

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

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	21 days	
	Frozen	21 days	

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.(1) 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).(2) 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.(3) Å Å

See [Connective Tissue Disease Cascade \(CTDC\)](#) in Special Instructions.

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 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

1. Banal F, Dougados M, Combes C, Gossec L: Sensitivity and specificity of the American College of Rheumatology 1987 criteria for the diagnosis of rheumatoid arthritis according to disease duration: a systemic literature review and meta-analysis. *Ann Rheum Dis* 2009 July;68:1184-1191
2. Schellekens GA, Visser H, De Jong BA, et al: The diagnostic properties of rheumatoid arthritis antibodies recognizing a cyclic citrullinated peptide. *Arthritis Rheum* 2000 Jan;43(1):155-163
3. Visser H, le Cessie S, Vos, K, et al: How to diagnose rheumatoid arthritis early: a prediction model for persistent (erosive) arthritis. *Arthritis Rheum* 2002 Feb;46(2):357-365

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

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, approved or is exempt 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

Test ID	Test Order Name	Order LOINC Value
CCP	Cyclic Citrullinated Peptide Ab, S	94874-5

Result ID	Test Result Name	Result LOINC Value
CCP	Cyclic Citrullinated Peptide Ab, S	94874-5