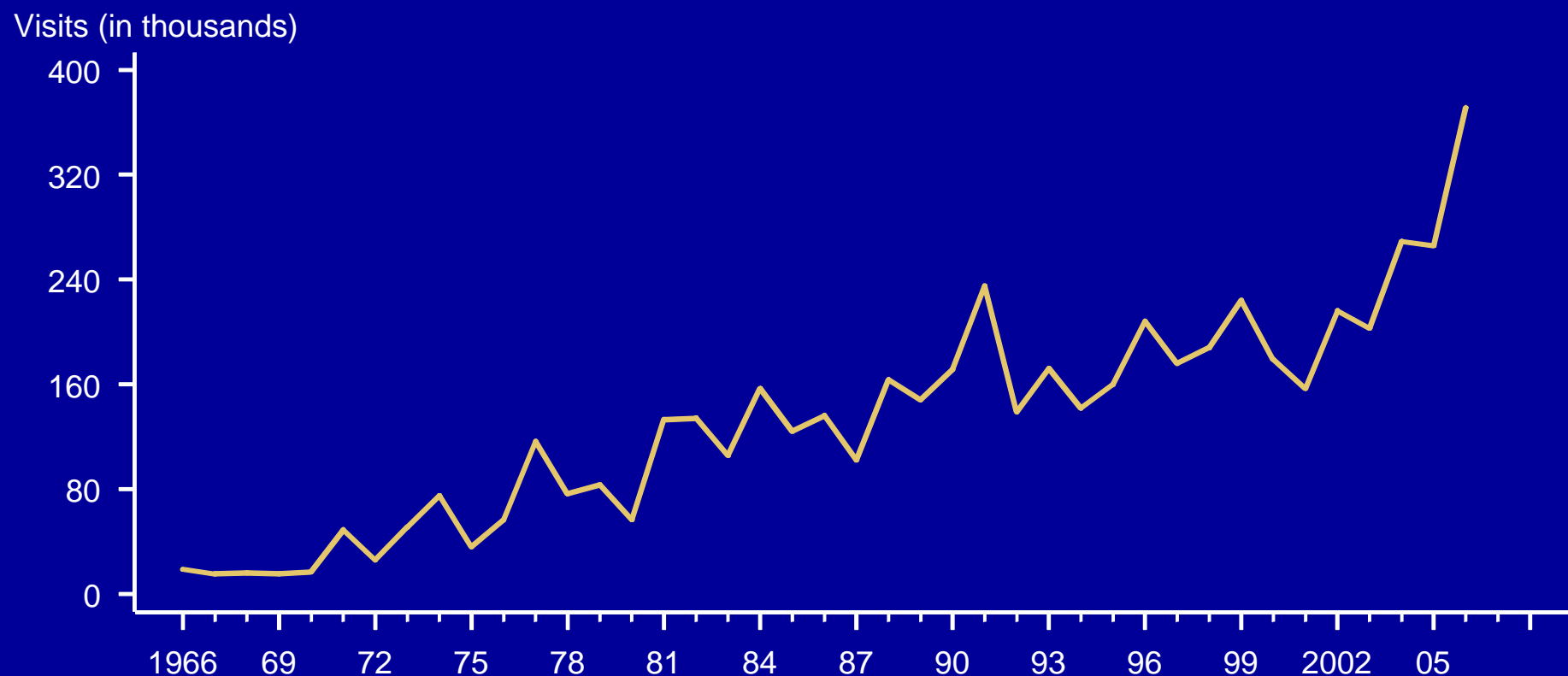




# Primary and Secondary Syphilis Rates by State



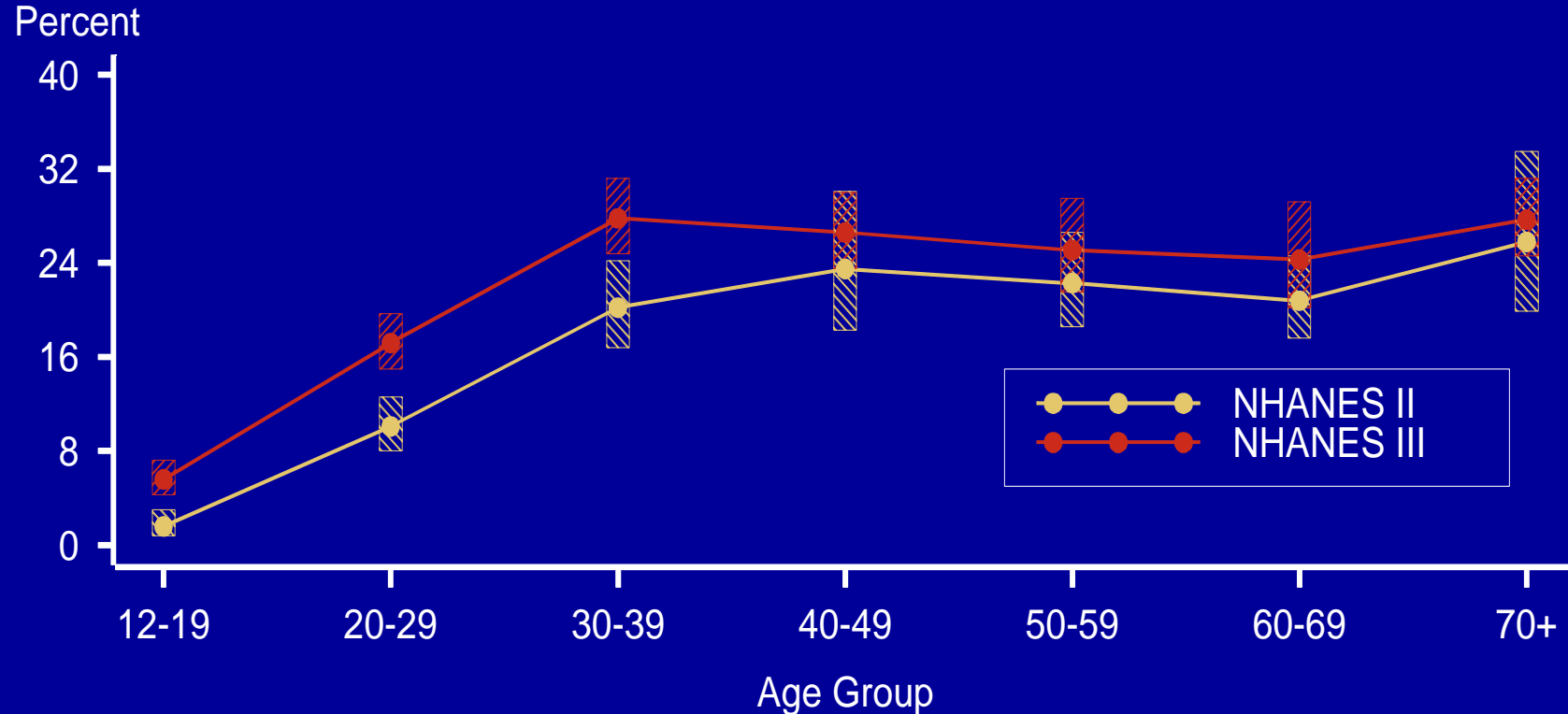
# Genital herpes — Initial visits to physicians' offices 1966–2006



Note: The relative standard error for genital herpes estimates range from 20% to 30%.

SOURCE: National Disease and Therapeutic Index (IMS Health)

# Genital HSV Type 2 — Seroprevalence in Two National Surveys 1976–1980 (NHANES II) and 1988–1994 (NHANES III)



# Empiric Management of Atypical GUD in 2008

- Do syphilis serology and HSV culture or PCR .
- If rapid reagin test is positive treat for primary syphilis. If negative in a relatively low risk patient then treat for HSV.
- Treat for primary syphilis in MSM and sex workers regardless of syphilis serology result.

# Secondary Syphilis

# Expected Results of Serologic Testing in Patients With Untreated Syphilis

	<u>% Positive at Disease Stage</u>	
	<u>Primary</u>	<u>Secondary</u>
Reagin test (e.g. RPR, VDRL)	70	100
Treponemal test (e.g. MHA-TP, new EIA automated assays)	85	100

A 40 year old male presents with dementia. On exam he has unequal pupils and the left pupil accommodates for distance but does not react to light. HIV antibody is negative as is the RPR. Neurosyphilis can be ruled-out in this case.

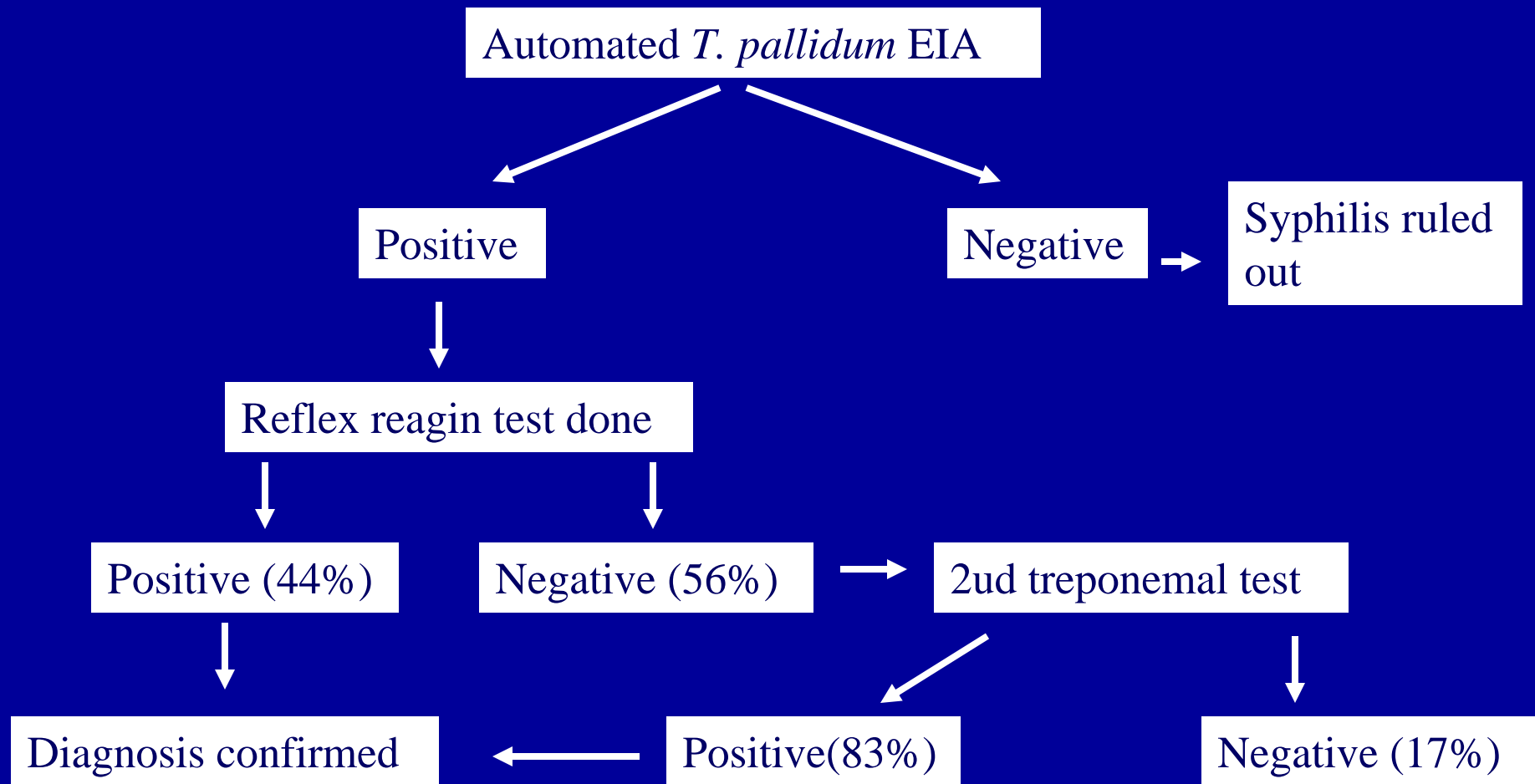
1. True
2. False

# Expected Results of Serologic Testing in Patients With Untreated Syphilis

	<u>% Positive at Disease Stage</u>		
	Primary	Secondary	Late
Reagin test (e.g. RPR, VDRL)	70	100	70
Treponemal test (e.g. MHA-TP, FTA-ABS)	85	100	98



# New Algorithm for Syphilis Serology Testing



## Approach to the patient with a positive treponemal test but a negative reagin test.

- Take a careful history.
- If there is no history of treatment repeat treponemal test using a different assay.
- If repeat test positive, do a second treponemal test
- If the second test is positive, treat for late latent syphilis.
- If the second test is negative don't treat or do a 3<sup>rd</sup> test??
- Counseling points – partners should be tested though infectivity of late latent disease is low.

# Serologic Testing for HSV-1 and HSV-2

- Until recently, herpes simplex virus serologic tests were nonspecific.
- The Biokit and SureVue HSV-2 point-of-care tests (Biokit USA) and the HerpeSelect tests (Focus Technology) are now commercially available and reliably distinguish between HSV-1 and -2.

# Potential Uses of Type Specific HSV Serologic Assays

- Patients with recurrent genital symptoms or atypical symptoms whose HSV cultures have been negative.
- Assessment of need for suppressive therapy for one member of an HSV discordant couple.
- Determination of infection status of exposed persons.
- Assessment of potential benefit of HSV suppressive therapy in HIV discordant couples??

# Relationship of HSV and HIV

- Strong association between HSV and HIV infection based on serology
- Prospective studies consistently show that HSV positive persons are 2-3 times more likely to acquire HIV infection
- HSV infection attracts CCR5 + CD4 cells and young dendritic cells, both targets for HIV infection, to mucosal surfaces.
- HSV suppressive treatment in dually infected patients reduces HIV viral loads in plasma and genital secretions.

# Randomized Trials of Acyclovir for the Prevention of HIV Infection in High Risk HSV Infected Women

- Watson-Jones D, et al. NEJM 2008; 358:1560
  - 821 high risk women took acyclovir 400 mg Bid or placebo for 1.5 years. Median adherence was 90%
  - HIV infection incidence rates were 4.4 and 4.1 per 100 person years in the two groups respectively.
- Celum C, et al. Lancet 2008; 371:2109
  - Study design nearly the same though MSM from Peru were included
  - Results identical – no effect in men and women.

# GUD Take Home Messages

- Don't forget the syphilis serologic test pearls.
- Automated *T. pallidum* EIA based syphilis testing has resulted in increased numbers of late latent syphilis cases.
- Empiric therapy of GUD depends on knowledge of current epidemiology of the causative agents.
- Type specific tests for HSV 2 are now available and should be useful in diagnosing discordantly infected couples.
- All that causes genital ulcers is not sexually transmitted!!

CDC STD Treatment Guidelines.  
MMWR 2006

<http://www.cdc.gov/std/treatment/>



# 2006 CDC STD Treatment Guidelines

## Early Syphilis

- Single dose **benzathine penicillin G** 2.4 million units IM
- Penicillin allergic
  - **Doxycycline** 100 mg orally 2 times a day for 14 days
  - **Tetracycline** 500 mg orally 4 times a day for 14 days

# 2006 CDC STD Treatment Guidelines

## Late Syphilis

- 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

# 2006 CDC STD Treatment Guidelines

## Late Syphilis

- Neurosyphilis
  - Recommended Regimen

18-24 million units **aqueous crystalline penicillin G** daily, administered as 3-4 million units IV every 4 hours, for 10-14 days
  - Alternative Regimen

2.4 million units **procaine penicillin** IM daily, plus **probenecid** 500 mg orally 4 times a day, both for 10-14 days

# 2006 CDC STD Treatment Guidelines

## Chancroid

**Azithromycin** 1 g orally in a single dose

**Ceftriaxone** 250 mg intramuscularly in a single dose

**Ciprofloxacin** 500 mg orally 2 times a day for 3 days

**Erythromycin base** 500 mg orally 4 times a day for 7 days

# 2006 CDC STD Treatment Guidelines

## Lymphogranuloma Venereum

- Recommended Regimen

**Doxycycline** 100 mg orally 2 times a day  
for 21 days

- Alternative Regimen

**Erythromycin base** 500 mg orally 4 times  
a day for 21 days

# 2006 CDC STD Treatment Guidelines

## First Episode Genital Herpes

**Acyclovir** 400 mg orally 3 times a day

**Acyclovir** 200 mg orally 5 times a day

**Famciclovir** 250 mg orally 3 times a day

**Valacyclovir** 1.0 gm orally 2 times a day

(all for 7-10 days)

# 2006 CDC STD Treatment Guidelines

## Recurrent Genital Herpes

**Acyclovir** 400 mg orally 3 times a day

**Acyclovir** 200 mg orally 5 times a day

**Acyclovir** 800 mg orally 2 times a day

**Famciclovir** 125 mg orally 2 times a day

**Valacyclovir** 500 mg orally 2 times a day

(all for 5 days)

# 2006 CDC STD Treatment Guidelines

## Suppression of Genital Herpes

**Acyclovir** 400 mg orally 2 times a day

**Famciclovir** 250 mg orally 2 times a day

**Valacyclovir** 500 mg orally once a day