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17 Tweets • 2021-01-16 12:33:29 UTC • See on Twitter

rattibha.com

1/ 📢Hello #MedTwitter
Let's talk about pediatric #MPGN / 'Immune complex GN' #ICGN today
A few pearls from the 1st @ASPNeph pathology webinar of 2021
#tweetorial #NephTwitter

Let's begin with a poll:
❓Which of the following is true about IC-MPGN?

2/ All the above

⚡There is limited data on epidemiology

⚡The estimated prevalence is 1 to 2/ million children, 5 to 15 years of age

3/💥MPGN denotes “pattern of injury” not etiology

⚡Characteristic mesangial & endocapillary cellularity

⚡Thickening of glomerular capillary walls due to subendothelial deposition of IC/complement factors

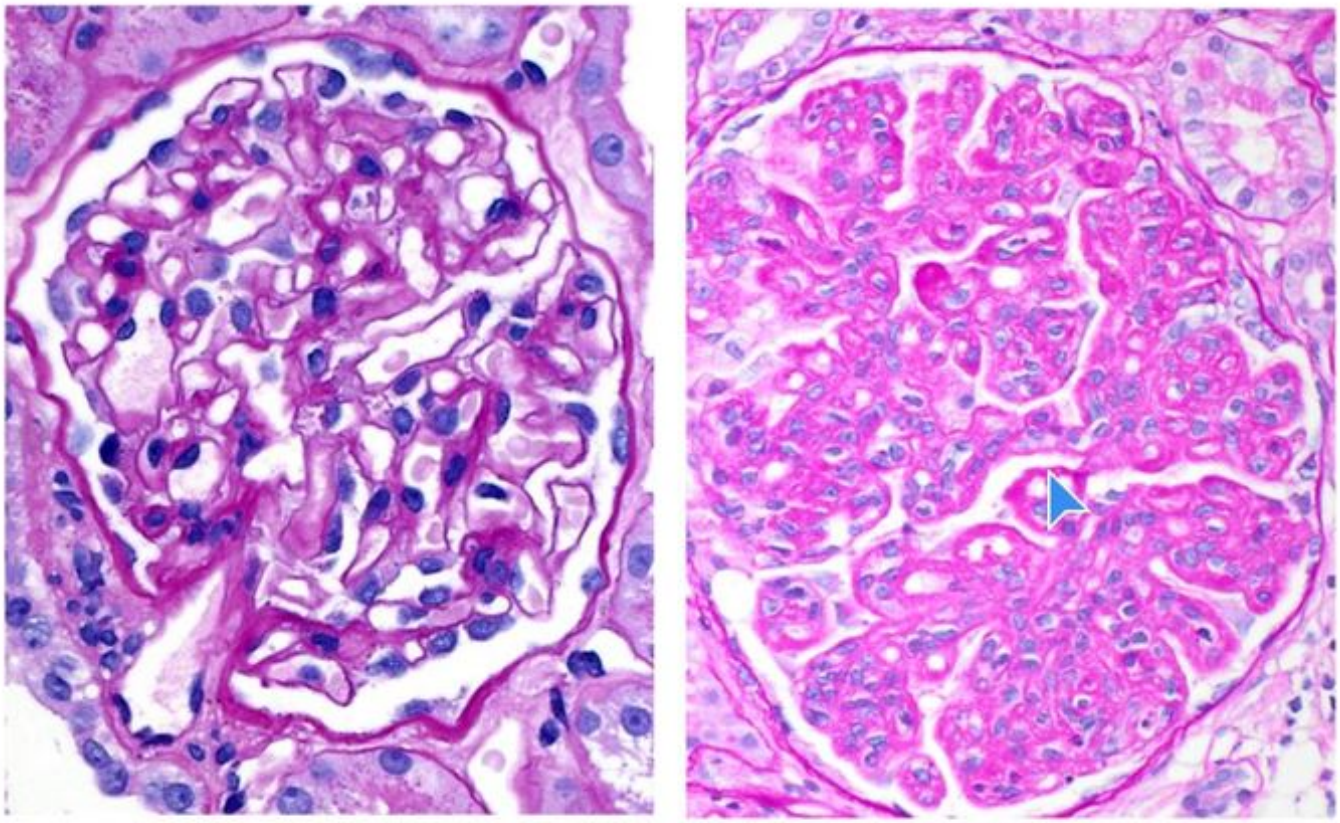


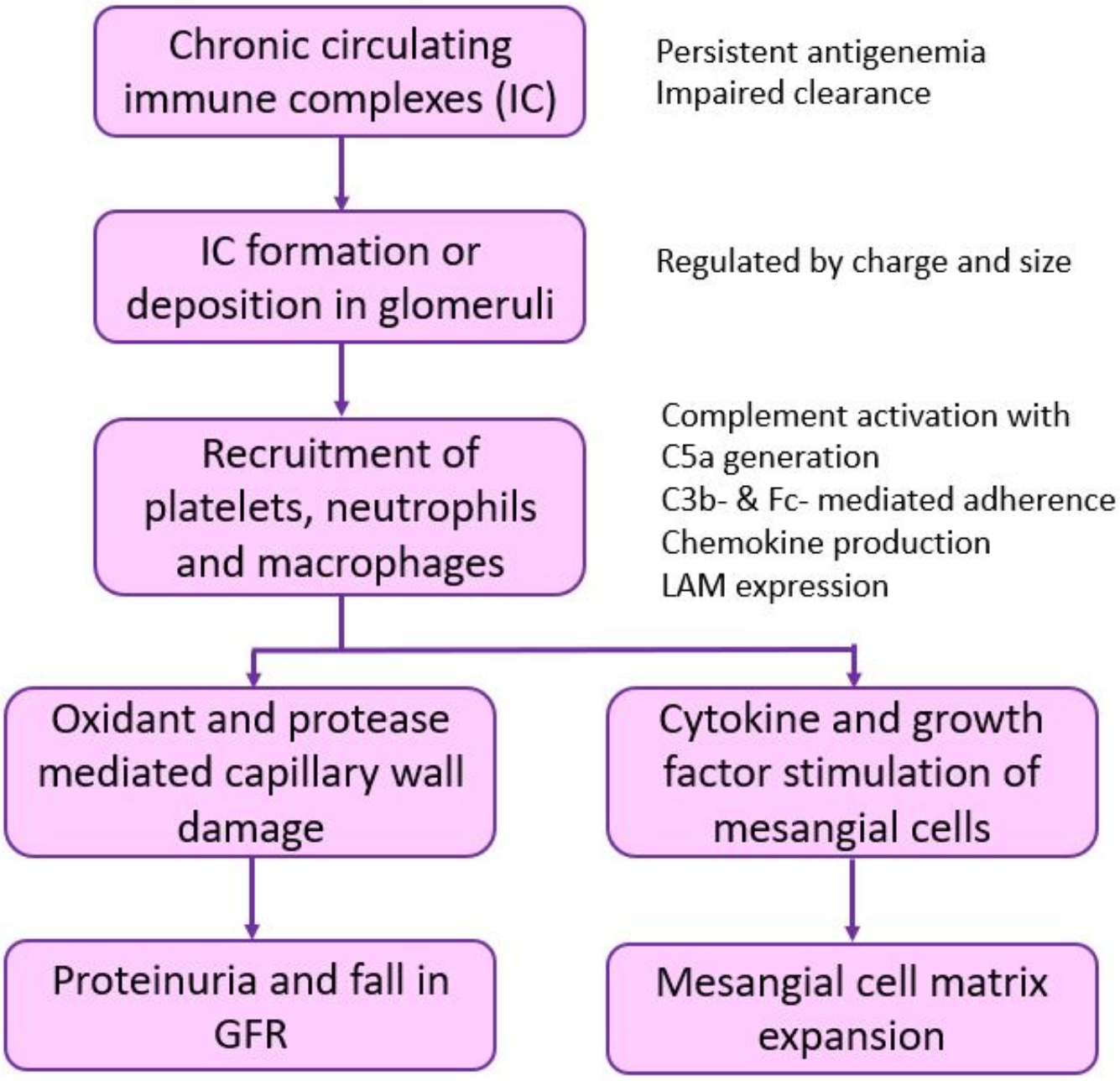
Image courtesy @Trumidor

4/ 💥Type III hypersensitivity reaction💥 is the hallmark of the disease

⚡”Anything” can form IC→IC deposition→activation of immune cells→ ‘complement activation’→ Glomerular injury

⚡complement dysregulation is the key🗝factor

Pathogenesis of IC-MPGN



@drM_sudha

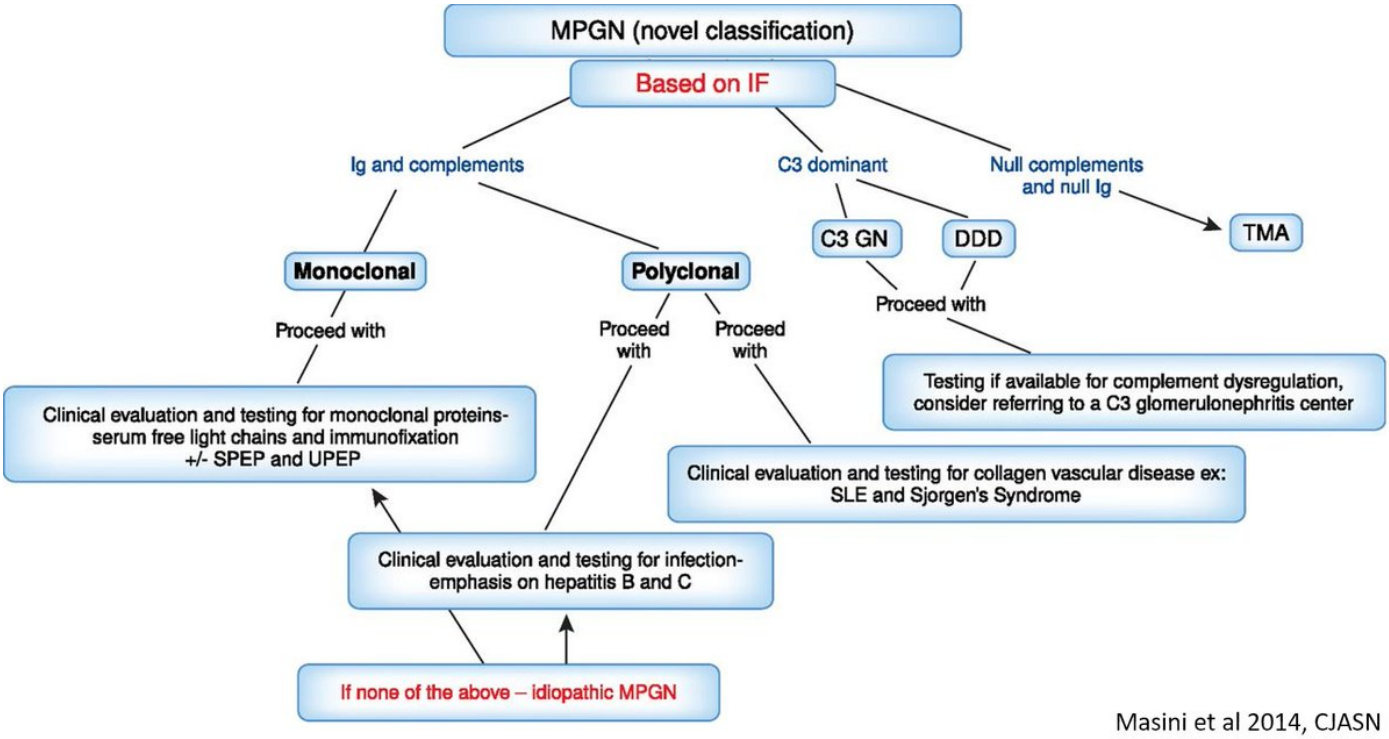
Adapted from comprehensive nephrology

5/ 💥Currently, “triggers/ risk factors” for host injury are unknown

⚡Damage is inversely proportional to Antigen (Ag) clearing
⚡In other words, chronic antigenemia = chronic inflammation

6/ 💥Latest classification is based on IF-

⚡C3 dominant deposits→ C3 Glomerulopathy (C3GN & DDD)- rare
⚡C3 + Ig deposits→ Ig- MPGN (Immunoglobulin asso. MPGN)
⚡No deposits MPGN→ Chr. TMA, transplant glomerulopathy, etc.



Masini et al 2014, CJASN

Immunoglobulin/ Immune Complex mediated	❖ Deposition of Ag-Ab complexes due to ▪ Infection ▪ autoimmune disease ❖ Deposition of monoclonal Ig due to plasma or B –cell disorder (>50y) ❖ Fibrillary GN
Complement- mediated	❖ C3GN and C3 DDD ❖ C4GN and C4 DDD
MPGN without IC or complement	❖ Transplant glomerulopathy ❖ Chronic TMA
Idiopathic	❖ None of the above are present

courtesy: Dr. Carla Nester

7/ 💥Etiopathogenesis:

⚡IC- MPGN is via CLASSICAL complement pathway activation,

⚡C3G is due to primary alternative complement pathway dysregulation

	IC- MPGN	C3G
Antigens	❖ Children- idiopathic ❖ Adults- secondary to infection, autoimmune disease, or monoclonal gammopathies	❖ autoantibodies that protect C3 convertase from degradation (C3, C4, or C5 nephritic factors) ❖ genetic mutations resulting in impaired function of alternative complement pathway regulators ❖ idiopathic
Complement	activation of CLASSICAL pathway	primary ALTERNATE pathway dysregulation

Kirpalani et al 2020

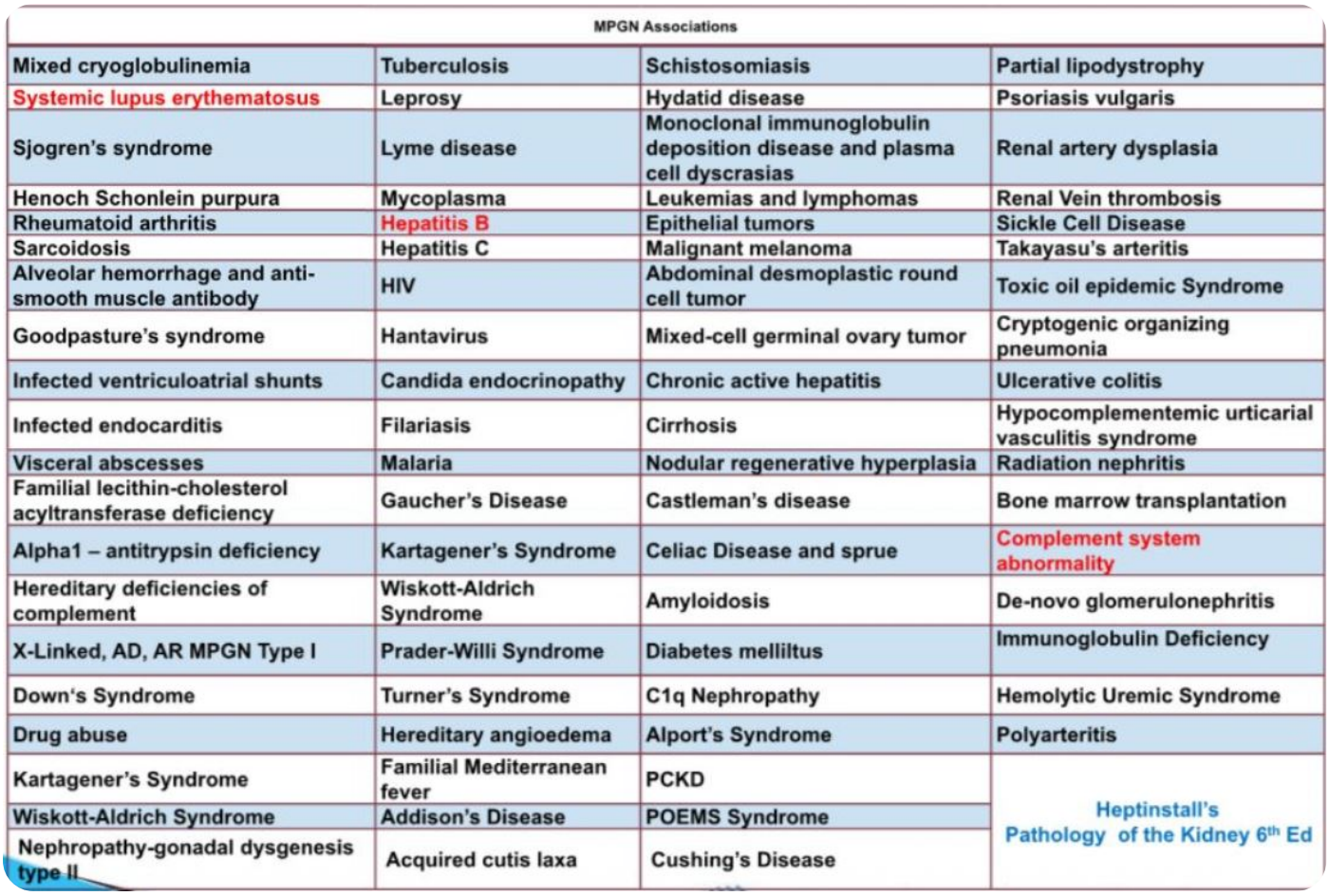
8/💥 MPGN is associated with a variety of disorders. Common one being

⚡Complement system abnormalities

⚡SLE

⚡Hepatitis B &C

⚡>50y -monoclonal gammopathies



MPGN Associations

Mixed cryoglobulinemia	Tuberculosis	Schistosomiasis	Partial lipodystrophy
Systemic lupus erythematosus	Leprosy	Hydatid disease	Psoriasis vulgaris
Sjogren's syndrome	Lyme disease	Monoclonal immunoglobulin deposition disease and plasma cell dyscrasias	Renal artery dysplasia
Henoch Schonlein purpura	Mycoplasma	Leukemias and lymphomas	Renal Vein thrombosis
Rheumatoid arthritis	Hepatitis B	Epithelial tumors	Sickle Cell Disease
Sarcoidosis	Hepatitis C	Malignant melanoma	Takayasu's arteritis
Alveolar hemorrhage and anti-smooth muscle antibody	HIV	Abdominal desmoplastic round cell tumor	Toxic oil epidemic Syndrome
Goodpasture's syndrome	Hantavirus	Mixed-cell germinal ovary tumor	Cryptogenic organizing pneumonia
Infected ventriculoatrial shunts	Candida endocrinopathy	Chronic active hepatitis	Ulcerative colitis
Infected endocarditis	Filariasis	Cirrhosis	Hypocomplementemic urticarial vasculitis syndrome
Visceral abscesses	Malaria	Nodular regenerative hyperplasia	Radiation nephritis
Familial lecithin-cholesterol acyltransferase deficiency	Gaucher's Disease	Castleman's disease	Bone marrow transplantation
Alpha1 – antitrypsin deficiency	Kartagener's Syndrome	Celiac Disease and sprue	Complement system abnormality
Hereditary deficiencies of complement	Wiskott-Aldrich Syndrome	Amyloidosis	De-novo glomerulonephritis
X-Linked, AD, AR MPGN Type I	Prader-Willi Syndrome	Diabetes mellitus	Immunoglobulin Deficiency
Down's Syndrome	Turner's Syndrome	C1q Nephropathy	Hemolytic Uremic Syndrome
Drug abuse	Hereditary angioedema	Alport's Syndrome	Polyarteritis
Kartagener's Syndrome	Familial Mediterranean fever	PCKD	Heptinstall's Pathology of the Kidney 6th Ed
Wiskott-Aldrich Syndrome	Addison's Disease	POEMS Syndrome	
Nephropathy-gonadal dysgenesis type II	Acquired cutis laxa	Cushing's Disease	

9/ 💥What is the most common presentation of IC-MPGN?

10/ Ans: Hematuria

💥Clinical presentation is heterogeneous

⚡ranges from asymptomatic hematuria to AKI

⚡In a pediatric study: hematuria> HTN > NS

https://www.kireports.org/article/S2468-0249(20)31534-5/fulltext#secsectitle0030

Table 3 Clinical parameters for the combined KidCOM and C3 Glomerulopathy and Membranoproliferative Glomerulonephritis: Pediatric Outcomes cohorts

Clinical parameters	Total cohort (*N* = 165)	IC-MPGN (*n* = 42)	C3G (*n* = 43)	*P* value (IC-MPGN vs. C3G)
Nephrotic syndrome at diagnosis	11.8%	22.0%	11.9%	NS (0.25)
Hypertension at diagnosis	57.5%	57.1%	57.6%	NS (0.38)
Hypertension at last follow-up	42.5%	70.4%	42.4%	NS (0.40)
P value	NS (0.05)	NS (0.31)	NS (0.44)	
Hematuria at diagnosis	80.9%	81.0%	61.9%	NS (0.19)
Hematuria at last follow-up	48.5%	57.1%	38.1%	NS (0.82)
P value	<0.0001[a]	0.0273[a]	0.0005[a]	

Kirpalani et al 2020

11/💥 A 14 yr old adolescent male patient presented with HTN, hematuria, nephrotic syndrome, and AKI. Kidney biopsy revealed IC-MPGN. What will be your initial workup?

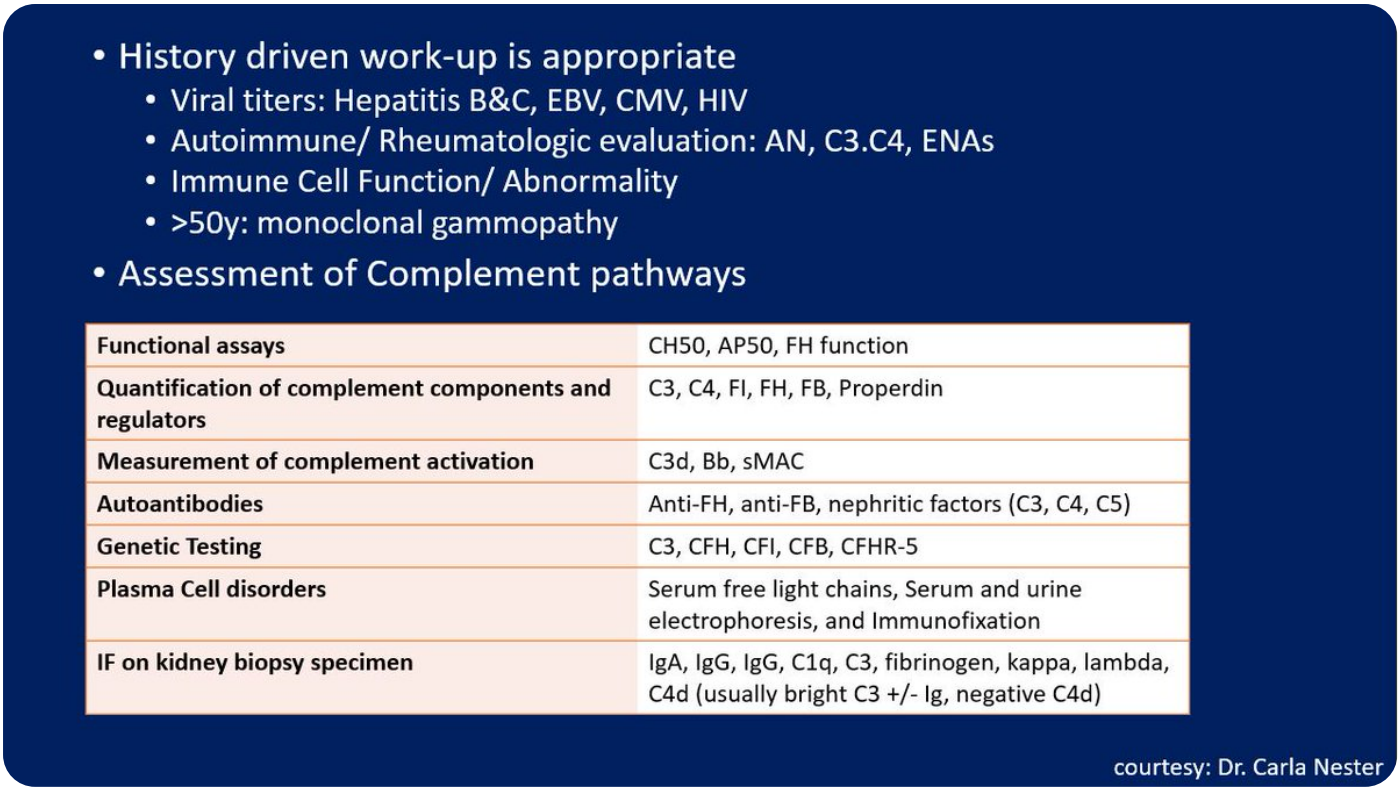
12/ 💥Ans: All the above

⚡GOAL: identifying Treatable Target⚡

📌Rule out PIGN prior to assigning IC-GN/ C3GN diagnosis

📌Hx driven work-up: Viral titers, Autoimmune/ Rheum. evaluation, Immune Cell Abnormality, etc

📌If no etiology is found--> assess complement dysregulation

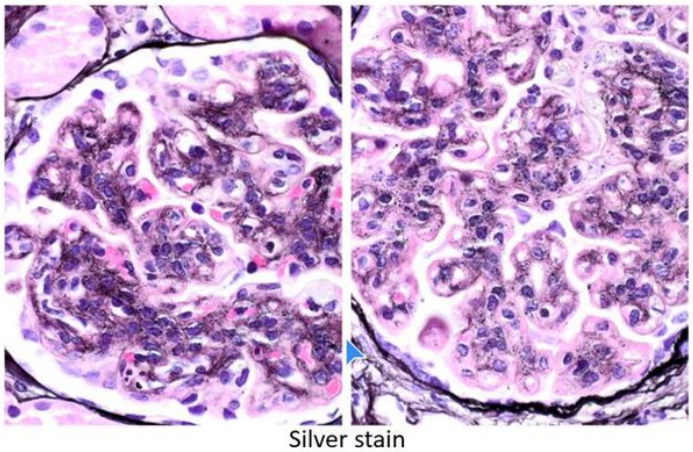


13/💥 Kidney Biopsy in IC-MPGN shows:

⚡LM: Mesangial proliferation and GBM thickening.
“smashed blueberry pancake” appearance - by @Trumidor

⚡IF: C3 deposits + Ig deposits

⚡EM: Mesangial proliferation, GBM thickening, mesangial deposits



Silver stain

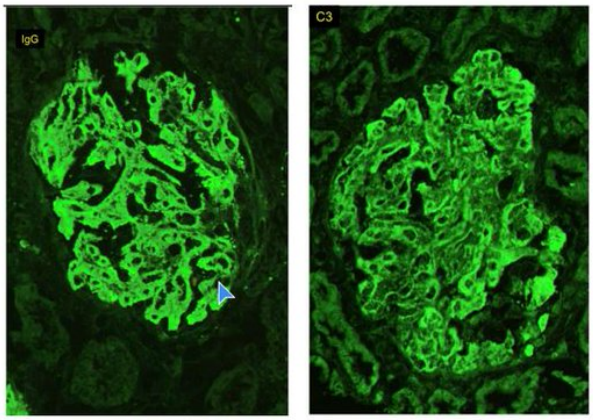


Image courtesy @Trumidor

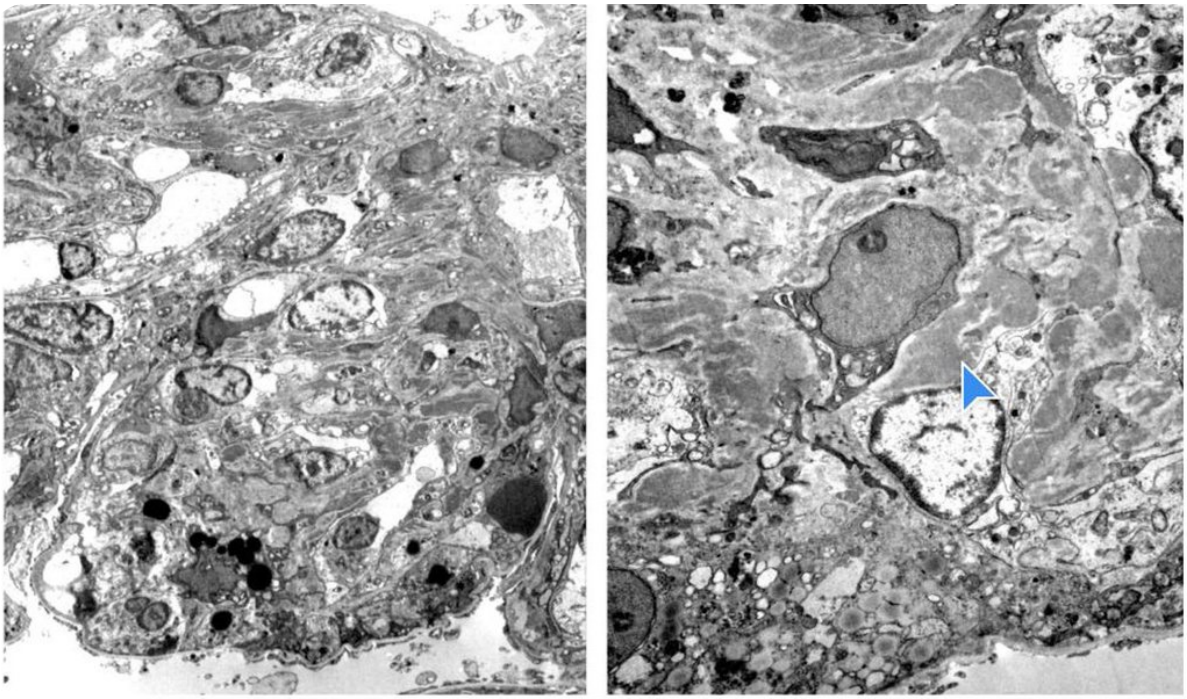


Image courtesy @Trumidor

14/ 💥Rx: treating the etiology, ↓ underlying immune dysregulation & burden of HTN & proteinuria

⚡No curative option

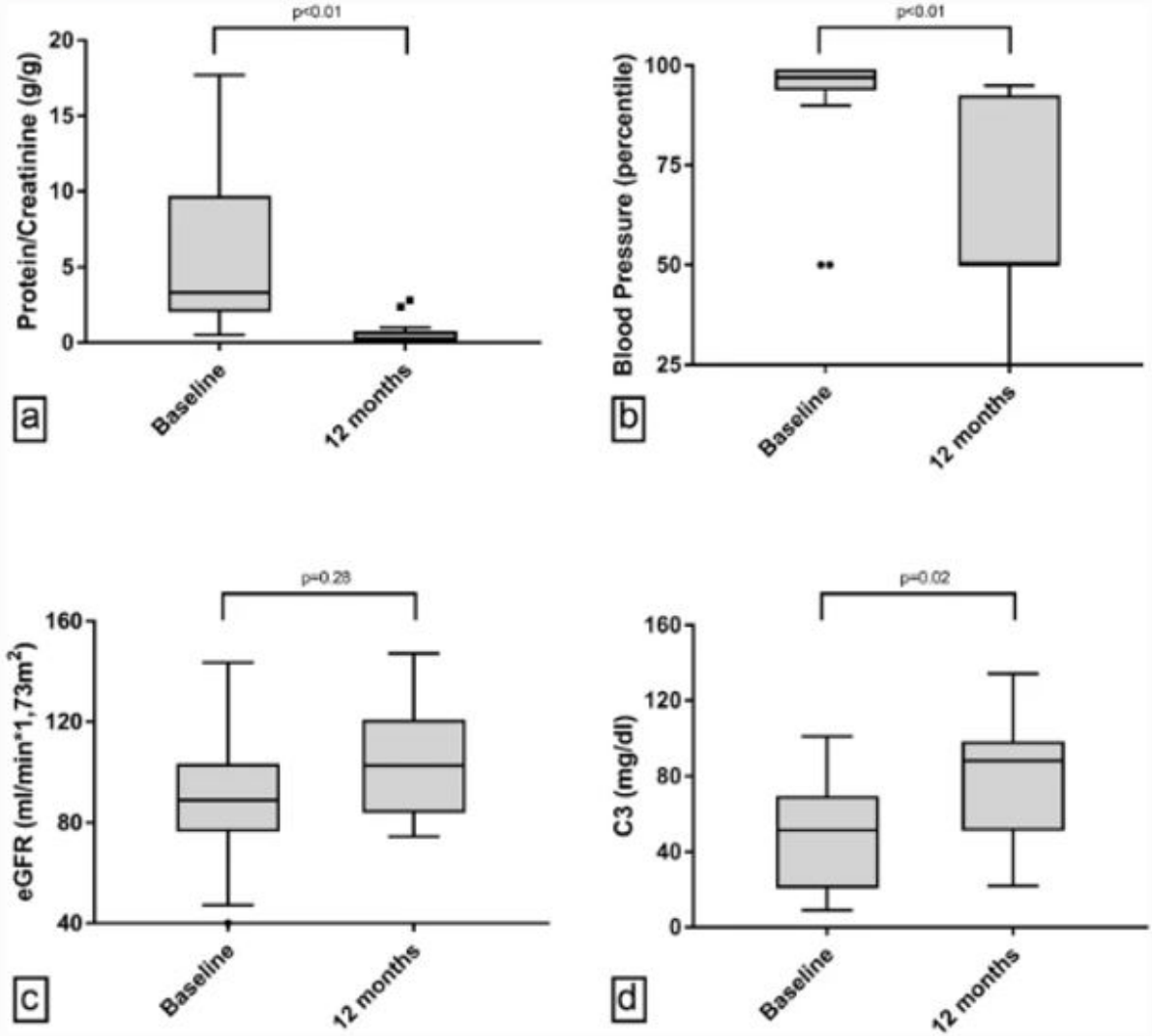
⚡Mostly expert-opinion based Rx data

⚡RAASi, HTN & Lipid-lowering agents - all

⚡Steroids, MMF & rarely CNI

⚡PLEX, Rituximab, Eculizumab- inconsistent data

Fig. 1



Clinical parameters at first presentation (n = 14) and after 1 year of follow-up (n = 13). Data are shown as median (line), interquartile range (box), and 1.5× interquartile range (whiskers). **a** Shows protein/creatinine ratio, **b** age-height-adapted blood pressure percentiles, **c** estimated glomerular filtration rate (eGFR) according to the Schwartz formula, and **d** serum C3 levels

Holle et al 2018

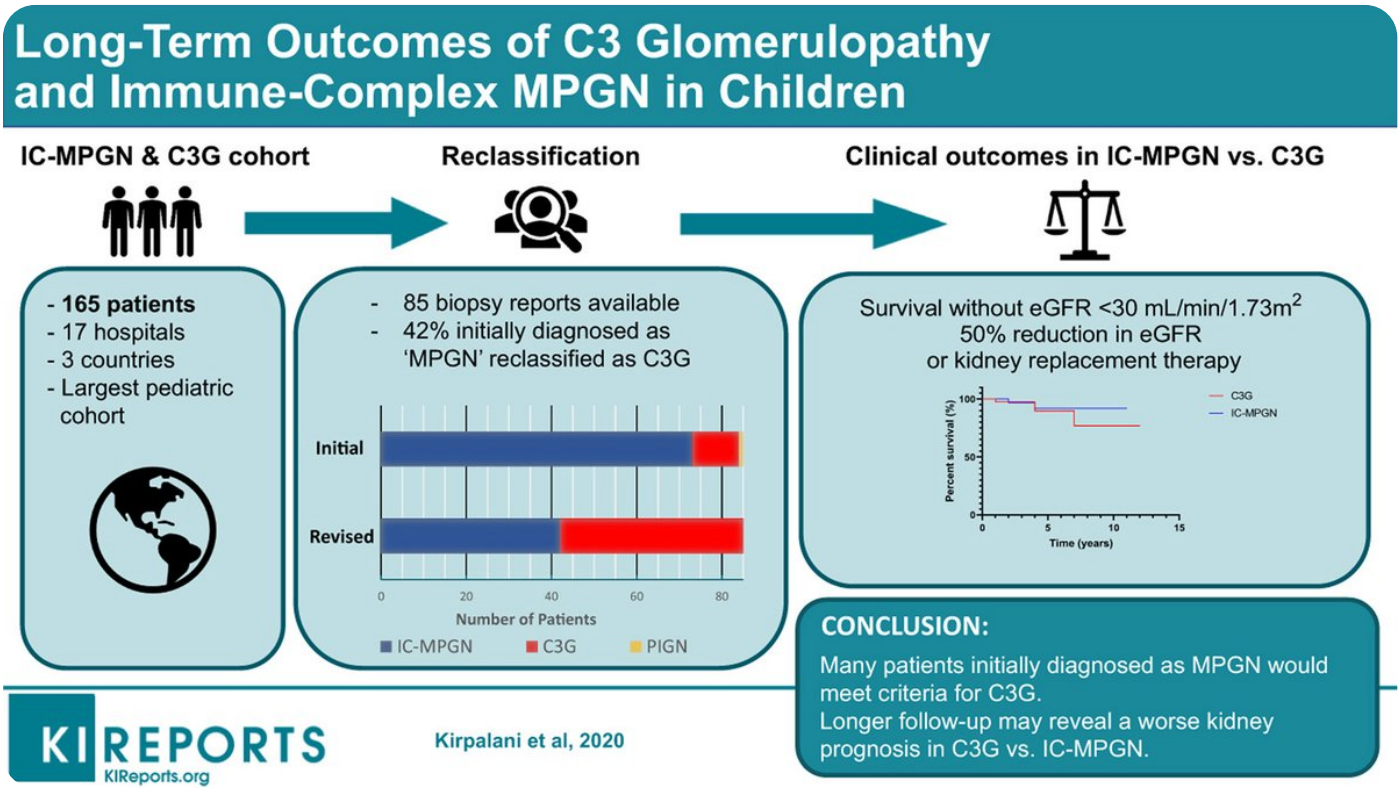
15/ 💥Prognosis:

⚡pediatric pts with IC-MPGN/ C3G have better outcomes than adults

⚡Progression to advanced CKD- rare in children

⚡HTN & proteinuria remain suboptimally controlled

⚡Poor prognosis: NS, low eGFR at the onset, persistent HTN & chronic changes on biopsy



16/💥Thank you for scrolling till the end!

For case-based discussion on this topic logon to @ASPNeph January pathology webinar
Until next time...
#MOC2credits

#FellowFOAMgroup #pediatricnephrology @pedsnephrology @Trumidor @kidnyhealth @priti899 @RoshanPGeorgeMD

@rattibha unroll please