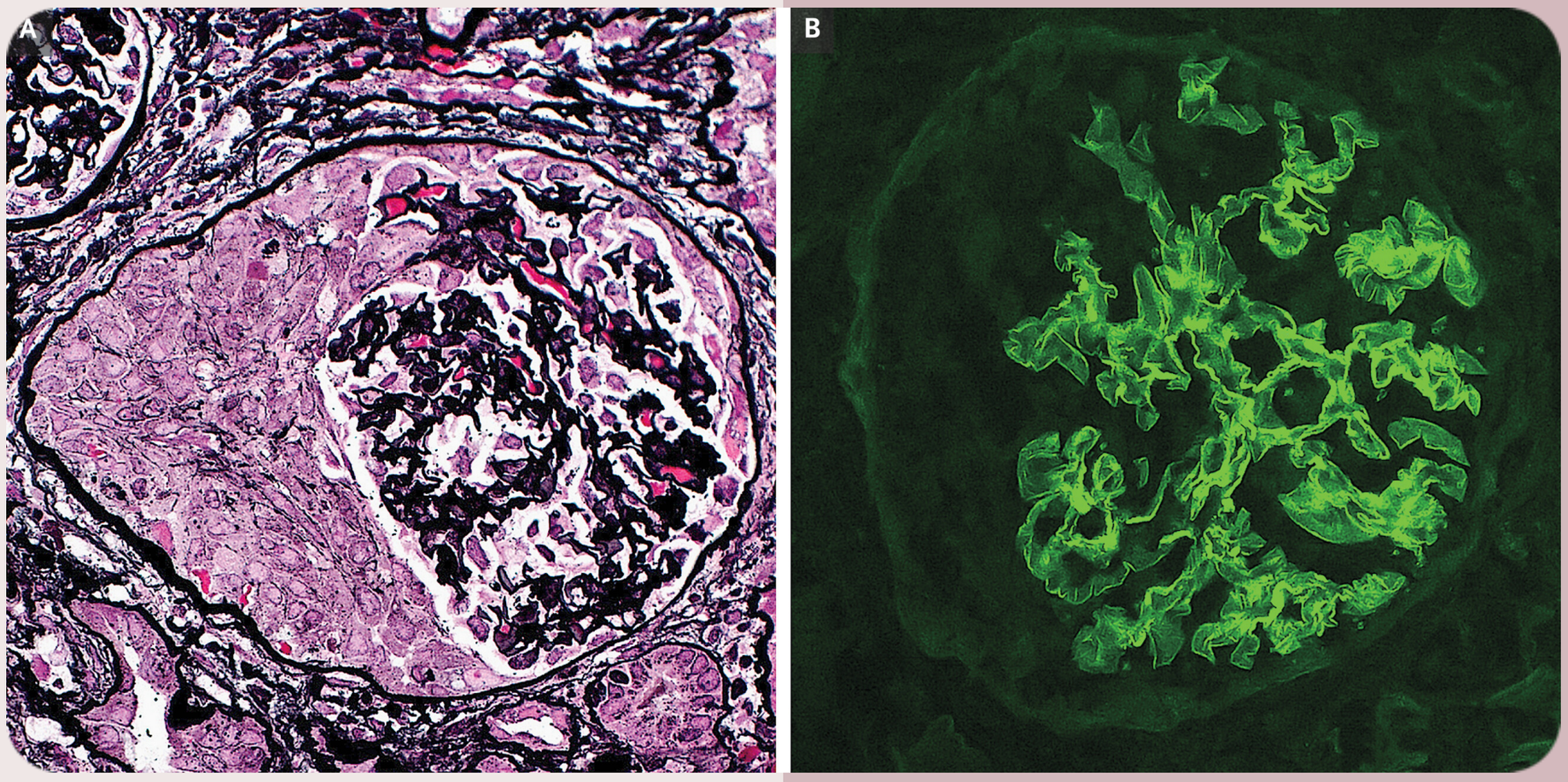
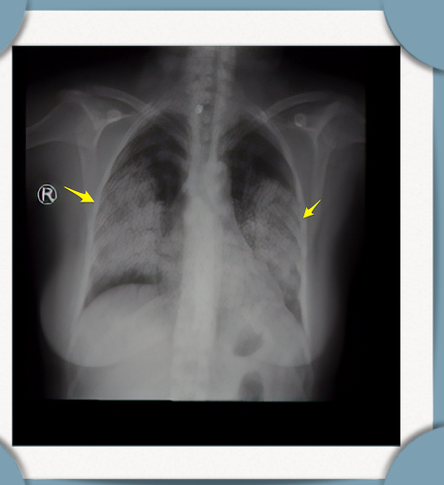
Ταχέως εξελισσόμενη σπειραματονεφρίτιδα

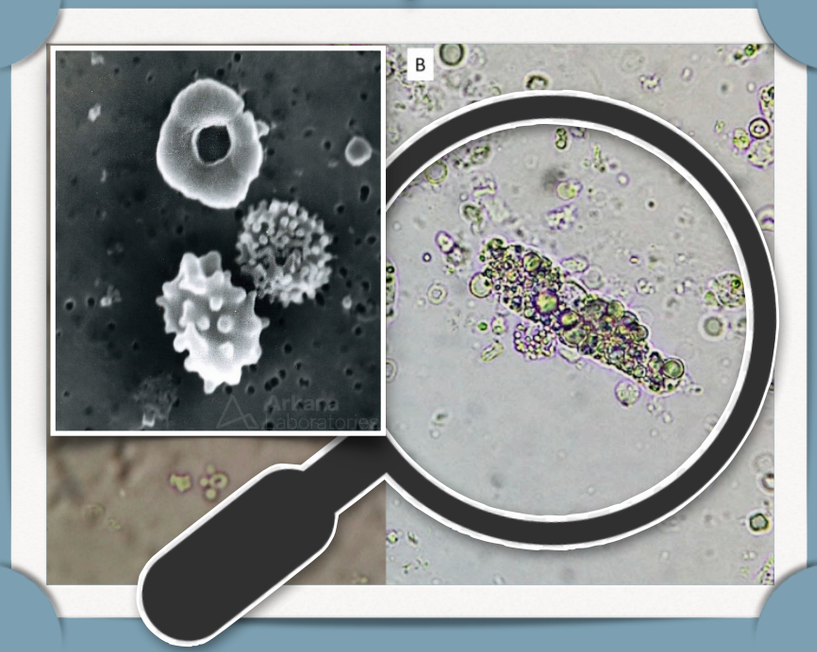


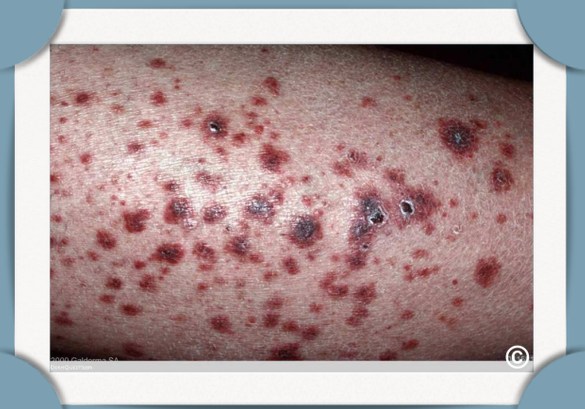
Rapidly progressive glomerulonephritis

Μάνου Ελένη, νεφρολόγος
ΓΝ Παπαγεωργίου, Θεσσαλονίκη

Αν θελήσουμε να δώσουμε τον ορισμό της θα πούμε ότι...





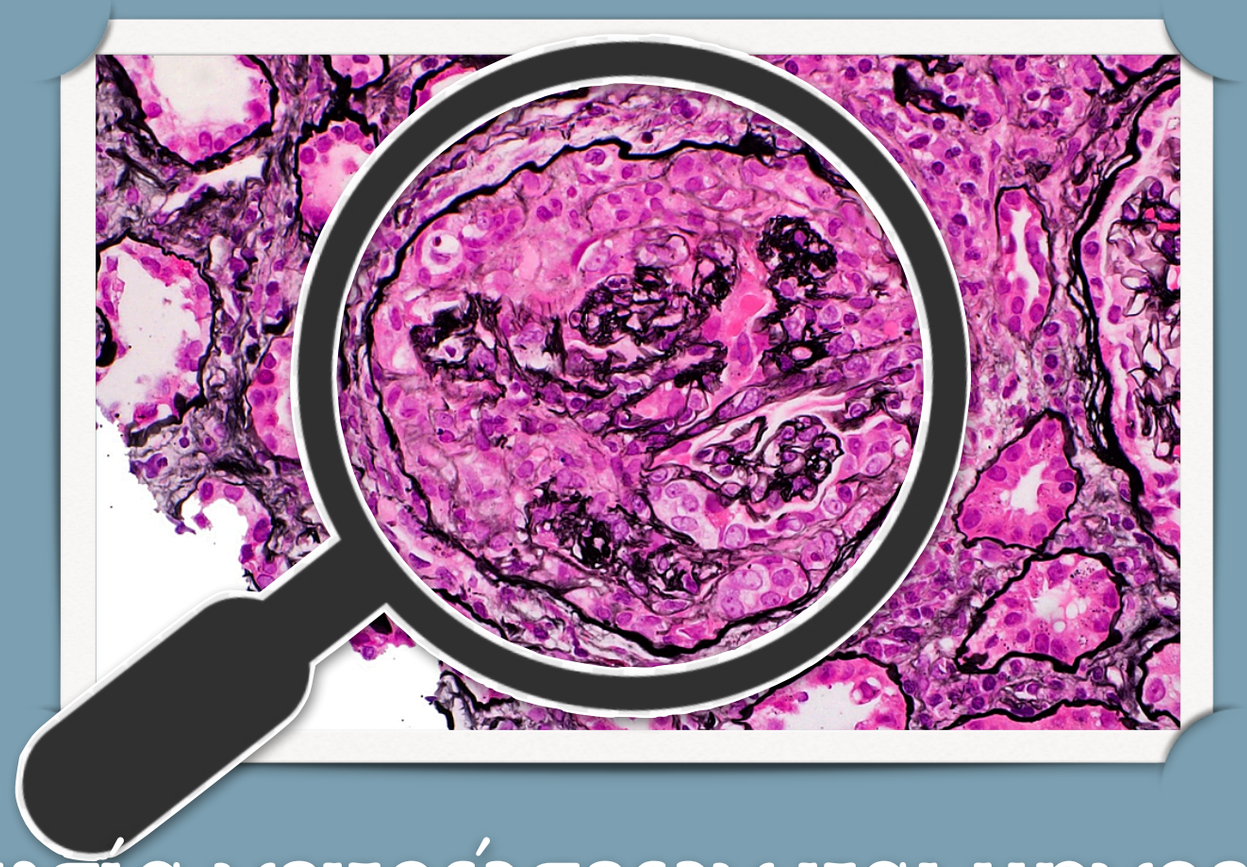


- Η ταχέως εξελισσόμενη σπειραματονεφρίτιδα (ΤΕΣΝ) αποτελεί ένα κλινικό **σύνδρομο** που χαρακτηρίζεται από ταχεία μείωση της νεφρικής λειτουργίας (συχνά κατά 50%), σε λίγες μόνο ημέρες ή εβδομάδες, συνοδευόμενη από **ενεργό** ίζημα ούρων (ερυθρά αιμοσφαίρια/αιμοσφαιρίνη ή ερυθροκυτταρικούς κυλίνδρους) και **λεύκωμα**, ενδεικτικά **σπειραματικής βλάβης**

- Συχνά συνυπάρχουν και σοβαρές ή λιγότερο σοβαρές **εξωνεφρικές** εκδηλώσεις

Αν θελήσουμε να δώσουμε τον ορισμό της θα πούμε ότι...

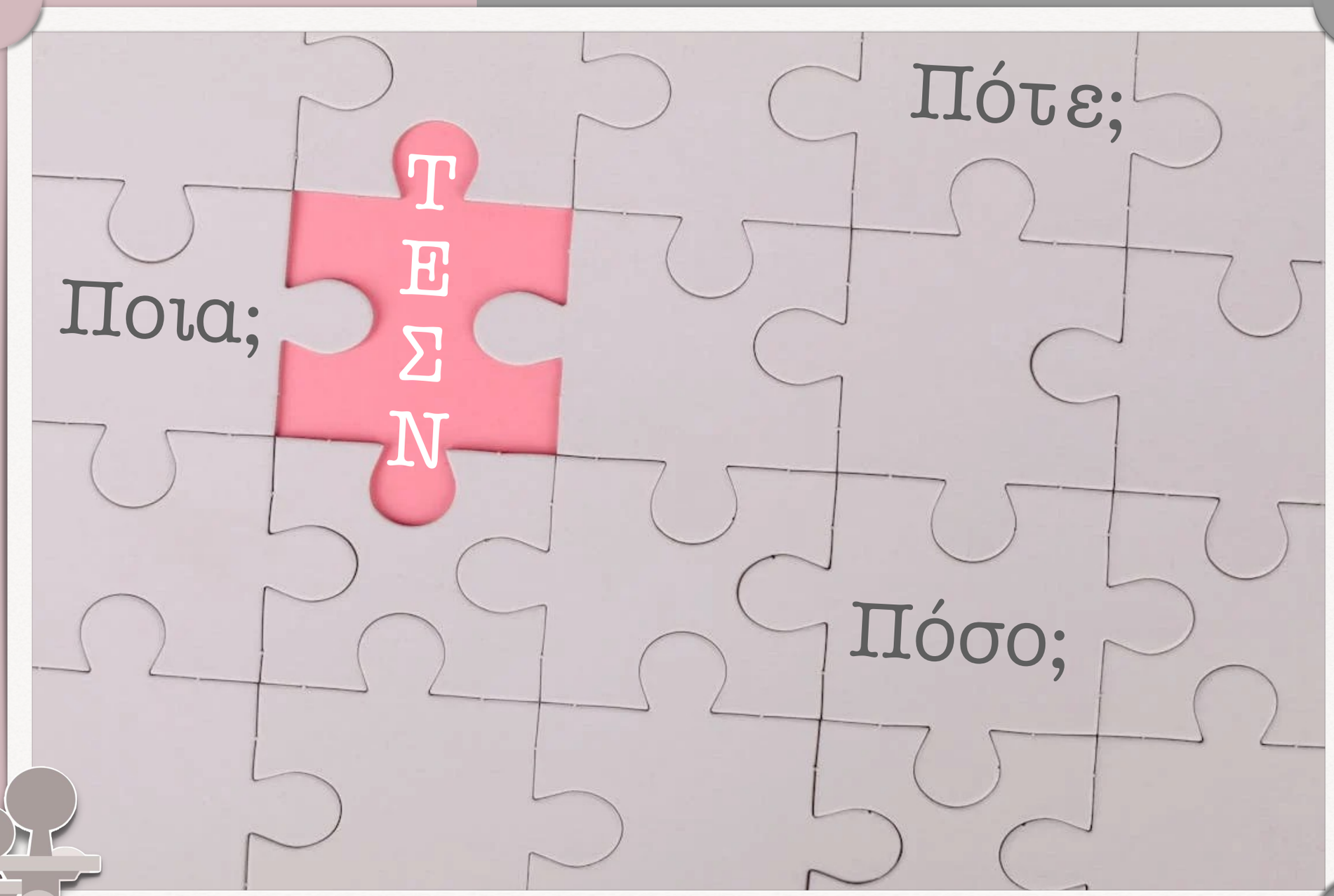
Η ΤΕΣΝ παρουσιάζει 2 χαρακτηριστικά ιστοπαθολογικά ευρήματα

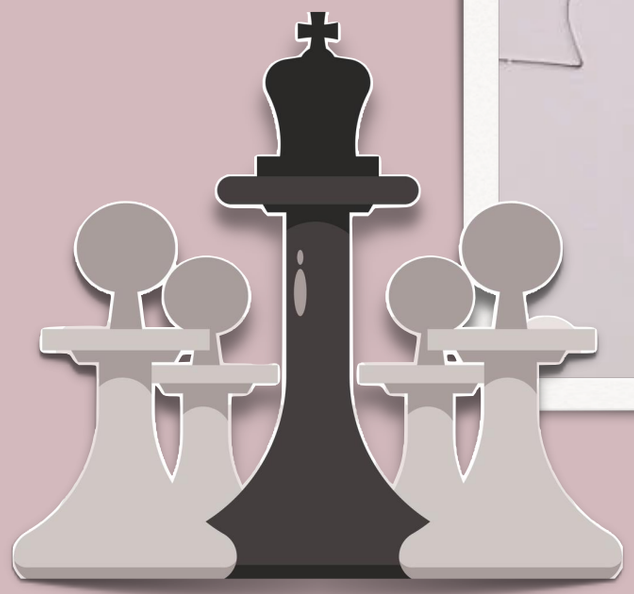


Παρουσία νεκρώσεων και μηνοειδών σχηματισμών (crescents)

Από την πλευρά της θεραπείας...

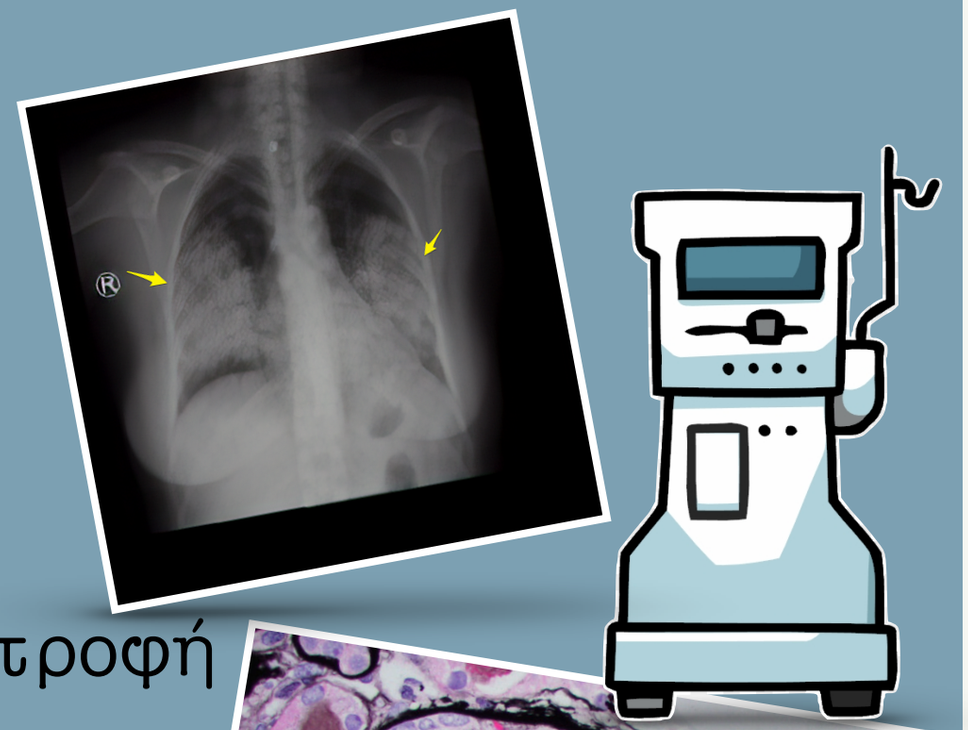
?

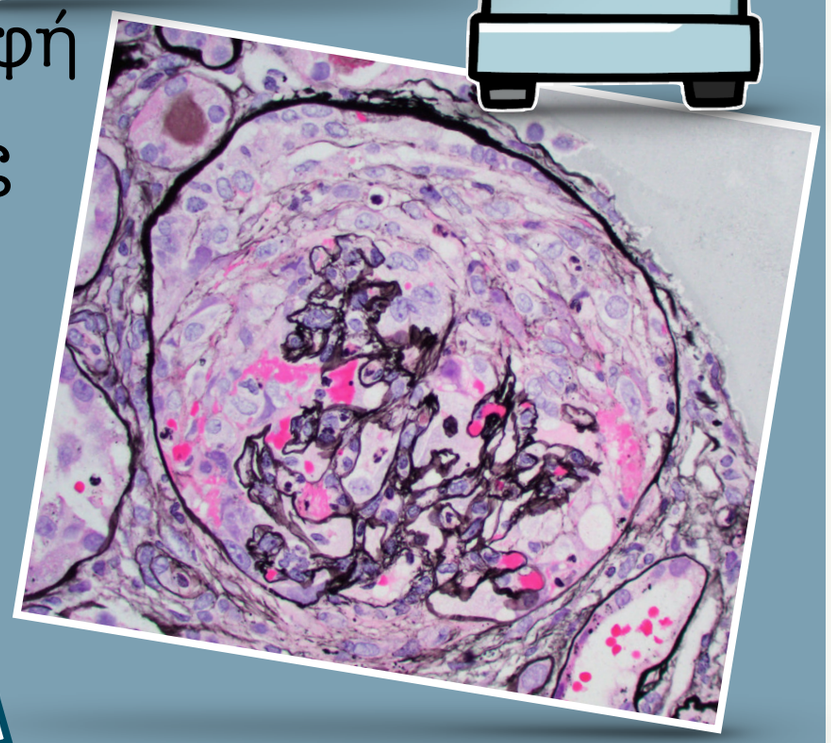


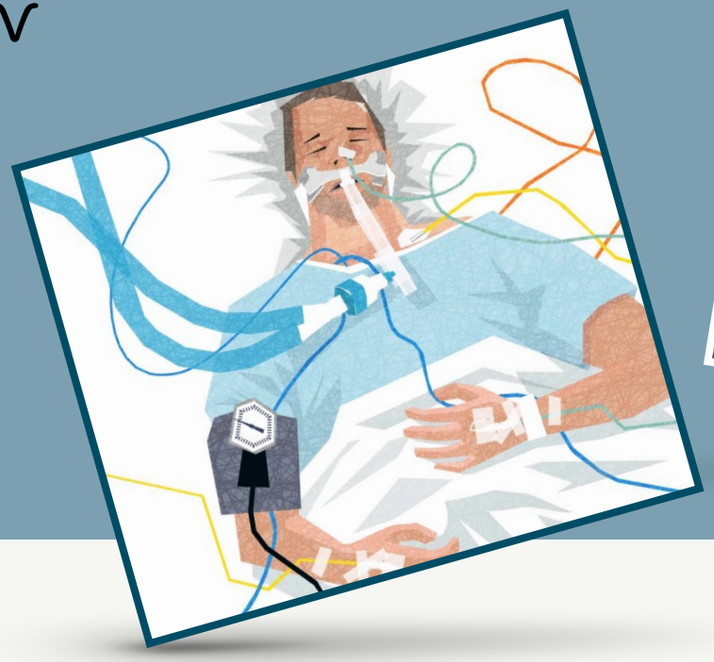


Η έγκαιρη διάγνωση και η άμεση θεραπευτική παρέμβαση είναι ζωτικής σημασίας για:

- Να ανακοπεί η ταχεία εξέλιξη της πορείας των νοσημάτων αυτών
- Να αποφευχθεί η μη αναστρέψιμη νεφρική βλάβη
- Να υπάρξει ιδανικά η πλήρης αναστροφή της συχνά βαριάς κλινικοεργαστηριακής εικόνας των ασθενών



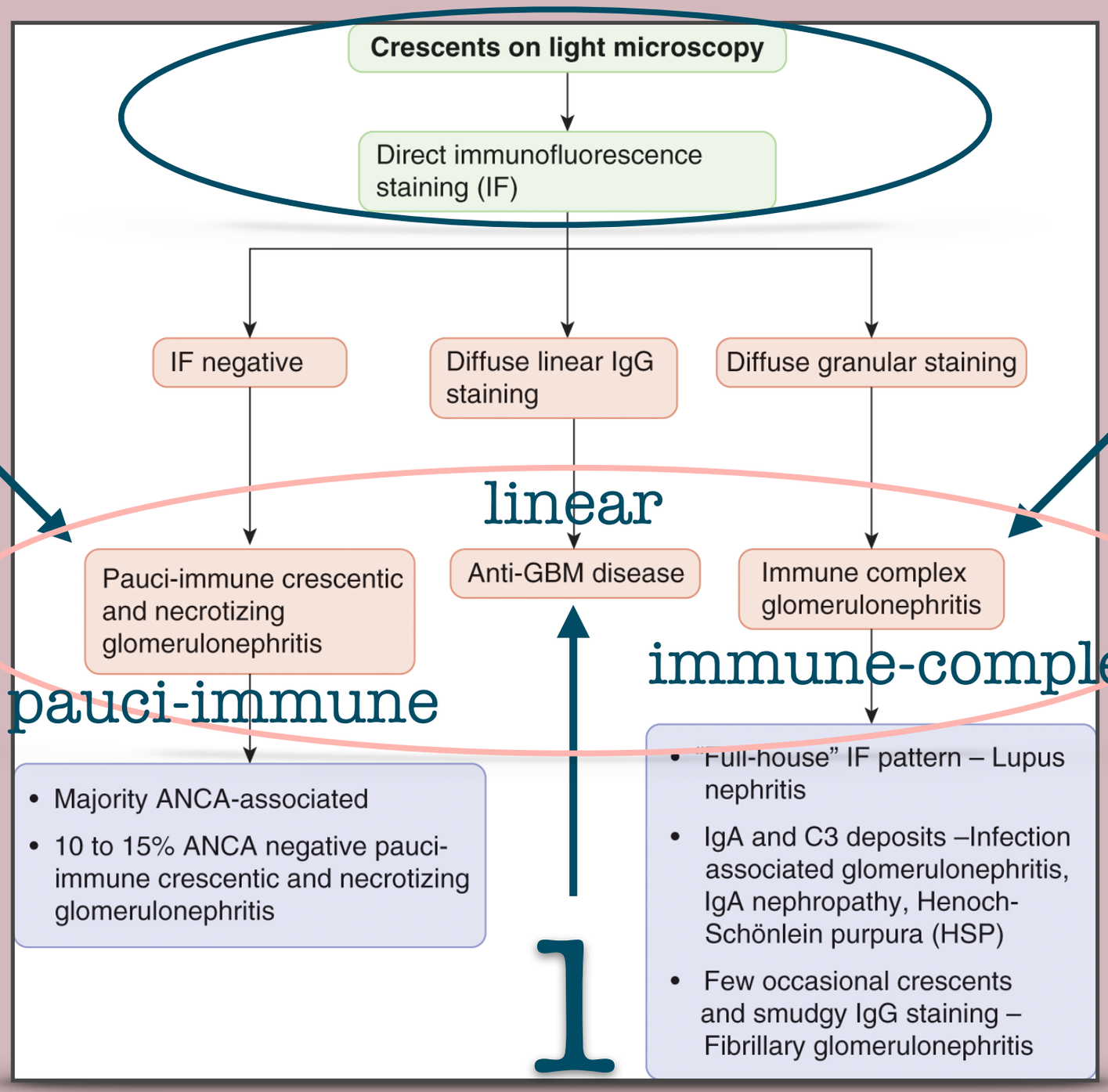




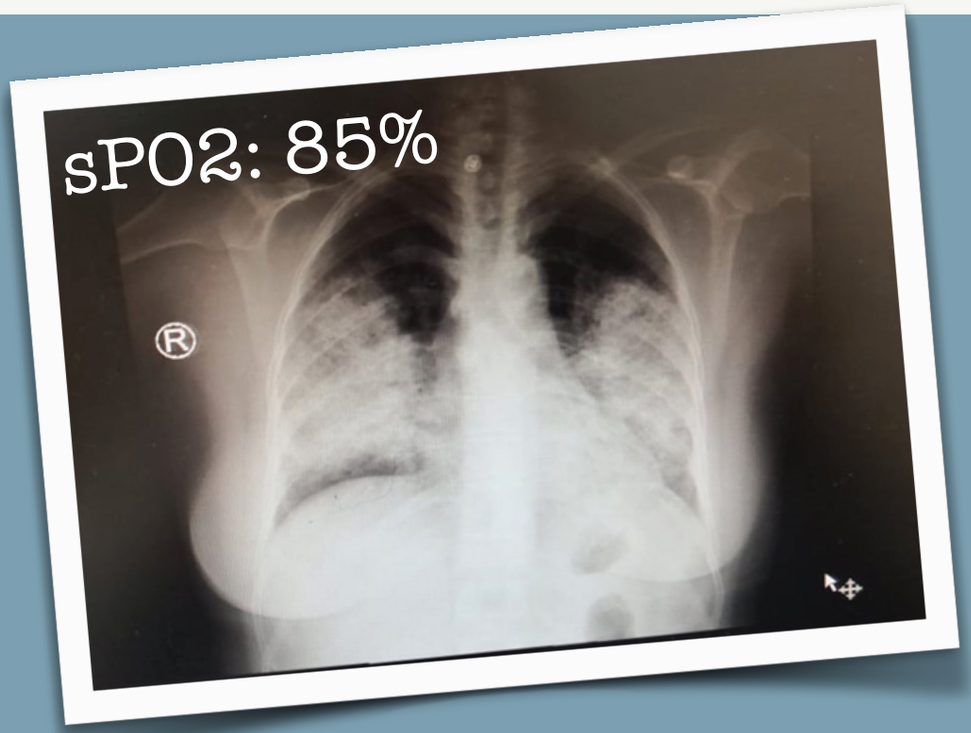
- Κλινικά συμπτώματα και σημεία…
  - Εκτενής εργαστηριακός έλεγχος…
    - Ιστολογική επιβεβαίωση με νεφρική βιοψία…

Όλοι όμως ξέρουμε καλά, ότι τέτοιου είδους διαγνώσεις συνήθως αργούν, συχνά αργούν πάρα πολύ…

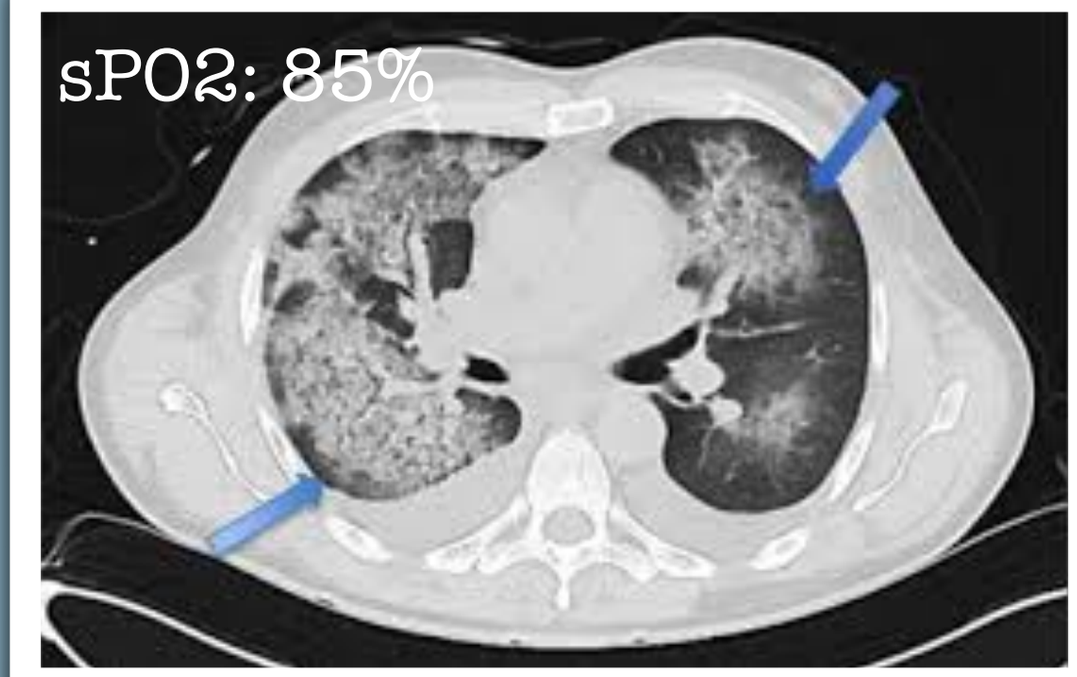
Ποια είναι τα νοσήματα που ανήκουν στο φάσμα της ΤΕΣΝ;



Ένας δικός μας ασθενής...



- Κρεατινίνη ορού: 4.5 mg/dl
- Ουρία ορού: 140 mg/dl
- Ht/Hb: 29%/10 gr/dl
- Γενική ούρων: λεύκωμα 100 mg/dl, αιμοσφαιρίνη +++, ερυθρά 30-50 κοπ
- ΤΚΕ: 120
- CRP: 15



Εύλογες ερωτήσεις...

1. Είναι ΤΕΣΝ;

2. Βρισκόμαστε μπροστά σε ένα **πνευμονονεφρικό σύνδρομο,** όπου όμως μας λείπει η εικόνα ενός αιμορραγικού εξανθήματος στα κάτω άκρα ή μας λείπουν οι έκδηλες αιμοπτύσεις;

3. Μήπως η εντυπωσιακή εικόνα από τον πνεύμονα είναι **λοίμωξη ή υπερφόρτωση με υγρά** λόγω μιας ΧΝΝ που δικαιολογεί και την αναιμία και αν ναι πώς θα δώσουμε εμείς ανοσοκαταστολή;

4. Θα **βρογχοσκοπηθεί** ο ασθενής για να παρθεί BAL;

5. Θα ξεκινήσουμε με **ώσεις κορτικοστεροειδών** ή **θα περιμένουμε** να προηγηθεί η διενέργεια **βιοψίας,** μήπως η κορτιζόνη μας αλλάξει την ιστολογική εικόνα;

6. Θα γίνει άμεσα νεφρική βιοψία;

Πιθανές απαντήσεις…

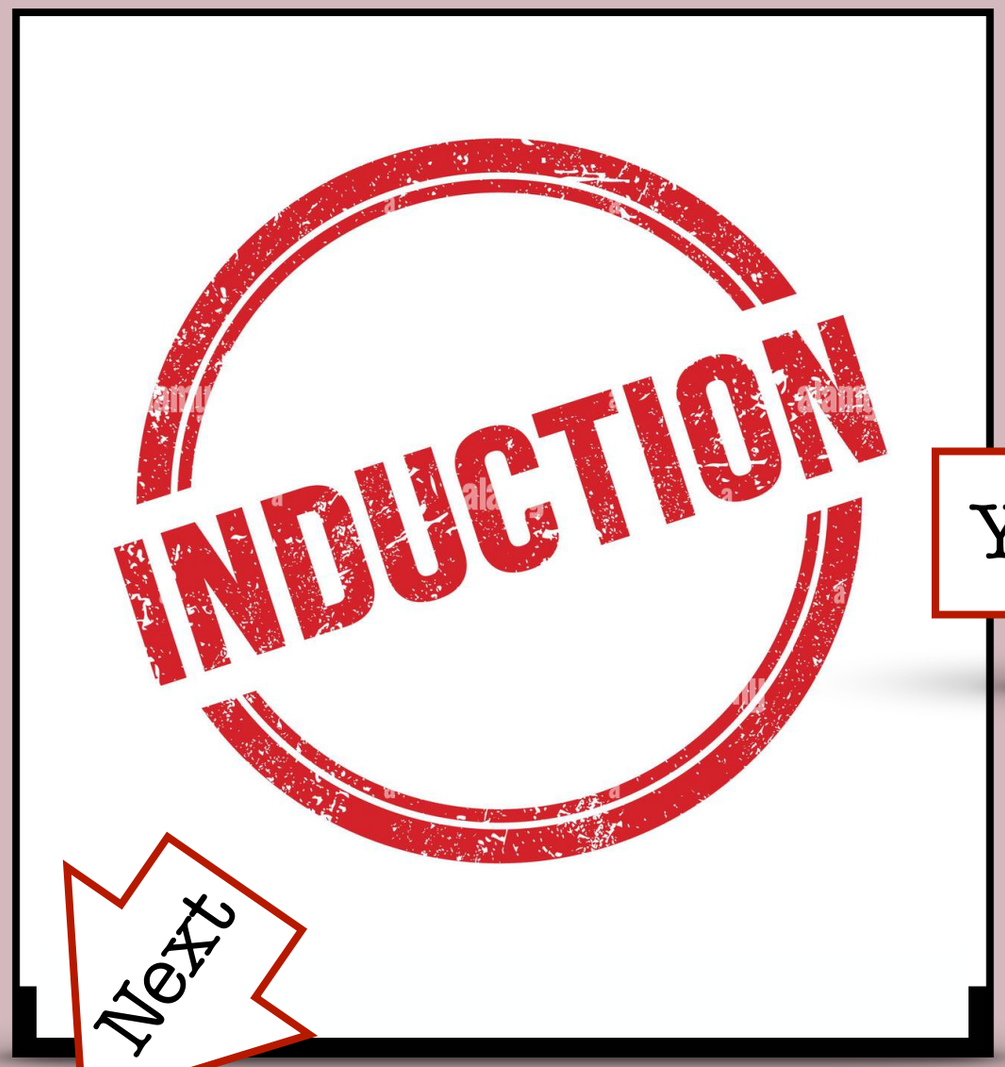
Ναι, ο ασθενής μας **είναι σε θέση** να υποβληθεί σε νεφρική βιοψία και ό,τι άλλο χρειαστεί …

Όχι, ο ασθενής μας **δεν είναι σε θέση** να υποβληθεί σε όλες τις παραπάνω δοκιμασίες, ούτε όμως και να περιμένει…

- Βρισκόμαστε μπροστά σε μια επείγουσα κατάσταση
- Όποια κι αν είναι η διάγνωση, θα δώσουμε τη βασική θεραπεία

Θεραπεία επαγωγής/εφόδου

Induction Therapy



Yes

Ύφεση

Remission

Next

Θεραπεία συντήρησης

Maintenance therapy

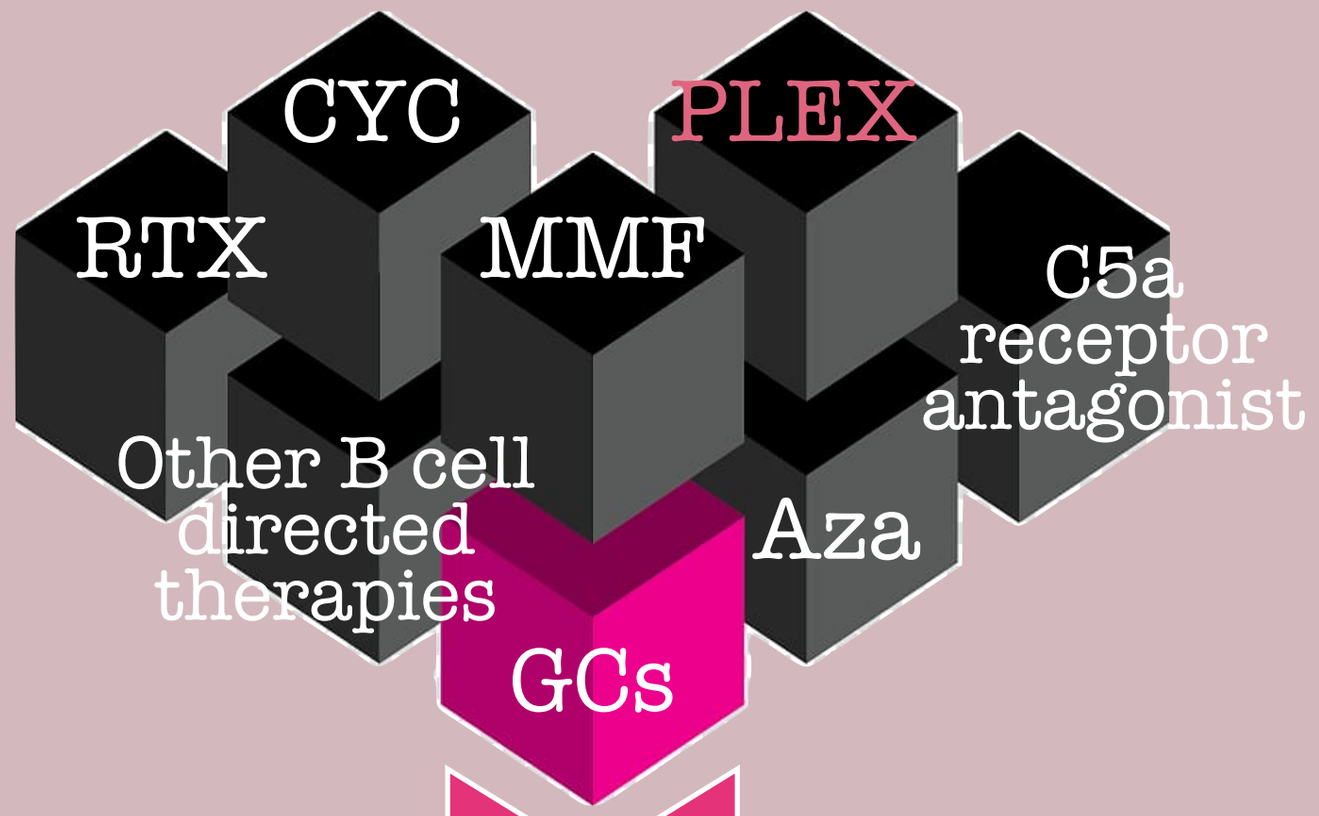
No

Υποτροπές

Relapses

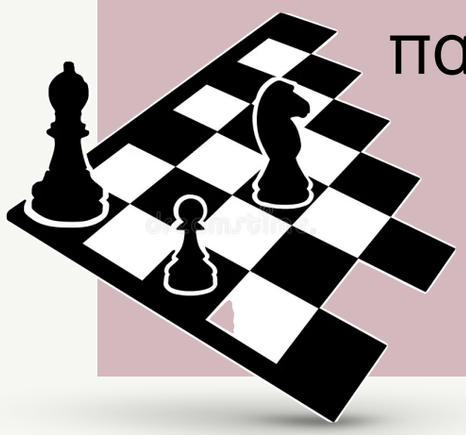
Induction

Τι επιλογές έχουμε σήμερα, πώς θα τις χρησιμοποιήσουμε;



Γνωστό προφίλ παρενεργειών

Προσπάθειες για steroid sparing θεραπείες

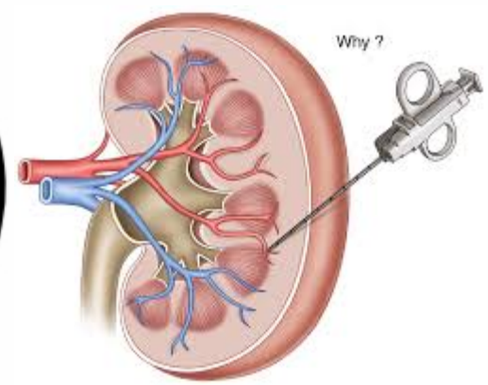


Κορτικοστεροειδή;

Maintenance

Θα προχωρήσουμε σε διενέργεια νεφρικής βιοψίας;

Εικόνα ΤΕΣΝ...



KDIGO 2024 Clinical Practice Guideline for the Management of Antineutrophil Cytoplasmic Antibody (ANCA)–Associated Vasculitis

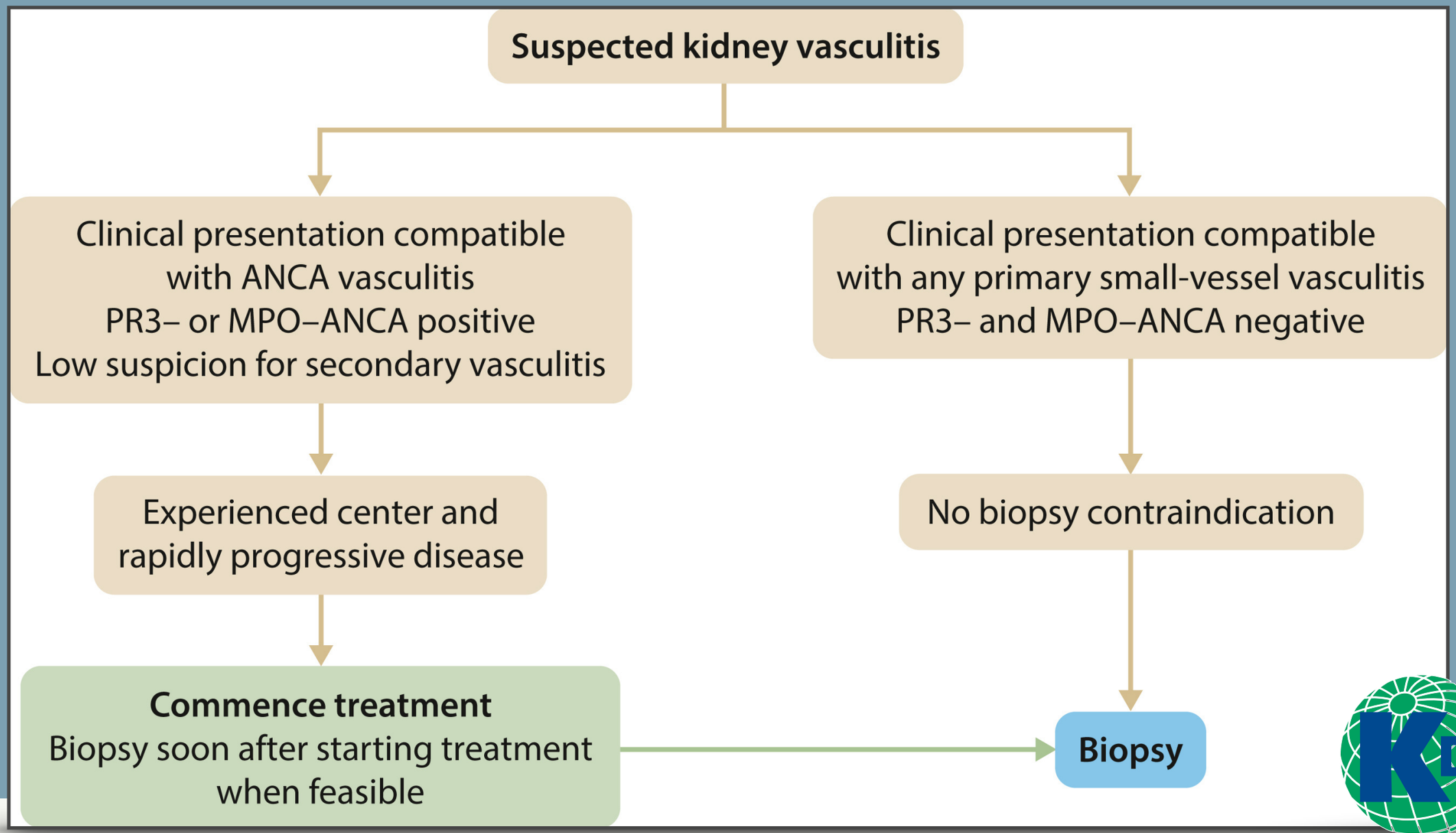
In the case of a clinical presentation compatible with small-vessel vasculitis in combination with positive myeloperoxidase (MPO)- or proteinase 3 (PR3)-ANCA serology, **waiting for a kidney biopsy to be performed or reported should not delay starting immunosuppressive therapy,** especially in patients who are rapidly deteriorating

⇩

An immediate biopsy **may not be necessary**...

KDIGO 2024 Clinical Practice Guideline for the Management of Antineutrophil Cytoplasmic Antibody (ANCA)–Associated Vasculitis

Treat or biopsy first?

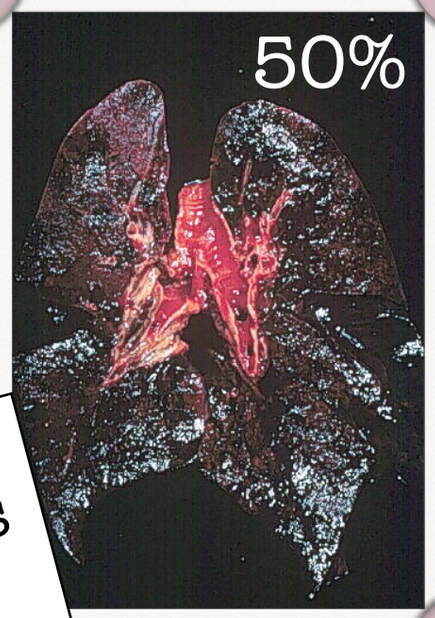


KDIGO 2021 Anti-GBM disease/Goodpasture syndrome

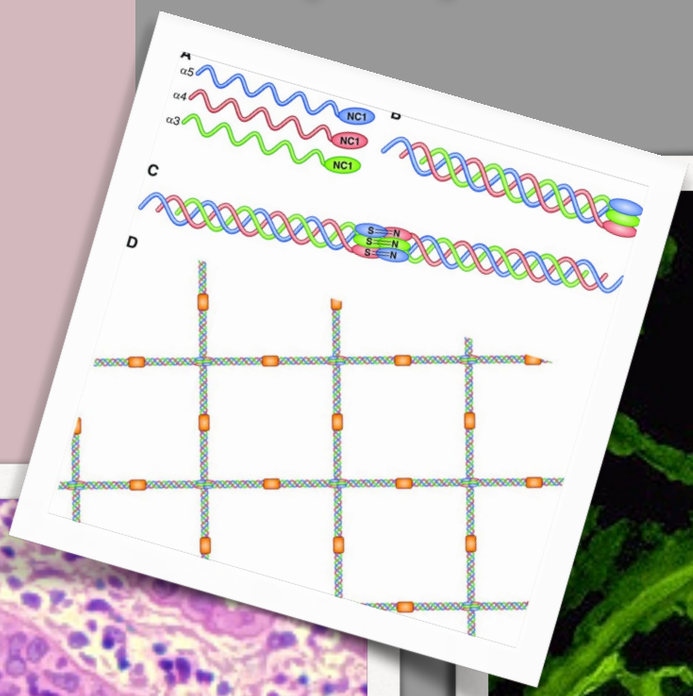
Diagnosis of anti-glomerular basement membrane (GBM) disease **should be made without delay** in all patients with suspected RPGN and treatment for anti-GBM disease **should start without delay if this diagnosis is suspected, even before the diagnosis is confirmed**

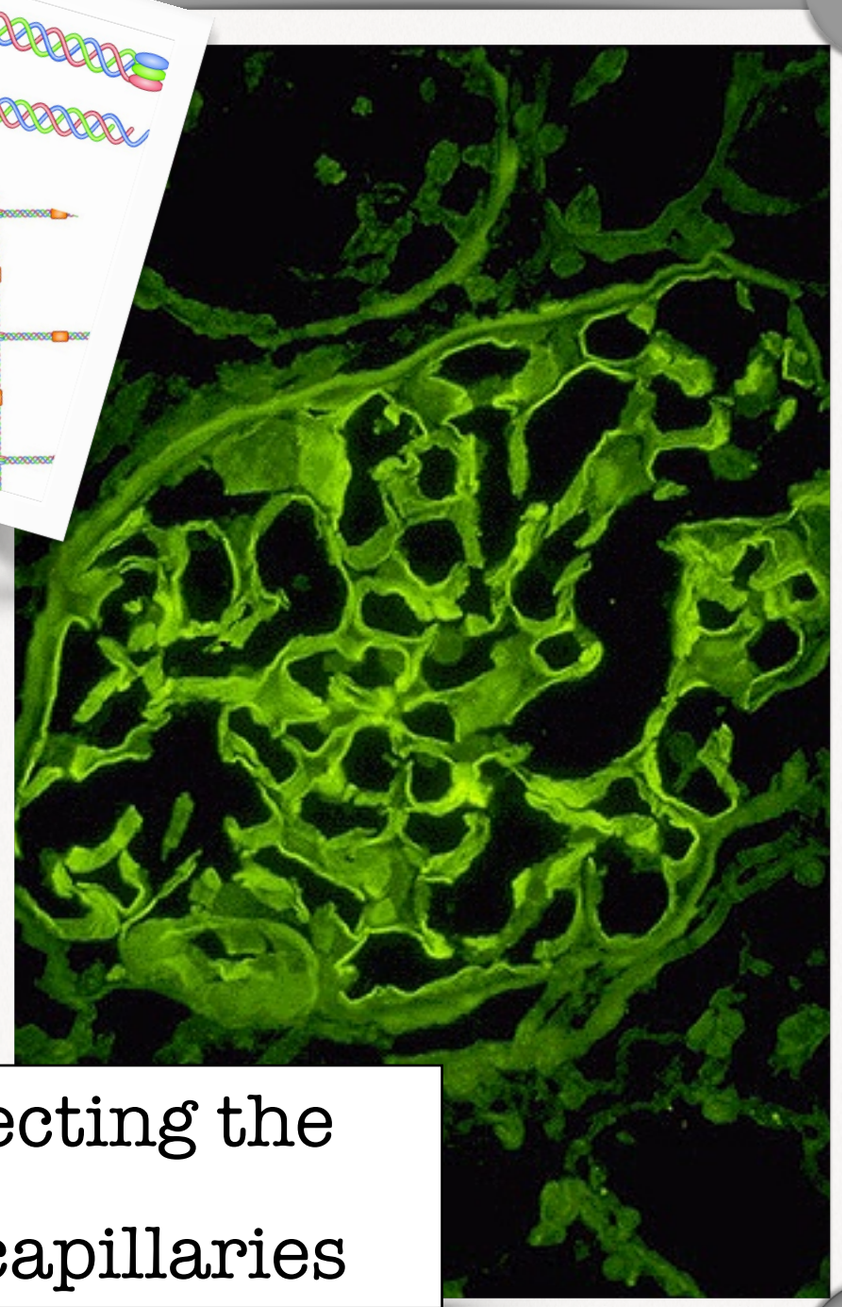
Anti-GBM νεφρίτιδα
Σύνδρομο Goodpasture

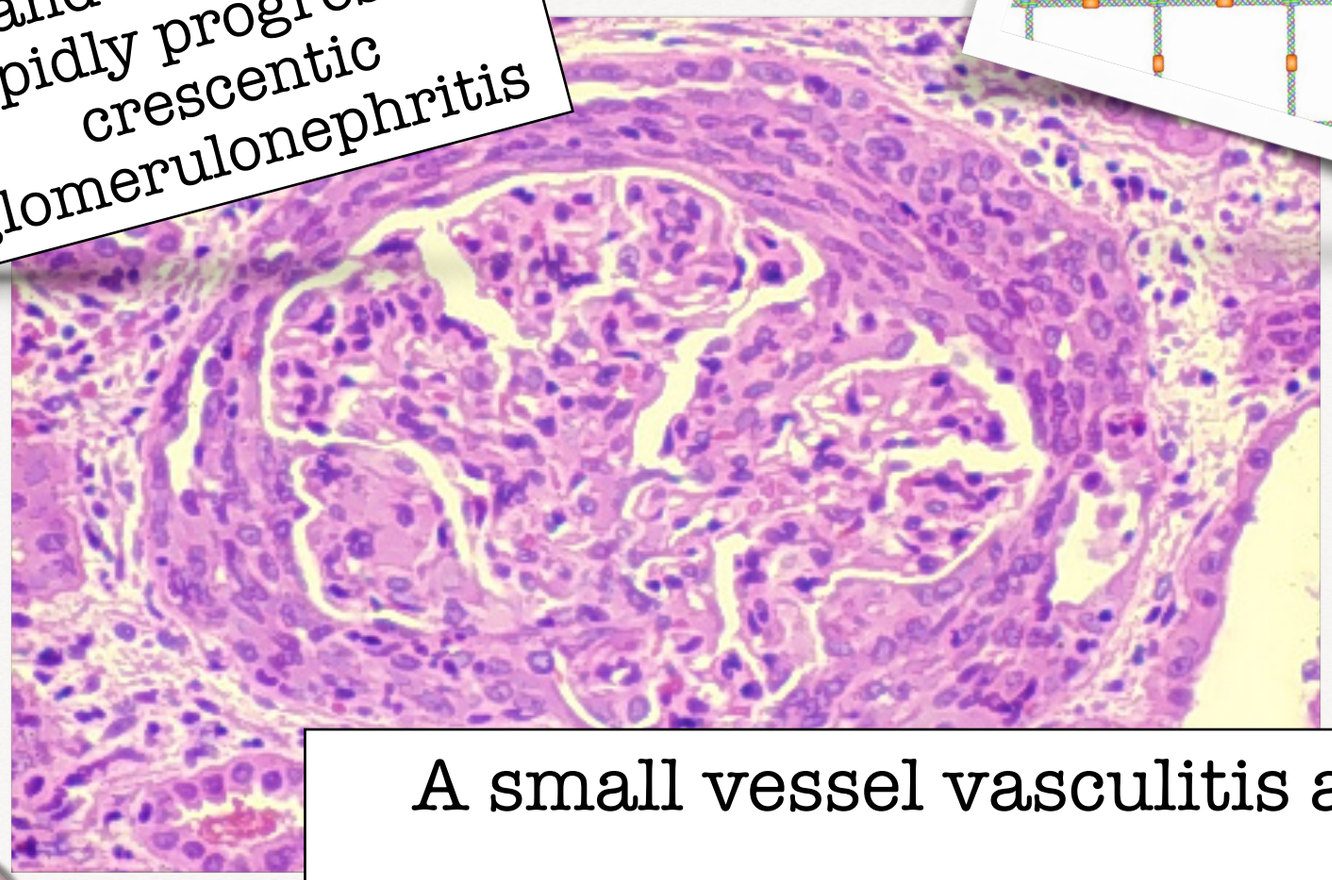
1



1-2% of acute glomerulonephritis and 10-15% of rapidly progressive crescentic glomerulonephritis







A small vessel vasculitis affecting the glomerular and pulmonary capillaries

Anti-GBM νεφρίτιδα
Σύνδρομο Goodpasture

Ο ακρογωνιαίος λίθος της θεραπείας είναι η ταχεία **απομάκρυνση** των παθογόνων αυτοαντισωμάτων και η **καταστολή** της παραγωγής τους για την πρόληψη περαιτέρω νεφρικής και πνευμονικής βλάβης

+

Μείωση της φλεγμονής

KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Disease

Anti-GBM νεφρίτιδα
Σύνδρομο Goodpasture

We **recommend** initiating immunosuppression with cyclophosphamide and glucocorticoids plus plasmapheresis **in all patients** with anti-GBM GN except those who are treated with dialysis at presentation, have 100% crescents or >50% global glomerulosclerosis in an adequate biopsy sample, and do not have pulmonary hemorrhage (1C)

KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Disease

"Rapid and accurate diagnosis is essential to guide appropriate therapy in anti-GBM disease..."

Όπου υπάρχει υψηλή κλινική υποψία και σοβαρές ενδείξεις νόσου, απειλητικής για ζωτικά όργανα ή και για την ίδια τη ζωή των ασθενών, **μπορεί και πρέπει** να ξεκινήσει **εμπειρική** θεραπεία όπως χορήγηση γλυκοκορτικοειδών ή/και πλασμαφαίρεσης εν αναμονή των οριστικών διαγνωστικών εξετάσεων

McAdoo SP and Pusey CD, Nephrol Dial Transplant 2026

IMMEDIATELY

We **recommend** initiating immunosuppression plus plasmapheresis...

♟Έκδηλη ενδοκυψελιδική αιμορραγία ανεξάρτητα της νεφρικής λειτουργίας

♟ΤΕΣΝ χωρίς άμεση διενέργεια αιμοκάθαρσης

♟ΤΕΣΝ που χρήζει αιμοκάθαρσης <u>αν ισχύουν τα παρακάτω</u>: *δεν είναι ολιγουρική, *από τη βιοψία δεν έχει καθολικές μήνες, έχει <50% σπειραματοσκλήρυνση ή έχει ευρήματα οξείας σωληναριακής νέκρωσης, *έχει διπλή θετικότητα (anti GBM και ANCA) και *η αιμοκάθαρση διενεργείται <72 ώρες

McAdoo SP and Pusey CD, Nephrol Dial Transplant 2026

Age related macular degeneration, dry	Rheopheresis	High-risk	II	2B
Amyloidosis, systemic	ß2-microglobulin column	Dialysis-related amyloidosis	II	2B
	TPE	Other causes	IV	2C
Anti-glomerular basement membrane disease (Goodpasture syndrome)	TPE	Diffuse alveolar hemorrhage (DAH)	I	1C
	TPE	Dialysis- independence	I	1B
	TPE	Dialysis-dependence, no DAH	III	2B
Atopic (neuro-) dermatitis (atopic eczema), recalcitrant	ECP		III	2A
	IA		III	2C
	TPE/DFPP		III	2C
Autoimmune hemolytic anemia, severe	TPE	Severe cold agglutinin disease	II	2C
	TPE	Severe warm autoimmune	III	2C
Babesiosis	RBC exchange	Severe	II	2C
Burn shock resuscitation	TPE		III	2B
Cardiac neonatal lupus	TPE		III	2C
Catastrophic antiphospholipid syndrome (CAPS)	TPE		I	2C

first-line therapy

American Society for Apheresis Grade I-III(1C-2B)

Age related macular degeneration, dry	Rheopheresis	High-risk	II	2B
Amyloidosis, systemic	ß2-microglobulin column	Dialysis-related amyloidosis	II	2B
	TPE	Other causes	IV	2C
Anti-glomerular basement membrane d syndrome)	TPE	Diffuse alveolar	I	1C
				1B
				2B
Atopic (neuro (atopic ecze				2A
				2C
				2C
Autoimmune severe				2C
				2C
Babesiosis	RBC exchange	Severe	II	2C
Burn shock resuscitation	TPE		III	2B
Cardiac neonatal lupus	TPE		III	2C
Catastrophic antiphospholipid syndrome (CAPS)	TPE		I	2C

RESEARCH ARTICLE · Volume 307, Issue 7962, P711-715

1976

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IMMUNOSUPPRESSION AND PLASMA-EXCHANGE IN THE TREATMENT OF GOODPASTURE'S SYNDROME

C.M Lockwood [a] · T.A Pearson [a] · A.J Rees [a] · D.J Evans [a] · D.K Peters [a] · C.B Wilson [b]

Affiliations & Notes · Article Info

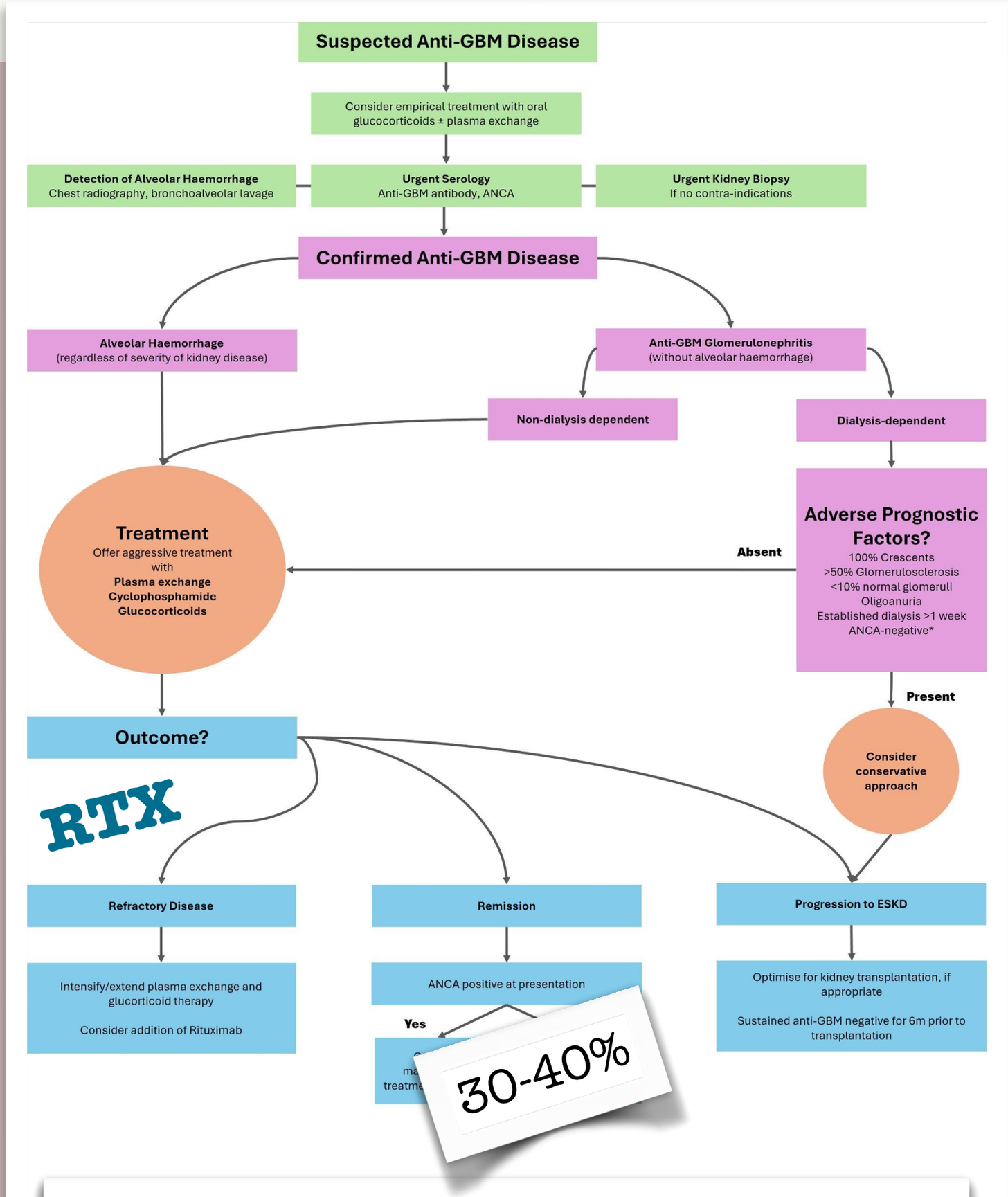
Μελέτες αναδρομικές, παρατήρησης παρά RCTs

KDIGO 2021 guidelines

Intervention	Dosing	Duration of treatment
Plasma exchange * Immuno adsorption	• 40–50 ml/kg ideal body weight exchange daily against 5% albumin • Add fresh frozen plasma at the end of plasma exchange in patients with alveolar hemorrhage and/or after kidney biopsy	Until circulating anti-GBM antibodies can no longer be detected; usually 14 days
Cyclophosphamide	• 2–3 mg/kg orally (reduce to 2 mg/kg in patients >55 years); experience with pulse intravenous cyclophosphamide is limited and efficacy is uncertain • Cyclophosphamide dosing should be reduced (or treatment interrupted) in cases of leukopenia • In patients not tolerating (or not responding to) cyclophosphamide rituximab or mycophenolate mofetil may be tried but experience is limited and efficacy uncertain	3 months
Glucocorticoids	• Pulse methylprednisolone may be given initially up to 1000 mg/d on 3 consecutive days • Prednisone 1 mg/kg orally • Reduce to 20 mg/d by 6 weeks	6 months

The parent drug cyclophosphamide has low molecular weight (~261 Da) and is water soluble, meaning that it is theoretically dialysable or removable by PLEX or hemodialysis before its metabolism

Anti-GBM disease



Relapse occurs in < 3% of patients

McAdoo SP and Pusey CD, Nephrol Dial Transplant 2026

Goodpasture

Suspected Anti-GBM Disease

↓

Consider empirical treatment with oral glucocorticoids + plasma exchange

Soveri I et al, Kidney Int 2019

IdeS

Imlifidase

GOOD-IDES-02 study

STOP

Restart of PLEX

anti-GBM kE/ml

anti-GBM U/ml

250 200 150 100 50 0

3000 2500 2000 1500 1000 500 0

-20 -15 -10 -5 0 5 10 15 20 25 30

pat 1 ref 1 pat 2 pat 3 ref 2

Relapse occurs in < 3% of patients

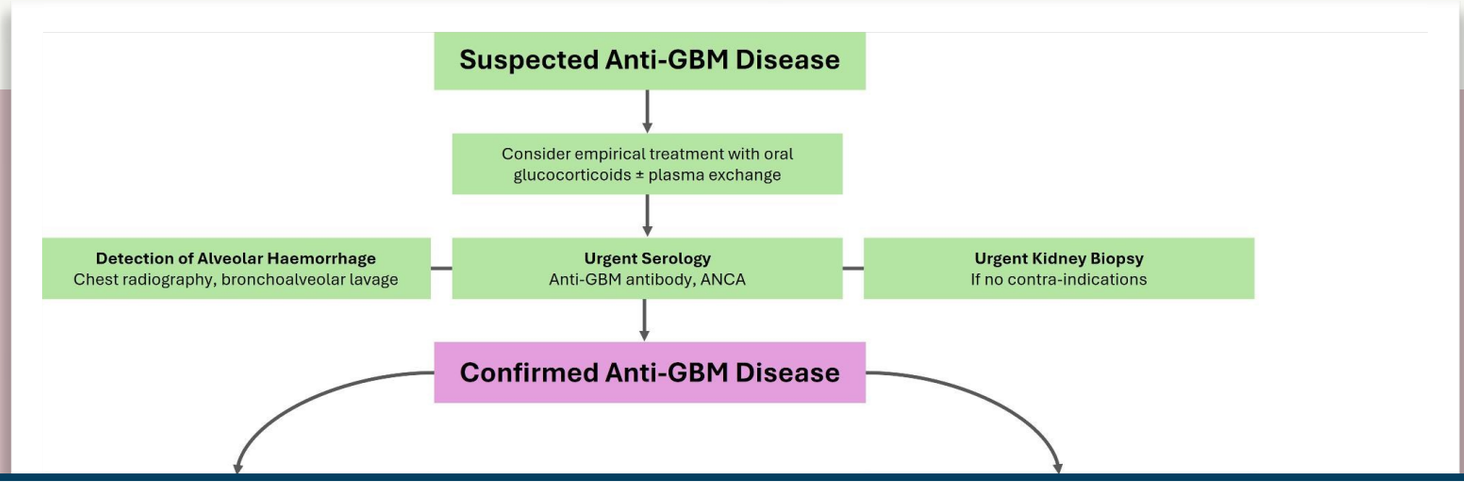


Table 1. Clinical characteristics and outcomes in case series of anti-GBM disease published after 2000

Reference	Country	Period	*n*	Age (years)	ANCA-positive (%)	Lung disease (%)	Patient survival[a] (%)	Renal survival[a] (%)
Levy *et al.* [15]	UK	1975–1999	81	40	Exclusion criterion	54	79	36
Li *et al.* [16]	China	1992–2003	10	59	20	40	80	20
Segelmark *et al.* [6]	Sweden	1987–1995	75	59	39	21	64	21
Cui *et al.* [14]	China	1997–2002	97	38	26	57	NA	15
Rutgers *et al.* [8]	Netherlands	1978–2003	24	57	46	NA	91	13
Kitagawa *et al.* [17]	Japan	1990–2005	16	61	25	25	88	31
Taylor *et al.* [10]	New Zealand	1998–2008	23	45	Exclusion criterion	39	89	48
Dammacco *et al.* [18]	Italy	2003–2012	10	49	33	60	80	60
Canney *et al.* [9]	Ireland	2003–2014	79	63	33	23	74	na
Alchi *et al.* [19]	UK	1991–2011	43	53	21	40	88	23
McAdoo *et al.* [13]	Czech Republic, UK, Sweden	2000–2013	78	61	47	38	86	42
van Daalen *et al.* [7]	Netherlands, UK, USA, New Zealand	1986–2015	123	51	40	35	NA	37

[a]Six-month or 1-year survival is given; some numbers not provided directly in the publications have been estimated through figures and diagrams.

RTX

30-40%

Relapse occurs in < 3% of patients

2

Anca-σχετιζόμενη αγγειίτιδα

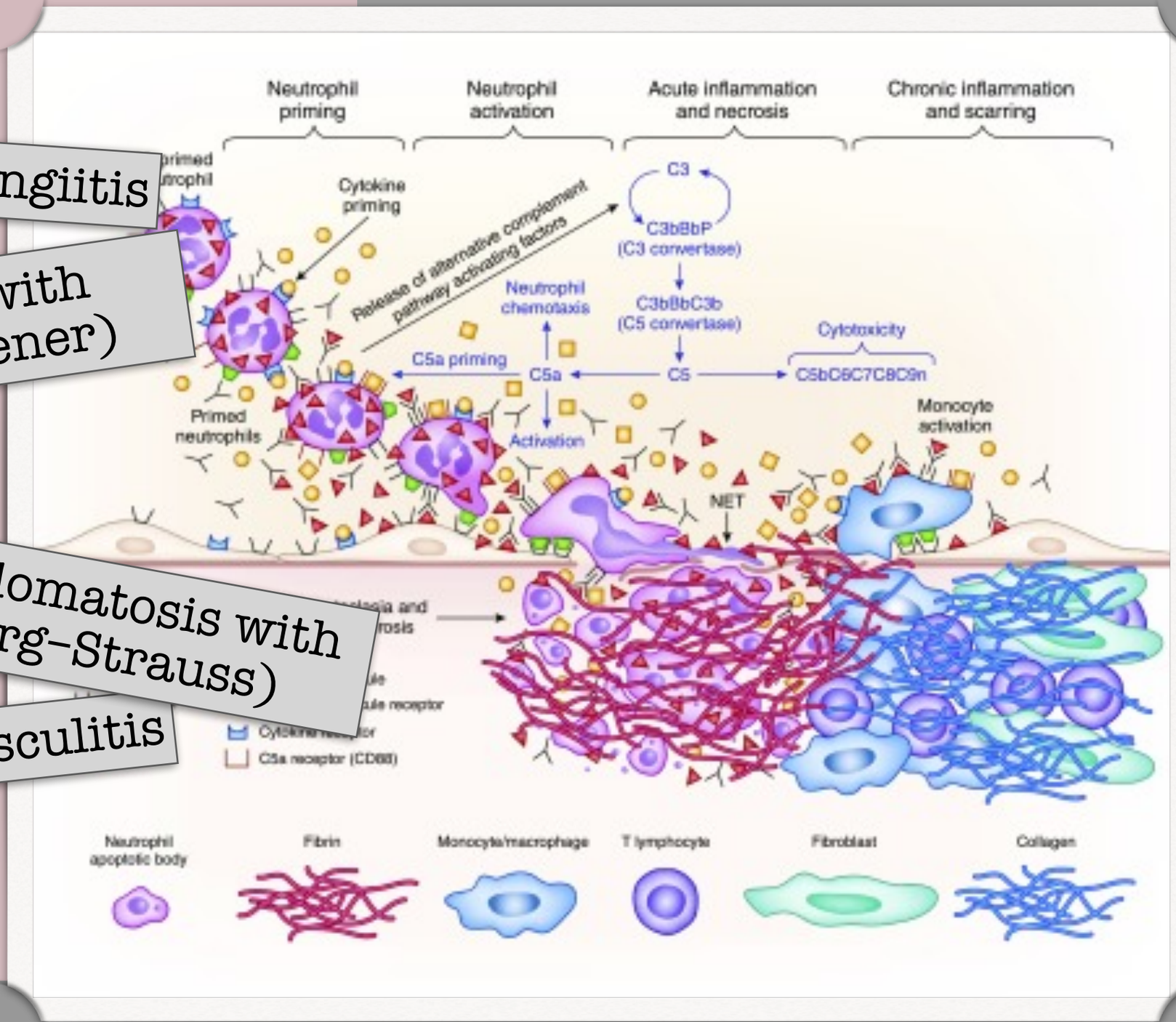
Pauci-immune necrotizing and crescentic

Microscopic polyangiitis

Granulomatosis with polyangiitis (Wegener)

Eosinophilic granulomatosis with polyangiitis (Churg–Strauss)

Renal-limited vasculitis

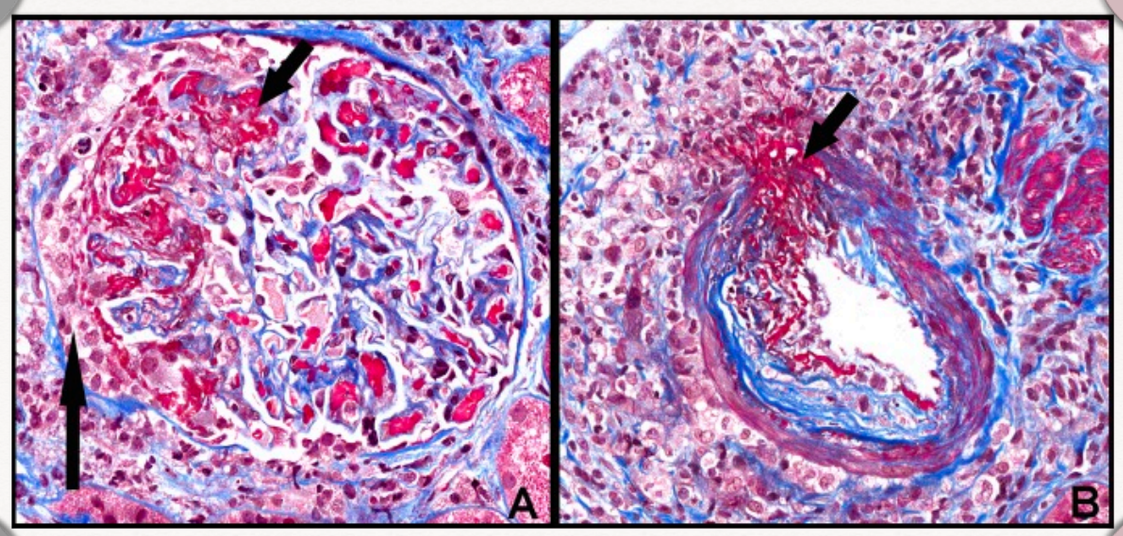


2

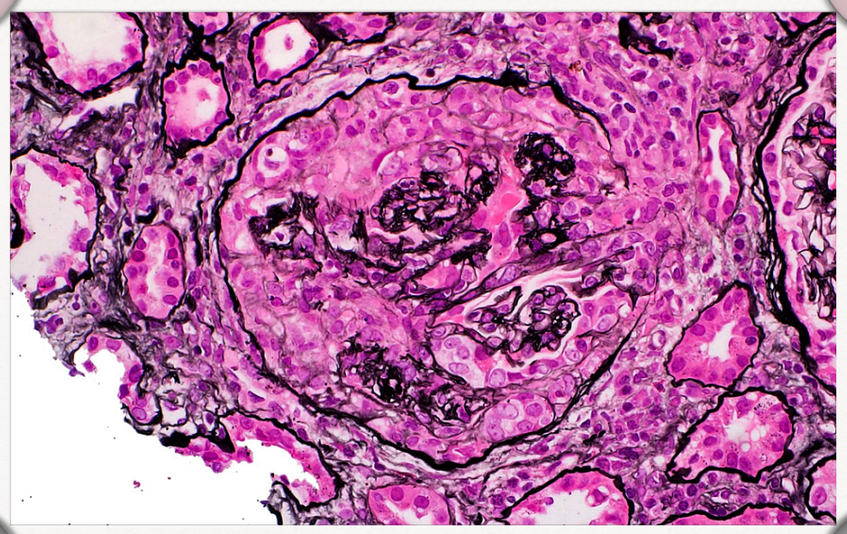
Anca-σχετιζόμενη αγγειίτιδα

Pauci-immune necrotizing and crescentic

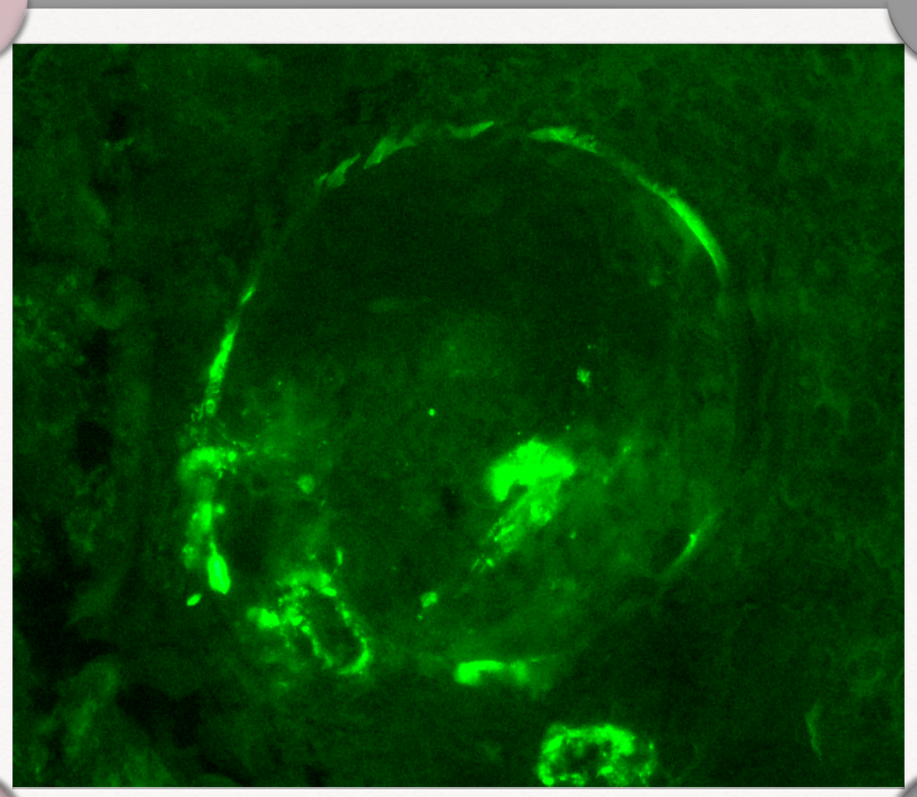
Necrotizing



Crescentic

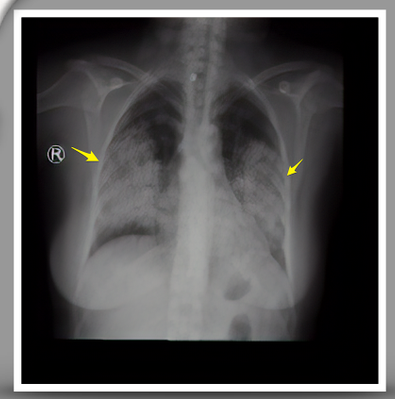


Pauci-immune



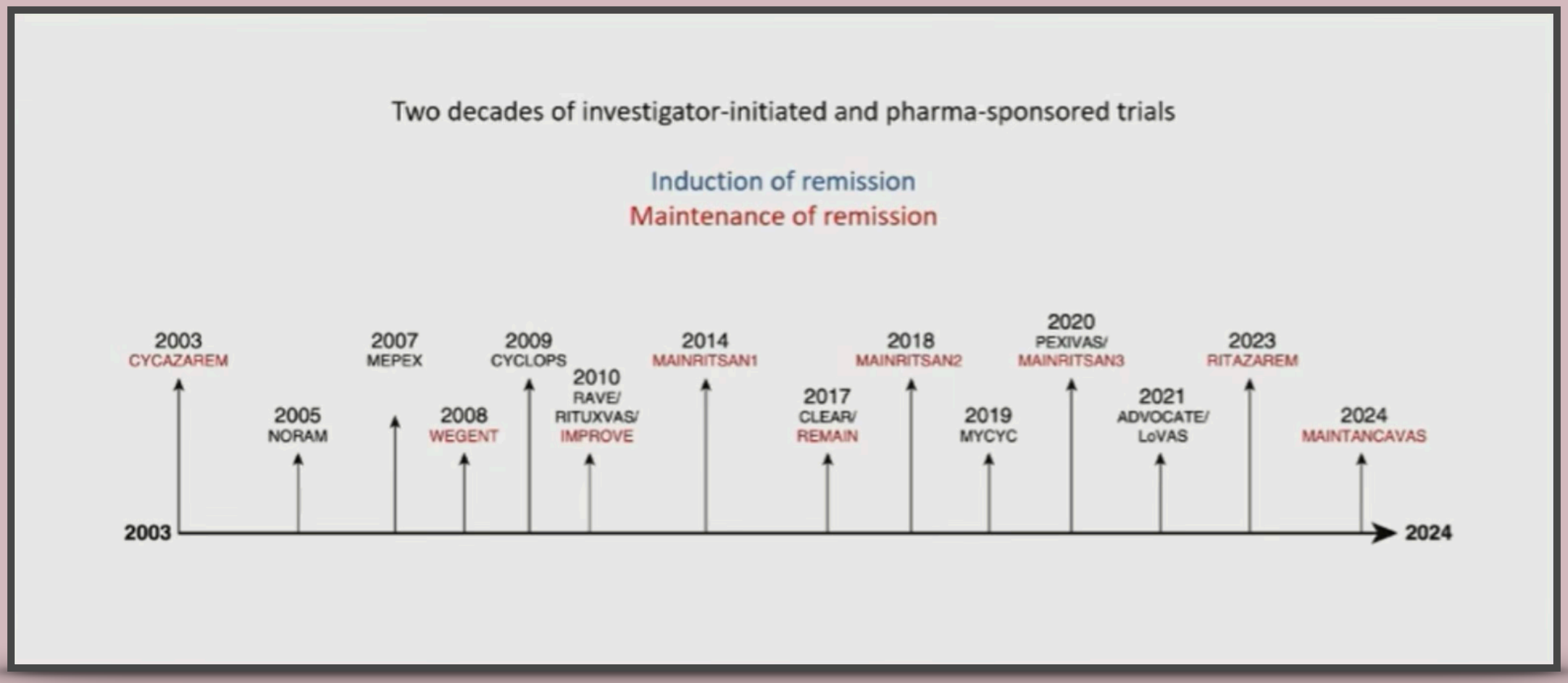
90% ANCA+

5% anti-GBM+



Pulmonary hemorrhage affects 10% of patients with AAV

Μεγάλες μελέτες επαγωγής και θεραπείας συντήρησης στις ANCA αγγειίτιδες



Kronbichler A et al, Brenner and Rector, 12th Edition Chapter 32

Kronbichler A, Glomcom 2026

Συγκριτικές κατευθυντήριες οδηγίες

Universitätsklinik für Innere Medizin IV
NEPHROLOGIE UND HYPERTENSIOLOGIE INNSBRUCK

Comparison Guidelines

MEDIZINISCHE UNIVERSITÄT INNSBRUCK

	EULAR 2022 [1]		KDIGO 2024 [2]		BSR 2025 [3]	
Severity	**Not organ-/life-threatening**	**Organ-/life-threatening**	**Not organ-/life-threatening**	**Organ-/life-threatening**	**Not organ-/life-threatening**	**Organ/life-threatening**
Induction of Remission	RTX > MTX/MMF	RTX or CYC	RTX or CYC	CYC > RTX	CYC, RTX or alternatives (MTX, MMF)	CYT, RTX or combination thereof
	PEXIVAS GC / consider avacopan		PEXIVAS GC / consider avacopan		LoVAS/PEXIVAS GC / consider avacopan	PEXIVAS GC / consider avacopan
Creatinine > 3.4 mg/dL (> 300 µmol/L)	Consider plasma exchange		Consider plasma exchange Consider a combination of RTX + CYC		Consider plasma exchange	
Prophylaxis	TMP/SMX and IVIG		TMP/SMX and IVIG		Not mentioned	
Maintenance of Remission	RTX > AZA/MTX		RTX > AZA + GC		RTX > AZA/MTX	

[1] European Alliance of Associations for Rheumatology, [2] Kidney Disease Improving Global Outcome, [3] British Society for Rheumatology Abbreviations: CYC (Cyclophosphamide), GC (Glucocorticoids), IVIG (Intravenous immunoglobulins), MMF (Mycophenolate mofetil), MTX (Methotrexate), RTX (Rituximab), TMP/SMX (Trimethoprim- Sulfamethoxazole).

Hellmich B, *et al*. Ann Rheum Dis 2024; **83**:30-47; Kidney Int 2024; **105**:447-449; Biddle K, *et al*. Rheumatology 2025; **64**:4470-4494.

Kronbichler A, Glomcom 2026

Πρωτοδιαγνωσθείσα ANCA αγγειίτιδα

9.3.1 Induction

Recommendation 9.3.1.1: We recommend that glucocorticoids in combination with rituximab or cyclophosphamide be used as initial treatment of new-onset AAV *(1B)*.

The best evidence is available for patients with new-onset AAV. In patients with severe kidney disease (SCr >4 mg/dl [>354 μmol/l]), limited data for induction therapy with rituximab are available.

RAVE study, NEJM 2010

RITUXIVAS study, NEJM 2010

CYCLOPS study, AnnRhDi 2009

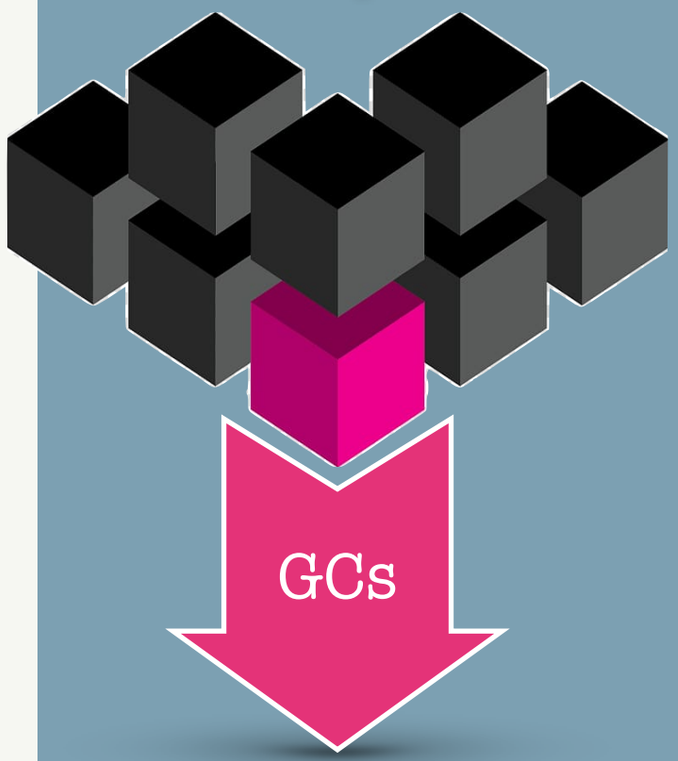
MYCYC study, AnnRhDi 2019

PEXIVAS study, NEJM 2020

LoVas study, JAMA 2021

ADVOCATE study, NEJM 2021

Πρωτοδιαγνωσθείσα ANCA αγγειίτιδα



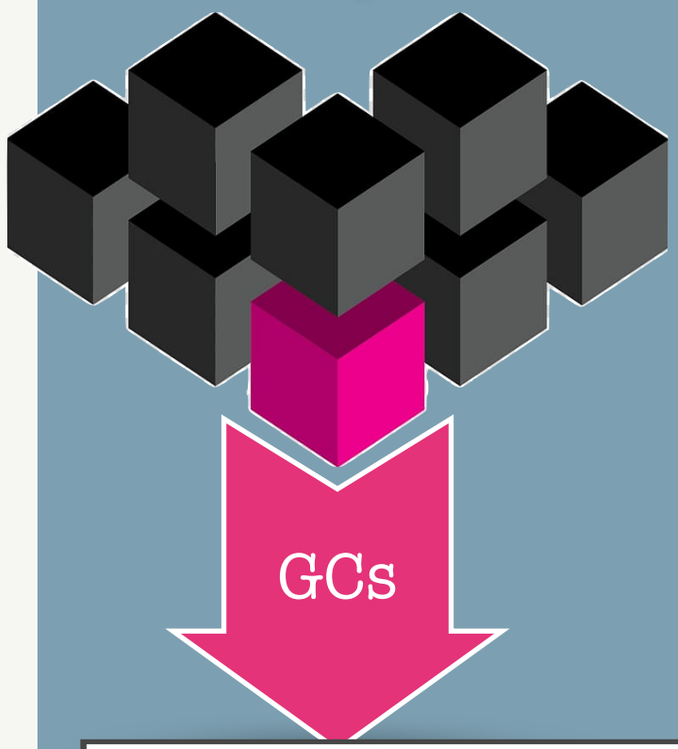
♟Τα από του στόματος γλυκοκορτικοειδή με ταχεία σταδιακή μείωση (tapering) φαίνεται ότι προτιμώνται έναντι του βραδύτερου tapering

♟Οι 2 μελέτες υποστηρίζουν ότι η χαμηλότερη δόση κορτικοστεροειδών (0.5 mg/kg/d) φαίνεται να μην υστερεί, συγκριτικά με τα παλιότερα σχήματα, μειώνοντας τις ανεπιθύμητες ενέργειες

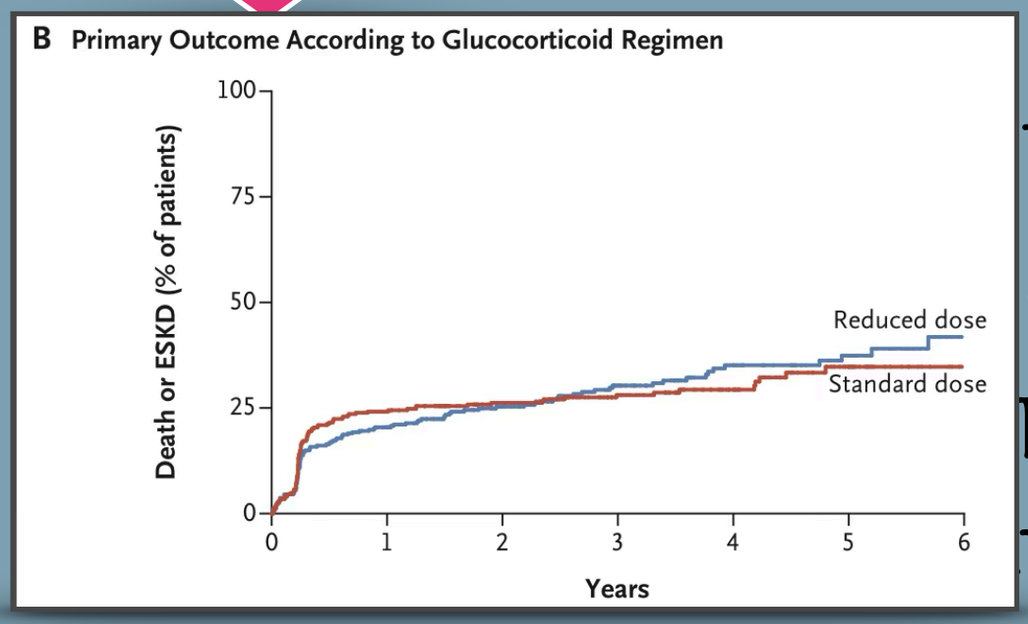
PEXIVAS study, NEJM 2020

LoVas study, JAMA 2021

Πρωτοδιαγνωσθείσα ANCA αγγειίτιδα



♟Τα από του στόματος γλυκοκορτικοειδή με ταχεία σταδιακή μείωση (tapering) φαίνεται ότι προτιμώνται έναντι του βραδύτερου tapering



ίζουν ότι η χαμηλότερη δόση 5 mg/kg/d) φαίνεται να μην με τα παλιότερα σχήματα, νεπιθύμητες ενέργειες

PEXIVAS study, NEJM 2020

LoVas study, JAMA 2021

Πρωτοδιαγνωσθείσα ANCA αγγειίτιδα

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 18, 2021 VOL. 384 NO. 7

Avacopan for the Treatment of ANCA-Associated Vasculitis

David R.W. Jayne, M.D., Peter A. Merkel, M.D., M.P.H., Thomas J. Schall, Ph.D., and Pirow Bekker, M.D, Ph.D.,
for the ADVOCATE Study Group*

Avacopan **was noninferior** but not superior to prednisone taper with respect to remission at week 26 and **was superior** to prednisone taper with respect to sustained remission at week 52

317 pts **CYC+RTX**

Πρωτοδιαγνωσθείσα ANCA αγγειίτιδα

Practice Point 9.3.1.9: Consider plasma exchange for patients with SCr >3.4 mg/dl (>300 μmol/l), patients requiring dialysis or with rapidly increasing SCr, and patients with diffuse alveolar hemorrhage who have hypoxemia.

Plasma exchange **increased the rate of renal recovery** in ANCA-associated systemic vasculitis that presented with renal failure when compared with intravenous methylprednisolone

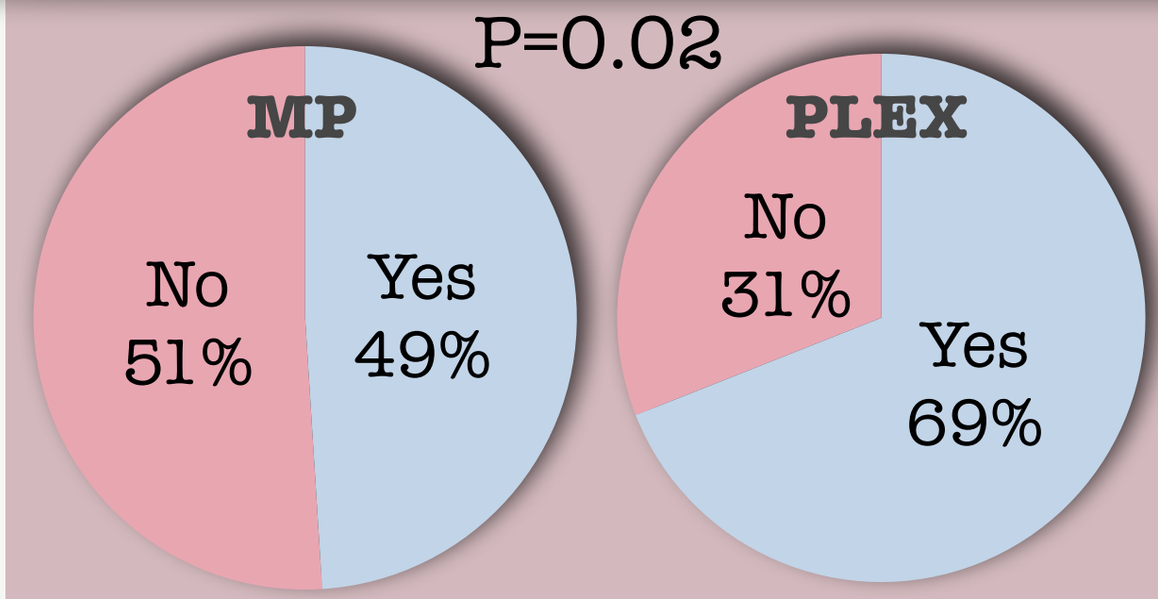
MEPEX study, JASN 2007

Among patients with severe ANCA-associated vasculitis, the use of plasma exchange **did not reduce the incidence of death or ESKD**

PEXIVAS study, NEJM 2020

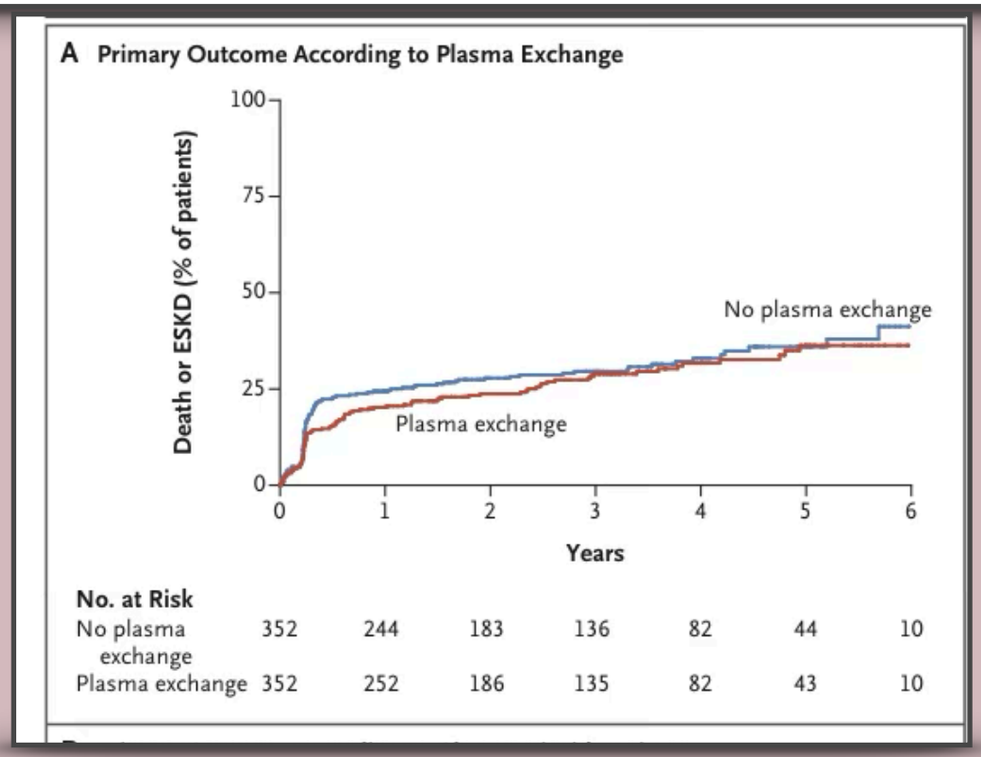
Πρωτοδιαγνωσθείσα ANCA αγγειίτιδα

Practice Point 9.3.1.9: Consider plasma exchange for patients with SCr >3.4 mg/dl (>300 μmol/l), patients requiring dialysis or with rapidly increasing SCr, and patients with diffuse alveolar hemorrhage who have hypoxemia.



Alive and Dialysis independent at 3 mo

MEPEX study, JASN 2007

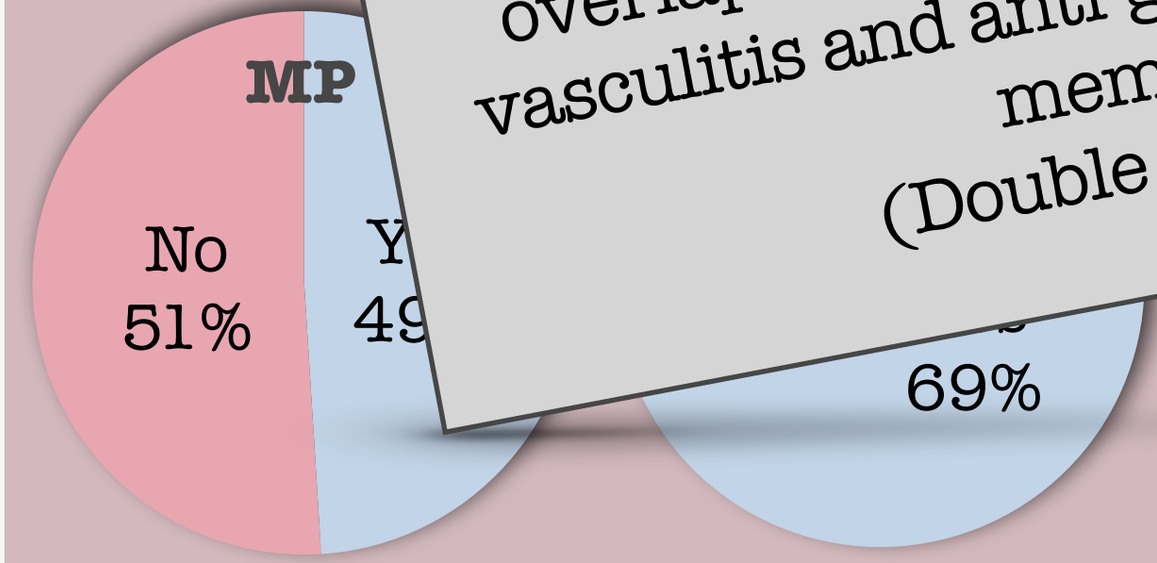


PEXIVAS study, NEJM 2020

Πρωτοδιαγνωσθείσα ANCA αγγειίτιδα

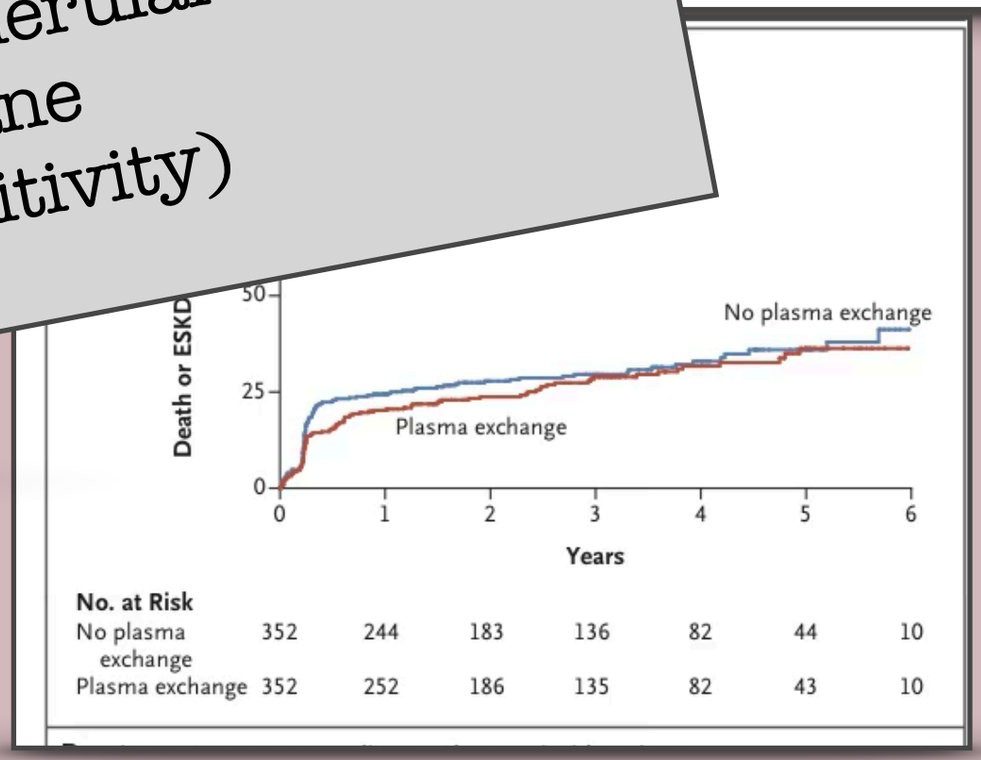
Practice Point 9.3.1.9: Consider plasma exchange for patients with SCr >3.4 mg/dl (>300 … requiring dialysis or with … ients with diffuse … .

Add plasma exchange for patients with an overlap syndrome of ANCA-associated vasculitis and anti-glomerular basement membrane (Double positivity)



Alive and Dialysis independent at 3 mo

MEPEX study, JASN 2007



PEXIVAS study, NEJM 2020

Πρωτοδιαγνωσθείσα ANCA αγγειίτιδα

Oral cyclophosphamide	Intravenous cyclophosphamide	Rituximab	Rituximab and i.v. cyclophosphamide	MMF	Avacopan
2 mg/kg/d for 3 months, continue for ongoing activity to a maximum of 6 months	15 mg/kg at weeks 0, 2, 4, 7, 10, 13 (16, 19, 21, 24 if required)	375 mg/m²/week × 4 weeks OR 1 g at weeks 0 and 2	Rituximab 375 mg/m²/week × 4 weeks, with i.v. cyclophosphamide 15 mg/kg at weeks 0 and 2 OR Rituximab 1 g at 0 and 2 weeks with i.v. cyclophosphamide 500 mg/2 weeks × 6	2000 mg/d (divided doses), may be increased to 3000 mg/d for poor treatment response	30 mg twice daily as alternative to glucocorticoids, in combination with rituximab or cyclophosphamide induction
Reduction for age: • 60 yr, 1.5 mg/kg/d • 70 yr, 1.0 mg/kg/d Reduce by 0.5 mg/kg/day for GFR <30 ml/min/1.73 m²	Reduction for age: • 60 yr 12.5 mg/kg • 70 yr, 10 mg/kg Reduce by 2.5 mg/kg for GFR <30 ml/min/1.73 m²				

Figure 10 | ...dosing for AAV. AAV, ANCA-associated vasculitis; ANCA, antineutrophil cytoplasmic antibody; GFR, ...s; MMF, mycophenolate mofetil.

Week	'Reduced-corticosteroid dose' in PEXIVAS trial		
	<50 kg	50–75 kg	>75 kg
1	50	60	75
2	25	30	40
3–4	20	25	30
5–6	15	20	25
7–8	12.5	15	20
9–10	10	12.5	15
11–12	7.5	10	12.5
13–14	6	7.5	10
15–16	5	5	7.5
17–18	5	5	7.5
19–20	5	5	5
21–22	5	5	5
23–52	5	5	5
>52	Investigators' local practice		

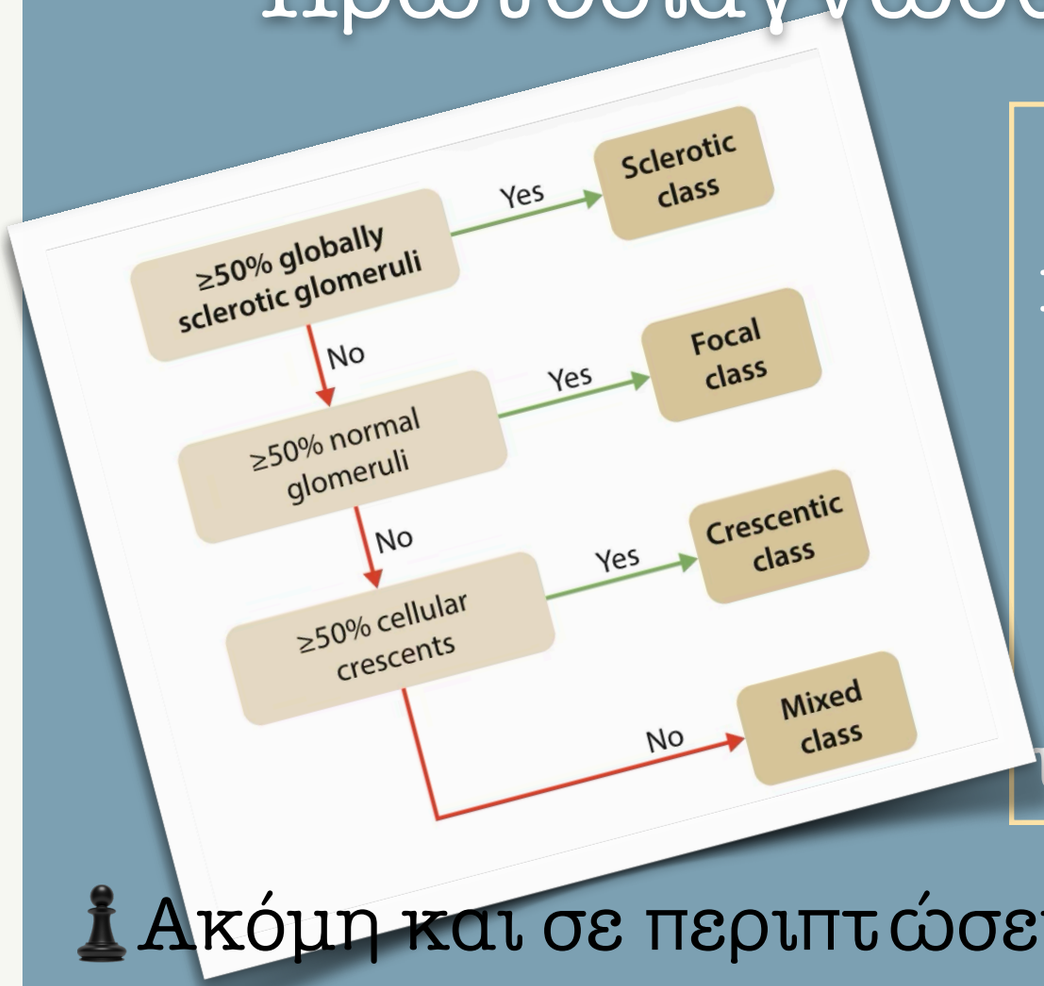
Figure 9 | Prednisolone tapering regimen for AAV. AAV, ANCA-associated vasculitis; ANCA, antineutrophil cytoplasmic antibody; PEXIVAS, Plasma Exchange and Glucocorticoids for the Treatment of ANCA-Associated Vasculitis.

ANCA vasculitis with severe kidney disease	Vasculitis with diffuse pulmonary hemorrhage	Vasculitis in association with anti-GBM antibodies
Seven treatments over a maximum of 14 days, 60 ml/kg volume replacement, albumin substitution	Daily until bleeding stops, replace albumin with fresh, frozen plasma	Daily for 14 days or until anti-GBM antibodies are undetectable

Figure 11 | Plasma exchange dosing and frequency for AAV. If a patient is at risk of bleeding, volume replacer... frozen plasma. AAV, ANCA-associated vasculitis; ANCA, antineutrophil cytoplasmic antibody; GBM, glomerular bas...

KDIGO

Πρωτοδιαγνωσθείσα ANCA αγγειίτιδα



Kidney recovery can be seen in the face of advanced kidney damage, and induction treatment should not be withheld on the basis of unfavorable histologic findings

♟Ακόμη και σε περιπτώσεις σοβαρής νεφρικής βλάβης, μπορεί να να παρατηρηθεί βελτίωση της νεφρικής λειτουργίας με την κατάλληλη αγωγή, και για αυτόν τον λόγο η θεραπεία επαγωγής **δε θα πρέπει να αναστέλλεται,** στη βάση δυσοίωνων ιστολογικών ευρημάτων

Όμως...

Practice Point 9.3.1.5: Consider discontinuation of immunosuppressive therapy after 3 months in patients who remain on dialysis and who do not have any extrarenal manifestations of disease.

- Ασθενείς που υποβάλλονται σε αιμοκάθαρση και δεν ανταποκρίνονται μετά από 3 μήνες επαγωγικής θεραπείας έχουν <5% πιθανότητα να απαλλαγούν από την αιμοκάθαρση

- Διακοπή ανοσοκαταστολής, εκτός αν έχουν προσβληθεί και άλλα σημαντικά όργανα

Η θέση της χημειοπροφύλαξης στη θεραπεία των ANCA αγγειιτίδων

EULAR 2022

As infections are the leading cause of death within the first year of induction therapy in patients with AAV,[206] infection prophylaxis with T/S (800/160 mg on alternate days or 400/80 mg daily) is recommended for all patients with AAV receiving CYC or RTX and patients where treatment with GCs at a dose of ≥30 mg/day for 4 weeks or longer is envisioned, irrespective of other concomitant immunosuppressants.

BSR 2025

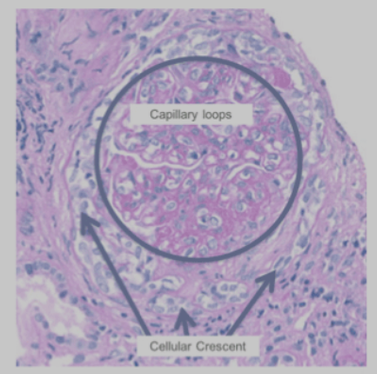
Co-trimoxazole is not recommended alone to prevent disease relapse but may be useful for infection-associated sinonasal disease activity. This treatment regimen is distinct from prophylactic co-trimoxazole for prevention of Pneumocystis jirovecii pneumonia (PJP) and other infections

Induction **Maintenance**

3 Ανοσοσυμπλεγματική ΤΕΣΝ

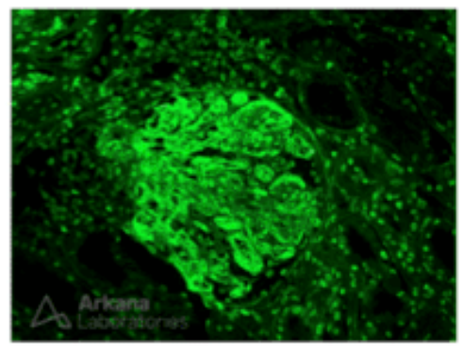
Rapidly Progressive Glomerulonephritis (RPGN)

- Loss of kidney function over a **short period of time**
- Urinalysis with evidence of glomerular disease (hematuria, proteinuria)
- Crescent formation (extra-capillary proliferation in Bowman's space)



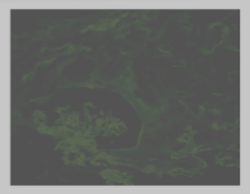
Immune-Complex Mediated

- **Presence of immune deposits in glomeruli**
  - Ex: IgA nephropathy, lupus nephritis, cryoglobulinemia, post-infectious GN



Pauci-Immune

- Minimal immune deposits, negative IF
- **Majority anti-neutrophil cytoplasmic antibody (ANCA) +**
  - **c-ANCA**: anti-proteinase 3 (CPR) → cytoplasmic neutrophilic staining
  - **p-ANCA**: anti-myeloperioxidase (MPO) → perinuclear cytoplasmic staining



NephSim
www.nephsim.com

3 Ανοσοσυμπλεγματική ΤΕΣΝ

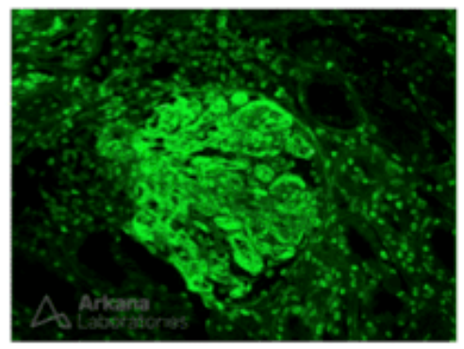
IgA/HSP

Lupus nephritis (vasculitis)

Membranoproliferative GN

Immune-Complex Mediated

- **Presence of immune deposits in glomeruli**
  - Ex: IgA nephropathy, lupus nephritis, cryoglobulinemia, post-infectious GN



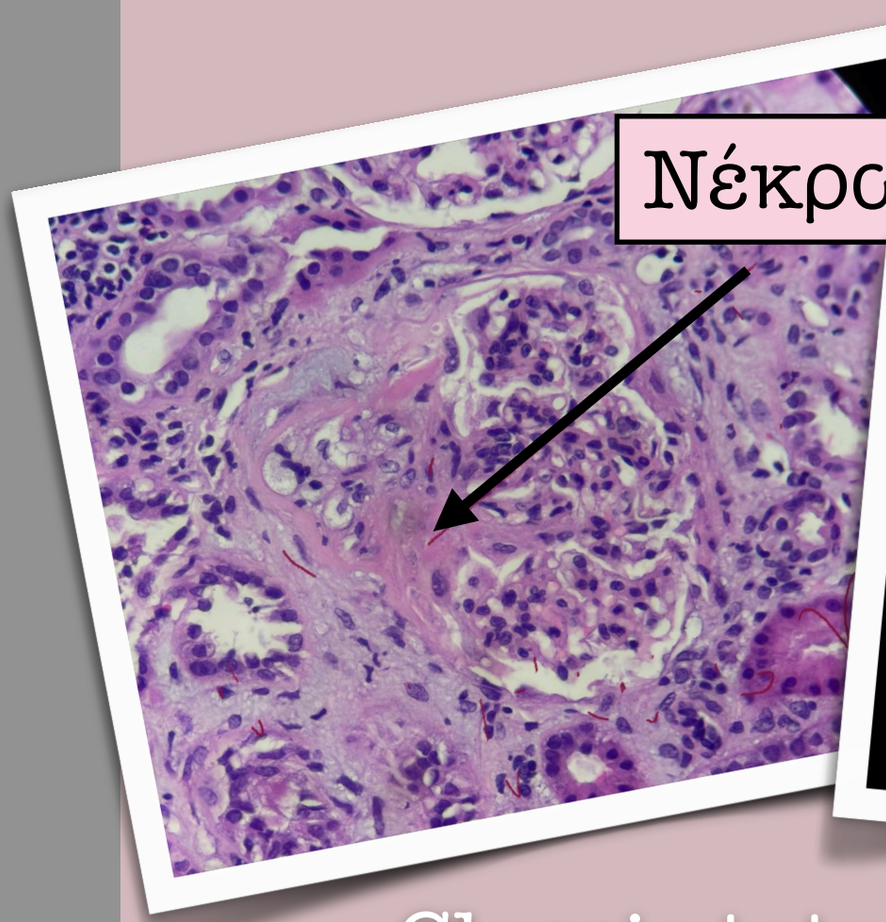
Cryoglobulinemia

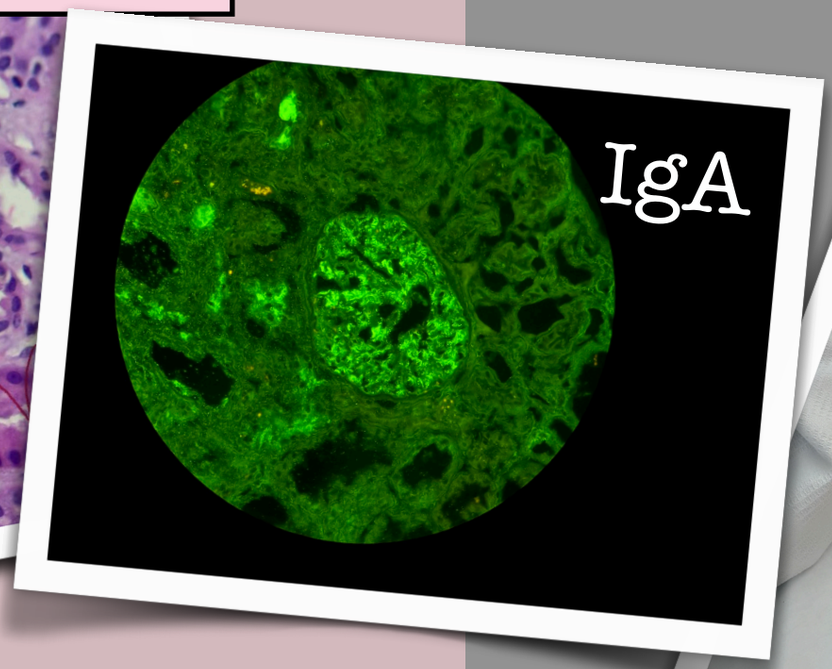
Infectious associated GN

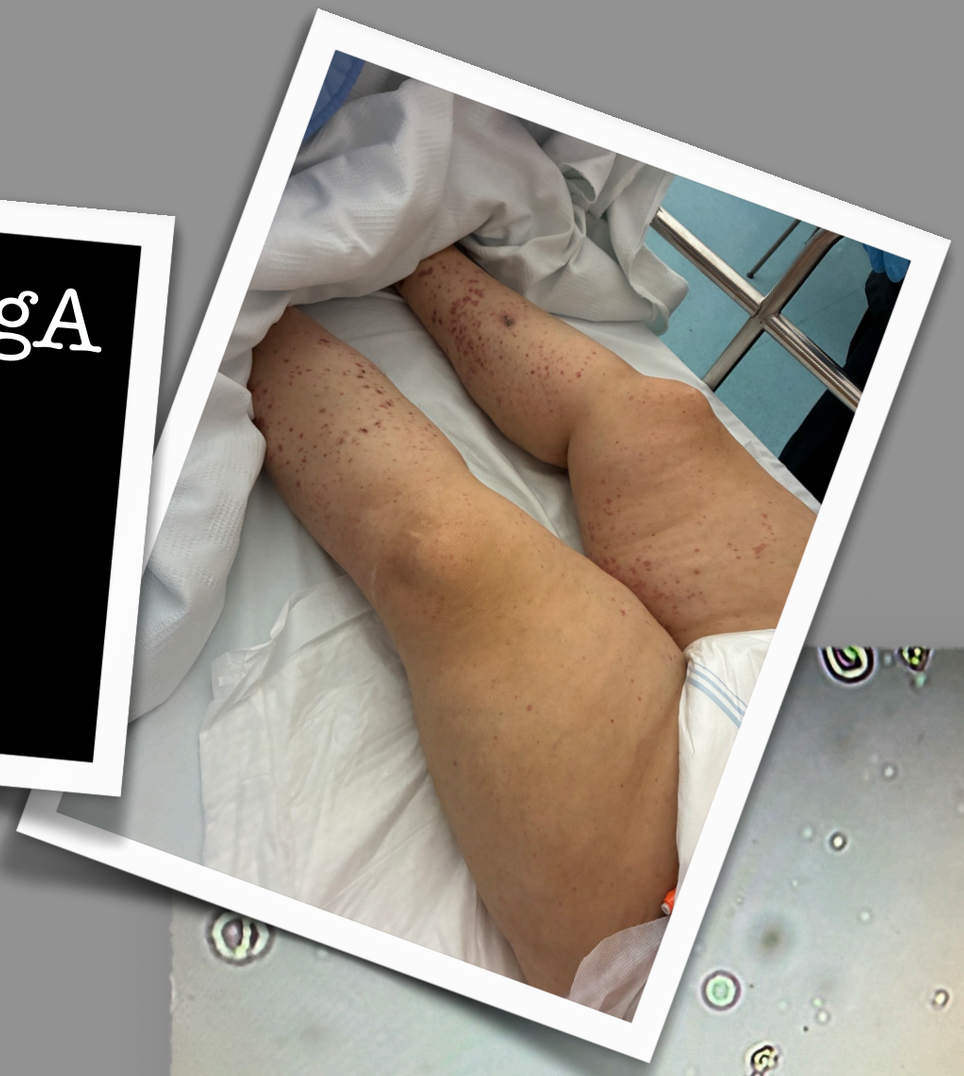
Fibrillary GN

IgA αγγειίτιδα

(Πορφύρα Henoch-Schönlein, HPS)

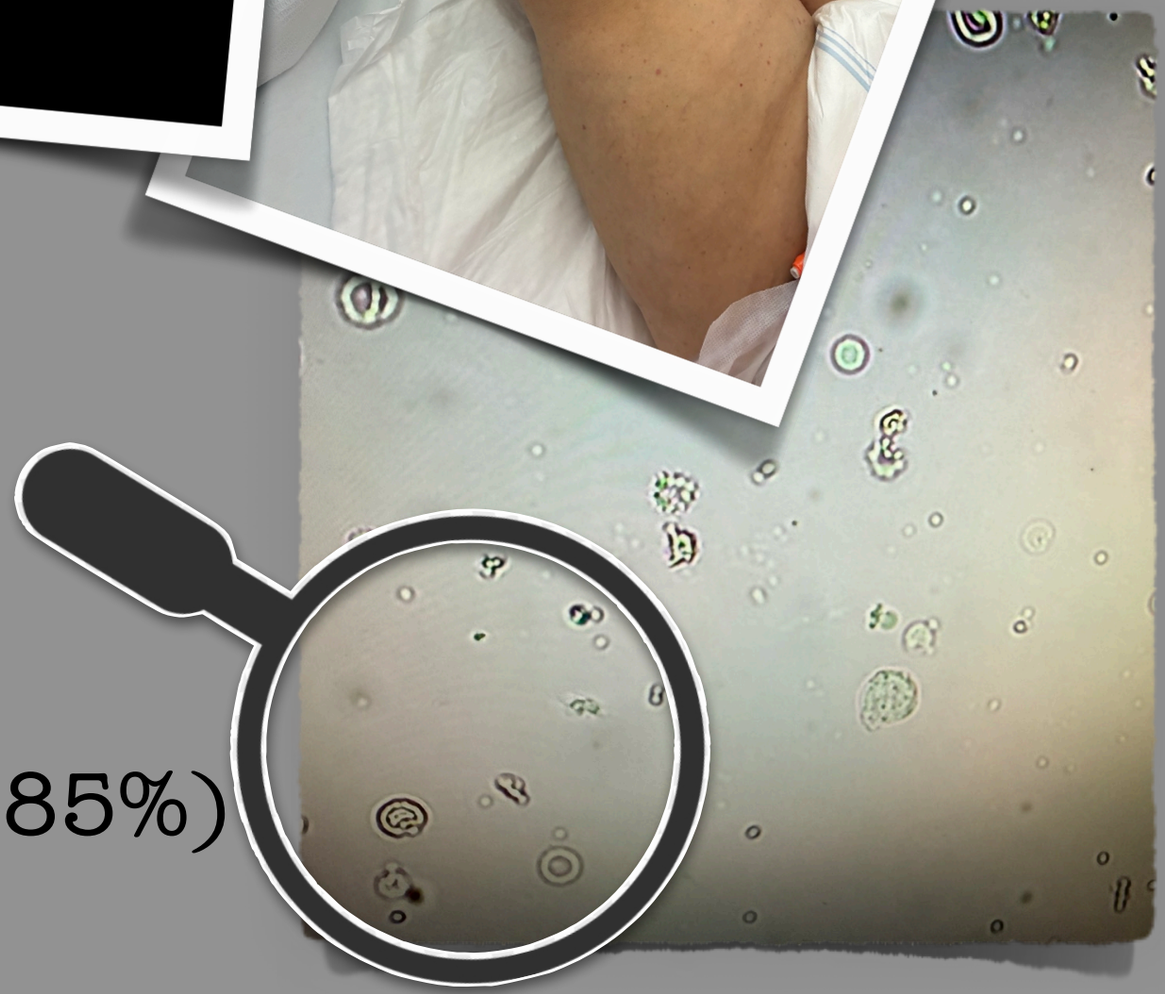






Classic tetrad

- Ψηλαφητή πορφύρα
- Εκδηλώσεις από το ΓΕΣ
- Αρθρίτιδα
- Σπειραματονεφρίτιδα (40-85%)



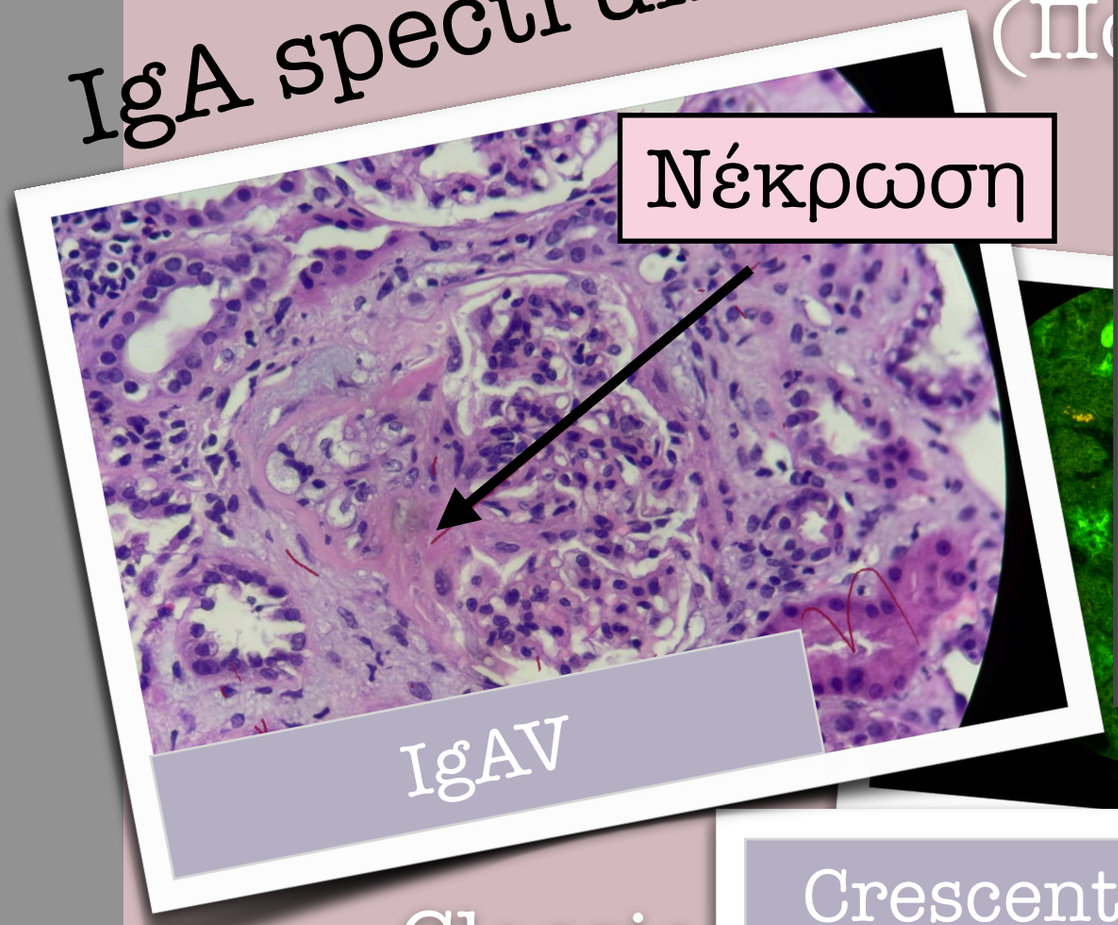
IgA αγγειίτιδα

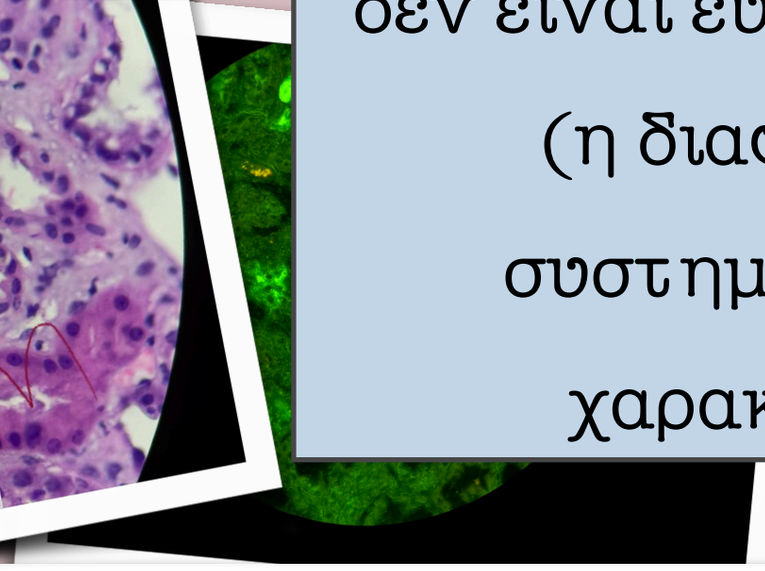
IgA spectrum disease

(Π

Τόσο η ιστοπαθολογική εικόνα όσο και η πορεία της IgAN-ΤΕΣΝ και της IgAV δεν είναι εύκολο να διαχωριστούν...

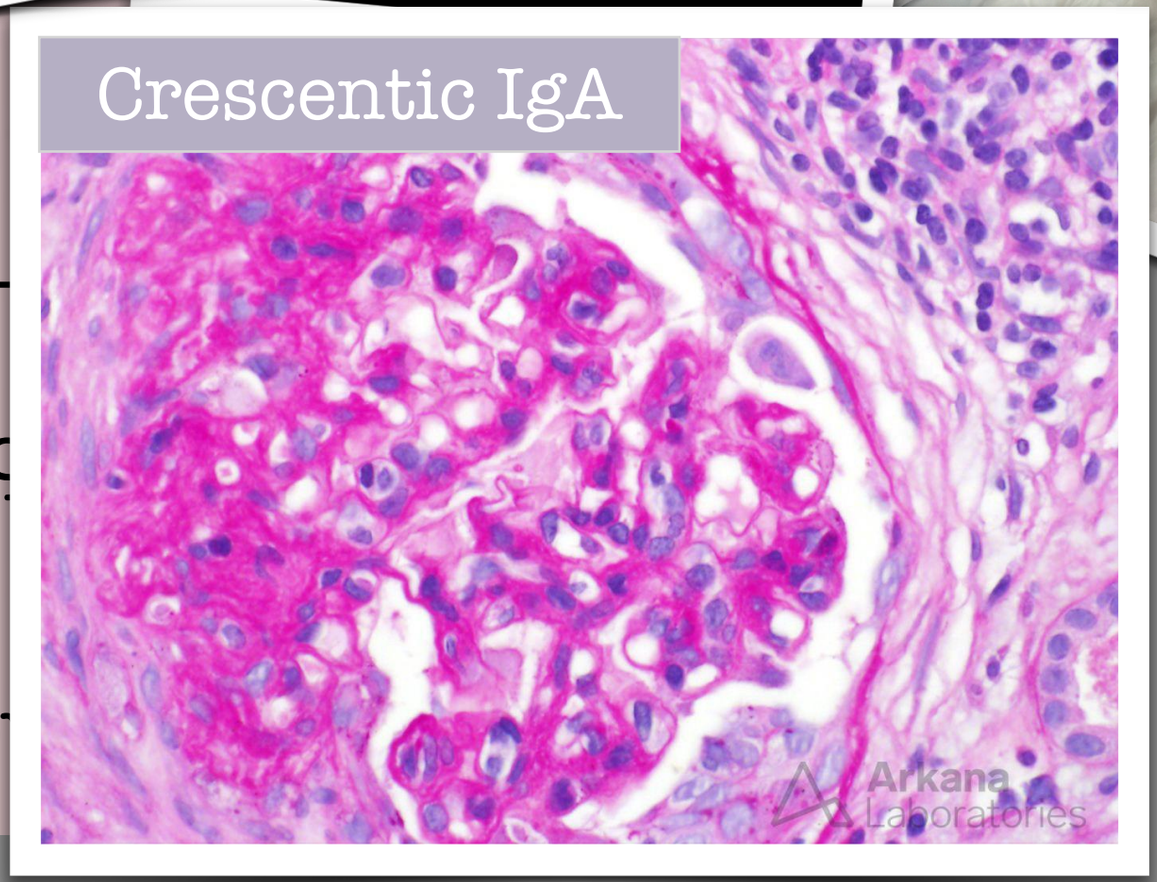
(η διαφορά βρίσκεται στη συστηματική προσβολή που χαρακτηρίζει την IgAV)





Classic

- Ψηλαφητή π
- Εκδηλώσεις
- Αρθρίτιδα
- Σπειραματο



IgA spectrum disease

IgAN/IgAV(HSP)

♟Η θεραπεία της IgAN-ΤΕΣΝ έχει ως στόχο τη μείωση του σχηματισμού των ανοσοσυμπλεγμάτων(IgA-IC) αλλά και της σπειραματικής βλάβης που προκαλείται από αυτά

♟Η θεραπεία της IgAV παραμένει αμφιλεγόμενη...

♟Η ανάγκη χρήσης ανοσοκατασταλτικής θεραπείας συνήθως υπογραμμίζεται από την παρουσία της νεφρικής συμμετοχής

IgA spectrum disease

IgAN/IgAV(HSP)

IgAN with RPGN

Patients with rapidly progressive IgAN should be offered treatment with cyclophosphamide and systemic glucocorticoids in accordance with the KDIGO 2024 Clinical Practice Guideline for the Management of Antineutrophil Cytoplasmic Antibody (ANCA)–Associated Vasculitis.[87]

IgAV with RPGN

Patients agreeing to the treatment should be treated in accordance with the KDIGO 2024 Clinical Practice Guideline for the Management of Antineutrophil Cytoplasmic Antibody (ANCA)–Associated Vasculitis.[87]

IgA spectrum disease

IgAN/IgAV(HSP)

IgAN with RPGN

Patients with rapidly progressive IgAN should be offe ys-
ten GO
202 ent
of Antineutrophil Cytoplasmic Antibody (ANCA)–
Associated Vasculitis.[87]

PLEX;

RTX (in refractory IgAV)

IgAV

Εξατομικευμένο θεραπευτικό πλάνο

Απουσία θεραπευτικών πρωτοκόλλων

Διαφορετικές πρακτικές

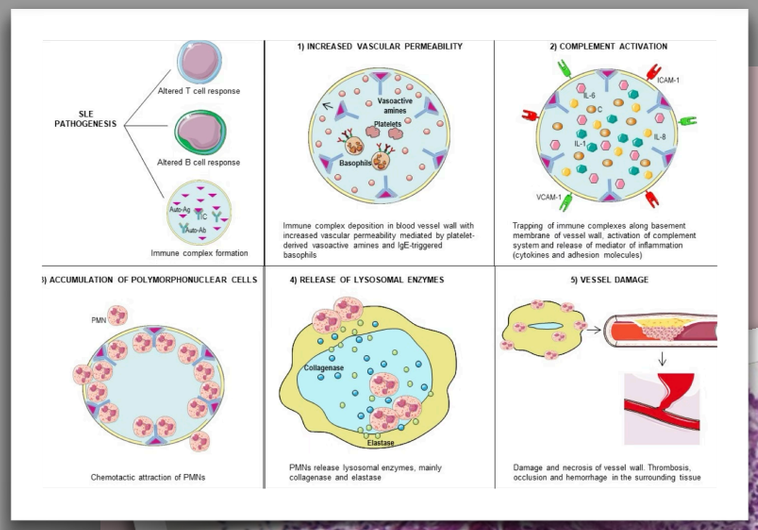
Extrapolation από μελέτες στην IgAN

Vasculitis.[87]

KDIGO

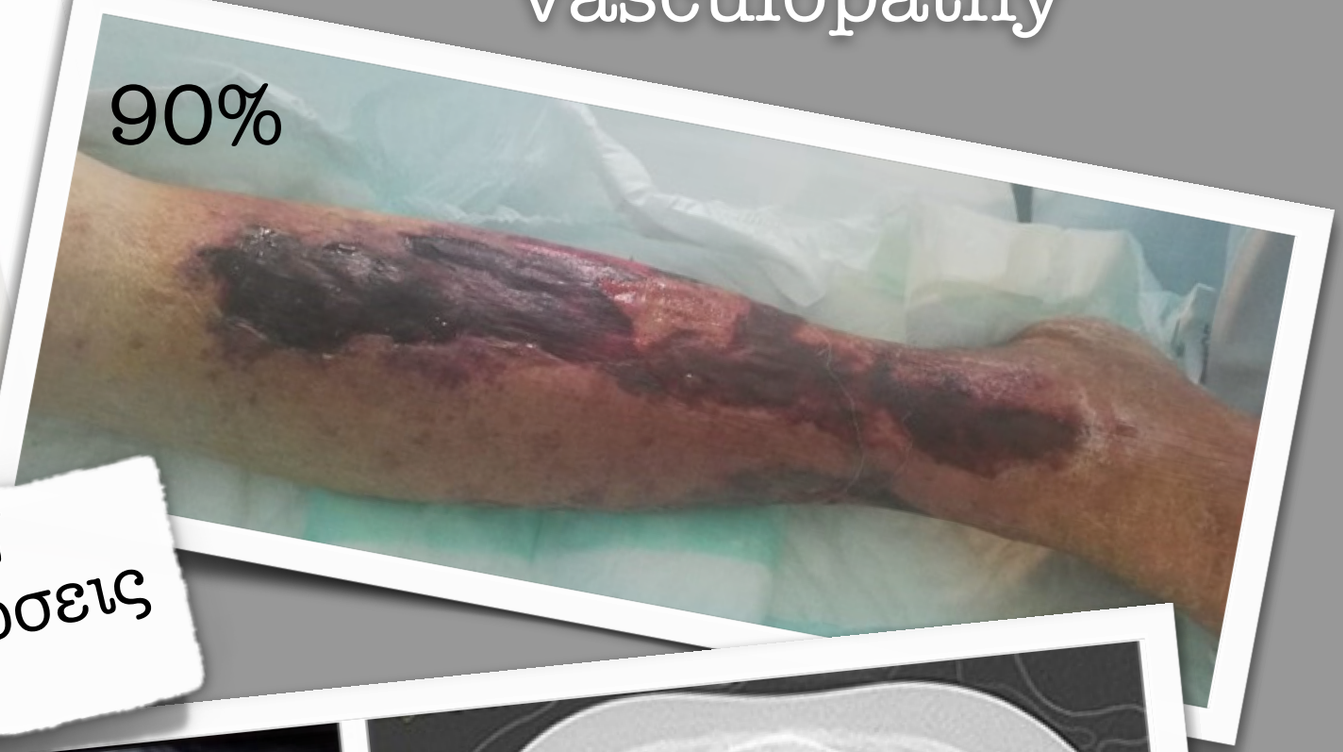
Αγγειίτιδα του λύκου

Lupus vasculitis-vasculopathy

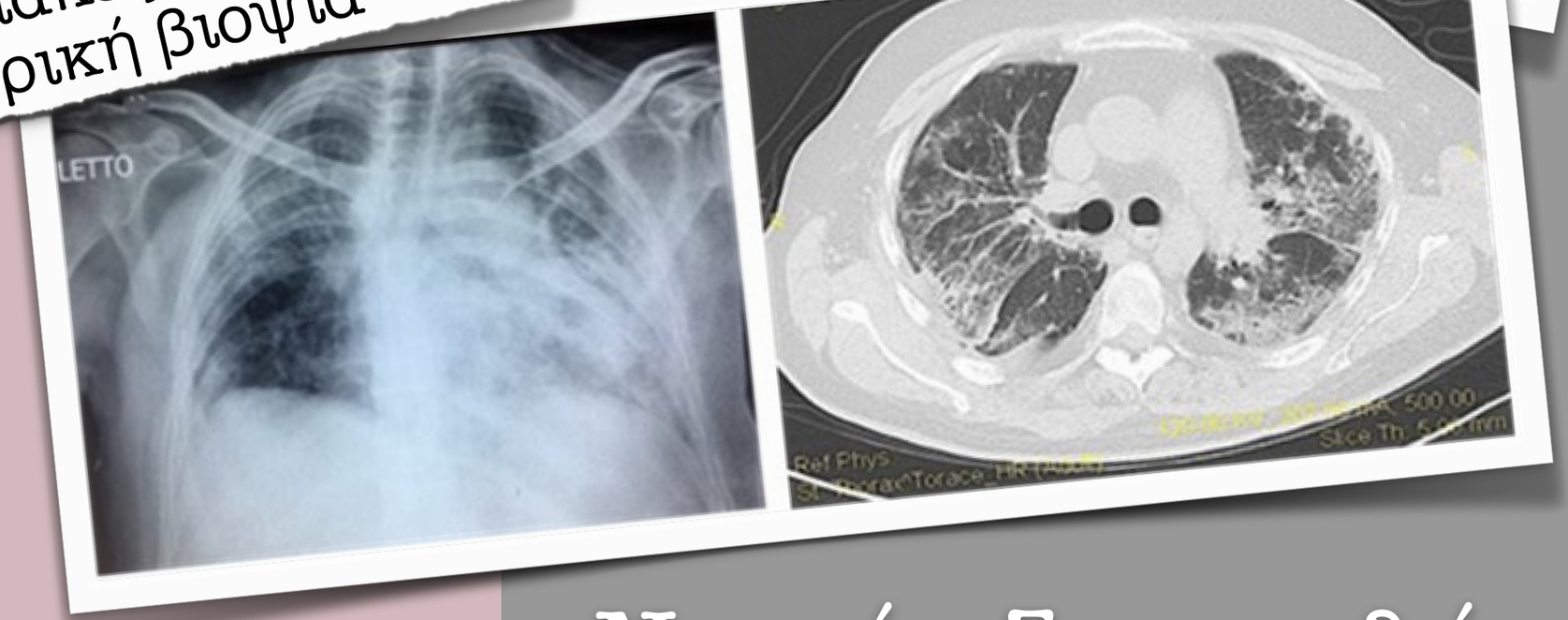


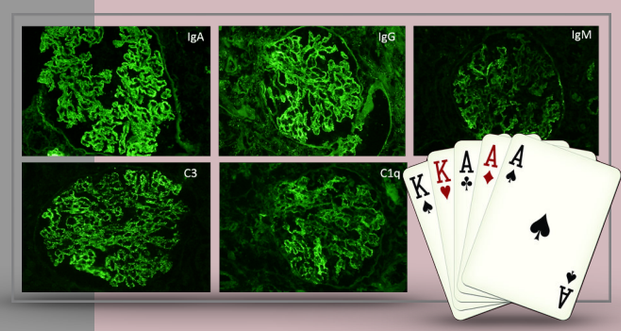
Νέκρωση

90%



10–40% των ασθενών με LN παρουσιάζουν αγγειακές αλλοιώσεις (LV) στη νεφρική βιοψία

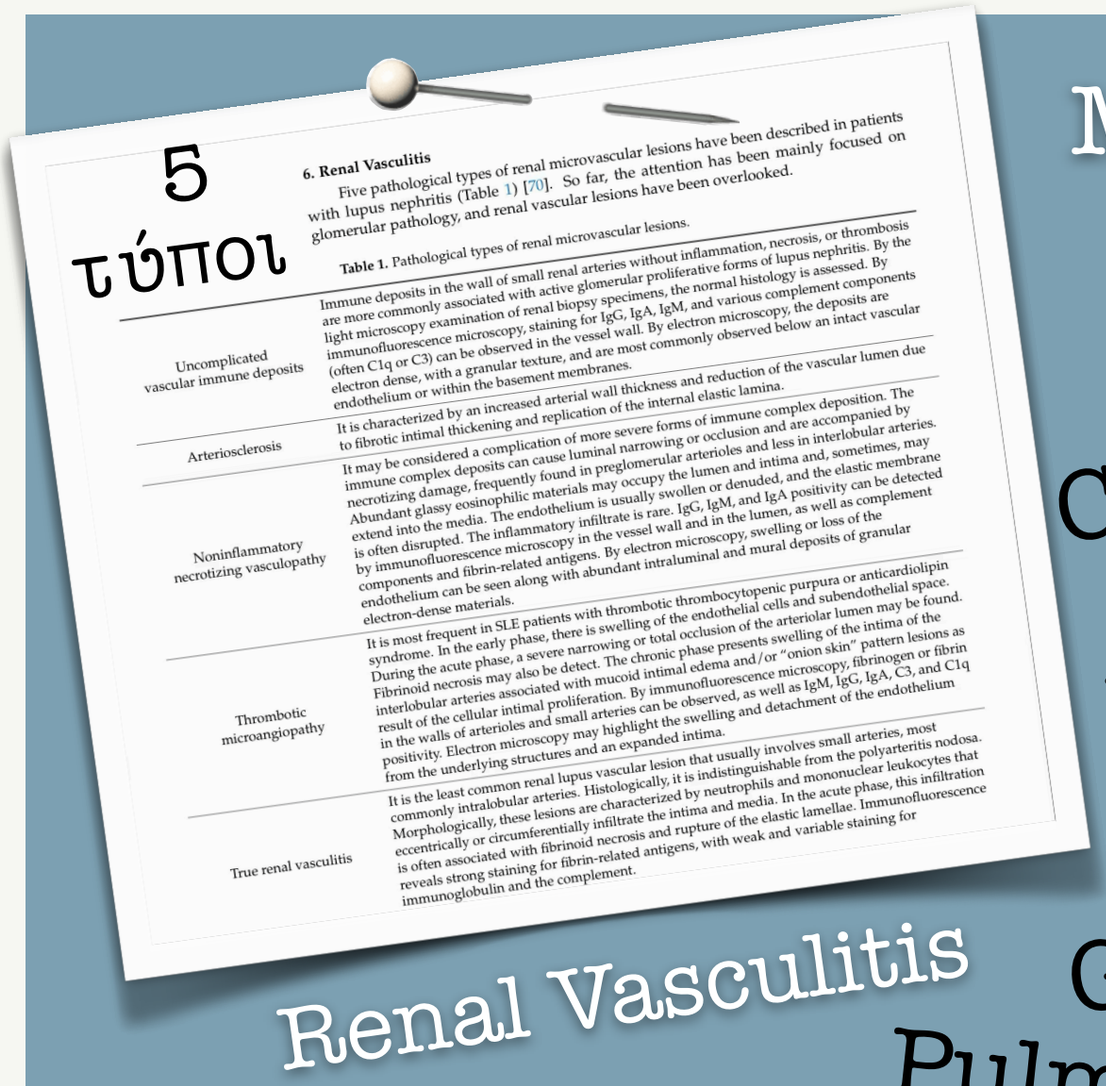




Νεφρίτιδα του λύκου

Μπορεί να προσβάλλει όλα τα συστήματα

5 τύποι



6. Renal Vasculitis

Five pathological types of renal microvascular lesions have been described in patients with lupus nephritis (Table 1) [70]. So far, the attention has been mainly focused on glomerular pathology, and renal vascular lesions have been overlooked.

Table 1. Pathological types of renal microvascular lesions.

Uncomplicated vascular immune deposits	Immune deposits in the wall of small renal arteries without inflammation, necrosis, or thrombosis are more commonly associated with active glomerular proliferative forms of lupus nephritis. By the light microscopy examination of renal biopsy specimens, the normal histology is assessed. By immunofluorescence microscopy, staining for IgG, IgA, IgM, and various complement components (often C1q or C3) can be observed in the vessel wall. By electron microscopy, the deposits are electron dense, with a granular texture, and are most commonly observed below an intact vascular endothelium or within the basement membranes.
Arteriosclerosis	It is characterized by an increased arterial wall thickness and reduction of the vascular lumen due to fibrotic intimal thickening and replication of the internal elastic lamina.
Noninflammatory necrotizing vasculopathy	It may be considered a complication of more severe forms of immune complex deposition. The immune complex deposits can cause luminal narrowing or occlusion and are accompanied by necrotizing damage, frequently found in preglomerular arterioles and less in interlobular arteries. Abundant glassy eosinophilic materials may occupy the lumen and intima and, sometimes, may extend into the media. The endothelium is usually swollen or denuded, and the elastic membrane is often disrupted. The inflammatory infiltrate is rare. IgG, IgM, and IgA positivity can be detected by immunofluorescence microscopy in the vessel wall and in the lumen, as well as complement components and fibrin-related antigens. By electron microscopy, swelling or loss of the endothelium can be seen along with abundant intraluminal and mural deposits of granular electron-dense materials.
Thrombotic microangiopathy	It is most frequent in SLE patients with thrombotic thrombocytopenic purpura or anticardiolipin syndrome. In the early phase, there is swelling of the endothelial cells and subendothelial space. During the acute phase, a severe narrowing or total occlusion of the arteriolar lumen may be found. Fibrinoid necrosis may also be detect. The chronic phase presents swelling of the intima of the interlobular arteries associated with mucoid intimal edema and/or "onion skin" pattern lesions as result of the cellular intimal proliferation. By immunofluorescence microscopy, fibrinogen or fibrin in the walls of arterioles and small arteries can be observed, as well as IgM, IgG, IgA, C3, and C1q positivity. Electron microscopy may highlight the swelling and detachment of the endothelium from the underlying structures and an expanded intima.
True renal vasculitis	It is the least common renal lupus vascular lesion that usually involves small arteries, most commonly intralobular arteries. Histologically, it is indistinguishable from the polyarteritis nodosa. Morphologically, these lesions are characterized by neutrophils and mononuclear leukocytes that eccentrically or circumferentially infiltrate the intima and media. In the acute phase, this infiltration is often associated with fibrinoid necrosis and rupture of the elastic lamellae. Immunofluorescence reveals strong staining for fibrin-related antigens, with weak and variable staining for immunoglobulin and the complement.

Cutaneous Vasculitis

Nervous System Vasculitis

Renal Vasculitis

Gastrointestinal Vasculitis

Pulmonary Vasculitis

Retinal Vasculitis

Coronary Vasculitis

Lupus Myocarditis

Lupus Vasculitis and APS

Leone P, Biomedicines 2021

Obinutuzumab Θεραπεία **Voclosporin**

Renal	Retrospective study	61	Cyclophosphamide or mycophenolate mofetil in combination with glucocorticoids for the induction phase. Mycophenolate mofetil or azathioprine combined with low-dose glucocorticoid regimens for the maintence phase.	N.R.	No severe adverse events	[113]
		9	Plasmapheresis and baseline immunosuppressive therapy	33	None	
	Systematic review (31 studies)	1259	Rituximab alone or in combination with cyclophosphamide or mycophenolate mofetil	77 Caucasian 38 East-Asian 28 Hispanic	N.R.	[114]
Renal	Systematic review (15 studies) and case report		Eculizumab			
	Case series	16	High-dose corticosteroid, followed by pulse methylprednisolone, plasmapheresis, pulse cyclophosphamide, and rituximab	N.R.	Infections	[86]
	Case series	34	High dose of methylprednisolone (>3 g) and cyclophosphamide	N.R.	N.R.	[96]
Pulmonary	Retrospective clinical trials	40 SLE			Mild (bleeding)	[116]
	Case control study				N.R.	[92]

RTX **CYC** **PLEX** **GCs** **MMF**

Complement inhibitors

Belimumab

Severe refractory lupus renal vasculitis

There is no consensus regarding the therapeutic approach to LV

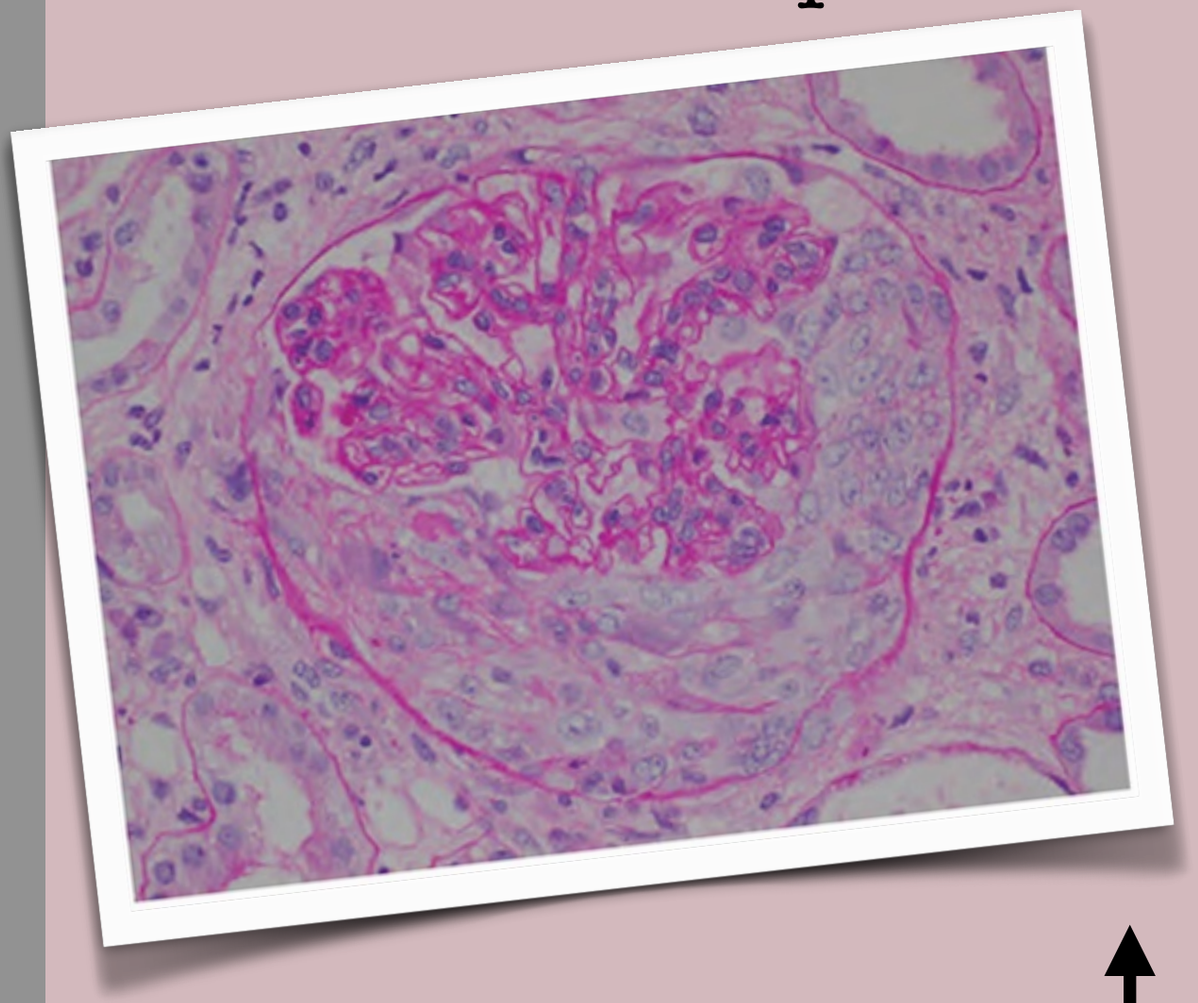
Leone P, Biomedicines 2021

32 ετών

Σχετιζόμενη με λοίμωξη ΤΕΣΝ

Infection-Related Rapidly Progressive Crescentic Glomerulonephritis

A rapidly progressive glomerulonephritis
in the setting of IV drug abuse, hepatitis C
and tricuspid valve MRSA endocarditis



Creat: 2.3 mg/dl

- C3 and C4 were low
- Cryuglobulins (-)
- Autoantibodies (-)

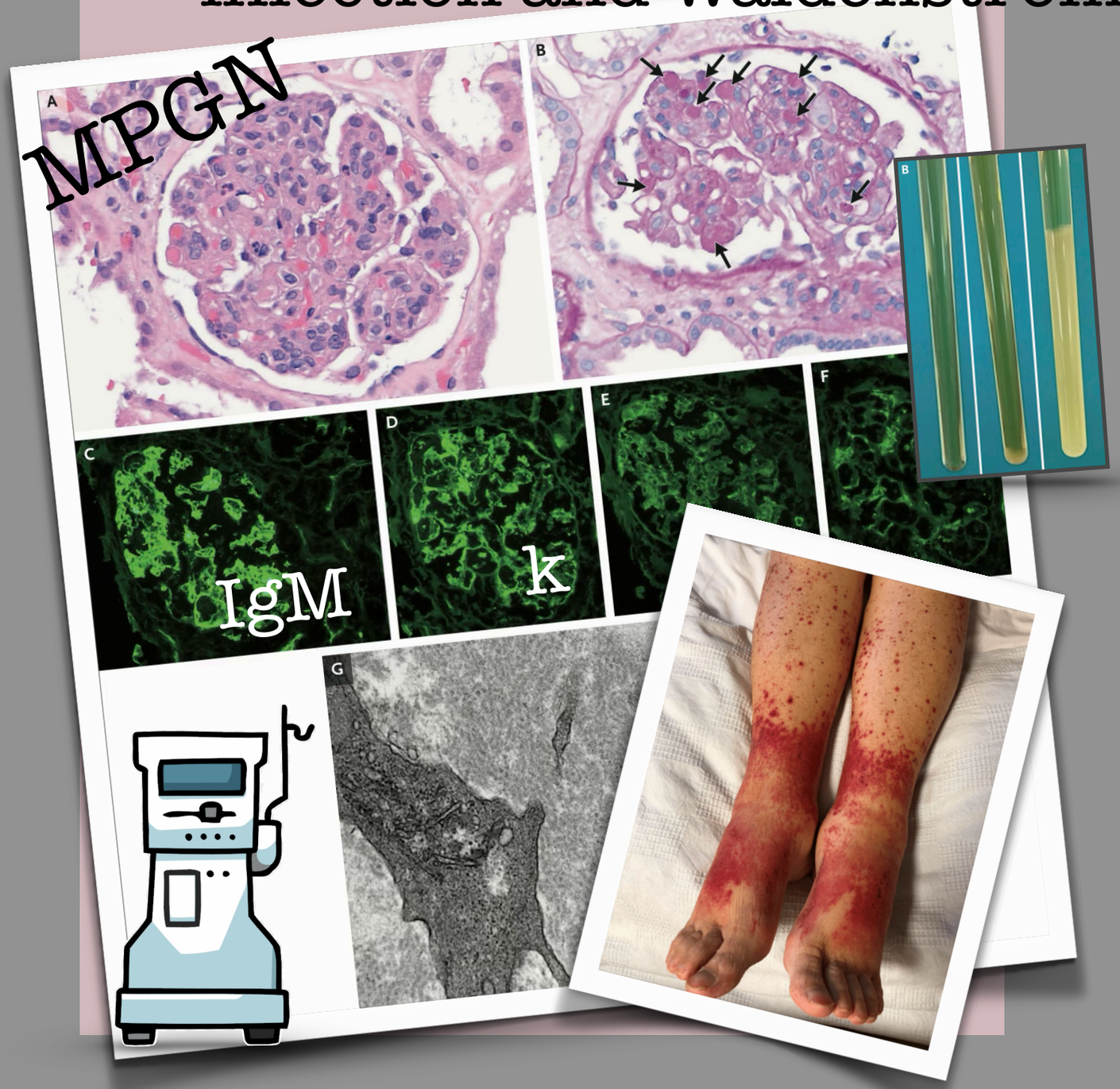
Antibiotics
Steroids
Immunosuppression

Henderson JR, Pembaur KB, JASN 2023

Κρυοσφαιριναιμία

76 ετών

A rapidly progressive glomerulonephritis associated with **type II cryoglobulinemic vasculitis,** in a patient with previous HCV infection and Waldenström macroglobulinemia



Creat: 2.6 > 4.4 mg/dl

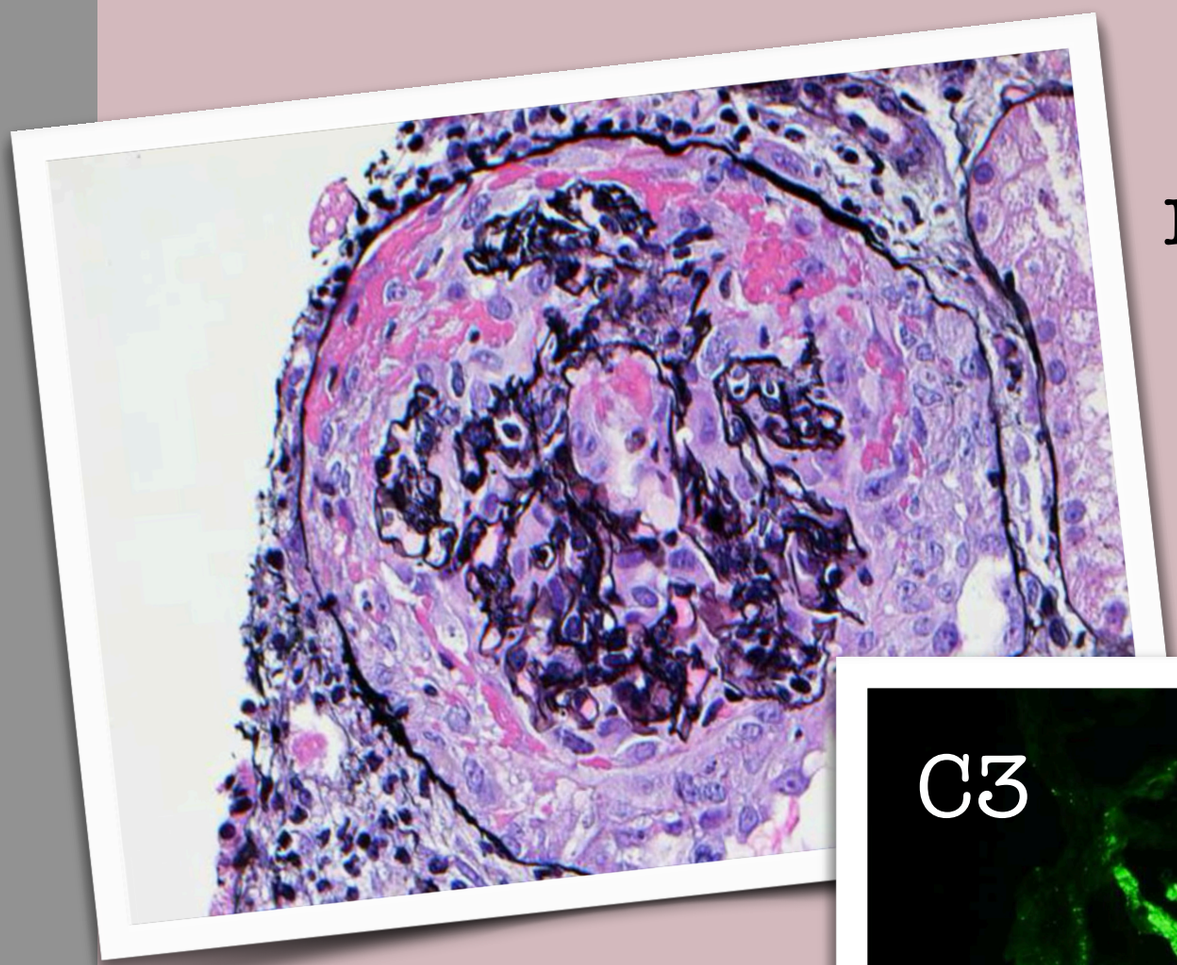
PLEX was initiated to rapidly reduce circulating IgM and cryoglobulin levels until clone-directed therapy took effect

Bortesomib
RTX
Dexamethasone

Cortazar FB et al, NEJM 2026

C3 σπειραματοπάθεια

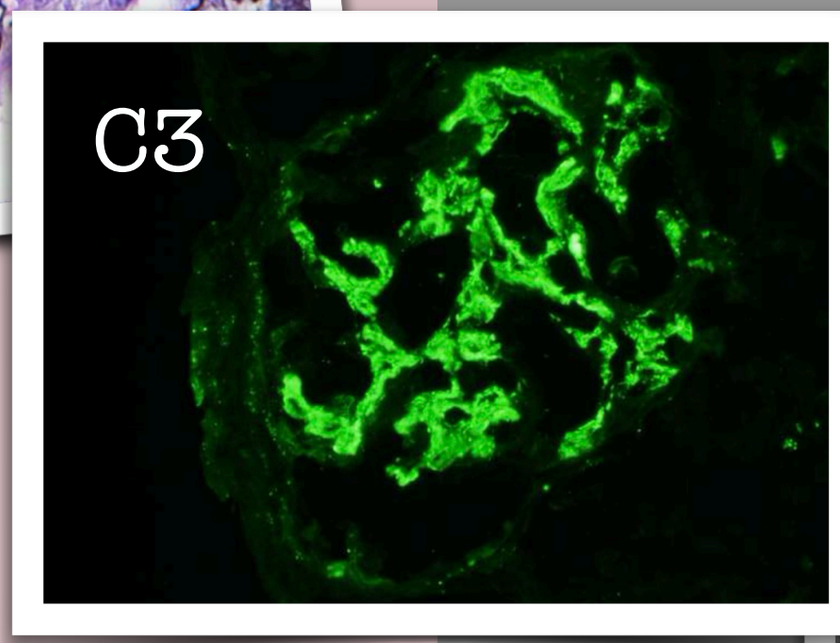
23 ετών

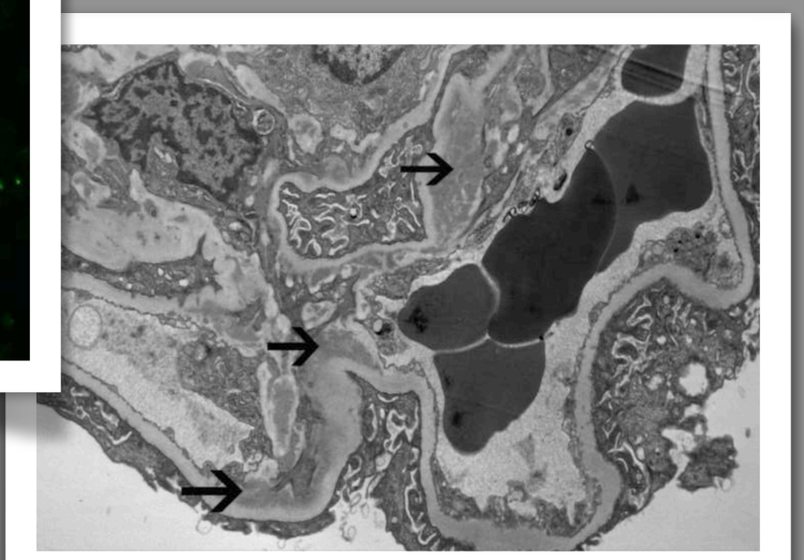


Association of a novel complement factor H mutation with severe crescentic and necrotizing glomerulonephritis

Steroids

IV/pos for 6 months



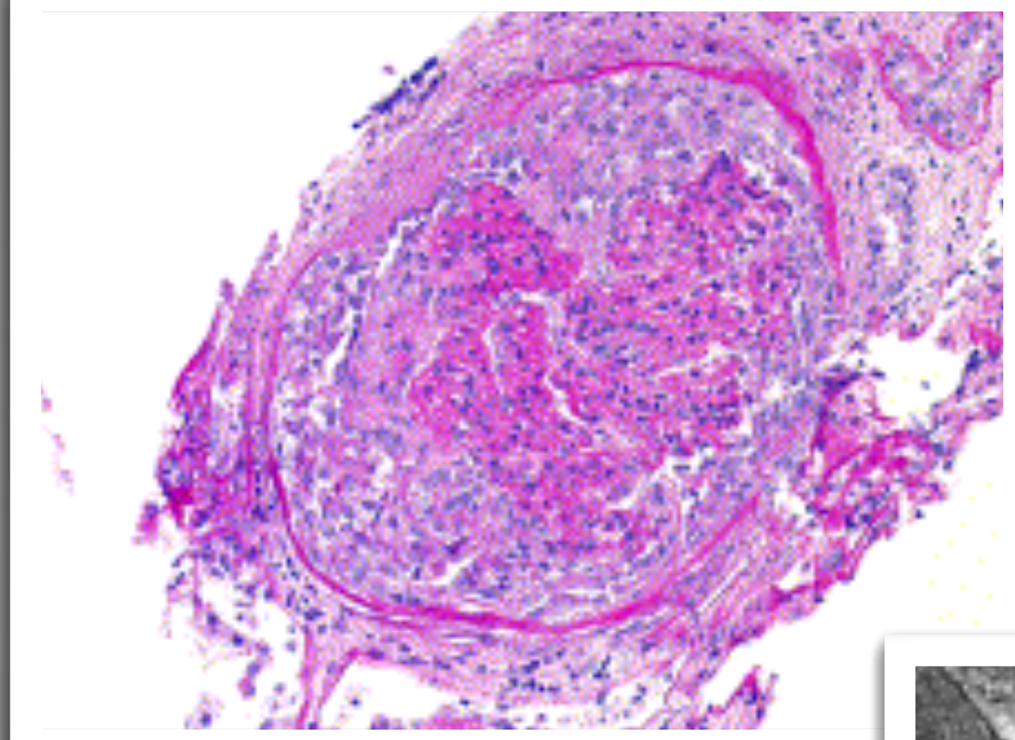


Creat: 1.8 mg/dl ↑

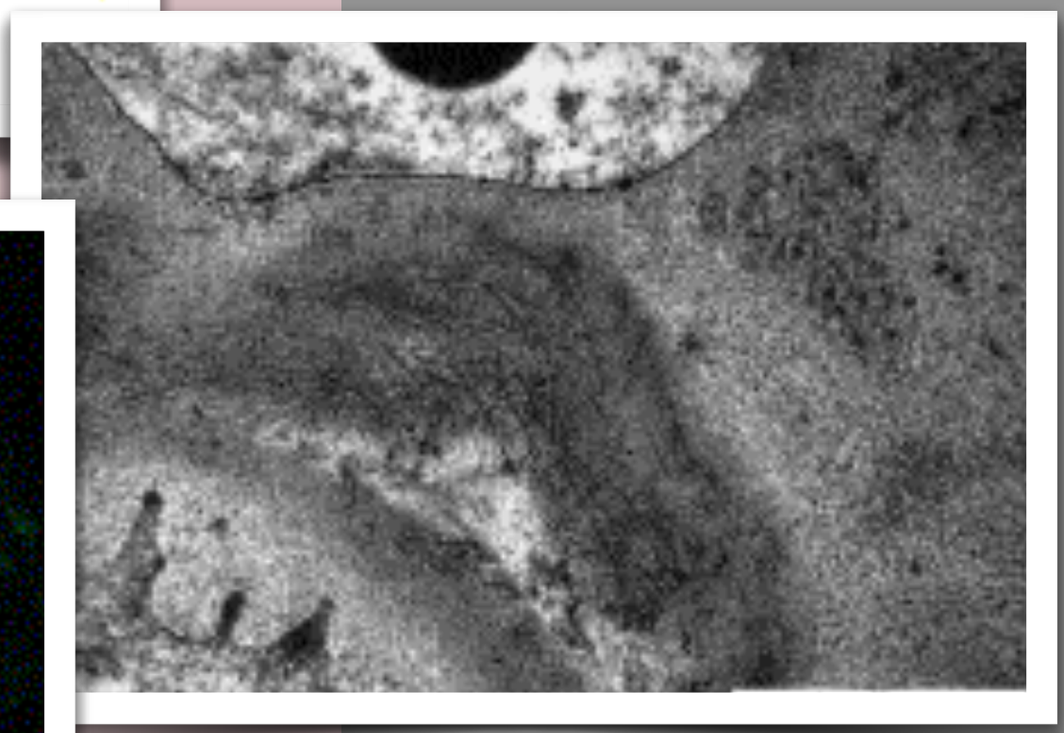
Fervenza FC et al, AJKD 2012

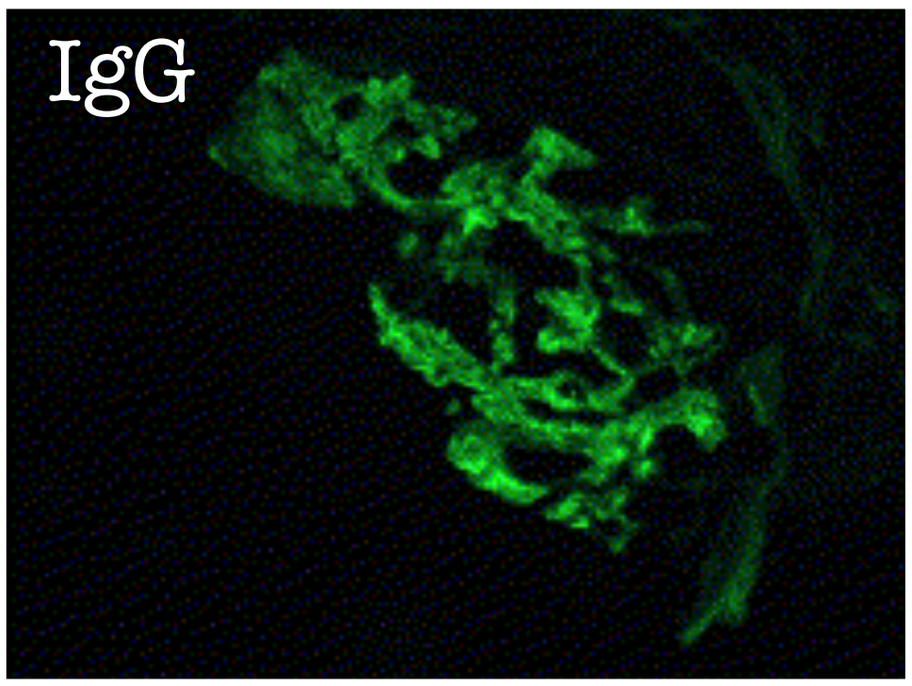
Ινιδιακή σπειραματονεφρίτιδα

61 ετών



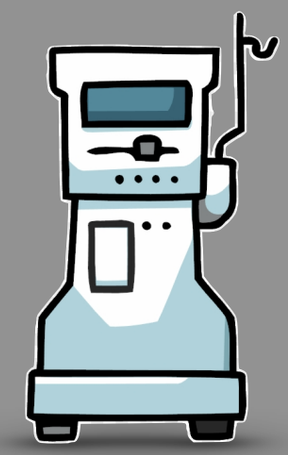
Μια σπάνια μορφή σπειραματονεφρίτιδας με εικόνα ΤΕΣΝ, γραμμικής εναπόθεσης IgG στον IF-όχι antiGMB-και χαρακτηριστικής εικόνας στο ΕΜ





Creat: 1.2 > 10 mg/dl

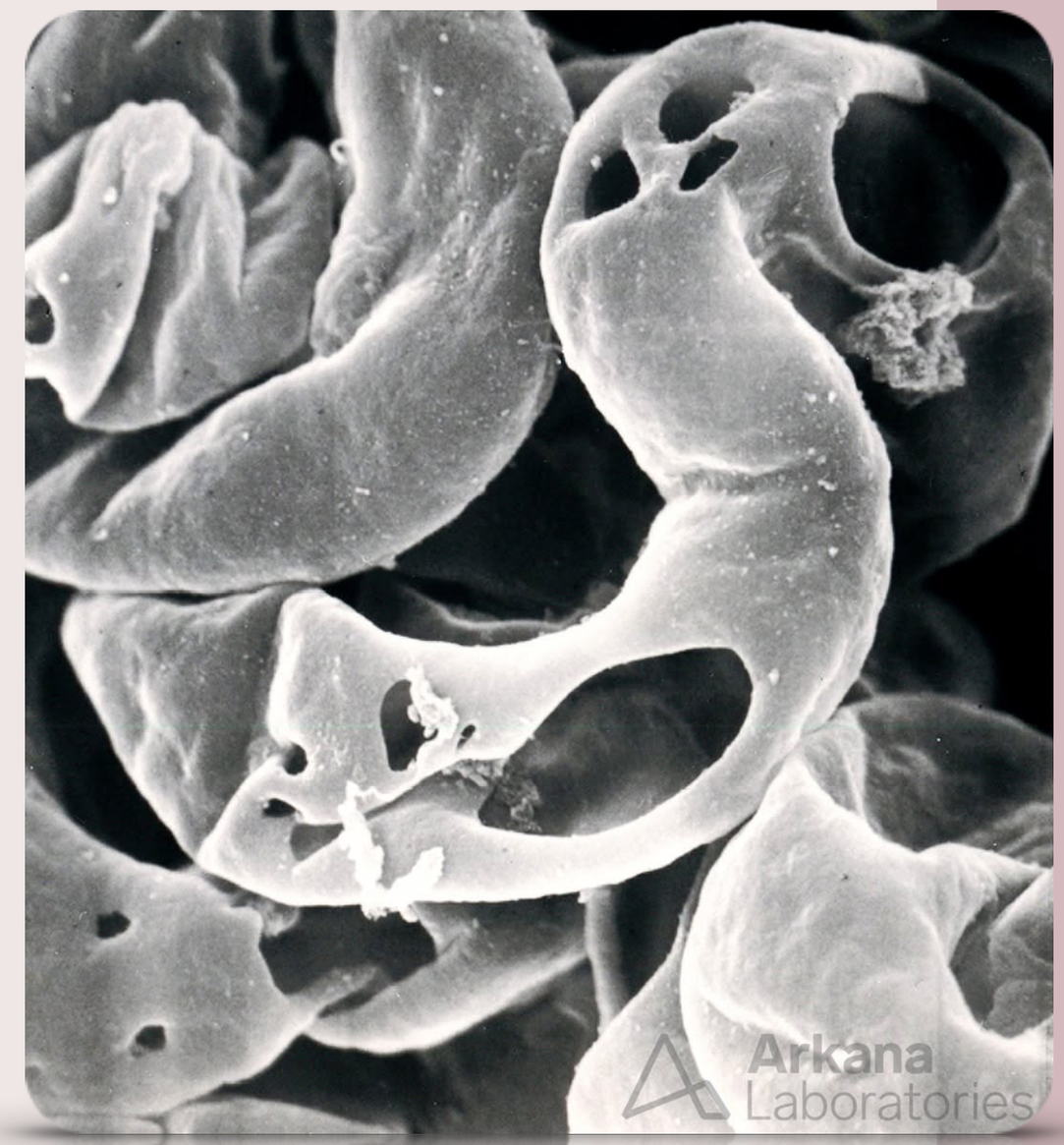
Steroids
CYC
PLEX



Sharma P et al, AJKD 2012

Επείγουσα Νεφρολογία

"Time is nephrons..."



Acellular scanning EM showing variably sized discrete GBM perforations in segmental necrotizing and crescentic glomerulonephritis

Ευχαριστώ πολύ