

**State of California Department of Health Services
DIVISION OF COMMUNICABLE DISEASE CONTROL
Microbial Diseases Laboratory
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A GUIDE TO SEROLOGIC SERVICES - MICROBIAL DISEASES LABORATORY (MDL)

1. Please use appropriate mailing containers and MDL laboratory report forms (syphilis serology, agglutination test, or special serology). Use one form for each specimen submitted. These materials are available from your local public health department laboratory.
2. Please provide all information requested on the laboratory report form. Include State history forms specific to Lyme disease and/or Bartonella testing, when required. Failure to do so may delay testing.
3. Submit adequate volumes: e.g., 5 ml whole clotted blood; 2 ml serum; 2 ml CSF. Collect specimens aseptically. Place in a sterile vial. Print patient's name and date taken on vial. Do not use preservatives or anticoagulants. Do not freeze whole blood (hemolyzed serum is unsatisfactory for testing). For STD blood specimens, avoid using pediatric vials, unless drawing children.
4. Specimens to be tested at the Centers for Disease Control (CDC) must be submitted through the MDL, and must be accompanied by pertinent information. See number 2 above and page 11 for information required.

DISEASE	TEST ⁽¹⁾	SOURCE ⁽²⁾	COMMENTS
Amebiasis	IHA	CDC	The IHA test detects antibody specific for <u>Entamoeba histolytica</u> at titers of 1:256 or greater in approximately 95% of patients with extra-intestinal amebiasis, 70% of patients with active intestinal infection, and in 10% of asymptomatic patients who are passing cysts of <u>E. histolytica</u> . Titers may persist for months or years even after successful treatment. Specificity is approximately 98%.
Amebic meningoencephalitis (Acanthamoeba) (Naegleria)	IFA	CDC	Experimental test for detection of antigen in tissue. Testing is not available without prior consultation with the Division of Parasitic Diseases, CDC, at (770) 488-4417.
Babesiosis	IFA	CDC	Titers may persist for 6-12 months after acute illness. Cross-reactions may occur with malaria infections.

DISEASE	TEST ⁽¹⁾	SOURCE ⁽²⁾	COMMENTS
Bartonellosis (Cat Scratch Fever)	IFA	CDC	Testing available only at the CDC on a limited basis. Acute and convalescent sera usually required (CSF not tested). A Bartonella history form is also required. NO LONGER AVAILABLE AT THE MDL. Contact Janice Lopez at (510) 412-3700
Blastomycosis	CF	CDC	Rise in CF titer is significant. Titer parallels severity. Test lacks sensitivity and specificity. Cross-reactions frequently occur with coccidioides and histoplasma infections.
	ID	CDC	Consistently anticomplementary sera are sent to CDC for ID testing. Demonstration of precipitin bands denotes recent or current infection.
Brucellosis <u>B. abortus</u> <u>B. melitensis</u> <u>B. suis</u> <u>B. canis</u>	TA	LOCAL, MDL	Availability of TA tests in local public health laboratories varies. Please contact your local laboratory for information regarding availability of tests and submission of specimens. Case history is required. Prior arrangement with the MDL is required for specimen submission, contact Janice Lopez at (510) 412-3700. <u>Brucella abortus</u> antigen is used for all tests, and will detect <u>B. abortus</u> , <u>B. melitensis</u> , or <u>B. suis</u> infections. Rise in titer is significant.
	MTA (Total AB) MTA (Ig G Titer)	CDC CDC	The Microtiter Agglutination test is available at the CDC only for testing specimens found to be positive in the TA test performed at the MDL. Specimens must have been previously tested with a positive result. Corroborating lab results must be submitted if tested elsewhere. The antigen used in this assay, <u>B. abortus</u> strain 1119-3, reacts with antibodies to naturally occurring strains of <u>B. abortus</u> , <u>B. melitensis</u> , and <u>B. suis</u> ; however, it does not detect antibodies to <u>B. canis</u> or other rough types, such as the vaccine strain <u>B. abortus</u> RB51.
	CF	CDC	The CF test can be used to detect IgG antibody which is considered indicative of active chronic infection. This test is done when clinical data are provided, and when specifically requested. NOTE: Antibodies developed in response to brucella vaccine or skin test antigens interfere with interpretation of test results. Cross-reactions may occur with <u>Vibrio cholerae</u> infection or immunization, <u>Francisella tularensis</u> infection, <u>Afipia clevelandensis</u> , <u>E. coli</u> O:157 infections, or <u>Yersinia enterocolitica</u> type 9 infection. <u>B. canis</u> serology is currently not offered at the CDC. Contact Janice Lopez for clarification 510-412-3700.

DISEASE	TEST ⁽¹⁾	SOURCE ⁽²⁾	COMMENTS
Candidiasis	ID LA ELISA	LOCAL, CDC	<p>A sero-conversion, an increase in the number of precipitin bands, or a four-fold rise in agglutinin titer provides presumptive evidence for candidiasis.</p> <p>Positive tests may indicate systemic candida infection or colonization with <u>Candida</u> sp., and results must be evaluated in relation to other clinical data.</p> <p>Cross-reactions may occur with torulopsis and cryptococcus infections.</p> <p>Experimental test. Detects mannan polysaccharide antigens produced by <u>Candida</u> sp. A positive test (2 ng/ml or greater) for antigenemia is presumptive evidence of invasive candidiasis and is of particular value in immunosuppressed patients. Precise interpretation of results awaits more extensive evaluation.</p>
Chagas' Disease (<i>T. cruzi</i>)	IFA	CDC	<p>Cross-reactions occur with other parasitic infections, particularly leishmaniasis. Tests become positive 3 weeks to 3 months after infection, reach maximum titers between 3 and 4 months after infection, and can remain positive for life at low titers.</p> <p>African trypanosomiasis: Immunodiagnostic tests for detection of <u>T. brucei rhodensiense</u> or <u>T. brucei gambiense</u> infections are <u>not available without prior consultation</u> with the Division of Parasitic Diseases, CDC, at (770) 488-4431.</p>
Coccidioidomycosis	CF ID	CDC CDC	<p>Rise in CF titer is significant. Titer parallels severity. Relatively specific. Cross-reactions rarely occur with blastomyces and histoplasma infections.</p> <p>Consistently anticomplementary sera are sent to CDC for ID testing. Demonstration of precipitin bands denotes recent, active, or inactive infection.</p>
Cryptococcosis			Testing is no longer available for cryptococcal antibody at the CDC or the MDL.

DISEASE	TEST ⁽¹⁾	SOURCE ⁽²⁾	COMMENTS
Cysticercosis	BLOT	CDC	Sensitivity is 98% in patients with neurocysticercosis with two or more cysts. Lower sensitivity (28% -72%) is found in patients with single or calcified cysts. Sensitivity is higher for serum samples than for CSF. <u>If submitting CSF, please also submit a serum sample at the same time.</u> Specificity is 100%.
Echinococcosis (Hydatid disease)	ELISA BLOT	CDC	Hydatid cysts in the lung and calcified cysts are less frequently detected by serological tests than active cysts in the liver. Antibody may persist for years after surgical removal of a hydatid cyst. False-positive reactions may occur in persons with other helminthic infections, cancer, or chronic immune disorder. Testing not performed on CSF. Positive reaction in the ELISA is ≥ 0.5 units. Sensitivity is 90%, specificity is 93%. Sensitivity and specificity of the BLOT are 86% and 99%, respectively.
Farmer's Lung (Hypersensitivity pneumonitis) (Thermophilic actinomycetes)	ID	CDC	Antigens include: <u>Micropolyspora faeni</u> , <u>Thermoactinomyces candidus</u> , and <u>T. vulgaris</u> . Demonstration of precipitin bands provides presumptive evidence of actinomycotic hypersensitivity pneumonitis.
Histoplasmosis	CF	CDC	Yeast-phase and mycelial-phase antigens are used. Rise in CF titer is significant. Titer parallels severity. Test lacks specificity. Cross-reactions frequently occur with blastomyces and coccidioides infection. Yeast-phase antigen is more sensitive, but less specific than mycelial phase.
	ID	CDC	Consistently anticomplementary sera are sent to CDC for ID testing. Two bands (H and M) have diagnostic value. The H band is generally associated with the M band, is not affected by skin testing, and is consistently found in patients with active histoplasmosis. The M band frequently appears alone, is affected by skin testing, and appears in acute or chronic infection. Demonstration of both bands is highly suggestive of active histoplasmosis. CAUTION: A single skin test may significantly increase antibody levels in sensitive individuals, making serologic test results uninterpretable.

DISEASE	TEST ⁽¹⁾	SOURCE ⁽²⁾	COMMENTS
Legionnaires' Disease	IFA	Available at Commercial Reference Labs	<p>NO LONGER AVAILABLE AT THE MDL.</p> <p>Antigen used is <u>Legionella pneumophila</u> serogroup 1 or multivalent Legionella species antigens. Antibody may appear late in infection - up to 6 to 8 weeks after onset.</p> <p><u>Acute and convalescent serum specimens required</u>, however a single convalescent specimen will be tested <u>if collected two or more weeks after onset</u> of symptoms.</p> <p>Serologic evidence supporting a recent infection is a 4-fold rise in antibody to a titer 1:128 or greater. Single or standing titers 1:256 or greater may indicate infection at an undetermined time.</p> <p>Negative results do not necessarily exclude infection.</p>
Leishmaniasis	IFA CF	CDC	<p>Cross-reactions frequently occur with Chagas' disease.</p> <p>Antibody detection is useful for diagnosing visceral leishmaniasis, but is less reliable for cutaneous leishmaniasis (tested with IFA only).</p>
Leptospirosis	MA IgM ELISA Dip-S-Ticks EIA	CDC CDC	<p>Testing consists of a quantitative microscopic agglutination assay using a battery of antigens.</p> <p>Cross-reactions with heterologous leptospiral antigens are frequently encountered in the acute stage. Rise in titer is significant.</p> <p><u>Paired sera</u> are usually required. Acute serum will be held until the convalescent serum is received and both tested in parallel.</p> <p>Assays detect IgM antibodies to <u>Leptospira</u> genus-specific antigens. The sensitivity on acute-phase specimens drawn ≤ 14 days after onset of symptoms was 64% by Dip-S-Ticks and 49% by IgM ELISA. Sensitivity on convalescent-phase specimens drawn > 14 days after onset was 93% by Dip-S-Ticks and 75% by IgM ELISA.</p> <p>A negative result does not exclude a diagnosis of leptospirosis. Some individuals may be immunologically unresponsive, or the serum specimen may have been drawn too early or late in the course of the disease.</p>

DISEASE	TEST ⁽¹⁾	SOURCE ⁽²⁾	COMMENTS
Paracoccidioidomycosis	ID	CDC	Demonstration of precipitin bands may denote active or inactive infection.
Paragonimiasis	BLOT	CDC	Sensitivity is 96%. Specificity is 99%.
Pertussis			Serological detection of antibody to Pertussis is no longer available at the CDC or the MDL.
Plague	PHA/HI ELISA	CDC CDC	<p>Prior arrangement must be made for specimen testing, contact Janice Lopez at (510) 412-3700.</p> <p>Rise in titer is significant. A titer of $\geq 1:10$ is considered positive. Serologic response is early in mild cases, but may be delayed in more severe cases. Serum specimens should be accompanied by pertinent history, including but not limited to, places of travel or residence, animal or arthropod contact. (See history form p.11).</p> <p>Experimental test: An IgG/IgM total antibody ELISA and an IgM capture ELISA is available to assist in the diagnosis of serum from persons who may be infected with plague.</p> <p>An ELISA IgG titer suggests past exposure, while a positive IgM Capture ELISA titer is consistent with current infection.</p>

DISEASE	TEST ⁽¹⁾	SOURCE ⁽²⁾	COMMENTS
Salmonellosis (Typhoid Fever)	TA	Available at Commercial Reference Labs	<p>NO LONGER AVAILABLE AT THE MDL. Do not submit specimens to the MDL for testing without prior approval.</p> <p>Note: CDC does <u>not</u> run this test routinely on non-outbreak related cases. Contact Bill Bibb at the CDC 404-639-3814 directly as to the availability of <i>Salmonella typhi</i> antibody and Vi testing. Additional testing / patient history will be required.</p> <p>Availability of TA tests in local public health laboratories varies. Please contact your local laboratory for information regarding availability of tests and submission of specimens.</p> <p>TA tests with H and O antigens may be useful if cultures are negative. A rise in titer is presumptive evidence of <u>Salmonella typhi</u> or other salmonellae infection.</p> <p>Titers are affected by: typhoid immunization; the presence of "normal" agglutinins; and antibiotic therapy.</p>
Schistosomiasis	FAST-ELISA BLOT	CDC	<p>Detects infection with <u>Schistosoma</u> species (specificity is 99%). A positive reaction is ≥ 9 units.</p> <p>99% Sensitivity for <u>S. mansoni</u> infection. 95% Sensitivity for <u>S. haematobium</u> infection.</p> <p>Immunoblot assays are species-specific. Detects <u>S. mansoni</u>, <u>S. haematobium</u>, or <u>S. japonicum/mekongi</u> infections (testing based on patient travel history).</p>
Sporotrichosis	LA TA	CDC	Titers 1:8 - 1:16 or greater provide presumptive evidence of infection, and are especially helpful in establishing a diagnosis of extracutaneous or systemic sporotrichosis.
Strongyloidiasis	ELISA	CDC	Sensitivity is 88%. Specificity is 80%. A positive titer is >8%.

DISEASE	TEST ⁽¹⁾	SOURCE ⁽²⁾	COMMENTS
Syphilis	Nontreponemal Treponemal	LOCAL, MDL CDC	Availability of the various serologic tests for syphilis varies widely. Please contact your local public health department laboratory for information regarding availability of tests, interpretation of results, and submission of specimens. Serologic tests do not differentiate syphilis from other treponematoses (yaws, pinta, bejel).
	Treponemal IgM 19S	CDC	Treponemal FTA-ABS (IgM 19S): Investigational test for the diagnosis of syphilis. Often used for neonatal congenital syphilis.
Trichinosis	ELISA	CDC	Positive reactions of >1.0 should be considered diagnostic of <u>Trichinella</u> infection acquired within the last year. Low level (0.4 - 1.0) positive reactions in ELISA may be false-positives, early infections, or residual antibody from an old infection. Specificity is 95%. False-negative results may occur in lightly infected patients or within the first 3-4 weeks of illness in moderately infected patients.
Tularemia	TA	LOCAL, MDL	Availability of tests in local public health laboratories varies. Please contact your local laboratory for information regarding availability of tests and submission of specimens. Exposure (insect, animal, camping, etc.) & any travel history are required. Prior arrangement must be made for specimen testing, contact Janice Lopez at (510) 412-3700. Rise in titer is significant. Titers remain elevated for years following infection. Cross-reactions may occur with brucella infections.
Visceral Larva Migrans (Toxocariasis)	ELISA	CDC	A titer of 1:32 or greater is indicative of infection at some time with <u>Toxocara</u> sp. Approximately 75% of patients with clinically-diagnosed visceral or ocular larva migrans have titers to <u>Toxocara canis</u> of 1:32 or greater. Specificity at titers of 1:32 or greater is 95%. Subclinical infection with <u>Toxocara</u> sp. is widespread, and titers of 1:32 or greater may be obtained in the serum of up to 10% of apparently normal persons. Titers of less than 1:32 are reported because of their possible value in assessing ocular infections, but must be interpreted with caution because of increased numbers of false-positive reactions.
Zygomycosis (Phycomycosis)	ID	CDC	Experimental test. Precise interpretation of results has not been established. Antigens used include: <u>Absidia corymifera</u> , <u>Mucor pusillus</u> , <u>Rhizopus oryzae</u> , and <u>R. arrhizus</u> .

- 1) BLOT = Immunoblot Assay
- CF = Complement Fixation Test
- Dip-S-Tick= Dipstick ELISA based Assay
- EIA = Enzyme immunoassay
- ELISA = Enzyme-Linked Immuno-Sorbent Assay
- ID = Immunodiffusion Test
- IFA = Indirect Fluorescent Antibody Test
- IHA = Indirect Hemagglutination Test
- LA = Latex Agglutination Test
- PHA/HI = Passive Hemagglutination/Hemagglutination Inhibition Tests
- MA = Microscopic Agglutination Test
- MTA = Microtiter Agglutination Test
- TA = Tube Agglutination Test
- WB = Western Blot Assay

Non-Treponemal Tests = RPR Card Test; VDRL Slide Test

Treponemal Tests = FTA-ABS Test; TP-PA Test, FADF Test

- 2) CDC = Centers for Disease Control and Prevention
- LOCAL = City or County Public Health Department or Clinical Laboratory
- MDL = Microbial Diseases Laboratory, State of California Department of Health Services
- VRDL = Viral and Rickettsial Disease Laboratory, State of California Department of Health Services

IMPORTANT. CDC NOW REQUIRES THAT PERTINENT PATIENT, CLINICAL, AND EPIDEMIOLOGICAL INFORMATION ACCOMPANY SPECIMENS SENT TO THEIR LABORATORIES FOR SEROLOGIC TESTS. SPECIMENS WILL NOT BE TESTED UNTIL THIS INFORMATION IS PROVIDED.

Items 1-11 are required. Items in **bold** are especially important. When pertinent, information requested in Items 12-13 must also be provided.

1. **NAME.**
2. **SEX.**
3. **BIRTHDATE.**
4. **TYPE OF SPECIMEN** (serum, CSF, etc.).
5. **DATE SPECIMEN TAKEN** (month, day, year).
6. **DATE OF ONSET** of Symptoms (month, day, and year illness started. If uncertain, give approximate date). **REQUIRED**
7. CLINICAL DIAGNOSIS (if none has been made, indicate why this test is required).
8. **MAJOR SIGNS AND SYMPTOMS.**
9. ASSOCIATED ILLNESS OR UNDERLYING CONDITIONS, IF PRESENT (e.g., immunodeficiency syndromes, cancer, arthritis, renal transplant, etc.).
10. **FATAL.**
11. PERTINENT LABORATORY FINDINGS (e.g., stool examination for ova and parasites negative, blood smear examination negative, etc.).
12. **EPIDEMIOLOGICAL DATA.** WHEN RELEVANT TO THE DISEASE SUSPECTED, GIVE PLACES OF TRAVEL OR RESIDENCE, ANIMAL OR ARTHROPOD CONTACT, SUSPECTED SOURCE OF INFECTION. ETC.
13. TREATMENT, IF RELEVANT (Administration of immune serum or globulin, or of antibiotics, which could affect detection of immune response. List drugs and give dates, if known.)
14. **PRIOR APPROVAL GIVEN BY:** If specified in the Guide to Serological Services, indicate who at the MDL (or the CDC) has approved this specimen for testing.

Please provide specimen and patient information (Items 1-5) on Special Serology form (MDL LAB FORM #413) for each specimen submitted. Information in Items 6-13 can be provided on the Serology form or as an attachment.