Bracketology

www.AJKDBlog.org

March 1-31, 2026

Slides Prepared by the NephMadness Executive Committee

- Matthew Sparks
- Anna Burgner
- Anna Vinnikova
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- Ana Catalina Alvarez-Elías
- Dia Waguespack
- Samira Farouk
- Krithika Mohan

What to do

- Review the Regions & Teams on *AJKD*Blog
- Submit your picks by March 31, 2026, on Tourneytopia
- Discuss on social media using #NephMadness
- Claim CME/MOC credit through NKF PERC

The BRP Has Chosen the Winning Bracket

To win, predict what the BRP thinks will bring the most practice change to nephrology!

- Timothy Yau
- Prabir Roy-Chaudhury
- Kirk Campbell
- Meredith Atkinson
- Lori-Ann Fisher
- William Whittier
- Yara Mouawad
- Christel Wekon-Kemeni
- Giftay Kingston

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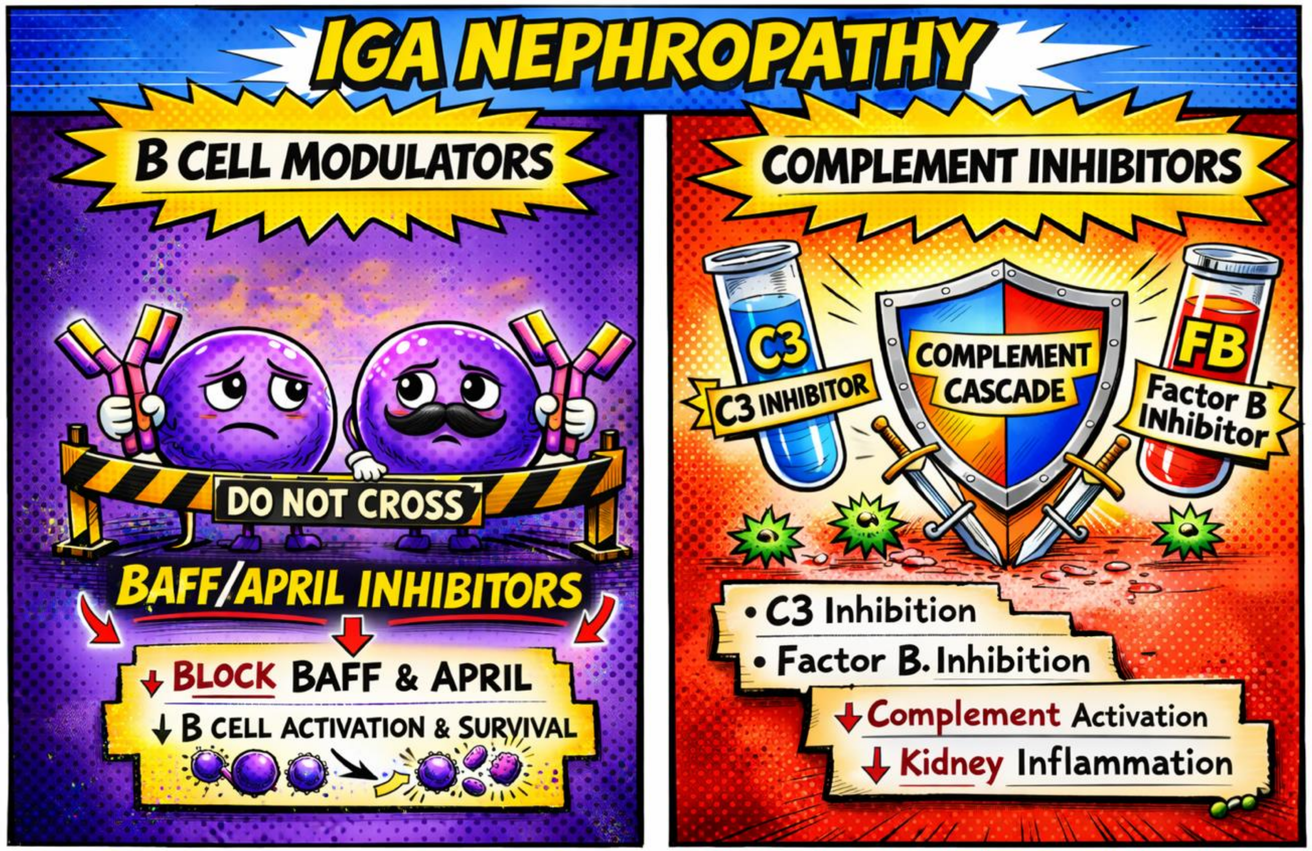
IgA Nephropathy



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Four-Hit Model in the Pathogenesis of IgA Nephropathy

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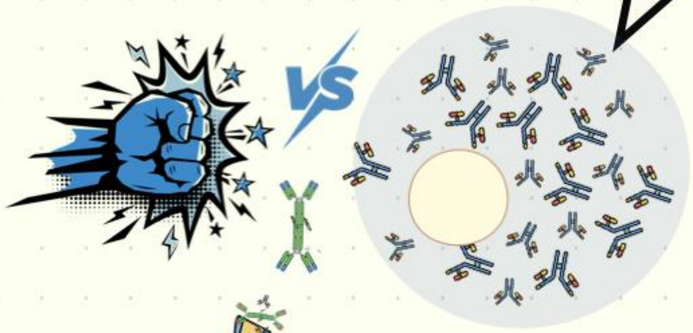
Hit 1

Increased production and circulation levels of a galactose-deficient IgA1 (Gd-IgA1)

Gd-IgA1 secreted by gut or respiratory tract

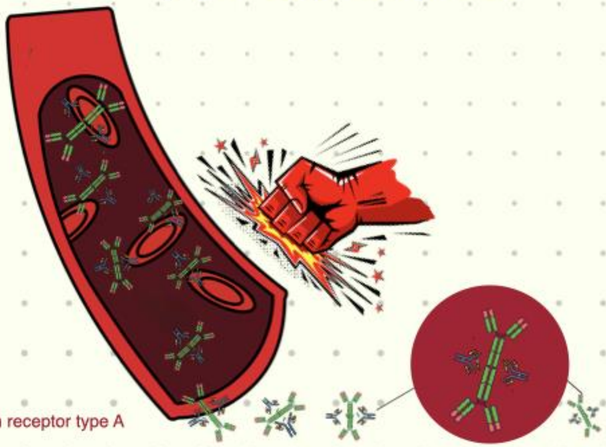
Hit 2

Production of auto-anti-antibodies against Gd-IgA1 (Self-antigen)



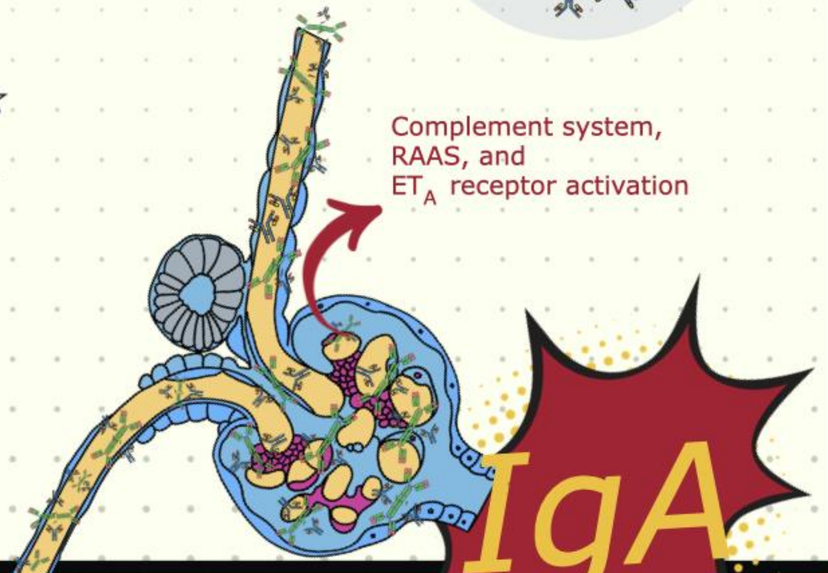
Hit 3

Formation of circulating nephritogenic immune complexes with anti-Gd-IgA1-IgG, IgA, and/or IgM



Hit 4

Binding of circulating immune complexes to mesangial cells



RAAS,renin-angiotensin-aldosterone system; ET , endothelin receptor type A
A

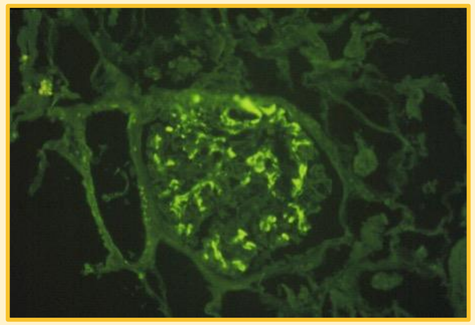
El Karoui K.et al.,CJASN, 2024

VA by **Elba Medina**

Conclusion: IgA nephropathy stems from deficient IgA1 galactosylation, which triggers a 'four-hit' process. This sequence involves Gd-IgA1 immune complex deposition in the mesangium, leading to glomerular and tubulointerstitial injury, intensified by activation of the complement system, RAAS, and endothelin pathway, ultimately provoking inflammation and fibrosis.

The Oxford classification, (MEST-C score), used as an initial assessment of disease severity.
5 key components:

- **M**esangial hypercellularity
- **E**ndocapillary hypercellularity
- **S**egmental glomerulosclerosis
- **T**ubular atrophy/interstitial fibrosis
- **C**rescent formation



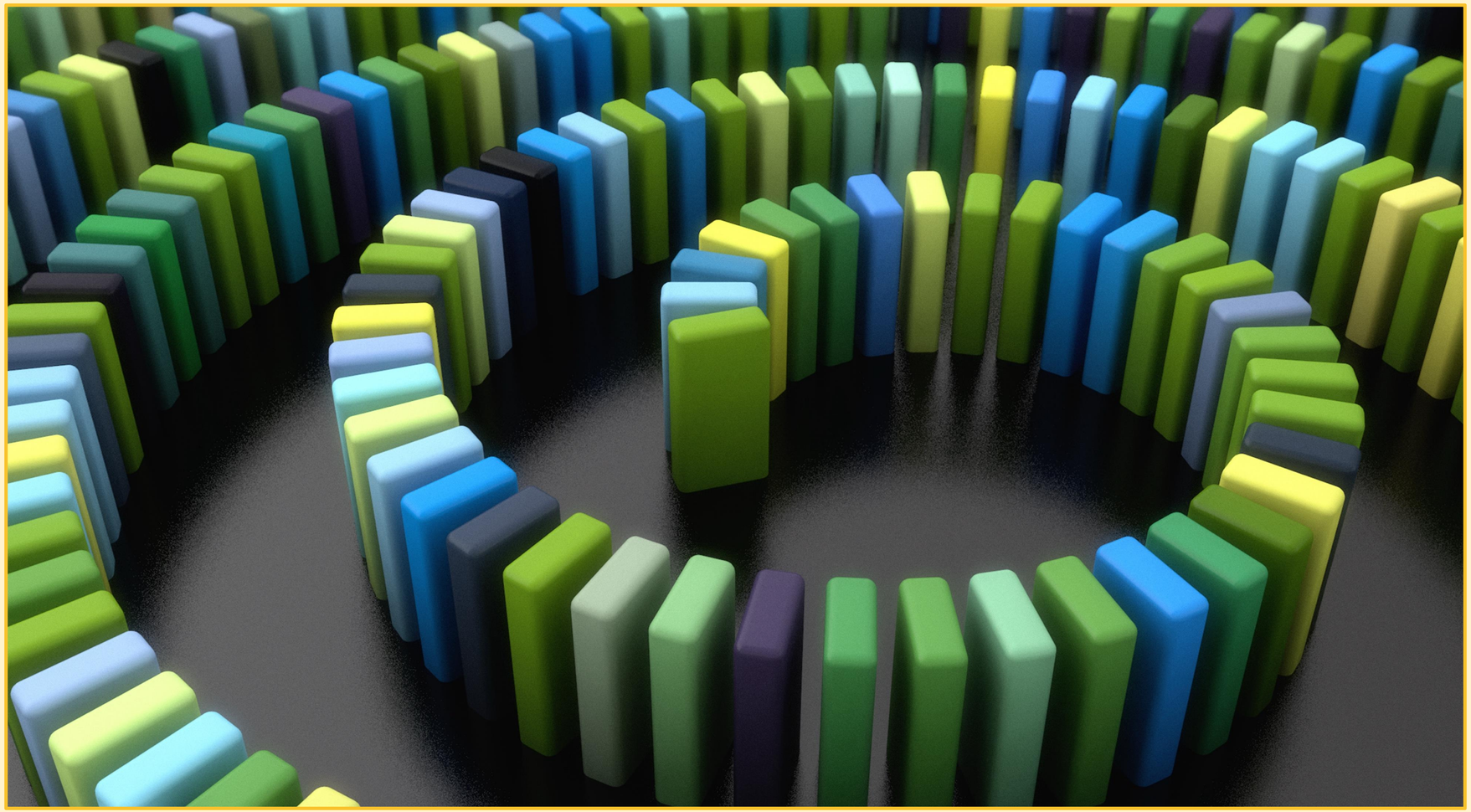
International IgAN Prediction Tool to help determine prognosis in adults with IgA nephropathy for up to two years following initial biopsy

2025 KDIGO Guidelines for IgA nephropathy

1. Stopping the production of pathogenic IgA and associated immune complex formation as well as resultant kidney injury
2. Reducing glomerular hyperfiltration and proteinuria
3. Managing hypertension.

Non-disease-specific interventions to manage BP, reduce glomerular hyperfiltration, proteinuria
-RAS inhibitors, -SGLT-2 inhibitors, -endothelin receptor antagonists (ERAs) or
-dual endothelin angiotensin receptor antagonists (DEARAs)
Disease modifying steroids, targeted-budesonide, **B-Cell modulators**, **anti-complement**

New B-Cell Targets



Team B-Cell Modulators

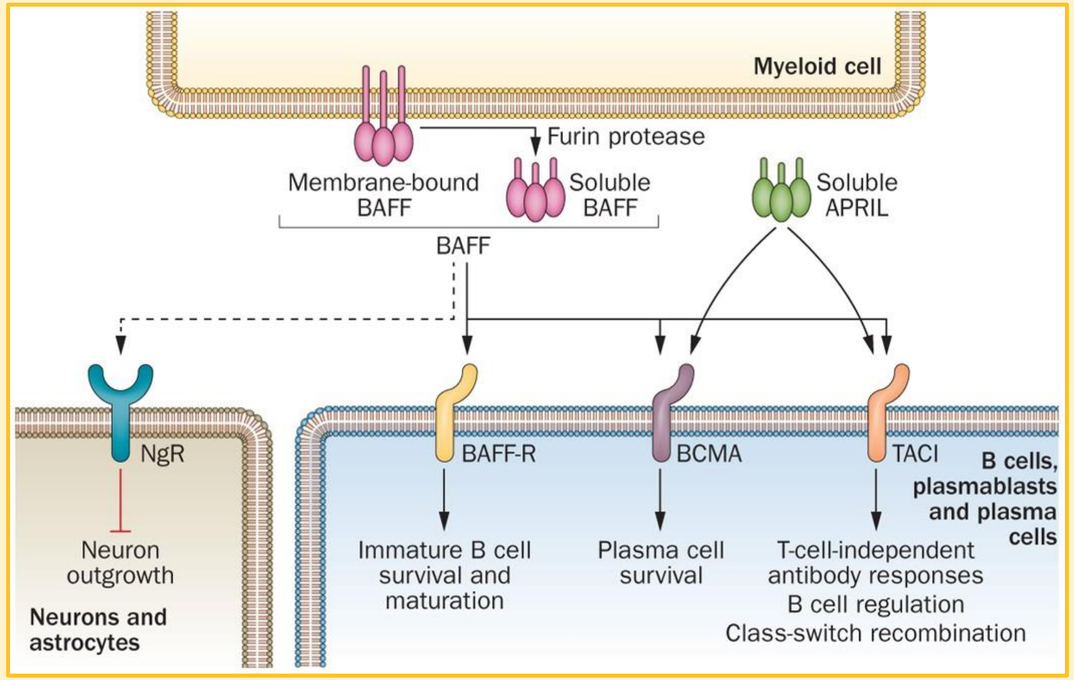
Let's meet our two cytokines that will be targeted. Both are important for B-Cell function.

BAFF- B-cell **A**ctivating **F**actor **F**amily
APRIL- A PRoliferation-**I**nducing **L**igand

BAFF facilitates peripheral B cell selection and survival, as well as helps maintain follicular- and marginal-zone B cell populations.

APRIL allows for antibody class-switching and ultimately their differentiation into antibody-secreting plasma cells.

Work by reducing aberrant IgA molecule (Gd-IgA1), reduce the production of IgG and IgA autoantibodies against Gd-IgA1, and reduce the formation of immune complexes containing IgG, IgA, and Gd-IgA1.



Vincent FB, et al Nat Rev Rheumatol. 2014 PMID: 24614588.

The players

Atacicept- A fully human recombinant fusion protein provided as a once-weekly subcutaneous injection, atacicept targets both BAFF and APRIL.
Ongoing phase 3 ORIGIN trial
- 203 patients were included in this prespecified analysis (106 in the atacicept and 97 in the placebo group)
- 46% reduction in proteinuria (7% in the placebo)
- Resolution of hematuria in 81% (21% in the placebo).

The phase 2 ORIGIN trial
- 60% decrease in circulating Gd-IgA1, 36% reduction in IgG, 64% in IgA, and 75% in IgM

The phase 2b extension trial
- sustained reduction in proteinuria (by 52%), hematuria, and circulating Gd-IgA1 levels at 96 weeks
- stabilization of eGFR (mean eGFR slope 0.6 mL/min/1.73 m2).
- We are awaiting FDA approval at the time of this publication.

Sibeprenlimab- A humanized monoclonal antibody that targets APRIL alone as a monthly subcutaneous injection. Has received conditional FDA approval.

VISIONARY: Safety and Efficacy of Sibeprenlimab in Patients with IgA Nephropathy

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- Multicenter (Phase 3)
- Double-blind
- IgA Nephropathy (Biopsy proven) n=320
- RASi SGLT2i

- 40 years Mean age
- 55% Male
- 40% White 55% Asian
- eGFR 63 Mean eGFR
- 1.2 g/g Mean UPCR

1:1 RANDOMIZATION

	Month 9	Reduction in 24 hr UPCR	Adverse Events	Gd IgA1 Levels (Week 48)	Reduction in APRIL (Week 48)
		PRIMARY OUTCOME	SECONDARY OUTCOMES		
Sibeprenlimab 400 mg SC/ 4 weeks n=152		-50%	3.5%	-67%	-96%
		p<0.001	No deaths		
Placebo n=168		+2%	4.4%	-1%	-26%

** UPCR, Urine protein-to-creatinine ratio; Gd IgA1, Galactose deficient IgA1, APRIL, A Proliferation Inducing Ligand*

Perkovic V, et al, NEJM, 2025

VA by **Edgar Lerma, MD**

Conclusion: Sibeprenlimab resulted in a significant reduction in proteinuria as compared with placebo in patients with IgA nephropathy

Complement Inhibition

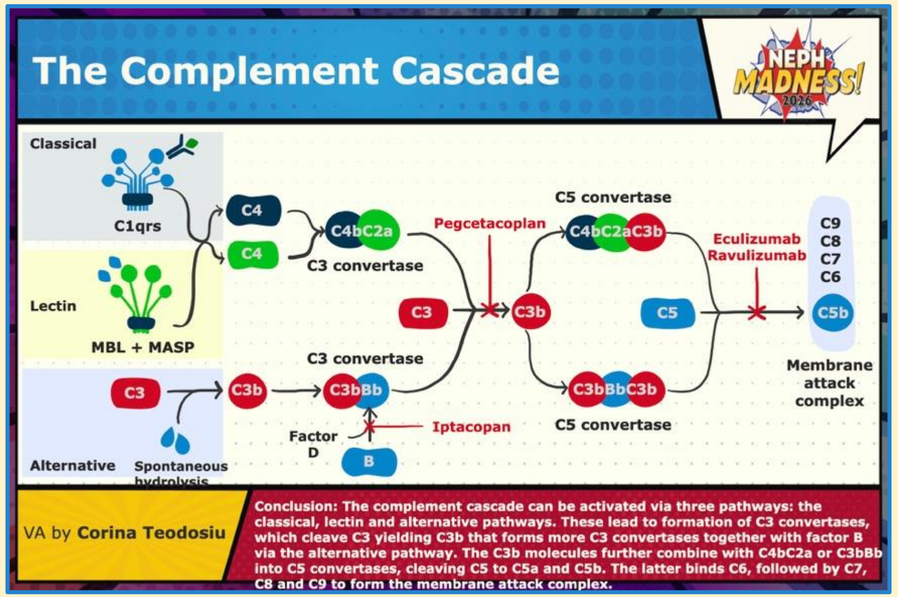
Team Complement Inhibitors

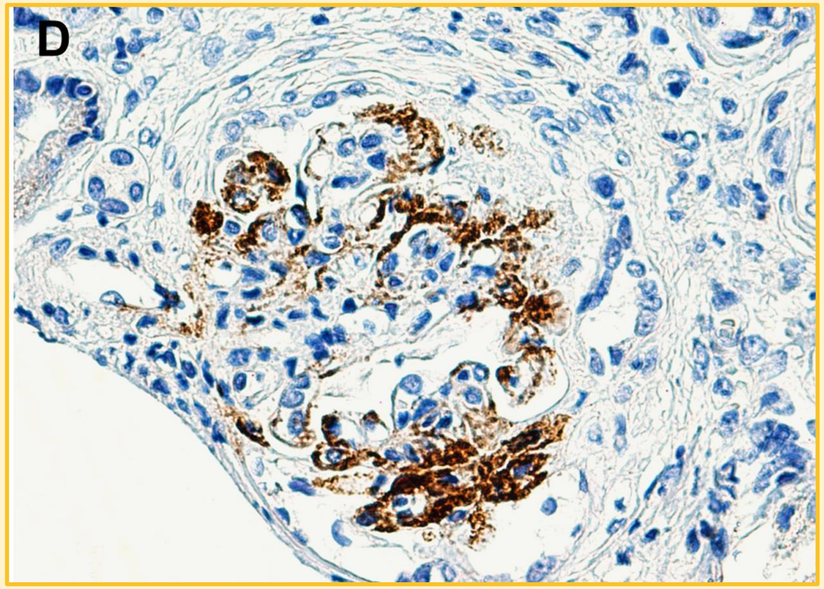
Evidence of complement deposition in glomeruli in IgA nephropathy is common.

The alternative and lectin pathways have been most implicated.

Role of complement inhibitors in the management of IgA nephropathy has gained significant traction.

Need vaccination to encapsulated bacteria- *Streptococcus pneumoniae, Neisseria meningitidis*





Faria B et al Am J Kidney Dis. 2020 PMID: 32439421.

Meet the players

- **Iptacopan** (ip-TAH-kopan)- An oral complement factor B inhibitor, works by blocking the alternative complement pathway, inhibiting Factor B preventing the formation of C3 convertase (C3bBb), inhibiting the cleavage of C3 dampening inflammation. Has received conditional FDA approval.
- **Pegcetacoplan** (Peg-sitta-co-plan) (a C3 inhibitor)- still under development.
- **Ravulizumab** (Rav-u-Liz-ooh-mab)(a long-acting C5 inhibitor similar to eculizumab)- Phase 3 I CAN Trial Starting

APPLAUSE-IgAN: Safety and Efficacy of Iptacopan in Patients with IgA Nephropathy

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- Multicenter (Phase 3)
- Double-blind
- IgA Nephropathy (Biopsy proven) n=443 *(n=250 in interim analysis)*

Prespecified Interim Analysis: When 1st 250 patients reached Month 9 or discontinued the study

- RASi
- SGLT2i

- 39 years Mean age
- 52% Male
- 51% Asian
- eGFR ≥30 Mean eGFR
- >1 g/g Mean UPCR

1:1 RANDOMIZATION

Month 9	Adjusted geometric Mean 24 hr UPCR	SAEs
	PRIMARY OUTCOME	
Iptacopan 200 mg BID n=125	44%	8% Mostly mild to moderate in severity and reversible
	38.3% (95% CI 26.0-48.6) *2-sided p <0.001*	
Placebo n=125	9%	5%

The reduction in proteinuria was supported by consistent results in secondary endpoint analyses

No increased risk of infection

* UPCR, Urine protein-to-creatinine ratio; SAEs. Serious Adverse Events

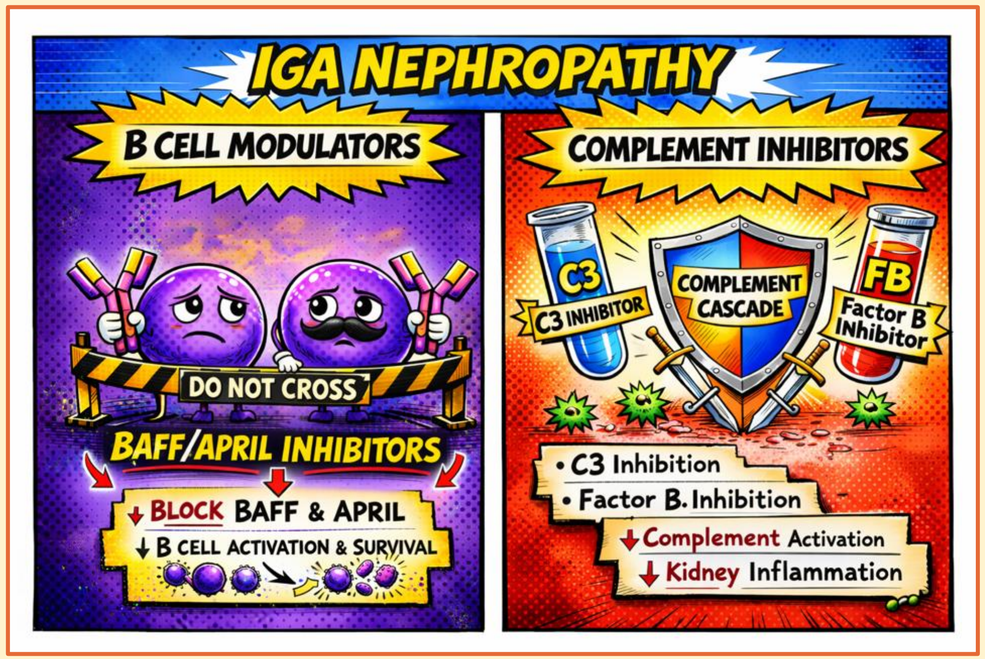
Perkovic V, et al, NEJM, 2025

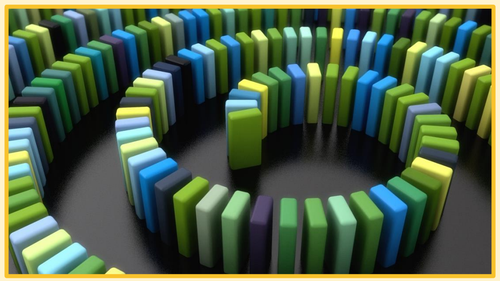
VA by **Edgar Lerma, MD**

Conclusion: Among patients with IgA nephropathy, treatment with iptacopan resulted in a significant and clinically meaningful reduction in proteinuria as compared with placebo.

EFFLUENT EIGHT ROUND

Pick Your Champion for the IgA Nephropathy Region





New B-Cell Targets

VS

Complement Inhibition

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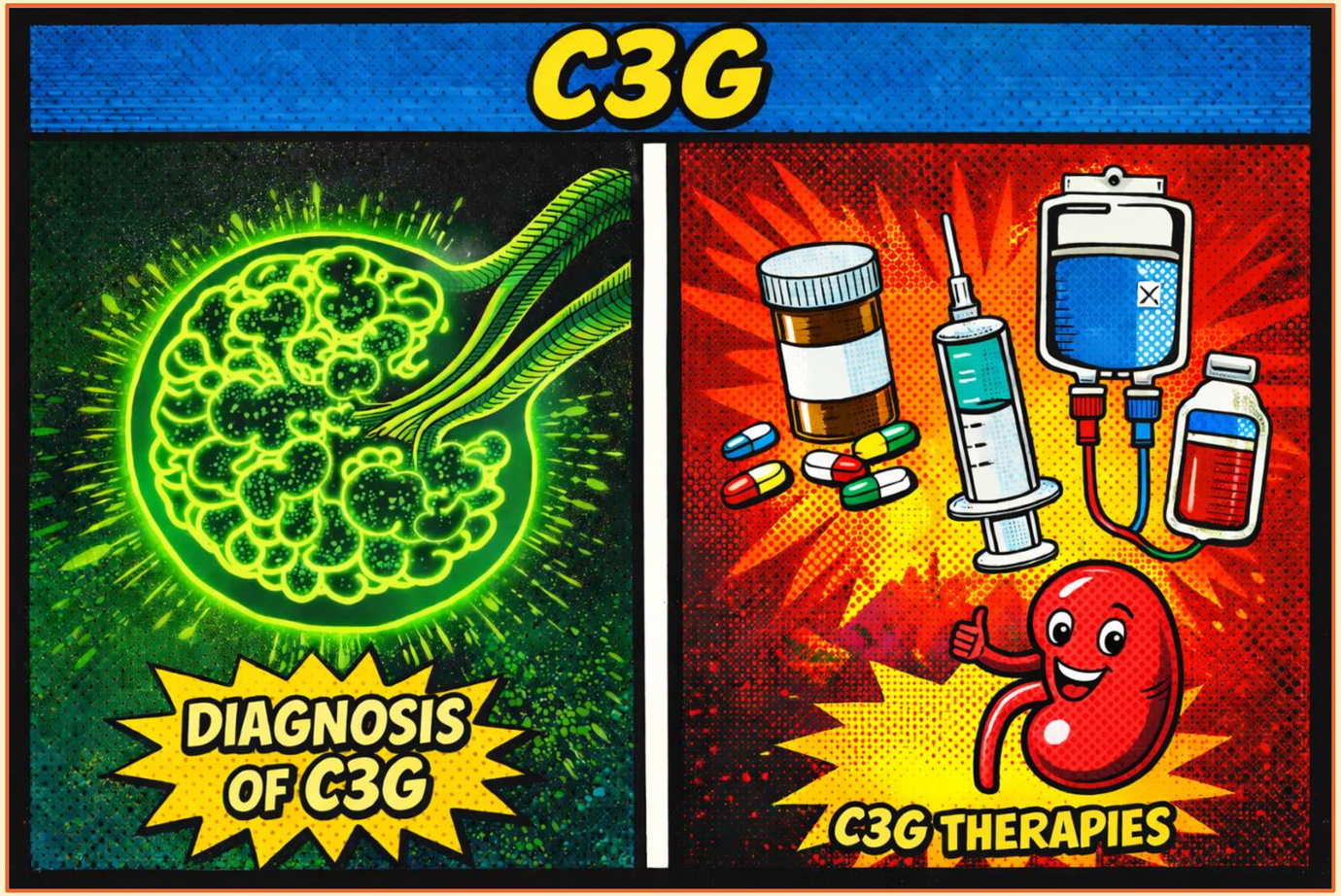
C3G



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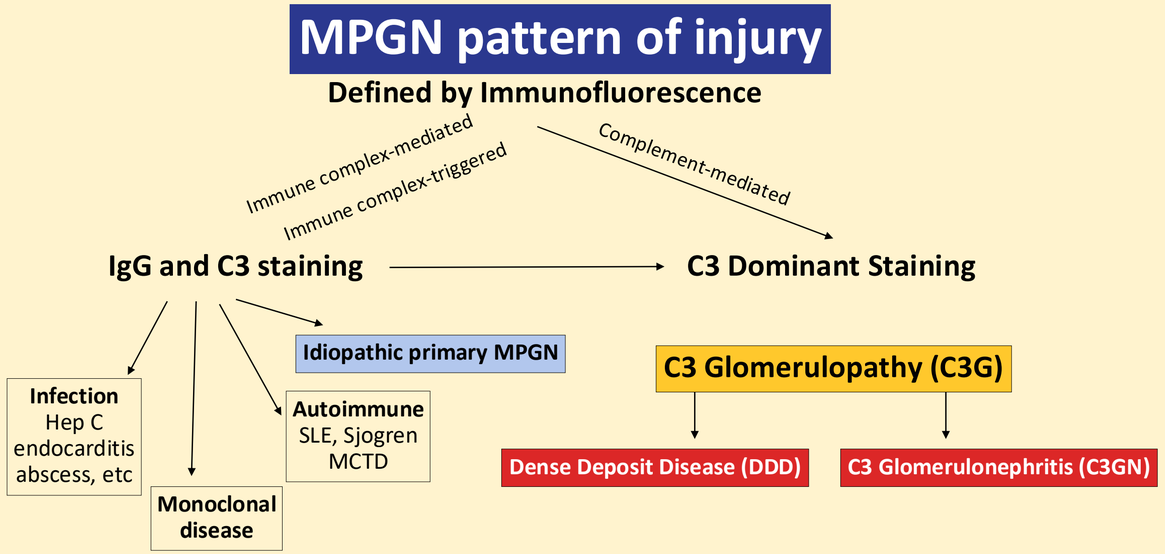
C3G Region

C3 glomerulopathy (C3G) is an ultra-rare disorder that encompasses
- C3 glomerulonephritis (C3GN)
- dense-deposit disease (DDD)

Results from dysregulation of the alternative complement pathway
- Leads **to C3 dominant complement deposition** in the kidney
- **50% progress to kidney failure** in 10 years after diagnosis
- **High rate of recurrence** in kidney transplantation
- Usually from autoantibodies (C3/4/5 nephritic factors), for Factor B/H autoantibodies & genetic mutations (workup on next slide)

Kidney biopsy is the main diagnostic tool
- Sits at the intersection of histologic overlap, subtle immunofluorescent interpretation, inadequate complement testing, and evolving terminology. (from infection, monoclonal diseases, to autoimmune diseases) (Figure to Right)
- Which is why diagnosis is highlighted as a distinct Team



Membranoproliferative glomerulonephritis (MPGN) underwent a nomenclature change in 2013 reflecting shift from morphology-based to pathogenesis-based classification. Pickering M et al. Kidney Int. 2013 PMID: 24172683

Treatment paradigm for C3G

- Past expert recommendations suggested use of MMF and steroids to dampen immune system
  -no RCTs -cohort retrospective studies provided mixed results
- Use of terminal (C5) complement inhibitor (eculizumab) with mixed results as well and no RCTs exist
- Use of plasma exchange and rituximab have both not demonstrated efficacy and no RCTs exist
- Recent RCTs have led to the FDA approval of two drugs, **pegcetacoplan** (C3 inhibitor) and **iptacopan** (Factor B inhibitor)
  -pegcetacoplan- ~65% reduction in proteinuria & reduction in C3 staining, -iptacoplan- ~35% proteinuria reduction
- mandated to have immunization to encapsulated bacteria (meningococcal and pneumococcal vaccine)
- Guidelines are still in development, but new approved drugs will likely dramatically alter this course of this disease

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C3G Diagnosis

Diagnostic approach to membranoproliferative glomerulonephritis

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Complement-mediated MPGN

C3GN and DDD

Low serum C3 and normal C4

IF: C3 staining at least 2 times greater than Ig
EM: Ribbon-like deposits within GBM in DDD, isolated subendothelial and mesangial deposits in C3GN

Additional tests to identify complement abnormality:

- Autoantibody testing (C3/C4/C5 nephritic factors, factor B/H autoantibodies)
- Genetic testing (mutations of factors B/H/I, C3, CFHR5)

DDD associates extra-kidney manifestations (ocular drusen, partial lipodystrophy)

Immune complex/monoclonal Ig-mediated MPGN

Post-infection associated GN

Low serum C3 and C4

IF: polyclonal Ig and complement components

Documentation of infection (bacterial, viral, fungal, protozoal or parasitic)

Screen for autoimmune disease (systemic lupus erythematosus, Sjögren's disease, rheumatoid arthritis)

Monoclonal Ig-mediated MPGN

Low serum C3 and C4

IF: monoclonal Ig and complement components

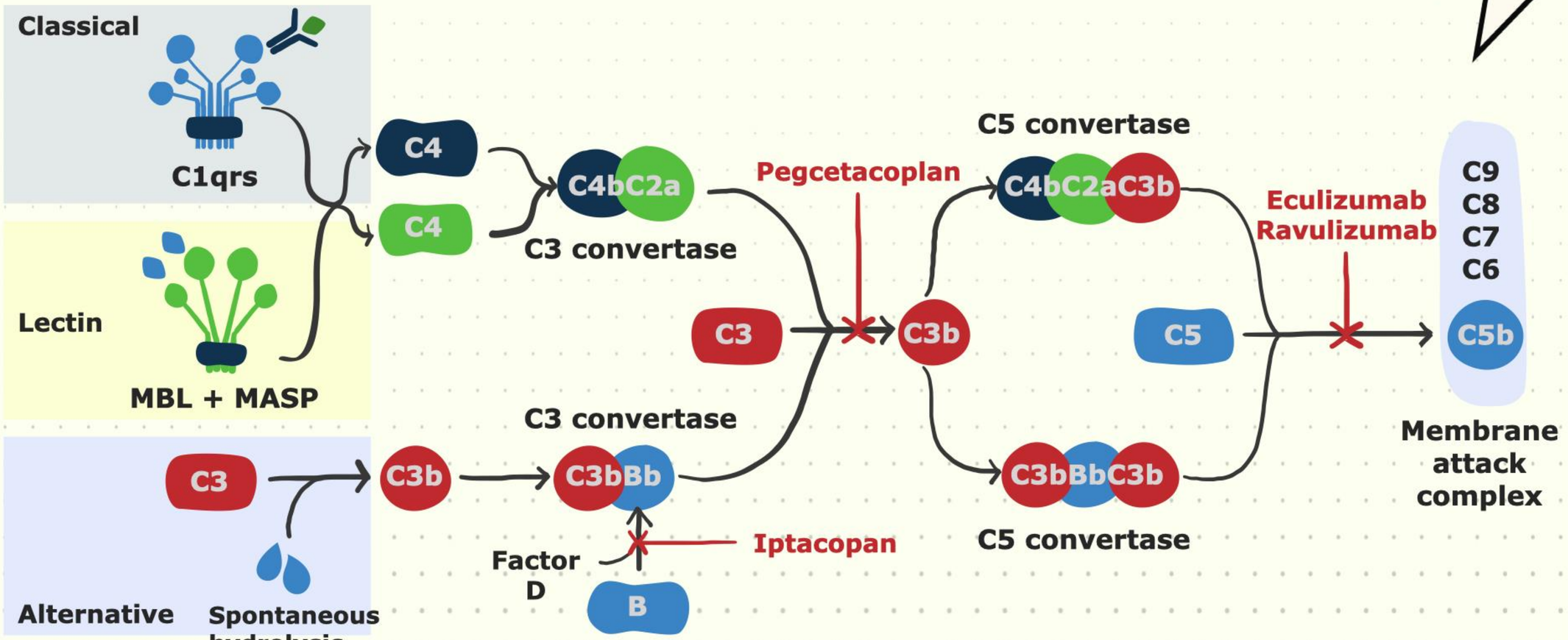
Identification of monoclonal protein (serum protein electrophoresis, serum free light chains, and/or immunofixation electrophoresis)

Bone marrow biopsy to identify plasma cell disorder

VA by **Corina Teodosiu**

Abbreviations: C3GN: C3 glomerulonephritis; CFHR: complement factor H-related; DDD: dense deposit disease; IF: immunofluorescence; EM: electron microscopy; GBM: glomerular basement membrane; Ig: immunoglobulin; MPGN: membrano-proliferative glomerulonephritis

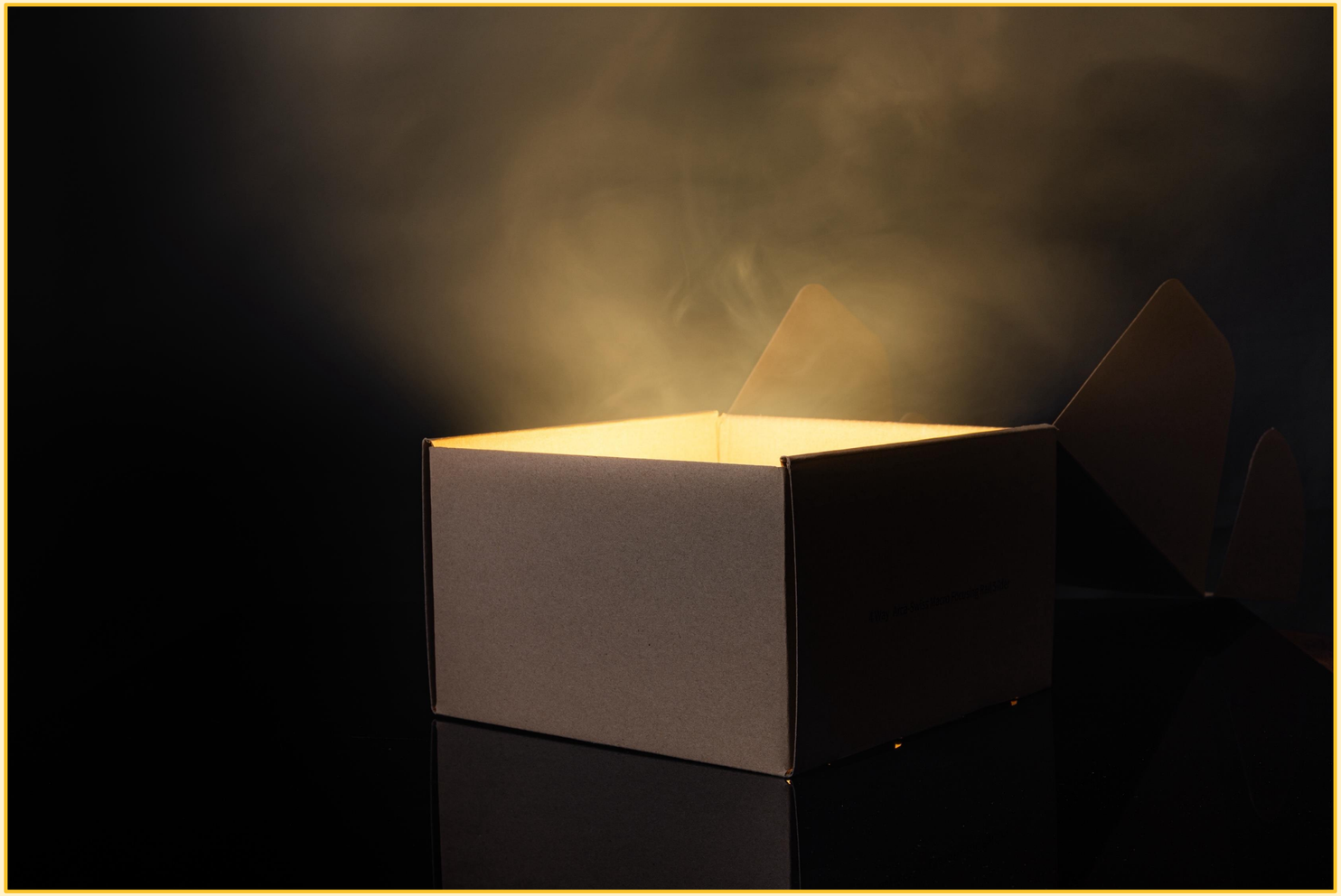
The Complement Cascade



VA by **Corina Teodosiu**

Conclusion: The complement cascade can be activated via three pathways: the classical, lectin and alternative pathways. These lead to formation of C3 convertases, which cleave C3 yielding C3b that forms more C3 convertases together with factor B via the alternative pathway. The C3b molecules further combine with C4bC2a or C3bBb into C5 convertases, cleaving C5 to C5a and C5b. The latter binds C6, followed by C7, C8 and C9 to form the membrane attack complex.

C3G Treatment



VALIANT trial: Is Pegcetacoplan in C3 Glomerulopathy and Immune-Complex MPGN Superior to Placebo?

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IC MPGN, immune complex membranoproliferative glomerulonephritis

Methods & Cohort

- **1:1 RCT, double blind**
- **International**
- **C3 glomerulopathy or primary IC MPGN**
  N = 124
- **Adolescents** (12-17 YO)
  Adults (≥ 18 YO)
- **05/2022 - 06/2024**

Design

Supportive care ± MMF & low dose glucocorticoids +...

Pegcetacoplan
1080mg 2x weekly
Weight adjusted ≤ 50kg
n = 63

vs

Placebo
n = 61

Results (at 26 weeks)

% Reduction UPCR (95% CI) (compared to placebo)	% change UPCR (95% CI)	% Stabilized eGFR & ≥50% reduction in UPCR	≥50% reduction in the UPCR
68.1 (57.3-76.2)	**– 67.2** (-74.9 to -57.2)	**49%**	**60%**
	– 2.9 (-8.6 to 15.9)	**3%**	**5%**

Fakhouri F, NEJM, 2025

VA by **Sophia L Ambruso**

Conclusion: Pegcetacoplan resulted in a significantly greater reduction in proteinuria than placebo among patients with C3 glomerulopathy or primary immune-complex MPGN.

APPEAR C3G: Is Iptacopan Superior to Placebo in C3 Glomerulopathy

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UPCR, urine protein creatinine ratio

Methods & Cohort

- 1:1 RCT, double blind
- International
- Biopsy confirmed C3 glomerulopathy

Inclusion criteria

- C3 <77 mg/dL at screen
- UPCR 1.0 g/g at days -75 & -15 before randomization
- eGFR ≥30ml/min/1.73m²

Design

July 28, 2021- Feb 15, 2023

	6 mos double blind	**6 mos** open label
	Iptacopan 200 mg BID n = 38	**Iptacopan** 200 mg BID
vs		
	Placebo n = 36	**Iptacopan** 200 mg BID

Results (at 6 mos)

Mean change in UPCR (g/g) (baseline → 6 mos)	**% Reduction 24-h UPCR** (95% CI) (compared to placebo)	**% change 24-h UPCR** (95% CI)
3.33→2.17	35% (13.8-51.1)	– 30% (42.8 to -14.8)
2.58 →2.8		– 8% (-11.9 to 31.3)

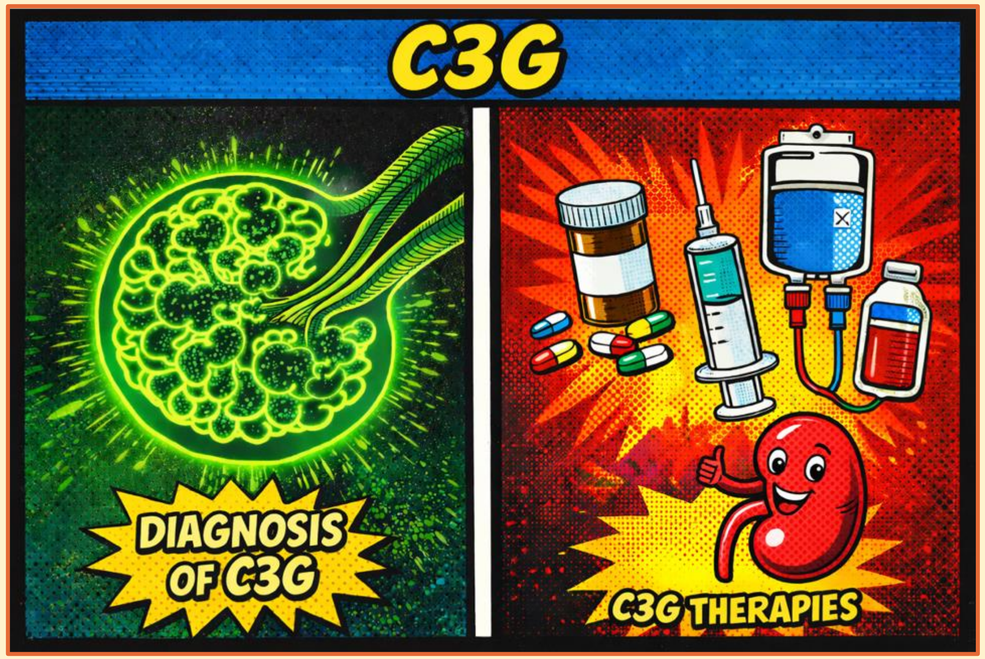
Kavanaugh D, Lancet, 2025

VA by **Sophia L Ambruso**

Conclusion: Iptacopan showed a statistically significant, clinically meaningful proteinuria reduction in addition to RAAS inhibitors and immunosuppression at 6 months. Iptacopan was well tolerated with an acceptable safety profile in patients with C3 glomerulopathy.

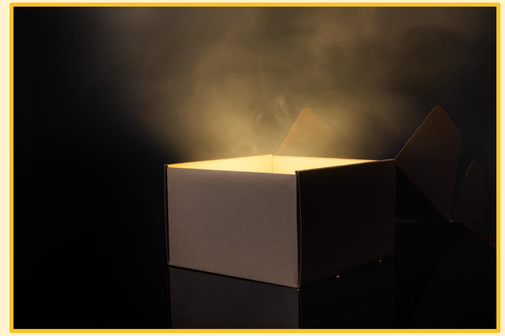
EFFLUENT EIGHT ROUND

Pick Your Champion for the C3G Region



C3G Diagnosis

VS



C3G Treatment

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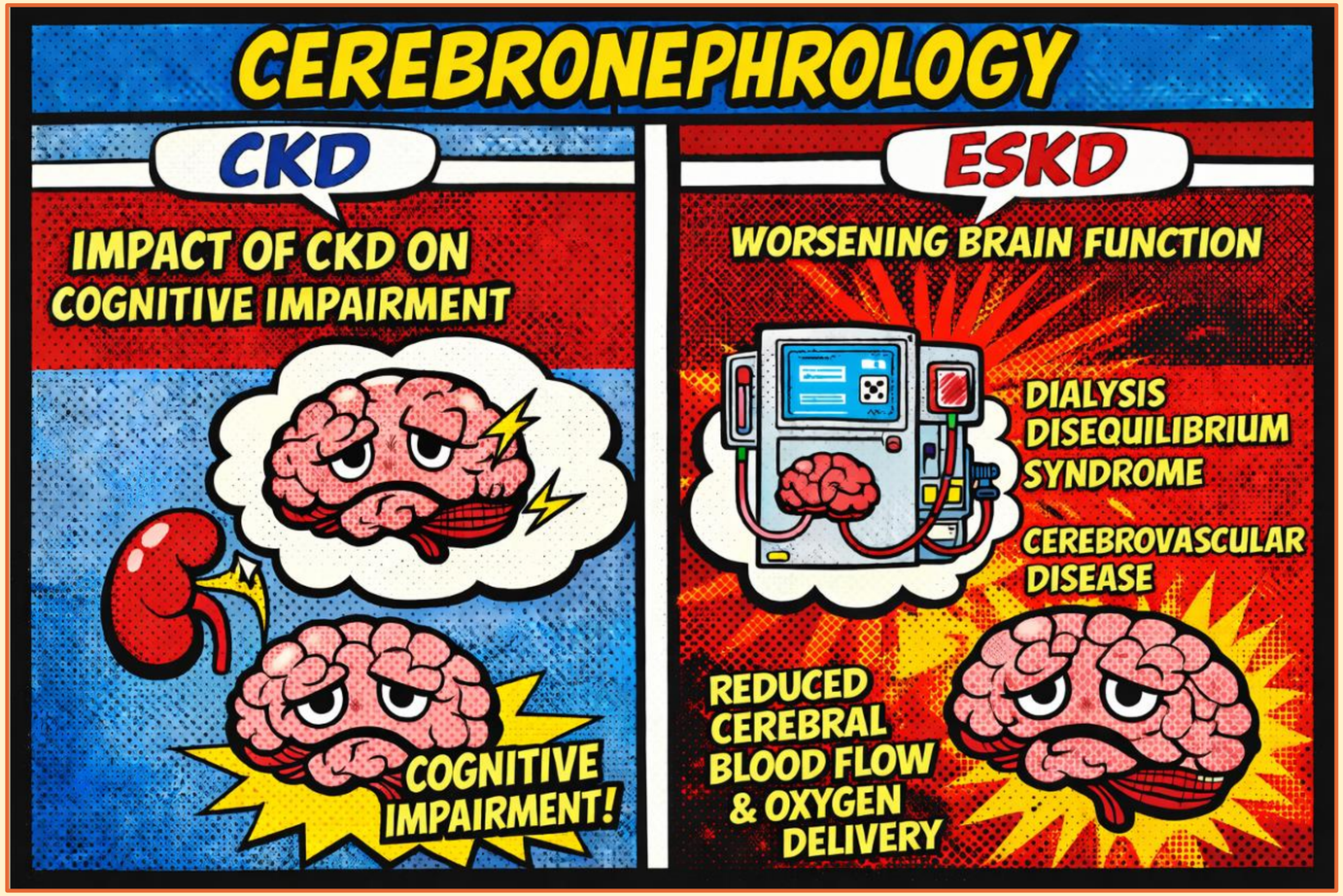
Cerebronephrology



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The Brain-Kidney Axis

- **Kidney & brain share vascular design**
  - Low-resistance, high-flow organs that rely on autoregulation → vulnerable to chronic BP/vascular injury
- **Bidirectional cross-talk**
  - CKD → ↑ cerebrovascular disease, blood–brain barrier disruption, exposure to uremic metabolites
  - Brain injury → ↑ sympathetic tone; impacts Na/H2O balance and kidney function
- **Why nephrologists should care**
  - Cognitive impairment can be an underrecognized CKD complication and impacts adherence, self-management, and outcomes

"**Team CKD**" (chronic microvascular + metabolic injury) vs "**Team ESKD**" (added dialysis-related hemodynamic/osmotic stress)

Cognition is not "extra-renal"—it's part of CKD/ESKD care.

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in CKD

Team CKD

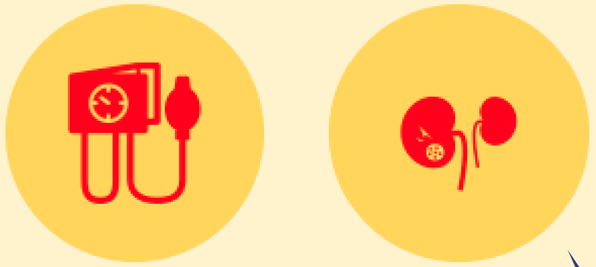
- **What it is**
  - Cognitive impairment = deficit in ≥1 domain (executive function, memory, attention, language, visuospatial, learning) spanning mild → dementia

- **How common / who's at risk**
  - CKD is common (especially in older adults), and cognitive impairment often goes unnoticed
  - Studies highlighted in the post: ~48% prevalence of neurocognitive impairment in older CKD cohorts
  - Risk rises with lower eGFR, higher albuminuria, and higher systolic BP

- **Pathophysiology - multifactorial**
  - Cerebral small vessel disease
  - Anemia/oxygen delivery mismatch: even with ↑ cerebral blood flow, oxygenation may be impaired
  - Glymphatic dysfunction (CNS waste clearance) and uremic metabolites accumulating earlier than "overt uremia"

Prevention focus:

control BP and albuminuria



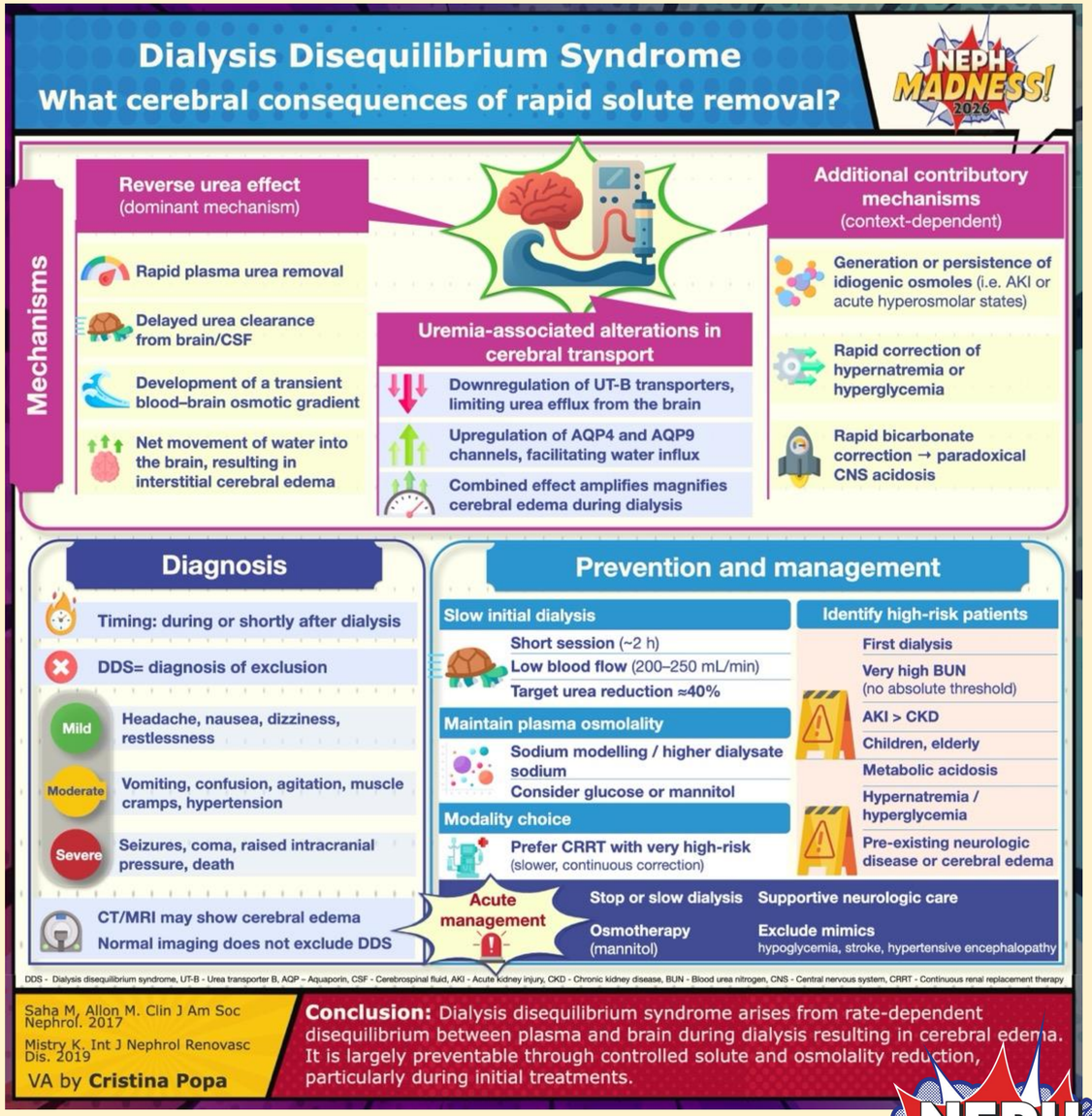
in ESKD

Team ESKD

- **Core concept**
  - Kidney replacement therapy necessarily lowers osmolality, intravascular volume, and MAP → can provoke transient ischemia + ICP fluctuations

- **Cerebrovascular + structural brain injury**
  - ESKD patients have high stroke/CVD burden
  - MRI/DTI studies: more atrophy/WMH and DTI shows reduced white matter integrity
  - PD vs CKD imaging: PD associated with lower gray matter volume and greater decline over 2 years

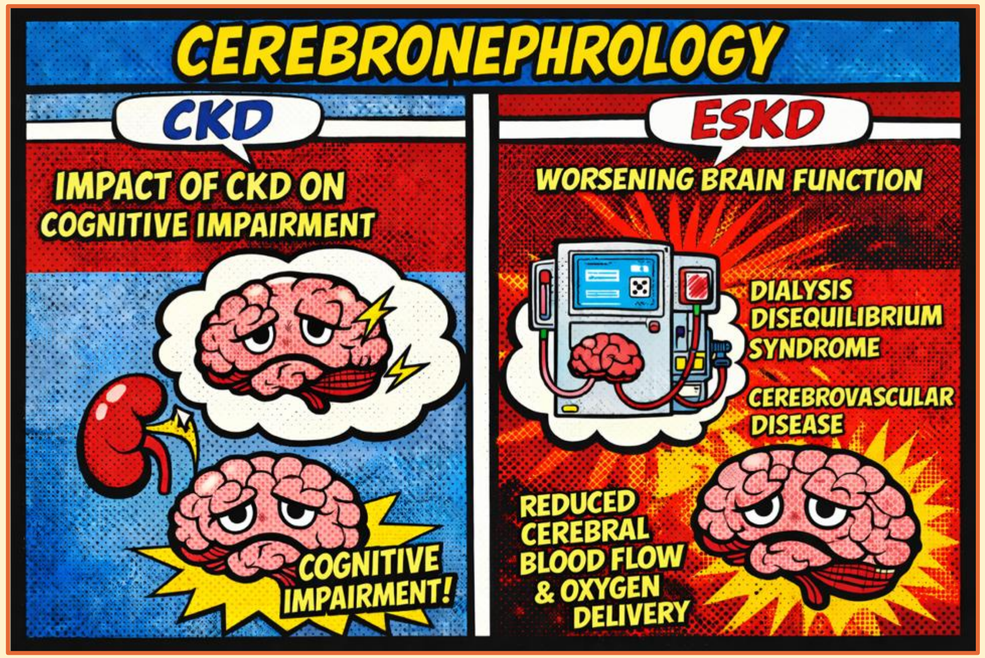
- **Hemodynamics during HD: often "silent" brain stress**
  - Near-infrared spectroscopy measurements with ≥15% cerebral oxygen drop; most episodes asymptomatic
  - Transcranial Doppler: mean flow velocity drops (~10%); correlates with UF and with subsequent cognitive/WMH signals
  - ICP monitoring and MRI data: HD can raise ICP and increase cerebral water



Dialysis physiology can stress the brain

EFFLUENT EIGHT ROUND

Pick Your Champion for the Cerebronephrology Region



in CKD

VS

in ESKD

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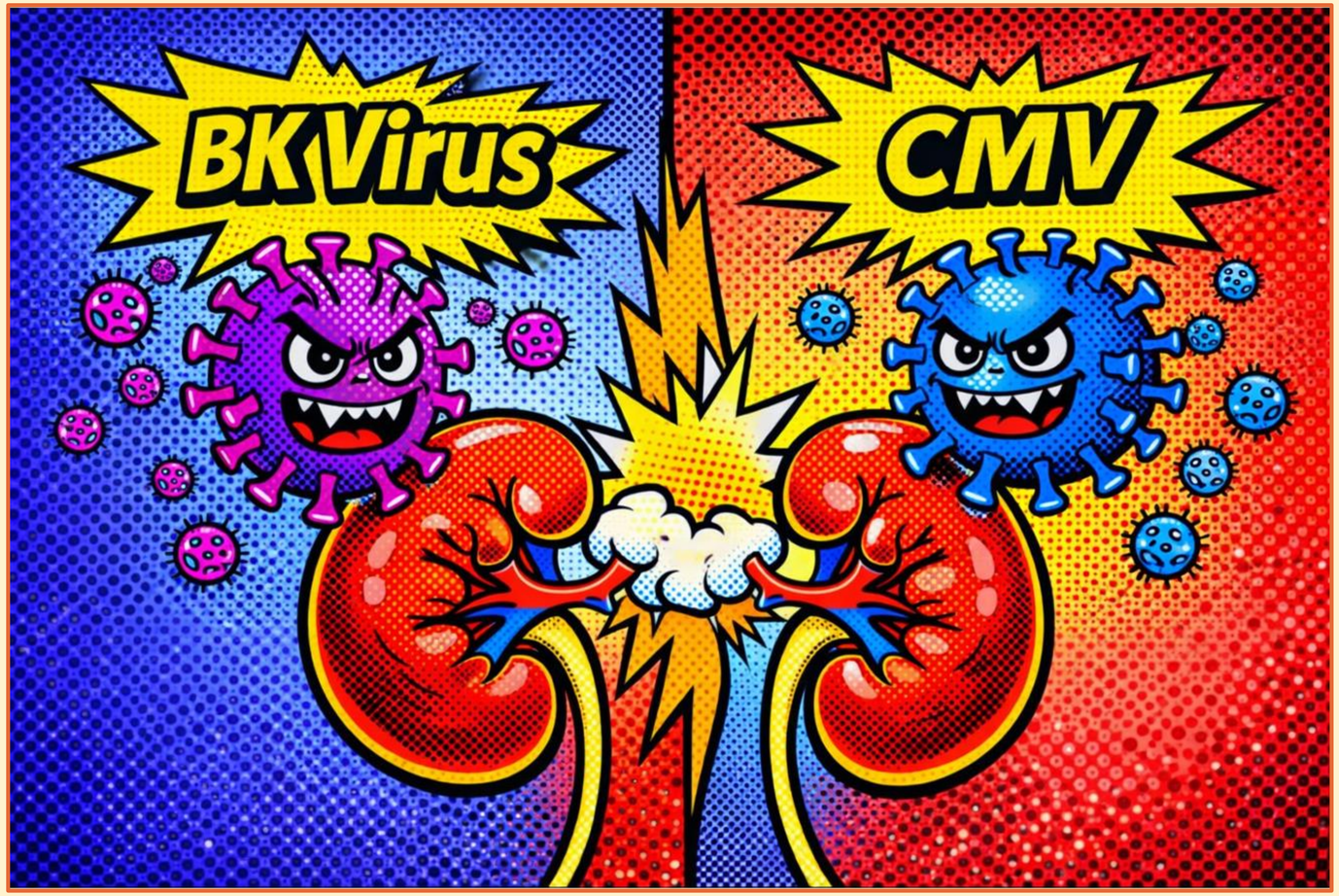
Trolls of Transplantation



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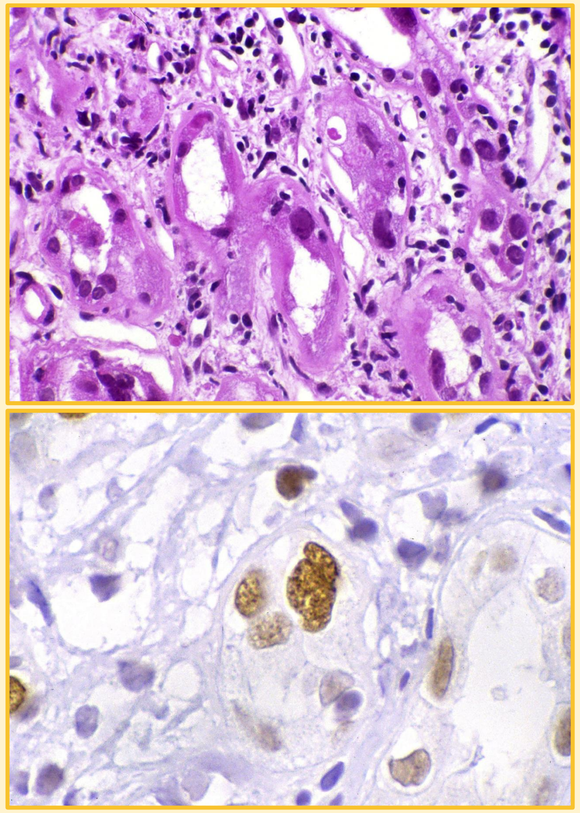
NEPH MADNESS! 2026

BK

NEPH MADNESS! 2026

BKV: A Silent Passenger With A Heavy Toll

- **Meet BK virus (BKV):** Identified in 1971 in Sudanese kidney transplant recipient (KTR) BK SD GB *(BKV = cousin of JCV: named for John Cunningham)*
- **BKV is a "sleeper":** 90% of adults seropositive; enters urothelial & tubular cells → lifelong latency in an episomal form (*as extra-chromosomal circles of DNA tucked into the nucleus without producing viral proteins*); can awaken/reactivate in immunosuppressed host
- Recipient age, prior KT, recent rejection, specific HLA class profiles: linked to BKV reactivation
- BK viremia *(we actually measure DNA-emia)* > 10K copies = presumptive BKVAN*
- BKVAN: in up to 10% of KTR; up to 50% allograft loss
- Donor-derived cell-free DNA assays have shown promise to distinguish viral injury from alloimmune rejection.
- Antivirals that have failed: fluoroquinolones, leflunomide, cidofovir. For now, KISS**: just lower immunosuppression!
- **Potentially promising therapies:** viral-like particle vaccines, monoclonal antibodies (potravitug, MAU868), BKV-specific T cells (e.g. posoleucel), targeting agnoprotein & viral mRNA splicing



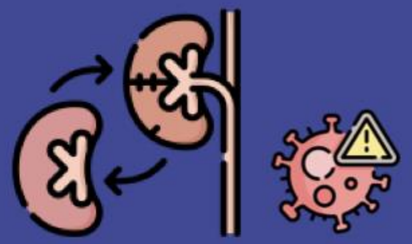
(Top) **Dark purple (basophils) inclusions** in tubular epithelial cells suggest BKV associated nephropathy; (Bottom) **SV40** Immunohistochemistry confirms BKV. Adapted from the *AJKD Atlas of Renal Pathology*

*BKV-associated nephropathy (BKVAN)
**Keep it simple stupid

NEPH MADNESS! 2026

Posoleucel in Kidney Transplant Recipients with BK Viremia: Multicenter, Randomized, Double-Blind, Placebo-Controlled Phase 2 Trial

NEPH MADNESS! 2026



61 kidney transplant recipients with BK viremia

Treated with Posoleucel (PSL) off-the-shelf, allogenic, multivirus-specific T-cell investigational therapy

Intervention

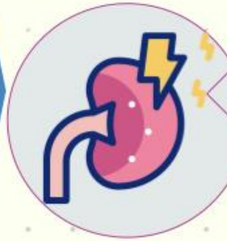
12 weeks Randomized 1:1:1

Number of patients achieving ≥1 log BKV viral load reduction

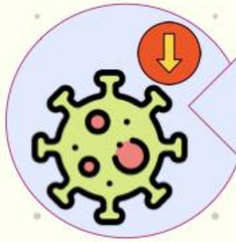
Group 1 PSL q 7d X 3 weeks then q 14d	**50% (10 of 20)**
Group 2 PSL q 7d X 3 weeks then q 28d	**28% (5 of 18)**
Placebo	**14% (2 of 14)**

12 weeks Follow-up after completing treatment

No deaths, graft-versus-host disease, or cytokine release syndrome



3 patients had allograft rejection, none deemed treatment-related



BK viremia reduction was associated with an increase in the circulating frequency of BKV-specific T cells in PSL groups

Anil Chandraker et al, JASN 2024 May 1;35(5):618-629

VA by Kajaree Giri

Conclusion: Posoleucel was generally safe, well tolerated, and associated with a larger reduction of BK viremia compared with placebo. Limitations of this study include the relatively short duration of follow-up and lack of power to detect significant differences in clinical outcomes.

CMV

CMV: Whether Asymptomatic or Deadly, Always Harmful

- **Meet cytomegalovirus (CMV):** AKA human herpes virus 5 (HHV5); Identified in 1956 in infants
- **Most common** opportunistic infection among KTR
- CMV genome: highest level of genetic diversity of all known HHV → antiviral resistance is a problem
- 2 phases: lytic (active viral replication and contagion) & latent (viral "hibernation")
- 2 preventative strategies
  - **Universal:** initiation on anti-viral drug for finite duration (valgancivlovir or letermovir ↓ leukopenia)
  - **Preemptive:** screen for CMV DNAemia, treat if you find it
- First line therapies: PO valganciclovir & IV ganciclovir (both activated by CMV kinase pUL97 & inhibit DNA polymerase pUL54)
- Options for refractory infections (+/- resistance): pUL54 inhibitors (foscarnet, cidofovir), pUL97 inhibitor (maribavir)
- Potential promising future therapies: CMV-specific T-cells, vaccines, monoclonal antibodies, adoptive T-cell therapies
- CMV-related kidney injury mimics BKV: tubulointerstitial nephritis, intranuclear glassy, basophilic inclusions with a surrounding halo ("owl's eye"). Collapsing FSGS has been reported

NEPH MADNESS! 2026

Efficacy and safety of letermovir + acyclovir vs valganciclovir for prevention of CMV disease in CMV-seronegative kidney transplant recipients

NEPH MADNESS! 2026

Randomized, double-masked, double-dummy, noninferiority, phase 3 trial

CMV-seronegative kidney transplant recipients who received an organ from a **CMV-seropositive donor**

94 participating sites

May 2018 - April 2021

1:1 ratio

Up to 200 days after transplant

	Prevention of CMV disease (week 52)	Quantifiable CMV DNAemia (week 28)	Leukopenia or neutropenia (week 28)	Discontinued prophylaxis (adverse events)
Letermovir 480mg + acyclovir n= 289	10%	2%	26%	4%
Valganciclovir 900mg n= 297	12%	9%	64%	13%

Time to onset of CMV disease was comparable between the groups HR 0.90 (0.56-1.47)

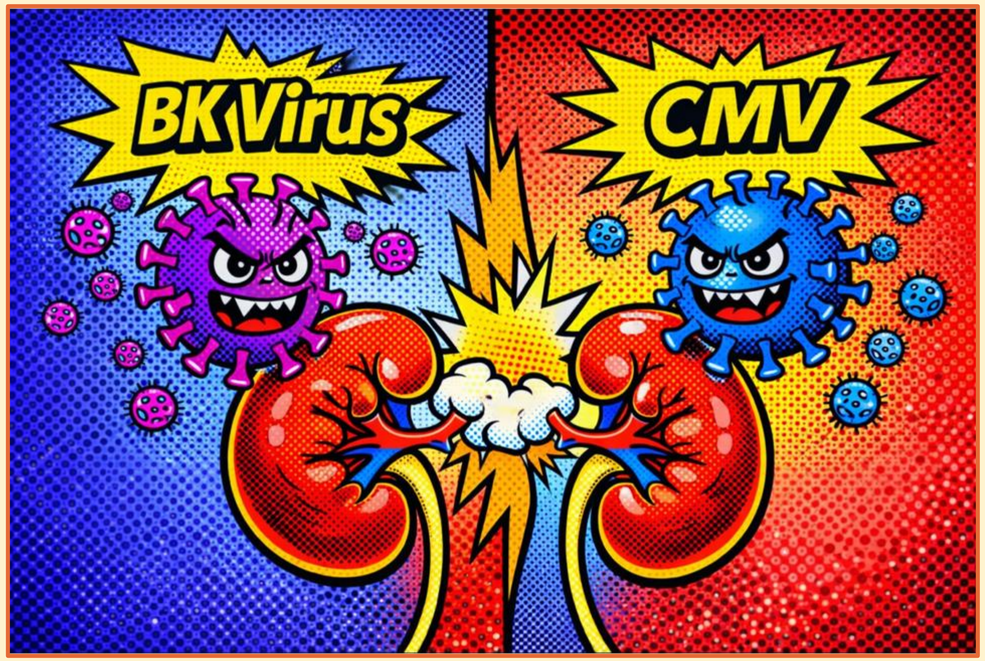
Limaye AP, JAMA, 2023;330;(1):33-42

VA by **Denisse Arellano**

Conclusion: Among adult CMV-seronegative kidney transplant recipients who received an organ from a CMV-seropositive donor, letermovir was noninferior to valganciclovir for prophylaxis of CMV disease over 52 weeks, with lower rates of leukopenia or neutropenia, supporting its use for this indication.

EFFLUENT EIGHT ROUND

Pick Your Champion for the Trolls of Transplantation Region



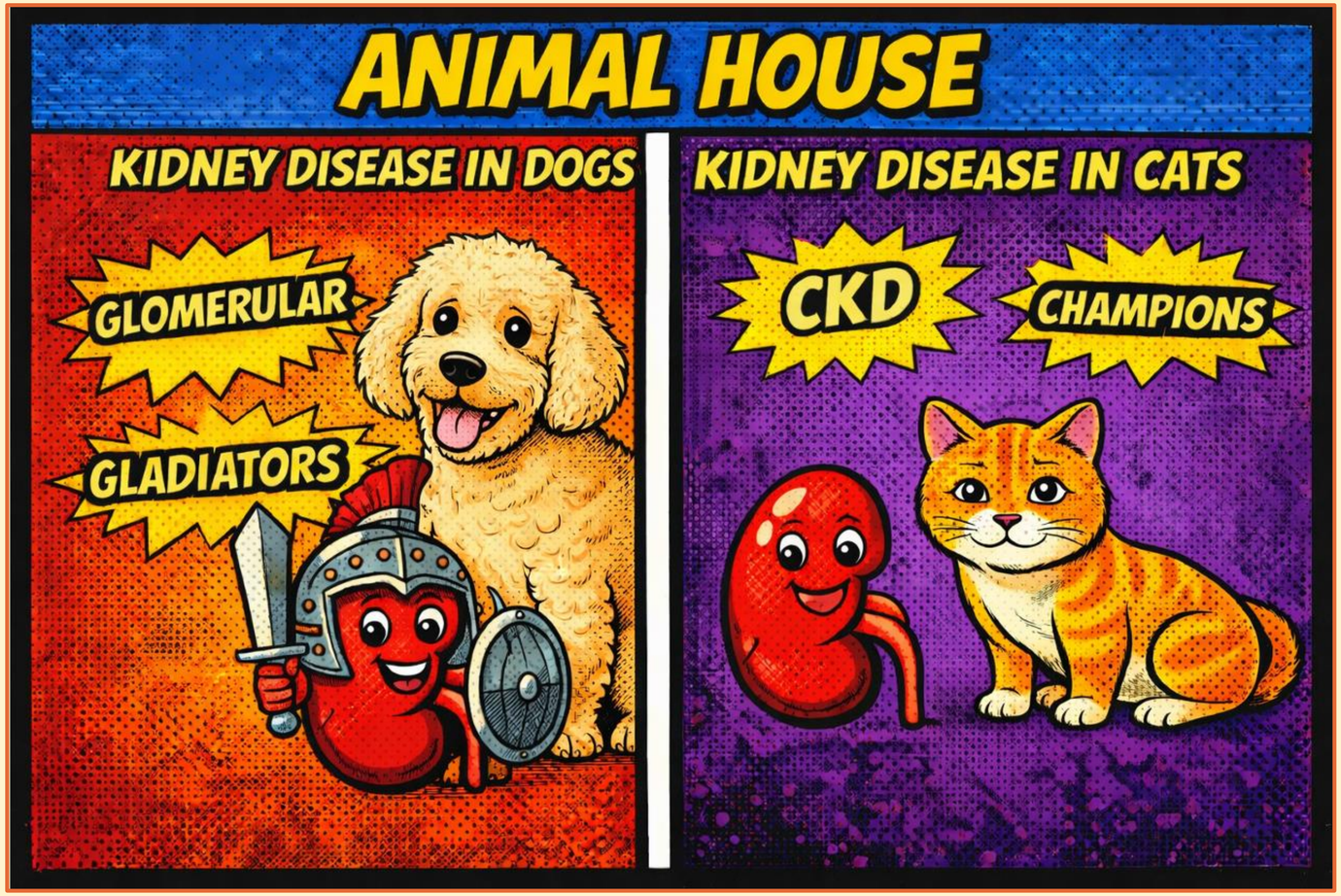
BK

VS

CMV

NEPH MADNESS! 2026

Animal House



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NEPH MADNESS! 2026

Dogs

Canine Kidney - A Bystander

NEPH MADNESS! 2026

Dogs are proteinuric powerhouses & glomerular gladiators

Physiology

- GFR 3.5-4.5 *mL/min/kg*
- Typical SG > 1.030

Anatomy

Bean shape, 2.5-3.5 times size of 2nd lumbar vertebra

Susceptible to glomerular diseases

Higher GFR per unit of body weight causes greater constant pressure on glomerular filtration barrier

Prone to immune complex mediated glomerulonephritis (Secondary to infections, chronic inflammation & neoplasia)

Cause immune complex deposition in the glomeruli activating the inflammatory cascade + decreased clearance

Proteinuria + glomerular damage

Acquired

Species	Disease	Primary lesion	Inheritance pattern	Gene mutation
Samoyed	Hereditary Nephropathy	Glomerular	XR	COL4A5
English Cocker Spaniel	Hereditary Nephritis	Glomerular	AR	COL4A4
Shih Tzu, Lhasa Apso	Renal Dysplasia	Tubulointerstitial, Glomerular	AR or AD with incomplete penetrance	Unknown, potentially COX-2 mutant alleles
Bull Terrier, Dalmatian	Hereditary Nephritis	Glomerular	AD	Not fully characterized
Chinese Shar-Pei	Familial Amyloidosis	Primarily Medullary/ Tubulointerstitial	Unknown, possibly AR	SAA gene variants studied, no direct link

SG specific gravity RAS renin angiotensin system XR x linked recessive AR autosomal recessive AD autosomal dominant ARB angiotensin receptor blocker

Etiology of glomerular damage

Inherited

Hypertension dependant on RAS
Drug of choice - ARB

Common kidney stones:
Male dogs- Ca oxalate > struvite >cystine
Female dogs- Struvite >>Ca oxalate

VA by **Krithika Mohan**

Ref : Debruyn et al, J Feline Med Surg. 2012 Oct 19 ;Brown et al, World small animal veterinary association world congress proceedings 2006 ;Ephraim et al, Food, science and nutrition, 2021; Vaden et al, Top companion anim med.2011, Aug (26) ;Day et al, Parasites & vectors, Sept 2016, Kopecny et al., J Vet Intern Med.2021 May

AKI, CKD and ESKD in 🐶 🐶

- **AKI:** driven by ischemic/inflammatory conditions (58%), infections (8%) unknown causes (24%) and nephrotoxins (6%)

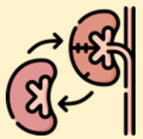
  - Common nephrotoxins are grapes, ethylene glycol, NSAIDs (especially human-use), antibiotics, vit D
  - IRIS AKI grading I-V uses creatinine, urine output and RRT requirement

- **CKD:** persistent urinary abnormalities > 3 mo
  - IRIS CKD staging 1-4 uses creatinine, proteinuria and blood pressure

- **Dialysis:** treatment of severe AKI and sometimes ESKD

  - Viewed as “bridge to recovery”, rarely “bridge to nowhere”(ESKD) (ethical dilemmas)
  - Cost: $3,000-5,000 for the first 2-3 treatments, $10,000-20,000 total including ICU care
  - Success rate: 50% survival to hospital discharge, higher in infections (eg. leptospirosis)
  - Prognosis: fair to good for reversible AKI

- **Transplant:**



  - High morbidity and mortality, rarely successful
  - Intense host immune response, rapid rejection
  - Requires potent, multi-agent protocols with severe side effects
  - Opportunistic infections are common due to dogs’ behavior and exploration of the environment
  - Cost upwards of $20,000 + high annual drug costs

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Cats

Feline Kidney - The Protagonist

NEPH MADNESS! 2026

Cats are desert animals, optimized for arid environments. And they are CKD champions!

Physiology

- GFR 2.5-3.5 *mL/min/kg*
- Typical SG > 1.035
- Superior ability to concentrate urine
- Max U.Osm 3000 *mOsm/kg*

Anatomy

Rounded shape, 2-3 times size of 2nd lumbar vertebra

Microscopy

- In cats, tubular cytoplasm & nuclei are larger due to higher metabolic activity
- Tubular lumens are narrower =>
- Higher risk of tubular obstruction in AKI in cats vs dogs
- Unique feature - islands of ascending branches of loop of Henle amid densely arranged papillary ducts

Predisposition to tubulointerstitial fibrosis

Cats maintain a highly efficient medullary concentration gradient that is metabolically demanding for tubular epithelial cells

+

High protein, low moisture diet increases solute load on tubules

↓

Continuous metabolic stress

↓

Chronic low grade cellular damage

↓

Tubulointerstitial inflammation & fibrosis *(TIF)*

↓

High risk of CKD (specially older cats)

Immune & genetic landscape

Cats are less commonly affected by vector-borne infections/ immune-mediated conditions

Greater genetic diversity within breeds may be contributing to natural resistance

Feline immune response targets metabolically stressed tubules >glomeruli

Inherited diseases

Polycystic kidney & amyloidosis replace normal tissues with cysts or deposits

More prone to kidney stones (struvite > calcium oxalate > uric acid)

Hypertension less dependant on RAS
Drug of choice - Calcium channel blockers

Glomerular diseases are less common

SG specific gravity RAS renin angiotensin system U.osm Urine osmolality

VA by **Krithika Mohan**

Ref : Debruyn et al, J Feline Med Surg. 2012 Oct 19 ;Brown et al, World small animal veterinary association world congress proceedings 2006 ;Ephraim et al, Food, science and nutrition, 2021; Vaden et al, Top companion anim med.2011, Aug (26) ;Day et al, Parasites & vectors, Sept 2016, Kopecny et al., J Vet Intern Med.May 2021, Kira et al., PLoS One, July 2024, Kopecny et al., J Vet Intern Med. May 2021

AKI, CKD and ESKD in  

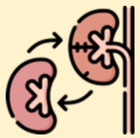
- **AKI: less common than CKD**
  - Common causes are trauma, obstruction, volume depletion and toxins such as lilies

- **CKD Champions: prevalence 20% in all cats and 80% in geriatric cats; treatment:**
  - Hydration (Hydra Care, water fountains, e-tubes)
  - Antiemetics and appetite stimulants
  - Darbepoetin or Molidustat for anemia
  - Phosphate binders
  - New: uremic toxin binders (Renaltec)

- **Dialysis: treatment of severe AKI and intoxications**

  - Cost: same as in dogs
  - Success rate: 50% survival to hospital discharge, less in intoxications (eg. lilies)
  - Prognosis: guarded to fair

- **Transplant:**



  - Survival 60-70% at 1 yr, 40% at 3 yrs
  - Tolerant immune response, cyclosporine is a key component of immunosuppressive regimen
  - Cost $8,000-15,000 for surgery + $500 - $1,500 annually for drugs
  - Ethical consensus: offered at specialized centers, donor must be adopted by recipient's owner

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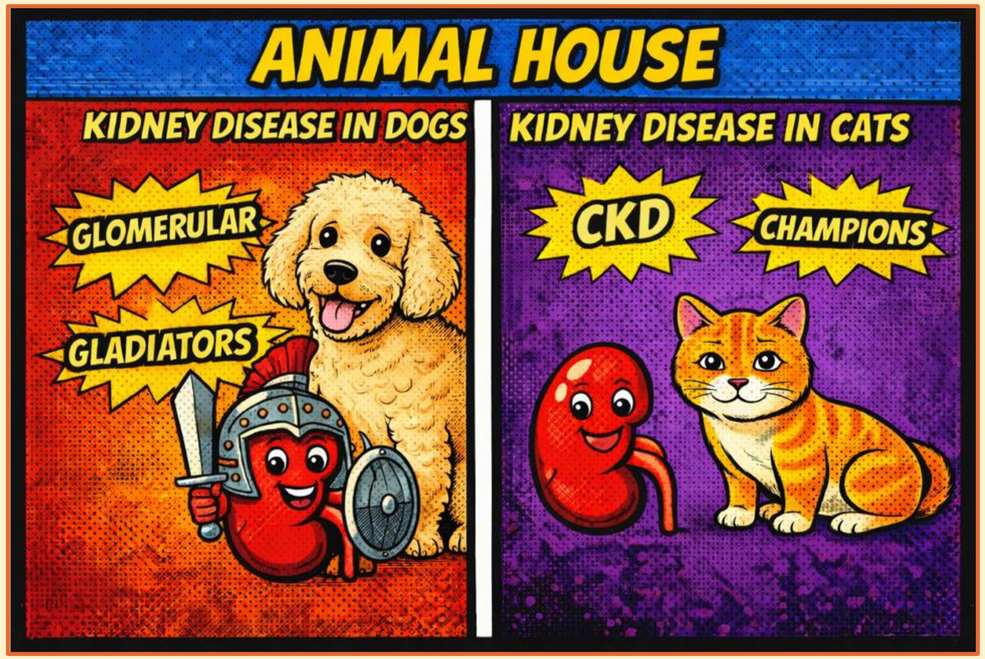
EFFLUENT EIGHT ROUND

Pick Your Champion for the Animal House Region



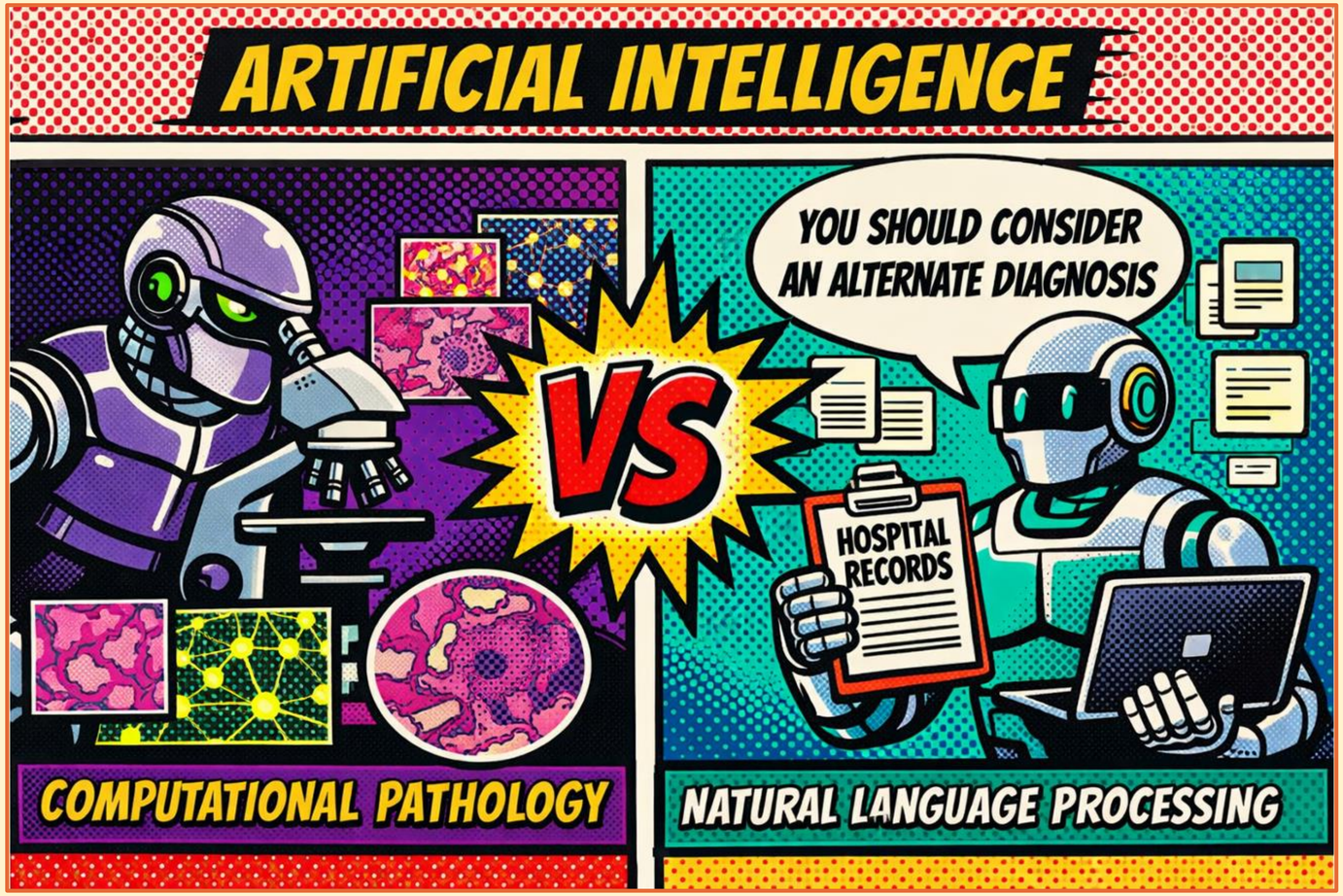
Dogs

vs

Cats

NEPH MADNESS! 2026

Artificial Intelligence



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Computational Pathology

Natural Language Processing

Artificial intelligence in nephrology
Clinical applications and real-world limits

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How AI is used?

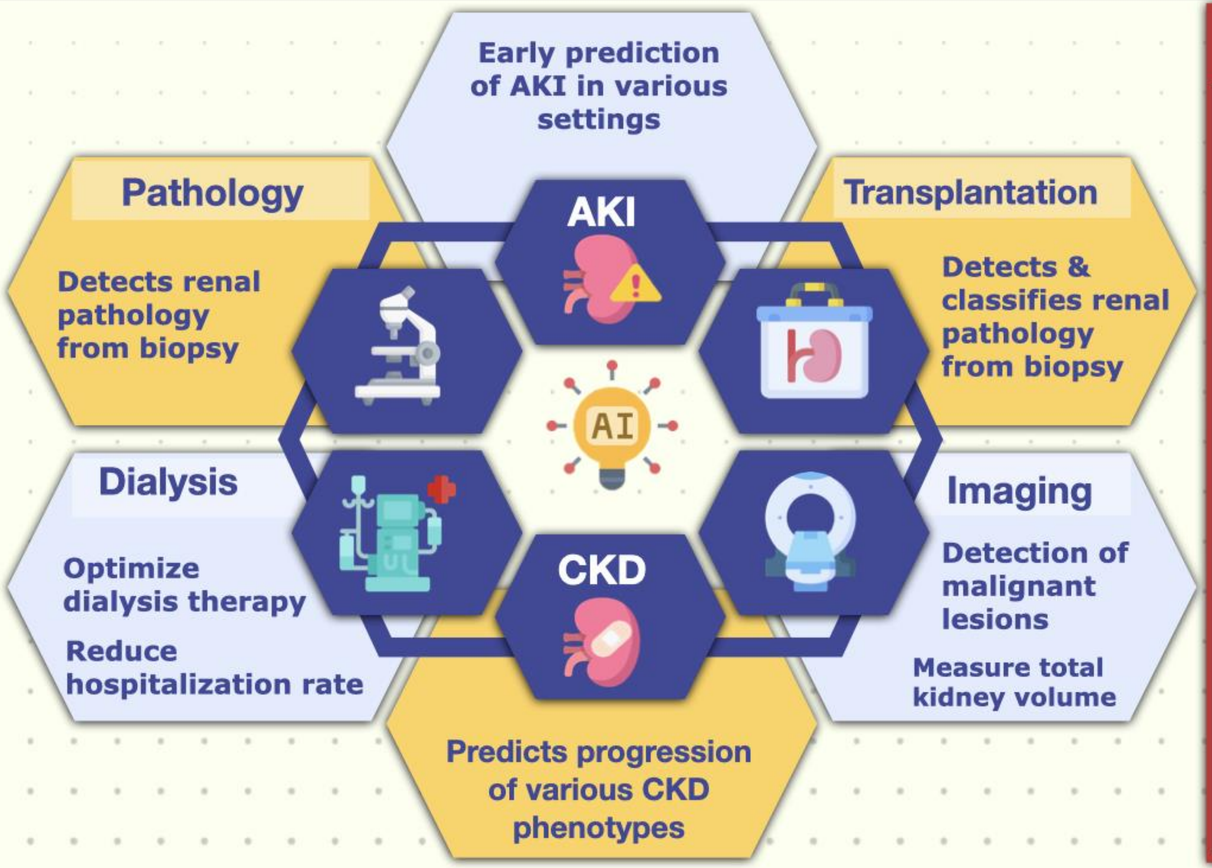
Supervised machine learning (ML)
predicts known outcomes

Deep learning
imaging, pathology, time-series

Unsupervised ML
phenotypes / clustering

Natural language processing
extracts signals from clinical notes

Reinforcement learning
conceptually useful; limited by ethics/ data in healthcare



AI challenges

Bias- non-representative data
Leads to inequity

Data quality
Missing/heterogenous/siloed

Black box- low transparency
Translating to low trust

Safety
Distribution shift after rollout

Standardization
EHR interoperability gaps

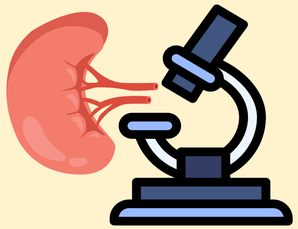
Medico/legal/ethics
Privacy, liability, governance

Singh P et al, Kidney Med, 2024

VA by **Cristina Popa**

Conclusion: AI is already shaping nephrology by helping spot risk earlier and bring more consistency to care. It highlights patterns and does not make decisions. The danger is using it blindly. Nephrologists need to understand what AI can and cannot do, so it supports clinical judgment rather than replacing it.

Two Different Engines, Two Different Problems



Computational Pathology

- Data source: Digitized histology images
- Unit of analysis: Pixels → Structures
- Strength: Quantification (fibrosis, lesions, segmentation)
- Best for: Morphology-driven questions

Natural Language Processing (NLP)

- Data source: Clinical documentation
- Unit of analysis: Words → Concepts
- Strength: Pattern extraction across time
- Best for: Phenotypes, medication signals, trajectories

AI in nephrology is not one tool — it is fundamentally different approaches solving different clinical problems

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Advances in Computational Nephropathology: Can Integration of AI Tools Improve the Digital Pathology Workflow?

NEPH MADNESS! 2026

Digital pathology workflow

Kidney biopsy

Tissue assessment

Tissue processing

Light microscopy
IHC/IF
Electron microscopy
Molecular analysis

Digitization and case assembly

Pathologist's assessment

Biomarkers

Classification

Prognostication

Report

Image-based applications

AI

Biopsy quality control

Multi-modal data fusion

Image quality control, AI-assisted case triage

Lesion detection, grading/ diagnosis, gene status prediction

Structure/cell segmentation

Outcome/ treatment prediction

Report generation/ speech recognition

Non-image applications

Molecular omics

Stain translation

Decision-free report

Feature analysis

Multimodal agents

Potentially integrating all above mentioned tasks (semi- or fully autonomous workflow)

ML/DL tasks

classification | segmentation and pathonomics | biostatistics | generative AI and NLP | classification+segmentation

Hölscher et al,
Kidney International, 2025

VA by **Kajaree Giri**

Conclusion: Computational nephropathology is transforming our ability to analyze kidney histopathology. By integrating artificial intelligence techniques into the digital and molecular workflow, we can enhance diagnostic precision and reveal novel morphomolecular relationships.

Natural Language Processing in Nephrology Clinical Care

NEPH MADNESS! 2026

Improve clinical trial candidate identification

Identify patients with symptoms under-documented in structured data

Identify novel features for outcome modelling

Link clinical concepts to outcomes for further testing

Improve disease identification

Compare CKD documentation vs ICD-coded CKD rates

Clinical decision support

Automated alerts or recommendations based on documentation

Automated patient interactions

Right-time recommendations to guide clinician decisions

Medical chatbots

Remind patients to take medications

Tielman et al, Adv Chronic Kidney Dis, 2023

VA by **Dr PS Vali**

Conclusion: Nephrology language processing (NLP) provides a way to access data, & has been used in research in nephrology. While there are challenges to the implementation of NLP into clinical care, NLP can enable the extraction of key patient characteristics from free text & allow for the inclusion of novel predictors into risk stratification models.

Where Do They Add Value?

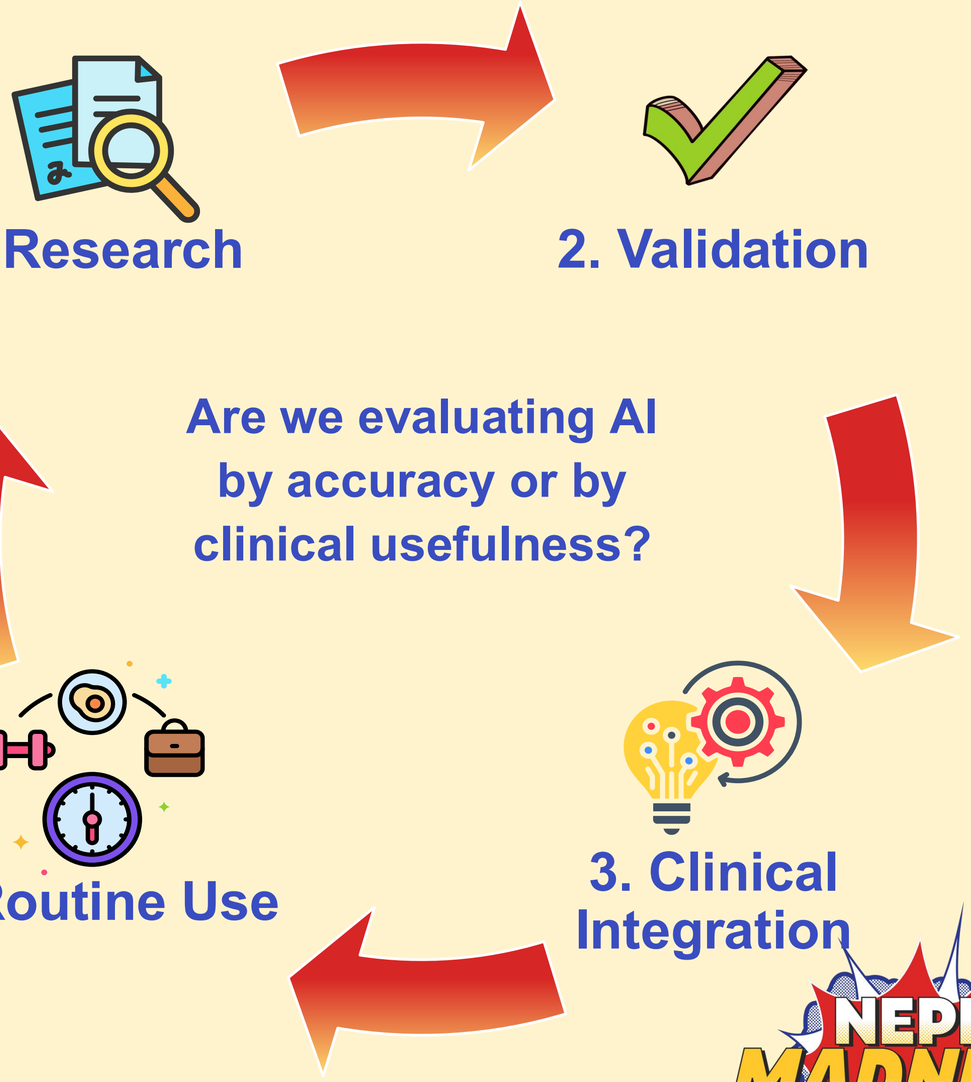
Clinical Domain	Computational Pathology		Natural Language Processing (NLP)	
Tissue-level diagnosis		Strong		Limited
Longitudinal risk detection		Emerging		Strong
Workflow efficiency		Lab-based		System-wide
Standardization		High reproducibility		Dependent on documentation

Different scalability paths:
Pathology AI = specialized centers, digital infrastructure
NLP = health system–wide deployment

From Innovation to Implementation

Shared implementation requirements for Computational Pathology and NLP:

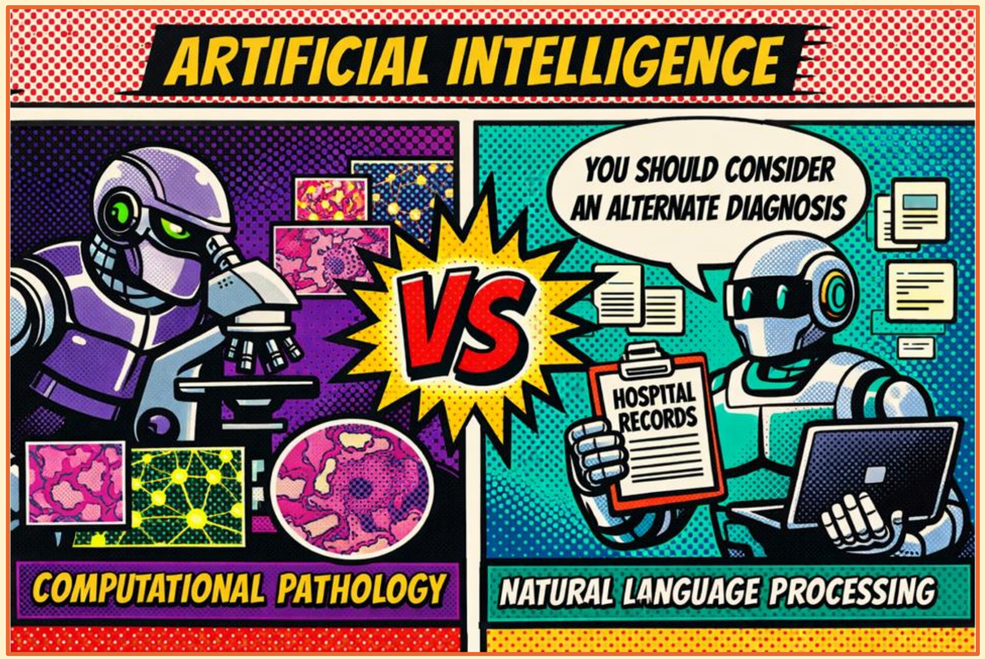
- External validation
- Bias Detection
- Data Governance
- Workflow integration
- Clinical Interpretability



Computational pathology and NLP are **complementary**, but **neither replaces clinical reasoning**.
Both must earn trust before routine adoption.

EFFLUENT EIGHT ROUND

Pick Your Champion for the Artificial Intelligence Region



Computational Pathology

vs

Natural Language Processing

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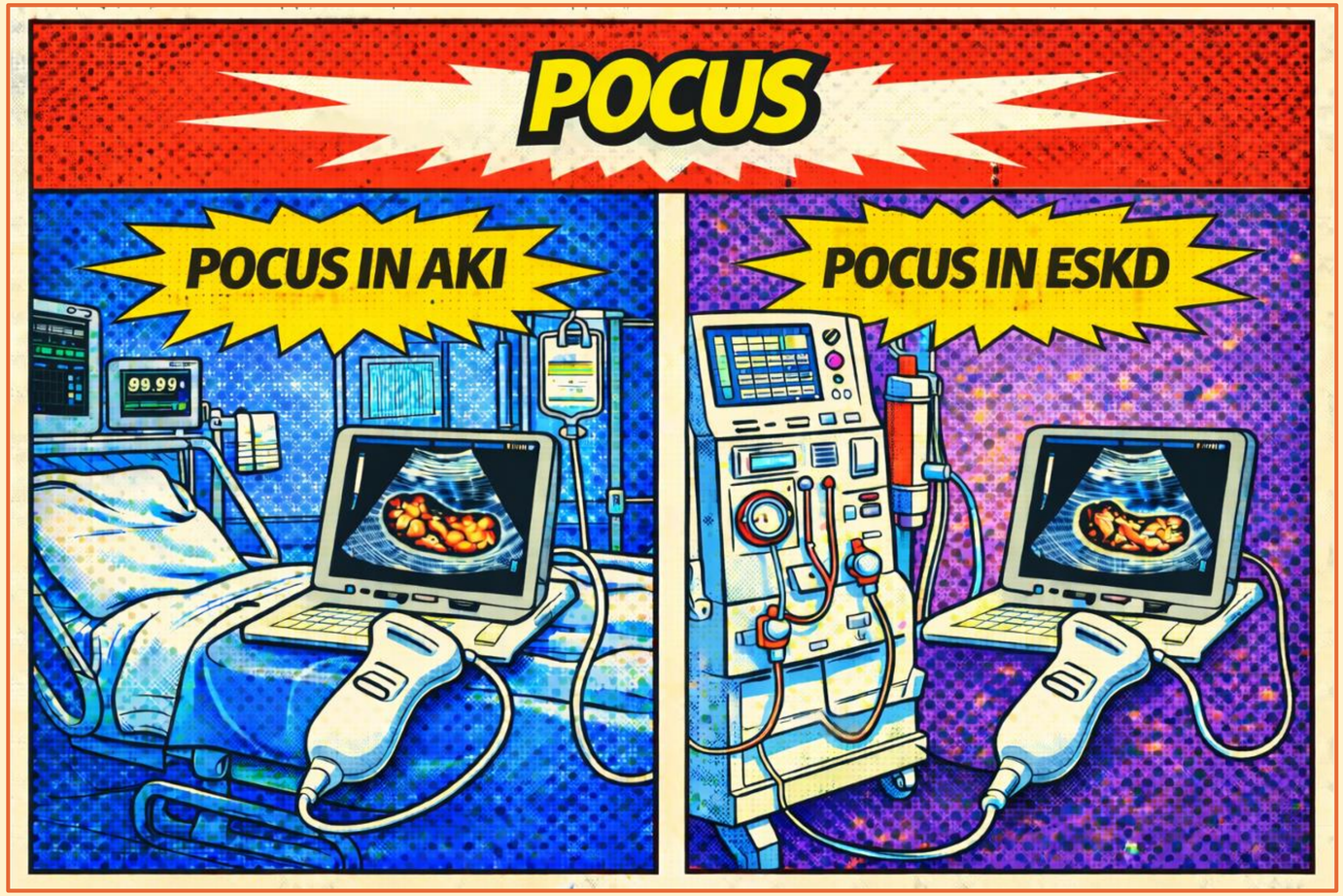
POCUS



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POCUS in AKI

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POCUS for Acute Kidney Injury

POCUS for Obstruction

- Obstructive Nephropathy Accounts for 5-10% of AKI

1. Formal renal-bladder ultrasounds can be unnecessary and costly in low-risk patients

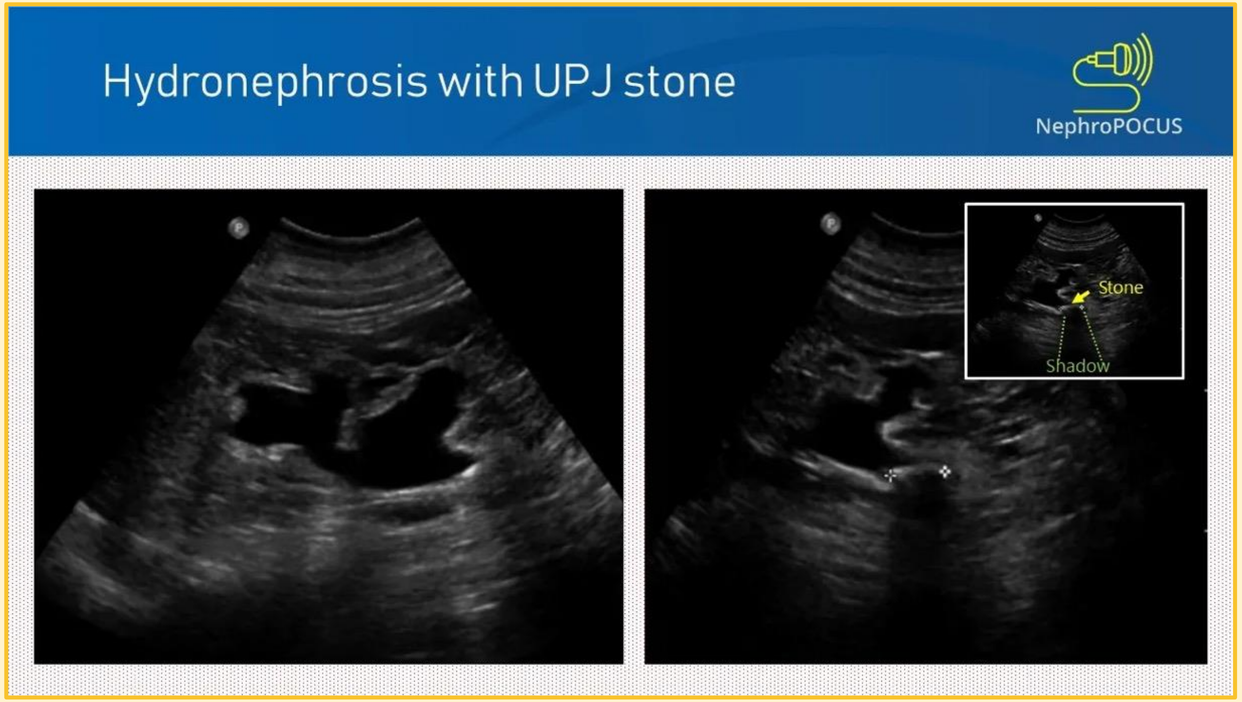
- POCUS of the Kidney can provide data regarding

1. Hydrouretonephrosis
2. Bladder Distention/Post-Void retention
3. Kidney Size (can give clues of acute vs chronic kidney disease)
4. Cortex Size and Echogenicity (acute vs chronic kidney disease)
5. Nephrolithiasis (echogenic focus with acoustic shadowing)

- Kidney POCUS has been demonstrated to be:

1. sensitive and specific (~90%) at identifying obstruction in the AKI population as Gold standard Studies (Renal Bladder Ultrasound and CT Abdomen)
2. Significantly faster at identifying obstruction
3. Particularly accurate in moderate – high risk patients

False negatives for obstructive Nephropathy may occur in early obstruction, volume depletion or retroperitoneal fibrosis



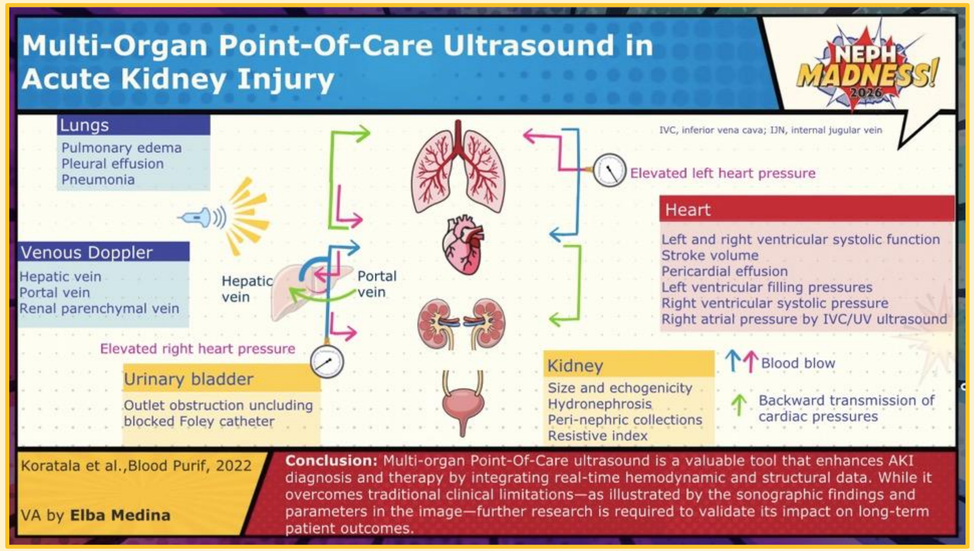
POCUS for Acute Kidney Injury

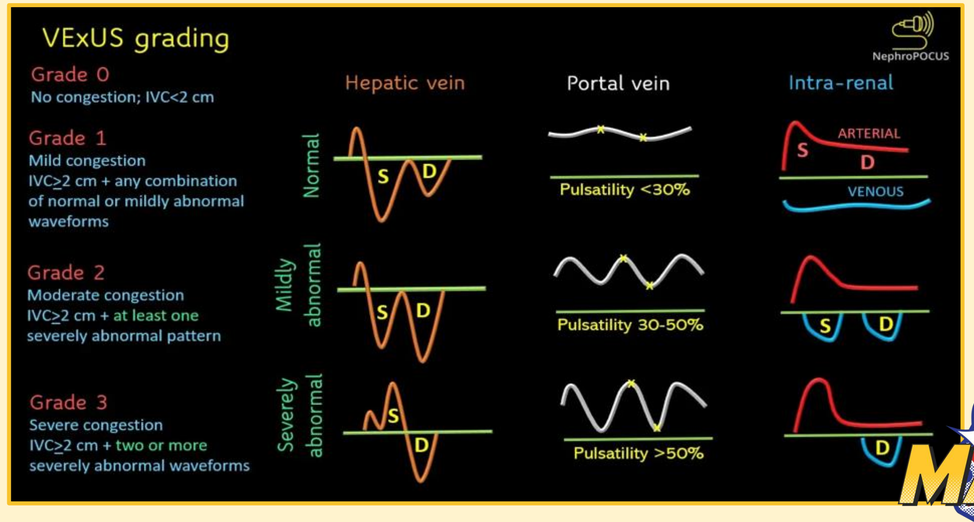
POCUS for Volume Assessment

- Volume assessment is physiologically complex, POCUS offers a comprehensive framework but requires understanding of the test strengths/limitations.

1. Cardiovascular Ultrasound – To assess left and right sided pressure/function
2. Lung/Abdominal Ultrasound– To assess for extravascular fluid
3. IVC ultrasound - marker for central venous pressure rather than fluid responsiveness.
4. VExUS– Assesses doppler flow patterns in larger proximal veins in liver/kidneys to assess for organ impacts of venous congestion

- VExUS > 2 has been validated in the post-cardiac surgery population as a risk factor for Acute Kidney Injury due to venous congestion
- A decrease in VExUS score in the critically ill population has shown improved kidney outcomes and lower in-hospital mortality in small prospective cohort studies





Modified Venous Excess Ultrasound :
A Dynamic Tool to Predict Mortality in Acute Decompensated Heart Failure

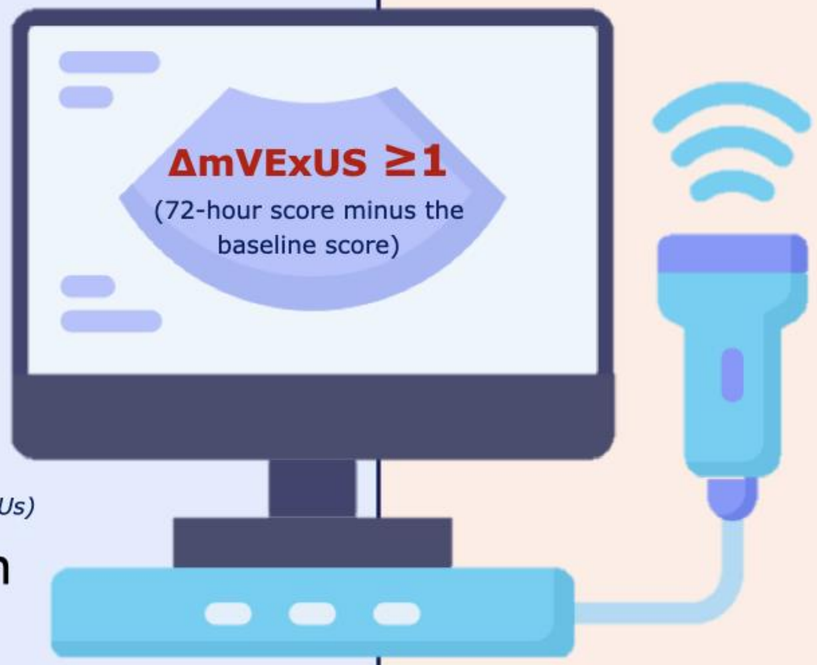
NEPH MADNESS! 2026

METHODS

Prospective Cohort Study

ADHF with **LVEF <50%** (**n = 104**)

Modified VExUS *(mVExUs)* at **≤24h** of admission & at **72h**



FINDINGS

↑ **Weight loss &**
↑ **Urine output**

Better **Clinical Congestion Score & Creatinine reduction**

↓ **In-hospital mortality**
aOR 0.31, 95% CI (0.14–0.68); p=0.004

Saadi et. al, JASE, 2025

VA by **Renz Pasilan**

Conclusion: A ≥1-point reduction in mVExUS over the first 72 hours (ΔVExUS ≥1) was independently associated with lower in-hospital mortality in patients with ADHF and LVEF <50%. This improvement tracked with more effective decongestion supporting serial mVExUS for bedside risk stratification and monitoring.

POCUS in ESKD

POCUS for End Stage Kidney Disease

POCUS for Volume
- Dry Weight determination remains imprecise

1. BP and Intradialytic weight gain are crude surrogates
2. No universally accepted gold standard.

VEXUS
1. No studies looking to date at long-term outcomes
2. One small cohort study showed that ultrafiltration did improve VExUS score over the course of a single dialysis session
3. Case reports have detailed how VExUS can guide Ultrafiltration in overloaded, hospitalized patients

IVC Ultrasound
1. Due to its limitations in interpretation, has only been studied in the critically ill dialysis population

POCUS for vascular access is accessible and may lead to earlier canulation with improved patient experience and outcomes
- Is used for perioperative vein assessment
- May lead to earlier cannulation

1. One study found POCUS led to a a quicker time to canulation for AVFs with a diameter >6mm, <6mm deep, and >6mm long when compared standard of care with no difference in complications between groups

- May lead to better AVF/AVG related outcomes, patient satisfaction and is Is teachable to dialysis unit staff

Lung Ultrasound (LUS)
1. Lung Ultrasound guided ultrafiltration has shown impove both dry weight/BP and cardiac parameters
2. A multicenter RCT (LUST Trial) evaluated a LUS guided UF protocol vs Standard of Care and found no significant difference in major adverse cardiovascular events between groups despite improved relief of lung congestion.

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Does POCUS shorten arterio-venous fistula cannulation time and CVC exposure?

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Single-center mixed design

- Prospective POCUS cohort
- Retrospective non-POCUS controls
- Population: Incident AVFs
- Follow-up: 1 year

Intervention

POCUS within 3–4 weeks post-surgery

Cannulation criteria

- Diameter >6 mm no >20% focal narrowing
- Depth <6 mm
- Cannulation length >6 cm
- ✗ **No flow measurements used**

With POCUS…

- **Earlier AVF cannulation**
  36 vs 63 days
- **Shorter CVC exposure**
  68 vs 98 days
- **No increase in early or late complications**
- **Fewer infections observed with POCUS**
  not statistically significant

POCUS- Point-of-Care Ultrasound, CVC-Central Venous Catheter, AVF- Arterio-Venous Fistula

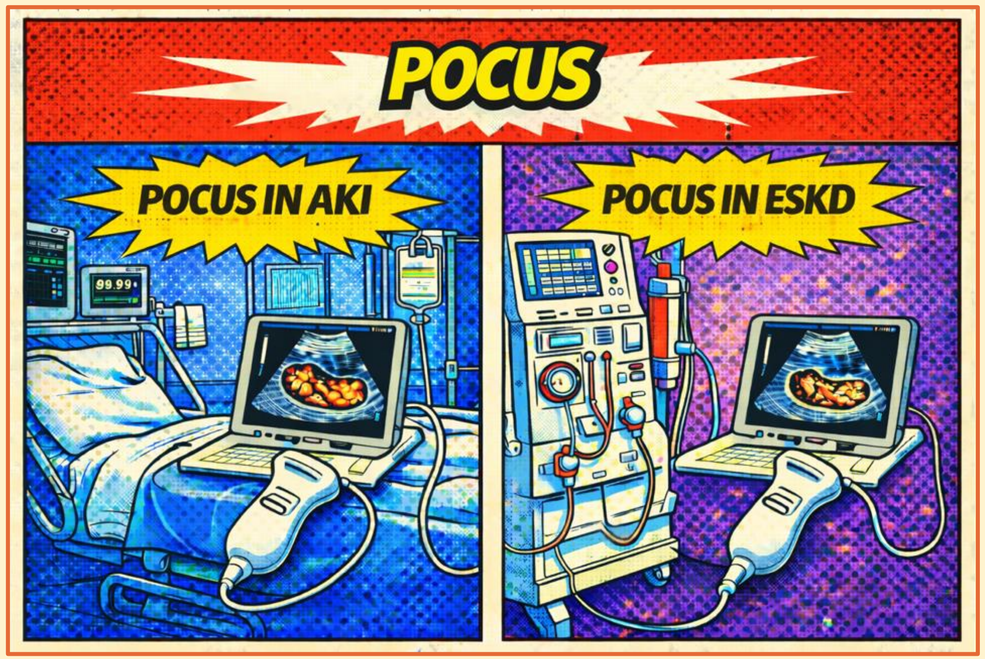
Coritsidis GN et al, J Vasc Access, 2020

VA by **Cristina Popa**

Conclusion: POCUS-guided assessment was associated with earlier AVF cannulation and shorter CVC duration, without increased complications. Due to the study's small size, single-center setting, and non-randomized design, effects on infection rates and long-term access outcomes cannot be definitively established.

EFFLUENT EIGHT ROUND

Pick Your Champion for the POCUS Region



POCUS in AKI

VS

POCUS in ESKD

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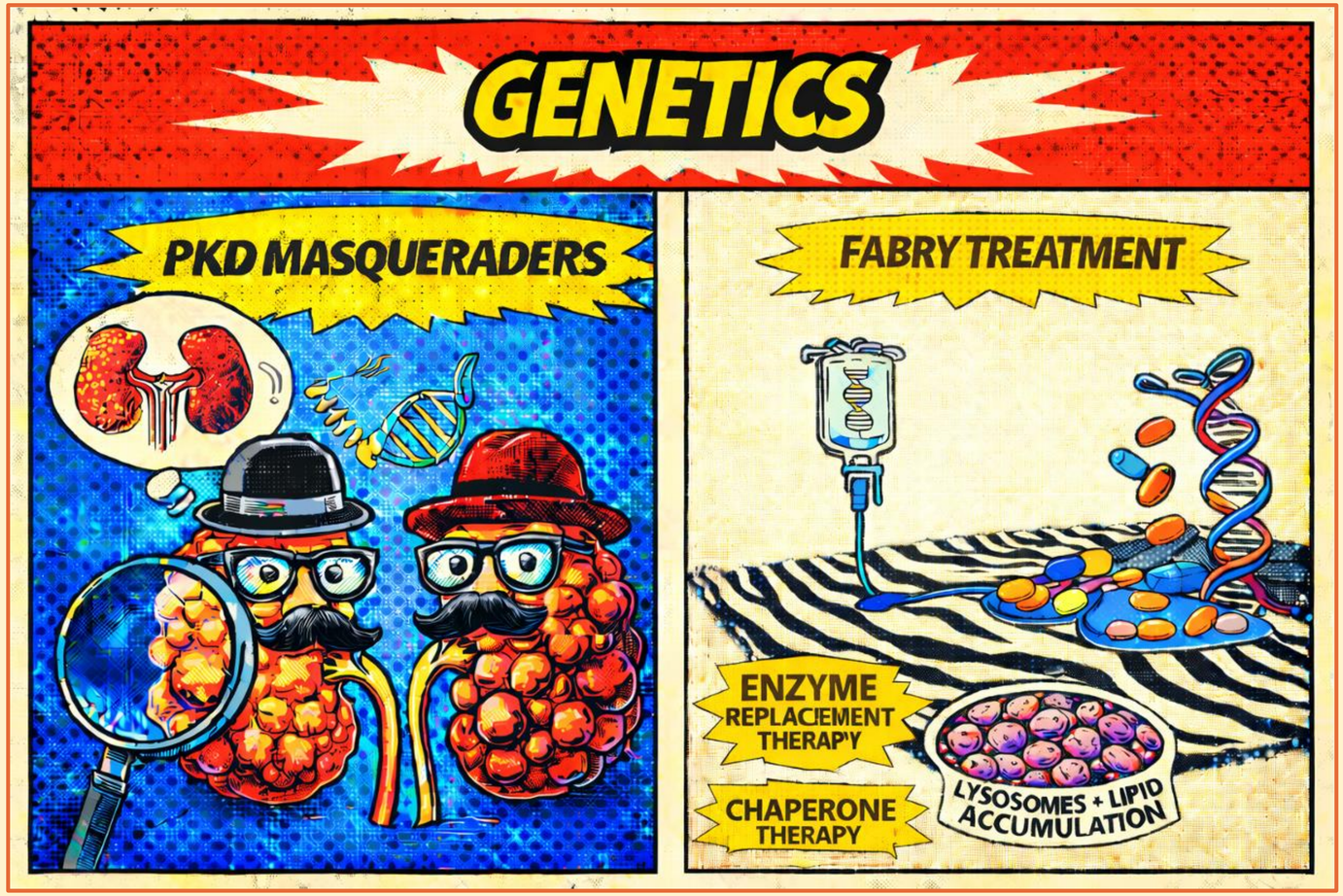
Genetics



Writers:
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Anna Burgner
Samira Farouk

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PKD Masqueraders

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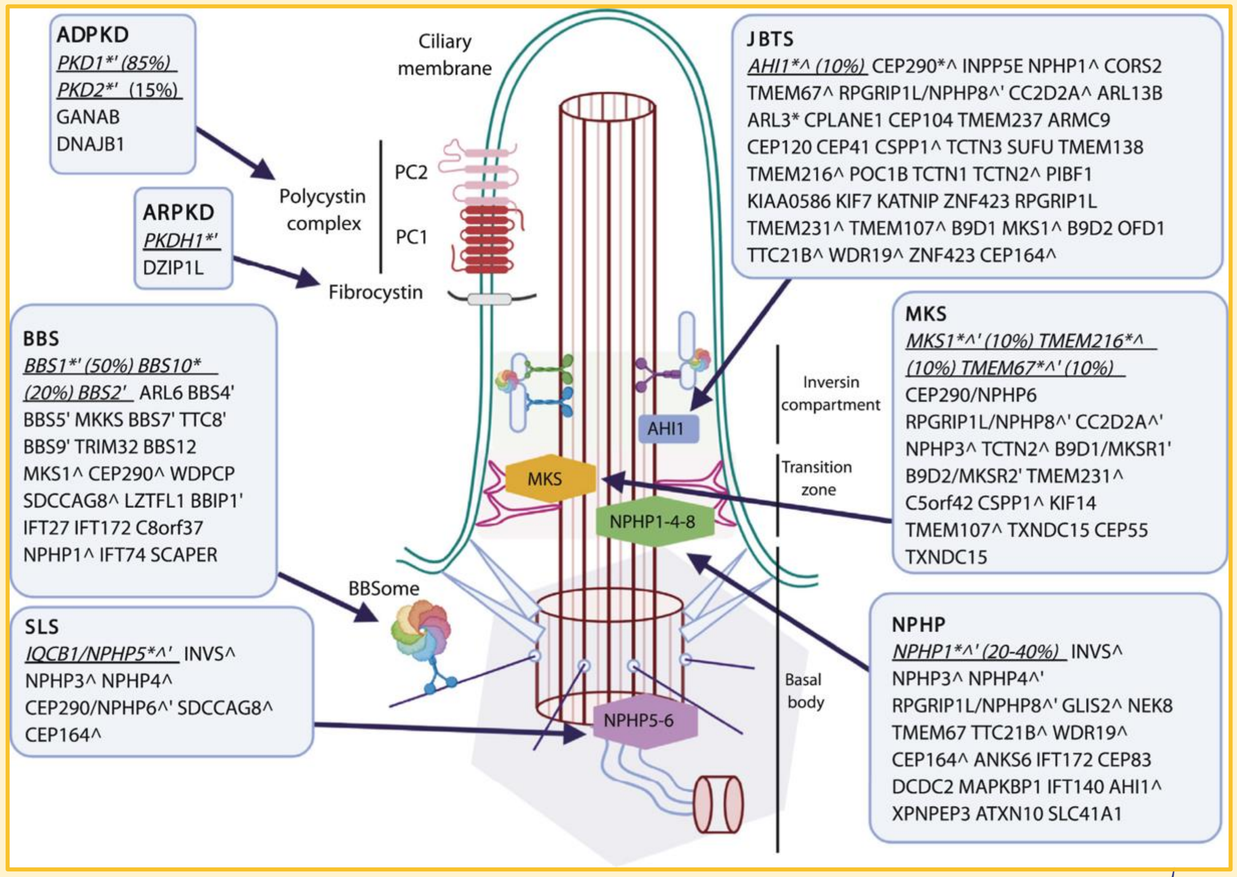
Ciliopathies and Their Cystic Kidney Diseases

- Cilia are hair-like organelles found on nearly all eukaryotic cells
  - Key roles in development including proliferation, differentiation, and migration.
  - Cilia Dysfunction →Ciliopathies are associated with diseases of multiple organ systems
  - Ciliopathies in the kidneys are associated with cystic kidney disease

- Polycystic Kidney Disease Masqueraders
  - Autosomal Dominant PKD
  - Autosomal Recessive PKD
  - Nephronophthisis
  - Medullary Sponge Kidney
  - HNF1*B* related Autosomal Dominant Tubulointerstitial Kidney Disease



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Our Understanding of the Genetics of Cystic Kidney Disease is Evolving

- Autosomal Dominant Polycystic Kidney Disease (ADPKD)
  - Mutations in the *PKD1* and *PKD2* genes are the most common cause
  - Threshold model → cyst formation is triggered if polycystin is reduced below a critical threshold in tubular epithelial cells
  - Leading to the discovery of multiple other gene mutations found that can cause ADPKD
    - *GANAB, DNAJB11, ALG8, ALG9, PRKCSH, SEC63, and SEC61B* among others

- *HNF1B* mutations
  - Also known as renal cysts and diabetes (RCAD) syndrome and HNF1B-MODY or MODY5
  - Kidney manifestations are highly variable, even within a family! (See next slide) →. the exact mutation doesn't predict the kidney disease!

How broad is the renal spectrum in HNF1B nephropathy?

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FAMILY

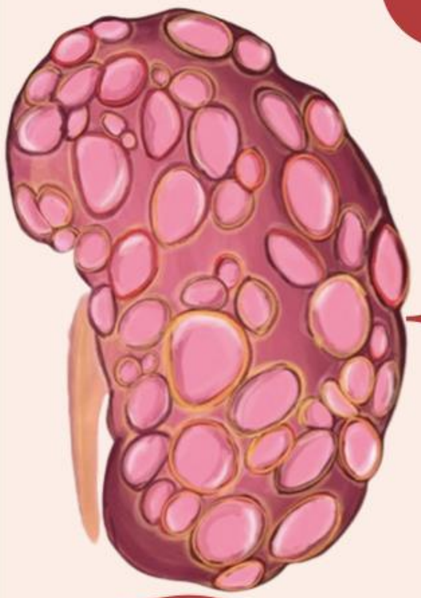
7 families
13 patients with genetically confirmed HNF1B nephropathy

Genetic testing

Targeted NGS panel + MLPA for whole-gene deletion

Segregation analysis

Systematic clinical, laboratory, imaging, and extrarenal phenotyping



Renal phenotypes

- Renal cysts and diabetes
- ADPKD-like cystic disease
- ADTKD ± hyperuricemia/gout (most common; bland urine, IF/TA)
- Congenital anomalies of kidney and urinary tract
- Nephrogenic diabetic insipidus with early polyuria

Marked inter-/ intrafamilial variability

Cysts in ~92%

Novel phenotype: medullary sponge kidney in 17q12 whole-gene deletion family

Genetics: 6 novel variants (3 frameshift, 2 missense, 1 nonsense) + whole-gene deletion

HNF1B- Hepatocyte nuclear factor-1β, ADPKD- Autosomal dominant polycystic kidney disease, ADTKD- Autosomal dominant tubulointerstitial kidney disease, NGS- Next-generation sequencing, MLPA- Multiplex ligation-dependent probe amplification. IF/TA- Interstitial fibrosis / tubular atrophy

Izzi C, et al, Kidney Int Rep, 2020

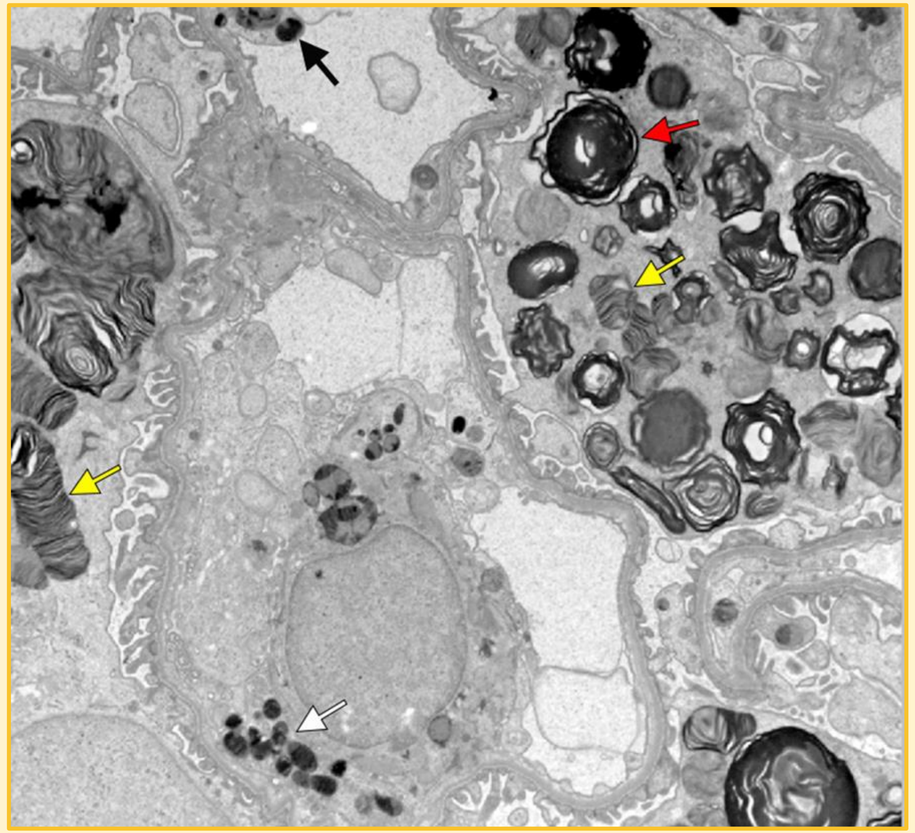
VA by **Cristina Popa**

Conclusion: Extreme renal phenotypic variability characterizes adult HNF1B nephropathy, now expanded to include medullary sponge kidney. The allelic spectrum is further broadened by newly identified pathogenic variants.

Fabry Treatment

Fabry Disease

- X-linked lysosomal storage disorder caused by mutations in the galactosidase A (GLA) gene
- Deficiency of lysosomal enzyme alpha galactosidase A → accumulation of lysosomal Gb3
- End Organ Disease
  - Proteinuric kidney diseased → kidney failure
  - Cardiomyopathy
  - Stroke
  - Neuropathy
  - Skin lesions (angiokeratomas)
- Other noteworthy symptoms:
  - Severe debilitating pain, irritable bowel syndrome-like symptoms, and anhidrosis (leading to heat intolerance)



Classic Zebra Bodies in Podocytes (Yellow Arrow)

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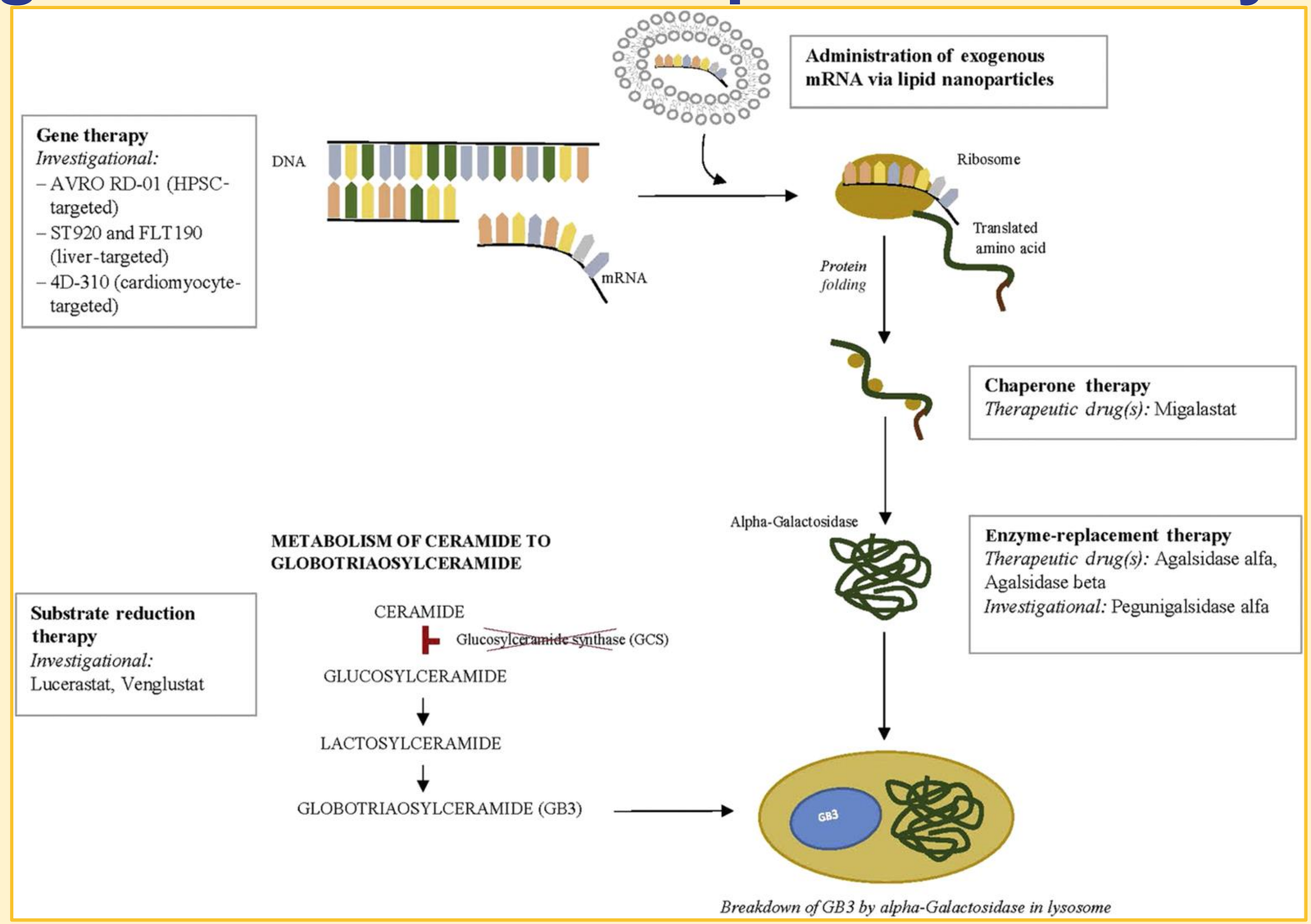
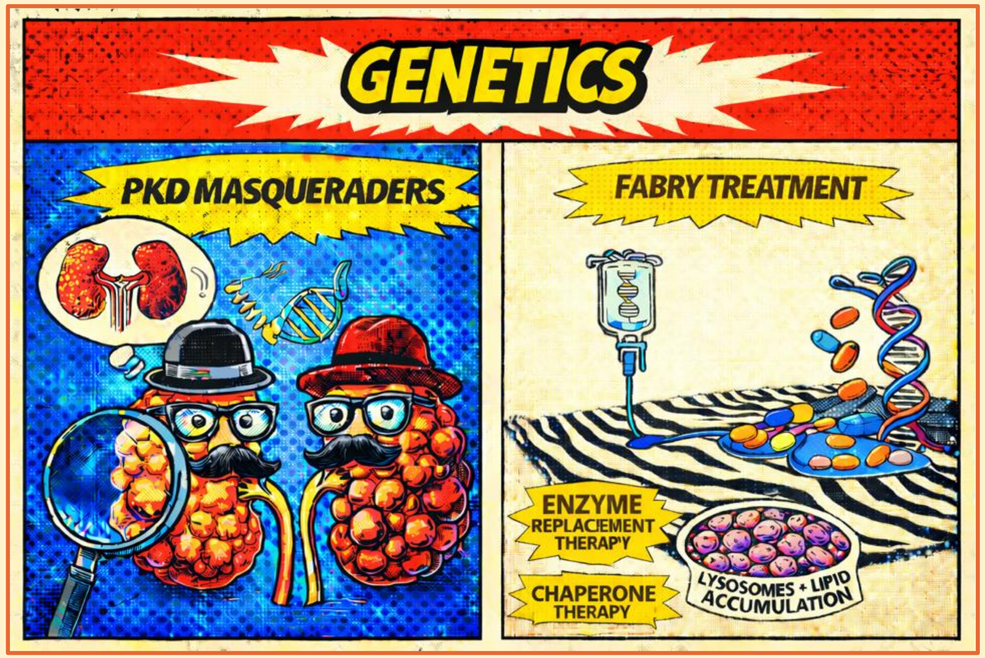
Growing List of Treatment Options for Fabry Disease



Felis A, Whitlow M, Kraus A, Warnock DG, Wallace E. Current and Investigational Therapeutics for Fabry Disease. Kidney Int Rep. 2019 Dec 6;5(4):407-413

EFFLUENT EIGHT ROUND

Pick Your Champion for the Genetics Region



PKD Masqueraders

vs

Fabry Treatment

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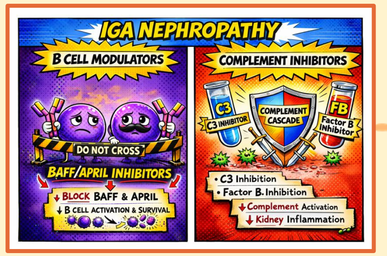
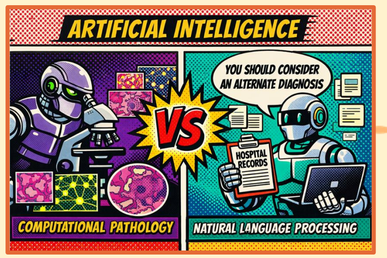
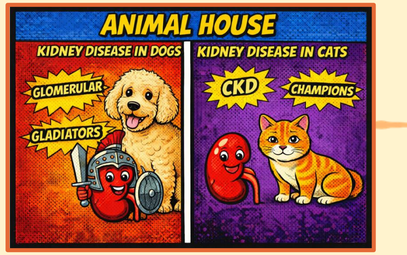
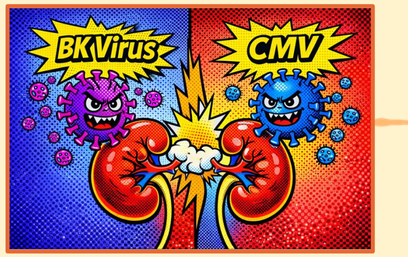
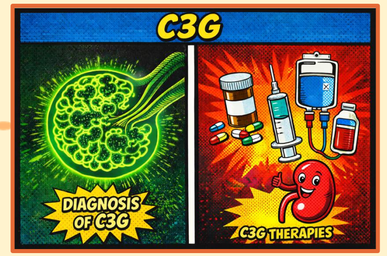
From your Effluent 8, pick your Filtered 4

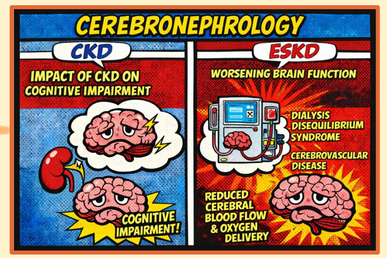


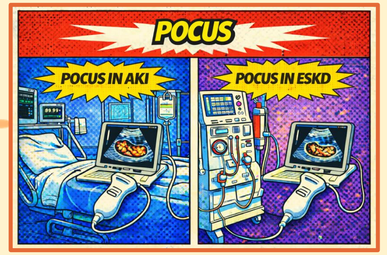


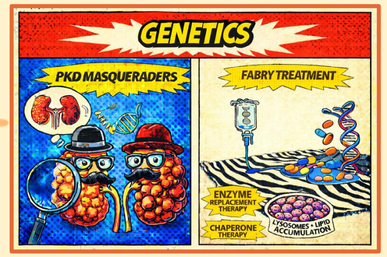












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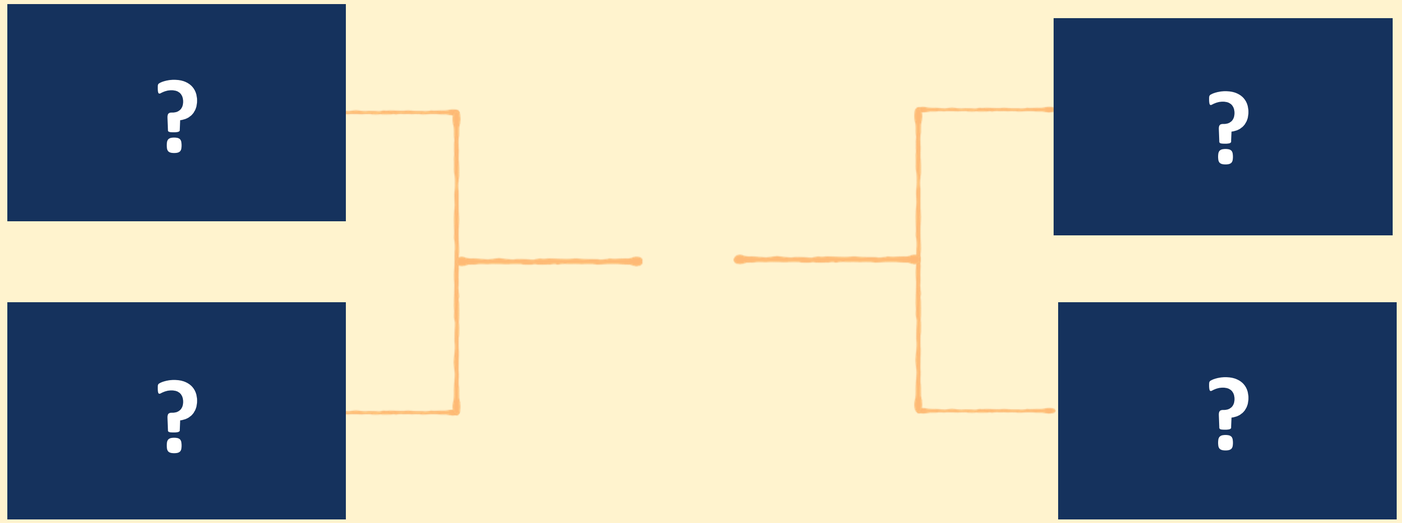
From your Filtered 4, pick your Left and Right Kidneys



Crown your NephMadness 2026 CHAMPION:

Thanks for playing and good luck!

- **Submit brackets by March 31, 2026 on Tourneytopia**
- **Claim CME and MOC credit through NKF PERC**
- **Discuss on social media using #NephMadness**

Important Dates:
March 1, Sunday (7:00 am Eastern): Bracket entry opens
March 31, Tuesday (11:59 pm Eastern): Deadline for entering contest
April 2, Thursday: Effluent 8 results
April 6, Monday: Filtered 4 results
April 8, Wednesday: Left & Right Kidney results
April 10, Friday: NephMadness Champion crowned