Women's Health PRN Focus Session—Bringing Sexy Back...Updates on Women's Health Focusing on Contraception and Sexually Transmitted Infections
Activity No. 0217-0000-11-074-L01-P (Application-Based Activity)

Monday, October 17
1:30 p.m.–3:30 p.m.
Convention Center: Rooms 302 & 303

Moderator: Alicia B. Forinash, Pharm.D., BCPS
Associate Professor of Pharmacy Practice, St. Louis College of Pharmacy, St. Louis, Missouri

Agenda

1:30 p.m.	What's New in Contraception? *Sally Rafie, Pharm.D.* Performance Improvement & Medication Safety Pharmacist, University of California–San Diego Health System, San Diego, California
2:00 p.m.	Who Is Eligible to Use Hormonal Contraception? Balancing Risk and Benefit for Contraception in Patients with Medical Conditions *Sarah P. Shrader, Pharm.D., BCPS* Associate Professor, South Carolina College of Pharmacy/Family Medicine (MUSC) Campus, Charleston, South Carolina
2:40 p.m.	Updates in Sexually Transmitted Infections *Kelly R. Ragucci, Pharm.D., FCCP, BCPS* Professor, Clinical Pharmacy and Outcomes Sciences/Family Medicine, South Carolina College of Pharmacy, Medical University of South Carolina, Charleston, South Carolina
3:20 p.m.	Questions and Answers

Faculty Conflict of Interest Disclosures

Sally Rafie: no conflicts to disclose.
Kelly R. Ragucci: no conflicts to disclose.
Sarah P. Shrader: no conflicts to disclose.

Learning Objectives

1. Describe new methods of hormonal contraception and specifically discuss the new quadriphasic oral contraceptive.
2. Discuss new methods of hormonal emergency contraception and specifically describe the new selective progesterone modulator.
3. Determine the new contraceptive methods' place in therapy.
4. Discuss the updated medical eligibility criteria for contraceptive use from the World Health Organization.

5. Devise a contraceptive management plan for a woman with common disease states encountered by pharmacists.
6. Design a contraceptive management plan for a women focusing on revisions and new information from the Centers of Disease Control and Prevention guidelines for medical eligibility.
7. Discuss the "Sexually Transmitted Disease Surveillance Data" and the impact STD's have in this country.
8. Describe prevention strategies for reduction of sexually transmitted diseases, including a discussion of Gardasil and Cervarix for HPV prevention.
9. Identify the therapeutic uses of various medications for common sexually transmitted diseases, focusing on changes within the 2010 guidelines.

Self-Assessment Questions

Self-assessment questions are available online at *www.accp.com/am*

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Updates in Hormonal Contraception

Sally Rafie, Pharm.D.

October 17, 2011

Conflicts of Interest

- No conflicts of interest to disclose.

Outline

*This is a case-based session, so slides are not available prior to session.

- New emergency contraception (ulipristal)
- New combined oral contraceptive (quadriphasic)
- Other new products
- Revised missed pill instructions
- Future directions in contraception

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Who is Eligible to use Hormonal Contraception? Balancing the Risk and Benefit for Contraception in Patients with Medical Conditions.

Sarah Shrader, Pharm.D., BCPS, CDE

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No Conflicts of Interest to Disclose.

Objectives

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- Discuss the updated medical eligibility criteria for contraceptive use from the World Health Organization.
- Devise a contraceptive management plan for a woman with common disease states encountered by pharmacists.
- Design a contraceptive management plan for a woman focusing on revisions and new information from the Centers of Disease Control and Prevention guidelines for medical eligibility.

WHO Document

- Medical Eligibility Criteria for Contraceptive Use. 4th edition, 2009. Dept. of Reproductive Health, World Health Organization.
- International working group representing 23 countries
- Goal is to provide policy and decision-makers and the scientific community with a set of recommendations that can be used for developing/revising national guidelines

http://whqlibdoc.who.int/publications/2010/9789241563888_eng.pdf. Accessed July 29, 2011.

U.S. Medical Eligibility Criteria for Contraceptive Use

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- CDC adapted the WHO document for use in the U.S.

Changes	Additions
Post-partum/Breast-feeding	Bariatric Surgery
Venous Thromboembolism	Peripartum Cardiomyopathy
Valvular Heart Disease	Rheumatoid Arthritis
Uterine Fibroids	Endometrial Hyperplasia
Ovarian Cancer	Inflammatory Bowel Disease
	Solid Organ Transplantation

Centers for Disease Control and Prevention. U.S. Medical Eligibility Criteria for Contraceptive Use. MMWR Early Release 2010;59:1-86.

Categories of Medical Eligibility Criteria

1= there is no restriction for the use of the contraceptive method
2= the advantages of using the contraceptive method generally outweigh theoretical or proven risks
3= the theoretical or proven risks usually outweigh the advantages of using the contraceptive method
4= unacceptable health risk if the contraceptive method is used

Centers for Disease Control and Prevention. U.S. Medical Eligibility Criteria for Contraceptive Use. MMWR Early Release 2010;59:1-86.

Considerations for Contraception

- Safety
  - Initiation vs. continuation?
- Efficacy
- Availability
- Acceptability

Efficacy Rates	Typical Pregnancy Rate	Perfect Pregnancy Rate
Most Effective		
Sterilization (male & female)	0.15-0.5%	0.15-0.5%
Implant	0.05%	0.05%
Injectable	3%	0.3%
Intrauterine device (hormonal)	0.2%	0.2%
Effective		
Hormonal contraception pills (combined & POP), transdermal patch, vaginal ring	8%	0.3%

Centers for Disease Control and Prevention. U.S. Medical Eligibility Criteria for Contraceptive Use. MMWR Early Release 2010;59:1-86.

Case 1

- EF is a 30 yo HF who just delivered her first child 1 week ago. She is breast-feeding w/o difficulty. She would like to plan for a second pregnancy in a year.
- PMH non-significant, 64 kg, no medications

Case 1

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- What contraception do you recommend today?

A. Etonogestrel/EE 15 mcg (NuvaRing)
B. Levonorgestrel IUD (Mirena)
C. Norethindrone/EE 35 mcg (Ortho-Novum 1/35)
D. Norethindrone (Micronor)

Postpartum (Not Breastfeeding)

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Time Since Delivery	CHC	POP	DMPA	Implant	LNG-IUD
< 21 days	3	1	1	1	2
> 21 days	1	1	1	1	1 *(if > 4 weeks post-delivery)*

Theoretical concern that within 3 weeks of delivery thrombosis risk is elevated.

Centers for Disease Control and Prevention. U.S. Medical Eligibility Criteria for Contraceptive Use. MMWR Early Release 2010;59:1-86.

Postpartum (Breastfeeding)

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Time Since Delivery	CHC	POP	DMPA	Implant	LNG-IUD
< 1 month	3	2	2	2	2
> 1 month	2	1	1	1	1 *(if > 4 weeks post-delivery)*

Conflicting evidence on effects of estrogen on milk production; theoretical concern that effects are greatest early postpartum when milk flow becoming established.

Centers for Disease Control and Prevention. U.S. Medical Eligibility Criteria for Contraceptive Use. MMWR Early Release 2010;59:1-86.

CHCs While Breastfeeding

- Cochrane Review
  - Evidence is inadequate to make a recommendation about CHC use during lactation
- "Strongest" evidence
  - CHC vs. Progestin-only contraception
  - Significant decrease in milk volume but no decrease in milk composition or infant growth in CHC group
  - Many limitations to this study

Cochrane Syst Rev. 2003;(2):CD003988.

Case 2

- TS is a 32 yo WF (just became sexually active again with a new boyfriend)
- PMH: DVT age 21, PE age 31, menorrhagia (worsened since on anticoagulation)
- 97 kg
- Meds: warfarin (INR trends therapeutic, this was restarted a year ago), APAP prn

Case 2

- What contraception do you recommend today?

A. Depot Medroxyprogesterone (Depo Provera)

B. Drospirenone/EE 30 mcg (Yasmin)

C. Norelgestromin/EE 20 mcg (Ortho Evra)

D. Levonorgestrel IUD (Mirena)

Venous Thromboembolism

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	CHC	POP	DMPA	Implant	LNG-IUD
VTE History (no AC)					
High Risk	4	2	2	2	2
Low Risk	3	2	2	2	2
Acute VTE	4	2	2	2	2
VTE + on AC x 3 months					
High Risk	4	2	2	2	2
Low Risk	3	2	2	2	2

Centers for Disease Control and Prevention. U.S. Medical Eligibility Criteria for Contraceptive Use. MMWR Early Release 2010;59:1-86.

Drospirenone VTE Controversy

- Previous studies report mixed results
- Incidence Rates:
  - 30.8 per 100,000 woman years of use for Drospirenone
  - 12.5 per 100,000 woman years of use for Levonorgestrel

Overall	No. Cases	No. Controls	Adjusted Odds Ratio
LNG	65	368	1.0
DSP	121	313	2.4 (95% CI, 1.7 to 3.4)

BMJ 2011;340:d2151.

Case 3

- CB is a 29 yo AAF (has 2 kids ages 4 + 6 from previous relationship)
- PMH: gestational DM, diagnosed T2DM at age 27, dyslipidemia, no evidence of micro/macrovascular complications
- Wt 95 kg (BMI 32), TC 180, LDL 102, HDL 39, TG 125, HbA1c 8%, BP 118/75
- Meds: Simvastation 40 mg QHS, Metformin 1 g BID, Glipizide XL 10 mg QAM
- Getting married in 1 month and uncertain about future children

Case 3

- What contraception do you recommend today?

A. Levonorgestrel/EE 30 mcg (Levlen)

B. Levonorgestrel IUD (Mirena)

C. Depot Medroxyprogesterone (Depo Provera)

D. Norgestrel/EE 50 mcg (Ogestrel)

Chronic Medical Conditions

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	CHC	POP	DMPA	Implant	LNG-IUD
BMI $\geq$ 30 kg/m^2	2	1	1	1	1
Hyperlipidemia	2/ 3	2	2	2	2
DM	2	2	2	2	2
DM w/ Vascular Disease or 20+ yrs	3/ 4	2	3	2	2
HTN < 160/100	3	1	2	1	1
HTN $\geq$ 160/100	4	2	3	2	2

Centers for Disease Control and Prevention. U.S. Medical Eligibility Criteria for Contraceptive Use. MMWR Early Release 2010;59:1-86.

Obesity and CHCs

- VTE Risk
  - BMI > 30 adjusted OR 5.1 (95% CI,3.8-6.9)
- Efficacy
  - Mixed results
  - CHC patch use precaution in women > 90 kg
  - Cochrane Review concluded that current evidence on effectiveness by BMI is limited but these contraceptive methods are still among the most effective

Contraception 2002;65:187-96.

Cochrane Syst Rev. 2010;(7):CD008452.

Case 3-three years later…

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- CB is a 32 yo AAF (has 3 kids ages 9, 7, + 2 – she is done!)
- PMH: gestational DM, diagnosed T2DM at age 27, dyslipidemia, no evidence of micro/macrovascular complications, bariatric surgery (laparoscopic gastric band)
- Wt 84 kg (BMI 29), TC 160, LDL 85, HDL 39, TG 95, HbA1c 6.4%, BP 118/75
- Meds: Metformin 500 mg BID, Levonorgestrel/EE 30 mcg (Levlen)

Case 3- three years later…

- What contraception do you recommend today?

A. Drospirenone/EE 30 mcg (Yasmin)

B. Continue Levonorgestrel/EE 30 mcg (Levlen)

C. Norethindrone (Micronor)

D. Levonorgestrel IUD (Mirena)

Bariatric Surgery

	CHC	POP	DMPA	Implant	LNG-IUD
Restrictive-decreased storage capacity of stomach	1	1	1	1	1
Malabsorptive-decreased absorption of nutrients/calories by decreasing small intestine	3 1 P/R	3	1	1	1

Centers for Disease Control and Prevention. U.S. Medical Eligibility Criteria for Contraceptive Use. MMWR Early Release 2010;59:1-86.

Bariatric Surgery

- LIMITED data!!
  - 40 women s/p BPD, 2 OC users became pregnant
  - 215 women s/p gastric banding, 0 pregnancies in OC users
  - 2 pharmacokinetic studies with mixed results in women s/p jejunoileal bypass
    - Lower progestin levels
    - Progestin levels were not decreased

Contraception 2010;82:86-94.

Case 4

- DL is a 17 yo WF (sexually active- 1 partner)
- PMH: epilepsy diagnosed 1 month ago
- Ht 5’4’’, 65 kg, Labs and Vitals WNL
- Meds: Phenytoin 300 mg QHS, Topiramate 100 mg BID, Levonorgestrel/EE 20 mcg (Alesse) Qday

Case 4

- What contraception do you recommend today?

A. Continue Levonorgestrel/EE 20 mcg (Alesse)

B. Levonorgestrel IUD (Mirena)

C. Norgestimate/EE 35 mcg (Sprintec)

D. Depot Medroxyprogesterone (Depo Provera)

Drug Interactions

	CHC	POP	DMPA	Implant	LNG-IUD
NRTIs	1	1	1	1	2/ 3
NNRTIs	2	2	1	2	2/ 3
Ritonavir Boosted PI	3	3	1	2	2/ 3

Limited data available

Clinical significance of NNRTI interaction is questionable

Ritonavir-boosted PI interaction significantly decreases hormone levels of CHC/POP

When COC is chosen select one containing at least 30 mcg EE

Centers for Disease Control and Prevention. U.S. Medical Eligibility Criteria for Contraceptive Use. MMWR Early Release 2010;59:1-86.

Drug Interactions

	CHC	POP	DMPA	Implant	LNG-IUD
Inducers (Phenytoin, CBZ, Barbiturates, Primidone, Topiramate, O-CBZ)	3	3	1	2	1
Lamotrigine	3	1	1	1	1

Typically recommended to use a non-oral progestin-only contraceptive for most

DMPA has some limited evidence that it may reduce seizure activity

When COC is chosen select one containing at least 30 mcg EE

Neurology 1984;34:1255-58.

Centers for Disease Control and Prevention. U.S. Medical Eligibility Criteria for Contraceptive Use. MMWR Early Release 2010;59:1-86.

Lamotrigine and CHCs

- Oral contraceptives increase metabolism of lamotrigine and significantly decrease lamotrigine levels
- No clinically significant interaction found when valproic acid used with lamotrigine
- Mechanism of induction of glucoronidation pathways involved in metabolism of EE and lamotrigine

Epilepsia 2007;48:484-489.

Drug Interactions

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	CHC	POP	DMPA	Implant	LNG-IUD
Broad Spectrum ABX	1	1	1	1	1
Antifungals	1	1	1	1	1
Antiparasitics	1	1	1	1	1
Rifampin or Rifabutin	3	3	1	2	1

Centers for Disease Control and Prevention. U.S. Medical Eligibility Criteria for Contraceptive Use. MMWR Early Release 2010;59:1-86.

Antimicrobial Drug Interactions

- Broad Spectrum ABX
  - Theoretical decrease of enterohepatic circulation
  - Anecdotal and case reports
  - Small PK studies- some in animal models with questionable clinical significance
  - Retrospective analysis mostly in dermatology practices in women using long-term ABX concluded no association with OC failure
- Clinical practice most are still conservative and recommend back-up for at least 7 days after ABX course is finished

J Am Acad Dermatol. 1997;36:705-710.

Antimicrobial Drug Interactions

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- Griseofulvin
  - Theoretical induction of metabolism of contraceptive steroids
  - Weak CYP3A4 inducer
  - Evidence based on case-reports
- Clinical practice most are still conservative and recommend back-up for at least 7 days after the course is finished

J Am Acad Dermatol. 1990;22:124-125.

Antimicrobial Drug Interaction

- Rifampin and Rifabutin
  - Induce metabolism of contraceptive steroids
  - Strong inducer of CYP3A4
  - Well documented evidence via “stronger” PK studies, case reports, and retrospective analysis associated with OC failure
- Clinical Practice use back-up for at least 7 days after course is finished or switch to different method

Clin Pharmacol Ther. 1999;65:428-38.

Fertil Steril. 1988;49(5 suppl 2):31S-38S.

Antimicrobial Drug Interactions

- CHC Transdermal Patch
  - Limited data available
  - Follow same recommendations as combined OCs
- CHC Vaginal Ring
  - Limited data available
  - Follow same recommendations as combined OCs
  - PK study demonstrated increase in contraceptive steroid levels when miconazole vaginal cream/suppository administered

www.orthoevra.com Accessed August 1, 2011.

www.nuvaring.com Accessed August 1, 2011.

Bottom Line for Most…

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- Postpartum Breastfeeding= progestin-only
- Postpartum Non-breastfeeding= can use CHC 3 weeks after delivery
- VTE= progestin-only
- Bariatric Surgery Restrictive= CHC or progestin-only
- Bariatric Surgery Malabsorptive= non-oral CHC or progestin-only
- DM or HTN (not “severe”)= CHC or progestin-only
- DM or HTN (“severe”)= progestin-only
- Drug Interactions= non-oral progestin-only or back-up for at least 7 days after interacting drug discontinued

Summary

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- Selection of contraceptive methods in women with co-existing medical conditions is challenging and the list of considerations is LONG
- Consider risks versus benefits for individual patients
- Consult the CDC Medical Eligibility Criteria for Contraceptive Use for helpful guidelines in addition to your clinical judgment!

Sexually Transmitted Diseases

Kelly R. Ragucci, Pharm.D., FCCP, BCPS, CDE
Assistant Dean and Professor
South Carolina College of Pharmacy, MUSC Campus

October 17, 2011

Objectives

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- Discuss the “Sexually Transmitted Disease Surveillance Data” and the impact STD’s have in this country
- Describe prevention strategies for reduction of sexually transmitted diseases, including a discussion of Gardasil and Cervarix for HPV prevention
- Identify the therapeutic uses of various medications for common sexually transmitted diseases, focusing on changes within the 2010 guidelines

Question #1

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MM is a 19 year old college student who presents to the medical office complaining of vaginal discharge x 2 days. She denies fever, chills, abdominal pain. She is sexually active and recently started a relationship with a new partner. Physical exam reveals mucopurulent cervical exudates and endocervical bleeding induced by gentle swabbing. A diagnosis of gonorrhea and chlamydia is made. Urine pregnancy test is positive. Which one of the following represents the most appropriate treatment plan for this patient?

1) Begin doxycycline (vibramycin) 100mg BID x 7 days and ofloxacin 400mg x 1 dose
2) Administer 125mg ceftriaxone (rocephin) IM and give metronidazole 500mg BID x 7 days
3) Begin erythromycin ethylsuccinate 400mg QID x 14 days and amoxicillin 500mg TID x 7 days
4) Administer 250mg ceftriaxone (rocephin) IM and give azithromycin (zithromax) 1 g x 1 dose

Question #2

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The mother of a teenage girl asks you to tell her more about the vaccine Gardasil. Which of the following is an accurate statement?

1) Gardasil will eliminate the need for regular Pap tests in women aged 11-26
2) Gardasil protects against four types of human papillomavirus and is recommended in girls age 11-12
3) Gardasil is not FDA approved for males or recommended in females over the age of 21
4) Gardasil protects against the two most common types of human papillomavirus and has cross-protection against other oncogenic types

Questions #3 and #4

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HK is a 26 year old female who complains of vaginal discharge and is subsequently diagnosed with bacterial vaginosis during a prenatal pelvic examination. She is in her 3rd trimester. Which one of the following represents the best treatment plan for this woman?

1) Metronidazole (Flagyl) 2 g as a single dose
2) No therapy is recommended
3) Metronidazole (Flagyl) 500mg BID x 7 days
4) Clindamycin (Cleocin) 2% cream intravaginally QHS x 7 days

How should HK's male partner be treated?

1) Metronidazole 500mg BID x 7 days
2) Tinidazole 2 g as a single dose
3) Clindamycin 300mg BID x 7 days
4) Treatment is not warranted

Question #5

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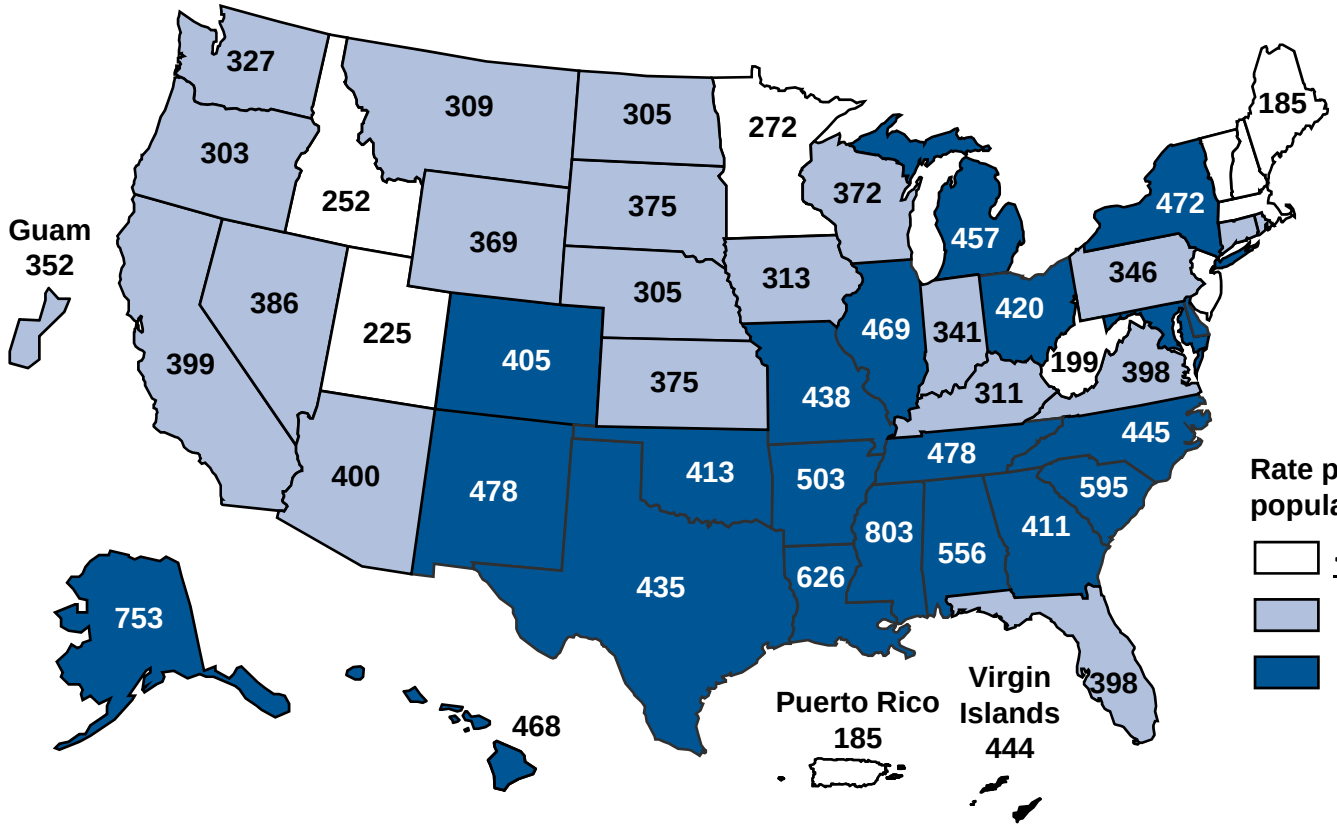
YO returns to your clinic 10 months after her initial herpes infection. She is becoming troubled by all of the recurrences she is having (seven to date). She does not currently have lesions. Which one of the following would be the most appropriate recommendation?

1) Valacyclovir 500mg BID x 5 days
2) Acyclovir 400mg TID x 10 days
3) Famciclovir 1g BID
4) Valacyclovir 500mg QD

Chlamydia—Rates by State, United States and Outlying Areas, 2009



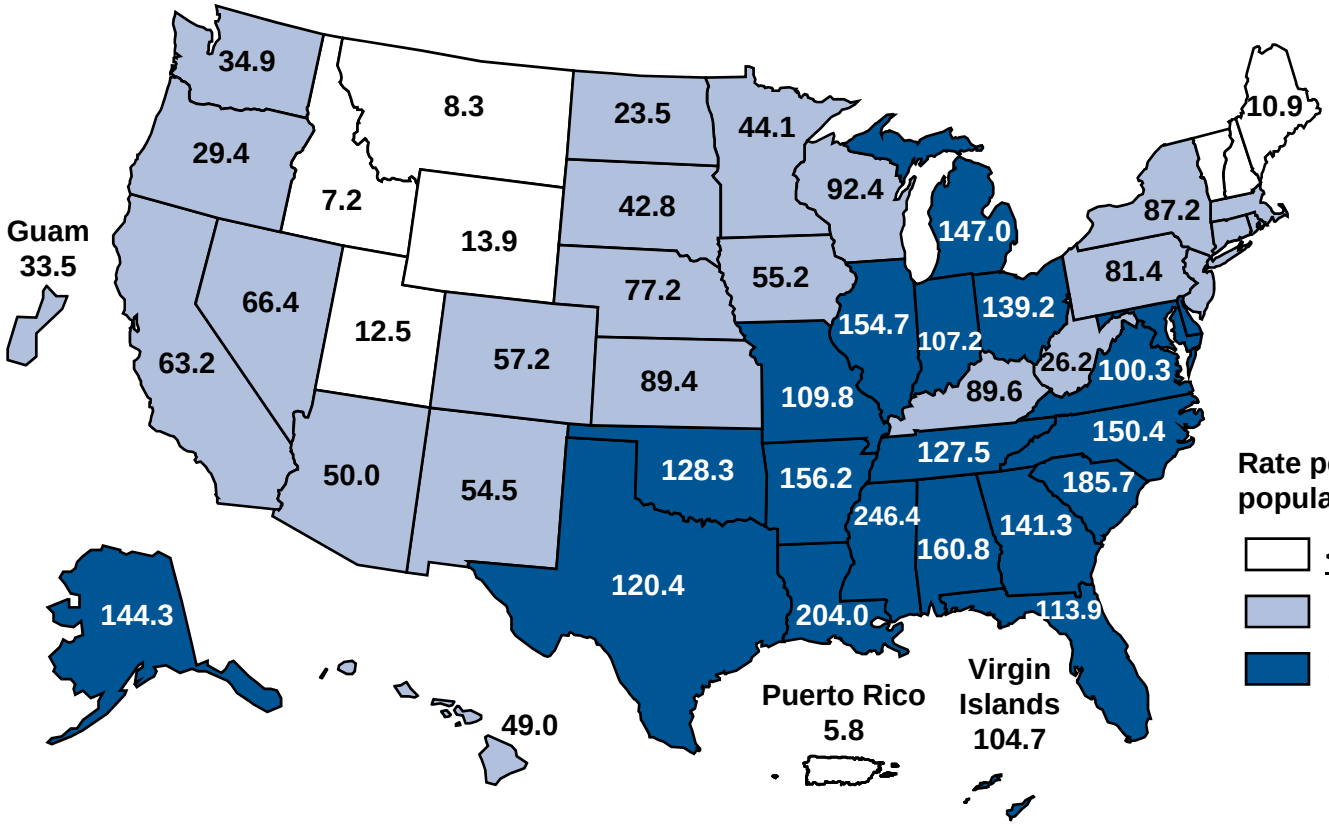
VT	191
NH	160
MA	297
RI	344
CT	346
NJ	276
DE	540
MD	422
DC	1,107

Rate per 100,000 population

- ≤300.0 (n = 10)
- 300.1–400.0 (n = 21)
- >400.0 (n = 23)

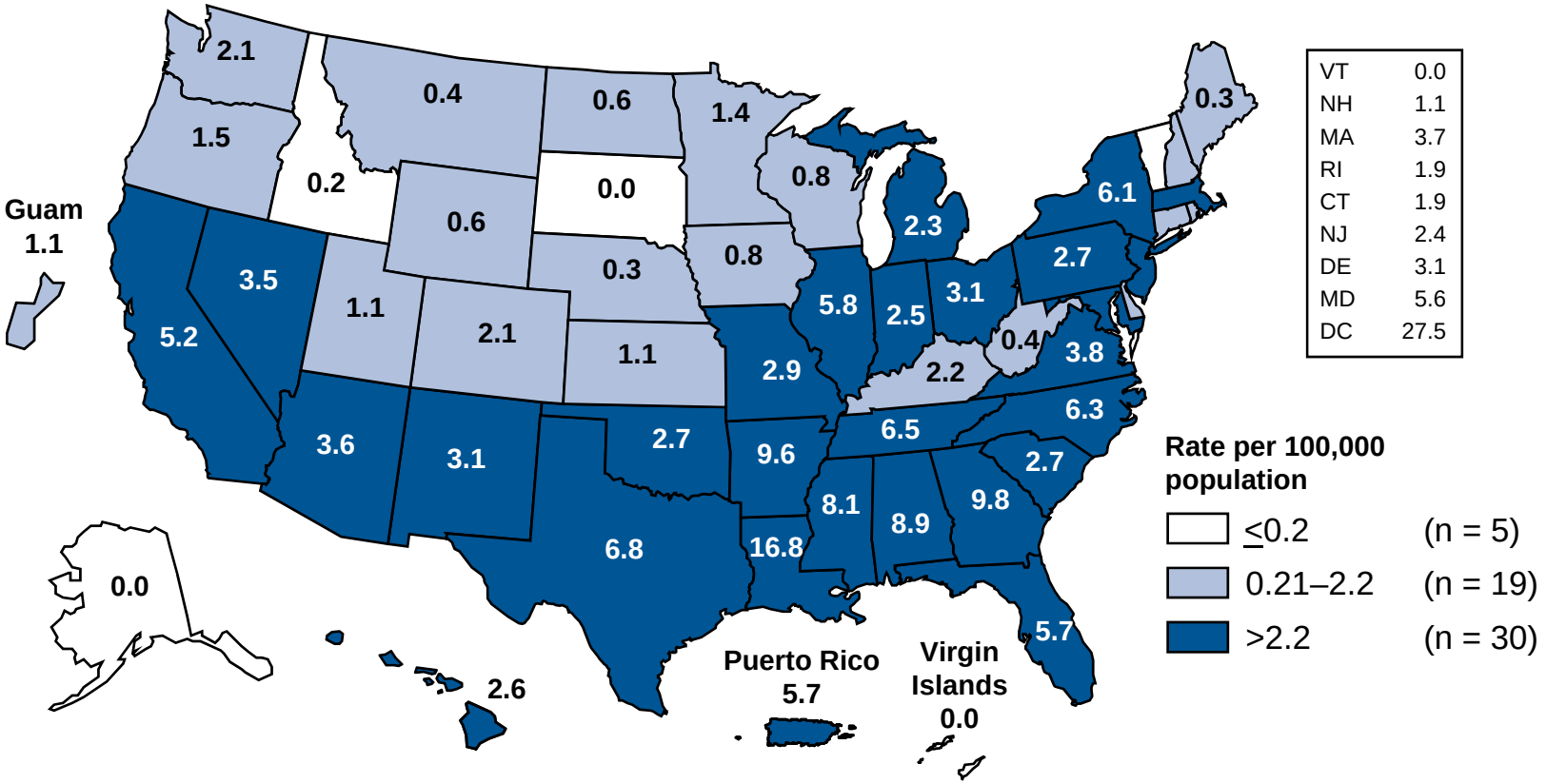
NOTE: The total rate of chlamydia for the United States and outlying areas (Guam, Puerto Rico, and Virgin Islands) was 406.3 per 100,000 population.

Gonorrhea—Rates by State, United States and Outlying Areas, 2009



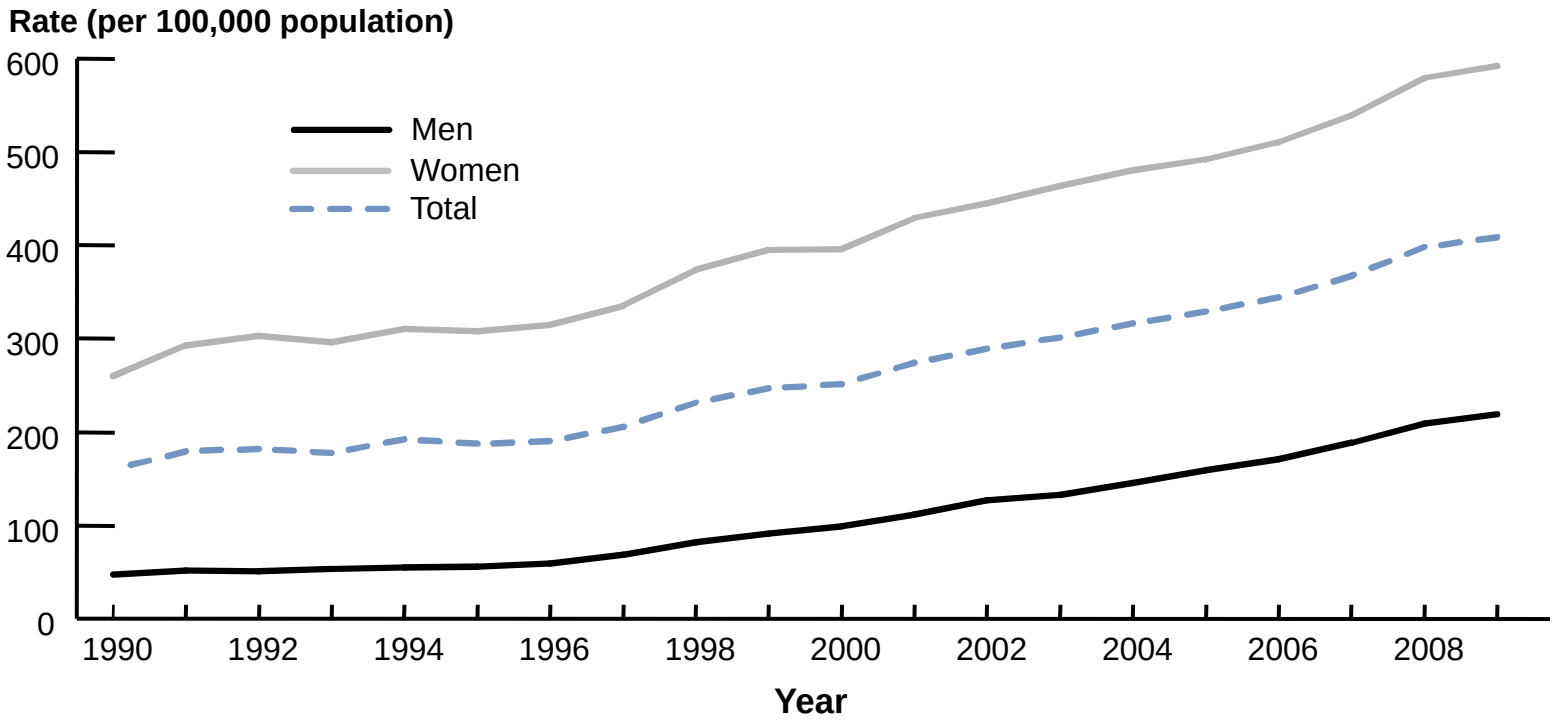
NOTE: The total rate of gonorrhea for the United States and outlying areas (Guam, Puerto Rico, and Virgin Islands) was 97.8 per 100,000 population.

Primary and Secondary Syphilis—Rates by State, United States and Outlying Areas, 2009



NOTE: The total rate of primary and secondary syphilis for the United States and outlying areas (Guam, Puerto Rico, and Virgin Islands) was 4.6 per 100,000 population.

Chlamydia—Rates by Sex, United States, 1990–2009



NOTE: As of January 2000, all 50 states and the District of Columbia had regulations that required chlamydia cases to be reported.

Chlamydia

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- Characteristics
  - Causative organism is *Chlamydia trachomatis*
  - Most commonly reported STD in U.S.
    - Highest prevalence in persons aged <25 years
  - Several serious sequelae can result in women
    - PID, ectopic pregnancy, infertility
- Annual Screening
  - Sexually active women </= 25 years old
  - Sexually active women > 25 years old with new or multiple sex partners

MMWR 2010;59(RR-12):1-109.

Chlamydia

- Recommended Regimens
  - Azithromycin 1g in single dose OR
  - Doxycycline 100mg BID x 7 days
- Alternative Regimens
  - Erythromycin base 500mg QID x 7 days OR
  - Erythromycin ethylsuccinate 800mg QID x 7 days OR
  - Ofloxacin 300mg BID x 7 days OR
  - Levofloxacin 500mg QD x 7 days
- Abstain from sexual intercourse for at least 7 days after single-dose regimen or after completion of multiple-dose regimen (all sexual partners within past 60 days should be evaluated and treated)
  - *CDC supports giving patients extra antibiotics for partner – if partner won't be seen*

MMWR 2010;59(RR-12):1-109.

Chlamydia

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- Recommended Regimens in Pregnancy
  - Azithromycin 1 g single dose OR
  - Amoxicillin 500mg TID x 7 days
- Alternative Regimen in Pregnancy
  - Erythromycin base 500mg QID x 7 days OR
  - Erythromycin base 250mg QID x 14 days OR
  - Erythromycin ethylsuccinate 800mg QID x 7 days OR
  - Erythromycin ethylsuccinate 400mg QID x 14 days

MMWR 2010;59(RR-12):1-109.

Chlamydia

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- Follow-up
  - Recommended treatment regimens are highly effective
  - In general, repeat testing 3 months after treatment is recommended for all infected men and women
    - Positive post-treatment cultures usually represent non-adherence, failure to treat sexual partners or lab error

MMWR 2010;59(RR-12):1-109.

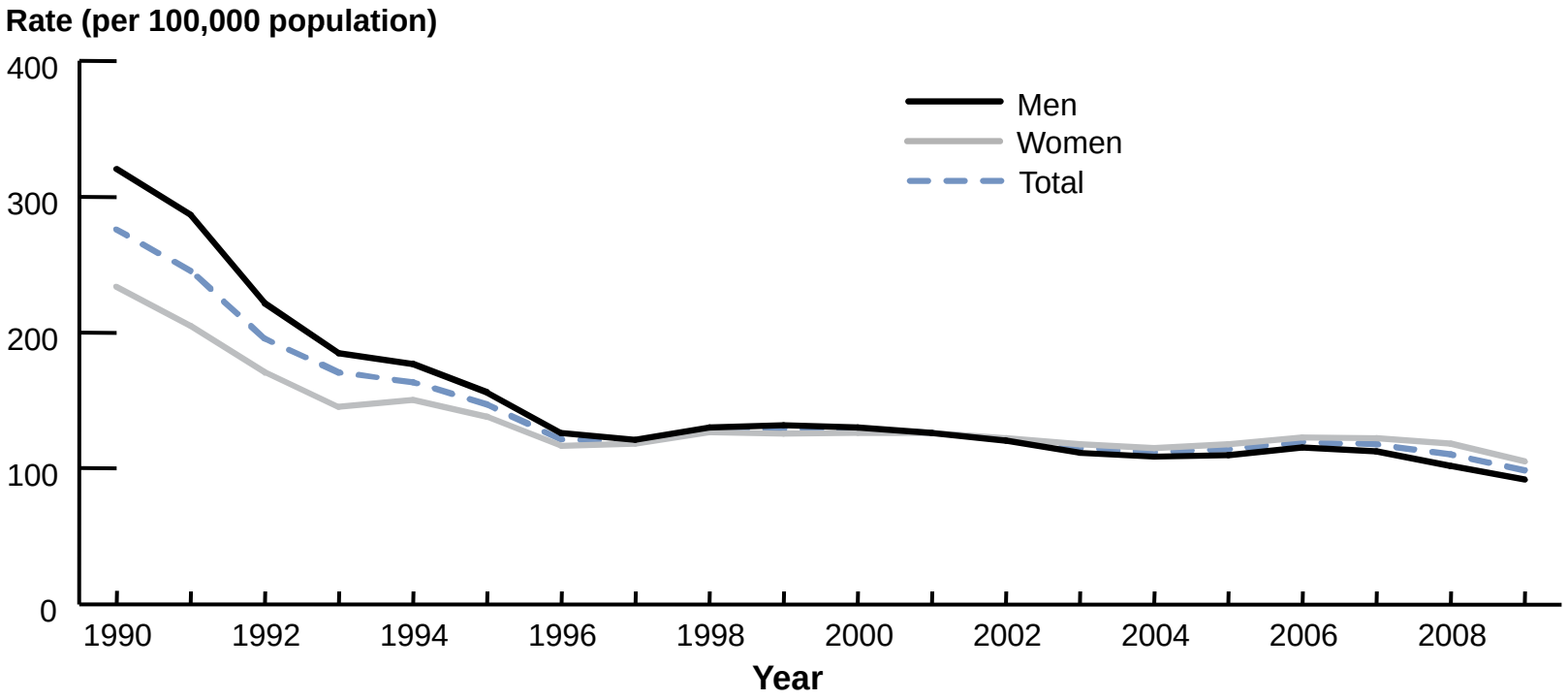
Lymphogranuloma venereum proctocolitis

- LGV being increasingly recognized especially among HIV-positive MSMs
- Caused by *C. trachomatis*
- In persons with painful perianal ulcers or those detected on anoscopy, presumptive therapy should be initiated
  - Recommended: Doxycycline 100mg PO BID x 21 days
  - Alternative: Erythromycin base 500mg PO QID x 21 days* OR Azithromycin 1 g PO QWK x 3 weeks

*Recommended during pregnancy

MMWR 2010;59(RR-12):1-109.

Gonorrhea—Rates by Sex, United States, 1990–2009



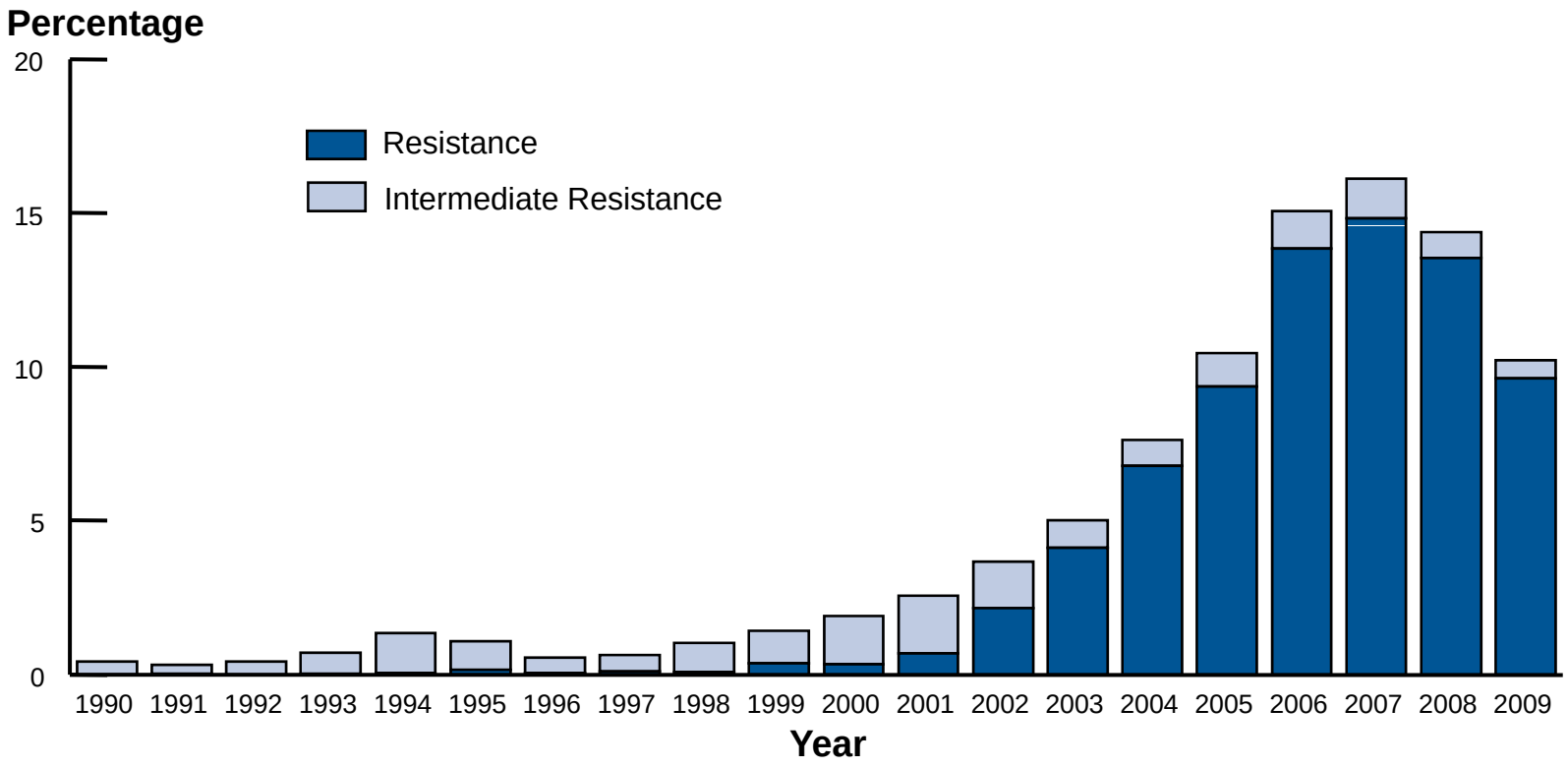
Gonorrhea

American College of Clinical Pharmacy

- Characteristics
  - Causative organism is *Neisseria gonorrhoeae*
  - Second most commonly reported bacterial STD in U.S.
  - Several serious sequelae can result in women
    - PID, ectopic pregnancy, infertility
- Screening
  - All sexually active women if at increased risk
    - <25 years old, previous infection, other STDs, new or multiple sex partners, inconsistent condom use, commercial sex work, drug use

MMWR 2010;59(RR-12):1-109.

Gonococcal Isolate Surveillance Project (GISP)—Percentage of *Neisseria gonorrhoeae* Isolates with Resistance or Intermediate Resistance to Ciprofloxacin, 1990–2009



NOTE: Resistant isolates have ciprofloxacin minimum inhibitory concentrations (MICs) >1 µg/ml. Isolates with intermediate resistance have ciprofloxacin MICs of 0.125–0.5 µg/ml. Susceptibility to ciprofloxacin was first measured in GISP in 1990.

Gonorrhea

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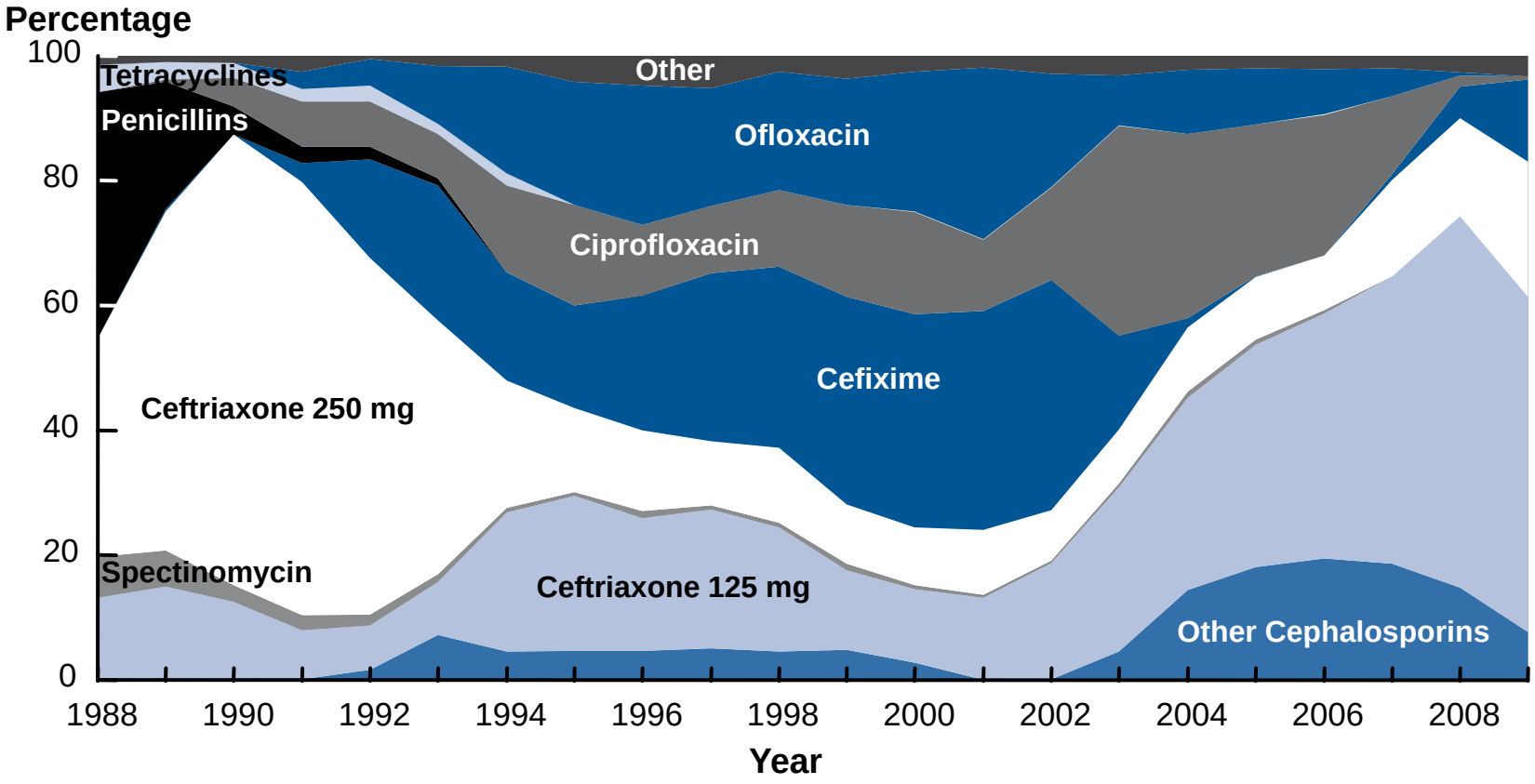
- Recommended Regimens
  - Ceftriaxone 250mg IM x 1 dose

  OR, IF NOT AN OPTION
  - Cefixime 400mg PO x 1 dose OR
  - Single-dose injectable cephalosporin PLUS azithromycin 1g PO x 1 dose OR doxycycline 100mg PO BID x 7 days
- Alternative Regimen
  - Azithromycin 2g x 1 dose

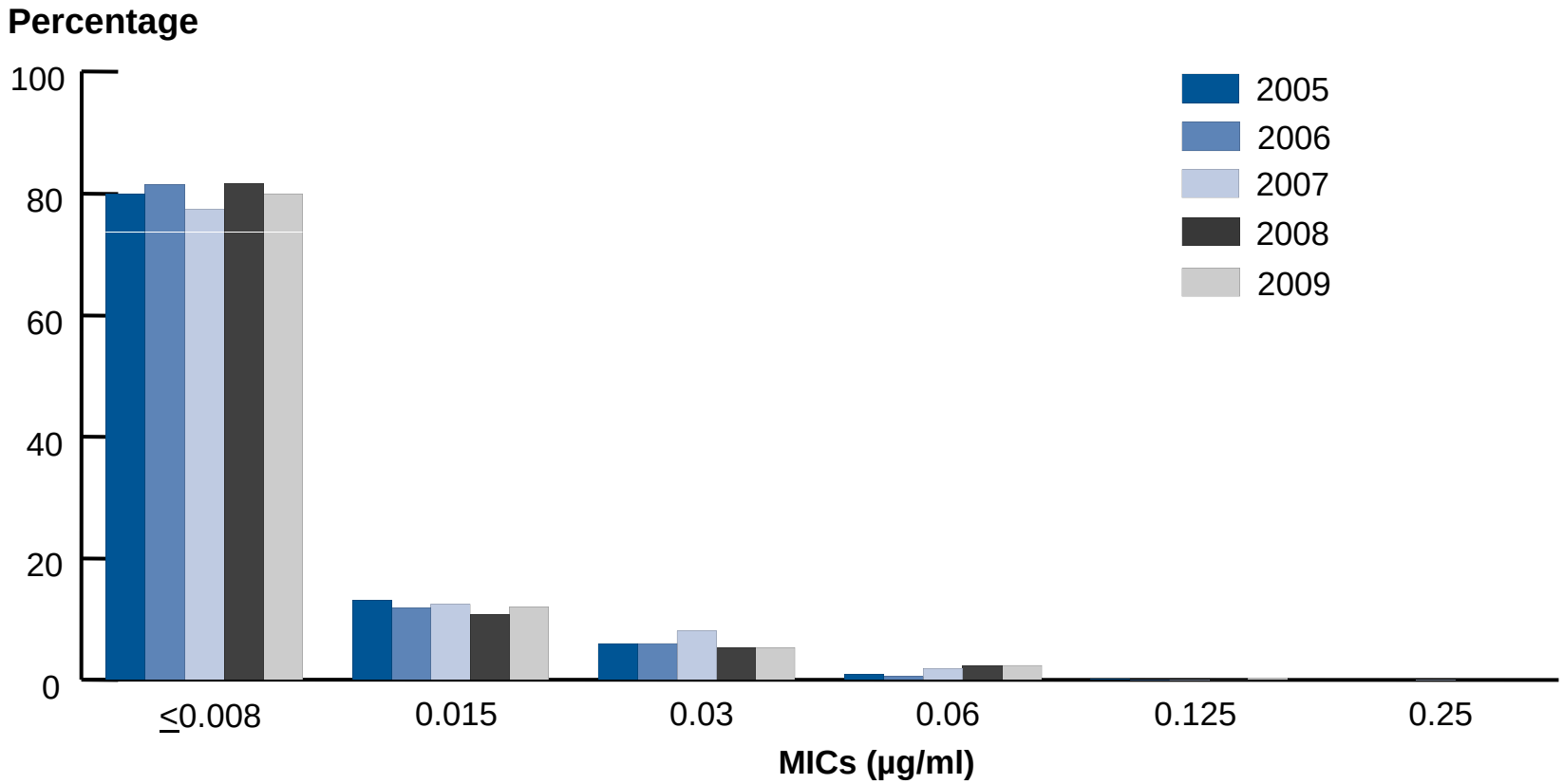
MMWR 2010;59(RR-12):1-109.

Gonococcal Isolate Surveillance Project (GISP)—Drugs Used to Treat Gonorrhea Among GISP Participants, 1988–2009

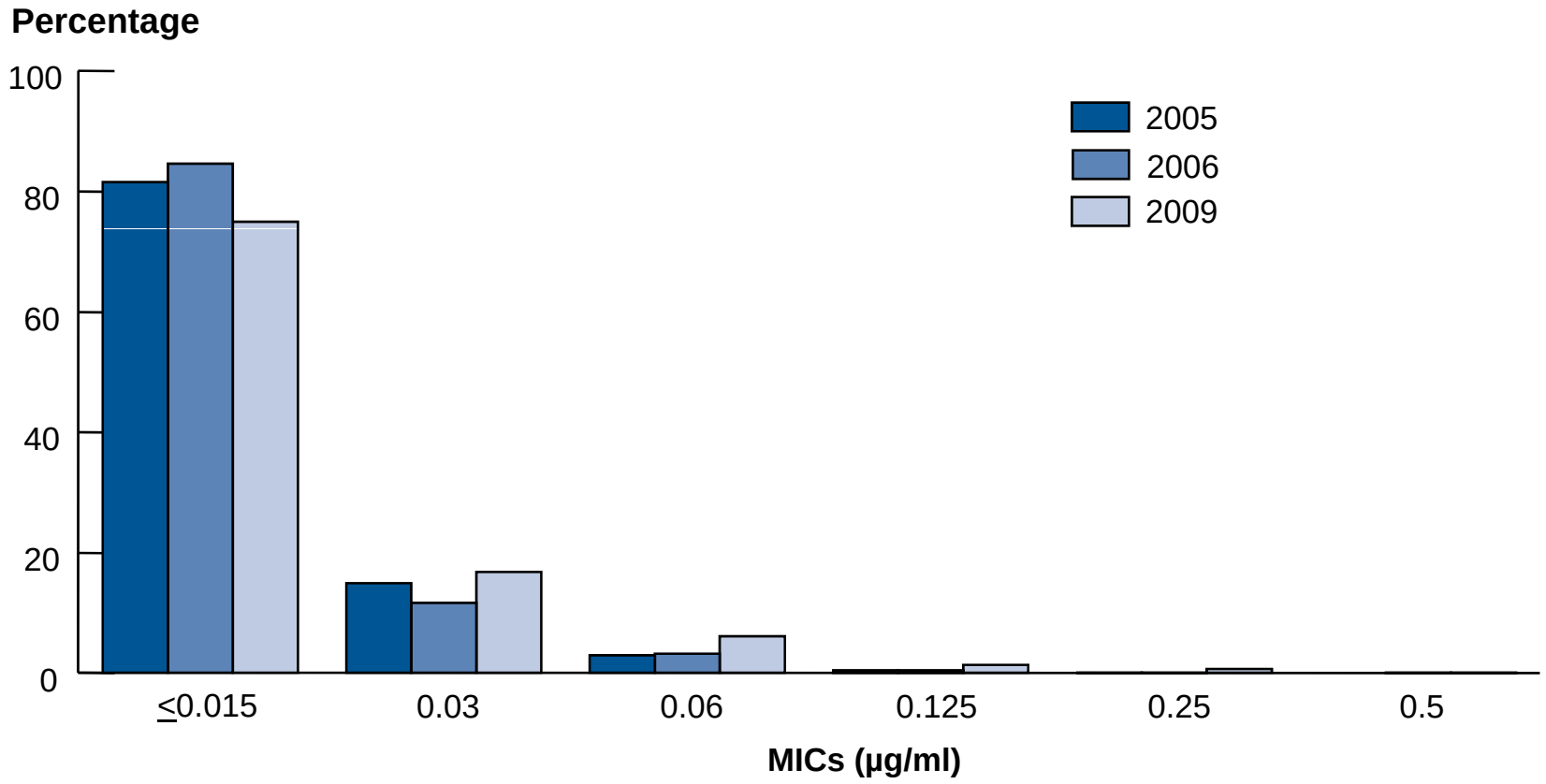


NOTE: For 2009, "Other" includes no therapy (1.5%), azithromycin 2 g (1.7%), and other less frequently used drugs.

Gonococcal Isolate Surveillance Project (GISP)—Distribution of Minimum Inhibitory Concentrations (MICs) to Ceftriaxone Among GISP Isolates, 2005–2009



Gonococcal Isolate Surveillance Project (GISP)—Distribution of Minimum Inhibitory Concentrations (MICs) to Cefixime Among GISP Isolates, 2005–2006 and 2009



NOTE: Isolates were not tested for cefixime susceptibility in 2007 and 2008.

Gonorrhea

- Patients should abstain from intercourse until therapy is completed and until they and their sex partners no longer have symptoms (all sexual partners within the past 60 days should be evaluated and treated)
  - *CDC supports giving patients extra antibiotics for partner – if partner won't be seen*

- Recommended Regimens in Pregnancy
  - Ceftriaxone, Cefixime
  - If cannot tolerate/allergy, azithromycin 2g PO x 1 dose

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Gonorrhea

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- Follow-up
  - In general, patients should be retested 3 months after treatment
  - Combination gonorrhea/chlamydia therapy rarely results in failure
    - Positive post-treatment cultures usually represent non-adherence, failure to treat sexual partners or lab error
    - Be cognizant of potential for resistance to cephalosporins

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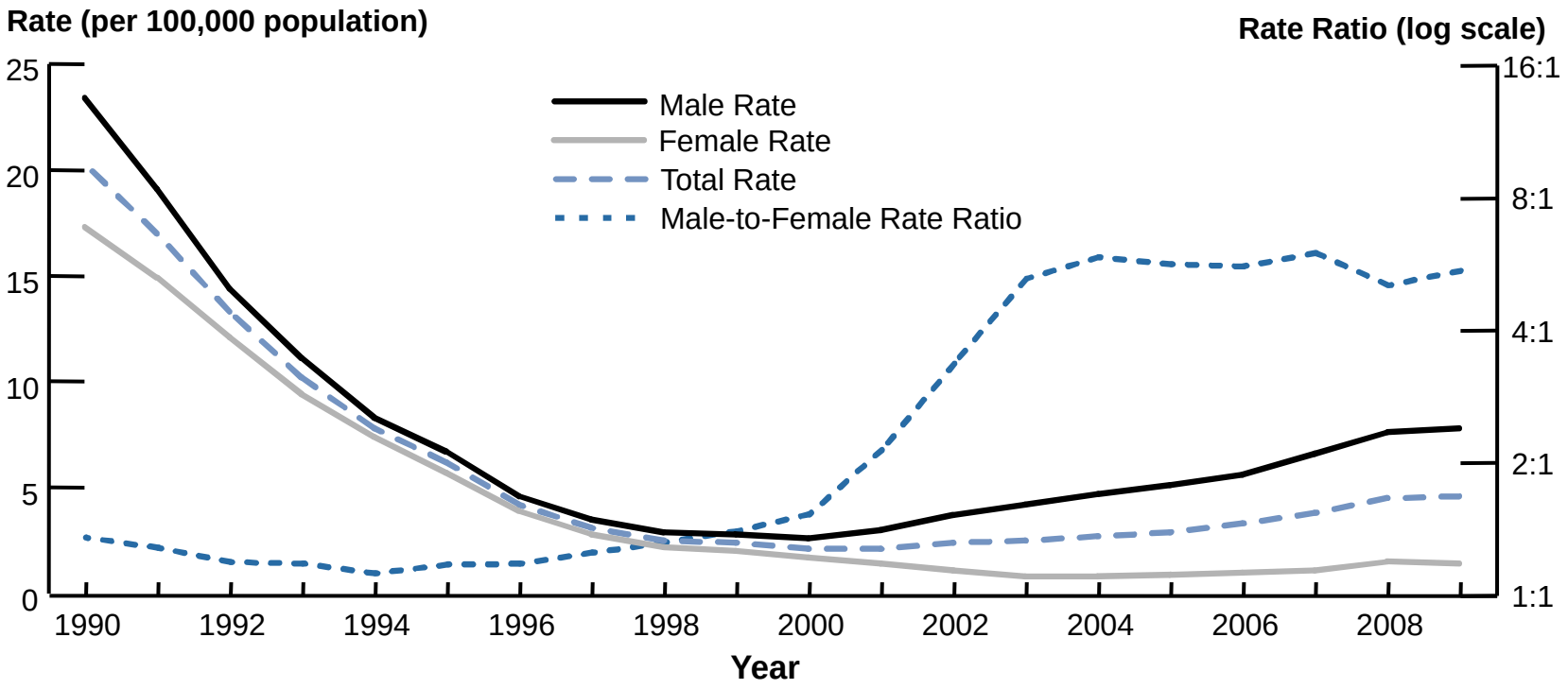
Primary and Secondary Syphilis—Rates by Sex and Male-to-Female Rate Ratios, United States, 1990–2009



Syphilis

- Characteristics
  - Causative organism is *Treponema pallidum*
  - Highly contagious disease and if left untreated, can progress to chronic systemic disease
  - Can be acquired by sexual contact with infected mucous membranes/lesions or rarely by accidental inoculation or blood transfusion

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Syphilis

- Recommended Regimens
  - Primary
    - Benzathine penicillin G 2.4 million units IM in a single dose (if allergic: Doxycycline 100mg BID or Tetracycline 500mg QID x 2 weeks or *Ceftriaxone 1 g IM/IV once daily x 8-10 days*)
  - Secondary/Early latent
    - Same as above
  - Tertiary/Late latent
    - Benzathine penicillin G 2.4 million units IM qweek x 3 (if allergic: Doxycycline 100mg BID or Tetracycline 500mg QID x 4 weeks)

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Syphilis

- Recommended Regimens
  - Neurosyphilis
    - Aqueous cystalline penicillin G 18-24 million units IV/day as 3-4 million units IV q4 hours or continuous infusion x 10-14 days (alternative: procaine penicillin 2.4 million units IM QD PLUS probenecid 500mg PO QID x 10-14 days)
    - If allergic, desensitize and give PCN

      (*NEJM 1985;312:1229-32)* OR Ceftriaxone 2g IM/IV QD x 10-14 days (cross-reactivity with PCN possible)

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TABLE 1. Oral desensitization protocol for patients with a positive skin test*

Penicillin V suspension dose†	Amount§ (units/mL)	mL	Units	Cumulative dose (units)
1	1,000	0.1	100	100
2	1,000	0.2	200	300
3	1,000	0.4	400	700
4	1,000	0.8	800	1,500
5	1,000	1.6	1,600	3,100
6	1,000	3.2	3,200	6,300
7	1,000	6.4	6,400	12,700
8	10,000	1.2	12,000	24,700
9	10,000	2.4	24,000	48,700
10	10,000	4.8	48,000	96,700
11	80,000	1.0	80,000	176,700
12	80,000	2.0	160,000	336,700
13	80,000	4.0	320,000	656,700
14	80,000	8.0	640,000	1,296,700

NOTE: Observation period: 30 minutes before parenteral administration of penicillin.

* Reprinted with permission from the *New England Journal of Medicine* (Wendel GO, Jr, Stark BJ, Jamison RB, Melina RD, Sullivan TJ. Penicillin allergy and desensitization in serious infections during pregnancy. N Engl J Med 1985;312:1229–32.).

† Interval between doses, 15 minutes; elapsed time, 3 hours and 45 minutes; cumulative dose, 1.3 million units.

§ The specific amount of drug was diluted in approximately 30 mL of water and then administered orally.

NEJM 1985;312:1229-32

Syphilis

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- Management of Sex Partners
  - Persons exposed within the 90 days preceding diagnosis should be treated presumptively
- Follow-up
  - Treatment failures can occur
  - Reexamine clinically and serologically
    - 6 and 12 months: primary and secondary syphilis
    - 6, 12 and 24 months: latent syphilis
    - CSF every 6 months until cell count normal: neurosyphilis

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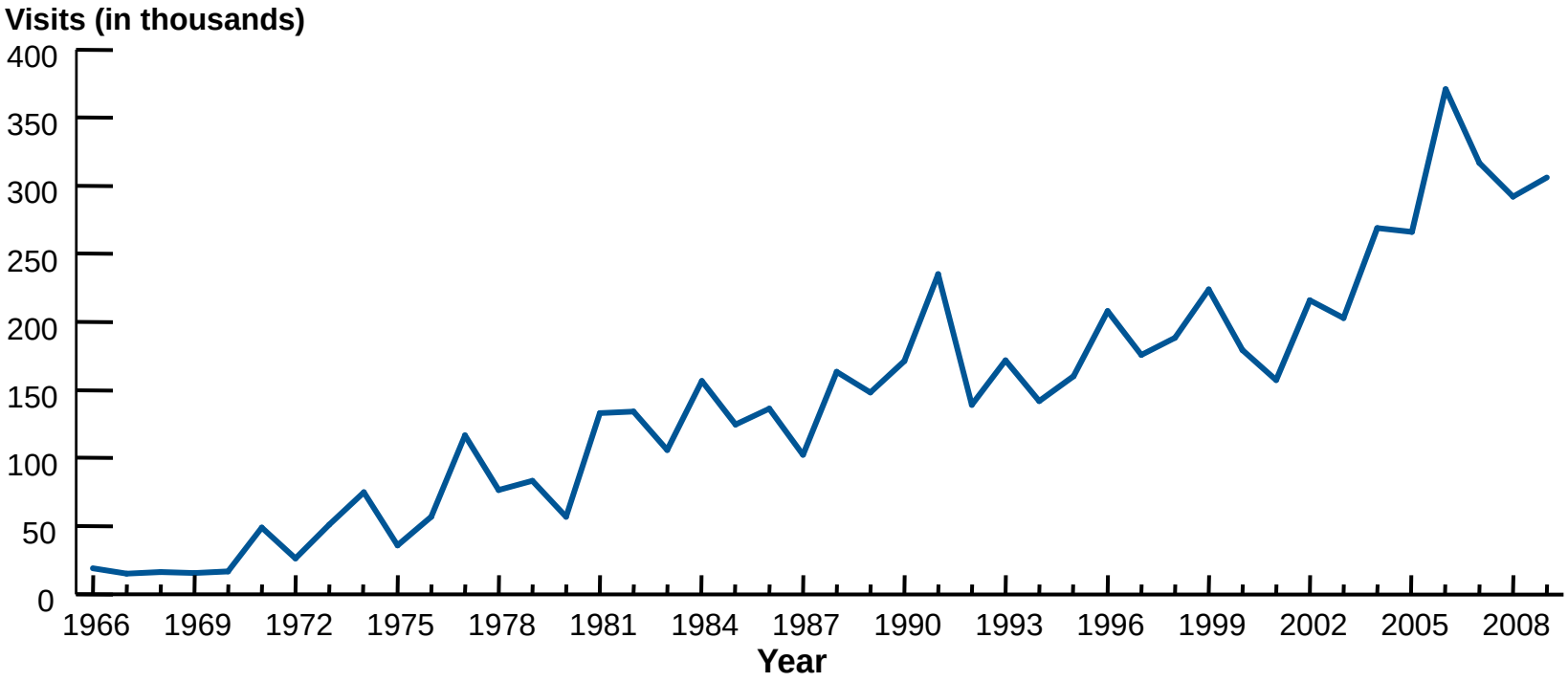
Genital Herpes—Initial Visits to Physicians' Offices, United States, 1966–2009



NOTE: The relative standard errors for genital herpes estimates of more than 100,000 range from 18% to 30%.

SOURCE: IMS Health, Integrated Promotional Services™. IMS Health Report, 1966–2009.

Herpes Simplex Virus (HSV)

- Characteristics
  - Diagnosed in at least 50 million people in U.S.
  - Recurrent, incurable viral disease
  - HSV-1/HSV-2
    - Most cases of recurrent genital herpes are caused by HSV-2, although HSV-1 becoming more common, especially anogenital herpetic infections
  - After primary infection, virus is latent in the sacral dorsal root ganglia
  - Treatment can partially control symptoms but it does not affect the risk, frequency, or severity of recurrences after treatment is stopped

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HSV

- Recommended Regimens
  - Initial infection
    - Acyclovir 400mg PO TID x 7-10 days* OR
    - Acyclovir 200mg PO 5x/day x 7-10 days* OR
    - Famciclovir 250mg PO TID x 7-10 days* OR
    - Valacyclovir 1g PO BID x 7-10 days*

      *(*Treatment can be extended if healing is incomplete after 10 days of therapy)*
  - Recurrent infection
    - Acyclovir 400mg PO TID x 5 days OR
    - Acyclovir 800mg PO TID x 2 days OR
    - Acyclovir 800mg PO BID x 5 days OR
    - Famciclovir 125mg PO BID x 5 days OR
    - Famciclovir 1 g BID x 1 day OR
    - Famciclovir 500mg once, followed by 250mg BID x 2 days OR
    - Valacyclovir 500mg PO BID x 3 days OR
    - Valacyclovir 1g PO QD x 5 days

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HSV

- Recommended Regimens
  - Daily suppressive therapy
    - Acyclovir 400mg PO BID OR
    - Famciclovir 250mg PO BID OR
    - Valacyclovir 500mg PO QD OR
    - Valacyclovir 1g PO QD

      *(*Valacyclovir 1g should be utilized in those with frequent recurrences - >=10 episodes per year)*
  - Severe disease
    - Acyclovir 5-10 mg/kg IV q8 hours x 2-7 days or until clinical improvement is observed, followed by oral antiviral therapy to complete at least 10 days total therapy
- Evaluation/counseling of sex partners

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HSV

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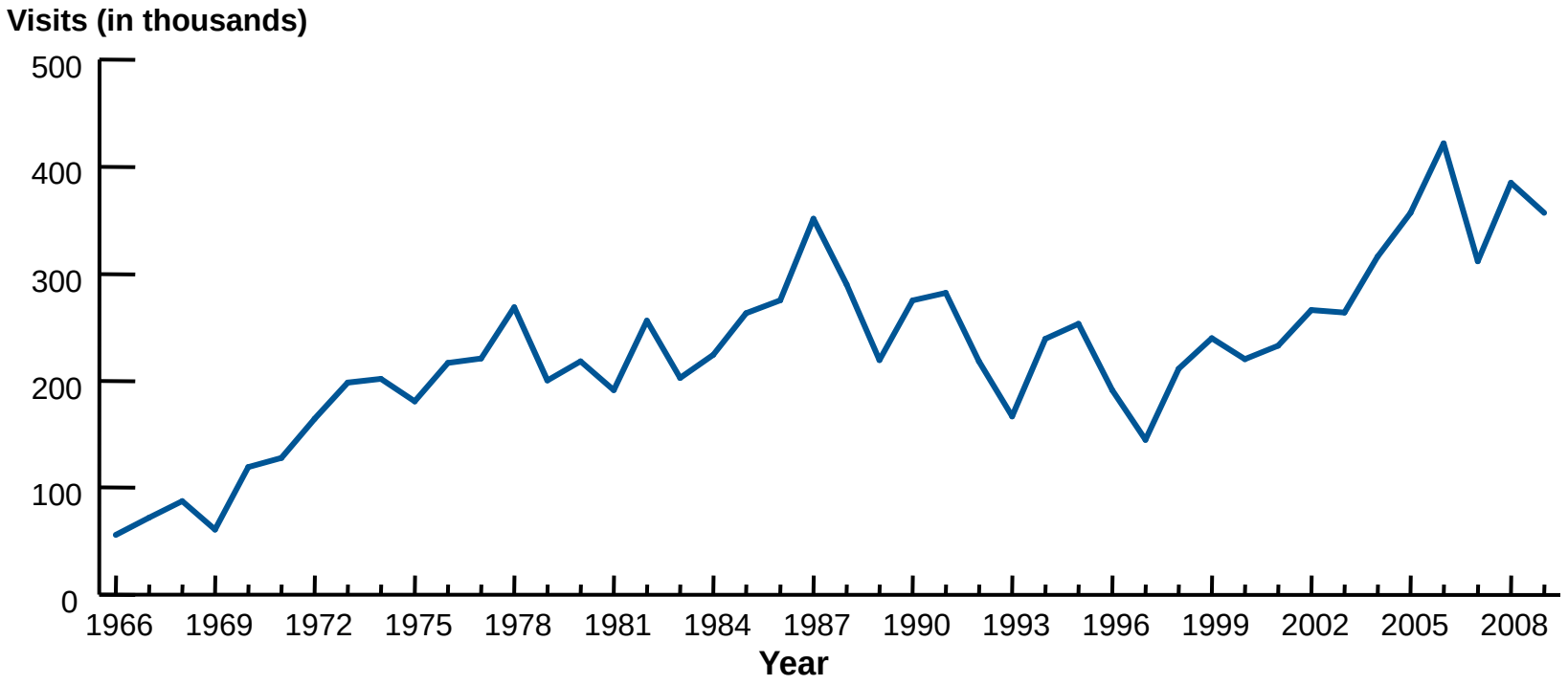
- Treatment during pregnancy
  - Available data do not indicate an increased risk of major birth defects compared with general population (less data with valacyclovir and famciclovir)
  - If first episode of herpes or for severe recurrent herpes, PO acyclovir (IV to pregnant women with severe HSV infection)
  - Acyclovir treatment late in pregnancy reduces frequency of cesarean sections among women who have recurrent genital herpes
  - No data to support use of antiviral therapy among HSV seropositive women without a history of genital herpes

MMWR 2010;59(RR-12):1-109.

Genital Warts—Initial Visits to Physicians' Offices, United States, 1966–2009



NOTE: The relative standard errors for genital warts estimates of more than 100,000 range from 18% to 30%.

SOURCE: IMS Health, Integrated Promotional Services™. IMS Health Report, 1966–2009.

Human Papilloma Virus (HPV)

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- Characteristics
  - More than 100 different types of HPV
    - Over 40 types infect mucosal surfaces
      - Cervix, vagina, vulva, rectum, urethra, penis, anus
      - Divided into “high-risk” and “low-risk” types
  - Most infections are asymptomatic, subclinical, or unrecognized
  - Treatment possibly reduces, but does not eliminate HPV infection or infectivity
    - If left untreated, visible genital warts might resolve on their own, remain unchanged or increase in size or number

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Types of HPV

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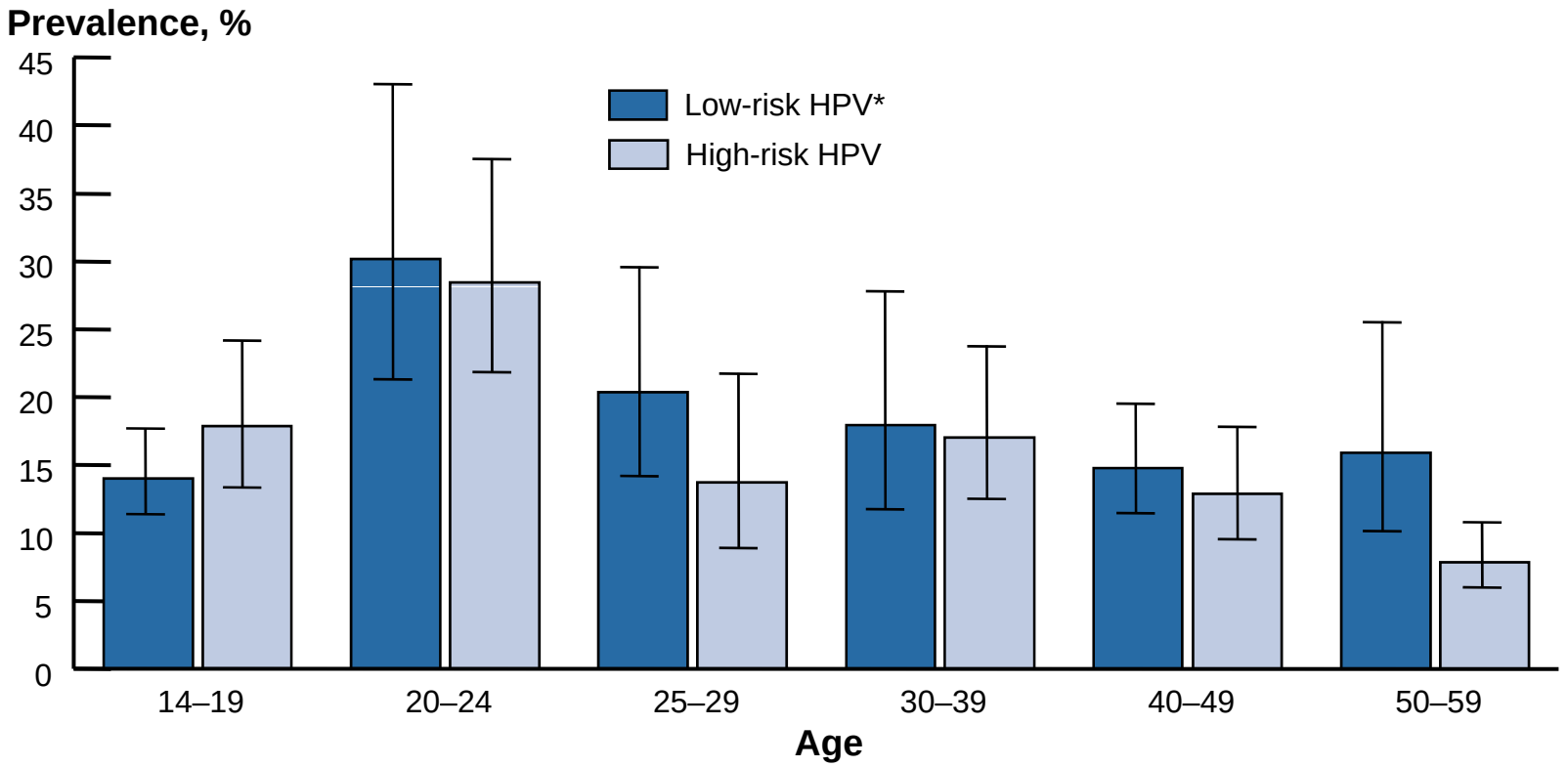
High-risk (oncogenic or cancer-associated) types	Low-risk (non-oncogenic) types
Common types: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 82	Common types: 6, 11, 40, 42, 43, 44, 54, 61, 72, 73, 81
•HPV 16 most common high-risk type, found in ~50% of all cervical cancers •HPV 18 is another common high-risk type, accounting for 10-12% of cervical cancers •HPV types 31, 33, 45, 52, 58 each account for 2-4% of cancers; all rest account for <1%	Can cause benign or low-grade cervical cell changes and genital warts but are rarely, if ever, found in association with invasive cancers •HPV 6 and 11 are the most commonly found in genital warts

www.cdc.gov/std/hpv/

Human Papillomavirus—Prevalence of High-risk and Low-risk Types Among Females Aged 14–59 Years, National Health and Nutrition Examination Survey, 2003–2004



* HPV = human papillomavirus.

NOTE: Error bars indicate 95% confidence intervals. Both high-risk and low-risk HPV types were detected in some females.

SOURCE: Dunne EF, Unger ER, Sternberg M, McQuillan G, Swan DC, Patel SS, et al. Prevalence of HPV infection among females in the United States. JAMA. 2007;297(8):813-9.

HPV

- Recommended Regimens
  - Patient-applied
    - Podofilox 0.5% solution or gel (apply BID x 3 days, followed by 4 days of no therapy. Repeat for 4 cycles) OR
    - Imiquimod 5% cream (apply QHS TIW x up to 16 weeks) OR
    - Sinecatechins (Veregen) 15% ointment (apply TID x up to 16 weeks)
  - Provider-administered
    - Podophyllin 10-25% in compound tincture of benzoin*OR
    - Tri(Bi)chloroacetic acid 80-90%* OR
    - Cryotherapy* OR
    - Surgical removal

    (*can repeat weekly)

NOTE: Should not use imiquimod, sinecatechins, podophyllin, podofilox during pregnancy

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HPV

- Management of Sex Partners
  - Examination of sex partners is not absolutely necessary
    - Role of reinfection is probably minimal and treatment to reduce transmission is not realistic; however, education/counseling may be beneficial
- Follow up
  - After visible warts have cleared, follow-up evaluation not mandatory
    - Patients concerned about recurrences should be offered follow-up evaluation 3 months after treatment

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HPV - Prevention

- Gardasil
  - Quadrivalent human papillomavirus (types 6, 11, 16, 18; some cross-protection against 31) recombinant vaccine; 0.5ml IM; adjuvant aluminum hydroxyphosphate sulfate
- Cervarix
  - Bivalent human papillomavirus (types 16 and 18; cross-protection against other oncogenic types – 31, 33,45) recombinant vaccine 0.5ml IM; adjuvant ASO4
- Dosing
  - First dose: at elected date
  - Second dose: 1-2 months after first dose
  - Third dose: 6 months after first dose

- CDC Advisory Committee recommends routine vaccination of girls 11-12 years of age (as young as 9) and for females aged 13-26 years if did not receive or complete vaccine series previously; Gardasil approved for use in males aged 9-26 years to prevent genital warts and anal cancer

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HPV - Prevention

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- Gardasil and Cervarix
  - Will not eliminate need for annual Pap tests
    - Cervical cancer can be caused by strains not covered by the vaccine
  - Duration of protection unclear
    - Current studies indicate effectiveness for at least 5 years (up to 10 years), with no evidence of waning immunity during that period
  - Cost
    - ~$120/dose ($360 total)
    - Federal Vaccines for Children (FVC) will provide free vaccines to those under 19 who are uninsured, Medicaid-eligible

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HPV - Prevention

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- Gardasil in Males
  - Pro
    - Further protection for females by preventing transmission from infected males
    - The more patients are vaccinated, lower chance of coming in contact with the virus (indirectly protects even the unimmunized - “herd immunity”)
    - Although only indicated for preventing genital warts in males, genital warts are associated with physical/psychological morbidity and place a burden on healthcare system
    - Although has not shown a reduction in cancers in males, HPV 16 and 18 have been associated with anal and oropharyngeal carcinomas; head and neck squamous cancers

HPV - Prevention

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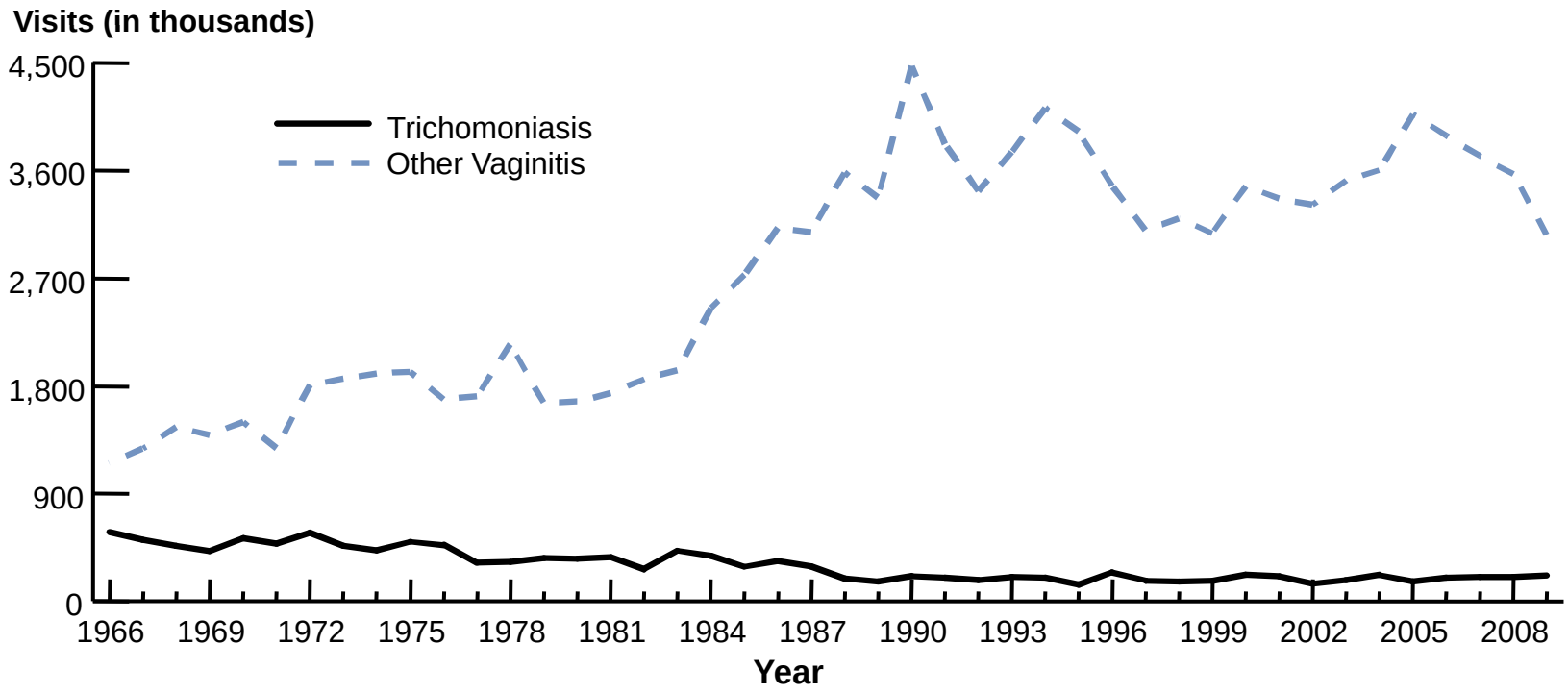
- Gardasil in Males
  - Con
    - Recent cost-benefit analysis concluded that including boys in an HPV vaccination program exceeds conventional thresholds of good value for money (however, they note that as more information becomes available, this conclusion could change)
  - CDC ACIP
    - Recommends against routine use of Gardasil to prevent genital warts in boys and young men
    - Recommends “permissive use” of Gardasil

State By State

- 41 states have introduced legislation to require, fund or educate public about HPV vaccine; 19 states have enacted this legislation
  - Colorado, Indiana, Iowa, Louisiana, Maine, Maryland, Michigan, Minnesota, Nevada, New Mexico, New York, North Carolina, North Dakota, Rhode Island, South Dakota, Texas, Utah, Virginia and Washington

http://www.ncsl.org/programs/health/HPVvaccine.htm
(updated July 2011)

Trichomoniasis and Other Vaginal Infections—Women—Initial Visits to Physicians' Offices, United States, 1966–2009



NOTE: The relative standard errors for trichomoniasis estimates range from 16% to 27% and for other vaginitis estimates range from 8% to 13%.

SOURCE: IMS Health, Integrated Promotional Services™, IMS Health Report, 1966–2009.

Trichomoniasis

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- Characteristics
  - Caused by *Trichomonas vaginalis*
  - May be associated with adverse pregnancy outcomes
    - Premature rupture of the membranes
    - Preterm delivery

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Trichomoniasis

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- Recommended Regimens
  - Metronidazole 2g PO x 1 dose* OR
  - Tinidazole 2 g PO x 1 dose

- Alternative Regimen
  - Metronidazole 500mg PO BID x 7 days

Patients should be advised to avoid consuming alcohol during treatment with metronidazole or tinidazole. Abstinence from alcohol use should continue for 24 hours after completion of metronidazole or 72 hours after completion of tinidazole

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Trichomoniasis

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- Management of Sex Partners
  - Should be treated. Avoid intercourse until patient and partner have completed therapy.

- Follow-up
  - Unnecessary in patients who become asymptomatic after treatment or who are initially asymptomatic
  - Repeated treatment failures
    - Metronidazole 2g PO QD x 5 days OR
    - Tinidazole 2g PO QD x 5 days

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Bacterial Vaginosis (BV)

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- Characteristics
  - Most common vaginal infection that presents to the primary care physicians office
  - Replacement of normal hydrogen peroxide-producing *Lactobacillus* sp. in the vagina with high concentrations of anaerobic bacteria
    - *Prevotella* sp. and *Mobiluncus* sp., *G. vaginalis, Mycoplasma hominus*
  - Cause not fully understood
    - Associated with having multiple sex partners, new sex partner, douching and lack of vaginal lactobacilli

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BV

- Recommended Regimens
  - Metronidazole 500mg PO BID x 7 days* OR
  - Clindamycin cream 2%, one full applicator (5g) intravaginally QHS x 7 days** OR
  - Metronidazole gel 0.75%, one full applicator (5g) intravaginally QD x 5 days

*Consuming alcohol should be avoided during treatment and for 24 hours thereafter

**Clindamycin cream is oil-based and might weaken latex condoms and diaphragms for 5 days after use

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BV

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- Alternative Regimens
  - Tinidazole 2g PO QD x 2 days OR
  - Tindazole 1 g PO QD x 5 days OR
  - Clindamycin 300mg PO BID x 7 days OR
  - Clindamycin ovules 100mg intravaginally QHS x 3 days

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BV

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- Pregnancy
  - Metronidazole 500mg PO BID x 7 days OR
  - Metronidazole 250mg PO TID x 7 days OR
  - Clindamycin 300mg PO BID x 7 days
- Management of Sex Partners
  - Routine treatment not recommended
- Follow-up
  - Unnecessary if symptoms resolve

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Question #1

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MM is a 19 year old college student who presents to the medical office complaining of vaginal discharge x 2 days. She denies fever, chills, abdominal pain. She is sexually active and recently started a relationship with a new partner. Physical exam reveals mucopurulent cervical exudates and endocervical bleeding induced by gentle swabbing. A diagnosis of gonorrhea and chlamydia is made. Urine pregnancy test is positive. Which one of the following represents the most appropriate treatment plan for this patient?

1) Begin doxycycline (vibramycin) 100mg BID x 7 days and ofloxacin 400mg x 1 dose
2) Administer 125mg ceftriaxone (rocephin) IM and give metronidazole 500mg BID x 7 days
3) Begin erythromycin ethylsuccinate 400mg QID x 14 days and amoxicillin 500mg TID x 7 days
4) Administer 250mg ceftriaxone (rocephin) IM and give azithromycin (zithromax) 1 g x 1 dose

Question #2

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The mother of a teenage girl asks you to tell her more about the vaccine Gardasil. Which of the following is an accurate statement?

1) Gardasil will eliminate the need for regular Pap tests in women aged 11-26
2) Gardasil protects against four types of human papillomavirus and is recommended in girls age 11-12
3) Gardasil is not FDA approved for males or recommended in females over the age of 21
4) Gardasil protects against the two most common types of human papillomavirus and has cross-protection against other oncogenic types

Questions #3 and #4

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HK is a 26 year old female who complains of vaginal discharge and is subsequently diagnosed with bacterial vaginosis during a prenatal pelvic examination. She is in her 3rd trimester. Which one of the following represents the best treatment plan for this woman?

1) Metronidazole (Flagyl) 2 g as a single dose
2) No therapy is recommended
3) Metronidazole (Flagyl) 500mg BID x 7 days
4) Clindamycin (Cleocin) 2% cream intravaginally QHS x 7 days

How should HK's male partner be treated?

1) Metronidazole 500mg BID x 7 days
2) Tinidazole 2 g as a single dose
3) Clindamycin 300mg BID x 7 days
4) Treatment is not warranted

Question #5

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YO returns to your clinic 10 months after her initial herpes infection. She is becoming troubled by all of the recurrences she is having (seven to date). She does not currently have lesions. Which one of the following would be the most appropriate recommendation?

1) Valacyclovir 500mg BID x 5 days
2) Acyclovir 400mg TID x 10 days
3) Famciclovir 1g BID
4) Valacyclovir 500mg QD

Questions?

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