Quest Diagnostics®

# **Understand autoimmune screening results** for faster diagnoses and care

**Your role as a primary care provider is pivotal.** Help improve patient outcomes by using a comprehensive screening approach.

To support faster autoimmune diagnoses with fewer steps, we've developed this tool to provide guidance on the clinical significance of results for ANA and over 20 disease-specific biomarkers.

1. Identify patients at risk
2. Screen beyond ANA
3. Interpret results
4. Provide informed referrals
5. Monitor risk

# **Confidently navigate** the autoimmune screening process

## Identify patients at risk

Vague, nonspecific symptoms can make autoimmune disease difficult to identify.

**Common symptoms include[1]:**

- Digestive problems
- Fever
- Fatigue
- Joint pain
- Muscle weakness or pain
- Rash
- Shortness of breath

## Screen beyond ANA

For some autoimmune diseases like rheumatoid arthritis (RA) and autoimmune thyroid disease (ATD), antinuclear antibodies (ANA) are only prevalent in a minority of patients with those conditions. Quest's autoimmune screening panels test for ANA plus the most informative disease-specific markers, so you can help empower a faster differential diagnosis, or identify patients with multiple autoimmune conditions.

### Antibody prevalence (%) in rheumatic and related diseases and healthy individuals[a]

| Biomarker | SLE[2,3] | MCTD[4] | SSc[5] | SS[6] | PM/DM[7] | APS[8] | ATD | RA[9] | | HI |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | Early RA[b] | All RA | |
| ANA[10-12] | 90-95 | 90-100 | 85-95[c] | 50-60 | 50-60 | 40-70 | 10-20 | 20 | 38 | 20-30 |
| B2GP1[13-16] | 7-22 | | 7 | 5 | | 78[d] | | | | 5 |
| C3 and C4 complement[17] | 73[e] | | | | | | | | | |
| Cardiolipin [4,13-16] | 7-21 | 15 | 10-14 | 4 | | 81[d] | | | | 1 |
| CCP[18-20] | 1 | | 3 | 1 | | | | 62 | 71 | 1 |
| CENP-B[11] | 2-5 | 2-5 | 20-40[c,f] | 5-10 | 1-3 | | | | | <3 |
| Chromatin[11] | 40-70 | 5-18 | <3 | <3 | <3 | | | | | <3 |
| dsDNA[11] | 40-70 | <3 | <3 | <3 | <3 | | | | | <3 |
| Jo-1[11] | 1-3 | <2[g] | 1-3 | <2 | 15-30 | | | | | <1 |
| MCV[18,19,21] | 12-36 | | 10 | 10 | | 27 | | 78 | 71 | ≤5 |
| RF[18-20,22] | 15-35 | 50-60 | 20-30 | 75-95 | 20 | | | 72 | 77 | 5-25 |
| RNP[11] | 10-40 | 100 | 5-15 | <3 | 5-15 | | | | | <3 |
| Scl-70[11] | 0-5 | <3[h] | 20-40[f] | <3 | <3 | | | | | <1 |
| Sm[11] | 5-20 | <2 | <2 | <1 | <1 | | | | | <1 |
| Sm/RNP[23,24] | 30 | 100 | 4 | 9 | 5 | | | | | |
| SS-A/Ro[11] | 40-70 | <3 | 3-10 | 60-90 | <3 | | | | | <3 |
| SS-B/La[11] | 15-30 | <3 | 1-5 | 60-80 | 5-15 | | | | | <3 |
| TPO[25-27] | 4-13 | | 5-21 | 10 | | | >90 | | | |

ANA, antinuclear antibody; APS, antiphospholipid syndrome; ATD, autoimmune thyroid disease (ie, Graves disease or Hashimoto thyroiditis); B2GP, beta-2-glycoprotein; CCP, cyclic citrullinated peptide; CENP-B, centromere B; dsDNA, double-stranded DNA; HI, healthy individual; Jo-1, histidyl-tRNA synthetase; MCTD, mixed connective tissue disease; MCV, mutated citrullinated vimentin; PM/DM, polymyositis/dermatomyositis; RA, rheumatoid arthritis; RF, rheumatoid factor; RNP, ribonucleoprotein; Scl-70, scleroderma-70 (topoisomerase 1); SLE, systemic lupus erythematosus; Sm, Smith; Sm/RNP, Smith/ribonucleoprotein; SS, Sjögren syndrome; SS-A, SS-B, Sjögren antibodies A and B; SSc, systemic sclerosis; TPO, thyroid peroxidase.

[a] **Highlighted antibodies or diagnostic criteria for the disease. Note that antibodies included in criteria are not always those with the highest prevalence in that disease.**
[b] Early RA defined as disease history of <1 year.
[c] CREST syndrome is a variant of systemic sclerosis defined by the presence of calcinosis cutis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia. Also known as limited cutaneous scleroderma. ANA is present in 70% of CREST patients, and CENP-B is present in 90% to 95%.[20]
[d] IgG type; 49% for cardiolipin IgM and 40% for B2GP IgM.[16]
[e] The prevalence of simultaneously low C3 and C4 levels was higher in 73% of patients with SLE.[17]
[f] The presence of scleroderma-related antibodies (centromere, Scl-70, or RNA polymerase III antibodies) is not necessary or sufficient for diagnosis, but is useful for classification in the absence of diagnostic clinical findings (ie, "skin thickening of the fingers extending proximal to the metacarpophalangeal joints"[5]).
[g] Especially in patients with features of muscle inflammation.
[h] Especially in patients with features of systemic sclerosis.

## **Interpret results:** what do they mean for your patient?

**Autoimmune disease may be complex, but getting answers doesn't have to be.** This table provides detailed guidance on what positive and negative screening results of ANA and 20+ specific antibodies mean for your patient.

- Included on ANAlyzeR™
- Included on Cascade
- Reflex test on Cascade

| Component | Clinical indication | Clinical significance |
|---|---|---|
| Antinuclear antibodies (ANA) ●● | General autoimmune disease | Although strongly associated with systemic lupus erythematosus (SLE), a positive ANA may also be present in a large number of autoimmune disorders. Quest's immunofluorescence test screens at a low titer in order to enhance sensitivity. A high titer (>1:160) strongly suggests autoimmune disease; a low titer (1:40 or 1:80) does not rule it out but may also be found in a minority of healthy individuals.[28] ANA patterns may help guide diagnosis, and Quest uses the International Consensus on ANA Patterns (ICAP) reporting guidelines.[29]<br>Individuals with negative results on the ANA IFA usually also have negative results when tested for specific antinuclear antibodies using immunoassay. Exceptions include Jo-1 antibody in some patients with myositis, and SS-A antibody in some patients with SLE or Sjögren syndrome.[30] |
| Rheumatoid factor (RF) ●● | Rheumatoid arthritis (RA) | Although strongly associated with RA, RF is found in a large variety of autoimmune and infectious disorders and even in healthy individuals. It is present in many patients with RA, but its poor specificity limits its use as a diagnostic marker of autoimmune disease.[22] |
| Cyclic citrullinated peptide (CCP) antibody (IgG) ●● | RA | The CCP antibody test detects a variety of antibodies against proteins which have undergone a modification in which some amino acids have been changed (into citrulline). These new parts of the proteins are highly immunogenic in patients with RA, and these antibodies are very specific for RA, although they are only found in half of patients.[9] Positivity for anti-CCP also increases the risk of more severe disease.[12] |
| Mutated citrullinated vimentin (MCV) antibody ●● | RA | Antibodies to MCV are a specific form of anti-CCP antibody which are directed against 1 specific target. Vimentin is a protein expressed by synovial cells in inflamed joints in RA in a mutated form which enhances citrullination. MCV antibodies are present in many patients with RA and may be positive in approximately 15% of CCP-negative patients, enhancing diagnostic sensitivity.[18] |
| dsDNA antibody ●○ | Systemic lupus erythematosus (SLE) | Antibodies to double-stranded DNA (dsDNA) are very specific for SLE. Their presence is associated with increased risk of lupus nephritis, and levels are useful for monitoring activity.[2] Quest has 2 assays for anti-dsDNA. The assay included in ANAlyzeR™ uses an organism called Crithidia luciliae which has an organelle with dsDNA. The other method is an immunoassay which may be more useful for monitoring patients.[31] |
| Chromatin ●○ | SLE | Chromatin refers to the assembly of DNA into organized structures (nucleosomes) which combine to make up the individual chromosomes. Most patients with anti-dsDNA antibodies also have anti-chromatin antibodies and their presence can help to confirm a diagnosis of SLE.[32] |
| Sm antibody ●○ | SLE | The Smith (Sm) antibody test detects antibodies to a protein component of small ribonucleoproteins. It is highly specific for SLE, although it is only detected in some patients.[2] |
| Complement components ● | SLE | Complement refers to a series of proteins which are part of the inflammatory response. The 2 major components are C3 and C4. Low levels of these proteins may be found in severe acute inflammatory disorders, especially active SLE and cryoglobulinemic vasculitis.[17] |
| Sm/RNP antibody ●○ | Lupus and mixed connective tissue disease | The Sm/RNP test detects an antibody against a unique target in small ribonucleoproteins which includes both Sm and RNP. It is present in a minority of patients with anti-Sm and/or anti-RNP, but its clinical significance is unclear.[33] |
| RNP antibody ●○ | Lupus and mixed connective tissue disease | RNP antibodies are directed against the RNA portion of small ribonucleoproteins. These antibodies are present in some patients with SLE and are also highly associated with an overlap syndrome called mixed connective tissue disease (MCTD).[34] |

## **Interpret results:** what do they mean for your patient?

| Component | Clinical indication | Clinical significance |
|---|---|---|
| Jo-1 antibody ●○ | Polymyositis and anti-synthetase syndrome | Jo-1 antibody is 1 of several myositis-specific antibodies associated with a particular type of myositis called anti-synthetase syndrome. This syndrome may include both skin and muscle pathology, as well as increased risk of chronic interstitial lung disease.[7] |
| Sjögren antibodies (SS-A,SS-B) ●○ | Sjögren syndrome | Sjögren syndrome is the combination of a systemic rheumatic disorder with a complex defined by inflammation of salivary and lacrimal glands. There are 2 associated antibodies: anti-SS-A and anti-SS-B (also known as Ro and La, respectively). Anti-SS-A is present in the majority of patients with Sjögren syndrome and may also be present in a minority of patients with SLE or RA. Anti-SS-B is present in a smaller percentage of Sjögren syndrome patients.[6] |
| Scleroderma antibodies ●○ | Systemic sclerosis | Two antibodies help to differentiate 2 types of scleroderma (progressive systemic sclerosis). Scl-70 antibody (also called anti-topoisomerase) is very specific for scleroderma, may be found in more than half of patients, and is associated with the diffuse type. Anti-centromere antibody may be found in some scleroderma patients and is associated with the limited type with CREST: calcinosis, Raynaud phenomenon, esophageal immotility, sclerodactyly, and telangiectasia.[5] |
| Centromere B antibody ●○ | CREST syndrome | Anti-centromere antibody is 1 of the 2 antibodies that help to differentiate 2 types of scleroderma (progressive systemic sclerosis). It may be found in many scleroderma patients and is associated with the limited type (with CREST: calcinosis, Raynaud phenomenon, esophageal immotility, sclerodactyly, and telangiectasia).[5] |
| Beta-2-glycoprotein 1 antibodies (IgG, IgA, IgM) ● | Antiphospholipid syndrome | Beta-2-glycoprotein 1 also known as apolipoprotein H is a cofactor in antiphospholipid antibody binding and is the critical antigen in the antiphospholipid antibody syndrome. The presence of high titer IgG/IgM beta-2-glycoprotein 1 antibodies is one criteria for the diagnosis of antiphospholipid antibody syndrome.[13] |
| Cardiolipin antibodies (IgA, IgG, IgM) ● | Antiphospholipid syndrome | The anti-cardiolipin antibody test also detects the presence of beta-2-glycoprotein 1 and other phospholipid bindings proteins. Positive results can help confirm the diagnosis of antiphospholipid syndrome. The testing in the ANAlyzeR panel includes IgG, IgA, and IgM antibodies.[13] |
| Thyroid peroxidase antibody ● | Autoimmune thyroid disease | Thyroid peroxidase (TPO) is an enzyme involved in the production of thyroid hormone. Anti-TPO antibodies are present in greater than 90% of patients with Hashimoto disease and many patients with Graves disease.[26] |

● Included on ANAlyzeR™
● Included on Cascade
○ Reflex test on Cascade

### Key tips to interpreting results

**The importance of positive and negative results.** If the ANA IFA result is positive, but specific antibody results in a panel, cascade, or individual supplement are negative, an autoimmune disease may still be present. While negative results won't lead to a differential diagnosis, they can be an important part of an informed referral to a rheumatologist.

**Knowing the ANA titer can be helpful in interpreting positive ANA results.** A high titer (>1:160) strongly suggests autoimmune disease; a low titer (1:40 or 1:80) does not rule it out but may also be found in a minority of healthy individuals. Higher titers are generally associated with greater likelihood of autoimmune disease.[38]

## Provide informed referrals

**Help rheumatologists know where to focus.** Comprehensive autoimmune screening delivers **more answers with a single test code,**[1] so you can empower faster and more informed referrals—and help limit disease progression.

- Recommended time after symptom onset to visit rheumatologist is **within 6 weeks**[35]
- Current reported wait times for new patients to see rheumatologist is **over 6 months**[36]

## Monitor and manage comorbidity risk

**25% of Americans with an autoimmune condition have more than 1 disease,**[37] making it critical for primary care providers to monitor comorbidities. Patients with an autoimmune disease may be at increased risk for other conditions, including but not limited to:

- Atherosclerosis
- Cancer
- Depression
- Heart disease
- Interstitial lung disease
- Kidney disease
- Osteoporosis
- Pregnancy complications

# Empower faster autoimmune diagnoses and referrals with **just 1 blood draw**

Expedite diagnoses and improve outcomes with comprehensive autoimmune testing that is more specific than ANA alone.[1]

## ANALyzeR™

ANA, IFA, with Reflex Titer/Pattern, Systemic Autoimmune Panel 1

**Test code 36378**

Fixed panel of 20+ analytes that gives a full-picture view (whether ANA is positive or negative), to support differential diagnosis, especially for patients with more than 1 autoimmune condition

## Cascade

ANA, IFA, Cascade and Rheumatoid Arthritis Panel 2, with Reflexes

**Test code 94954**

Automatic reflex panel that tests for the 8 most common autoimmune diseases using a tiered cascade approach when ANA results are positive

The component tests may also be ordered individually.

**ANALyzeR™:**
ANA Screen,IFA, with Reflex to Titer/Pattern (249); dsDNA Antibody, Crithidia IFA with Reflex to Titer (37092); Complement Component C3c and C4c (351, 353); Chromatin (nucleosomal) Antibody (34088); Sm Antibody (37923); Sm/RNP Antibody (38567); RNP Antibody (19887); Rheumatoid Factor Antibodies (IgA, IgG, IgM) (19705); Mutated Citrullinated Vimentin (MCV) antibody (13238); Cyclic Citrullinated Peptide (CCP) Antibody (IgG) (11173); Sjogren Antibodies (SS-A, SS-B) (38568, 38569); Scleroderma Antibody (Scl-70) (4942); Jo-1 Antibody (5810); Centromere B Antibody; Beta-2-Glycoprotein I Antibodies (IgG, IgA, IgM) (36552, 36553, 36554); Cardiolipin Antibodies (IgA, IgG, IgM) (4661, 4662, 4663); Thyroid Peroxidase Antibodies (TPO) (5081)

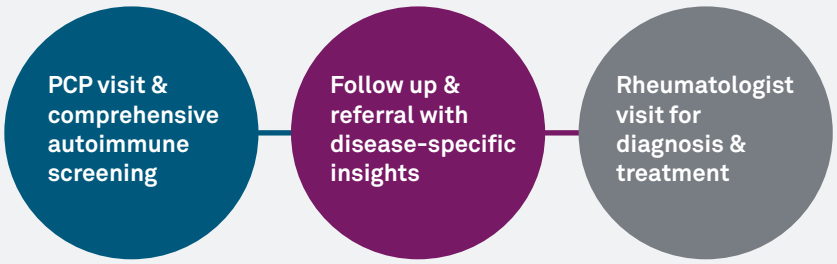
**Cascade:**
ANA screen, IFA, with Reflex to Titer/Pattern (249); and ANA Multiplex with Reflex to 11 Antibody Cascade (19946); Cyclic Citrullinated Peptide (CCP) Antibody (IgG) (11173); Mutated Citrullinated Vimentin (MCV) Antibody (13238)

**ANA screening alone cannot diagnose the specific autoimmune condition.[39]**

In fact, positive ANA results do not definitively rule out healthy patients either,[10] so referrals based only on ANA results can lead to unnecessary rheumatologist visits.

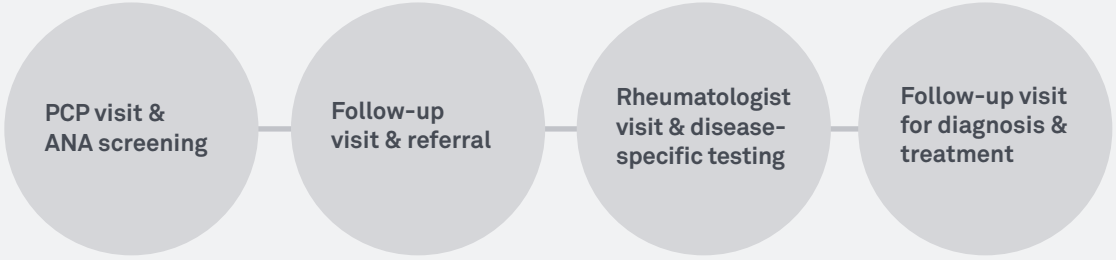
**Comprehensive autoimmune screening**

1 blood draw, fewer steps to treatment[a]




**Screening with ANA alone**

Multiple blood draws, more steps to treatment[a]




[a]The number of visits, referrals, and ordered tests may vary based on the specific patient case and the clinician's decisions.

References

1. MedlinePlus. Autoimmune diseases. Updated October 15, 2021. Accessed September 18, 2023. https://medlineplus.gov/autoimmunediseases.html
2. Aringer M, Costenbader K, Daikh D, et al. 2019 European League Against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus. *Ann Rheum Dis.* 2019;78(9):1151-1159. doi:10.1136/annrheumdis-2018-214819
3. Petri M, Orbai AM, Alarcón GS, et al. Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. *Arthritis Rheum.* 2012;64(8):2677-2686. doi:10.1002/art.34473
4. Ortega-Hernandez OD, Shoenfeld Y. Mixed connective tissue disease: an overview of clinical manifestations, diagnosis and treatment. *Best Pract Res Clin Rheumatol.* 2012;26(1):61-72. doi:10.1016/j.berh.2012.01.009
5. van den Hoogen F, Khanna D, Fransen J, et al. 2013 classification criteria for systemic sclerosis: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Arthritis Rheum.* 2013;65(11):2737-2747. doi:10.1002/art.38098
6. Shiboski CH, Shiboski SC, Seror R, et al. 2016 American College of Rheumatology/European League Against Rheumatism classification criteria for primary Sjögren's syndrome: a consensus and data-driven methodology involving three international patient cohorts. *Ann Rheum Dis.* 2017;76(1):9-16. doi:10.1136/annrheumdis-2016-210571
7. Lundberg IE, Tjärnlund A, Bottai M, et al. 2017 European League Against Rheumatism/American College of Rheumatology classification criteria for adult and juvenile idiopathic inflammatory myopathies and their major subgroups. *Ann Rheum Dis.* 2017;76(12):1955-1964. doi:10.1136/annrheumdis-2017-211468
8. Miyakis S, Lockshin MD, Atsumi T, et al. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). *J Thromb Haemost.* 2006;4(2):295-306. doi:10.1111/j.1538-7836.2006.01753.x
9. Aletaha D, Neogi T, Silman AJ, et al. 2010 rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Arthritis Rheum.* 2010;62(9):2569-2581. doi:10.1002/art.27584
10. Kavanaugh A, Tomar R, Reveille J, et al. Guidelines for clinical use of the antinuclear antibody test and tests for specific autoantibodies to nuclear antigens: American College of Pathologists. *Arch Pathol Lab Med.* 2000;124(1):71-81. doi:10.5858/2000-124-0071-GFCUOT
11. Mahler M, Meroni PL, Bossuyt X, et al. Current concepts and future directions for the assessment of autoantibodies to cellular antigens referred to as anti-nuclear antibodies. *J Immunol Res.* 2014;2014:315179. doi:10.1155/2014/315179
12. Rönnelid J, Turesson C, Kastbom A. Autoantibodies in rheumatoid arthritis - laboratory and clinical perspectives. *Front Immunol.* 2021;12:685312. doi:10.3389/ fimmu.2021.685312
13. Marchetti T, Ribi C, Perneger T, et al. Prevalence, persistence and clinical correlations of classic and novel antiphospholipid antibodies in systemic lupus erythematosus. *Rheumatology (Oxford).* 2018;57(8):1350-1357. doi:10.1093/rheumatology/key095
14. Morrisroe KB, Stevens W, Nandurkar H, et al. The association of antiphospholipid antibodies with cardiopulmonary manifestations of systemic sclerosis. *Clin Exp Rheumatol.* 2014;32(6) (suppl 86):S133-S137.
15. Pasoto SG, Chakkour HP, Natalino RR, et al. Lupus anticoagulant: a marker for stroke and venous thrombosis in primary Sjögren's syndrome. *Clin Rheumatol.* 2012;31(9):1331-1338. doi:10.1007/s10067-012-2019-z
16. Rodríguez-Pintó I, Moitinho M, Santacreu I, et al. Catastrophic antiphospholipid syndrome (CAPS): descriptive analysis of 500 patients from the International CAPS Registry. *Autoimmun Rev.* 2016;15(12):1120-1124. doi:10.1016/j.autrev.2016.09.010
17. Li H, Lin S, Yang S, et al. Diagnostic value of serum complement C3 and C4 levels in Chinese patients with systemic lupus erythematosus. *Clin Rheumatol.* 2015;34(3):471-477. doi:10.1007/s10067-014-2843-4
18. Liu X, Jia R, Zhao J, et al. The role of anti-mutated citrullinated vimentin antibodies in the diagnosis of early rheumatoid arthritis. *J Rheumatol.* 2009;36(6):1136-1142. doi:10.3899/jrheum.080796
19. Zhu JN, Nie LY, Lu XY, et al. Meta-analysis: compared with anti-CCP and rheumatoid factor, could anti-MCV be the next biomarker in the rheumatoid arthritis classification criteria? *Clin Chem Lab Med.* 2019;57(11):1668-1679. doi:10.1515/cclm-2019-0167
20. van Paassen P, Damoiseaux J, Tervaert JWC. Laboratory assessment in musculoskeletal disorders. *Best Pract Res Clin Rheumatol.* 2003;17(3):475-494. doi:10.1016/s1521-6942(03)00029-9
21. Alessandri C, Agmon-Levin N, Conti F, et al. Anti-mutated citrullinated vimentin antibodies in antiphospholipid syndrome: diagnostic value and relationship with clinical features. *Immunol Res.* 2017;65(2):524-531. doi:10.1007/s12026-017-8899-x
22. Ingegnoli F, Castelli R, Gualtierotti R. Rheumatoid factors: clinical applications. *Dis Markers.* 2013;35(6):727-734. doi:10.1155/2013/726598
23. Satoh M, Vázquez-Del Mercado M, Chan EK. Clinical interpretation of antinuclear antibody tests in systemic rheumatic diseases. *Mod Rheumatol.* 2009;19(3):219-228. doi:10.1007/s10165-009-0155-3
24. Scholz J, Grossmann K, Knütter I, et al. Second generation analysis of antinuclear antibody (ANA) by combination of screening and confirmatory testing. *Clin Chem Lab Med.* 2015;53(12):1991-2002. doi:10.1515/cclm-2015-0083
25. Lazarus JH. Chronic (Hashimoto's) thyroiditis. In: Jameson JL, De Groot LJ, eds. *Endocrinology.* 6th ed. Saunders Elsevier; 2010:1583-1594.
26. Posselt RT, Coelho VN, Pigozzo DC, et al. Prevalence of thyroid autoantibodies in patients with systematic autoimmune rheumatic diseases: cross-sectional study. *Sao Paulo Med J.* 2017;135(6):535-540. doi:10.1590/1516-3180.2017.0089110617
27. Koszarny A, Majdan M, Dryglewska M, et al. Prevalence of selected organ-specific autoantibodies in rheumatoid arthritis and primary Sjögren's syndrome patients. *Reumatologia.* 2015;53(2):61-68. doi:10.5114/reum.2015.51504
28. Wener MH, Fink SL, Morishima C, Chaudhary A, Hutchinson K. Anti-nuclear antibody quantitation: Calibration and harmonization adjustment via population interrogation. *J Appl Lab Med.* 2022; 7:46-56. doi:10.1093/jalm/jfab142
29. Damoiseaux J, Andrade LEC, Carballo OG, et al. Clinical relevance of Hep-2 indirect immunofluorescence patterns: the International Consensus on ANA Patterns (ICAP) perspective. *Ann Rheum Dis.* 2019; 78:879-889. doi:10.1136/annrheumdis-2018-214436
30. Fritzler MJ. Choosing wisely: review and commentary on anti-nuclear antibody (ANA) testing. *Autoimmunity Rev.* 2016;15:272-280. doi:10.1016/j.autrev.2015.12.002
31. Orme ME, Voreck A, Aksouh R, et al. Anti-dsDNA testing specificity for systemic lupus erythematosus: a systemic review. *J Appl Lab Med.* 2022; 7:221-239. doi:10.1093/jalm/jfab146
32. Gómez-Puerta JA, Burlingame RW, Cervera R. Anti-chromatin (anti-nucleosome) antibodies: diagnostic and clinical value. *Autoimmun Rev.* 2008;7(8):606-611. doi:10.1016/j.autrev.2008.06.005
33. Tebo AE, Peterson LK, Snyder MR, et al. Clinical significance of anti-U1 ribonucleoprotein antibody is analyte dependent. Implications for laboratory reporting, interpretation, and interassay correlation. *Arch Pathol Lab Med.* 2023;147:1461-1465. doi:10.5858/arpa.2022-0316-OA
34. Kattah NH, Kattah MG, Utz PJ. The U1-snRNP complex: structural properties relating to autoimmune pathogenesis in rheumatic diseases. *Immunol Rev.* 2010;233:126-145. doi:10.1111/j.0105-2896.2009.00863.x
35. Niemantsverdriet E, Dougados M, Combe B, et al. Referring early arthritis patients within 6 weeks versus 12 weeks after symptom onset: an observational cohort study. *Lancet Rheumatol.* 2020;2(6):e332-e338. doi:10.1016/s2665-9913(20)30061-8
36. American College of Rheumatology. American College of Rheumatology responds to the Senate Health, Education, Pension, & Labor Committee (HELP) request for information (RFI) on the healthcare workforce shortage. March 20, 2023. Accessed July 18, 2023. https://assets.contentstack.io/v3/assets/bltee37abb6b278ab2c/bltf9244a31c1fd18fe/acr-help-workforce-rfiresponse.pdf
37. Autoimmune Association. Rare autoimmune disease: individually rare, collectively common. Accessed March 15, 2023. https://autoimmune.org/resourcecenter/about-autoimmunity
38. Tozzoli R, Bizzaro N, Tonutti E, et al. Guidelines for the laboratory use of autoantibody tests in the diagnosis and monitoring of autoimmune rheumatic diseases. *Am J Clin Pathol.* 2002;117(2):316-324. doi:10.1309/Y5VF-C3DM-L8XV-U053
39. Yazdany J, Schmajuk G, Robbins M, et al. Choosing wisely: the American College of Rheumatology's Top 5 list of things physicians and patients should question. *Arthritis Care Res (Hoboken).* 2013;65:329-339. doi:10.1002/acr.21930

Learn more about Quest's autoimmune screening solutions by visiting **DiagnoseAutoimmune.com**

Test codes may vary by location. Please contact your local laboratory for more information.

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