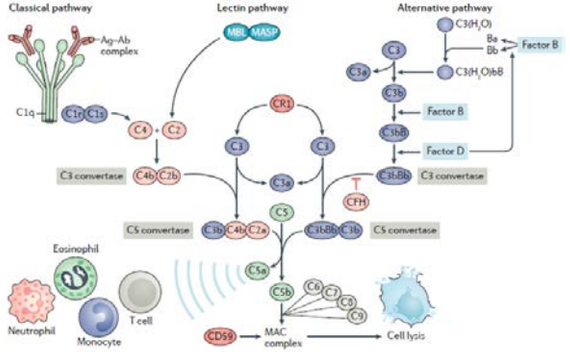
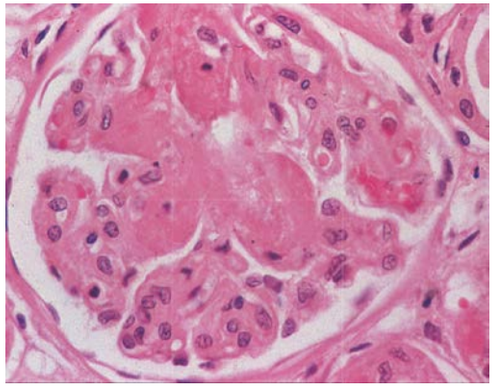
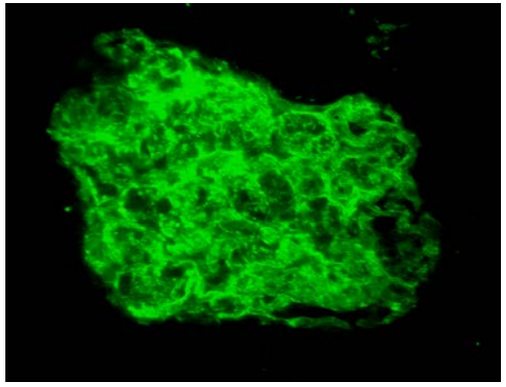
20ο Πανελλήνιο Συνέδριο Νεφρολογίας
Ελληνική Νεφρολογική Εταιρεία
3-6 Μαΐου 2018
Μέγαρο Διεθνές Συνεδριακό Κέντρο Αθηνών, **Αθήνα**



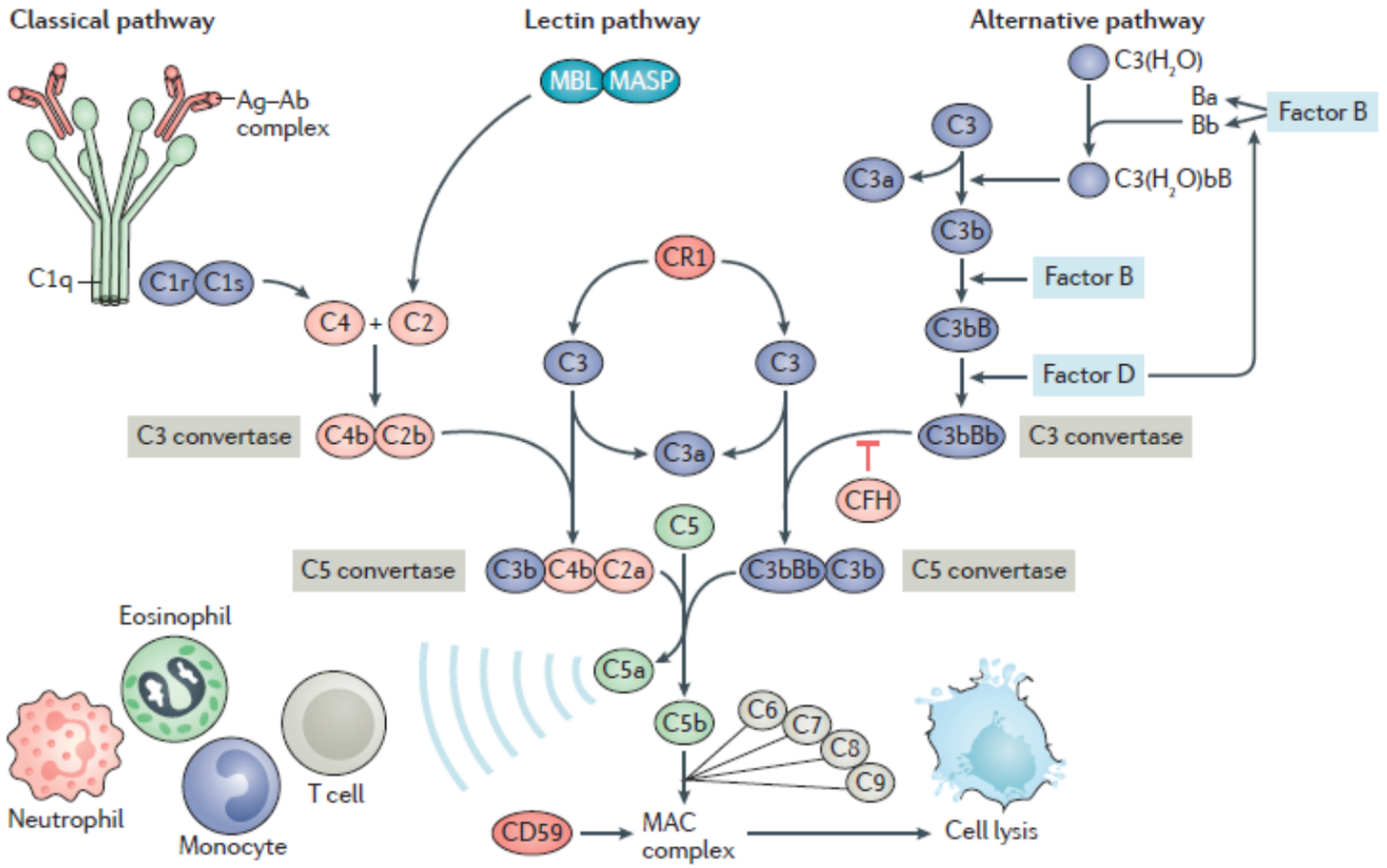
Σπειραματοπάθειες από διαταραχή της εναλλακτικής οδού του συμπληρώματος





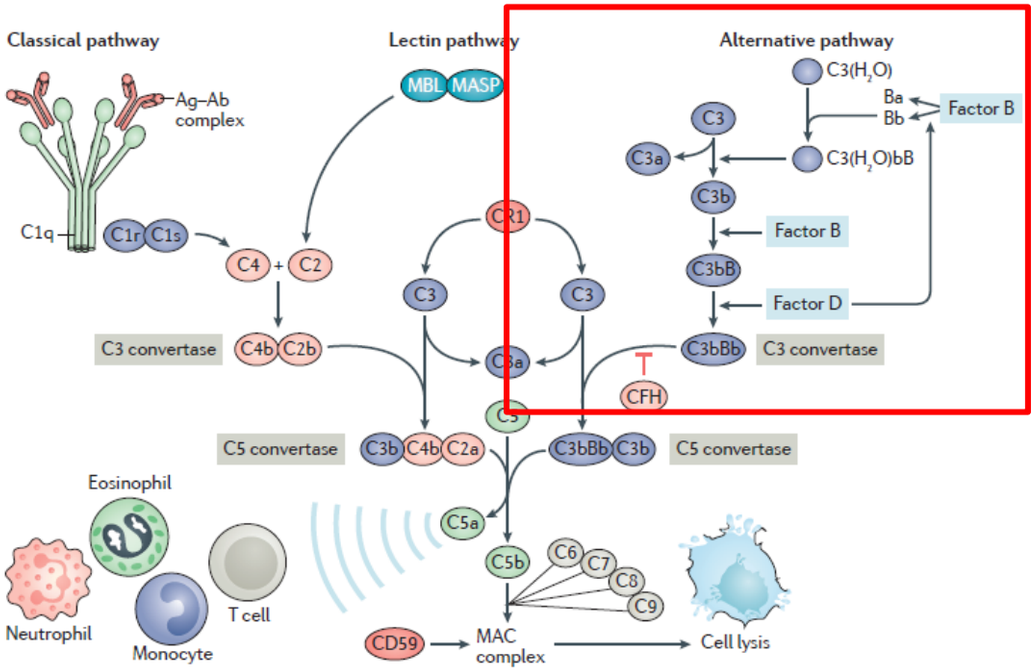
Π. Πατεινάκης
Νεφρολόγος Επ Α’
ΓΝΘ «Παπαγεωργίου»

Συμπλήρωμα



Chen M, Nature Reviews Nephrology 13, 359–367 (2017)

Διαταραχή εναλλακτικής οδού και σπειραματοπάθεια



Θρομβωτική μικροαγγειοπάθεια

Άτυπο ουραιμικό αιμολυτικό σύνδρομο (aHUS)

Σπειραματική εναπόθεση αποκλειστικά C3

C3 σπειραματοπάθεια (C3ΣΠ – C3G)

Ορισμός: αHUS

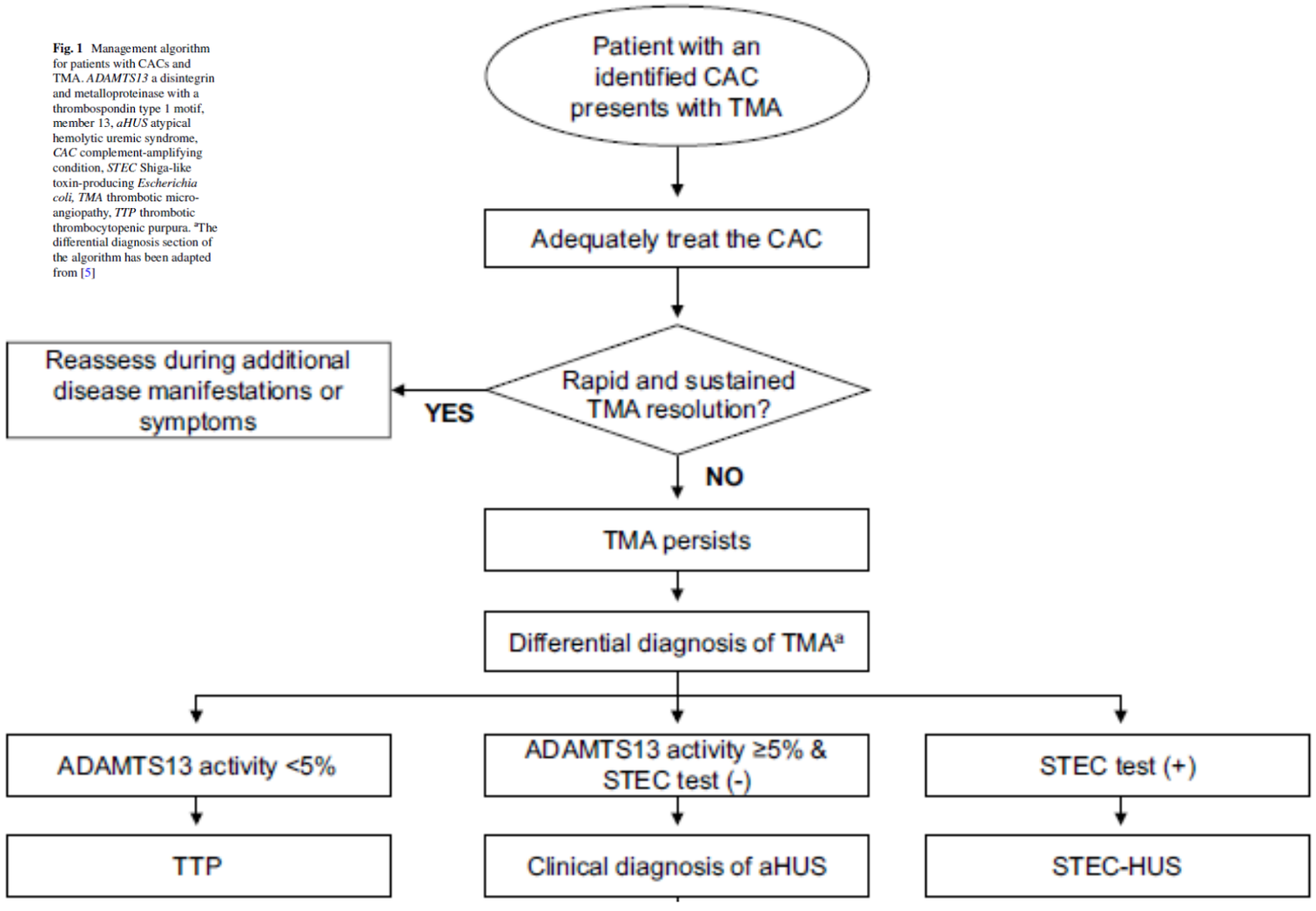


Fig. 1 Management algorithm for patients with CACs and TMA. *ADAMTS13* a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13, *aHUS* atypical hemolytic uremic syndrome, *CAC* complement-amplifying condition, *STEC* Shiga-like toxin-producing *Escherichia coli*, *TMA* thrombotic micro-angiopathy, *TTP* thrombotic thrombocytopenic purpura. [a]The differential diagnosis section of the algorithm has been adapted from [5]

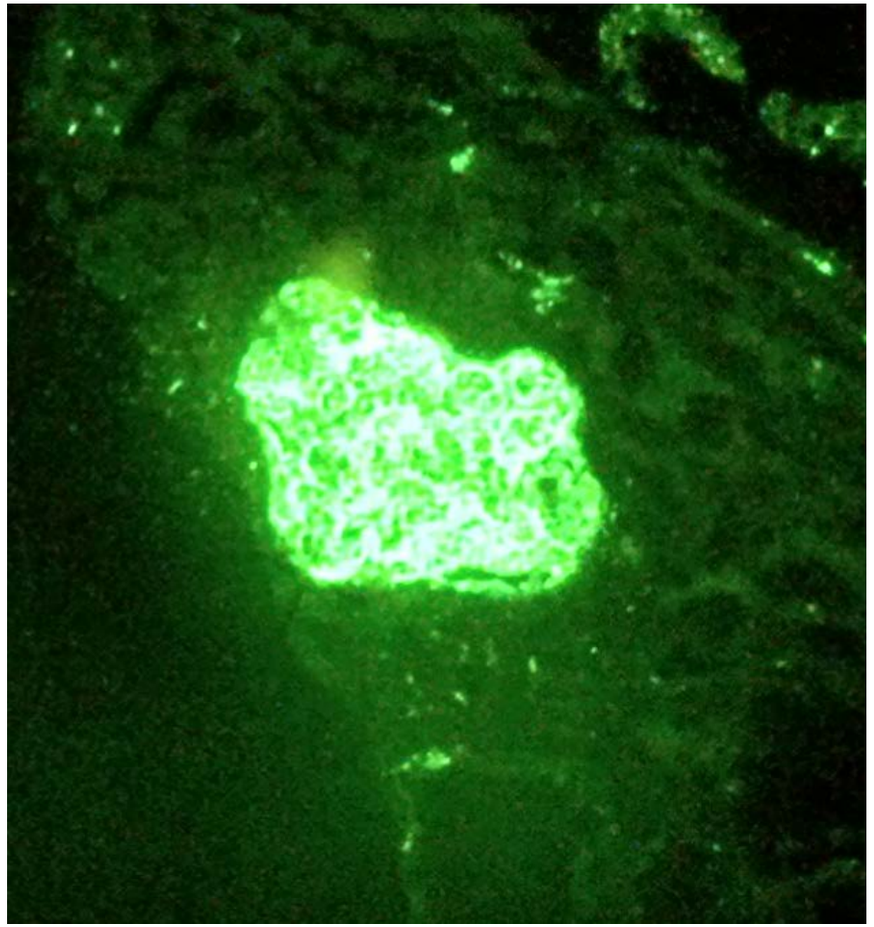
J Nephrol (2017) 30:347–362

- Κλινικός ορισμός
- Ουριαμία, αιμόλυση
- Θομβωτική μικροαγγειοπάθεια που **δεν** οφείλεται σε ανεπάρκεια ADAMTS13 (TTP) ή σε STEC (κλασσικό/D+ HUS)
- >50% των περιστατικών οφείλεται σε διαταραχές ρύθμισης της εναλλακτικής οδού

Clin J Am Soc Nephrol 13: 300–317, 2018

Ορισμός: C3 σπειραματοπάθεια

- Ανοσοϊστολογικός ορισμός
- Σπειραματική βλάβη με κυρίαρχη εναπόθεση C3 στον ανοσοφθορισμό



Kidney International (2017) 91, 539–551

16-1578

Επιδημιολογία

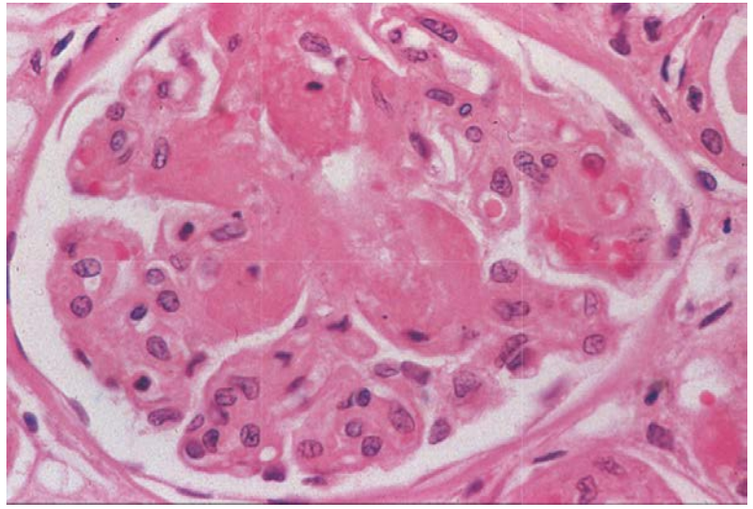
- aHUS
- C3ΣΠ

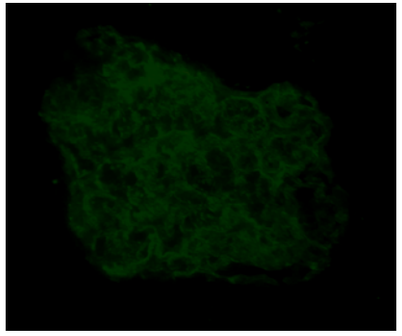
~1/1,000,000/έτος

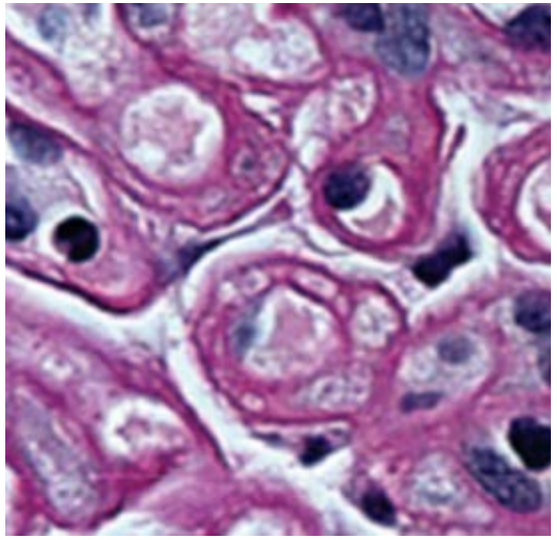
Kidney International (2017) 91, 539–551

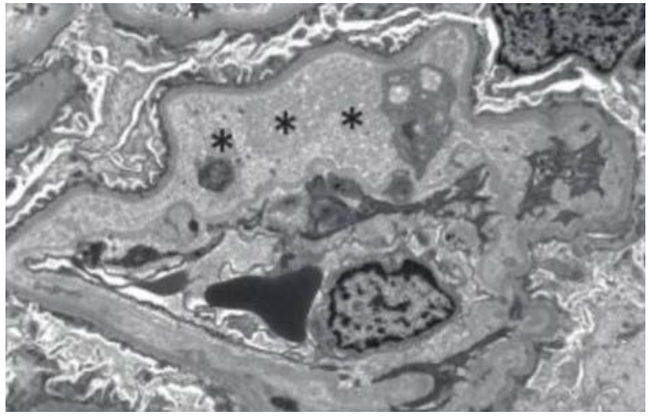
Ιστοπαθολογία

aHUS









- Η βιοψία **δεν** είναι απαραίτητη για τη διάγνωση
- Μη ειδικές αλλοιώσεις

- Θρομβωτική μικροαγγειοπάθεια
- Οξεία
  - Ενδοτριχοειδικοί θρόμβοι
- Χρόνια
  - Διπλή παρυφή
- Ανοσοφθορισμός αρνητικός για Igs και C3, C1q
- ΗΜ: ενδοθηλιακή βλάβη, χωρίς εναποθέσεις

C3ΣΠ - Ιστοχημεία

Table 2 | Morphological features of C3G

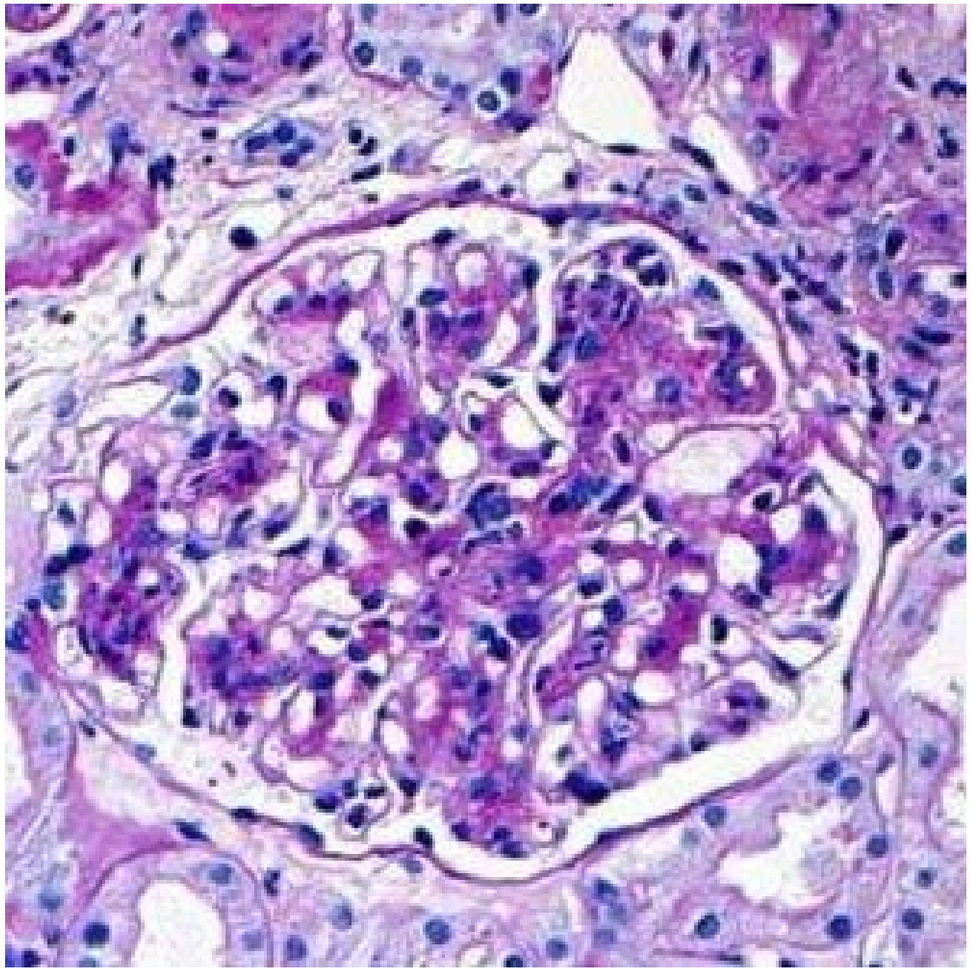
Light microscopy

Active lesions

- Mesangial expansion with or without hypercellularity

C3G, C3 glomerulopathy; DDD, dense deposit disease; C3GN, C3 glomerulonephritis.

Kidney International (2017) 91, 539–551



Kidney International (2012) 82, 465–473

C3ΣΠ - Ιστοχημεία

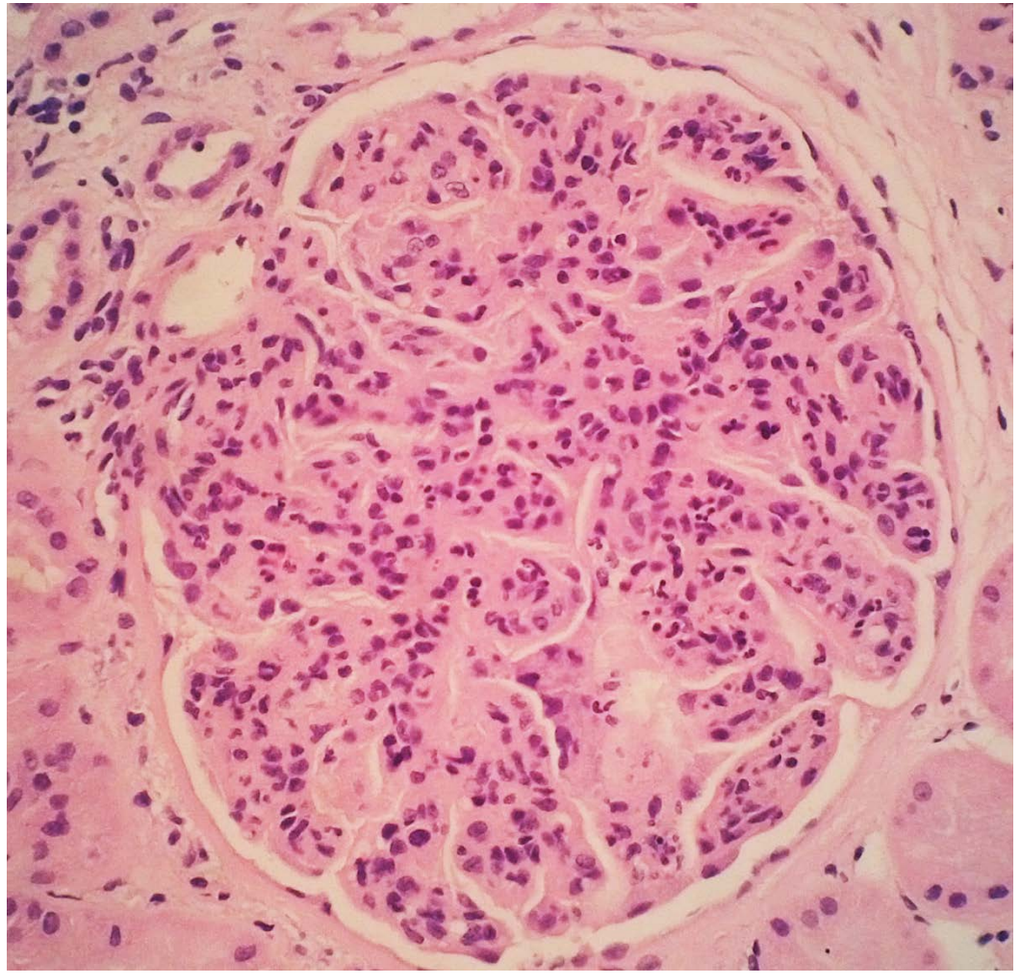
Table 2 | Morphological features of C3G

Light microscopy

Active lesions

- Mesangial expansion with or without hypercellularity
- Endocapillary hypercellularity including monocytes and/or neutrophils

C3G, C3 glomerulopathy; DDD, dense deposit disease; C3GN, C3 glomerulonephritis.



Kidney International (2017) 91, 539–551

16-1578

C3ΣΠ - Ιστοχημεία

Table 2 | Morphological features of C3G

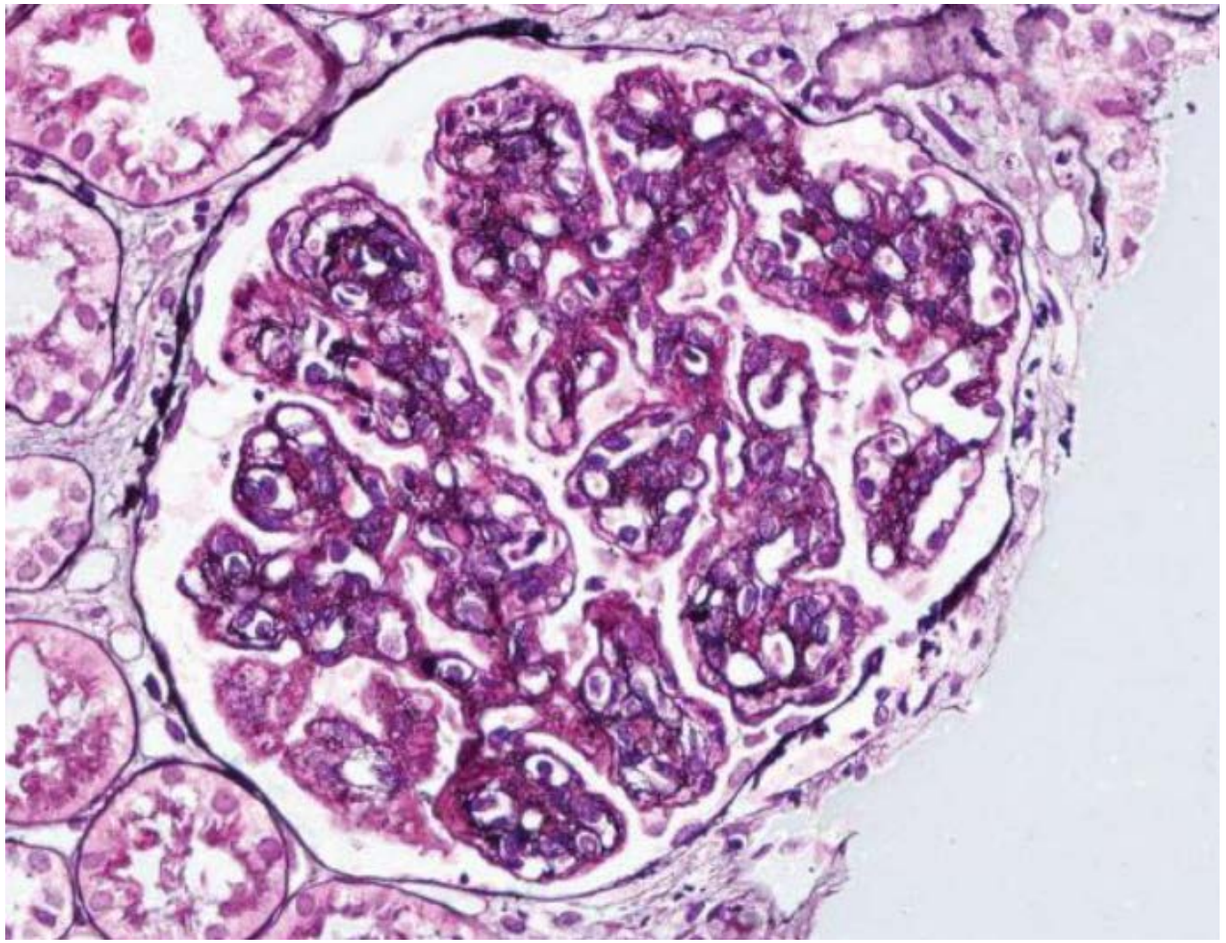
Light microscopy

Active lesions

- Mesangial expansion with or without hypercellularity
- Endocapillary hypercellularity including monocytes and/or neutrophils
- Capillary wall thickening with double contours (the combination of capillary wall thickening and mesangial increase is referred to as a membranoproliferative pattern)

C3G, C3 glomerulopathy; DDD, dense deposit disease; C3GN, C3 glomerulonephritis.

Kidney International (2017) 91, 539–551



Heptinstall Pathology of the Kidney 7th Edition

C3ΣΠ - Ιστοχημεία

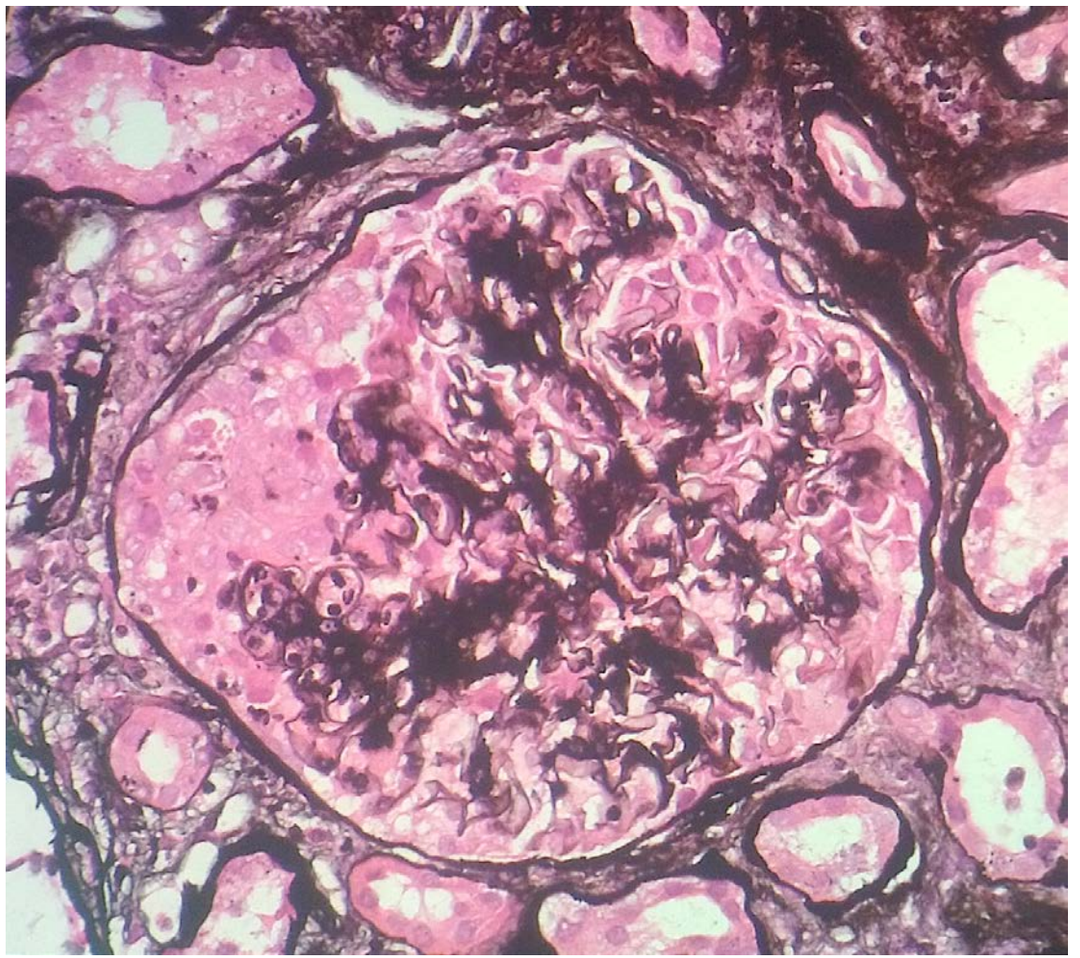
Table 2 | Morphological features of C3G

Light microscopy

Active lesions

- Mesangial expansion with or without hypercellularity
- Endocapillary hypercellularity including monocytes and/or neutrophils
- Capillary wall thickening with double contours (the combination of capillary wall thickening and mesangial increase is referred to as a membranoproliferative pattern)
- Necrosis
- Cellular/fibrocellular crescents

C3G, C3 glomerulopathy; DDD, dense deposit disease; C3GN, C3 glomerulonephritis.



Kidney International (2017) 91, 539–551

16-2249

C3ΣΠ - Ιστοχημεία

Table 2 | Morphological features of C3G

Light microscopy

Active lesions

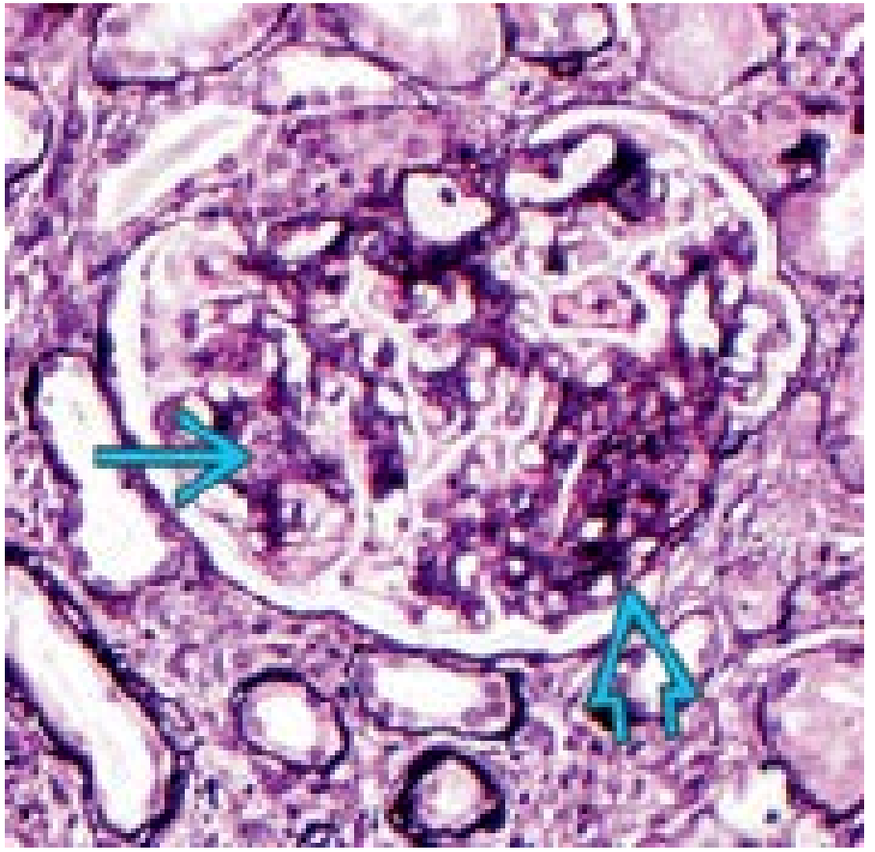
- Mesangial expansion with or without hypercellularity
- Endocapillary hypercellularity including monocytes and/or neutrophils
- Capillary wall thickening with double contours (the combination of capillary wall thickening and mesangial increase is referred to as a membranoproliferative pattern)
- Necrosis
- Cellular/fibrocellular crescents

Chronic lesions

- Segmental or global glomerulosclerosis
- Fibrous crescents

C3G, C3 glomerulopathy; DDD, dense deposit disease; C3GN, C3 glomerulonephritis.

Kidney International (2017) 91, 539–551



2016 Diagnostic Pathology Kidney Diseases 2nd Edition

C3ΣΠ - Ανοσοφθορισμός

Table 2 | Morphological features of C3G

Light microscopy

Active lesions

- Mesangial expansion with or without hypercellularity
- Endocapillary hypercellularity including monocytes and/or neutrophils
- Capillary wall thickening with double contours (the combination of capillary wall thickening and mesangial increase is referred to as a membranoproliferative pattern)
- Necrosis
- Cellular/fibrocellular crescents

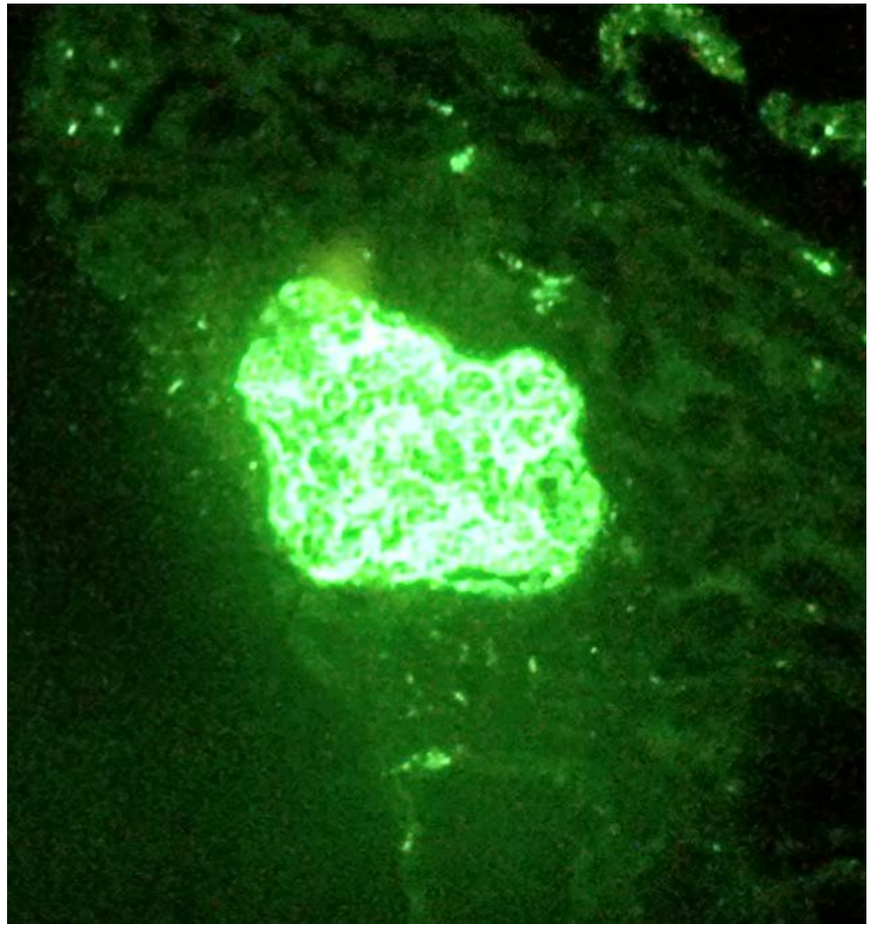
Chronic lesions

- Segmental or global glomerulosclerosis
- Fibrous crescents

Immunofluorescence microscopy

- Typically dominant C3 staining

C3G, C3 glomerulopathy; DDD, dense deposit disease; C3GN, C3 glomerulonephritis.



Kidney International (2017) 91, 539–551

16-1578

C3ΣΠ – ΗΜ: DDD (dese deposit disease)

Table 2 | Morphological features of C3G

Light microscopy

Active lesions

- Mesangial expansion with or without hypercellularity
- Endocapillary hypercellularity including monocytes and/or neutrophils
- Capillary wall thickening with double contours (the combination of capillary wall thickening and mesangial increase is referred to as a membranoproliferative pattern)
- Necrosis
- Cellular/fibrocellular crescents

Chronic lesions

- Segmental or global glomerulosclerosis
- Fibrous crescents

Immunofluorescence microscopy

- Typically dominant C3 staining

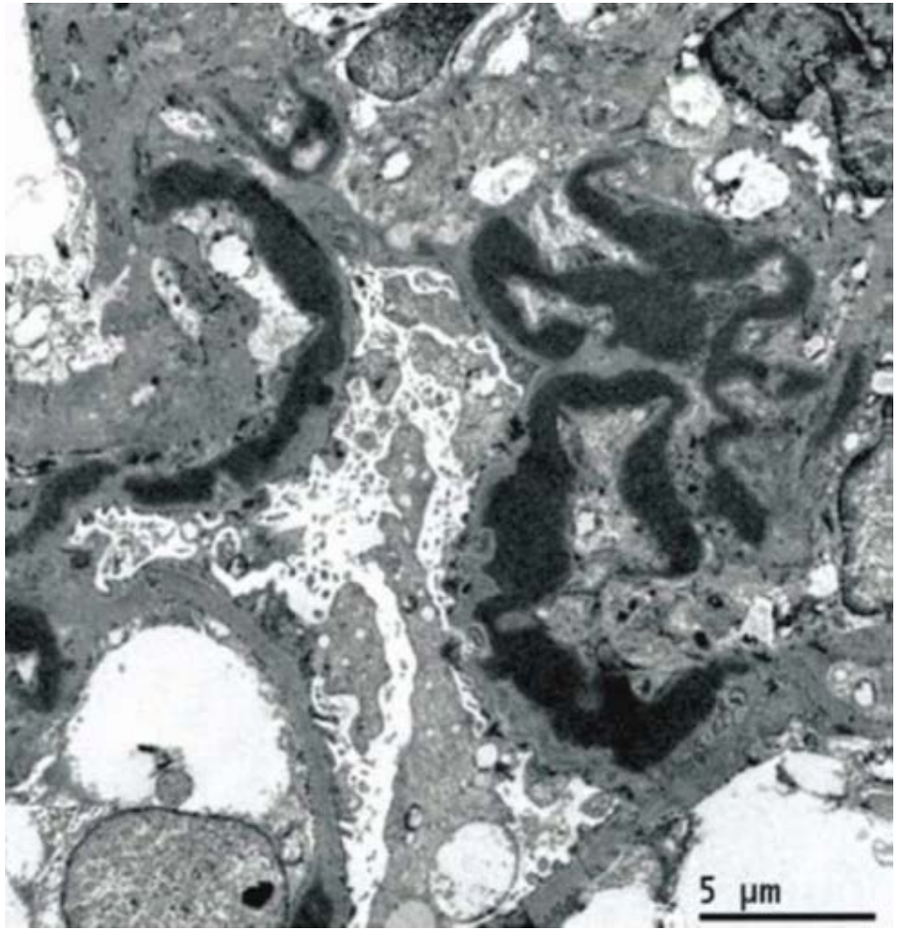
Electron microscopy

- DDD: Dense osmiophilic mesangial and intramembranous electron dense deposits

Τέως μεμβρανοπαραγωγική τύπου ΙΙ

C3G, C3 glomerulopathy; DDD, dense deposit disease; C3GN, C3 glomerulonephritis.

Kidney International (2017) 91, 539–551



Modern Pathology (2007) 20, 605–616

C3ΣΠ– ΗΜ: C3ΣΝ (C3 σπειραμαμονεφρίτιδα)

Table 2 | Morphological features of C3G

Light microscopy

Active lesions

- Mesangial expansion with or without hypercellularity
- Endocapillary hypercellularity including monocytes and/or neutrophils
- Capillary wall thickening with double contours (the combination of capillary wall thickening and mesangial increase is referred to as a membranoproliferative pattern)
- Necrosis
- Cellular/fibrocellular crescents

Chronic lesions

- Segmental or global glomerulosclerosis
- Fibrous crescents

Immunofluorescence microscopy

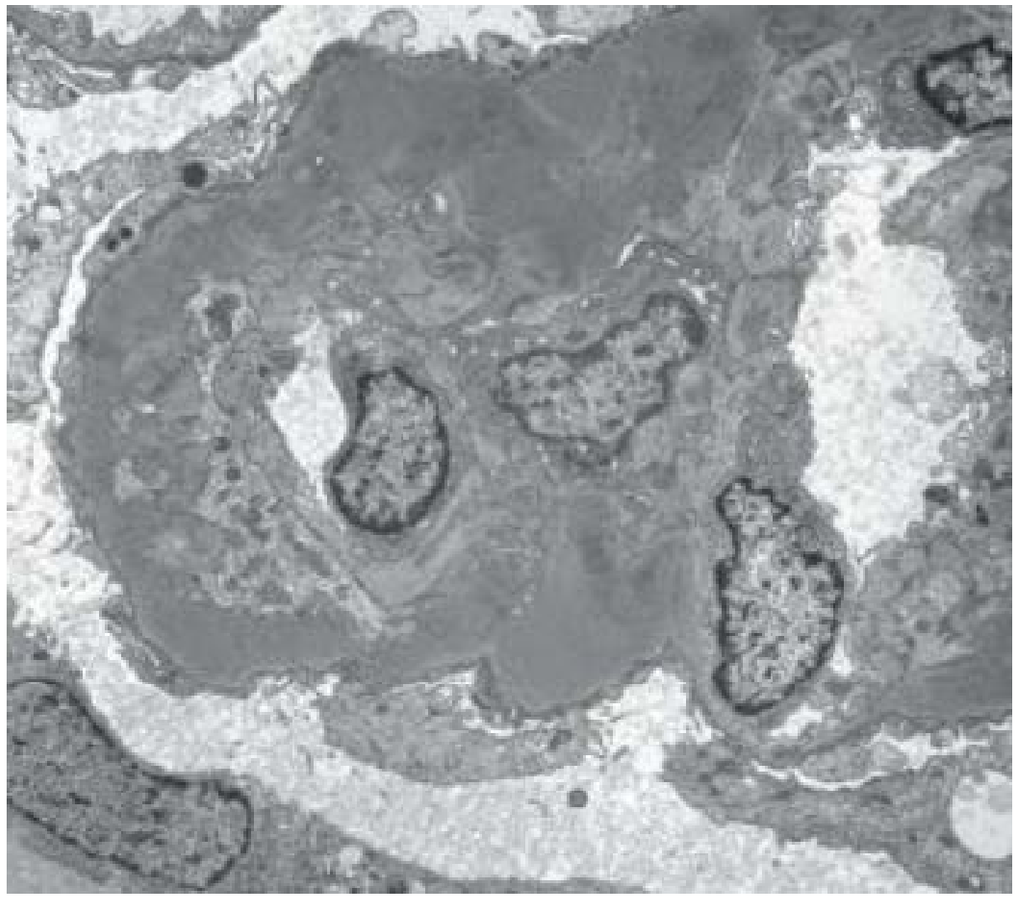
- Typically dominant C3 staining

Electron microscopy

- DDD: Dense osmiophilic mesangial and intramembranous electron dense deposits
- C3GN: Amorphous mesangial with or without capillary wall deposits

C3G, C3 glomerulopathy; DDD, dense deposit disease; C3GN, C3 glomerulonephritis.

Kidney International (2017) 91, 539–551



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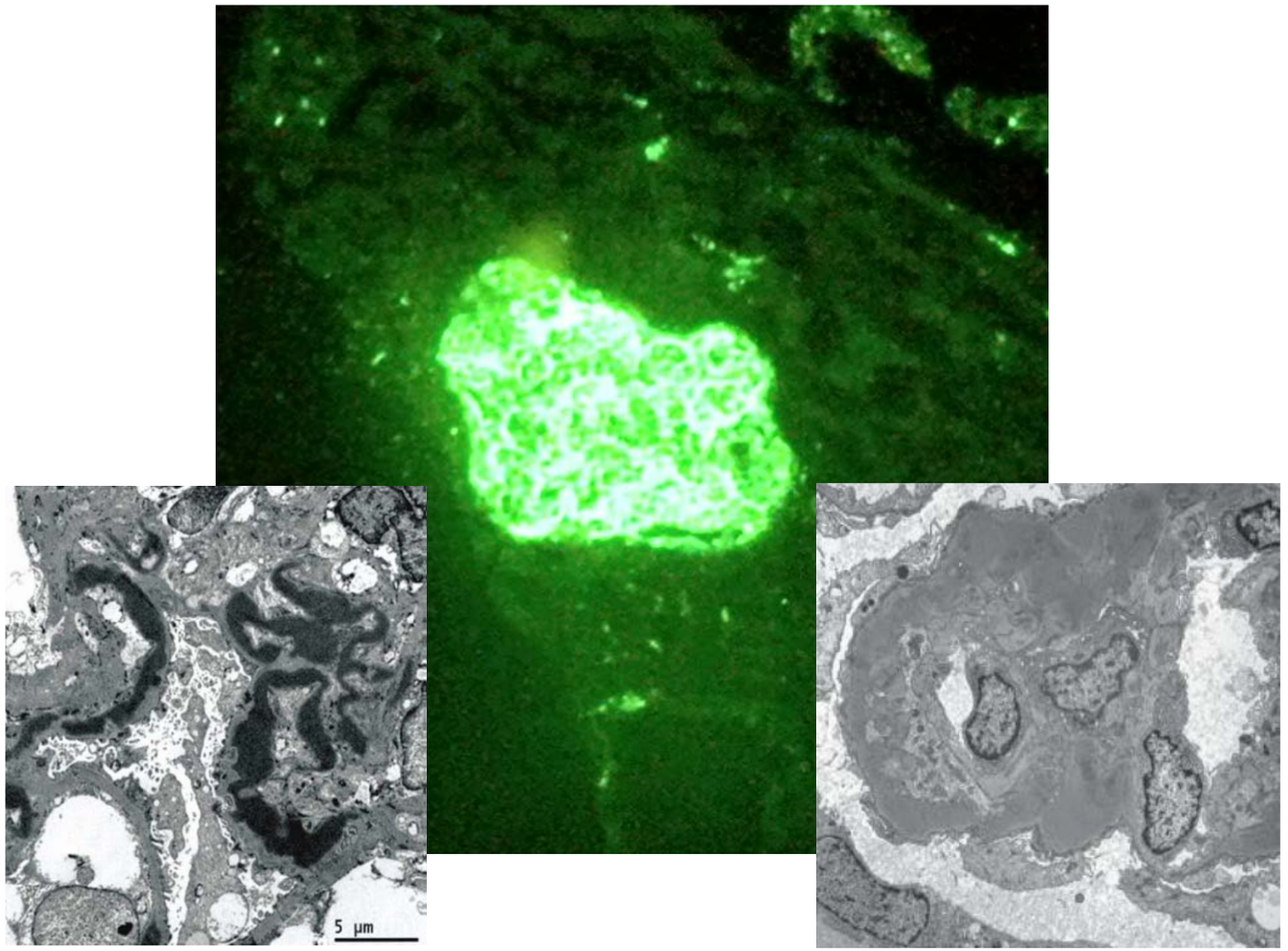
C3ΣΠ (σπειραματοπάθεια - C3G) =
DDD + C3 ΣΝ (σπειραματονεφρίτιδα – C3GN)



C3ΣΠ Ιστολογική εικόνα – ΗΜ: humps

Table 2 | Morphological features of C3G

Light microscopy

Active lesions

- Mesangial expansion with or without hypercellularity
- Endocapillary hypercellularity including monocytes and/or neutrophils
- Capillary wall thickening with double contours (the combination of capillary wall thickening and mesangial increase is referred to as a membranoproliferative pattern)
- Necrosis
- Cellular/fibrocellular crescents

Chronic lesions

- Segmental or global glomerulosclerosis
- Fibrous crescents

Immunofluorescence microscopy

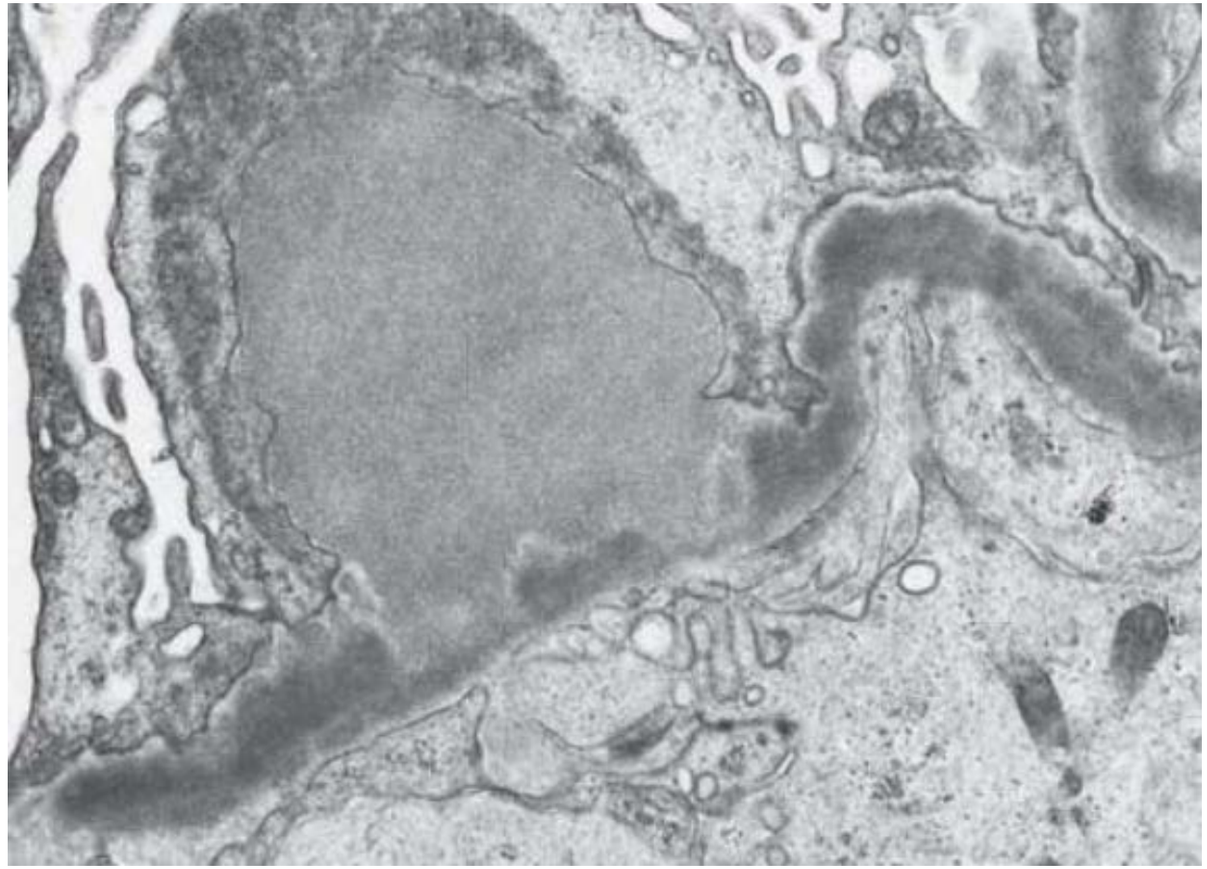
- Typically dominant C3 staining

Electron microscopy

- DDD: Dense osmiophilic mesangial and intramembranous electron dense deposits
- C3GN: Amorphous mesangial with or without capillary wall deposits including subendothelial, intramembranous and subepithelial electron dense deposits
- Subepithelial "humps" may be seen in both DDD and C3GN

C3G, C3 glomerulopathy; DDD, dense deposit disease; C3GN, C3 glomerulonephritis.

Kidney International (2017) 91, 539–551



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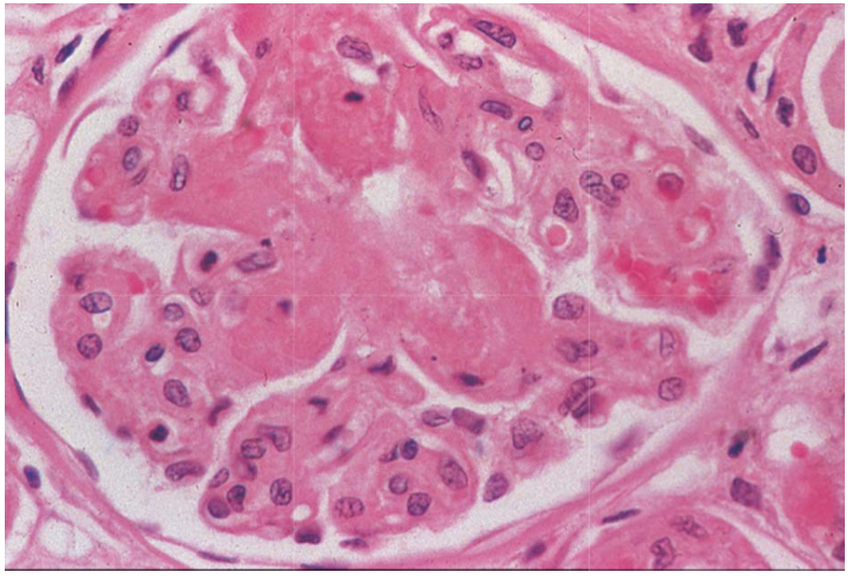
Κλινικοεργαστηριακές εκδηλώσεις

Κλινικοεργαστηριακές εκδηλώσεις: αHUS



- Συνήθως οξεία έναρξη
- Νεφρική ανεπάρκεια
- Μικροαγγειοπαθητική αιμολυτική αναιμία
- Θρομβοπενία
- Υπέρταση «κακοήθης»
- Χαμηλό C3 σε έως 50% των περιπτώσεων

Kidney International (2017) 91, 539–551

Semin Nephrol 33:508-530, 2013

Κλινικοεργαστηριακές εκδηλώσεις: C3ΣΠ

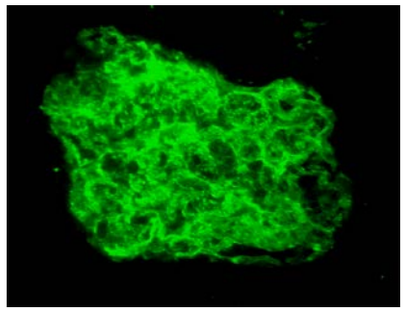
Table 1. Clinical and laboratory findings at the time of renal biopsy in patients with C3 glomerulopathy

Category	Total (*N*=80)	DDD (*n*=21)	C3GN (*n*=59)	*P* Value
Age (yr)				
Median	21 (10–47)	12 (8–20)	26 (12–53)	0.002
<16	32 (40)	14 (68)	18 (31)	
C3 (*n*=69 total; 19 DDD, 50 C3GN) (0.65–1.65 g/L)				
Normal	28 (41)	2 (11)	26 (52)	0.003
Low	41 (59)	17 (79)	24 (48)	

Clin J Am Soc Nephrol 9: 46–53, 2014

- Υποξεία, χρόνια ή υποκλινική πορεία
- Μικροαιματουρία, λευκωματουρία, νεφρωσικό
- Σπανίως ταχέως εξελισόμενη νεφρική νόσος
- Υπέρταση

- Χαμηλό C3 (75% DDD, 30-50% C3GN)
- C3Nef (85% DDD, 45% C3GN)
- η DDD σε μικρότερες ηλικίες



Kidney International (2012) 82, 454–464

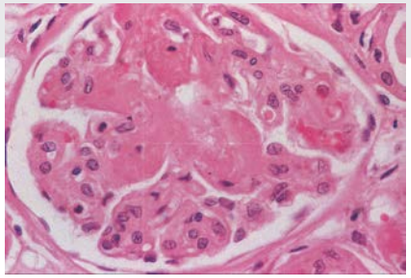
Kidney International (2017) 91, 539–551

Εξωνεφρικές εκδηλώσεις: αHUS

Table 9. Extrarenal Manifestations Associated With aHUS

Extrarenal manifestation	Reference
Digital gangrene	220–222
Cerebral artery thrombosis/stenosis	222–224
Extracerebral artery stenosis	223
Cardiac involvement/myocardial infarction	51,225
Ocular involvement	226
Pulmonary involvement	51,94
Pancreatic involvement	51
Neurologic involvement	51,94,103

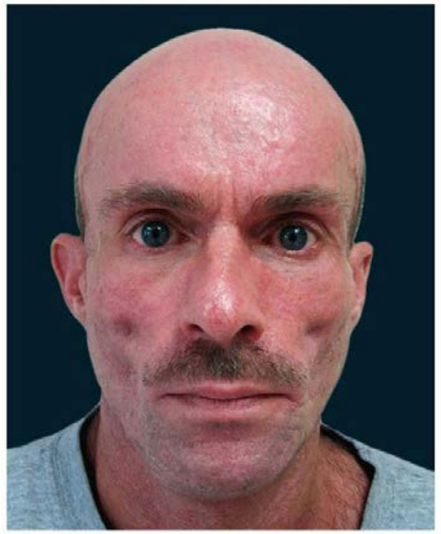
Semin Nephrol 33: 508-530, 2013



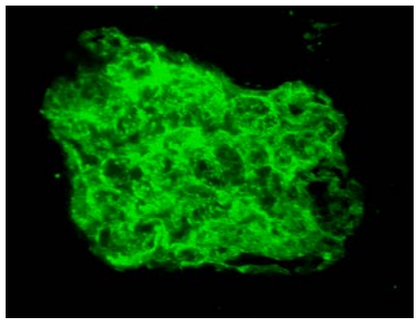
- 10-20%
- Νευρολογικές (10%)
  - Διέγερση, κρίσεις Ε, PRES, κώμα
  - ? αποτέλεσμα ΘΜΑ ή υπερτασικής κρίσης, ουραιμίας
- ΟΕΜ
- Γάγγραινα δακτύλων
- Συμμετοχή παγκρέατος, πνευμόνων, οφθαλμών

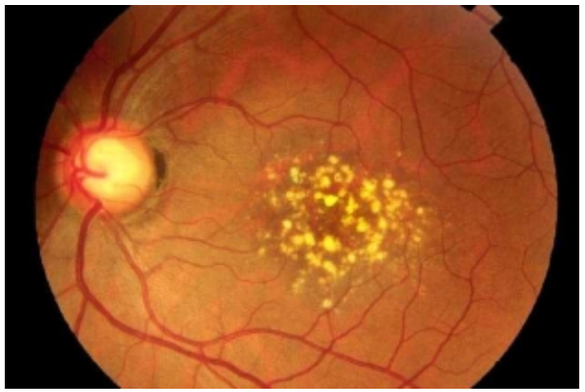
PRES: posterior reversible encephalopathy syndrome

Εξωνεφρικές εκδηλώσεις: C3ΣΠ



- Επίκτητη μερική λιποδυστροφία
  - παράγοντας D σε λιποκύτταρα,
  - καταστροφή λιποκυττάρων μέσω εναλλακτικής οδού



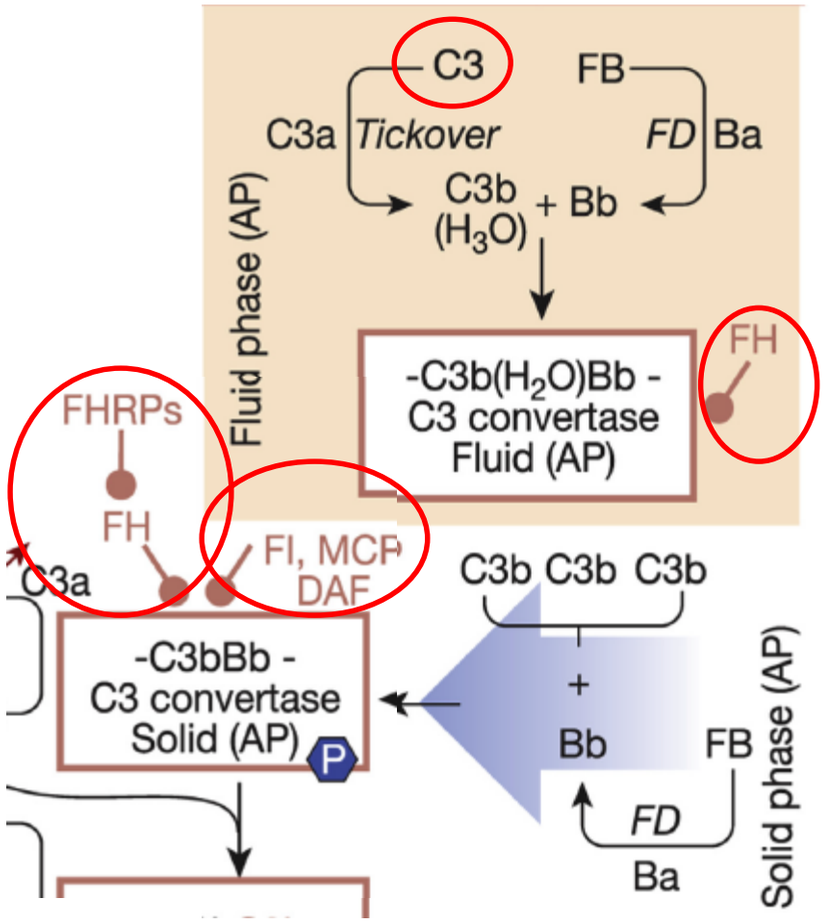


- Drusen
  - Συσώρρευση πρωτεϊνών συμπληρώματος και λιπιδίων

Kidney International (2017) 91, 539–551

Παθογένεια

Παθογένεια



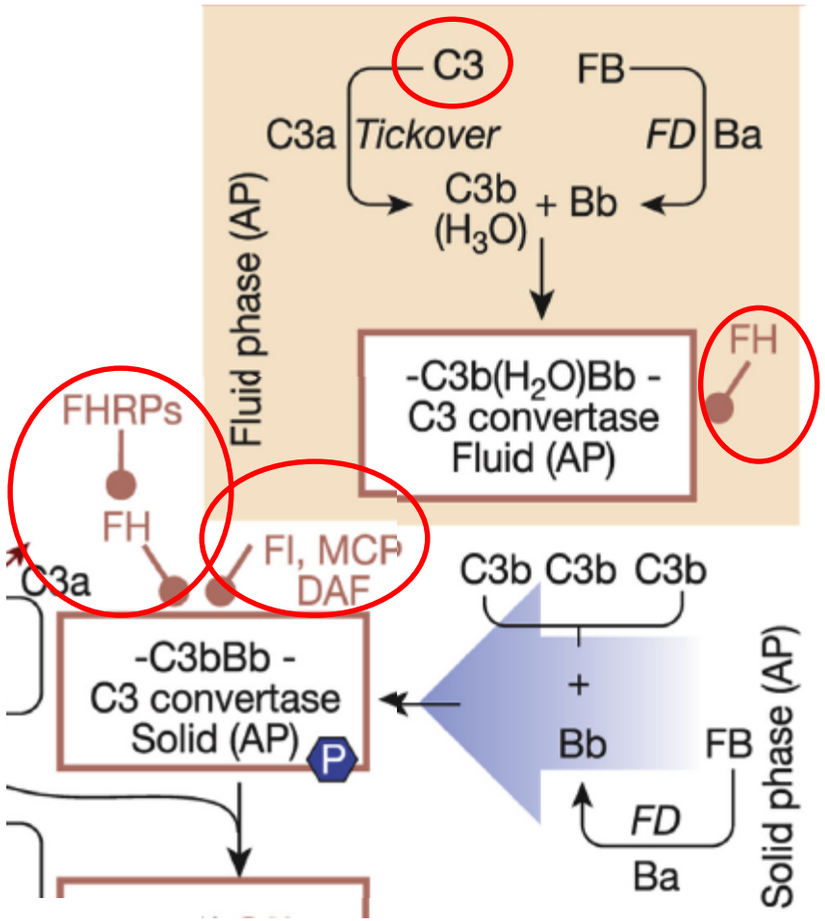
- Διαταραχή στη ρύθμιση αυτοενεργοποίησης της εναλλακτικής οδού
- Δυσλειτουργία των ρυθμιστικών παραγόντων

  C3 MCP CFI CFH/CFHRP

MCP: Membrane Cofactor Protein
CFI: Complement Factor I
CFH: Complement Factor H
CFHRP: Complement Factor H Regulating/Related Proteins

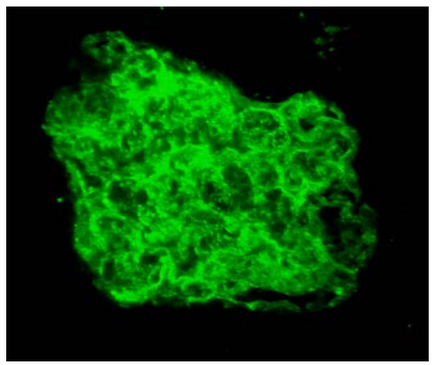
Kidney International (2016) 89, 278–288

Παθογένεια



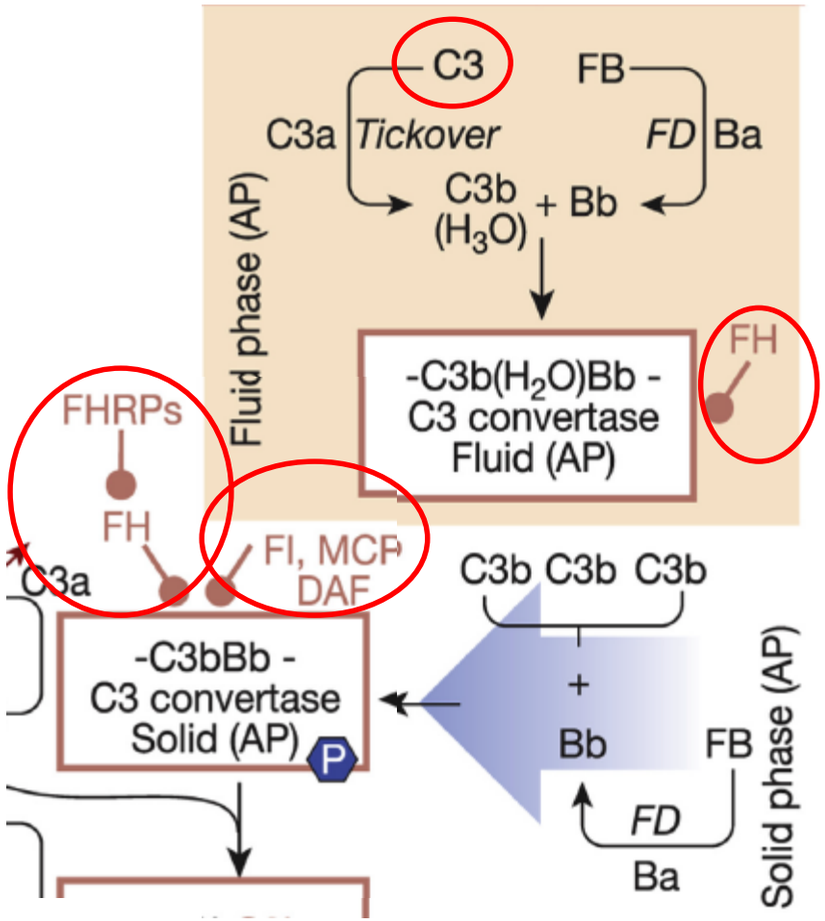
Ενεργοποίηση στον ορό

C3 σπειραματοπάθεια



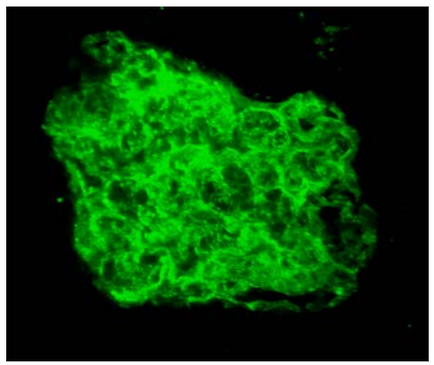
Kidney International (2016) 89, 278–288

Παθογένεια



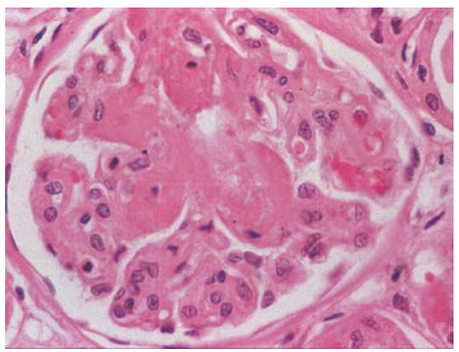
Ενεργοποίηση στον ορό

C3 σπειραματοπάθεια



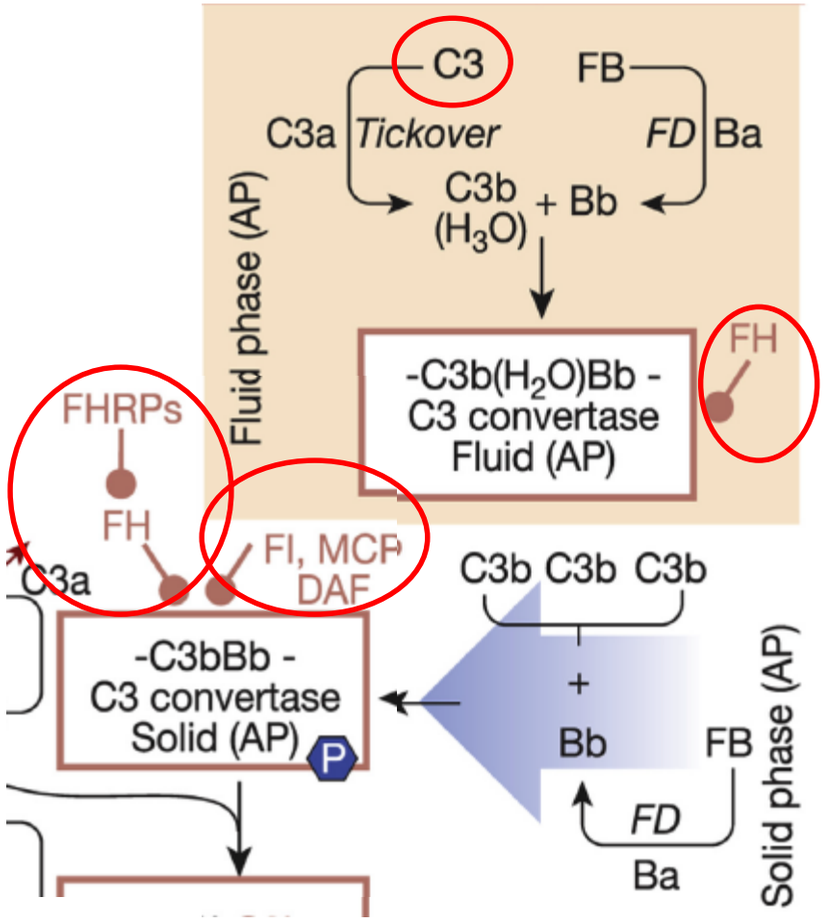
Ενεργοποίηση στο ενδοθήλιο

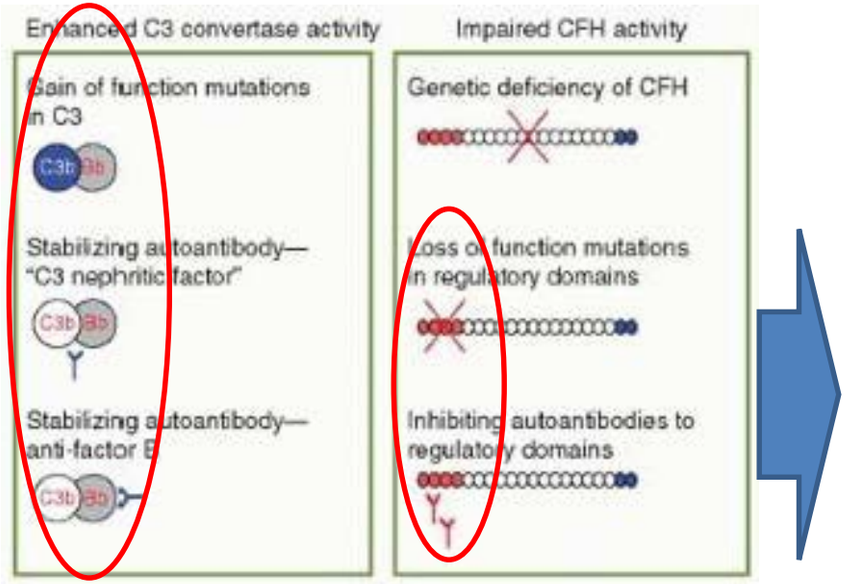
άτυπο HUS

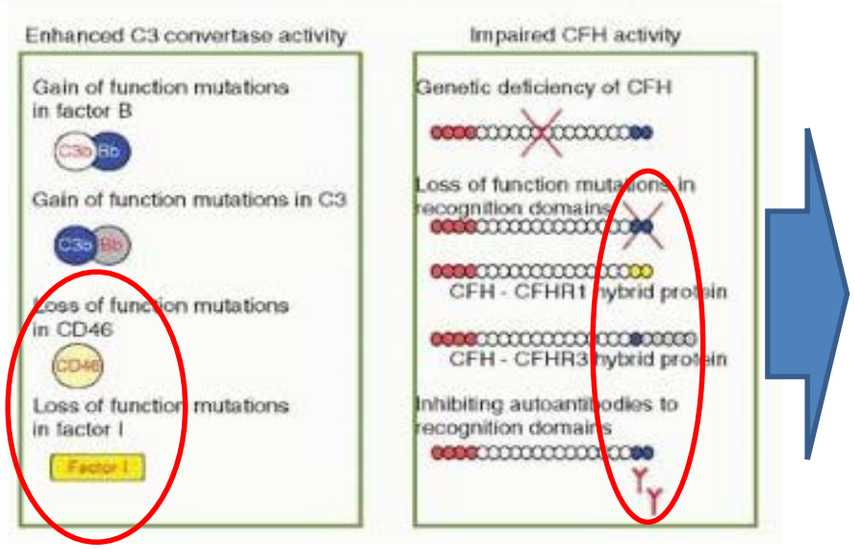


Kidney International (2016) 89, 278–288

Παθογένεια







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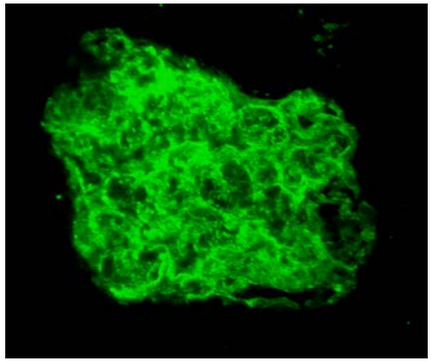

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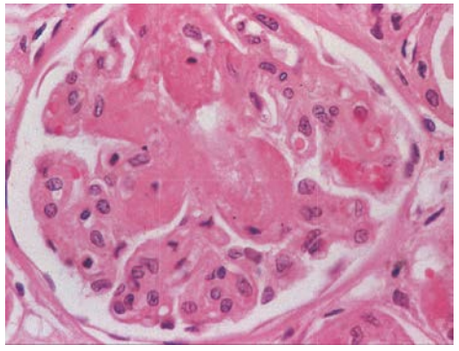
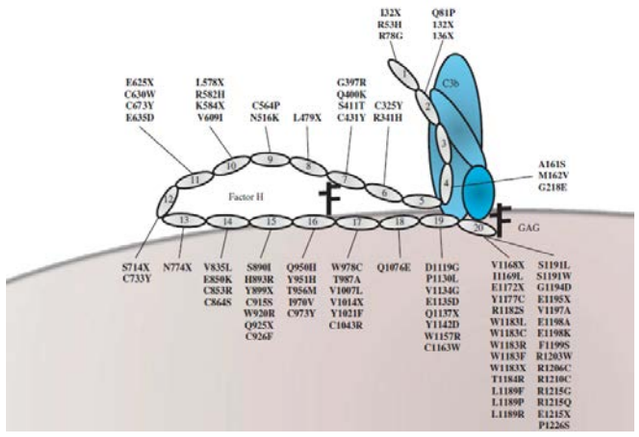
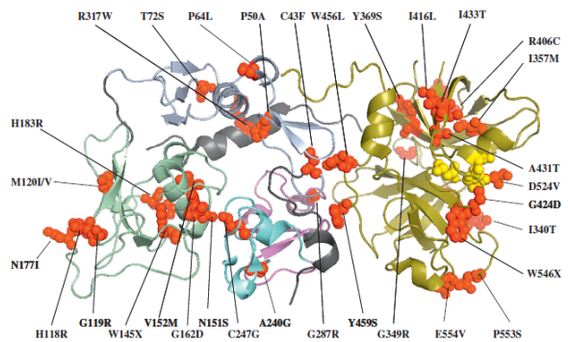
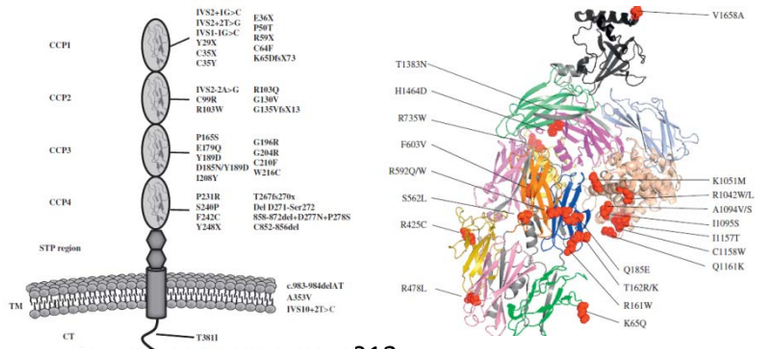


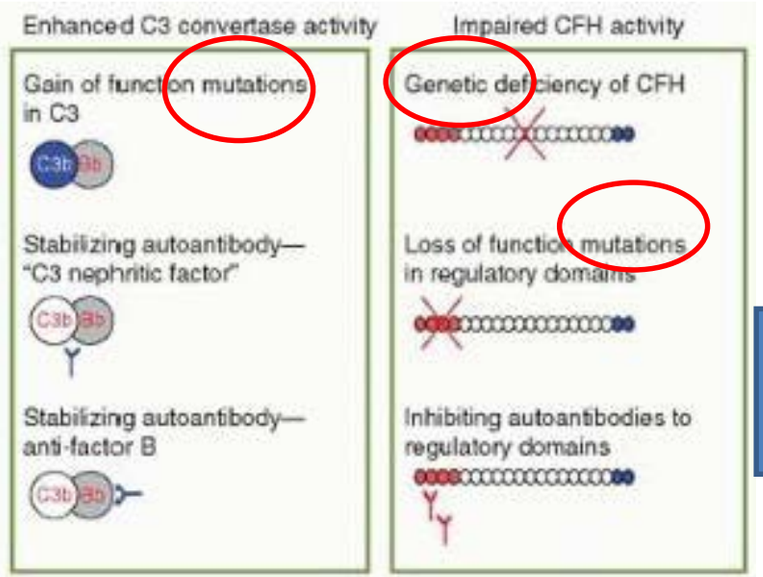
Kidney International (2016) 89, 278–288

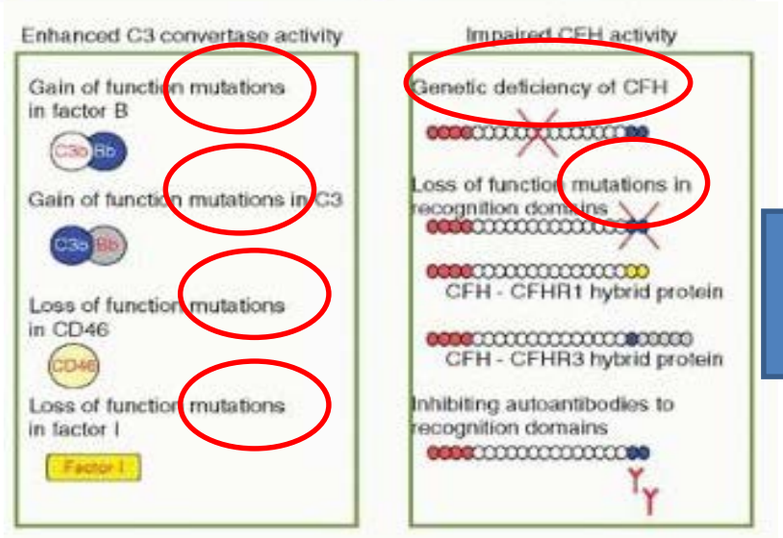
Αίτια: γενετικά











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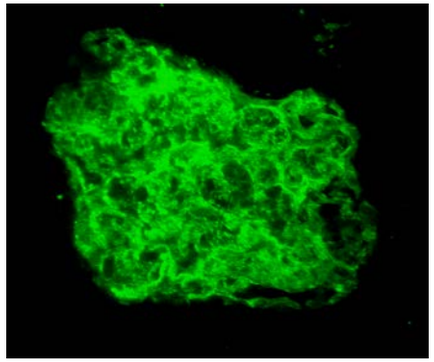

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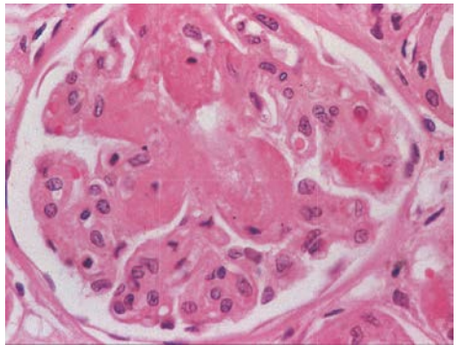
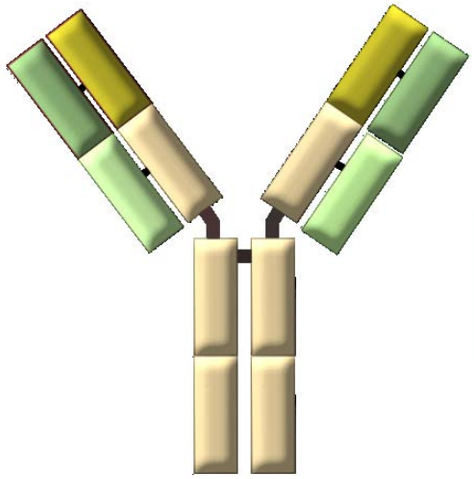
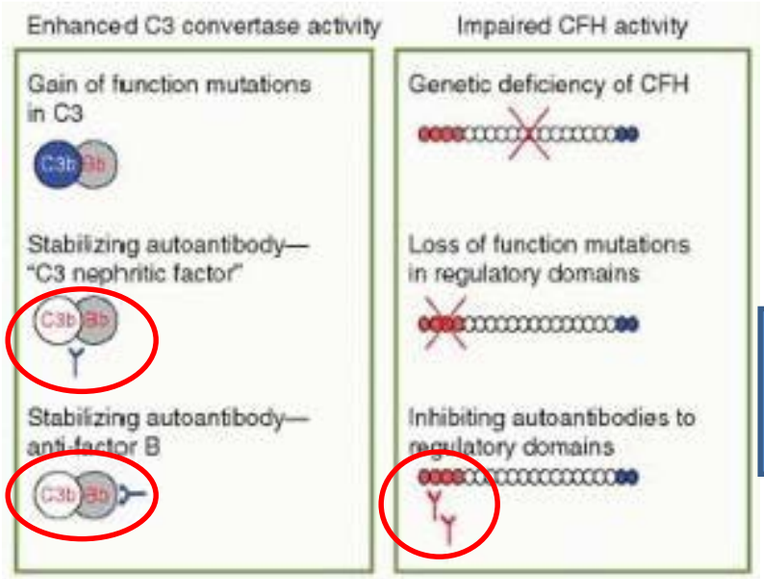


Semin Nephrol33:508-530, 2013

Αίτια: επίκτητα





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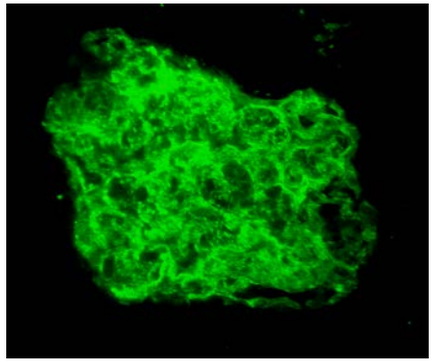

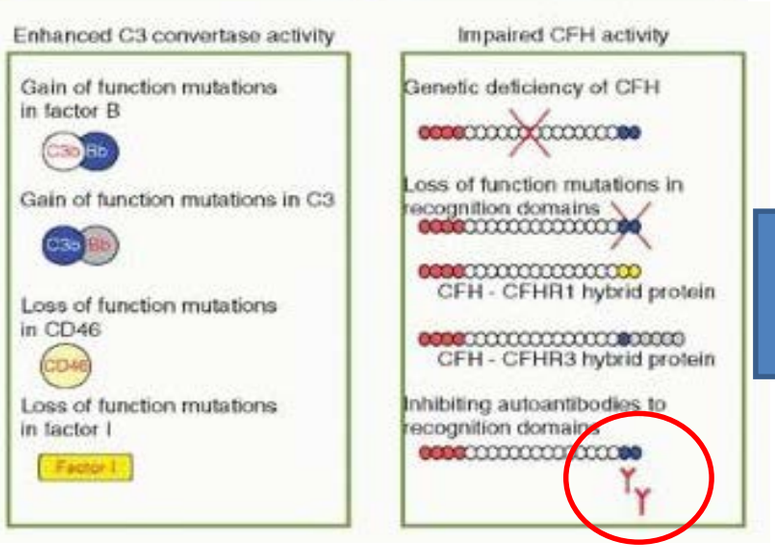

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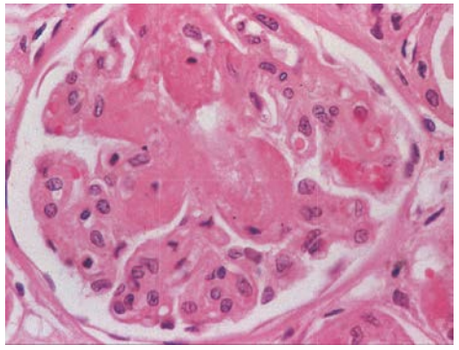
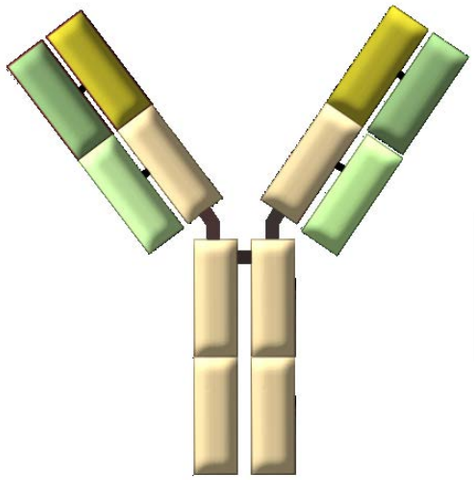
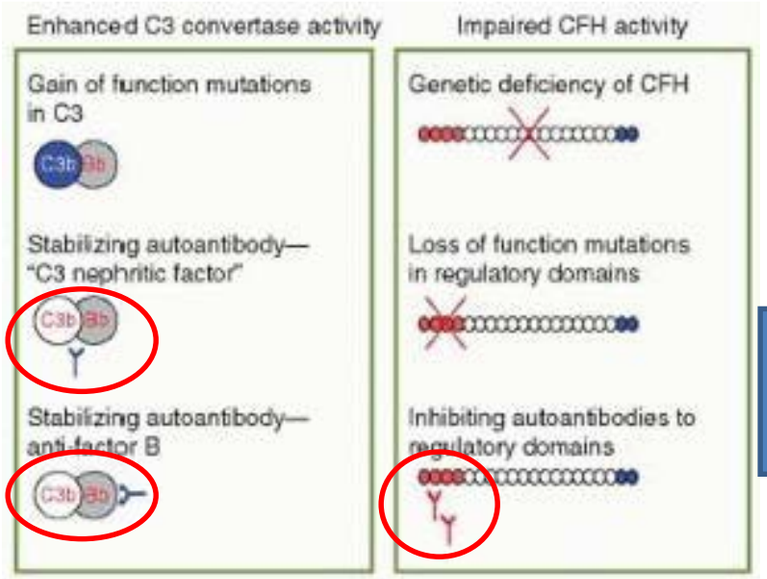


Αίτια: επίκτητα

C3nefritic factors (C3Nefs)





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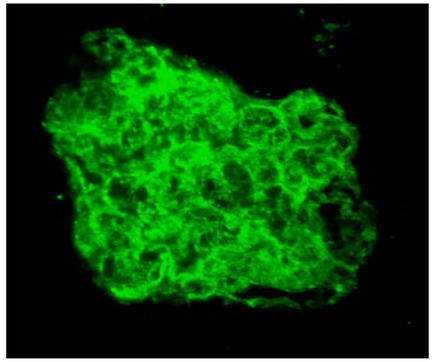

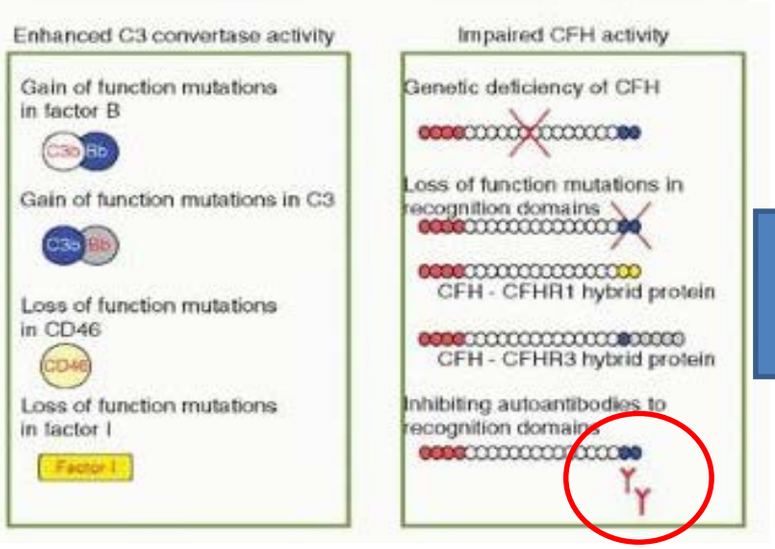

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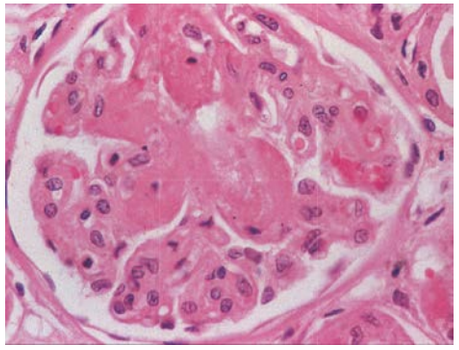

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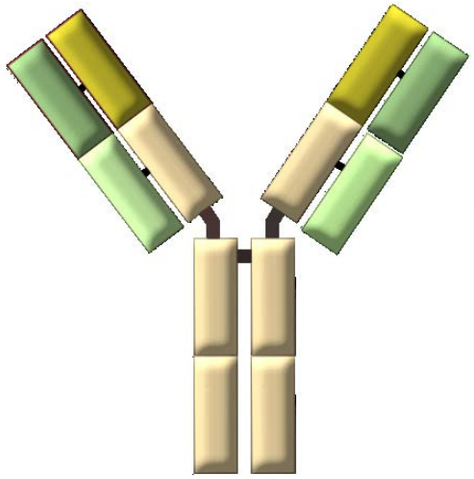
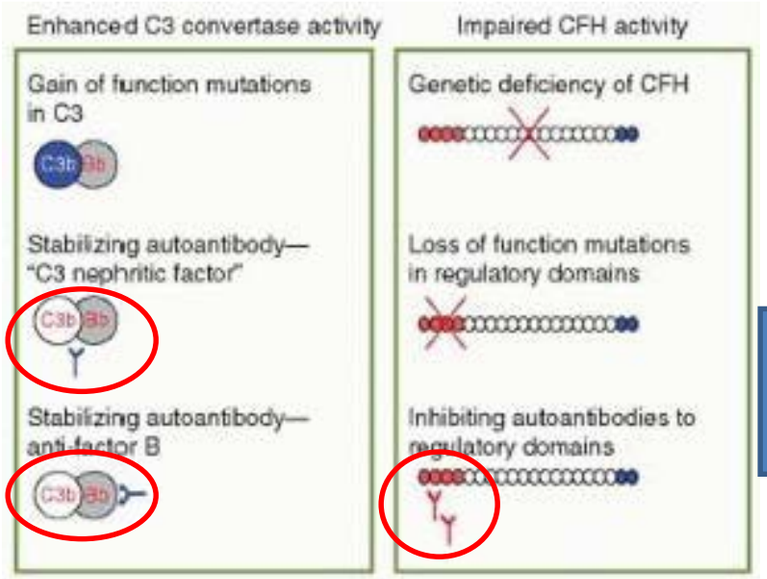
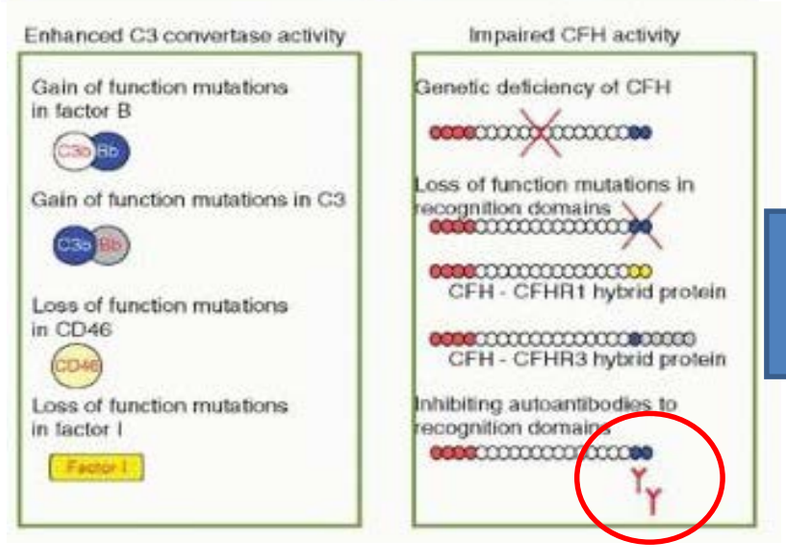


Anti FH

Παραπρωτεΐνες





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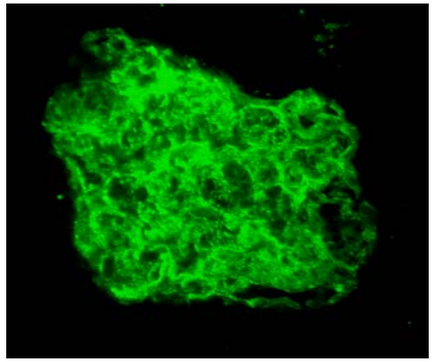

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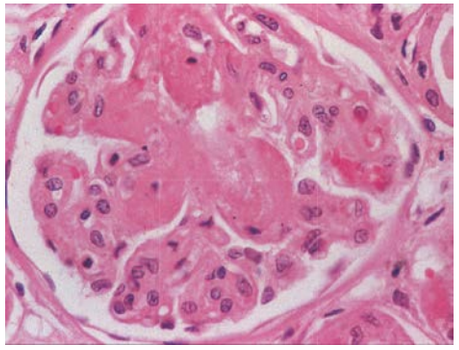
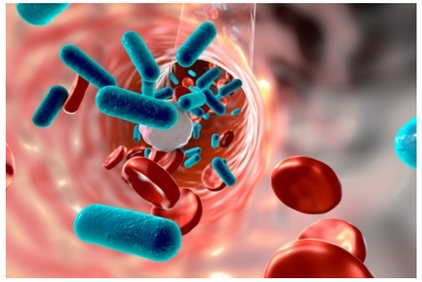
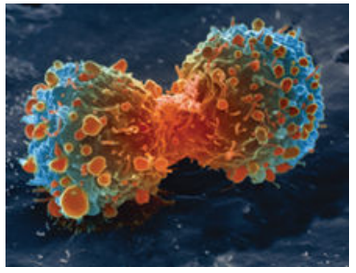


Εκλυτικά αίτια aHUS





- Λοιμώξεις
- Κύηση
- Φάρμακα
- Κακοήθειες

- Εκδήλωση aHUS

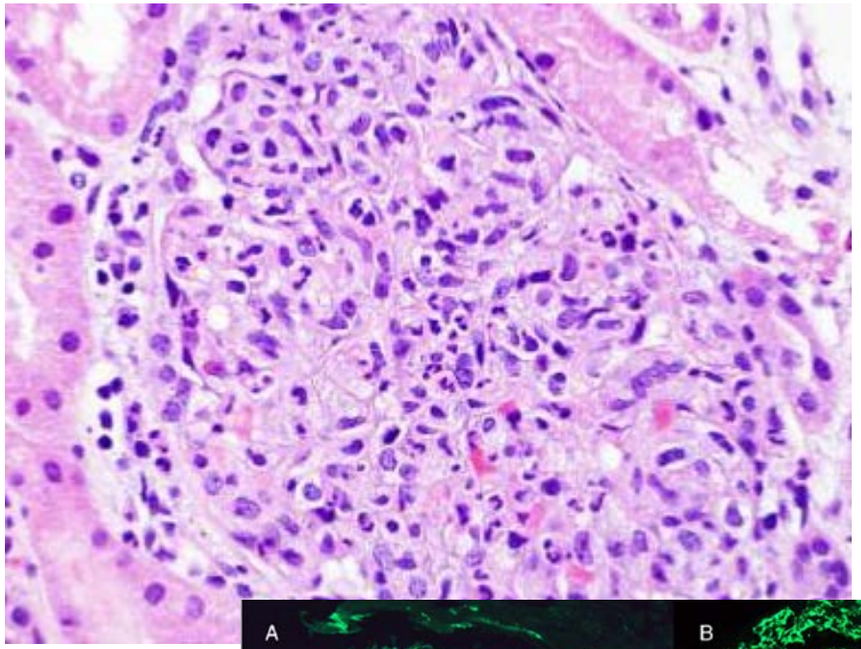
? σε έδαφος μεταλλάξεων που σχετίζονται με λανθάνουσα διαταραχή της ενεργοποίησης του συμπληρώματος

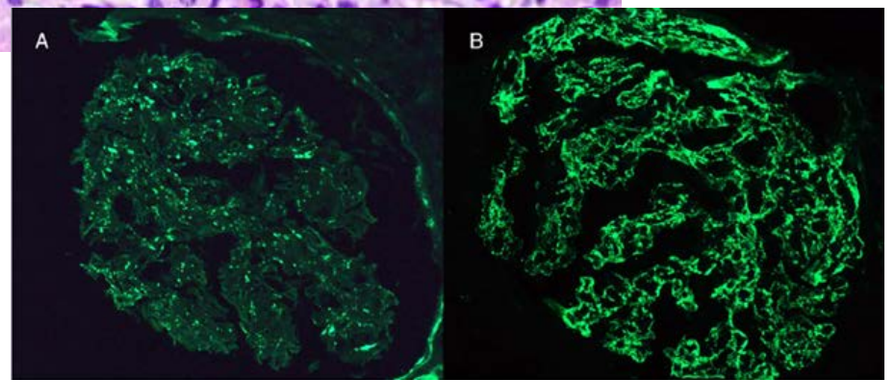
? άμεση επίδραση στην εναλλακτική οδό

Semin Nephrol 33:508-530

Kidney International (2016) 89, 537–538;

Λοιμώξεις και C3ΣΠ





- Ιστολογική εικόνα C3 ΣΠ μετά από λοίμωξη, συχνά στρεπτοκοκκική
- ? C3ΣΠ ή όψιμη μεταλοιμώδης με μόνο C3 στον ανοσοφθορισμό

- Σχεδόν αδύνατη η ΔΔ τη στιγμή της βιοψίας
- Κλινική πορεία και εφόσον δεν αυτοεπεριορίζεται διερεύνηση διαταραχών εναλλακτικής οδού

Clinical Kidney Journal, 2016, vol. 9, no. 3, 397–402

Διερεύνηση

Διερεύνηση επίκτητων αιτίων C3ΣΠ και aHUS

Supplementary Table 8. Acquired drivers of disease in aHUS and C3G: screening recommendations

Acquired factor	aHUS	C3G
C3 nephritic factor	No	Yes
Anti-factor H autoantibodies	Yes	Yes
Monoclonal gammopathy	Yes	Yes

Abbreviation: aHUS, atypical hemolytic uremic syndrome; C3G, C3 glomerulopathy

Kidney International (2017) 91, 539–551

Supplementary Table 3. Complement studies for aHUS and C3G

Test	aHUS	C3G
Complement protein levels	C3, C4, FB*, C5*	C3, C4, FB*, C5*
Complement regulatory protein levels	FH, FI, Properdin*, CD46#	FH, FI, Properdin*
Complement split products	C3c*, C3d*, Bb*, sC5b-9*	C3c*, C3d*, Bb*, sC5b-9*
Complement functional assays	CH50, AH50, hemolytic assays, FH assays*	CH50, AH50, hemolytic assays, FH assays*
Autoantibodies	Anti-FH	Anti-FH, anti-FB*, C3Nef*, C4Nef*
Tests to detect plasma cell dyscrasia	-	Serum free light chains, SEP
Genetic screening	*CFH, CFI, C3, CD46, CFB* Genomic rearrangements across the *FH-FHR* locus (e.g., by MLPA) Sequencing of coding regions and assessment of CNV Non-complement genetic screening includes *THBD* and *DGKE*	*CFH, CFI, C3, CFB* Genomic rearrangements across the *FH-FHR* locus (e.g. by MLPA) Sequencing of coding regions and assessment of CNV Non-complement genetic screening includes *DGKE*

*Currently available only at specific laboratories; they are research and not clinically validated assays
#CD46 is also known as MCP

Abbreviations: AH50, alternative pathway hemolytic assay; C3, complement component 3; C3Nef, C3 nephritic factor; C4, complement component 4; C4Nef, C4 nephritic factor; C5, complement component 5; *CFB*, complement factor B gene; *CFH*, complement factor H gene; *CFHR*, complement factor H related genes; *CFI*, complement factor I gene; CH50, classical pathway hemolytic assay; CNV, copy number variation; *DGKE* gene, diacylglycerol kinase epsilon gene; FB, complement factor B; FH, complement factor H; FI, complement factor I; MLPA, multiplex ligation-dependent probe amplification; sC5b-9, soluble C5b-9; SEP, serum protein electrophoresis; THBD, thrombomodulin.

Kidney International (2017) 91, 539–551

aHUS: Συσχέτιση γονότυπου – φαινότυπου

Supplementary Table 5. Genotype-phenotype correlations in aHUS*

Gene	Risk of death or ESRD at onset or first year	Risk of recurrence	Risk of death or ESRD after 3-5yr	Risk of recurrence in allograft
CFH or CFH-CFHR1/3 hybrid genes	50-70%	50%	75%	75-90%
CFI	50%	10-30%	50-60%	45-80%
MCP single	0-6%	70-90%	6-38%	<20%
MCP combined*	30-40%	50%	50%	50-60%
C3	60%	50%	75%	40-70%
CFB	50%	3/3	75%	100%
THBD	50%	30%	54%	?
Anti-FH	30-40%	40-60%	35-60%	Depends on antibody titers

*Data refer to the period *before* introduction of eculizumab

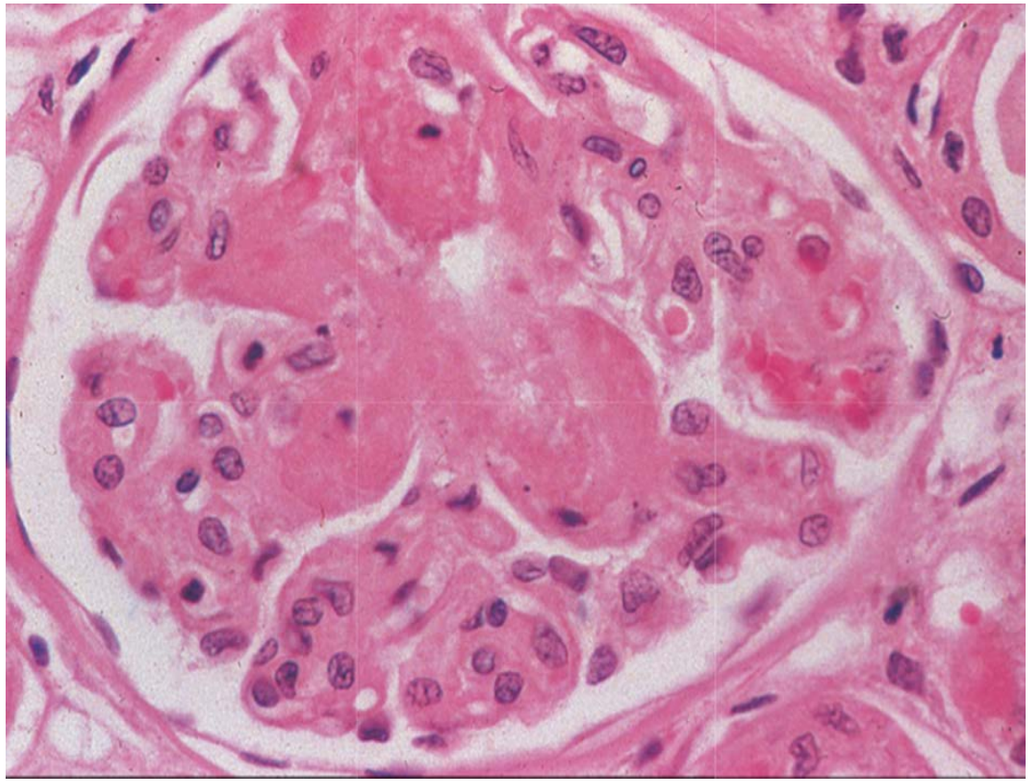
**Combined with *CFH* or *CFI* or *C3* mutations

Abbreviations: aHUS, atypical hemolytic uremic syndrome; CFB, complement factor B gene; CFH, complement factor H gene; CFHR, complement factor H-related genes; CFI, complement factor I gene; ESRD, end-stage renal disease; FH, factor H protein; THBD, thrombomodulin gene

Kidney International (2017) 91, 539–551

Αντιμετώπιση

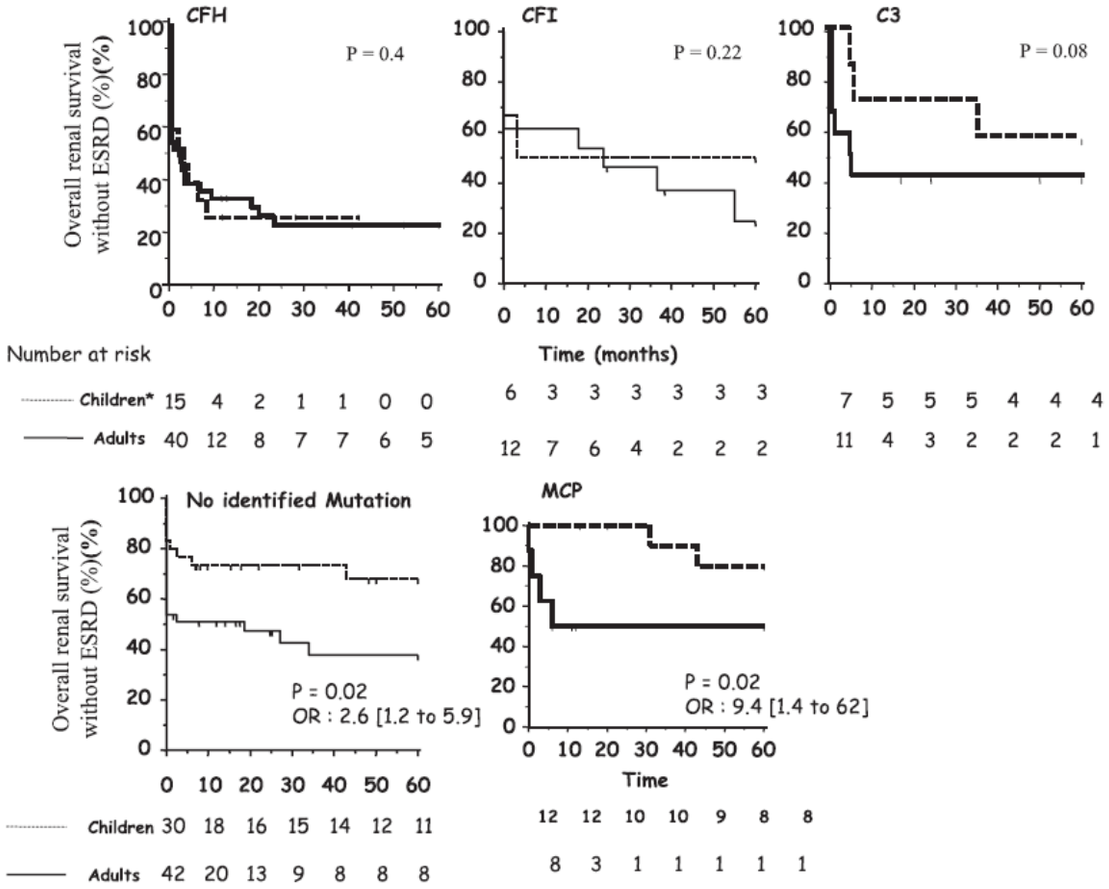
Αντιμετώπιση: αHUS



- Πλασμαφαίρεση
- Eculizumab (anti-C5)

Clin J Am Soc Nephrol 13: 300–317, 2018

aHUS: Πλασμαφαίρεση



- ΤΣΧΝΝ στα 3-5 έτη

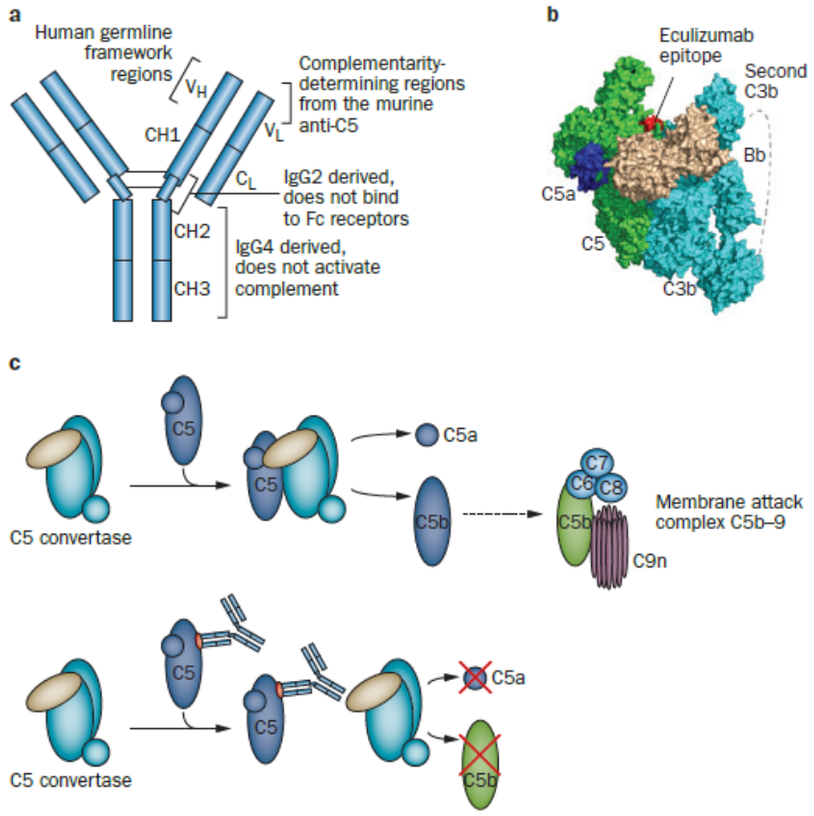
  35-50% σε παιδιά

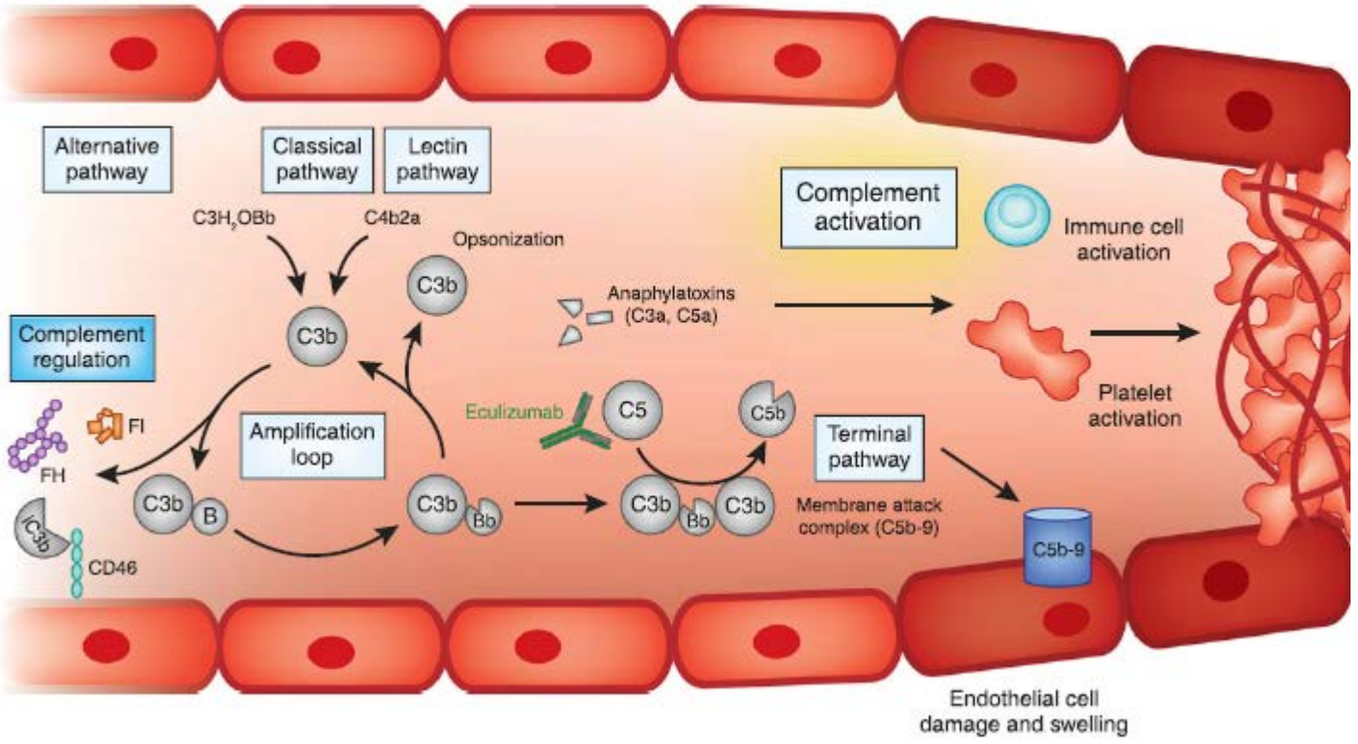
  65% σε ενήλικες

Clin J Am Soc Nephrol 8: 554–562, 2013

Clinical Kidney Journal, 2017, vol. 10, no. 5, 600–624

Eculizimab (anti C5)

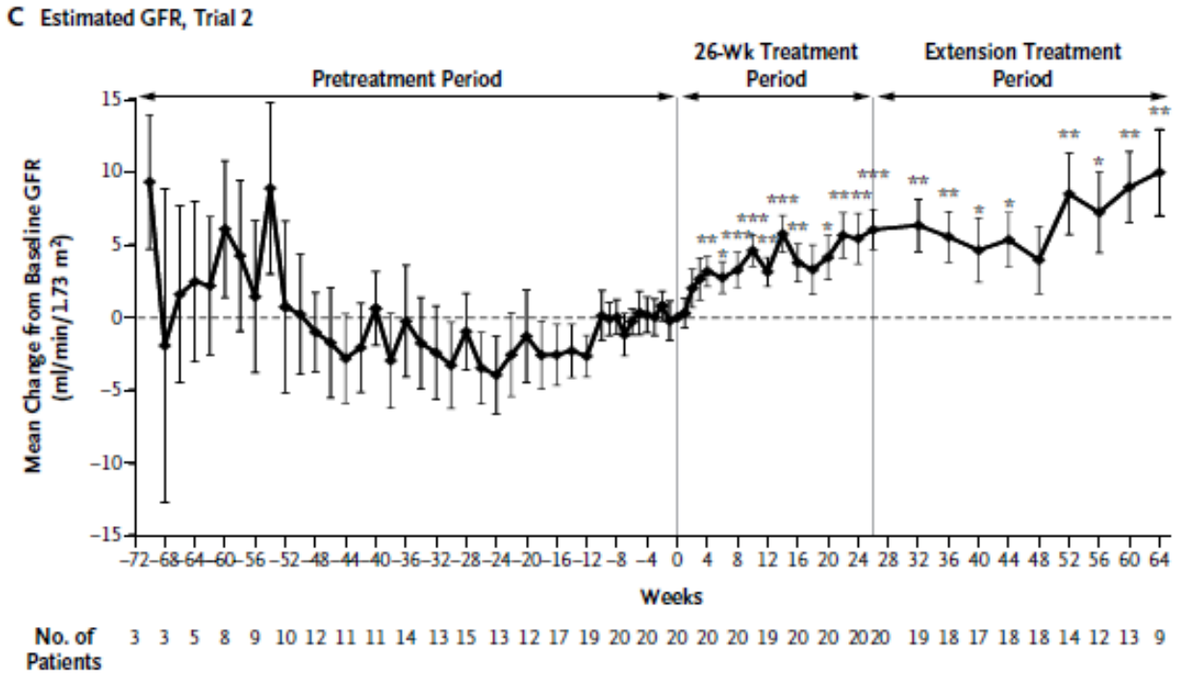




Nat. Rev. Nephrol. 8, 643–657 (2012)

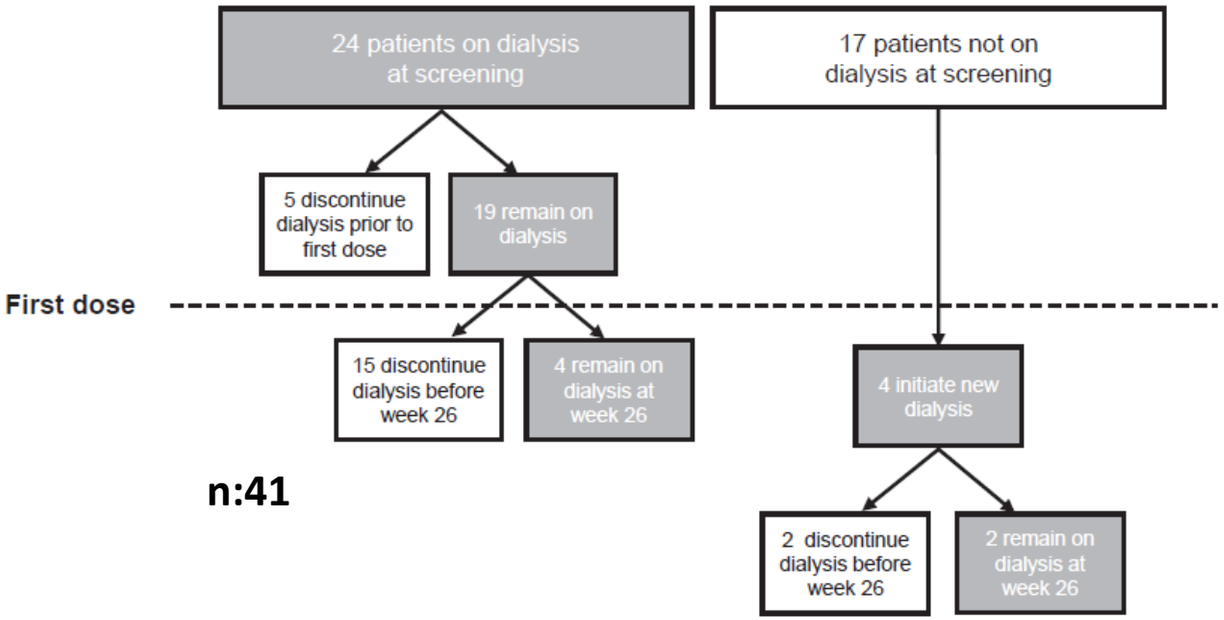
Clin J Am Soc Nephrol 13: 300–317, 2018

aHUS και eculizimab



80% απένταξη από ΑΚ

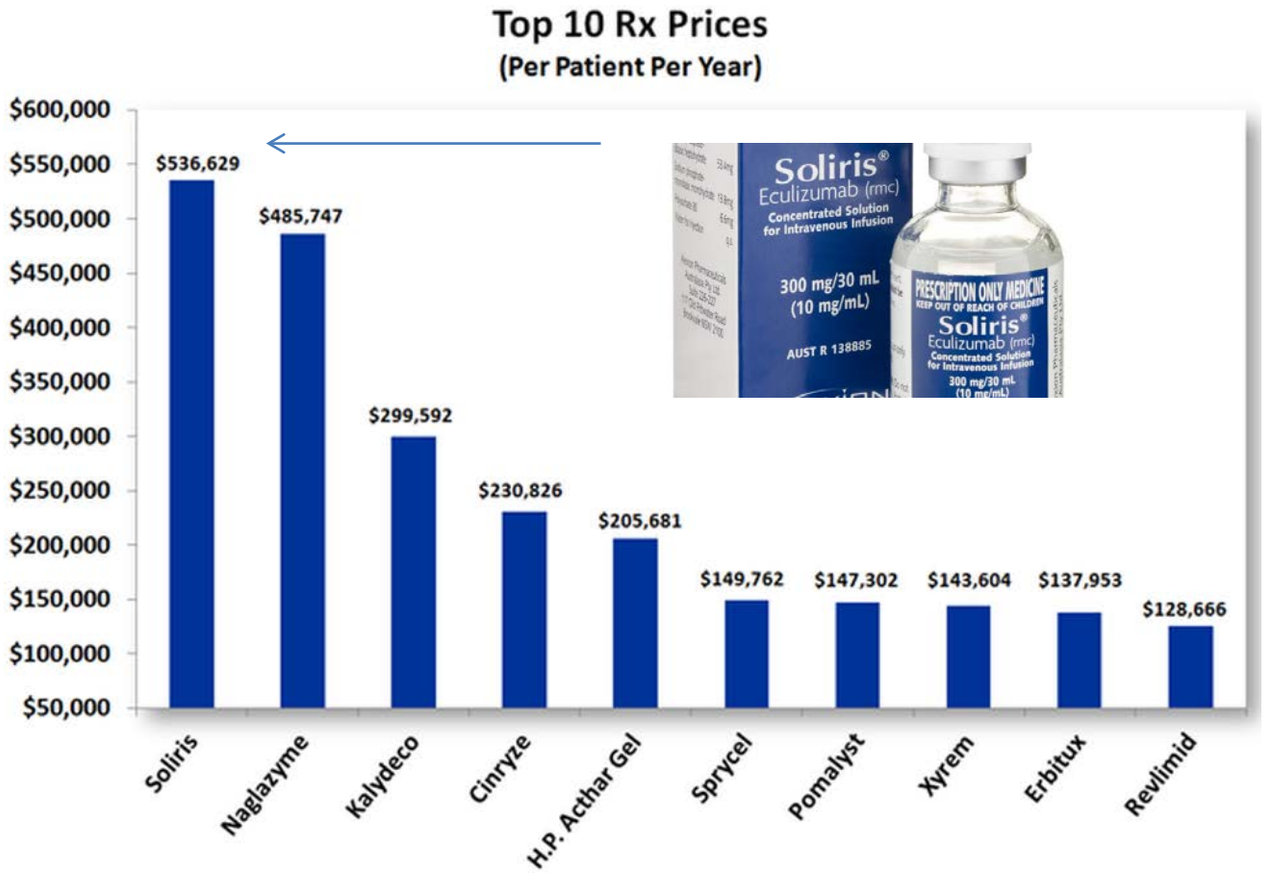
N Engl J Med 2013;368:2169-81



- 79% απένταξη από ΑΚ
- 15% ΤΣΧΝΝ στα 2 έτη

Am J Kidney Dis. 2016;68(1):84-93

Eculizimab: χορήγηση



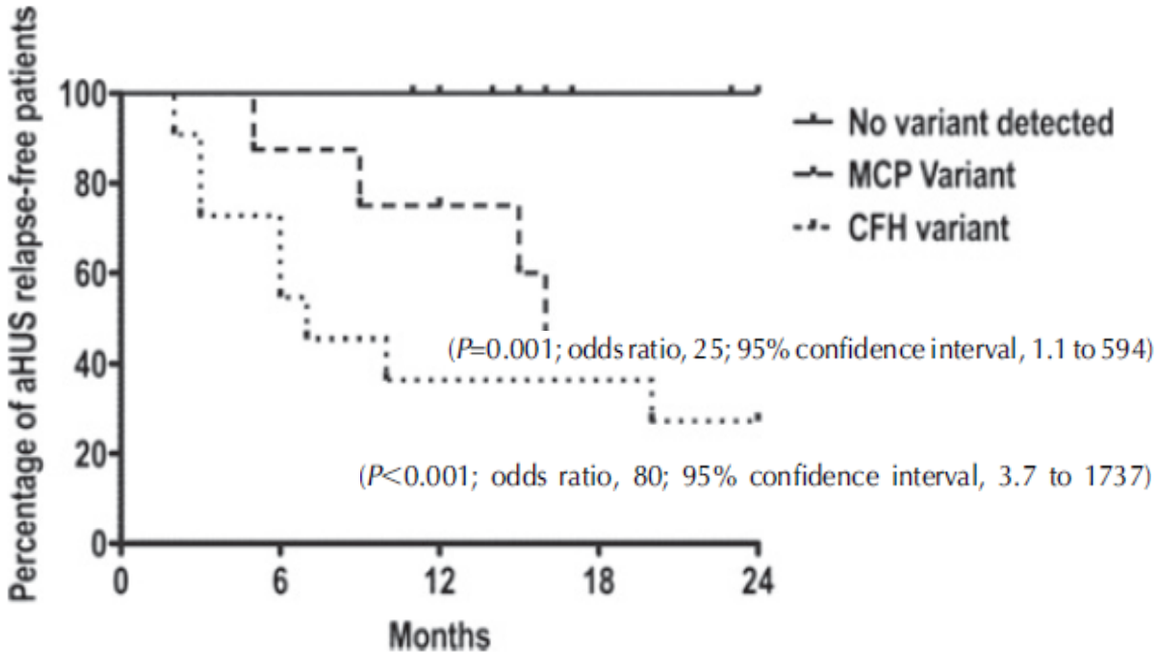
- 4 εβδομαδιαίες δόσεις και μετά

  2 το μήνα
- Για πάντα (SPC)
- Μηνιγγιτιδόκοκκος:

  εμβόλιο χημειοπροφύλαξη
- >$500.000/έτος για ενήλικα

Am J Kidney Dis. 2014;64(4):633-637

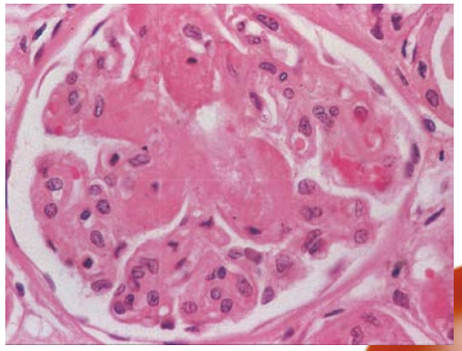
Γονίδια και υποτροπή μετά από διακοπή eculizumab

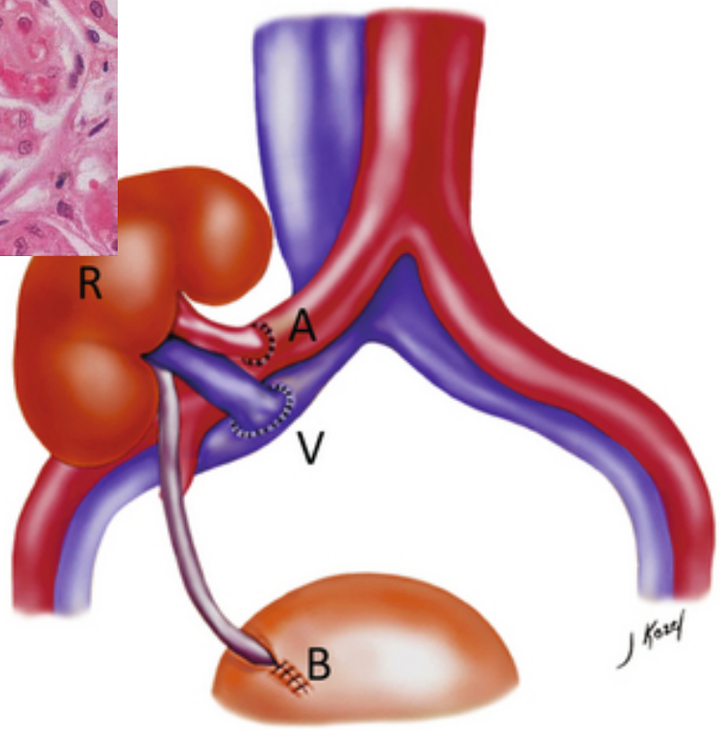


- 108 treated
- 38 discontinued
- median follow-up of 22 months
- **12 patients (31%) experienced relapse**
- **8/11 (72%)** with complement **factor H** variants
- **4/8 (50%)** with **membrane cofactor protein** variants
- **0% with no variant**

Clin J Am Soc Nephrol 12: 50–59, 2017

aHUS και μεταμόσχευση νεφρού





- Αποκλεισμός γενετικού υπόβαθρου σε ζώντα συγγενή δότη
- Υποτροπή σε 60-80%

Αυξημένος κίνδυνος σε διαταραχές CFH, CFI, CFB, C3 ή σε προηγούμενη υποτροπή

Χαμηλός σε MCP

- Trigger : Ενδοθηλιακή βλάβη

Ισχαιμία επαναιμάτωση

Αναστολείς καλσινευρίνης

- Καλή απάντηση σε eculizumab
- ?προφυλλακτική χορήγηση eculizumab?

Am J Kidney Dis. 2017;70(6):754-757

Atypical hemolytic uremic syndrome and C3 glomerulopathy: conclusions from a "Kidney Disease: Improving Global Outcomes" (KDIGO) Controversies Conference

OPEN

Timothy H.J. Goodship[1], H. Terence Cook[2], Fadi Fakhouri[3], Fernando C. Fervenza[4], Véronique Frémeaux-Bacchi[5], David Kavanagh[1], Carla M. Nester[6,7], Marina Noris[8], Matthew C. Pickering[2], Santiago Rodríguez de Córdoba[9], Lubka T. Roumenina[10,11,12], Sanjeev Sethi[13] and Richard J.H. Smith[6,7]; for Conference Participants[14]

Kidney International (2017) 91, 539–551

Table 4 | Prophylaxis against aHUS recurrence in allografts based on a risk-assessment strategy[a]

Recurrence risk	Treatment regimen
High risk (50-100%) • Previous early recurrence • Pathogenic mutation[a] • Gain-of-function mutation	Prophylactic eculizumab[b,c] Note: Start on the day of transplantation due to potential for severe recurrence and limited recovery of function in renal grafts compared with native kidneys
Moderate risk • No mutation identified • Isolated *CFI* mutations • Complement gene mutation of unknown significance • Persistent low titer FH autoantibody	Prophylactic eculizumab or plasma exchange[d]
Low risk (<10%) • Isolated *MCP* mutations • Persistently negative FH autoantibodies	No prophylaxis

aHUS, atypical hemolytic uremic syndrome; CFI, complement factor I gene; FH, complement factor H protein; MCP, membrane cofactor protein gene.
[a]Requires complete screening of all genes implicated in aHUS.
[b]Prophylactic regimens are based on local center protocols; no trial data exist to support superiority of 1 protocol over another.
[c]Liver transplantation can be considered for renal transplant recipients with liver-derived complement protein abnormalities, uncontrolled disease activity despite eculizumab therapy, or financial considerations regarding cost of long-term eculizumab therapy.
[d]The decision to perform or not to perform prophylactic plasma exchange or complement inhibition is left to the discretion of the clinician.

MTM σε aHUS – χωρίς eculizumab

Variant Classification[d]	Previous Tx/HUS Recurrence After Previous Tx	Recurrence Risk According to KDIGO Guideline	Pt No.	Kidney Function at End of F/U: F/U, mo	Scr, μmol/L	eGFR, mL/min/1.73 m²	Proteinuria, mg/10 mmol Scr	aHUS Recurrence	
Pathogenic	N/N	High risk	1	68	132[a]	39	0	No	No
Likely pathogenic			2	66	80	71	0.06	No	No
Pathogenic	Y/Y	High risk	3	66	106	46	0	No	No
			4	63	104	65	0.1	No	No
Pathogenic	N/N	High risk	5	45	76	72	0.07	No	No
Pathogenic	Y/Y	High risk							
Pathogenic	N/N	High risk	6	43	158[a]	39	0.27	No	No
Pathogenic	Y/Y	High risk	7	32	84	59	0	No	No
Pathogenic	Y (2×)/N	High risk	8	32	91[a]	64	0.05	No	Yes
			9	25	166[a]	36	0.12	No	Yes
Likely pathogenic	N/N	High risk							
Pathogenic	N/N	High risk	10	14	143	35	0.05	Yes	No
Likely pathogenic	Y/Y	High risk							
Pathogenic	N/N	High risk							
—	N/N	Moderate risk	11	9	151[a]	30	0.14	No	Yes
Pathogenic	N/N	High risk							
Likely pathogenic	N/N	High risk							
			12	7	140[a]	51	0.09	No	No
Pathogenic	N/N	High risk	13	7	67	86	0.06	No	No
Likely pathogenic	Y/Y	High risk	14	13	77	76	0.31	No	No
			15	22	145	50	0.10	No	No
Likely pathogenic			16	10	79	72	0.17	No	No
Likely pathogenic	N/N	High risk	17	7	175[a]	28	0.44	No	No

- N=17
- ***Ζώντες** δότες (3 συγγενείς)
- Basiliximab
- High MMF
- ***Low tac**
- ***Statin ACEi**
- FU: 25m (7-68)

***προστασία ενδοθηλίου**

Am J Kidney Dis. 2017;70(6):770-777

MTM σε aHUS – χωρίς eculizumab

Variant Classification[d]	Previous Tx/HUS Recurrence After Previous Tx	Recurrence Risk According to KDIGO Guideline	Pt No.	Kidney Function at End of F/U: F/U, mo	Scr, μmol/L	eGFR, mL/min/1.73 m²	Proteinuria, mg/10 mmol Scr	aHUS Recurrence	
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- N=17
- ***Ζώντες** δότες (3 συγγενείς)
- Basiliximab
- High MMF
- ***Low tac**
- ***Statin ACEi**
- FU: 25m (7-68)
- 1 υποτροπή
- $22 million κέρδος

***προστασία ενδοθηλίου**

Am J Kidney Dis. 2017;70(6):770-777

MTM σε aHUS – χωρίς eculizumab

Variant Classification[d]	Previous Tx/HUS Recurrence After Previous Tx	Recurrence Risk According to KDIGO Guideline	Pt No.	F/U, mo	Kidney Function at End of F/U: Scr, μmol/L	eGFR, mL/min/1.73 m²	Proteinuria, mg/10 mmol Scr	aHUS Recurrence
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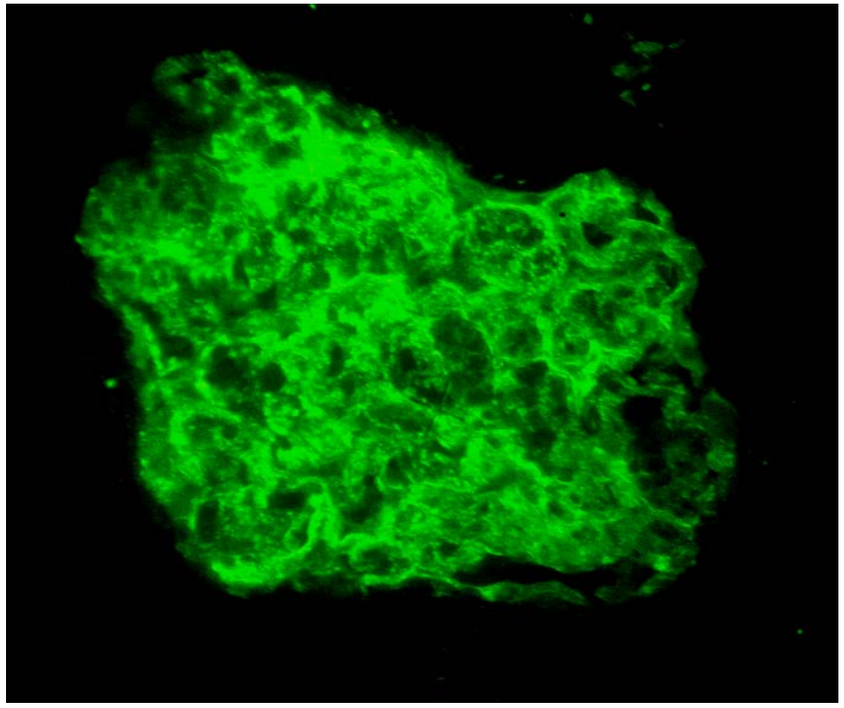
Am J Kidney Dis. 2017;70(6):770-777

Αντιμετώπιση: C3ΣΠ

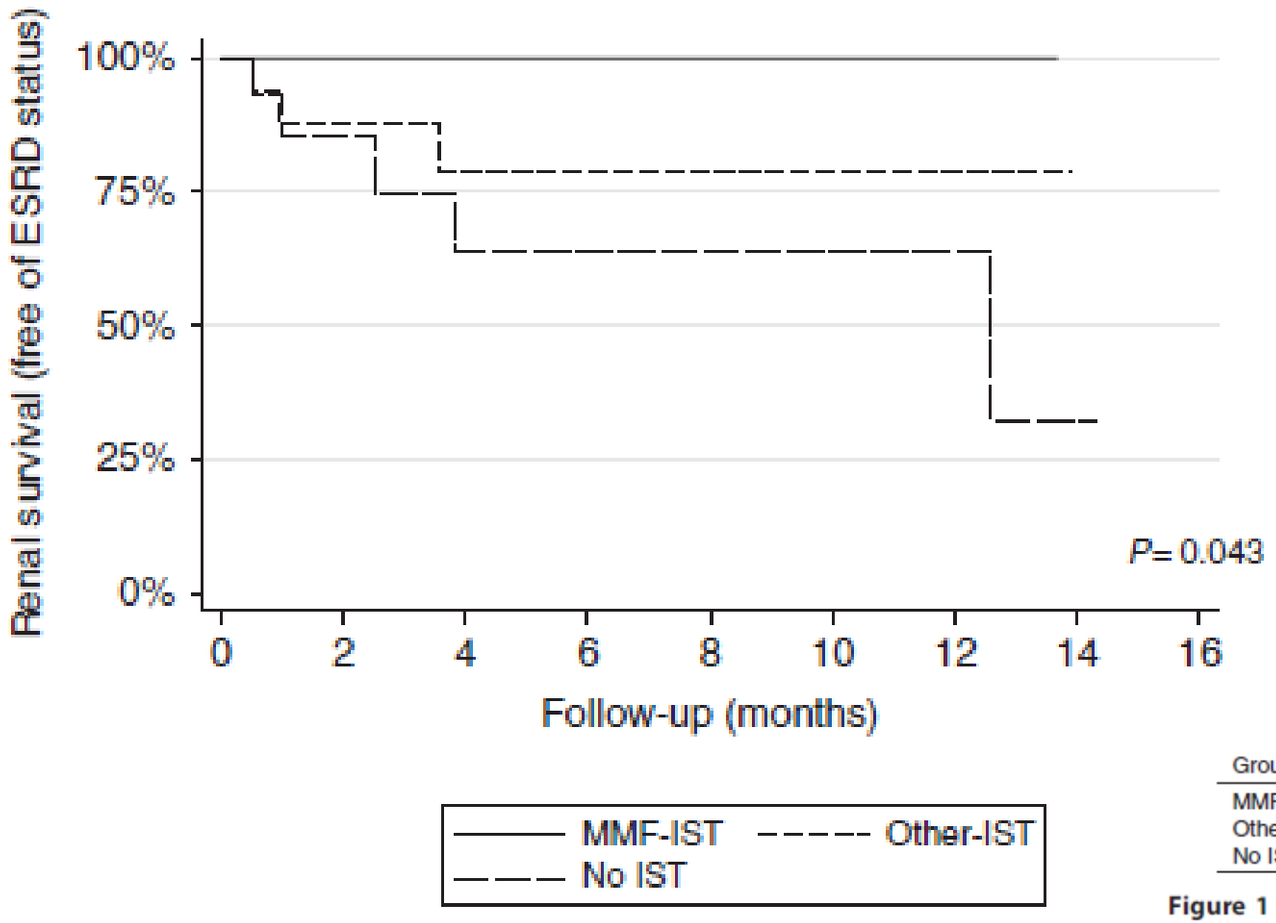


- Αντιμετώπιση αιτιολογική?
  παραπρωτεΐνη
  λεμφοϋπερπλαστικό νόσημα
- Αντιμετώπιση «εμπειρική»

- 10ετής νεφρική επιβίωση 50%

Kidney International (2017) 91, 539–551

MMF σε C3ΣN



''we studied a series of 60 patients in whom a complete registry of treatments was available''

Αναδρομική μελέτη

Patients at risk according to months of follow-up

Group of treatment	0	2	4	6	8	10	12	14	16
MMF-IST	22	15	10	5	4	4	2	1	1
Other-IST	18	13	10	6	4	2	2	1	1
No IST	20	14	11	7	6	6	5	4	3

Figure 1 | Renal survival (defined by a status free of end-stage renal disease) in patients treated with MMF (MMF-IST), other IST (other-IST), and no IST (non-IST). ESRD, end-stage renal disease; IST, immunosuppressive treatments; MMF, mycophenolate mofetil.

Kidney International (2015) 88, 1153–1160

Eculizumab και C3G

Table 3. Published reports of eculizumab use in C3 glomerulopathy and MPGN

Report (year)	Study design	Reported diagnosis (age at treatment/sex)	C3NeF	Treatment duration (months)	Clinical response
Daina *et al.* (2012) [18]	Case report	DDD (22F)	+	11	Yes
Vivarelli *et al.* (2012) [19]	Case report	DDD (17M)	+	18 + 9	Yes
Radhakrishnan *et al.* (2012) [20]	Case report	MPGN Type 1 (16F)	+	1.5	Yes
McCaughan *et al.* (2012) [21]	Case report	Allograft recurrent DDD (29F)	+	2.5	Yes
Bomback *et al.* (2012) [22]	Prospective, open-label, uncontrolled trial	DDD (22M)	−	12	Yes
		DDD (42M)	+	9	No
		Allograft recurrent DDD (32M)	−	12	Yes
		C3GN (25M)	−	12	No
		Allograft recurrent C3GN (22M)	+	12	No
		Allograft recurrent C3GN (20M)	+	12	Yes
Gurkan *et al.* (2013) [23]	Case report	Allograft recurrent C3GN (21M)	+	12	Yes
Besbas *et al.* (2013) [24]	Case report	C3 glomerulopathy (16F)	−	10	No
Kerns *et al.* (2013) [25]	Case report	C3 glomerulopathy (16M)	−	3.5	Yes
Rousset-Rouvière *et al.* (2014) [26]	Case report	DDD (10M)	+	6.5	Yes
Ozkaya (2014) *et al.* [27]	Case report	DDD (14F)	+	7	Yes
Berthe-Aucejo *et al.* (2014) [28]	Case report	DDD (17M)	+	3.5	No
Sánchez-Moreno *et al.* (2014) [29]	Case report	Allograft recurrent DDD (14F)	+	30	Yes

50%

82%

Nephrol Dial Transplant (2016) 31: 717–725

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Kidney International (2017) 91, 539–551

Table 5 | Recommended treatment approach for C3G[a]

	Description	Recommendation
Moderate disease	• Urine protein over 500 mg/24 h despite supportive therapy *or* • Moderate inflammation on renal biopsy *or* • Recent increase in serum creatinine suggesting risk for progressive disease	• Prednisone • Mycophenolate mofetil

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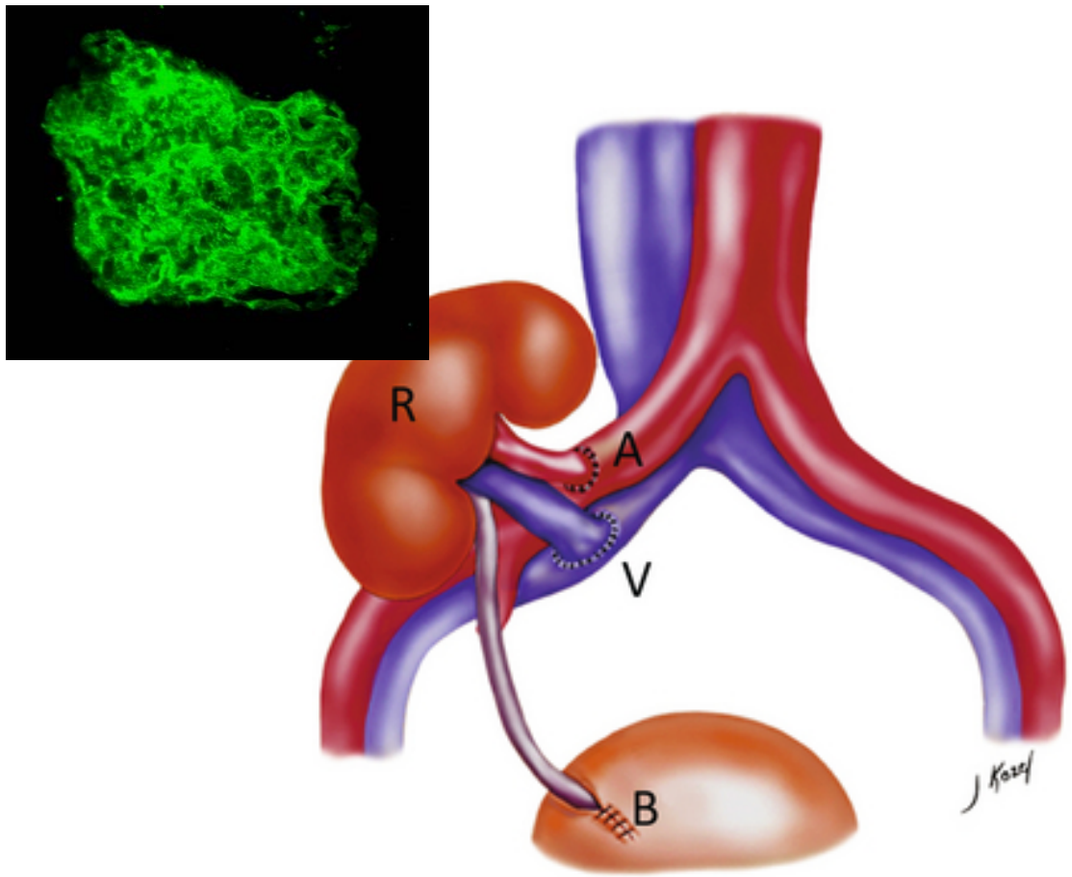
Kidney International (2017) 91, 539–551

Table 5 | Recommended treatment approach for C3G[a]

	Description	Recommendation
Severe disease	• Urine protein over 2000 mg/24 h despite immunosuppression and supportive therapy *or* • Severe inflammation represented by marked endo- or extracapillary proliferation with or without crescent formation despite immunosuppression and supportive therapy *or* • Increased serum creatinine suggesting risk for progressive disease at onset despite immunosuppression and supportive therapy	• Methylprednisolone pulse dosing as well as other anti-cellular immune suppressants have had limited success in rapidly progressive disease • Data are insufficient to recommend eculizumab as a first-line agent for the treatment of rapidly progressive disease

C3ΣΠ και μεταμόσχευση

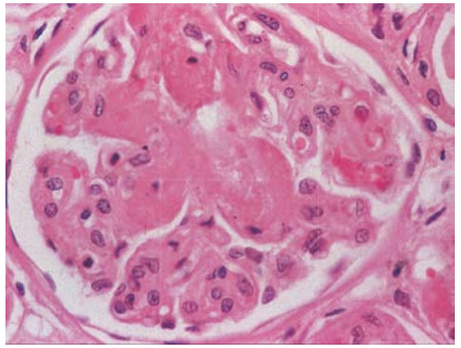


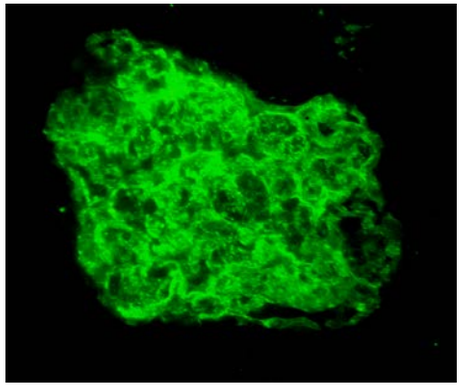
- Ελάχιστα δεδομένα
- Συχνή υποτροπή
  (σχεδόν 100% σε DDD)
- 50% απώλεια μοσχεύματος

Kidney International (2017) 91, 539–551


Summary
1
2
3

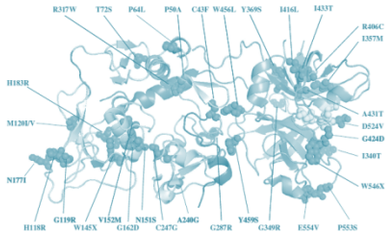
Ανακεφαλαίωση

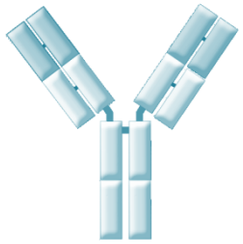


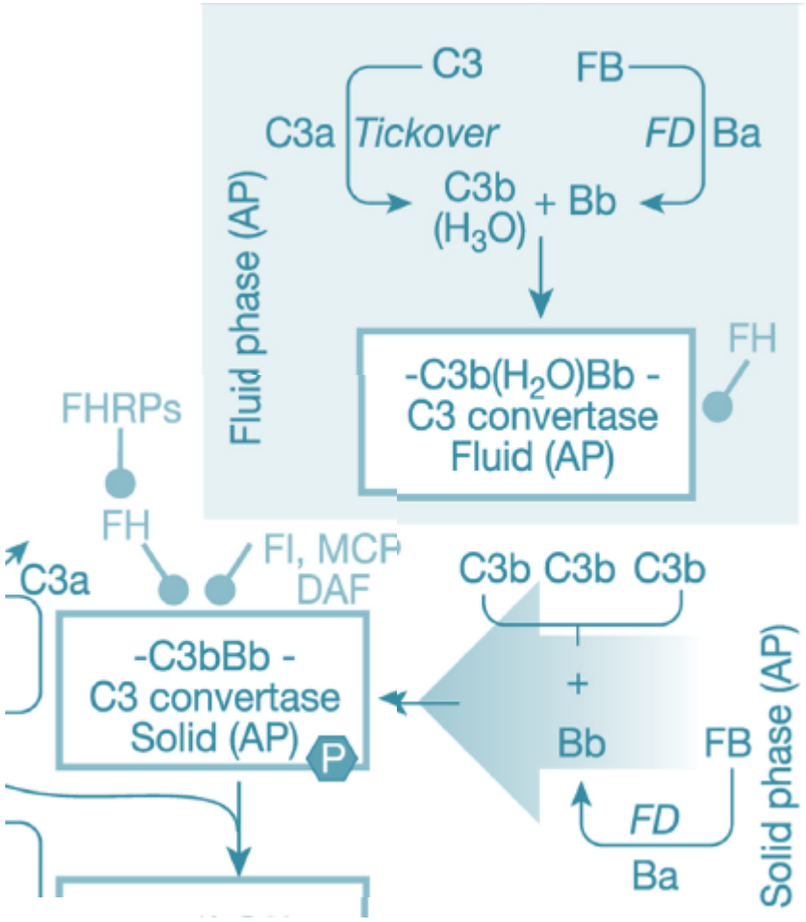


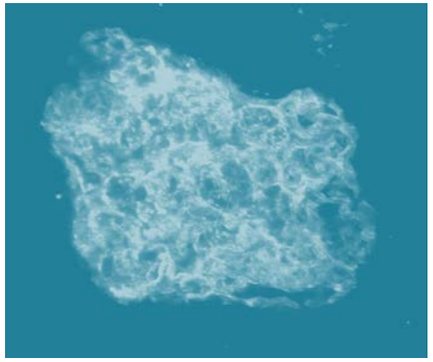
- Άτυπο HUS (aHUS), C3 σπειραματοπάθεια (C3G=DDD+C3GN)
- Σπειραματική προσβολή από διαταραχή αυτορρύθμισης της εναλλακτικής οδού
- στο ενδοθήλιο (aHUS) και στην υγρή φάση (C3G)
- Γενετικό υπόβραθρο ή/και επίκτητοι παράγοντες (παραπρωτεϊνη)
- Περισσότερα τα δεδομένα για το aHUS
- Θεραπεία eculizumab πολλά υποσχόμενη (aHUS)

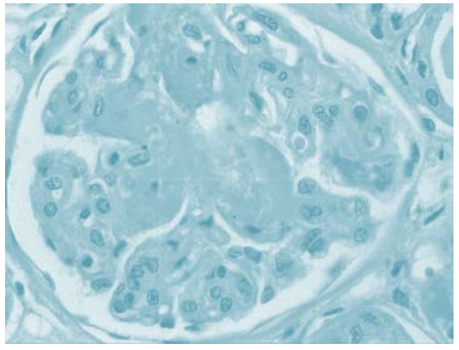
  αλλά ακριβή και με ερωτηματικά για την ενδεδειγμένη διάρκεια
- Σημαντικός στη διαχείρηση ο γενετικός έλεγχος

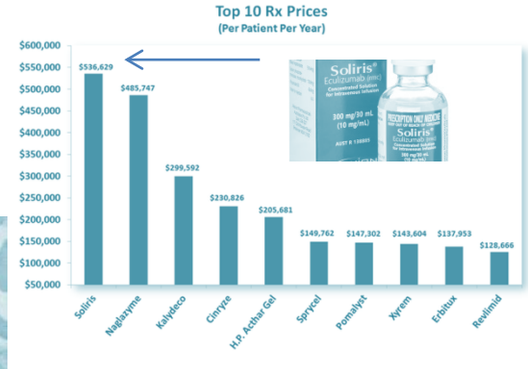


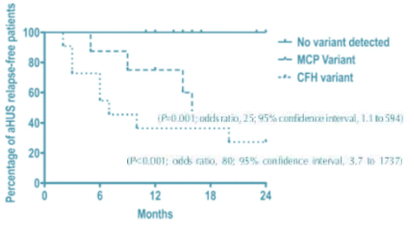












Ευχαριστώ για την προσοχή σας