EDUCATIONAL COMMENTARY – 2003 2nd TEST EVENT
Immunology
The Use of Rheumatoid Factor in Diagnosis of Rheumatoid Arthritis

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Learning Outcomes
Upon completion of this exercise, the participant will be able to:

• Describe the disease process and symptoms of rheumatoid arthritis.
• Discuss the incidence of the disease.
• Discuss the rheumatoid factor test as related to the diagnosis of rheumatoid arthritis.
• List diseases which may result in false-positive rheumatoid factor tests.

Rheumatoid arthritis (RA) is an autoimmune disease. It manifests itself as a chronic inflammatory disease of the joints and the area surrounding the joint tissues that is characterized by swelling, stiffness, pain, and loss of function of the joints. Symptoms vary considerably from patient to patient but often include fever and fatigue. Over 2 million adults in the United States have RA. The onset of the disease occurs most commonly in middle age, though children and young adults may also develop it. The highest incidence of the disease occurs in women between the ages of 30 and 50 and it occurs twice as often in women than in men.

A description of rheumatoid arthritis as a disease process requires an understanding of the anatomy of the joint. A joint is the point at which two bones meet. Cartilage covers the ends of the bones to prevent deterioration that is caused by friction. Joints are surrounded by a protective capsule lined with a tissue called synovium. The synovium produces a lubricating fluid known as synovial fluid. Patients with RA have chronic inflammation of the synovium which eventually results in abnormal growth of the synovial tissue. The increased thickness of the synovium and the inflammatory process are responsible for the swelling, redness, and warmth that occur in the area of the joint. Continued growth of synovial tissue results in destruction of the cartilage and bone. The disease is systemic, meaning that the sites of inflammation may include almost any body tissue and may occur in multiple sites in an individual. The joints are most susceptible but other tissues, such as the sac surrounding the heart and the lining of the lungs and blood vessels, may also be affected.

Diagnosis of RA is often difficult due to the variation of symptoms that may be present and the fact that the symptoms are similar to those of other diseases that affect the joints. The slow progression of the disease also adds to the difficulty in diagnosis. Diagnosis of RA requires evaluation of the clinical symptoms, physical examination of the joints of the patient, and laboratory testing. X-rays may or may not be used in diagnosing RA, but are utilized after bone destruction has occurred. X-rays can be performed periodically after diagnosis to monitor the progression of the disease.
Seventy to eighty percent of patients diagnosed with RA have rheumatoid factor (RF) in their serum and synovial fluid. A negative result does not rule out a diagnosis of RA. Positive results for RF are also demonstrated in most patients with RA-associated diseases, such as Sjogren’s syndrome. Sjogren’s syndrome is an autoimmune disease which results in abnormal dryness of the eyes, mouth, and other mucous membranes and it occurs in a significant percentage of RA patients. Low titers of rheumatoid factor may be present in individuals with other disease states, such as systemic lupus erythematosus, endocarditis, tuberculosis, viral infections, chronic infections, hepatitis, chronic hepatic disease, and syphilis. Rheumatoid factor levels may disappear when infections have been treated with antibiotics. Patients with sarcoidosis may exhibit high titers of RF. Patients with juvenile RA are usually negative for RF.

The most commonly performed laboratory test for RA is the assay for rheumatoid factor. Rheumatoid factor is a macroglobulin which acts like an antibody and will react with gamma globulin. Most laboratories utilize a rapid slide test, but tube tests are also available. The assay may be performed on serum or synovial fluid. In the assay, visible agglutination occurs when reagent gamma globulin (antigen) that is attached to a particulate carrier reacts with rheumatoid factor in the patient specimen. The particulate carrier for the antigen may be latex particles (latex agglutination) or erythrocytes (hemagglutination). Assays using erythrocytes as the particulate carrier are more specific, while assays using latex as the carrier are more sensitive. Low titers of RF may be demonstrated in individuals without apparent disease (false positives). Incidence of RF also increases as individuals age. Each method will state a minimum titer that must be present to indicate a disease state. In comparison to latex agglutination, hemagglutination procedures have better specificity and produce fewer false positives. Some false positives may occur in hemagglutination procedures due to interference by heterophile antibodies, as in individuals with infectious mononucleosis. ELISA and nephelometric procedures may also be performed to detect RF.

Other laboratory tests that may be increased in RA are erythrocyte sedimentation rates and C-reactive protein. Complement levels may vary. In active disease, increases of complement levels may result from increased synthesis, or decreased complement levels may occur due to depletion of circulating components. Often complement levels are within normal limits. Low titers of antinuclear antibodies may also be present in individuals with RA. Patients often also have a normochromic, normocytic anemia.

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