Yersinia IgG & IgA by Western blot

USEFUL IN DIAGNOSING *YERSINIA*-INDUCED REACTIVE ARTHRITIS

Clinical Background

The genus *Yersinia* includes three different gram-negative coccobacilli species that are pathogenic to humans: *Y. enterocolitica*, *Y. pseudotuberculosis*, and *Y. pestis*. Infections with *Y. enterocolitica* are transmitted primarily to humans through soil, water, animals, and food. Infection with *Y. enterocolitica* occurs most often in young children. The infection manifests in the gastrointestinal tract causing symptoms of diarrhea; loose, watery, or bloody stools; abdominal pain; and fever. *Y. pseudotuberculosis* is the least pathogenic of the *Yersinia* species and causes a zoonotic disease with symptoms similar to those of *Y. enterocolitica*. Infections with *Y. enterocolitica* and *Y. pseudotuberculosis* can be asymptomatic, mild, or severe, with infection resolving within a few weeks, with or without the use of antibiotics, depending on the severity of the infection. However, complications with the development of an inflammatory arthritis, known as reactive arthritis, can manifest one to four weeks post-infection, with increased risk if the individual is positive for the MHC HLA-B27 allele. *Y. pestis*, the causative agent of the bubonic and pneumonic plague, is transmitted to humans through flea bites or inhalation. There is no known association between a *Y. pestis* infection and the development of reactive arthritis.

The incidence of reactive arthritis in Scandinavia following *Y. enterocolitica* infection among adults is estimated to be 10-30 percent. The incidence is much lower in most other countries, including the United States. The most commonly affected joints are the knees and ankles, but other joints such as toes, fingers, and wrists can be involved. In most cases, two to four joints become involved sequentially and asymmetrically over a period of a few days to two weeks. Monoarticular arthritis occurs less commonly. In two-thirds of cases, the acute arthritis persists for one to four months. Chronic joint disease or ankylosing spondylitis occurs rarely. Less common nonsuppurative sequelae of *Y. enterocolitica* infections include reactive uveitis, iritis, conjunctivitis, glomerulonephritis, and urethritis. Reiter's syndrome (arthritis, conjunctivitis, and urethritis) is seen in only 5 to 10 percent of patients with *Yersinia*-induced arthritis.

Serologic tests can be used to support a diagnosis of yersiniosis. Since *Yersinia* can crossreact with other bacteria (e.g., *Bartonella henselae*, *Borrelia burgdorferi*, *Brucella*, *Chlamydia pneumoniae*, *Francisella tularensis, Rickettsia rickettsii,* and *Vibrio* species) and with serum from some patients with Graves disease, results should be interpreted with caution. With yersiniosis, antibody levels begin to rise within the first week of illness, peak in the second week, and then return to normal within three to six months. Antibodies may remain detectable for several years. PCR tests to detect yersinial DNA in clinical specimens are experimental at this time.

In *Yersinia*-induced reactive arthritis, the synovial fluid is sterile. The white blood cell count of the synovial fluid ranges from a few hundred to 60,000/µL, with a majority being neutrophils. Antinuclear antibodies and rheumatoid factor are usually absent. The isolation of a pathogenic *Yersinia* strain from feces is the most specific test for the diagnosis of yersiniosis. However, culture is not very sensitive in reactive arthritis and serologic tests for *Yersinia* can be helpful diagnostically in cases with a high index of clinical suspicion. In cases of *Yersinia*-induced reactive arthritis, IgA antibodies tend to persist for longer periods than in cases without arthritis. IgA antibodies can persist for 14 to 16 months after the onset of infection, with peak levels correlating directly with the severity of arthritis. IgG antibodies can also persist longer in patients with reactive arthritis, but not as consistently as IgA antibodies. It is recommended that IgG and IgA antibodies be tested in cases of acute and chronic reactive arthritis.

Indications for Use

This test detects IgG and IgA antibodies against *Yersinia* in serum samples.

Interpretation

A positive result with consistent clinical symptoms and history is supportive of a diagnosis of *Yersinia* infection.

Limitations

- Serologic results from this assay aid in diagnosis and should not be used as the sole method of diagnosis.
- Extensive crossreactivity has been shown to exist between *Yersinia*, *Bartonella henselae*, *Borrelia burgdorferi*, *Brucella*, *Chlamydia pneumoniae*, and *Rickettsia rickettsii* species. The literature suggests that crossreactivity between *Yersinia*, *Francisella tularensis*, *Vibrio,* and thryoid-stimulating immunoglobulin may also exist. Therefore, results should be interpreted with caution and correlated with clinical information.

Methodology

Samples are assayed using Western blot methodology. Diluted serum is incubated with nitrocellulose strips that contain the purified *Yersinia* outer membrane protein antigens. If antibodies against *Yersinia* are present in the serum, they bind to the immobilized antigens on the strip. Following the incubation period, the strips are washed with a diluted wash buffer to remove any unbound material. Next, the strips are incubated for 15 minutes with a diluted alkaline-phosphatase conjugated anti-human immunoglobulin (IgA and IgG specific). The conjugate binds to any antigen-antibody complexes that formed during the first incubation. The strips are then rewashed to remove any unbound conjugate. Finally, a chromogen substrate solution is incubated with the strips for five to 15 minutes. During this time, the chromogen substrate causes a reaction with the bound alkaline phosphatase of the conjugate to develop a color band on the blots. The color development is terminated by washing in deionized or distilled water. The intensity of each band on each strip is compared to the 35 kDa cut-off band on the cut-off strip. Antibodies against the pathogenic strains of *Y. enterocolitica* and *Y. pseudotuberculosis* will be detected with the *Yersinia* Western blot. Further studies are currently being performed to indicate whether the *Yersinia* Western blot will detect specific antibodies to *Y. pestis*.

Test Highlights

- Utilizes *Yersinia* outer membrane protein (Yops) antigens for the detection of *Yersinia* antibodies.
- This test offers differentiation of IgG and IgA antibodies, which may indicate the state of the disease.
- This assay will detect antibodies against *Y. enterocolitica* and *Y. pseudotuberculosis* species.
- More sensitive and specific than current complement fixation method.

Related Tests

- Stool culture is recommended during acute infection when the patient has diarrhea.

REFERENCES

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- Colmegna I, et al. HLA-B27-associated reactive arthritis: pathogenetic and clinical considerations. Clin Micro Rev 2004; 17:348-69.
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- Leirisalo-Repo M. *Yersinia* arthritis. Contrib Microbiol Immunol 1987; 9:145-54.

For specific collection, transport, and testing information, refer to *Yersian* Species Antibodies, IgA & IgG by Western Blot (0051230) the ARUP Web site at www.aruplab.com.