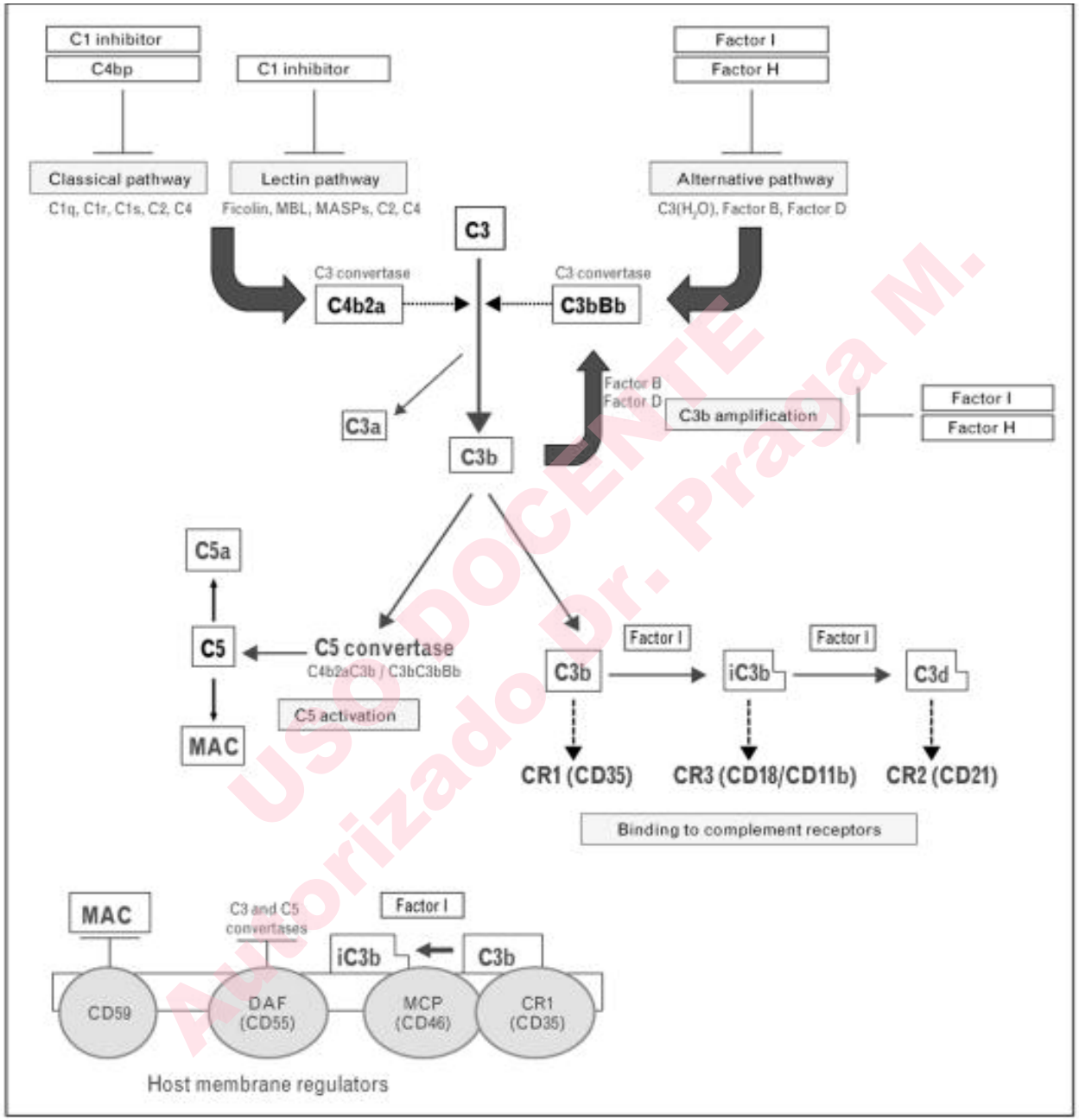
Patología renal asociada al Complemento: de la Microangiopatía Trombótica a la Glomerulopatía C3

Montevideo, Uruguay

14-15 Septiembre 2015



Complement and glomerular disease: new insights.
Pickering, Matthew; Cook, H
Current Opinion in Nephrology & Hypertension. 20(3):271-277, May 2011.

Clinical Case

- ***17 year old man***
- ***Following a cold, asthenia and progressive weakness in the last weeks. Dark (coca-cola) urine.***
- ***Blood Pressure 180/105 mmHg.***
- ***Analysis:***

  Hemoglobin 7 g/dl.

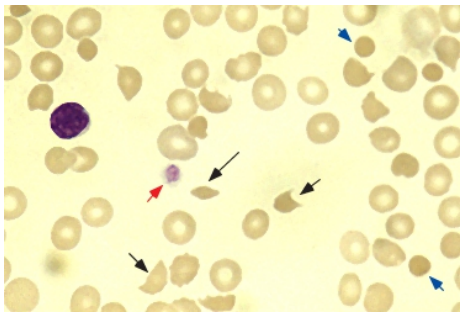
  Platelet count 65.000/mm3.

  LDH >1000 UI.

  Serum Creatinine 3.1 mg/dl.

  Hematuria (+++), Proteinuria 2 g/day.

  Schystocytes >5.



Thrombotic Microangiopathy (TMA)

CLINICAL PRESENTATION

Microangiopathic hemolytic anemia

-Anemia

-Schystocytes in peripheral blood frotis

-Increased LDH

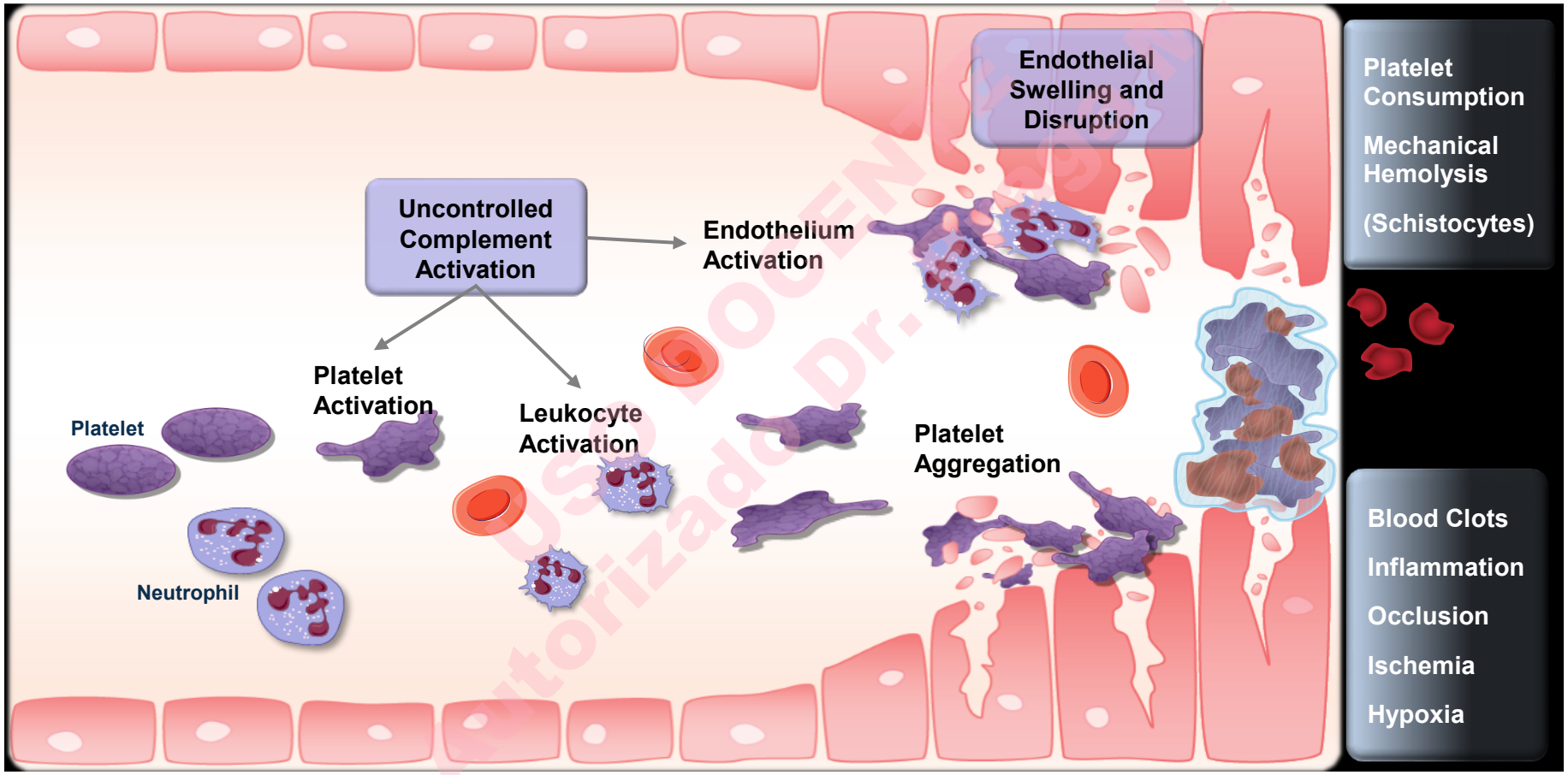
Thrombocytopenia

<150.000/mm3

-Coombs Test (-)

-Decreased serum haptoglobin

Chronic Uncontrolled Complement Activation Causes Platelet, Endothelial, Leukocyte Activation Leading to Inflammation and Systemic Small Vessel Occlusion



from Desch K et al. *JASN*. 2007;18:2457-60. Modified from Licht C et al. *Blood*. 2009;114:4538-4545. Modified from Noris M et al. *NEJM*. 2009; 361:1676-87. Modified from Stahl A, et al. *Blood* 2008;111:5307-15. Modified from Camous L et al. *Blood*. 2011;117:1340-9.

Common misconceptions in TMA diagnosis

Microangiopathic hemolytic anemia

-**Anemia:** ***«Attributed to the AKI…….»***

-**LDH increase:** ***«No specific……»***

-**Schystocytes:** ***«Variable, dependent on the interest and collaboration of hematologist on duty…..»***

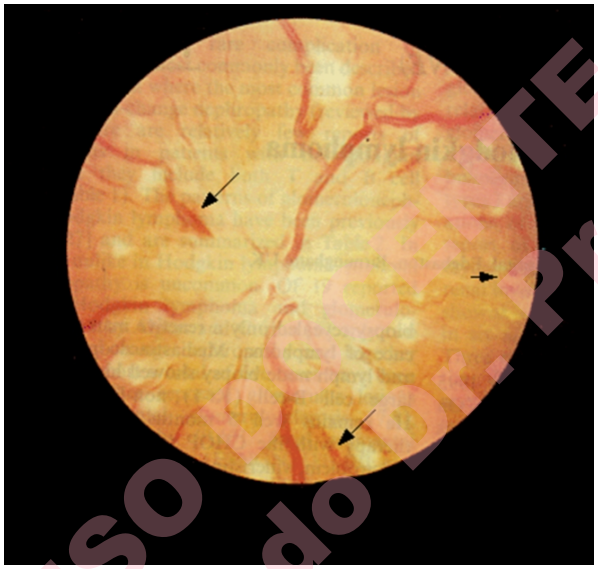
-**Haptoglobin decrease**: **Very useful to confirm diagnosis but it is variable and not always requested**

Thrombocytopenia

«20% of aHUS without thrombocytopenia»

Our Patient

- ***Blood Pressure 180/105 mmHg.***



Definition of Malignant Hypertension: Very Severe Increase of Blood Pressure and Funduscopy examination showing Hypertensive retinopathy grades III (hemorrhages, exudates) or III+IV (grade III+ papilledema)

Common Misconceptions in TMA diagnosis

- Severe Hypertension, frequently fullfilling Malignant Hypertension criteria, is a characteristic and very common ingredient of TMA, including aHUS

- Any patient with essential or secondary hypertension (renovascular, primary hyperaldosteronism, pheochromocytoma…) can present episodes of Malignant hypertension, but severe TMA is uncommon in these conditions

LONG-TERM RENAL SURVIVAL IN MALIGNANT HYPERTENSION

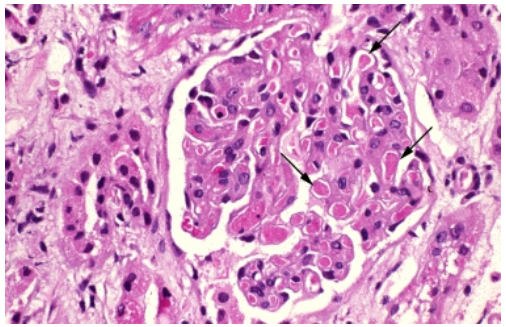
González R, Morales E, Segura J, Ruilope LM, Praga M.

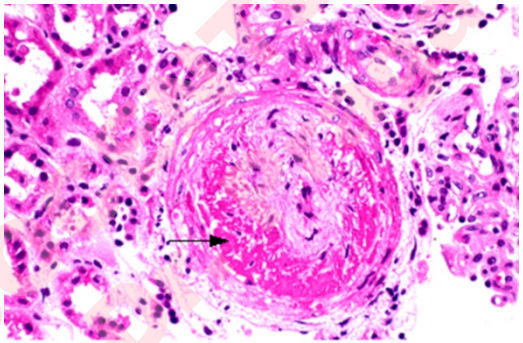
Nephrology Dialysis Transplantation 25: 3266-72, 2010

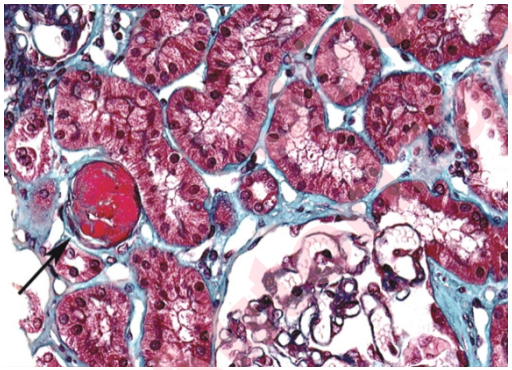
- 197 patients with essential hypertension who developed Malignant Hypertension
- **TMA (Microangiopathic hemolytic anemia and thrombocytopenia) was uncommon in patients with essential malignant hypertension (3%)**
- Renal function impairment was detected at admission in 144 patients (63%).
- Renal function improvement or stabilization in a majority of patients (early treatment with RAAS blockade)

Our Patient

A percutaneous renal biopsy was performed







Diagnosis: Thrombotic Microangiopathy

The Role of Renal Biopsy in TMA

Advantages

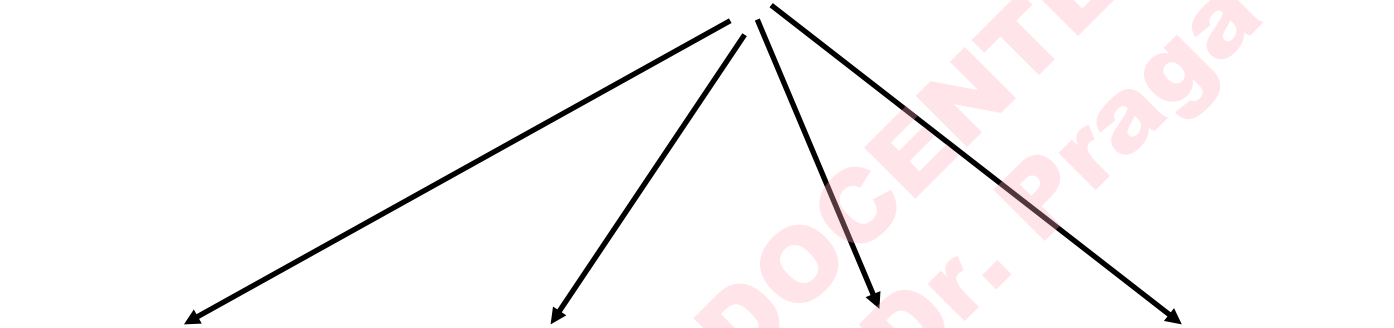
- Confirm diagnosis of TMA
- Evaluation of chronic, irreversible parenchymal damage (Prognosis)
- Rule out C3 Glomerulopathies, IgA nephropathy and (in some cases) lupus nephritis or other systemic diseases

Drawbacks

- TMA histological lesions: No pathognomonic of any entity causing TMA (unspecific findings)
- Risk of bleeding (hypertension, thrombocytopenia, AKI…)

TMA Differential Diagnosis

Microangiopathic hemolytic anemia, Thrombocitopenia, AKI, Hypertension



Secondary TMA

TTP

Thrombotic Thrombocytopenic Purpura

STEC-HUS

Shiga-Toxin E.Coli-HUS

aHUS

Atypical-HUS

SECONDARY TMA

Systemic Diseases

SLE
Vasculitis
Sclerodermia
Antiphospholipid syndrome

Glomerulonephritis

Complement-mediated GN (C3GN)

Infections

HIV
HCV
Influenza
Other

Tumors

TMA in Pregnancy/Postpartum

Preeclampsia
Eclampsia
HELLP

Drugs

Quinine
Interpheron
Ticlopidin, Clopidogrel
Valaciclovir
Oral Anticonceptivos orales

Antitumoral Drugs

Mitomicin, Gemcitabine, Cisplatin
VEGF inhibitors, Tyrosin-Kinase inhibitors

Immunosuppressive drugs

Calcineurin Inhibitors (cyclosporin, tacrolimus)
mTOR inhibitors (sirolimus, everolimus)

Bone-Marrow trasplantation

Organ Transplantation

Other

Cobalamin deficiency
DGKE mutations
Intestinal Lymphangiectasia

Common misconceptions in TMA diagnosis

- Classic differential diagnosis between HUS and TTP based on non-specific clinical and laboratory findings:

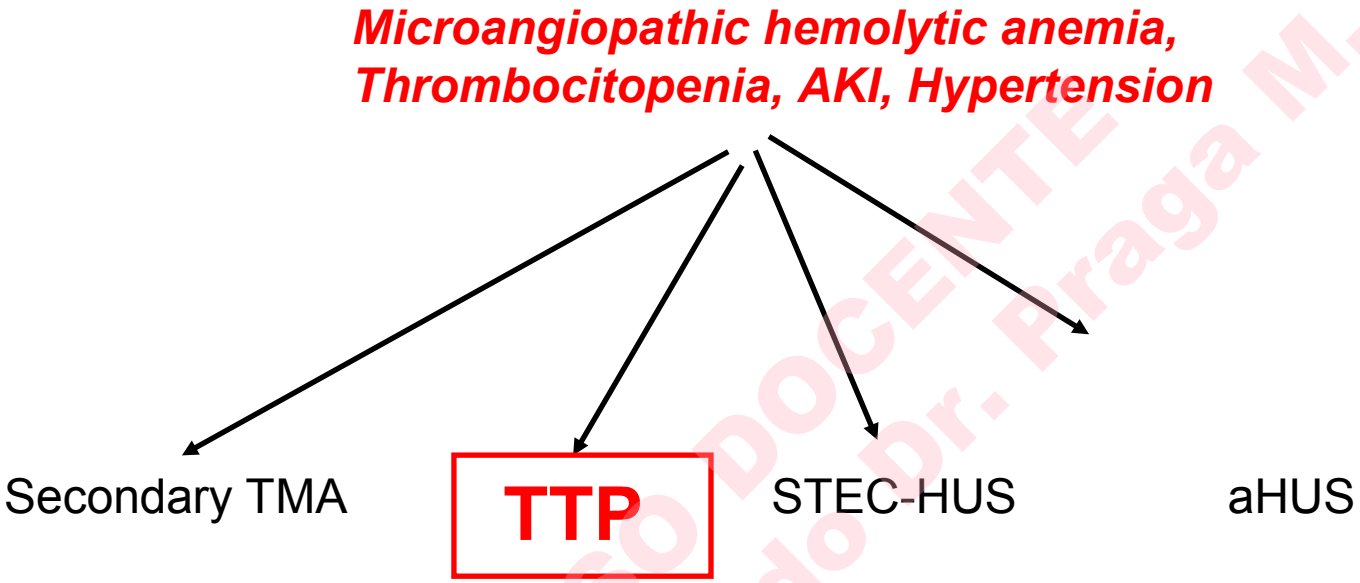
- *HUS: Predominance of AKI (Serum creatinine >2.5 mg/dl)*
- *TTP: Predominance of neurological manifestations*

  More severe thrombocytopenia

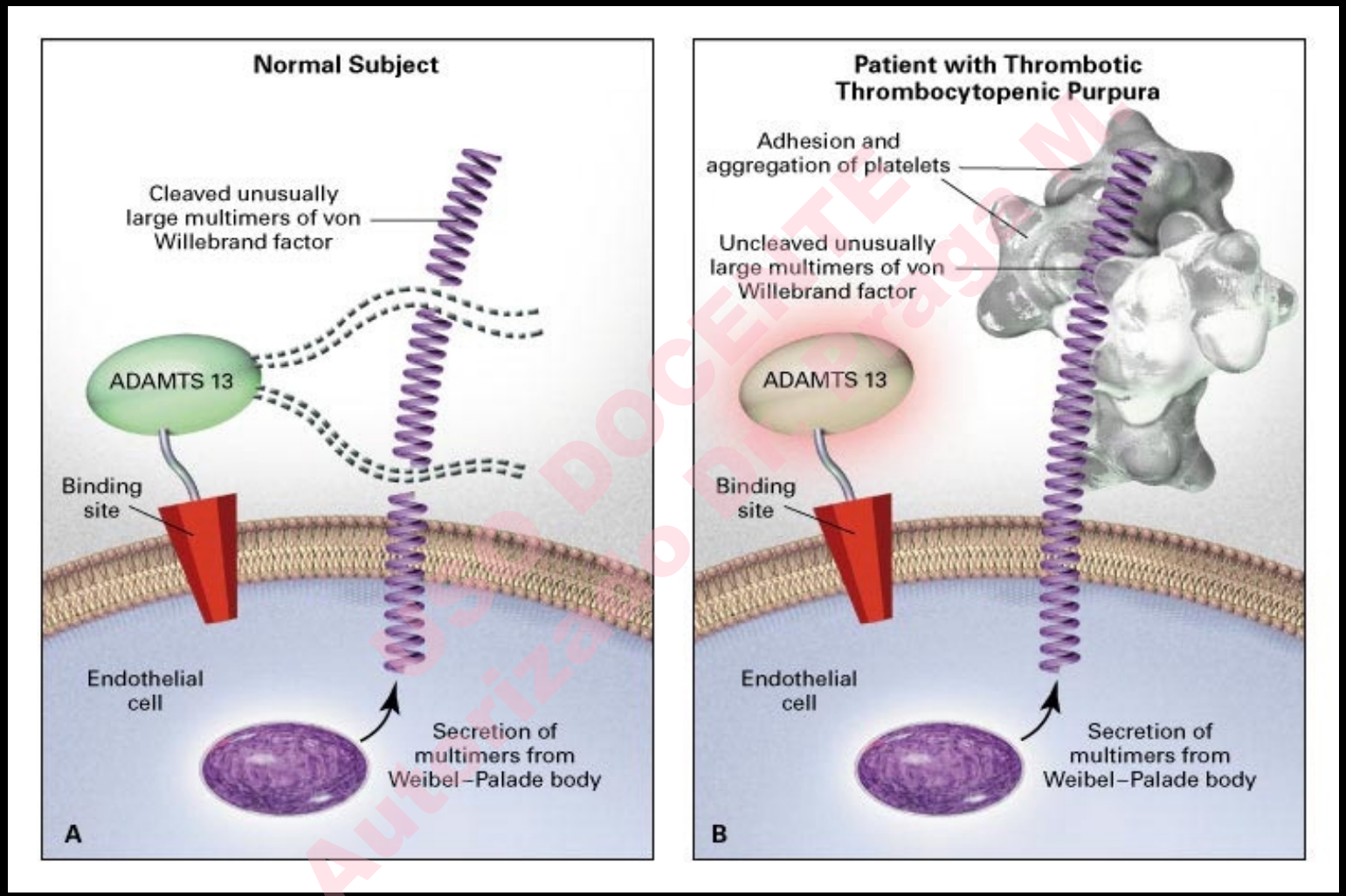
BUT

- ***Many TTP patients can present severe AKI***
- ***Many HUS patients present severe neurological manifestations***

TMA Differential Diagnosis



ADAMTS-13



Moake JL. N Engl J Med 2002;347:589-600.

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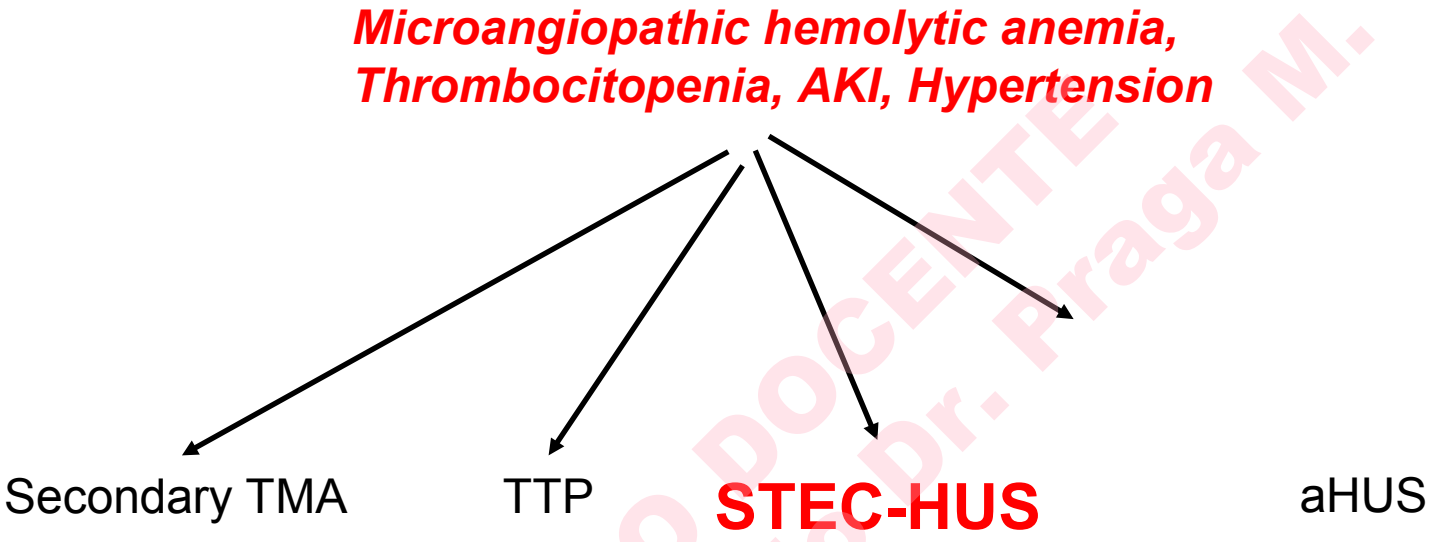
ADAMTS-13

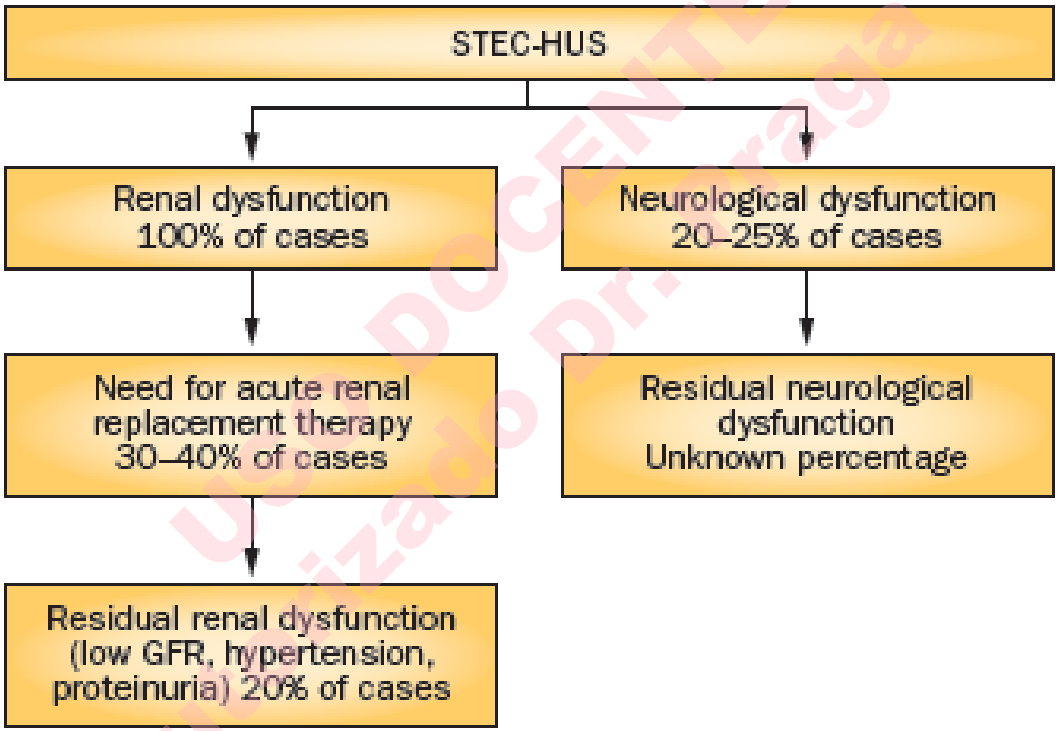
- A very rapid and reliable way to differentiate HUS and TTP
- ADAMTS-13 values <5-10% in TTP
- ADAMTS-13 deficiency due to genetic abnormalities (uncommon) or acquired (drugs, autoantibodies)

TMA Differential Diagnosis



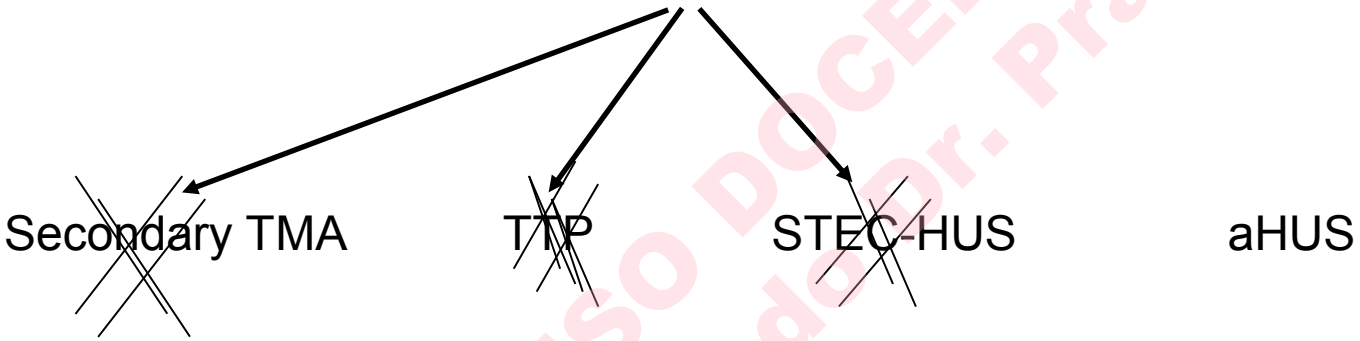
Renal and neurological involvement in typical Shiga toxin-associated HUS

Howard Trachtman, Catherine Austin, Maria Lewinski and Rolf A. K. Stahl



TMA Differential Diagnosis

Microangiopathic hemolytic anemia,
Thrombocytopenia, Increased LDH,
Schystocytes, Low serum haptoglobin
AKI, Hypertension



Complement system study looking for Complement Mutations or autoantibodies

Our Patient
Treatment

- Enalapril / amlodipin for blood pressure control
- Plasma exchange (3 sessions)
- Mild improvement of anemia (hemoglobin 8.3 g/dl) and thrombocytopenia (80.000/mmm3)
- Renal function continued to deteriorate (serum creatinine 4.9 mg/dl)

Table 2. Genetic Abnormalities and Clinical Outcome in Patients with Atypical Hemolytic–Uremic Syndrome.*

Gene	Protein Affected	Main Effect	Frequency	Response to Short-Term Plasma Therapy†	Long-Term Outcome‡	Outcome of Kidney Transplantation
			%			
CFH	Factor H	No binding to endothelium	20–30	Rate of remission: 60% (dose and timing dependent)	Rate of death or ESRD: 70–80%	Rate of recurrence: 80–90%§
CFHR1/3	Factor HR1, R3	Anti–factor H antibodies	6	Rate of remission: 70–80% (plasma exchange combined with immunosuppression)	Rate of ESRD: 30–40%	Rate of recurrence: 20%¶
MCP	Membrane cofactor protein	No surface expression	10–15	No definitive indication for therapy	Rate of death or ESRD: <20%	Rate of recurrence: 15–20%¶
CFI	Factor I	Low level or low cofactor activity	4–10	Rate of remission: 30–40%	Rate of death or ESRD: 60–70%	Rate of recurrence: 70–80%§
CFB	Factor B	C3 convertase stabilization	1–2	Rate of remission: 30%	Rate of death or ESRD: 70%	Recurrence in one case
C3	Complement C3	Resistance to C3b inactivation	5–10	Rate of remission: 40–50%	Rate of death or ESRD: 60%	Rate of recurrence: 40–50%
THBD	Thrombomodulin	Reduced C3b inactivation	5	Rate of remission: 60%	Rate of death or ESRD: 60%	Recurrence in one case

* ESRD denotes end-stage renal disease.
† Remission was defined as either complete remission or partial remission (i.e., hematologic remission with renal sequelae).
‡ The long-term outcome was defined as the outcome 5 to 10 years after onset.
§ Patients in this category were eligible for combined liver and kidney transplantation.
¶ Patients in this category were eligible for single kidney transplantation.

Noris M and Remuzzi G, *N Engl J Med* 2009; 361:1676-1687

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Noris M and Remuzzi G, *N Engl J Med* 2009; 361:1676-1687

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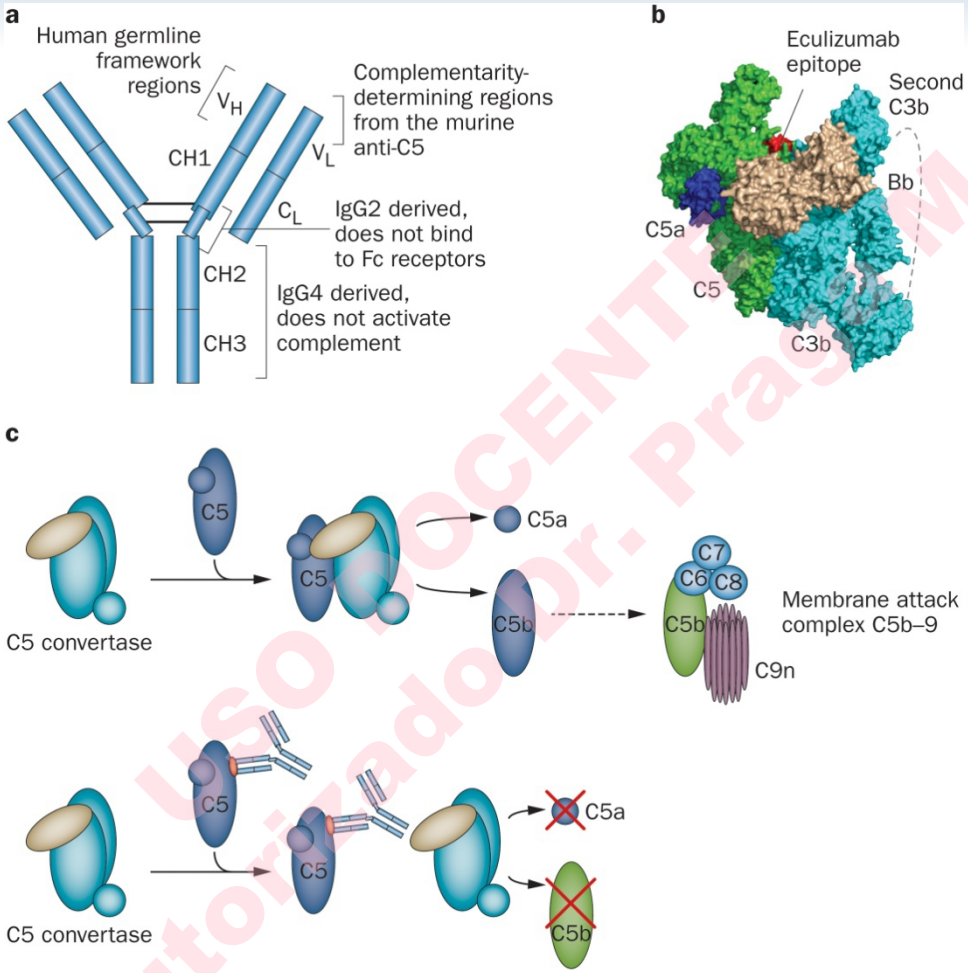
➢ **Diagnosis of aHUS on clinical grounds: Onset of Eculizumab (10 days after admission)**

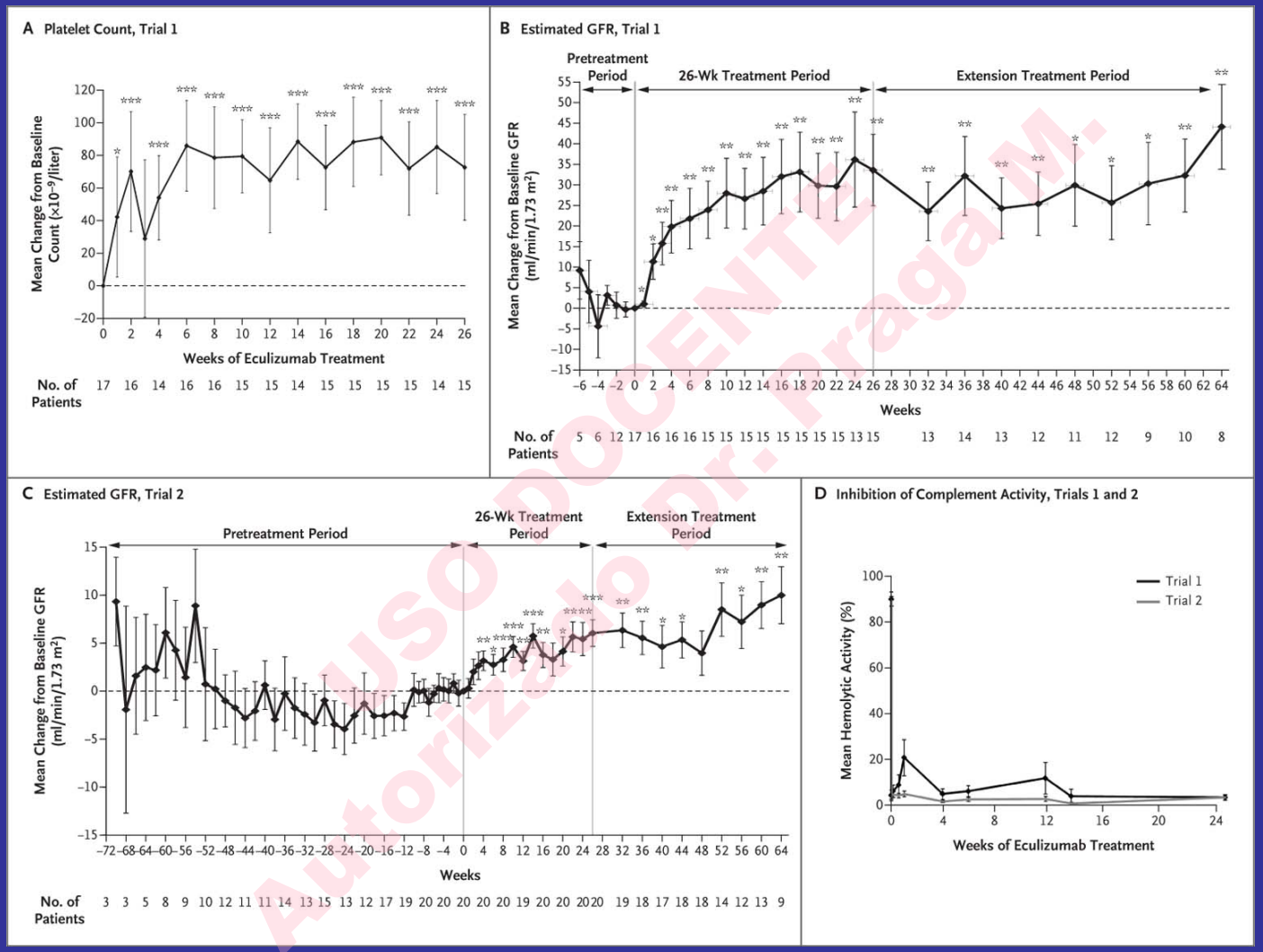
Figure 1 Eculizumab: molecular structure and mode of action



Zuber, J. *et al.* (2012) Use of eculizumab for atypical haemolytic uraemic syndrome and C3 glomerulopathies *Nat. Rev. Nephrol.* doi:10.1038/nrneph.2012.214

nature REVIEWS NEPHROLOGY

End Points.



Legendre CM et al. N Engl J Med 2013;368:2169-2181

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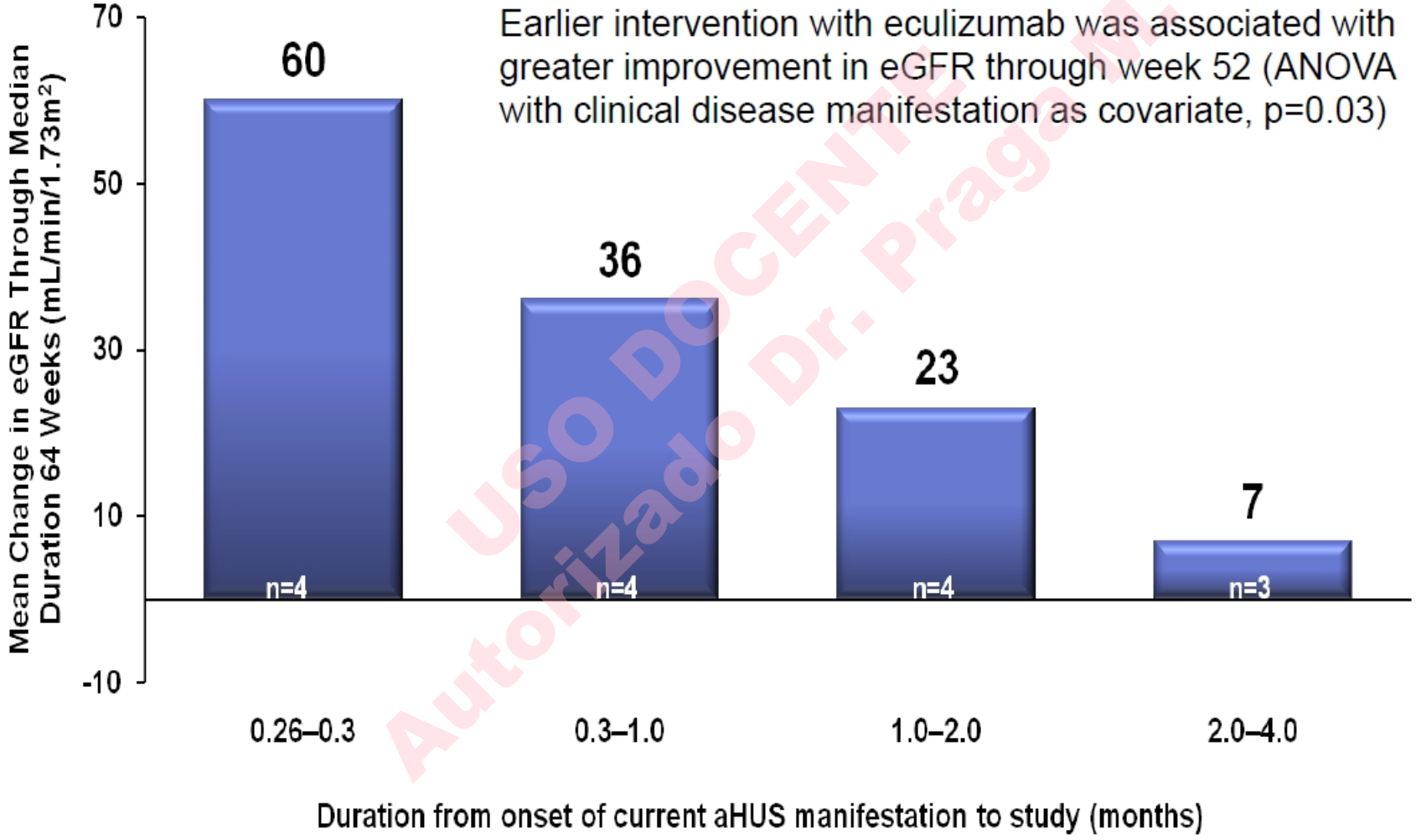
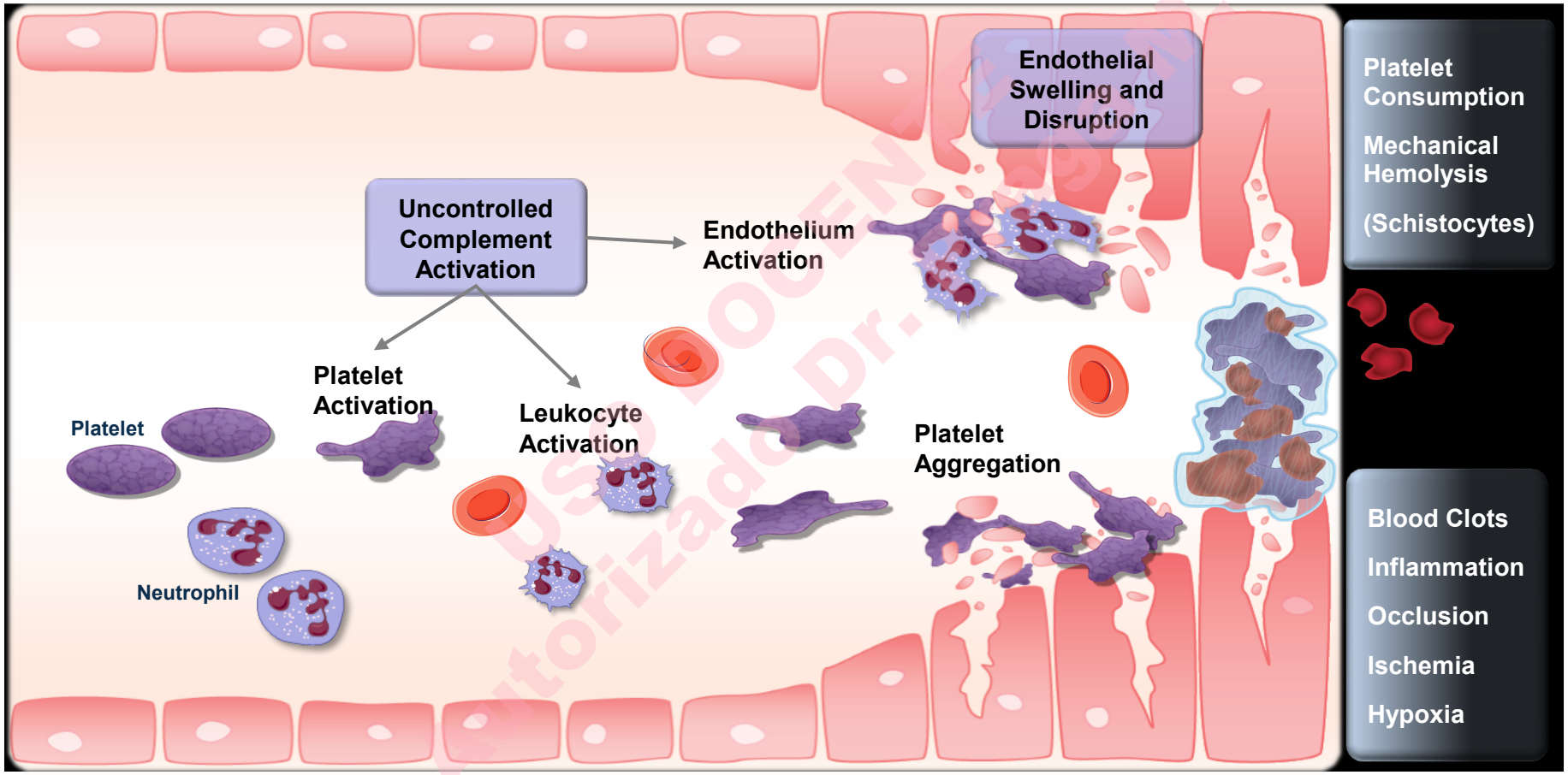
Earlier treatment with eculizumab leads to greater improvement in renal function



Median duration of aHUS current clinical manifestation to study was 0.75 months (range, 0.2–4.0)

Legendre CM et al. N Engl J Med 2013;368:2169-81

Chronic Uncontrolled Complement Activation Causes Platelet, Endothelial, Leukocyte Activation Leading to Inflammation and Systemic Small Vessel Occlusion



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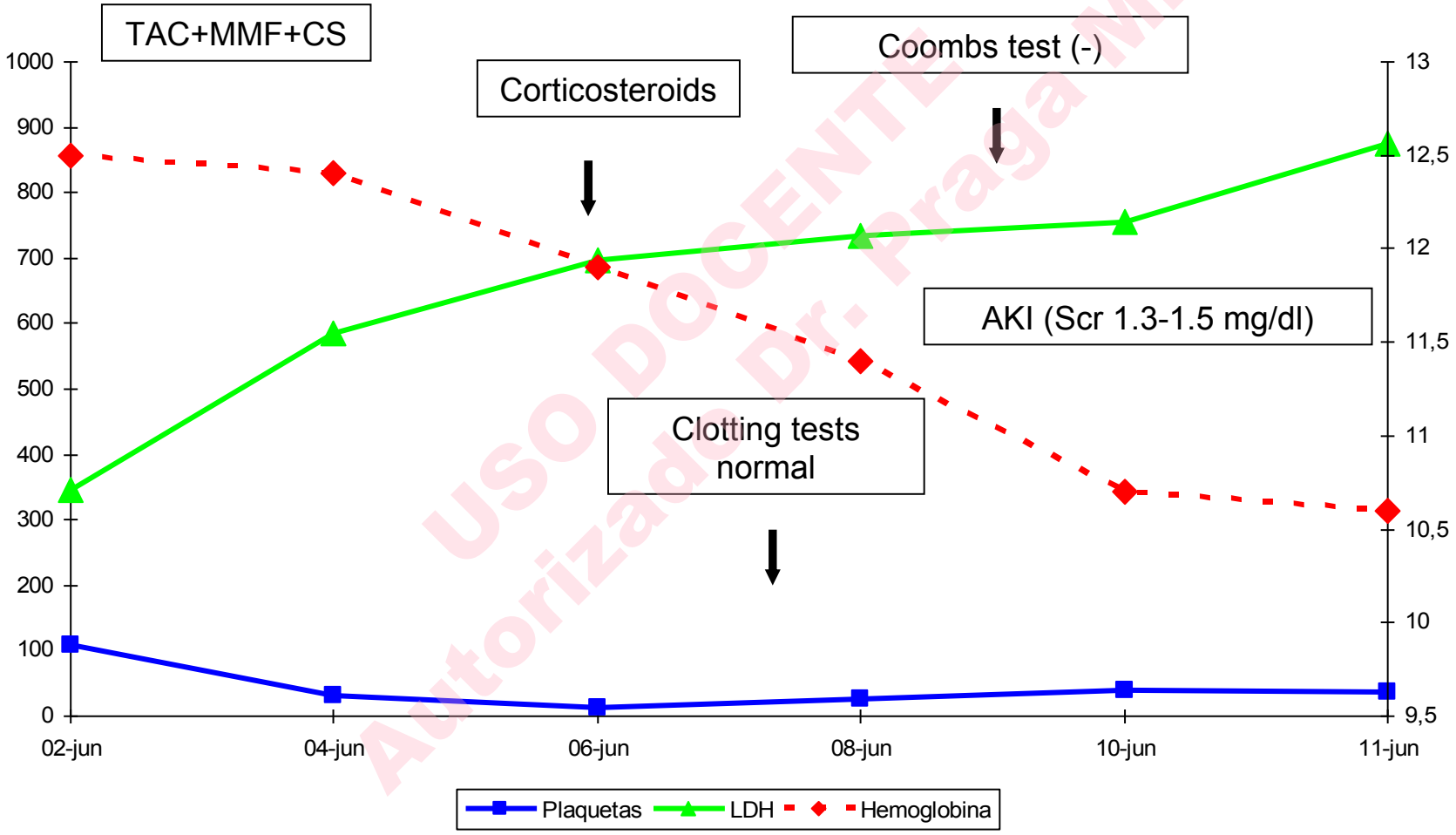
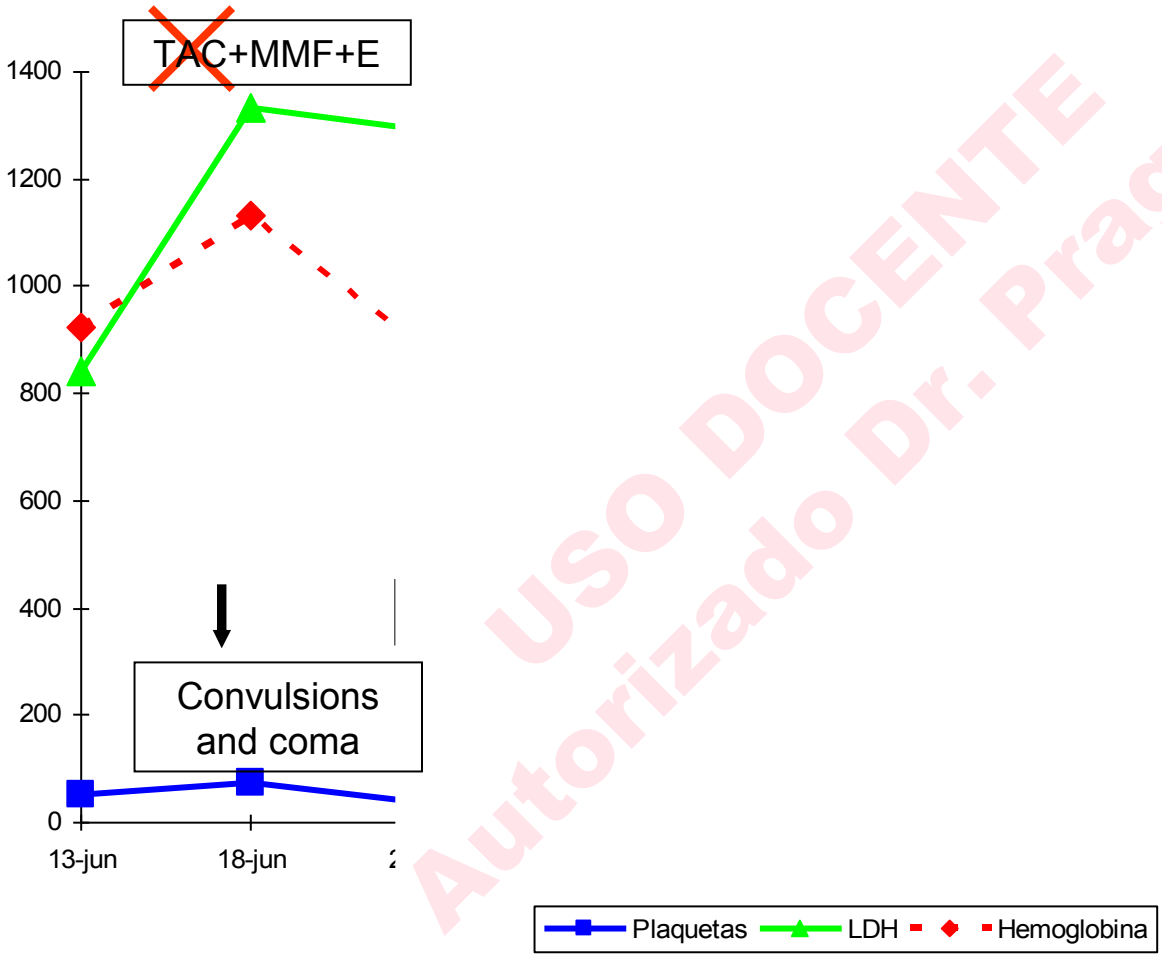
Clinical Case 3

- 42 years old woman
- Familiar hypertrophic nonobstructive myocardiopathy evolving to severe heart failure
- Waiting list for heart transplantation
- Heart transplant 01/06/2014

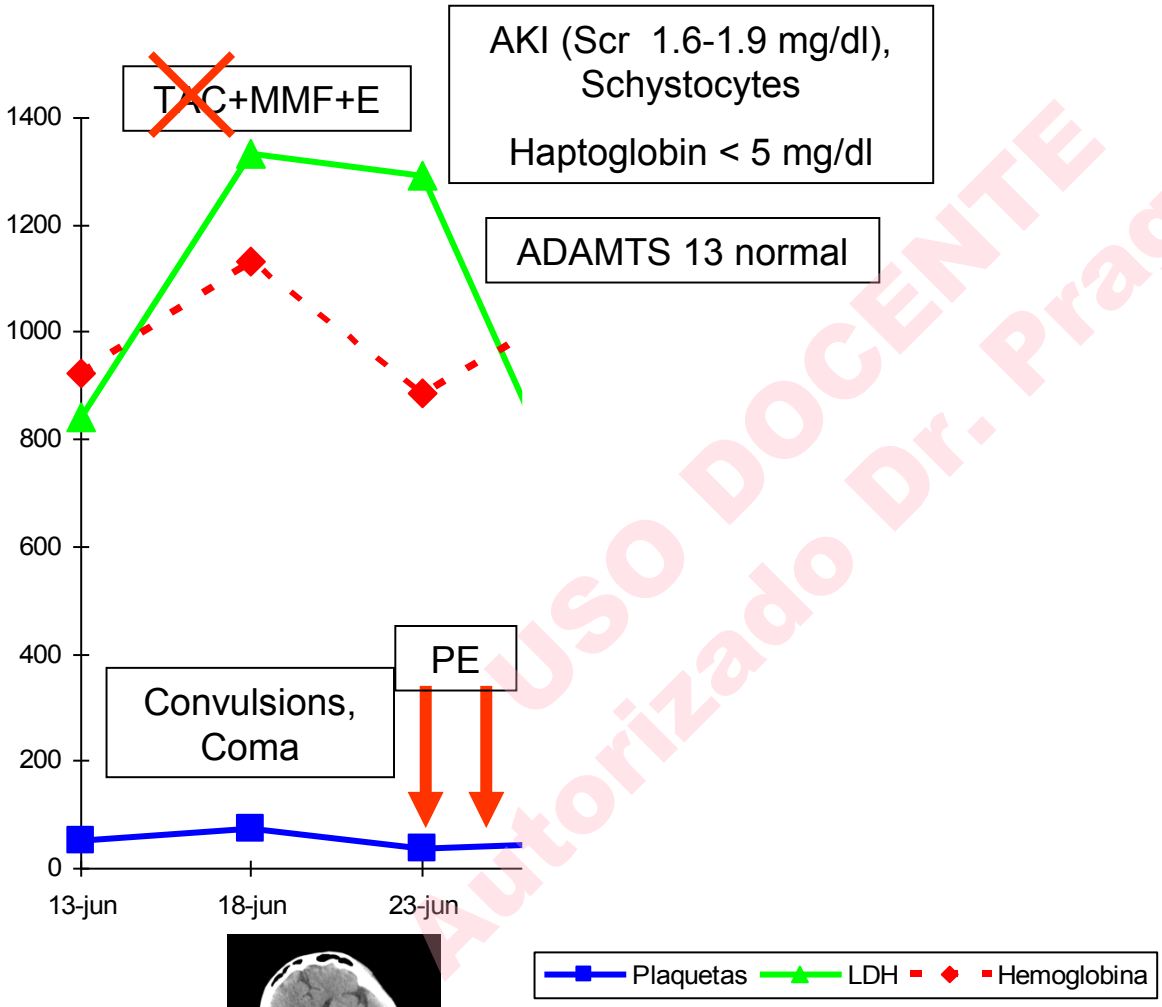
Clinical Case 3

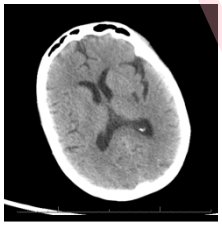


Clinical Case 3



Clinical Case 3





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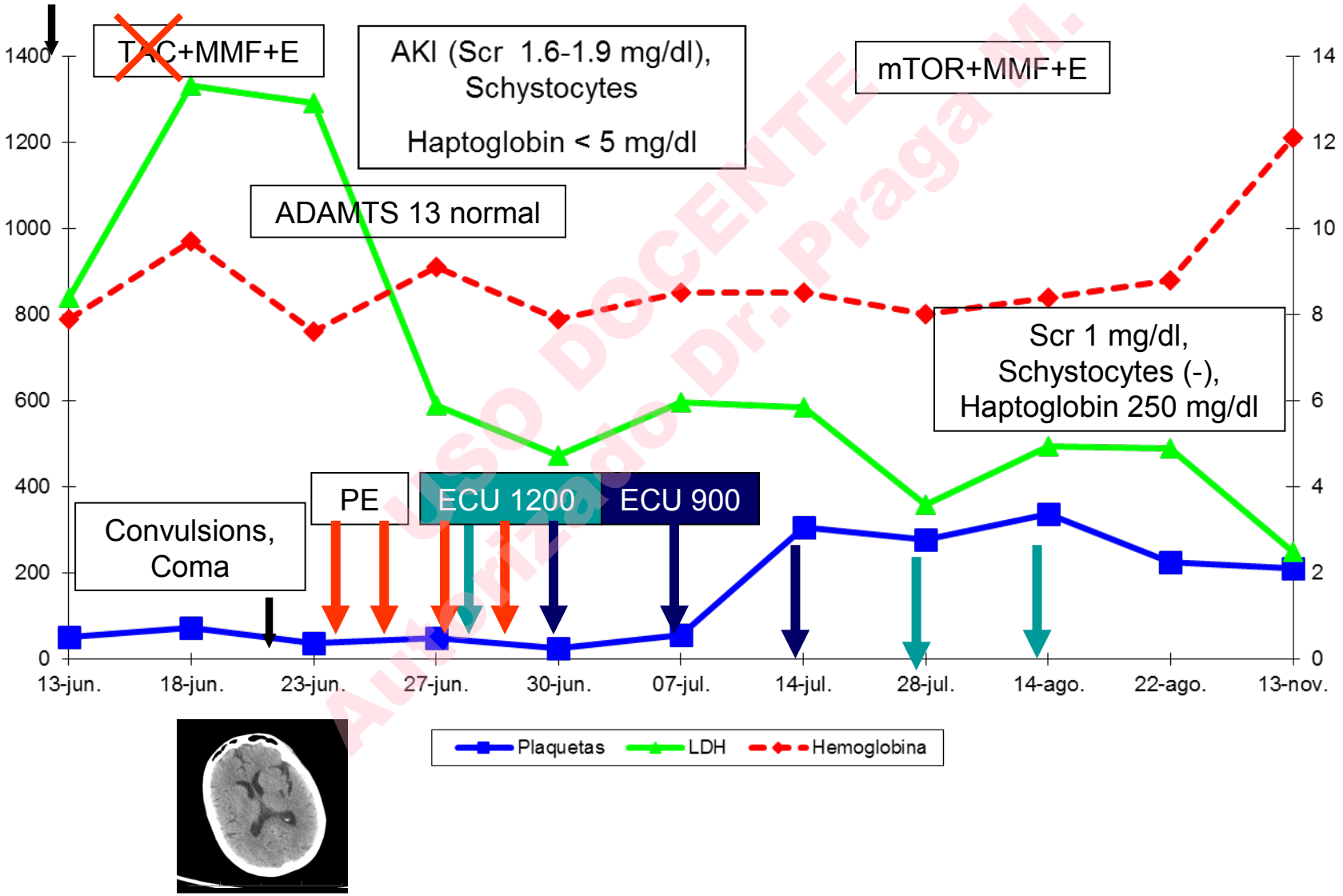
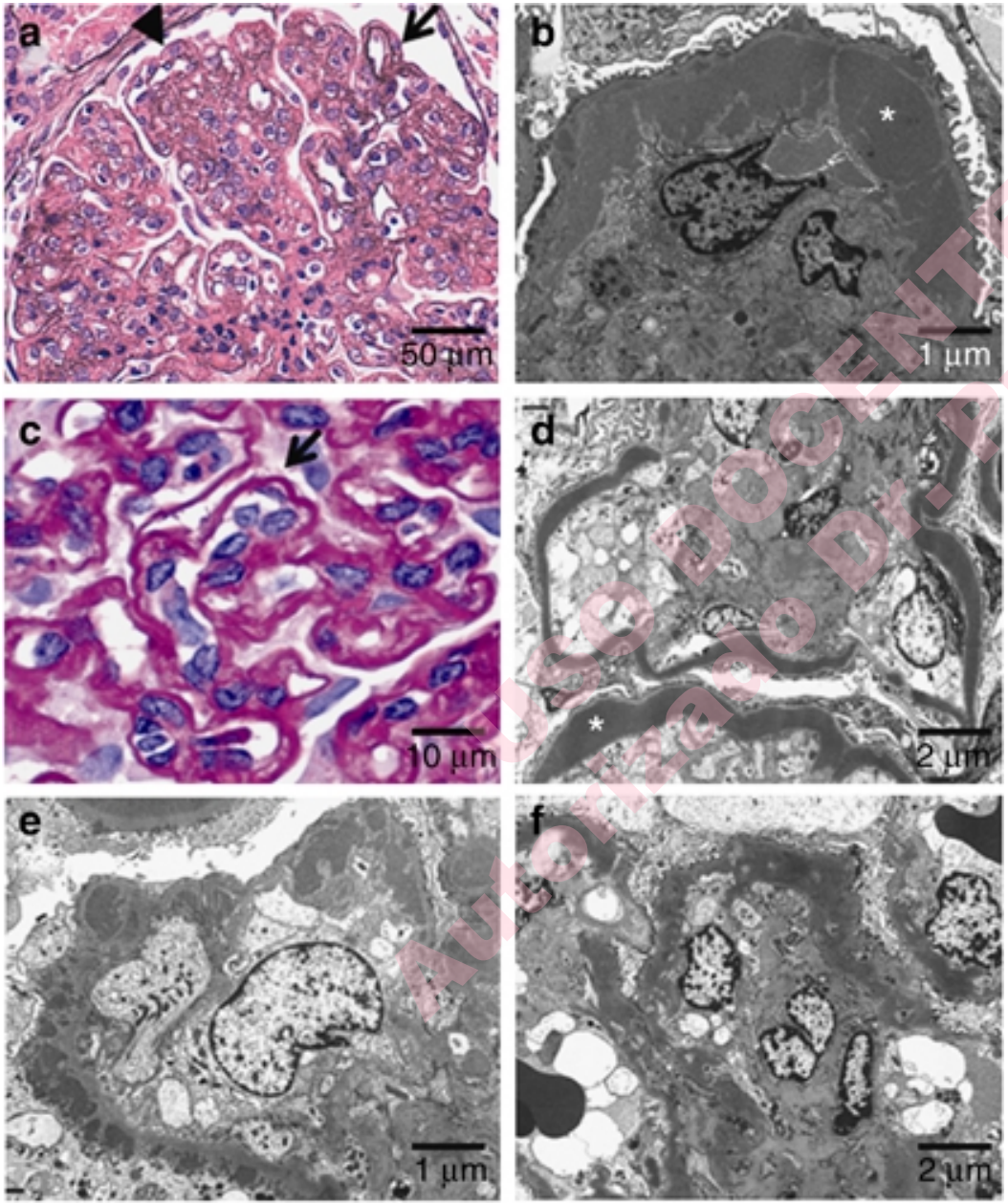


Complemento, MAT, otras enfermedades renales

- Púrpura Trombótica Trombocitopénica*
- Shiga-Toxin HUS*
- MAT por fármacos*
- MAT asociada a Lupus Eritematoso Diseminado*
- Síndrome antifosfolípido catastrófico*
- Nefritis Lúpica
- MAT del Trasplante de Médula Ósea*
- Vasculitis ANCA +
- Glomerulopatia C3*
- Nefropatía IgA*
- Prevención del rechazo humoral en Hiperinmunizados
- Prevención del retraso en la función del injerto

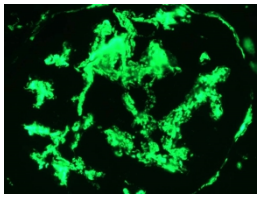
Toward a working definition of C3 glomerulopathy by immunofluorescence

Jean Hou[1], Glen S. Markowitz[1], Andrew S. Bomback[2], Gerald B. Appel[2], Leal C. Herlitz[1], M. Barry Stokes[1] and Vivette D. D'Agati[1]



Type 1 MPGN

- **DDD (type 2)**
- **Dysregulation of the alternative Complement Pathway**

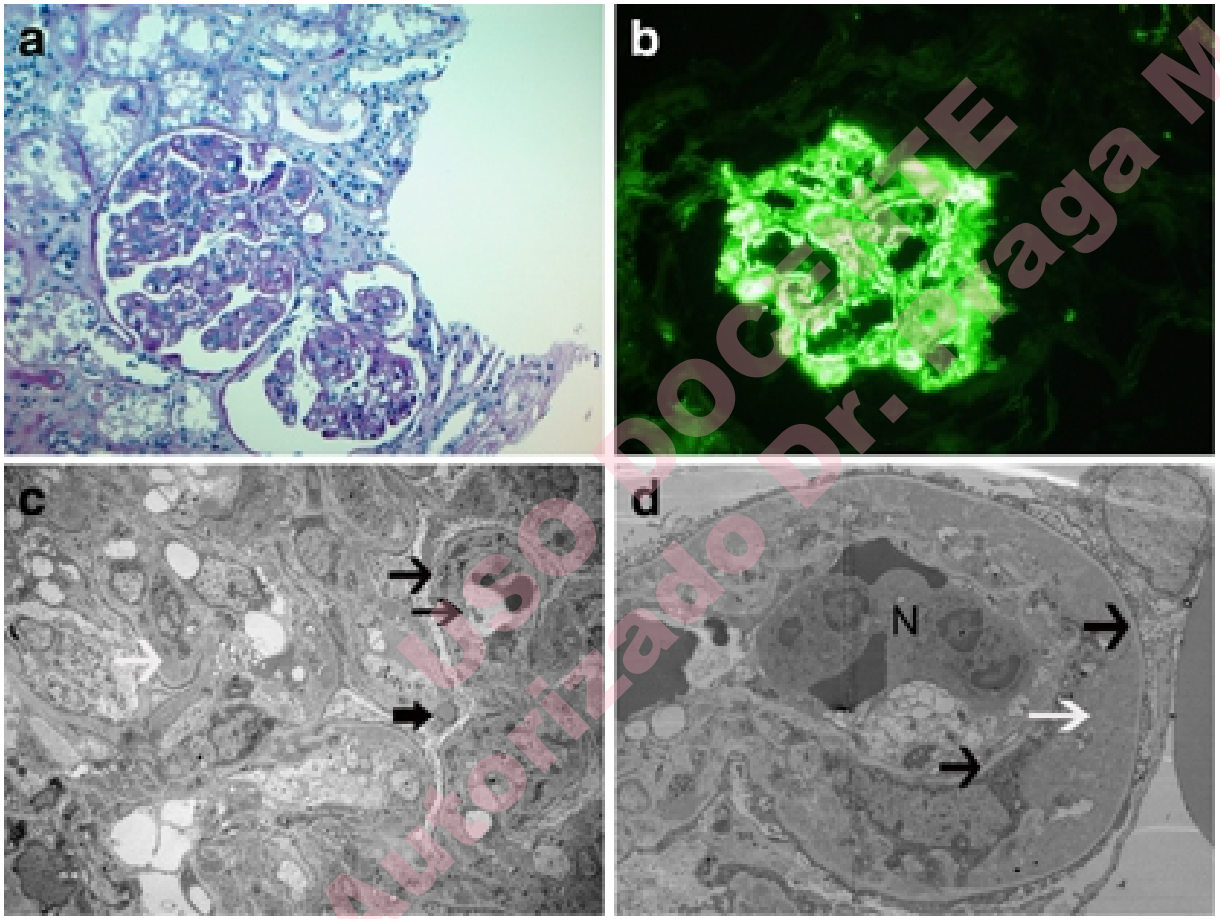


Isolated C3 deposits on IF

Type 3 MPGN

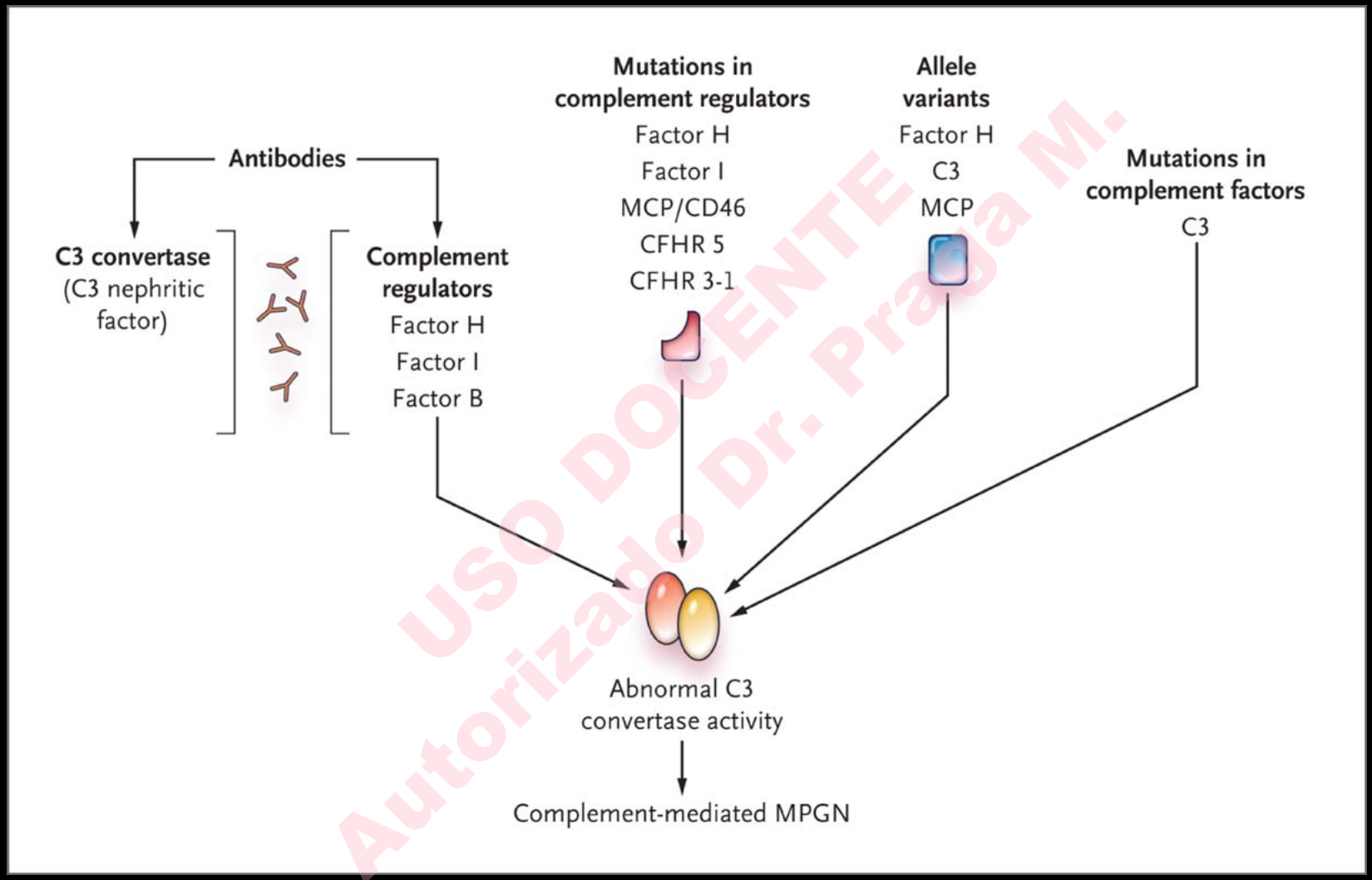
Membranoproliferative glomerulonephritis and C3 glomerulopathy: resolving the confusion

Sanjeev Sethi[1], Carla M. Nester[2,3,4] and Richard J.H. Smith[2,3,4]



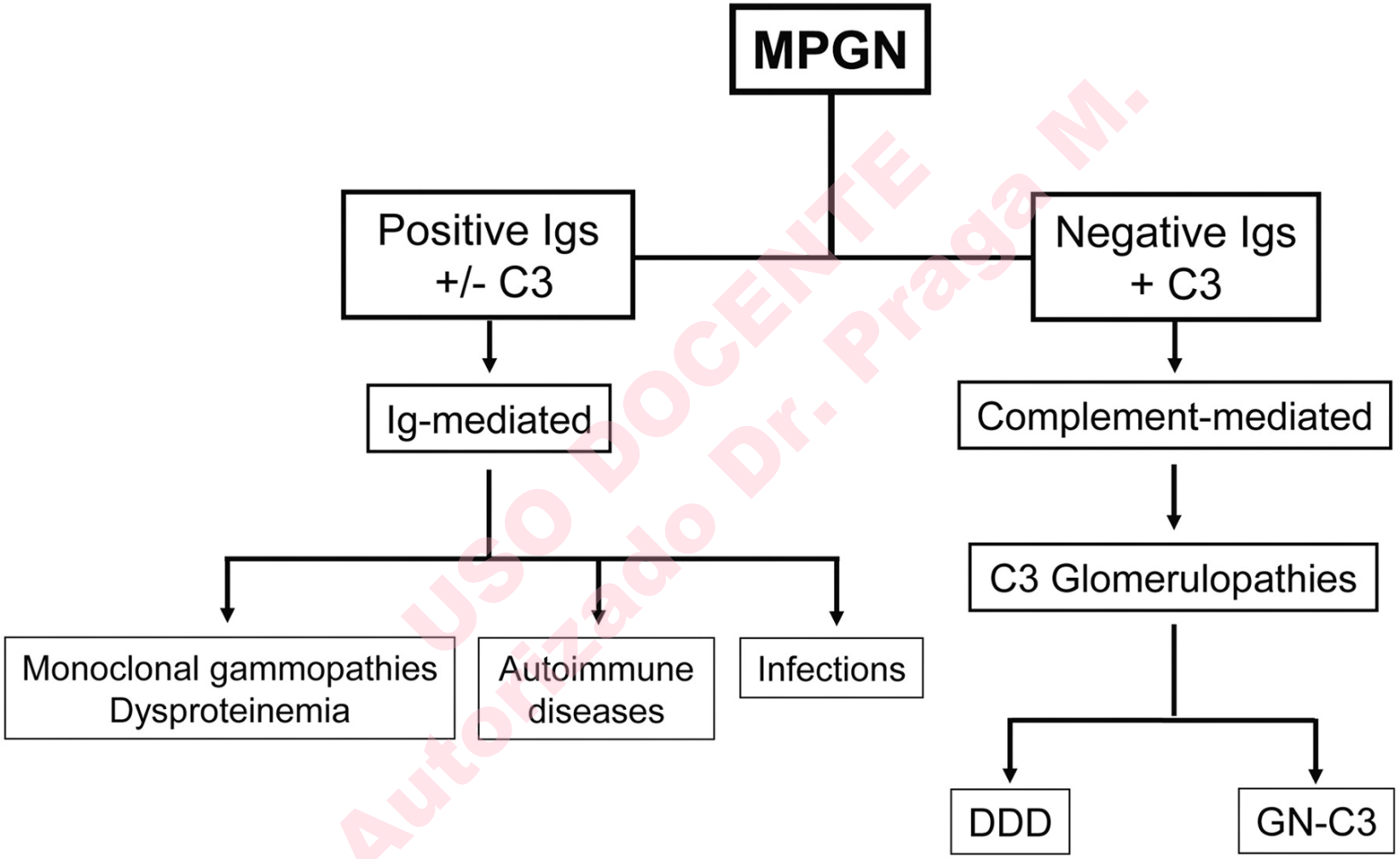
Kidney Int 2012

Acquired and Genetic Abnormalities Associated with Complement-Mediated MPGN.



Sethi S, Fervenza FC. N Engl J Med 2012;366:1119-1131

Proposed evaluation scheme for MPGN based on the presence or absence of immunoglobulins by immunofluorescence.



Sethi S et al. CJASN 2011;6:1009-1017

AJKD
Case Report

Association of a Novel Complement Factor H Mutation With Severe Crescentic and Necrotizing Glomerulonephritis

Fernando C. Fervenza, MD, PhD,[1] Richard J.H. Smith, MD,[2,3,4] and Sanjeev Sethi, MD, PhD[5]

To summarize, we present a case of severe crescen- tic and necrotizing GN associated with a novel muta- tion in *CFH* and the presence of 2 copies of the H402 allele of *CFH* and 2 copies of the G102 and 1 copy of the L314 alleles of *C3*. Crescentic and necrotizing GN with extensive glomerular C3 staining on immunoflu- orescence studies warrants an in-depth evaluation of the alternative pathway.

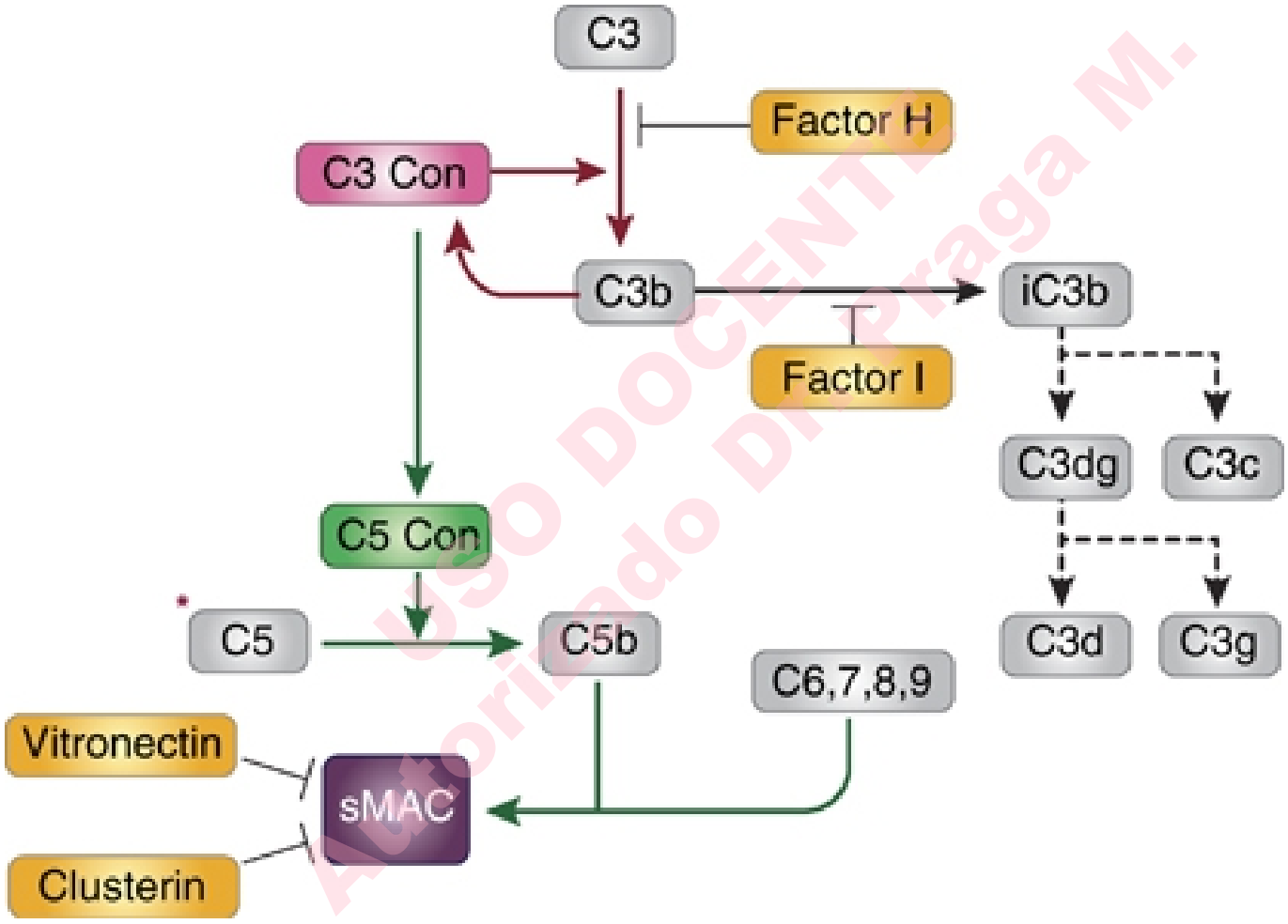
AJKD
Kidney Biopsy Teaching Case

Secondary Focal and Segmental Glomerulosclerosis Associated With Single-Nucleotide Polymorphisms in the Genes Encoding Complement Factor H and C3

Sanjeev Sethi, MD, PhD,[1] Fernando C. Fervenza, MD, PhD,[2] Yuzhou Zhang, PhD,[3,4,5,6] and Richard J.H. Smith, MD[3,4,5,6]

To summarize, although genetic causes of FSGS typically involve mutations of the podocyte proteins and occasionally the glomerular basement membranes, we describe a case of FSGS associated with single-nucleotide polymorphisms in CFH and C3, suggesting that FSGS can be caused by dysregulation of the alternative pathway of complement. Evidence of vascular injury in FSGS warrants an in-depth evaluation of the alternative pathway of complement.

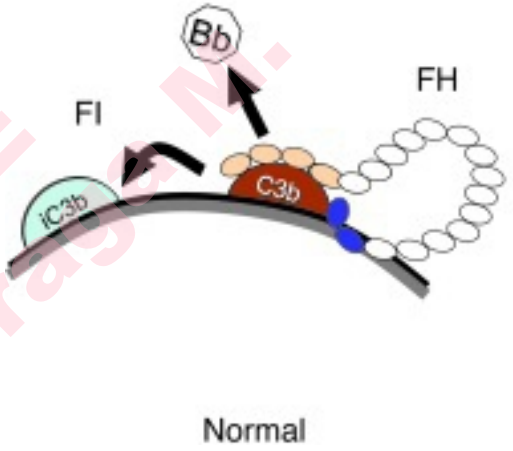
C3 G. Pathogenesis

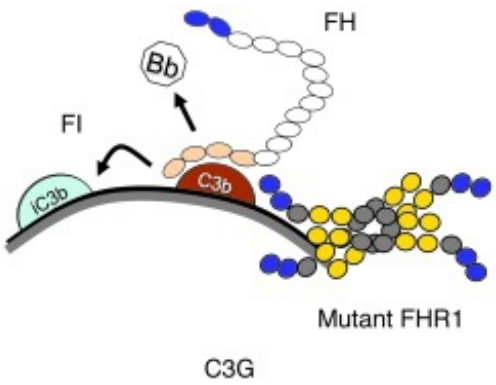


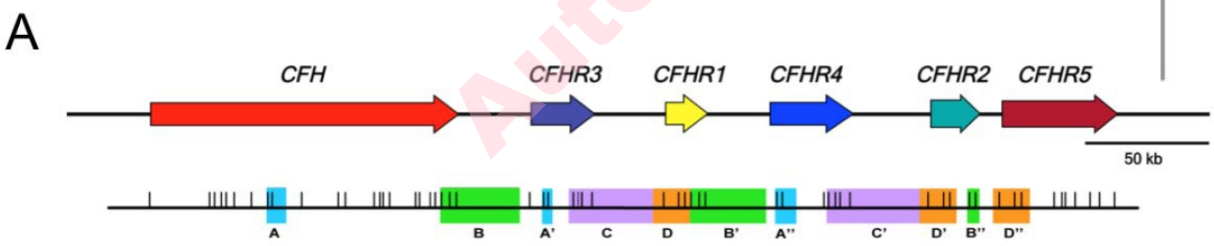
Sethi S et al Kidney Int 2012

Genetic Complement Abnormalities in C3G

- **Mutations and rare variants in CFH, CFI, MCP (*Servais et al, Kidney Int 2012)***
- **Mutations in CFHR 5 *(Gale DP, Lancet 2010; Athanasiou Y, CJASN 2011)***
- **Mutations in CFHR 1-3**







Acquired Autoantibodies; C3NeF

Autoantibody that binds and stabilizes C3 convertase (C3bBb) , Increasing and prolonging its C3-cleaving action

Table 1 | C3 nephritic factor prevalence in DDD and C3GN

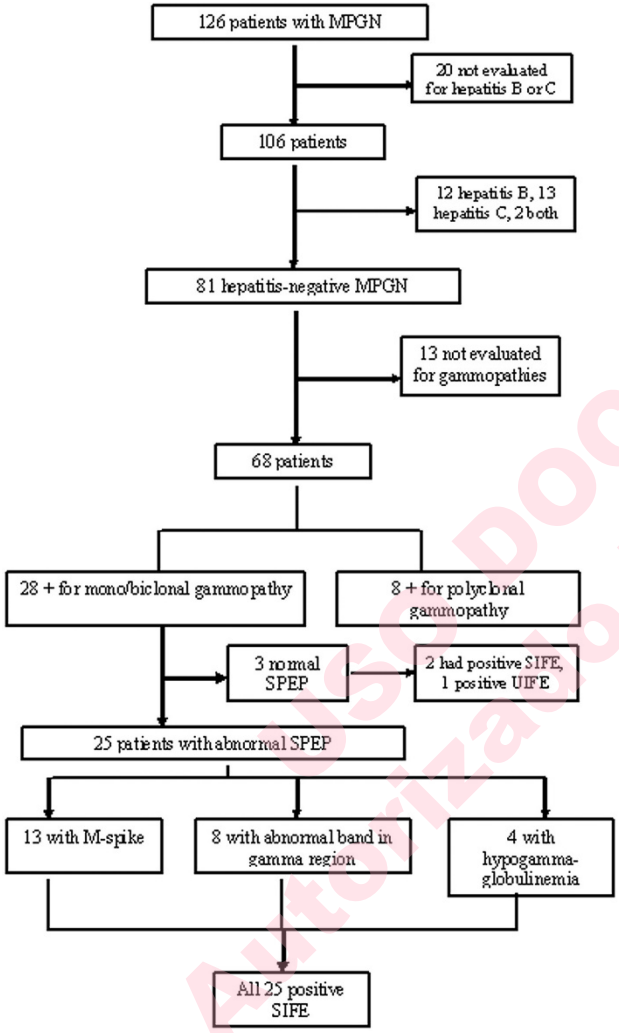
Reference	*n*	DDD (%)	C3GN (%)
Servais *et al.* (2007)[17]	17	N/A	41
Nasr *et al.* (2009)[52]	9	78	N/A
Zhang *et al.* (2012)[14]	32	78	N/A
Servais *et al.* (2012)[38]	75	86	45
Sethi *et al.* (2012)[30]	10	N/A	50

Abbreviations: C3GN, C3 glomerulonephritis; DDD, dense deposit disease; N/A, not applicable.

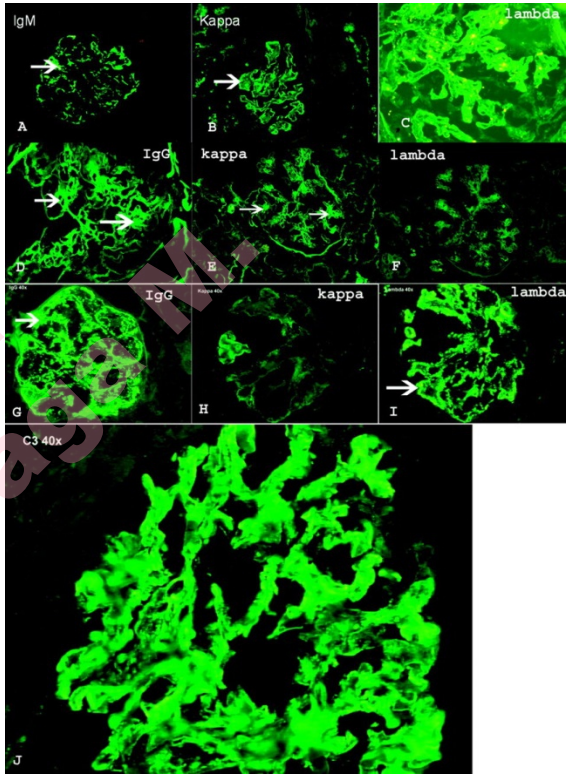
Bomback, A. S. & Appel, G. B. *Nat. Rev. Nephrol.* 8, 634–642 (2012);

Other Autoantibodies: Anti-Factor B, Anti Factor H

Summary of workup of patients with MPGN.



Sethi S et al. CJASN 2010;5:770-782



Nephritogenic lambda light chain dimer: a unique human miniautoantibody against complement factor H

Jokiranta TS; J Immunol 1999; 166:4590

Monoclonal Ig lambda light chain in a hypocomplementemic MPGN. The paraprotein was found to bind to Factor H, activating the alternative pathway of complement

C3G vs aHUS

- Common Pathogenesis: Abnormal activation of the alternative pathway of complement

- C3G (C3GN and DDD): Activation in the fluid phase, leading to increased production of Complement breakdown products (iC3b, C3d, C3g) that are deposited in the glomeruli

- aHUS: Activation in the solid phase (cell surface) causing endothelial cell damage and lesions of thrombotic microangiopathy

Coexistence of C3G and TMA

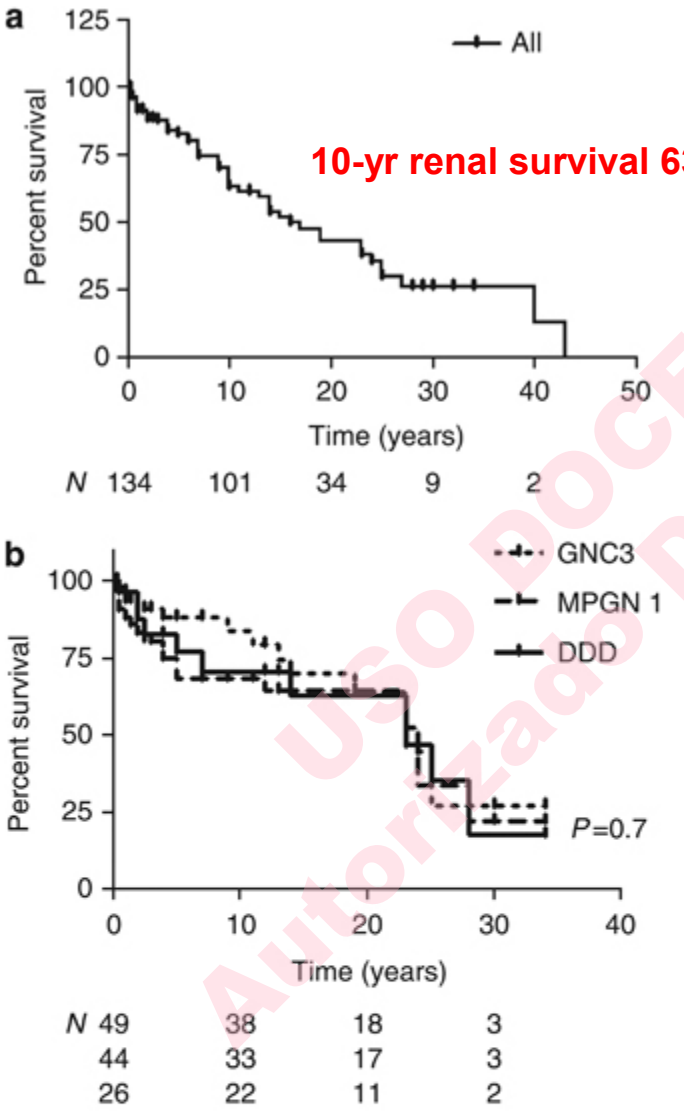
- ***Coexistence of C3G and TMA (Servais, Kidney Int 2012)***

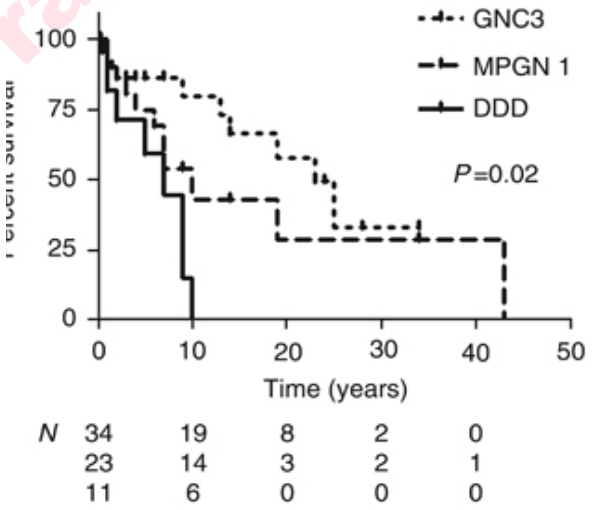
- ***Appearance of TMA in patients with previous C3G (Van Doorn, Clin Kidney J 2013)***

- ***TMA after kidney transplantation in patients with C3G in native kidneys (Lorcy N, NDT 2011; Servais, Kidney Int 2012)***

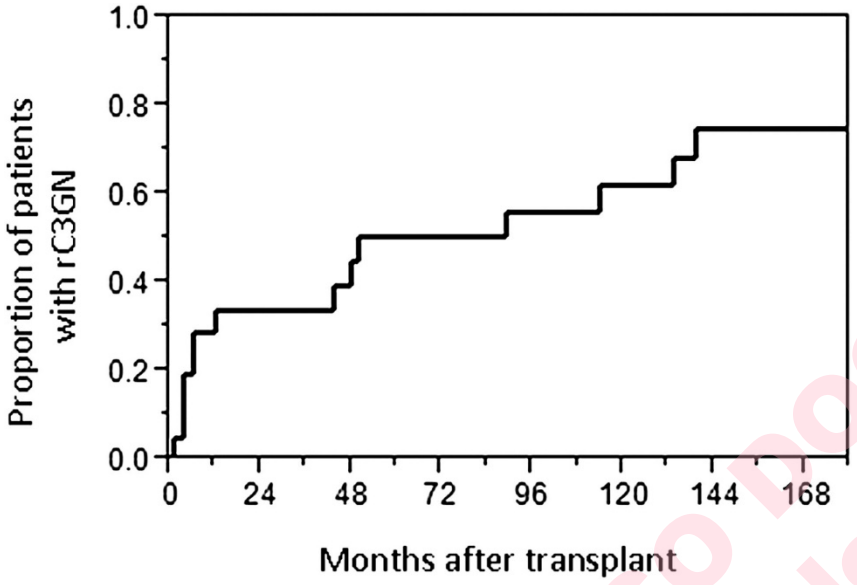
Renal survival in GNC3, MPGN 1 and DDD

Servais et al, Kidney Int 2012



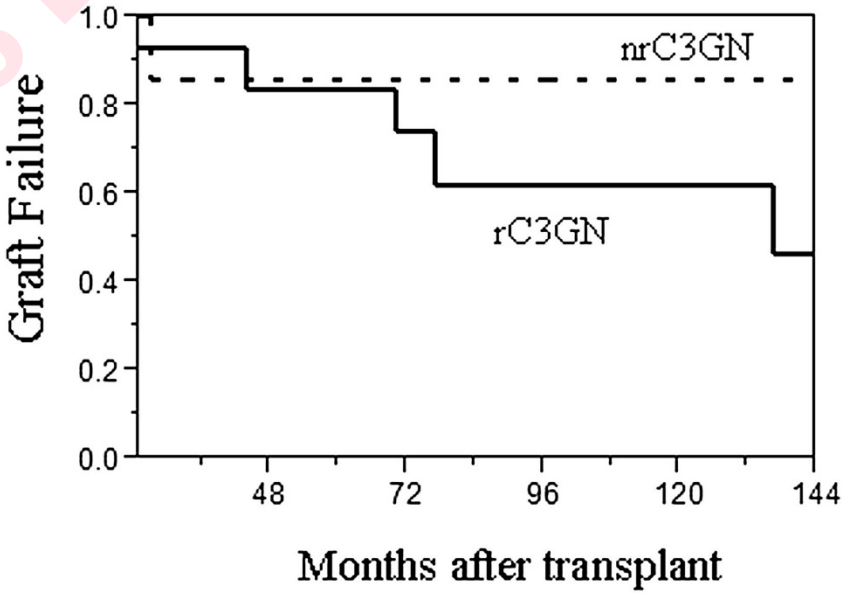


Recurrence of C3GN after Kidney Transplantation



21 patients with C3GN who received a kidney graft

Recurrence of the disease in 66%



Zand L et al. JASN 2014;25:1110-1117

Treatment

- **Immunosuppresion (IS) considered as ineffective, but information is very scarce and of poor quality**
- **Response to eculizumab in some but not all patients**
- **Possible indications of eculizumab (*Zuber et al NRN 2012):***
  - ***Short duration of the disease***
  - ***Predominant Inflammatory changes***
  - ***Increase in circulating C5b-9***

Table 2 | Reports of eculizumab therapy in C3 glomerulopathies

Reference	*n*	Disease	Native or in transplant?	C3Nef	Response
McCaughan *et al.* (2012)[59]	1	DDD	Transplant	+	↓ SCr ↓ Proteinuria
Daina *et al.* (2012)[58]	1	DDD	Native	+	↓ SCr ↓ Proteinuria ↑ SAlb
Vivarelli *et al.* (2012)[57]	1	DDD	Native	+	↓ Proteinuria ↑ SAlb
Radhakrishnan *et al.* (2012)[36]	1	MPGN type I	Native	+	↓ SCr ↓ Proteinuria ↑ SAlb
Bomback *et al.* (2012)[31]	6	DDD (*n*=3) C3GN (*n*=3)	Native (*n*=3) Transplant (*n*=3)	+ in 3/6	↓ SCr in 2/6 ↓ Proteinuria in 1/6 ↑ SAlb in 1/6

Effectiveness of mycophenolate mofetil in C3 glomerulonephritis

Cristina Rabasco[1], Teresa Cavero[1], Elena Román[2], Jorge Rojas-Rivera[3], Teresa Olea[4], Mario Espinosa[5], Virginia Cabello[6], Gema Fernández-Juarez[7], Fayna González[8], Ana Ávila[9], José María Baltar[10], Montserrat Díaz[11], Raquel Alegre[3], Sandra Elías[12], Monserrat Antón[13], Miguel Angel Frutos[14], Alfonso Pobes[15], Miguel Blasco[16], Francisco Martín[17], Carmen Bernis[18], Manuel Macías[19], Sergio Barroso[20], Alberto de Lorenzo[21], Gema Ariceta[22], Manuel López-Mendoza[6], Begoña Rivas[4], Katia López-Revuelta[7], José María Campistol[16], Santiago Mendizábal[2], Santiago Rodríguez de Córdoba[23] and Manuel Praga[1,24] for the Spanish Group for the Study of Glomerular Diseases (GLOSEN)

Table 1 | Characteristics of patients at baseline and clinical presentation

	All patients ($n=60$)	Non-IST ($n=20$)	IST ($n=40$)	P-value[a]	MMF-IST ($n=22$)	Other-IST ($n=18$)	P-value[b]
Age (years)[c]	27 (13–57)	29 (18–49)	24 (12–62)	0.594	35 (13–66)	18 (10–41)	0.109
Gender, no. (%), male	34 (57)	14 (70)	20 (50)	0.174	14 (64)	6 (33)	0.111
Hypertension, no. (%)	27 (45)	11 (55)	16 (40)	0.288	9 (41)	7 (39)	1.0
Clinical presentation, no. (%)				<0.001			0.126
Nephrotic syndrome	31 (52)	4 (20)	27 (67)		17 (77)	10 (55)	
Nephritic syndrome	19 (32)	7 (35)	12 (30)		4 (18)	8 (44)	
Asymptomatic urinary abnormalities	10 (17)	9 (45)	1 (2)		1 (4)	0 (0.0)	
SCr (mg/dl)[c]	1.4 (0.7–2.8)	1.3 (0.8–2.0)	1.4 (0.7–2.9)	0.772	1.3 (0.6–2.9)	1.6 (0.8–2.9)	0.838
eGFR (ml/min per 1.73 m^2)[c]	66 (25–104)	65 (34–96)	66 (24–113)	0.963	67 (23–119)	66 (26–112)	0.870
Proteinuria (g/24 h)[c]	3.8 (1.4–7.0)	1.4 (0.9–3.1)	5.2 (3.4–7.4)	0.001	6.5 (3.9–8.6)	4.3 (1.5–5.6)	0.099
Serum albumin (g/dl)[c]	3 (2.6–3.5)	3.6 (2.9–4.3)	2.8 (2.4–3.1)	<0.001	2.8 (2.1–3.1)	2.9 (2.5–3.1)	0.340
Hypocomplementemia C3, no. (%)	38 (63)	8 (40)	29 (72)	0.024	15 (68)	14 (78)	0.723
Follow-up (months)[c]	47 (16–93)	38 (11–136)	50 (20–77)	0.605	44 (22–66)	54 (13–78)	0.744

C3 Glomerulonephritis

Spanish Group for the Study of Glomerular Diseases (GLOSEN)

- Age : 37 (13-57); Gender: 34 M, 26 F
- Renal Biopsy: Membranoproliferative GN 74%
  Mesangioproliferative GN 14%
  Endocapillar proliferatioin GN 8%
  Focal segmental glomerulosclerosis 2%
  Extracapillar proliferation 2%
- Clinical presentation
  Nephrotic syndrome (NS): 50%
  Nephritic syndrome (NephS): 33%
  Asymptomatic urinary abnormalities (AUA): 17%
- Low C3 serum levels: 63%

C3 Glomerulonephritis

Spanish Group for the Study of Glomerular Diseases (GLOSEN)

- ACEI, ARB: 54/60 (90%)
- Immunosuppressive treatments (IS) 40/60 (66%)

Corticosteroids+MMF	22 (55%)
Corticosteroids+Others	9 (22%)
Corticosteroids only	9 (22%)

- Definition of Response

Complete response: eGFR>60 ml/m/1.73 or return to basal values, proteinuria <0.5 g/d, inactive sediment, serum albumin >3 g/d

Partial response: Proteinuria < 3.5 g/d in those with nephrotic-range proteinuria; proteinuria decrease >50% in those with proteinuria <3.5 g/d, and improvement or stabilization (±25%) of renal function with respect to initial values

Follow-up: 73 (16-94) months

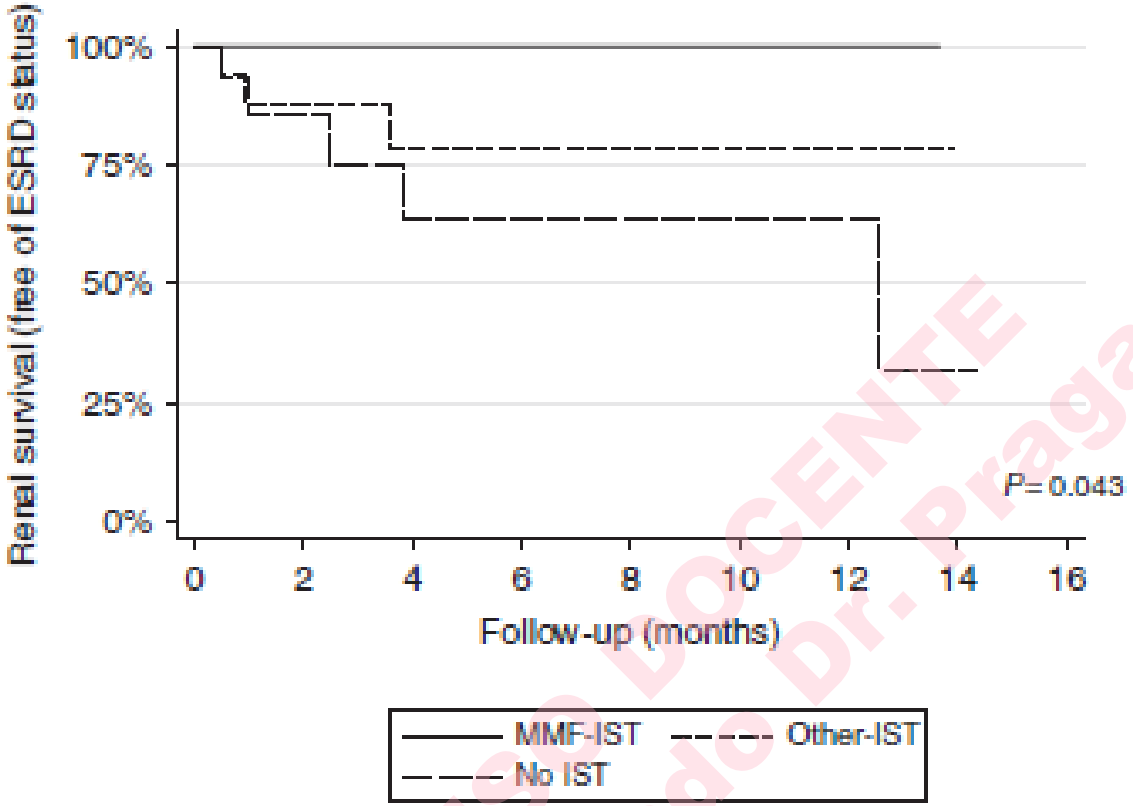


Table 4 | Response to treatment according to immunological and genetic abnormalities

	C3NeF (+) ($n=11$)	C3NeF (−) ($n=12$)
No IST, no. (%)	1 (9)	4 (33)
IST, no. (%)	10 (91)	8 (67)
Remission, no. (%)	8 (80)	3 (37)
ESRD, no. (%)	2 (20)	5 (63)[a]

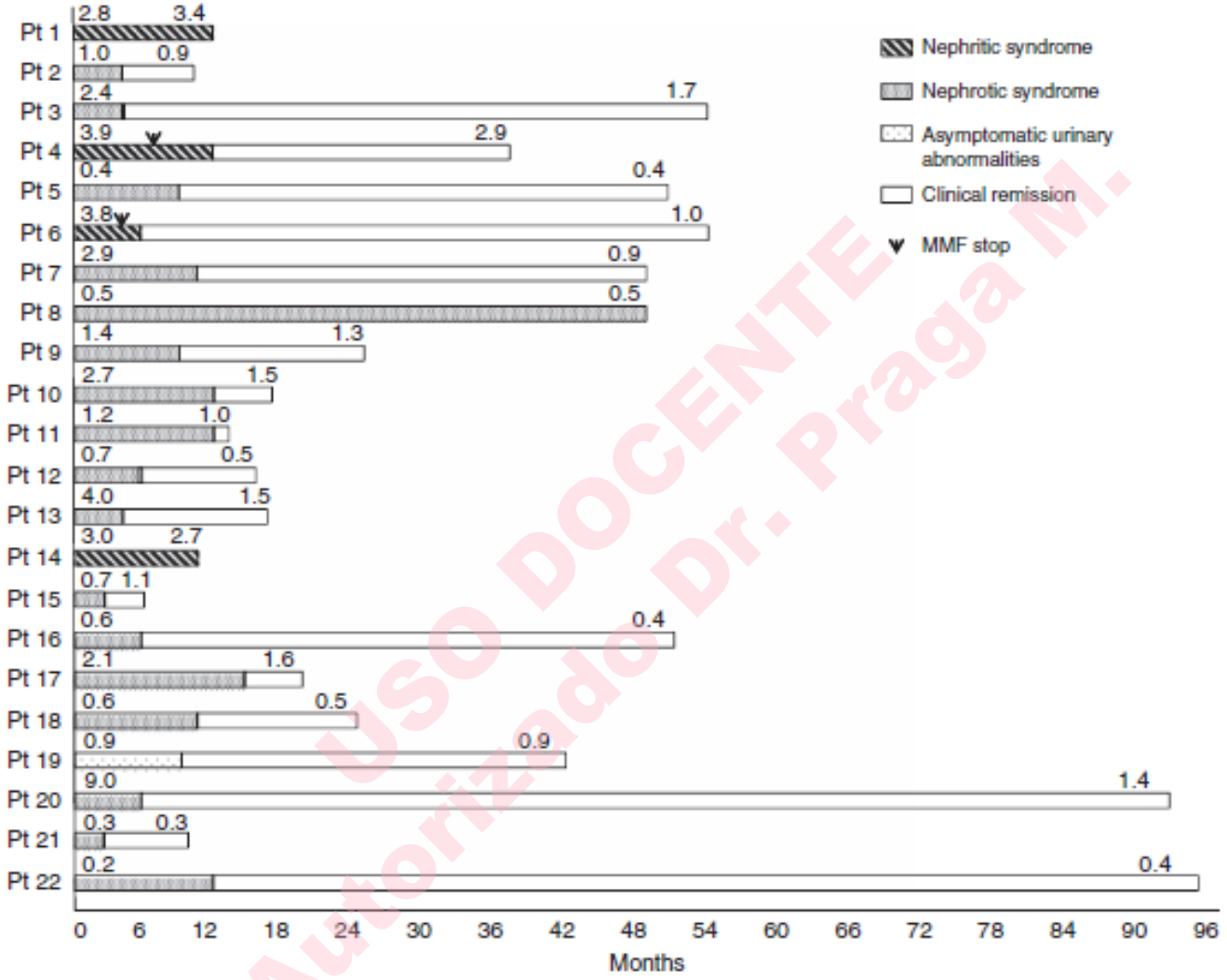


Figure 2 | Individual clinical course of 22 C3 glomerulonephritis (C3GN) patients treated with mycophenolate mofetil (MMF). '0' represents the onset of MMF treatment. Numbers represent serum creatinine values (mg/dl) at the onset of MMF and at the last follow-up visit in every patient. MMF was discontinued only in patients 4 and 6; the remaining 20 patients were receiving MMF at the last visit.

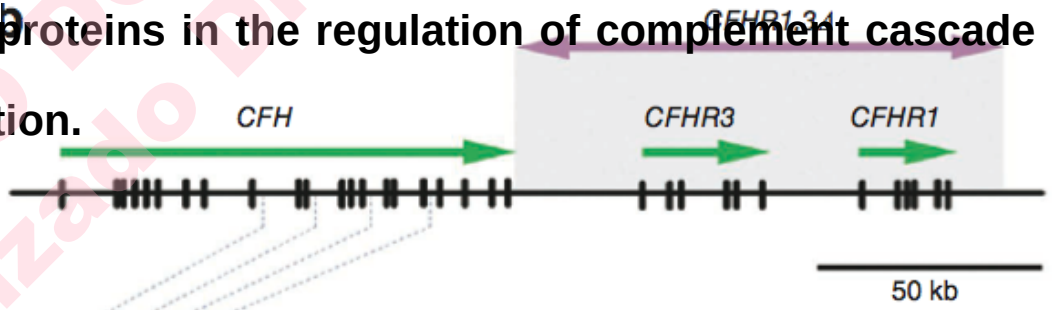
Genome-wide association study identifies susceptibility loci for IgA nephropathy

nature genetics

- Carriers of a common deletion encompassing the neighboring **CFHR1 and CFHR3 genes had an approximately 30% decreased risk of developing IgAN**. The risk was almost 60% lower in the rare individuals who carry two copies of this deletion.

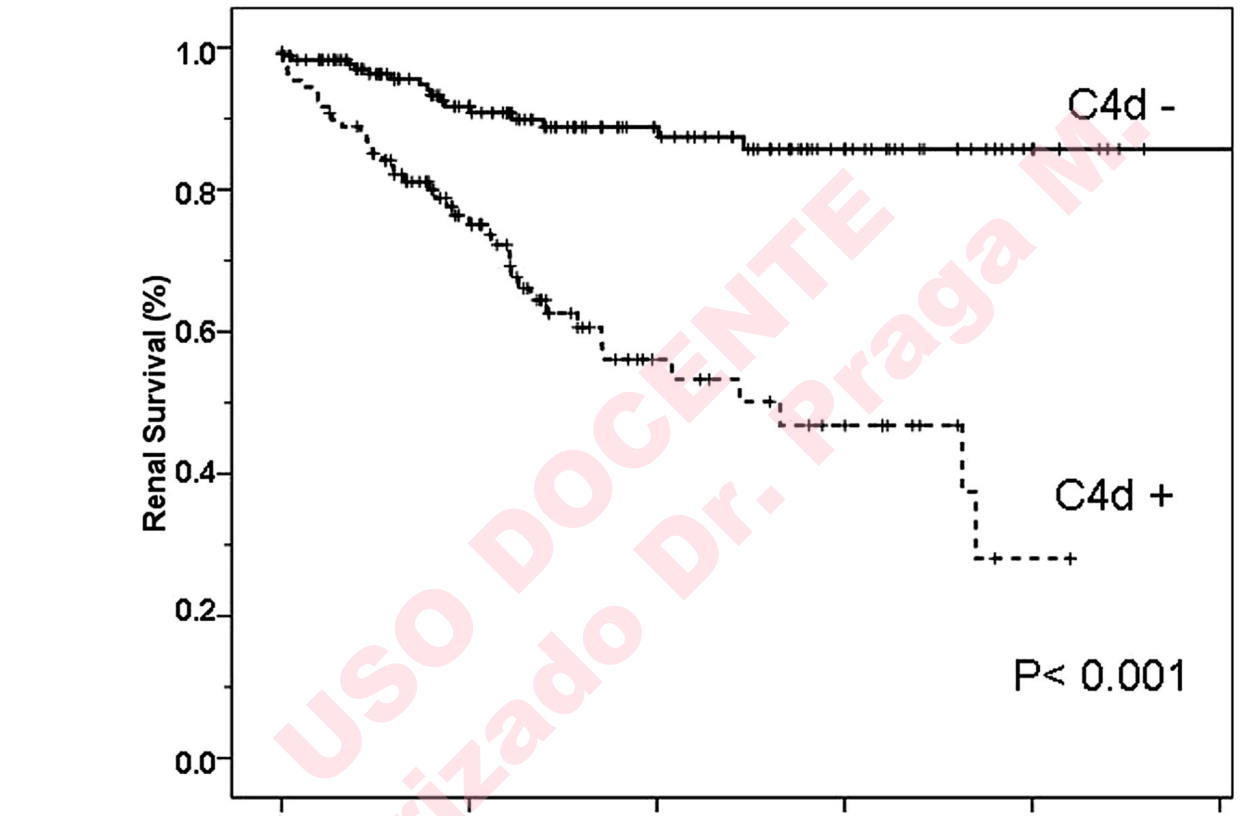
- **The role of CFHR1 and CFHR3 proteins in the regulation of complement cascade is currently under active investigation.**

- Therefore, a relative loss of CFHR1 and CFHR3 may **enhance the inhibitory action of CFH and thus convey protection against local inflammation.**



	rs10801555	rs6677604	rs2284664	rs1065489	Freq. cases	Freq. controls	OR (95% CI)	Published associations:
H-1:	A	G	G	G	0.075	0.075	1.00 (reference)	AMD (risk)
H-2:	G	A	G	G	0.038	0.070	0.56 (0.40–0.79)***	AMD (protective), AHUS (risk)
H-3:	G	G	G	T	0.529	0.477	1.11 (0.88–1.39)	*N. meningitidis* (protective)
H-4:	G	G	A	G	0.344	0.361	0.96 (0.76–1.21)	Unknown
H-5:	G	G	G	G	0.013	0.017	0.82 (0.48–1.40)	Unknown

Renal survival according to C4d staining.



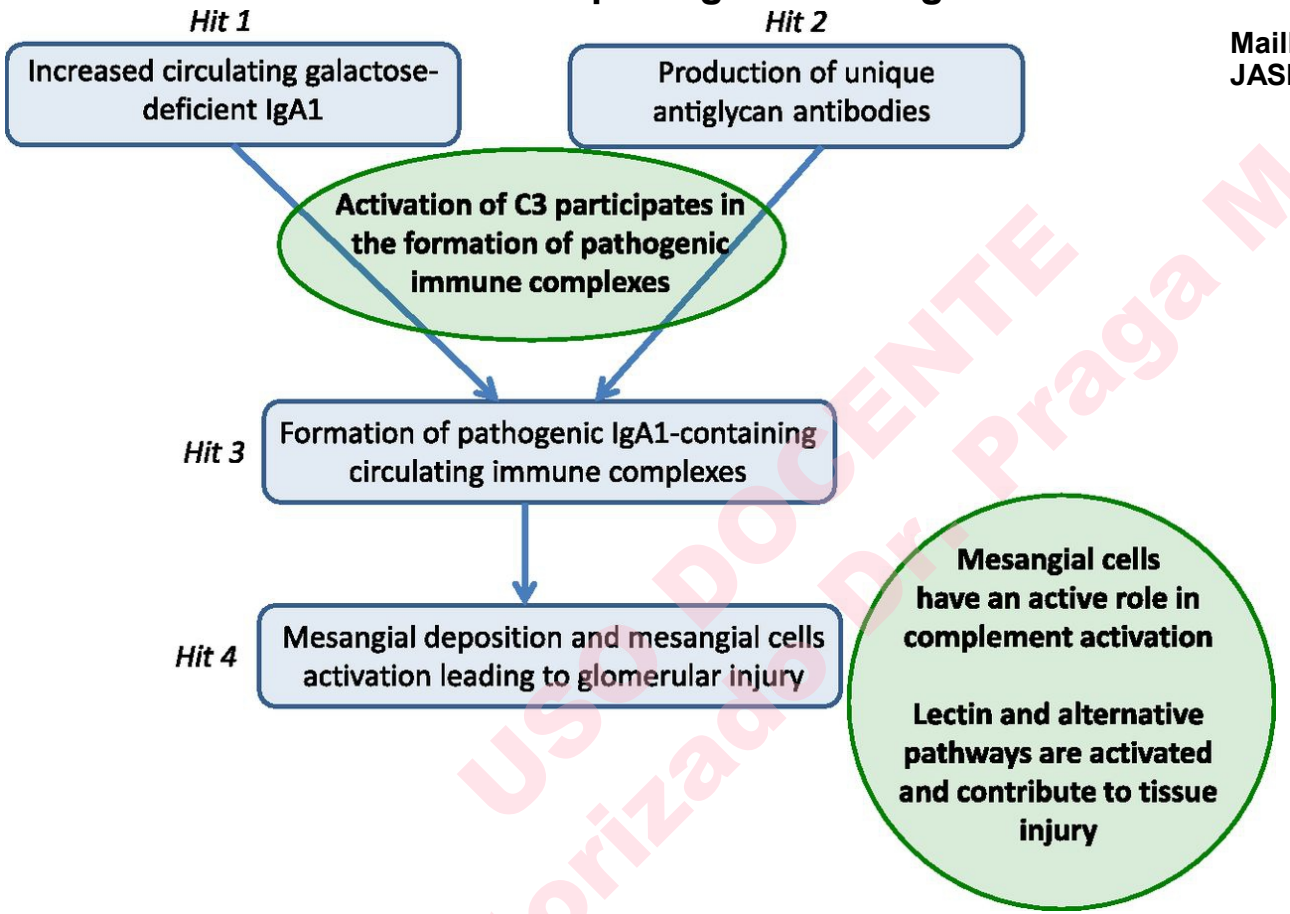
Subjects at risk

C4d -	174	109	63	31	10	1
C4d+	109	58	19	11	2	0

Espinosa M et al. CJASN doi:10.2215/CJN.09710913

CJASN

Integrative view of the role of complement activation in the four-hit model of the pathogenesis of IgAN.



Maillard et al.
JASN 2015;26:1503-1512

Brief Report

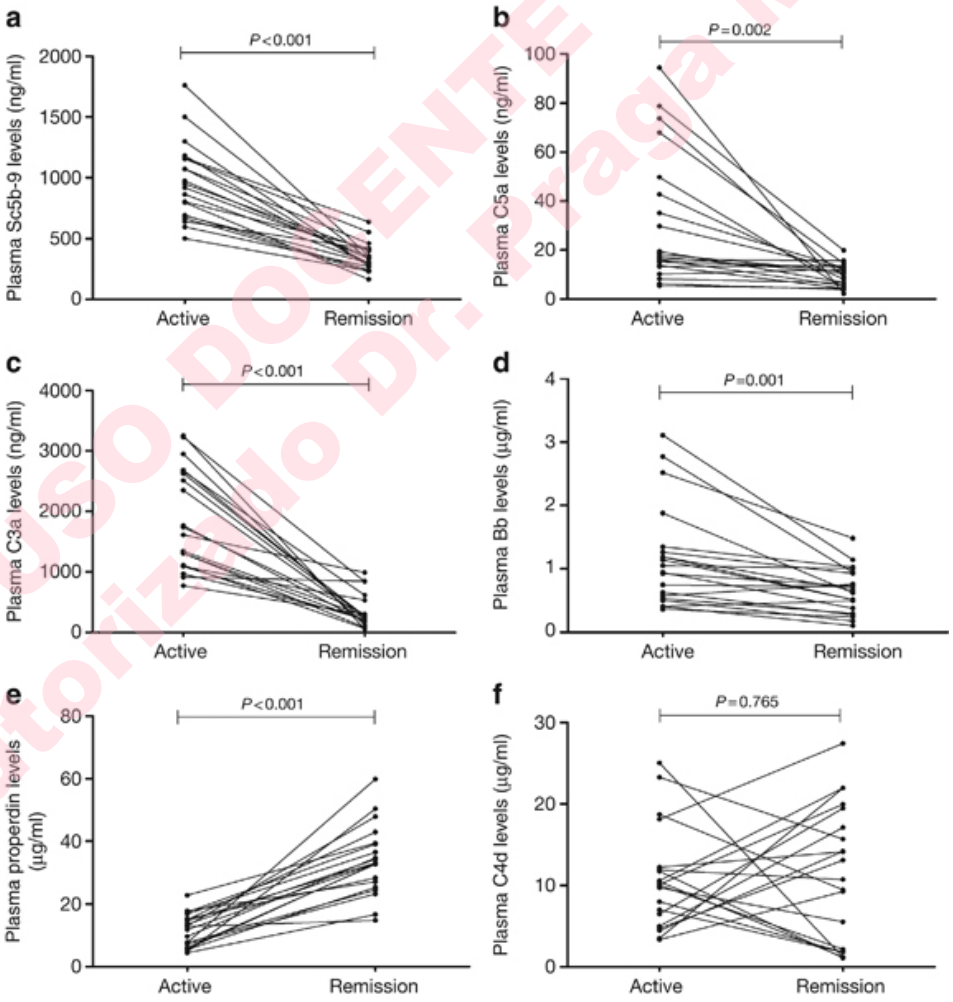
Pediatric Nephrology, 29 :2225-2228, 2014

Rosenbland T et al. Eculizumab treatment for rescue of renal function in IgA nephropathy

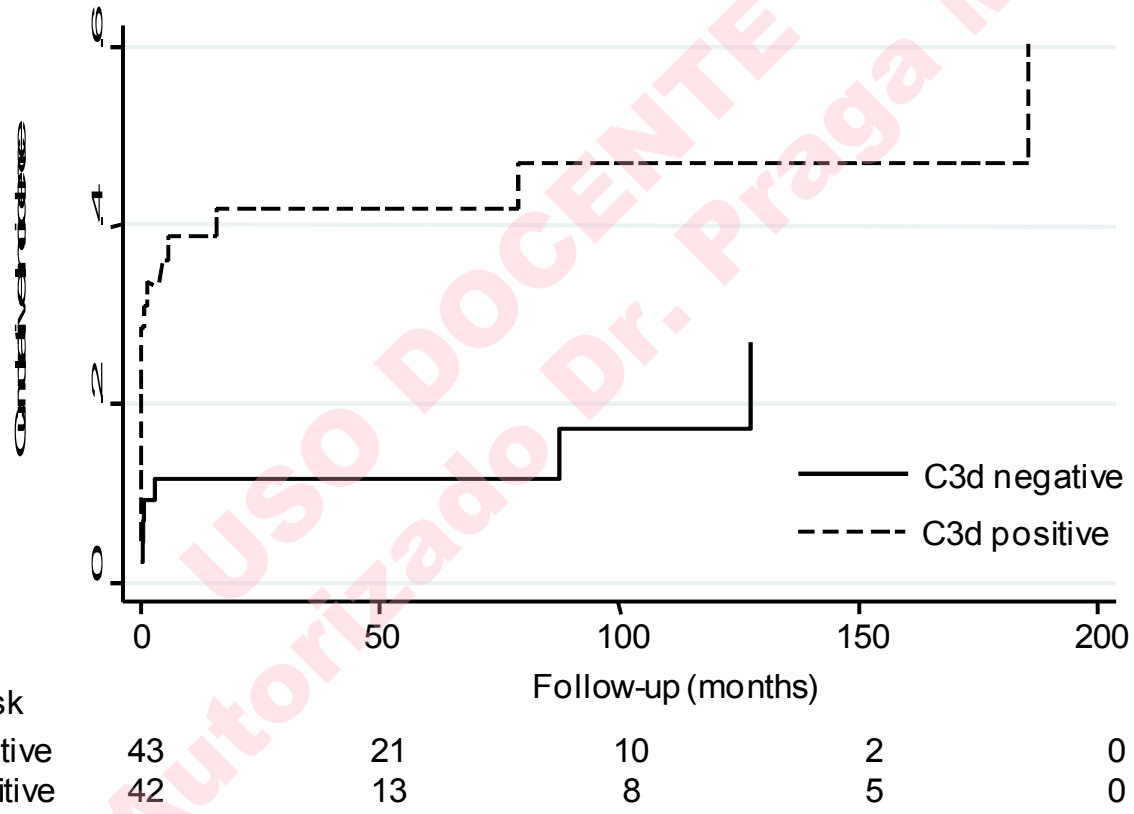
see commentary on page 16

Circulating complement activation in patients with anti-neutrophil cytoplasmic antibody–associated vasculitis

Shen-Ju Gou[1,3], Jun Yuan[1,2,3], Min Chen[1], Feng Yu[1] and Ming-Hui Zhao[1]



Cumulative incidence curves of ESRD according to according to C3d stainir
In patients with ANCA+ vasculitis.



Cortesía Dra Fernández-Juárez

Complemento, MAT, otras enfermedades renales

- Púrpura Trombótica Trombocitopénica*
- Shiga-Toxin HUS*
- MAT por fármacos*
- MAT asociada a Lupus Eritematoso Diseminado*
- Síndrome antifosfolípido catastrófico*
- Nefritis Lúpica
- MAT del Trasplante de Médula Ósea*
- Vasculitis ANCA +
- Glomerulopatia C3*
- Nefropatía IgA*
- Prevención del rechazo humoral en Hiperinmunizados
- Prevención del retraso en la función del injerto

THANK YOU

FOR YOUR ATTENTION

C3 Glomerulonephritis. (GLOSEN)

-Mycophenolate Mofetil appears to be effective in an important number of patients with C3GN

Hypothesis

Immunosuppressive treatment effective in patients with autoantibodies (C3 Nef, Others)?

- **Coexistence of C3Nef with genetic abnormalities in a considerable proportion of patients**
- **Fluctuations in C3Nef activity without correlation with clinical activity or prognosis**

CONCLUSIONS

- Diagnosis of C3GN based on IF
- Genotype-phenotype correlations, significance of antibodies C3NeF
- Prospective clinical trials
- New treatments (new complement inhibitors)
- Mycophenolate mofetil + Corticosteroids, effective in an important number of patients
- Eculizumab in selected patients