Προσεγγίζοντας τον ασθενή με μικροσκοπική αιματουρία

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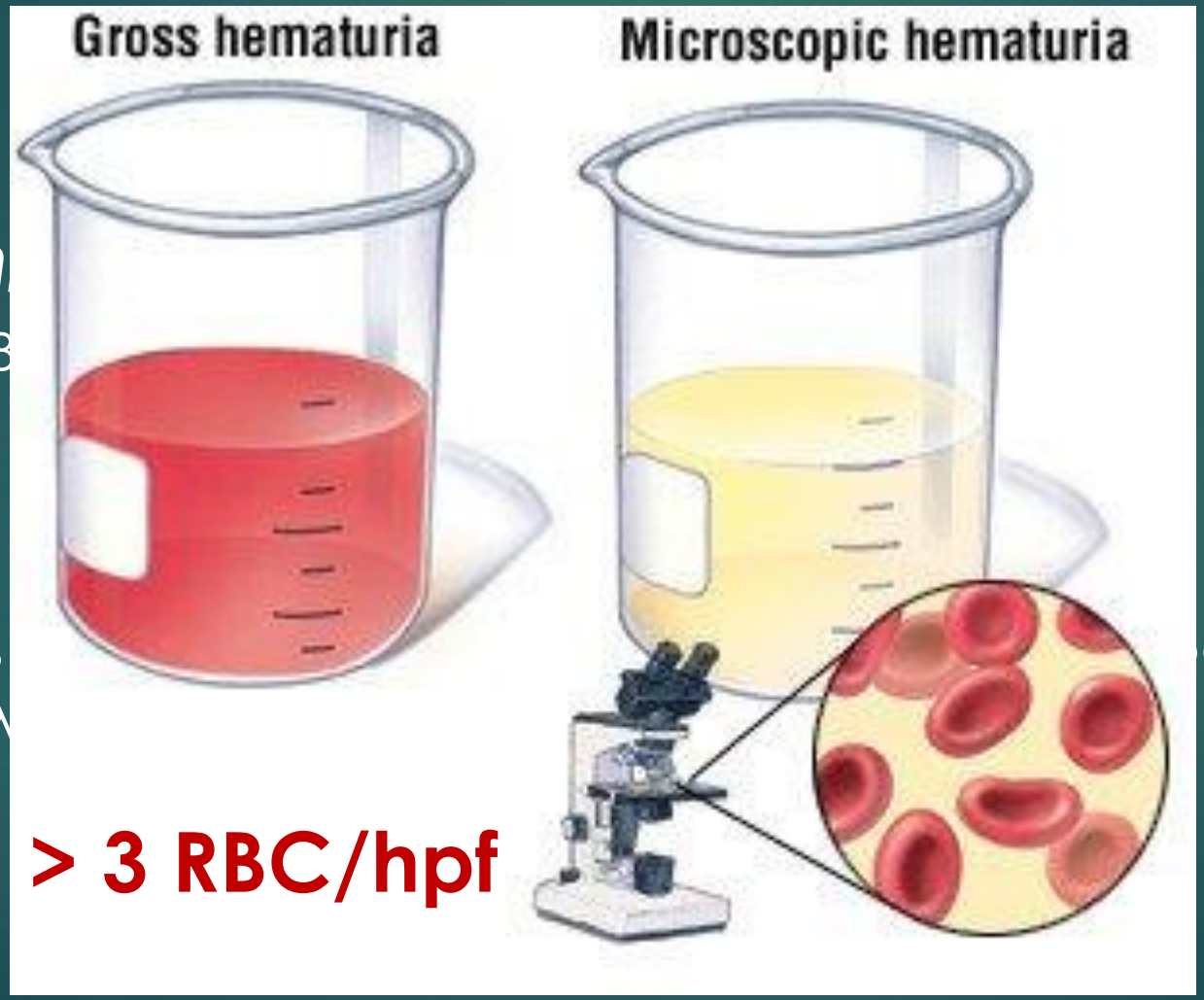
ΕΜΕΠΥ, 30/09/2023

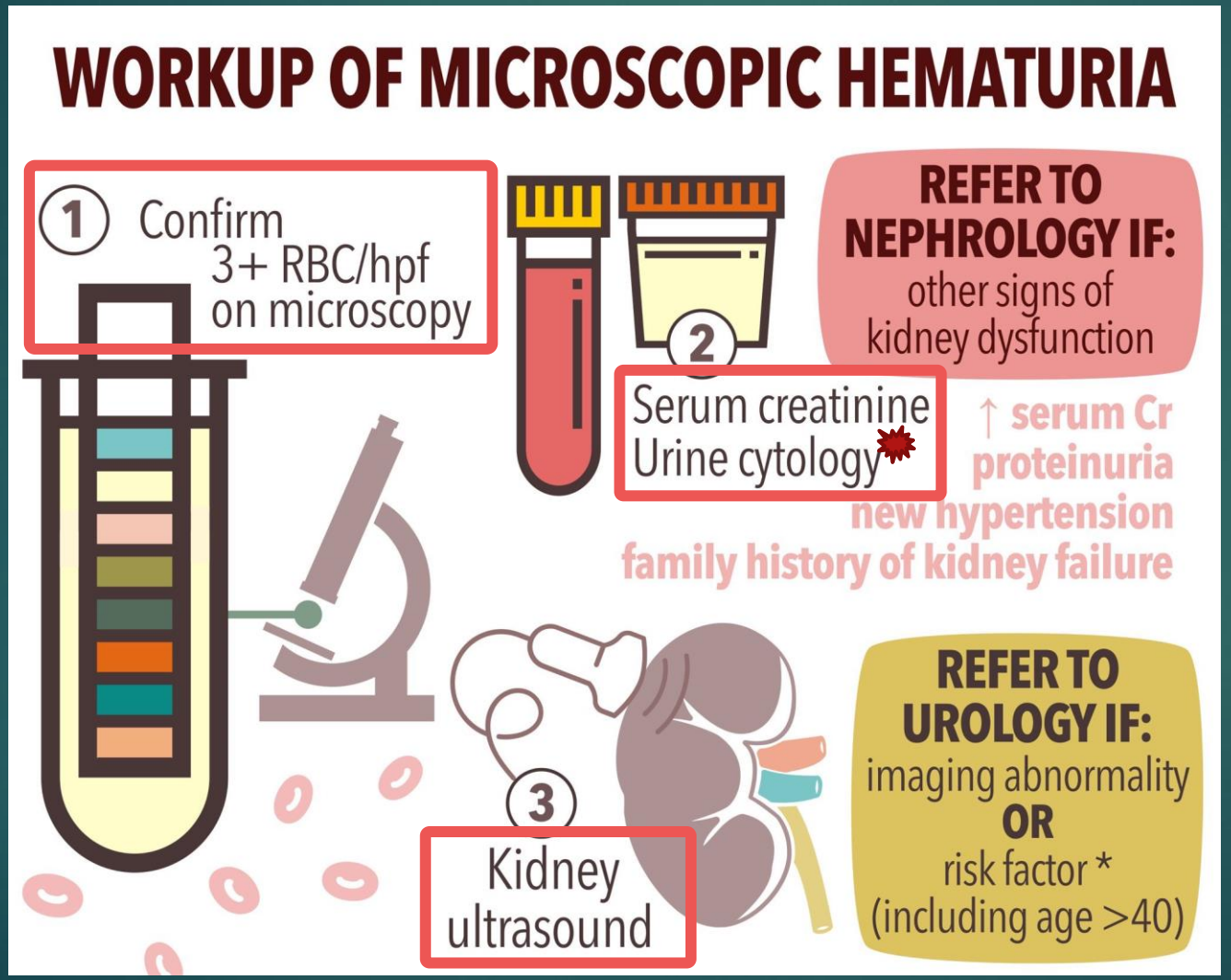
Μικροσκοπική αιματουρία

- *Σιωπη*
  - ✓ 0.18 παιδιών
- 63.7% αματικής προέλ
  - ✓ Πιο



Glomerular Hematuria: Cause or Consequence of Renal Inflammation? Moreno JA et. Al., Int J Mol Sci. 2019 May 5;20(9):2205. doi: 10.3390/ijms20092205. PMID: 31060307; PMCID: PMC6539976.

Μικροσκοπική αιματουρία



Διαφοροδιάγνωση αιματουρίας

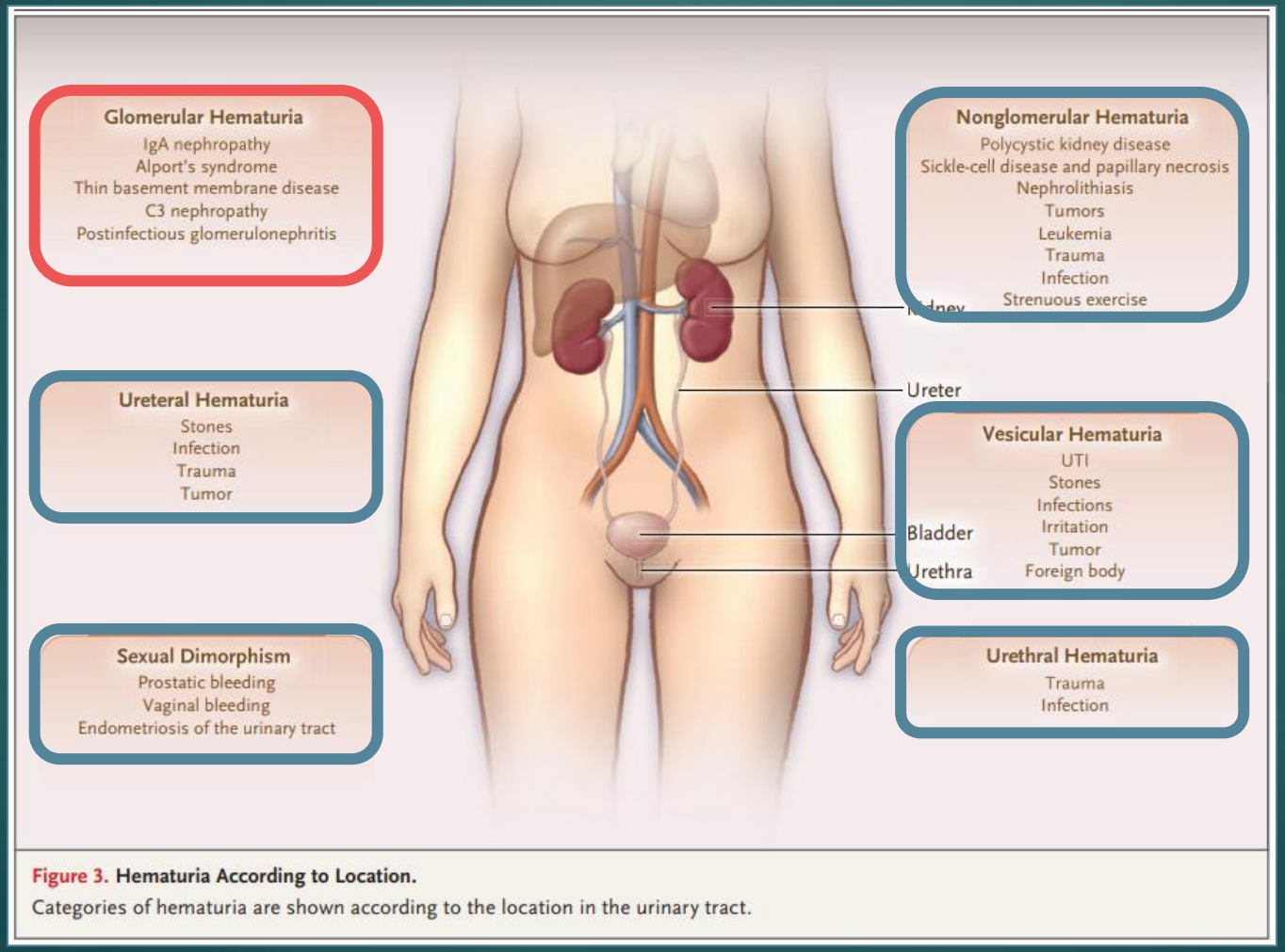
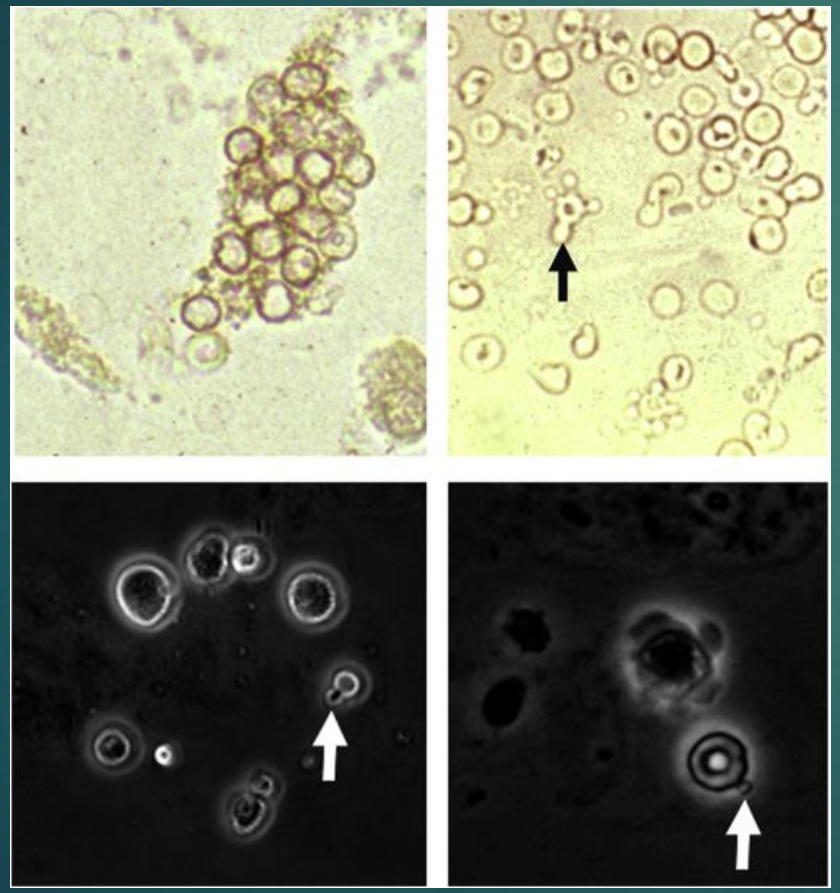
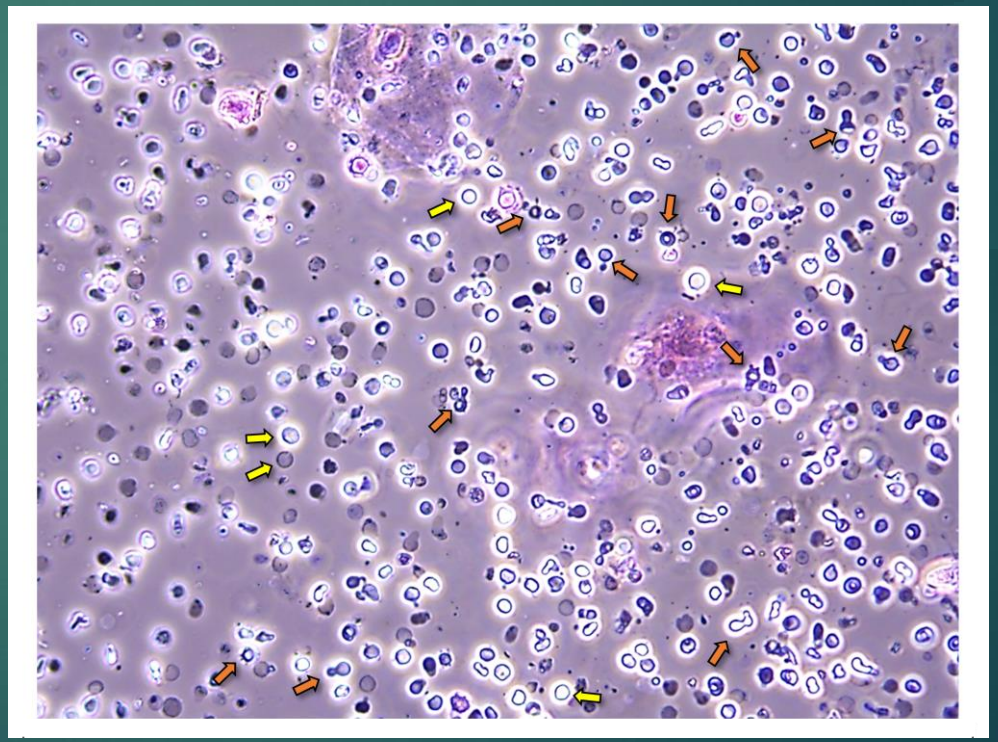


Figure 3. Hematuria According to Location.
Categories of hematuria are shown according to the location in the urinary tract.

Hematuria in Adults, *Julie R. Ingelfinger, M.D., N Engl J Med 2021; 385:153-163*
DOI: 10.1056/NEJMra1604481

Ίζημα ούρων: *πάσχει ή δεν πάσχει ο νεφρός;*





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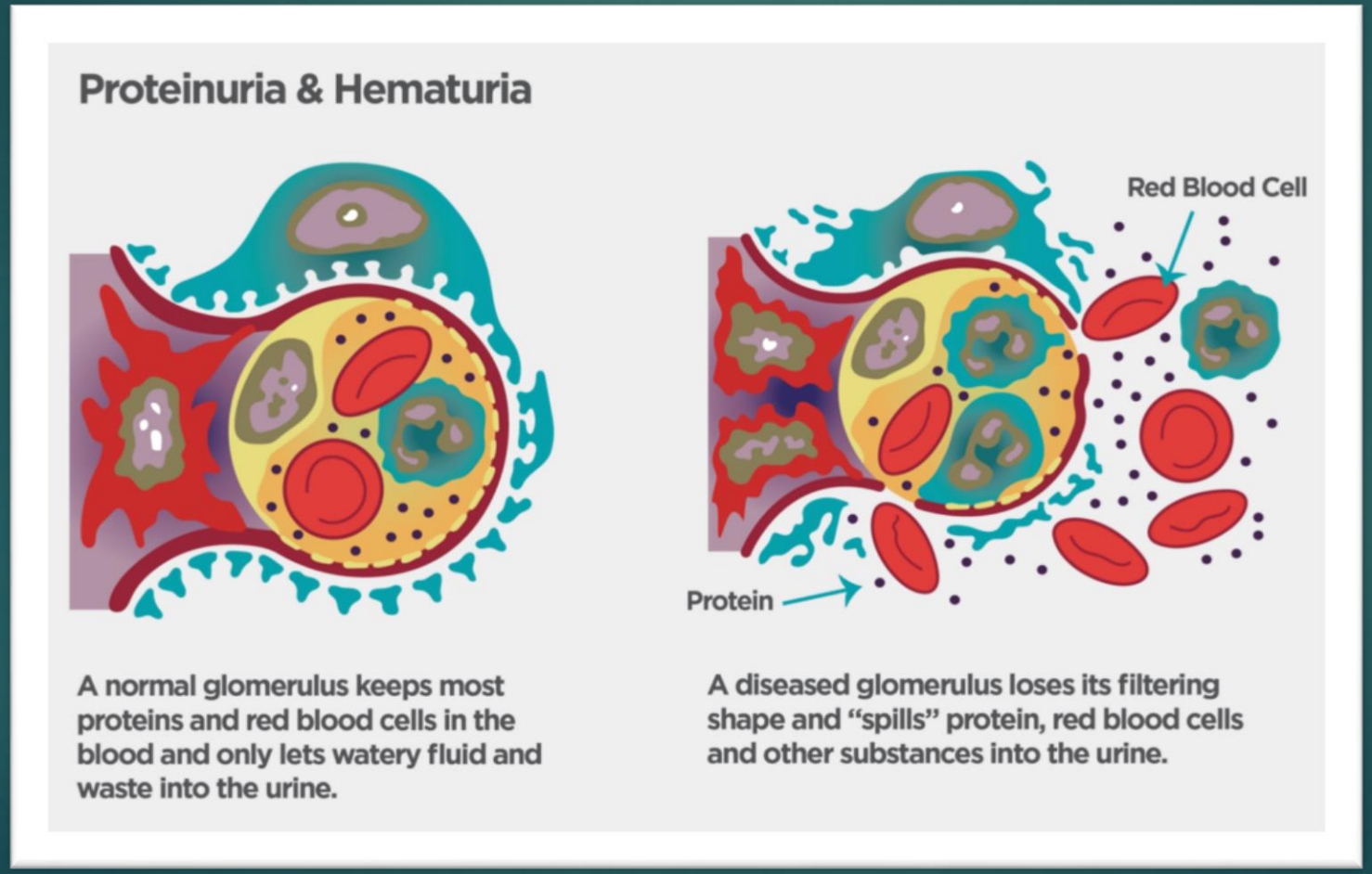
Παθογένεση της σπειραματικής αιματουρίας



Pathogenesis of glomerular haematuria, *Yuste C et.al.. World J Nephrol. 2015 May 6;4(2):185-95. doi: 10.5527/wjn.v4.i2.185. PMID: 25949932; PMCID: PMC4419128.*

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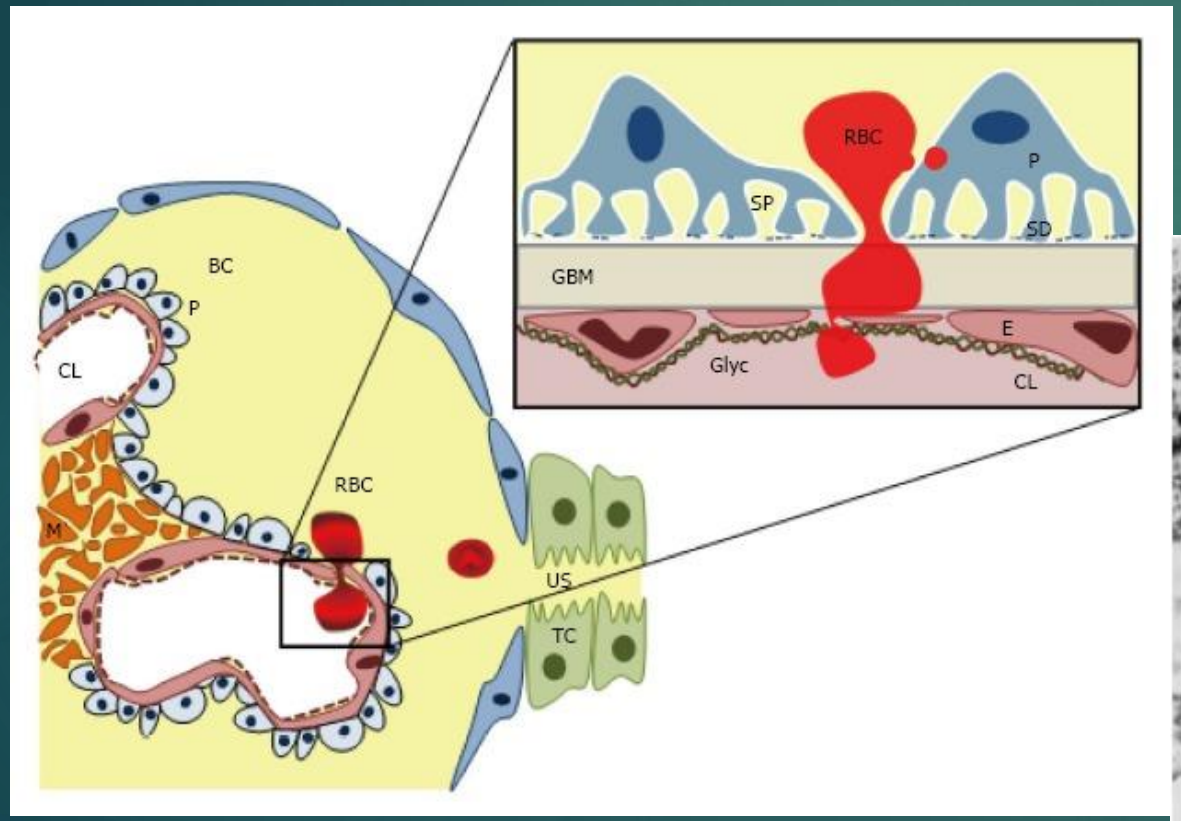

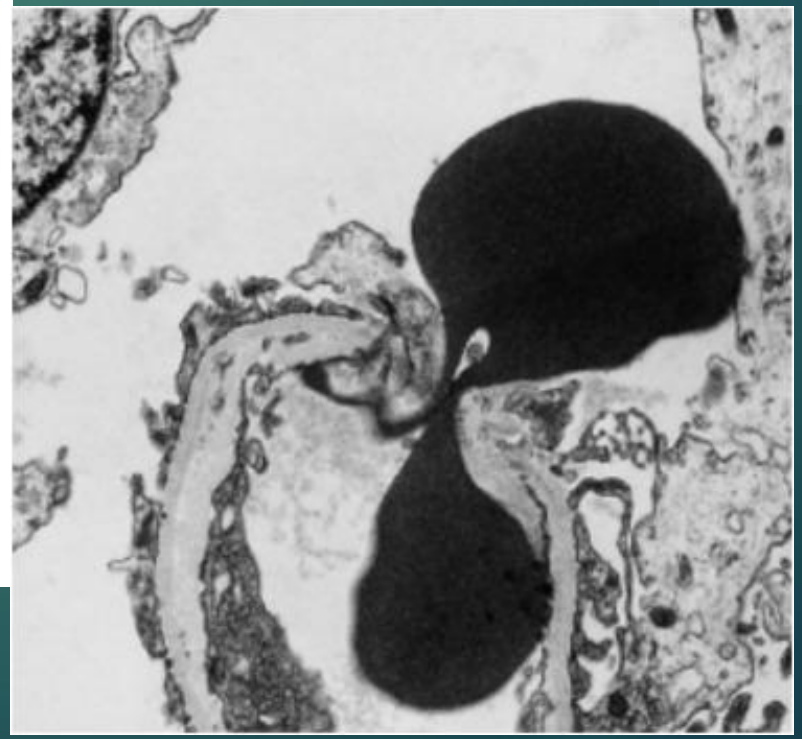

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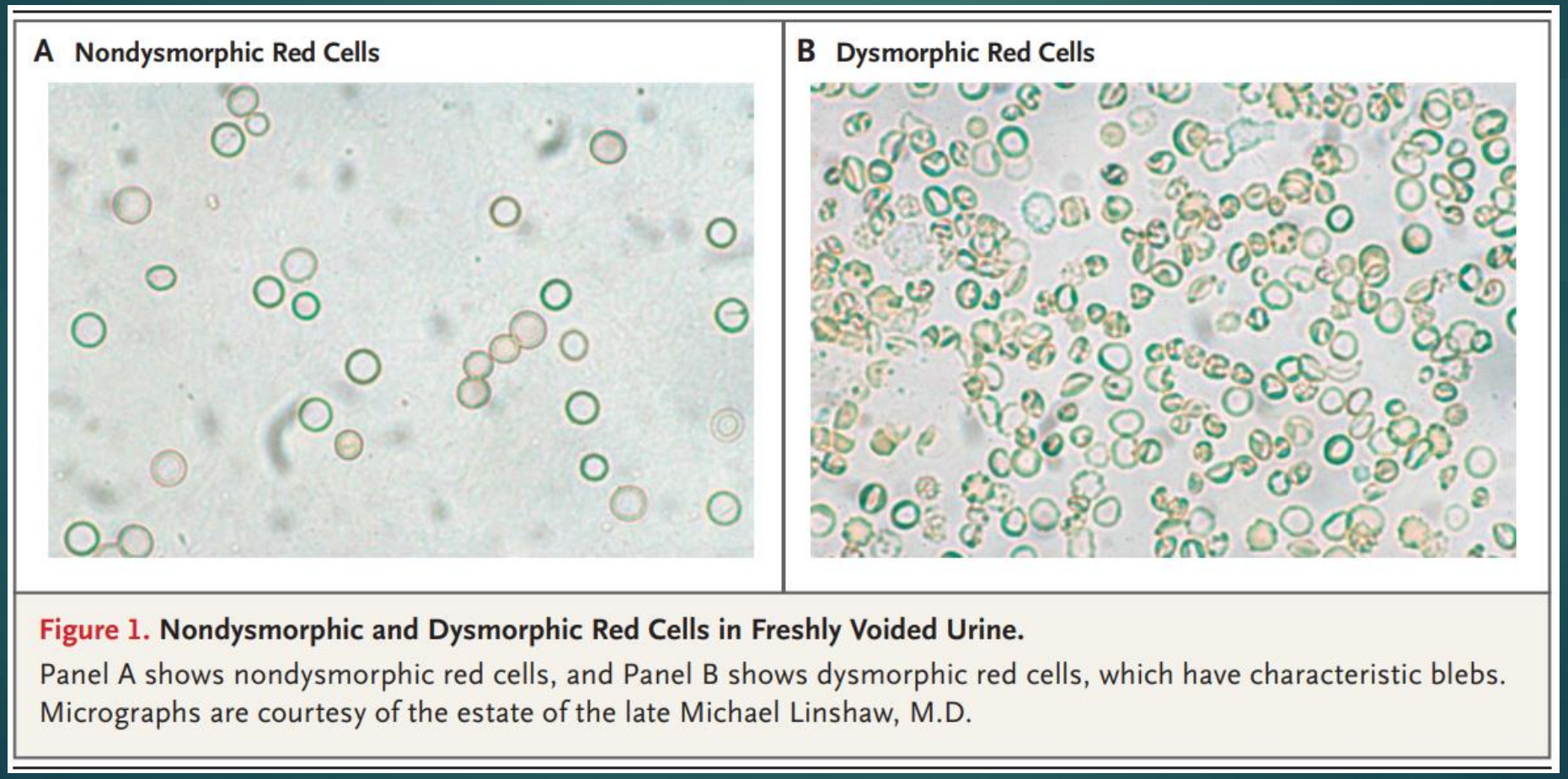

Figure 1. Nondysmorphic and Dysmorphic Red Cells in Freshly Voided Urine.
Panel A shows nondysmorphic red cells, and Panel B shows dysmorphic red cells, which have characteristic blebs. Micrographs are courtesy of the estate of the late Michael Linshaw, M.D.

Hematuria in Adults, *Julie R. Ingelfinger, M.D., N Engl J Med 2021; 385:153-163*
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Αιματουρία σε ασθενή με ΣΕΛ

- Ασθενής ♀, 33 ετών, με α/α ΣΕΛ υπό HCQ, εμφανίζει στη γ/ο (++) αιματουρία, με «ενεργό» ίζημα ούρων

uPCR ~1gr/gr

uPCR ~120mg/gr

Βιοψία νεφρού

Βιοψία νεφρού
ή
Follow up ???

Μπορεί το ίζημα ούρων να είναι παθογνωμικό;

Lupus (2001) 10, 418–423
© 2001 Arnold All rights reserved 0961–2033

Κλινική ΣΕΛ Πανεπιστημίου του Τορόντο → όλα τα επεισόδια μεμονωμένης αιματουρίας ή μεμονωμένης πυουρίας την περίοδο 1970 – 2000

- ✓ ***Μεμονωμένη αιματουρία → RBC >5 /κοπ,***
  μεμονωμένη άσηπτη πυουρία → WBC >5 /κοπ
- ✓ **nrSLEDAI στο 1° επεισόδιο μεμονωμένης αιματουρίας ή πυουρίας**
- ✓ **Ενεργότητα νεφρίτιδας του λύκου στις βιοψίες νεφρού που πραγματοποιήθηκαν εντός 3 μηνών**

Significance of isolated hematuria and isolated pyuria in systemic lupus erythematosus. ***Lupus***, Rahman, P et. al. (2001), *10*(6), 418–423. doi:10.1191/096120301678646164

Μπορεί το ίζημα ούρων να είναι παθογνωμικό;

Table 1 Prior and subsequent renal involvement in lupus patients with significant hematuria and pyuria

	Isolated hematuria	*Isolated pyuria*
Total number of episodes	989	408
Total number of patients	323	215
Age at onset of SLE	32.2 (14.1)	31.2 (13.8)
Disease duration at first episode	5.8 (6.0)	7.0 (7.2)
Non-renal SLEDAI at first episode	5.25 (5.8)	4.77 (5.0)
Total number with prior renal disease	140	127
Urinary characteristics of those with prior renal disease[a]		
proteinuria	69.3%	66.9%
casts	22.9%	25.2%
azotemia	10%	8.7%
hematuria	51.4	82.7%
pyuria	60%	45.7
Total number with first renal manifestation	183	88
Total number with subsequent renal disease	129	59
Urinary characteristics of those with		

Διαταραχές anti-ds-DNA ή/και συμπληρώματος σε >60% των ασθενών

Table 2 Renal biopsies within 3 months of detecting isolated hematuria and pyuria

	Isolated hematuria	*Isolated pyuria*
Total number of biopsies	22	12
Class I[a]	1 (4.5%)	0 (0%)
Class II	12 (56%)	6 (50%)
Class III	4 (18%)	4 (33%)
Class IV	4 (18%)	2 (17%)
Class V	1 (4.5%)	0 (0%)
Active renal biopsy[b]	12 (54%)	9 (75%)

[a]According to WHO classification.
[b]According to NIH activity index.

Significance of isolated hematuria and isolated pyuria in systemic lupus erythematosus. **Lupus**, Rahman, P et. al. (2001), *10*(6), 418–423. doi:10.1191/096120301678646164

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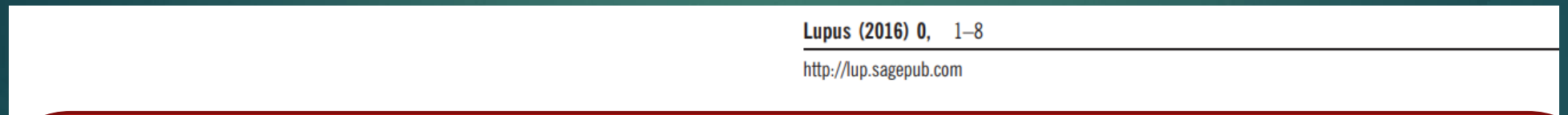
Lupus (2016) 0, 1–8
http://lup.sagepub.com

Ασθενείς με LN που επρόκειτο να υποβληθούν σε βιοψία νεφρού, λήψη δείγματος ούρων από κάθε ασθενή το πρωί προ της βιοψίας

- ✓ **Κρεατινίνη και uPCR**
- ✓ **Μέτρηση κυττάρων στα ούρα**
- ✓ **Μορφολογία ερυθροκυττάρων**
- ✓ **Βιοψία νεφρού**

Urinary sediment suggests lupus nephritis histology. MU Martínez-Martínez et. al., (2016). *Lupus*, (), 096120331666924 1–. doi:10.1177/0961203316669241

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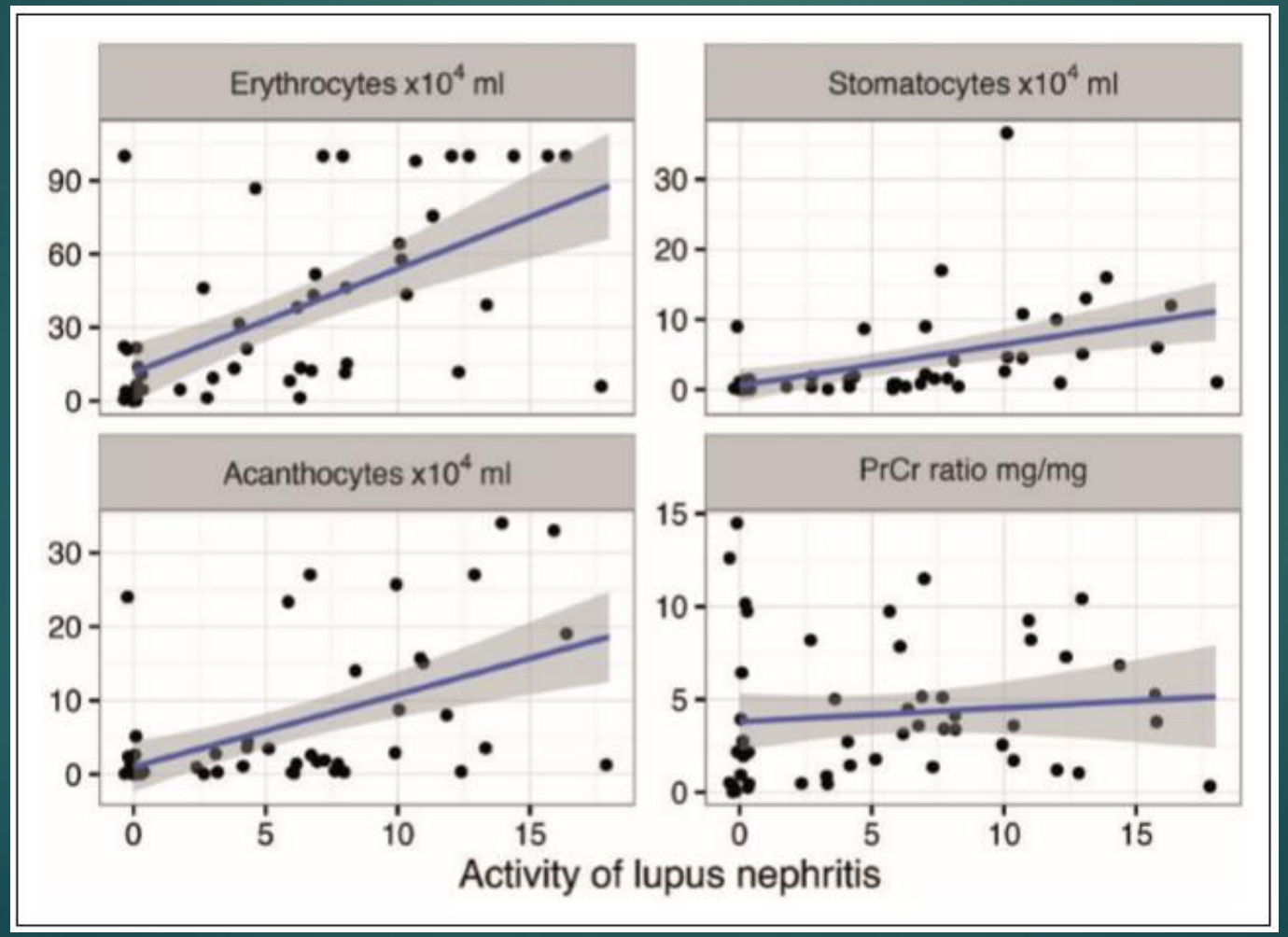

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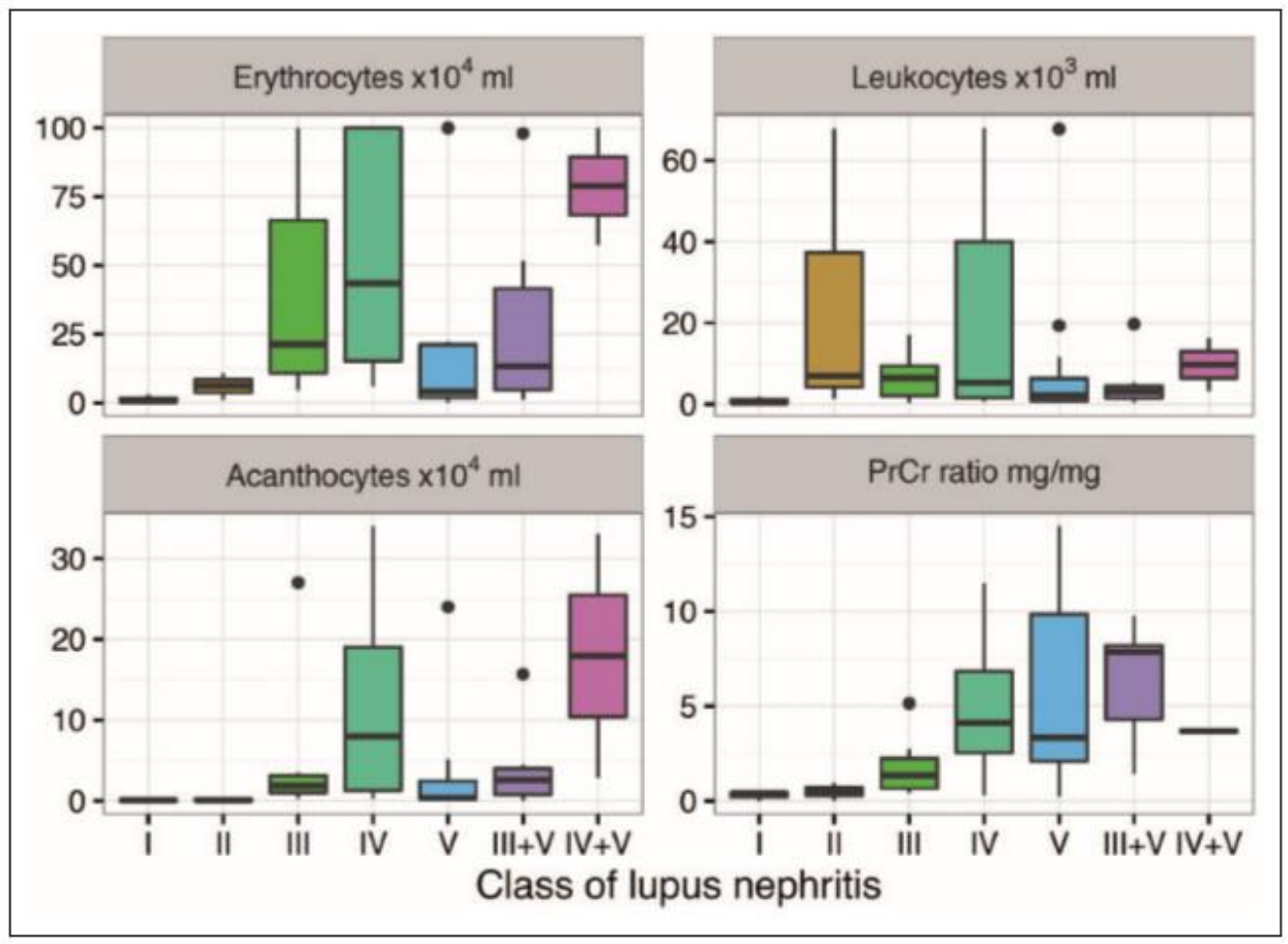

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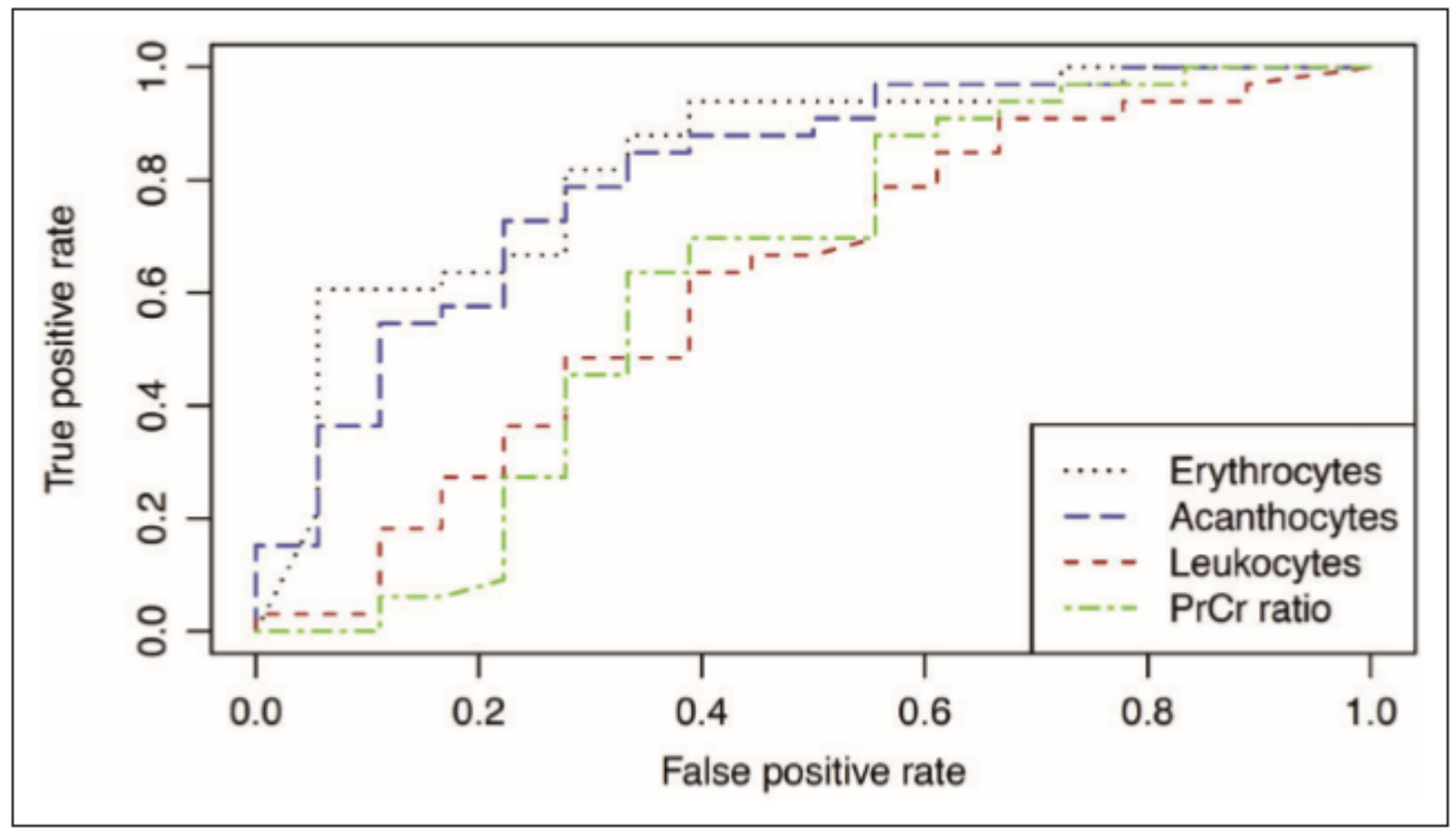

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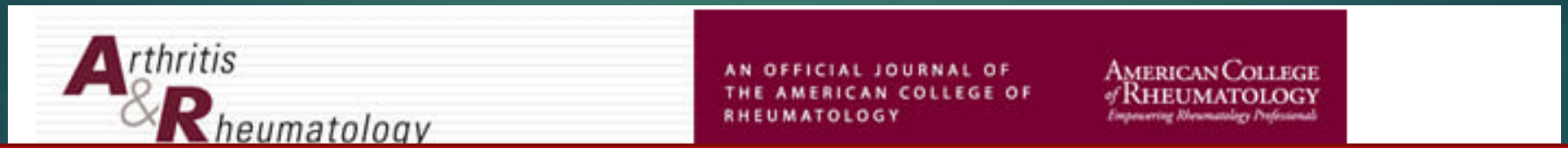


76 ασθενής από τη Euro-Lupus Nephritis Trial

- ✓ **Πρωτεϊνουρία**
- ✓ **serum Cr**
- ✓ **urinary RBC**

➢ **στους 3, 6, 12 μήνες, με παρακολούθηση τουλάχιστον 7 έτη**

Glomerular Hematuria: Cause or Consequence of Renal Inflammation? *Moreno JA et. Al., Int J Mol Sci. 2019 May 5;20(9):2205. doi: 10.3390/ijms20092205. PMID: 31060307; PMCID: PMC6539976.*

Μπορεί το ίζημα ούρων να είναι παθογνωμικό;

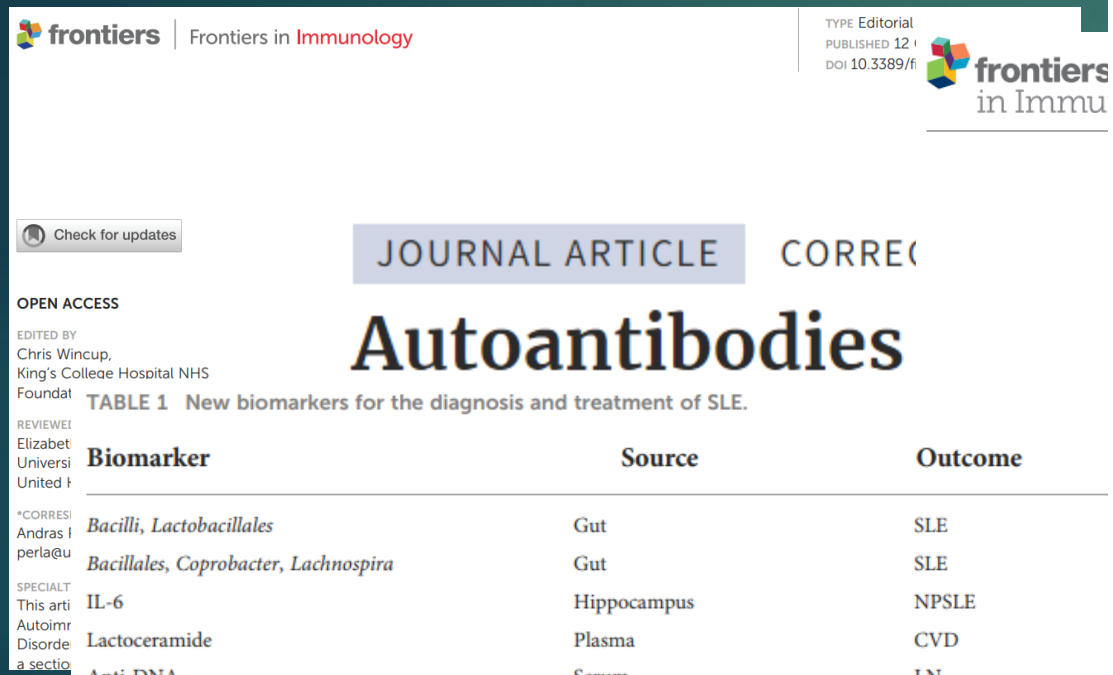
Table 1. Evaluation of selected predictors of good long-term renal function at 12 months*

Predictor, at 12 months	Sensitivity estimate (95% CI)	Specificity estimate (95% CI)	PPV estimate (95% CI)	NPV estimate (95% CI)
Single-criterion predictors				
Proteinuria ≤0.5 gm/day	0.64 (0.49–0.77)	0.83 (0.61–0.95)	0.88 (0.73–0.97)	0.53 (0.35–0.70)
Proteinuria <0.8 gm/day	0.81 (0.67–0.91)	0.78 (0.56–0.93)	0.88 (0.75–0.96)	0.67 (0.46–0.83)
Serum Cr ≤0.8 mg/dl	0.58 (0.43–0.72)	0.83 (0.61–0.95)	0.88 (0.71–0.96)	0.49 (0.32–0.65)
Serum Cr ≤1.0 mg/dl	0.90 (0.77–0.97)	0.48 (0.27–0.69)	0.78 (0.65–0.88)	0.69 (0.41–0.89)
Urinary RBCs ≤5/hpf	0.62 (0.47–0.76)	0.64 (0.41–0.83)	0.78 (0.61–0.90)	0.45 (0.27–0.64)
Composite predictors				
Proteinuria <0.8 gm/day *and* serum Cr ≤1.0 mg/dl	0.70 (0.55–0.83)	0.87 (0.66–0.97)	0.92 (0.78–0.98)	0.59 (0.41–0.75)
Proteinuria <0.8 gm/day *and* urinary RBCs ≤5/hpf	0.47 (0.32–0.62)	0.87 (0.66–0.97)	0.88 (0.69–0.97)	0.44 (0.30–0.60)
Proteinuria <0.8 gm/day *and* serum Cr ≤1.0 mg/dl *and* urinary RBCs ≤5/hpf	0.40 (0.26–0.56)	0.91 (0.72–0.99)	0.90 (0.70–0.99)	0.43 (0.29–0.58)
LUNAR study complete response†	0.32 (0.19–0.47)	0.91 (0.72–0.99)	0.88 (0.64–0.99)	0.40 (0.26–0.54)

* 95% CI = 95% confidence interval; PPV = positive predictive value; NPV = negative predictive value; Cr = creatinine; RBCs = red blood cells; hpf = high-power field.
† A complete response according to the Lupus Nephritis Assessment of Rituximab (LUNAR) study was a proteinuria value of ≤0.5 gm/day, a serum Cr level within 15% of baseline, and urinary RBCs ≤5/hpf.

Glomerular Hematuria: Cause or Consequence of Renal Inflammation? *Moreno JA et. Al., Int J Mol Sci. 2019 May 5;20(9):2205. doi: 10.3390/ijms20092205. PMID: 31060307; PMCID: PMC6539976.*

Βιοδείκτες για το ΣΕΛ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Autoantibodies

TABLE 1 New biomarkers for the diagnosis and treatment of SLE.

Biomarker	Source	Outcome
Bacilli, Lactobacillales	Gut	SLE
Bacillales, Coprobacter, Lachnospira	Gut	SLE
IL-6	Hippocampus	NPSLE
Lactoceramide	Plasma	CVD
Anti-DNA	Serum	LN
ABCB1, IFI27, PLSCR1	PBMC	SLE
P3H1, PHACTR4, RGS12	Serum	LN
ALCAM, VCAM-1 and PF4	Urine	LN
S100A8	Kidney	SLEDAI, LN
S100A8	Blood, Urine, Saliva	SLEDAI, LN
Adiponectin, MCP-1, sVCAM-1,PF4	Urine	LN
CD11c, T-bet, and CD21high B cells	Blood	LN

LN, lupus nephritis.

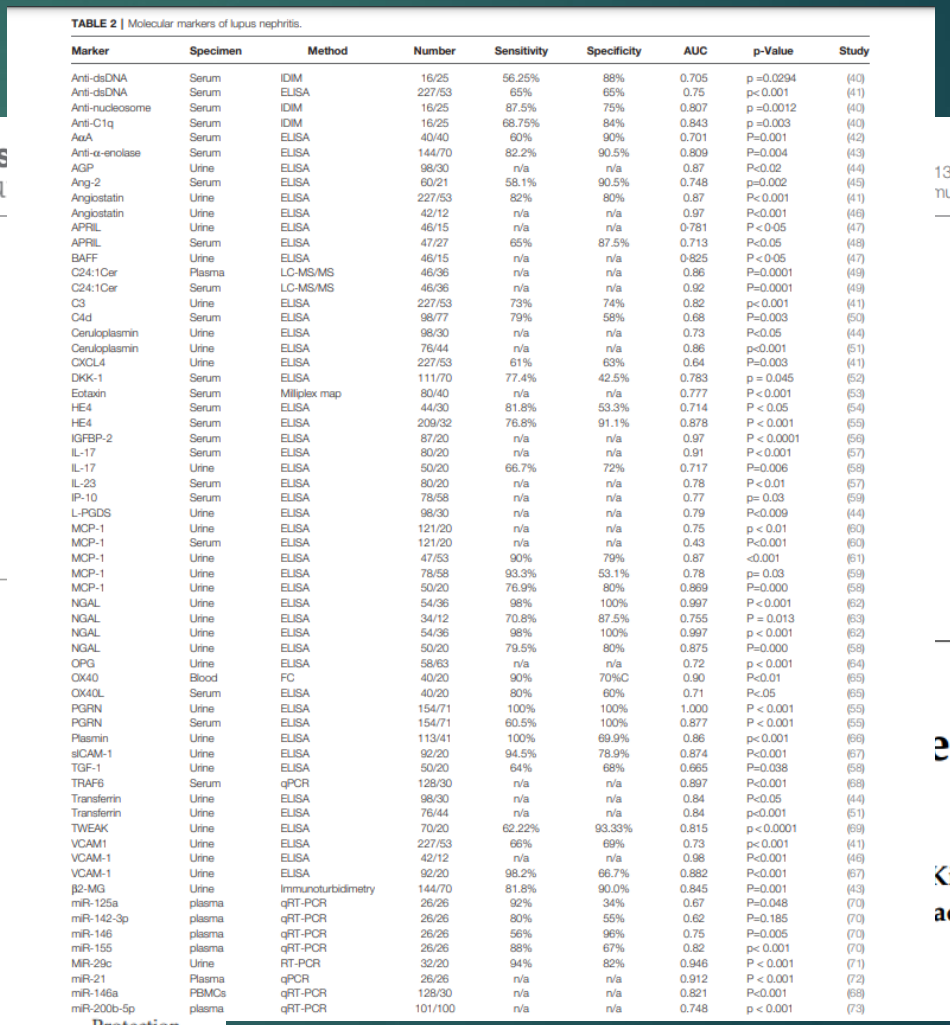


TABLE 2 | Molecular markers of lupus nephritis.

Marker	Specimen	Method	Number	Sensitivity	Specificity	AUC	p-Value	Study
Anti-dsDNA	Serum	IDIM	16/25	56.25%	88%	0.705	p =0.0294	(40)
Anti-dsDNA	Serum	ELISA	227/53	65%	65%	0.75	p< 0.001	(41)
Anti-nucleosome	Serum	IDIM	16/25	87.5%	75%	0.807	p =0.0012	(40)
Anti-C1q	Serum	IDIM	16/25	68.75%	84%	0.843	p =0.003	(40)
AqaA	Serum	ELISA	40/40	60%	90%	0.701	P=0.001	(42)
Anti-α-enolase	Serum	ELISA	144/70	82.2%	90.5%	0.809	P=0.004	(43)
AGP	Urine	ELISA	98/30	n/a	n/a	0.87	P<0.02	(44)
Ang-2	Serum	ELISA	60/21	58.1%	90.5%	0.748	p=0.002	(45)
Angiostatin	Urine	ELISA	227/53	82%	80%	0.87	P< 0.001	(41)
Angiostatin	Urine	ELISA	42/12	n/a	n/a	0.97	P<0.001	(46)
APRIL	Urine	ELISA	46/15	n/a	n/a	0·781	P < 0·05	(47)
APRIL	Serum	ELISA	47/27	65%	87.5%	0.713	P<0.05	(48)
BAFF	Urine	ELISA	46/15	n/a	n/a	0·825	P < 0·05	(47)
C24:1Cer	Plasma	LC-MS/MS	46/36	n/a	n/a	0.86	P=0.0001	(49)
C24:1Cer	Serum	LC-MS/MS	46/36	n/a	n/a	0.92	P=0.0001	(49)
C3	Urine	ELISA	227/53	73%	74%	0.82	p< 0.001	(41)
C4d	Serum	ELISA	98/77	79%	58%	0.68	P=0.003	(50)
Ceruloplasmin	Urine	ELISA	98/30	n/a	n/a	0.73	P<0.05	(44)
Ceruloplasmin	Urine	ELISA	76/44	n/a	n/a	0.86	p<0.001	(51)
CXCL4	Urine	ELISA	227/53	61%	63%	0.64	P=0.003	(41)
DKK-1	Serum	ELISA	111/70	77.4%	42.5%	0.783	p = 0.045	(52)
Eotaxin	Serum	Milliplex map	80/40	n/a	n/a	0.777	P < 0.001	(53)
HE4	Serum	ELISA	44/30	81.8%	53.3%	0.714	P < 0.05	(54)
HE4	Serum	ELISA	209/32	76.8%	91.1%	0.878	P < 0.001	(55)
IGFBP-2	Serum	ELISA	87/20	n/a	n/a	0.97	P < 0.0001	(56)
IL-17	Serum	ELISA	80/20	n/a	n/a	0.91	P < 0.001	(57)
IL-17	Urine	ELISA	50/20	66.7%	72%	0.717	P=0.006	(58)
IL-23	Serum	ELISA	80/20	n/a	n/a	0.78	P < 0.01	(57)
IP-10	Serum	ELISA	78/58	n/a	n/a	0.77	p= 0.03	(59)
L-PGDS	Urine	ELISA	98/30	n/a	n/a	0.79	P<0.009	(44)
MCP-1	Urine	ELISA	121/20	n/a	n/a	0.75	p < 0.01	(60)
MCP-1	Serum	ELISA	121/20	n/a	n/a	0.43	P<0.001	(60)
MCP-1	Urine	ELISA	47/53	90%	79%	0.87	<0.001	(61)
MCP-1	Urine	ELISA	78/58	93.3%	53.1%	0.78	p= 0.03	(59)
MCP-1	Urine	ELISA	50/20	76.9%	80%	0.869	P=0.000	(58)
NGAL	Urine	ELISA	54/36	98%	100%	0.997	P < 0.001	(62)
NGAL	Urine	ELISA	34/12	70.8%	87.5%	0.755	P = 0.013	(63)
NGAL	Urine	ELISA	54/36	98%	100%	0.997	p < 0.001	(62)
NGAL	Urine	ELISA	50/20	79.5%	80%	0.875	P=0.000	(58)
OPG	Urine	ELISA	58/63	n/a	n/a	0.72	p < 0.001	(64)
OX40	Blood	FC	40/20	90%	70%C	0.90	P<0.01	(65)
OX40L	Serum	ELISA	40/20	80%	60%	0.71	P<.05	(65)
PGRN	Urine	ELISA	154/71	100%	100%	1.000	P < 0.001	(55)
PGRN	Serum	ELISA	154/71	60.5%	100%	0.877	P < 0.001	(55)
Plasmin	Urine	ELISA	113/41	100%	69.9%	0.86	p< 0.001	(66)
sICAM-1	Urine	ELISA	92/20	94.5%	78.9%	0.874	P<0.001	(67)
TGF-1	Urine	ELISA	50/20	64%	68%	0.665	P=0.038	(58)
TRAF6	Serum	qPCR	128/30	n/a	n/a	0.897	P<0.001	(68)
Transferrin	Urine	ELISA	98/30	n/a	n/a	0.84	P<0.05	(44)
Transferrin	Urine	ELISA	76/44	n/a	n/a	0.84	p<0.001	(51)
TWEAK	Urine	ELISA	70/20	62.22%	93.33%	0.815	p < 0.0001	(69)
VCAM1	Urine	ELISA	227/53	66%	69%	0.73	p< 0.001	(41)
VCAM-1	Urine	ELISA	42/12	n/a	n/a	0.98	P<0.001	(46)
VCAM-1	Urine	ELISA	92/20	98.2%	66.7%	0.882	P<0.001	(67)
β2-MG	Urine	Immunoturbidimetry	144/70	81.8%	90.0%	0.845	P=0.001	(43)
miR-125a	plasma	qRT-PCR	26/26	92%	34%	0.67	P=0.048	(70)
miR-142-3p	plasma	qRT-PCR	26/26	80%	55%	0.62	P=0.185	(70)
miR-146	plasma	qRT-PCR	26/26	56%	96%	0.75	P=0.005	(70)
miR-155	plasma	qRT-PCR	26/26	88%	67%	0.82	p< 0.001	(70)
MR-29c	Urine	RT-PCR	32/20	94%	82%	0.946	P < 0.001	(71)
miR-21	Plasma	qPCR	26/26	n/a	n/a	0.912	P < 0.001	(72)
miR-146a	PBMCs	qRT-PCR	128/30	n/a	n/a	0.821	P<0.001	(68)
miR-200b-5p	plasma	qRT-PCR	101/100	n/a	n/a	0.748	p < 0.001	(73)

Protection

REVIEW
13 January 2022
nu.2021.808839

Check for updates

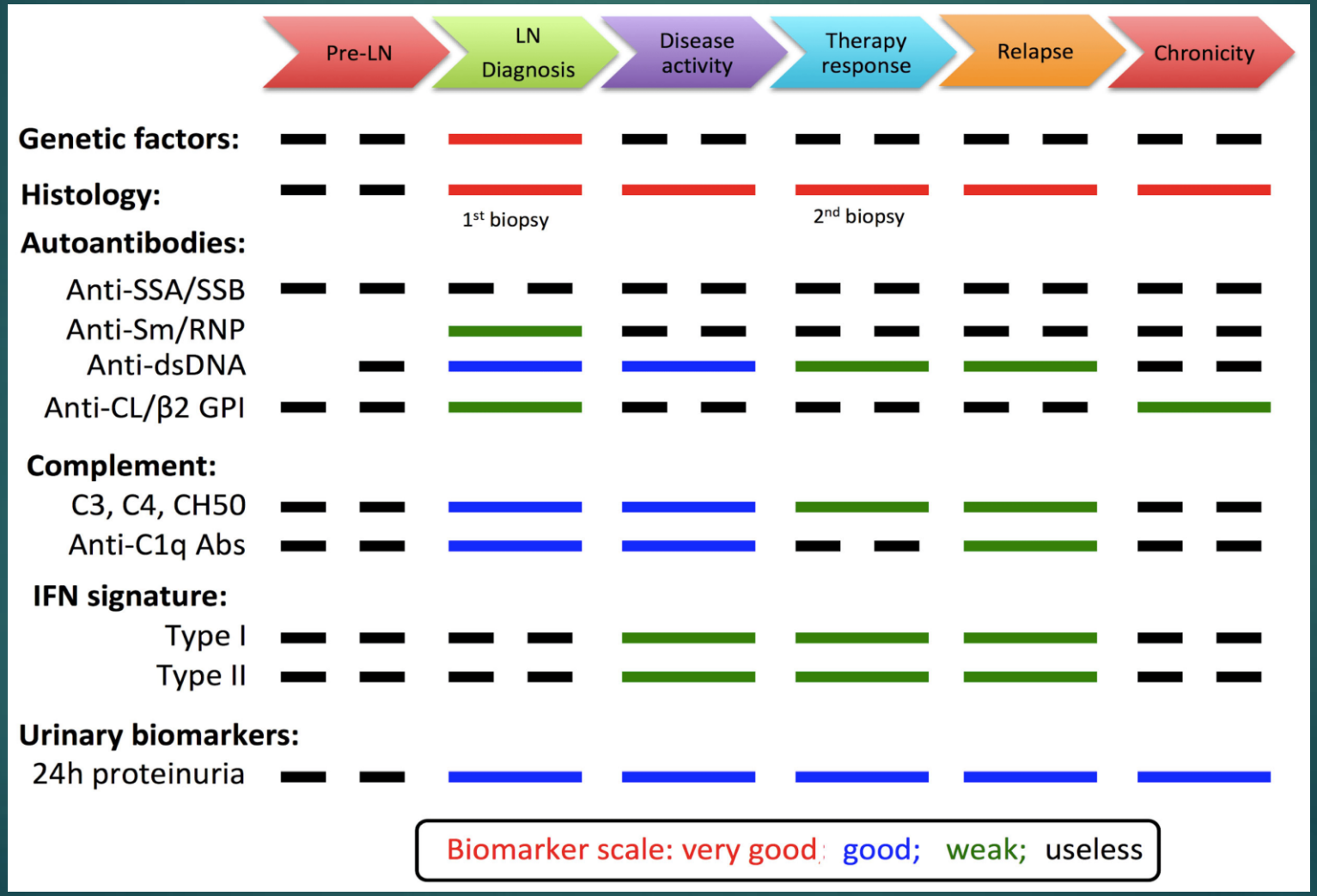
ch & Therapy

MDPI

ers of

Kit-Chung Ng [1], ac-Moune Lai [3]

Βιοδείκτες για το ΣΕΛ



Lupus Nephritis Risk Factors and Biomarkers: An Update., Renaudineau, Y. et. al.. Int. J. Mol. Sci. **2023**, 24, 14526. https://doi.org/10.3390/ijms241914526

Βιοψία ή όχι;

Recommendation

2019 Update of the Joint European League Against Rheumatism and European Renal Association–European Dialysis and Transplant Association (EULAR/ERA–EDTA) recommendations for the management of lupus nephritis

Antonis Fanouriakis ,[1,2] Myrto Kostopoulou,[3] Kim Cheema,[4] Hans-Joachim Anders,[5] Martin Aringer ,[6] Ingeborg Bajema,[7] John Boletis,[8] Eleni Frangou,[9] Frederic A Houssiau ,[10] Jane Hollis,[11] Adexandre Karras,[12] Francesca Marchiori,[13] Stephen D Marks,[14] Gabriella Moroni ,[15] Marta Mosca,[16] Ioannis Parodis ,[17] Manuel Praga,[18] Matthias Schneider,[19] Josef S Smolen,[20] Vladimir Tesar,[21] Maria Trachana,[22] Ronald F van Vollenhoven ,[23] Alexandre E Voskuyl,[24] Y K Onno Teng,[25] Bernadette van Leew,[26] George Bertsias,[27] David Jayne,[4] Dimitrios T Boumpas [1,28]

Glomerular Hematuria: Cause or Consequence of Renal Inflammation? Moreno JA et. Al., Int J Mol Sci. 2019 May 5;20(9):2205. doi: 10.3390/ijms20092205. PMID: 31060307; PMCID: PMC6539976.

Βιοψία ή όχι;

Table 2 Overarching principles and recommendations for the management of patients with LN

Overarching principles		
Kidney involvement in SLE, … physician decisions.		… shared patient–
Vigilance for symptoms and …		…timal outcomes.
Goals of treatment include … and improvement in disease		…f comorbidities
Management of active phas… intensive therapy to consoli…		…sually less
Recommendation/statem…		**…oA, mean (SD)**
1. Investigation of the patie…		
1.1 Kidney biopsy should be … ≥0.5 g/24 hours (or UPCR ≥… and/or an unexplained decr…		…84 (0.54)
1.2 Kidney biopsy remains indispensable and its diagnostic and prognostic value cannot be substituted by other clinical or laboratory variables.	2b/B	9.96 (0.20)

Recommendations

Investigation of the patient with suspected LN

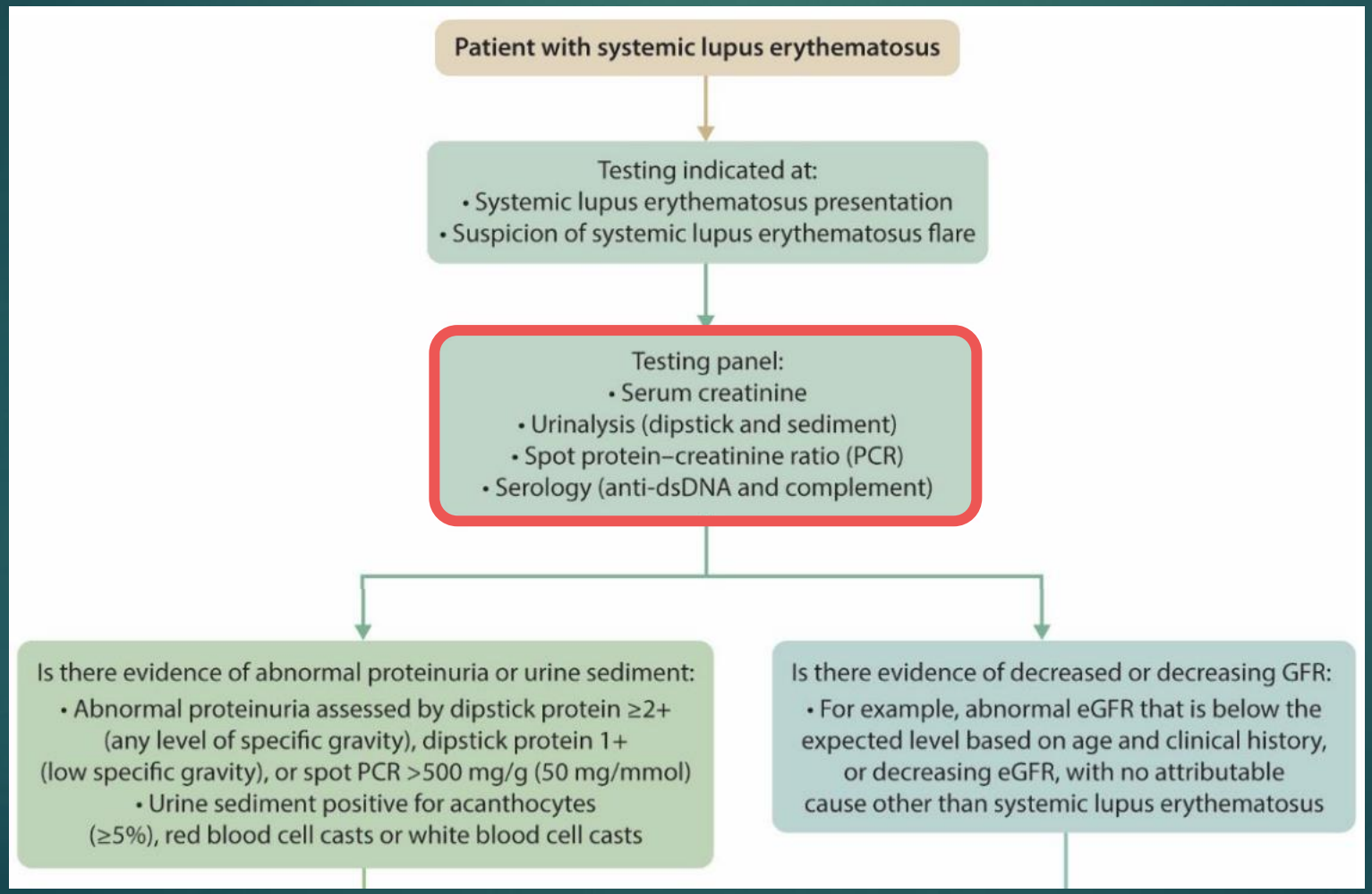
Patients with SLE with any sign of kidney involvement (glomerular haematuria and/or cellular casts, proteinuria >0.5 g/24 hours (or spot urine protein-to-creatine ratio (UPCR) >500 mg/g), unexplained decrease in glomerular filtration rate (GFR)) are candidates for kidney biopsy. Mild clinical presentations (eg, subnephrotic proteinuria) can nonetheless be associated with active histological lesions.[9–11] In a review of kidney biopsies

2019 Update of the Joint European League Against Rheumatism and European Renal Association-European Dialysis and Transplant Association (EULAR/ERA-EDTA) recommendations for the management of lupus nephritis. *Fanouriakis A et. al., Ann Rheum Dis. 2020 Jun;79(6):713-723. doi: 10.1136/annrheumdis-2020-216924. Epub 2020 Mar 27. PMID: 32220834.*

Βιοψία ή όχι;

KDIGO 2023 CLINICAL PRACTICE GUIDELINE FOR THE MANAGEMENT OF LUPUS NEPHRITIS

Βιοψία ή όχι;



KDIGO 2023 CLINICAL PRACTICE GUIDELINE FOR THE MANAGEMENT OF LUPUS NEPHRITIS

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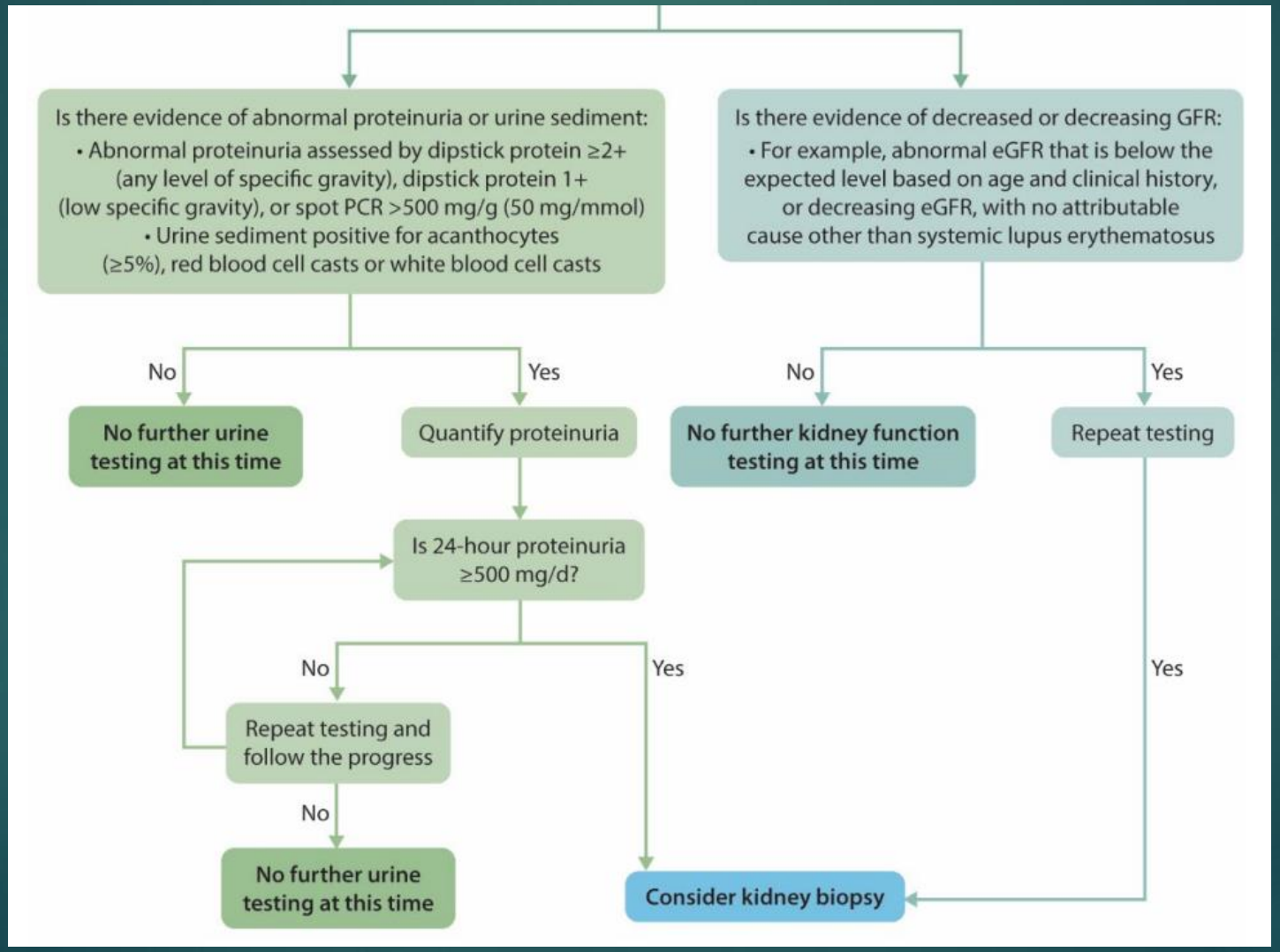

KDIGO 2023 CLINICAL PRACTICE GUIDELINE FOR THE MANAGEMENT OF LUPUS NEPHRITIS

Αιματουρία σε ασθενή με ΣΕΛ

- Ασθενής ♀, 33 ετών, με α/α ΣΕΛ υπό HCQ, εμφανίζει στη γ/ο (++) αιματουρία, με «ενεργό» ίζημα ούρων

uPCR ~1gr/gr

Βιοψία νεφρού

uPCR ~120mg/gr

Βιοψία νεφρού
ή
Follow up ???

Αιματουρία σε ασθενή με ΣΕΛ

- Ενεργότητα ΣΕΛ
- Ιστορικό LN
- Θεραπεία που λαμβάνει ήδη ο/η ασθενής
- Ίζημα ούρων
- Πρωτεϊνουρία, νεφρική λειτουργία
- Anti-ds-DNA, συμπληρώματα