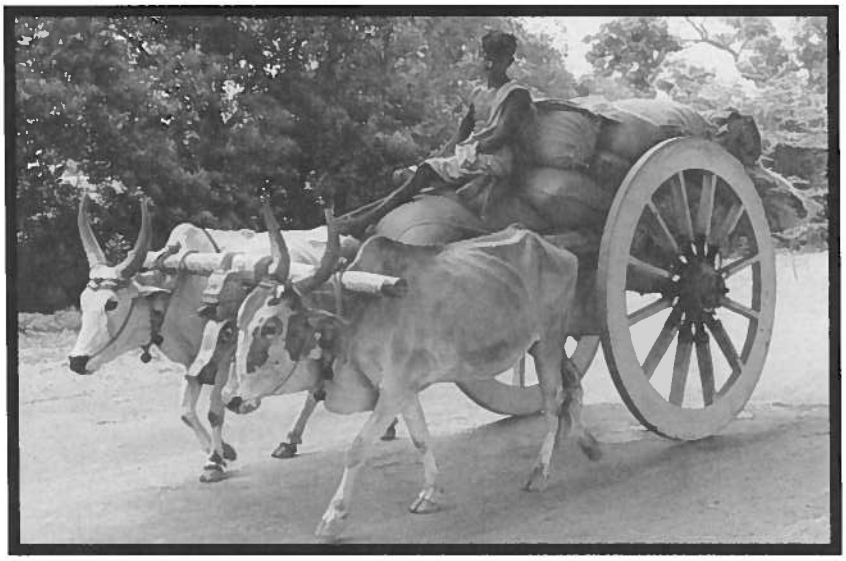
Sexually Transmitted Diseases



Screening for Sexually Transmitted Diseases during the Domestic Medical Examination for Newly Arrived Refugees

Background

Sexually transmitted infections (STIs) are a major cause of acute illness and infertility worldwide. The World Health Organization (WHO) estimates that 448 million new cases of curable STIs occur annually worldwide in adults aged 15–49 years. The largest number of new infections occurs in the region of South and Southeast Asia, followed by sub-Saharan Africa, Latin America, and the Caribbean. In low-income countries, STIs rank in the top five disease categories for which adults seek health care.

The prevalence of STIs in refugee populations is not well characterized and likely varies among populations. Because certain refugee groups are at potentially high risk for STIs, it is important to screen for certain STIs to minimize or prevent acute and chronic sequelae, as well as prevent transmission to others.

Medical Screening

Overseas Pre-Departure Screening and Testing

Refugees undergo health screening prior to resettlement in the United States to identify conditions that exclude resettlement until after treatment. For refugees 15 years of age or older, clinical evaluation (laboratory for syphilis) and treatment for identified infection are considered mandatory for the following infections:

- Syphilis (laboratory testing required)
- Gonorrhea
- Chancroid
- Granuloma inguinale
- Lymphogranuloma venereum

Note: HIV has been removed from the list of excludable infections and is no longer routinely tested overseas beginning January, 2010 (see domestic guidelines for HIV testing during refugee new arrival screening: http://www.cdc.gov/immigrantrefugeehealth/guidelines/refugee-guidelines.html).

A complete overseas screening medical examination for syphilis consists of a medical history, physical examination, and serologic testing. Further testing is performed as necessary to confirm a suspected diagnosis. For the other STIs (i.e., gonorrhea, chancroid, lymphogranuloma venereum, and granuloma inguinale), the evaluation includes a medical history and physical examination. Therefore, with the exception of syphilis, negative overseas STI screening does not exclude STIs.

Recommendations for Post-Arrival Screening and Evaluation

The Office of Refugee Resettlement and the Centers for Disease Control and Prevention recommend that all refugees receive a new-arrival medical evaluation on arrival to the United States. The following STIs should be considered during this examination:

- Syphilis
- Gonorrhea
- Chlamydia
- Chancroid
- Granuloma inguinale/donovanosis
- Lymphogranuloma venereum
- Genital herpes
- Genital warts
- HIV
- Trichomoniasis

A complete screening medical examination for all STIs includes a thorough medical history, physical examination and, for specific disorders, diagnostic testing. Although history taking is challenging due to language and cultural barriers, the optimal medical history should include inquiries regarding sexual contact with a person who has or had a known STI or symptoms of an STI, signs and symptoms of current infection (e.g., genital discharge, dysuria, genital lesion, ulcer, or rash), and/or prior diagnostic evaluation and treatment of STIs. Information on treatment of sex partners should be obtained to assess risk of re-infection.

Pertinent elements of the physical examination for STIs include palpation of lymph nodes and an external anal and genital examination, including inspection for discharge, ulcers, or rashes. In previously traumatized refugees (e.g., sexual assault victims), the anal and genital examination may be postponed until the refugee establishes a trusting relationship with a provider. Signs and symptoms and specific information on diagnostic testing available for select STIs are described below. With exception of the routine testing for syphilis (for refugees $\geq$ 15 years of age) and chlamydia testing (for females <25 years of age or older with risk factors as in U.S. CDC guidelines: www.cdc.gov/mmwr/preview/mmwrhtml/rr5912a1.htm?s_cid=rr5912a1_w, no data support the utility of routine testing for other non-HIV STIs in refugees. Further study to elucidate prevalence rates and the utility of screening in refugee populations is encouraged. The following summarizes the currently recommended testing:

- Syphilis: Venereal Disease Research Laboratory (VDRL) or rapid plasma reagin (RPR) or equivalent test.
  - All persons $\geq$15 years of age, regardless of the overseas results.
  - Children < 15 years of age who meet one or more of the following criteria:
    - Sexually active or history of sexual assault.
    - All children who are at risk (i.e., mother who tests positive for syphilis) should be evaluated according to current guidelines, found at www.cdc.gov/mmwr/preview/mmwrhtml/rr5912a1.htm?s_cid=rr5912a1_w.

        - All refugees from countries that are endemic for treponemal subspecies (e.g., yaws, bejel, pinta).
    - Confirmatory testing [i.e., fluorescent treponemal antibody (FTA), treponema pallidum particle agglutination assay (TPPA), or enzyme-linked immunosorbent assay (EIA)] should be performed on all refugees who test positive by VDRL or RPR. Further evaluation, including evaluation for neurosyphilis, and treatment should be instituted according to current guidelines, found at www.cdc.gov/std/treatment/.
- Chlamydia: Nucleic acid amplification tests
    - Females ≤ 25 years old who are sexually active or those with risk factors (e.g., new sexual partner or multiple sexual partners).
    - Consider for children who have a history of sexual assault. However, management and evaluation of such children require consultation with an expert (www.cdc.gov/mmwr/preview/mmwrhtml/rr5912a1.htm?s_cid=rr5912a1_w).
    - Persons with symptoms or leukoesterase (LE) detected in urine sample.
- Gonorrhea: Nucleic acid amplification tests
    - Consider for children who have a history of sexual assault. However, management and evaluation of such individuals require consultation with an expert (www.cdc.gov/mmwr/preview/mmwrhtml/rr5912a1.htm?s_cid=rr5912a1_w).
    - Persons who have symptoms or leukoesterase (LE) detected in urine sample.

NOTE: HIV testing is strongly encouraged in newly arriving refugee populations according to current CDC guidelines (www.cdc.gov/immigrantrefugeehealth/guidelines/refugee-guidelines.html). However, testing for HIV is particularly important and encouraged for any refugee with a confirmed non-HIV STI.

Further information on STIs, including treatment guidelines, is available at www.cdc.gov/STD/ and www.cdc.gov/mmwr/preview/mmwrhtml/rr5912a1.htm?s_cid=rr5912a1_w [1]. In addition, updated laboratory guidance for syphilis, gonorrhea and chlamydia is available at: http://www.aphl.org/aphlprograms/infectious/std/Pages/stdtestingguidelines.aspx

Syphilis

Syphilis, which is caused by the bacterium *Treponema pallidum,* has often been called the "great imitator" because so many of its signs and symptoms are indistinguishable from those of other diseases.

Typical signs and symptoms of various stages of syphilis include—

- Primary stage

    - Generally occurs 10–90 days after exposure
    - Ulcer or chancre at the infection site, usually the genitals, rectum, tongue or lips
- Secondary stage
    - Generally occurs 2–10 weeks after the chancre appears
    - Skin rash marked by red or reddish-brown macules on the palms and soles or other parts of the body, mucocutaneous lesions, lymphadenopathy, anorexia, fever, headaches, weight loss, fatigue
- Latent stage (early latent and late latent)
    - No signs and symptoms present
    - Begins when primary and secondary symptoms disappear and may last for years
    - Early latent syphilis can relapse to secondary syphilis and become infectious (again)
- Tertiary stage
    - Generally occurs 10–20 years after infection
    - Cardiac or ocular manifestations (e.g., aortitis, optic atrophy, uveitis, gradual blindness), auditory abnormalities (e.g., asymmetric deafness, tinnitus), neurologic manifestations (e.g., tabes dorsalis, meningitis, dementia), gumma
- Neurosyphilis may occur at any stage of disease.
- Congenital syphilis
    - Prevention and detection of congenital syphilis depend on identification of syphilis in pregnant women by serology. For specific guidelines on screening and identification of congenital syphilis, see the 2010 congenital section of the syphilis treatment guidelines (www.cdc.gov/mmwr/preview/mmwrhtml/rr5912a1.htm?s_cid=rr5912a1_w).

Diagnostic Testing

Syphilis Serology

Serologic tests for syphilis include screening tests that use nonspecific cardiolipin antigens and confirmatory tests that use specific *T. pallidum* antigens (Table 1). A nontreponemal test such as Venereal Disease Research Laboratory (VDRL), rapid plasma reagin (RPR) or an equivalent test may be used for screening. Positive results on these nontreponemal tests should be confirmed by using a treponemal test, such as fluorescent treponemal antibody absorption (FTA-ABS) or other treponemal test.

Screening tests such as the VDRL and RPR are relatively simple to perform and provide rapid results. However, interpretation of results demands trained personal and in addition laboratory equipment and quality control can present challenges in non-U.S. settings (Table 2). Both VDRL and RPR quantitative titer usually correlate with disease activity and are used to monitor the effect of treatment. If treatment is successful, the antibody

titer gradually declines. A fourfold change in titer (e.g., from 1:16 to 1:4) is necessary to demonstrate a clinically significant difference between two nontreponemal tests. Sequential serologic tests in individuals should be performed by using the same testing method, because quantitative results from the two tests cannot be compared directly; RPR titers are frequently slightly higher than VDRL titers. The timing of follow-up testing is dictated by the clinical presentation and the stage of infection, as well as the HIV status of the refugee, and are detailed in the current treatment guidelines (1).

Table 1. Serology tests for syphilis.

Nontreponemal (reagin) test	Treponemal (specific) test
Rapid plasma reagin (RPR) test Venereal Disease Research Laboratory (VDRL) test Toluidine red unheated serum test (TRUST)	Fluorescent treponemal antibody-absorption (FTA-ABS) test *Treponema pallidum* immobilization (TPI) test *Treponema pallidum* particle agglutination assay (TPPA) Enzyme immune assay (EIA) or enzyme-linked immunosorbent assay (ELISA) Chemiluminescence immunoassay Chromatographic point of contact (POC) tests

Unlike nontreponemal tests, treponemal tests (e.g., FTA) do not usually revert to nonreactivity after successful treatment of syphilis. Screening with treponemal tests (i.e., use of rapid syphilis tests) is not recommended in high-prevalence settings, because these tests will be reactive in persons with previous successful treatment as well as those with untreated or incompletely treated infection. Therefore, treatment of persons with treponemal positive tests, without previous positive nontreponemal testing (i.e. VDRL, RPR), may result in overtreatment.

Table 2. Interpretation of results for syphilis serology tests.

Nontreponemal test (e.g., RPR, VDRL)	Treponemal (specific) test (e.g., FTA-ABS, TPPA)	Likely interpretations and comments
Nonreactive*	Not routinely done if screening is nonreactive	• No evidence of syphilis

Reactive	Reactive	• Untreated syphilis OR • Previously treated late syphilis OR • Other spirochetal diseases
Reactive	Nonreactive	• False positive. Seen in certain acute or chronic infections (e.g., tuberculosis, hepatitis, malaria, early HIV infection), autoimmune diseases (e.g., systemic lupus, rheumatoid arthritis), drug addiction, pregnancy, and following vaccination (e.g. smallpox, MMR).
Nonreactive*	Reactive	• Very early untreated syphilis OR • Previously treated syphilis OR • Very late untreated syphilis • Note: After successful treatment, a positive nontreponemal test usually becomes negative, whereas the treponemal test remains positive for life.

* Note: Nontreponemal testing may have a false-negative result during primary syphilis in the very early stages, tertiary syphilis in the very late stages, or syphilis with concomitant HIV infection. Suggest retesting or alternative testing if clinical suspicion is high. See treatment guidelines for details.[1]

Cerebrospinal Fluid Examination

Involvement of the central nervous system can occur during any stage of syphilis. Therefore, any person who has clinical evidence of neurologic involvement (e.g., motor or sensory deficits, cranial nerve palsies, or symptoms and signs of meningitis) and a positive treponemal test should have a lumbar puncture performed to obtain cerebrospinal fluid (CSF). A reactive VDRL performed on a CSF sample, in combination with elevated CSF white blood cells ($\geq$10 wbc/mm^3) or protein, is suggestive of neurosyphilis. Because VDRL-CSF might be nonreactive even when neurosyphilis is present, an FTA-ABS test on CSF may be helpful if the result of the VDRL-CSF test is negative.

Neurosyphilis may be a difficult diagnosis, particularly in HIV-positive individuals. The treatment guidelines provide in-depth information on diagnosis and treatment, and expert consultation may be needed when deciding how to evaluate an individual or interpret testing [1].

Other Diagnostic Tests

Syphilis infection must be correctly diagnosed to ensure that the refugee with syphilis receives correct treatment and to prevent further spread of the disease. When clinical findings are suggestive of primary syphilis but serologic tests are nonreactive or their interpretation is unclear, alternative tests should be considered (e.g., biopsy of a lesion, darkfield microscopy, or direct fluorescent antibody staining of lesion exudate or tissue).

The diagnosis of congenital syphilis is complicated by transplacental transfer of maternal nontreponemal and treponemal IgG antibodies to the fetus, making it difficult to interpret reactive serologic tests for syphilis in newborns born to mothers seropositive for syphilis. Pathologic examination of the placenta or umbilical cord by using specific fluorescent antitreponemal antibody staining is recommended. Darkfield microscopic examination or direct fluorescent antibody staining of suspicious lesions or body fluids should also be performed (e.g., nasal discharge). Other tests (e.g., complete blood count with platelets, bone radiographs) may be performed to support a diagnosis of congenital syphilis.

Other Treponema pallidum *infection*

Infection with other *T. pallidum* subspecies (e.g., *T. pallidum* subsp. *pertenue*, *T. pallidum* subsp. *endemicum*, and *T. carateum*) is acquired through contact with infected skin and results in rashes and may cause disfiguring skin lesions. Unlike syphilis, these infections are not considered sexually transmitted. Long-term infection can lead to deformations of bone and nasopharyngeal tissue. Infection with any of these subspecies can produce positive results for both treponemal and nontreponemal tests used for diagnosis of syphilis. Therefore, it is important to obtain a thorough history of both sexual and nonsexual exposures to assist in differentiating between syphilis and other *T. pallidum* subspecies infections. Lesions should be evaluated for treponemes by darkfield or fluorescence microscopy. Note: Darkfield microscopy of oral lesions will not allow distinction between syphilitic and nonsyphilitic treponemes.

Because the diseases caused by *T. pallidum* subsp. *pertenue*, *T. pallidum* subsp. *endemicum*, and *T. carateum* (i.e., yaws, bejel/endemic syphilis, and pinta, respectively) usually occur during childhood, CDC recommends that all refugee children from areas where treponemes are known to be endemic (Table 3) undergo nontreponemal serologic testing at the initial health screening [2]. If the screening test is positive, a treponemal confirmatory test should be performed.

Table 3. Regions and countries endemic for *Treponema pallidum* subspecies

Region	Country	
Africa	Angola	Liberia
	Benin	Mali
	Botswana	Mauritania
	Burkina Faso	Niger
	Cameroon	Republic of the Congo
	Central African Republic	Rwanda
	Chad	Senegal
	Côte d'Ivoire	Somalia

	Democratic Republic of the Congo Ethiopia Gabon Ghana	South Africa Sudan Togo
Americas	Colombia Ecuador Haiti Guyana	Martinique Mexico Surinam Venezuela
Asia	Cambodia India Indonesia	Pakistan Sri Lanka
Middle East	Saudi Arabia	
Western Pacific	Papua New Guinea Solomon Islands Vanuatu	

Chlamydia

Chlamydia, the most frequently reported STI in the United States, has the highest prevalence in persons 15-25 years of age. Asymptomatic infection is common in the U.S. and, in accordance with current CDC guidelines (www.cdc.gov/mmwr/preview/mmwrhtml/rr5912a1.htm?s_cid=rr5912a1_w) screening of sexually active refugee women ≤ 25 years old, or of women older than 25 with risk factors (e.g., new sexual partner or multiple sexual partners) is recommended. In women, untreated infection can cause pelvic inflammatory disease, ectopic pregnancy, and infertility. Rarely, genital chlamydia infection can cause arthritis that can be accompanied by skin lesions and inflammation of the eye and urethra (Reiter's syndrome).

Women with symptoms may have an abnormal vaginal discharge or burning sensation when urinating. Other symptoms include abdominal pain, low back pain, nausea, fever, pain during intercourse (dyspareunia), or bleeding between menstrual periods. Men with signs or symptoms might have penile discharge, burning and itching or burning sensation when urinating. Pain and swelling of the testicles occur but are uncommon. Autoinoculation may occur in men or women and can be associated with conjunctivitis.

Chlamydia trachomatis infection in infants most frequently presents as conjunctivitis that develops 5–12 days after birth. It can also cause an afebrile pneumonia with onset 1–3 months after birth. Signs of *C. trachomatis* pneumonia include a repetitive staccato cough with tachypnea and hyperinflation and bilateral diffuse infiltrates on chest radiograph.

Diagnostic Testing for Chlamydia

Diagnosis of *C. trachomatis* urogenital infection in women can be made by testing urine or cervical specimens. Urethral *C. trachomatis* infection in men can be diagnosed by testing urethral swab or urine specimens.

Nucleic acid amplification tests (NAATs) are the most sensitive tests available for detection of *C. trachomatis.* These tests can be performed on cervical, urethral, urine, or self-collected vaginal swab specimens. Direct immunofluorescent antibody test is used to detect *C. trachomatis* from nasopharyngeal specimens, tracheal aspirates, and lung biopsy tissue in infants. Further information on diagnostic testing can be obtained at (www.cdc.gov/std).

Gonorrhea

Gonorrhea, which is caused by the bacterium *Neisseria gonorrhoeae*, is the second most commonly reported bacterial STI in the United States. The majority of gonococcal urethral infections in men produce symptoms. However, among women, 30%-40% or more of infections do not produce recognizable symptoms. Untreated infection can result in complications such as pelvic inflammatory disease (PID), infertility, and ectopic pregnancy.

Signs and symptoms of gonorrhea may appear 2–10 days or as long as 30 days after exposure to an infected person.

In men, signs and symptoms may include—

- Pain or burning sensation when urinating
- Penile discharge
- Painful or swollen testicles
- Rectal infection: typically asymptomatic, but discharge, anal itching, soreness, bleeding, or painful bowel movements may occur

In women, signs and symptoms may include—

- Pain or burning sensation when urinating
- Vaginal discharge
- Itching or burning of the vagina
- Intermenstrual bleeding
- Rectal infection: typically asymptomatic, but discharge, anal itching, soreness, bleeding, or painful bowel movements may occur

Other sites of infection include the eyes (gonococcal conjunctivitis) and pharynx. Disseminated gonococcal infection is associated with intermittent fever, arthralgia, and skin lesions ranging from maculopapular or pustular to hemorrhagic. Arthritis and tenosynovitis, particularly involving the wrists, knees, and ankles, may occur.

Gonococcal infection among infants usually results from exposure to infected cervical exudate at birth. It is usually an acute illness that develops 2–5 days after birth and may present as ophthalmia neonatorum that can result in perforation of the globe of the eye

and blindness. Ophthalmic prophylaxis at birth is effective at preventing this complication. Other manifestations in infants are scalp abscesses, rhinitis, vaginitis, urethritis, arthritis, meningitis, and sepsis.

Diagnostic Testing for Gonorrhea

Specific diagnostic testing for gonorrhea may be performed on endocervical, vaginal, male urethral or urine specimens. For screening purposes, urine samples tested by nucleic acid amplification tests (NAAT) are highly sensitive and specific. No data support routine screening in refugees. A gram stain of discharge or on a urethral swab showing gram-negative diplococci supports the diagnosis and may be sufficient to confirm gonorrhea in symptomatic men.

Because nonculture-based tests do not permit antimicrobial susceptibility testing, in cases of persistent gonococcal infection following treatment, bacterial culture and antimicrobial susceptibility testing should be assessed.

Persons infected with *N. gonorrhoeae* are frequently coinfected with *Chlamydia trachomatis*. Therefore, persons who test positive for *N. gonorrhoeae* should also receive treatment for chlamydia.

Chancroid

Chancroid can be a cause of genital ulcer, especially in Asia, Africa and the Caribbean, and an important cofactor of HIV transmission in countries most severely affected by HIV. Infection with the bacterium *Haemophilus ducreyi* results in painful, superficial ulcers, often with regional lymphadenopathy.

Genital ulcers may be single or multiple, or in women lesions may be located within the vagina or on the cervix. Unlike a syphilitic chancre, which is painless, the chancroid ulcer is painful, tender, and nonindurated. Symptoms usually occur 4–10 days after exposure. The lesion at the site of infection is initially a pustule that breaks down to form a painful, soft, ulcer with a necrotic base with irregular borders. Multiple lesions and inguinal adenopathy often develop. With lymph node involvement, fever, chills and malaise may also develop. Other symptoms of chancroid include painful urination, vaginal discharge, rectal bleeding, pain with bowel movements, and dyspareunia.

Diagnostic Testing for Chancroid

The combination of a painful genital ulcer and tender suppurative inguinal adenopathy suggests the diagnosis of chancroid. A probable diagnosis of chancroid can be made if all the following criteria are met:

- One or more painful genital ulcers (regional lymphadenopathy is also typical)
- No evidence of *T. pallidum* infection by darkfield examination of ulcer exudate or by syphilis serologic testing performed at least 7 days after onset of ulcers
- Test for herpes simplex virus performed on the ulcer exudate is negative

A definitive diagnosis of chancroid requires the identification of *H. ducreyi* on special culture media that is not widely available from commercial sources. Nucleic acid amplification tests can be performed in clinical laboratories that have developed their own tests.

Granuloma inguinale/donovanosis

Granuloma inguinale is a chronic, relapsing granulomatous anogenital infection caused by the bacterium *Calymmatobacterium (Donovania) granulomatis*, which is endemic in tropical and developing areas, including India, Guyana, New Guinea, central Australia, and southern Africa. Symptoms usually occur 1–12 weeks after infection. The infection begins with the appearance of relative painless nodules that break down into shallow, sharply demarcated ulcers with a beefy-red friable base of granulation tissue. The lesions may occur on the skin, genitalia, or perineal areas and slowly spread to the lower abdomen and thighs. The lesions may develop secondary bacterial infection or may be coinfected with another sexually transmitted pathogen.

Diagnostic Testing for Granuloma inguinale/donovanosis

Diagnosis requires visualization of Donovan bodies (numerous bacilli in the cytoplasm of macrophage demonstrated with Giemsa or Wright's stain) in smears of scrapings from the ulcer base or histologic sections. Culture of *C. granulomatis* is difficult to perform and not routinely available.

Lymphogranuloma venereum

Lymphogranuloma venereum (LGV) is caused by three subtypes of *C. trachomatis*, serovars L1, L2, or L3. It is most often seen in tropical areas of Asia, Africa, South America, and the Caribbean. Symptoms appear 3–30 days after infection and usually present as a painless ulcer or papule at the site of inoculation. Inguinal and femoral lymphadenopathy may also occur. Rectal exposure can result in mucoid or hemorrhagic rectal discharge, painful bowel movement, and constipation. Late manifestations include rectal and perirectal inflammation that can lead to rectal strictures and rectovaginal and perianal fistulas. Constitutional symptoms such as fever may occur.

Diagnostic Testing for LGV

Diagnosis is based on clinical suspicion, epidemiologic information, and *C. trachomatis* testing. Genital and lymph node specimens (e.g., lesion swab, aspirate) may be tested for *C. trachomatis* by culture, direct immunofluorescence, or nucleic acid detection. To differentiate LGV from non-LGV *C. trachomatis,* special testing is generally necessary (e.g., genotyping) and may necessitate consultation with laboratory experts. Chlamydia serology (complement fixation titers >1:64) can support the diagnosis in the appropriate clinical context.

Genital herpes

Genital herpes is a chronic, lifelong infection caused by herpes simplex virus (HSV), type 1 and type 2. Most cases of recurrent genital herpes are caused by HSV-2. Many persons with HSV-1 or HSV-2 have mild or unrecognized infections but intermittently shed the virus in the genital tract. When genital ulcers do occur, they appear typically as one or more blisters on or around the genitals or rectum. The blisters break, leaving tender ulcers that may take 2–4 weeks to heal the first time they occur. Other symptoms, such as fever, headache, muscle aches, malaise, and swollen lymph glands, may occur before appearance of the lesions. After the first episode of genital herpes, symptoms usually recur, but they tend to be milder and briefer. After the lesions erupt, they typically heal in 6–10 days.

Neonatal herpes is a rare but serious condition occurring among infants exposed to HSV during birth. Although the disease may be limited to skin, eyes, or mucus membranes, disseminated disease involving the lungs, liver, adrenal glands and central nervous system disease (e.g., encephalitis) may also occur and is associated with serious consequences.

Diagnostic Testing for Genital Herpes

Both virologic and type-specific serologic tests for HSV are available for diagnosis. Isolation of HSV in cell culture is the preferred virologic test for genital lesions. However, the sensitivity of the culture is low, especially for recurrent lesions. Polymerase chain reaction (PCR) tests for HSV DNA are more sensitive but are not FDA-approved for testing genital specimens. Viral culture isolates can be typed to determine if HSV-1 or HSV-2 is the cause of the infection.

Type-specific serologic tests (e.g., ELISA, immunoblot) may be useful—

- In clinical diagnosis of genital herpes without laboratory confirmation
- For recurrent genital symptoms or atypical symptoms with negative HSV culture
- When a sexual partner has known genital herpes

Genital warts

Genital warts are the most recognized sign of genital human papillomavirus (HPV) infection. HPV types 6 and 11 are usually associated with genital warts. Other HPV types that affect the anogenital region (e.g., types 16, 18, 31, 33, and 35) are associated with cervical neoplasia.

Genital warts are usually flat, papular, or pedunculated growths on the genital mucosa and often occur in clusters. They can appear on the penis, vulva, the vagina, cervix or rectum, rectum, groin or thigh within weeks or months after sexual contact with an infected person.

Diagnostic Testing for Genital Warts

Diagnosis of genital warts is made by visual inspection. Biopsy may confirm the diagnosis but is generally needed only when the lesions do not respond to appropriate

therapy or worsen during therapy.

A definitive diagnosis of HPV infection is based on detection of viral nucleic acid (i.e., DNA or RNA) or capsid protein. Tests that detect several types of HPV DNA in cells scraped from the cervix are available but are only indicated for use in very limited circumstances (see www.cdc.gov/std).

Trichomoniasis

Trichomoniasis, caused by the protozoan *Trichomonas vaginalis*, is the most common curable STI in sexually active women. The most common sites of infection are the vagina in women and urethra in men.

Some men with trichomoniasis do not have signs or symptoms. Others may have an irritation inside the penis, mild discharge, or slight burning after urination. Many infected women have frothy, malodorous yellow-green vaginal discharge with irritation and itching of the genital area. There can also be small red ulcerations on the vaginal wall or cervix. Symptoms usually appear within 5–28 days after exposure.

Diagnostic Testing for Trichomoniasis

Diagnosis of vaginal trichomoniasis is usually performed by microscopy of vaginal secretions and evaluation of wet preparation slide for trichomonads. Other tests for trichomoniasis in women include immunochromatographic capillary flow dipstick test and nucleic acid probe test. Although these tests tend to be more sensitive than vaginal wet preparations, false positives may occur, especially in low-prevalence populations. Culture is the most sensitive method of diagnosis. In women in whom trichomoniasis is suspected but not confirmed by microscopy, vaginal secretions may be cultured for *T. vaginalis*. In men, a wet preparation is insensitive, and culture testing of urethral swab, urine, and semen is required for optimal sensitivity. Frequently, this infection is treated presumptively based on clinical signs and symptoms when testing is not available.

Counseling

The health-care provider must counsel all refugees with STIs and their contacts to reduce their risk of future STIs. Preventive measures should include using barrier protection methods such as condoms, reducing the number of sexual partners, and knowing the health status and HIV infection status of partners.

Further information on the prevention of STIs is available at CDC's website at http://www.cdc.gov/STD/.

References:

1. Centers for Disease Control and Prevention. Sexually Transmitted Diseases Treatment Guidelines, 2010. Morb Mort Wkly Rep (MMWR) 2010;59(12): 1-

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2. Centers for Disease Control and Prevention. Notice to readers: Recommendations regarding screening of refugee children for treponemal infection. MMWR Morb Mortal Wkly Rep 2005;54(37):933-934.

Screening for HIV-Infection During the Refugee Domestic Medical Examination

Key Points

Post-arrival screening:

- Beginning January 4th, 2010, refugees are no longer tested for HIV-infection prior to arrival in the U.S.
- Current CDC guidelines for the United States recommend HIV screening in health-care settings for all persons 13-64 years of age [1]. Screening of all refugees 13-64 years of age is recommended in accordance with this policy. Screening of all refugees on arrival, including those ≤12 years and ≥64 years of age, is also encouraged.
- Repeat screening 3-6 months following resettlement is recommended for refugees with a recent exposure or high-risk activity to identify individuals who may be in the "window period" when they arrive in the United States. Subsequent screening should be done in accordance with CDC guidelines.
- Specific testing for HIV-2 should be conducted for refugees who screen positive for HIV and are native to or have transited through the following countries: Angola, Benin, Burkina Faso, Cape Verde, Côte d'Ivoire (Ivory Coast), Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Mali, Mauritania, Mozambique, Niger, São Tomé, Senegal, Sierra Leone, and Togo.
- Screening should be performed on all refugees unless they decline (opt out). Refugees should be clearly informed orally or in writing that HIV testing will be performed. Oral or written information should include an explanation of HIV infection and the meanings of positive and negative test results, and the patient should be offered an opportunity to ask questions. With such notification, consent for HIV screening should be incorporated into the patient's general informed consent for medical care on the same basis as other screening or diagnostic tests. Where separate consent is mandated by State law, a separate consent form for HIV testing must be utilized. (A compendium of requirements in specific jurisdictions is available at http://nccc.ucsf.edu/.)
- Efforts should be made to understand the context of HIV testing, diagnosis, and care within specific cultural and societal norms. Information about HIV and HIV testing should be provided in the languages of the commonly encountered populations within the service area. The competence of interpreters and bilingual staff to provide language assistance to patients with limited English proficiency must be ensured.
- When a refugee declines an HIV test, this decision should be documented in the medical record.
- All HIV-infected individuals should receive culturally sensitive and appropriate counseling in their primary spoken language.
- Appropriate referral for care, treatment, and preventive services should be made for all individuals confirmed to be HIV-infected.

Special pediatric considerations:

- Children <13 years of age should be screened unless negative HIV status for the mother of the child can be confirmed and the child is otherwise thought to be at low risk of infection (no history of high-risk exposures such as previous blood product transfusions, early sexual activity, or history of sexual violence or abuse). In most situations, complete risk information will not be available, and thus most children <13 years of age should be screened.
- Children <18 months of age who test positive for HIV antibodies should receive further testing with DNA or RNA assays. Results of positive antibody tests in this age group can be unreliable because they may detect persistent maternal antibody.
- All children born to or breast-fed by an HIV-infected mother should receive chemoprophylactic trimethoprim/sulfamethoxazole beginning >6 weeks of age until they are confirmed to be uninfected.

Special considerations for pregnant women:

- The identification and treatment of HIV-infected pregnant women can prevent HIV infection in their infants. All refugee women who are pregnant should undergo routine HIV screening as part of their post-arrival and prenatal medical screening and care.

Background

The Global Burden of HIV

The HIV/AIDS pandemic remains one of the most serious global health challenges today [2, 3]. More than 30 million people were living with HIV at the end of 2007, with approximately 2.1 million deaths annually due to AIDS [2]. In addition, an estimated 2.7 million new HIV infections occurred in 2007 [2]. While HIV/AIDS affects individuals throughout the world, certain regions, such as sub-Saharan Africa, have disproportionally high prevalence rates (exceeding 20% in some countries). In addition, HIV/AIDS disproportionately affects certain vulnerable population groups, such as young adults, women, and children.

Refugees and HIV infection

The increasing global rates of new HIV infections, despite efforts in prevention, coupled with the increasing mobility of populations, make HIV/AIDS an important issue in every country. Although the link between HIV and migration is complex and nonlinear, multiple factors heighten the HIV risk for refugees. Economic distress, conflict, sexual abuse and violence, oppression, discrimination, exploitation, gender bias, and sociopolitical marginalization contribute to conditions in which transmission of HIV may be enhanced [4, 5]. However, few studies have been performed that document actual increased risk behaviors in specific refugee populations [5]. In addition, refugees are frequently excluded from the national health care systems of host countries where they reside, and, until recently, voluntary counseling and testing (VCT) was not provided in many camp settings or to urban refugee populations [6,7]. Even when VCT is available, many barriers may exist for refugee populations that make testing less accessible (e.g., mistrust in how asylum countries may use information, difficulty in maintaining confidentiality in refugee settings) [8].

Approximately 14% of the incoming refugees to the United States arrive from countries with HIV prevalence >5% [9-11]. These figures are based on country-specific HIV prevalence data from the end of 2006 and may underestimate true infection rates because of underreporting or lack of surveillance data. In addition, prior to resettlement, refugees may have traveled to or lived in other countries with high HIV prevalence rates. Refugees may also have been victims of physical and sexual violence and may be at risk of HIV acquisition through rape, blood product transfusions, or other medical procedures leading to infection, or through drug use [12-14]. Disclosure of these exposures may not be forthcoming during initial intake assessments. It is imperative that a scientific and rational approach to the screening, diagnosis, support and care of these individuals be developed and implemented.

Pre-departure medical screening

Prior to departure to the United States, all refugees undergo a pre-departure medical screening process. This process generally includes screening for inadmissible medical conditions (e.g., active tuberculosis), as well as presumptive pre-departure treatment for malaria and intestinal parasites, when appropriate. HIV has been removed from the list of inadmissible conditions, and refugees are no longer routinely tested for HIV prior to departure to the United States.

HIV screening during the domestic medical screening examination

Identifying HIV infection has implications for the individual refugee, the clinical provider, and the public health system. Early entry into care and treatment for HIV has been associated with improved survival [15]. The use of highly active antiretroviral therapy (HAART) has led to substantial declines in morbidity and mortality experienced by HIV-infected persons. In addition, knowing one's HIV status has important implications for the prevention of transmission to others.

Studies specifically examining the cost-effectiveness of screening refugees in the era of HAART in the United States are currently lacking. However, the cost-effectiveness of routine HIV screening in health-care settings is comparable with that of other commonly accepted screening interventions, even in populations with relatively low seroprevalence [16, 17]. The current guidance from CDC recommends testing for HIV as a routine part of medical care and stresses an "opt out" approach in which a patient is notified that testing will be performed unless the patient declines [1]. The current CDC guidelines are available at: www.cdc.gov/mmwr/preview/mmwrhtml/rr5514a1.htm.

Considerations for testing

Testing for HIV infection has historically been complicated by the diversity of the HIV genome and the inability of various assays to detect all types and subtypes of HIV. Currently, available assays are largely able to overcome these limitations, although an understanding of both population differences and variability in assay performance is important.

Two types of HIV are known to infect humans: HIV-1 and HIV-2. HIV-1 is the cause of the majority of HIV infections globally [18]. HIV-2 accounts for less than 1% of HIV

infections worldwide and is found mostly in West Africa, although cases have been reported from India, Europe, Brazil, and the United States [19]. While most available tests in use in the United States screen for both HIV-1 and HIV-2, specific testing for HIV-2 infection should be performed in individuals from areas where HIV-2 is common, if their HIV screening test is reactive.

HIV-1 is divided into three groups: Group M (major), Group N (nonmajor), and Group O (outlier) [20,21]. Group O is found in West and Central Africa and is of particular importance to HIV screening, as some assays fail to detect Group O infections. Group M constitutes 90% of current HIV infections and is further divided into phylogenetically distinct subtypes (A1-4, B, C, D, F1-2, G, H, J and K) [22]. Subtype B, found predominantly in the United States and Europe, has been the most studied subtype, although it represents less than 12% of worldwide infections. Globally, the most prevalent subtype is C, constituting half of all known infections. See below for a table of geographic distribution of subtypes [22].

Subtype	**Location**	**Proportion of known infections**
A	East and Central Africa, central Asia, eastern Europe (including Russia)	12.3%
B	Americas, Western Europe, East Asia, Oceania (including Japan)	10.2%
C	India, Nepal, Eastern and Southern Africa	49.9%
D	East and Central Africa	2.5%
G	West Africa, East Africa, Central Europe	6.3%
F, H, J, K	Various locations	<1% each
Circulating recombinant forms (CRFs)	Various locations	remainder

Available testing methods

Conventional Antibody Testing

EIA test results are classified as reactive or nonreactive. Specimens with a nonreactive result from the initial EIA are considered HIV-negative. Specimens with a reactive EIA result are retested in duplicate. If the result of either duplicate test is reactive, the specimen is reported as repeatedly reactive and undergoes confirmatory testing with a more specific supplemental test such as Western blot, immunofluorescence assay (IFA), or RNA testing [26]. Some laboratories report only a final result (not an initial reactive EIA result that is not confirmed). This reporting may have implications, particularly for individuals with very recent infections or for Group O infections.

The HIV-1 Western blot is a solid-phase EIA with immobilized viral antigens to detect IgG antibodies to specific HIV proteins. A Western blot is interpreted as positive if bands appear at the site of two or more of the following HIV antigens: p24, gp41, or gp120/160. Specimens that are repeatedly reactive by EIA and Western blot are considered HIV-positive. The Western blot is considered indeterminate if bands are present, but fewer than two of the latter bands are present. Specimens that are repeatedly EIA-reactive occasionally provide an indeterminate Western blot result, due either to an incomplete antibody response to HIV in an infected person or to nonspecific reactions in an uninfected person [27]. The Western blot is interpreted as negative only if no bands are present. Repeat Western blot or RNA testing, performed on a subsequent blood specimen, will distinguish persons with early infections from uninfected persons with persistent indeterminate results.

Current HIV EIAs are >99% sensitive and specific for HIV infection and are able to detect nearly all non-B subtypes and most group O infections [28]. However, Western blot may fail to detect group O in 10%-20% of specimens [29]. Individuals from areas with high rates of group O infection (e.g., Cameroon) with reactive EIAs but a negative Western blot should undergo further testing with assays known to detect group O (RNA testing).

Rapid Diagnostic Tests

Diagnostic testing for HIV also includes rapid antibody assays, whose sensitivity and specificity are high (≥ 99%) [31, 32]. Rapid tests may be particularly useful for screening individuals who may not return for the results of conventional screening tests. A rapid antibody test produces results in 20 minutes or less. Six FDA-approved rapid tests detect the presence of antibodies to HIV in blood, serum, or oral fluid specimens [33]. As with the conventional EIA, a reactive rapid HIV test result must be confirmed with a follow-up supplemental test (e.g., Western blot or RNA) before a final diagnosis of HIV infection can be made [33]. If confirmatory testing yields negative or indeterminate results, follow-up testing should be performed on a blood specimen collected 4 weeks after the initial reactive rapid HIV test result. Most rapid HIV-1 tests are capable of detecting all major subtypes of group M, although not all rapid HIV screening assays detect Group O. Four rapid tests are FDA-approved for detection of both HIV-1 and HIV-2, one of which can differentiate HIV-1 from HIV-2 [30].

Nucleic Acid Tests

A qualitative RNA test has been FDA-approved for diagnosis of acute HIV infection in antibody-negative persons. This test may also be used to confirm a reactive antibody screening test. Quantitative tests for HIV RNA are available, but are not FDA-approved for diagnosis. These RNA tests are routinely used to quantify viral load for monitoring progression of HIV disease [33]. HIV-1 RNA tests do not detect HIV-2, and the FDA has not approved an HIV-2 RNA or DNA test [30]. Plasma viral load is characteristically low in HIV-2 infection and RNA testing is unreliable for the detection of HIV-2. DNA testing for HIV-2 can be performed to confirm HIV-2 infection.

Pediatric screening considerations:

HIV disproportionately affects children of foreign-born mothers [34]. A 2002-2003 report of the Ministerial Council on HIV/AIDS in Canada estimated that 70% of all maternal HIV transmission to children in Canada occurred among women of African and Caribbean origin [34]. Despite HIV disease progression being more rapid in children and data suggesting that infected children have significantly improved survival when antiretroviral therapy is initiated early, HIV screening in children <15 years of age has often been restricted to those with identifiable risk factors (receipt of blood products, HIV-infected mother, or other risk factors identified by provider).

The diagnosis of HIV in children is complicated by the presence of passively acquired maternal anti-HIV immunoglobulin (IgG) in children born to HIV-infected mothers. Maternal antibody has been demonstrated in children up to 18 months of age, complicating interpretation of positive antibody test results [35]. The American Academy of Pediatrics recommends that infants born to HIV-positive mothers undergo DNA or RNA testing at day 14, again at 1-2 months of age, and then at 3-6 months of age. A positive RNA or DNA result at any age is a presumptive indicator of HIV infection but must be confirmed. The diagnosis of a HIV-infection is made if two DNA or RNA tests are positive. CDC guidelines state that HIV is definitively excluded by two negative RNA or DNA tests (at 1 month and >4 months) or two negative antibody tests from separate specimens obtained at age >6 months. Given that HIV can be transmitted from mother to child through breastfeeding, many clinicians confirm the absence of HIV-1 with a negative HIV-1 antibody assay at 12-18 months of age or after the child is no longer breastfeeding [35].

Summary:

Refugees represent a population vulnerable to HIV infection and disease. Given the known benefits of early detection, counseling, provision of antiretroviral therapy, and prevention of mother-to-child transmission, HIV screening should be offered to all refugees resettling in the United States.

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Press Release

CDC Expands Testing Recommendations For Chronic Hepatitis B Virus Infection

New Guidance Also Issued on Patient Management for Those Infected

For Immediate Release: September 18, 2008
Contact: National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Phone: 404-639-8895

The U.S. Centers for Disease Control and Prevention (CDC) today published new recommendations for health care providers that are designed to increase routine testing in the United States for chronic hepatitis B, a major cause of liver disease and liver cancer. CDC recommends testing all individuals born in Asia and Africa, as well as testing additional at-risk populations, including men who have sex with men (MSM) and injection-drug users (IDUs). The recommendations, published today in CDC's Morbidity and Mortality Weekly Report (MMWR) Recommendations & Reports, also for the first time give health professionals guidance for effective management of chronically infected hepatitis B patients.

"Chronic hepatitis B affects the lives of more than one million Americans, many of whom do not even know they are infected. These new recommendations are critical to identifying people who are living with the disease without the benefits of medical attention," said John W. Ward, M.D., director of CDC's Division of Viral Hepatitis. "Testing is the first step to identify infected persons so that they can receive lifesaving care and treatment, which can break the cycle of transmission, slow disease progression, and prevent deaths from liver cancer."

In the United States, chronic hepatitis B is the underlying cause of an estimated 2,000 – 4,000 deaths each year from cirrhosis and liver cancer. The CDC recommendations are key to increasing the early diagnosis of chronic hepatitis B virus (HBV) infection, since many of the estimated 800,000 – 1.4 million Americans with chronic HBV infection have no symptoms and are unaware of their disease.

Highlights of the recommendations

The new testing recommendations build upon and reinforce past recommendations to test all pregnant women, infants born to infected mothers, household contacts and sex partners of infected individuals, and people with HIV.

Along with continued testing of those groups, routine testing is now recommended for additional populations, including:

- Individuals born in Asia, Africa, and other geographic regions with 2 percent or higher prevalence of chronic HBV infections: Previous CDC recommendations called for testing of people born in areas with 8 percent prevalence or higher. Expanded testing is essential since the rate of liver cancer deaths and chronic HBV in the United States remains high among foreign-born U.S. populations from these areas. For example, nearly one in 12 Asian Americans and Pacific Islanders living in the United States is HBV-infected, and one-third or more are unaware.
- Men who have sex with men and injection drug users: Routine testing is needed for these persons since both have a higher prevalence of chronic HBV infection than the overall U.S. population. Up to 3 percent of MSM and up to 6 percent of IDUs are estimated to be chronically infected with HBV, compared to three tenths of one percent of the general population.
- Persons with abnormal liver function tests (not explained by other conditions) and persons who require immunosuppressive therapy (e.g., chemotherapy for malignant diseases).

The new CDC report also gives recommendations for referral of HBV-infected persons to specialists for ongoing monitoring and medical care. Such guidelines are needed now to assist providers, since most of the effective medications for chronic HBV treatment have become available only in the last five years. In addition, the recommendations advise healthcare providers to provide culturally-sensitive ongoing patient education, begin lifelong monitoring for progression of liver disease, and ensure protection of household members and other close contacts of infected persons.

Testing recommendations are a critical component of CDC's strategy to eliminate HBV transmission. CDC continues to work with the medical community to promote comprehensive prevention and treatment efforts for HBV, which include vaccination for all infants and at-risk adults; catch-up vaccination of previously unvaccinated children; routine screening for all pregnant women; treatment of newborns of infected or untested mothers; and testing household contacts and sex partners of HBV-infected persons.

For more information chronic hepatitis B infection, visit www.cdc.gov/hepatitis/HBV/TestingChronic.htm or www.cdc.gov/hepatitis/.

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