Overview

Useful For
Evaluating patients suspected of having rheumatoid arthritis (RA)

Differentiating RA from other connective tissue diseases that may present with arthritis

Testing Algorithm
See Connective Tissue Disease Cascade (CTDC) in Special Instructions.

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.

Specimen Minimum Volume
0.4 mL

Reject Due To

<table>
<thead>
<tr>
<th>Rejected Reason</th>
<th>Acceptability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemolysis</td>
<td>Mild OK; Gross reject</td>
</tr>
<tr>
<td>Lipemia</td>
<td>Mild OK; Gross reject</td>
</tr>
<tr>
<td>Icterus</td>
<td>Mild OK; Gross OK</td>
</tr>
<tr>
<td>Other</td>
<td>NA</td>
</tr>
</tbody>
</table>

Specimen Stability Information
Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by chronic joint inflammation that ultimately leads to joint destruction. RA affects approximately 1% of the world's population. The diagnosis of RA is established primarily on clinical criteria and serologic findings. Historically, rheumatoid factor (RF), which is an antibody specific for the Fc portion of human IgG, has been considered a marker for RA. RF is, in fact, one of the diagnostic criteria for RA that was established by the American College of Rheumatology. Although 50% to 90% of patients with RA are RF-positive, the specificity of the RF test is known to be relatively poor. RF is found in many patients with other autoimmune diseases, infectious diseases and some healthy individuals. Consequently, a search for better diagnostic markers, with improved specificity for RA, ensued. Antiperinuclear factor (APF) and antikeratin antibodies (AKA), identified by immunofluorescence, were found to have a specificity of close to 90% for RA, but testing for these autoantibodies has never become popular. It was subsequently determined that APF and AKA react with the same antigen, specifically a citrullinated form of filaggrin (citrulline is an unusual amino acid formed by posttranslational modification of arginine residues by the enzyme peptidyl arginine deaminase). Recombinant filaggrin fragments, after enzymatic deamination in vitro, react with autoantibodies in RA sera. Synthetic cyclic citrullinated peptide (CCP) variants also react with anti-filaggrin autoantibodies and serve as the substrate for detecting anti-CCP antibodies serologically. Most studies of anti-CCP antibodies demonstrated that these autoantibodies have much improved specificity for RA compared to RF.

**Clinical and Interpretive**

**Clinical Information**

Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by chronic joint inflammation that ultimately leads to joint destruction. RA affects approximately 1% of the world's population. The diagnosis of RA is established primarily on clinical criteria and serologic findings. Historically, rheumatoid factor (RF), which is an antibody specific for the Fc portion of human IgG, has been considered a marker for RA. RF is, in fact, one of the diagnostic criteria for RA that was established by the American College of Rheumatology. Although 50% to 90% of patients with RA are RF-positive, the specificity of the RF test is known to be relatively poor. RF is found in many patients with other autoimmune diseases, infectious diseases and some healthy individuals. Consequently, a search for better diagnostic markers, with improved specificity for RA, ensued. Antiperinuclear factor (APF) and antikeratin antibodies (AKA), identified by immunofluorescence, were found to have a specificity of close to 90% for RA, but testing for these autoantibodies has never become popular. It was subsequently determined that APF and AKA react with the same antigen, specifically a citrullinated form of filaggrin (citrulline is an unusual amino acid formed by posttranslational modification of arginine residues by the enzyme peptidyl arginine deaminase). Recombinant filaggrin fragments, after enzymatic deamination in vitro, react with autoantibodies in RA sera. Synthetic cyclic citrullinated peptide (CCP) variants also react with anti-filaggrin autoantibodies and serve as the substrate for detecting anti-CCP antibodies serologically. Most studies of anti-CCP antibodies demonstrated that these autoantibodies have much improved specificity for RA compared to RF.

See Connective Tissue Diseases Cascade (CTDC) in Special Instructions.

**Reference Values**

- <20.0 U (negative)
- 20.0-39.9 U (weak positive)
- 40.0-59.9 U (positive)
- ≥60.0 U (strong positive)

Reference values apply to all ages.

**Interpretation**

A positive result for cyclic citrullinated peptide (CCP) antibodies indicates a high likelihood of rheumatoid arthritis (RA).

A Mayo 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). CCP antibodies have also been reported in approximately 40% of seronegative RA patients, and, like rheumatoid factor (RF), a positive CCP antibody result indicates an increased likelihood of erosive disease in patients with RA.

High levels of CCP antibodies may be useful to identify patients with aggressive disease, but further studies are needed to document this association. The level of CCP antibodies may also correlate with disease activity in RA, but
further studies are needed to document this clinical application.

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 the Mayo study mentioned above, the false-positive rate in this subgroup was approximately 10%.

Antirheumatic 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 (Quanta Lite CCP3 IgG ELISA, INOVA Diagnostics). 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 CCP3 IgG ELISA. INOVA Diagnostics. San Diego, CA 11/2010)

PDF Report

No

Day(s) and Time(s) Test Performed

Monday through Saturday; 4 p.m.

Analytic Time

Same day/1 day

Maximum Laboratory Time

3 days

Specimen Retention Time

14 days

Performing Laboratory Location

Rochester
Test Definition: CCP
Cyclic Citrullinated Peptide Ab, S

Fees and Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification
This test has been cleared or approved by the U.S. 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

LOINC® Information

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Test Order Name</th>
<th>Order LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCP</td>
<td>Cyclic Citrullinated Peptide Ab, S</td>
<td>32218-0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Result ID</th>
<th>Test Result Name</th>
<th>Result LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCP</td>
<td>Cyclic Citrullinated Peptide Ab, S</td>
<td>32218-0</td>
</tr>
</tbody>
</table>