HLA-B27 Antigen

Test Code: 528(X)

Specimen Requirements: 5 mL room-temperature whole blood (sodium heparin [green-top tube]); 1 mL minimum

CPT Code*: 86812

CLINICAL USE

- Diagnose spondyloarthritis

CLINICAL BACKGROUND

The term "spondyloarthritis" (SpA) encompasses a group of inflammatory rheumatic diseases that cause arthritis; these include ankylosing spondylitis, reactive arthritis, psoriatic arthritis, and inflammatory bowel disease-associated arthritis. SpA can be sub-divided into axial SpA, which involves the spine and sacroiliac joints, and peripheral SpA, which involves peripheral arthritis, enthesitis, and dactylitis.[1,2] Inflammation caused by SpA is treatable with nonsteroidal anti-inflammatory drugs and tumor necrosis factor inhibitors.[3] Identification of individuals with SpA is important, because treatment can slow radiographic progression.[4]

Testing for human leukocyte antigen (HLA)-B27 can help identify individuals with SpA.[1,2] In some populations, over 80% of patients with ankylosing spondylitis and almost 75% of patients with nonradiographic axial SpA (lacking in radiographically defined sacroiliitis) have HLA-B27.[5] However, not every HLA-B27-positive person develops SpA; one study found that less than 14% of people with HLA-B27 have the disorder.[6] Thus, HLA-B27 testing is not diagnostic by itself and must be used in combination with other clinical and radiographic criteria.

The Assessment of SpondyloArthritis international Society (ASAS) released classification criteria for axial SpA in 2009[2] and peripheral SpA in 2011.[1] The ASAS criteria were developed to be applicable to nonradiographic and early stage SpA.[2] The axial SpA criteria have radiographic (imaging) and clinical arms, both of which incorporate HLA-B27 testing (Table); these criteria have a sensitivity of 82.9% and a specificity of 84.4%.[2] The peripheral SpA criteria also incorporate HLA-B27 testing and have a sensitivity of 77.8% and a specificity of 82.2%.[1]

Quest Diagnostics offers an antigen test and a molecular test for the detection of HLA-B27. However, HLA-B27 antigen testing is sufficient for SpA classification.

INDIVIDUALS SUITABLE FOR TESTING

- Individuals with clinical or radiographic indications of SpA

METHOD

- Detection of HLA-B27 antigen using antigen-antibody binding and flow cytometry

Table. ASAS Classification Criteria for Spondyloarthritis

Axial SpA[2]		**Peripheral SpA[1]**
Patients with back pain for ≥3 months who are <45 years at onset and meet criteria in clinical or imaging arm		Patients with peripheral manifestations only
Clinical Arm HLA-B27 and ≥2 SpA other features from footnote a	*Imaging Arm* Sacroiliitis on imaging and ≥1 SpA feature from footnote a	Arthritis, enthesitis, or dactylitis *and* ≥1 SpA feature from footnote b *or* ≥2 other SpA features from footnote c

[a] HLA-B27, inflammatory back pain, arthritis, enthesitis, uveitis, dactylitis, psoriasis, Crohn's or ulcerative colitis, response to NSAIDs, family history of SpA, elevated C-reactive protein levels.

[b] HLA-B27, uveitis, psoriasis, Crohn's or ulcerative colitis, preceding infection, sacroiliitis on imaging.

[c] Arthritis, enthesitis, dactylitis, inflammatory back pain, family history of SpA.

REFERENCE RANGE

Negative or not detected

INTERPRETIVE INFORMATION

A positive HLA-B27 result is consistent with SpA (ankylosing spondylitis, reactive arthritis, psoriatic arthritis, or inflammatory bowel disease-associated arthritis), acute anterior uveitis, or juvenile idiopathic arthritis. However, most people who are HLA-B27 positive do not develop an associated condition. Thus, diagnosis and classification should be based on multiple criteria.[1,2]

A negative HLA-B27 result does not rule out conditions associated with HLA-B27; the allele is not always present in patients with these conditions.

References

1. Rudwaleit M, van der Heijde D, Landewe R, et al. The Assessment of SpondyloArthritis International Society classification criteria for peripheral spondyloarthritis and for spondyloarthritis in general. *Ann Rheum Dis.* 2011;70:25-31.
2. Rudwaleit M, van der Heijde D, Landewe R, et al. The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part II): validation and final selection. *Ann Rheum Dis.* 2009;68:777-783.
3. Tsui FW, Tsui HW, Akram A, et al. The genetic basis of ankylosing spondylitis: new insights into disease pathogenesis. *Appl Clin Genet*. 2014;7:105-115.
4. Poddubnyy D, Rudwaleit M, Haibel H, et al. Effect of non-steroidal anti-inflammatory drugs on radiographic spinal progression in patients with axial spondyloarthritis: results from the German Spondyloarthritis Inception Cohort. *Ann Rheum Dis.* 2012;71:1616-1622.
5. Rudwaleit M, Haibel H, Baraliakos X, et al. The early disease stage in axial spondylarthritis: results from the German Spondyloarthritis Inception Cohort. *Arthritis Rheum.* 2009;60:717-727.
6. Braun J, Bollow M, Remlinger G, et al. Prevalence of spondylarthropathies in HLA-B27 positive and negative blood donors. *Arthritis Rheum.* 1998;41:58-67.

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