Table 1. Organisms Responsible for Bacterial Infections in Drug Users.*

Skin, soft-tissue, and skeletal infections
Staphylococcus aureus (including community-associated MRSA)
Streptococcus species — groups A, C, and G; *Streptococcus anginosus* (*milleri*)†; and α-hemolytic streptococci†
Pseudomonas aeruginosa
Other gram-negative bacteria (*Escherichia coli*, enterobacter, klebsiella, proteus, serratia)
Oral anaerobes (bacteroides species, *Eikenella corrodens*, fusobacterium species, peptostreptococcus species)†
Mycobacterium tuberculosis
Infective endocarditis‡
S. aureus (including community-associated MRSA)
Streptococcus species (groups A, B, G, and others)
P. aeruginosa and other gram-negative bacteria
Toxin-mediated disease
Clostridium botulinum, *C. tetani*
Other clostridia species (*C. sordellii*, *C. novyi*, *C. perfringens*)
Group A streptococcus and *S. aureus*
Pulmonary infection
Community-acquired pneumonia
S. pneumoniae, *S. aureus*, *Haemophilus influenzae*, *Klebsiella pneumoniae*, *Chlamydia pneumoniae*, *Mycoplasma pneumoniae*, *Legionella pneumophila*
Oropharyngeal flora (i.e., due to aspiration)
Opportunistic pulmonary infections (associated with HIV disease)
M. tuberculosis (including multidrug-resistant tuberculosis), *M. avium* complex, *P. aeruginosa*, nocardia species, *Rhodococcus equi*
Sexually transmitted infections
Chlamydia trachomatis, *Neisseria gonorrhoeae*, *Treponema pallidum*, and others

* This is a selection of likely bacterial pathogens. Other bacterial or nonbacterial pathogens may also be present and should be considered in the differential diagnosis. MRSA denotes methicillin-resistant *S. aureus*.
† These organisms are more likely to be pathogens when oral contamination is present.
‡ Injection-drug users have an increased risk of polymicrobial infective endocarditis.

Source: Gordon, R. J. and F. D. Lowy (2005). "Bacterial infections in drug users." N Engl J Med 353(18): 1945-1954.

SYLLABUS MATERIAL: Medical Complications of Addiction

Table 2. Initial Management of Bacterial Infectious Syndromes among Suspected Drug Users.*

Clinical Scenario	Selected Diagnostic Tests	Empirical Treatment Options†	
		Oral	Parenteral
Skin or soft-tissue infection in which *S. aureus* is a likely pathogen	Send drainage for Gram's staining, culture, and susceptibility testing.	Incision and drainage plus wound care may suffice for uncomplicated abscesses	
		For methicillin-susceptible *S. aureus*: dicloxacillin or cephalexin,‡ 500 mg every 6 hr	For methicillin-susceptible *S. aureus*: nafcillin or oxacillin, 1–2 g every 4–6 hr; cefazolin,‡ 1–2 g every 8 hr
		If MRSA suspected: TMP-SMX,‡ 6–10 mg/kg of body weight/day (TMP) in divided doses given every 8–12 hr; clindamycin,§ 300 mg every 6 hr or 450 mg every 8 hr; doxycycline or minocycline, 100 mg every 12 hr; linezolid, 600 mg every 12 hr	If MRSA suspected: vancomycin,‡ 15 mg/kg every 12 hr; teicoplanin,‡¶ 6 mg/kg every 12 hr for 3 doses, then 6 mg/kg every 24 hr; linezolid, 600 mg every 12 hr; daptomycin,‡ 4 mg/kg every 24 hr
Infections in which oral contamination is suspected, including skin or soft-tissue and skeletal infections (septic arthritis and bursitis, tenosynovitis, and osteomyelitis)	Send specimens for Gram's staining, culture, and susceptibility testing. Consider imaging to diagnose or define deep-seated infections. A bone biopsy is important when osteomyelitis is suspected regardless of whether blood-culture results are positive. Specimens for anaerobic culture require special handling.	Incision and drainage when appropriate; wound care	
		Amoxicillin–clavulanate,‡ 875 mg every 12 hr; For serious penicillin allergy: clindamycin and quinolone (dose and route based on type and severity of infection)	Ampicillin–sulbactam,‡ 1.5–3.0 g every 6 hr, plus gentamicin,‡ 1.5–2.0 mg/kg every 8 hr for serious or complicated infections; piperacillin–tazobactam,‡ 3.375 g every 4–6 hr or 4.5 g every 6–8 hr; ticarcillin–clavulanate,‡ 3.1 g every 4–6 hr; cefepime,‡ 1–2 g every 12 hr; For osteomyelitis, serious infections, and possible MRSA infection, add vancomycin‡ or teicoplanin‡¶
Acute right-sided infective endocarditis	Diagnosis is based on the modified Duke criteria.[71] Culture of multiple blood specimens before the initiation of antibiotic therapy is the optimal approach.	Vancomycin,‡ 15 mg/kg IV every 12 hr (or teicoplanin,‡¶ 12 mg/kg every 12 hr for 3 doses, then 12 mg/kg every 24 hr), plus gentamicin,‡ 1 mg/kg every 8 hr or consider nafcillin or oxacillin, 2 g IV every 4 hr, plus gentamicin,‡ 1 mg/kg every 8 hr, if MRSA not present in the community; consider broadening coverage (pseudomonal, gram-negative, or fungal antibiotics) on the basis of patient risk factors‖	
Pulmonary infection (community-acquired pneumonia and aspiration pneumonia, pulmonary tuberculosis, and other opportunistic pathogens) in drug users, including those with HIV or AIDS or risk factors for HIV infection	Radiographic imaging: Gram's and AFB staining of sputum and cultures of sputum and blood. Bronchoscopy may be needed to diagnose pneumocystis pneumonia. In certain cases, performing a PPD test or checking for *Streptococcus pneumoniae* and legionella urinary antigens may be useful.	Hospitalized with community-acquired pneumonia: ceftriaxone, 1–2 g IV every 24 hr, and azithromycin, 500 mg IV every 24 hr or respiratory fluoroquinolone**	
		Aspiration pneumonia likely: clindamycin, 600–900 mg IV every 8 hr	
		Pneumocystis pneumonia suspected: TMP–SMX,‡ 15–20 mg/kg/day (TMP dose), given in divided doses every 6–8 hr (with or without corticosteroids)	
		For tuberculosis, see treatment guidelines at www.thoracic.org or www.who.int/tb/en/index.html	
Presentation involving septic or neurologic findings of unknown cause with or without skin or soft-tissue infection	Gram's staining, culture, and susceptibility testing should be done if applicable.	For botulism: trivalent antitoxin (type A, B, or E), 1 vial, available from the appropriate public health authority; and penicillin G,‡ 3 million U IV every 6 hr	
		For tetanus-prone wounds or tetanus: human tetanus immune globulin and tetanus toxoid; metronidazole, 500 mg orally or IV every 8 hr	
		For other clostridia species (may be polymicrobial): débridement of skin or soft-tissue infections; ampicillin–sulbactam,‡ 3 g IV every 6 hr plus vancomycin,‡ 15 mg/kg IV every 12 hr (or teicoplanin‡¶)††	
Sexually transmitted infections	Examination and workup are conducted according to local health department guidelines. RPR and VDRL tests may be false positive; confirm results with FTA-ABS test.	Follow CDC treatment guidelines or those of public health authorities (available at www.who.int/topics/sexually_transmitted_infections/en/)	

* MRSA denotes methicillin-resistant *S. aureus*, TMP-SMX trimethoprim–sulfamethoxazole, AFB acid-fast bacilli, RPR rapid plasma reagin, VDRL Venereal Disease Research Laboratory, FTA-ABS fluorescent treponemal antibody absorption, IV intravenously, and CDC Centers for Disease Control and Prevention.
† Therapy should be adjusted on the basis of the culture results and antibiotic susceptibilities.
‡ The dose must be adjusted in patients with reduced creatinine clearance.
§ Clindamycin should not be used if the isolate is resistant to erythromycin.
¶ This drug is not available in the United States.
‖ Therapy is generally continued for four to six weeks. Baddour et al.[72] provide specific recommendations.
** Respiratory quinolones include gatifloxacin, levofloxacin, and moxifloxacin.
†† Hyperbaric oxygen has also been used.

Source: Gordon, R. J. and F. D. Lowy (2005). "Bacterial infections in drug users." N Engl J Med 353(18): 1945-1954.

HIV Transmission Risk

June 2014

The risk of getting HIV varies widely depending on the type of exposure. Some exposures, such as exposure to HIV during a blood transfusion, carry a much higher risk of transmission than other exposures, such as oral sex. For some exposures, risk of transmission, while biologically plausible, is so low that it is not possible to provide a precise number.

Different factors can increase or decrease transmission risk. For example, taking antiretroviral therapy (i.e., medicines for HIV infection) can reduce the risk of an HIV-infected person transmitting the infection to another by as much as 96%[1], and consistent use of condoms reduces the risk of getting or transmitting HIV by about 80%[2]. Using both condoms and antiretroviral therapy reduces the risk of HIV acquisition from sexual exposure by 99.2%[3]. Conversely, having a sexually transmitted infection or a high level of HIV virus in the blood (which happens in early and late-stage infection) may increase transmission risk.

The table below lists the risk of transmission per 10,000 exposures for various types of exposures.

Estimated Per-Act Probability of Acquiring HIV from an Infected Source, by Exposure Act*

Type of Exposure	Risk per 10,000 Exposures
Parenteral[3]	
Blood Transfusion	9,250
Needle-sharing during injection drug use	63
Percutaneous (needle-stick)	23
Sexual[3]	
Receptive anal intercourse	138
Insertive anal intercourse	11
Receptive penile-vaginal intercourse	8
Insertive penile-vaginal intercourse	4
Receptive oral intercourse	low
Insertive oral intercourse	low
Other^	
Biting	negligible[4]
Spitting	negligible
Throwing body fluids (including semen or saliva)	negligible
Sharing sex toys	negligible

* Factors that may increase the risk of HIV transmission include sexually transmitted diseases, acute and late-stage HIV infection, and high viral load. Factors that may decrease the risk include condom use, male circumcision, antiretroviral treatment, and pre-exposure prophylaxis. None of these factors are accounted for in the estimates presented in the table.

^ HIV transmission through these exposure routes is technically possible but unlikely and not well documented.

[1] Cohen MS, Chen YQ, McCauley M, et al; HPTN 052 Study Team. Prevention of HIV-1 Infection with early antiretroviral therapy. *N Engl J Med* 2011;365(6):493-505.

[2] Weller SC, Davis-Beaty K. Condom effectiveness in reducing heterosexual HIV transmission (Review). The Cochrane Collaboration. Wiley and Sons, 2011.

[3] Patel P, Borkowf CB, Brooks JT. Et al. Estimating per-act HIV transmission risk: a systematic review. AIDS. 2014. doi: 10.1097/QAD.0000000000000298.

[4] Pretty LA, Anderson GS, Sweet DJ. Human bites and the risk of human immunodeficiency virus transmission. Am J Forensic Med Pathol 1999;20(3):232-239.

NON-OCCUPATIONAL POSTEXPOSURE PROPHYLAXIS: Follow the algorithm to determine whether the patient should be offered nPEP medications. If the patient is a candidate for treatment, provide counseling about the potential risks and benefits of nPEP.

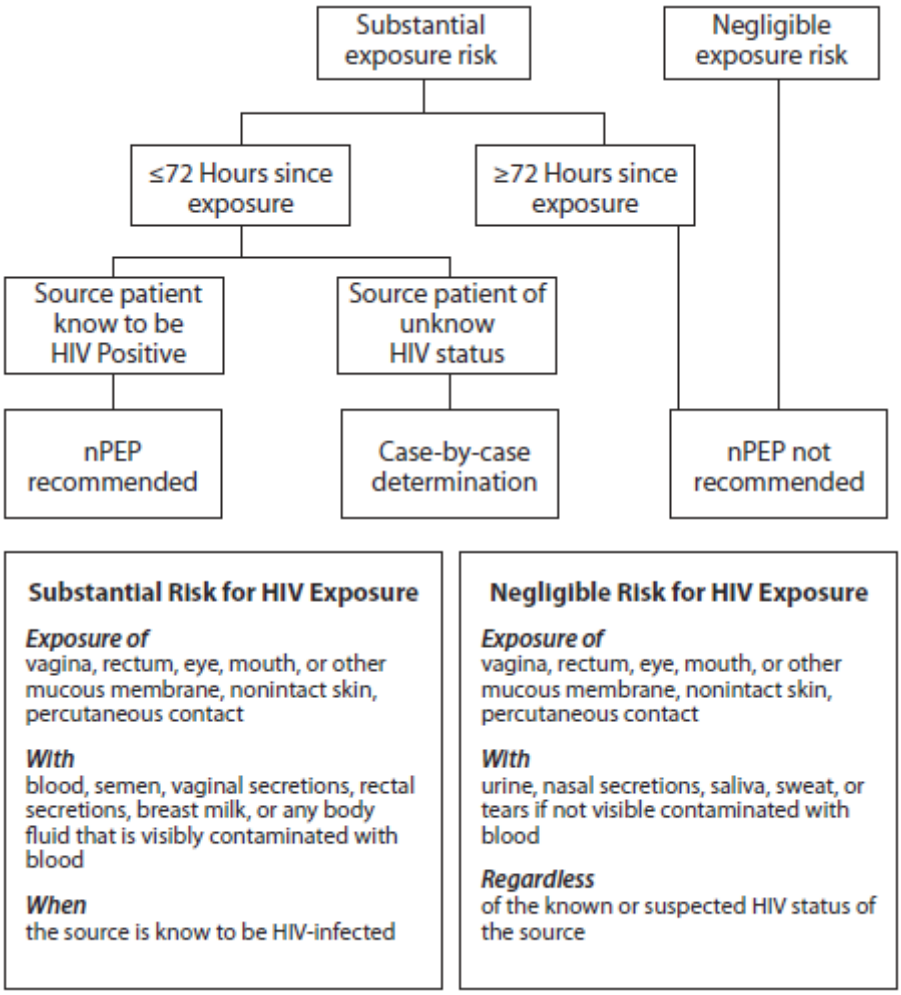

Figure 1. Algorithm for evaluation and treatment of possible non-occupational HIV exposure
Source: DHHS, http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5402a1.htm

RECOMMENDED nPEP REGIMEN: The preferred PEP regimen is raltegravir 400 mg BID + tenofovir/emtricitabine 1 tablet once daily. The first dose should be given as soon as possible after exposure, ideally within 2 hours. The recommended duration of PEP is 28 days.

Treating clinicians who do not have access to experienced HIV clinicians should call the National Clinicians' Consultation Center PEPline at 1-888-448-4911.

Source: New York State Department of Public Health, http://www.hivguidelines.org/clinical-guidelines/post-exposure-prophylaxis/hiv-prophylaxis-following-non-occupational-exposure/

Pre-exposure Prophylaxis (PrEP) for HIV Prevention

May 2014

Fast Facts

- Pre-exposure prophylaxis, or PrEP, is a way to help prevent HIV by taking a pill every day.
- People who are at substantial risk for HIV should talk to their doctor about PrEP.
- PrEP must be taken every day to be most effective.

Pre-exposure prophylaxis, or PrEP, is a way for people who do not have HIV to help prevent HIV infection by taking a pill every day. The pill contains two medicines that are also used, in combination with other medicines, to treat HIV. When someone is exposed to HIV through sex or injection drug use, PrEP can help stop the virus from establishing a permanent infection.

When used consistently, PrEP has been shown to greatly reduce the risk of HIV infection in people who are at substantial risk. PrEP is much less effective when it is not taken consistently.

PrEP is a powerful HIV prevention tool, and can be combined with condoms and other prevention methods to provide even greater protection than when used alone. People who use PrEP must commit to taking the drug daily and seeing their health care provider every 3 months for HIV testing and other follow-up.

PrEP Medicines

Most PrEP clinical trials have tested a combination of two antiretroviral drugs, tenofovir disoproxil fumarate (also called TDF, or tenofovir) and emtricitabine (also called FTC), taken in a single pill daily for HIV prevention. This combination pill (brand name **Truvada**) was approved by the US Food and Drug Administration (FDA) for use as an HIV treatment in 2004, and was approved as PrEP in July 2012. Some clinical studies have also evaluated the use of tenofovir on its own as a preventive drug, but this drug alone is not FDA-approved for PrEP.

Research Supporting PrEP Use

On May 14, 2014, the US Public Health Service released the first comprehensive clinical practice guidelines for PrEP (www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf). This follows the earlier publication of brief interim guidelines that were based on findings from several large national and international clinical trials. These trials evaluated PrEP among gay and bisexual men, heterosexual men and women, and injection drug users. All participants in these trials received pills containing either PrEP or placebo, along with intensive counseling on safe-sex behavior, regular testing for sexually transmitted diseases (STDs), and a regular supply of condoms.

In all of these studies, the risk of getting HIV infection was lower—up to 92% lower—for **participants who took the medicines consistently** than for those who did not take the medicines. (See our PrEP web page at www.cdc.gov/hiv/prevention/research/prep/ for a brief description of the clinical trials, with links to the published studies.)

Guidelines for PrEP Use

The new federal guidelines for health care providers recommend that PrEP be considered for people who are HIV-negative and **at substantial risk for HIV infection**.

For sexual transmission, this includes anyone who is in an ongoing relationship with an HIV-positive partner. It also includes anyone who 1) is not in a mutually monogamous relationship with a partner who recently tested HIV-negative, and 2) is a

- gay or bisexual man who has had anal sex without a condom or been diagnosed with an STD in the past 6 months; or
- heterosexual man or woman who does not regularly use condoms during sex with partners of unknown HIV status who are at substantial risk of HIV infection (e.g., people who inject drugs or have bisexual male partners).

For people who inject drugs, this includes those who have injected illicit drugs in past 6 months and who have shared injection equipment or been in drug treatment for injection drug use in the past 6 months.

Health care providers should also discuss PrEP with heterosexual couples in which one partner is HIV-positive and the other is HIV-negative as one of several options to protect the partner who is HIV-negative during conception and pregnancy.

For a summary of clinical indications and treatment recommendations for PrEP, see the Table on the next page.

Summary of Guidance for PrEP Use

	Men Who Have Sex With Men	Heterosexual Women and Men	Injection Drug Users
Detecting substantial risk of acquiring HIV infection:	• Sexual partner with HIV • Recent bacterial STD • High number of sex partners • History of inconsistent or no condom use • Commercial sex work	• Sexual partner with HIV • Recent bacterial STD • High number of sex partners • History of inconsistent or no condom use • Commercial sex work • Lives in high-prevalence area or network	• HIV-positive injecting partner • Sharing injection equipment • Recent drug treatment (but currently injecting)
Clinically eligible:	• Documented negative HIV test before prescribing PrEP • No signs/symptoms of acute HIV infection • Normal renal function, no contraindicated medications • Documented hepatitis B virus infection and vaccination status		
Prescription	Daily, continuing, oral doeses of TDF/FTC (Truvada), ≤90 day supply		
Other services:	• Follow-up visits at least every 3 months to provide: • HIV test, medication adherence counseling, behavioral risk reduction support, side effect assessment, STD symptom assessment • At 3 months and every 6 months after, assess renal function • Every 6 months test for bacterial STDs		
	• Do oral/rectal STD testing	• Assess pregnancy intent • Pregnancy test every 3 months	• Access to clean needles/ syringes and drug treatment services

Source: US Public Health Service. Preexposure prophylaxis for the prevention of HIV infection in the United States —2014: a clinical practice guideline.

Because no prevention strategy for sexually active people is 100% effective, patients taking PrEP are encouraged to use other effective prevention strategies to maximally reduce their risk, including:

- Using condoms consistently and correctly.
- Getting HIV testing with partners.
- Choosing less risky sexual behaviors, such as oral sex.
- For people who inject drugs, getting into drug treatment programs and using sterile equipment.

The more prevention options patients choose, the greater their protection. Some HIV prevention strategies, such as using condoms, can also provide protection against other STDs, which PrEP does not prevent.

PrEP is only for people who are at ongoing substantial risk of HIV infection. For people who need to prevent HIV after a single high-risk event of potential HIV exposure—such as unprotected sex, needle-sharing injection drug use, or sexual assault —there is another option called postexposure prophylaxis, or PEP. PEP must begin within 72 hours of exposure. See our PEP Q&A (www.cdc.gov/hiv/basics/pep.html) for more information.

Supporting PrEP Uptake

To support the new guidelines and provider's supplement, CDC is leading efforts on multiple fronts to improve PrEP awareness and delivery in community settings. For example, the agency is implementing a pilot study examining practical requirements, costs, and impact of PrEP delivered at four federally qualified health centers, and will support state and local health departments by providing webinars and program guidance on using CDC funds to support PrEP implementation.

Many other groups will also play a vital role in achieving the full promise of PrEP. Health care providers can prescribe PrEP to those patients with indications for its use and increase awareness and uptake of PrEP for their patients who are at substantial risk. Advocates can raise PrEP awareness in at-risk populations, and groups implementing HIV prevention efforts can integrate PrEP education into existing programs.

Resources

- Basic PrEP Q&As (www.cdc.gov/hiv/basics/prep.html)
- Clinical Practice Guidelines (www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf)
- Clinical Practice Guidelines—Providers' Supplement (www.cdc.gov/hiv/pdf/guidelines/PrEPProviderSupplement2014.pdf)
- Basic PEP Q&As (www.cdc.gov/hiv/basics/pep.html)

Additional Resources

CDC-INFO
1-800-CDC-INFO (232-4636)
www.cdc.gov/info

CDC HIV Website
www.cdc.gov/hiv

CDC Act Against AIDS Campaign
www.cdc.gov/actagainstaids

Update to Interim Guidance for Preexposure Prophylaxis (PrEP) for the Prevention of HIV Infection: PrEP for Injecting Drug Users

On June 12, 2013, the Thailand Ministry of Health and CDC published results from a randomized controlled trial of a daily oral dose of 300 mg of tenofovir disoproxil fumarate (TDF) that showed efficacy in reducing the acquisition of human immunodeficiency virus (HIV) infection among injecting drug users (IDUs) (*1*). Based on these findings, CDC recommends that preexposure prophylaxis (PrEP) be considered as one of several prevention options for persons at very high risk for HIV acquisition through the injection of illicit drugs.

Background

Among the approximately 50,000 new HIV infections acquired each year in the United States, 8% were attributed to injection-drug use in 2010 (*2*). The National HIV Behavioral Surveillance System, surveying IDUs in 20 U.S. cities in 2009, found high frequencies of both injection-drug use and sexual practices that are associated with HIV acquisition (*3*). Among IDUs without HIV infection, 34% reported having shared syringes in the preceding 12 months, and 58% reported having shared injection equipment; 69% reported having unprotected vaginal sex and 23% reported having unprotected male-female anal sex. Among HIV-uninfected male IDUs, 7% reported previous male-male anal sex, and 5% reported unprotected male-male anal sex. However, only 19% of male and female IDUs reported participating in an intervention to reduce risk behaviors. These findings underscore a need to provide effective interventions to further reduce HIV infections among IDUs in the United States.

Several clinical trials have demonstrated safety and efficacy of daily oral antiretroviral PrEP for the prevention of HIV acquisition among men who have sex with men (MSM) (*4*) and heterosexually active men and women (*5,6*), although two trials were unable to show efficacy, likely because of low adherence (*7,8*) (Table). CDC previously has issued interim guidance for PrEP use with MSM (*9*) and heterosexually active adults (*10*) and now provides interim guidance for PrEP use in IDUs.

During 2009–2013, CDC convened workgroup meetings and consulted with external subject matter experts, including clinicians, epidemiologists, academic researchers, health department policy and program staff members, community representatives, and HIV and substance abuse subject matter experts at federal health agencies, to 1) review the results of PrEP trials and other data as they became available and 2) deliberate and recommend content for interim guidance and comprehensive U.S. Public Health Service guidelines for PrEP use in the United States. The expert opinions from the IDU workgroup and other workgroups were used to develop this interim guidance on PrEP use with IDUs.

Rationale and Evidence

The Bangkok Tenofovir Study enrolled HIV-uninfected persons who reported injecting illicit drugs in the prior year into a phase-III randomized, double-blind, placebo-controlled trial to determine the safety and efficacy of daily oral TDF to reduce the risk for HIV acquisition. In all, 2,413 eligible, consenting men and women aged 20–60 years were randomized to receive either daily oral doses of 300 mg of TDF (n = 1,204) or a placebo tablet (n = 1,209). Participants could elect to receive tablets daily by directly observed therapy or receive a 28-day supply of daily doses to take home; they could switch medication supply method at their monthly follow-up visits. At follow-up visits every 28 days, individualized adherence and risk-reduction counseling, HIV testing, pregnancy testing for women, and assessment for adverse events were conducted. An audio computer-assisted self-interview was conducted every 3 months to assess risk behaviors. Blood was collected at enrollment; months 1, 2, and 3; and then every 3 months for laboratory testing to screen for adverse reactions to the medication. At study clinics (operated by the Bangkok Metropolitan Administration), social services, primary medical care, methadone, condoms, and bleach (for cleaning injection equipment) were provided free of charge.

The study was conducted during 2005–2012, with a mean follow-up time of 4.6 years (maximum: 6.9 years) and a 24% loss to follow-up or voluntary withdrawal in the TDF group and a 23% loss in the placebo group. Participants took their study drug an average of 83.8% of days and were on directly observed therapy 86.9% of the time.

After enrollment, 50 patients acquired HIV infection: 17 in the TDF group and 33 in the placebo group. In the modified "intent-to-treat" analysis (excluding two participants later found to have been HIV-infected at enrollment), HIV incidence was 0.35 per 100 person-years in the TDF group and 0.68 per 100 person-years in the placebo group, representing a 48.9% reduction in HIV incidence (95% confidence interval [CI] = 9.6%–72.2%). Among those in an unmatched case-control study that included the 50 persons with incident HIV infection (case-patients) and 282 HIV-uninfected participants from four clinics (controls), detection of tenofovir in plasma was associated with a 70% reduction in the risk for HIV infection (CI = 2.3%–90.6%).

TABLE. Results from randomized, placebo-controlled, clinical trials of the efficacy of daily oral antiretroviral preexposure prophylaxis (PrEP) for preventing human immunodeficiency virus (HIV) infection

Clinical trial	Participants	Type of medication	mITT efficacy*		Adherence-adjusted efficacy based on TDF detection in blood	
			%	(95% CI)	%	(95% CI)
Bangkok Tenofovir Study	Injecting drug users	TDF	49	(10–72)	70	(2–91)
Partners PrEP	HIV discordant couples	TDF	67	(44–81)	86	(67–94)
		TDF/FTC	75	(55–87)	90	(58–98)
TDF2	Heterosexually active men and women	TDF/FTC	62	(22–83)	84	NS
iPrEx	Men who have sex with men	TDF/FTC	42	(18–60)	92	(40–99)
Fem-PrEP	Heterosexually active women	TDF/FTC	NS	—	NA	—
VOICE	Heterosexually active women	TDF	NS	—	NA	—
		TDF/FTC	NS	—	NA	—

Abbreviations: mITT = modified intent to treat analysis, excluding persons determined to have had HIV infection at enrollment; CI = confidence interval; TDF = tenofovir disoproxil fumarate; FTC = emtricitabine; NS = not statistically significant; NA = data not available.
* % reduction in acquisition of HIV infection.

The rates of adverse events, serious adverse events, deaths, grade 3–4 laboratory abnormalities, and elevated serum creatinine did not differ significantly between the two groups. Reports of nausea and vomiting were higher in the TDF group than the placebo group in the first 2 months of medication use but not thereafter. No HIV infections with mutations associated with TDF resistance were identified among HIV-infected participants.

Comparing rates at enrollment with rates at 12 months of follow-up, risk behaviors decreased significantly for injecting drugs (from 62.7% to 22.7%), sharing needles (18.1% to 2.3%), and reporting multiple sexual partners (21.7% to 11.0%), and these risk behaviors remained below baseline throughout the entire period of the trial (all three comparisons, $p<0.001$). Rates were similar in the TDF and placebo groups.

PrEP Recommendation for IDUs

On July 16, 2012, based on the results of trials in MSM and heterosexually active women and men, the Food and Drug Administration approved a label indication for the use of the fixed dose combination of TDF 300 mg and emtricitabine (FTC) 200 mg (Truvada) as PrEP against sexual HIV acquisition by MSM and heterosexually active women and men (*11*). These trials did not evaluate safety and efficacy among injecting-drug users.

CDC recommends that daily TDF/FTC be the preferred PrEP regimen for IDUs for the following reasons: 1) TDF/FTC contains the same dose of TDF (300 mg) proven effective for IDUs, 2) TDF/FTC showed no additional toxicities compared with TDF alone in PrEP trials that have provided both regimens, 3) IDUs also are at risk for sexual HIV acquisition for which TDF/FTC is indicated, and 4) TDF/FTC has an approved label indication for PrEP to prevent sexual HIV acquisition in the United States. Its use to prevent parenteral HIV acquisition in those without sexual acquisition risk is currently an "off-label" use. Reported injection practices that place persons at very high risk for HIV acquisition include sharing of injection equipment, injecting one or more times a day, and injection of cocaine or methamphetamine. CDC recommends that prevention services provided for IDUs receiving PrEP include those targeting both injection and sexual risk behaviors (12).

In all populations, PrEP use 1) is contraindicated in persons with unknown or positive HIV status or with an estimated creatinine clearance <60 mL/min, 2) should be targeted to adults at very high risk for HIV acquisition, 3) should be delivered as part of a comprehensive set of prevention services, and 4) should be accompanied by quarterly monitoring of HIV status, pregnancy status, side effects, medication adherence, and risk behaviors, as outlined in previous interim guidance (*9,10*). Adherence to daily PrEP is critical to reduce the risk for HIV acquisition, and achieving high adherence was difficult for many participants in PrEP clinical trials (Table).

Comment

Providing PrEP to IDUs at very high risk for HIV acquisition could contribute to the reduction of HIV incidence in the United States. In addition, if PrEP delivery is integrated with prevention and clinical care for the additional health concerns faced by IDUs (e.g., hepatitis B and C infection, abscesses, and overdose), substance abuse treatment and behavioral health care, and social services, PrEP will contribute additional benefits to a population with multiple life-threatening physical, mental, and social health challenges (*12,13*). CDC, in collaboration with other federal agencies, is preparing comprehensive U.S. Public Health Service guidelines on the use of PrEP with MSM, heterosexually active men and women, and IDUs, currently scheduled for release in 2013.

Reported by

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The ABCs of Hepatitis

	HEPATITIS A is caused by the Hepatitis A virus (HAV)	**HEPATITIS B** is caused by the Hepatitis B virus (HBV)	**HEPATITIS C** is caused by the Hepatitis C virus (HCV)
U.S. Statistics	• Estimated 17,000 new infections in 2010	• Estimated 38,000 new infections in 2010 • Estimated 1.2 million people with chronic HBV infection	• Estimated 17,000 new infections in 2010 • Estimated 3.2 million people with chronic HCV infection
Routes of Transmission	Ingestion of fecal matter, even in microscopic amounts, from: • Close person-to-person contact with an infected person • Sexual contact with an infected person • Ingestion of contaminated food or drinks	Contact with infectious blood, semen, and other body fluids, primarily through: • Birth to an infected mother • Sexual contact with an infected person • Sharing of contaminated needles, syringes or other injection drug equipment • Needlesticks or other sharp instrument injuries	Contact with blood of an infected person, primarily through: • Sharing of contaminated needles, syringes, or other injection drug equipment Less commonly through: • Sexual contact with an infected person • Birth to an infected mother • Needlestick or other sharp instrument injuries
Persons at Risk	• Travelers to regions with intermediate or high rates of Hepatitis A • Sex contacts of infected persons • Household members or caregivers of infected persons • Men who have sex with men • Users of certain illegal drugs (injection and non-injection) • Persons with clotting-factor disorders	• Infants born to infected mothers • Sex partners of infected persons • Persons with multiple sex partners • Persons with a sexually transmitted disease (STD) • Men who have sex with men • Injection drug users • Household contacts of infected persons • Healthcare and public safety workers exposed to blood on the job • Hemodialysis patients • Residents and staff of facilities for developmentally disabled persons • Travelers to regions with intermediate or high rates of Hepatitis B (HBsAg prevalence of ≥2%)	• Current or former injection drug users • Recipients of clotting factor concentrates before 1987 • Recipients of blood transfusions or donated organs before July 1992 • Long-term hemodialysis patients • Persons with known exposures to HCV (e.g., healthcare workers after needlesticks, recipients of blood or organs from a donor who later tested positive for HCV) • HIV-infected persons • Infants born to infected mothers
Incubation Period	15 to 50 days (average: 28 days)	45 to 160 days (average: 120 days)	14 to 180 days (average: 45 days)
Symptoms of Acute Infection	**Symptoms of all types of viral hepatitis are similar and can include one or more of the following:** • Fever • Fatigue • Loss of appetite • Nausea • Vomiting • Abdominal pain • Gray-colored bowel movements • Joint pain • Jaundice		
Likelihood of Symptomatic Acute infection	• < 10% of children < 6 years have jaundice • 40%–50% of children age 6–14 years have jaundice • 70%–80% of persons > 14 years have jaundice	• < 1% of infants < 1 year develop symptoms • 5%–15% of children age 1-5 years develop symptoms • 30%–50% of persons > 5 years develop symptoms **Note:** Symptoms appear in 5%–15% of newly infected adults who are immunosuppressed	• 20%–30% of newly infected persons develop symptoms of acute disease
Potential for Chronic Infection	None	• Among unimmunized persons, chronic infection occurs in >90% of infants, 25%–50% of children aged 1–5 years, and 6%–10% of older children and adults	• 75%–85% of newly infected persons develop chronic infection • 15%–25% of newly infected persons clear the virus
Severity	Most persons with acute disease recover with no lasting liver damage; rarely fatal	• Most persons with acute disease recover with no lasting liver damage; acute illness is rarely fatal • 15%–25% of chronically infected persons develop chronic liver disease, including cirrhosis, liver failure, or liver cancer • Estimated 3,000 persons in the United States die from HBV-related illness per year	• Acute illness is uncommon. Those who do develop acute illness recover with no lasting liver damage. • 60%–70% of chronically infected persons develop chronic liver disease • 5%–20% develop cirrhosis over a period of 20–30 years • 1%–5% will die from cirrhosis or liver cancer • Estimated 12,000 persons in the United States die from HCV-related illness per year
Serologic Tests for Acute Infection	• IgM anti-HAV	• HBsAg in acute and chronic infection • IgM anti-HBc is positive in acute infection only	• No serologic marker for acute infection

	HEPATITIS A	HEPATITIS B	HEPATITIS C
Serologic Tests for Chronic Infection	• Not applicable—no chronic infection	• HBsAg (and additional markers as needed)	• Screening assay (EIA or CIA) for anti-HCV • Verification by an additional, more specific assay (e.g., nucleic acid testing (NAT) for HCV RNA)
Screening Recomendations for Chronic Infection	• Not applicable—no chronic infection Note: Screening for past acute infection is generally not recommended	Testing is recommended for: • All pregnant women • Persons born in regions with intermediate or high rates of Hepatitis B (HBsAg prevalence of ≥2%) • U.S.–born persons not vaccinated as infants whose parents were born in regions with high rates of Hepatitis B (HBsAg prevalence of ≥8%) • Infants born to HBsAg-positive mothers • Household, needle-sharing, or sex contacts of HBsAg-positive persons • Men who have sex with men • Injection drug users • Patients with elevated liver enzymes (ALT/AST) of unknown etiology • Hemodialysis patients • Persons needing immunosuppressive or cytotoxic therapy • HIV-infected persons • Donors of blood, plasma, organs, tissues, or semen	Testing is recommended for: • Persons born from 1945–1965 • Persons who currently inject drugs or who have injected drugs in the past, even if once or many years ago • Recipients of clotting factor concentrates before 1987 • Recipients of blood transfusions or donated organs before July 1992 • Long-term hemodialysis patients • Persons with known exposures to HCV (e.g., healthcare workers after needlesticks, recipients of blood or organs from a donor who later tested positive for HCV) • HIV-infected persons • Children born to infected mothers (do not test before age 18 mos.) • Patients with signs or symptoms of liver disease (e.g., abnormal liver enzyme tests) • Donors of blood, plasma, organs, tissues, or semen
Treatment	• No medication available • Best addressed through supportive treatment	• Acute: No medication available; best addressed through supportive treatment • Chronic: Regular monitoring for signs of liver disease progression; some patients are treated with antiviral drugs	• Acute: Antivirals and supportive treatment • Chronic: Regular monitoring for signs of liver disease progression; some patients are treated with antiviral drugs
Vaccination Recommendations	Hepatitis A vaccine is recommended for: • All children at age 1 year • Travelers to regions with intermediate or high rates of Hepatitis A • Men who have sex with men • Users of certain illegal drugs (injection and non-injection) • Persons with clotting-factor disorders • Persons who work with HAV-infected primates or with HAV in a research laboratory • Persons with chronic liver disease, including HBV- and HCV-infected persons with chronic liver disease • Family and care givers of recent adoptees from countries where Hepatitis A is common • Anyone else seeking long-term protection	Hepatitis B vaccine is recommended for: • All infants at birth • Older children who have not previously been vaccinated • Susceptible sex partners of infected persons • Persons with multiple sex partners • Persons seeking evaluation or treatment for an STD • Men who have sex with men • Injection drug users • Susceptible household contacts of infected persons • Healthcare and public safety workers exposed to blood on the job • Persons with chronic liver disease, including HCV-infected persons with chronic liver disease • Persons with HIV infection • Persons with end-stage renal disease, including predialysis, hemodialysis, peritoneal dialysis, and home dialysis patients • Residents and staff of facilities for developmentally disabled persons • Travelers to regions with intermediate or high rates of Hepatitis B (HBsAg prevalence of ≥2%) • Unvaccinated adults with diabetes mellitus 19–59 (for those aged ≥60 years, at the discretion of clinician) • Anyone else seeking long-term protection	There is no Hepatitis C vaccine.
Vaccination Schedule	2 doses given 6 months apart	• Infants and children: 3 to 4 doses given over a 6- to 18-month period depending on vaccine type and schedule • Adults: 3 doses given over a 6-month period (most common schedule)	No vaccine available

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Testing for HCV Infection: An Update of Guidance for Clinicians and Laboratorians

On May 7, 2013, this report was posted as an MMWR *Early Release on the* MMWR *website (http://www.cdc.gov/mmwr).*

In the United States, an estimated 4.1 million persons have been infected with hepatitis C virus (HCV), of whom an estimated 3.2 (95% confidence interval [CI] = 2.7–3.9) million are living with the infection (*1*). New infections continue to be reported particularly among persons who inject drugs and persons exposed to HCV-contaminated blood in health-care settings with inadequate infection control (*2*).

Since 1998, CDC has recommended HCV testing for persons with risks for HCV infection (*3*). In 2003, CDC published guidelines for the laboratory testing and result reporting of antibody to HCV (*4*). In 2012, CDC amended testing recommendations to include one-time HCV testing for all persons born during 1945–1965 regardless of other risk factors (*1*).

CDC is issuing this update in guidance because of 1) changes in the availability of certain commercial HCV antibody tests, 2) evidence that many persons who are identified as reactive by an HCV antibody test might not subsequently be evaluated to determine if they have current HCV infection (*5*), and 3) significant advances in the development of antiviral agents with improved efficacy against HCV (*6*). Although previous guidance has focused on strategies to detect and confirm HCV antibody (*3,4*), reactive results from HCV antibody testing cannot distinguish between persons whose past HCV infection has resolved and those who are currently HCV infected. Persons with current infection who are not identified as currently infected will not receive appropriate preventive services, clinical evaluation, and medical treatment. Testing strategies must ensure the identification of those persons with current HCV infection.

This guidance was written by a workgroup convened by CDC and the Association of Public Health Laboratories (APHL), comprising experts from CDC, APHL, state and local public health departments, and academic and independent diagnostic testing laboratories, in consultation with experts from the Veterans Health Administration and the Food and Drug Administration (FDA). The workgroup reviewed laboratory capacities and practices relating to HCV testing, data presented at the CDC 2011 symposium on identification, screening and surveillance of HCV infection (*7*), and data from published scientific literature on HCV testing. Unpublished data from the American Red Cross on validation of HCV antibody testing also were reviewed.

Changes in HCV Testing Technologies

Since the 2003 guidance was published (*4*), there have been two developments with important implications for HCV testing:

1. Availability of a rapid test for HCV antibody. The OraQuick HCV Rapid Antibody Test (OraSure Technologies) is a rapid assay for the presumptive detection of HCV antibody in fingerstick capillary blood and venipuncture whole blood. Its sensitivity and specificity are similar to those of FDA–approved, laboratory-conducted HCV antibody assays (*8*). In 2011, a Clinical Laboratory Improvements Amendments waiver was granted to the test by FDA. The waiver provides wider testing access to persons at risk for HCV infection, permitting use of the assay in nontraditional settings such as physician offices, hospital emergency departments, health department clinics, and other freestanding counseling and testing sites.
2. Discontinuation of RIBA HCV. The Chiron RIBA HCV 3.0 Strip Immunoblot Assay (Novartis Vaccines and Diagnostics) that was recommended (*4*) for supplemental testing of blood samples after initial HCV antibody testing is no longer available. As a result, the only other FDA-approved supplemental tests for HCV infection are those that detect HCV viremia.

Identifying Current HCV Infections

In 2011, FDA approved boceprevir (Victrelis, Merck & Co.) and telaprevir (Incivek, Vertex Pharmaceuticals) for treatment of chronic hepatitis C genotype 1 infection, in combination with pegylated interferon and ribavirin, in adult patients with compensated liver disease. Boceprevir and telaprevir interfere directly with HCV replication. Persons who complete treatment using either of these drugs combined with pegylated interferon and ribavirin are more likely to clear virus (i.e., have virologic cure), compared to those given standard therapy based on pegylated interferon and ribavirin (*9*). Viral clearance, when sustained, stops further spread of HCV and is associated with reduced risk for hepatocellular carcinoma (*10*) and all-cause mortality (*11*). Other compounds under study in clinical trials hold promise for even more effective therapies (*6*).

Because antiviral treatment is intended for persons with current HCV infection, these persons need to be distinguished from persons whose infection has resolved. HCV RNA in blood, by nucleic acid testing (NAT), is a marker for HCV viremia and is detected only in persons who are currently infected. Persons with reactive results after HCV antibody testing should be evaluated for the presence of HCV RNA in their blood.

Benefits of Testing for Current HCV Infection

Accurate testing to identify current infection is important to 1) help clinicians and other providers correctly identify persons infected with HCV, so that preventive services, care and treatment can be offered; 2) notify tested persons of their infection status, enabling them to make informed decisions about medical care and options for HCV treatment, take measures to limit HCV-associated disease progression (e.g., avoidance or reduction of alcohol intake, and vaccination against hepatitis A and B), and minimize risk for transmitting HCV to others; and 3) inform persons who are not currently infected of their status and the fact that they are not infectious.

Recommended Testing Sequence

The testing sequence in this guidance is intended for use by primary care and public health providers seeking to implement CDC recommendations for HCV testing (*1,3,4*). In most cases, persons identified with HCV viremia have chronic HCV infection. This testing sequence is not intended for diagnosis of acute hepatitis C or clinical evaluation of persons receiving specialist medical care, for which specific guidance is available (*12*).

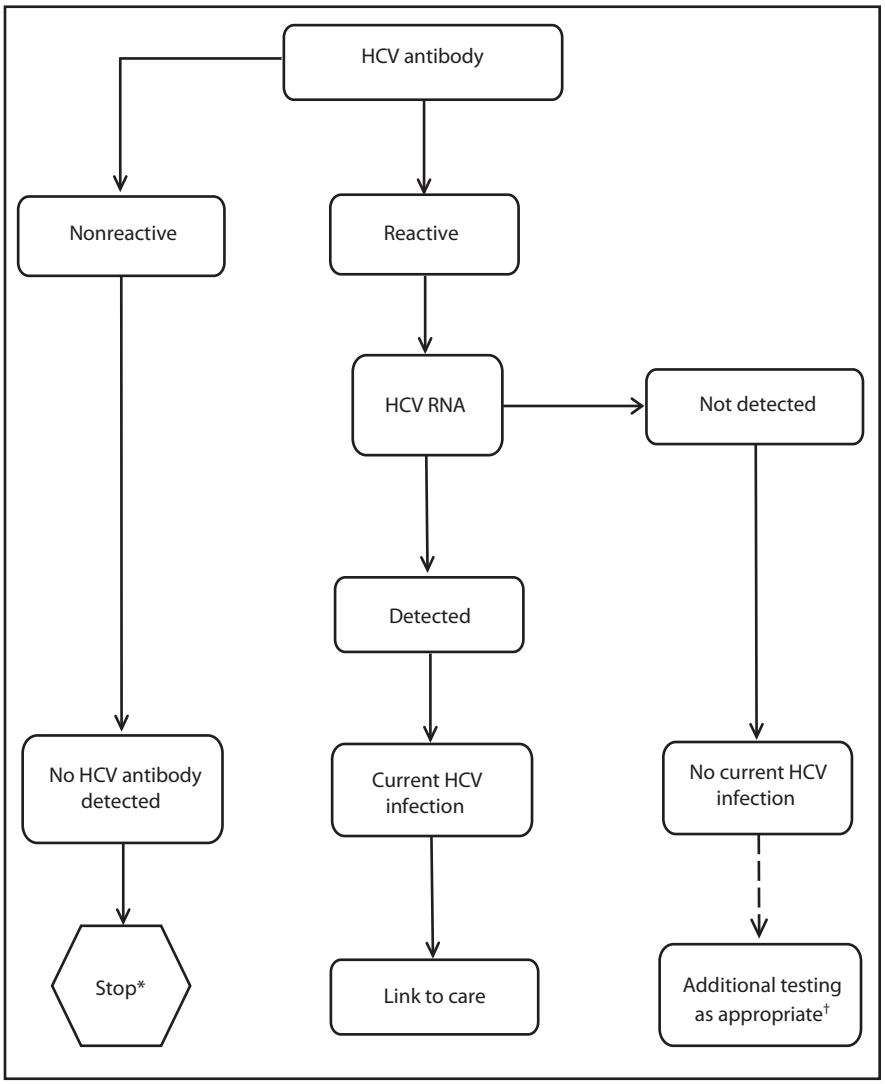
Testing for HCV infection begins with either a rapid or a laboratory-conducted assay for HCV antibody in blood (Figure). A nonreactive HCV antibody result indicates no HCV antibody detected. A reactive result indicates one of the following: 1) current HCV infection, 2) past HCV infection that has resolved, or 3) false positivity. A reactive result should be followed by NAT for HCV RNA. If HCV RNA is detected, that indicates current HCV infection. If HCV RNA is not detected, that indicates either past, resolved HCV infection, or false HCV antibody positivity.

Initial Testing for HCV Antibody. An FDA-approved test for HCV antibody should be used. If the OraQuick HCV Rapid Antibody Test is used, the outcome is reported as reactive or nonreactive. If a laboratory-based assay is used, the outcome is reported as reactive or nonreactive without necessarily specifying signal-to-cutoff ratios.

Testing for HCV RNA. An FDA-approved NAT assay intended for detection of HCV RNA in serum or plasma from blood of at-risk patients who test reactive for HCV antibody should be used. There are several possible operational steps toward NAT after initial testing for HCV antibody:

1. Blood from a subsequent venipuncture is submitted for HCV NAT if the blood sample collected is reactive for HCV antibody during initial testing.
2. From a single venipuncture, two specimens are collected in separate tubes: one tube for initial HCV antibody testing; and a second tube for HCV NAT if the HCV antibody test is reactive.

FIGURE. Recommended testing sequence for identifying current hepatitis C virus (HCV) infection



* For persons who might have been exposed to HCV within the past 6 months, testing for HCV RNA or follow-up testing for HCV antibody is recommended. For persons who are immunocompromised, testing for HCV RNA can be considered.

† To differentiate past, resolved HCV infection from biologic false positivity for HCV antibody, testing with another HCV antibody assay can be considered. Repeat HCV RNA testing if the person tested is suspected to have had HCV exposure within the past 6 months or has clinical evidence of HCV disease, or if there is concern regarding the handling or storage of the test specimen.

3. The same sample of venipuncture blood used for initial HCV antibody testing, if reactive, is reflexed to HCV NAT without another blood draw for NAT (*13*).
4. A separate venipuncture blood sample is submitted for HCV NAT if the OraQuick HCV Rapid Antibody Test for initial testing of HCV antibody has used fingerstick blood.

Supplemental Testing for HCV Antibody

If testing is desired to distinguish between true positivity and biologic false positivity for HCV antibody, then, testing may be done with a second HCV antibody assay approved by FDA for diagnosis of HCV infection that is different from the assay used for initial antibody testing. HCV antibody assays vary according to their antigens, test platforms, and performance characteristics, so biologic false positivity is unlikely to be exhibited by more than one test when multiple tests are used on a single specimen (*14*).

Test Interpretation and Further Action

See Table.

Laboratory Reporting

"Acute hepatitis C" and "hepatitis C (past or present)" are nationally notifiable conditions, and are subject to mandated reporting to health departments by clinicians and laboratorians, as determined by local, state or territorial law and regulation. Surveillance case definitions are developed by the Council of State and Territorial Epidemiologists in collaboration with CDC (*15*). In all but a few jurisdictions, positive results from HCV antibody and HCV RNA testing that are indicative of acute, or past or present HCV infection, are reportable. Specific policies for laboratory reporting are found at health department websites (*16*).

Future Studies

Research, development, validation, and cost-effectiveness studies are ongoing to inform the best practices for detecting HCV viremia and for distinguishing between resolved HCV infection and biologic false positivity for HCV antibody in persons in whom HCV RNA is not detected. Outcomes of these studies will provide comprehensive guidance on testing, reporting, and clinical management, and will improve case definitions for disease notification and surveillance.

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TABLE. Interpretation of results of tests for hepatitis C virus (HCV) infection and further actions

Test outcome	Interpretation	Further action
HCV antibody nonreactive	No HCV antibody detected	Sample can be reported as nonreactive for HCV antibody. No further action required. If recent HCV exposure in person tested is suspected, test for HCV RNA.*
HCV antibody reactive	Presumptive HCV infection	A repeatedly reactive result is consistent with current HCV infection, or past HCV infection that has resolved, or biologic false positivity for HCV antibody. Test for HCV RNA to identify current infection.
HCV antibody reactive, HCV RNA detected	Current HCV infection	Provide person tested with appropriate counseling and link person tested to medical care and treatment.†
HCV antibody reactive, HCV RNA not detected	No current HCV infection	No further action required in most cases. If distinction between true positivity and biologic false positivity for HCV antibody is desired, and if sample is repeatedly reactive in the initial test, test with another HCV antibody assay. In certain situations§ follow up with HCV RNA testing and appropriate counseling.

* If HCV RNA testing is not feasible and person tested is not immunocompromised, do follow-up testing for HCV antibody to demonstrate seroconversion. If the person tested is immunocompromised, consider testing for HCV RNA.
† It is recommended before initiating antiviral therapy to retest for HCV RNA in a subsequent blood sample to confirm HCV RNA positivity.
§ If the person tested is suspected of having HCV exposure within the past 6 months, or has clinical evidence of HCV disease, or if there is concern regarding the handling or storage of the test specimen.

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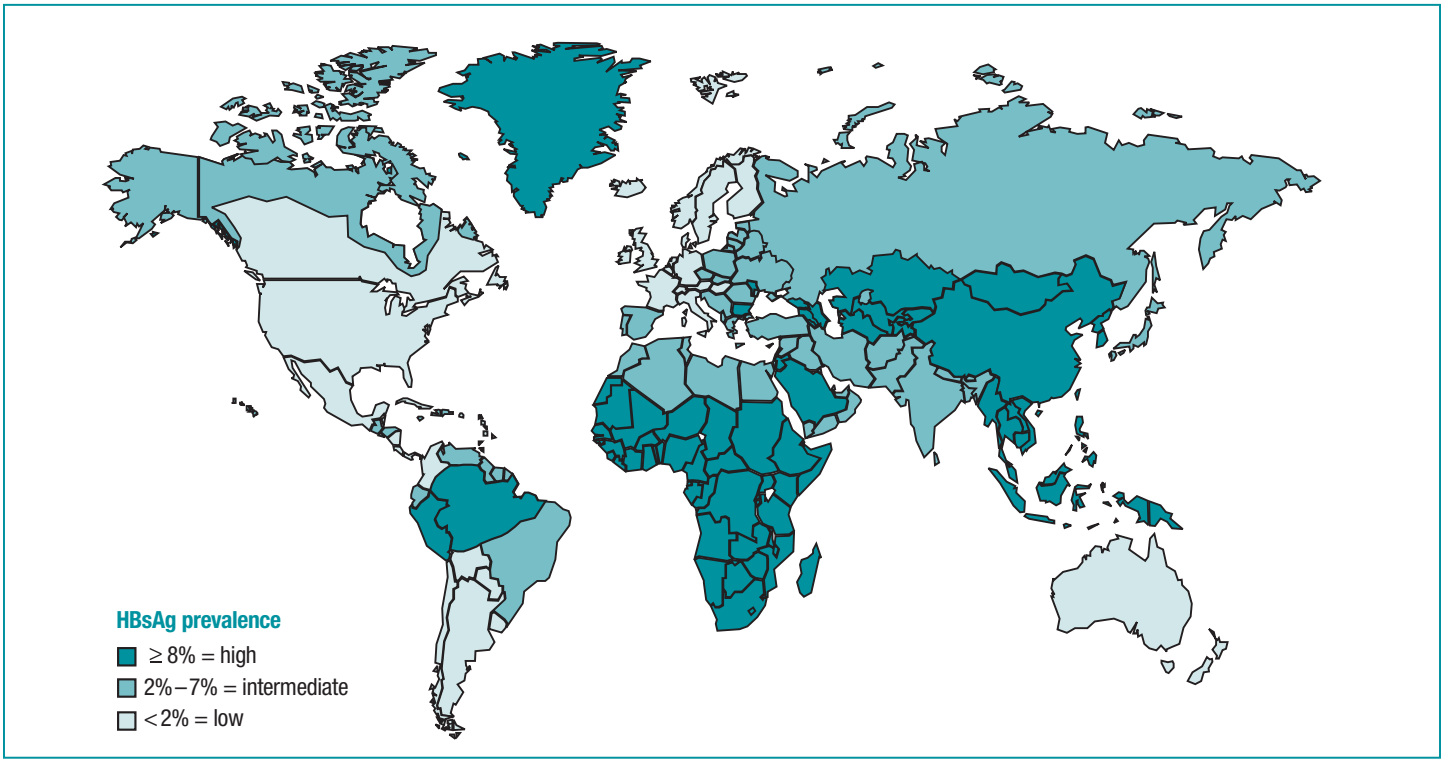
Recommendations for Routine Testing and Follow-up for Chronic Hepatitis B Virus (HBV) Infection

Population	Recommendation	
	Testing	Vaccination/Follow-up
Persons born in regions of high and intermediate HBV endemicity (HBsAg prevalence ≥2%)	Test for HBsAg, regardless of vaccination status in their country of origin, including – immigrants – refugees – asylum seekers – internationally adopted children	If HBsAg-positive, refer for medical management. If negative, assess for on-going risk for hepatitis B and vaccinate if indicated.
US born persons not vaccinated as infants whose parents were born in regions with high HBV endemicity (≥8%)	Test for HBsAg regardless of maternal HBsAg status if not vaccinated as infants in the United States.	If HBsAg-positive, refer for medical management. If negative, assess for on-going risk for hepatitis B and vaccinate if indicated.

Continues on back

Geographic Distribution of Chronic HBV Infection — Worldwide, 2006*



* For multiple countries, estimates of prevalence of hepatitis B surface antigen (HBsAg), a marker of chronic HBV infection, are based on limited data and might not reflect current prevalence in countries that have implemented childhood hepatitis B vaccination. In addition, HBsAg prevalence might vary within countries by subpopulation and locality.

Source: CDC. Travellers' Health; Yellow Book. http://wwwn.cdc.gov/travel/yellowbookch4-HepB.aspx.

Routine Testing and Follow-up for Chronic HBV Infection (continued)

Population	Recommendation	
	Testing	Vaccination/Follow-up
Injection-drug users	Test for HBsAg, as well as for anti-HBc or anti-HBs to identify susceptible persons.	First vaccine dose should be given at the same visit as testing. Susceptible persons should complete a 3-dose hepatitis B vaccine series to prevent infection from ongoing exposure.
Men who have sex with men	Test for HBsAg, as well as for anti-HBc or anti-HBs to identify susceptible persons.	First vaccine dose should be given at the same visit as testing. Susceptible persons should complete a 3-dose hepatitis B vaccine series to prevent infection from ongoing exposure.
Persons needing immunosuppressive therapy, including chemotherapy, immunosuppression related to organ transplantation, and immunosuppression for rheumatologic or gastroenterologic disorders	Test for all markers of HBV infection (HBsAg, anti-HBc, and anti-HBs).	Treat persons who are HBsAg-positive. Monitor closely persons who are anti-HBc positive for signs of liver disease.
Persons with elevated ALT/AST of unknown etiology	Test for HBsAg along with other appropriate medical evaluation.	Follow-up as indicated.
Donors of blood, plasma, organs, tissues, or semen	Test for HBsAg, anti-HBc, and HBV-DNA as required.	
Hemodialysis patients	Test for all markers of HBV infection (HBsAg, anti-HBc, and anti-HBs). Test vaccine nonresponders monthly for HBsAg. HBsAg-positive hemodialysis patients should be cohorted.	Vaccinate against hepatitis B to prevent transmission and revaccinate when serum anti-HBs titer falls below 10mIU/mL.
All pregnant women	Test for HBsAg during each pregnancy, preferably in the first trimester. Test at the time of admission for delivery if prenatal HBsAg test result is not available or if mother was at risk for infection during pregnancy.	If HBsAg-positive, refer for medical management. To prevent perinatal transmission, infants of HBsAg-positive mothers and unknown HBsAg status mothers should receive vaccination and postexposure immunoprophylaxis in accordance with recommendations and within 12 hours of delivery.
Infants born to HBsAg-positive mothers	Test for HBsAg and anti-HBs 1–2 mos after completion of at least 3 doses of a licensed hepatitis B vaccine series (i.e., at age 9–18 months, generally at the next well-child visit to assess effectiveness of postexposure immunoprophylaxis). Testing should not be performed before age 9 months or within 1 month of the most recent vaccine dose.	Vaccinate in accordance with recommendations.
Household, needle-sharing, or sex contacts of persons known to be HBsAg positive	Test for HBsAg, as well as anti-HBc or anti-HBs to identify susceptible persons.	First vaccine dose should be given at the same visit as testing. Susceptible persons should complete a 3-dose hepatitis B vaccine series to prevent transmission from ongoing exposure.
Persons who are the sources of blood or body fluids resulting in an exposure (e.g., needlestick, sexual assault) that might require postexposure prophylaxis	Test source for HBsAg.	Vaccinate healthcare and public safety workers with reasonably anticipated occupational exposures to blood or infectious body fluids. Provide postexposure prophylaxis to exposed person if needed.
HIV-positive persons	Test for HBsAg, as well as for anti-HBc or anti-HBs to identify susceptible persons.	Vaccinate susceptible persons against hepatitis B to prevent transmission.

Adapted from: Centers for Disease Control and Prevention. Recommendations for Identification and Public Health Management of Persons with Chronic Hepatitis B Virus Infection. MMWR 2008; 57 (No. RR-8).

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Interpretation of Hepatitis B Serologic Test Results

Hepatitis B serologic testing involves measurement of several hepatitis B virus (HBV)-specific antigens and antibodies. Different serologic "markers" or combinations of markers are used to identify different phases of HBV infection and to determine whether a patient has acute or chronic HBV infection, is immune to HBV as a result of prior infection or vaccination, or is susceptible to infection.

HBsAg **anti-HBc** **anti-HBs**	negative negative negative	Susceptible
HBsAg **anti-HBc** **anti-HBs**	negative positive positive	Immune due to natural infection
HBsAg **anti-HBc** **anti-HBs**	negative negative positive	Immune due to hepatitis B vaccination
HBsAg **anti-HBc** **IgM anti-HBc** **anti-HBs**	positive positive positive negative	Acutely infected
HBsAg **anti-HBc** **IgM anti-HBc** **anti-HBs**	positive positive negative negative	Chronically infected
HBsAg **anti-HBc** **anti-HBs**	negative positive negative	Interpretation unclear; four possibilities: 1. Resolved infection (most common) 2. False-positive anti-HBc, thus susceptible 3. "Low level" chronic infection 4. Resolving acute infection

Adapted from: A Comprehensive Immunization Strategy to Eliminate Transmission of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. Part I: Immunization of Infants, Children, and Adolescents. MMWR 2005;54(No. RR-16).

- **Hepatitis B surface antigen (HBsAg):** A protein on the surface of hepatitis B virus; it can be detected in high levels in serum during acute or chronic hepatitis B virus infection. The presence of HBsAg indicates that the person is infectious. The body normally produces antibodies to HBsAg as part of the normal immune response to infection. HBsAg is the antigen used to make hepatitis B vaccine.
- **Hepatitis B surface antibody (anti-HBs):** The presence of anti-HBs is generally interpreted as indicating recovery and immunity from hepatitis B virus infection. Anti-HBs also develops in a person who has been successfully vaccinated against hepatitis B.
- **Total hepatitis B core antibody (anti-HBc):** Appears at the onset of symptoms in acute hepatitis B and persists for life. The presence of anti-HBc indicates previous or ongoing infection with hepatitis B virus in an undefined time frame.
- **IgM antibody to hepatitis B core antigen (IgM anti-HBc):** Positivity indicates recent infection with hepatitis B virus (≤6 mos). Its presence indicates acute infection.

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APPENDIX 1 HIV TEST TABLES

Table 11: FDA-Approved HIV Rapid Tests Typically Used for Point-of-Care testing or in Clinicians Offices[64,129] (as of February 2014)

Test Name	CLIA-Waived Testing[a]	CLIA-Moderately Complex Testing[a]	Approximate window period to HIV detection
OraQuick Advance Rapid HIV-1/2 Antibody Test	Oral fluid; fingerstick whole blood; EDTA, ACD, or heparin venipuncture whole blood	Plasma	4–5 weeks (blood) >4 weeks (oral fluid)
Alere Determine HIV-1/2 Ag/Ab Combo Test	Not approved for CLIA-Waived testing	Fingerstick whole blood; EDTA, ACD, or heparin venipuncture whole blood	2–4 weeks
Uni-Gold Recombigen HIV-1	Fingerstick whole blood; EDTA, ACD, or heparin venipuncture whole blood	Plasma/ Serum	4–5 weeks
Clearview HIV-1/2 STAT-PAK	Fingerstick whole blood; EDTA, ACD, or heparin venipuncture whole blood	Plasma/ Serum	4–5 weeks
Clearview Complete HIV-1/2	Fingerstick whole blood; EDTA, ACD, or heparin venipuncture whole blood	Plasma/ Serum	4–5 weeks
INSTI HIV-1 Antibody Test Kit	Fingerstick whole blood; EDTA, ACD, or heparin venipuncture whole blood	Plasma	4–5 weeks
Chembio DPP HIV-1/2 Assay	Not approved for CLIA-Waived testing	Fingerstick whole blood; EDTA, ACD, or heparin venipuncture whole blood; oral fluid; Plasma/Serum	3–4 weeks
Multispot HIV-1/HIV-2 Rapid Test (differentiates HIV-1 and HIV-2)	Not approved for CLIA-Waived testing	Plasma/Serum	3–4 weeks
Reveal Rapid HIV-1 Antibody Test	Not approved for CLIA-Waived testing	Plasma/Serum	3–4 weeks

CLIA, Clinical Laboratory Improvement Amendments

[a] Only unprocessed (not centrifuged) specimens can be used by sites with a CLIA Certificate of Waiver. However labs with certificates for moderate or high complexity testing can use centrifuged blood for testing. Many laboratories use rapid tests as part of their testing strategy.

Table 12: FDA-Approved Diagnostic Laboratory Based HIV Tests (CLIA-High Complexity Tests)[64,129] (as of February 2014)

Trade Name	Testing Format	Samples Used	Approximate Window Period to HIV Detection
GS HIV Combo Ag/Ab EIA Assay	Manual and semi-automated EIA	Serum/Plasma	2–3 weeks
Abbott ARCHITECT HIV Ag/Ab Combo	Fully automated chemiluminescent microparticle immunoassay	Serum/Plasma	2–3 weeks
ADVIA Centaur HIV 1/O/2 Enhanced (EHIV)	Fully automated chemiluminescent microparticle immunoassay	Serum/Plasma	2–3 weeks
Vitros Anti-HIV 1+2 Assay	Fully automated chemiluminescent microparticle immunoassay	Serum/Plasma	2–3 weeks
GS HIV-1/HIV-2 Plus O EIA	Manual and semi-automated EIA	Serum/Plasma	2–3 weeks
APTIMA HIV-1 RNA Qualitative Assay	Manual TMA	Serum/Plasma	1–2 weeks
GS HIV-1 Western Blot[a]	Manual Western blot	Serum/Plasma, Dried Blood Spot	4–5 weeks
Fluorognost HIV-1 IFA[a]	Manual immunofluorescent antibody	Serum/Plasma, Dried Blood Spot	4–5 weeks

[a] These are supplemental tests not intended for primary diagnostic screening; they are used to confirm the test result of a diagnostic screening test.

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Syphilis

Syphilis - CDC Fact Sheet

Basic Fact Sheet (STDFact-Syphilis.htm) | **Detailed Version** | View Images of Symptoms (images.htm)

Detailed fact sheets are intended for physicians and individuals with specific questions about sexually transmitted diseases. Detailed fact sheets include specific testing and treatment recommendations as well as citations so the reader can research the topic more in depth.

What is syphilis?

Syphilis is a sexually transmitted disease (STD) caused by the bacterium *Treponema pallidum*. Syphilis can cause long-term complications if not adequately treated.

How common is syphilis?

CDC estimates that, annually, 55,400 people in the United States get new syphilis infections. During 2012, there were 49,903 reported new cases of syphilis, compared to 48,298 estimated new diagnoses of HIV infection in 2011 and 334,826 cases of gonorrhea in 2012. Of syphilis cases, 15,667 were of primary and secondary (P&S) syphilis, the earliest and most transmissible stages of syphilis. During the 1990s, syphilis primarily occurred among heterosexual men and women of racial and ethnic minority groups; during the 2000s, however, cases increased among men who have sex with men (MSM). 1 (http://www.cdc.gov/std/syphilis/STDFact-Syphilis-detailed.htm#_ENREF_1) In 2002, rates of P&S syphilis were highest among men 30–39 years-old, but in 2012, were highest among men 20–29 years-old. 2 (http://www.cdc.gov/std/syphilis/STDFact-Syphilis-detailed.htm#_ENREF_2) , 3 (http://www.cdc.gov/std/syphilis/STDFact-Syphilis-detailed.htm#_ENREF_3) This epidemiologic shift reflects increasing cases reported among young MSM in recent years. 4 (http://www.cdc.gov/std/syphilis/STDFact-Syphilis-detailed.htm#_ENREF_4) MSM accounted for 75% of all P&S syphilis cases in 2012.

Black, Hispanic, and other racial/ethnic minorities are disproportionately affected by P&S syphilis in the United States, with black Americans accounting for most of P&S syphilis among individuals who are not MSM. 3 (#_ENREF_3)

While the rate of congenital syphilis (syphilis passed from pregnant women to their babies) has decreased in recent years, 3 (http://www.cdc.gov/std/syphilis/STDFact-Syphilis-detailed.htm#_ENREF_3) more cases of congenital syphilis are reported in the United States than cases of perinatal HIV infection. During 2012, 322 cases of congenital syphilis were reported, compared to an estimated 162 cases of perinatal HIV infection during 2010. 5 (http://www.cdc.gov/std/syphilis/STDFact-Syphilis-detailed.htm#_ENREF_5) Congenital syphilis rates were 14.1 times and 3.8 times higher among infants born to black and Hispanic mothers (29.6 and 7.9 cases per 100,000 live births, respectively) compared to white mothers (2.1 cases per 100,000 live births). 6 (http://www.cdc.gov/std/syphilis/STDFact-Syphilis-detailed.htm#_ENREF_6)

How do people get syphilis?

Syphilis is transmitted from person to person by direct contact with a syphilitic sore, known as a chancre. Chancres occur mainly on the external genitals, vagina, anus, or in the rectum. Chancres also

can occur on the lips and in the mouth. Transmission of syphilis occurs during vaginal, anal, or oral sex. Pregnant women with the disease can transmit it to their unborn child.

How quickly do symptoms appear after infection?

The average time between infection with syphilis and the start of the first symptom is 21 days, but can range from 10 to 90 days.

What are the signs and symptoms in adults?

Syphilis has been called "The Great Pretender", as its symptoms can look like many other diseases. However, syphilis typically follows a progression of stages that can last for weeks, months, or even years:

Primary Stage

The appearance of a single chancre marks the primary (first) stage of syphilis symptoms, but there may be multiple sores. The chancre is usually firm, round, and painless. It appears at the location where syphilis entered the body. Possibly because these painless chancres can occur in locations that make them difficult to find (e.g., the vagina or anus), smaller proportions of MSM and women are diagnosed in primary stage than men having sex with women only. [3 (#_ENREF_3)] The chancre lasts 3 to 6 weeks and heals regardless of whether a person is treated or not. However, if the infected person does not receive adequate treatment, the infection progresses to the secondary stage.

Secondary Stage

Skin rashes and/or mucous membrane lesions (sores in the mouth, vagina, or anus) mark the second stage of symptoms. This stage typically starts with the development of a rash on one or more areas of the body. Rashes associated with secondary syphilis can appear when the primary chancre is healing or several weeks after the chancre has healed. The rash usually does not cause itching. The characteristic rash of secondary syphilis may appear as rough, red, or reddish brown spots both on the palms of the hands and the bottoms of the feet. However, rashes with a different appearance may occur on other parts of the body, sometimes resembling rashes caused by other diseases. Sometimes rashes associated with secondary syphilis are so faint that they are not noticed. Large, raised, gray or white lesions, known as condyloma lata, may develop in warm, moist areas such as the mouth, underarm or groin region. In addition to rashes, symptoms of secondary syphilis may include fever, swollen lymph glands, sore throat, patchy hair loss, headaches, weight loss, muscle aches, and fatigue. The symptoms of secondary syphilis will go away with or without treatment, but without treatment, the infection will progress to the latent and possibly late stages of disease.

Latent and Late Stages

The latent (hidden) stage of syphilis begins when primary and secondary symptoms disappear. Without treatment, the infected person will continue to have syphilis infection in their body even though there are no signs or symptoms. *Early latent syphilis* is latent syphilis where infection occurred within the past 12 months. *Late latent syphilis* is latent syphilis where infection occurred more than 12 months ago. Latent syphilis can last for years.

The late stages of syphilis can develop in about 15% of people who have not been treated for syphilis, and can appear 10–20 years after infection was first acquired. In the late stages of syphilis, the disease may damage the internal organs, including the brain, nerves, eyes, heart, blood vessels, liver, bones, and joints. Symptoms of the late stage of syphilis include difficulty coordinating muscle movements, paralysis, numbness, gradual blindness, and dementia. This damage may be serious enough to cause death.

Neurosyphilis

Syphilis can invade the nervous system at any stage of infection, and causes a wide range of symptoms varying from no symptoms at all, to headache, altered behavior, and movement problems that look like Parkinson's or Huntington's disease. [7 (#_ENREF_7)] This invasion of the nervous system is called "neurosyphilis."

Note: Health departments report syphilis by its stage of infection, noting "neurological manifestations," rather than using the term neurosyphilis. [3 (#_ENREF_3)]

HIV infection and syphilis symptoms

Individuals who are HIV-positive can develop symptoms very different from the symptoms described above, including hypopigmented skin rashes. [8 (#_ENREF_8)] HIV can also increase the chances of developing syphilis with neurological involvement. [9 (#_ENREF_9)]

How does syphilis affect a pregnant woman and her baby?

The syphilis bacterium can infect the baby of a woman during her pregnancy. All pregnant women should be tested for syphilis at the first prenatal visit. The syphilis screening test should be repeated during the third trimester (28 to 32 weeks gestation) and at delivery in women who are at high risk for syphilis, live in areas of high syphilis morbidity, are previously untested, or had a positive screening test in the first trimester. [10 (#_ENREF_10)]

Depending on how long a pregnant woman has been infected, she may have a high risk of having a stillbirth (a baby born dead) or of giving birth to a baby who dies shortly after birth; untreated syphilis in pregnant women results in infant death in up to 40 percent of cases. [6 (#_ENREF_6)] Any woman who delivers a stillborn infant after 20 week's gestation should also be tested for syphilis.

An infected baby born alive may not have any signs or symptoms of disease. However, if not treated immediately, the baby may develop serious problems within a few weeks. Untreated babies may become developmentally delayed, have seizures, or die. All babies born to mothers who test positive for syphilis during pregnancy should be screened for syphilis and examined thoroughly for evidence of congenital syphilis. [10 (#_ENREF_10)]

For pregnant women only penicillin therapy can be used to treat syphilis and prevent passing the disease to her baby; treatment with penicillin is extremely effective (success rate of 98%) in preventing mother-to-child transmission. [11 (#_ENREF_11)] Pregnant women who are allergic to penicillin should be referred to a specialist for desensitization to penicillin.

How is syphilis diagnosed?

The definitive method for diagnosing syphilis is visualizing the spirochete via darkfield microscopy. This technique is rarely performed today because it is a technologically difficult method. Diagnoses are thus more commonly made using blood tests. There are two types of blood tests available for syphilis: 1) nontreponemal tests and 2) treponemal tests.

Nontreponemal tests (e.g., VDRL and RPR) are simple, inexpensive, and are often used for screening. However, they are not specific for syphilis, can produce false-positive results, and, by themselves, are insufficient for diagnosis. VDRL and RPR should each have their antibody titer results reported quantitatively. Persons with a reactive nontreponemal test should receive a treponemal test to confirm a syphilis diagnosis. This sequence of testing (nontreponemal, then treponemal test) is considered the "classical" testing algorithm.

Treponemal tests (e.g., FTA-ABS, TP-PA, various EIAs, and chemiluminescence immunoassays)

detect antibodies that are specific for syphilis. Treponemal antibodies appear earlier than nontreponemal antibodies and usually remain detectable for life, even after successful treatment. If a treponemal test is used for screening and the results are positive, a nontreponemal test with titer should be performed to confirm diagnosis and guide patient management decisions. Based on the results, further treponemal testing may be indicated. For further guidance, please refer to the 2010 STD Treatment Guidelines. 10 (#_ENREF_10) This sequence of testing (treponemal, then nontreponemal, test) is considered the "reverse" sequence testing algorithm.Reverse sequence testing can be more convenient for laboratories, but its clinical interpretation is problematic, as this testing sequence can identify individuals not previously described (e.g., treponemal test positive, nontreponemal test negative), making optimal management choices difficult. 12 (#_ENREF_12)

Special note: Because untreated syphilis in a pregnant woman can infect and possibly kill her developing baby, every pregnant woman should have a blood test for syphilis. All women should be screened at their first prenatal visit. For patients who belong to communities and populations with high prevalence of syphilis and for patients at high risk, blood tests should also be performed during the third trimester (at 28–32 weeks) and at delivery. For further information on screening guidelines, please refer to the 2010 STD Treatment Guidelines. 10 (#_ENREF_10)

All infants born to mothers who have reactive nontreponemal and treponemal test results should be evaluated for congenital syphilis. A quantitative nontreponemal test should be performed on infant serum and, if reactive, the infant should be examined thoroughly for evidence of congenital syphilis. Suspicious lesions, body fluids, or tissues (e.g., umbilical cord, placenta) should be examined by darkfield microscopy and/or special stains. Other recommended evaluations may include analysis of cerebrospinal fluid by VDRL, cell count and protein, CBC with differential and platelet count, and long-bone radiographs. For further guidance on evaluation of infants for congenital syphilis, please refer to the 2010 STD Treatment Guidelines. 10 (#_ENREF_10)

What is the link between syphilis and HIV?

Genital sores caused by syphilis make it easier to transmit and acquire HIV infection sexually. There is an estimated 2- to 5-fold increased risk of acquiring HIV if exposed to that infection when syphilis is present. 13 (#_ENREF_13)

Ulcerative STDs that cause sores, ulcers, or breaks in the skin or mucous membranes, such as syphilis, disrupt barriers that provide protection against infections. The genital ulcers caused by syphilis can bleed easily, and when they come into contact with oral and rectal mucosa during sex, increase the infectiousness of and susceptibility to HIV. Studies have observed that infection with syphilis was associated with subsequent HIV infection among MSM. 14 (#_ENREF_14) , 15 (#_ENREF_15)

Having other STDs can also indicate increased risk for becoming HIV infected. 14 (#_ENREF_14)

What is the treatment for syphilis?

There are no home remedies or over-the-counter drugs that will cure syphilis, but syphilis is easy to cure in its early stages. A single intramuscular injection of long acting **Benzathine penicillin G** (2.4 million units administered intramuscularly) will cure a person who has primary, secondary or early latent syphilis. Three doses of long acting Benzathine penicillin G (2.4 million units administered intramuscularly) at weekly intervals is recommended for individuals with late latent syphilis or latent syphilis of unknown duration. Treatment will kill the syphilis bacterium and prevent further damage, but it will not repair damage already done.

Selection of the appropriate penicillin preparation is important to properly treat and cure syphilis. **Combinations of some penicillin preparations (e.g., Bicillin C-R, a combination of**

benzathine penicillin and procaine penicillin) are not appropriate treatments for syphilis, as these combinations provide inadequate doses of penicillin. 16 (#_ENREF_16)

Although data to support the use of alternatives to penicillin is limited, options for non-pregnant patients who are allergic to penicillin may include doxycycline, tetracycline, and for neurosyphilis, potentially probenecid. These therapies should be used only in conjunction with close clinical and laboratory follow-up to ensure appropriate serological response and cure. 10 (#_ENREF_10)

Persons who receive syphilis treatment must abstain from sexual contact with new partners until the syphilis sores are completely healed. Persons with syphilis must notify their sex partners so that they also can be tested and receive treatment if necessary.

Who should be tested for syphilis?

Any person with signs or symptoms of primary infection, secondary infection, neurologic infection, or tertiary infection should be tested for syphilis.

Providers should routinely test persons who

- are pregnant;
- are members of an at-risk subpopulation (i.e., persons in correctional facilities and MSM);
- describe sexual behaviors that put them at risk for STDs (i.e., having unprotected vaginal, anal, or oral sexual contact; having multiple sexual partners; using drugs and alcohol, and engaging in commercial or coerced sex);
- have partner(s) who have tested positive for syphilis ;

are sexually active and live in areas with high syphilis morbidity.

Will syphilis recur?

Syphilis does not recur. However, having syphilis once does not protect a person from becoming infected again. Even following successful treatment, people can be *re*-infected. Patients with signs or symptoms that persist or recur or who have a sustained fourfold increase in nontreponemal test titer probably failed treatment or were reinfected. These patients should be retreated.

Because chancres can be hidden in the vagina, rectum, or mouth, it may not be obvious that a sex partner has syphilis. Unless a person knows that their sex partners have been tested and treated, they may be at risk of being reinfected by an untreated partner. For further details on the management of sex partners, refer to the 2010 STD Treatment Guidelines. 10 (#_ENREF_10)

How can syphilis be prevented?

Correct and consistent use of latex condoms can reduce the risk of syphilis only when the infected area or site of potential exposure is protected. However, a syphilis sore outside of the area covered by a latex condom can still allow transmission, so caution should be exercised even when using a condom. For persons who have latex allergies, synthetic non-latex condoms can be used but it is important to note that they have higher breakage rates than latex condoms. 17 (#_ENREF_17) Natural membrane condoms are not recommended for STD prevention. 18 (#_ENREF_18) Other individual-based interventions, such as the use of microbicide or male circumcision, do not prevent syphilis. 19 (#_ENREF_19)

The surest way to avoid transmission of sexually transmitted diseases, including syphilis, is to abstain from sexual contact or to be in a long-term mutually monogamous relationship with a partner who has been tested and is known to be uninfected.

Partner-based interventions include partner notification – a critical component in preventing the

spread of syphilis. Sexual partners of infected patients should be considered at risk and provided treatment per the 2010 STD Treatment Guidelines. 10 (#_ENREF_10)

Transmission of an STD, including syphilis, cannot be prevented by washing the genitals, urinating, and/or douching after sex. Any unusual discharge, sore, or rash, particularly in the groin area, should be a signal to refrain from having sex and to see a doctor immediately.

Avoiding alcohol and drug use may also help prevent transmission of syphilis because these activities may lead to risky sexual behavior. It is important that sex partners talk to each other about their HIV status and history of other STDs so that preventive action can be taken.

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Sexually Transmitted Diseases: *Updated Summary of 2010 CDC Treatment Guidelines*

These summary guidelines reflect the August 2012 update to the 2010 CDC Guidelines for Treatment of Sexually Transmitted Diseases. CDC issues new recommendations for treating uncomplicated gonorrhea in this update. This summary is intended as a source of clinical guidance. An important component of STD treatment is partner management. Providers can arrange for the evaluation and treatment of sex partners either directly or with assistance from state and local health departments. Complete guidelines can be viewed online at www.cdc.gov/std/treatment/2010.

DISEASE	RECOMMENDED Rx		DOSE/ROUTE	ALTERNATIVES
Bacterial Vaginosis Nonpregnant women	metronidazole oral[1] metronidazole gel 0.75%[1] clindamycin cream 2%[1,2]	OR OR	500 mg orally 2x/day for 7 days One 5 g applicator intravaginally 1x/day for 5 days One 5 g applicator intravaginally at bedtime for 7 days	◆ tinidazole 2 g orally 1x/day for 2 days OR ◆ tinidazole 1 g orally 1x/day for 5 days OR clindamycin 300 mg orally 2x/day for 7 days OR clindamycin ovules 100 mg intravaginally at bedtime for 3 days
Pregnancy[3,4]	metronidazole oral[1] clindamycin oral	OR	500 mg orally 2x/day for 7 days or 250 mg orally 3x/day for 7 days 300 mg orally 2x/day for 7 days; See complete guidelines for dosing	
Cervicitis[5]	azithromycin doxycycline[6]	OR	1 g orally in a single dose 100 mg orally 2x/day for 7 days	
Chlamydial Infections Adults, adolescents, and children aged ≥8 years	azithromycin doxycycline[6]	OR	1 g orally in a single dose 100 mg orally 2x/day for 7 days	erythromycin base[7] 500 mg orally 4x/day for 7 days OR erythromycin ethylsuccinate[8] 800 mg orally 4x/day for 7 days OR levofloxacin[9] 500 mg orally 1x/day for 7 days OR ofloxacin[9] 300 mg orally 2x/day for 7 days
Pregnancy[3]	azithromycin[10] amoxicillin	OR	1 g orally in a single dose 500 mg orally 3x/day for 7 days	erythromycin base[7,11] 500 mg orally 4x/day for 7 days OR erythromycin base 250 mg orally 4x/day for 14 days OR erythromycin ethylsuccinate 800 mg orally 4x/day for 7 days OR erythromycin ethylsuccinate 400 mg orally 4x/day for 14 days
Children (<45 kg): urogenital, rectal	erythromycin base[12] or ethylsuccinate		50 mg/kg/day orally (4 divided doses) daily for 14 days	
Neonates: ophthalmia neonatorum, pneumonia	erythromycin base[12] or ethylsuccinate		50 mg/kg/day orally (4 divided doses) daily for 14 days	
Epididymitis[13,14] *For acute epididymitis most likely due to enteric organisms or with negative GC culture or NAAT:*	ceftriaxone doxycycline	PLUS	250 mg IM in a single dose 100 mg orally 2x/day for 10 days	
	levofloxacin ofloxacin	OR	500 mg orally 1x/day for 10 days 300 mg orally 2x/day for 10 days	
Genital Herpes Simplex First clinical episode of genital herpes	acyclovir acyclovir famciclovir[15] valacyclovir[15]	OR OR OR	400 mg orally 3x/day for 7-10 days[16] 200 mg orally 5x/day for 7-10 days[16] 250 mg orally 3x/day for 7-10 days[16] 1 g orally 2x/day for 7-10 days[16]	
Episodic therapy for recurrent genital herpes	acyclovir acyclovir acyclovir famciclovir[15] famciclovir[15] famciclovir[15] valacyclovir[15] valacyclovir[15]	OR OR OR OR OR OR OR	400 mg orally 3x/day for 5 days 800 mg orally 2x/day for 5 days 800 mg orally 3x/day for 2 days 125 mg orally 2x/day for 5 days 1000 mg orally 2x/day for 1 day[16] ◆ 500 mg orally once, followed by 250 mg 2x/day for 2 days 500 mg orally 2x/day for 3 days 1 g orally 1x/day for 5 days	
Suppressive therapy[17] for recurrent genital herpes	acyclovir famciclovir[15] valacyclovir[15] valacyclovir[15]	OR OR OR	400 mg orally 2x/day 250 mg orally 2x/day 500 mg orally once a day 1 g orally once a day	
Recommended regimens for episodic infection in persons with HIV infection	acyclovir famciclovir[15] valacyclovir[15]	OR OR	400 mg orally 3x/day for 5-10 days 500 mg orally 2x/day for 5-10 days 1 g orally 2x/day for 5-10 days	
Recommended regimens for daily suppressive therapy in persons with HIV infection	acyclovir famciclovir[15] valacyclovir[15]	OR OR	400-800 mg orally 2-3x/day 500 mg orally 2x/day 500 mg orally 2x/day	
Genital Warts[18] (Human Papillomavirus) External genital and perianal warts	**Patient Applied** podofilox 0.5%[15] solution or gel imiquimod 5%[15] cream ◆ sinecatechins 15% ointment[2,15] **Provider Administered** Cryotherapy podophyllin resin 10%-25%[15] trichloroacetic acid or bichloroacetic acid 80%-90% surgical removal	OR OR OR OR OR	Apply to visible warts 2x/day for 3 days, rest 4 days, 4 cycles max. Apply once h.s., wash off after 6-10 hours 3x/week QOD, 16 weeks max. Apply 3x/day, 16 weeks max; See complete CDC guidelines. Apply small amount, dry, wash off in 1-4 hours. Repeat weekly if necessary Apply small amount, dry, apply weekly if necessary	Intralesional interferon OR Laser surgery
★ ***Gonococcal Infections***[19] Adults, adolescents, and children >45 kg: urogenital, rectal	ceftriaxone PLUS azithromycin[6] doxycycline[9]	OR OR	◆ 250 mg IM in a single dose 1 g orally in a single dose 100 mg orally 2x/day for 7 days	cefixime[20] 400 mg orally in a single dose PLUS azithromycin[10] 1 g orally in a single dose OR doxycycline[6] 100 mg 2x/day for 7 days PLUS test-of-cure If the patient has severe cephalosporin allergy: azithromycin 2 g orally in a single dose PLUS test-of-cure
◆ Pharyngeal[21]	ceftriaxone PLUS azithromycin[6] doxycycline[9]	 OR	250 mg IM in a single dose 1 g orally in a single dose 100 mg orally 2x/day for 7 days	
Pregnancy[3]	See complete CDC guidelines.			
Adults and adolescents: conjunctivitis	ceftriaxone		1 g IM in a single dose, irrigate infected eye with saline solution once	
Children (≤ 45 kg): urogenital, rectal, pharyngeal	ceftriaxone[22]		◆ 125 mg IM in a single dose	
Lymphogranuloma venereum	doxycycline[6]		100 mg orally 2x/day for 21 days	erythromycin base 500 mg orally 4x/day for 21 days
Nongonococcal Urethritis *(NGU)*	azithromycin[10] doxycycline[6]	OR	1 g orally in a single dose 100 mg orally 2x/day for 7 days	erythromycin base[7] 500 mg orally 4x/day for 7 days OR erythromycin ethylsuccinate[8] 800 mg orally 4x/day for 7 days OR levofloxacin 500 mg 1x/day for 7 days OR ofloxacin 300 mg 2x/day for 7 days
Recurrent NGU[3,23,24]	metronidazole[25] tinidazole azithromycin (if not used for initial episode)	OR PLUS	2 g orally in a single dose 2 g orally in a single dose 1 g orally in a single dose	
Pediculosis Pubis	permethrin 1% cream rinse pyrethrins with piperonyl butoxide	OR	Apply to affected area, wash off after 10 minutes Apply to affected area, wash off after 10 minutes	malathion 0.5% lotion, applied 8-12 hrs then washed off OR ivermectin 250 µg/kg, orally repeated in 2 weeks
Pelvic Inflammatory Disease[13]	1. ceftriaxone doxycycline WITH OR WITHOUT metronidazole 2. cefoxitin doxycycline WITH OR WITHOUT metronidazole 3. Other parenteral third-generation cephalosporin (e.g. ceftizoxime or cefotaxime) doxycycline WITH OR WITHOUT metronidazole	PLUS PLUS PLUS 	250 mg IM in a single dose 100 mg orally 2x/day for 14 days 500 mg orally 2x/day for 14 days 2 g IM in a single dose and probenecid, 1 g, orally administered concurrently in a single dose 100 mg orally 2x/day for 14 days 500 mg orally 2x/day for 14 days 100 mg orally 2x/day for 14 days 500 mg orally 2x/day for 14 days	
	Alternative oral regimens are listed in CDC's 2010 STD Treatment Guidelines.			
Scabies	permethrin 5% cream ivermectin	OR	Apply to all areas of body from neck down, wash off after 8-14 hours 200 µg/kg orally, repeated in 2 weeks	lindane 1%[26,27] 1 oz. of lotion or 30 g of cream, applied thinly to all areas of the body from the neck down, wash off after 8 hours
Syphilis Primary, secondary, or early latent <1 year	benzathine penicillin G		2.4 million units IM in a single dose	doxycycline[6,28] 100 mg 2x/day for 14 days OR tetracycline[6,28] 500 mg orally 4x/day for 14 days
Latent >1 year, latent of unknown duration	benzathine penicillin G		2.4 million units IM in 3 doses each at 1 week intervals (7.2 million units total)	doxycycline[6,28] 100 mg 2x/day for 28 days OR tetracycline[6,28] 500 mg orally 4x/day for 28 days
Pregnancy[3]	See complete CDC guidelines.			
Neurosyphilis	aqueous crystalline penicillin G		3 to 4 million units IV every 4 hours for 10-14 days (18-24 million units/day)	procaine penicillin G 2.4 MU IM 1x daily PLUS probenecid 500 mg orally 4x/day, both for 10-14 days.
Congenital syphilis	aqueous crystalline penicillin G procaine penicillin G	OR	100,000-150,000 units/kg/day (50,000 units/kg/dose IV every 12 hours) during the first 7 days of life and every 8 hours thereafter for a total of 10 days 50,000 units/kg/dose IM in a single dose for 10 days	
Children: primary, secondary, or early latent <1 year	benzathine penicillin G		50,000 units/kg IM in a single dose (maximum 2.4 million units)	
Children: latent >1 year, latent of unknown duration	benzathine penicillin G		50,000 units/kg IM for 3 doses at 1 week intervals (maximum total 7.2 million units)	
Trichomoniasis	metronidazole[25] tinidazole[29]	OR	2 g orally in a single dose 2 g orally in a single dose	metronidazole[25] 500 mg 2x/day for 7 days

1. The recommended regimens are equally efficacious.
2. These creams are oil-based and may weaken latex condoms and diaphragms. Refer to product labeling for further information.
3. Please refer to the complete 2010 CDC Guidelines for recommended regimens.
4. Existing data do not support the use of topical agents in pregnancy.
5. Consider concurrent treatment for gonococcal infection if prevalence of gonorrhea is >5% (younger age).
6. Should not be administered during pregnancy, lactation, or to children <8 years of age.
7. If patient cannot tolerate high-dose erythromycin base schedules, change to 250 mg 4x/day for 14 days.
8. If patient cannot tolerate high-dose erythromycin ethylsuccinate schedules, change to 400 mg orally 4 times a day for 14 days.
9. Contraindicated for pregnant or lactating women.
10. Clinical experience and published studies suggest that azithromycin is safe and effective.
11. Erythromycin estolate is contraindicated during pregnancy.
12. Effectiveness of erythromycin treatment is approximately 80%; a second course of therapy may be required.
13. Patients who do not respond to oral therapy (within 72 hours) should be re-evaluated.
14. For patients with suspected sexually transmitted epididymitis, close follow-up is essential.
15. No definitive information available on prenatal exposure.
16. Treatment may be extended if healing is incomplete after 10 days of therapy.
17. Consider discontinuation of treatment after one year to assess frequency of recurrence.
18. Vaginal, cervical, urethral meatal, and anal warts may require referral to an appropriate specialist.
19. CDC recommends that treatment for uncomplicated gonococcal infections of the cervix, urethra, and/or rectum should include dual therapy, i.e. both a cephalosporin (e.g. ceftriaxone) plus azithromycin (preferred) or doxycycline
20. CDC recommends that cefixime in combination with azithromycin or doxycycline be used as an alternative when ceftriaxone is not available.
21. Only ceftriaxone is recommended for the treatment of pharyngeal infection. Providers should inquire about oral sexual exposure
22. Use with caution in hyperbilirubinemic infants, especially those born prematurely.
23. MSM are unlikely to benefit from the addition of nitroimidazoles.
24. Moxifloxacin 400mg orally 1x/day for 7 days effective against *Mycoplasma genitalium*
25. Pregnant patients can be treated with 2 g single dose.
26. Contraindicated for pregnant or lactating women, or children <2 years of age.
27. Do not use after a bath; should not be used by persons who have extensive dermatitis.
28. Pregnant patients allergic to penicillin should be treated with penicillin after desensitization.
29. Randomized controlled trials comparing single 2 g doses of metronidazole and tinidazole suggest that tinidazole is equivalent to, or superior to, metronidazole in achieving parasitologic cure and resolution of symptoms.

◆ Indicates revision from the 2006 CDC Guidelines for the Treatment of Sexually Transmitted Diseases.

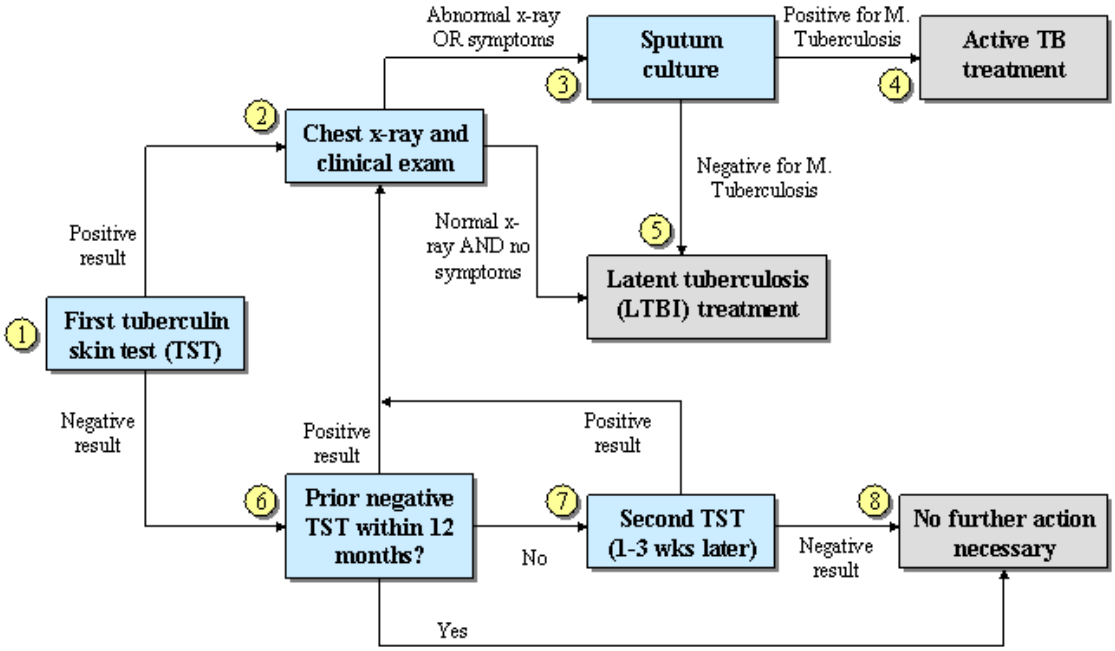
★ Indicates update from the 2010 CDC Guidelines for the Treatment of Sexually Transmitted Diseases; see MMWR Morb Mortal Wkly Rep. 2012 Aug 10; 61(31):590-594 for details.

Reviewed by the CDC 8/2012

SYLLABUS MATERIAL: Medical Complications of Addiction

TUBERCULOSIS:

Figure 1. Two-step Tuberculin Skin Testing (TST) Flow Chart



Source: Centers for Disease Control and Prevention. Targeted tuberculin testing and treatment of latent tuberculosis infection. Morbidity and Mortality Weekly Report 2000;49(RR-6):1-51.

TB Elimination

Targeted Tuberculosis Testing and Interpreting Tuberculin Skin Test Results

Introduction

Targeted tuberculosis (TB) testing is used to focus program activities, provider practices, and financial resources on groups at the highest risk for latent tuberculosis infection (LTBI). Once TB disease has been ruled out, those who would benefit from treatment of LTBI should be offered this option regardless of their age.

Every effort should be made to test only those persons at the highest risk, interpret tuberculin skin test (TST) reactions and TB blood test results accurately, and ensure appropriate treatment and completion of the recommended regimen.

Table 1: Criteria for Classifying Positive TST Reactions

Positive IGRA result or a TST reaction of 5 or more millimeters of induration is considered positive in

- HIV-infected persons
- Recent contacts of a TB case
- Persons with fibrotic changes on chest radiograph consistent with old TB
- Organ transplant recipients
- Persons who are munosuppressed for other reasons (e.g., taking the equivalent of >15 mg/day of prednisone for 1 month or longer, taking TNF-α antagonists)

Positive IGRA result or a TST reaction of 10 or more millimeters of induration is considered positive in

- Recent immigrants (< 5 years) from high-prevalence countries
- Injection drug users
- Residents and employees of high-risk congregate settings (e.g., correctional facilities, nursing homes, homeless shelters, hospitals, and other health care facilities)
- Mycobacteriology laboratory personnel
- Children under 4 years of age, or children and adolescents exposed to adults in high-risk categories

Positive IGRA result or a TST Reaction of 15 or more millimeters of induration is considered positive in

- Persons with no known risk factors for TB*

** Although skin testing programs should be conducted only among high-risk groups, certain individuals may require TST for employment or school attendance. An approach independent of risk assessment is not recommended by CDC or the American Thoracic Society.*

Persons at Risk for Developing TB Disease

Generally, persons at high risk for developing TB disease fall into two categories: those who have an increased likelihood of exposure to persons with TB disease, and those with clinical conditions that increase the risk of progression from LTBI to TB disease.

Persons at risk for exposure to persons with TB disease include:

- Close contacts of a person with infectious TB disease
- Persons who have immigrated from areas of the world with high rates of TB
- Residents and employees of high-risk congregate settings (e.g., correctional facilities, homeless shelters, health care facilities)

Persons more likely to progress from LTBI to TB disease include:

- Recent converters (those with an increase of 10 mm or more in size of TST reaction within a 2-year period)
- HIV-infected persons
- Young children who have a positive TST result
- Those with a history of prior, untreated TB or fibrotic lesions on chest radiograph
- Injection drug users
- Those receiving TNF-α antagonists for treatment of rheumatoid arthritis or Crohn's disease

Clinical conditions that increase the risk of progression from LTBI to TB disease:

- HIV infection
- Low body weight (>10% below ideal)
- Silicosis
- Diabetes mellitus

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- Chronic renal failure or being on hemodialysis
- Gastrectomy
- Jejunoileal bypass
- Solid organ transplant
- Head and neck cancer

Special Considerations

Questions often arise about the interpretation of TST results in persons with a history of Bacille Calmette-Gurin (BCG) vaccine, HIV infection, and recent contacts to an infectious TB case.

BCG vaccine is currently used in many parts of the world to protect infants and children from severe TB disease, especially TB meningitis. It does not confer lifelong immunity, and its significance in persons receiving the TST causes confusion in the medical and lay community.

- History of BCG vaccine is NOT a contraindication for tuberculin skin testing
- TST reactivity caused by BCG vaccine generally wanes with time
- If more than 5 years have elapsed since administration of BCG vaccine, a positive TST reaction is most likely a result of *M. tuberculosis* infection

Persons who are HIV infected have a much greater risk for progression to TB disease if they have LTBI.

- Individuals with HIV infection may be unable to mount an immune response to the TST and may have false-negative TST results
- Usefulness of anergy testing in TST-negative persons who are HIV infected has not been demonstrated

Persons with a positive TST result who are contacts of an individual with infectious TB should be treated regardless of age.

- Some TST-negative persons should also be considered for treatment (i.e., young children, immunosuppressed)
- Repeat TST in 8-10 weeks if initial test result is negative. A delayed-type hypersensitivity response to tuberculin is detected 2–8 weeks after infection

Additional Information

1. ATS/CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49 (No. RR- 6). http://www.cdc.gov/mmwr/preview/mmwrhtml/rr4906a1.htm
2. Targeted Tuberculosis (TB) Testing and Treatment of Latent TB Infection (slide set). http://www.cdc.gov/tb/publications/slidesets/LTBI/default.htm
3. ATS/CDC. Update: Adverse Event Data and Revised American Thoracic Society/CDC Recommendations Against the Use of Rifampin and Pyrazinamide for Treatment of Latent Tuberculosis Infection. *MMWR* 2003; 52 (No. 31). http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5231a4.htm
4. CDC. Tuberculosis Associated with Blocking Agents Against Tumor Necrosis Factor - Alpha - California, 2002–2003. *MMWR* 2004; 53 (No. 30). http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5330a4.htm
5. ATS/CDC. Treatment of tuberculosis. *MMWR* 2003; 52(No. RR-11). http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5211a1.htm
6. TB Education and Training Resources website http://www.findtbresources.org/
7. World Health Organization (WHO) website http://www.who.int/en/
8. CDC Division of TB Elimination website http://www.cdc.gov/tb
9. Treatment of Latent Tuberculosis Infection: Maximizing Adherence (factsheet). http://www.cdc.gov/tb/publications/factsheets/treatment/LTBIadherence.htm
10. Treatment Options for Latent Tuberculosis Infection (factsheet). http://www.cdc.gov/tb/publications/factsheets/treatment/LTBItreatmentoptions.htm

http://www.cdc.gov/tb

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TB Elimination
Treatment Options for Latent Tuberculosis Infection

Introduction

Treatment of latent tuberculosis (TB) infection (LTBI) is essential to controlling and eliminating TB in the United States, because it substantially reduces the risk that TB infection will progress to TB disease. Certain groups are at very high risk of developing TB disease once infected. Once the diagnosis of LTBI has been made, health care providers must choose the most appropriate and effective treatment regimen, and make every effort to ensure those persons complete the entire course of treatment for LTBI.

However, if exposed to and infected by a person with multidrug-resistant TB (MDR TB) or extensively drug-resistant TB (XDR TB), preventive treatment may not be an option.

Pretreatment Evaluation

To decide whether an individual who has a positive tuberculin skin test (TST) or interferon gamma release assay (IGRA) result is a candidate for treatment of LTBI

- Determine the benefits of treatment by evaluating the individual's risk for developing TB disease
- Assess the person's level of commitment to completion of treatment and resources available to ensure adherence

Once the decision is made to treat an individual for LTBI, the health care provider must establish rapport with the patient and

- Discuss benefits and risks of treatment
- Review possible medication side effects or drug interactions
- Emphasize importance of adherence
- Identify potential barriers to adherence
- Establish a plan to ensure adherence

Table1: **Candidates for the Treatment of Latent TB Infection**

Groups Who Should be Given High Priority for Latent TB Infection	
People who have a positive IGRA result or a TST reaction of 5 or more millimeters	People who have a positive IGRA result or a TST reaction of 10 or more millimeters
• HIV-infected persons • Recent contacts of a TB case • Persons with fibrotic changes on chest radiograph consistent with old TB • Organ transplant recipients • Persons who are immunosuppressed for other reasons (e.g., taking the equivalent of >15 mg/day of prednisone for 1 month or longer, taking TNF-α antagonists)	• Recent immigrants (< 5 years) from high-prevalence countries • Injection drug users • Residents and employees of high-risk congregate settings (e.g., correctional facilities, nursing homes, homeless shelters, hospitals, and other health care facilities) • Mycobacteriology laboratory personnel • Children under 4 years of age, or children and adolescents exposed to adults in high-risk categories

Persons with no known risk factors for TB may be considered for treatment of LTBI if they have either a positive IGRA result or if their reaction to the TST is 15 mm or larger. However, targeted TB testing programs should only be conducted among high-risk groups. All testing activities should be accompanied by a plan for follow-up care for persons with TB infection or disease.

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Choosing the Most Effective Regimen

Treatment of LTBI should be initiated after the possibility of TB disease has been excluded. Persons suspected of having TB disease should receive the recommended multidrug regimen for treatment of disease until the diagnosis is confirmed or ruled out.

Consultation with a TB expert is advised if the known source of TB infection has drug-resistant TB.

Table 2. **Latent TB Infection Treatment Regimens**

Drugs	Duration	Interval	Minimum doses
Isoniazid	9 months	Daily	270
		Twice weekly*	76
Isoniazid	6 months	Daily	180
		Twice weekly*	52
Isoniazid & Rifapentine	3 months	Once weekly*	12
Rifampin	4 months	Daily	120

**Use Directly Observed Therapy (DOT).*
Note: *Due to the reports of severe liver injury and deaths, CDC recommends that the combination of rifampin (RIF) and pyrazinamide (PZA) should generally not be offered for the treatment of latent TB infection.*

Although regimens are broadly applicable, there are modifications that should be considered under special circumstances (e.g., HIV infection, suspected drug resistance, pregnancy, or treatment of children). Table 2 lists the current recommended regimens. *Refer to Targeted Tuberculin Testing and Recommendations for Use of an Isoniazid–Rifapentine Regimen with Direct Observation to Treat Latent Mycobacterium tuberculosis Infection* for detailed information about the treatment of LTBI.

Isoniazid (INH)

The standard treatment regimen for LTBI is nine months of daily INH. This regimen is very effective and is the preferred regimen for HIV-infected people taking antiretroviral therapy, and children aged 2-11 years of age.

Isoniazid (INH) and Rifapentine (RPT) Regimen

The 12-dose regimen of INH and RPT does not replace other recommended LTBI treatment regimens; it is another effective regimen option for otherwise healthy patients aged ≥12 years who have predictive factor for greater likelihood of TB developing, which includes recent exposure to contagious TB, conversion from negative to positive on an indirect test for infection (i.e., interferon-γ release assay or tuberculin test), and radiographic findings of healed pulmonary TB.

This regimen is not recommended for

- Children younger than 2 years old,
- People with HIV/AIDS who are taking antiretroviral treatment,
- People presumed to be infected with INH or RIF-resistant *M. tuberculosis*, and
- Pregnant women or women expecting to become pregnant within the 12-week regimen.

Adverse Drug Reactions

Patients on treatment for LTBI should be instructed to report any signs and symptoms of adverse drug reactions to their health care provider, including

- Unexplained anorexia, nausea or vomiting, dark urine*, or icterus
- Persistent paresthesia of hands or feet
- Persistent weakness, fatigue, fever, or abdominal tenderness
- Easy bruising or bleeding

**Advise patients taking RIF or RPT that they will notice a normal orange discoloration of body fluids, including urine and tears. Contact lenses may be permanently stained.*

Obtain a list of patient's current medications to avoid drug interactions. Some interactions to note:

- INH increases blood levels of phenytoin (Dilantin) and disulfiram (Antabuse)
- RIF and RPT decrease blood levels of many drugs including oral contraceptives, warfarin, sulfonureas, and methadone
- RIF and RPT are contraindicated in HIV-infected individuals being treated with protease inhibitors (PIs) and most nonnucleoside reverse transcriptase inhibitors (NNRTIs)

Monitoring During Treatment

Baseline and routine laboratory monitoring during treatment of LTBI are indicated only when there is a history of liver disease, HIV infection, pregnancy (or within 3 months post delivery), or regular alcohol use. Baseline hepatic measurements of serum AST, ALT, and bilirubin are used in the situations mentioned above and to evaluate symptoms of hepatotoxicity. Laboratory testing should be performed to evaluate possible adverse reactions that occur during the treatment regimen.

Clinical monitoring, including a brief physical examination, should occur at monthly visits to assess adherence, rationale for treatment, and to identify signs or symptoms of adverse drug reactions.

CDC collects reports of all severe adverse events (e.g., liver injury, metabolic acidosis, anaphylaxis, seizure, severe dermatitis) leading to hospitalization or death of a person receiving treatment for LTBI. Report these adverse events to the Division of Tuberculosis Elimination by sending an email to LTBIdrugevents@cdc.gov.

Additional Information

1. ATS/CDC. Targeted tuberculin testing and treatment of latent TB infection. (PDF) *MMWR* 2000;49(No. RR- 6). http://www.cdc.gov/MMWR/PDF/rr/rr4906.pdf
2. CDC. Recommendations for Use of an Isoniazid–Rifapentine Regimen with Direct Observation to Treat Latent *Mycobacterium tuberculosis* Infection. *MMWR* 2011; 60:1650 –1653. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6048a3.htm?s_cid=mm6048a3_w
3. CDC. Update: Adverse Event Data and Revised American Thoracic Society/CDC Recommendations Against the Use of Rifampin and Pyrazinamide for Treatment of Latent Tuberculosis Infection. *MMWR* 2003; 52 (No. 31). http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5231a4.htm
4. Updated Guidelines for the Use of Rifamycins for the Treatment of Tuberculosis Among HIV-Infected Patients Taking Protease Inhibitors or Nonnucleoside Reverse Transcriptase Inhibitors. *MMWR* 2004: 53 (No. 2). http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5302a6.htm
5. Latent Tuberculosis Infection: A Guide for Primary Health Care Providers. http://www.cdc.gov/tb/publications/LTBI/default.htm
6. Targeted Tuberculosis (TB) Testing and Treatment of Latent TB Infection. http://www.cdc.gov/tb/publications/slidesets/LTBI/default.htm
7. Treatment of Latent Tuberculosis Infection: Maximizing Adherence. http://www.cdc.gov/tb/publications/factsheets/treatment/LTBIadherence.htm
8. CDC Division of Tuberculosis Elimination website http://www.cdc.gov/tb

http://www.cdc.gov/tb