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1993 Sexually Transmitted Diseases Treatment Guidelines

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Abbreviations Used in This Publication

ACIP	Advisory Committee on Immunization Practices
ACS	American Cancer Society
AIDS	Acquired immunodeficiency syndrome
ASCUS	Atypical squamous cells of undetermined significance
BV	Bacterial vaginosis
CMV	Cytomegalovirus
CSF	Cerebrospinal fluid
DDC	Dideoxycytodine
DDI	Didanosine
DGI	Disseminated gonococcal infection
DTH	Delayed-type hypersensitivity
FDA	Food and Drug Administration
FTA-ABS	Fluorescent treponemal antibody absorbed
HBc	Hepatitis B core antigen
HBIG	Hepatitis B immune globulin
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
Hib	*Haemophilus influenzae* type b
HIV	Human immunodeficiency virus
HPV	Human papillomavirus
HSV	Herpes simplex virus
IFA	Immunofluorescence assay
IM	Intramuscularly
IV	Intravenous or intravenously
KOH	Potassium hydroxide
LET	Leukocyte esterase test
LGV	Lymphogranuloma venereum
MPC	Mucopurulent cervicitis
NIAID	National Institute of Allergy and Infectious Diseases
NGU	Nongonococcal urethritis
OTC	Over-the-counter
Pap	Papanicolaou
PCP	*Pneumocystis carinii* pneumonia
PID	Pelvic inflammatory disease
PPD	Purified protein derivative
PPV	Positive predictive value
RPR	Rapid plasma reagin
RVVC	Recurrent vulvovaginal candidiasis
SIL	Squamous intraepithelial lesions
STD	Sexually transmitted disease
TB	Tuberculosis
TCA	Trichloroacetic acid
TMP-SMX	Trimethoprim-sulfamethoxazole
VDRL	Venereal Disease Research Laboratory
VVC	Vulvovaginal candidiasis

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1993 Sexually Transmitted Diseases Treatment Guidelines

Summary

These guidelines for the treatment of patients with sexually transmitted diseases (STDs) were developed by staff members of CDC after consultation with a group of invited experts who met in Atlanta on January 19–21, 1993. Included are new recommendations for single-dose oral therapy for gonococcal infections, chlamydial infections, and chancroid; new regimens for the treatment of bacterial vaginosis (BV) and outpatient management of pelvic inflammatory disease (PID); a new patient-applied medication for treatment of genital warts; and a revised approach to the management of victims of sexual assault. This report includes new sections on subclinical human papillomavirus (HPV) infections and cervical cancer screening for women who attend STD clinics or who have a history of STDs. These recommendations also include expanded sections on the management of patients with asymptomatic human immunodeficiency virus (HIV) infection; vulvovaginal candidiasis (VVC); STDs among patients coinfected with HIV; and STDs among infants, children, and pregnant women.

INTRODUCTION

Physicians and other health-care providers have a critical role in the effort to prevent and treat sexually transmitted diseases (STDs). These recommendations for the treatment of STDs are intended to assist with that effort. They were developed by CDC staff members in consultation with a group of invited experts.*

This report was produced through a multi-stage process. Beginning in the spring of 1992, CDC personnel systematically reviewed literature on each of the major STDs, focusing on data and reports that have become available since the 1989 *STD Treatment Guidelines* were published. Background papers were written and tables of evidence constructed summarizing the type of study (e.g., randomized controlled trial, case series), the study population and setting, the treatments or other interventions, outcome measures assessed, reported findings, and weaknesses and biases in study design and analysis. For these reviews and tables, published abstracts and peer-reviewed journal articles were considered. CDC personnel then developed a draft document based on those reviews.

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In January 1993, invited consultants assembled in Atlanta for a 3-day meeting. CDC personnel presented the key questions on STD treatment suggested from their literature reviews and presented the data available to answer those questions. Where relevant, the questions focused on four principal outcomes of STD therapy: a) microbiologic cure, b) alleviation of signs and symptoms, c) prevention of sequelae, and d) prevention of transmission. The consultants then assessed whether the questions identified were the appropriate ones, ranked them in order of priority, and attempted to arrive at answers using the available evidence. In addition, the consultants evaluated the quality of evidence supporting the answers based on the number and types of studies and the quality of those studies.

In several areas, the process diverged from that described above. The section on STD/HIV prevention guidelines was reviewed for comment by experts who had not been present at the January meeting, as well as by additional experts on STD/HIV prevention at CDC. The recommendations for STD screening during pregnancy were developed after CDC staff reviewed the published recommendations of other expert groups that were convened by CDC and other organizations. The sections on HIV infection and early intervention and hepatitis B virus (HBV) also are principally a compilation of recommendations developed by other experts and are provided in this report for the convenience of those who use this document.

Throughout this document the evidence used as the basis for specific recommendations is briefly discussed. More comprehensive, annotated discussions of such evidence will appear in background papers that will be submitted for publication in 1994.

These recommendations were developed in consultation with experts whose experience is primarily with the treatment of patients in public STD clinics. These recommendations also should be applicable to other patient-care settings, including family planning clinics, private doctor's offices, and other primary-care facilities. When using these guidelines, consideration should be given to the disease prevalence and to other characteristics of the practice setting. These recommendations should not be construed as standards or as inflexible rules, but as a source of clinical guidance within the United States.

These recommendations focus on the treatment and counseling of individual patients and do not address other community services and interventions that also play important roles in STD/HIV prevention. Clinical and laboratory diagnoses are described when such information is related to therapy. For a more comprehensive discussion of diagnosis, refer to CDC's *STD Clinical Practice Guidelines, 1991* (*1*).

STD/HIV PREVENTION GUIDELINES

Prevention and control of STDs is based on four major concepts: first, education of those at risk on the means for reducing the risk for transmission; second, detection of asymptomatically infected individuals and of persons who are symptomatic but unlikely to seek diagnostic and treatment services; third, effective diagnosis and treatment of those who are infected; fourth, evaluation, treatment, and counseling of sex partners of persons who have an STD. Although this document deals largely with secondary prevention, namely clinical aspects of STD control, primary prevention of STDs is based on changing the sexual behaviors that place patients at risk.

Physicians and other health-care providers have an important role in the prevention of STDs. In addition to interrupting transmission by treating persons who have bacterial and parasitic STDs, clinicians have the opportunity to provide patient education and counseling and to participate in identifying and treating infected sex partners.

Prevention Methods

Condoms

When used consistently and correctly, condoms are very effective in preventing a variety of STDs, including HIV infection. Multiple cohort studies, including those of serodiscordant couples, have demonstrated a strong protective effect of condom use against HIV infection. Condoms are regulated as medical devices and subject to random sampling and testing by the Food and Drug Administration (FDA). Each latex condom manufactured in the United States is tested electronically for holes before packaging. Condom breakage rates during use are low in the United States (≤2 per 100 condoms tested). Condom failure usually results from inconsistent or incorrect use rather than condom breakage.

Patients should be advised that condoms must be used consistently and correctly to be effective in preventing STDs. Patients should also be instructed in the correct use of condoms. The following recommendations ensure the proper use of condoms:

- Use a new condom with each act of intercourse.
- Carefully handle the condom to avoid damaging it with fingernails, teeth, or other sharp objects.
- Put the condom on after the penis is erect and before any genital contact with the partner.
- Ensure that no air is trapped in the tip of the condom.
- Ensure that there is adequate lubrication during intercourse, possibly requiring the use of exogenous lubricants.
- Use only water-based lubricants (e.g., K-Y Jelly™ or glycerine) with latex condoms (oil-based lubricants [e.g., petroleum jelly, shortening, mineral oil, massage oils, body lotions, or cooking oil] that can weaken latex should never be used).
- Hold the condom firmly against the base of the penis during withdrawal, and withdraw while the penis is still erect to prevent slippage.

Condoms and Spermicides

The effectiveness of spermicides in preventing HIV transmission is unknown. No data exist to indicate that condoms lubricated with spermicides are more effective than other lubricated condoms in protecting against the transmission of HIV infection and other STDs. Therefore, latex condoms with or without spermicides are recommended.

Female Condoms

Laboratory studies indicate that the female condom (Reality™)—a lubricated polyurethane sheath with a ring on each end that is inserted into the vagina—is an effective mechanical barrier to viruses, including HIV. Aside from a small study of trichomoniasis, no clinical studies have been completed to evaluate protection from

HIV infection or other STDs. However, an evaluation of the female condom's effectiveness in pregnancy prevention was conducted during a 6-month period for 147 women in the United States. The estimated 12-month failure rate for pregnancy prevention among the 147 women was 26%.

Vaginal Spermicides, Sponges, Diaphragms

As demonstrated in several cohort studies, vaginal spermicides (i.e., film, gel, suppositories; contraceptive foam has not been studied) used alone without condoms reduce the risk for cervical gonorrhea and chlamydia, but protection against HIV infection has not been established in human studies. The vaginal contraceptive sponge protects against cervical gonorrhea and chlamydia, but increases the risk for candidiasis as evidenced by cohort studies. Diaphragm use has been demonstrated to protect against cervical gonorrhea, chlamydia, and trichomoniasis, but only in case-control and cross-sectional studies; no cohort studies have been performed. Gonorrhea and chlamydia among women usually involve the cervix as a portal of entry, whereas other STD pathogens (including HIV) may infect women through the vagina or vulva, as well as the cervix. Protection of women against HIV infection should not be assumed from the use of vaginal spermicides, vaginal sponges, or diaphragms. The role of spermicides, sponges, and diaphragms for preventing STDs among men has not been studied.

Nonbarrier Contraception, Surgical Sterilization, Hysterectomy

Women who are not at risk for pregnancy may incorrectly perceive themselves to be at no risk for STDs, including HIV infection. Nonbarrier contraceptive methods offer no protection against HIV or other STDs. Women using hormonal contraception (oral contraceptives, Norplant™ , Depo-Provera™), who have been surgically sterilized or who have had hysterectomies should be counseled regarding the use of condoms and the risk for STDs, including HIV infection.

Prevention Messages

Preventing the spread of STDs requires that persons at risk for transmitting or acquiring infections change their behaviors. When risks have been identified, the health-care provider has an opportunity to deliver prevention messages. Counseling skills are essential to the effective delivery of prevention messages (i.e., respect, compassion, and a nonjudgmental attitude). Techniques that can be effective in developing rapport with the patient include using open-ended questions, using language that the patient understands, and reassuring the patient that treatment will be provided regardless of considerations such as ability to pay, citizenship or immigration status, language spoken, or lifestyle.

Prevention messages should be tailored to the patient, with consideration given to his or her specific risks. Messages should include a description of measures, such as the following, that the person can take to avoid acquiring or transmitting STDs:

- The most effective way to prevent sexual transmission of HIV infection and other STDs is to avoid sexual intercourse with an infected partner.

- If a person chooses to have sexual intercourse with a partner whose infection status is unknown or who is infected with HIV or other STDs, men should use a new latex condom with each act of intercourse.
- When a male condom cannot be used, couples should consider using a female condom.

Injection Drug Users

Prevention messages appropriate for injection drug users are the following:

- Enroll or continue in a drug treatment program.
- Do not, under any circumstances, use injection equipment (needles, syringes) that has been used by another person.
- Persons who continue to use injection equipment that has been used by other persons should first clean the equipment with bleach and water. (Disinfecting with bleach does not sterilize the equipment and does not guarantee that HIV is inactivated. However, thoroughly and consistently cleaning injection equipment with bleach should reduce the rate of HIV transmission when equipment is shared.)

HIV Prevention Counseling

Knowledge of one's HIV status and appropriate counseling are thought to play an important role in initiating behavior change. Counseling associated with HIV testing has two main components: pretest and posttest counseling.

During *pretest counseling*, the clinician should conduct a personalized risk assessment, explain the meaning of positive and negative test results, ask for informed consent for the HIV test, and help the person to develop a realistic, personalized risk reduction plan.

During *posttest counseling*, the clinician should inform the patient of the results, review the meaning of the results, and reinforce prevention messages. If the patient is HIV positive, posttest counseling should include referral for follow-up medical services and for social and psychological services, if needed. HIV- seronegative persons at continuing risk for HIV infection also may benefit from referral for additional counseling and prevention services.

HIV counseling is considered to be an important HIV-prevention strategy, although its efficacy in reducing risk behavior is still under evaluation. By ensuring that counseling is empathic and "client-centered," clinicians will be able to develop a realistic appraisal of the person's risk and help him or her to develop a specific and realistic HIV-prevention plan (*2*).

Partner Notification and Management of Sex Partners

Patients with STDs should ensure that their sex partners, including those without symptoms, are referred for evaluation. Providers should be prepared to assist in that effort. In most circumstances, partners of patients with STDs should be examined.

When a diagnosis of a treatable STD is considered likely, appropriate antibiotics should be administered even though there may be no clinical signs of infection and before laboratory test results are available. In most states, the local or state health department can assist in notifying the partners of patients with selected STDs, especially HIV, syphilis, gonorrhea, and chlamydia.

Breaking the chain of transmission is crucial to STD control. For treatable STDs, further transmission and reinfection can be prevented by referral of sex partners for diagnosis, treatment, and counseling. The following two strategies are used for partner notification: a) patient referral (index patients notify their partners), and b) provider referral (partners named by infected patients are notified and counseled by health department staff). When a physician refers an infected person to a local or state health department, trained professionals may interview the patient to obtain names and locating information about all of his or her sex partners. Every health department protects the privacy of patients in partner notification activities. Because of the advantage of confidentiality, many patients prefer that public health officials notify partners.

If a patient with HIV infection refuses to notify partners while continuing to place them at risk, the physician has an ethical and legal responsibility to inform persons that they are at risk of HIV infection. This duty-to-warn may be most applicable to primary care physicians, who often have knowledge about a patient's social and familial relationships. The decision to invoke the duty-to-warn measure should be a last resort—applicable only in cases in which all efforts to persuade the patient to disclose positive test results to those who need to know have failed.

Although compelling ethical, theoretical, and public health reasons exist to undertake partner notification, the efficacy of partner notification as an STD prevention strategy is under evaluation, and its effectiveness may be disease-specific.

Clinical guidelines for sex partner management and recommendations for partner notification for specific STDs are included for each STD addressed in this report.

Reporting and Confidentiality

The accurate identification and timely reporting of STDs form an integral part of successful disease control. Reporting assists local health authorities in identifying sex partners who may be infected. Reporting also is important for assessing morbidity trends. *STD/HIV and acquired immunodeficiency syndrome (AIDS) cases should be reported in accordance with local statutory requirements and in a timely manner*.

Syphilis, gonorrhea, and AIDS are reportable diseases in every state. The requirements for reporting other STDs and asymptomatic HIV infection differ from state to state, and clinicians should be familiar with local STD reporting requirements.

Reporting may be provider- and/or laboratory-based. Clinicians who are unsure of local reporting requirements should seek advice from local health departments or state STD programs.

STD and HIV reports are held in strictest confidence and in many jurisdictions are protected by statute from subpoena. Further, before any follow-up of a positive STD test is conducted by program representatives, these persons consult with the patient's health-care provider to verify the diagnosis and treatment.

SPECIAL POPULATIONS

Pregnant Women

Intrauterine or perinatally transmitted STDs can have fatal or severely debilitating effects on a fetus. Pregnant women and their sex partners should be questioned about STDs and should be counseled about the possibility of neonatal infections.

Recommended Screening Tests

The following screening tests are recommended for pregnant women:

- A serologic test for syphilis

All women should be screened serologically for syphilis during the early stages of pregnancy. In populations in which utilization of prenatal care is not optimal, rapid plasma reagin (RPR)-card test screening and treatment, if that test is reactive, should be performed at the time a pregnancy is diagnosed. For patients at high risk, screening should be repeated in the third trimester and again at delivery. (Some states mandate screening all women at delivery.) No infant should be discharged from the hospital without the syphilis serologic status of its mother having been determined at least once during pregnancy and, preferably, again at delivery. Any woman who delivers a stillborn infant after 20 weeks gestation should be tested for syphilis.

- A serologic test for hepatitis B surface antigen (HBsAg)
- A test for *Neisseria gonorrhoeae*
- A test for *Chlamydia trachomatis*

Pregnant women at increased risk (<25 years of age, or with a new or more than one partner) should be tested and treated, if necessary, during the third trimester to prevent maternal postnatal complications and chlamydial infection among infants. Screening during the first trimester might permit prevention of adverse effects of chlamydia during pregnancy. However, the evidence for adverse effects during pregnancy is minimal. If screening is performed only during the first trimester, a longer period exists for acquiring infection before delivery.

- A test for HIV infection

Patients with risk factors for HIV or with a high-risk sex partner should be tested for HIV infection. Some authorities recommend offering HIV tests to all pregnant women, particularly in areas of high HIV seroprevalence. Appropriate counseling should be provided, and informed consent for HIV testing should be obtained.

Other Issues

Other STD-related issues to be considered are as follows:

- Pregnant women with primary genital herpes, HBV, primary cytomegalovirus (CMV) infection, group B streptococcal infection, and women who have syphilis and who are allergic to penicillin may need to be referred to an expert for management.
- In the absence of lesions during the third trimester, routine serial cultures for herpes simplex virus (HSV) are not indicated for women with a history of recurrent genital herpes. However, obtaining cultures from such women at the time of delivery may be useful in guiding neonatal management. "Prophylactic" caesarean section is not indicated for women who do not have active genital lesions at the time of delivery.
- The presence of genital warts is not considered an indication for caesarean section.

For a more detailed discussion of these issues, as well as for infections not transmitted sexually, refer to *Guidelines for Perinatal Care* (*3*).

NOTE: The sources for these guidelines for screening of pregnant women include *Guide to Clinical Preventive Services* (*4*), *Guidelines for Perinatal Care* (*3*), and *Recommendations for the Prevention and Management of* Chlamydia trachomatis *Infections, 1993* (*5*). These sources are not entirely consistent in their recommendations. The *Guide to Clinical Preventive Services* recommends routine testing for gonorrhea at the first prenatal visit, with repeat testing for those at increased risk, and selective screening for chlamydia at the first prenatal visit. The *Guidelines for Perinatal Care* does not specifically recommend screening for either gonorrhea or chlamydia, but recommends screening for STDs in the third trimester for women at risk. The *Recommendations for the Prevention and Management of* Chlamydia trachomatis *Infections, 1993* recommend screening for chlamydia during the third trimester for all pregnant women <25 years of age or for any woman with a new sex partner or multiple partners. Recommendations to screen pregnant women for STDs are based on disease severity and sequelae, prevalence in the population, costs, medical/legal considerations (including state laws), and other factors. The screening recommendations in this report are more comprehensive (i.e., if followed, more women will be screened for more STDs than would be screened by following other recommendations) and are compatible with other CDC guidelines. Physicians should select a screening strategy compatible with their practice population and setting.

Adolescents

Health-care providers who provide care for patients with sexually transmitted infections should be aware of several issues that relate specifically to adolescents. The rates of many STDs are highest among adolescents; e.g., the rate of gonorrhea is highest among persons 15–19 years of age. Clinic-based studies have demonstrated that the prevalence of chlamydial infections, and possibly of HPV infections, also is highest among adolescents.

All adolescents in the United States can consent to the confidential diagnosis and treatment of STDs. Medical care for these conditions can be provided to adolescents without parental consent or knowledge. Furthermore, in many states adolescents can consent to HIV counseling and testing.

The style and content of counseling and health education should be adapted for adolescents. Discussions should be appropriate for the patient's developmental level and should identify risky behaviors, such as sex and drug use behaviors. Care and counseling should be direct and nonjudgmental.

Children

Management of children with STDs requires close cooperation between the clinician, laboratory, and child-protection authorities. Investigations, when indicated, should be initiated promptly. Some diseases, such as gonorrhea, syphilis, and chlamydia, if acquired after the neonatal period, are almost 100% indicative of sexual contact. For other diseases, such as HPV infection and vaginitis, the association with sexual contact is not as clear (see Sexual Assault and STDs).

Persons with HIV Infection

The management of patients infected with HIV and patients infected with both HIV and other STDs presents complex clinical and behavioral issues. For that reason, these issues are addressed throughout this report (see HIV Infection and Early Intervention and specific disease sections). Because of its effects on the immune system, HIV infection may alter the natural histories of many STDs and the effect of antimicrobial therapy. Such effects are likely to occur as the degree of immunosuppression advances; frequent or severe episodes of some STDs or failure to respond appropriately to therapy should lead the health-care provider to consider HIV infection as a cause. Close clinical follow-up of patients infected with both HIV and STDs is imperative.

STD infection among patients with or without HIV is a sentinel event, often indicating unprotected sexual activity. Further patient counseling is needed in such situations.

HIV INFECTION AND EARLY INTERVENTION

Infection with HIV produces a spectrum that progresses from no apparent illness to AIDS as a late manifestation. The pace of disease progression is variable. The median time between infection with HIV and the development of AIDS among adults is 10 years, with a range from a few months to ≥12 years. Most adults and adolescents infected with HIV remain symptom-free for long periods, but viral replication can be detected in asymptomatic persons and increases substantially as the immune system deteriorates. Most people who are infected with HIV will eventually have symptoms related to the infection. In cohort studies of adults infected with HIV, data indicated that symptoms developed in 70%–85% of infected adults, and AIDS developed in 55%–62% within 12 years after infection. Additional cases are expected to occur among those who have remained AIDS-free for >12 years.

Greater awareness of risky behaviors by both patients and health-care providers has led to increased testing for HIV and earlier diagnosis of early HIV infection, often before symptoms develop (though emotional or psychological problems may occur). Such early identification of HIV infection is important for several reasons. Treatments are available to slow the decline of immune system function. Persons who are infected with HIV and altered immune function also are at increased risk for infections such as tuberculosis (TB), bacterial pneumonia, and *Pneumocystis carinii* pneumonia (PCP), for which preventive measures are available. Because of its effect on the immune system, HIV affects the diagnosis, evaluation, treatment, and follow-up of many other diseases and may affect the efficacy of antimicrobial therapy for some STDs. Close clinical follow-up after treatment for STDs is imperative.

During early infection, persons with HIV and their families can be educated about the disease and become linked with a support network that addresses their needs and with care systems effective in maintaining good health and delaying the onset of symptoms. Early diagnosis also offers the opportunity for counseling and for assistance in preventing the transmission of HIV infection to others.

For the purpose of these recommendations, early intervention for HIV is defined as care for persons infected with HIV who are without symptoms. However, recently detected HIV infection may not have been recently acquired. Persons newly diagnosed with HIV may be at many different stages of the infection. Therefore, early intervention also involves assuming the responsibility for coordinating care and for arranging access to resources necessary to meet the medical, psychological, and social needs of persons with more advanced HIV infection.

Diagnostic Testing for HIV-1 and HIV-2

HIV infection is most often diagnosed by using HIV-1 antibody tests. Antibody testing begins with a sensitive screening test such as the enzyme-linked immunosorbent assay (ELISA) or a rapid assay. If confirmed by Western blot or other supplemental test, a positive antibody test means that a person is infected with HIV and is capable of transmitting the virus to others. HIV antibody is detectable in ≥95% of patients within 6 months of infection. Although a negative antibody test usually means a person is not infected, antibody tests cannot rule out infection that occurred <6 months before the test.

Since there is transplacental passage of maternal HIV antibody, antibody tests for HIV are expected to be positive in the serum of both infected and uninfected infants born to a seropositive mother. Passively acquired HIV antibody falls to undetectable levels among most infants by 15 months of age. A definitive determination of HIV infection for an infant <15 months of age should be based either on the presence of antibody to HIV in conjunction with a compatible immunologic profile and clinical course or on laboratory evidence of HIV in blood or tissues by culture, nucleic acid, or antigen detection.

Specific recommendations for the diagnostic testing of HIV are listed below:

- Informed consent must be obtained before an HIV test is performed. Some states require written consent. See HIV Prevention Counseling for a discussion of pretest and posttest counseling.

- Positive screening tests for HIV antibody must be confirmed by a more specific confirmatory test (either the Western blot assay or indirect immunofluorescence assay [IFA]) before being considered definitive for confirming HIV infection.
- Persons with positive HIV tests must receive medical and psychosocial evaluation and monitoring services, or be referred for these services.

The prevalence of HIV-2 in the United States is extremely low, and CDC does not recommend routine testing for HIV-2 in settings other than blood centers, unless demographic or behavioral information suggests that HIV-2 infection might be present. Those at risk for HIV-2 infection include persons from a country in which HIV-2 is endemic or the sex partners of such persons. (As of July 1992, HIV-2 was endemic in parts of West Africa and an increased prevalence of HIV-2 had been reported in Angola, France, Mozambique, and Portugal.) Additionally, testing for HIV-2 should be conducted when there is clinical evidence or suspicion of HIV disease in the absence of a positive test for antibodies to HIV-1 (*6*).

Counseling for Patients with HIV Infection

Behavioral and psychosocial services are an integral part of HIV early intervention. Patients usually experience emotional distress when first being informed of a positive HIV test result, and also later when notified of changes in immunologic markers, when antiviral or prophylactic therapy is initiated, and when symptoms develop. Patients face several major adaptive challenges: a) accepting the possibility of a curtailed life span, b) coping with others' reactions to a stigmatizing illness, c) developing strategies for maintaining physical and emotional health, and d) initiating changes in behavior to prevent HIV transmission. Many patients also require assistance with making reproductive choices, gaining access to health services and health insurance, and confronting employment discrimination.

Interrupting HIV transmission depends upon changes in behavior by those persons at risk for transmitting or acquiring infection. Though some viral culture studies suggest that antiviral treatment reduces viral burden, clinical data are insufficient to determine whether therapy might reduce the probability of transmission. Infected persons, as potential sources of new infections, must receive extra attention and support to help break chains of transmission and to prevent infection of others. Targeting behavior change programs toward HIV-infected persons and their sex partners, or those with whom they share needles, is an important adjunct to current AIDS prevention efforts.

Specific recommendations for counseling patients with HIV infection are listed below:

- Persons who test positive for HIV antibody should be counseled by a person who is able to discuss the medical, psychological, and social implications of HIV infection.
- Appropriate social support and psychological resources should be available, either on site or through referral, to assist patients in coping with emotional distress.

- Persons who continue to be at risk for transmitting HIV should receive assistance in changing or avoiding behaviors that can transmit infection to others.

Initial Evaluation and Planning for Care

Practice settings for offering early HIV care are variable, depending upon local resources and needs. Primary-care providers and outpatient facilities must ensure that appropriate resources are available for each patient and must avoid fragmentation of care; it is preferable for persons with HIV infection to receive care from a single source that is able to provide comprehensive care for all stages of HIV infection. But the limited availability of such resources often results in the need to coordinate care among outpatient, inpatient, and specialist providers in different locations. Because of the progressive nature of HIV and the increased risk for bacterial infections, including TB—even before HIV infection becomes advanced—it is essential to establish specific provisions for handling the medical, psychological, and social problems likely to arise at any stage of infection. An important component of early intervention is effective linkage with referral settings where off-hours care and specialty services are available. Development of an appropriate plan for care involves the following:

- Identification of patients in need of immediate medical care (e.g., patients with symptomatic HIV infection or emotional crisis) and of those in need of antiretroviral therapy or prophylaxis for opportunistic infections (e.g., PCP).
- Evaluation for the presence of diseases associated with HIV, such as TB and STDs.
- Administration of recommended vaccinations.
- Case management or referral for case management.
- Counseling (see Counseling for Patients with HIV Infection).

The CD4+ T-lymphocyte count is the best laboratory indicator of clinical progression, and comprehensive management strategies for HIV infection are typically stratified by CD4 count. Either the absolute number or the percentage of CD4+ T cells may be determined. CD4+ percentage is more consistent than absolute CD4+ count with successive measurements for the same person and less variable with delays in specimen processing. However, most clinical trials have used absolute CD4+ count to evaluate the need for and timing of therapeutic interventions. Patients with CD4+ counts >500/μL usually do not demonstrate evidence of clinical immunosuppression. Patients with 200–500 CD4+ cells/μL are more likely to develop HIV-related symptoms and to require medical intervention. Patients with CD4+ counts <200 cells/μL, and those with higher CD4+ counts who develop thrush or unexplained fever (temperature >37.8 C for ≥2 weeks) are at increased risk for developing complicated HIV disease. Such patients should be managed in a comprehensive treatment setting with access to specialty resources and hospitalization.

Providers unable to offer therapeutic management of HIV may use the initial evaluation to identify the need for prompt referral to appropriate resources. The initial evaluation of HIV-positive patients should include the following essential components:

- A detailed history, including sexual history, substance abuse history, and a review of systems for specific HIV-related symptoms.
- A physical examination; for females, this examination should include a gynecologic examination.
- For females, testing for *N. gonorrhoeae*, *C. trachomatis*, a Papanicolaou (Pap) smear, and wet mount examination of vaginal secretions.
- A syphilis serology.
- A CD4+ T-lymphocyte analysis.
- Complete blood and platelet counts.
- A purified protein derivative (PPD) tuberculin skin test by the Mantoux method and anergy testing with two delayed-type hypersensitivity (DTH) antigens (*Candida*, mumps, or tetanus toxoid) administered by the Mantoux method or a multipuncture device.
- A thorough psychosocial evaluation, including ascertainment of behavioral factors indicating risk for transmitting HIV and elucidation of information about any partners who should be notified about possible exposure to HIV.

Preventive Therapy for TB

Studies conducted among persons with and without HIV infection have suggested that HIV infection can depress tuberculin reactions before signs and symptoms of HIV infection develop. Cutaneous anergy (defined as skin test response of ≤3 mm to all DTH antigens) may be present among ≥10% of asymptomatic persons with CD4+ counts >500 cells/μL, and among >60% of persons with CD4+ counts <200.

HIV-positive persons with a PPD reaction ≥5 mm induration are considered to be infected with *M. tuberculosis* and should be evaluated for preventive treatment with isoniazid after active TB has been excluded. Anergic persons whose risk for tuberculous infection is estimated to be ≥10%, based on available prevalence data, also should be considered for preventive therapy. For further details regarding evaluation of patients for TB, refer to *Purified Protein Derivative (PPD-tuberculin anergy) and HIV Infection: Guidelines for Anergy Testing and Management of Anergic Persons at Risk of Tuberculosis* (*7*).

The preliminary results from a randomized clinical trial suggest that treatment with isoniazid is effective for preventing active TB among HIV-infected persons. The usual regimen is isoniazid 10 mg/kg daily, up to a maximum adult dose of 300 mg daily. Twelve months of isoniazid preventive treatment is recommended for persons with HIV infection. For further details regarding preventive therapy for TB, refer to *The Use of Preventive Therapy for Tuberculous Infection in the United States* (*8*) and *Management of Persons Exposed to Multidrug-Resistant Tuberculosis* (*9*).

Recommended Immunizations for Adults and Adolescents

Specific recommendations for immunization of persons infected with HIV are listed below:

- Pneumococcal vaccination and an annual influenza vaccination should be administered.
- Persons at increased risk for acquiring HBV and who lack evidence of immunity may receive a three-dose schedule of hepatitis B vaccine, with postvaccination serologic testing between 1 and 6 months after the vaccination series.

Recommendations for vaccinating HIV-infected persons are based on expert opinions and consensus of the Advisory Committee on Immunization Practices (ACIP). No clinical data exist to document the efficacy of inactivated vaccines among HIV-infected persons, and pneumococcal vaccine failures have been reported. However, the use of inactivated vaccines may be beneficial for persons with HIV infection and there is no evidence that they are harmful. Immunogenicity studies have suggested a generally poorer response among HIV-infected persons, with higher response rates among asymptomatic persons than among those with advanced HIV disease.

Current evidence indicates that HIV infection does not increase susceptibility to HBV, nor does it increase the severity of clinical disease. The presence of HIV infection is not an indication for hepatitis B vaccine, but HIV-infected persons are at increased risk for becoming chronic carriers after hepatitis B infection. Because the routes of transmission of HBV parallel those of HIV, efforts to modify risky behaviors must be the primary focus of prevention efforts. However, vaccine should be administered to HIV-infected patients who continue to have a high likelihood for HBV exposure.

Persons with HIV infection also are at increased risk for invasive *Haemophilus influenzae* type B (Hib) disease and for complications from measles. Immunization against Hib and measles should be considered for asymptomatic HIV-infected persons who may have an increased risk for exposure to these infections. For further details on immunization of HIV-infected patients, refer to *Recommendations of the Advisory Committee on Immunization Practices (ACIP): Use of Vaccines and Immune Globulins in Persons with Altered Immunocompetence* (*10*).

Follow-Up Evaluation

There have been no controlled studies to serve as the basis for recommending specific follow-up tests or follow-up intervals. The suggested frequency of monitoring is based on the slow decrease in CD4+ counts observed among patients in cohort studies, but should be modified depending on the patient's psychological status, the presence of symptoms, or both. Repeat evaluation for STDs also is important in the follow-up of HIV-infected persons and should be performed on all persons who continue to be sexually active. Follow-up evaluation should be performed every 6 months and should include the following:

- An interim history and physical examination;
- A complete blood count, platelet count, and lymphocyte subset analysis;

- Re-evaluation of psychosocial status and behavioral factors indicating risk for transmitting HIV.

To follow CD4+ measurements, providers should use the same laboratory and, optimally, obtain each specimen at the same time each day. When unexpected or discrepant results are obtained or when major treatment decisions are to be made, health-care providers should consider repeating the CD4+ measurement after at least 1 week.

More frequent laboratory monitoring, every 3–4 months, is indicated if CD4+ results indicate a patient is close to a point when a clinical intervention may be indicated.

Continuing Management of Patients with Early HIV Infection

Providing comprehensive, continuing management of patients with early HIV infection can include additional diagnostic studies (e.g., chest x-ray, serum chemistry, antibody testing for toxoplasmosis and hepatitis B), antiretroviral therapy and monitoring, and PCP prophylaxis. Treatment of HIV infection and prophylaxis against opportunistic infections continue to evolve rapidly. This treatment should be undertaken in consultation with physicians who are familiar with the care of persons with HIV infection. The complete therapeutic management of HIV infection is beyond the scope of this document.

Antiretroviral Therapy

The optimal time for initiating antiretroviral therapy has not yet been established. Zidovudine (ZDV) at a dose of 500 mg/day (100 mg orally every 4 hours while the patient is awake) has been recommended for symptomatic persons with <500 CD4+ T-cells/μL, and for asymptomatic persons with <300 CD4+ T-cells/μL. This recommendation is based on results of short-term follow-up in three randomized clinical trials demonstrating that the initiation of ZDV therapy delays progression to advanced disease. Evidence for improved long-term survival after early treatment is less conclusive. The effects of ZDV may be transient, possibly because of the development of viral resistance or other factors. Sequential or combination therapy with other antiretroviral agents could be more efficacious.

Whether other daily dosages, dose schedules, or dosages based on body weight would result in greater therapeutic benefit or few side effects is not known. Providers should work with patients to design a treatment strategy that is both clinically sound and appropriate for each individual patient's needs, priorities, and circumstances. An initial dose of 600 mg in divided doses has been recommended by a panel of experts convened by the National Institute of Allergy and Infectious Diseases (NIAID). Preliminary data suggest ZDV can yield therapeutic results when the dosing interval is increased to 8 hours, and at doses of 200 mg three times daily. Antiretroviral efficacy is diminished at doses <300 mg/day, and it has been suggested that higher oral doses may be required to achieve effective levels in the central nervous system.

There are no data to support the use of antiretroviral drugs other than ZDV as initial therapy. Didanosine (DDI) is recommended for persons who are intolerant of ZDV or who experience progression of symptoms despite ZDV. Two 100 mg tablets of DDI are recommended every 12 hours for persons who weigh ≥ 60 kg; the recommended dose for adults <60 kg is one 100 mg tablet and one 25 mg tablet every 12 hours. Two tablets are recommended at each dose so that adequate buffering is provided to prevent gastric acid degradation of the drug.

Benefits have been reported from other antiretroviral regimens, including treatment with combinations of ZDV, DDC (dideoxycytidine [zalcitabine]), and DDI, or switching therapy to DDI after long-term therapy with ZDV. Experience with these alternatives is insufficient to serve as a basis for recommendations. Providers managing patients who are taking antiretroviral therapy should be familiar with evidence being developed in several clinical trials. Current information is available from the NIAID AIDS Clinical Trials Information Service, 1-800-TRIALS-A.

Side effects that are serious (e.g., anemia, cytopenia, pancreatitis, and peripheral neuropathy) and uncomfortable (e.g., nausea, vomiting, headaches, and insomnia) are common during antiretroviral therapy. Although hematologic toxicity from ZDV is less common with the lower doses recommended, approximately 2% of patients who receive 500 mg/day manifest severe anemia by the 18th month of treatment—most within the 3rd through 8th month of treatment. Careful hematologic monitoring of patients receiving ZDV is recommended.

PCP Prophylaxis

Adults and adolescents with <200 CD4+ T-cells/μL or with constitutional symptoms, such as thrush or unexplained fever >100 F for ≥2 weeks, and any patient with a previous episode of PCP should receive PCP prophylaxis. Prophylaxis should be continued for the lifetime of the patient.

Based upon evidence from randomized controlled clinical trials, the Public Health Service Task Force on Antipneumocystis Prophylaxis has recommended the following regimens for PCP prophylaxis among adults and adolescents:

- Oral trimethoprim-sulfamethoxazole (TMP-SMX) at a dose of one double-strength tablet (800 mg SMX and 160 mg TMP) orally once a day.
- For patients unable to tolerate TMP-SMX: aerosol pentamidine administered by either the Respirgard II nebulizer regimen (300 mg once a month) or the Fisoneb nebulizer (initial loading regimen of five 60 mg doses during a 2-week period, followed by a 60 mg dose every 2 weeks).

The efficacy of alternatives for patients unable to tolerate TMP-SMX, including dapsone 100 mg orally once a day and sulfa desensitization, has not been studied extensively. For further details on PCP prophylaxis, refer to *Recommendations for Prophylaxis Against* Pneumocystis carinii *pneumonia for adults and adolescents infected with human immunodeficiency virus* (*11*).

Management of Sex Partners

The rationale for implementing partner notification is that early diagnosis and treatment of HIV infection may reduce morbidity and offers the opportunity to encourage risk-reducing behaviors. Two complementary notification processes, patient referral and provider referral, can be used to identify partners. With patient referral, patients inform their own partners directly of their exposure to HIV infection. With provider referral, trained health department personnel locate partners on the basis of the names, descriptions, and addresses provided by the patient. During the notification process, the anonymity of patients is protected; their names are not revealed to sex or needle-sharing partners who are notified. Many state health departments provide assistance with provider referral partner notification upon request.

One randomized trial suggested that provider referral is more effective in notifying partners than patient referral. In that trial, 50% of partners in the provider referral group were notified, yet only 7% of partners were notified by subjects in the patient referral group. However, few data demonstrate whether behavioral change takes place as a result of partner notification and many patients are reluctant to disclose the names of partners because of concern about discrimination, disruption of relationships, and loss of confidentiality for the partners.

When referring to those persons infected with HIV, the term "partner" includes not only sex partners but also injecting drug users who share needles or other injecting equipment. Partner notification is a means of identifying and concentrating risk-reduction efforts on persons at high risk for contracting or transmitting HIV infection. Partner notification for HIV infection must be confidential and should depend upon the voluntary cooperation of the patient.

Specific recommendations for implementing partner notification procedures are listed below:

- Persons who are HIV-positive should be encouraged to notify their partners and to refer them for counseling and testing. Providers should assist in this process, if desired by the patient, either directly or through referral to health department partner notification programs.
- If patients are unwilling to notify their partners or if it cannot be assured that their partners will seek counseling, physicians or health department personnel should use confidential procedures to assure that the partners are notified.

Special Considerations

Pregnancy

Women who are HIV-infected should be specifically informed about the risk for perinatal infection. Current evidence indicates that 15%–39% of infants born to HIV-infected mothers are infected with HIV, and the virus also can be transmitted from an infected mother by breastfeeding. Pregnancy among HIV-infected patients does not appear to increase maternal morbidity or mortality.

Women should be counseled about their options regarding pregnancy. The objective of counseling is to provide HIV-infected women with current information for making reproductive decisions, analogous to the model used in genetic counseling. Contraceptive, prenatal, and abortion services should be available on site or by referral.

Minimal information is available on the use of ZDV or other antiretroviral drugs during pregnancy. Trials to evaluate its efficacy in preventing perinatal transmission and its safety during pregnancy are being conducted. A case series of 43 pregnant women has been published; dosages of ZDV ranged from 300 to 1,200 mg/day. ZDV was well tolerated and there were no malformations among the newborns in this series. Although this observation is encouraging, this series of negative case reports cannot be used to infer that ZDV is not teratogenic.

Burroughs Wellcome Co. and Hoffmann-LaRoche, Inc., in cooperation with CDC, maintain a registry to assess the effects of the use of ZDV and DDC during pregnancy. Women who receive either ZDV or DDC during pregnancy should be reported to this registry (1-800-722-9292, ext. 58465).

HIV Infection Among Infants and Children

Infants and young children with HIV infection differ from adults and adolescents with respect to the diagnosis, clinical presentation, and management of HIV disease. For example, total lymphocytes and absolute CD4+ cell counts are much higher in infants and children than in healthy adults and are age dependent. Specific indications and dosages for both antiretroviral and prophylactic therapy have been developed for children (*12*). Other modifications must be made in health services that are recommended for infants and children, such as avoiding vaccination with live oral polio vaccine when a child (or close household contact) is infected with HIV.

State laws differ regarding consent of minor persons (<18 years of age) for HIV counseling and testing, evaluation, treatment services, and participation in clinical trials. Although most adolescents receive adult doses of antiretroviral and prophylactic therapy, there are no data on modification of these dosages during puberty. Management of infants, children, and adolescents—who are known or suspected to be infected with HIV—requires referral to, or close consultation with, physicians familiar with the manifestations and treatment of pediatric HIV infection.

DISEASES CHARACTERIZED BY GENITAL ULCERS

Management of the Patient with Genital Ulcers

In the United States, most patients with genital ulcers have genital herpes, syphilis, or chancroid. The relative frequency of each varies by geographic area and patient population, but in most areas of the United States genital herpes is the most common of these diseases. More than one of these diseases may be present among at least 3%–10% of patients with genital ulcers. Each disease has been associated with an increased risk for HIV infection.

A diagnosis based only on history and physical examination is often inaccurate. Therefore, evaluation of all persons with genital ulcers should include a serologic test for syphilis and possibly other tests. Although ideally all of these tests should be conducted for each patient with a genital ulcer, use of such tests (other than a serologic test for syphilis) may be based on test availability and clinical or epidemiologic suspicion. Specific tests for the evaluation of genital ulcers are listed below:

- Darkfield examination or direct immunofluorescence test for *Treponema pallidum*,
- Culture or antigen test for HSV, and
- Culture for *Haemophilus ducreyi*.

HIV testing should be considered in the management of patients with genital ulcers, especially for those with syphilis or chancroid.

A health-care provider often must treat a patient before test results are available (even after complete testing, at least one quarter of patients with genital ulcers have no laboratory-confirmed diagnosis). In that circumstance, the clinician should treat for the diagnosis considered most likely. Many experts recommend treatment for both chancroid and syphilis if the diagnosis is unclear or if the patient resides in a community in which chancroid morbidity is notable (especially when diagnostic capabilities for chancroid and syphilis are not ideal).

Chancroid

Chancroid is endemic in many areas of the United States and also occurs in discrete outbreaks. Chancroid has been well established as a co-factor for HIV transmission and a high rate of HIV infection among patients with chancroid has been reported in the United States and in other countries. As many as 10% of patients with chancroid may be coinfected with *T. pallidum* or HSV.

Definitive diagnosis of chancroid requires identification of *H. ducreyi* on special culture media that are not commercially available; even using these media, sensitivity is no higher than 80% and is usually lower. A probable diagnosis, for both clinical and surveillance purposes, may be made if the person has one or more painful genital ulcers, and a) no evidence of *T. pallidum* infection by darkfield examination of ulcer exudate or by a serologic test for syphilis performed at least 7 days after onset of ulcers, and b) either the clinical presentation of the ulcer(s) is not typical of disease caused by HSV or the HSV test results are negative. The combination of a painful ulcer with tender inguinal adenopathy (which occurs among one-third of patients) is suggestive of chancroid, and when accompanied by suppurative inguinal adenopathy is almost pathognomonic.

Treatment

Successful treatment cures infection, resolves clinical symptoms, and prevents transmission to others. In extensive cases, scarring may result despite successful therapy.

Recommended Regimens

Azithromycin 1 g orally in a single dose

or

Ceftriaxone 250 mg intramuscularly (IM) in a single dose

or

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

All three regimens are effective for the treatment of chancroid among patients without HIV infection. Azithromycin and ceftriaxone offer the advantage of single-dose therapy. Antimicrobial resistance to ceftriaxone and azithromycin has not been reported. Although two isolates resistant to erythromycin were reported from Asia a decade ago, similar isolates have not been reported.

Alternative Regimens

Amoxicillin 500 mg plus **clavulanic acid** 125 mg orally 3 times a day for 7 days,

or

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

NOTE: Ciprofloxacin is contraindicated for pregnant and lactating women, children, and adolescents ≤17 years of age.

These regimens have not been evaluated as extensively as the recommended regimens; neither has been studied in the United States.

Other Management Considerations

Patients should be tested for HIV infection at the time of diagnosis. Patients also should be tested 3 months later for both syphilis and HIV, if initial results are negative.

Follow-Up

Patients should be re-examined 3–7 days after initiation of therapy. If treatment is successful, ulcers improve symptomatically within 3 days and improve objectively within 7 days after therapy. If no clinical improvement is evident, the clinician must consider whether a) the diagnosis is correct, b) coinfection with another STD agent exists, c) the patient is infected with HIV, d) treatment was not taken as instructed, or e) the *H. ducreyi* strain causing infection is resistant to the prescribed antimicrobial. The time required for complete healing is related to the size of the ulcer; large ulcers may require ≥2 weeks. Clinical resolution of fluctuant lymphadenopathy is slower than that of ulcers and may require needle aspiration through adjacent intact skin—even during successful therapy.

Management of Sex Partners

Persons who had sexual contact with a patient who has chancroid within the 10 days before onset of the patient's symptoms should be examined and treated. The examination and treatment should be administered even in the absence of symptoms.

Special Considerations

Pregnancy

The safety of azithromycin for pregnant and lactating women has not been established. Ciprofloxacin is contraindicated during pregnancy. No adverse effects of chancroid on pregnancy outcome or on the fetus have been reported.

HIV Infection

Patients coinfected with HIV should be closely monitored. These patients may require courses of therapy longer than those recommended in this report. Healing may be slower among HIV-infected persons and treatment failures do occur, especially after shorter-course treatment regimens. Since data on therapeutic efficacy with the recommended ceftriaxone and azithromycin regimens among patients infected with HIV are limited, those regimens should be used among persons known to be infected with HIV only if follow-up can be assured. Some experts suggest using the erythromycin 7-day regimen for treating HIV-infected persons.

Genital Herpes Simplex Virus Infections

Genital herpes is a viral disease that may be recurrent and has no cure. Two serotypes of HSV have been identified: HSV-1 and HSV-2; most cases of genital herpes are caused by HSV-2. On the basis of serologic studies, approximately 30 million persons in the United States may have genital HSV infection.

Most infected persons never recognize signs suggestive of genital herpes; some will have symptoms shortly after infection and then never again. A minority of the total infected U.S. population will have recurrent episodes of genital lesions. Some cases of first clinical episode genital herpes are manifested by extensive disease that requires hospitalization. Many cases of genital herpes are acquired from persons who do not know that they have a genital infection with HSV or who were asymptomatic at the time of the sexual contact.

Randomized trials show that systemic acyclovir provides partial control of the symptoms and signs of herpes episodes when used to treat first clinical episodes, or when used as suppressive therapy. However, acyclovir neither eradicates latent virus nor affects subsequent risk, frequency, or severity of recurrences after administration of the drug is discontinued. Topical therapy with acyclovir is substantially less effective than the oral drug and its use is discouraged. Episodes of HSV infection among HIV-infected patients may require more aggressive therapy. Immunocompromised persons may have prolonged episodes with extensive disease. For these persons, infections caused by acyclovir-resistant strains require selection of alternate antiviral agents.

First Clinical Episode of Genital Herpes

Recommended Regimen

Acyclovir 200 mg orally 5 times a day for 7–10 days or until clinical resolution is attained.

First Clinical Episode of Herpes Proctitis

Recommended Regimen

Acyclovir 400 mg orally 5 times a day for 10 days or until clinical resolution is attained.

Recurrent Episodes

When treatment is instituted during the prodrome or within 2 days of onset of lesions, some patients with recurrent disease experience limited benefit from therapy. However, since early treatment can seldom be administered, most immunocompetent patients with recurrent disease do not benefit from acyclovir treatment, and it is not generally recommended.

Recommended Regimen

Acyclovir 200 mg orally 5 times a day for 5 days,

or

Acyclovir 400 mg orally 3 times a day for 5 days,

or

Acyclovir 800 mg orally 2 times a day for 5 days.

Daily Suppressive Therapy

Daily suppressive therapy reduces the frequency of HSV recurrences by at least 75% among patients with frequent recurrences (i.e., six or more recurrences per year). Suppressive treatment with oral acyclovir does not totally eliminate symptomatic or asymptomatic viral shedding or the potential for transmission. Safety and efficacy have been documented among persons receiving daily therapy for as long as 5 years. Acyclovir-resistant strains of HSV have been isolated from some persons receiving suppressive therapy, but these strains have not been associated with treatment failure among immunocompetent patients. *After 1 year of continuous suppressive therapy, acyclovir should be discontinued to allow assessment of the patient's rate of recurrent episodes.*

Recommended Regimen

Acyclovir 400 mg orally 2 times a day.

Alternative Regimen

Acyclovir 200 mg orally 3–5 times a day.

The goal of the alternative regimen is to identify for each patient the lowest dose that provides relief from frequently recurring symptoms.

Severe Disease

Intravenous (IV) therapy should be provided for patients with severe disease or complications necessitating hospitalization (e.g., disseminated infection that includes encephalitis, pneumonitis, or hepatitis).

Recommended Regimen

Acyclovir 5–10 mg/kg body weight IV every 8 hours for 5–7 days or until clinical resolution is attained.

Other Management Considerations

Other considerations for managing patients with genital HSV infection are as follows:

- Patients should be advised to abstain from sexual activity while lesions are present.
- Patients with genital herpes should be told about the natural history of the disease, with emphasis on the potential for recurrent episodes, asymptomatic viral shedding, and sexual transmission. Sexual transmission of HSV has been documented to occur during periods without evidence of lesions. Many cases are transmitted during such asymptomatic periods.

The use of condoms should be encouraged during all sexual exposures. The risk for neonatal infection should be explained to all patients—male and female—with genital herpes. Women of childbearing age who have genital herpes should be advised to inform health-care providers who care for them during pregnancy about their HSV infection.

Management of Sex Partners

Sex partners of patients who have genital herpes are likely to benefit from evaluation and counseling. Symptomatic sex partners should be managed in the same manner as any patient with genital lesions. However, the majority of persons with genital HSV infection do not have a history of typical genital lesions. These asymptomatic persons may benefit from evaluation and counseling; thus, even asymptomatic

partners should be queried about histories of typical and atypical genital lesions and encouraged to examine themselves for lesions in the future.

Commercially available HSV type-specific antibody tests have not demonstrated adequate performance characteristics; their use is not currently recommended. Sensitive and specific type-specific serum antibody assays now utilized in research settings might contribute to future intervention strategies. Should tests with adequate sensitivity and specificity become commercially available, it might be possible to accurately identify asymptomatic persons infected with HSV-2, to focus counseling on how to detect lesions by self-examination, and to reduce the risk for transmission to sex partners.

Special Considerations

Allergy, Intolerance, or Adverse Reactions

Effective alternatives to therapy with acyclovir are not available.

HIV Infection

Lesions caused by HSV are relatively common among patients infected with HIV. Intermittent or suppressive therapy with oral acyclovir may be needed.

The acyclovir dosage for HIV-infected persons is controversial, but experience strongly suggests that immunocompromised patients benefit from increased dosage. Regimens such as 400 mg orally 3 to 5 times a day, as used for other immunocompromised persons, have been found useful. Therapy should be continued until clinical resolution is attained.

For severe disease, IV acyclovir therapy may be required. If lesions persist among patients undergoing acyclovir treatment, resistance to acyclovir should be suspected. These patients should be managed in consultation with an expert. For severe disease because of proven or suspected acyclovir-resistant strains, hospitalization should be considered. Foscarnet, 40 mg/kg body weight IV every 8 hours until clinical resolution is attained, appears to be the best available treatment.

Pregnancy

The safety of systemic acyclovir therapy among pregnant women has not been established. Burroughs Wellcome Co., in cooperation with CDC, maintains a registry to assess the effects of the use of acyclovir during pregnancy. Women who receive acyclovir during pregnancy should be reported to this registry (1-800-722-9292, ext. 58465).

Current registry findings do not indicate an increase in the number of birth defects identified among the prospective reports when compared with those expected in the general population. Moreover, no consistent pattern of abnormalities emerges among retrospective reports. These findings provide some assurance in counseling women who have had inadvertent prenatal exposure to acyclovir. However, accumulated case histories comprise a sample of insufficient size for reaching reliable and definitive conclusions regarding the risks of acyclovir treatment to pregnant women and to their fetuses.

In the presence of life-threatening maternal HSV infection (e.g., disseminated infection that includes encephalitis, pneumonitis, or hepatitis), acyclovir administered IV is indicated. Among pregnant women without life-threatening disease, systemic acyclovir should not be used to treat recurrences nor should it be used as suppressive therapy near-term (or at other times during pregnancy) to prevent reactivation.

Perinatal Infections

Most mothers of infants who acquire neonatal herpes lack histories of clinically evident genital herpes. The risk for transmission to the neonate from an infected mother appears highest among women with first episode genital herpes near the time of delivery, and is low (≤3%) among women with recurrent herpes. The results of viral cultures during pregnancy do not predict viral shedding at the time of delivery, and such cultures are not routinely indicated.

At the onset of labor, all women should be carefully questioned about symptoms of genital herpes and should be examined. Women without symptoms or signs of genital herpes infection (or prodrome) may deliver their babies vaginally. Among women who have a history of genital herpes, or who have a sex partner with genital herpes, cultures of the birth canal at delivery may aid in decisions relating to neonatal management.

Infants delivered through an infected birth canal (proven by virus isolation or presumed by observation of lesions) should be followed carefully, including virus cultures obtained 24–48 hours after birth. Available data do not support the routine use of acyclovir as anticipatory treatment for asymptomatic infants delivered through an infected birth canal. Treatment should be reserved for infants who develop evidence of clinical disease and for those with positive postpartum cultures.

All infants with evidence of neonatal herpes should be treated with systemic acyclovir or vidarabine; refer to the *Report of the Committee on Infectious Diseases, American Academy of Pediatrics* (*13*). For ease of administration and to lower toxicity, acyclovir (30 mg/kg/day for 10-–14 days) is the preferred drug. The care of these infants should be managed in consultation with an expert.

Lymphogranuloma Venereum

Lymphogranuloma venereum (LGV), a rare disease in the United States, is caused by serovars L_1, L_2, or L_3 of *C. trachomatis*. The most common clinical manifestation of LGV among heterosexuals is tender inguinal lymphadenopathy that is most commonly unilateral. Women and homosexually active men may have proctocolitis or inflammatory involvement of perirectal or perianal lymphatic tissues resulting in fistulas and strictures. When patients seek care, most no longer have the self-limited genital ulcer that sometimes occurs at the site of inoculation. The diagnosis is usually made serologically and by exclusion of other causes of inguinal lymphadenopathy or genital ulcers.

Treatment

Treatment cures infection and prevents ongoing tissue damage, although tissue reaction can result in scarring. Buboes may require aspiration or incision and drainage through intact skin. Doxycycline is the preferred treatment.

Recommended Regimen

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

Alternative Regimens

Erythromycin 500 mg orally 4 times a day for 21 days

or

Sulfisoxazole 500 mg orally 4 times a day for 21 days or equivalent sulfonamide course.

Follow-Up

Patients should be followed clinically until signs and symptoms have resolved.

Management of Sex Partners

Persons who have had sexual contact with a patient who has LGV within the 30 days before onset of the patient's symptoms should be examined, tested for urethral or cervical chlamydial infection, and treated.

Special Considerations

Pregnancy

Pregnant and lactating women should be treated with the erythromycin regimen.

HIV infection

Persons with HIV infection and LGV should be treated following the regimens previously cited.

Syphilis

General Principles

Background

Syphilis is a systemic disease caused by *T. pallidum*. Patients with syphilis may seek treatment for signs or symptoms of primary infection (ulcer or chancre at site of infection), secondary infection (manifestations that include rash, mucocutaneous lesions, and adenopathy), or tertiary infection (cardiac, neurologic, ophthalmic, auditory, or gummatous lesions). Infections also may be detected during the latent stage by serologic testing. Patients with latent syphilis who are known to have been infected within the preceding year are considered to have early latent syphilis; others have late latent syphilis or syphilis of unknown duration. Theoretically, treatment for late latent syphilis (as well as tertiary syphilis) requires therapy of longer duration because organisms are dividing more slowly; however, the validity of this division and its timing are unproven.

Diagnostic Considerations and Use of Serologic Tests

Darkfield examinations and direct fluorescent antibody tests of lesion exudate or tissue are the definitive methods for diagnosing early syphilis. Presumptive diagnosis is possible with the use of two types of serologic tests for syphilis: a) nontreponemal (e.g., Venereal Disease Research Laboratory [VDRL] and RPR, and b) treponemal (e.g., fluorescent treponemal antibody absorbed [FTA-ABS] and microhemagglutination assay for antibody to *T. pallidum* [MHA-TP]). The use of one type of test alone is not sufficient for diagnosis. Nontreponemal test antibody titers usually correlate with disease activity, and results should be reported quantitatively. A fourfold change in titer, equivalent to a change of two dilutions (e.g., from 1:16 to 1:4, or from 1:8 to 1:32), is necessary to demonstrate a substantial difference between two nontreponemal test results that were obtained using the same serologic test. A patient who has a reactive treponemal test usually will have a reactive test for a lifetime, regardless of treatment or disease activity (15%–25% of patients treated during the primary stage may revert to being serologically nonreactive after 2–3 years). Treponemal test antibody titers correlate poorly with disease activity and should not be used to assess response to treatment.

Sequential serologic tests should be performed using the same testing method (e.g., VDRL or RPR) by the same laboratory. The VDRL and RPR are equally valid, but quantitative results from the two tests cannot be directly compared because RPR titers are often slightly higher than VDRL titers.

Abnormal results of serologic testing (unusually high, unusually low, and fluctuating titers) have been observed among HIV-infected patients. For such patients, use of other tests (e.g., biopsy and direct microscopy) should be considered. However, serologic tests appear to be accurate and reliable for the diagnosis of syphilis and for evaluation of treatment response for the vast majority of HIV-infected patients.

No single test can be used to diagnose neurosyphilis among all patients. The diagnosis of neurosyphilis can be made based on various combinations of reactive serologic test results, abnormalities of cerebrospinal fluid (CSF) cell count or protein, or a reactive VDRL-CSF (RPR is not performed on CSF) with or without clinical manifestations. The CSF leukocyte count is usually elevated (>5 WBC/mm^3) when active neurosyphilis is present, and it is also a sensitive measure of the effectiveness of therapy. The VDRL-CSF is the standard serologic test for CSF; when reactive in the absence of substantial contamination of the CSF with blood, it is considered diagnostic of neurosyphilis. However, the VDRL-CSF may be nonreactive when neurosyphilis is present. Some experts recommend performing an FTA-ABS test on CSF. The CSF FTA-ABS is less specific (i.e., yields more false positives) for neurosyphilis than the VDRL-CSF; however, the test is believed to be highly sensitive.

Treatment

Parenteral penicillin G is the preferred drug for treatment of all stages of syphilis. The preparation(s) used (i.e., benzathine, aqueous procaine, or aqueous crystalline), the dosage, and the length of treatment depend on the stage and clinical manifestations of disease.

The efficacy of penicillin for the treatment of syphilis was well established through clinical experience before the value of randomized controlled clinical trials was recognized. Therefore, nearly all the recommendations for the treatment of syphilis are

based on expert opinion reinforced by case series, open clinical trials, and 50 years of clinical experience.

Parenteral penicillin G is the only therapy with documented efficacy for neurosyphilis or for syphilis during pregnancy. Patients with neurosyphilis and pregnant women with syphilis in any stage who report penicillin allergy should almost always be treated with penicillin, after desensitization, if necessary. Skin testing for penicillin allergy may be useful for some patients and in some settings (see Management of the Patient With a History of Penicillin Allergy). However, minor determinants needed for penicillin skin testing are not available commercially.

The **Jarisch-Herxheimer reaction** is an acute febrile reaction—accompanied by headache, myalgia, and other symptoms—that may occur within the first 24 hours after any therapy for syphilis; patients should be advised of this possible adverse reaction. The Jarisch-Herxheimer reaction is common among patients with early syphilis. Antipyretics may be recommended, but there are no proven methods for preventing this reaction. The Jarisch-Herxheimer reaction may induce early labor or cause fetal distress among pregnant women. This concern should not prevent or delay therapy (see Syphilis During Pregnancy).

Management of Sex Partners

Sexual transmission of *T. pallidum* occurs only when mucocutaneous syphilitic lesions are present; such manifestations are uncommon after the first year of infection. However, persons sexually exposed to a patient with syphilis in any stage should be evaluated clinically and serologically according to the following recommendations:

- Persons who were exposed to a patient with primary, secondary, or latent (duration <1 year) syphilis within the preceding 90 days might be infected even if seronegative, and therefore should be treated presumptively.
- Persons who were sexually exposed to a patient with primary, secondary, or latent (duration <1 year) syphilis >90 days before examination should be treated presumptively if serologic test results are not available immediately, and the opportunity for follow-up is uncertain.
- For purposes of partner notification and presumptive treatment of exposed sex partners, patients who have syphilis of unknown duration and who have high nontreponemal serologic test titers (≥1:32) may be considered to be infected with early syphilis.
- Long-term sex partners of patients with late syphilis should be evaluated clinically and serologically for syphilis.

The time periods before treatment used for identifying at-risk sex partners are 3 months plus duration of symptoms for primary syphilis, 6 months plus duration of symptoms for secondary syphilis, and 1 year for early latent syphilis.

Primary and Secondary Syphilis

Treatment

Four decades of experience indicate that parenteral penicillin G is effective in achieving local cure (healing of lesions and prevention of sexual transmission) and in preventing late sequelae. However, no adequately conducted comparative trials have been performed to guide the selection of an optimal penicillin regimen (i.e., dose, duration, and preparation). Substantially fewer data on nonpenicillin regimens are available.

Recommended Regimen for Adults

Nonallergic patients with primary or secondary syphilis should be treated with the following regimen:

Benzathine penicillin G, 2.4 million units IM in a single dose.

NOTE: Recommendations for treating pregnant women and HIV-infected persons for syphilis are discussed in separate sections.

Recommended Regimen for Children

After the newborn period, children diagnosed with syphilis should have a CSF examination to exclude a diagnosis of neurosyphilis, and birth and maternal medical records should be reviewed to assess whether the child has congenital or acquired syphilis (see Congenital Syphilis). Children with acquired primary or secondary syphilis should be evaluated (including consultation with child-protection services) and treated using the following pediatric regimen (see Sexual Assault or Abuse of Children).

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

Other Management Considerations

All patients with syphilis should be tested for HIV. In areas with high HIV prevalence, patients with primary syphilis should be retested for HIV after 3 months.

Patients who have syphilis and who also have symptoms or signs suggesting neurologic disease (e.g., meningitis) or ophthalmic disease (e.g., uveitis) should be fully evaluated for neurosyphilis and syphilitic eye disease (including CSF analysis and ocular slit-lamp examination). Such patients should be treated appropriately according to the results of this evaluation.

Invasion of CSF by *T. pallidum* with accompanying CSF abnormalities is common among adults who have primary or secondary syphilis. However, few patients develop neurosyphilis after treatment with the regimens described in this report. Therefore, unless clinical signs or symptoms of neurologic involvement are present (e.g., auditory, cranial nerve, meningeal, or ophthalmic manifestations), lumbar puncture is not recommended for routine evaluation of patients with primary or secondary syphilis.

Follow-Up

Treatment failures can occur with any regimen. However, assessing response to treatment is often difficult, and no definitive criteria for cure or failure exist. Serologic test titers may decline more slowly among patients with a prior syphilis infection. Patients should be re-examined clinically and serologically at 3 months and again at 6 months.

Patients with signs or symptoms that persist or recur or who have a sustained fourfold increase in nontreponemal test titer compared with either the baseline titer or to a subsequent result, can be considered to have failed treatment or to be reinfected. These patients should be re-treated after evaluation for HIV infection. Unless reinfection is likely, lumbar puncture also should be performed.

Failure of nontreponemal test titers to decline fourfold by 3 months after therapy for primary or secondary syphilis identifies persons at risk for treatment failure. Those persons should be evaluated for HIV infection. Optimal management of such patients is unclear if they are HIV negative. At a minimum, these patients should have additional clinical and serologic follow-up. If further follow-up cannot be assured, re-treatment is recommended. Some experts recommend CSF examination in such situations.

When patients are re-treated, most experts recommend re-treatment with three weekly injections of benzathine penicillin G 2.4 million units IM, unless CSF examination indicates that neurosyphilis is present.

Management of Sex Partners

Refer to General Principles, Management of Sex Partners.

Special Considerations

Penicillin Allergy

Nonpregnant penicillin-allergic patients who have primary or secondary syphilis should be treated with the following regimen.

Doxycycline 100 mg orally 2 times a day for 2 weeks

or

Tetracycline 500 mg orally 4 times a day for 2 weeks.

There is less clinical experience with doxycycline than with tetracycline, but compliance is likely to be better with doxycycline. Therapy for a patient who cannot tolerate either doxycycline or tetracycline should be based upon whether the patient's compliance with the therapy regimen and with follow-up examinations can be assured.

For nonpregnant patients whose compliance with therapy and follow-up can be assured, an alternative regimen is erythromycin 500 mg orally 4 times a day for 2 weeks. Various ceftriaxone regimens also may be considered.

Patients whose compliance with therapy or follow-up cannot be assured should be desensitized, if necessary, and treated with penicillin. Skin testing for penicillin allergy may be useful in some situations (see Management of the Patient With a History of Penicillin Allergy).

Erythromycin is less effective than other recommended regimens. Data on ceftriaxone are limited, and experience has been too brief to permit identification of late failures. Optimal dose and duration have not been established for ceftriaxone, but regimens that provide 8–10 days of treponemicidal levels in the blood should be used. *Single dose ceftriaxone therapy is not effective for treating syphilis*.

Pregnancy

Pregnant patients who are allergic to penicillin should be treated with penicillin, after desensitization, if necessary (see Management of the Patient With a History of Penicillin Allergy and Syphilis During Pregnancy).

HIV Infection

Refer to Syphilis Among HIV-Infected Patients.

Latent Syphilis

Latent syphilis is defined as those periods after infection with *T. pallidum* when patients are seroreactive, but show no other evidence of disease. Patients who have latent syphilis and who have acquired syphilis within the preceding year are classified as having early latent syphilis. Patients can be demonstrated to have acquired syphilis within the preceding year on the basis of documented seroconversion, a fourfold or greater increase in titer of a nontreponemal serologic test, history of symptoms of primary or secondary syphilis, or if they had a sex partner with primary, secondary, or latent syphilis (documented independently as duration <1 year). Nearly all others have latent syphilis of unknown duration and should be managed as if they had late latent syphilis.

Treatment

Treatment of latent syphilis is intended to prevent occurrence or progression of late complications. Although clinical experience supports belief in the effectiveness of penicillin in achieving those goals, limited evidence is available for guidance in choosing specific regimens. There is very little evidence to support the use of nonpenicillin regimens.

Recommended Regimens for Adults

These regimens are for nonallergic patients with normal CSF examination (if performed).

Early Latent Syphilis

Benzathine penicillin G, 2.4 million units IM in a single dose.

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.

Recommended Regimens for Children

After the newborn period, children diagnosed with syphilis should have a CSF examination to exclude neurosyphilis, and birth and maternal medical records should be reviewed to assess whether the child has congenital or acquired syphilis (see Congenital Syphilis). Older children with acquired latent syphilis should be evaluated as described for adults and treated using the following pediatric regimens (see Sexual Assault or Abuse of Children). These regimens are for nonallergic children who have acquired syphilis and who have had a normal CSF examination.

Early Latent Syphilis

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

Late Latent Syphilis or Latent Syphilis of Unknown Duration

Benzathine penicillin G, 50,000 units/kg IM, up to the adult dose of 2.4 million units, for three total doses (total 150,000 units/kg up to adult total dose of 7.2 million units).

Other Management Considerations

All patients with latent syphilis should be evaluated clinically for evidence of tertiary disease (e.g., aortitis, neurosyphilis, gumma, and iritis). Recommended therapy for patients with latent syphilis may not be optimal therapy for the persons with asymptomatic neurosyphilis. However, the yield from CSF examination, in terms of newly diagnosed cases of neurosyphilis, is low.

Patients with any one of the criteria listed below should have a CSF examination before treatment:

- Neurologic or ophthalmic signs or symptoms;
- Other evidence of active syphilis (e.g., aortitis, gumma, iritis);

- Treatment failure;
- HIV infection;
- Serum nontreponemal titer ≥1:32, unless duration of infection is known to be <1 year; or
- Nonpenicillin therapy planned, unless duration of infection is known to be <1 year.

If dictated by circumstances and patient preferences, CSF examination may be performed for persons who do not meet the criteria listed above. If a CSF examination is performed and the results show abnormalities consistent with CNS syphilis, the patient should be treated for neurosyphilis (see Neurosyphilis).

- All syphilis patients should be tested for HIV.

Follow-Up

Quantitative nontreponemal serologic tests should be repeated at 6 months and again at 12 months. Limited data are available to guide evaluation of the response to therapy for a patient with latent syphilis. If titers increase fourfold, or if an initially high titer (≥1:32) fails to decline at least fourfold (two dilutions) within 12–24 months, or if the patient develops signs or symptoms attributable to syphilis, the patient should be evaluated for neurosyphilis and re-treated appropriately.

Management of Sex Partners

Refer to General Principles, Management of Sex Partners.

Special Considerations

Penicillin Allergy

For patients who have latent syphilis and who are allergic to penicillin, nonpenicillin therapy should be used only after CSF examination has excluded neurosyphilis. Nonpregnant, penicillin-allergic patients should be treated with the following regimens.

Doxycycline 100 mg orally 2 times a day

or

Tetracycline 500 mg orally 4 times a day.

Both drugs are administered for 2 weeks if duration of infection is known to have been <1 year; otherwise, for 4 weeks.

Pregnancy

Pregnant patients who are allergic to penicillin should be treated with penicillin, after desensitization, if necessary (see Management of the Patient With a History of Penicillin Allergy and Syphilis During Pregnancy).

HIV Infection

Refer to Syphilis Among HIV-Infected Patients.

Late Syphilis

Late (tertiary) syphilis refers to patients with gumma and patients with cardiovascular syphilis, but not to neurosyphilis. Nonallergic patients without evidence of neurosyphilis should be treated with the following regimen.

Recommended Regimen

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

Other Management Considerations

Patients with symptomatic late syphilis should undergo CSF examination before therapy. Some experts treat all patients who have cardiovascular syphilis with a neurosyphilis regimen. The complete management of patients with cardiovascular or gummatous syphilis is beyond the scope of these guidelines. These patients should be managed in consultation with experts.

Follow-Up

There is minimal evidence regarding follow-up of patients infected with late syphilis. Clinical response depends partly on the nature of the lesions.

Management of Sex Partners

Refer to General Principles, Management of Sex Partners.

Special Considerations

Penicillin Allergy

Patients allergic to penicillin should be treated according to treatment regimens recommended for late latent syphilis.

Pregnancy

Pregnant patients who are allergic to penicillin should be treated with penicillin, after desensitization, if necessary (see Management of the Patient With a History of Penicillin Allergy and Syphilis During Pregnancy).

HIV Infection

Refer to Syphilis Among HIV-Infected Patients.

Neurosyphilis

Treatment

Central nervous system disease can occur during any stage of syphilis. A patient with clinical evidence of neurologic involvement (e.g., ophthalmic or auditory symptoms, cranial nerve palsies) with syphilis warrants a CSF examination. Although four decades of experience have confirmed the effectiveness of penicillin, the evidence to guide the choice of the best regimen is limited.

Syphilitic eye disease is frequently associated with neurosyphilis, and patients with this disease should be treated according to neurosyphilis treatment recommendations. CSF examination should be performed on all such patients to identify those patients with CSF abnormalities who should have follow-up CSF examinations to assess response to treatment.

Patients who have neurosyphilis or syphilitic eye disease (e.g., uveitis, neuroretinitis, or optic neuritis) and who are not allergic to penicillin should be treated with the following regimen.

Recommended Regimen

12–24 million units **aqueous crystalline penicillin G** daily, administered as 2–4 million units IV every 4 hours, for 10–14 days.

If compliance with therapy can be assured, patients may be treated with the following alternative regimen.

Alternative Regimen

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

The durations of these regimens are shorter than that of the regimen used for late syphilis in the absence of neurosyphilis. Therefore, some experts administer benzathine penicillin, 2.4 million units IM after completion of these neurosyphilis treatment regimens to provide a comparable total duration of therapy.

Other Management Considerations

Other considerations in the management of the patient with neurosyphilis are the following:

- All patients with syphilis should be tested for HIV.
- Many experts recommend treating patients with evidence of auditory disease caused by syphilis in the same manner as for neurosyphilis, regardless of the findings on CSF examination.

Follow-Up

If CSF pleocytosis was present initially, CSF examination should be repeated every 6 months until the cell count is normal. Follow-up CSF examinations also may be used to evaluate changes in the VDRL-CSF or CSF protein in response to therapy, though changes in these two parameters are slower and persistent abnormalities are of less certain importance. If the cell count has not decreased at 6 months, or if the CSF is not entirely normal by 2 years, re-treatment should be considered.

Management of Sex Partners

Refer to General Principles, Management of Sex Partners.

Special Considerations

Penicillin Allergy

No data have been collected systematically for evaluation of therapeutic alternatives to penicillin for treatment of neurosyphilis. Therefore, patients who report being allergic to penicillin should be treated with penicillin, after desensitization if necessary, or should be managed in consultation with an expert. In some situations, skin testing to confirm penicillin allergy may be useful (see Management of the Patient With a History of Penicillin Allergy).

Pregnancy

Pregnant patients who are allergic to penicillin should be treated with penicillin, after desensitization if necessary (see Syphilis During Pregnancy).

HIV Infection

Refer to Syphilis Among HIV-Infected Patients.

Syphilis Among HIV-Infected Patients

Diagnostic Considerations

Unusual serologic responses have been observed among HIV-infected persons who also have syphilis. Most reports involved serologic titers that were higher than expected, but false-negative serologic test results or delayed appearance of seroreactivity have also been reported. *Nevertheless, both treponemal and nontreponemal serologic tests for syphilis are accurate for the majority of patients with syphilis and HIV coinfection*.

When clinical findings suggest that syphilis is present, but serologic tests are nonreactive or confusing, it may be helpful to perform such alternative tests as biopsy of a lesion, darkfield examination, or direct fluorescent antibody staining of lesion material.

Neurosyphilis should be considered in the differential diagnosis of neurologic disease among HIV-infected persons.

Treatment

Although adequate research-based evidence is not available, published case reports and expert opinion suggest that HIV-infected patients with early syphilis are at increased risk for neurologic complications and have higher rates of treatment failure with currently recommended regimens. The magnitude of these risks, although not precisely defined, is probably small. No treatment regimens have been demonstrated to be more effective in preventing development of neurosyphilis than those recommended for patients without HIV infection. *Careful follow-up after therapy is essential*.

Primary and Secondary Syphilis Among HIV-Infected Patients

Treatment

Treatment with benzathine penicillin G 2.4 million units IM, as for patients without HIV infection, is recommended. Some experts recommend additional treatments, such as multiple doses of benzathine penicillin G as suggested for late syphilis, or other supplemental antibiotics *in addition to* benzathine penicillin G 2.4 million units IM.

Other Management Considerations

CSF abnormalities are common among HIV-infected patients who have primary or secondary syphilis, but these abnormalities are of unknown prognostic significance. Most HIV-infected patients respond appropriately to currently recommended penicillin therapy; however, some experts recommend CSF examination before therapy and modification of treatment accordingly.

Follow-Up

Patients should be evaluated clinically and serologically for treatment failure at 1 month and at 2, 3, 6, 9, and 12 months after therapy. Although of unproven benefit, some experts recommend performing CSF examination after therapy (i.e., at 6 months).

HIV-infected patients who meet the criteria for treatment failure should undergo CSF examination and be retreated just as for patients without HIV infection. CSF examination and re-treatment also should be strongly considered for patients in whom the suggested fourfold decrease in nontreponemal test titer does not occur within 3 months for primary or secondary syphilis. Most experts would re-treat patients with benzathine penicillin G 7.2 million units (as 3 weekly doses of 2.4 million units each) if the CSF examination is normal.

Special Considerations

Penicillin Allergy

Penicillin regimens should be used to treat HIV-infected patients in all stages of syphilis. Skin testing to confirm penicillin allergy may be used (see Management of the Patient With a History of Penicillin Allergy), but data on the utility of that approach

among immunocompromised patients are inadequate. Patients may be desensitized, then treated with penicillin.

Latent Syphilis Among HIV-Infected Patients

Diagnostic Considerations

Patients who have both latent syphilis (regardless of apparent duration) and HIV infection should undergo CSF examination before treatment.

Treatment

A patient with latent syphilis, HIV infection, and a normal CSF examination can be treated with benzathine penicillin G 7.2 million units (as 3 weekly doses of 2.4 million units each).

Special Considerations

Penicillin Allergy

Penicillin regimens should be used to treat all stages of syphilis among HIV-infected patients. Skin testing to confirm penicillin allergy may be used (see Management of the Patient With a History of Penicillin Allergy), but data on the utility of that approach in immunocompromised patients are inadequate. Patients may be desensitized, then treated with penicillin.

Syphilis During Pregnancy

All women should be screened serologically for syphilis during the early stages of pregnancy. In populations in which utilization of prenatal care is not optimal, RPR-card test screening and treatment, if that test is reactive, should be performed at the time a pregnancy is diagnosed. In communities and populations with high syphilis prevalence or for patients at high risk, serologic testing should be repeated during the third trimester and again at delivery. (Some states mandate screening at delivery for all women.) Any woman who delivers a stillborn infant after 20 weeks gestation should be tested for syphilis. No infant should leave the hospital without the serologic status of the infant's mother having been determined at least once during pregnancy.

Diagnostic Considerations

Seropositive pregnant women should be considered infected unless treatment history is clearly documented in a medical or health department record and sequential serologic antibody titers have appropriately declined.

Treatment

Penicillin is effective for preventing transmission to fetuses and for treating established infection among fetuses. Evidence is insufficient, however, to determine whether the specific, recommended penicillin regimens are optimal.

Recommended Regimens

Treatment during pregnancy should be the penicillin regimen appropriate for the woman's stage of syphilis. Some experts recommend additional therapy (e.g., a second dose of **benzathine penicillin** 2.4 million units IM) 1 week after the initial dose, particularly for those women in the third trimester of pregnancy and for women who have secondary syphilis during pregnancy.

Other Management Considerations

Women who are treated for syphilis during the second half of pregnancy are at risk for premature labor or fetal distress, or both, if their treatment precipitates the Jarisch-Herxheimer reaction. These women should be advised to seek medical attention following treatment if they notice any change in fetal movements or if they have contractions. Stillbirth is a rare complication of treatment; however, since therapy is necessary to prevent further fetal damage, that concern should not delay treatment. All patients with syphilis should be tested for HIV.

Follow-Up

Serologic titers should be checked monthly until adequacy of treatment has been assured. The antibody response should be appropriate for the stage of disease.

Management of Sex Partners

Refer to General Principles, Management of Sex Partners.

Special Considerations

Penicillin Allergy

There are no proven alternatives to penicillin. A pregnant woman with a history of penicillin allergy should be treated with penicillin, after desensitization, if necessary. Skin testing may be helpful for some patients and in some settings (see Management of the Patient With a History of Penicillin Allergy).

Tetracycline and doxycycline are contraindicated during pregnancy. Erythromycin should not be used because it cannot be relied upon to cure an infected fetus.

Congenital Syphilis

Diagnostic Considerations

Who Should Be Evaluated

Infants should be evaluated for congenital syphilis if they were born to seropositive (nontreponemal test confirmed by treponemal test) women who meet the following criteria:

- Have untreated syphilis;* or
- Were treated for syphilis during pregnancy with erythromycin; or
- Were treated for syphilis <1 month before delivery; or
- Were treated for syphilis during pregnancy with the appropriate penicillin regimen, but nontreponemal antibody titers did not decrease sufficiently after therapy to indicate an adequate response (≥ fourfold decrease); or
- Do not have a well-documented history of treatment for syphilis; or
- Were treated appropriately before pregnancy but had insufficient serologic follow-up to assure that they had responded appropriately to treatment and are not currently infected (≥ fourfold decrease for patients treated for early syphilis; stable or declining titers ≤1:4 for other patients).

No infant should leave the hospital without the serologic status of the infant's mother having been documented at least once during pregnancy. Serologic testing also should be performed at delivery in communities and populations at risk for congenital syphilis. Serologic tests can be nonreactive among infants infected late during their mother's pregnancy.

Evaluation of the Infant

The clinical and laboratory evaluation of infants born to women described above should include the following:

- A thorough physical examination for evidence of congenital syphilis;
- A quantitative nontreponemal serologic test for syphilis performed on the infant's sera (not on cord blood);
- CSF analysis for cells, protein, and VDRL;
- Long bone x-rays;
- Other tests as clinically indicated (e.g., chest x-ray, complete blood count, differential and platelet count, liver function tests);
- For infants who have no evidence of congenital syphilis on the above evaluation, determination of presence of specific antitreponemal IgM antibody by a testing method recognized by CDC as having either provisional or standard status;
- Pathologic examination of the placenta or amniotic cord using specific fluorescent antitreponemal antibody staining.

* A woman treated with a regimen other than those recommended for treatment of syphilis (for pregnant women or otherwise) in these guidelines should be considered untreated.

Treatment

Therapy Decisions

Infants should be treated for presumed congenital syphilis if they were born to mothers who, at delivery, had untreated syphilis or who had evidence of relapse or reinfection after treatment (see Congenital Syphilis, Diagnostic Considerations). Additional criteria for presumptively treating infants with congenital syphilis are as follows:

- Physical evidence of active disease;
- X-ray evidence of active disease;
- A reactive VDRL-CSF or, for infants born to seroreactive mothers, an abnormal* CSF white blood cell count or protein, regardless of CSF serology;
- A serum quantitative nontreponemal serologic titer that is at least fourfold greater than the mother's titer†;
- Specific antitreponemal IgM antibody detected by a testing method that has been given provisional or standard status by CDC;
- If they meet the previously cited criteria for "Who Should Be Evaluated," but have not been fully evaluated (see Congenital Syphilis, Diagnostic Considerations).

NOTE: Infants with clinically evident congenital syphilis should have an ophthalmologic examination.

Recommended Regimens

Aqueous crystalline penicillin G, 100,000–150,000 units/kg/day (administered as 50,000 units/kg IV every 12 hours during the first 7 days of life and every 8 hours thereafter) for 10–14 days,

or

Procaine penicillin G, 50,000 units/kg IM daily in a single dose for 10–14 days.

If more than 1 day of therapy is missed, the entire course should be restarted. An infant whose complete evaluation was normal and whose mother was a) treated for syphilis during pregnancy with erythromycin, or b) treated for syphilis <1 month before delivery, or c) treated with an appropriate regimen before or during pregnancy

*In the immediate newborn period, interpretation of CSF test results may be difficult; normal values vary with gestational age and are higher in preterm infants. Other causes of elevated values also should be considered when an infant is being evaluated for congenital syphilis. Though values as high as 25 white blood cells(WBC)/mm^3 and 150 mg protein/dL occur among normal neonates, some experts recommend that lower values (5 WBC/mm^3 and 40 mg/dL) be considered the upper limits of normal. The infant should be treated if test results cannot exclude infection.

†The absence of a fourfold greater titer for an infant *cannot* be used as evidence *against* congenital syphilis.

but did not yet have an adequate serologic response should be treated with benzathine penicillin G, 50,000 units/kg IM in a single dose. In some cases, infants with a normal complete evaluation for whom follow-up can be assured can be followed closely without treatment.

Treatment of Older Infants and Children with Congenital Syphilis

After the newborn period, children diagnosed with syphilis should have a CSF examination to exclude neurosyphilis and records should be reviewed to assess whether the child has congenital or acquired syphilis (see Primary and Secondary Syphilis and Latent Syphilis). Any child who is thought to have congenital syphilis (or who has neurologic involvement) should be treated with aqueous crystalline penicillin G, 200,000–300,000 units/kg/day IV or IM (administered as 50,000 units/kg every 4–6 hours) for 10–14 days.

Follow-Up

A seroreactive infant (or an infant whose mother was seroreactive at delivery) who is not treated for congenital syphilis during the perinatal period should receive careful follow-up examinations at 1 month and at 2, 3, 6, and 12 months after therapy. Nontreponemal antibody titers should decline by 3 months of age and should be nonreactive by 6 months of age if the infant was not infected and the titers were the result of passive transfer of antibody from the mother. If these titers are found to be stable or increasing, the child should be re-evaluated, including CSF examination, and fully treated. Passively transferred treponemal antibodies may be present for as long as 1 year. If they are present >1 year, the infant should be re-evaluated and treated for congenital syphilis.

Treated infants also should be followed every 2–3 months to assure that nontreponemal antibody titers decline; these infants should have become nonreactive by 6 months of age (response may be slower for infants treated after the neonatal period). Treponemal tests should not be used to evaluate response to treatment because test results can remain positive despite effective therapy if the child was infected. Infants with CSF pleocytosis should undergo CSF examination every 6 months, or until the cell count is normal. If the cell count is still abnormal after 2 years, or if a downward trend is not present at each examination, the child should be re-treated. The VDRL-CSF also should be checked at 6 months; if still reactive, the infant should be re-treated.

Follow-up of children treated for congenital syphilis after the newborn period should be the same as that prescribed for congenital syphilis among neonates.

Special Considerations

Penicillin Allergy

Children who require treatment for syphilis after the newborn period, but who have a history of penicillin allergy, should be treated with penicillin after desensitization, if necessary. Skin testing may be helpful in some patients and settings (see Management of the Patient With a History of Penicillin Allergy).

HIV Infection

Mothers of infants with congenital syphilis should be tested for HIV. Infants born to mothers who have HIV infection should be referred for evaluation and appropriate follow-up.

No data exist to suggest that infants with congenital syphilis whose mothers are coinfected with HIV require different evaluation, therapy, or follow-up for syphilis than is recommended for all infants.

Management of the Patient With a History of Penicillin Allergy

No proven alternatives to penicillin are available for treating neurosyphilis, congenital syphilis, or syphilis among pregnant women. Penicillin also is recommended for use, whenever possible, with HIV-infected patients. Unfortunately, 3%–10% of the adult population in the United States have experienced urticaria, angioedema, or anaphylaxis (upper airway obstruction, bronchospasm, or hypotension) with penicillin therapy. Re-administration of penicillin can cause severe immediate reactions among these patients. Because anaphylactic reactions to penicillin can be fatal, every effort should be made to avoid administering penicillin to penicillin-allergic patients, unless the anaphylactic sensitivity has been removed by acute desensitization.

However, only approximately 10% of persons who report a history of severe allergic reactions to penicillin are still allergic. With the passage of time after an allergic reaction to penicillin, most persons who have experienced a severe reaction stop expressing penicillin-specific IgE. These persons can be treated safely with penicillin. Many studies have found that skin testing with the major and minor determinants can reliably identify persons at high risk for penicillin reactions. Although these reagents are easily generated and have been available in academic centers for >30 years, currently only penicilloyl-poly-L-lysine (Pre-Pen, the major determinant) and penicillin G are available commercially. Experts estimate that testing with only the major determinant and penicillin G detects 90%–97% of the currently allergic patients. However, because skin testing without the minor determinants would still miss 3%–10% of allergic patients, and serious or fatal reactions can occur among these minor determinant positive patients, experts suggest caution when the full battery of skin test reagents listed in the table is not available.

Recommendations

If the full battery of skin-test reagents is available, including the major and minor determinants (see Penicillin Allergy Skin Testing), patients who report a history of penicillin reaction and are skin-test negative can receive conventional penicillin therapy. Skin-test positive patients should be desensitized.

If the full battery of skin-test reagents, including the minor determinants, is not available, the patient should be skin tested using penicilloyl (the major determinant, Pre-Pen) and penicillin G. Those with positive tests should be desensitized. Some experts believe that persons with negative tests, in that situation, should be regarded as probably allergic and should be desensitized. Others suggest that those with negative

skin tests can be test-dosed gradually with oral penicillin in a monitored setting in which treatment for anaphylactic reaction is possible.

Penicillin Allergy Skin Testing

Patients at high risk for anaphylaxis (i.e., a history of penicillin-related anaphylaxis, asthma or other diseases that would make anaphylaxis more dangerous, or therapy with beta-adrenergic blocking agents) should be tested with 100-fold dilutions of the full-strength skin-test reagents before testing with full-strength reagents. In these situations, patients should be tested in a monitored setting in which treatment for an anaphylactic reaction is possible. If possible, the patient should not have taken antihistamines (e.g., chlorpheniramine maleate or terfenadine during the past 24 hours, diphenhydramine HCl or hydroxyzine during the past 4 days, or astemizole during the past 3 weeks).

Reagents (Adapted from Beall [*14*])*

Major Determinant

- Benzylpenicilloyl poly-L-lysine (Pre-Pen [Taylor Pharmacal Company, Decatur, Illinois]) (6×10^{-5}M).

Minor Determinant Precursors†

- Benzylpenicillin G (10^{-2}M, 3.3 mg/mL, 6000 U/mL),
- Benzylpenicilloate (10^{-2}M, 3.3 mg/mL),
- Benzylpenilloate (or penicilloyl propylamine)(10^{-2}M, 3.3 mg/mL).

Positive Control

- Commercial histamine for epicutaneous skin testing (1 mg/mL).

Negative Control

- Diluent used to dissolve other reagents, usually phenol saline.

Procedures

Dilute the antigens 100-fold for preliminary testing if the patient has had a life-threatening reaction, or 10-fold if the patient has had another type of immediate, generalized reaction within the past year.

Epicutaneous (prick) tests. Duplicate drops of skin-test reagent are placed on the volar surface of the forearm. The underlying epidermis is pierced with a 26-gauge needle without drawing blood.

*Reprinted with permission from G.N. Beall in *Annals of Internal Medicine*.
†Aged penicillin is not an adequate source of minor determinants. Penicillin G should be freshly prepared or should come from a fresh-frozen source.

An epicutaneous test is positive if the average wheal diameter after 15 minutes is 4 mm larger than that of negative controls; otherwise, the test is negative. The histamine controls should be positive to assure that results are not falsely negative because of the effect of antihistaminic drugs.

Intradermal test. If epicutaneous tests are negative, duplicate 0.02 mL intradermal injections of negative control and antigen solutions are made into the volar surface of the forearm using a 26- or 27-gauge needle on a syringe. The crossed diameters of the wheals induced by the injections should be recorded.

An intradermal test is positive if the average wheal diameter 15 minutes after injection is 2 mm or larger than the initial wheal size and also is at least 2 mm larger than the negative controls. Otherwise, the tests are negative.

Desensitization

Patients who have a positive skin test to one of the penicillin determinants can be desensitized. This is a straightforward, relatively safe procedure that can be done orally or IV. Although the two approaches have not been compared, oral desensitization is thought to be safer, simpler, and easier. Patients should be desensitized in a hospital setting because serious IgE-mediated allergic reactions, although unlikely, can occur. Desensitization can usually be completed in about 4 hours, after which the first dose of penicillin is given (Table 1). STD programs should have a referral center where patients with positive skin tests can be desensitized. After desensitization, patients must be maintained on penicillin continuously for the duration of the course of therapy.

TABLE 1. Oral desensitization protocol for patients with a positive skin test (*15*)*

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

Observation period: 30 minutes before parenteral administration of penicillin.

*Reprinted with permission from the *New England Journal of Medicine*.
†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.

DISEASES CHARACTERIZED BY URETHRITIS AND CERVICITIS

Management of the Patient with Urethritis

Urethritis, or inflammation of the urethra, is caused by an infection characterized by the discharge of mucoid or purulent material and by burning during urination. However, asymptomatic infections are common. The two bacterial agents primarily responsible for urethritis among men are *N. gonorrhoeae* and *C. trachomatis*. Testing to determine the specific diagnosis is recommended because both of these infections are reportable to state health departments and because with a specific diagnosis, treatment compliance may be better and the likelihood of partner notification may be improved. If diagnostic tools (e.g., Gram stain and microscope) are unavailable, health-care providers should treat patients for both infections. The added expense of treating a person with nongonococcal urethritis (NGU) for both infections also should encourage the health-care provider to make a specific diagnosis. (See Nongonococcal Urethritis, Chlamydial Infections, and Gonococcal Infections.)

Nongonococcal Urethritis

NGU, or inflammation of the urethra not caused by gonococcal infection, is characterized by a mucoid or purulent urethral discharge. In the presence or absence of a discharge, NGU may be diagnosed by ≥5 polymorphonuclear leukocytes per oil immersion field on a smear of an intraurethral swab specimen. Increasingly, the leukocyte esterase test (LET) is being used to screen urine from asymptomatic males for evidence of urethritis (either gonococcal or nongonococcal). The diagnosis of urethritis among males tested with LET should be confirmed with a Gram-stained smear of a urethral swab specimen. *C. trachomatis* is the most frequent cause of NGU (23%–55% of cases); however, prevalence varies among age groups, with lower prevalence found among older men. *Ureaplasma urealyticum* causes 20%–40% of cases, and *Trichomonas vaginalis* 2%–5%. HSV is occasionally responsible for cases of NGU. The etiology of the remaining cases of NGU is unknown.

Complications of NGU among men infected with *C. trachomatis* include epididymitis and Reiter's syndrome. Female sex partners of men who have NGU are at risk for chlamydial infection and associated complications.

Recommended Regimen

Doxycycline 100 mg orally 2 times a day for 7 days.*

Alternative Regimens

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

or

* Azithromycin 1 g in a single dose, according to manufacturer's data, is equivalent to doxycycline. However, this study has not been published in a peer-reviewed journal. For a discussion comparing azithromycin and doxycyline, refer to Chlamydial Infections.

Erythromycin ethylsuccinate 800 mg orally 4 times a day for 7 days.

If a patient cannot tolerate high-dose erythromycin schedules, one of the following regimens may be used:

Erythromycin base 250 mg orally 4 times a day for 14 days

or

Erythromycin ethylsuccinate 400 mg orally 4 times a day for 14 days.

Treatment with the recommended regimen has been demonstrated in most cases to result in alleviation of symptoms and in microbiologic cure of infection. If the etiologic organism is susceptible to the antimicrobial agent used, sequelae specific to that organism will be prevented, as will further transmission; this is especially important for cases of NGU caused by *C. trachomatis*.

Follow-Up

Patients should be instructed to return for evaluation if symptoms persist or recur after completion of therapy. Patients with persistent or recurrent urethritis should be re-treated with the initial regimen if they failed to comply with the treatment regimen or if they were re-exposed to an untreated sex partner. Otherwise, a wet mount examination and culture of an intraurethral swab specimen for *T. vaginalis* should be performed; if negative, the patient should be retreated with an alternative regimen extended to 14 days (e.g., erythromycin base 500 mg orally 4 times a day for 14 days). The use of alternative regimens ensures treatment of possible tetracycline-resistant *U. urealyticum*.

Effective regimens have not been identified for treating patients who experience persistent symptoms or frequent recurrences following treatment with doxycycline and erythromycin. Urologic examinations do not usually reveal a specific etiology. Such patients should be assured that, although they have persistent or frequently recurring urethritis, the condition is not known to cause complications among them or their sex partners and is not known to be sexually transmitted. However, men exposed to a new sex partner should be re-evaluated. Symptoms alone, without documentation of signs or laboratory evidence of urethral inflammation, are not a sufficient basis for re-treatment.

Management of Sex Partners

Patients should be instructed to refer sex partners for evaluation and treatment. Since exposure intervals have received limited evaluation, the following recommendations are somewhat arbitrary. Sex partners of symptomatic patients should be evaluated and treated if their last sexual contact with the index patient was within 30 days of onset of symptoms. If the index patient is asymptomatic, sex partners whose last sexual contact with the index patient was within 60 days of diagnosis should be evaluated and treated. If the patient's last sexual intercourse preceded the time intervals previously described, the most recent sex partner should be treated. A

specific diagnosis may facilitate partner referral and partner cooperation. Therefore, testing for both gonorrhea and chlamydia is encouraged.

Patients should be instructed to abstain from sexual intercourse until patient and partners are cured. In the absence of microbiologic test-of-cure, this means when therapy is completed and patient and partners are without symptoms or signs.

Special Considerations

HIV Infection

Persons with HIV infection and NGU should receive the same treatment as patients without HIV infection.

Management of the Patient With Mucopurulent Cervicitis

Mucopurulent cervicitis (MPC) is characterized by a yellow endocervical exudate visible in the endocervical canal or in an endocervical swab specimen. Some experts also make the diagnosis on the basis of an increased number of polymorphonuclear leukocytes on cervical Gram stain. The condition is asymptomatic among many women, but some may experience an abnormal vaginal discharge and abnormal vaginal bleeding (e.g., following intercourse). The condition can be caused by *C. trachomatis* or *N. gonorrhoeae*, although in most cases neither organism can be isolated. Patients with MPC should have cervical specimens tested for *C. trachomatis* and cultured for *N. gonorrhoeae*. MPC is not a sensitive predictor of infection; however, most women with *C. trachomatis* or *N. gonorrhoeae* do not have MPC.

Treatment

The results of tests for *C. trachomatis* or *N. gonorrhoeae* should determine the need for treatment, unless the likelihood of infection with either organism is high or unless the patient is unlikely to return for treatment. Treatment for MPC should include the following:

- Treatment for gonorrhea and chlamydia in patient populations with high prevalence of both infections, such as patients seen at many STD clinics.
- Treatment for chlamydia only, if the prevalence of *N. gonorrhoeae* is low but the likelihood of chlamydia is substantial.
- Await test results if the prevalence of both infections are low and if compliance with a recommendation for a return visit is likely.

Follow-Up

Follow-up should be as recommended for the infections for which the woman is being treated.

Management of Sex Partners

Management of sex partners of women with MPC should be appropriate for the STD (*C. trachomatis* or *N. gonorrhoeae*) identified. Partners should be notified, examined, and treated on the basis of test results. However, partners of patients who are treated presumptively should receive the same treatment as the index patient.

Special Considerations

HIV Infection

Persons with HIV infection and MPC should receive the same treatment as patients without HIV infection.

Chlamydial Infections

Chlamydial genital infection is common among adolescents and young adults in the United States. Asymptomatic infection is common among both men and women. Testing sexually active adolescent girls for chlamydial infection should be routine during gynecologic examination, even if symptoms are not present. Screening of young adult women 20–24 years of age also is suggested, particularly for those who do not consistently use barrier contraceptives and who have new or multiple partners. Periodic surveys of chlamydial prevalence among these groups should be conducted to confirm the validity of using these recommendations in specific clinical settings.

Chlamydial Infections Among Adolescents and Adults

The following recommended treatment regimens or the alternative regimens relieve symptoms and cure infection. Among women, several important sequelae may result from *C. trachomatis* infection, the most serious among them being PID, ectopic pregnancy, and infertility. Some women with apparently uncomplicated cervical infection already have subclinical upper reproductive tract infection. Treatment of cervical infection is believed to reduce the likelihood of sequelae, although few studies have demonstrated that antimicrobial therapy reduces the risk of subsequent ascending infections or decreases the incidence of long-term complications of tubal infertility and ectopic pregnancy.

Treatment of infected patients prevents transmission to sex partners, and for infected pregnant women may prevent transmission of *C. trachomatis* to infants during birth. Treatment of sex partners will help to prevent re-infection of the index patient and infection of other partners.

Because of the high prevalence of coinfection with *C. trachomatis* among patients with gonococcal infection, presumptive treatment for chlamydia of patients being treated for gonorrhea is appropriate, particularly if no diagnostic test for *C. trachomatis* infection will be performed (see Gonococcal Infections).

Recommended Regimens

Doxycycline 100 mg orally 2 times a day for 7 days,

or

Azithromycin 1 g orally in a single dose.

Alternative Regimens

Ofloxacin 300 mg orally 2 times a day for 7 days

or

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

or

Erythromycin ethylsuccinate 800 mg orally 4 times a day for 7 days

or

Sulfisoxazole 500 mg orally 4 times a day for 10 days (inferior efficacy to other regimens).

Doxycycline and azithromycin appear similar in efficacy and toxicity; however, the safety and efficacy of azithromycin for persons ≤15 years of age have not been established. Doxycycline has a longer history of extensive use, safety, efficacy, and the advantage of low cost. Azithromycin has the advantage of single-dose administration. Ofloxacin is similar in efficacy to doxycycline and azithromycin, but is more expensive than doxycycline, cannot be used during pregnancy or with persons ≤17 years of age, and offers no advantage in dosing. Ofloxacin is the only quinolone with proven efficacy against chlamydial infection. Sulfisoxazole is the least desirable treatment because of inferior efficacy.

Follow-Up

Patients do not need to be retested for chlamydia after completing treatment with doxycycline or azithromycin unless symptoms persist or re-infection is suspected. Retesting may be considered 3 weeks after completion of treatment with erythromycin, sulfisoxazole, or amoxicillin. This is usually unnecessary if the patient was treated with doxycycline, azithromycin, or ofloxacin. The validity of chlamydial culture testing performed at <3 weeks following completion of therapy among patients failing therapy has not been established. False-negative results may occur because of small numbers of chlamydial organisms. In addition, nonculture tests conducted at <3 weeks following completion of therapy for patients successfully treated may sometimes be false-positive because of the continued excretion of dead organisms.

Some studies have demonstrated high rates of infection among women retested several months following treatment, presumably because of reinfection. Rescreening women several months following treatment may be an effective strategy for detecting further morbidity in some populations.

Management of Sex Partners

Patients should be instructed to refer their sex partners for evaluation and treatment. Because exposure intervals have received limited evaluation, the following recommendations are somewhat arbitrary. Sex partners of symptomatic patients with *C. trachomatis* should be evaluated and treated for chlamydia if their last sexual contact with the index patient was within 30 days of onset of the index patient's symptoms. If the index patient is asymptomatic, sex partners whose last sexual contact with the index patient was within 60 days of diagnosis should be evaluated and treated. Health-care providers should treat the last sex partner even if last sexual intercourse took place before the foregoing time intervals.

Patients should be instructed to avoid sex until they and their partners are cured. In the absence of microbiologic test-of-cure, this means until therapy is completed and patient and partner(s) are without symptoms.

Special Considerations

Pregnancy

Doxycycline and ofloxacin are contraindicated for pregnant women, and sulfisoxazole is contraindicated for women during pregnancy near-term and for women who are nursing. The safety and efficacy of azithromycin among pregnant and lactating women have not been established. Repeat testing, preferably by culture, after completing therapy with the following regimens is recommended because there are few data regarding the effectiveness of these regimens, and the frequent gastrointestinal side effects of erythromycin may discourage a patient from complying with the prescribed treatment.

Recommended Regimen for Pregnant Women

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

Alternative Regimens for Pregnant Women

Erythromycin base 250 mg orally 4 times a day for 14 days

or

Erythromycin ethylsuccinate 800 mg orally 4 times a day for 7 days

or

Erythromycin ethylsuccinate 400 mg orally 4 times a day for 14 days

or

If erythromycin cannot be tolerated:

Amoxicillin 500 mg orally 3 times a day for 7–10 days.

NOTE: Erythromycin estolate is contraindicated during pregnancy because of drug-related hepatotoxicity. Few data exist concerning the efficacy of amoxicillin.

HIV Infection

Persons with HIV infection and chlamydial infection should receive the same treatment as patients without HIV infection.

Chlamydial Infections Among Infants

Prenatal screening of pregnant women can prevent chlamydial infection among neonates. Pregnant women <25 years of age and those with new or multiple sex partners should, in particular, be targeted for screening. Periodic surveys of chlamydial prevalence can be conducted to confirm the validity of using these recommendations in specific clinical settings.

C. trachomatis infection of neonates results from perinatal exposure to the mother's infected cervix. The prevalence of *C. trachomatis* infection generally exceeds 5% among pregnant women, regardless of race/ethnicity or socioeconomic status. Neonatal ocular prophylaxis with silver nitrate solution or antibiotic ointments is ineffective in preventing perinatal transmission of chlamydial infection from mother to infant. However, ocular prophylaxis with those agents does prevent gonococcal ophthalmia and should be continued for that reason (see Prevention of Ophthalmia Neonatorum).

Initial *C. trachomatis* perinatal infection involves mucous membranes of the eye, oropharynx, urogenital tract, and rectum. *C. trachomatis* infection among neonates can most often be recognized because of conjunctivitis developing 5–12 days after birth. Chlamydia is the most frequent identifiable infectious cause of ophthalmia neonatorum. *C. trachomatis* also is a common cause of subacute, afebrile pneumonia with onset from 1 to 3 months of age. Asymptomatic infections of the oropharynx, genital tract, and rectum among neonates also occur.

Ophthalmia Neonatorum Caused by C. trachomatis

A chlamydial etiology should be considered for all infants with conjunctivitis through 30 days of age.

Diagnostic Considerations

Sensitive and specific methods to diagnose chlamydial ophthalmia for the neonate include isolation by tissue culture and nonculture tests, direct fluorescent antibody tests, and immunoassays. Giemsa-stained smears are specific for *C. trachomatis*, but are not sensitive. Specimens must contain conjunctival cells, not exudate alone. Specimens for culture isolation and nonculture tests should be obtained from the everted eyelid using a dacron-tipped swab or the swab specified by the manufacturer's test kit. A specific diagnosis of *C. trachomatis* infection confirms the need for chlamydial treatment not only for the neonate, but also for the mother and her sex partner(s). Ocular exudate from infants being evaluated for chlamydial conjunctivitis should also be tested for *N. gonorrhoeae*.

Recommended Regimen

Erythromycin 50 mg/kg/day orally divided into 4 doses for 10–14 days.

Topical antibiotic therapy alone is inadequate for treatment of chlamydial infection and is unnecessary when systemic treatment is undertaken.

Follow-Up

The possibility of chlamydial pneumonia should be considered. The efficacy of erythromycin treatment is approximately 80%; a second course of therapy may be required. Follow-up of infants to determine resolution is recommended.

Management of Mothers and Their Sex Partners

The mothers of infants who have chlamydial infection and the mother's sex partners should be evaluated and treated following the treatment recommendations for adults with chlamydial infections (see Chlamydial Infections Among Adolescents and Adults).

Infant Pneumonia Caused by C. trachomatis

Characteristic signs of chlamydial pneumonia among infants include a repetitive staccato cough with tachypnea, and hyperinflation and bilateral diffuse infiltrates on a chest roentgenogram. Wheezing is rare, and infants are typically afebrile. Peripheral eosinophilia, documented in a complete blood count, is sometimes observed among infants with chlamydial pneumonia. Because variation from this clinical presentation is common, initial treatment and diagnostic tests should encompass *C. trachomatis* for all infants 1–3 months of age who have possible pneumonia.

Diagnostic Considerations

Specimens should be collected from the nasopharynx for chlamydial testing. Tissue culture remains the definitive standard for chlamydial pneumonia; nonculture tests can be used with the knowledge that nonculture tests of nasopharyngeal specimens produce lower sensitivity and specificity than nonculture tests of ocular specimens. Tracheal aspirates and lung biopsy specimens, if collected, should be tested for *C. trachomatis*.

The microimmunofluorescence test for *C. trachomatis* antibody is useful but not widely available. An acute IgM antibody titer ≥1:32 is strongly suggestive of *C. trachomatis* pneumonia.

Because of the delay in obtaining test results for chlamydia, inclusion of an agent active against *C. trachomatis* in the antibiotic regimen must frequently be decided on the basis of the clinical and radiologic findings. Conducting tests for chlamydial infection is worthwhile, not only to assist in the management of an infant's illness, but also to determine the need for treatment of the mother and her sex partners.

Recommended Regimen

Erythromycin 50 mg/kg/day orally divided into 4 doses for 10–14 days.

Follow-Up

The effectiveness of erythromycin treatment is approximately 80%; a second course of therapy may be required. Follow-up of infants is recommended to determine that the pneumonia has resolved. Some infants with chlamydial pneumonia have had abnormal pulmonary function tests later in childhood.

Management of Mothers and Their Sex Partners

Mothers of infants who have chlamydial infection and the mother's sex partners should be evaluated and treated according to the recommended treatment of adults with chlamydial infections (see Chlamydial Infections Among Adolescents and Adults).

Infants Born to Mothers Who Have Chlamydial Infection

Infants born to mothers who have untreated chlamydia are at high risk for infection and should be evaluated and treated as for infants with ophthalmia neonatorum caused by *C. trachomatis*.

Chlamydial Infections Among Children

Sexual abuse must be considered a cause of chlamydial infection among preadolescent children, although perinatally transmitted *C. trachomatis* infection of the nasopharynx, urogenital tract, and rectum may persist beyond 1 year (see Sexual Assault or Abuse of Children). Because of the potential for a criminal investigation and legal proceedings for sexual abuse, diagnosis of *C. trachomatis* among preadolescent children requires the high specificity provided by isolation in cell culture. The cultures should be confirmed by microscopic identification of the characteristic intracytoplasmic inclusions, preferably by fluorescein-conjugated monoclonal antibodies specific for *C. trachomatis*.

Diagnostic Considerations

Nonculture chlamydia tests should not be used because of the possibility of false-positive test results. With respiratory tract specimens, false-positive test results can occur because of cross-reaction of test reagents with *Chlamydia pneumoniae*; with genital and anal specimens, false-positive test results occur because of cross-reaction with fecal flora.

Recommended Regimen

Children who weigh <45 kg

Erythromycin 50 mg/kg/day divided into four doses for 10–14 days.

NOTE: The effectiveness of erythromycin treatment is approximately 80%; a second course of therapy may be required.

Children who weigh ≥45 kg but who are <8 years of age

Use the same treatment regimens for these children as the adult regimens of **erythromycin** (see Chlamydial Infections Among Adolescents and Adults).

Children ≥8 years of age

Use the same treatment regimens for these children as the adult regimens of **doxycycline** or **tetracycline** (see Chlamydial Infections Among Adolescents and Adults). Adult regimens of **azithromycin** also may be considered for adolescents.

Other Management Considerations

See Sexual Assault or Abuse of Children.

Follow-Up

Follow-up cultures are necessary to ensure that treatment has been effective.

Gonococcal Infections

Gonococcal Infections Among Adolescents and Adults

An estimated 1 million new infections with *N. gonorrhoeae* occur in the United States each year. Most infections among men produce symptoms that cause the person to seek curative treatment soon enough to prevent serious sequelae—but not soon enough to prevent transmission to others. Many infections among women do not produce recognizable symptoms until complications such as PID have occurred. PID, whether symptomatic or asymptomatic, can cause tubal scarring leading to infertility or ectopic pregnancy. Because gonococcal infections among women are often asymptomatic, a primary measure for controlling gonorrhea in the United States has been the screening of high-risk women.

Uncomplicated Gonococcal Infections

Recommended Regimens

Ceftriaxone 125 mg IM in a single dose

or

Cefixime 400 mg orally in a single dose

or

Ciprofloxacin 500 mg orally in a single dose

or

Ofloxacin 400 mg orally in a single dose

PLUS

A regimen effective against possible coinfection with *C. trachomatis* , such as **doxycycline** 100 mg orally 2 times a day for 7 days.

Many antibiotics are safe and effective for treating gonorrhea, eradicating *N. gonorrhoeae*, ending the possibility of further transmission, relieving symptoms, and reducing the chances of sequelae.

Selection of a treatment regimen for *N. gonorrhoeae* infection requires consideration of the anatomic site of infection, resistance of *N. gonorrhoeae* strains to antimicrobials, the possibility of concurrent infection with *C. trachomatis*, and the side effects and costs of the various treatment regimens.

Because coinfection with *C. trachomatis* is common, persons treated for gonorrhea should be treated presumptively with a regimen that is effective against *C. trachomatis* (see Chlamydial Infections).

Most experts agree that other regimens recommended for the treatment of *C. trachomatis* infection are also likely to be satisfactory for the treatment of coinfection (see Chlamydial Infections). However, studies have not been conducted to investigate possible interactions between other treatments for *N. gonorrhoeae* and *C. trachomatis*, including interactions influencing the effectiveness and side effects of cotreatment.

In clinical trials, these recommended regimens cured >95% of anal and genital infections; any of the regimens may be used for uncomplicated anal or genital infection. Published studies indicate that ceftriaxone 125 mg and ciprofloxacin 500 mg can cure ≥90% of pharyngeal infections. *If pharyngeal infection is a concern, one of these two regimens should be used*.

Ceftriaxone in a single dose of either 125 mg or 250 mg provides sustained, high bactericidal levels in the blood. Extensive clinical experience indicates that both doses are safe and effective for the treatment of uncomplicated gonorrhea at all sites. In the past, the 250 mg dose has been recommended on the supposition that the routine use of a higher dose may forestall the development of resistance. However, on the basis of ceftriaxone's activity against *N. gonorrhoeae*, its pharmacokinetics, and the results in

clinical trials of doses as low as 62.5 mg, the 125 mg dose appears to have a therapeutic reserve at least as large as that of other accepted treatment regimens. No ceftriaxone-resistant strains of *N. gonorrhoeae* have been reported. The drawbacks of ceftriaxone are that it is expensive, currently unavailable in vials of <250 mg, and must be administered by injection. Some health-care providers believe that the discomfort of the injection may be reduced by using 1% lidocaine solution as a diluent. Ceftriaxone also may abort incubating syphilis, a concern when gonorrhea treatment is not accompanied by a 7–day course of doxycycline or erythromycin for the presumptive treatment of chlamydia.

Cefixime has an antimicrobial spectrum similar to that of ceftriaxone, but the 400 mg oral dose does not provide as high nor as sustained a bactericidal level as does 125 mg of ceftriaxone. Cefixime appears to be effective against pharyngeal gonococcal infection, but few patients with pharyngeal infection have been included in studies. No gonococcal strains resistant to cefixime have been reported. The advantage of cefixime is that it can be administered orally. It is not known if the 400 mg dose can cure incubating syphilis.

Ciprofloxacin at a dose of 500 mg provides sustained bactericidal levels in the blood. Clinical trials have demonstrated that both 250 mg and 500 mg doses are safe and effective for the treatment of uncomplicated gonorrhea at all sites. Most clinical experience in the United States has been with the 500 mg dose. Ciprofloxacin can be administered orally and is less expensive than ceftriaxone. No resistance has been reported in the United States, but strains with decreased susceptibility to some quinolones are becoming common in Asia and have been reported in North America. The 500 mg dose is recommended, rather than the 250 mg dose, because of the trend toward decreasing susceptibility to quinolones and because of rare reports of treatment failure. Quinolones are contraindicated for pregnant or nursing women and for persons ≤17 years of age on the basis of information from animal studies. Quinolones are not active against *T. pallidum* .

Ofloxacin is active against *N. gonorrhoeae,* has favorable pharmacokinetics, and the 400 mg dose has been effective for the treatment of uncomplicated anal and genital gonorrhea. In published studies a 400 mg dose cured 22 (88%) of 25 pharyngeal infections.

Alternative Regimens

- **Spectinomycin** 2 g IM in a single dose. Spectinomycin has the disadvantages of being injectable, expensive, inactive against *T. pallidum* , and relatively ineffective against pharyngeal gonorrhea. In addition, resistant strains have been reported in the United States. However, spectinomycin remains useful for the treatment of patients who can tolerate neither cephalosporins nor quinolones.
- **Injectable cephalosporin** regimens other than ceftriaxone 125 mg that have demonstrated efficacy against uncomplicated anal or genital gonococcal infections include these injectable cephalosporins: ceftizoxime 500 mg IM in a single dose; cefotaxime 500 mg IM in a single dose; cefotetan 1 g IM in a single dose; and cefoxitin 2 g IM in a single dose.

None of these injectable cephalosporins offers any advantage compared with ceftriaxone, and there is less clinical experience with them for the treatment of uncomplicated gonorrhea. Of these four regimens, ceftizoxime 500 mg appears to be the most effective according to cumulative experience in published clinical trials.

- **Oral cephalosporin** regimens other than cefixime 400 mg include cefuroxime axetil 1 g orally in a single dose and cefpodoxime proxetil 200 mg orally in a single dose. These two regimens have anti-gonococcal activity and pharmacokinetics less favorable than the 400 mg cefixime regimen, and there is less clinical experience with them in the treatment of gonorrhea. They have not been very effective against pharyngeal infections among the few patients studied.
- **Quinolone** regimens other than ciprofloxacin 500 mg and ofloxacin 400 mg include enoxacin 400 mg orally in a single dose; lomefloxacin 400 mg orally in a single dose; and norfloxacin 800 mg orally in a single dose. They appear to be safe and effective for the treatment of uncomplicated gonorrhea, but none appears to offer any advantage over ciprofloxacin at a dose of 500 mg or ofloxacin at 400 mg.

  Enoxacin and norfloxacin are active against *N. gonorrhoeae* , have favorable pharmacokinetics, and have been effective in clinical trials, but there is minimal experience with their use in the United States. Lomefloxacin is effective against *N. gonorrhoeae* and has very favorable pharmacokinetics, but there are few published clinical studies to support its use for the treatment of gonorrhea, and there is little experience with its use in the United States.

Many other antimicrobials are active against *N. gonorrhoeae*. These guidelines are not intended to be a comprehensive list of all effective treatment regimens.

Other Management Considerations

Persons treated for gonorrhea should be screened for syphilis by serology when gonorrhea is first detected. Gonorrhea treatment regimens that include ceftriaxone or a 7-day course of either doxycycline or erythromycin may cure incubating syphilis, but few data relevant to this topic are available.

Follow-Up

Persons who have uncomplicated gonorrhea and who are treated with any of the regimens in these guidelines need not return for a test-of-cure. Those persons with symptoms persisting after treatment should be evaluated by culture for *N. gonorrhoeae*, and any gonococci isolated should be tested for antimicrobial susceptibility. Infections detected after treatment with one of the recommended regimens more commonly occur because of reinfection rather than treatment failure, indicating a need for improved sex partner referral and patient education. Persistent urethritis, cervicitis, or proctitis also may be caused by *C. trachomatis* and other organisms.

Management of Sex Partners

Patients should be instructed to refer sex partners for evaluation and treatment. Sex partners of symptomatic patients who have *N. gonorrhoeae* infection should be evaluated and treated for *N. gonorrhoeae* and *C. trachomatis* infections, if their last sexual contact with the patient was within 30 days of onset of the patient's symptoms. If the index patient is asymptomatic, sex partners whose last sexual contact with the patient was within 60 days of diagnosis should be evaluated and treated. Health-care providers should treat the most recent sex partner, if last sexual intercourse took place before those time periods.

Patients should be instructed to avoid sexual intercourse until patient and partner(s) are cured. In the absence of microbiologic test-of-cure, this means until therapy is completed and patient and partner(s) are without symptoms.

Special Considerations

Allergy, Intolerance, or Adverse Reactions

Persons who cannot tolerate cephalosporins should, in general, be treated with quinolones. Those who can take neither cephalosporins nor quinolones should be treated with spectinomycin, except for those patients who are suspected or known to have pharyngeal infection. For pharyngeal infections among persons who can tolerate neither a cephalosporin nor quinolones, some studies suggest that trimethoprim/sulfamethoxazole may be effective at a dose of 720 mg trimethoprim/3,600 mg sulfamethoxazole orally once a day for 5 days.

Pregnancy

Pregnant women should not be treated with quinolones or tetracyclines. Those infected with *N. gonorrhoeae* should be treated with a recommended or alternate cephalosporin. Women who cannot tolerate a cephalosporin should be administered a single dose of 2 g of spectinomycin IM. Erythromycin is the recommended treatment for presumptive or diagnosed *C. trachomatis* infection during pregnancy (see Chlamydial Infections).

HIV Infection

Persons with HIV infection and gonococcal infection should receive the same treatment as persons not infected with HIV.

Gonococcal Conjunctivitis

Only one North American study of the treatment of gonococcal conjunctivitis among adults has been published in recent years. In that study, 12 of 12 patients responded favorably to a single 1 g IM injection of ceftriaxone. The recommendations that follow reflect the opinions of expert consultants.

Treatment

Recommended Regimen

A single, 1 g dose of **ceftriaxone** should be administered IM, and the infected eye should be lavaged with saline solution once.

Management of Sex Partners

As for uncomplicated infections, patients should be instructed to refer sex partner(s) for evaluation and treatment (see Uncomplicated Gonococcal Infections, Management of Sex Partners).

Disseminated Gonococcal Infection

Disseminated gonococcal infection (DGI) results from gonococcal bacteremia, often resulting in petechial or pustular acral skin lesions, asymmetrical arthalgias, tenosynovitis or septic arthritis—and is occasionally complicated by hepatitis and, rarely, by endocarditis or meningitis. Strains of *N. gonorrhoeae* that cause DGI tend to cause little genital inflammation. These strains have become uncommon in the United States during the past decade.

No North American studies of the treatment of DGI have been published recently. The recommendations that follow reflect the opinions of expert consultants.

Treatment

Hospitalization is recommended for initial therapy, especially for patients who cannot be relied on to comply with treatment, for those for whom the diagnosis is uncertain, and for those who have purulent synovial effusions or other complications. Patients should be examined for clinical evidence of endocarditis and meningitis. Patients treated for DGI should be treated presumptively for concurrent *C. trachomatis* infection.

Recommended Initial Regimen

Ceftriaxone 1 g IM or IV every 24 hours.

Alternative Initial Regimens

Cefotaxime 1 g IV every 8 hours

or

Ceftizoxime 1 g IV every 8 hours

or

For persons allergic to ß-lactam drugs:

Spectinomycin 2 g IM every 12 hours.

All regimens should be continued for 24–48 hours after improvement begins; then therapy may be switched to one of the following regimens to complete a full week of antimicrobial therapy:

Cefixime 400 mg orally 2 times a day

or

Ciprofloxacin 500 mg orally 2 times a day.

NOTE: Ciprofloxacin is contraindicated for children, adolescents ≤17 years of age, and pregnant and lactating women.

Management of Sex Partners

Gonococcal infection is often asymptomatic in sex partners of patients with DGI. As for uncomplicated infections, patients should be instructed to refer sex partner(s) for evaluation and treatment (see Uncomplicated Gonococcal Infections, Management of Sex Partners).

Gonococcal Meningitis and Endocarditis

Recommended Initial Regimen

1–2 g of **ceftriaxone** IV every 12 hours.

Therapy for meningitis should be continued for 10–14 days and for endocarditis for at least 4 weeks. Treatment of complicated DGI should be undertaken in consultation with an expert.

Management of Sex Partners

As for uncomplicated infections, patients should be instructed to refer sex partners for evaluation and treatment (see Uncomplicated Gonococcal Infections, Management of Sex Partners).

Gonococcal Infections Among Infants

Gonococcal infection among neonates usually results from peripartum exposure to infected cervical exudate of the mother. Gonococcal infection among neonates is usually an acute illness beginning 2–5 days after birth. The incidence of *N. gonorrhoeae* among neonates varies in U.S. communities, depends on the prevalence of infection among pregnant women, on whether pregnant women are screened for gonorrhea, and on whether newborns receive ophthalmia prophylaxis. The prevalence of infection is <1% in most prenatal patient populations, but may be higher in some settings.

Of greatest concern are complications of ophthalmia neonatorum and sepsis, including arthritis and meningitis. Less serious manifestations at sites of infection include rhinitis, vaginitis, urethritis, and inflammation at sites of intrauterine fetal monitoring.

Ophthalmia Neonatorum Caused by N. gonorrhoeae

In most patient populations in the United States, *C. trachomatis* and nonsexually transmitted agents are more common causes of neonatal conjunctivitis than *N. gonorrhoeae*. However, *N. gonorrhoeae* is especially important because gonococcal ophthalmia may result in perforation of the globe and in blindness.

Diagnostic Considerations

Infants at high risk for gonococcal ophthalmia in the United States are those who do not receive ophthalmia prophylaxis, whose mothers have had no prenatal care, or whose mothers have a history of STDs or substance abuse. The presence of typical Gram-negative diplococci in a Gram-stained smear of conjunctival exudate suggests a diagnosis of *N. gonorrhoeae* conjunctivitis. Such patients should be treated presumptively for gonorrhea after obtaining appropriate cultures for *N. gonorrhoeae*; appropriate chlamydial testing should be done simultaneously. The decision not to treat presumptively for *N. gonorrhoeae* among patients without evidence of gonococci on a Gram-stained smear of conjunctival exudate, or among patients for whom a Gram-stained smear cannot be performed, must be made on a case-by-case basis after considering the previously described risk factors.

A specimen of conjunctival exudate also should be cultured for isolation of *N. gonorrhoeae*, since culture is needed for definitive microbiologic identification and for antibiotic susceptibility testing. Such definitive testing is required because of the public health and social consequences for the infant and mother that may result from the diagnosis of gonococcal ophthalmia. *Moraxella catarrhalis* and other *Neisseria* species are uncommon causes of neonatal conjunctivitis that can mimic *N. gonorrhoeae* on Gram-stained smear. To differentiate *N. gonorrhoeae* from *M. catarrhalis* and other *Neisseria* species, the laboratory should be instructed to perform confirmatory tests on any colonies that meet presumptive criteria for *N. gonorrhoeae*.

Recommended Regimen

Ceftriaxone 25–50 mg/kg IV or IM in a single dose, not to exceed 125 mg.

NOTE: Topical antibiotic therapy alone is inadequate and is unnecessary if systemic treatment is administered.

Other Management Considerations

Simultaneous infection with *C. trachomatis* has been reported and should be considered for patients who do not respond satisfactorily. The mother and infant should be tested for chlamydial infection at the same time that gonorrhea testing is done (see

Ophthalmia Neonatorum Caused by *C. trachomatis*). Ceftriaxone should be administered cautiously among infants with elevated bilirubin levels, especially premature infants.

Follow-Up

Infants should be admitted to the hospital and evaluated for signs of disseminated infection (e.g., sepsis, arthritis, and meningitis). One dose of ceftriaxone is adequate for gonococcal conjunctivitis, but many pediatricians prefer to maintain infants on antibiotics until cultures are negative at 48–72 hours. The decision on duration of therapy should be made with input from experienced physicians.

Management of Mothers and Their Sex Partners

The mothers of infants with gonococcal infection and their sex partners should be evaluated and treated following the recommendations for treatment of gonococcal infections in adults (see Gonococcal Infections Among Adolescents and Adults).

Disseminated Gonococcal Infection Among Infants

Sepsis, arthritis, meningitis, or any combination thereof are rare complications of neonatal gonococcal infection. Gonococcal scalp abscesses also may develop as a result of fetal monitoring. Detection of gonococcal infection among neonates who have sepsis, arthritis, meningitis, or scalp abscesses requires cultures of blood, CSF, and joint aspirate on chocolate agar. Cultures of specimens from the conjunctiva, vagina, oropharynx, and rectum onto gonococcal selective medium are useful to identify sites of primary infection, especially if inflammation is present. Positive Gram-stained smears of exudate, CSF, or joint aspirate provide a presumptive basis for initiating treatment for *N. gonorrhoeae*. Diagnoses based on positive Gram-stained smears or presumptive isolation by cultures should be confirmed with definitive tests on culture isolates.

Recommended Regimen

Ceftriaxone 25–50 mg/kg/day IV or IM in a single daily dose for 7 days, with a duration of 10–14 days, if meningitis is documented;

or

Cefotaxime 25 mg/kg IV or IM every 12 hours for 7 days, with a duration of 10–14 days, if meningitis is documented.

Prophylactic Treatment for Infants Whose Mothers Have Gonococcal Infection

Infants born to mothers who have untreated gonorrhea are at high risk for infection.

Recommended Regimen in the Absence of Signs of Gonococcal Infection

Ceftriaxone 25–50 mg/kg IV or IM, not to exceed 125 mg, in a single dose.

Other Management Considerations

If simultaneous infection with *C. trachomatis* has been reported, mother and infant should be tested for chlamydial infection.

Follow-Up

Follow-up examination is not required.

Management of Mothers and Their Sex Partners

The mothers of infants with gonococcal infection and the mother's sex partners should be evaluated and treated following the recommendations for treatment of gonococcal infections among adults (see Gonococcal Infections).

Gonococcal Infections Among Children

After the neonatal period, sexual abuse is the most common cause of gonococcal infection among preadolescent children (see Sexual Assault or Abuse of Children). Vaginitis is the most common manifestation of gonococcal infection among preadolescent children. PID following vaginal infection appears to be less common than among adults. Among sexually-abused children, anorectal and pharyngeal infections with *N. gonorrhoeae* are common and are frequently asymptomatic.

Diagnostic Considerations

Because of the potential medical/legal use of the test results for *N. gonorrhoeae* among children, only standard culture systems for the isolation of *N. gonorrhoeae* should be used to diagnose *N. gonorrhoeae* for these children. Nonculture gonococcal tests, including Gram-stained smear, DNA probes, or EIA tests should not be used; none of these tests have been approved by the FDA for use in the oropharynx, rectum, or genital tract of children. Specimens from the vagina, urethra, pharynx, or rectum should be streaked onto selective media for isolation of *N. gonorrhoeae*. All presumptive isolates of *N. gonorrhoeae* should be confirmed by at least two tests that involve different principles, e.g., biochemical, enzyme substrate, or serologic. Isolates should be preserved to permit additional or repeated analysis.

Recommended Regimen for Children

Children Who Weigh ≥45 kg

Children who weigh ≥45 kg should be administered the same treatment regimens as those recommended for adults (see Gonococcal Infections).

Children Who Weigh <45 kg

The following treatment recommendations are for children with uncomplicated gonococcal vulvovaginitis, cervicitis, urethritis, pharyngitis, or proctitis.

Ceftriaxone 125 mg IM in a single dose.

Alternative Regimen

Spectinomycin 40 mg/kg (maximum 2 g) IM in a single dose.

Children Who Weigh <45 kg and Who Have Bacteremia, Arthritis, or Meningitis

Recommended Regimen

Ceftriaxone 50 mg/kg (maximum 1 g) IM or IV in a single dose daily for 7 days.

NOTE: For meningitis, increase the duration of treatment to 10–14 days and the maximum dose to 2 g.

Follow-Up

Follow-up cultures of specimens from infected sites are necessary to ensure that treatment has been effective.

Other Management Considerations

Only parenteral cephalosporins are recommended for use among children. Ceftriaxone is approved for all gonococcal indications among children; cefotaxime is approved for gonococcal ophthalmia only. Oral cephalosporins (cefixime, cefuroxime axetil, cefpodoxime) have not received adequate evaluation in the treatment of gonococcal infections among pediatric patients to recommend their use. The pharmacokinetic activity of these drugs among adults cannot be extrapolated to children.

All children with gonococcal infections should be evaluated for coinfection with syphilis and *C. trachomatis*. For a discussion of issues regarding sexual assault, refer to Sexual Assault or Abuse of Children.

Ophthalmia Neonatorum Prophylaxis

Instillation of a prophylactic agent into the eyes of all newborn infants is recommended to prevent gonococcal ophthalmia neonatorum and is required by law in most states. Although all the regimens that follow effectively prevent gonococcal eye disease, their efficacy in preventing chlamydial eye disease is not clear. Furthermore, they do not eliminate nasopharyngeal colonization with *C. trachomatis*. Treatment of gonococcal and chlamydial infections among pregnant women is the best method for preventing neonatal gonococcal and chlamydial disease. However, ocular prophylaxis

should continue because it can prevent gonococcal ophthalmia and, in some populations, >10% of pregnant women may receive no prenatal care.

Prophylaxis

Recommended Preparations

Silver nitrate (1%) aqueous solution in a single application

or

Erythromycin (0.5%) ophthalmic ointment in a single application

or

Tetracycline ophthalmic ointment (1%) in a single application.

One of the above preparations should be instilled into the eyes of every neonate as soon as possible after delivery. If prophylaxis is delayed (i.e., not administered in the delivery room), hospitals should establish a monitoring system to see that all infants receive prophylaxis. All infants should be administered ocular prophylaxis, whether delivery is vaginal or caesarian. Single-use tubes or ampules are preferable to multiple-use tubes. Bacitracin is *not* effective.

DISEASES CHARACTERIZED BY VAGINAL DISCHARGE

Management of the Patient with Vaginitis

Vaginitis is characterized by a vaginal discharge (usually) or vulvar itching and irritation; a vaginal odor may be present. The three common diseases characterized by vaginitis include trichomoniasis (caused by *T. vaginalis*), BV (caused by a replacement of the normal vaginal flora by an overgrowth of anaerobic microorganisms and *Gardnerella vaginalis*), and candidiasis (usually caused by *Candida albicans*). MPC caused by *C. trachomatis* or *N. gonorrhoeae* may uncommonly cause a vaginal discharge. Although vulvovaginal candidiasis is not usually transmitted sexually, it is included here because it is a common infection among women being evaluated for STDs.

The diagnosis of vaginitis is made by pH and microscopic examination of fresh samples of the discharge. The pH of the vaginal secretions can be determined by narrow-range pH paper for the elevated pH (>4.5) typical of BV or trichomoniasis. One way to examine the discharge is to dilute a sample in 1–2 drops of 0.9% normal saline solution on one slide and 10% potassium hydroxide (KOH) solution on a second slide. An amine odor detected immediately after applying KOH suggests either BV or trichomoniasis. A cover slip is placed on each slide and they are examined under a microscope at low- and high-dry power. The motile *T. vaginalis* or the clue cells of BV are usually easily identified in the saline specimen. The yeast or pseudohyphae of *Candida* species are more easily identified in the KOH specimen. The presence of objective signs of vulvar inflammation in the absence of vaginal pathogens, along with a minimal amount of discharge, suggests the possibility of mechanical or

chemical irritation of the vulva. Culture for *T. vaginalis* or *Candida* species is more sensitive than microscopic examination, but the specificity of culture for *Candida* species to diagnose vaginitis is less clear. Laboratory testing fails to identify a cause among a substantial minority of women.

Bacterial Vaginosis

BV is a clinical syndrome resulting from replacement of the normal H_2O_2-producing *Lactobacillus* spp in the vagina with high concentrations of anaerobic bacteria (e.g., *Bacteroides* spp, *Mobiluncus* spp), *G. vaginalis*, and *Mycoplasma hominis*. This condition is the most prevalent cause of vaginal discharge or malodor. However, half the women who meet clinical criteria for BV have no symptoms. The cause of the microbial alteration is not fully understood. Although BV is associated with sexual activity in that women who have never been sexually active are rarely affected and acquisition of BV is associated with having multiple sex partners, BV is not considered exclusively an STD. Treatment of the male sex partner has not been found beneficial in preventing the recurrence of BV.

Diagnostic Considerations

BV may be diagnosed by the use of clinical or Gram stain criteria. Clinical criteria require three of the following symptoms or signs:

- A homogeneous, white, noninflammatory discharge that adheres to the vaginal walls;
- The presence of clue cells on microscopic examination;
- pH of vaginal fluid >4.5;
- A fishy odor of vaginal discharge before or after addition of 10% KOH (whiff test).

When Gram stain is used, determining the relative concentration of the bacterial morphotypes characteristic of the altered flora of BV is an acceptable laboratory method for diagnosing BV. Culture of *G. vaginalis* is not recommended as a diagnostic tool because it is not specific. *G. vaginalis* can be isolated from vaginal cultures among half of normal women.

Treatment

The principal goal of therapy is to relieve vaginal symptoms and signs. Therefore, only women with symptomatic disease require treatment. Because male sex partners of women with BV are not symptomatic, and because treatment of male partners has not been shown to alter either the clinical course of BV in women during treatment or the relapse/reinfection rate, preventing transmission to men is not a goal of therapy.

Many bacterial flora characterizing BV have been recovered from the endometrium or salpinx of women with PID. BV has been associated with endometritis, PID, or vaginal cuff cellulitis following invasive procedures such as endometrial biopsy, hysterectomy, hysterosalpingography, placement of IUD, caesarian section, or uterine curettage. A randomized controlled trial found that treatment of BV with

metronidazole substantially reduced post-abortion PID. Based on these data, it may be reasonable to consider treatment of BV (symptomatic or asymptomatic) before performing surgical abortion procedures. However, more data are needed to consider treatment of asymptomatic patients with BV when performing other invasive procedures.

Recommended Regimen

Metronidazole 500 mg orally 2 times a day for 7 days.

NOTE: Patients should be advised to avoid using alcohol during treatment with metronidazole and for 24 hours thereafter.

Alternative Regimens

Metronidazole 2 g orally in a single dose.

The following alternative regimens have been effective in clinical trials, although experience with these regimens is limited.

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

or

Metronidazole gel, 0.75%, one full applicator (5 g) intravaginally, 2 times a day for 5 days;

or

Clindamycin 300 mg orally 2 times a day for 7 days.

Oral metronidazole has been shown in numerous studies to be efficacious for the treatment of BV, resulting in relief of symptoms and improvement in clinical course and flora disturbances. Based on efficacy data from four randomized-controlled trials, the overall cure rates are 95% for the 7-day regimen and 84% for the 2 g single-dose regimen.

Some health-care providers remain concerned about the possibility of metronidazole mutagenicity, which has been suggested by experiments on animals using extremely high and prolonged doses. However, there is no evidence for mutagenicity in humans. Some health-care providers prefer the intravaginal route because of lack of systemic side effects such as mild-to-moderate gastrointestinal upset and unpleasant taste (mean peak serum concentrations of metronidazole following intravaginal administration are <2% those of standard 500 mg oral doses and mean bioavailability of clindamycin cream is about 4%).

Follow-Up

Follow-up visits are not necessary if symptoms resolve. Recurrence of BV is common. The alternative treatment regimens suitable for BV treatment may be used for treatment of recurrent disease. No long-term maintenance regimen with any therapeutic agent is currently available.

Management of Sex Partners

Treatment of sex partners in clinical trials has not influenced the woman's response to therapy, nor has it influenced the relapse or recurrence rate. Therefore, routine treatment of sex partners is *not* recommended .

Special Considerations

Allergy or Intolerance to the Recommended Therapy

Clindamycin cream is preferred in case of allergy or intolerance to metronidazole. Metronidazole gel can be considered for patients who do not tolerate systemic metronidazole, but patients allergic to oral metronidazole should not be administered metronidazole vaginally.

Pregnancy

Because metronidazole is contraindicated during the first trimester of pregnancy, clindamycin vaginal cream is the preferred treatment for BV during the first trimester of pregnancy (clindamycin cream is recommended instead of oral clindamycin because of the general desire to limit the exposure of the fetus to medication). During the second and third trimesters of pregnancy, oral metronidazole can be used, although the vaginal metronidazole gel or clindamycin cream may be preferable.

BV has been associated with adverse outcomes of pregnancy (e.g., premature rupture of the membranes, preterm labor, preterm delivery), and the organisms found in increased concentration in BV are also commonly present in postpartum or post-caesarean endometritis. Whether treatment of BV among pregnant women would reduce the risk of adverse pregnancy outcomes is unknown; randomized controlled trials have not been conducted.

HIV infection

Persons with HIV and BV should receive the same treatment as persons without HIV.

Trichomoniasis

Trichomoniasis is caused by the protozoan *T. vaginalis*. The majority of men infected with *T. vaginalis* are asymptomatic, but many women are symptomatic. Among women, *T. vaginalis* typically causes a diffuse, malodorous, yellow-green discharge with vulvar irritation. There is recent evidence of a possible relationship between vaginal trichomoniasis and adverse pregnancy outcomes, particularly premature rupture of the membranes and preterm delivery.

Recommended Regimen

Metronidazole 2 g orally in a single dose.

Alternative Regimen

Metronidazole 500 mg twice daily for 7 days.

Only metronidazole is available in the United States for the treatment of trichomoniasis. In randomized clinical trials, both of the recommended metronidazole regimens have resulted in cure rates of approximately 95%. Treatment of the patient and sex partner results in relief of symptoms, microbiologic cure, and reduction of transmission. Metronidazole gel has been approved for the treatment of BV but it has not been studied for the treatment of trichomoniasis. Earlier preparations of metronidazole for topical vaginal therapy demonstrated low efficacy against trichomoniasis.

Follow-Up

Follow-up is unnecessary for men and for women who become asymptomatic after treatment.

Infections by strains of *T. vaginalis* with diminished susceptibility to metronidazole occur. However, most of these organisms respond to higher doses of metronidazole. If failure occurs with either regimen, the patient should be retreated with metronidazole 500 mg 2 times a day for 7 days. If repeated failure occurs, the patient should be treated with a single 2 g dose of metronidazole once daily for 3–5 days.

Patients with culture-documented infection who do not respond to the regimens described in this report and in whom reinfection has been excluded, should be managed in consultation with an expert. Evaluation of such cases should include determination of the susceptibility of *T. vaginalis* to metronidazole.

Management of Sex Partners

Sex partners should be treated. Patients should be instructed to avoid sex until patient and partner(s) are cured. In the absence of microbiologic test-of-cure, this means when therapy has been completed and patient and partner(s) are without symptoms.

Special Considerations

Allergy, Intolerance, or Adverse Reactions

Effective alternatives to therapy with metronidazole are not available.

Pregnancy

The use of metronidazole is contraindicated in the first trimester of pregnancy. Patients may be treated after the first trimester with 2 g of metronidazole in a single dose.

HIV Infection

Persons with HIV infection and trichomoniasis should receive the same treatment as persons without HIV.

Vulvovaginal Candidiasis

Vulvovaginal candidiasis (VVC) is caused by *C. albicans* or, occasionally, by other *Candida* spp, *Torulopsis* sp, or other yeasts. An estimated 75% of women will experience at least one episode of VVC during their lifetime, and 40%–45% will experience two or more episodes. A small percentage of women (probably <5%) experience recurrent VVC (RVVC). Typical symptoms of VVC include pruritus and vaginal discharge. Other symptoms may include vaginal soreness, vulvar burning, dyspareunia, and external dysuria. None of these symptoms is specific for VVC. VVC usually is not sexually acquired or transmitted.

Diagnostic Considerations

A diagnosis of *Candida* vaginitis is suggested clinically by pruritus in the vulvar area together with erythema of the vagina or vulva; a white discharge may occur. The diagnosis can be made when a woman has signs and symptoms of vaginitis, and when a wet preparation or Gram stain of vaginal discharge demonstrates yeasts or pseudohyphae, or when a culture or other test yields a positive result for a yeast species. Vaginitis solely because of *Candida* infection is associated with a normal vaginal pH (≤4.5). Use of 10% KOH in wet preparations improves the visualization of yeast and mycelia by disrupting cellular material that may obscure the yeast or pseudohyphae. Identifying *Candida* in the absence of symptoms should not lead to treatment, because approximately 10%–20% of women normally harbor *Candida* spp and other yeasts in the vagina. VVC may be present concurrently with STDs.

Treatment

Topical formulations provide effective treatment for VVC. The topically applied azole drugs are more effective than nystatin. Treatment with azoles results in relief of symptoms and negative cultures among 80%–90% of patients after therapy is completed.

Recommended Regimens

The following intravaginal formulations are recommended for the treatment of VVC.

Butoconazole 2% cream 5 g intravaginally for 3 days;*

or

Clotrimazole 1% cream 5 g intravaginally for 7–14 days;†

or

*These creams and suppositories are oil-based and may weaken latex condoms and diaphragms. Refer to product labeling for further information.

†Over-the-counter (OTC) preparations.

Clotrimazole 100 mg vaginal tablet for 7 days;†

or

Clotrimazole 100 mg vaginal tablet, two tablets for 3 days;

or

Clotrimazole 500 mg vaginal tablet, one tablet single application;

or

Miconazole 2% cream 5 g intravaginally for 7 days;*†

or

Miconazole 200 mg vaginal suppository, one suppository for 3 days;*

or

Miconazole 100 mg vaginal suppository, one suppository for 7 days;*†

or

Tioconazole 6.5% ointment 5 g intravaginally in a single application;*

or

Terconazole 0.4% cream 5 g intravaginally for 7 days;

or

Terconazole 0.8% cream 5 g intravaginally for 3 days;

or

Terconazole 80 mg suppository, 1 suppository for 3 days.*

Although information is not conclusive, single-dose treatments should probably be reserved for cases of uncomplicated mild-to-moderate VVC. Multi-day regimens (3- and 7-day) are the preferred treatment for severe or complicated VVC.

Preparations for intravaginal administration of both miconazole and clotrimazole are now available over-the-counter (OTC [nonprescription]), and women with VVC can choose one of those preparations. The duration for treatment with either preparation is 7 days. Self-medication with OTC preparations should be advised only for women who have been diagnosed previously with VVC and who experience a recurrence of the same symptoms. Any woman whose symptoms persist after using an OTC preparation or who experiences a recurrence of symptoms within 2 months should seek medical care.

*These creams and suppositories are oil-based and may weaken latex condoms and diaphragms. Refer to product labeling for further information.
†Over-the-counter (OTC) preparations.

Alternative Regimens

Several trials have demonstrated that oral azole agents such as fluconazole, ketoconazole, and itraconazole may be as effective as topical agents. The optimum dose and duration of oral therapy have not been established, but a range of 1–5 days of treatment, depending on the agent, has been effective in clinical trials. The ease of administration of oral agents is an advantage over topical therapies. However, the potential for toxicity associated with using a systemic drug, particularly ketoconazole, must be considered. No oral agent is approved currently by the FDA for the treatment of acute VVC.

Follow-Up

Patients should be instructed to return for follow-up visits only if symptoms persist or recur. Women who experience three or more episodes of VVC per year should be evaluated for predisposing conditions (see Recurrent Vulvovaginal Candidiasis).

Management of Sex Partners

VVC is not acquired through sexual intercourse; treatment of sex partners has not been demonstrated to reduce the frequency of recurrences. Therefore, routine notification or treatment of sex partners is not warranted. A minority of male sex partners may have balanitis, which is characterized by erythematous areas on the glans in conjunction with pruritus or irritation. These partners may benefit from treatment with topical antifungal agents to relieve symptoms.

Special Considerations

Allergy or Intolerance to the Recommended Therapy

Topical agents are usually free of systemic side effects, although local burning or irritation may occur. Oral agents occasionally cause nausea, abdominal pain, and headaches. Therapy with the oral azoles has been associated rarely with abnormal elevations of liver enzymes. Hepatotoxicity secondary to ketoconazole therapy has been estimated to appear in 1:10,000 to 1:15,000 exposed persons. Clinically important interactions may occur when these oral agents are administered with other drugs, including terfenadine, rifampin, astemizole, phenytoin, cyclosporin A, coumarin-like agents, or oral hypoglycemic agents.

Pregnancy

VVC is common during pregnancy. Only topical azole therapies should be used for the treatment of pregnant women. The most effective treatments that have been studied for pregnant women are clotrimazole, miconazole, butoconazole, and terconazole. Many experts recommend 7 days of therapy during pregnancy.

HIV Infection

Acute VVC occurs frequently among women with HIV infection and may be more severe for these women than for other women. However, insufficient information exists to determine the optimal management of VVC in HIV-infected women. Until such

information becomes available, women with HIV infection and acute VVC should be treated following the same regimens as for women without HIV infection.

Recurrent Vulvovaginal Candidiasis

RVVC, usually defined as three or more episodes of symptomatic VVC annually, affects a small proportion of women (probably <5%). The natural history and pathogenesis of RVVC are poorly understood. Risk factors for RVVC include diabetes mellitus, immunosuppression, broad spectrum antibiotic use, corticosteroid use, and HIV infection, although the majority of women with RVVC have no apparent predisposing conditions. Clinical trials addressing the management of RVVC have involved continuing therapy between episodes.

Treatment

The optimal treatment for RVVC has not been established. Ketoconazole 100 mg orally, once daily for up to 6 months reduces the frequency of episodes of RVVC. Current studies are evaluating weekly intravaginal administration of clotrimazole, as well as oral therapy with itraconazole and fluconazole, in the treatment of RVVC. All cases of RVVC should be confirmed by culture before maintenance therapy is initiated.

Although patients with RVVC should be evaluated for predisposing conditions, routinely performing HIV testing for women with RVVC who do not have HIV risk factors is unwarranted.

Follow-Up

Patients who are receiving treatment for RVVC should receive regular follow-up to monitor the effectiveness of therapy and the occurrence of side effects.

Management of Sex Partners

Treatment of sex partners does not prevent recurrences, and routine therapy is not warranted. However, partners with symptomatic balanitis or penile dermatitis should be treated with a topical agent.

Special Considerations

HIV Infection

Insufficient information exists to determine the optimal management of RVVC among HIV-infected women. Until such information becomes available, management should be the same as for other women with RVVC.

PELVIC INFLAMMATORY DISEASE

PID comprises a spectrum of inflammatory disorders of the upper genital tract among women and may include any combination of endometritis, salpingitis, tubo-ovarian abscess, and pelvic peritonitis. Sexually transmitted organisms, especially *N. gonorrhoeae* and *C. trachomatis*, are implicated in the majority of cases; however, microorganisms that can be part of the vaginal flora, such as anaerobes, *G. vaginalis*,

H. influenzae, enteric Gram-negative rods, and *Streptococcus agalactiae* also can cause PID. Some experts also believe that *M. hominis* and *U. urealyticum* are etiologic agents of PID.

Diagnostic Considerations

Because of the wide variation in many symptoms and signs among women with this condition, a clinical diagnosis of acute PID is difficult. Many women with PID exhibit subtle or mild symptoms that are not readily recognized as PID. Consequently, delay in diagnosis and effective treatment probably contributes to inflammatory sequelae in the upper reproductive tract. Laparoscopy can be used to obtain a more accurate diagnosis of salpingitis and a more complete bacteriologic diagnosis. However, this diagnostic tool is often neither readily available for acute cases nor easily justifiable when symptoms are mild or vague. Moreover, laparoscopy will not detect endometritis and may not detect subtle inflammation of the fallopian tubes. Consequently, the diagnosis of PID is usually made on the basis of clinical findings.

The clinical diagnosis of acute PID is also imprecise. Data indicate that a clinical diagnosis of symptomatic PID has a positive predictive value (PPV) for salpingitis of 65%–90% when compared with laparoscopy as the standard. The PPV of a clinical diagnosis of acute PID varies depending on epidemiologic characteristics and the clinical setting, with higher PPV among sexually active young (especially teenage) women and among patients attending STD clinics or from settings with high rates of gonorrhea or chlamydia. In all settings, however, no single historical, physical, or laboratory finding is both sensitive and specific for the diagnosis of acute PID (i.e., can be used both to detect all cases of PID and to exclude all women without PID). Combinations of diagnostic findings that improve either sensitivity (detect more women who have PID) or specificity (exclude more women who do not have PID) do so only at the expense of the other. For example, requiring two or more findings excludes more women without PID but also reduces the number of women with PID who are detected.

Many episodes of PID go unrecognized. Although some women may have asymptomatic PID, others are undiagnosed because the patient or the health-care provider fails to recognize the implications of mild or nonspecific symptoms or signs, such as abnormal bleeding, dyspareunia, or vaginal discharge (“atypical PID”). Because of the difficulty of diagnosis and the potential for damage to the reproductive health of women even by apparently mild or atypical PID, experts recommend that providers maintain a low threshold of diagnosis for PID. Even so, the long-term outcome of early treatment of women with asymptomatic or atypical PID on important clinical outcomes is unknown. The following recommendations for diagnosing PID are intended to help health-care providers recognize when PID should be suspected and when they need to obtain additional information to increase diagnostic certainty. These recommendations are based in part on the fact that diagnosis and management of other common causes of lower abdominal pain (e.g., ectopic pregnancy, acute appendicitis, and functional pain) are unlikely to be impaired by initiating empiric antimicrobial therapy for PID.

Minimum Criteria

Empiric treatment of PID should be instituted on the basis of the presence of all of the following three minimum clinical criteria for pelvic inflammation and in the absence of an established cause other than PID:

- Lower abdominal tenderness,
- Adnexal tenderness, and
- Cervical motion tenderness.

Additional Criteria

For women with severe clinical signs, more elaborate diagnostic evaluation is warranted because incorrect diagnosis and management may cause unnecessary morbidity. These additional criteria may be used to increase the specificity of the diagnosis.

Listed below are the **routine** criteria for diagnosing PID:

- Oral temperature >38.3 C,
- Abnormal cervical or vaginal discharge,
- Elevated erythrocyte sedimentation rate,
- Elevated C-reactive protein,
- Laboratory documentation of cervical infection with *N. gonorrhoeae* or *C. trachomatis*.

Listed below are the **elaborate** criteria for diagnosing PID:

- Histopathologic evidence of endometritis on endometrial biopsy,
- Tubo-ovarian abscess on sonography or other radiologic tests,
- Laparoscopic abnormalities consistent with PID.

Although initial treatment decisions can be made before bacteriologic diagnosis of *C. trachomatis* or *N. gonorrhoeae* infection, such a diagnosis emphasizes the need to treat sex partners.

Treatment

PID therapy regimens must provide empiric, broad-spectrum coverage of likely pathogens. Antimicrobial coverage should include *N. gonorrhoeae*, *C. trachomatis*, Gram-negative facultative bacteria, anaerobes, and streptococci. Although several antimicrobial regimens have proven effective in achieving clinical and microbiologic cure in randomized clinical trials with short-term follow-up, few studies have been done to assess and compare elimination of infection of the endometrium and fallopian tubes, or the incidence of long-term complications such as tubal infertility and ectopic pregnancy.

No single therapeutic regimen has been established for persons with PID. When selecting a treatment regimen, health-care providers should consider availability, cost, patient acceptance, and regional differences in antimicrobial susceptibility of the likely pathogens.

Many experts recommend that all patients with PID be hospitalized so that supervised treatment with parenteral antibiotics can be initiated. Hospitalization is especially recommended when the following criteria are met:

- The diagnosis is uncertain, and surgical emergencies such as appendicitis and ectopic pregnancy cannot be excluded,
- Pelvic abscess is suspected,
- The patient is pregnant,
- The patient is an adolescent (among adolescents, compliance with therapy is unpredictable),
- The patient has HIV infection,
- Severe illness or nausea and vomiting preclude outpatient management,
- The patient is unable to follow or tolerate an outpatient regimen,
- The patient has failed to respond clinically to outpatient therapy,
- Clinical follow-up within 72 hours of starting antibiotic treatment cannot be arranged.

Inpatient Treatment

Experts have experience with both of the following regimens. Also, there are multiple randomized trials demonstrating the efficacy of each regimen.

Regimen A

Cefoxitin 2 g IV every 6 hours or **cefotetan** 2 g IV every 12 hours,

PLUS

Doxycycline 100 mg IV or orally every 12 hours.

NOTE: This regimen should be continued for at least 48 hours after the patient demonstrates substantial clinical improvement, after which doxycycline 100 mg orally 2 times a day should be continued for a total of 14 days. Doxycycline administered orally has bioavailability similar to that of the IV formulation and may be administered if normal gastrointestinal function is present.

Clinical data are limited for other second- or third-generation cephalosporins (e.g., ceftizoxime, cefotaxime, and ceftriaxone), which might replace cefoxitin or cefotetan, although many authorities believe they also are effective therapy for PID. However, they are less active than cefoxitin or cefotetan against anaerobic bacteria.

Regimen B

Clindamycin 900 mg IV every 8 hours,

PLUS

Gentamicin loading dose IV or IM (2 mg/kg of body weight) followed by a maintenance dose (1.5 mg/kg) every 8 hours.

NOTE: This regimen should be continued for at least 48 hours after the patient demonstrates substantial clinical improvement, then followed with doxycycline 100 mg orally 2 times a day or clindamycin 450 mg orally 4 times a day to complete a total of 14 days of therapy. When tubo-ovarian abscess is present, many health-care providers use clindamycin for continued therapy rather than doxycycline, because it provides more effective anaerobic coverage. Clindamycin administered intravenously appears to be effective against *C. trachomatis* infection; however, the effectiveness of oral clindamycin against *C. trachomatis* has not been determined.

Alternative Inpatient Regimens. Limited data support the use of other inpatient regimens, but two regimens have undergone at least one clinical trial and have broad-spectrum coverage. Ampicillin/sulbactam plus doxycycline has good anaerobic coverage and appears to be effective for patients with a tubo-ovarian abscess. Intravenous ofloxacin has been studied as a single agent. A regimen of ofloxacin plus either clindamycin or metronidazole provides broad-spectrum coverage. Evidence is insufficient to support the use of any single agent regimen for inpatient treatment of PID.

Outpatient Treatment

Clinical trials of outpatient regimens have provided little information regarding intermediate and long-term outcomes. The following regimens provide coverage against the common etiologic agents of PID, but evidence from clinical trials supporting their use is limited. The second regimen provides broader coverage against anaerobic organisms but costs substantially more than the other regimen. Patients who do not respond to outpatient therapy within 72 hours should be hospitalized to confirm the diagnosis and to receive parenteral therapy.

Regimen A

Cefoxitin 2 g IM plus **probenecid**, 1 g orally in a single dose concurrently, or **ceftriaxone** 250 mg IM or other parenteral third-generation **cephalosporin** (e.g., **ceftizoxime** or **cefotaxime**),

PLUS

Doxycycline 100 mg orally 2 times a day for 14 days.

Regimen B

Ofloxacin 400 mg orally 2 times a day for 14 days,
PLUS

Either **clindamycin** 450 mg orally 4 times a day, or **metronidazole** 500 mg orally 2 times a day for 14 days.

Clinical trials have demonstrated that the cefoxitin regimen is effective in obtaining short-term clinical response. Fewer data support the use of ceftriaxone or other third-generation cephalosporins, but, based on their similarities to cefoxitin, they also are considered effective. No data exist regarding the use of oral cephalosporins for the treatment of PID.

Ofloxacin is effective against both *N. gonorrhoeae* and *C. trachomatis*. One clinical trial demonstrated the effectiveness of oral ofloxacin in obtaining short-term clinical response with PID. Despite results of this trial, there is concern related to ofloxacin's lack of anaerobic coverage; the addition of clindamycin or metronidazole provides this coverage. Clindamycin, but not metronidazole, further enhances the Gram-positive coverage of the regimen.

Alternative Outpatient Regimens. Information regarding other outpatient regimens is limited. The combination of amoxicillin/clavulanic acid plus doxycycline was effective in obtaining short-term clinical response in one clinical trial, but many of the patients had to discontinue the regimen because of gastrointestinal symptoms.

Follow-Up

Hospitalized patients receiving IV therapy should show substantial clinical improvement (e.g., defervescence, reduction in direct or rebound abdominal tenderness, and reduction in uterine, adnexal, and cervical motion tenderness) within 3–5 days of initiation of therapy. Patients who do not demonstrate improvement within this time period usually require further diagnostic workup or surgical intervention, or both.

If the provider elects to prescribe outpatient therapy, follow-up examination should be performed within 72 hours, using the criteria for clinical improvement previously described.

Because of the risk for persistent infection, particularly with *C. trachomatis*, patients should have a microbiologic re-examination 7–10 days after completing therapy. Some experts also recommend rescreening for *C. trachomatis* and *N. gonorrhoeae* 4–6 weeks after completing therapy.

Management of Sex Partners

Evaluation and treatment of sex partners of women who have PID is imperative because of the risk for re-infection and the high likelihood of urethral gonococcal or chlamydial infection of the partner.

Since nonculture, and perhaps culture, tests for *C. trachomatis* and *N. gonorrhoeae* are thought to be insensitive among asymptomatic men, sex partners should be treated empirically with regimens effective against both of these infections—regardless of the apparent etiology of PID or pathogens isolated from the infected woman.

Even in clinical settings in which only women are seen, special arrangements should be made to provide care for male sex partners of women with PID. When this is not feasible, health-care providers should ensure that sex partners are appropriately referred for treatment.

Special Considerations

Pregnancy

Pregnant women with suspected PID should be hospitalized and treated with parenteral antibiotics.

HIV Infection

Differences in the clinical manifestations of PID between HIV-infected women and noninfected women have not been described clearly. However, in one study, HIV-infected women with PID tended to have a leukopenia or a lesser leukocytosis than women who were not HIV-infected, and they were more likely to require surgical intervention. HIV-infected women who develop PID should be managed aggressively. Hospitalization and inpatient therapy with one of the IV antimicrobial regimens described in this report is recommended.

EPIDIDYMITIS

Among men <35 years of age, epididymitis is most often caused by *N. gonorrhoeae* or *C. trachomatis*. Epididymitis caused by sexually transmitted *Escherichia coli* infection also occurs among homosexual men who are the insertive partners during anal intercourse. Sexually transmitted epididymitis is usually accompanied by urethritis, which is often asymptomatic. Nonsexually transmitted epididymitis associated with urinary tract infections caused by Gram-negative enteric organisms is more common among men >35 years of age, and among men who have recently undergone urinary tract instrumentation or surgery.

Diagnostic Considerations

Men with epididymitis typically have unilateral testicular pain and tenderness; palpable swelling of the epididymis is usually present. Testicular torsion, a surgical emergency, should be considered in all cases but is more frequent among adolescents. Emergency testing for torsion may be indicated when the onset of pain is sudden, pain is severe, or test results available during the initial visit do not permit a diagnosis of urethritis or urinary tract infection. The evaluation of men for epididymitis should include the following procedures:

- A Gram-stained smear of urethral exudate or intraurethral swab specimen for *N. gonorrhoeae* and for NGU (≥5 polymorphonuclear leukocytes per oil immersion field),
- A culture of urethral exudate or intraurethral swab specimen for *N. gonorrhoeae*,
- A test of an intraurethral swab specimen for *C. trachomatis*,

- Culture and Gram-stained smear of uncentrifuged urine for Gram-negative bacteria.

Treatment

Empiric therapy is indicated before culture results are available. Treatment of epididymitis caused by *C. trachomatis* or *N. gonorrhoeae* will result in microbiologic cure of infection, improve signs and symptoms, and prevent transmission to others.

Patients with suspected sexually transmitted epididymitis should be treated with an antimicrobial regimen effective against *C. trachomatis* and *N. gonorrhoeae*; confirmation of these agents by testing will assist in partner notification efforts, but current tests for *C. trachomatis* are not sufficiently sensitive to exclude infection with that agent.

Recommended Regimen

Ceftriaxone 250 mg IM in a single dose
and
Doxycycline 100 mg orally 2 times a day for 10 days.

The effect of substituting the 125 mg dose of ceftriaxone recommended for treatment of uncomplicated *N. gonorrhoeae*, or the azithromycin regimen recommended for treatment of *C. trachomatis*, is unknown.

As an adjunct to therapy, bed rest and scrotal elevation are recommended until fever and local inflammation have subsided.

Alternative Regimen

Ofloxacin 300 mg orally 2 times a day for 10 days.

NOTE: Ofloxacin is contraindicated for persons ≤17 years of age.

Follow-Up

Failure to improve within 3 days requires re-evaluation of both the diagnosis and therapy, and consideration of hospitalization. Swelling and tenderness that persist after completing antimicrobial therapy should be evaluated for testicular cancer and tuberculous or fungal epididymitis.

Management of Sex Partners

Patients with epididymitis that is known or suspected to be caused by *N. gonorrhoeae* or *C. trachomatis* should be instructed to refer sex partners for evaluation and treatment. Sex partners of these patients should be referred if their contact with the index patient was within 30 days of onset of symptoms.

Patients should be instructed to avoid sexual intercourse until patient and partner(s) are cured. In the absence of microbiologic test-of-cure, this means until therapy is completed and patient and partner(s) are without symptoms.

Special Considerations

HIV Infection

Persons with HIV infection and uncomplicated epididymitis should receive the same treatment as persons without HIV. Fungal and mycobacterial causes of epididymitis are more common, however, among patients who are immunocompromised.

HUMAN PAPILLOMAVIRUS INFECTION

Genital Warts

Exophytic genital and anal warts are benign growths most commonly caused by HPV types 6 or 11. Other types that may be present in the anogenital region (e.g., types 16, 18, 31, 33, and 35) have been strongly associated with genital dysplasia and carcinoma. These types are usually associated with subclinical infection, but occasionally are found in exophytic warts.

Treatment

The goal of treatment is removal of exophytic warts and the amelioration of signs and symptoms—not the eradication of HPV. No therapy has been shown to eradicate HPV. HPV has been identified in adjacent tissue after laser treatment of HPV-associated cervical intraepithelial neoplasia and after attempts to eliminate subclinical HPV by extensive laser vaporization of the anogenital area.

Genital warts are generally benign growths that cause minor or no symptoms aside from their cosmetic appearance. Treatment of external genital warts is not likely to influence the development of cervical cancer. A multitude of randomized clinical trials and other treatment studies have demonstrated that currently available therapeutic methods are 22%–94% effective in clearing external exophytic genital warts, and that recurrence rates are high (usually at least 25% within 3 months) with all modalities. Several well-designed studies have indicated that treatment is more successful for genital warts that are small and that have been present <1 year. No studies have assessed if treatment of exophytic warts reduces transmission of HPV. Many experts speculate that exophytic warts may be more infectious than subclinical infection, and therefore, the risk for transmission might be reduced by "debulking" genital warts. Most experts agree that recurrences of genital warts more commonly result from reactivation of subclinical infection than reinfection by a sex partner. The effect of treatment on the natural history of HPV is unknown. If left untreated, genital warts may resolve on their own, remain unchanged, or grow. In placebo-controlled studies, genital warts have cleared spontaneously without treatment in 20%–30% of patients within 3 months.

Regimens

Treatment of genital warts should be guided by the preference of the patient. Expensive therapies, toxic therapies, and procedures that result in scarring should be avoided. A specific treatment regimen should be chosen with consideration given to

anatomic site, size, and number of warts as well as the expense, efficacy, convenience, and potential for adverse effects. Extensive or refractory disease should be referred to an expert.

Carbon dioxide laser and conventional surgery are useful in the management of extensive warts, particularly for those patients who have not responded to other regimens; these alternatives are not appropriate for treatment of limited lesions. One randomized trial of laser therapy indicated efficacy of 43%, with recurrence among 95% of patients. A randomized trial of surgical excision demonstrated efficacy of 93%, with recurrences among 29% of patients. These therapies and more cost-effective treatments do not eliminate HPV infection.

Interferon therapy is not recommended because of its cost and its association with a high frequency of adverse side effects, and efficacy is no greater than that of other available therapies. Two randomized trials established systemic interferon alpha to be no more effective than placebo. Efficacy of interferon injected directly into genital warts (intralesional therapy) during two randomized trials was 44%–61%, with recurrences among none to 67% of patients.

Therapy with 5-fluorouracil cream has not been evaluated in controlled studies, frequently causes local irritation, and is not recommended for the treatment of genital warts.

External Genital/Perianal Warts

Cryotherapy with liquid nitrogen or cryoprobe.

or

Podofilox 0.5% solution for self-treatment (*genital warts only*). Patients may apply podofilox with a cotton swab to warts twice daily for 3 days, followed by 4 days of no therapy. This cycle may be repeated as necessary for a total of 4 cycles. Total wart area treated should not exceed 10 cm^2, and total volume of podofilox should not exceed 0.5 mL per day. The health-care provider should demonstrate the proper application technique and identify which warts should be treated. If possible, the health-care provider should apply the initial treatment to demonstrate the proper application technique and identify which warts should be treated. *The use of podofilox is contraindicated during pregnancy* .

or

Podophyllin 10%–25%, in compound tincture of benzoin. To avoid the possibility of problems with systemic absorption and toxicity, some experts recommend that application be limited to ≤0.5 mL or ≤10 cm^2 per session. Thoroughly wash off in 1–4 hours. Repeat weekly if necessary. If warts persist after six applications, other therapeutic methods should be considered. *The use of podophyllin is contraindicated during pregnancy.*

or

Trichloroacetic acid (TCA) 80%–90%. Apply only to warts; powder with talc or sodium bicarbonate (baking soda) to remove unreacted acid. Repeat weekly if necessary. If warts persist after six applications, other therapies should be considered.

or

Electrodesiccation or **electrocautery**. Electrodesiccation and electrocautery are contraindicated for patients with cardiac pacemakers or for lesions proximal to the anal verge.

Cryotherapy is relatively inexpensive, does not require anesthesia, and does not result in scarring if performed properly. Special equipment is required, and most patients experience moderate pain during and after the procedure. Efficacy during four randomized trials was 63%–88%, with recurrences among 21%–39% of patients.

Therapy with 0.5% podofilox solution is relatively inexpensive, simple to use, safe, and is self-applied by patients at home. Unlike podophyllin, podofilox is a pure compound with a stable shelf-life and does not need to be washed off. Most patients experience mild/moderate pain or local irritation after treatment. Heavily keratinized warts may not respond as well as those on moist mucosal surfaces. To apply the podofilox solution safely and effectively, the patient must be able to see and reach the warts easily. Efficacy during five recent randomized trials was 45%–88%, with recurrences among 33%–60% of patients.

Podophyllin therapy is relatively inexpensive, simple to use, and safe. Compared with other available therapies, a larger number of treatments may be required. Most patients experience mild to moderate pain or local irritation after treatment. Heavily keratinized warts may not respond as well as those on moist mucosal surfaces. Efficacy in four recent randomized trials was 32%–79%, with recurrences among 27%–65% of patients.

Few data on the efficacy of TCA are available. One randomized trial among men demonstrated 81% efficacy and recurrence among 36% of patients; the frequency of adverse reactions was similar to that seen with the use of cryotherapy. One study among women showed efficacy and frequency of patient discomfort to be similar to podophyllin. No data on the efficacy of bichloroacetic acid are available.

Few data on the efficacy of electrodesiccation are available. One randomized trial of electrodesiccation demonstrated an efficacy of 94%, with recurrences among 22% of patients; another randomized trial of diathermocoagulation demonstrated an efficacy of 35%. Local anesthesia is required, and patient discomfort is usually moderate.

Cervical Warts

For women with (exophytic) cervical warts, dysplasia must be excluded before treatment is begun. Management should be carried out in consultation with an expert.

Vaginal Warts

Cryotherapy with liquid nitrogen. The use of a cryoprobe in the vagina is not recommended because of the risk for vaginal perforation and fistula formation.

or

TCA 80%–90%. Apply only to warts; powder with talc or sodium bicarbonate (baking soda) to remove unreacted acid. Repeat weekly as necessary. If warts persist after six applications, other therapeutic methods should be considered.

or

Podophyllin 10%–25% in compound tincture of benzoin. Apply to the treatment area, which must be dry before removing the speculum. Treat ≤2 cm^2 per session. Repeat application at weekly intervals. Because of concern about potential systemic absorption, some experts caution against vaginal application of podophyllin. *The use of podophyllin is contraindicated during pregnancy* .

Urethral Meatus Warts

Cryotherapy with liquid nitrogen.

or

Podophyllin 10%–25% in compound tincture of benzoin. The treatment area must be dry before contact with normal mucosa. Podophyllin must be washed off in 1–2 hours. Repeat weekly if necessary. If warts persist after six applications, other therapeutic methods should be considered. *The use of podophyllin is contraindicated during pregnancy*.

Anal Warts

Cryotherapy with liquid nitrogen.

or

TCA 80%–90%. Apply only to warts; powder with talc or sodium bicarbonate (baking soda) to remove unreacted acid. Repeat weekly if necessary. If warts persist after six applications, other therapeutic methods should be considered.

or

Surgical removal.

NOTE: Management of warts on rectal mucosa should be referred to an expert.

Oral Warts

Cryotherapy with liquid nitrogen
or
Electrodesiccation or **electrocautery**
or
Surgical removal.

Follow-Up

After warts have responded to therapy, follow-up is not necessary. Annual cytologic screening is recommended for women with or without genital warts. The presence of genital warts is not an indication for colposcopy.

Management of Sex Partners

Examination of sex partners is not necessary for management of genital warts because the role of reinfection is probably minimal. Many sex partners have obvious exophytic warts and may desire treatment; also, partners may benefit from counseling. Patients with exophytic anogenital warts should be made aware that they are contagious to uninfected sex partners. The majority of partners, however, are probably already subclinically infected with HPV, even if they do not have visible warts. No practical screening tests for subclinical infection are available. Even after removal of warts, patients may harbor HPV in surrounding normal tissue, as may persons without exophytic warts. The use of condoms may reduce transmission to partners likely to be uninfected, such as new partners; however, the period of communicability is unknown. Experts speculate that HPV infection may persist throughout a patient's lifetime in a dormant state and become infectious intermittently. Whether patients with subclinical HPV infection are as contagious as patients with exophytic warts is unknown.

Special Considerations

Pregnancy

The use of podophyllin and podofilox are contraindicated during pregnancy. Genital papillary lesions have a tendency to proliferate and to become friable during pregnancy. Many experts advocate removal of visible warts during pregnancy.

HPV types 6 and 11 can cause laryngeal papillomatosis among infants. The route of transmission (transplacental, birth canal, or postnatal) is unknown, and laryngeal papillomatosis has occurred among infants delivered by caesarean section. Hence, the preventive value of caesarean delivery is unknown. Caesarean delivery must not be performed solely to prevent transmission of HPV infection to the newborn. However, in rare instances, caesarean delivery may be indicated for women with genital warts if the pelvic outlet is obstructed or if vaginal delivery would result in excessive bleeding.

HIV Infection

Persons infected with HIV may not respond to therapy for HPV as well as persons without HIV.

Subclinical Genital HPV Infection (Without Exophytic Warts)

Subclinical genital HPV infection is much more common than exophytic warts among both men and women. Infection is often indirectly diagnosed on the cervix by Pap smear, colposcopy, or biopsy and on the penis, vulva, and other genital skin by the appearance of white areas after application of acetic acid. Acetowhitening is not a specific test for HPV infection, and false-positive tests are common. Definitive diagnosis of HPV infection relies on detection of viral nucleic acid (DNA or RNA) or capsid proteins. Pap smear diagnosis of HPV generally does not correlate well with detection of HPV DNA in cervical cells. Cell changes attributed to HPV in the cervix are similar to those of mild dysplasia and often regress spontaneously without treatment. Tests for the detection of several types of HPV DNA in cells scraped from the cervix are now widely available, but the clinical utility of these tests for managing patients is not known. Management decisions should not be made on the basis of HPV DNA tests. Screening for subclinical genital HPV infection using DNA tests or acetic acid is not recommended.

Treatment

In the absence of coexistent dysplasia, treatment is not recommended for subclinical genital HPV infection diagnosed by Pap smear, colposcopy, biopsy, acetic acid soaking of genital skin or mucous membranes, or the detection of HPV nucleic acids (DNA or RNA) or capsid antigen, because diagnosis often is questionable and no therapy has been demonstrated to eradicate infection. HPV has been demonstrated in adjacent tissue after laser treatment of HPV-associated dysplasia and after attempts to eliminate subclinical HPV by extensive laser vaporization of the anogenital area of men and women.

In the presence of coexistent dysplasia, management should be based on the grade of dysplasia.

Management of Sex Partners

Examination of sex partners is not necessary. The majority of partners are probably already infected subclinically with HPV. No practical screening tests for subclinical infection are available. The use of condoms may reduce transmission to partners likely to be uninfected, such as new partners; however, the period of communicability is unknown. Experts speculate that HPV infection may persist throughout a patient's lifetime in a dormant state and become infectious intermittently. Whether patients with subclinical HPV infection are as contagious as patients with exophytic warts is unknown.

CERVICAL CANCER SCREENING FOR WOMEN WHO ATTEND STD CLINICS OR WHO HAVE A HISTORY OF STDs

Women who have a history of STDs are at increased risk for cervical cancer, and women attending STD clinics may have additional characteristics that place them at even higher risk. Prevalence studies have found that precursor lesions for cervical cancer occur approximately five times more often among women attending STD clinics than among women attending family planning clinics.

The Pap smear (cervical smear) is an effective and relatively low-cost screening test for invasive cervical cancer and squamous intraepithelial lesions (SIL)*, the precursors of cervical cancer. The screening guidelines of both the American College of Obstetricians and Gynecologists and the American Cancer Society recommend annual Pap smears for sexually active women. Although these guidelines take the position that Pap smears can be obtained less frequently in some situations, women who attend STD clinics or who have a history of STDs should be screened annually because of their increased risk for cervical cancer. Moreover, reports from STD clinics indicate that many women do not understand the purpose or importance of Pap smears, and many women who have had a pelvic examination believe they have had a Pap smear when they actually have not.

Recommendations

Whenever a woman has a pelvic examination for STD screening, the health-care provider should inquire about the result of her last Pap smear and should discuss the following information with the patient:

- Purpose and importance of the Pap smear,
- Whether a Pap smear was obtained during the clinic visit,
- Need for a Pap smear each year,
- Names of local providers or referral clinics that can obtain Pap smears and adequately follow up results *(if a Pap smear was not obtained during this examination)*.

If a woman has *not* had a Pap smear during the previous 12 months, a Pap smear should be obtained as part of the routine pelvic examination in most situations. Health-care providers should be aware that, after a pelvic examination, many women may believe they have had a Pap smear when they actually have not, and therefore may report they have had a recent Pap smear.

In STD clinics, a Pap smear should be obtained during the routine clinical evaluation of women who have not had a documented normal smear within the past 12 months.

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* The 1988 Bethesda System for Reporting Cervical/Vaginal Cytologic Diagnoses introduced the new terms *low-grade squamous intraepithelial lesion* (SIL) and *high-grade SIL*. Low-grade SIL encompasses cellular changes associated with HPV and mild dysplasia/cervical intraepithelial neoplasia 1 (CIN 1). High-grade SIL includes moderate dysplasia/CIN 2, severe dysplasia/CIN 3, and carcinoma in situ (CIS)/CIN 3 (*16*).

A woman may benefit from receiving printed information about Pap smears and a report containing a statement that a Pap smear was obtained during her clinic visit. Whenever possible, a copy of the Pap smear result should be sent to the patient for her records.

Follow-Up

If a Pap smear shows severe inflammation with reactive cellular changes, the woman should be advised to have another Pap smear within 3 months. If possible, underlying infection should be treated before the repeat Pap smear is obtained.

If a Pap smear shows either SIL (or equivalent) or atypical squamous cells of undetermined significance (ASCUS), the woman should be notified promptly and appropriate follow-up initiated.

Appropriate follow-up of Pap smears showing a high-grade SIL (or equivalent) on Pap smears should always include referral to a health-care provider who has the capacity to provide a colposcopic examination of the lower genital tract and, if indicated, colposcopically directed biopsies. Because clinical follow-up of abnormal Pap smears with colposcopy and biopsy is beyond the scope of many public clinics, including most STD clinics, in most situations women with Pap smears demonstrating these abnormalities will need to be referred to other local providers or clinics. Women with either a low-grade SIL or ASCUS also need similar follow-up, although some experts believe that, in some situations, a repeat Pap smear may be a satisfactory alternative to referral for colposcopy and biopsy.

Other Management Considerations

Other considerations in performing Pap smears are the following:

- The Pap smear is not an effective screening test for STDs;
- If a woman is *menstruating*, a Pap smear should be postponed and the woman should be advised to have a Pap smear at the earliest opportunity;
- If a woman has an obvious severe cervicitis, the Pap smear may be deferred until after antibiotic therapy has been completed to obtain an optimum smear;
- A woman with external genital warts does not require Pap smears more frequently than a woman without warts, unless otherwise indicated.

Special Considerations

Pregnancy

Women who are pregnant should have a Pap smear as part of routine prenatal care. A cytobrush may be used for obtaining Pap smears from pregnant women, although care should be taken not to disrupt the mucous plug.

HIV Infection

Recent studies have documented an increased prevalence of SIL among women infected with HIV. Also, HIV may hasten the progression of precursor lesions to invasive cervical cancer; however, evidence supporting such a progression is limited. The

following provisional recommendations for Pap smear screening among HIV-infected women are based partially on consultation with experts in the care and management of cervical cancer and HIV infection among women.

These provisional recommendations may be altered in the future as more information regarding cervical disease among HIV-infected women becomes available:

- Women who are HIV-infected should be advised to have a comprehensive gynecologic examination, including a Pap smear, as part of their initial medical evaluation.
- If initial Pap smear results are within normal limits, at least one additional Pap smear should be obtained in approximately 6 months to rule out the possibility of false-negative results on the initial Pap smear. If the repeat Pap smear is normal, HIV-infected women should be advised to have a Pap smear obtained annually.
- If the initial or follow-up Pap smear shows severe inflammation with reactive squamous cellular changes, another Pap smear should be collected within 3 months.
- If the initial or follow-up Pap smear shows SIL (or equivalent) or ASCUS, the woman should be referred for a colposcopic examination of the lower genital tract and, if indicated, colposcopically directed biopsies.

HIV infection is not an indication for colposcopy among women with normal Pap smears.

HEPATITIS B

Hepatitis B is a common STD. Sexual transmission accounts for an estimated one-third to two-thirds of the estimated 200,000 to 300,000 new HBV infections that occurred annually in the United States during the past 10 years. Of persons infected as adults, 6%–10% become chronic HBV carriers. These persons are capable of transmitting HBV to others and are at risk for developing fatal complications. HBV leads to an estimated 5,000 deaths annually in the United States from cirrhosis of the liver and hepatocellular carcinoma.

The risk of perinatal HBV infection among infants born to HBV-infected mothers ranges from 10% to 85%, depending on the mother's hepatitis B e antigen status. Infected newborns usually become HBV carriers and are at high risk for developing chronic liver disease.

Prevention

Infection of both adults and neonates can be readily prevented with a safe and effective vaccine that has been used in the United States for more than 10 years. Universal vaccination of newborns is now recommended (*17*). The use of hepatitis B immune globulin (HBIG) combined with vaccination can prevent infection among persons exposed sexually to HBV if administered within 14 days of exposure.

Vaccination Eligibility

Persons known to be at high risk for acquiring HBV (e.g., persons with multiple sex partners, sex partners of HBV carriers, or injecting drug users) should be advised of their risk for HBV infection (as well as HIV infection) and the means to reduce their risk (i.e., exclusivity in sexual relationships, use of condoms, avoidance of nonsterile drug injection equipment, and HBV vaccination).

Selected high-risk groups for which HBV vaccination is recommended by the ACIP include the following persons:

- Sexually active homosexual and bisexual men,
- Men and women diagnosed as having recently acquired another STD,
- Persons who have had more than one sex partner in the preceding 6 months.

Such persons should be vaccinated unless they are immune to HBV as a result of past infection or vaccination. Refer to *Hepatitis B Virus: A Comprehensive Strategy for Eliminating Transmission in the United States Through Universal Child Vaccination, Recommendations of the Advisory Committee on Immunization Practices (ACIP)* (*17*).

Screening for Antibody Versus Vaccination Without Screening

The prevalence of past HBV infection among sexually active homosexual men and among injecting drug users is high. Serologic screening for evidence of past infection before vaccinating members of these groups may be cost-effective, depending on the relative costs of laboratory testing and vaccine. Among those attending STD clinics, it may be cost-effective to screen older persons for past infection. During a recent study of 2,000 STD clinic patients who accepted HBV vaccination, 28% of those ≥25 years of age had evidence of past infection, whereas only 7% of persons <25 years of age had evidence of past infection. Past infection with HBV can be detected with a serologic test for antibody to the hepatitis B core antigen (anti-HBc). Immunity can be demonstrated by a test for antibody to the hepatitis B surface antigen (anti-HBs). The HBV carrier state can be detected by a test for HBsAg. If only a test for anti-HBc is used to screen for susceptibility to infection, persons immune because of prior vaccination will be falsely classified as susceptible. If only a test for anti-HBs is used, carriers will be falsely classified as susceptible.

Vaccination Schedules

The usual vaccination schedule is three doses of vaccine at 0, 1, and 6 months. An alternative schedule of 0, 1, 2, and 12 months also has been approved for one vaccine. The dose is 1 mL for adults, which must be administered IM in the deltoid—not in a buttock. For persons 11–19 years of age, the dose is either 0.5 or 1 mL, depending on the manufacturer of the vaccine.

Management of Persons Exposed to HBV

Susceptible persons exposed to HBV through sexual contact with a person who has acute or chronic HBV infection should receive postexposure prophylaxis with 0.06 mL/kg of HBIG in a single IM dose within 14 days of their last exposure; early administration may be more effective. HBIG administration should be followed by the

standard three-dose immunization series with HBV vaccine beginning at the time of HBIG administration.

Special Considerations

Pregnancy

Pregnancy is not a contraindication to HBV or HBIG vaccine administration.

HIV Infection

Among HIV-infected persons, HBV infection is more likely to lead to chronic HBV carriage. HIV infection also impairs the response to HBV vaccine. Therefore, HIV-infected persons who are vaccinated should be tested for anti-HBs 1–2 months after the third vaccine dose. Revaccination with one or more doses should be considered for those who do not respond to vaccination initially. Those who do not respond to additional doses should be advised that they may remain susceptible.

PROCTITIS, PROCTOCOLITIS, AND ENTERITIS

Sexually transmitted gastrointestinal syndromes include proctitis, proctocolitis, and enteritis. Proctitis occurs predominantly among persons who participate in anal intercourse, and enteritis occurs among those whose sexual practices include oral-fecal contact. Proctocolitis may be acquired by either route depending on the pathogen. Evaluation should include appropriate diagnostic procedures, such as anoscopy or sigmoidoscopy, stool examination, and culture.

Proctitis is an inflammation limited to the rectum (the distal 10 cm–12 cm) that is associated with anorectal pain, tenesmus, and rectal discharge. *N. gonorrhoeae*, *C. trachomatis* (including LGV serovars), *T. pallidum*, and HSV are the most common sexually transmitted pathogens involved. Among patients coinfected with HIV, herpes proctitis may be especially severe.

Proctocolitis is associated with symptoms of proctitis plus diarrhea and/or abdominal cramps and inflammation of the colonic mucosa extending to 12 cm. Pathogenic organisms include *Campylobacter* spp, *Shigella* spp, *Entamoeba histolytica*, and, rarely, *C. trachomatis* (LGV serovars). CMV or other opportunistic agents may be involved among immunosuppressed patients with HIV infection.

Enteritis usually results in diarrhea and abdominal cramping without signs of proctitis or proctocolitis. In otherwise healthy patients, *Giardia lamblia* is most commonly implicated. Among patients with HIV infection, other infections that are not generally sexually transmitted may occur, including CMV, *Mycobacterium avium-intracellulare*, *Salmonella* spp, *Cryptosporidium*, *Microsporidium*, and *Isospora*. Multiple stool examinations may be necessary to detect *Giardia*, and special stool preparations are required to diagnose cryptosporidiosis and microsporidiosis. Additionally, enteritis may be a primary effect of HIV infection.

When laboratory diagnostic capabilities are available, treatment should be based on the specific diagnosis. Diagnostic and treatment recommendations for all enteric infections are beyond the scope of these guidelines.

Treatment

Acute proctitis of recent onset among persons who have recently practiced receptive anal intercourse is most often sexually transmitted. Such patients should be examined by anoscopy and should be evaluated for infection with HSV, *N. gonorrhoeae*, *C. trachomatis*, and *T. pallidum*. If anorectal pus is found on examination, or if polymorphonuclear leukocytes are found on a Gram-stained smear of anorectal secretions, the following therapy may be prescribed pending results of further laboratory tests.

Recommended Regimen

Ceftriaxone 125 mg IM (or another agent effective against anal and genital gonorrhea)

and

Doxycycline 100 mg orally 2 times a day for 7 days.

NOTE: For patients with herpes proctitis, refer to Genital Herpes Simplex Virus Infections.

Follow-Up

Follow-up should be based on specific etiology and severity of clinical symptoms. Reinfection may be difficult to distinguish from treatment failure.

Management of Sex Partners

Partners of patients with sexually transmitted enteric infections should be evaluated for any diseases diagnosed in the index patient.

ECTOPARASITIC INFECTIONS

Pediculosis Pubis

Patients with pediculosis pubis (pubic lice) usually seek medical attention because of pruritus. Commonly, they also notice lice on pubic hair.

Recommended Regimens

Lindane 1% shampoo applied for 4 minutes and then thoroughly washed off (not recommended for pregnant or lactating women or for children <2 years of age)

or

Permethrin 1% creme rinse applied to affected areas and washed off after 10 minutes

or

Pyrethrins with **piperonyl butoxide** applied to the affected area and washed off after 10 minutes.

The lindane regimen remains the least expensive therapy; toxicity (as indicated by seizure and aplastic anemia) has not been reported when treatment is limited to the recommended 4-minute period. Permethrin has less potential for toxicity in the event of inappropriate use.

Other Management Considerations

The recommended regimens should *not* be applied to the eyes. Pediculosis of the eyelashes should be treated by applying occlusive ophthalmic ointment to the eyelid margins two times a day for 10 days.

Bedding and clothing should be decontaminated (machine washed or machine dried using heat cycle or dry-cleaned) or removed from body contact for at least 72 hours. Fumigation of living areas is not necessary.

Follow-Up

Patients should be evaluated after 1 week if symptoms persist. Re-treatment may be necessary if lice are found or if eggs are observed at the hair-skin junction. Patients who are not responding to one of the recommended regimens should be retreated with an alternative regimen.

Management of Sex Partners

Sex partners within the last month should be treated.

Special Considerations

Pregnancy

Pregnant and lactating women should be treated with permethrin or pyrethrins with piperonyl butoxide.

HIV Infection

Persons with HIV infection and pediculosis pubis should receive the same treatment as those without HIV infection.

Scabies

The predominant symptom of scabies is pruritus. For pruritus to occur, sensitization to *Sarcoptes scabiei* must occur. Among persons with their first infection, sensitization takes several weeks to develop, while pruritus may occur within 24 hours after reinfestation. Scabies among adults may be sexually transmitted, although scabies among children is usually not sexually transmitted.

Recommended Regimen

Permethrin cream (5%) applied to all areas of the body from the neck down and washed off after 8–14 hours,

or

Lindane (1%) 1 oz. of lotion or 30 g of cream applied thinly to all areas of the body from the neck down and washed off thoroughly after 8 hours.

NOTE: Lindane should not be used following a bath, and it should not be used by persons with extensive dermatitis, pregnant or lactating women, and children <2 years of age.

Alternative Regimen

Crotamiton (10%) applied to the entire body from the neck down, nightly for 2 consecutive nights, and washed off 24 hours after the second application.

Permethrin is effective and safe but costs more than lindane. Lindane is effective in most areas of the country, but lindane resistance has been reported in some areas of the world, including parts of the United States. Seizures have occurred when lindane was applied after a bath or used by patients with extensive dermatitis. Aplastic anemia following lindane use also has been reported.

Other Management Considerations

Bedding and clothing should be decontaminated (machine washed or machine dried using hot cycle or dry-cleaned) or removed from body contact for at least 72 hours. Fumigation of living areas is not necessary.

Follow-Up

Pruritus may persist for several weeks. Some experts recommend re-treatment after 1 week for patients who are still symptomatic; other experts recommend re-treatment only if live mites can be observed. Patients who are not responding to the recommended treatment should be retreated with an alternative regimen.

Management of Sex Partners

Both sexual and close personal or household contacts within the last month should be examined and treated.

Special Considerations

Pregnant Women, Infants, and Young Children

Infants, young children, and pregnant and lactating women should *not* be treated with lindane. They may be treated with permethrin or crotamiton regimens.

HIV Infection

Persons with HIV infection and uncomplicated scabies should receive the same treatment as persons without HIV infection. Persons with HIV infection and others who are immunosuppressed are at increased risk for Norwegian scabies, a disseminated dermatologic infection. Such patients should be managed in consultation with an expert.

SEXUAL ASSAULT AND STDs

Adults and Adolescents

Recommendations in this report are limited to the identification and treatment of sexually transmitted infections and conditions commonly identified in the management of such infections. The documentation of findings and collection of specimens for forensic purposes and the management of potential pregnancy or physical and psychological trauma are beyond the scope of these recommendations. Among sexually active adults, the identification of sexually transmitted infections following assault is usually more important for the psychological and medical management of the patient than for legal purposes, if the infection could have been acquired before the assault.

Trichomoniasis, chlamydia, gonorrhea, and BV appear to be the infections most commonly diagnosed among women following sexual assault. Since the prevalence of these conditions is substantial among sexually active women, their presence (post-assault) does not necessarily signify acquisition during the assault. Chlamydial and gonococcal infection among females are of special concern because of the possibility of ascending infection.

Evaluation for Sexually Transmitted Infections

Initial Examination

An initial examination should include the following procedures:

- Cultures for *N. gonorrhoeae* and *C. trachomatis* from specimens collected from any sites of penetration or attempted penetration.

If chlamydial culture is not available, nonculture tests for chlamydia are an acceptable substitute, although false-negative test results are more common with nonculture tests and false-positive test results may occur. If a nonculture test is used, a positive test result should be verified with a second test based on a different diagnostic principle or with a blocking antibody or competitive probe procedure.

- Wet mount and culture of a vaginal swab specimen for *T. vaginalis* infection. If vaginal discharge or malodor is evident, the wet mount should also be examined for evidence of BV and yeast infection.
- Collection of a serum sample to be preserved for subsequent analysis if follow-up serologic tests are positive (see Follow-up Examination 12 Weeks After Assault).

Follow-Up Examination 2 Weeks After Assault

Examination for sexually transmitted infections should be repeated 2 weeks after the assault. Because infectious agents acquired through assault may not have produced sufficient concentrations of organisms to result in positive tests at the initial examination, culture and wet mount tests should be repeated at the 2-week visit unless prophylactic treatment has already been provided.

Follow-Up Examination 12 Weeks After Assault

Serologic tests for syphilis and HIV infection should be performed 12 weeks after the assault. If positive, testing of the sera collected at the initial examination will assist in determining whether the infection antedated the assault.

Prophylaxis

Although not all experts agree, most patients probably benefit from prophylaxis because a) follow-up of patients who have been sexually assaulted can be difficult, and b) patients may be reassured if offered treatment or prophylaxis for possible infection. The following prophylactic measures address the more common microorganisms:

- HBV vaccination (see HEPATITIS B).
- Antimicrobial therapy: empiric regimen for chlamydial, gonococcal, and trichomonal infections and for BV.

Recommended Regimen

Ceftriaxone 125 mg IM in a single dose

PLUS

Metronidazole 2 g orally in a single dose

PLUS

Doxycycline 100 mg orally 2 times a day for 7 days.

NOTE: For patients requiring alternative treatments, see the appropriate sections of this report addressing those agents.

Other Management Considerations

At the initial examination and, as indicated, at follow-up examinations, patients should be counseled regarding the following:

- Symptoms of STDs and the need for immediate examination if symptoms occur, and
- Use of condoms for sexual intercourse until STD prophylactic treatment is completed.

Risk for Acquiring HIV Infection

Although HIV-antibody seroconversion has been reported among persons whose only known risk factor was sexual assault or sexual abuse, the risk for acquiring HIV infection through sexual assault is minimal in most instances. Although the overall rate of transmission of HIV from an HIV-infected person during a single act of heterosexual intercourse is thought to be low (<1%), this risk depends on many factors. Prophylactic treatment for HIV is not known to be effective and is not generally recommended in this situation. However, all persons should be offered HIV counseling and testing after the assault.

Raising the issue of the potential for HIV infection during the initial medical evaluation may add to the acute psychological stress the patient may be experiencing because of the assault. An alternative is to address the issue at the 2-week follow-up appointment when the patient may be better able to receive this information and give informed consent for HIV testing. All persons electing to be tested for HIV should receive pretest and posttest counseling.

Sexual Assault or Abuse of Children

Recommendations in this report are limited to the identification and treatment of sexually transmitted infections. Management of the psychosocial and legal aspects of the sexual assault or abuse of children are important, but are beyond the scope of these recommendations.

The identification of sexually transmissible agents among children beyond the neonatal period suggests sexual abuse. However, there are exceptions; for example, rectal or genital infection with *C. trachomatis* among young children may be the result of perinatally acquired infection and may persist for as long as 3 years. In addition, BV and genital mycoplasmas have been identified among children who have been abused and among those who have not been abused. A finding of genital warts, although suggestive of assault, is not specific for sexual abuse without other evidence. When the only evidence of sexual abuse is the isolation of an organism or the detection of antibodies to a sexually transmissible agent, findings should be confirmed and the implications carefully considered.

Evaluation for Sexually Transmitted Infections

Examinations of children for sexual assault or abuse should be conducted so as to minimize trauma to the child. The decision to evaluate the child for STDs must be made on an individual basis. Situations involving a high risk for STDs and a strong indication for testing include the following:

- A suspected offender is known to have an STD or to be at high risk for STDs (e.g., multiple partners or past history of STD),
- The child has symptoms or signs of an STD,
- There is a high STD prevalence in the community.

Obtaining the indicated specimens requires skill to avoid psychological and physical trauma to the child. The clinical manifestations of some sexually transmitted infections are different among children when compared with adults. Examinations and specimen collection should be conducted by practitioners who have experience and training in the evaluation of abused or assaulted children.

A principal purpose of the examination is to obtain evidence of an infection that is likely to have been sexually transmitted. However, because of the legal and psychosocial consequences of a false-positive diagnosis, only tests with high specificities should be used. Additional cost and time are justified to obtain such tests.

The scheduling of examinations should depend on the history of assault or abuse. If initial exposure is recent, infectious agents acquired through the exposure may not have produced sufficient concentrations of organisms to result in positive tests. A follow-up visit approximately 2 weeks after the last sexual exposure should include a repeat physical examination and collection of additional specimens. To allow sufficient time for antibody to develop, another follow-up visit approximately 12 weeks after the last sexual exposure also is necessary to collect sera. A single examination may be sufficient if the child was abused for an extended period of time, or if the last suspected episode of abuse took place some time before the child received the medical evaluation.

The following recommendation for scheduling examinations is a general guide. The exact timing and nature of follow-up contacts should be determined on an individual basis and should be considerate of the patient's psychological and social needs. Compliance with follow-up appointments may be improved when law enforcement personnel or child protective services are involved.

Initial and 2-Week Examinations

During the initial examination and 2-week follow-up examination (if indicated), the following should be performed:

- Cultures for *N. gonorrhoeae* specimens collected from the pharynx and anus in both sexes, the vagina in girls, and the urethra in boys. Cervical specimens are not recommended for prepubertal girls. For boys, a meatal specimen of urethral discharge is an adequate substitute for an intraurethral swab specimen when discharge is present. Only standard culture systems for the isolation of *N. gonorrhoeae* should be used. All presumptive isolates of *N. gonorrhoeae* should be confirmed by at least two tests that involve different principles (e.g., biochemical, enzyme substrate, or serologic methods). Isolates should be preserved in case additional or repeated testing is needed.

- Cultures for *C. trachomatis* from specimens collected from the anus in both sexes and from the vagina in girls. Limited information suggests that the likelihood of recovering chlamydia from the urethra of prepubertal boys is too low to justify the trauma involved in obtaining an intraurethral specimen. A urethral specimen should be obtained if urethral discharge is present. Pharyngeal specimens for *C. trachomatis* also are not recommended for either sex because the yield is low, perinatally acquired infection may persist beyond infancy, and culture systems in some laboratories do not distinguish between *C. trachomatis* and *C. pneumoniae*.

Only standard culture systems for the isolation of *C. trachomatis* should be used. The isolation of *C. trachomatis* should be confirmed by microscopic identification of inclusions by staining with fluorescein-conjugated monoclonal antibody specific for *C. trachomatis*. Isolates should be preserved. Nonculture tests for chlamydia are not sufficiently specific for use in circumstances involving possible child abuse or assault.

- Culture and wet mount of a vaginal swab specimen for *T. vaginalis* infection. The presence of clue cells in the wet mount suggests BV among children with vaginal discharge. The significance of clue cells or other indicators of BV as an indicator of sexual exposure is unclear. The clinical significance of clue cells or other indicators of BV in the absence of vaginal discharge also is not clear.
- Collection of a serum sample to be preserved for subsequent analysis if follow-up serologic tests are positive. If the last sexual exposure occurred >8 weeks before the initial examination, sera should be tested immediately for antibody to sexually transmitted agents. Agents for which suitable tests are available include *T. pallidum*, HIV, and HBV. The choice of agents for serologic tests should be made on a case-by-case basis (see Examination 12 Weeks After Assault).

Examination 12 Weeks After Assault

An examination approximately 12 weeks after the last suspected sexual exposure is recommended to allow time for antibodies to infectious agents to develop. Serologic tests for the agents listed below should be considered:

- *T. pallidum*,
- HIV,
- HBV.

The prevalence of these infections varies greatly among communities, and depends upon whether risk factors are known to be present in the abuser or assailant. Also, results of HBV tests must be interpreted carefully, because HBV may be transmitted by nonsexual modes as well as sexually. The choice of tests must be made on a case-by-case basis.

Presumptive Treatment

There are few data upon which to establish the risk of a child's acquiring a sexually transmitted infection as a result of sexual abuse. The risk is believed to be low in most circumstances, although documentation to support this position is inadequate.

Presumptive treatment for children who have been sexually assaulted or abused is not widely recommended because girls appear to be at lower risk for ascending infection than adolescent or adult women, and regular follow-up can usually be assured. However, some children or their parents or guardians may be very concerned about the possibility of contracting an STD, even if the risk is perceived by the health-care practitioner to be low. Addressing patient concerns may be an appropriate indication for presumptive treatment in some settings.

Reporting

Every state, the District of Columbia, Puerto Rico, Guam, the Virgin Islands, and American Samoa have laws that require the reporting of child abuse. The exact requirements vary from state to state but, generally, if there is reasonable cause to suspect child abuse, it must be reported. Health-care providers should contact their state or local child protective service agency about child abuse reporting requirements in their areas.

References

1. CDC. Sexually Transmitted Diseases Clinical Practice Guidelines, 1991.
2. CDC. Technical guidance on HIV counseling. MMWR 1993;42(RR–2):8–17.
3. American Academy of Pediatrics, American College of Obstetrics and Gynecology (ACOG). Guidelines for Perinatal Care, third edition, 1992.
4. Guide to Clinical Preventive Services, Report of the U.S. Preventive Services Task Force. Williams and Wilkins:Baltimore, MD., 1989.
5. CDC. Recommendations for the prevention and management of *Chlamydia trachomatis* infections, 1993. MMWR 1993;42(RR-12):1-39.
6. CDC. Testing for antibodies to human immunodeficiency virus type 2 in the United States. MMWR 1992;41(RR–12):1–9.
7. CDC. Purified protein derivative (PPD-tuberculin anergy) and HIV infection: Guidelines for anergy testing and management of anergic persons at risk of tuberculosis. MMWR 1991;40 (RR–5):27–33.
8. CDC. The use of preventive therapy for tuberculous infection in the United States. MMWR 1990;39(RR–8):6–8.
9. CDC. Management of persons exposed to multidrug-resistant tuberculosis. MMWR 1992;41(RR–11):59–71.
10. Recommendations of the Advisory Committee on Immunization Practices (ACIP): Use of vaccines and immune globulins in persons with altered immunocompetence. MMWR 1993;42(RR–4):1–18.
11. CDC. Recommendations for prophylaxis against *Pneumocystis carinii* pneumonia for adults and adolescents infected with human immunodeficiency virus. MMWR 1992;41(RR–4):1–11.
12. CDC. Guidelines for prophylaxis against *Pneumocystis carinii* pneumonia for children infected with human immunodeficiency virus. MMWR 1991;40(RR–2):1–13.
13. Committee on Infectious Diseases, American Academy of Pediatrics. Report of the Committee on Infectious Diseases, 22nd edition, 1991.
14. Beall GN. Penicillins. In: Saxon A, moderator. Immediate hypersensitivity reactions to beta lactam antibiotics. Ann Intern Med 1987;107:204-15.
15. Oral desensitization protocol for patients with a positive skin test (Table). N Engl J Med 1985:312;1229-32.
16. National Cancer Institute Workshop. The 1988 Bethesda System for reporting cervical/vaginal cytological diagnoses. JAMA 1989;262:931-4.
17. CDC. Hepatitis B virus: A comprehensive strategy for eliminating transmission in the United States through universal childhood vaccination, Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1991;40(RR–13):1–25.

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