Complement investigations in C3 glomerulopathy

Tests recommended in all patients	
	Comment
Measurement of serum C3 and C4	Low C3 with normal C4 indicates alternative pathway activation
Measurement of C3 nephritic factor	C3 nephritic factors are associated with C3 glomerulopathy; their correlation with disease course is unclear
Measurement of serum factor H	Factor H deficiency is associated with C3 glomerulopathy and is invariably associated with reduction in serum C3
Serum paraprotein detection	Paraproteinemia associated with C3 glomerulopathy, specialist tests required to determine whether paraprotein is a cause of uncontrolled
Screening for *CFHR5* mutation	CFHR5 nephropathy is a well-characterized cause of C3 glomerulopathy, and thus screening for this mutation is clinically informative
Tests that should be considered on a case-by-case basis as they require expert interpretation and/or clinical validation	
	Comment
Measurement of serum factor B	Uncontrolled alternative pathway activation may be associated with reduced factor B levels
Measurement of serum C5	May be reduced in terminal pathway activation and could indicate group most likely to benefit from therapeutic C5 inhibition
Measurement of markers of C3 activation, e.g., C3d, C3c, C3adesArg	Activated C3 components are more sensitive markers of C3 activation than antigenic levels of intact C3
Measurement of markers of C5 activation, e.g., C5adesArg, soluble C5b-9	Activated C5 components are more sensitive markers of C5 activation than antigenic levels of intact C5
Measurement of anti-factor H autoantibodies	Anti-factor H autoantibodies are associated with C3 glomerulopathy; correlation with disease course is unclear; especially important to measure in patients with low C3 and negative C3 nephritic factor
Anti-factor B autoantibodies	Anti-factor B autoantibodies are associated with C3 glomerulopathy; correlation with disease course is unclear
Mutation screening of complement regulatory genes (e.g., *CFH, CFI, CD46*), activation protein genes (*C3, CFB*) and assessment of copy number variation across the *CFH-CFHR* locus	Mutations in these genes associated with C3 glomerulopathy; especially important to screen for *CFH* mutations in patients with low C3 and negative C3 nephritic factor

From: C3 glomerulopathy: consensus report. Pickering MC, D'Agati VD, Nester CM, Smith RJ, Haas M, Appel GB, Alpers CE, Bajema IM, Bedrosian C, Braun M, Doyle M, Fakhouri F, Fervenza FC, Fogo AB, Frémeaux-Bacchi V, Gale DP, Goicoechea de Jorge E, Griffin G, Harris CL, Holers VM, Johnson S, Lavin PJ, Medjeral-Thomas N, Paul Morgan B, Nast CC, Noel LH, Peters DK, Rodríguez de Córdoba S, Servais A, Sethi S, Song WC, Tamburini P, Thurman JM, Zavros M, Cook HT. Kidney Int. 2013 Dec;84(6):1079-89. http://www.ncbi.nlm.nih.gov/pubmed/24172683