

Febrile Antibodies Panel

REPLACES THE FEBRILE AGGLUTININS PANEL WITH UP-TO-DATE SEROLOGICAL ASSAYS FOR RICKETTSIA ANTIBODIES

Test Highlights

- The indirect fluorescent assay (IFA) specific for *Rickettsia rickettsii* (Rocky Mountain spotted fever) and *Rickettsia typhi* (typhus fever) antibodies replace the nonspecific and insensitive Weil-Felix test offered in the traditional Febrile Agglutinins Panel.
- *Brucella* antibodies and *Salmonella typhi* antibodies (Widal agglutinins or typhoid fever antibodies) are assayed by the traditional direct agglutination assay.
- There are several reasons for a change from the Weil-Felix methodology to better methods. The Weil-Felix test relies on the agglutination of certain strains of the enteric bacterium, *Proteus vulgaris* (Proteus OX-19 Abs; Proteus OX-2 Abs; Proteus OX-K Abs), which shares cross-reactive antigens with certain *Rickettsia*. The results of the Weil-Felix test are nonspecific and insensitive, yet many hospitals use it despite the availability of better methods. Patients with prior infections due to *Proteus sp.* (i.e., urinary tract or wound infections) will have false-positive results with this method.

Clinical Background

- *Rickettsiae* are gram-negative, obligate, intracellular organisms. Diagnosis of infection is by serology since *Rickettsia* is difficult to culture. Any antibody reactivity to *Rickettsia rickettsii* should be considered group reactive to any species in the spotted fever group of *Rickettsia*, including *R. conorii*, *R. honei*, *R. akari*, *R. japonica*, *R. australis*, and *R. sibirica*. Antibody reactivity to *Rickettsia typhi* should be considered group reactive to both *R. prowazekii* and *R. typhi*.
- *Brucella* are gram-negative coccobacilli that commonly infect cows (*B. abortus*), pigs (*B. suis*), and goats (*B. melitensis*), along with wild animals such as deer, elk, buffalo, and moose. *Brucella sp.* can be cultured in the bacteriology laboratory; however, serologic tests are generally used for the diagnosis of brucellosis because isolation of the organism is difficult. The agglutination test is the principal serologic test employed, but *Brucella* IgG-specific and IgM-specific ELISA tests are now available.
- *Salmonella sp.* are gram-negative enteric bacteria that are readily cultured in the bacteriology laboratory. Typhoid fever is best diagnosed by isolation of the organism from blood culture, which is positive in the first week of illness in 80 percent of patients who have not taken antibiotics. Cultures of bone marrow occasionally are positive when blood cultures are not. Serology may be helpful in cases where culture is not possible or difficult. Stool culture is not reliable because it may be positive in gastroenteritis without typhoid fever.

Disease Overview

- The incubation period for most rickettsioses is three to 14 days. Most patients develop nonspecific symptoms and signs. Fever and headache are the most common symptoms, but chills, myalgias, arthralgias, malaise, and anorexia also are noted. Rash is a hallmark of infection for both Rocky Mountain spotted fever and typhus. The absence of rash, however, should not rule out a possible rickettsial serology.
- Brucellosis has an incubation period of one to three weeks. Fever, sweats, headache, back pain, and weakness are clinical symptoms of mild infections, but severe complications such as CNS infections of endocarditis occur in about 5 percent of cases.

- The incubation period for typhoid fever is five to 14 days. Infection begins when organisms cross the intestinal mucosa. Symptoms include increasing malaise, headache, cough, and sore throat. Abdominal pain and constipation are often present while the fever ascends in a stepwise fashion. After about seven to 10 days, the fever reaches a plateau and the patient is much more ill, with exhaustion and prostration. Marked constipation may develop into “pea soup” diarrhea. Splenomegaly, abdominal distention and tenderness, relative bradycardia, dicrotic pulse, and occasionally meningismus appear. The rash (rose spots) commonly appears during the second week of disease.

Epidemiology

- Rocky Mountain spotted fever (RMSF) is a tick-borne disease, while typhus is transmitted by lice. Typhus is often seen in conditions of poor hygiene and overcrowding such as refugee camps and war zones throughout the world. In the southeast United States, typhus has been transmitted to humans from flying squirrels that are often kept as pets.
- Over 70 percent of reported cases of brucellosis occur in the meat-processing and livestock industries. Infection is generally via skin wounds, but the organisms can also be inhaled. A common route of *Brucella* infection is to eat or drink infected dairy products that have not been pasteurized.
- Approximately 400 cases of typhoid fever occur per year in the United States, mostly among travelers. An estimated 21 million cases of typhoid fever and 200,000 deaths occur worldwide. Infection is transmitted by consumption of contaminated food or water.

Indications for Ordering

- This profile is useful for the laboratory support of infections associated with *Rickettsia* (eg., RMSF), *Brucella sp.*, and *Salmonella typhi*.
- Some studies have indicated that febrile agglutinins panels are overutilized and are often difficult to interpret.
- These studies conclude it is better to make a diagnosis based on clinical findings and epidemiological criteria and select specific tests to confirm the diagnosis.

Additional Ordering Notes

- Antibodies against *Francisella tularensis* (tularemia) are sometimes included in a febrile agglutinins panel and may be ordered as a separate test if clinically indicated.
- An ELISA assay is also offered for the detection of *Brucella* IgM and IgG antibodies.

Interpretation

- Positive IgM antibodies to *Rickettsia rickettsii* and *R. typhi* are indicative of an acute infection with these organisms. A low-positive IgM value, however, needs to be interpreted with caution. A positive IgG for the *Rickettsia* organisms may indicate past or current infection. Rising or falling values may be needed to confirm an acute infection when using the IgG value alone.
- High-positive titers to the *Salmonella* and *Brucella* agglutinins may be indicative of an acute infection. Low titers may indicate past infection. Rising or falling acute and convalescent titers may be needed to confirm an acute infection.

Limitations

- Antibodies are often negative during the acute stage of the illness.
- Acute and convalescent titers measured one to two weeks apart are often needed to confirm an acute infection.

Methodology

- Direct agglutination is used for detection of antibodies to *Brucella* and the O and H antigens of *S. typhi* and *paratyphi*.
- An IFA is used for the detection of IgM and IgG antibodies to *Rickettsia typhi* and *Rickettsia rickettsii*.

Related Tests

- *Brucella* Antibodies, IgM and IgG (0050333)
- *Francisella tularensis* Antibodies, Total (0092305)

References

1. Zuerlein TJ, Smith PW. The diagnostic utility of the febrile agglutinin tests. *JAMA* 1985; 254(9):1211-4.
2. Chow CB, Wang PS, Cheung MW, Yan WW, Leung NK. Diagnostic value of the Widal test in childhood typhoid fever. *Pediatr Infect Dis J* 1987; 6(10):914-7.
3. Burke DS, Brown SL. Lack of diagnostic utility of "febrile agglutinin" screens. *Mil Med* 1980; 145(9):624-7.
4. Pang T, Puthucheary SD. Significance and value of the Widal test in the diagnosis of typhoid fever in an endemic area. *J Clin Pathol* 1983; 36(4):471-5.

Test Information

0051638

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For specific collection, transport, and testing information, refer to the ARUP Web site at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at www.arupconsult.com.