

NOVEL INFLAMMATORY MARKER

Serum amyloid A (SAA)

In rheumatology, inflammatory markers are crucial for diagnosing and monitoring inflammatory diseases.



Serum amyloid A (SAA) is a well-characterized acute phase reactant (APR) protein that can be used as a highly sensitive marker of both acute and chronic inflammation.¹ Elevation of SAA is critical for an appropriate immune response and resolution of tissue injury.¹ Consistent with other APR proteins, including the well-characterized C-reactive protein, levels of SAA are tightly linked to inflammation and will quickly rise in response to APR onset and fall as inflammation resolves.²

Clinical usefulness of SAA

The quantification of SAA has broad clinical relevance to various acute and chronic inflammatory conditions.^{1,3-6}



It is used in a variety of disease states to differentiate, diagnose, or monitor inflammatory rheumatic diseases, including rheumatoid arthritis, systemic lupus erythematosus, vasculitis, inflammatory bowel disease and microbial infections, among others.^{3,4,7-9}

Elevated SAA levels are associated with these inflammatory conditions, acute infections, an increased risk of atherosclerosis, and cardiovascular disease.¹⁰⁻¹⁴

Prolonged elevation of SAA can also lead to amyloidosis, the deposits of non-soluble amyloid A in tissues such as the liver and kidneys, which can result in fatal organ damage.¹⁴

Amyloidosis incidence is relatively uncommon but is significantly elevated in populations prone to episodic inflammation or prolonged subclinical inflammation, including in individuals with familial Mediterranean fever (FMF), mevalonate kinase deficiency (hyper-IgD syndrome), tumor necrosis factor receptor-associated periodic syndrome (TRAPS), cryopyrin associated periodic syndromes (CAPS), Blau syndrome, PAPAS (pyogenic sterile arthritis, pyoderma gangrenosum, and acne syndrome).¹⁵⁻²¹

Monitoring SAA levels in these autoinflammatory diseases aids management in confirming adequate suppression of inflammation and prevention of AA amyloidosis, including amyloid nephropathy.²²⁻²⁴

For example, during attack-free periods of FMF, SAA levels usually normalize; however, in about 30% of FMF patients, SAA remains elevated, and these patients may benefit from adjustment of the colchicine dose.²⁵

Labcorp offers supplemental genetic testing to help you diagnose and identify carriers of FMF.

Considerations for an enhanced inflammation assessment using SAA

SAA has diverse uses as a biomarker to assess inflammation;^{2,3,8,13,15} however, SAA should not be used to determine the causes of inflammation or when differentiating between clinical manifestations of inflammation. Other factors can influence SAA levels, particularly in the subclinical range. These factors include age, sex, and adiposity.² Subclinical elevation of SAA is best interpreted with an understanding of an individual's baseline SAA levels and complete medical history.



Test Number	Test Name
520380	Serum Amyloid A (SAA)

Related genetic testing for FMF

Test Number	Test Name
482500	GeneSeq® PLUS, MEFV
630763	GeneSeq® Immuno: Periodic Fever Syndromes Panel

References

- Sack GH. Serum amyloid A – a review. *Mol Med.* 2018;24(1):46
- Liu Q, Fu J, Wang X, et al. Distribution of serum amyloid A and establishment of reference intervals in healthy adults. *J Clin Lab Anal.* 2020;34(4):e23120
- Curtis JR, Weinblatt ME, Shadick NA, et al. Validation of the adjusted multi-biomarker disease activity score as a prognostic test for radiographic progression in rheumatoid arthritis: a combined analysis of multiple studies. *Arthritis Res Ther.* 2021;23(1):1
- den Hartigh LJ, May KS, Zhang XS, Chait A, Blaser MJ. Serum amyloid A and metabolic disease: evidence for a critical role in chronic inflammatory conditions. *Front Cardiovasc Med.* 2023;10:1130196
- Çakan M, Karadağ ŞG, Tanatar A, Sönmez HE, Ayaz NA. The value of serum amyloid A levels in familial Mediterranean fever to identify occult inflammation during asymptomatic periods. *J Clin Rheumatol.* 2021;27(1):1-4
- Zinellu A, Paliogiannis P, Carru C, Mangoni AA. Serum amyloid A concentrations, COVID-19 severity and mortality: an updated systematic review and meta-analysis. *Int J Infect Dis.* 2021;105:668-674
- Chen R, Xiao Y, Chen M, et al. Serum amyloid protein A in inflammatory bowel disease: from bench to bedside. *Cell Death Discov.* 2023;9(1):1-10
- Sorić Hosman I, Kos I, Lamot L. Serum amyloid A in inflammatory rheumatic diseases: a compendious review of a renowned biomarker. *Front Immunol.* 2021;11:631299
- Wang CM, Deng JH, Mao GF, He YL, Shi X. Serum amyloid A: a potential biomarker assessing disease activity in systemic lupus erythematosus. *Med Sci Monit.* 2020;26:e923290
- Stonik JA, Remaley AT, Demosky SJ, Neufeld EB, Bocharov A, Brewer HB. Serum amyloid A promotes ABCA1-dependent and ABCA1-independent lipid efflux from cells. *Biochem Biophys Res Commun.* 2004;321(4):936-941
- Dong Z, Wu T, Qin W, et al. Serum amyloid A directly accelerates the progression of atherosclerosis in apolipoprotein E-deficient mice. *Mol Med.* 2011;17(11):1357-1364
- Johnson BD, Kip KE, Marroquin OC, et al. Serum amyloid A as a predictor of coronary artery disease and cardiovascular outcome in women. *Circulation.* 2004;109(6):726-732
- Thompson JC, Wilson PG, Shridas P, et al. A brief elevation of serum amyloid A is sufficient to increase atherosclerosis. *J Lipid Res.* 2015;56(2):286-293
- Thorne JC, Amin S, Nasr SH, et al. Serum amyloid A protein-associated kidney disease: presentation, diagnosis, and management. *Kidney Med.* 2022;4(9):100504
- Çakan M, Karadağ ŞG, Tanatar A, Sönmez HE, Ayaz NA. Serum amyloid A as a biomarker in differentiating attacks of familial Mediterranean fever from acute febrile infections. *Clin Rheumatol.* 2020;39(1):249-253
- Lofly HM, Marzouk H, Farag Y, Nabih M, Khalifa IA, Mostafa N, Salah A, Rashed L, El Garf K. Serum Amyloid A Level in Egyptian Children with Familial Mediterranean Fever. *Int J Rheumatol.* 2016;2016:7354018.
- Moghaddas F, Llamas R, De Nardo D, Martinez-Banaclocha H, Martinez-Garcia JJ, Mesa-Del-Castillo P, Baker PJ, Gargallo V, Mensa-Vilaro A, Canna S, Wicks IP, Pelegrin P, Arostegui JJ, Masters SL. A novel Pyrin-Associated Autoinflammation with Neutrophilic Dermatitis mutation further defines 14-3-3 binding of pyrin and distinction to Familial Mediterranean Fever. *Ann Rheum Dis.* 2017;76(12):2085-2094.
- Lane T, Loeffler JM, Rowczenio DM, Gilbertson JA, Bybee A, Russell TL, Gillmore JD, Wechalekar AD, Hawkins PN, Lachmann HJ. AA amyloidosis complicating the hereditary periodic fever syndromes. *Arthritis Rheum.* 2013;65(4):1116-21.
- Deutch N, Cudrici C, Ombrello A, Aksentjevich I. TNF Receptor-Associated Periodic Fever Syndrome. 2022 Nov 10. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Amemiya A, editors. *GeneReviews® [Internet]*. Seattle (WA): University of Washington, Seattle; 1993-2025.
- Pastore S, Paloni G, Caorsi R, Ronfani L, Taddio A, Lepore L; CAPS Italian Register. Serum amyloid protein A concentration in cryopyrin-associated periodic syndromes patients treated with interleukin-1 beta antagonist. *Clin Exp Rheumatol.* 2014 Jul-Aug;32(4 Suppl 84):S63-6.
- Kötter I, Schedel J, Kümmerle-Deschner JB. Periodische Fiebersyndrome/autoinflammatorische Syndrome [Periodic fever syndrome/autoinflammatory syndrome]. *Z Rheumatol.* 2009 Mar;68(2):137-48; quiz 149. German.
- Zhang C, Peng J, Liu Z, Zhou Q. Kidney Involvement in Autoinflammatory Diseases. *Kidney Dis (Basel).* 2023 Feb 28;9(3):157-172.
- Thorne J, Clark D, Geldenhuys L, More K, Vinson A, Tennankore K. Serum Amyloid A Protein-Associated Kidney Disease: Presentation, Diagnosis, and Management. *Kidney Med.* 2022;4(8):100504.
- Papa R, Lachmann HJ. Secondary, AA, Amyloidosis. *Rheum Dis Clin North Am.* 2018;44(4):585-603.
- Berkun Y, Padeh S, Reichman B, et al. A single testing of serum amyloid A levels as a tool for diagnosis and treatment dilemmas in familial Mediterranean fever. *Semin Arthritis Rheum.* 2007;37(3):182-188. doi:10.1016/j.semarthrit.2007.03.005

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