Laboratory Medicine Update

February 26th, 2020

Goodpasture and Vasculitis Diseases Screening

We are notifying you that on Wednesday the 26th of February 2020, the Special Immunochemistry Section of the Clinical Biochemistry Laboratory at the Health Science Center will begin offering a new screening test panel for Goodpasture and Vasculitis Diseases Screening (GVDS). This test panel will screen for Glomerular basement membrane autoantibody (GBM), and Antineutrophil cytoplasmic antibodies (C-ANCA (PR3), and P-ANCA (MPO)) on all samples.

One orderable test will be available:

Test Name	Aliases	Provincial Mnemonic
Goodpasture and Vasculitis Diseases Screening (GVDS)	Glomerular basement membrane autoantibody (GBM autoantibody), C-ANCA (PR3 autoantibody), P-ANCA (MPO autoantibody)	VASCUP

Testing will be performed once a week. Approval for STAT requests require approval by the clinical biochemist on-call. Any positive test result on the GVDS test panel will be reported and reflexively referred out for quantitative measurement of GBM, MPO or PR3 autoantibody testing based on the workflow algorithm below. All screening for vasculitis or Goodpasture's disease should begin with the GVDS test panel. All requests for ANCA, vasculitis screening, GBM autoantibody, PR3 autoantibody, or MPO antibody will have the GVDS test panel performed. Specific orders for referred out quantitative tests for GBM, MPO or PR3 autoantibody will be required rarely and will be orderable separately only by Rheumatologist or by the clinical biochemist approval of a filled LTSA form.

Antineutrophil Cytoplasmic Antibody (ANCA) Associated Vasculitis (AAV)

ANCA-associated vasculitis (AAV) are classified into distinct diseases based on clinical and pathological features: granulomatosis with polyangiitis (GPA, Wegener's granulomatosis), microscopic polyangiitis (MPA), eosinophilic granulomatosis with polyangiitis (EGPA, Churg–Strauss syndrome), and renal-limited vasculitis (RLV) with pauci-immune necrotizing glomerulonephritis. Etiology and pathogenesis of AAV are multifactorial.

ANCA targeting proteinase 3 (PR3) and myeloperoxidase (MPO) expressed by innate immune cells are salient diagnostic and pathogenic features of small vessel vasculitis. AAV is most prevalent in individuals >50 years old and less than 10% of patients with clinical and pathologic features of GPA, MPA, EGPA and RLV are negative for ANCA using current clinical assays. PR3-ANCA vasculitis has more upper respiratory tract disease and is highly associated with GPA whereas MPO-ANCA vasculitis has more renal disease and is generally associated with MPA, EGPA and RLV. Other organs frequently affected are peripheral and central nervous system, skin, gut, and heart. PR3-ANCA vasculitis has more granulomatous inflammation and MPO-ANCA vasculitis less granulomatous inflammation. At the time of biopsy, PR3-ANCA glomerulonephritis (GN) has more necrosis and MPO-ANCA GN has more sclerosis.

MPO and PR3 autoantibodies testing (GVDS test) should be ordered for patient with at least one of the following clinical signs or symptoms: glomerulonephritis, pulmonary hemorrhage, cutaneous vasculitis with systemic features, multiple lung nodules, chronic destructive disease of the upper airways, long-standing sinusitis or otitis, subglottic tracheal stenoses, mononeuritis multiplex or other peripheral neuropathy, retro-orbital mass or scleritis.

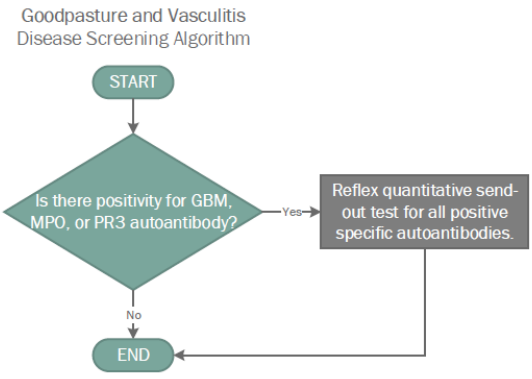
The revised consensus on the use of ANCA testing now recommends high-quality immunoassays as primary screening method and to reflex positive sample for a second analysis using a different immunoassay methodology. We provide this through the reflexive testing strategy described above.

Anti-Glomerular Basement Membrane (GBM) Autoantibody in Goodpasture's Disease.

Goodpasture's disease is a rare organ-specific autoimmune disease that is mediated by anti-glomerular basement membrane (GBM) autoantibody. Clinically, Goodpasture's disease presents with rapidly progressive glomerulonephritis and renal failure, accompanied by pulmonary hemorrhage that may be life-threatening. Both pulmonary and renal involvement occur in 60 to 80% of the patients. Renal manifestations alone are seen in 20 to 40% and are referred to as anti-GBM glomerulonephritis. The etiology of Goodpasture's disease is unknown.

The diagnosis of Goodpasture's disease relies on the detection of GBM autoantibodies in tissues or circulation in combination with the detection of glomerulonephritis and/or alveolitis. GBM autoantibodies are highly specific and sensitive markers of the disease and are by definition present in all patients with Goodpasture's disease. GBM autoantibody testing is crucial for early diagnosis of the disease. Clinical progression of the disease correlates with antibody concentrations, with high concentrations of circulating GBM autoantibodies indicating an unfavorable prognosis. The relevant antigenic target is the non-collagenous domain 1 (NC1) of the α-3 chain of type IV collagen within the glomerular basement membrane or the alveolar basal membrane. Distribution of this molecule in the human body is limited to specific organs, such as kidneys and lungs, thereby explaining the main manifestations of the syndrome.

Twenty to 35 percent of patients with GBM autoantibodies also have ANCA, mostly with specificity for myeloperoxidase (MPO autoantibody). Since Goodpasture's disease and ANCA Associated Vasculitis (AAV) may have the same clinical presentation, it is recommended that GBM and ANCA (MPO and PR3) autoantibodies should be analyzed in parallel in patients with renal disease. This screening approach is provided through the new GVDS test panel.



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