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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
CENTERS FOR DISEASE CONTROL

CENTERS FOR DISEASE CONTROL

September 1, 1989 / Vol. 38 / No. S-8

MMWR

Recommendations and Reports

MORBIDITY AND MORTALITY WEEKLY REPORT

1989 Sexually Transmitted Diseases Treatment Guidelines

U.S. Department of Health and Human Services
Public Health Service
Division of Sexually Transmitted Diseases
Center for Prevention Services
Centers for Disease Control
Atlanta, Georgia 30333

The *MMWR* series of publications is published by the Epidemiology Program Office, Centers for Disease Control, Public Health Service, U.S. Department of Health and Human Services, Atlanta, Georgia 30333.

SUGGESTED CITATION
Centers for Disease Control. 1989 Sexually Transmitted Diseases Treatment Guidelines. *MMWR* 1989;38(No. S-8):[inclusive page numbers].

Contents

Introduction

These guidelines for the treatment of patients with sexually transmitted diseases (STD) were established after consultation with a group of outside experts and staff of CDC.* These guidelines are based on available efficacy data, practical applicability, and cost. The recommendations should not be construed as rules, but rather as a source of clinical guidance within the United States. The guidelines focus on the treatment and counseling of individual patients and do not address other community services and interventions that may play roles in STD prevention. Clinical and laboratory diagnosis are briefly alluded to when appropriate in the context of therapy.

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User's Guide

STD and their therapies have been categorized by etiologic agent, if possible. Some syndromes overlap; for example, urethritis may be caused by *Neisseria gonorrhoeae* or *Chlamydia trachomatis*. Table 1 correlates symptoms syndromes with etiologic organisms and directs the user to the appropriate section in this document.

TABLE 1. Correlation of symptoms/signs, organism/syndrome, and document section.

Symptoms/signs	Organism/syndrome	Document section
Infections in Men		
Urethritis	*Neisseria gonorrhoeae*	Gonorrhea
	Chlamydia trachomatis	Chlamydia
	Herpes simplex virus (HSV)	Herpes (primary)
	Mycoplasma hominis	Nongonococcal urethritis (NGU)
	Ureaplasma urealyticum	NGU
	Uncharacterized	NGU
Epididymitis		See specific section
Infections in Women		
Cervicitis	*N. gonorrhoeae*	Gonorrhea
	C. trachomatis	Chlamydia
	HSV	Herpes
Mucopurulent cervicitis		See specific section
Pelvic inflammatory disease		See specific section
Vaginal infections	*Trichomonas vaginalis*	Trichomoniasis
	Candida albicans	Candida infections
	Bacterial vaginosis (BV)	See specific section
Perinatal infections	*Treponema pallidum*	Syphilis
	N. gonorrhoeae	Gonorrhea
	C. trachomatis	Chlamydia
	HSV	Herpes
	BV	BV
	Candida	Candida infections
	T. vaginalis	Trichomoniasis
	Human immunodeficiency virus (HIV)	HIV
	Human papillomavirus (HPV)	Genital warts
	Hepatitis B	Hepatitis B
	Cytomegalovirus (CMV)	CMV
Genital ulcer disease	*T. pallidum*	Syphilis
	Haemophilus ducreyi	Chancroid
	HSV	Herpes
	C. trachomatis	Lymphogranuloma venereum (LGV)
Genital warts	HPV	Genital warts
Enteric infection		See specific section
Proctitis (See also enteric infections)	*N. gonorrhoeae*	Gonorrhea
	C. trachomatis	Chlamydia
	T. pallidum	Syphilis
	HSV	Herpes
	Other	See Enteric Infection section
Ophthalmic disease (See specific section for general prevention)	*N. gonorrhoeae*	Gonorrhea
	C. trachomatis	Chlamydia

Abbreviations Used in This Publication

AIDS	Acquired immunodeficiency syndrome
BV	Bacterial vaginosis
CMRNG	Chromosomally mediated resistant *Neisseria gonorrhoeae*
CMV	Cytomegalovirus
CSF	Cerebrospinal fluid
DGI	Disseminated gonococcal infection
DIS	Disease Intervention Specialist(s)
ELISA	Enzyme-linked immunosorbent assay
FTA-ABS	Fluorescent treponemal antibody absorbed
HBIG	Hepatitis B immune globulin
HBsAg	Hepatitis B surface antigen
HIV	Human immunodeficiency virus
HPV	Human papillomavirus
HSV	Herpes simplex virus
IM	Intramuscularly
IV	Intravenous
LGV	Lymphogranuloma venereum
MHATP	Microhemagglutination assay for antibody to *Treponema pallidum*
MPC	Mucopurulent cervicitis
NGU	Nongonococcal urethritis
PID	Pelvic inflammatory disease
PPD	Purified protein derivative
PPNG	Penicillinase-producing *N. gonorrhoeae*
RPR	Rapid plasma reagin
STD	Sexually transmitted disease(s)
TCA	Trichloroacetic acid
TRNG	Tetracycline-resistant *N. gonorrhoeae*
VDRL	Venereal Disease Research Laboratory
ZDV	Zidovudine

Clinician Guidelines And Public Health Considerations

Control of STD is based on four major concepts: 1) education of persons at risk on the modes of disease transmission and the means for reducing the risk of transmission; 2) detection of infection in asymptomatic persons and in persons who are symptomatic but unlikely to seek diagnostic and treatment services; 3) effective diagnosis and treatment of persons who are infected; and 4) evaluation, treatment, and counseling of sex partners of persons with an STD. Although this document deals largely with clinical aspects of STD control, the prevention of STD is based primarily on changing the sexual behaviors that put patients at risk.

Clinical Considerations

For persons requesting health services for evaluation of an STD, appropriate care consists of the following components (the temporal order of the interventions may vary, depending on the specific case and diagnosis):

History
Medical and behavioral risk assessment
Physical examination
Laboratory investigations
Diagnosis
Curative or palliative therapy
Counseling and education
  Present episode of STD
  Prevention of future episodes
Reporting of case when required
Sex partner identification, notification, and evaluation
Clinical follow-up when appropriate

Persons who are seeking health-care services for other reasons, but who are at risk for acquisition of STD*, should undergo the following as part of their routine health care:

- STD risk assessment
- Directed physical examination based on elicited symptoms
- Screening for asymptomatic infections

In special situations, such as prenatal visits and legally induced abortions, screening for STD may have greater impact in preventing complications of STD. For specific recommendations in cases of sexual assault or child abuse, see "Sexual Assault and STD."

Specific guidelines for screening in each situation are beyond the scope of this document. However, whenever possible, the following laboratory screening tests for STD should be available:

*Persons at higher risk for STD include sexually active persons under 25 years of age, those who have had multiple sexual partners within the previous 6 months, and those with a history of STD. In addition, prostitutes and persons having sexual contact with prostitutes, users of illicit drugs, and inmates of detention centers have increased rates of STD and should be evaluated when seeking medical care.

HIV antibody test (screening + confirmatory test)
Syphilis serology (nontreponemal test + treponemal confirmatory test)
Culture for *N. gonorrhoeae*
Culture or antigen test for *C. trachomatis*
Light microscopy for Gram's stain, wet mounts of vaginal secretions
Dark-field microscopy for *Treponema pallidum*

Diagnosis of an STD should be considered a "sentinel event" reflecting unprotected sexual activity. Patients with one STD are at high risk for having others. Therefore, patients should be closely evaluated for other STD infections, including syphilis and human immunodeficiency virus (HIV) serology (if not performed within the previous 3 months), gonorrhea and chlamydial testing from appropriate anatomic sites, and physical examination. Women wishing to prevent unplanned pregnancy and who are not using contraception should be counseled about contraception services; ideally, contraceptives and pregnancy testing should be available at the same facility providing STD services. Annual Pap smear evaluation should also be available.

Primary Prevention

Clinics and practitioners who treat patients with STD should have resources available for educating patients about risk assessment and behavioral choices. Behavioral assessment is an integral part of the STD history, and patients should be counseled on methods to lower their risk of acquiring STD, including abstinence, careful selection of partners, use of condoms and spermicides, and periodic examination. Specific recommendations for behavioral assessment and counseling are beyond the scope of these guidelines.

Condoms and Spermicides

Condoms and spermicides should be available in any facility providing clinical STD services. Instruction in proper use should also be provided. Although condoms do not provide absolute protection from any infection, if properly used, they reduce the risk of infection. Recommendations for the proper use of condoms (Table 2) have been made by CDC and other public health organizations.

Special Populations

Pregnant Women

Intrauterine or perinatally transmitted STD can have fatal or severely debilitating effects on the fetus. Routine prenatal care should include an assessment for STD, which in most cases includes serologic screening for syphilis and hepatitis B, testing for chlamydia, and gonorrhea culture (see specific sections for management of clinical disease). Prenatal screening for HIV is indicated for all patients with risk factors for HIV or with a high-risk sexual partner; some authorities recommend HIV screening of all pregnant women.

Practical management issues are discussed in the sections pertaining to specific diseases. Pregnant women and their sexual partners should be questioned about STD and counseled about possible neonatal infections. Pregnant women with primary genital herpes infection, hepatitis B, primary cytomegalovirus (CMV) infection, or Group B streptococcal infection may need to be referred to an expert for management. In the absence of lesions or other evidence of active disease, tests for herpes simplex virus (HSV) and cesarean delivery are *not* routinely indicated for women with a history of recurrent genital herpes infection during pregnancy. Routine HPV screening is not recommended. For a fuller discussion of these issues, as well as for infections not transmitted sexually, refer to "Guidelines for Perinatal Care" (second edition, 1988), jointly written and published by the American Academy of Pediatrics and the American College of Obstetricians and Gynecologists.

Children

Management of STD in children 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; in other diseases, such as HPV infection and vaginitis, the association with sexual contact is not so clear (see "Sexual Assault and STD").

TABLE 2. Recommendations for use of condoms

1. Latex condoms should be used because they may offer greater protection against HIV and other viral STD than natural membrane condoms.
2. Condoms should be stored in a cool, dry place out of direct sunlight.
3. Condoms in damaged packages or those that show obvious signs of age (e.g., those that are brittle, sticky, or discolored) should not be used. They cannot be relied upon to prevent infection or pregnancy.
4. Condoms should be handled with care to prevent puncture.
5. The condom should be put on before any genital contact to prevent exposure to fluids that may contain infectious agents. Hold the tip of the condom and unroll it onto the erect penis, leaving space at the tip to collect semen, yet ensuring that no air is trapped in the tip of the condom.
6. Only water-based lubricants should be used. Petroleum- or oil-based lubricants (such as petroleum jelly, cooking oils, shortening, and lotions) should not be used because they weaken the latex and may cause breakage.
7. Use of condoms containing spermicides may provide some additional protection against STD. However, vaginal use of spermicides along with condoms is likely to provide still greater protection.
8. If a condom breaks, it should be replaced immediately. If ejaculation occurs after condom breakage, the immediate use of spermicide has been suggested. However, the protective value of postejaculation application of spermicide in reducing the risk of STD transmission is unknown.
9. After ejaculation, care should be taken so that the condom does not slip off the penis before withdrawal; the base of the condom should be held throughout withdrawal. The penis should be withdrawn while still erect.
10. Condoms should never be reused.

Adapted from *MMWR* 1988;37:133-7.

Patients with Multiple Episodes of STD ("Repeaters")

These patients have a disproportionately high rate of STD and should be targeted for intensive counseling on methods to reduce risk. More research is needed into methods of behavior modification for these patients, including the role of outreach and support services. In many cases, periodic call-back for STD evaluation may be indicated.

STD Core Groups

Populations of core STD transmitters account for most STD morbidity. Although substantial regional variation occurs, in most urban areas the core groups consist largely of ethnic minority populations with low levels of education and socioeconomic attainment. In many such environments, illicit drug use and prostitution are common. Core groups are often geographically limited, permitting definition of core geographic areas as well as populations. STD programs should evaluate the occurrence of STD in their jurisdictions to define core populations and core areas for targeted education, screening, clinical outreach, call-back reexamination programs, and other control measures.

Illicit Drug Users

STD appear to be increasingly linked to illicit drug use. Illicit drug users may be at higher risk for sexual behaviors that put them at risk for STD. In addition, illicit drug users account for an increasing proportion of HIV infections. Further research is needed into the behaviors associated with drug use and STD, particularly to facilitate behavioral and clinical interventions targeted at drug users. Outreach programs in the community and in cooperation with drug treatment programs should be considered.

Prison and Detention Populations

Residents of short-term correctional and detention facilities often have high prevalence rates of STD. Screening and treatment for infections that are highly prevalent in the community should be provided for all inmates. In many situations, screening and treatment in the prison population is central to effective STD control. In addition, for many patients, correctional health services may be the only opportunity for interaction with health-care providers.

Patients with HIV Infection and STD

The management of patients with STD who are coinfected with HIV presents complex clinical and behavioral issues. Because of its effect on the immune system, HIV may alter the natural histories of many STD, as well as the effect of antimicrobial therapy. Close clinical follow-up is imperative. STD infection in patients with and without HIV is a sentinel event, often indicating continued unprotected sexual activity. Further patient counseling is indicated in these situations.

STD Reporting and Confidentiality

Disease surveillance activities, which include the accurate identification and timely reporting of STD, form an integral part of successful disease control. Reporting assists local health authorities in identifying sexual contacts who may be infected (see next section). Reporting is also important for assessing morbidity trends.

Reporting may be provider- and/or laboratory-based. Cases should be reported in accordance with local statutory requirements and in as timely a manner as possible. Clinicians who are unsure of local reporting requirements are encouraged to seek advice through their local health departments or state STD programs.

STD reports are held in strictest confidence and in many jurisdictions are protected by statute from subpoena. Before any follow-up of a positive STD test is conducted by STD program representatives, these personnel consult with the provider to verify the diagnosis and treatment. Most local health departments offer STD partner notification and follow-up services for selected STD.

Management of Sex Partners and Partner Notification

Clinical guidelines for management of sex partners are included in each disease section.

Breaking the chain of transmission is crucial to STD control. Further transmission and reinfection are prevented by referral of sex partners for diagnosis and treatment. Patients should ensure that their sex partners, including those without symptoms, are referred for evaluation. Partners of patients with STD should be examined; treatment should not be provided for partners who are not examined, except in rare instances such as when the partner is at a site remote from medical care. Appropriate referral for sex partners should be provided if care will not or cannot be provided by the initial health-care provider. Disease Intervention Specialists (DIS), i.e., public health professionals trained in STD management, can assist patients and practitioners in this process through interviewing and confidential field outreach procedures. Local and state health departments offer DIS referral services. Physicians and other community health personnel are encouraged to use DIS services to ensure complete case management. Health department managers should allocate DIS resources based on local morbidity patterns, outbreak situations, and available resources.

Medical Resources

Health-care providers caring for STD patients should ensure that medical resources for the following are available either on site or through referral:

- Medical evaluation and treatment facilities for HIV-infected patients
- Hospitalization facilities for patients with complicated STD infection, such as pelvic inflammatory disease (PID) and disseminated gonococcal infection (DGI)
- Medical, pediatric, infectious disease, dermatologic, and gynecological/obstetrical referral services
- Family planning services
- Substance abuse treatment services

AIDS and HIV Infection in The General STD Setting

The acquired immunodeficiency syndrome (AIDS) is a late manifestation of infection with human immunodeficiency virus (HIV). Most people infected with HIV remain asymptomatic for long periods. HIV infection is most often diagnosed by using HIV antibody tests. Detectable antibody usually develops within 3 months after infection. A confirmed positive antibody test means that a person is infected with HIV and is capable of transmitting the virus to others. Although a negative antibody test usually means a person is not infected, antibody tests cannot rule out infection from a recent exposure. If antibody testing is related to a specific exposure, the test should be repeated 3 and 6 months after the exposure.

Antibody testing for HIV begins with a screening test, usually an enzyme-linked immunosorbent assay (ELISA). If the screening test is positive, it is followed by a more specific confirmatory test, most commonly the Western blot assay. New antibody tests are being developed and licensed that are either easier to perform or more accurate. Positive results from screening tests must be confirmed before being considered definitive.

The time between infection with HIV and development of AIDS ranges from a few months to $\geq$10 years. Most people who are infected with HIV will eventually have some symptoms related to that infection. In one cohort study, AIDS developed in 48% of a group of gay men $\leq$10 years after infection; but additional AIDS cases are expected among those who have remained AIDS-free for >10 years.

Therapy with zidovudine (ZDV—previously known as azidothymidine) has been shown to benefit persons in the later stages of disease (AIDS or AIDS-related conditions along with a CD4 [T4] lymphocyte count less than 200/mm^3). Serious side effects, usually anemias and cytopenias, have been common during therapy with ZDV; therefore, patients taking ZDV require careful follow-up in consultation with physicians who are familiar with ZDV therapy. Clinical trials are currently evaluating ZDV therapy for persons with asymptomatic HIV infection to see if it decreases the rate of progression to AIDS. Other trials are evaluating new drugs or combinations of drugs for persons with different stages of HIV infection, including asymptomatic infections. The complete therapeutic management of HIV infection is beyond the scope of this document.

Preventing the Sexual Transmission of HIV

The only way to prevent AIDS is to prevent the initial infection with HIV. Prevention of sexual transmission of HIV can be ensured in only two situations: 1) sexual abstinence or 2) choosing only sex partners who are not infected with HIV.

Many HIV-infected persons are asymptomatic and are unaware that they are infected. Therefore, without an antibody test, infected persons are difficult to identify. AIDS case surveillance and HIV seroprevalence studies allow estimation of risk for persons in different areas; however, these population estimates may have a limited impact on an individual's sexual decisions. Although knowledge of antibody status is desirable before a sexual relationship is initiated, this information may not be

available. Therefore, individuals should be counseled that when they initiate a sexual relationship they should use sexual practices that reduce the risk of HIV transmission.

Sexual practices may influence the likelihood of HIV transmission during sexual contact with an infected partner. Women who practice anal intercourse with an infected partner are more likely to acquire infection than women who have only vaginal intercourse. The relative risk of transmission by oral-genital contact is probably somewhat lower than the risk of transmission by vaginal intercourse. Other STD or local trauma that breaks down the mucosal barrier to infection would be expected to increase the risk of HIV transmission. Condoms supplement natural barriers to infection and therefore reduce the risk of HIV transmission (see "Clinician Guidelines and Public Health Considerations").

When to Test for HIV

Voluntary, confidential, HIV antibody testing should be done routinely when the results may contribute either to the medical management of the person being tested or to the prevention of further transmission.

Testing is important for persons with symptoms of HIV-related illnesses or with diseases such as syphilis, chancroid, herpes, or tuberculosis, for which a positive test result might affect the recommended diagnostic evaluation, treatment, or follow-up. HIV counseling and testing for persons with STD is a particularly important part of an HIV prevention program, because patients who have acquired an STD have demonstrated their potential risk for acquiring HIV.

Because no vaccine or cure is available, HIV prevention requires changes in behavior by people at risk for transmitting or acquiring infection. Therefore, patient counseling must be an integral part of any HIV testing program in an STD clinic. Counseling should be done both before and after HIV testing.

Pretest Counseling

Pretest counseling should include assessment of the patient's risk for HIV infection and measures to reduce that risk.

Intravenous (IV) drug users should be advised to stop using drugs. If they do not stop, they should not share needles. If needle-sharing continues, injection equipment should be cleaned with bleach between uses. Sexually active persons who have multiple partners should be advised to consider sexual abstinence or to enter a mutually monogamous relationship with a partner who has also been tested for HIV. Condoms should be used consistently if either or both partners are infected or have other partners. Similarly, heterosexuals with STD other than HIV should be encouraged to bring their partners in for HIV testing and to use condoms if they are not in a mutually monogamous relationship with an uninfected partner.

Posttest Counseling and Evaluation

Persons who have negative HIV antibody tests should be told their test result by a person who understands the need to reduce unsafe sexual behaviors and can explain ways to modify sexual practices to reduce risks.

Antibody tests cannot detect infections that occurred in the several weeks before the test (see above). Persons who have negative tests should understand that the negative test result does not signify protection from acquiring infection. They should be advised about the ways the virus is transmitted and how to avoid infection. Their partners' risks for HIV infection should be discussed, and partners at risk should be encouraged to be tested for HIV.

Persons who test positive for HIV antibody should be told their test result by a person who is able to discuss the medical, psychological, and social implications of HIV infection. Routes of HIV transmission and methods to prevent further transmission should be emphasized.

Risks to past sexual and needle-sharing partners of HIV antibody-positive patients should be discussed, and they should be instructed in how to notify their partners and to refer them for counseling and testing. If they are unable to notify their partners or they are not sure that their partners will seek counseling, physicians or health department personnel should assist, using confidential procedures, to ensure that the partners are notified. Infected women should be advised of the risk of perinatal transmission (see below), and methods of contraception should be discussed and provided. Additional follow-up, counseling, and support systems should be available to facilitate psychosocial adjustment and changes in behavior among HIV antibody-positive persons.

Perinatal Infections

Infants born to women with HIV infection may also be infected with HIV; this risk is estimated to be 30%-40%. The mother in such a case may be asymptomatic and her HIV infection not recognized at delivery. Infected neonates are usually asymptomatic, and currently HIV infection cannot be readily or easily diagnosed at birth. (A positive antibody test may reflect passively transferred maternal antibodies, and the infant must be observed over time to determine if neonatal infection is present.) Infection may not become evident until the child is 12-18 months of age. All pregnant women with a history of STD should be offered HIV counseling and testing. Recognition of HIV infection in pregnancy permits health-care workers to inform patients about the risks of transmission to the infant and the risks of continuing pregnancy.

Asymptomatic HIV Infections

As more HIV-infected persons are identified, primary health-care providers will need to assume increased responsibility for these patients. Most internists, pediatricians, family practitioners, and gynecologists should be qualified to provide initial evaluation of HIV-infected individuals and follow-up of those with uncomplicated HIV infection. These services should be available in all public health clinics.

Health-care professionals who identify HIV-positive patients should provide posttest counseling; medical evaluation (either on site or by referral)—including a physical examination, complete blood count, lymphocyte subset analysis, syphilis serology, and a purified protein derivative (PPD) skin test for tuberculosis. Psychosocial counseling resources should also be available.

All clinics and providers should establish and maintain contacts with resources in their regions for persons concerned about HIV infection, and they should refer patients when necessary. Possible resources for referral include counseling services, support groups, social workers, physicians, and clinics.

Diseases Characterized by Genital Ulcers or Inguinal Lymphadenopathy

In the United States, most patients with genital ulcers have genital herpes, syphilis, or chancroid. Inguinal lymphadenopathy is common in these infections. More than one of these diseases may be present in a patient. Patients who have genital ulcers may be at increased risk for HIV infection.

Diagnosis based only on history and physical examination is often inaccurate. Thus, evaluation of most persons with genital ulcers should include one or more of the following:

- Dark-field examination or direct immunofluorescence test for *T. pallidum*
- Serologic test(s) for syphilis
- Culture or antigen test for HSV
- Culture for *Haemophilus ducreyi*

Chancroid

Because of recent spread of *H. ducreyi*, chancroid has become an important STD in the United States. Its importance is enhanced by the knowledge that outside the United States chancroid has been associated with increased infection rates for HIV. Chancroid must be considered in the differential diagnosis of any patient with a painful genital ulcer. Painful inguinal lymphadenopathy is present in about half of all chancroid cases.

Recommended Regimen

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

or

Ceftriaxone 250 mg intramuscularly (IM) in a single dose.

Alternative Regimen

Trimethoprim/sulfamethoxazole 160/800 mg (one double-strength tablet) orally 2 times a day for 7 days.

Comment: The susceptibility of *H. ducreyi* to this combination of antimicrobial agents varies throughout the world; clinical efficacy should be monitored, preferably in conjunction with monitoring of susceptibility patterns.

or

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

Comment: Not evaluated in the United States.

or

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

Comment: Although a regimen of 500 mg orally once was effective outside the United States, based on pharmacokinetics and susceptibility data, 2- or 3-day regimens of the same dose may be prudent, especially for patients coinfected with HIV. Quinolones, such as ciprofloxacin, are contraindicated during pregnancy and in children 16 years of age or younger.

Management of Sex Partners

Sex partners, within the 10 days preceding onset of symptoms in an infected patient, whether symptomatic or not, should be examined and treated with a recommended regimen.

Follow-Up

If treatment is successful, ulcers due to chancroid symptomatically improve within 3 days and objectively improve (evidenced by resolution of lesions and clearing of exudate) within 7 days after institution of therapy. Clinical resolution of lymphadenopathy is slower than that of ulcers and may require needle aspiration (through healthy, adjacent skin), even during successful therapy. Patients should be observed until the ulcer is completely healed. Because of the epidemiologic association with syphilis, serological testing for syphilis should be considered within 3 months after therapy.

Treatment Failures

If no clinical improvement is evident by 7 days after therapy, the clinician should consider whether 1) antimicrobials were taken as prescribed, 2) the *H. ducreyi* causing infection is resistant to the prescribed antimicrobial, 3) the diagnosis is correct, 4) coinfection with another STD agent exists, or 5) the patient is also infected with HIV. Preliminary information indicates that patients coinfected with HIV do not respond to antimicrobial therapy as well as patients not infected with HIV, especially when single-dose treatment is used. Antimicrobial susceptibility testing should be performed on *H. ducreyi* isolated from patients who do not respond to recommended therapies.

Syphilis

General principles

Serologic Tests

Dark-field examinations and direct fluorescent antibody tests on lesions or tissue are the definitive methods for diagnosing early syphilis. Presumptive diagnosis is possible by using two types of serologic tests for syphilis: 1) treponemal (e.g., fluorescent treponemal antibody absorbed [FTA-ABS], microhemagglutination assay

for antibody to *T. pallidum* [MHATP]) and 2) nontreponemal (e.g., Venereal Disease Research Laboratory [VDRL], rapid plasma reagin [RPR]). Neither test alone is sufficient for diagnosis. Treponemal antibody tests, once positive, usually remain so for life, regardless of treatment or disease activity. Treponemal antibody titers do not correlate with disease activity and should be reported as positive or negative. Nontreponemal antibody titers do tend to correlate with disease activity, usually rising with new infection and falling after treatment. Nontreponemal antibody test results should be reported quantitatively and titered out to a final end point rather than reported as greater than an arbitrary cutoff (e.g., >1:512). With regard to changes in nontreponemal test results, a fourfold change in titers is equivalent to a two-dilution change—e.g., from 1:16 to 1:4, or from 1:8 to 1:32.

For sequential serologic tests, the same test (e.g., VDRL or RPR) should be used, and it should be run by the same laboratory. The VDRL and RPR are equally valid, but RPR titers are often slightly higher than VDRL titers and therefore are not comparable.

Neurosyphilis cannot be accurately diagnosed from any single test. Cerebrospinal fluid (CSF) tests should include cell count, protein, and VDRL (not RPR). The CSF leukocyte count is usually elevated (>5 WBC/mm^3) when neurosyphilis is present and is a sensitive measure of the efficacy of therapy. VDRL is the standard test for CSF; ***when positive*** it is considered ***diagnostic*** of neurosyphilis. However, it may be negative when neurosyphilis is present and cannot be used to rule out neurosyphilis. Some experts also order an FTA-ABS; this may be less specific (more false positives) but is highly sensitive. The positive predictive value of the CSF-FTA-ABS is lower, but ***when negative***, this test provides evidence ***against*** neurosyphilis.

Penicillin Therapy

Penicillin is the preferred drug for treating patients with syphilis. Penicillin is the only proven therapy that has been widely used for patients with neurosyphilis, congenital syphilis, or syphilis during pregnancy. For patients with penicillin allergy, skin testing—with desensitization, if necessary—is optimal. Sample guidelines for skin testing and desensitization are included (see Appendix to this section). However, the minor determinant mixture for penicillin is not currently available commercially.

Jarisch-Herxheimer Reaction

The Jarisch-Herxheimer reaction is an acute febrile reaction, often accompanied by headache, myalgia, and other symptoms, that may occur after any therapy for syphilis, and patients should be so warned. Jarisch-Herxheimer reactions are more common in patients with early syphilis. Antipyretics may be recommended, but no proven methods exist for preventing this reaction. Pregnant patients, in particular, should be warned that early labor may occur.

Persons Exposed to Syphilis (Epidemiologic Treatment)

Persons sexually exposed to a patient with early syphilis should be evaluated clinically and serologically. If the exposure occurred within the previous 90 days, the person may be infected yet seronegative and therefore should be presumptively

treated. (It may be advisable to presumptively treat persons exposed more than 90 days previously if serologic test results are not immediately available and follow-up is uncertain.) Patients who have other STD may also have been exposed to syphilis and should have a serologic test for syphilis. The dual therapy regimen currently recommended for gonorrhea (ceftriaxone and doxycycline) is probably effective against incubating syphilis. If a different, nonpenicillin antibiotic regimen is used to treat gonorrhea, the patient should have a repeat serologic test for syphilis in 3 months.

Early Syphilis

Primary and Secondary Syphilis and Early Latent Syphilis of Less than 1 Year's Duration

Recommended Regimen

Benzathine penicillin G, 2.4 million units IM, in one dose.

Alternative Regimen for Penicillin-Allergic Patients (Nonpregnant)

Doxycycline, 100 mg orally 2 times a day for 2 weeks

or

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

Doxycycline and **tetracycline** are equivalent therapies. There is less clinical experience with **doxycycline**, but compliance is better. In patients who cannot tolerate doxycycline or tetracycline, three options exist:

- If follow-up or compliance cannot be ensured, the patient should have skin testing for penicillin allergy and be desensitized if necessary (see Appendix).
- If compliance and follow-up are ensured, **erythromycin**, 500 mg orally 4 times a day for 2 weeks, can be used.
- Patients who are allergic to penicillin may also be allergic to cephalosporins; therefore, caution must be used in treating a penicillin-allergic patient with a cephalosporin. However, preliminary data suggest that **ceftriaxone**, 250 mg IM once a day for 10 days, is curative—but careful follow-up is mandatory.

Follow-Up

Treatment failures can occur with any regimen. Patients should be reexamined clinically and serologically at 3 months and 6 months. If nontreponemal antibody titers have not declined fourfold by 3 months with primary or secondary syphilis, or by 6 months in early latent syphilis, or if signs or symptoms persist and reinfection has been ruled out, patients should have a CSF examination and be retreated appropriately.

HIV-infected patients should have more frequent follow-up, including serologic testing at 1, 2, 3, 6, 9, and 12 months. In addition to the above guidelines for 3 and 6 months, any patient with a fourfold increase in titer at any time should have a CSF examination and be treated with the neurosyphilis regimen unless reinfection can be established as the cause of the increased titer.

Lumbar Puncture in Early Syphilis

CSF abnormalities are common in adults with early syphilis. Despite the frequency of these CSF findings, very few patients develop neurosyphilis when the treatment regimens described above are used. Therefore, unless clinical signs and symptoms of neurologic involvement exist, such as optic, auditory, cranial nerve, or meningeal symptoms, lumbar puncture is not recommended for routine evaluation of early syphilis. This recommendation also applies to immunocompromised and HIV-infected patients, since no clear data currently show that these patients need increased therapy.

HIV Testing

All syphilis patients should be counseled concerning the risks of HIV and be encouraged to be tested for HIV.

Late Latent Syphilis of More Than 1 Year's Duration, Gummas, and Cardiovascular Syphilis

All patients should have a thorough clinical examination. Ideally, all patients with syphilis of more than 1 year's duration should have a CSF examination; however, performance of lumbar puncture can be individualized. In older asymptomatic individuals, the yield of lumbar puncture is likely to be low; however, CSF examination is clearly indicated in the following specific situations:

- Neurologic signs or symptoms
- Treatment failure
- Serum nontreponemal antibody titer $\geq$1:32
- Other evidence of active syphilis (aortitis, gumma, iritis)
- Nonpenicillin therapy planned
- Positive HIV antibody test

Note: If CSF examination is performed and reveals findings consistent with neurosyphilis, patients should be treated for neurosyphilis (see next section).

Some experts also treat cardiovascular syphilis patients with a neurosyphilis regimen.

Recommended Regimen

Benzathine penicillin G, 7.2 million units total, administered as 3 doses of 2.4 million units IM, given 1 week apart for 3 consecutive weeks.

Alternative Regimen for Penicillin-Allergic Patients (Nonpregnant)

Doxycycline, 100 mg orally 2 times a day for 4 weeks

or

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

If patients are allergic to penicillin, alternate drugs should be used only after CSF examination has excluded neurosyphilis. Penicillin allergy is best determined by careful history taking, but skin testing may be used if the major and minor determinants are available (see Appendix).

Follow-Up

Quantitative nontreponemal serologic tests should be repeated at 6 months and 12 months. If titers increase fourfold, if an initially high titer ($\geq$1:32) fails to decrease, or if the patient has signs or symptoms attributable to syphilis, the patient should be evaluated for neurosyphilis and retreated appropriately.

HIV Testing

All syphilis patients should be counseled concerning the risks of HIV and be encouraged to be tested for HIV antibody.

Neurosyphilis

Central nervous system disease may occur during any stage of syphilis. Clinical evidence of neurologic involvement (e.g., optic and auditory symptoms, cranial nerve palsies) warrants CSF examination.

Recommended Regimen

Aqueous crystalline penicillin G, 12-24 million units administered 2-4 million units every 4 hours IV, for 10-14 days.

Alternative Regimen (If Outpatient Compliance Can Be Ensured)

Procaine penicillin, 2-4 million units IM daily

and

Probenecid, 500 mg orally 4 times a day, both for 10-14 days.

Many authorities recommend addition of **benzathine penicillin G**, 2.4 million units IM weekly for three doses after completion of these neurosyphilis treatment regimens. No systematically collected data have evaluated therapeutic alternatives to penicillin. Patients who cannot tolerate penicillin should be skin tested and desensitized, if necessary, or managed in consultation with an expert.

Follow-Up

If an initial CSF pleocytosis was present, CSF examination should be repeated every 6 months until the cell count is normal. If it has not decreased at 6 months, or is not normal by 2 years, retreatment should be strongly considered.

HIV Testing

All syphilis patients should be counseled concerning the risks of HIV and be encouraged to be tested for HIV antibody.

Syphilis in Pregnancy

Screening

Pregnant women should be screened early in pregnancy. Seropositive pregnant women should be considered infected unless treatment history and sequential serologic antibody titers are showing an appropriate response. In populations in

which prenatal care utilization is not optimal, patients should be screened, and if necessary, treatment provided at the time pregnancy is detected. In areas of high syphilis prevalence, or in patients at high risk, screening should be repeated in the third trimester and again at delivery.

Treatment

Patients should be treated with the penicillin regimen appropriate for the woman's stage of syphilis. Tetracycline and doxycycline are contraindicated in pregnancy. Erythromycin should not be used because of the high risk of failure to cure infection in the fetus. Pregnant women with histories of penicillin allergy should first be carefully questioned regarding the validity of the history. If necessary, they should then be skin tested and either treated with penicillin or referred for desensitization (see Appendix). Women who are treated in the second half of pregnancy are at risk for premature labor and/or fetal distress if their treatment precipitates a Jarisch-Herxheimer reaction. They should be advised to seek medical attention following treatment if they notice any change in fetal movements or have any contractions. Stillbirth is a rare complication of treatment; however, since therapy is necessary to prevent further fetal damage, this concern should not delay treatment.

Follow-Up

Monthly follow-up is mandatory so that retreatment can be given if needed. The antibody response should be the same as for nonpregnant patients.

HIV Testing

All syphilis patients should be counseled concerning the risks of HIV and be encouraged to be tested for HIV antibody.

Congenital Syphilis

Who Should be Evaluated

Infants should be evaluated if they were born to seropositive (nontreponemal test confirmed by treponemal test) women who:

- Have untreated syphilis; ***or***
- Were treated for syphilis less than 1 month before delivery; ***or***
- Were treated for syphilis during pregnancy with a non-penicillin regimen; ***or***
- Did not have the expected decrease in nontreponemal antibody titers after treatment for syphilis; ***or***
- Do not have a well-documented history of treatment for syphilis; ***or***
- Were treated but had insufficient serologic follow-up during pregnancy to assess disease activity.

An infant should not be released from the hospital until the serologic status of its mother is known.

Evaluation of the Infant

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

- A thorough physical examination for evidence of congenital syphilis
- Nontreponemal antibody titer
- CSF analysis for cells, protein, and VDRL
- Long bone x-rays
- Other tests as clinically indicated (e.g., chest x-ray)
- If possible, FTA-ABS on the purified 19S-IgM fraction of serum (e.g., separation by Isolab columns)

Therapy Decisions

Infants should be treated if they have:

- Any evidence of active disease (physical examination or x-ray); ***or***
- A reactive CSF-VDRL; ***or***
- An abnormal CSF finding (white blood cell count >5/mm^3 or protein >50 mg/dl)* regardless of CSF serology; ***or***
- Quantitative nontreponemal serologic titers that are fourfold (or greater) higher than their mother's; ***or***
- Positive FTA-ABS-19S-IgM antibody, if performed.

Even if the evaluation is normal, infants should be treated if their mothers have untreated syphilis or evidence of relapse or reinfection after treatment. Infants, who meet the criteria listed in "Who Should be Evaluated" but are not fully evaluated, should be assumed to be infected, and treated.

Treatment

Treatment should consist of: 100,000-150,000 units/kg of **aqueous crystalline penicillin G** daily (administered as 50,000 units/kg IV every 8-12 hours) *or* 50,000 units/kg of **procaine penicillin** daily (administered once IM) for 10-14 days. If more than 1 day of therapy is missed, the entire course should be restarted. All symptomatic neonates should also have an ophthalmologic examination.

Infants who meet the criteria listed in "Who Should be Evaluated" but who after evaluation do not meet the criteria listed in "Therapy Decisions," **are at low risk for congenital syphilis. If their mothers were treated with erythromycin during pregnancy**, or if close follow-up cannot be assured, they should be treated with **benzathine penicillin G,** 50,000 units/kg IM as a one-time dose.

Follow-Up

Seropositive untreated infants must be closely followed at 1, 2, 3, 6, and 12 months of age. In the absence of infection, nontreponemal antibody titers should be decreasing by 3 months of age and should have disappeared by 6 months of age. If

*In the immediate newborn period, interpretation of these tests may be difficult; normal values vary with gestational age and are higher in preterm infants. Other causes of elevated values should also be considered. However, *when an infant is being evaluated for congenital syphilis,* the infant should be treated if test results cannot exclude infection.

these titers are found to be stable or increasing, the child should be reevaluated and fully treated. Additionally, in the absence of infection, treponemal antibodies may be present up to 1 year. If they are present beyond 1 year, the infant should be treated for congenital syphilis.

Treated infants should also be observed to ensure decreasing nontreponemal antibody titers; these should have disappeared by 6 months of age. Treponemal tests should not be used, since they may remain positive despite effective therapy if the child was infected. Infants with documented CSF pleocytosis should be reexamined 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 infant should be retreated. The CSF-VDRL should also be checked at 6 months; if it is still reactive, the infant should be retreated.

Therapy of Older Infants and Children

After the newborn period, children discovered to have syphilis should have a CSF examination to rule out congenital syphilis. Any child who is thought to have congenital syphilis or who has neurologic involvement should be treated with 200,000-300,000 units/kg/day of **aqueous crystalline penicillin G** (administered as 50,000 units/kg every 4-6 hours) for 10-14 days. Older children with definite acquired syphilis and a normal neurologic examination may be treated with **benzathine penicillin G,** 50,000 units/kg IM, up to the adult dose of 2.4 million units. Children with a history of penicillin allergy should be skin tested and, if necessary, desensitized (see Appendix). Follow-up should be performed as described previously.

HIV Testing

In cases of congenital syphilis, the mother should be counseled concerning the risks of HIV and be encouraged to be tested for HIV; if her test is positive, the infant should be referred for follow-up.

Syphilis in HIV-Infected Patients

Diagnosis

- All sexually active patients with syphilis should be encouraged to be counseled and tested for HIV because of the frequency of association of the two diseases and the implications for clinical assessment and management.
- Neurosyphilis should be considered in the differential diagnosis of neurologic disease in HIV-infected persons.
- When clinical findings suggest that syphilis is present but serologic tests are negative or confusing, alternative tests, such as biopsy of lesions, dark-field examination, and direct fluorescent antibody staining of lesion material, should be used.
- In cases of congenital syphilis, the mother should be encouraged to be counseled and tested for HIV; if her test is positive, the infant should be referred for follow-up.

Treatment and Follow-Up

- Penicillin regimens should be used whenever possible for all stages of syphilis in HIV-infected patients. Skin testing to confirm penicillin allergy may be used if minor and major determinants are available (see Appendix). However, data on its use in HIV-infected individuals are inadequate. Patients may be desensitized and treated with penicillin.
- No change in therapy for early syphilis for HIV-coinfected patients is recommended. However, some authorities advise CSF examination and/or treatment with a regimen appropriate for neurosyphilis for all patients coinfected with syphilis and HIV, regardless of the clinical stage of syphilis. In all cases, careful follow-up is necessary to ensure adequacy of treatment.
- HIV-infected patients treated for syphilis should be followed clinically and with quantitative nontreponemal serologic tests (VDRL, RPR) at 1, 2, 3, 6, 9, and 12 months after treatment. Patients with early syphilis whose titers increase or fail to decrease (see section on "Follow-Up, Early Syphilis") fourfold within 6 months should undergo CSF examination and be retreated. In such patients, CSF abnormalities could be due to HIV-related infection, neurosyphilis, or both. STD clinics and other providers of STD treatment should ensure adequate follow-up.

Appendix

Management of Patients with Histories of Penicillin Allergy

Currently, no proven alternative therapies to penicillin are available for treating patients with neurosyphilis, congenital syphilis, or syphilis in pregnancy. Therefore, skin testing—with desensitization, if indicated—is recommended for these patients.

Skin Testing

Skin testing is a rapid, safe, and accurate procedure (see below). It is also productive; 90% of patients with histories of "penicillin allergy" have negative skin tests and can be given penicillin safely. The other 10% with positive skin tests have an increased risk of being truly penicillin-allergic and should undergo desensitization. Clinics involved in STD management should be equipped and prepared to do skin testing or should establish referral mechanisms to have skin tests performed.

Skin testing is quick; four determinants, along with positive and negative controls, can be placed and read in an hour (Table 3). Skin testing is also safe, if properly performed. Patients who have had a severe, life-threatening reaction in the past year should be tested in a controlled environment, such as a hospital setting, and the determinant antigens diluted 100-fold. Other patients can be skin-tested safely in a physician-staffed clinic. Patients with a history of penicillin allergy but with no reaction to penicillin skin tests, who are not on antihistamines and who had a positive histamine control on skin testing (Table 3), should be given **penicillin**, 250 mg orally, and observed for one hour. Patients who tolerate this dose well may be treated with penicillin as needed.

Desensitization

Patients who have a positive skin test to one of the penicillin determinants can be desensitized. This is a straightforward, relatively safe procedure. Although the procedure can be done orally or intravenously, oral desensitization is thought to be safer, simpler, and easier. Desensitization should be done in a hospital setting because serious IgE-mediated allergic reaction, although unlikely, can occur. Desensitization can be completed in 4 hours, after which the first dose of penicillin is given (Table 4). STD programs should have a referral center where patients with positive skin tests can be desensitized. After desensitization, patients must be maintained on penicillin for the duration of therapy.

TABLE 3. Penicillin allergy skin testing (adapted from Beall*)

Note: If there has been a severe generalized reaction to penicillin in the previous year, the antigens should be diluted 100-fold, and patients should be tested in a controlled environment. Both major and minor determinants should be available for the tests to be interpretable. The patient should not have taken antihistamines in the previous 48 hours.

Reagents

Major determinants:

Benzylpenicilloyl-polylysine (major, Pre-Pen [Taylor Pharmacal Co., Decatur, Illinois], 6×10^{-5}M)

Benzylpenicillin (10^{-2}M or 6000 U/mL)

Minor determinants:

Benzylpenicilloic acid (10^{-2}M)

Benzylpenilloic acid (10^{-2}M)

Positive control (histamine, 1 mg/mL)

Negative control (buffered saline solution)

Dilute the antigens 100-fold for preliminary testing if there has been an immediate generalized reaction within the past year.

Procedure

Epicutaneous (scratch or prick) test: apply one drop of material to volar forearm and pierce epidermis without drawing blood; observe for 20 minutes. If there is no wheal $\geq$4 mm, proceed to intradermal test.

Intradermal test: inject 0.02 ml *intradermally* with a 27-gauge short-bevelled needle; observe for 20 minutes.

Interpretation

For the test to be interpretable, the negative (saline) control must elicit no reaction and the positive (histamine) control must elicit a positive reaction.

Positive test: a wheal >4 mm in mean diameter to any penicillin reagent; erythema must be present.

Negative test: the wheals at the site of the penicillin reagents are equivalent to the negative control.

Indeterminate: all other results.

*Reprinted with permission from Beall GN, Penicillins, pp 205-9. In: Saxon A, moderator. Immediate hypersensitivity reactions to beta lactam antibiotics. Ann Intern Med 1987;107: 204-15.

TABLE 4. Oral-desensitization protocol (from Wendel)

Dose*	Penicillin V Suspension (units/ml)	Amount†		Cumulative dose (units)
		ml	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.

*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 given orally.

Adapted with permission from the *New England Journal of Medicine* 1985;312:1229-32.

Lymphogranuloma Venereum

Lymphogranuloma venereum (LGV) is caused by *C. trachomatis* (LGV serovars). Inguinal lymphadenopathy is the most common clinical manifestation. Diagnosis is often made clinically and may be confused with chancroid. LGV is not a common cause of inguinal lymphadenopathy in the United States.

Treatment: Genital, inguinal, or anorectal

Recommended Regimen

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

Alternative Regimen

Tetracycline 500 mg orally 4 times a day for 21 days

or

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.

Genital Herpes Simplex Virus Infections

Genital herpes is a viral disease that may be chronic and recurring and for which no known cure exists. Systemic acyclovir treatment provides partial control of the symptoms and signs of herpes episodes; it accelerates healing but does not eradicate the infection nor affect the subsequent risk, frequency, or severity of recurrences after the drug is discontinued. Topical therapy with acyclovir is substantially less effective than therapy with the oral drug.

First Clinical Episode of Genital Herpes

Recommended Regimen

Acyclovir 200 mg orally 5 times a day for 7-10 days or until clinical resolution occurs.

First Clinical Episode of Herpes Proctitis

Recommended Regimen

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

Inpatient Therapy

For patients with severe disease or complications necessitating hospitalization.

Recommended Regimen

Acyclovir 5 mg/kg body weight IV every 8 hours for 5-7 days or until clinical resolution occurs.

Recurrent Episodes

Most episodes of recurrent herpes do not benefit from therapy with acyclovir. In severe recurrent disease, some patients who start therapy at the beginning of the prodrome or within 2 days after onset of lesions may benefit from therapy, although this has not been proven.

Recommended Regimen

Acyclovir 200 mg orally 5 times a day for 5 days

or

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

Daily Suppressive Therapy

Daily treatment reduces frequency of recurrences by at least 75% among patients with frequent (more than six per year) recurrences. Safety and efficacy have been clearly documented among persons receiving daily therapy for up to 3 years. Acyclovir-resistant strains of HSV have been isolated from persons receiving suppressive therapy, but they have not been associated with treatment failure among immunocompetent patients. After 1 year of continuous daily suppressive therapy, acyclovir should be discontinued so that the patient's recurrence rate may be reassessed.

Recommended Regimen

Acyclovir 200 mg orally 2 to 5 times a day*

or

Acyclovir 400 mg orally 2 times a day.*

Genital Herpes among HIV-Infected Patients

The need for higher-than-standard doses of oral acyclovir among HIV-infected but immunocompetent patients has not been established. Immune status, not HIV infection alone, is the likely predictor of disease severity and response to therapy. Case reports strongly suggest that patients with clinical immunodeficiency have a more severe clinical course of anogenital herpes than do immunocompetent patients, and some health-care providers are using increased doses of acyclovir for patients with immunodeficiency. However, neither the need for nor the proper increased dosage of acyclovir has been conclusively established. Immunocompromised as well as immunocompetent hosts who fail initial therapy may benefit from an increased dosage of acyclovir. The indications for suppressive therapy among immunocompromised patients, and the dose required, are controversial. Clinical benefits to the patient must be weighed against the potential for selecting HSV strains that are resistant to acyclovir. Patients whose therapy for a recurrence fails because of resistant strains of HSV should be managed in consultation with an expert.

Acyclovir for Treating Pregnant Patients

The safety of systemic acyclovir therapy among pregnant women has not been established. In the presence of life-threatening maternal HSV infection (e.g., disseminated infection that includes encephalitis, pneumonitis, and/or hepatitis) acyclovir administered IV is probably of value. Among pregnant women without life-threatening disease, systemic acyclovir treatment ***should not*** be used for recurrent genital herpes episodes or as suppressive therapy to prevent reactivation near term.

Perinatal Infections

Most mothers of infants who acquire neonatal herpes lack histories of clinically evident genital herpes. The risk of transmission to the neonate from an infected mother is highest among women with primary herpes infection near the time of

*Dosage must be individualized for each patient.

delivery, and it is low among women with recurrent herpes. The results of viral cultures during pregnancy do not predict viral shedding at the time of delivery; such cultures are not routinely indicated.

At the onset of labor, all women should be examined and carefully questioned about symptoms. Women without symptoms or signs of genital herpes infection or prodrome may have vaginal deliveries. For 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 be helpful in decisions about neonatal management. Infants delivered through an infected birth canal (proven by culture or presumed by observation of lesions) should be cultured and observed carefully. Although data are limited concerning the use of acyclovir for asymptomatic infants, some experts presumptively treat infants who were exposed to HSV at delivery. Herpes cultures should be obtained from infants before therapy; positive cultures obtained 24-48 hours or more after birth indicate active viral infection.

Counseling and Management of Sex Partners

Patients with genital herpes should be told about the natural history of their disease, with emphasis on the potential for recurrent episodes. Patients should be advised to abstain from sexual activity while lesions are present. Sexual transmission of HSV has been documented during periods without recognized lesions. Suppressive treatment with oral acyclovir reduces the frequency of recurrences but does not totally eliminate viral shedding. Genital herpes and other diseases causing genital ulcers have been associated with an increased risk of acquiring HIV infections; therefore, condoms should be used during all sexual exposures. If sex partners of patients with genital herpes have genital lesions, they may benefit from evaluation; however, evaluation of asymptomatic partners is of little value in preventing transmission of HSV.

The risk of neonatal infection should be explained to all patients—male and female—with genital herpes. Women of child-bearing age with genital herpes should be advised to inform their clinicians of their history during any future pregnancy.

Infections of Epithelial Surfaces

Genital Warts

Exophytic genital and anal warts are caused by certain types (most frequently types 6 and 11) of HPV. Other types sometimes present in the anogenital region (most commonly types 16, 18, and 31) have been found to be strongly associated with genital dysplasia and carcinoma. For this reason, a biopsy is needed in all instances of atypical, pigmented, or persistent warts. All women with anogenital warts should have an annual Pap smear.

Some subclinical HPV infections may be detected by Pap smear and colposcopy. Application of acetic acid may also indicate otherwise subclinical lesions, but false-positive tests occur. Tests for the detection of HPV-DNA are now widely

available. The clinical use of these tests in managing individual patients is not known. Therefore, therapeutic decisions should not be made on the basis of these HPV-DNA tests.

No therapy has been shown to eradicate HPV. HPV has been demonstrated 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. The benefit of treating patients with subclinical HPV infection has not been demonstrated, and recurrence is common. The effect of genital wart treatment on HPV transmission and the natural history of HPV is unknown. ***Therefore, the goal of treatment is removal of exophytic warts and the amelioration of signs and symptoms, not the eradication of HPV.***

Expensive therapies, toxic therapies, and procedures that result in scarring should be avoided. Sex partners should be examined for evidence of warts. Patients with anogenital warts should be made aware that they are contagious to uninfected sex partners. The use of condoms is recommended to help reduce transmission.

In most clinical situations, cryotherapy with liquid nitrogen or cryoprobe is the treatment of choice for external genital and perianal warts. Cryotherapy is nontoxic, does not require anesthesia, and—if used properly—does not result in scarring. Podophyllin, trichloroacetic acid (TCA), and electrodesiccation/electrocautery are alternative therapies. Treatment with interferon is not recommended because of its relatively low efficacy, high incidence of toxicity, and high cost.

The carbon dioxide laser and conventional surgery are useful in the management of extensive warts, particularly for patients who have not responded to cryotherapy; these alternatives are not appropriate for limited lesions. Like more cost-effective treatments, these therapies do not eliminate HPV and often are associated with the recurrence of clinical cases.

Pregnant Patients and Perinatal Infections

Cesarean delivery for prevention of transmission of HPV infection to the newborn is not indicated. In rare instances, however, cesarean delivery may be indicated for women with genital warts if the pelvic outlet is obstructed or if vaginal delivery would result in excessive bleeding.

Genital papillary lesions have a tendency to proliferate and to become friable during pregnancy. Many experts advocate removal of visible warts during pregnancy, although data on this subject are limited.

HPV can cause laryngeal papillomatosis in infants. The route of transmission (transplacental, birth canal, or postnatal) is unknown; therefore, the preventive value of cesarean delivery is unknown. The perinatal transmission rate is also unknown, although it must be very low, given the relatively high prevalence of genital warts and the rarity of laryngeal papillomas. Neither routine HPV screening tests nor cesarean delivery are indicated to prevent transmission of HPV infection to the newborn.

Treatment Recommendations

External Genital/Perianal Warts

Recommended Regimen

Cryotherapy with liquid nitrogen or cryoprobe.

Alternative Regimen

Podophyllin 10%-25% in compound tincture of benzoin. Limit the total volume of podophyllin solution applied to <0.5 ml per treatment session. Thoroughly wash off in 1-4 hours. Treat <10 cm^2 per session. Repeat applications at weekly intervals. Mucosal warts are more likely to respond than highly keratinized warts on the penile shaft, buttocks, and pubic areas. ***Contraindicated in pregnancy***.

Trichloroacetic acid (80%-90%). Apply only to warts; powder with talc or sodium bicarbonate (baking soda) to remove unreacted acid. Repeat application at weekly intervals.

Electrodesiccation/electrocautery. Electrodesiccation is contraindicated in patients with cardiac pacemakers, or for lesions proximal to the anal verge. Extensive or refractory disease should be referred to an expert.

Cervical Warts

Recommended Regimen

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

Vaginal Warts

Recommended Regimen

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

Alternative Regimen

Trichloroacetic acid (80%-90%). Apply only to warts; powder with talc or sodium bicarbonate (baking soda) to remove unreacted acid. Repeat application at weekly intervals.

Podophyllin 10%-25% in compound tincture of benzoin. Treatment area must be dry before speculum is removed. Treat <2 cm^2 per session. Repeat application at weekly intervals. ***Contraindicated in pregnancy***. Extensive or refractory disease should be referred to an expert.

Urethral Meatus Warts

Recommended Regimen

Cryotherapy with liquid nitrogen.

Alternative Regimen

Podophyllin 10%-25% in compound tincture of benzoin. Treatment area must be dry before contact with normal mucosa, and podophyllin must be washed off in 1-2 hours. ***Contraindicated in pregnancy***. Extensive or refractory disease should be referred to an expert.

Anal Warts

Recommended Regimen

Cryotherapy with liquid nitrogen. Extensive or refractory disease should be referred to an expert.

Alternative Regimen

Trichloroacetic acid (80%-90%).

Surgical removal.

Oral Warts

Recommended Regimen

Cryotherapy with liquid nitrogen.

Alternative Regimen

Electrodesiccation/electrocautery.

Surgical removal. Extensive or refractory disease should be referred to an expert.

Gonococcal Infections

Treatment of gonococcal infections in the United States is influenced by the following trends: 1) the spread of infections due to antibiotic-resistant *N. gonorrhoeae*, including penicillinase-producing *N. gonorrhoeae* (PPNG), tetracycline-resistant *N. gonorrhoeae* (TRNG), and strains with chromosomally mediated resistance to multiple antibiotics; 2) the high frequency of chlamydial infections in persons with gonorrhea; 3) recognition of the serious complications of chlamydial and gonococcal infections; and 4) the absence of a fast, inexpensive, and highly accurate test for chlamydial infection.

All gonorrhea cases should be diagnosed or confirmed by culture to facilitate antimicrobial susceptibility testing. The susceptibility of *N. gonorrhoeae* to antibiotics is likely to change over time in any locality. Therefore, gonorrhea control programs should include a system of regular antibiotic sensitivity testing of a surveillance sample of *N. gonorrhoeae* isolates as well as all isolates associated with treatment failure.

Because of the wide spectrum of antimicrobial therapies effective against *N. gonorrhoeae*, these guidelines are *not* intended to be a comprehensive list of all possible treatment regimens.

Treatment of Adults

Uncomplicated Urethral, Endocervical, or Rectal Infections

Single-dose efficacy is a major consideration in choosing an antibiotic regimen to treat persons infected with *N. gonorrhoeae*. Another important concern is coexisting chlamydial infection, documented in up to 45% of gonorrhea cases in some populations. Until universal testing for chlamydia with quick, inexpensive, and highly accurate tests becomes available, persons with gonorrhea should also be treated for presumptive chlamydial infections. Generally, patients with gonorrhea infections should be treated simultaneously with antibiotics effective against both *C. trachomatis* and *N. gonorrhoeae*. Simultaneous treatment may lessen the possibility of treatment failure due to antibiotic resistance.

Recommended Regimen

Ceftriaxone 250 mg IM once

plus

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

Some authorities prefer a dose of 125 mg **ceftriaxone** IM because it is less expensive and can be given in a volume of only 0.5 ml, which is more easily administered in the deltoid muscle. However, the 250-mg dose is recommended because it may delay the emergence of ceftriaxone-resistant strains. At this time, both doses appear highly effective for mucosal gonorrhea at all sites.

Alternative Regimens

For patients who cannot take ceftriaxone, the preferred alternative is **Spectinomycin** 2 g IM, in a single dose (***followed by*** **doxycycline**).

Other alternatives, for which experience is less extensive, include **ciprofloxacin*** 500 mg orally once; **norfloxacin*** 800 mg orally once; **cefuroxime axetil** 1 g orally once with **probenecid** 1 g; **cefotaxime** 1 g IM once; and **ceftizoxime** 500 mg IM once. All of these regimens are ***followed by*** **doxycycline** 100 mg orally, twice daily for 7 days. If infection was acquired from a source proven *not* to have penicillin-resistant gonorrhea, a penicillin such as **amoxicillin** 3 g orally with 1 g **probenecid** ***followed by*** **doxycycline** may be used for treatment.

Doxycycline or tetracycline alone is no longer considered adequate therapy for gonococcal infections but is added for treatment of coexisting chlamydial infections. Tetracycline may be substituted for doxycycline; however, compliance may be worse since **tetracycline** must be taken at a dose of 500 mg 4 times a day between meals, whereas **doxycycline** is taken at a dose of 100 mg 2 times a day without regard to meals. Moreover, at current prices, tetracycline costs only a little less than generic doxycycline.

*Quinolones, such as ciprofloxacin and norfloxacin, are contraindicated during pregnancy and in children 16 years of age or younger.

For patients who cannot take a **tetracycline** (e.g., pregnant women), **erythromycin** may be substituted (**erythromycin** base or stearate at 500 mg orally 4 times a day for 7 days ***or*** **erythromycin ethylsuccinate**, 800 mg orally 4 times a day for 7 days). See "Chlamydial Infections" for further information on management of chlamydial infection.

Special Considerations

All patients with gonorrhea should have a serologic test for syphilis and should be offered confidential counseling and testing for HIV infection. Most patients with incubating syphilis (those who are seronegative and have no clinical signs of syphilis) may be cured by any of the regimens containing β-lactams (e.g., ceftriaxone) or tetracyclines.

Spectinomycin and the quinolones (ciprofloxacin, norfloxacin) have not been shown to be active against incubating syphilis. Patients treated with these drugs should have a serologic test for syphilis in 1 month.

Patients with gonorrhea and documented syphilis and gonorrhea patients who are sex partners of syphilis patients should be treated for syphilis (see "Syphilis") as well as for gonorrhea.

Some practitioners report that mixing 1% lidocaine (without epinephrine) with ceftriaxone reduces the discomfort associated with the injection (see package insert). No adverse reactions have been associated with use of lidocaine diluent.

Management of Sex Partners

Persons exposed to gonorrhea within the preceding 30 days should be examined, cultured, and treated presumptively.

Follow-Up

Treatment failure following combined **ceftriaxone/doxycycline** therapy is rare; therefore, a follow-up culture ("test-of-cure") is not essential. A more cost-effective strategy may be a reexamination with culture 1-2 months after treatment ("rescreening"); this strategy detects both treatment failures and reinfections. Patients should return for examination if symptoms persist after treatment. Because there is less long-term experience with drugs other than ceftriaxone, patients treated with regimens other than ceftriaxone/doxycycline should have follow-up cultures obtained for 4-7 days after completion of therapy.

Treatment Failures

Persistent symptoms after treatment should be evaluated by culture for *N. gonorrhoeae*, and any gonococcal isolate should be tested for antibiotic sensitivity. Symptoms of urethritis may also be caused by *C. trachomatis* and other organisms associated with nongonococcal urethritis (see "Nongonococcal Urethritis"). Additional treatment for patients with gonorrhea should be **ceftriaxone**, 250 mg, ***followed by*** **doxycycline**. Infections occurring after treatment with one of the recommended regimens are commonly due to reinfection rather than to treatment failure and indicate a need for improved sex-partner referral and patient education.

Pharyngeal Gonococcal Infection

Patients with uncomplicated pharyngeal gonococcal infection should be treated with **ceftriaxone** 250 mg IM once. Patients who cannot be treated with ceftriaxone should be treated with **ciprofloxacin** 500 mg orally as a single dose. Since experience with this regimen is limited, such patients should be evaluated with repeat culture 4-7 days after treatment.

Treatment of Gonococcal Infections in Pregnancy

Pregnant women should be cultured for *N. gonorrhoeae* (and tested for *C. trachomatis* and syphilis) at the first prenatal-care visit. For women at high risk of STD, a second culture for gonorrhea (as well as tests for chlamydia and syphilis) should be obtained late in the third trimester.

Recommended Regimen

Ceftriaxone 250 mg IM once

plus

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

Pregnant women allergic to β-lactams should be treated with **spectinomycin** 2 g IM once (***followed by*** **erythromycin**). Follow-up cervical and rectal cultures for *N. gonorrhoeae* should be obtained 4-7 days after treatment is completed.

Ideally, pregnant women with gonorrhea should be treated for chlamydia on the basis of chlamydial diagnostic studies. If chlamydial diagnostic testing is not available, treatment for chlamydia should be given. Tetracyclines (including doxycycline) and the quinolones are contraindicated in pregnancy because of possibly adverse effects on the fetus. Treatments for pregnant patients with chlamydial infection, acute salpingitis, and disseminated gonorrhea in pregnancy are described in respective sections.

Disseminated Gonococcal Infection (DGI)

Hospitalization is recommended for initial therapy, especially for patients who cannot reliably comply with treatment, have uncertain diagnoses, or have purulent synovial effusions or other complications. Patients should be examined for clinical evidence of endocarditis or meningitis.

Recommended Regimens—DGI Inpatient

Ceftriaxone 1 g, IM or IV, every 24 hours

or

Ceftizoxime 1 g, IV, every 8 hours

or

Cefotaxime 1 g, IV, every 8 hours.

Patients who are allergic to β-lactam drugs should be treated with **spectinomycin** 2 g IM every 12 hours.

*__Erythromycin__ stearate 500 mg or **erythromycin ethylsuccinate** 800 mg or equivalent may be substituted for erythromycin base.

When the infecting organism is proven to be penicillin-sensitive, parenteral treatment may be switched to **ampicillin** 1 g every 6 hours (or equivalent).

Patients treated for DGI should be tested for genital *C. trachomatis* infection. If chlamydial testing is not available, patients should be treated empirically for coexisting chlamydial infection.

Reliable patients with uncomplicated disease may be discharged 24-48 hours after all symptoms resolve and may complete the therapy (for a total of 1 week of antibiotic therapy) with an oral regimen of **cefuroxime axetil** 500 mg 2 times a day *or* **amoxicillin** 500 mg with clavulanic acid 3 times a day *or*, if not pregnant, **ciprofloxacin** 500 mg 2 times a day.

Meningitis and Endocarditis

Meningitis and endocarditis caused by *N. gonorrhoeae* require high-dose IV therapy with an agent effective against the strain causing the disease, such as **ceftriaxone** 1-2 g IV every 12 hours. Optimal duration of therapy is unknown, but most authorities treat patients with gonococcal meningitis for 10-14 days and with gonococcal endocarditis for at least 4 weeks. Patients with gonococcal nephritis, endocarditis or meningitis, or recurrent DGI should be evaluated for complement deficiencies. Treatment of complicated DGI should be undertaken in consultation with an expert.

Adult Gonococcal Ophthalmia

Adults and children over 20 kg with nonsepticemic gonococcal ophthalmia should be treated with **ceftriaxone** 1 g IM once. Irrigation of the eyes with saline or buffered ophthalmic solutions may be useful adjunctive therapy to eliminate discharge. All patients must have careful ophthalmologic assessment, including slit-lamp examination for ocular complications. Topical antibiotics alone are insufficient therapy and are unnecessary when appropriate systemic therapy is given. Simultaneous ophthalmic infection with *C. trachomatis* has been reported and should be considered for patients who do not respond promptly.

Gonococcal Infections of Infants and Children

Child abuse should be carefully considered and evaluated (see "Sexual Assault and Abuse of Children") for any child with documented gonorrhea.

Treatment of Infants Born to Mothers with Gonococcal Infection

Infants born to mothers with untreated gonorrhea are at high risk of infection (e.g., ophthalmia and DGI) and should be treated with a single injection of **ceftriaxone** (50 mg/kg IV or IM, not to exceed 125 mg). Ceftriaxone should be given cautiously to

hyperbilirubinemic infants, especially premature infants. Topical prophylaxis for neonatal ophthalmia is not adequate treatment for documented infections of the eye or other sites.

Treatment of Infants with Gonococcal Infection

Infants with documented gonococcal infections at any site (e.g., eye) should be evaluated for DGI. This evaluation should include a careful physical examination, especially of the joints, as well as blood and CSF cultures. Infants with gonococcal ophthalmia or DGI should be treated for 7 days (10 to 14 days if meningitis is present) with one of the following regimens:

Recommended Regimen

Ceftriaxone 25-50 mg/kg/day IV or IM in a single daily dose

or

Cefotaxime 25 mg/kg IV or IM every 12 hours.

Alternative Regimen

Limited data suggest that uncomplicated gonococcal ophthalmia among infants may be cured with a single injection of **ceftriaxone** (50 mg/kg up to 125 mg). A few experts use this regimen for children who have no clinical or laboratory evidence of disseminated disease.

If the gonococcal isolate is proven to be susceptible to penicillin, **crystalline penicillin G** may be given. The dose is 100,000 units/kg/day given in 2 equal doses (4 equal doses per day for infants more than 1 week old). The dose should be increased to 150,000 units/kg/day for meningitis.

Infants with gonococcal ophthalmia should receive eye irrigations with buffered saline solutions until discharge has cleared. Topical antibiotic therapy alone is inadequate. Simultaneous infection with *C. trachomatis* has been reported and should be considered for patients who do not respond satisfactorily. Therefore, the mother and infant should be tested for chlamydial infection.

Gonococcal Infections of Children

Children who weigh ≥45 kg should be treated with adult regimens. Children who weigh <45 kg who have uncomplicated vulvovaginitis, cervicitis, urethritis, pharyngitis, or proctitis should be treated as follows:

Recommended Regimen

Ceftriaxone 125 mg IM once.

Patients who cannot tolerate ceftriaxone may be treated with:
Spectinomycin 40 mg/kg IM once.

Patients weighing <45 kg with bacteremia or arthritis should be treated with **ceftriaxone** 50 mg/kg (maximum 1 g) once daily for 7 days. For meningitis, the duration of treatment is increased to 10-14 days and the maximum dose is 2 g.

Children ≥8 years of age should also be given **doxycycline** 100 mg 2 times a day for 7 days. All patients should be evaluated for coinfection with syphilis and *C. trachomatis*. Follow-up cultures are necessary to ensure that treatment has been effective.

Prevention of Ophthalmia Neonatorum

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 regimens listed below 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 in pregnant women is the best method for preventing neonatal gonococcal and chlamydial disease.

Recommended Regimen

Erythromycin (0.5%) ophthalmic ointment, once

or

Tetracycline (1%) ophthalmic ointment, once

or

Silver nitrate (1%) aqueous solution, once.

One of these should be instilled into the eyes of every neonate as soon as possible after delivery, and definitely within 1 hour after birth. Single-use tubes or ampules are preferable to multiple-use tubes.

The efficacy of tetracycline and erythromycin in the prevention of TRNG and PPNG ophthalmia is unknown, although both are probably effective because of the high concentrations of drug in these preparations. Bacitracin is ***not*** recommended.

Chlamydial Infections

Culture and nonculture methods for diagnosis of *C. trachomatis* are now available. Appropriate use of these diagnostic tests is strongly encouraged, especially for screening asymptomatic high-risk women in whom infection would otherwise be undetected. However, in clinical settings where testing for chlamydia is not routine or available, treatment often is prescribed on the basis of clinical diagnosis or as cotreatment for gonorrhea (see "Gonococcal Infections"). In clinical settings, periodic surveys should be performed to determine local chlamydial prevalence in patients with gonorrhea. Priority groups for chlamydia testing, if resources are limited, are high-risk pregnant women, adolescents, and women with multiple sexual partners.

Results of chlamydial tests should be interpreted with care. The sensitivity of all currently available laboratory tests for *C. trachomatis* tests is substantially less than 100%; thus, false-negative tests are possible. Although the specificity of nonculture

tests has improved substantially, false-positive test results may still occur with nonculture tests. Persons with chlamydial infections may remain asymptomatic for extended periods of time.

Treatment of Uncomplicated Urethral, Endocervical, or Rectal *C. trachomatis* Infections

Recommended Regimen

Doxycycline 100 mg orally 2 times a day for 7 days

or

Tetracycline 500 mg orally 4 times a day for 7 days.

Alternative Regimen

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

or

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

If erythromycin is not tolerated because of side effects, the following regimen may be effective:

Sulfisoxazole 500 mg orally 4 times a day for 10 days or equivalent.

Test of Cure

Because antimicrobial resistance of *C. trachomatis* to recommended regimens has not been observed, test-of-cure evaluation is not necessary when treatment has been completed.

Treatment of *C. trachomatis* in Pregnancy

Pregnant women should undergo diagnostic testing for *C. trachomatis, N. gonorrhoeae,* and syphilis, if possible, at their first prenatal visit and, for women at high risk, during the third trimester. Risk factors for chlamydial disease during pregnancy include young age (<25 years), past history or presence of other STD, a new sex partner within the preceding 3 months, and multiple sex partners. Ideally, pregnant women with gonorrhea should be treated for chlamydia on the basis of diagnostic studies, but if chlamydial testing is not available, treatment should be given because of the high likelihood of coinfection.

Recommended Regimen

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

If this regimen is not tolerated, the following regimens are recommended:

Alternative Regimen

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.

Alternative if Erythromycin Cannot Be Tolerated

Amoxicillin 500 mg orally 3 times a day for 7 days (limited data exist concerning this regimen).

Erythromycin estolate is contraindicated during pregnancy, since drug-related hepatoxicity can result.

Sex Partners of Patients with *C. trachomatis* Infections

Sex partners of patients who have *C. trachomatis* infection should be tested and treated for *C. trachomatis* if their contact was within 30 days of onset of symptoms. If testing is not available, they should be treated with the appropriate antimicrobial regimen.

Bacterial STD Syndromes

Nongonococcal Urethritis

Among men with urethral symptoms, nongonococcal urethritis (NGU) is diagnosed by Gram stain demonstrating abundant polymorphonuclear leukocytes without intracellular gram-negative diplococci. *C. trachomatis* has been implicated as the cause of NGU in about 50% of cases. Other organisms that cause 10%-15% of cases include *Ureaplasma urealyticum*, *T. vaginalis*, and herpes simplex virus. The cause of other cases is unknown.

Recommended Regimen

Doxycycline 100 mg orally 2 times a day for 7 days

or

Tetracycline 500 mg orally 4 times a day for 7 days.

Alternative Regimen

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

or

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

If high-dose erythromycin schedules are not tolerated, the following regimen is recommended:

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

or

Erythromycin base 250 mg orally 4 times a day or equivalent salt for 14 days.

Management of Sex Partners

Sex partners of men with NGU should be evaluated for STD and treated with an appropriate regimen based on the evaluation.

Recurrent NGU Unresponsive to Conventional Therapy

Recurrent NGU may be due to lack of compliance with an initial antibiotic regimen, to reinfection due to failure to treat sex partners, or to factors currently undefined. If noncompliance or reinfection cannot be ruled out, repeat doxycycline (100 mg orally 2 times a day for 7 days) ***or*** tetracycline (500 mg orally 4 times a day for 7 days).

If compliance with the initial antimicrobial agent is likely, treat with one of the above listed regimens.

If objective signs of urethritis continue after adequate treatment, these patients should be evaluated for evidence of other causes of urethritis and referred to a specialist.

Mucopurulent Cervicitis

The presence of mucopurulent endocervical exudate often suggests mucopurulent cervicitis (MPC) due to chlamydial or gonococcal infection. Presumptive diagnosis of MPC is made by the finding of mucopurulent secretion from the endocervix, which may appear yellow when viewed on a white cotton-tipped swab (positive swab test). Patients with MPC should have Gram stain and culture for *N. gonorrhoeae*, test for *C. trachomatis*, and a wet mount examination for *T. vaginalis*.

Recommended Regimen

If *N. gonorrhoeae* is found on Gram stain or culture of endocervical or urethral discharge, treatment should be the same as that recommended for uncomplicated gonorrhea in adults, including cotreatment for chlamydial infection.

If *N. gonorrhoeae* is not found, treatment should be the same as that recommended for chlamydial infection in adults.

Management of Sex Partners

Sex partners of women with MPC should be evaluated for STD and treated with an appropriate regimen based on the evaluation.

Epididymitis

Among sexually active heterosexual men <35 years of age, epididymitis is most likely caused by *N. gonorrhoeae* or *C. trachomatis*. Specimens should be obtained for a urethral smear for Gram stain and culture for *N. gonorrhoeae* and *C. trachomatis* and for a urine culture. Empiric therapy based on the clinical diagnosis is recommended before culture results are available.

Recommended Regimen

Ceftriaxone 250 mg IM once

and

Doxycycline 100 mg orally 2 times a day for 10 days

or

Tetracycline 500 mg orally 4 times a day for 10 days.

Pelvic Inflammatory Disease

Treatment Guidelines

Pelvic inflammatory disease (PID) comprises a spectrum of inflammatory disorders of the upper genital tract in women. PID may include endometritis, salpingitis, tubo-ovarian abscess, and pelvic peritonitis. Sexually transmitted organisms, especially *N. gonorrhoeae* and *C. trachomatis*, are implicated in most cases; however, endogenous organisms, such as anaerobes, gram-negative rods, streptococci, and mycoplasmas, may also be etiologic agents of disease.

A confirmed diagnosis of salpingitis and more accurate bacteriologic diagnosis is made by laparoscopy. Since laparoscopy is not always available, the diagnosis of PID is often based on imprecise clinical findings and culture or antigen detection tests of specimens from the lower genital tract.

Guidelines for the treatment of patients with PID have been designed to provide flexibility in therapeutic choices. PID therapy regimens are designed to provide empiric, broad-spectrum coverage of likely etiologic pathogens. Antimicrobial coverage should include *N. gonorrhoeae, C. trachomatis*, gram-negatives, anaerobes, Group B streptococcus, and the genital mycoplasmas. Limited data demonstrate that effective treatment of the upper genital tract pyogenic process will decrease the incidence of long-term complications such as tubal infertility and ectopic pregnancy.

Ideally, as for all intra-abdominal infections, hospitalization is recommended whenever possible, and particularly when 1) the diagnosis is uncertain; 2) surgical emergencies such as appendicitis and ectopic pregnancy cannot be excluded; 3) a pelvic abscess is suspected; 4) the patient is pregnant; 5) the patient is an adolescent (the compliance of adolescent patients with therapy is unpredictable, and the long-term sequelae of PID may be particularly severe in this group); 6) severe illness precludes outpatient management; 7) the patient is unable to follow or tolerate an outpatient regimen; 8) the patient has failed to respond to outpatient therapy; or 9) clinical follow-up within 72 hours of starting antibiotic treatment cannot be arranged. Many experts recommend that all patients with PID be hospitalized so that treatment with parenteral antibiotics can be initiated.

Selection of a treatment regimen must consider institutional availability, cost-control efforts, patient acceptance, and regional differences in antimicrobial susceptibility.

These treatment regimens are recommendations only and the specific antibiotics named are examples. Treatments used for PID will continue to be broad spectrum and empiric until more definitive studies are performed.

Inpatient treatment

One of the following:

Recommended Regimen A

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

plus

Doxycycline 100 mg every 12 hours orally or IV.

The above regimen is given for at least 48 hours after the patient clinically improves.

After discharge from hospital, continuation of:

Doxycycline 100 mg orally 2 times a day for a total of 10-14 days.

Recommended Regimen B

Clindamycin IV 900 mg every 8 hours

plus

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

The above regimen is given for at least 48 hours after the patient improves. After discharge from hospital, continuation of:

Doxycycline 100 mg orally 2 times a day for 10-14 days total.

Continuation of **clindamycin**, 450 mg orally, 5 times daily, for 10 to 14 days, may be considered as an alternative. Continuation of medication after hospital discharge is important for the treatment of possible *C. trachomatis* infection. Clindamycin has more complete anaerobic coverage. Although limited data suggest that clindamycin is effective against *C. trachomatis* infection, doxycycline remains the treatment of choice for patients with chlamydial disease. When *C. trachomatis* is strongly suspected or confirmed as an etiologic agent, doxycycline is the preferable alternative. In such instances, doxycycline therapy may be started during hospitalization if initiation of therapy before hospital discharge is thought likely to improve the patient's compliance.

Rationale

Clinicians have extensive experience with both the cefoxitin/doxycycline and clindamycin/aminoglycoside combinations. Each of these regimens provides broad coverage against polymicrobial infection. Cefotetan has properties similar to those of cefoxitin and requires less frequent dosing. Clinical data are limited on third-generation cephalosporins (ceftizoxime, cefotaxime, ceftriaxone), although many authorities believe they are effective. Doxycycline administered orally has bioavailability similar to that of the IV formulation and may be given if normal gastrointestinal function is present.

*Other cephalosporins such as ceftizoxime, cefotaxime, and ceftriaxone, which provide adequate gonococcal, other facultative gram-negative aerobic, and anaerobic coverage, may be utilized in appropriate doses.

Experimental studies suggest that aminoglycosides may not be optimal treatment for gram-negative organisms within abscesses, but clinical studies suggest that they are highly effective in the treatment of abscesses when administered in combination with clindamycin.

Although short courses of aminoglycosides in healthy young women usually do not require serum-level monitoring, many practitioners may elect to monitor levels.

Ambulatory Management of PID

Recommended Regimen

Cefoxitin 2 g IM ***plus*** **probenecid**, 1 g orally concurrently ***or*** **ceftiaxone** 250 mg IM, ***or*** equivalent **cephalosporin**

plus

Doxycycline 100 mg orally 2 times a day for 10-14 days

or

Tetracycline 500 mg orally 4 times a day for 10-14 days.

Alternative for Patients Who Do Not Tolerate Doxycycline

Erythromycin, 500 mg orally 4 times a day for 10-14 days may be substituted for doxycycline/tetracycline.

This regimen, however, is based on limited clinical data.

Rationale

These empiric regimens provide broad-spectrum coverage against the common etiologic agents of PID. Parenteral β-lactam antibiotics are recommended in all cases. The cephalosporins are effective in the treatment of gram-negative organisms, including enteric rods, anaerobic organisms, and gonococci. Although decreased susceptibility of gonococci to cefoxitin has been recently noted, treatment failure has not yet been a clinical problem. Patients who do not respond to therapy within 72 hours should be hospitalized for parenteral therapy. Doxycycline provides definitive therapy for chlamydial infections. Patients treated on an ambulatory basis need to be monitored closely and reevaluated in 72 hours.

Management of Sex Partners

Sex partners of women with PID should be evaluated for STD. After evaluation, sex partners should be empirically treated with regimens effective against *N. gonorrhoeae* and *C. trachomatis* infections.

Intrauterine Device (IUD)

The intrauterine device is a risk factor for the development of pelvic inflammatory disease. Although the exact effect of removing an IUD on the response of acute salpingitis to antimicrobial therapy and on the risk of recurrent salpingitis is unknown, removal of the IUD is recommended soon after antimicrobial therapy has been initiated. When an IUD is removed, contraceptive counseling is necessary.

Sexually Transmitted Enteric Infections

Sexually transmitted gastrointestinal syndromes include proctitis, proctocolitis, and enteritis. With the exception of rectal gonococcal infection, these syndromes occur predominantly in homosexual men who participate in receptive anal intercourse. Evaluation should include additional diagnostic procedures, such as anoscopy or sigmoidoscopy, stool examination, and culture.

Proctitis is inflammation limited to the rectum (the distal 10-12 cm) and is associated with anorectal pain, tenesmus, constipation, and discharge. *N. gonorrhoeae, C. trachomatis,* 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 the colonic mucosa is inflamed proximal to 12 cm. Etiologic organisms include *Campylobacter jejuni, Shigella* spp., amebiasis, and, rarely, *T. pallidum* or *C. trachomatis* (often LGV serovars). CMV may be involved in patients coinfected with HIV.

Enteritis in homosexual men usually results in diarrhea without signs of proctitis or proctocolitis. In otherwise healthy patients, *Giardia lamblia* is most commonly implicated. In patients also coinfected with HIV, CMV. *Mycobacterium avium-intracellulare, Salmonella* spp., *Cryptosporidium,* and *Isospora* must be considered. Special stool preparations are required to diagnose giardiasis or cryptosporidiosis. Additionally, some cases of enteritis may be a primary effect of HIV infection.

All patients with sexually transmitted enteric infections should be counseled and tested for HIV infection.

Treatment recommendations for all enteric infections are beyond the scope of these guidelines. However, acute proctitis of recent onset in an individual who has recently practiced unprotected receptive anal intercourse is most often sexually transmitted. Such patients should be examined by anoscopy and should be evaluated for infection with *N. gonorrhoeae, C. trachomatis,* HSV, and *T. pallidum.* Treatment can be based on specific etiologic diagnosis or can be empiric.

Empiric Treatment for Sexually Transmitted Proctitis

Recommended Regimen

Ceftriaxone 250 mg IM ***plus*** **doxycycline** 100 mg orally 2 times a day for 7 days provides adequate treatment for gonorrhea and chlamydial infection.

Vaginal Diseases

Trichomoniasis

Trichomoniasis is almost always a sexually transmitted infection. Diagnosis is usually made by direct microscopic visualization (wet preparation) or by culture. Diagnosis by cervical cytology or fixed preparation should be confirmed by direct visualization or culture. Symptomatic and asymptomatic patients should be treated.

Recommended Regimen

Metronidazole 2 g orally in a single dose.

Alternative Regimen

Metronidazole 500 mg twice daily for 7 days.

If failure occurs with either regimen, the patient should be retreated with **metronidazole** 500 mg twice daily for 7 days. If repeated failure occurs, the patient should be treated with a single 2-g dose of **metronidazole** daily for 3-5 days.

Cases of additional culture-documented treatment failure in which reinfection has been excluded should be managed in consultation with an expert. Evaluation of such cases should include determination of the susceptibility of *Trichomonas vaginalis* to metronidazole.

Treatment of Sex Partners

Sex partners should be treated with either the single dose or the 7-day metronidazole regimen.

Trichomoniasis During Pregnancy

Metronidazole is contraindicated in the first trimester of pregnancy, and its safety in the rest of pregnancy is not established. However, no other adequate therapy exists. For patients with severe symptoms after the first trimester, treatment with 2 g of **metronidazole** in a single dose may be considered.

Vulvovaginal Candidiasis

Generally not considered a sexually transmitted disease, vulvovaginal candidiasis is frequently diagnosed in women presenting with symptoms involving the genitalia. Treatment with antibiotics predisposes women to the development of vulvovaginal candidiasis.

Treatment

Many treatment regimens are effective, but 3- and 7-day regimens are superior to a single-dose therapy.

Recommended Regimen

Examples of effective regimens include the following:

Miconazole nitrate (vaginal suppository 200 mg), intravaginally at bedtime for 3 days

or

Clotrimazole (vaginal tablets 200 mg), intravaginally at bedtime for 3 days

or

Butaconazole (2% cream 5 g), intravaginally at bedtime for 3 days

or

Teraconazole 80 mg suppository or 0.4% cream, intravaginally at bedtime for 3 days.

hepatitis B (such as homosexual men), prevaccination screening for antibody to hepatitis B is cost effective. Prevaccination screening in moderate-risk groups (such as heterosexual persons with STD) is usually not indicated.

Hepatitis B Vaccination

Recommendation for Hepatitis B Vaccination

Hepatitis B vaccine (several FDA-approved recombinant or plasma-derived preparations are available) in dosages as recommended by the manufacturer. The vaccination series requires an initial visit and two follow-up visits.

Vaccine should ***not*** be administered in the gluteal (buttocks) or quadriceps (thigh) muscle. After vaccination, testing for antibody response is not routinely indicated unless the patient is infected with HIV.

Post-Exposure Prophylaxis

Prophylactic treatment with hepatitis B immune globulin should be considered in the following situations: sexual contact with a patient who has active hepatitis B or who contracts hepatitis B; sexual contact with a hepatitis B carrier (blood test positive for hepatitis B surface antigen). Prophylactic treatment for sexual exposure should be given within 14 days of sexual contact. Assay for preexisting immunity to HBV may be cost effective if individuals concerned are from populations at high risk for HBV.

Recommendation for Post-Exposure Prophylaxis

Hepatitis B immune globulin (HBIG) .06 ml/kg, IM in a single dose
followed by
Initiation of **hepatitis B vaccine series** as described above.

Perinatal Infections

Pregnant women with HBV infection can transmit hepatitis B to their infants at delivery. Infants infected at birth are at high risk for contracting chronic hepatitis B infection. Such infection can be prevented by administering HBIG and hepatitis B vaccine to the infant. Therefore, all pregnant women should be screened during their first obstetrical visit for the presence of HBsAg. If they are found to be HBsAg-positive, their newborns should be given HBIG ***as soon as possible*** after birth and subsequently should be immunized with hepatitis B vaccine.

Hepatitis guidelines are updated periodically by the Immunization Practices Advisory Committee, and are published in the *MMWR*. Reference to the most current recommendations is advised.

Persons at risk for sexual transmission of hepatitis B are also at risk for HIV and other STD. HIV coinfection reduces the humoral response to HB vaccine.

Cytomegalovirus

Cytomegalovirus (CMV) is a common infection in pregnant women, and 0.5%-2% of all infants of CMV-infected women are congenitally infected, although most of these infants are only mildly affected. Another 5%-10% of infants are perinatally infected; these infections are without known sequelae. The risk of severe congenital disease (retardation, deafness, visual problems) is highest when primary CMV infection occurs during pregnancy, although recurrent CMV may also cause severe congenital infection. Because severe congenital infection occurs before delivery, and because CMV infection is widespread, the route of delivery should not be influenced by viral shedding. No accepted routine therapy exists for either maternal or neonatal infection.

Ectoparasitic Infections

Pediculosis Pubis

Recommended Regimen

Permethrin (1%) creme rinse applied to affected area and washed off after 10 minutes

or

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

or

Lindane 1% shampoo applied for 4 minutes and then thoroughly washed off. (Not recommended for pregnant or lactating women.)

Patients should be reevaluated after 1 week if symptoms persist. Retreatment may be necessary if lice are found or eggs are observed at the hair-skin junction.

Sex partners should be treated as above.

Special Considerations. Pediculosis of the eyelashes should be treated by the application of occlusive ophthalmic ointment to the eyelid margins, 2 times a day for 10 days, to smother lice and nits. Lindane or other drugs should not be applied to the eyes. Clothing or bed linen that may have been contaminated by the patient within the past 2 days should be washed and/or dried by machine (hot cycle in each) or dry cleaned.

Scabies

Recommended Regimen (Adults and Older Children)

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. (Not recommended for pregnant or lactating women.)

Alternative Regimen

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

Infants, Children 2 Years Of Age or Less, Pregnant and Lactating Women. For these groups, lindane is contraindicated. The crotamiton regimen should be used.

Contacts. Sex partners and close household contacts should be treated as above.

Special Considerations. Pruritus may persist for several weeks after adequate therapy. A single reeatment after 1 week may be appropriate if no clinical improvement occurs. Additional weekly treatments are warranted only if live mites can be demonstrated.

Clothing or bed linen that may have been contaminated by the patient within the past 2 days should be washed and dried by machine (hot cycle in each) or dry cleaned.

Sexual Assault and STD

Recommendations are limited to the identification and treatment of sexually transmitted infections. Matters concerning the sensitive management of potential pregnancy and of physical and psychological trauma are important and they should be addressed, but are beyond the scope of these guidelines. Victims of sexual assault are evaluated both to provide necessary medical services and to identify and collect forensic evidence. Although some information may be useful for the medical management of a victim, this information may not be admissible in court.

Some STD, such as gonorrhea and syphilis, are almost exclusively transmitted sexually and may be useful markers of sexual assault. BV is commonly found after assault, but is highly prevalent in most populations, which limits its usefulness as a marker of assault. Nonculture tests have lower sensitivity and specificity than culture techniques.

Sexual Assault

Any sexually transmissible agent, including HIV, may be transmitted during an assault. Few data exist on which to establish the risk of an assaulted person's acquiring an STD. The risk of acquiring gonococcal and/or chlamydial infections appears to be highest. Inferences about STD risk may be based on the known prevalences of these diseases in the community. If the suspected assailant is identified, that individual should be evaluated for STD to the extent possible under the law.

The presence of STD within 24 hours of the assault may represent prior infection and not assault-acquired disease. Furthermore, some syndromes, such as BV, may be nonsexually transmitted.

Evaluation

The victim should be initially evaluated for STD within 24 hours of the assault, if possible, and evaluation should include the following (see also subsection of "Test Selection and Specimen Handling"):

- Cultures for *N.gonorrhoeae* and *C. trachomatis* from specimens from any sites of penetration or attempted penetration
- Collection of a blood sample for a serologic test for syphilis and for storage of a serum sample for possible future testing. Serologic testing for HIV and hepatitis B infection should be considered
- For women, examination of vaginal specimens for *T. vaginalis* and for evidence of BV
- Pregnancy test

Follow-up evaluations should be scheduled after 14-21 days, to repeat studies other than those for syphilis and viral STD. A third visit may be scheduled at 8-12 weeks to repeat initial serologic studies, including tests for antibodies to syphilis and/or hepatitis B, and/or HIV.

Treatment

Treatment should be given for any infection identified on examination or for any infection identified in the assailant. Although the risk of infection is frequently low, use of presumptive treatment is controversial. Some experts recommend presumptive treatment for all victims of sexual assault, whereas some reserve presumptive treatment for special circumstances, for example, when follow-up examination of the victim cannot be ensured or when treatment is specifically requested by the patient. Although no regimen covers all potential pathogens, the following regimens should be effective against gonorrhea, chlamydia, and, most likely, syphilis.

Empiric Regimen for Victims of Sexual Assault

Ceftriaxone, 250 mg, given IM,

to be followed by either

Doxycycline 100 mg orally 2 times a day for 7 days

or

Tetracycline HCl 500 mg orally 4 times a day for 7 days.

Sexual Assault and Abuse of Children

The identification of a sexually transmissible agent from a child beyond the neonatal period suggests sexual abuse. However, exceptions do exist, e.g., rectal and genital infection with *C. trachomatis* in young children may be due to persistent perinatally acquired infection, which may persist for up to 3 years. In addition, BV and genital mycoplasmas have been identified in both abused and nonabused children.

A finding of genital warts, although suggestive of assault, is nonspecific without other evidence of sexual abuse. When the only evidence of sexual abuse is the isolation of an organism or the detection of antibodies, findings should be carefully confirmed.

Evaluation

Among sexually abused children, the prevalence of STD appears relatively low; in most studies, *C. trachomatis* is the most frequently isolated organism. Sexually abused children are best managed by a team of professionals experienced in dealing with the many needs of children. Although testing for the diseases appropriate for children (Table 5) is essentially the same as that for adults, the special needs of children must be taken into account.

Recommended evaluation of suspected child abuse/assault

- Since a child's report of assault may not be complete, specimens for culture for *N. gonorrhoeae* and *C. trachomatis* should be collected from the pharynx and rectum as well as from the vagina (girls) or urethra (boys).
- Internal pelvic examinations usually should not be performed unless indicated by the presence of a foreign body or by trauma.
- Follow-up visits should be scheduled so as to minimize trauma to the child; for asymptomatic children, an initial visit and one visit at 8-12 weeks may be sufficient.
- In cases of continuing abuse, the alleged offender may be available for medical evaluation. In such instances, care for the child may be modified when results of the evaluation of the offender are known.

Treatment

Treatment before diagnosis is not indicated unless evidence shows that the assailant is infected. Presumptive treatment after assault may be given if the victim or victim's family requests it or if follow-up examination of the victim cannot be ensured.

TABLE 5. Recommended laboratory procedures at initial and follow-up evaluation of sexually abused children (prepubertal)

Gram stain of any genital or anal discharge*
Culture for *Neisseria gonorrhoeae*†
Culture for *Chlamydia trachomatis*†
Wet preparation of vaginal secretion for trichomonads
Culture of lesions for herpes simplex virus (HSV)
Serologic test for syphilis
Serologic test for human immunodeficiency virus (HIV)§
Frozen serum sample
Note: Syphilis and HIV serology should be repeated in 12 weeks. All other tests should be repeated 10-14 days after the initial examination.

*Care should be taken in the interpretation of results of any Gram stain of any anal discharge.
†Cultures of pharynx, rectum, and vagina/urethra should be done.
§ Testing for HIV should be based on the prevalence of infection and on suspected risk.

Test Selection and Specimen Handling

When a sexually transmitted agent is identified from a sexually abused adult or child, the positive laboratory report may be required in pending legal action. Isolation of gonorrhea and chlamydia organisms by culture, and their confirmation by recognized techniques, is standard. All presumptive isolates of *N. gonorrhoeae* from children should be confirmed by at least two tests that involve different principles, e.g., biochemical, enzyme substrate, or serologic. Direct specimen antigen-detection tests or DNA probe tests are ***not recommended*** for use on specimens from any victim of sexual abuse. These tests may be used to diagnose *C. trachomatis* in adults only in areas where culture is not available. Results of nonculture tests may be used to guide medical management but should not be used for forensic purposes. The potential for an inaccurate result is greatest in children, and nonculture tests are not recommended in the evaluation of sexual assault or sexual abuse in children. Isolates should be stored at -70 C for possible future studies, and the use of a reference laboratory should be considered. Expert laboratory consultations are recommended for testing as well as for chain-of-evidence issues.

*U.S. GOVERNMENT PRINTING OFFICE: 1989 731-011/04983 Region 4