Overview

Useful For
Evaluating patients suspected of having rheumatoid arthritis (RA)
Differentiating RA from other inflammatory arthritis or connective tissue diseases

Testing Algorithm
See Connective Tissue Disease Cascade (CTDC)

Special Instructions
- Connective Tissue Disease Cascade (CTDC)

Method Name
Enzyme-Linked Immunosorbent Assay (ELISA)

NY State Available
Yes

Specimen

Specimen Type
Serum

Specimen Required
Container/Tube:
Preferred: Serum gel
Acceptable: Red top

Specimen Volume: 0.5 mL

Forms
If not ordering electronically, complete, print, and send a General Request (T239) with the specimen.

Reject Due To

| Gross hemolysis | Reject |
| Gross lipemia   | Reject |
| Gross icterus   | OK     |
| Heat-treated specimen | Reject |

Specimen Minimum Volume
0.4 mL

Specimen Stability Information

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum</td>
<td>Refrigerated (preferred)</td>
<td>21 days</td>
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Clinical & Interpretive

Clinical Information
Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease characterized by interactions between the environment, specific genetic risk factors, and the human immune system. It affects about 0.6% of the US population with a global prevalence of 0.24%.(1) Clinically, RA is typified by progressive damage of synovial joints, inflammation, production of diverse autoantibodies, and variable extra-articular manifestations.(2-4) Patients with RA may be categorized based on the phase of disease (early versus established), presence or absence of antibodies (seropositive versus seronegative), clinical manifestations (joint erosion, interstitial lung disease, or cardiovascular), or specific risks (genes, gender, or smoking).(2-4) Delayed diagnosis of RA is associated with joint erosion, destruction or deformities, poor response to treatment with ultimate increase in morbidity, and mortality.(3,4)

Although late RA prognosis may be linked to adverse consequences, early diagnosis has been reported to improve outcomes; notably reduced joint destruction or deformity, delayed radiologic progression, and decreased functional disability.(3-5) To facilitate early diagnosis, the American College of Rheumatology/European League Against Rheumatism 2010 RA classification criteria recommend testing for rheumatoid factor (RF) and anticitrullinated protein antibodies (ACPA).(2) RF is an autoantibody directed against the Fc portion of immunoglobulin while ACPA are directed against peptides and proteins containing citrulline, a modified form of the amino acid arginine.(6,7) In addition to the use of RA and ACPA IgG to diagnose RA, RF and ACPA isotype antibodies and other serologic biomarkers have been used to predict if, and when, an individual who has inflammatory arthritis (IA) may develop future clinically apparent IA and access genetic and/or environmental risks.(3,4,8,9)

Compared to early serologic tests for RA including RF, several studies have demonstrated that ACPA have much improved specificity for RA.(4,6,10) A systemic review and meta-analysis of 33 studies including patients with RA and healthy or disease controls demonstrated the sensitivity of anti-mutated citrullinated vimentin, anticyclic citrullinated peptide, and RF of 71%, 71%, 77%, with the specificity of 89%, 95%, 73%, and the area under the curve of the summary receiver operating characteristic of 89%, 95%, 82%, respectively.(10) Based on these studies, there exist a subset of patients with RA who are negative for RF and ACPA IgG (seronegative) who must be diagnosed clinically or with use of emerging diagnostic tests.(4,7,9)

See Connective Tissue Disease Cascade (CTDC).

Reference Values
<20.0 U (negative)
20.0-39.9 U (weak positive)
40.0-59.9 U (positive)
> or =60.0 U (strong positive)
Reference values apply to all ages.

Interpretation
A positive result for cyclic citrullinated peptide (CCP) antibodies may be suggestive of rheumatoid arthritis (RA) if compatible clinical features of disease are present. Significantly elevated levels of CCP antibodies may be useful to identify RA patients with erosive joint disease.

A Mayo Clinic prospective clinical evaluation of the CCP antibody test showed a diagnostic sensitivity for RA of 78% with fewer than 5% false positive results in healthy controls (see Cautions).
Cautions
Positive results for cyclic citrullinated peptide (CCP) antibodies may occur in some patients with systemic lupus erythematosus or other autoimmune, connective tissue diseases. In a Mayo Clinic study (see Interpretation), the false-positive rate in this subgroup was approximately 10%.
Anti-rheumatic therapy should not be initiated based solely on a positive test for CCP antibodies, and changes in treatment should not be based upon the levels of CCP antibodies.

Clinical Reference

Performance

Method Description
Cyclic citrullinated peptide (CCP) antibodies in serum are detected by binding to the wells of a commercial microtiter plate coated with synthetic CCP. During the first incubation, serum antibodies bind to adsorbed, solid phase CCP. The wells are then washed to remove unbound serum constituents, and horse radish peroxidase-labeled goat anti-human IgG antibody is added. After further incubation and washing to remove unbound conjugate, substrate (3,3',5,5' tetramethylbenzidine) is added and allowed to incubate. The reaction between enzyme and substrate is stopped and color in the wells is measured in a microtiter plate reader. The concentration of CCP antibodies is determined by comparison to a 5-point standard curve (15.6-250 U). Testing is performed on the Agility instrument by Dynex. (Package insert: Quanta Lite CCP IgG ELISA. INOVA Diagnostics; 02/2020)
Test Definition: CCP
Cyclic Citrullinated Peptide Ab, S

PDF Report
No

Specimen Retention Time
14 days

Performing Laboratory Location
Rochester

Fees & Codes

Test Classification
This test has been cleared, approved, or is exempt by the US Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information
86200