ERKNet
The European Rare Kidney Disease Reference Network

european society for paediatric nephrology

WELCOME TO

ESPN/ERKNet
Educational Webinars on Pediatric Nephrology & Rare Kidney Diseases

Date: **13 April 2021**

Topic: **IgA nephropathy and Henoch-Schönlein nephritis**

(IgA vasculitis nephritis)

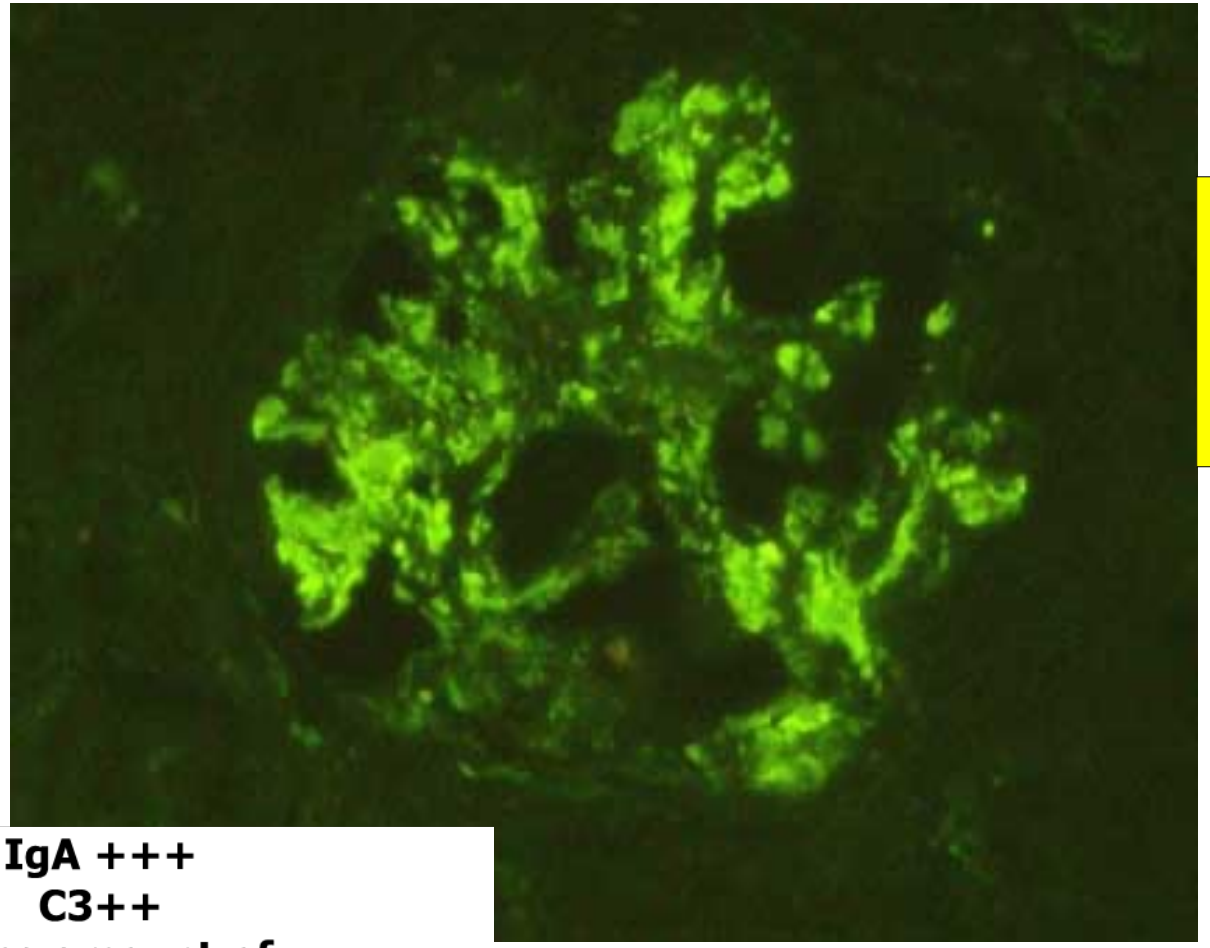
Speaker: **Rosanna Coppo**

Moderator: **Elena Levtchenko**

IgA nephropathy:

is defined by detection of immunoglobulin IgA in glomeruli as dominant or co-dominant in respect to the other immunoglobulins.

Primary IgAN (IgAN)
Berger's GN



IgA +++
C3++
trace amount of other Immunoglobulins

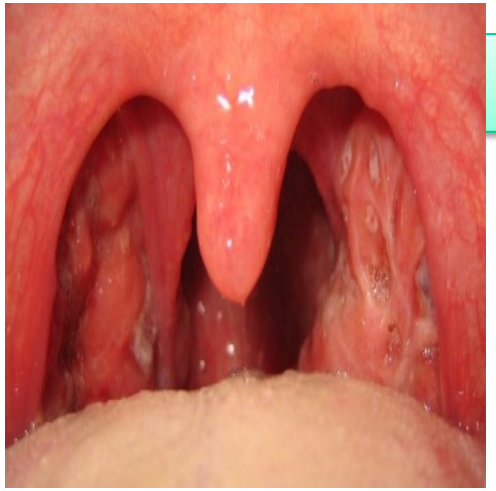
IgAN secondary to vasculitis (IgAVN)
Henoch-Schoenlein GN

Question n 1

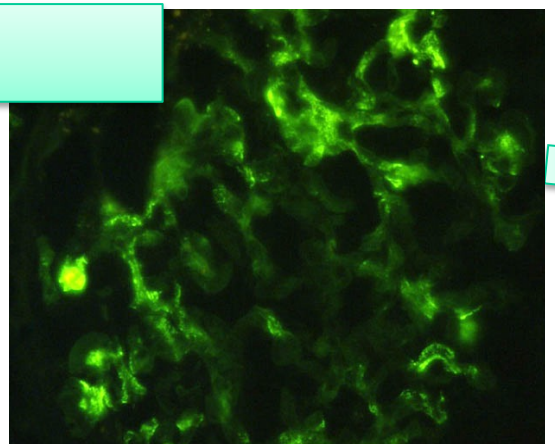
How many patients with primary IgA nephropathy have you seen?

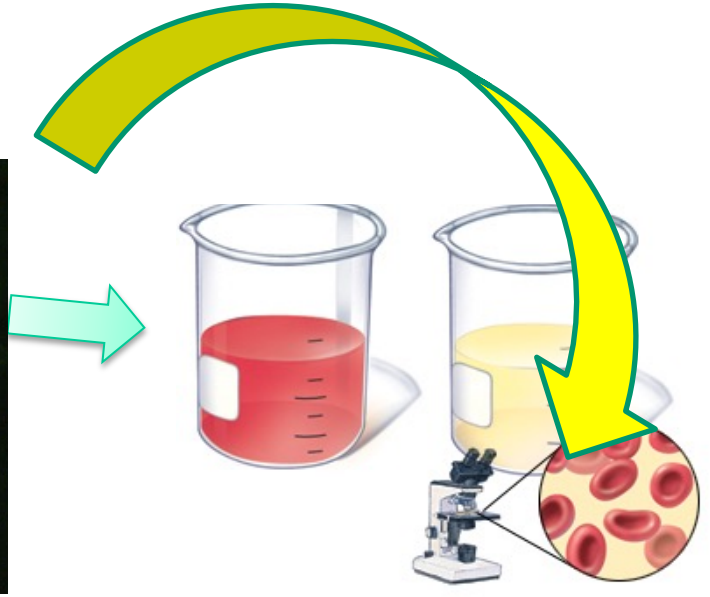
How many patients with IgA vasculitis nephritis (Henoch-Schoenlein purpura nephritis) have you seen?

Primary IgAN



IgA





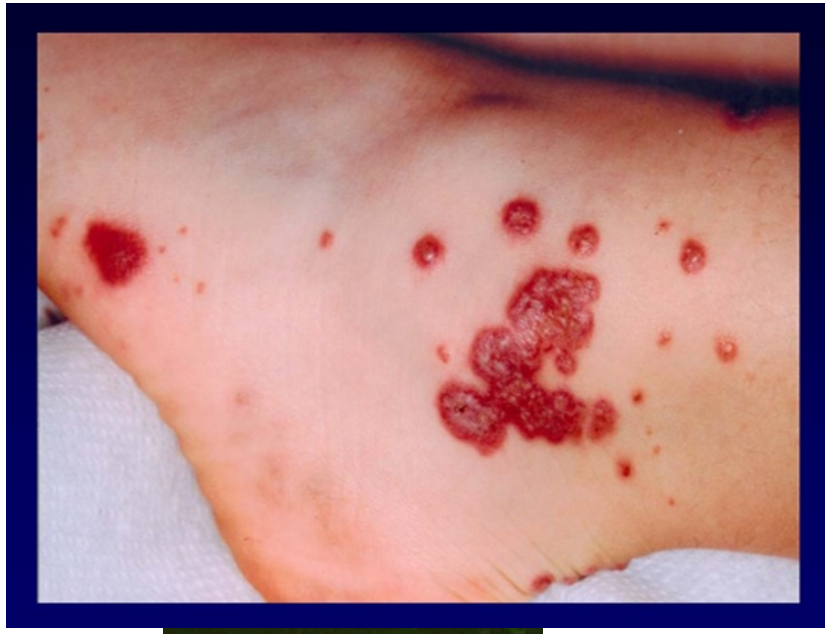
Onset:

- **Gross hematuria following an upper respiratory tract infection**
- **Microscopic hematuria without or with associated proteinuria**

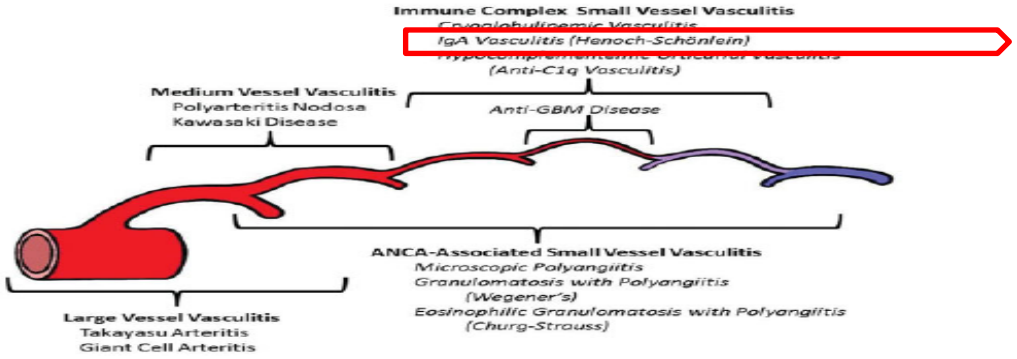
Natural history:

- **Most common in young adults. Relentless progression.**
- **In children possibility of remission, unfrequent progression over decades.**

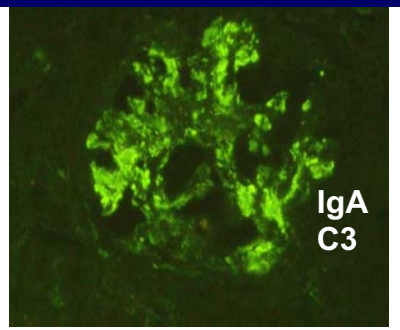
IgA Vasculitis (Henoch-Schoenlein purpura) is a vasculitis whit IgA-dominant immune deposits affecting small vessels (capillaries, venules, arterioles) Involving skin, gut and glomeruli and associated with arthralgia or arthritis



4 JENNETTE ET AL



IgAVN



Onset:

- **Palpable purpura and multiorgan signs with hematuria and proteinuria**

Natural history.

- **Most common in children**
- **In children most frequent remission, in rare cases rapid progression, possible progression over decades.**

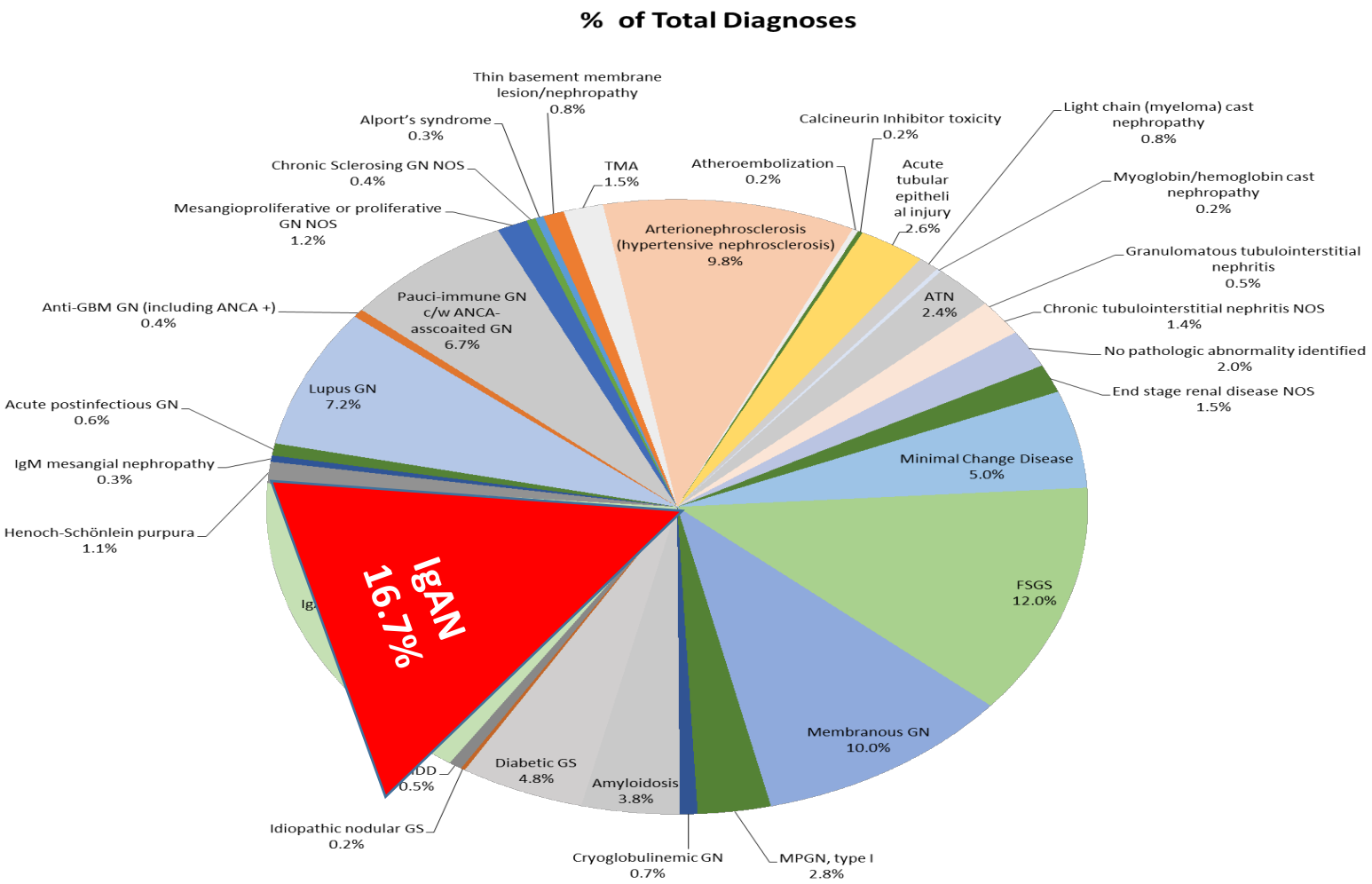
Primary IgA nephropathy (IgAN)

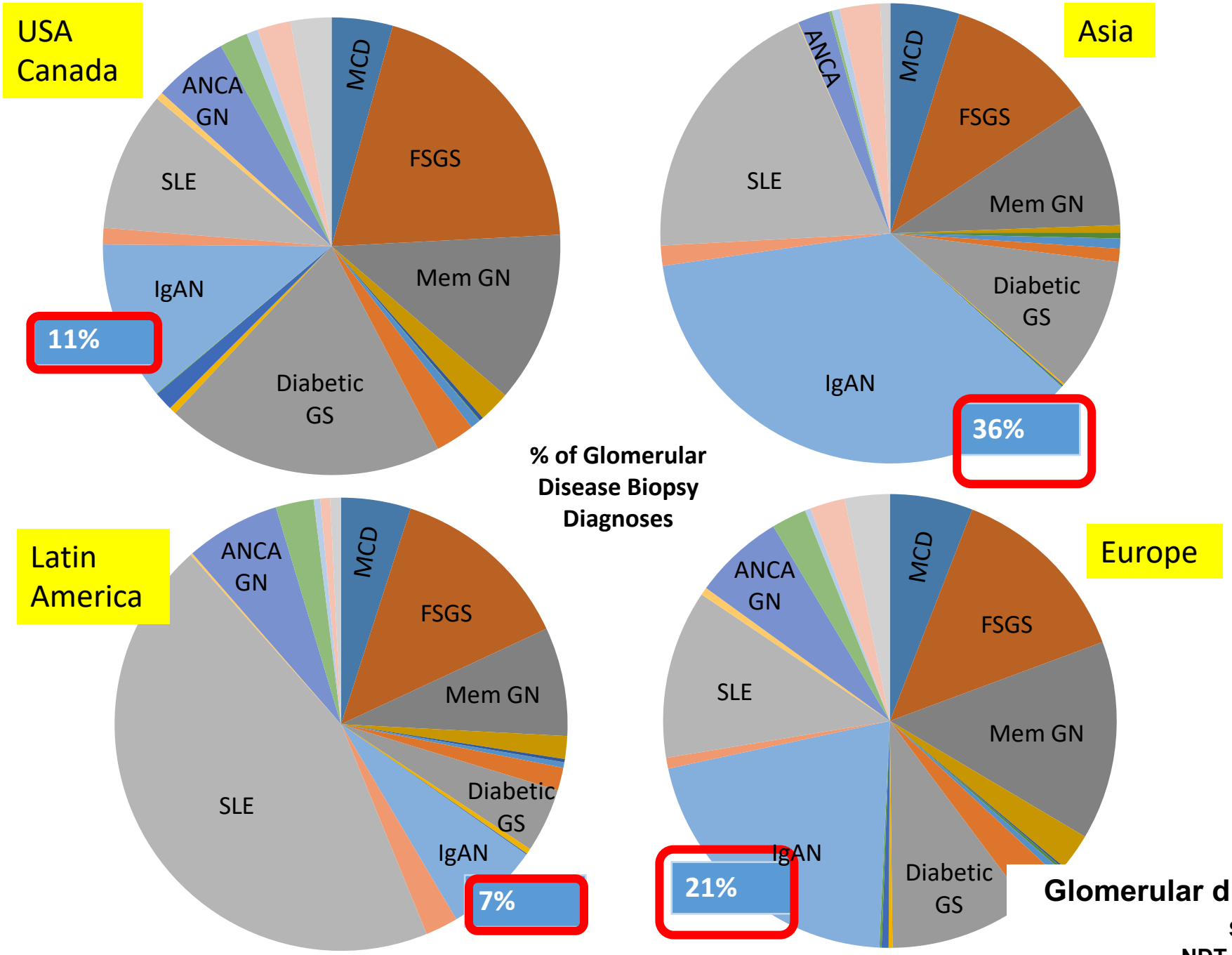
NDT 2018 1;33:661-669

International Kidney Biopsy Survey

on 42,603 renal biopsies of glomerular diseases in 4 Continents

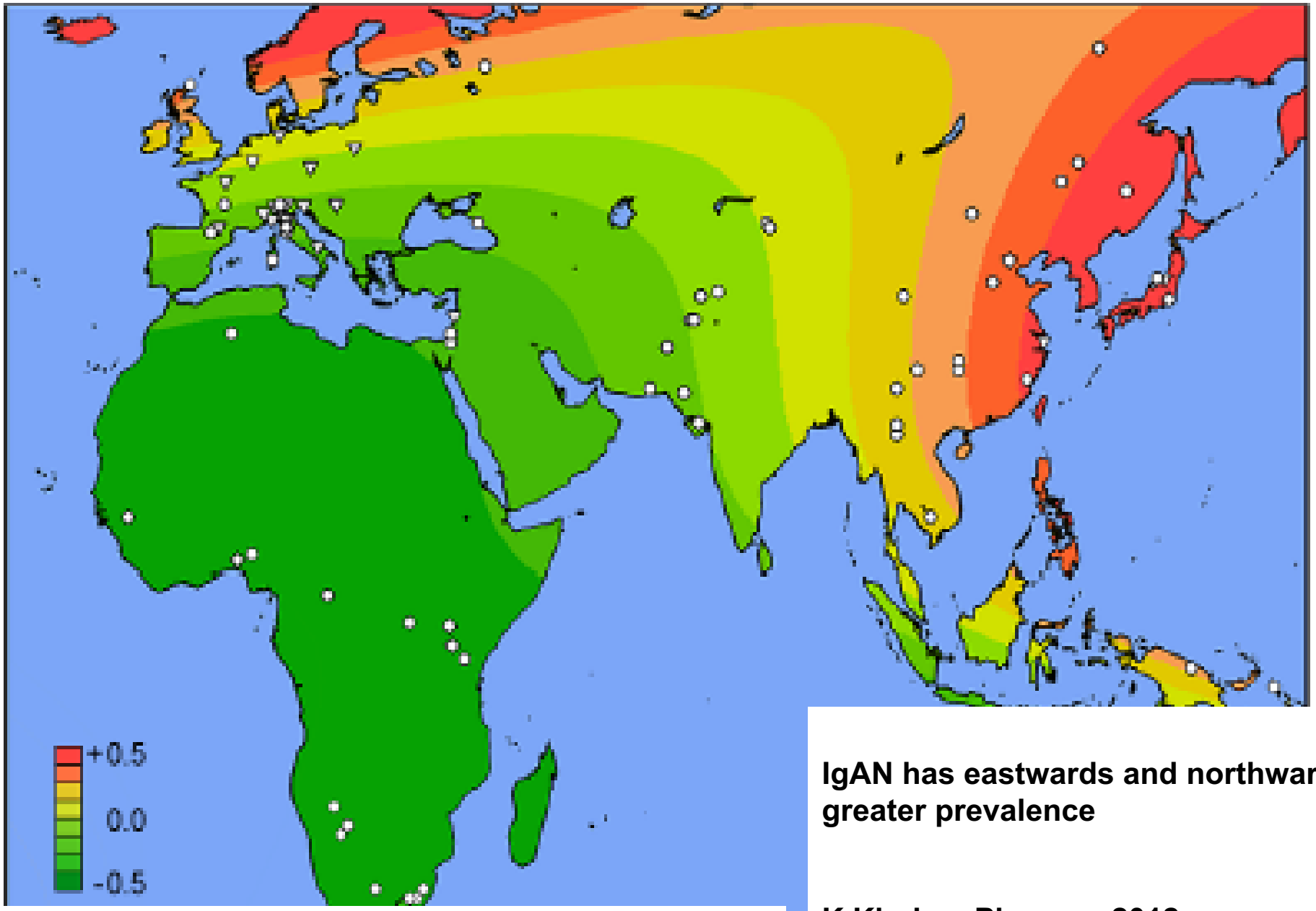
IgAN frequency





Glomerular disease international survey

NDT 2018; 33: 261



IgAN has eastwards and northwards greater prevalence

K Kiryluc Plos one 2012

OPEN ACCESS Freely available online

PLoS GENETICS

Geographic Differences in Genetic Susceptibility to IgA Nephropathy: GWAS Replication Study and Geospatial Risk Analysis

Detection of IgAN:
diagnosis ONLY by renal biopsy

The frequency of IgAN
depends on the indications to perform renal biopsy

Screening programs

Isolated microscopic hematuria

Microscopic hematuria and proteinuria

After gross hematuria

Incidence.

Adults: 10-40 pmp/y, in median 25 pmp/y

USA:10 cases pmp/y

Asia: 20-40 cases pmpy

Europe: 8-25 cases pmp/y

Children: 5-50 cases /pmpy

3-5 cases/year/pm children in Europe,

up to 140 cases/year/pmch Asia

clinical investigation http://www.kidney-international.org
© 2014 International Society of Nephrology

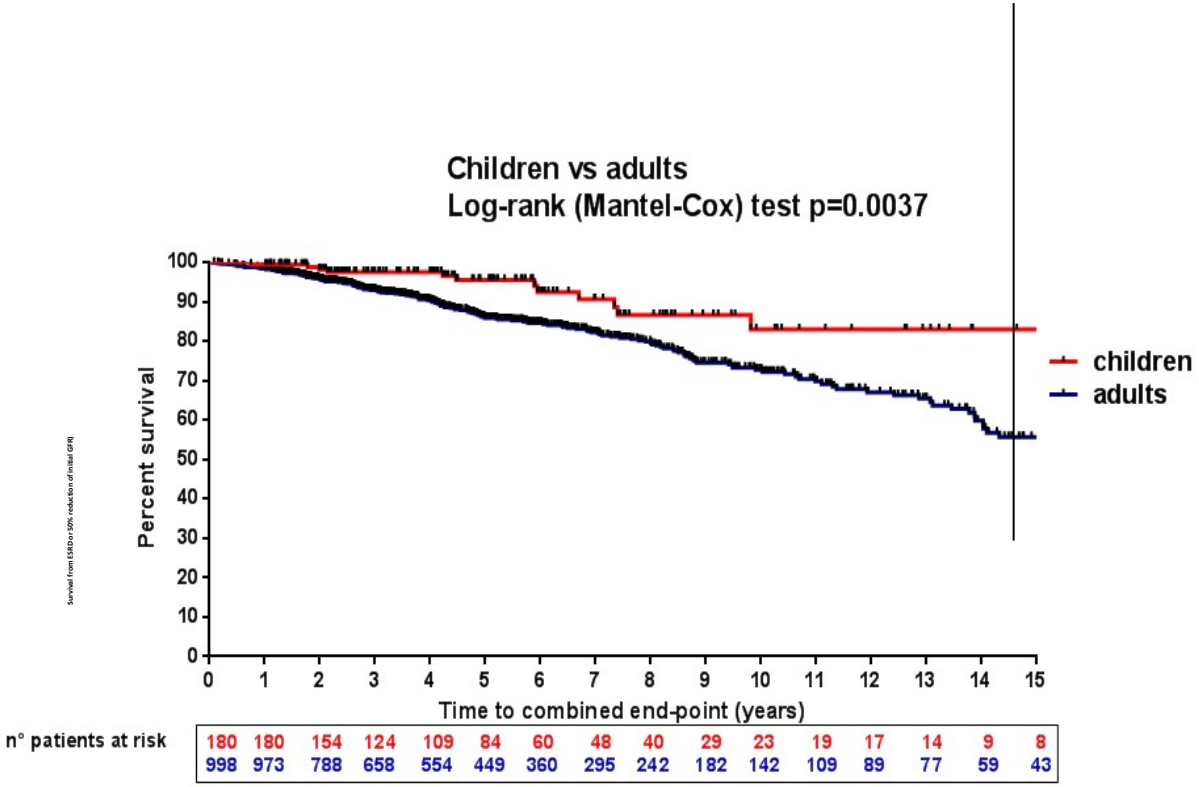
OPEN

Validation of the Oxford classification of IgA nephropathy in cohorts with different presentations and treatments

Rosanna Coppo[1,7], Stéphan Troyanov[2,7], Shubha Bellur[3,8], Daniel Cattran[4,7], H. Terence Cook[5,7], John Feehally[6,7], Ian S.D. Roberts[3,7], Laura Morando[8], Roberta Camilla[8], Vladimir Tesar[8], Sigrid Lunberg[8], Loreto Gesualdo[8], Francesco Emma[8], Cristiana Rollino[8], Alessandro Amore[8], Manuel Praga[8], Sandro Feriozzi[8], Giuseppe Segoloni[8], Antonello Pani[8], Giovanni Cancarini[8], Magalena Durlik[8], Elisabetta Moggia[8], Gianna Mazzucco[8], Costantinos Giannakakis[8], Eva Honsova[8], B. Brigitta Sundelin[8], Anna Maria Di Palma[8], Franco Ferrario[8], Eduardo Gutierrez[8], Anna Maria Asunis[8], Jonathan Barratt[8], Regina Tardanico[8] and Agnieszka Perkowska-Ptasinska[8], on behalf of the VALIGA study of the ERA-EDTA Immunonephrology Working Group[8]

55 Centers of Nephrology and Renal Pathology
13 European Countries

VALIGA
1147 IgAN
follow-up : 4.7 years

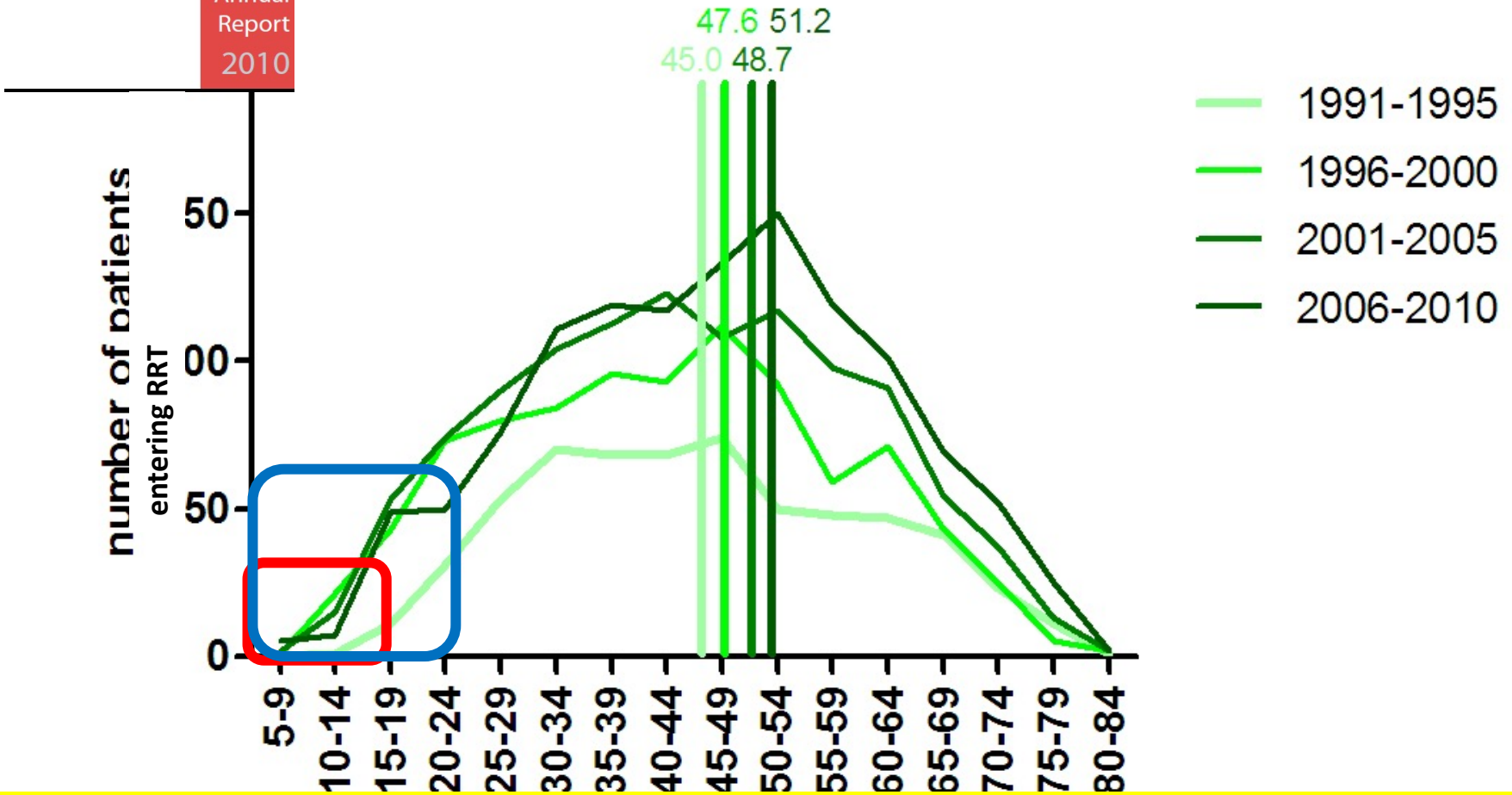


ERA-EDTA Registry

Annual Report 2010

Age at start of RRT for IgAN in Europe

50% of IgAN patients enter dialysis before 51 years of age



several progressive IgAN begin in childhood and youth

30-60% of children with IgAN will never experience any decline in GFR over a long and healthy life

10% at 10 years and 20% at 20 years after renal biopsy progress to end stage renal failure (ESRD) or loss of 50% of GFR

In most adult subjects the diagnosis of IgAN follows chance finding investigations for hypertension and/or reduced GFR

Need to identify children with IgAN at risk of progression

Clinical and histological risk factors for progression of IgA nephropathy: an update in children, young and adult patients
R. Coppo
J.Nephrol 2017, 30:339-346

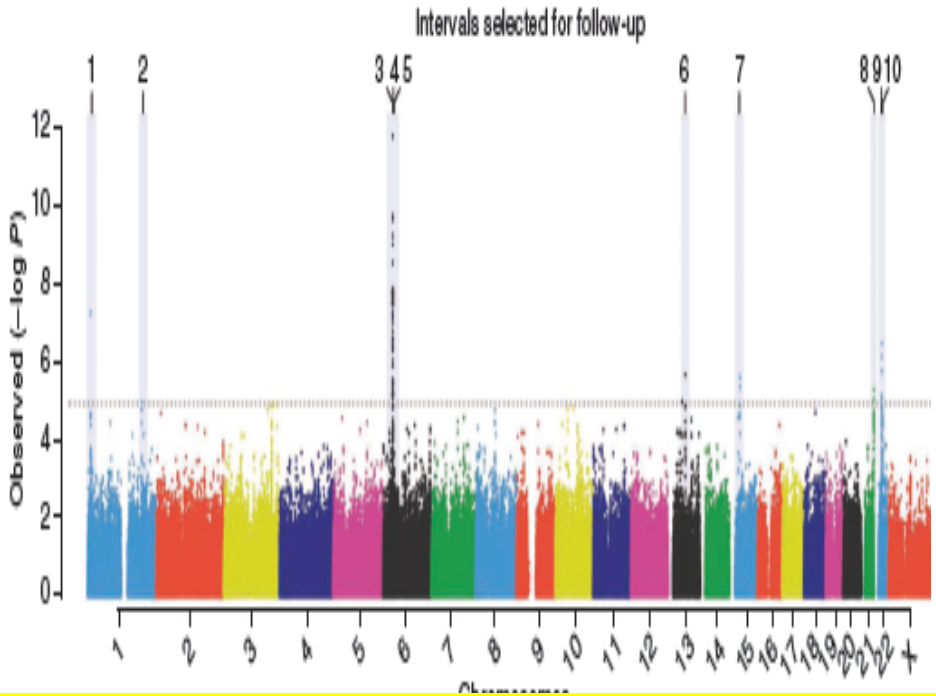
Genetic conditioning

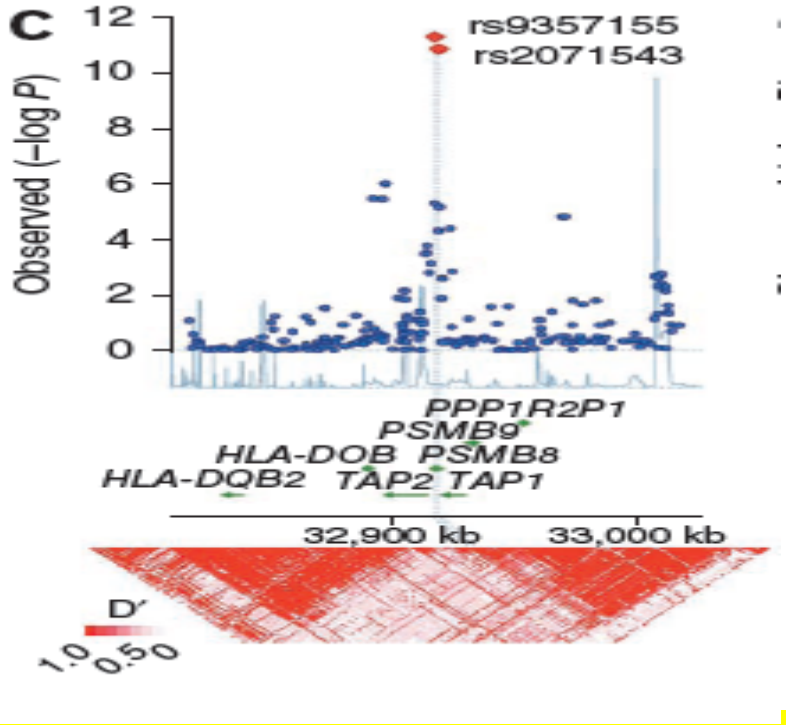
nature genetics

NATURE GENETICS VOLUME 43 | NUMBER 4 | APRIL 2011

Genome-wide association study identifies susceptibility loci for IgA nephropathy

Ali G Gharavi[1], Krzysztof Kiryluk[1], Murim Choi[2], Yifu Li[1], Ping Hou[1,3], Jingyuan Xie[1,4], Simone Sanna-Cherchi[1], Clara J Men[2], Bruce A Julian[5], Robert J Wyatt[6], Jan Novak[5], John C He[7], Haiyan Wang[3], Jicheng Lv[3], Li Zhu[3], Weiming Wang[4], Zhaohui Wang[4], Kasuhito Yasuno[2], Murat Gunel[2], Shrikant Mane[2,8], Sheila Umlauf[2,8], Irina Tikhonova[2,8], Isabel Beerman[2], Silvana Savoldi[9], Riccardo Magistroni[10], Gian Marco Ghiggeri[11], Monica Bodria[11], Francesca Lugani[1,11], Pietro Ravani[12], Claudio Ponticelli[13], Landino Allegri[14], Giuliano Boscutti[15], Giovanni Frasca[16], Alessandro Amore[17], Licia Peruzzi[17], Rosanna Coppo[17], Claudia Izzi[18], Battista Fabio Viola[19], Elisabetta Prati[20], Maurizio Salvadori[21], Renzo Mignani[22], Loreto Gesualdo[23], Francesca Bertinetto[24], Paola Mesiano[24], Antonio Amoroso[24], Francesco Scolari[18], Nan Chen[4], Hong Zhang[3] & Richard P Lifton[2]





3 areas of SNPs
were significantly different in IgAN and healthy control and encode for

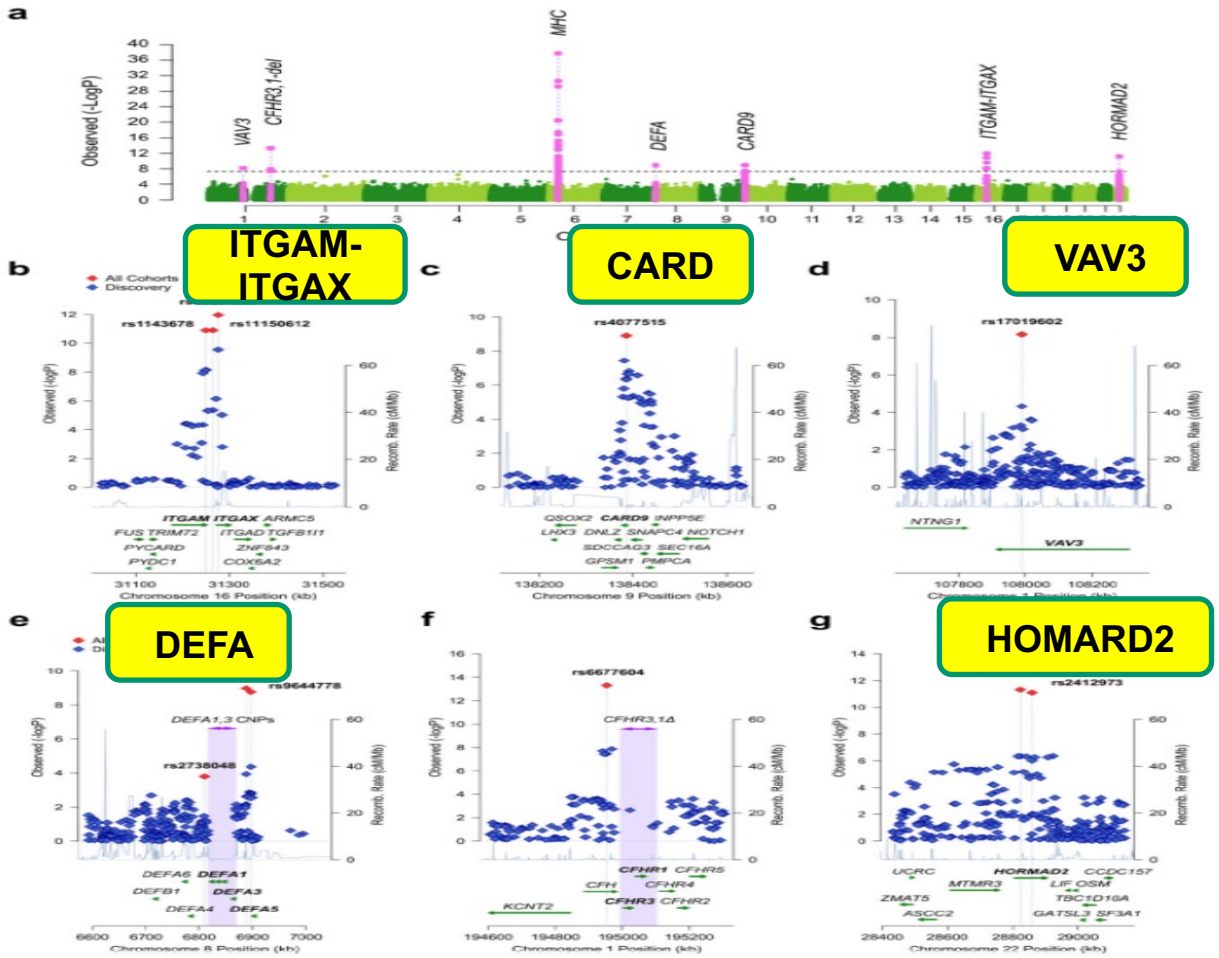
1) HLA
2) complement
3) lymphomononuclear cells interplay

nature genetics

NATURE GENETICS VOLUME 46 | NUMBER 11 | NOVEMBER 2014

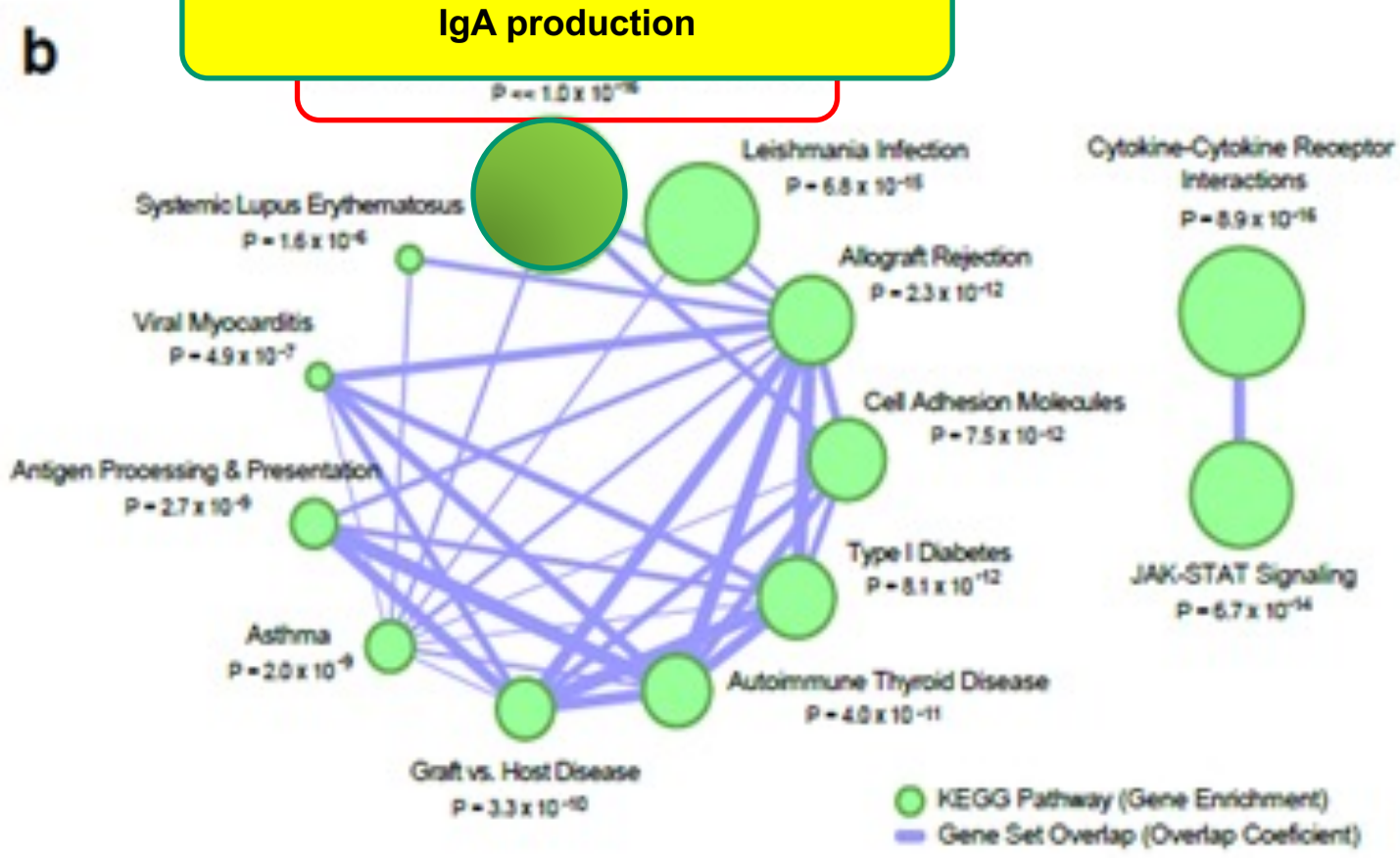
Discovery of new risk loci for IgA nephropathy implicates genes involved in immunity against intestinal pathogens

[5], Miguel Verbitsky[1],
J Snyder[1],
, Cristina Barlassina[8],
Marcella Rocchietti[11],
rani[14,15],
icesca Lugani[17],
, Giovanni Frasca[20],
Marcantoni[25],
eriozzi[28],
amboli[32],
Frank Eitner[35,36],
Leszek Pączek[39],
Pawlaczyk[42],
anaud[47,48],
rita[54], Yasar Caliskan[55],
, Bruce A Julian[61],
ravi[1]



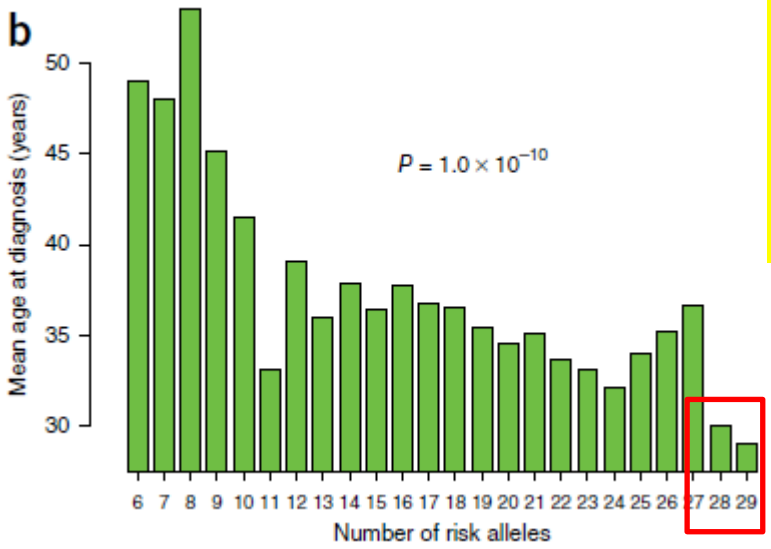
innate immunity against intestinal pathogens

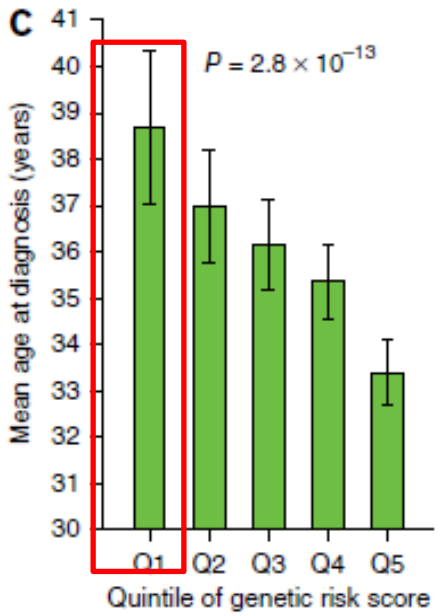
intestinal immune network for IgA production



most loci associated with IgAN
are also associated with risk of inflammatory bowel diseases or maintenance of the intestinal barrier in response to intestinal pathogens

high frequency of risk alleles
in 15 loci
is associated with early IgAN onset

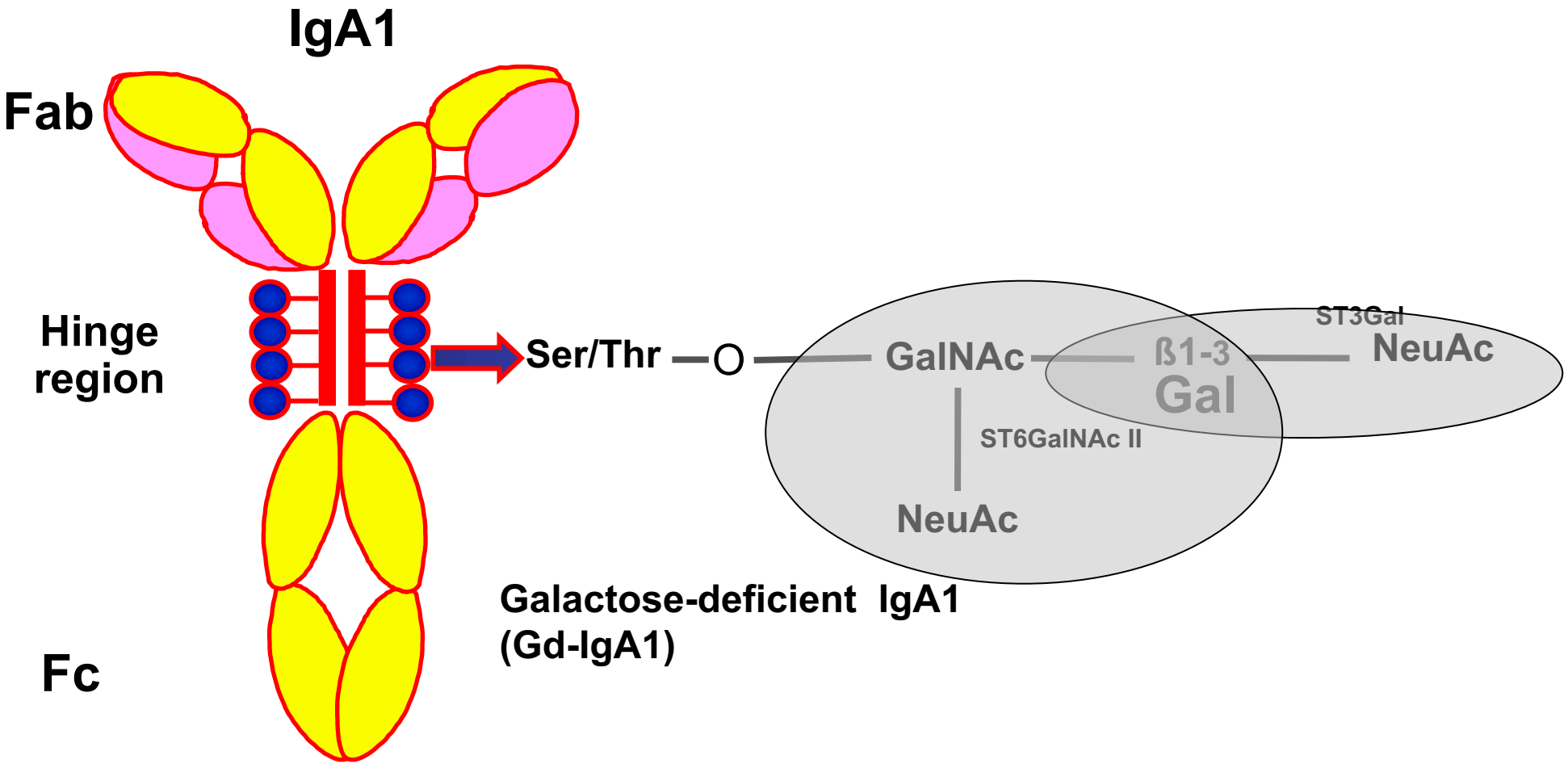




Pathogenetical mechanisms for the development of IgAN

IgAN
immune system

Yeo SC et al Pediatr Nephrol 2018; 33: 763–777



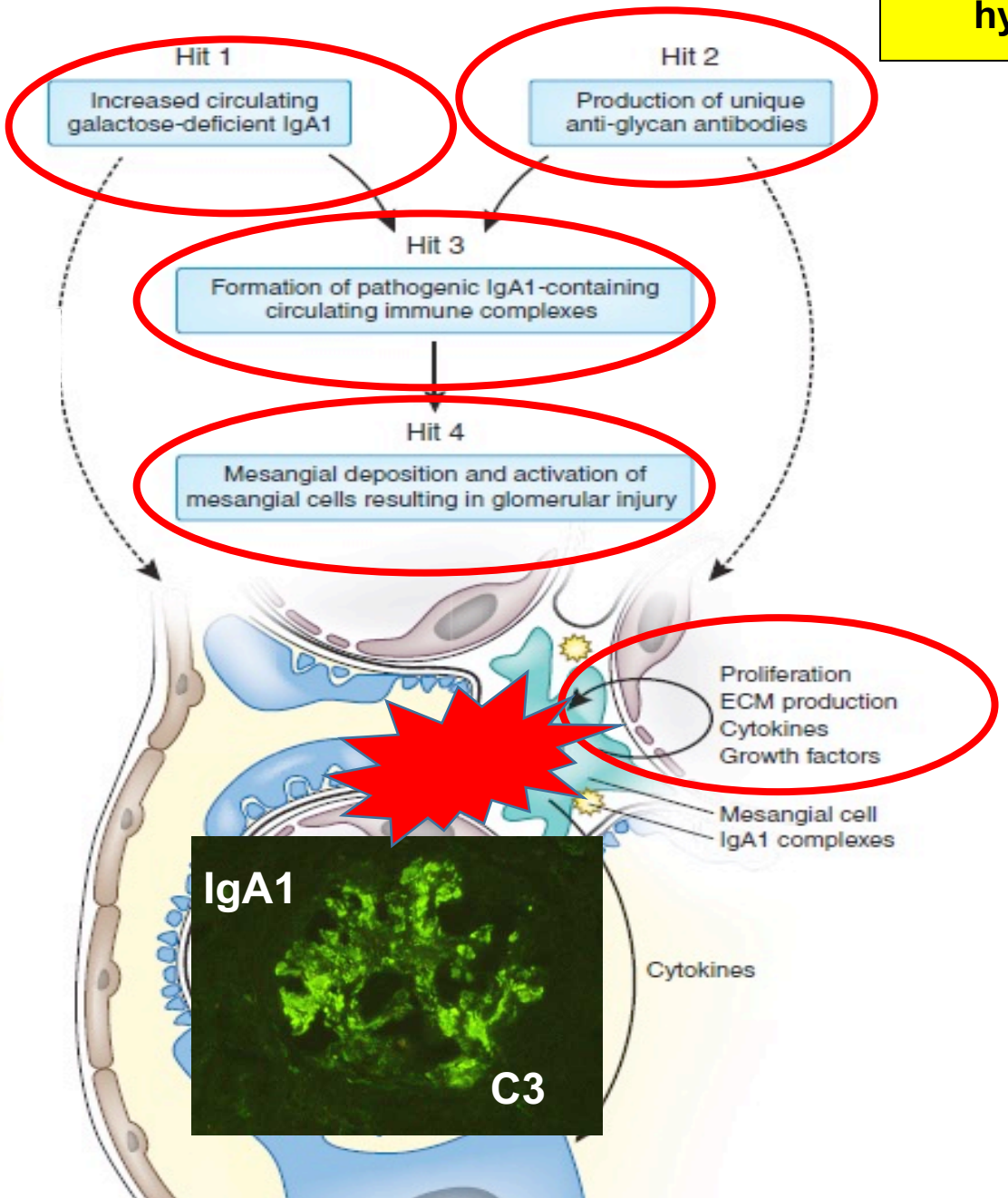
IgAN: 4 hits hypothesis

BRIEF REVIEW www.jasn.org

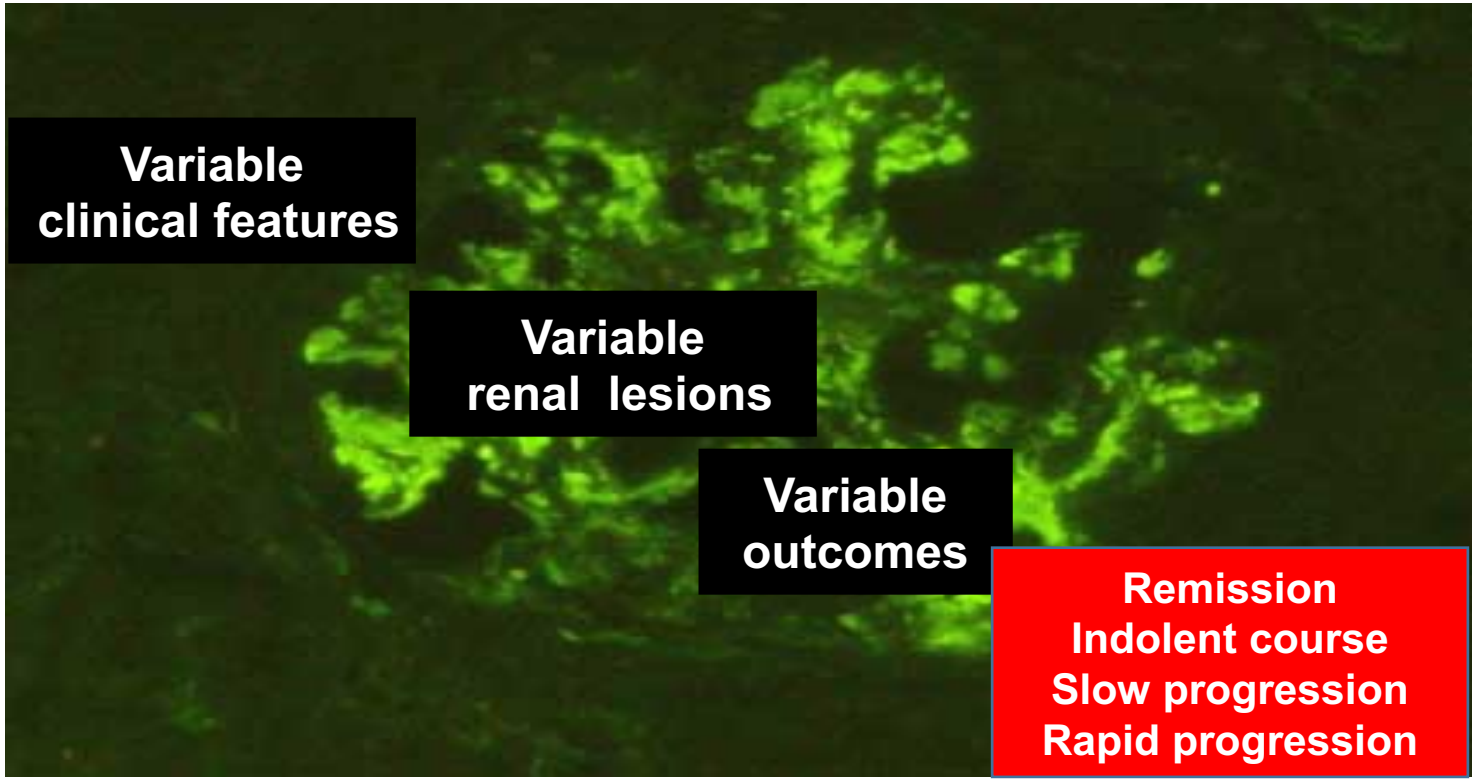
The Pathophysiology of IgA Nephropathy

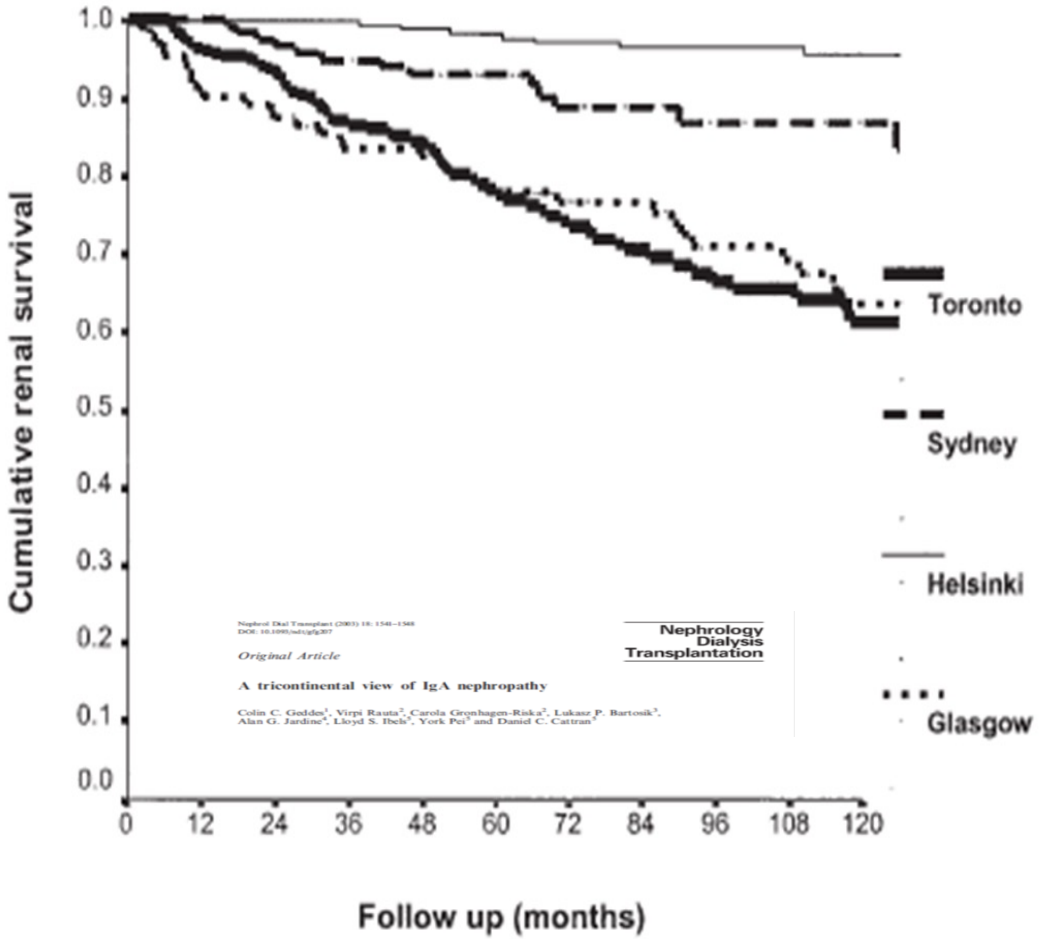
Hitoshi Suzuki,*‡ Krzysztof Kiryluk,† Jan Novak,‡ Zina Moldoveanu,‡ Andrew B. Herr,¶ Matthew B. Renfrow,§ Robert J. Wyatt,** Francesco Scolari,†† Jiri Mestecky,‡‖ Ali G. Gharavi,† and Bruce A. Julian‡‖

J Am Soc Nephrol 2011; 22: 1795–1803



IgA nephropathy





In adults most frequently IgA nephropathy is a relentlessly progressive renal disease

The potential progression of IgAN in children varies according to the indications to perform renal biopsy

- Screening programs
- Controls for sports
- Familiary history of kidney diseases
- Post- gross hematuria urinary tests
- Change in urine colour
- Oedema, fatigue, polyuria hypertension

Long-term outcome of childhood IgA nephropathy with minimal proteinuria

Higa A et al and Yoshikawa N , Ped Nephrol 2015

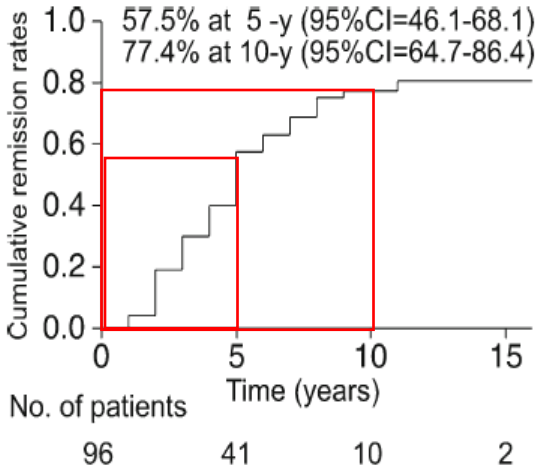
Pediatr Nephrol (2013) 28:71–76
DOI 10.1007/s00467-012-2294-6

ORIGINAL ARTICLE

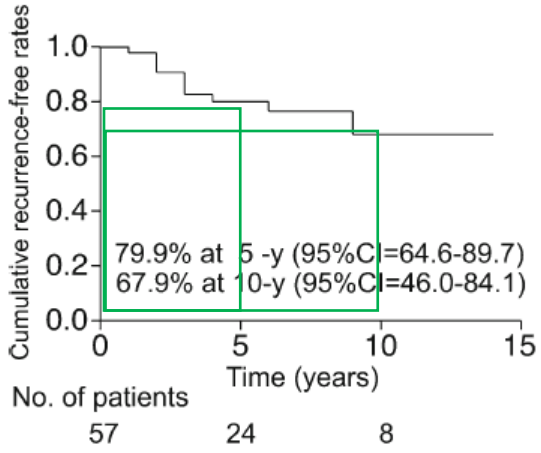
Spontaneous remission in children with IgA nephropathy

Yuko Shima · Koichi Nakanishi · Taketsugu Hama · Hironobu Mukaiyama · Hiroko Togawa · Mayumi Sako · Hiroshi Kaito · Kandai Nozu · Ryojiro Tanaka · Kazumoto Iijima · Norishige Yoshikawa

96 children
with minimal glomerular abnormalities
who did not receive medication:
remission



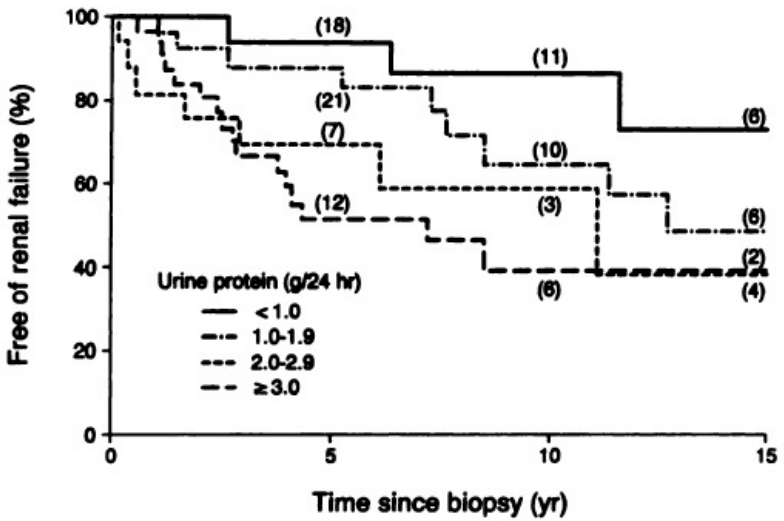
recurrence
In 20% at 5 years
and 32 % at 10 years
after remission



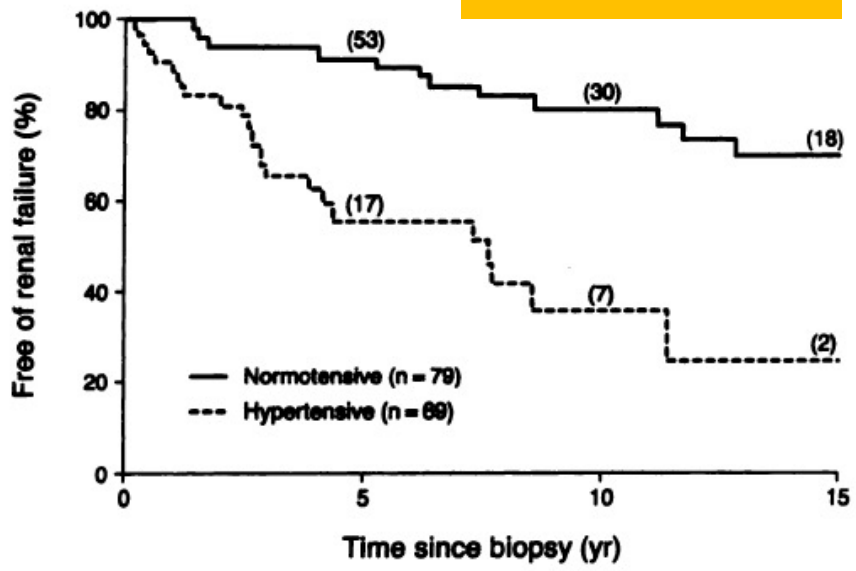
Clinical risk factors for progression of IgAN

Clinical Risk factors for progression of IgAN in adults

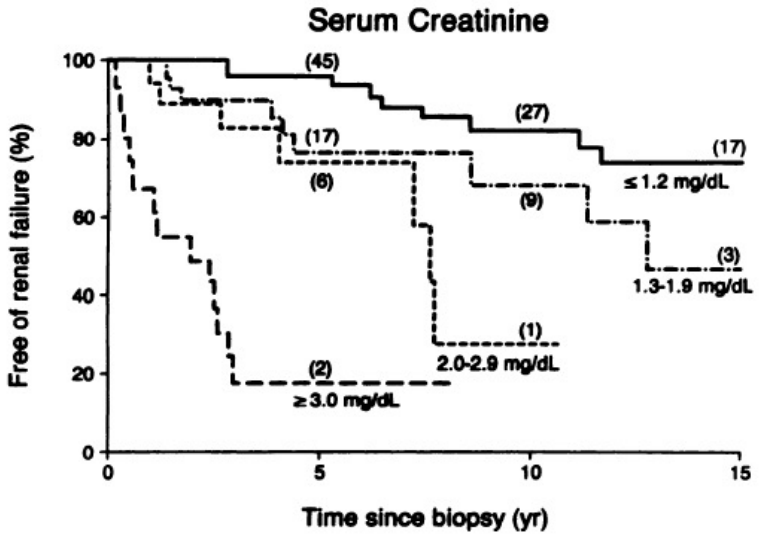
PROTEINURIA



HYPERTENSION



RENAL FUNCTION AT PRESENTATION



Journal of the American Society of Nephrology

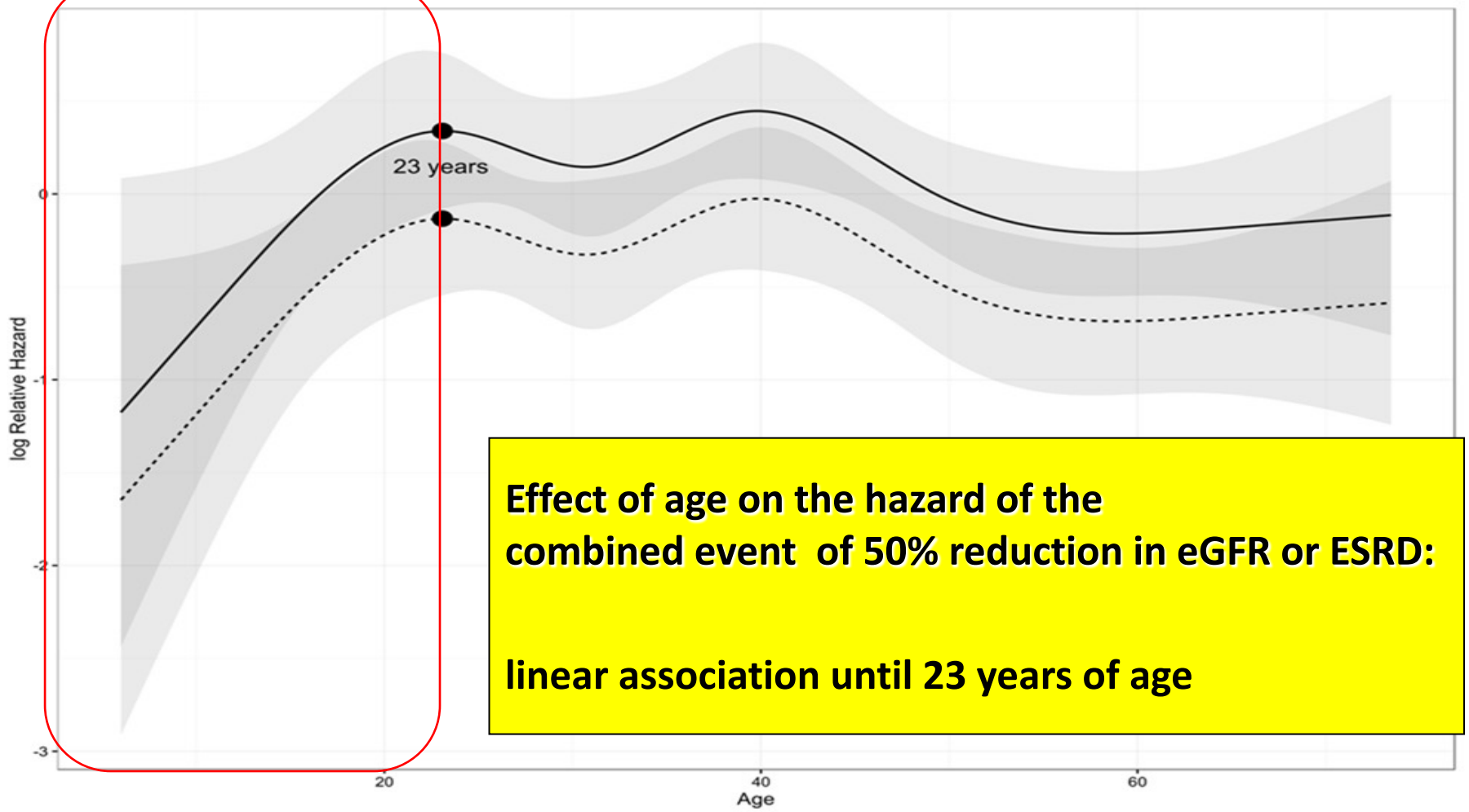
8: 199–207, 1997

Coppo R et al Pediatr Nephrol. 2017 Jan;32(1):139-150.

ORIGINAL ARTICLE

Risk factors for progression in children and young adults with IgA nephropathy: an analysis of 261 cases from the VALIGA European cohort

Rosanna Coppo[1] · Danilo D Lofaro[2] · Roberta R Camilla[1] · Shubha Bellur[3] · Daniel Cattran[4] ·



Effect of age on the hazard of the combined event of 50% reduction in eGFR or ESRD:

linear association until 23 years of age

Risk factors for progression in children with IgAN
European multicenter cohort

Clinical data at renal biopsy (proteinuria, hypertension, reduced GFR)

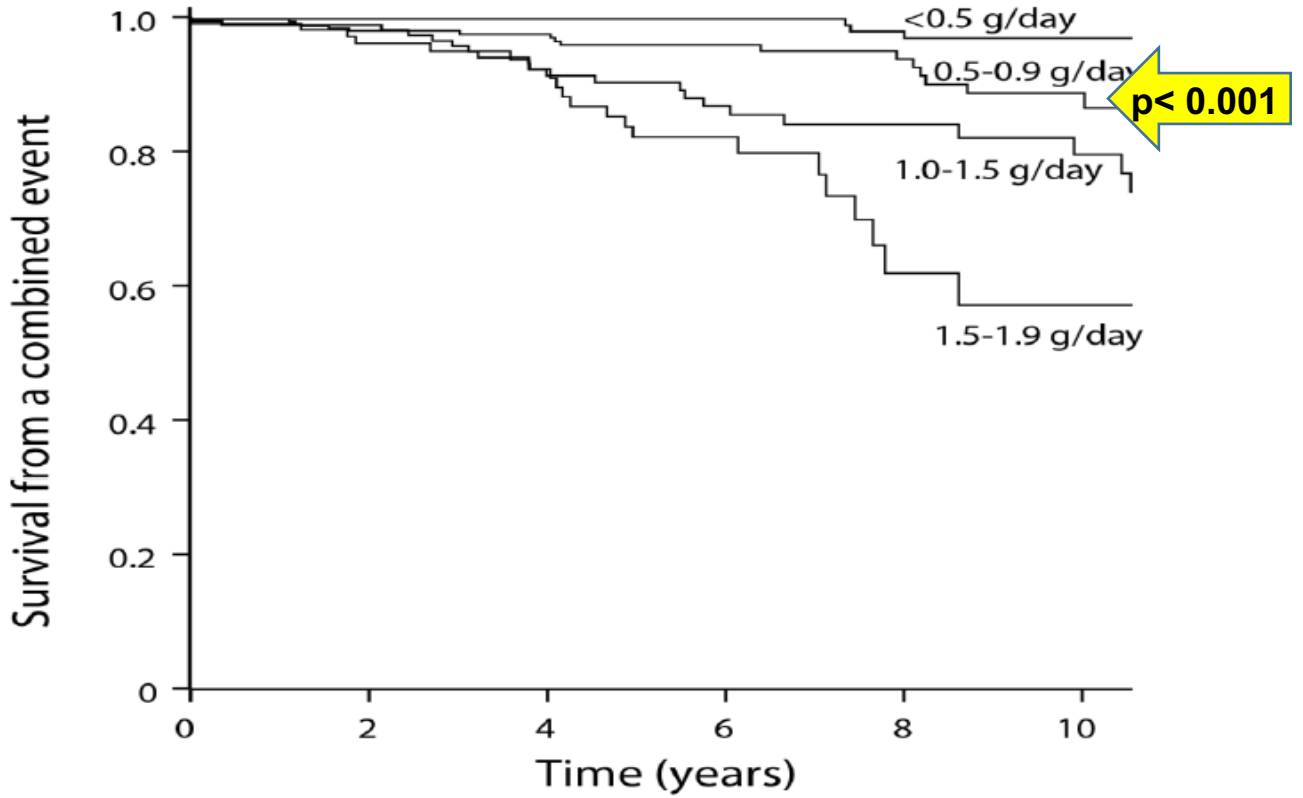
are not significant predictor of outcome,

Follow-up (time averaged) proteinuria and BP values are significant indicators of progression.

Children with IgAN followed for a median of 4.6 y

had a median time-averaged proteinuria of 0.55 g/day/.73m2 despite treatments

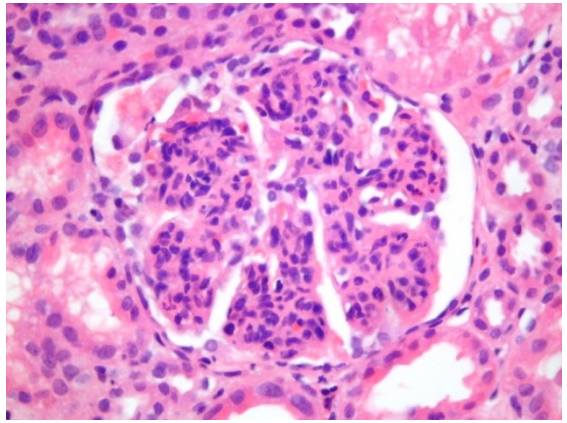
In the European Study VALIGA
(1147 patients with IgAN)
time average proteinuria >0.5 < 1 g/day
is a significant risk factor for progression

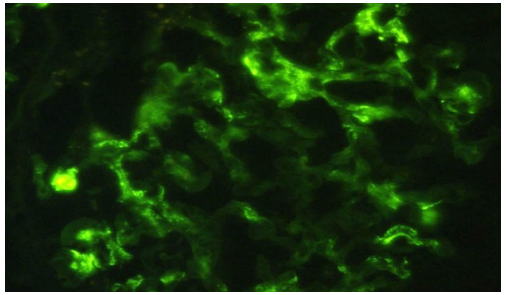


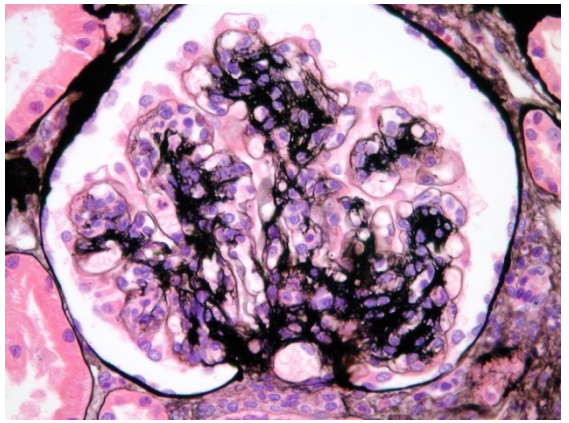
<0.5 g/day	338	198
0.5-0.9 g/day	315	185
1.0-1.5 g/day	167	97
1.5-1.9 g/day	107	68

Coppo R et al 2014 Kidney Int

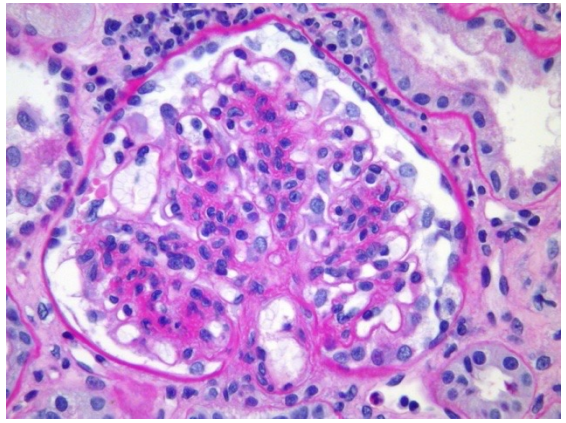
Renal lesions as risk factors for progression of IgA nephropathy

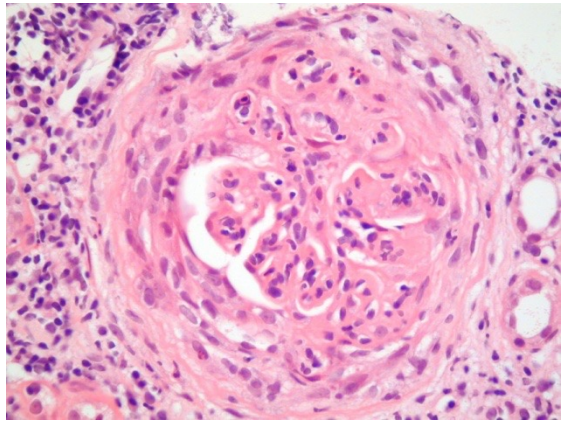


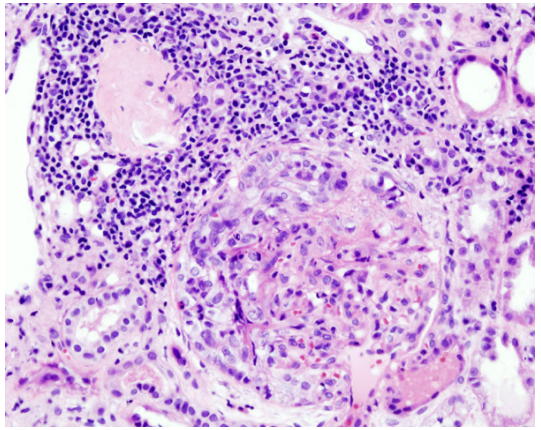




Variability of pathology lesions in IgA nephropathy







International Consensus on clinico-pathological Classification of IgAN: Oxford Classification

Kidney International (2009) 76, 546–556- Kidney International (2009) 76, 534–545

4 histologic features
risk factors for progression
independent from
clinical data at renal biopsy and follow-up

Mesangial hypercellularity
Endocapillary hypercellularity
Segmental glomerular sclerosis
Tubular atrophy/interstitial fibrosis

Crescents

IS THERE LONG-TERM VALUE OF PATHOLOGY SCORING IN IgA NEPHROPATHY? A VALIGA UPDATE

R.Coppo et al NDT 2020, 35: 1002-9

1130 patients (174 children)
follow-up 7.1 (4.1-10.8) years up to 35 years

Multivariable Cox regression analysis for the risk of 50% decline in eGFR or kidney failure.

	All patients (n=1130)
M1	**1.34 (1.02-1.75), p=0.037**
E1	1.17 (0.79-1.74), p=0.43
S1	**1.61 (1.10-2.36), p=0.01**
T1-2	**2.46 (1.80-3.36), p<0.001**
Crescents (C1-2)	0.85 (0.55-1.30), p=0.44
Arteriosclerosis	1.19 (0.89-1.58), p=0.24
Age	1.00 (0.99-1.01), p=0.60
Gender (male)	0.90 (0.67-1.22), p=0.51

It was independent of age, and valid for children as well as for adults.

Dependent variable: 50% decrease in eGFR or ESRD
Data are presented as hazard ratio, 95% CI and P value

IS THERE LONG-TERM VALUE OF PATHOLOGY SCORING IN IgA NEPHROPATHY? A VALIGA UPDATE

R.Coppo et al NDT 2020, 35: 1002-9

1130 patients (174 children)
follow-up 7.1 (4.1-10.8) years up to 35 years

Multivariable linear regression analysis of the rate of renal function decline (eGFR slope).

	All patients (n=1130)	Patients never treated with corticosteroid/immunosuppressors during the follow-up (n=582)
M1	-0.03 (p=0.28)	-0.06 (p=0.18)
E1	-0.06 (p=0.07)	0.08 (p=0.07)
S1	-0.05 (p=0.14)	-0.07 (p=0.14)
T1-2	**-0.16 (P<0.001)**	**-0.14; p=0.003**
Arteriosclerosis	-0.002 (p=0.94)	0.03 (p=0.51)
Crescents (C1-2)	**0.002 (p=0.95)**	**-0.11 p =0.01**
Gender (male)	0.02 (p=0.42)	-0.006 (p=0.89)
Age	-0.01 (0.76)	0.004 (0.94)

It was independent of age, and valid for children as well as for adults.

Dependent variable: rate of renal function decline.
Data are presented as standardized regression coefficient (beta) and P value

Value of combined

clinical and pathology risk factors

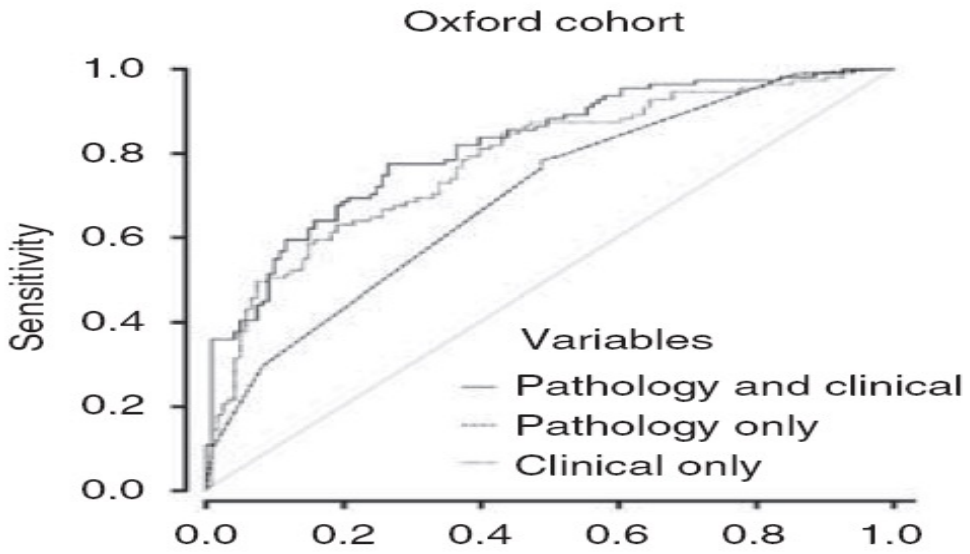
Kidney International (2009) **76,** 534–545; doi:10.1038/ki.2009.243;
published online 1 July 2009

The Oxford classification of IgA nephropathy: rationale, clinicopathological correlations, and classification

A Working Group of the International IgA Nephropathy Network and the Renal Pathology Society:
Daniel C. Cattran[1,†], Rosanna Coppo[2,†], H. Terence Cook[3,†], John Feehally[4,†], Ian S.D. Roberts[5,†], Stéphan Troyanov[6,†], Charles E. Alpers[7], Alessandro Amore[2], Jonathan Barratt[4], Francois Berthoux[8], Stephen Bonsib[9], Jan A. Bruijn[10], Vivette D'Agati[11], Giuseppe D'Amico[12], Steven Emancipator[13], Francesco Emma[14], Franco Ferrario[15], Fernando C. Fervenza[16], Sandrine Florquin[17], Agnes Fogo[18], Colin C. Geddes[19], Hermann-Josef Groene[20], Mark Haas[21], Andrew M. Herzenberg[22], Prue A. Hill[23], Ronald J. Hogg[24], Stephen I. Hsu[25], J. Charles Jennette[26], Kensuke Joh[27], Bruce A. Julian[28], Tetsuya Kawamura[29], Fernand M. Lai[30], Chi Bon Leung[31], Lei-Shi Li[32], Philip K.T. Li[31], Zhi-Hong Liu[32], Bruce Mackinnon[19], Sergio Mezzano[33], F. Paolo Schena[34], Yasuhiko Tomino[35], Patrick D. Walker[36], Haiyan Wang[37], Jan J. Weening[38], Nori

Mesangial hypercellularity
Endocapillary hypercellularity
Segmental glomerular sclerosis
Tubular atrophy/interstitial fibrosis
Crescents

JASN 2017;28:691-701



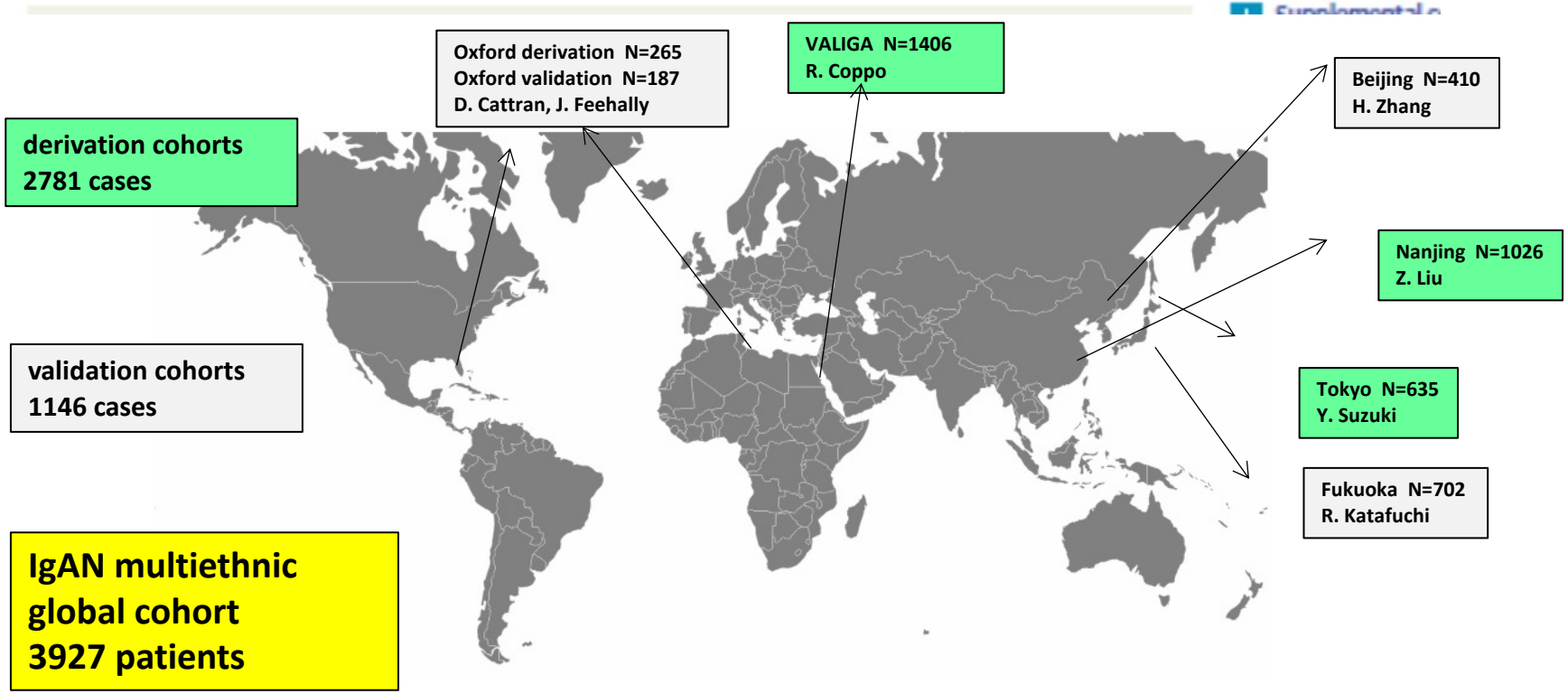
Added value of pathology variables in predicting a more rapid rate of renal-function decline.

JAMA Internal Medicine | Original Investigation

Evaluating a New International Risk-Prediction Tool in IgA Nephropathy

JAMA Intern Med. 2019 Apr 13. doi: 10.1001/

Sean J. Barbour, MD, MSc; Rosanna Coppo, MD, FERA; Hong Zhang, MD, PhD; Zhi-Hong Liu, MD; Yusuke Suzuki, MD, PhD; Kelichi Matsuzaki, MD, PhD; Ritsuko Katafuchi, MD, PhD; Lee Er, MSc; Gabriela Espino-Hernandez, MSc; S. Joseph Kim, MD, PhD; Heather N. Reich, MD, PhD; John Feehally, FRCP; Daniel C. Cattran, MD, FRCPC; for the International IgA Nephropathy Network



International IgAN Network collaboration

How can the IgAN Prediction Tool be accessed?

- A mobile-app calculator is available **on *Calculate by QxMD,*** which you can access through your App store on your mobile device.
- A web-based calculator is available at **https://qxcalc.app.link/igarisk.**

JAMA Intern Med. 2019 Apr 13. doi: 10.1001

KDIGO CLINICAL PRACTICE GUIDELINE ON GLOMERULAR DISEASES

Age (years)	35
Sex	M
Race	C
eGFR (ml/Prior min/1.73m^2)	80
SBP (mmHg)	140
DBP (mmHg)	80
Proteinuria (g/d)	2
Use RASB	no
Prior immunosuppression	no
MEST	M1E0S1T1

JAMA Intern Med. 2019 Apr 13. doi: 10.1001

Risk of progression (% of patients reaching the end-point over 5 years) and rate of eGFR decline (ml/min/1.73m2/year)

Risk Subgroup	Mean Predicted 5-year Risk	eGFR Decline (ml/min/1.73m^2/year)		
		Mean	95% CI	P-value
Full Model With Race (similar results without race)				
Low risk	1.5%	-1.24	-1.63, -0.85	<0.0001
Intermediate risk	4.7%	-1.76	-2.01, -1.50	
Higher risk	13.9%	-2.35	-2.35, -2.10	
Highest risk	46.5%	-3.43	-3.80, -3.06	

Updating the International IgA Nephropathy Prediction Tool for use in children

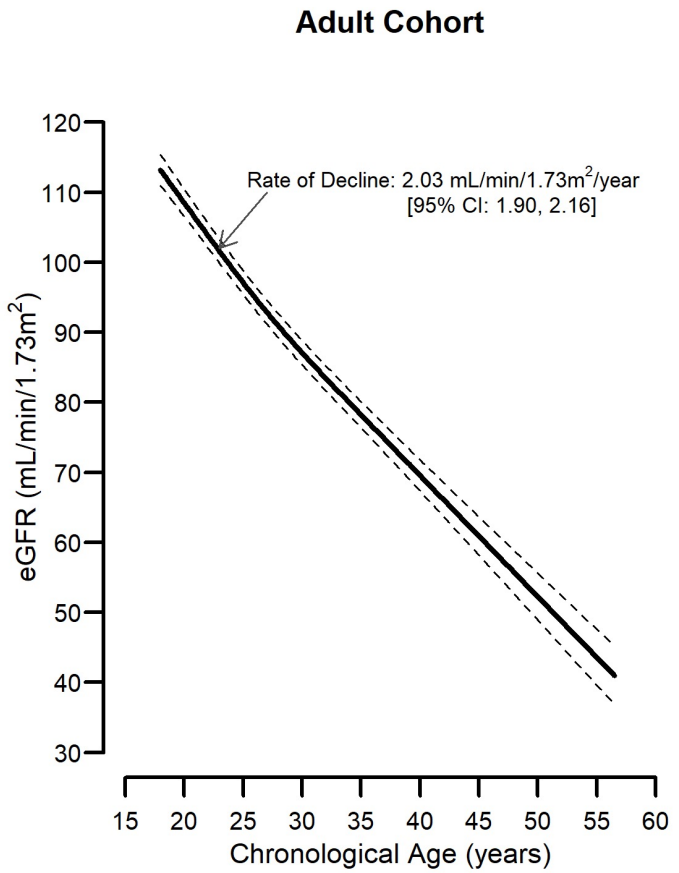
Sean J. Barbour[1,2,17], Rosanna Coppo[3,17], Lee Er[2], Maria Luisa Russo[3], Zhi-Hong Liu[4], Jie Ding[5], Ritsuko Katafuchi[6], Norishige Yoshikawa[7], Hong Xu[8], Shoji Kagami[9], Yukio Yuzawa[10], Francesco Emma[11], Alexandra Cambier[12], Licia Peruzzi[3,13], Robert J. Wyatt[14] and Daniel C. Cattran[15,17]; for the International IgA Nephropathy Network[16]

Kidney Int. 2020 Nov 18:S0085-2538(20)31385-5. doi: 10.1016/j.kint.2020.10.033. Epub ahead of print.

International IgAN Network pediatric collaboration

IgAN global pediatric cohort
1060 children <18 y old

eGFR trajectory in patients with IgA nephropathy : children vs adults



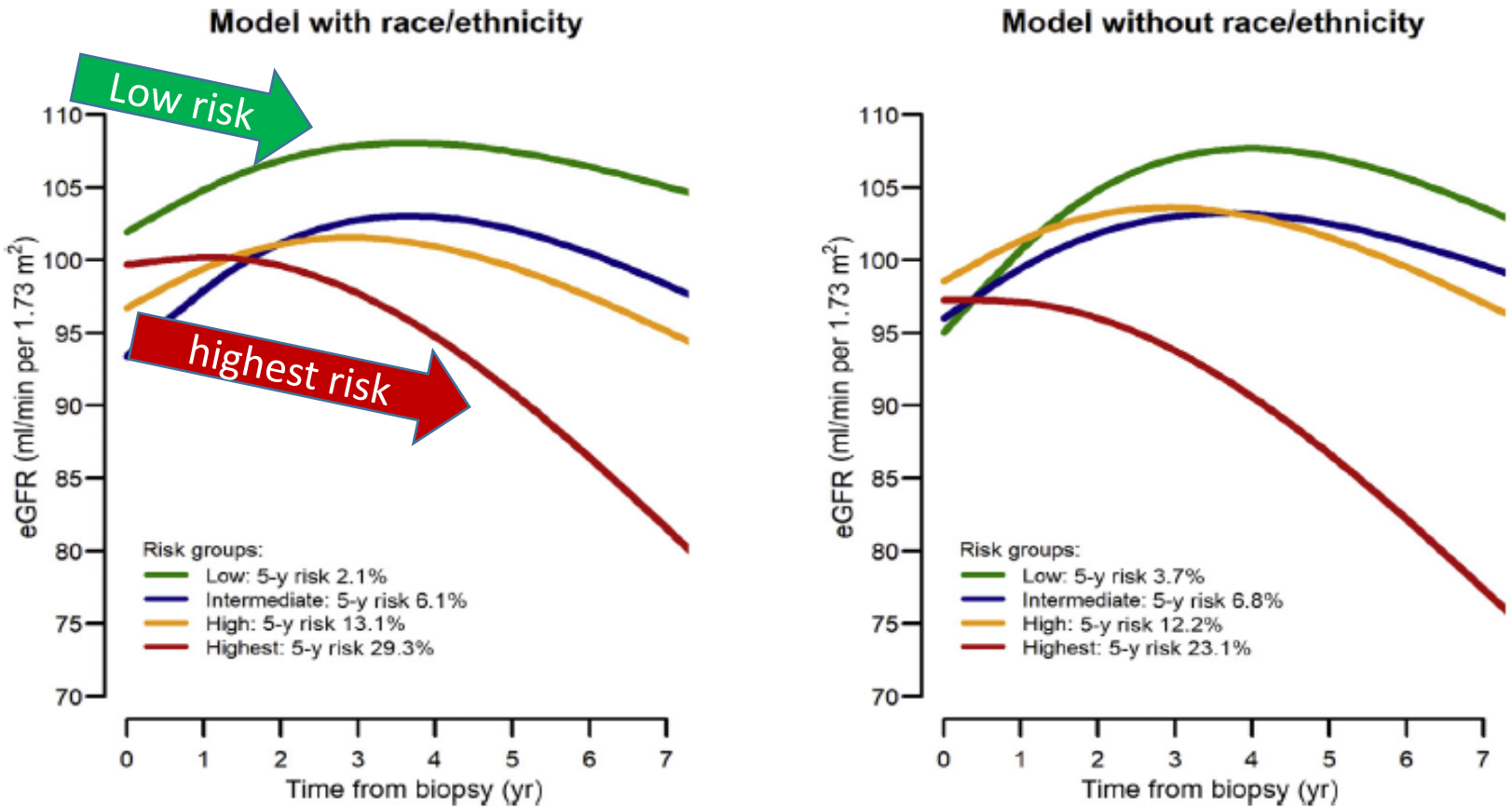


Figure 3 | Trajectories of estimated glomerular filtration rate (eGFR) according to time from biopsy within risk subgroups based on the fully updated pediatric International IgA Nephropathy Prediction Tool. Risk subgroups are based on percentiles of the linear predictor (low risk, <16th [green]; intermediate risk, 16th–50th [blue]; high risk, 50th–84th [orange]; and highest risk, >84th [red]). Using the fully updated pediatric Prediction Tool, the mean 5-year risk of the secondary outcome (30% decline in eGFR or end-stage kidney disease) is provided for each sub

https://qxcalc.app.link/igarisk

Treatments

KDIGO 2020 GN

General recommendation for IgAN: target BP and proteinuria using RAS inhibitors

Goal systolic blood pressure is <120 mm Hg using standardized office BP measurement (adults).

Goal mean arterial pressure is ≤50% age/sex (children)

In children:
Start RASB when proteinuria >0.2 g/24h/1.73m2

Recommendation 2.3.2. We recommend that all patients with proteinuria >0.5 g/24h, irrespective of whether they have hypertension, are treated with either an ACEi or ARB *(1B)*.

KDIGO Clinical Practice Guideline for Glomerulonephritis

Kidney Int 2012; 2 (Suppl 2): 139–274

10.3.1: We suggest that patients with persistent proteinuria ≥1 g/d, despite 3–6 months of optimized supportive care (including ACE-I or ARBs and blood pressure control), and GFR >50 ml/min per 1.73 m^2, receive a 6-month course of corticosteroid therapy. (2C)

Table 2. Corticosteroid monotherapy

Trial	Pozzi *et al.*, Italy[37,36]	Katafuchi *et al.*, Japan[38]	Hogg *et al.*, United States[26]	Manno *et al.*, Italy[35]	Lv *et al.*, China[34]
Corticosteroid regimen	Intravenous methylprednisolone 1 g/d for 3 consecutive days at the beginning of months 1, 3, and 5, plus oral prednisone 0.5 mg/kg every other day for 6 months	Oral prednisolone 20 mg/d tapered to 5 mg/d at 18 months	Oral prednisone every other day 60 mg/m^2 for 3 months, then 40 mg/m^2 for 9 months, and then 30 mg/m^2 for 12 months	Oral prednisone for 6 months (1 mg/kg/day for 2 months, then reduced by 0.2 mg/kg/day per month)	Oral prednisone for 6–8 months (0.8–1 mg/kg/day for 2 months, then reduced by 5–10 mg every 2 wk)
Control regimen	Supportive only	Dipyridamole	Placebo	Supportive only	Supportive only
RAS blockade	14% at baseline, allowed during follow-up	2% at baseline; allowed during follow-up	Enalapril if hypertensive	Ramipril in all patients	Cilazapril in all patients
Key outcome in steroid group *versus* control	Ten-year renal survival (=absent doubling of serum creatinine), 53% in controls *versus* 97% in the steroid group	Significant reduction in proteinuria but not ESRD frequency	No benefit in the steroid group *versus* placebo at 2 years	Mean annual loss of GFR 6.2 ml/min in controls *versus* 0.6 ml/min in the steroid group	Significantly fewer patients with a 50% increase in serum creatinine in the steroid group

Therapeutic regimens and outcomes in randomized controlled trials in IgAN patients. RAS, renin-angiotensin system; ESRD, end-stage renal disease.

Cochrane Database Syst Rev. 2020 Mar

Cochrane Library

Cochrane Database of Systematic Reviews

58 studies (3933 patients)
6 in children

Corticosteroid therapy probably prevents decline in GFR

in adults and children with IgA nephropathy and proteinuria.

Kidney Int. 2019 Feb;95(2):268-280.

Kidney Int. 2019 ;95:268-280.

STOP-IgAN

KDIGO executive conclusions www.kidney-international.org

Management and treatment of glomerular diseases (part 1): conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference

Check for updates

OPEN

Jürgen Floege[1], Sean J. Barbour[2,3,4], Daniel C. Cattran[5], Jonathan J. Hogan[6], Patrick H. Nachman[7], Sydney C.W. Tang[8], Jack F.M. Wetzels[9], Michael Cheung[10], David C. Wheeler[11], Wolfgang C. Winkelmayer[12] and Brad H. Rovin[13]; for Conference Participants[14]

Optimized supportive care induced a very slow decline in GFR

Corticosteroid/Immunosuppressive therapy (CS/IS) induced a transient reduction in proteinuria over 3 years but had no impact on eGFR

Significant increase in adverse events in CS-IS.

Kidney Int. 2019 Feb;95(2):268-280.

Kidney Int. 2019 ;95:268-280.

KDIGO executive conclusions www.kidney-international.org

Management and treatment of glomerular diseases (part 1): conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference

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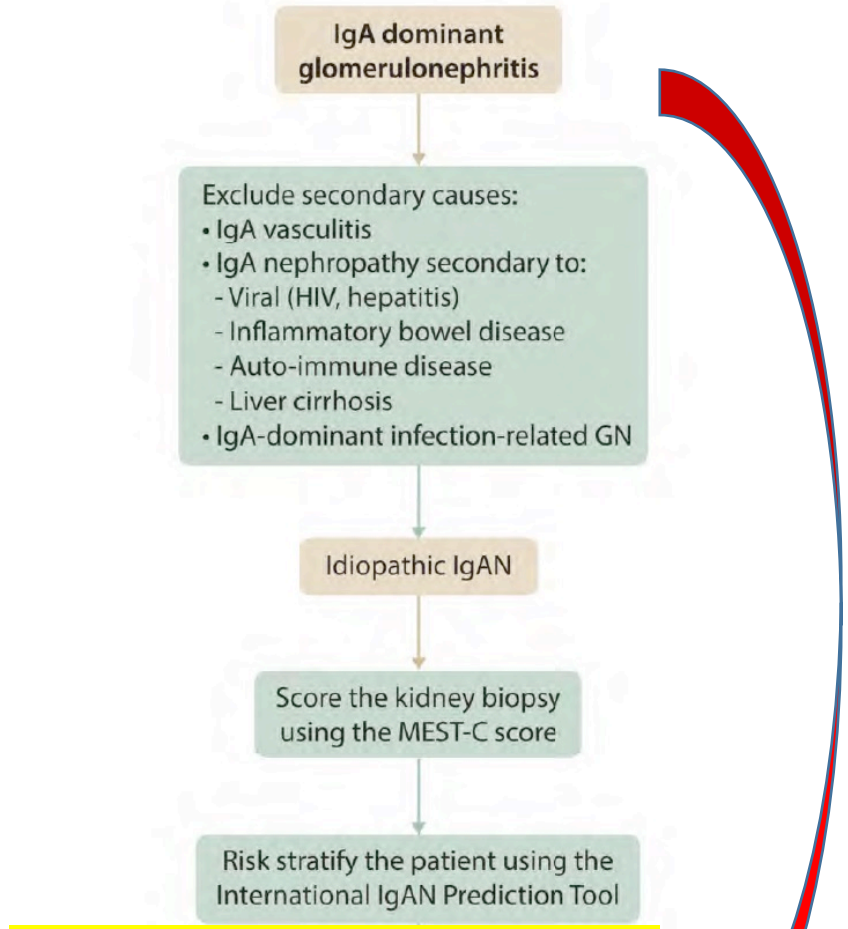
TESTING
IgAN

Discontinuation due to high risk of adverse events

Significant increase in infections including two deaths

Significant protection from 40% eGFR decline

Figure IgAN1. Initial assessment and management of the patient with IgAN



KDIGO 2020 GN

Optimized supportive care (SUP)
Rigorous BP control
Maximally tolerated ACEi/ARB

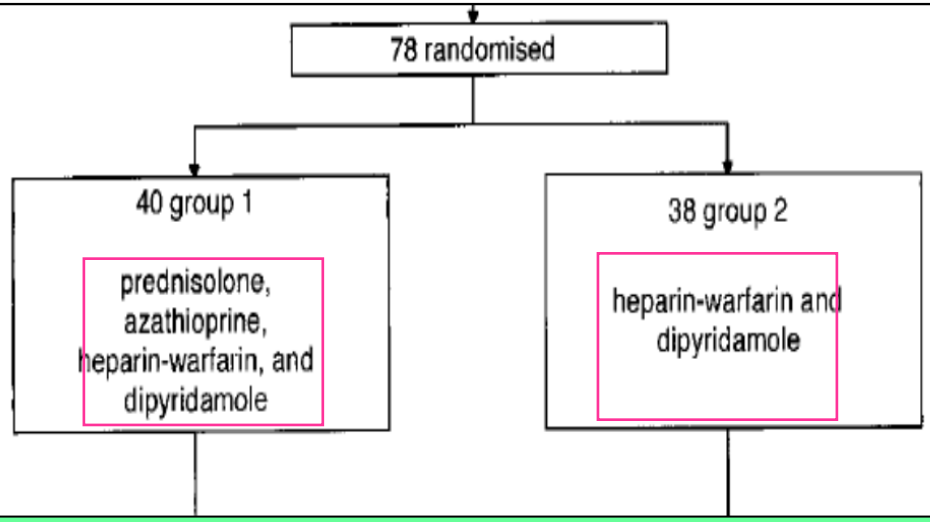
If supportive care does not induce proteinuria reduction, Corticosteroids for 6 months are recommended, after recognition of adverse effects

J Am Soc Nephrol 10: 101–109, 1999

A Controlled Trial of Combined Therapy for Newly Diagnosed Severe Childhood IgA Nephropathy

NORISHIGE YOSHIKAWA,* HIROSHI ITO,† TADASU SAKAI,§

124 children newly diagnosed IgAN
>80% mesangial proliferation



After 2 years in corticosteroid treated children
Mesangial proliferation reversed in 63%
Glomerular sclerosis did not increase
Mean proteinuria was reduced from 1.3 to 0.22 g/d

Side effects in 2 cases
Leukopenia, glaucoma, cataract, peptic ulce, depression

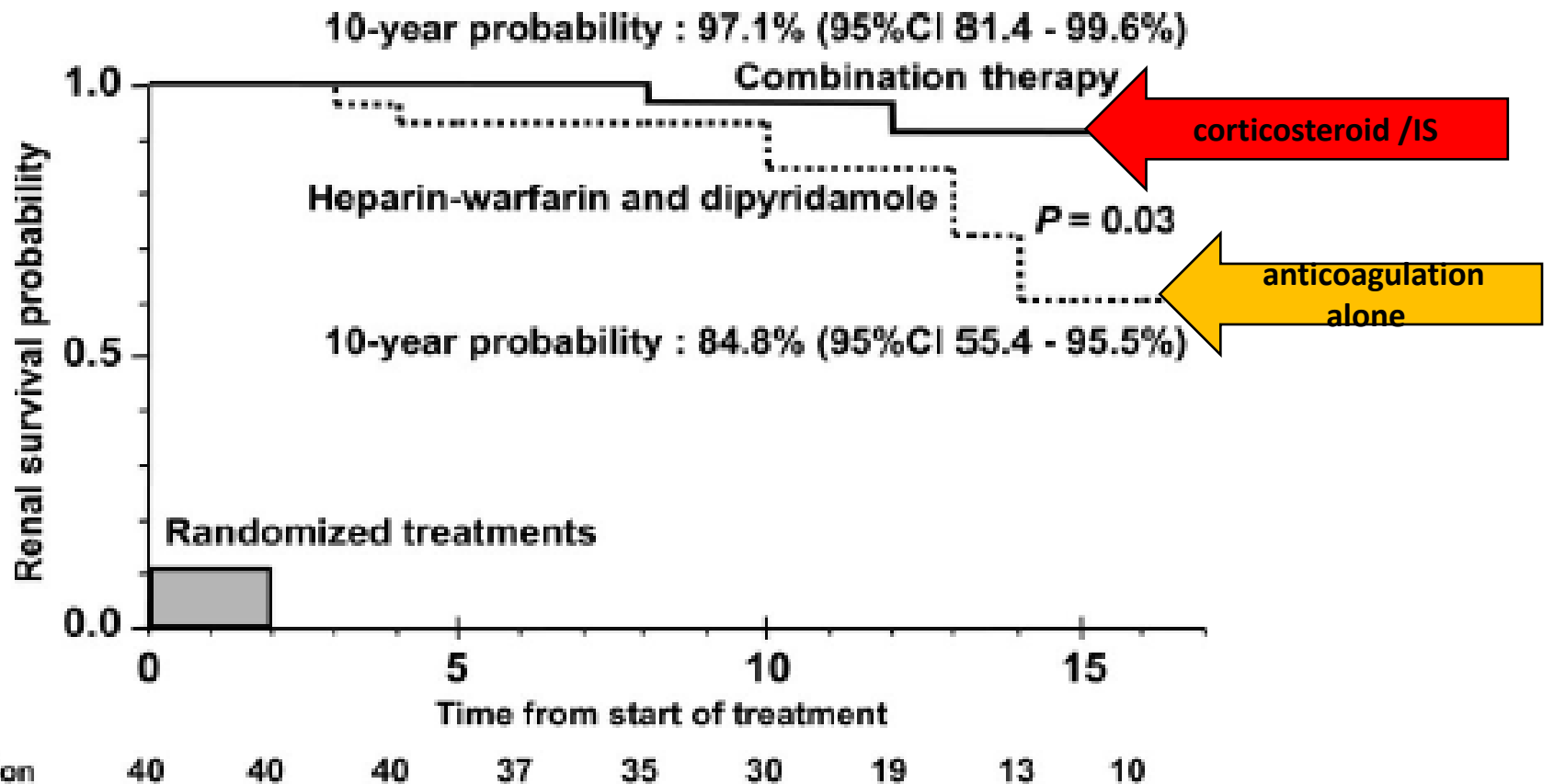
Clin J Am Soc Nephrol 6: 1301–1307, 2011.

Long-Term Results of a Randomized Controlled Trial in Childhood IgA Nephropathy

Koichi Kamei, Koichi Nakanishi,† Shuichi Ito,* Mari Saito,‡ Mayumi Sako,‡ Kenji Ishikura,§ Hiroshi Hataya,§ Masataka Honda,§ Kazumoto Iijima,‖ and Norishige Yoshikawa,† for the Japanese Pediatric IgA Nephropathy Treatment Study Group*

Mesangial proliferation targeted CS/IS treatment

2 years trial, followed by
10 years of uncontrolled treatment



Heterogeneous results of corticosteroid / immunosuppressive therapy in children with IgAN

\+ **Waldo FB**, Alexander R, Wyatt RJ, Kohaut EC.
Alternate-day prednisone therapy in children with IgAN. Am J Kidney Dis. 1989
6 children for 36 mo. A normal urinalysis was found at follow-up in all treated patients, compared with one of 15 untreated patients (P = 0.003)

Pediatr Nephrol. 1993
13 children 60 mg/m2 for 3 month, was reduced to 30 mg/m2 by 1 year and 15 mg/m2 by 2 years. Similar benefits over long-term FU

\- **Welch** TR, et al. Double-blind, controlled trial of short-term prednisone therapy inIgAN . J Pediatr. 1992.
12 chidreln for 12 week cross-over study: no benefit.

\+ **Kang** Z, et al Mycophenolate mofetil therapy for steroid-resistant IgANwith the nephrotic syndrome in children. Pediatr Nephrol. 2015
prednisone 2 mg/kg per day for 8 weeks. Steroid-resistant patients MMF and prednisone for 6-12 months.
Good response but not in children with T lesions.

\- **Hogg RJ,** et al Am J Kidney Dis. 2015
Randomized controlled trial of mycophenolate mofetil in children, adolescents, and adults with IgA nephropathy.
Trial terminated because no patient in remission at 6 mo.

\+ Shima Y, et al IgA N with presentation of nephrotic syndrome at onset in children. Pediatr Nephrol. 201
Favorable results of CS (sometimes with IS).

\+ Coppo R,et al . Plasmapheresis in a patient with rapidly progressive IgAN: removal of IgAIC and clinical recovery.
Nephron 1985
Treatment of rapidly progressive IgA nephropathy. Contrib Nephrol. 1995

\+ Niaudet P et al Actualité Necker 1993:
12 children with crescentic IgAN;: MP pulses 1 g/1.73 m2, followed by 12 months oral P
PE in 2, Cyclophosphamide in 3.
After 1-9 years none i ESRD, 6 in remission.

KDIGO 2020 GN

Practice Point 2.4.5. IgAN in children:

IgAN children with proteinuria >200 mg/d should receive ACEi or ARB blockade,

RASB when proteinuria > 0.2 g/day/1.73m2

- In children with proteinuria >1 g/d and mesangial hypercellularity (Oxford M1) most pediatric nephrologists will treat with corticosteroids in addition to RAS blockade from time of diagnosis.[10, 11, 13, 17]

Proteinuria > 1g/1.73m2 and M1: CS + RASB

- As in adults, children with rapidly progressive IgAN have a poor outcome and, despite limited evidence, this subgroup should be offered treatment with corticosteroids (usually as methylprednisolone pulses) and oral cyclophosphamide.[11, 13, 18]

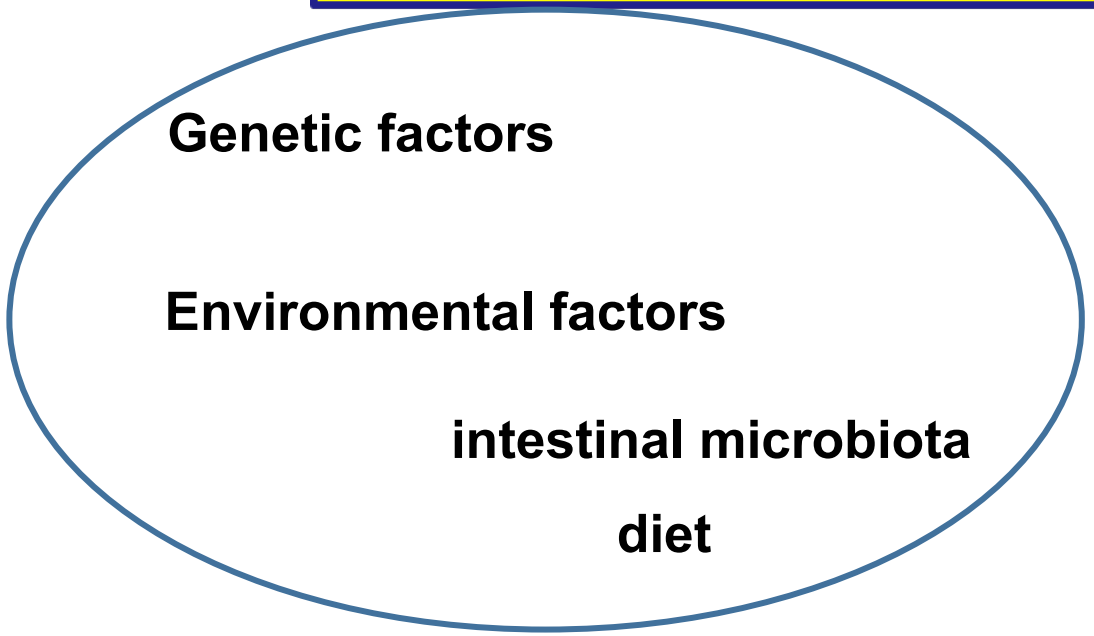
IgAN with rapidly progressive course: prompt use of CS/IS

- Continue to follow patients even after complete remission as they can relapse even after many years.[19]

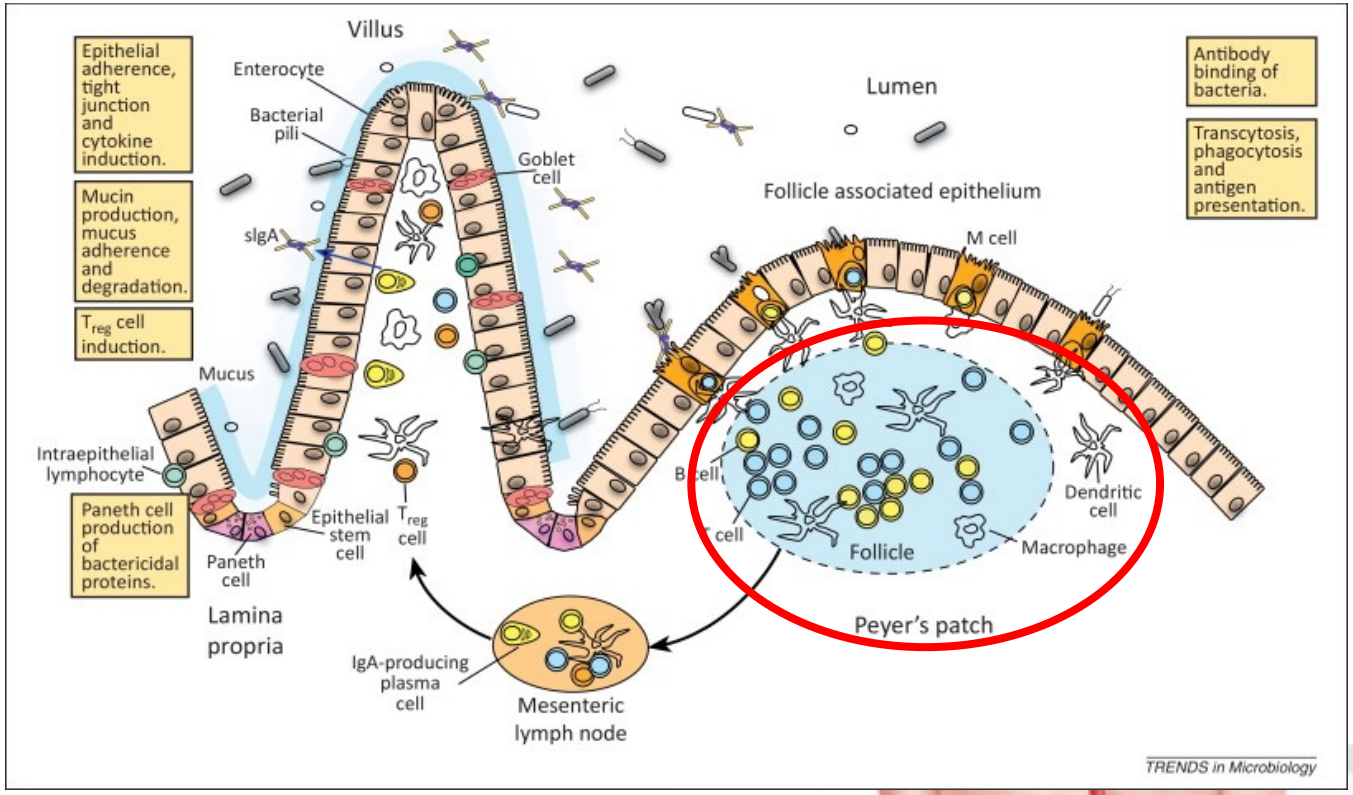
Other therapeutic approaches to IgAN treatment

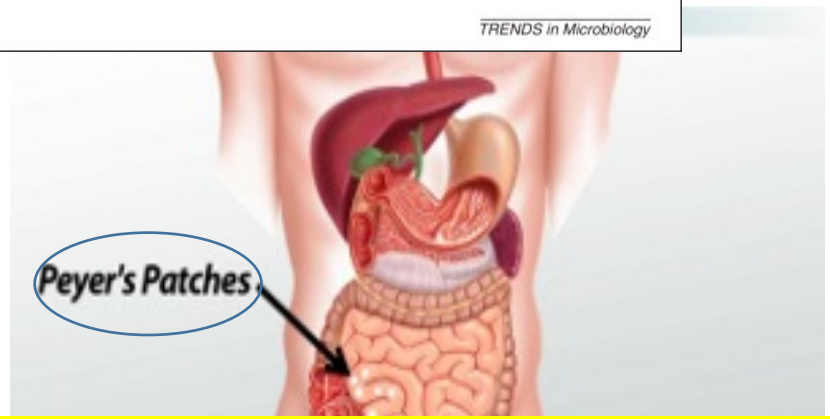
Target the gut associated lymphoid tissue (GALT)

Gut-kidney axis in IgAN: pathogenetical role and target for treatment



Activation of intestinal immunity in IgAN: subclinical intestinal mucosa inflammation leading to IgA dysregulated synthesis





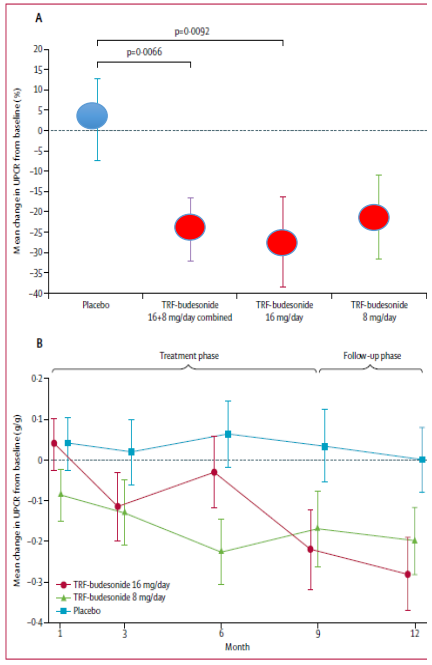
A targeted-release formulation of the glucocorticoid budesonide developed to deliver the drug at the ileo-cecal junction, rich in Payer's patches

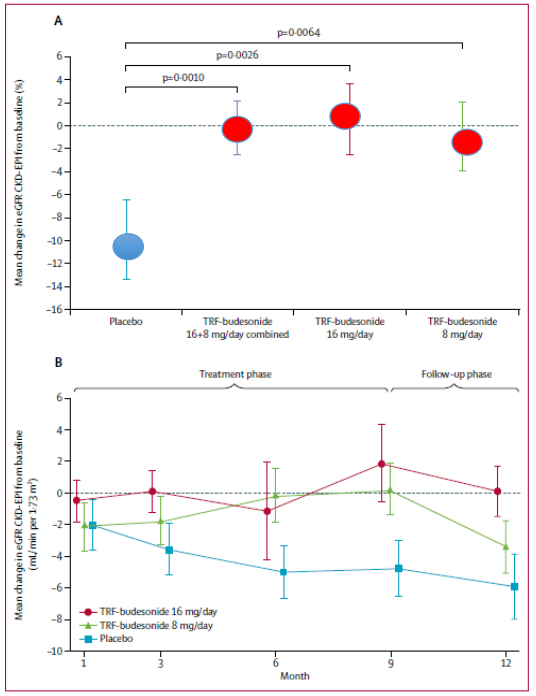
Targeted-release budesonide versus placebo in patients with IgA nephropathy (NEFIGAN): a double-blind, randomised, placebo-controlled phase 2b trial

Lancet. 2017; 389:2117-2127.

Bengt C Fellström, Jonathan Barratt, Heather Cook, Rosanna Coppo, John Feehally, Johan W de Fijter, Jürgen Floege, Gerd Hetzel, Alan G Jardine, Francesco Locatelli, Bart D Maes, Alex Mercer, Fernanda Ortiz, Manuel Praga, Søren S Sørensen, Vladimir Tesar, Lucia Del Vecchio, for the NEFIGAN Trial Investigators

- **Nefecon 16 mg/day, 8 mg/day**
- **Placebo**





Other therapeutic approaches to IgAN treatment

Targeted-.release formulation of budesonide

Tonsillectomy

Mycophenolate Mofetil

Cyclophosphamide

Rituximab

Hydroxychloroquine

Anti edothelin associated with RASB

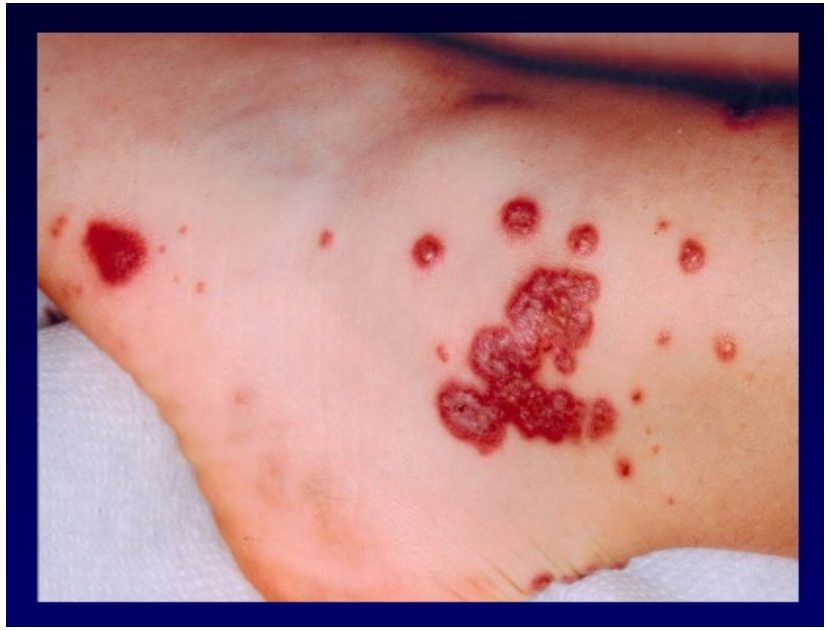
Inhibitors of BAFF-TNF receptor family (BAFF, APRIL TACI).

Anti-complement factors. C5, C5a receptor, C3 , factor D, MASP-2 inhibitors

Question n 2

Are IgAN and IgAVN the same disease with different expression?

IgAVN



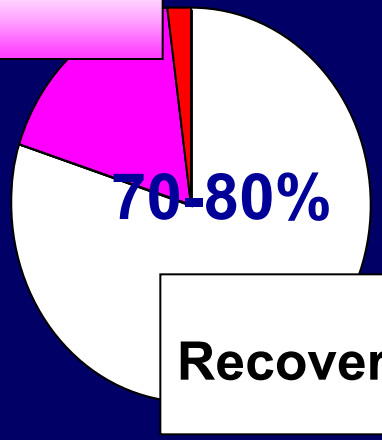
in children HSP
is the most common vasculitis

Incidence in children
60-140 cases / mp children (peak 6 y)
IgAVN develops in 20-80%, in median 30% (15-70 cases pmpy)

Incidence in adults 4-13 cases pmpy (peak 45 y)
IgAVN develops in 80%

in children IgAVN
renal involvement
is highly variable

In 20-28% abnormal urinary sediment
for >1 month



In 2-3% progression
to ESRF in long-term follow-up.

Recovery in 4 weeks

Frequent rapid regression of IgAVN in children

IgAVN (Henoch Schoenlein purpura nephritis)

- **Today rarely children with IgAVN reach kidney failure within the pediatric age.**
- **However, IgAVN may have progression of subclinical damage and develop chronic kidney damage (CKD) as well as hypertension**

BRIEF REVIEW www.jasn.org

The Pathophysiology of IgA Nephropathy

Hitoshi Suzuki,*‡ Krzysztof Kiryluk,† Jan Novak,‡ Zina Moldoveanu,‡ Andrew B. Herr,¶ Matthew B. Renfrow,§ Robert J. Wyatt,** Francesco Scolari,†† Jiri Mestecky,‡‖ Ali G. Gharavi,† and Bruce A. Julian‡‖

J Am Soc Nephrol 22: 1795–1803, 2011.

Galactose- deficient IgA1 (Gd-IgA1)

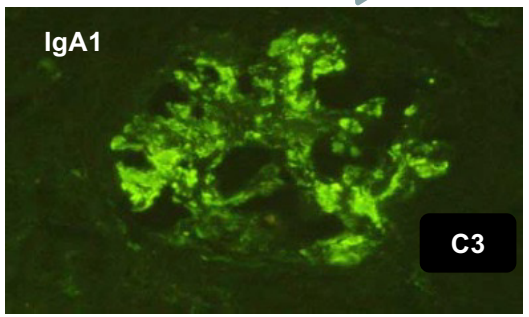
IgG anti Gd-IgA1

Circulating IgA-IgG IC

mesangial deposition of macromolecular IgA1 inflammation tissue damage

IgAVN

IgAN



Variable clinical expression and outcome possibly due to differences in

- **genetics**
- **initial promoting factors**
- **inflammatory mediators**

Autoimmunity Reviews 17 (2018) 301–315

Contents lists available at ScienceDirect

Autoimmunity Reviews

journal homepage: www.elsevier.com/locate/autrev

Review

Genetics of immunoglobulin-A vasculitis (Henoch-Schönlein purpura): An updated review

Raquel López-Mejías [a,*], Santos Castañeda [b], Fernanda Genre [a], Sara Remuzgo-Martínez [a], F. David Carmona [c,d],

Gene analyzed	Results obtained
Genetic studies on IgAV susceptibility	
HLA class II	*HLA-DRB1*01* ↑ susceptibility mainly due to the HLA-*DRB1*0103* allele. Intergenic region, between HLA-DQA1 and HLA-DQB1, ↑ susceptibility
HLA class I	*HLA-B*4102* ↑ susceptibility independent of the HLA class II
HSPA2	1267 GG genotype ↑ susceptibility
IL6	No association of rs1800795-174 [G/C], rs2069827 [G/T], and rs2069840 [C/G]
IL1β	No association of rs16944-511 [C/T]
MCP1	−2518 TT genotype and −2518 T allele ↑ susceptibility
Agt	rs699 M235 T-M allele ↓ whereas rs699 M235 T-TT genotype ↑ susceptibility
ACE	I6D-DD ↑ susceptibility
PTPN22	No association of rs2476601 [G/A] (R620W) and rs33996649 [C/T] (R263Q)
CSK	No association of rs34933034 [G/A] and rs1378942 [A/C]
Genetic studies on IgAV severity	
IL6	No association of rs1800795-174 [G/C], rs2069827 [G/T], and rs2069840 [C/G]
IL1β	rs16944-511 TT genotype and T allele ↑ severe nephropathy and renal sequelae
CCL5	rs2107538-403 TC and TT genotype ↑ renal manifestations
MCP1	−2518TT ↑ skin lesions, GI complications and joint pain
ACE	I16D-DD ↑ nephritis
PTPN22	No association of rs2476601 [G/A] (R620W) and rs3399664
CSK	No association of rs34933034 [G/A] and rs1378942 [A/C]
PAX2	798 [C/T]/909 [A/C] ↑ renal manifestations
eNOS	−786 TT genotype ↑ nephritis

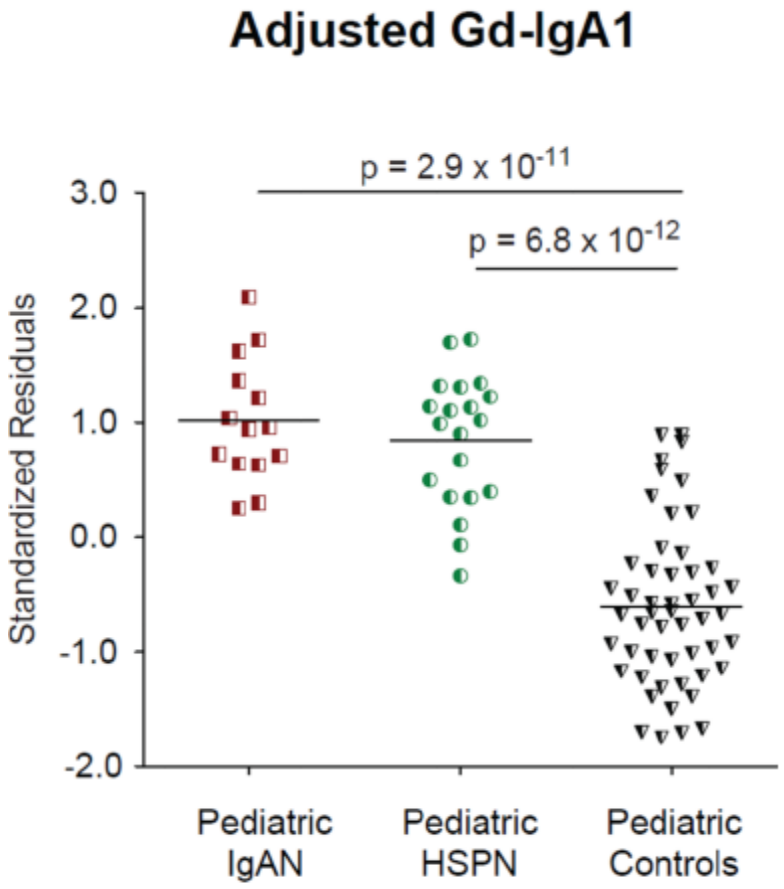
IgAV immunoglobulin A vasculitis, *HLA* human leukocyte antigen, *HSPA2* 70 kDa heat shock
IL6 interleukin 6, *IL1β* interleukin 1 ß, *MCP1* chemokine monocyte chemoattractant protein
ACE angiotensin-converting enzyme, *PTPN22* protein tyrosine phosphatase nonreceptor 22,
kinase, *CCL5* chemokine (C-C motif) ligand 5, *PAX2* paired box 2, *eNOS* endothelial nitric

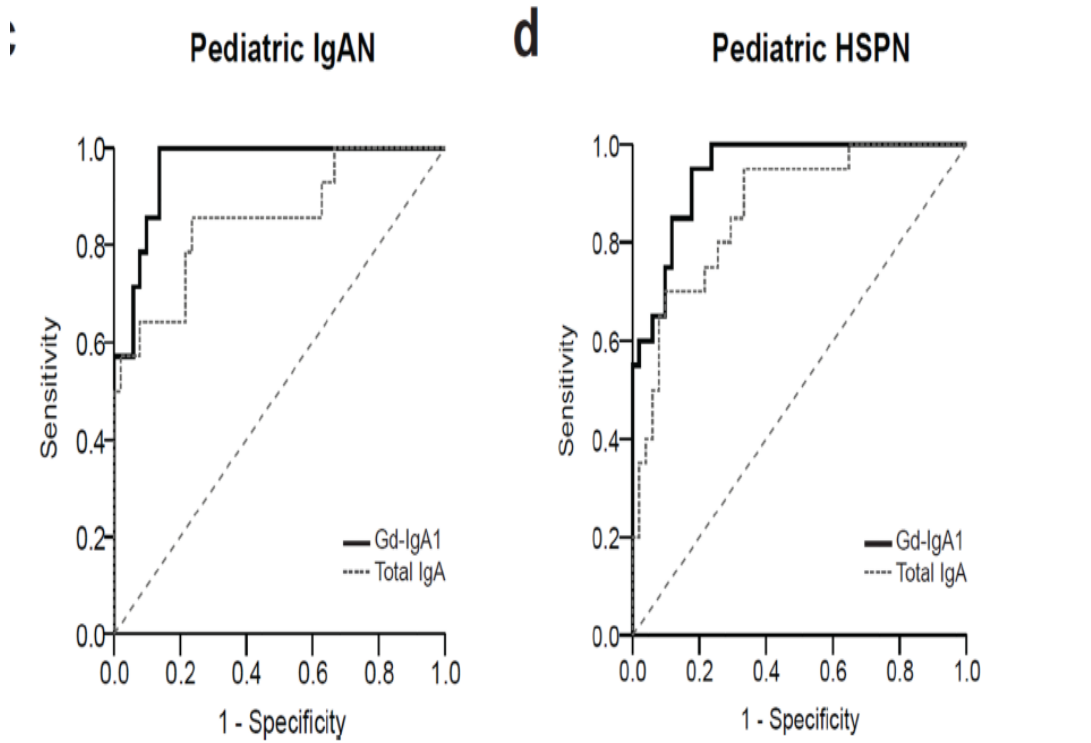
HLA Class II DRB1, and HLA class I B
and genes encoding for
- IgA galactosylation
- cytokines, chemokines, adhesion molecules,T cells,
- nitric oxide, neoangiogenesis, RAS, homocysteine

Published in final edited form as:
Kidney Int. 2011 July ; 80(1): 79–87. doi:10.1038/ki.2011.16.

Aberrant Glycosylation of IgA1 is Inherited in Pediatric IgA Nephropathy and Henoch-Schönlein Purpura Nephritis

Krzysztof Kiryluk[1], Zina Moldoveanu[2], John T. Sanders[4,5], T. Matthew Eison[4,5], Hitoshi Suzuki[2,3], Bruce A. Julian[2], Jan Novak[2], Ali G. Gharavi[1], and Robert J. Wyatt[4,5]





Levels of Gd-IgA1 are similar in IgAN, IgAVN, children and adults

Nephrol Dial Transplant (2018) 33: 1579–1590
doi: 10.1093/ndt/gfx300
Advance Access publication 3 November 2017

Value of biomarkers for predicting immunoglobulin A vasculitis nephritis outcome in an adult prospective cohort

Laureline Berthelot[1,2,3,4,5], Agnès Jamin[1,2,3,4], Denis Viglietti[6], Jonathan M. Chemouny[1,2,3,4,7], Hamza Ayari[1,2,3,4], Melissa Pierre[1,2,3,4], Pierre Housset[1,2,3,4], Virginia Sauvaget[1,2,3,4], Margarita Hurtado-Nedelec[1,2,3,4,8], François Vrtovsnik[1,2,3,4,7], Eric Daugas[1,2,3,4,7], HSPrognosis Group, Renato C. Monteiro[1,2,3,4,8] and Evangeline Pillebout[1,2,3,4,6]

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Prospective study in 85 adult IgAV (60 with IgAVN)
Patients were reexamined after 1 year for outcome

Markers of IgAN
Gd-IgA1
IgA-CD89 complexes
IgA-IgG immune complexes

IgA in serum and urine

Mediators of renal damage
Cytokines in plasma and urine
IL-1β
IL-6
IL-8
IL-10
IL-12p70
TNF-α

All biomarkers are increased in IgAVN versus IgAV without nephritis

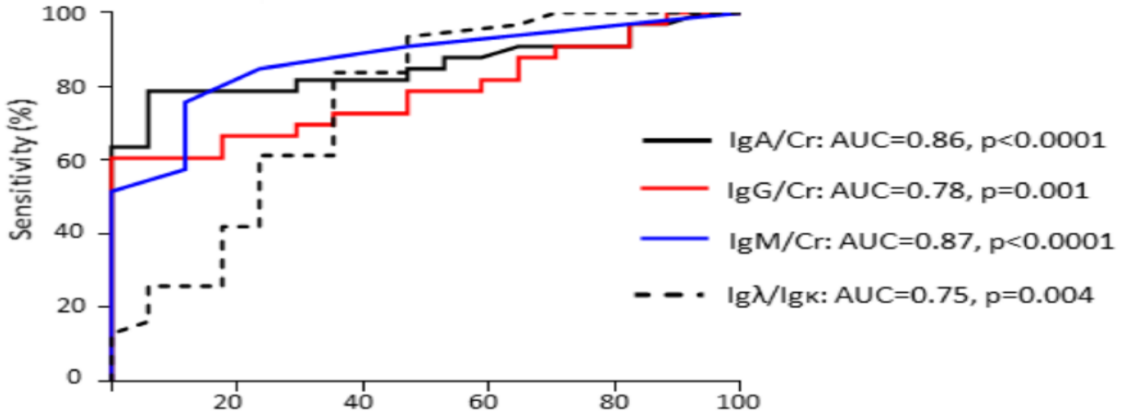
RESEARCH ARTICLE

Biomarkers of IgA vasculitis nephritis in children

Evangeline Pillebout[1,2,3,4,5]*, Agnès Jamin[1,2,3,4], Hamza Ayari[1,2,3,4], Pierre Housset[1,2,3,4], Melissa Pierre[1,2,3,4], Virginia Sauvaget[1,2,3,4], Denis Viglietti[5], Georges Deschenes[1,2,3,4,6], Renato C. Monteiro[1,2,3,4,7☯]*, Laureline Berthelot[1,2,3,4,8☯]*, for the HSPrognosis group[¶]

1 INSERM 1149, Center of Research on Inflammation (CRI), Paris, France, **2** Inflamex, Laboratory of Excellence, Bichat Medical Faculty, Paris, France, **3** University Paris Diderot, Sorbonne Paris Cité, Paris, France, **4** CNRS ERL8252, Paris, France, **5** Department of nephrology, Saint-Louis Hospital, AP-HP, Paris, France, **6** Department of Pediatric Nephrology, Robert Debré Hospital, AP-HP, DHU Fire, Paris, France, **7** Department of Immunology, Bichat Hospital, AP-HP, DHU Fire, Paris, France, **8** Centre de Recherche en Transplantation et Immunologie (CRTI), UMR 1064, INSERM, Université de Nantes, Nantes, France

IgA, IL-6 , IL-8 in urine
In adults and in children
with IgAV N were
biomarkers valid at univariate analysis



Biomarkers of pediatric IgAV nephritis

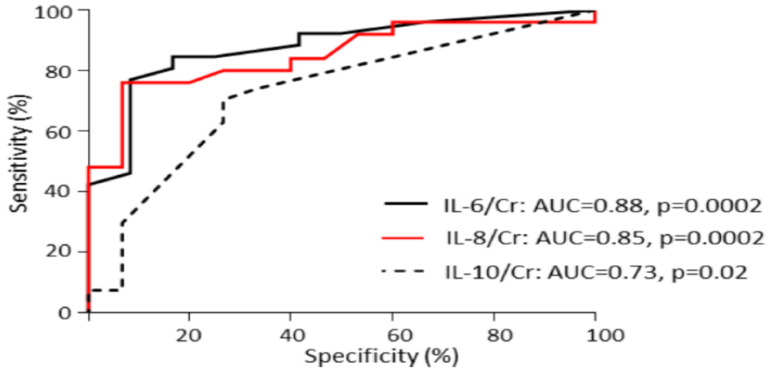


Fig 4. ROC curves of urinary cytokines comparing the IgAV-woN and IgAV-N groups.

At multivariable analysis
no effect on
disease expression or progression

Davin, J.-C. & Coppo, R. *Nat. Rev. Nephrol.*

July 2014; doi:10.1038/

Table 3 | Immune system reactants involved in the pathogenesis of HSP nephritis

Reactant*	Details
Circulating IgA molecules	Galactose-deficient IgA_1 Autoaggregated galactose-deficient IgA_1 IgG antibodies to galactose-deficient IgA_1 IgG–IgA_1 circulating immune complexes IgA_1–soluble CD89 complexes
Receptors for IgA_1	Myeloid FcαRI (also known as CD89) Transferrin receptor (also known as CD71) on mesangial cells
Cytokines‡	IL-17 (increased ratio of IL-17:T_{REG} cells), TNF, IL-1β, IL-2, IL-6, IL-8, TGF-β, VEGF, TWEAK, low IFN-γ and IL-12, increased IL-4 (imbalance of T_H1:T_H2)
Mesangial cell receptors§	C3, FcγRI, TNF, TGF-β, PDGF-RB, IL-1, IL-6, IFN-γ, fibronectin receptor, integrins, angiotensin II receptor, CD71, EGF, TLR-3, TLR-4, chemokines
Products of mesangial cells	Cytokines: TNF, IL-1β, IL-6, TGF-β Chemokines: IL-8, RANTES, MCP-1 Prostanoids, angiotensin II, nitric oxide, reactive oxygen species

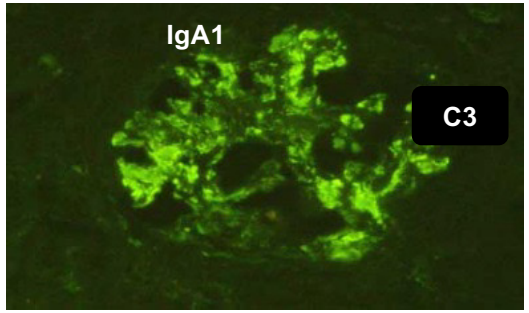
IgAN

Galactose- deficient IgA1
(Gd-IgA1)

IgG anti Gd-IgA1

Circulating IgA-IgG IC

mesangial
deposition of
macromolecular IgA1
inflammation
tissue damage



IgAVN

IgAV is a vasculitis

Complement
Endothelial activation
Coagulation activation
Crescent formation

COMPLEMENT ACTIVATION

IN SERA and/or IN RENAL TISSUE

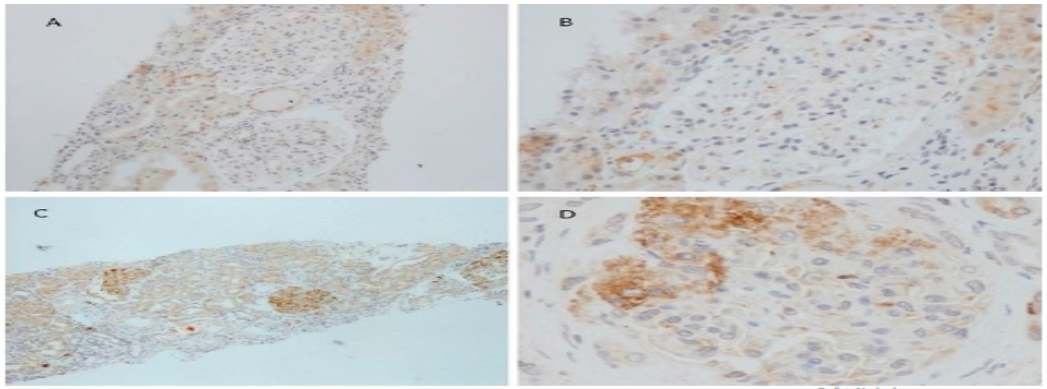
	IgAVN	PRIMARY IgAN
• C3d	↑↑	↑
• C4d	↑	↑
• C5b-9	↑↑	↑
• Mannose binding lectin	↑	↑
• MASP-1	↑	↑↑

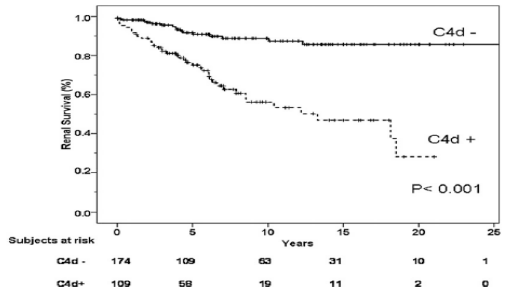
COAGULATION ACTIVATION

	IgAVN	PRIMARY IgAN
• Factor XIII	↓	-
• Lipoprotein a (LPA)	↑	-
• PAI-1	↑	-
• Thrombomodulin	↑	-
• S Protein	↑	-
• C Protein	↑	-

Association of C4d Deposition with Clinical Outcomes in IgA Nephropathy

Mario Espinosa, Rosa Ortega, Marina Sánchez, Alfons Segarra, Maria Teresa Salcedo, Fayna Gonzâlez, Rafael Camacho, Miguel Angel Valdivia, Rocio Cabrera, Katia López, Fernando Pinedo, Eduardo Gutierrez, Alfonso Valera, Miryam Leon, Maria Angeles Cobo, Rosa Rodriguez, Jose Ballarín, Yolanda Arce, Beatriz García, María Dolores Muñoz, and Manuel Praga for the Spanish Group for the Study of Glomerular Diseases (GLOSEN)



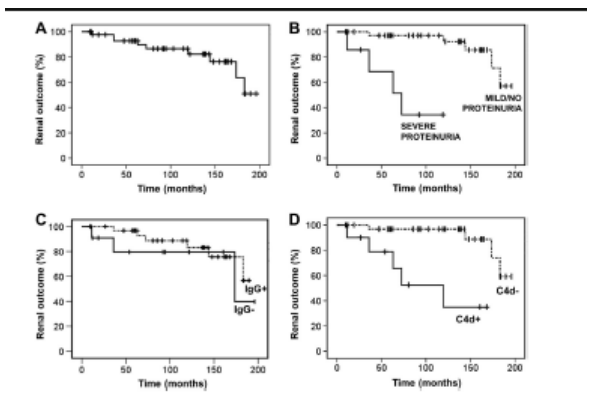


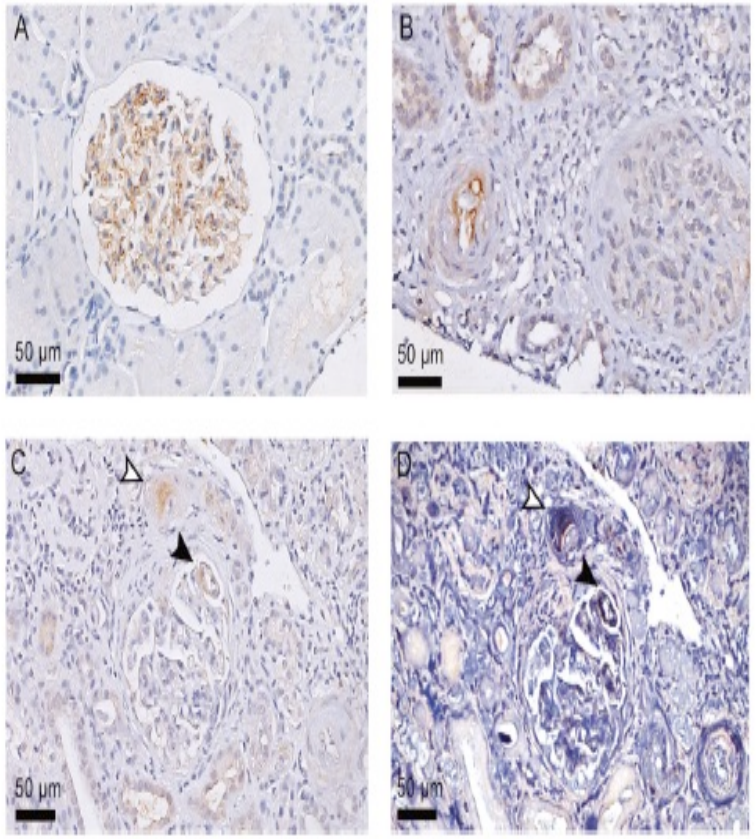
Pediatr Nephrol
DOI 10.1007/s00467-017-3610-y

ORIGINAL ARTICLE

Mesangial C4d deposition may predict progression of kidney disease in pediatric patients with IgA nephropathy

Rafaela Cabral Gonçalves Fabiano[1] · Stanley de Almeida Araújo[2] · Eduardo Alves Bambirra[2] · Eduardo Araújo Oliveira[3] · Ana Cristina Simões e Silva[3,4] · Sérgio Veloso Brant Pinheiro[3,5]





Modern Pathology
https://doi.org/10.1038/s41379-019-0259-z

ARTICLE

Complement-mediated microangiopathy in IgA nephropathy and IgA vasculitis with nephritis

Jamie S. Chua[1] · Malu Zandbergen[1] · Ron Wolterbeek[2] · Hans J. Baelde[1] · Leendert A. van Es[1] · Johan W. de Fijter[3] · Jan A. Bruijn[1] · Ingeborg M. Bajema[1]

Mod Pathol. 2019 Jul;32:1147-1157..

Co-localization of C4d and microangiopathy lesions

	Microangiopathy absent $n=94$	Microangiopathy present $n=22$	Total $n=116$	p value
C4d positive, n (%)	16 (17)	17 (77)	33 (28)	<0.001
In glomeruli, n (%)	14 (15)	12 (55)	26 (22)	<0.001
In arterioles, n (%)	5 (5)	11 (50)	16 (14)	<0.001

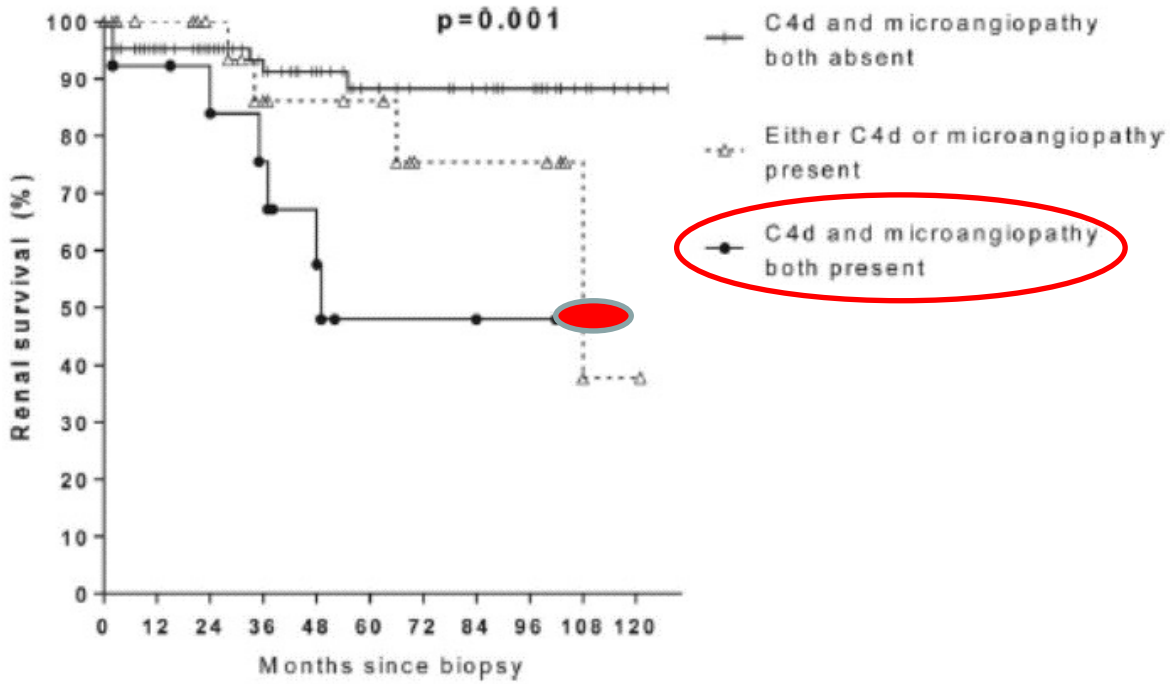


Table 4 Risk factors for renal replacement therapy

Variable	Hazard ratio	95% confidence interval	*p* value
Both microangiopathy and C4d absent	Reference (1.000)	NA	0.028
Either microangiopathy or C4d present	2.007	0.600–7.193	0.249
Both microangiopathy and C4d present	4.439	1.492–13.207	0.007
Hypertension present	2.779	0.746–10.504	0.127

Multivariable Cox proportional hazard regression analyses. The hazard ratios for requiring renal replacement therapy are shown for microangiopathy and C4d staining, corrected for hypertension. *NA* not applicable

Nephrol Dial Transplant (2019) 1–6
doi: 10.1093/ndt/gfz241

Nephrol Dial Transplant. 2021 Mar 29;36(4):581-586.

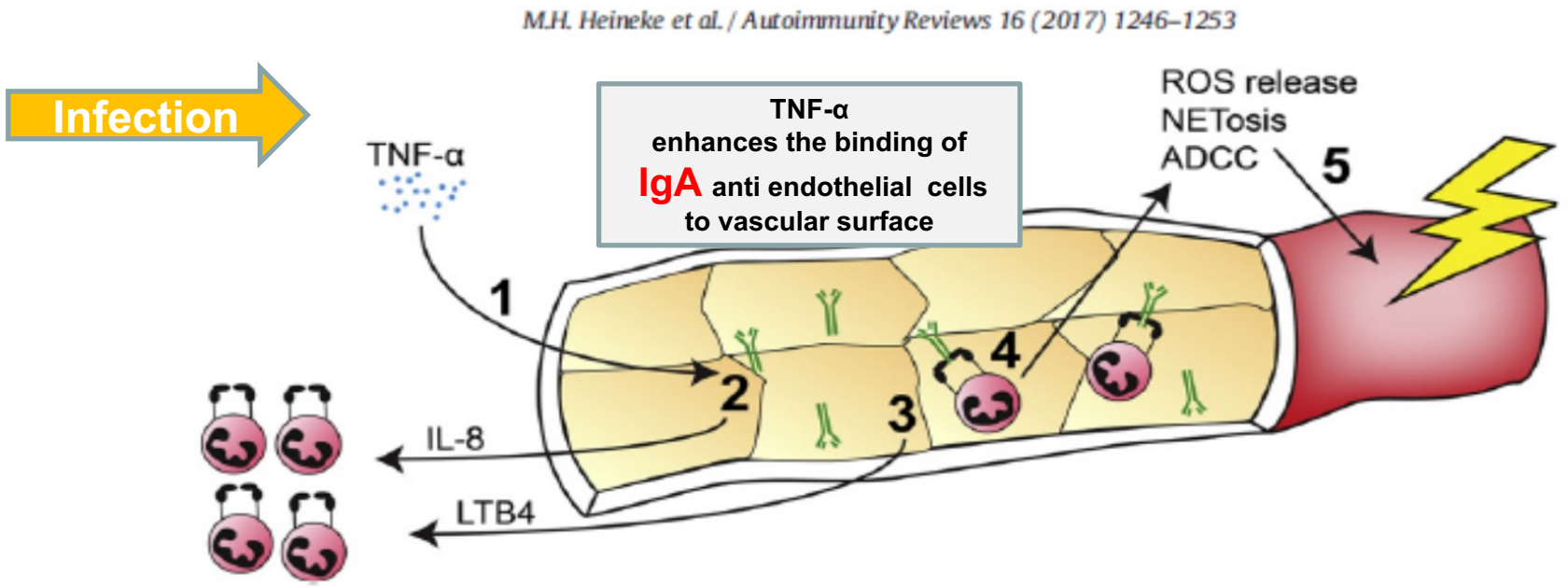
ndt
Nephrology Dialysis Transplantation

Glomerular endothelial activation, C4d deposits and microangiopathy in immunoglobulin A nephropathy

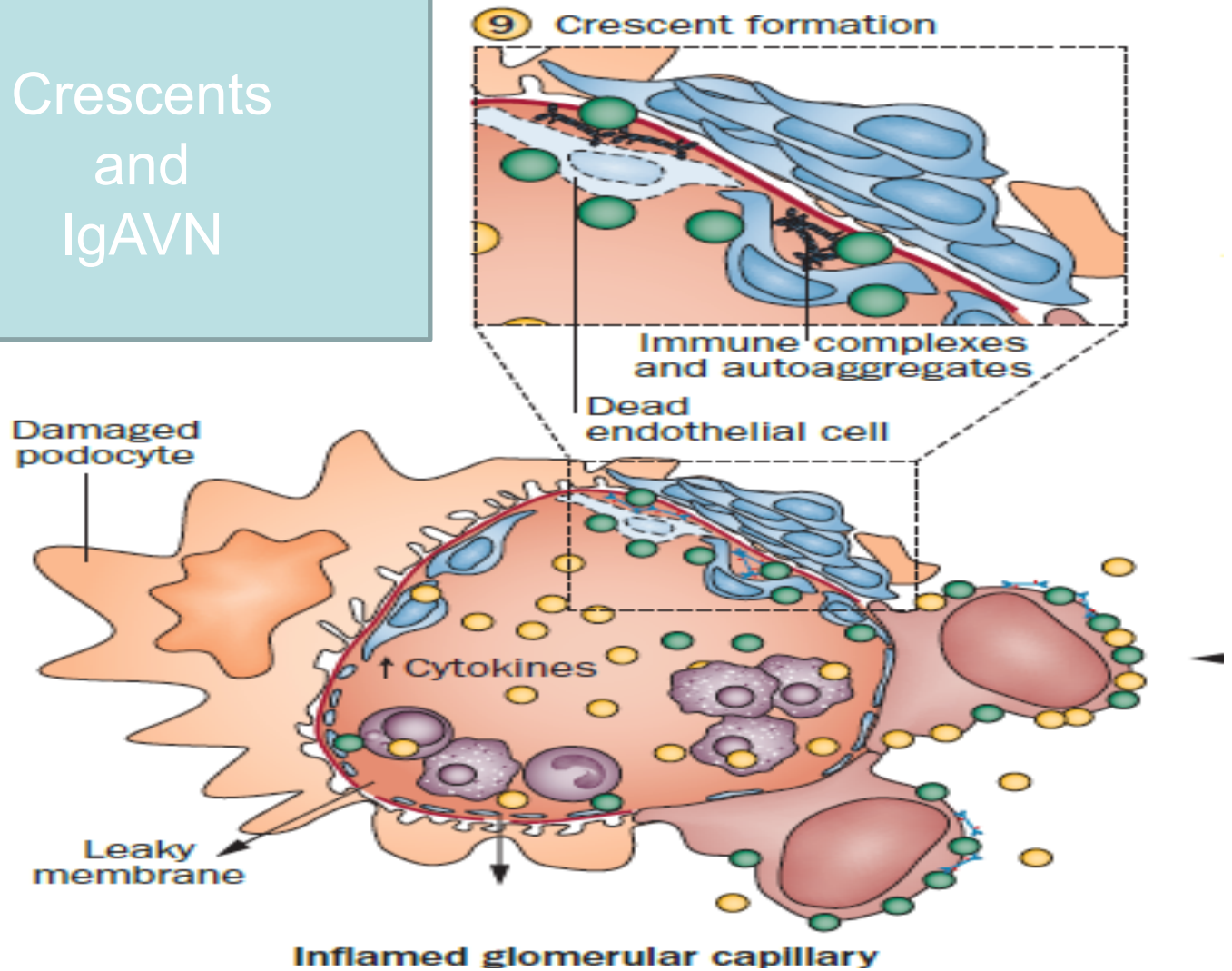
Hernán Trimarchi [1] and Rosanna Coppo[2]

role of IgA anti endothelial cells

Endothelial cell activation in IgA Vasculitis



Crescents and IgAVN



Davin, J.-C. & Coppo, R. *Nat. Rev. Nephrol.*

ISKDC International study kidney diseases in children classification of IgAVN (HSPN)

- I: Minimal histologic alterations
- II: Pure mesangial proliferation
- III: Focal (IIIa) or diffuse (IIIb) mesangial proliferation with <50% crescentic glomeruli
- IV: Focal (IVa) or diffuse (IVb) mesangial proliferation with 50–75% crescentic glomeruli
- V: Focal (Va) or diffuse (Vb) mesangial proliferation with >75% crescentic glomeruli
- VI: Membranoproliferative-like glomerulonephritis

Nephrol Dial Transplant (1997) 12: 2277–2283

Long-term prognosis of Henoch–Schönlein nephritis in adults and children*

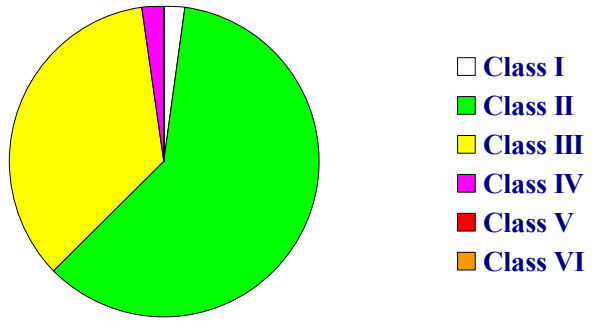
R. Coppo, G. Mazzucco, L. Cagnoli[1], A. Lupo[2], F. P. Schena[3], for the Italian Group of Renal Immunopathology Collaborative Study on Henoch–Schönlein purpura

Predictors of Outcome in Henoch-Schönlein Nephritis in Children and Adults

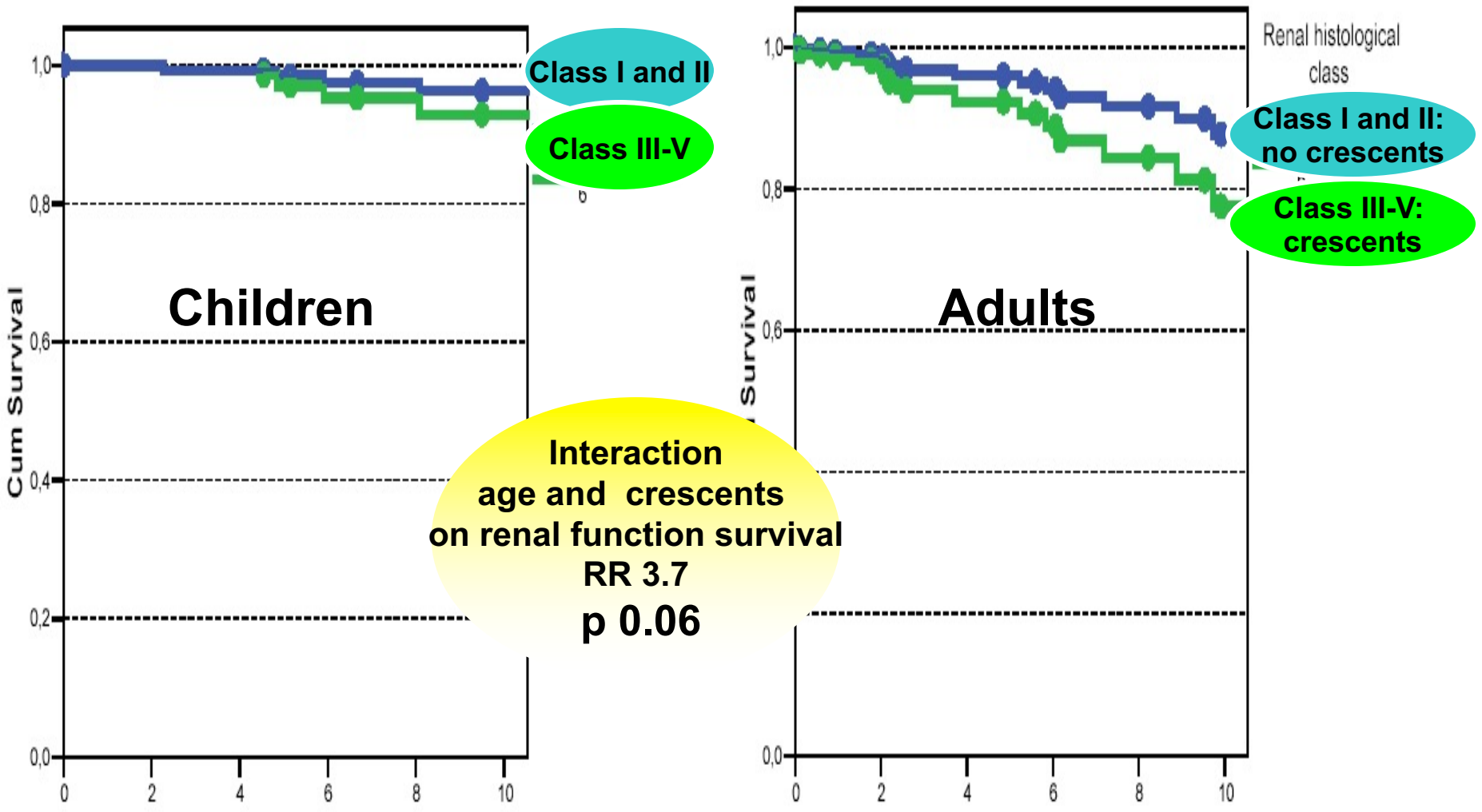
Rosanna Coppo, MD, Simeone Andrulli, MD, Alessandro Amore, MD, Bruno Gianoglio, MD, Giovanni Conti, MD, Licia Peruzzi, MD, Francesco Locatelli, MD, and Leonardo Cagnoli, MD

American Journal of Kidney Diseases, Vol 47, No 6 (June), 2006: pp 993-1003

219 patients (83 children) with IgAVN assessed by renal histology
Class II ISKD: no crescents
Class III <50% crescents



Histologic class: children and adults



Survival time to dialysis (years)

Survival time to dialysis (years)

Predictors of Outcome in Henoch-Schönlein Nephritis in Children and Adults

Rosanna Coppo, MD, Simeone Andrulli, MD, Alessandro Amore, MD, Bruno Gianoglio, MD, Giovanni Conti, MD, Licia Peruzzi, MD, Francesco Locatelli, MD, and Leonardo Cagnoli, MD

American Journal of Kidney Diseases, Vol 47, No 6 (June), 2006: pp 993-1003

Table 5. Predictor Variables Related to Survival at Multivariate Cox Regression Analysis by Using Doubling of Baseline Creatinine Level (Corrected for Body Surface Area in Children) and Dialysis Therapy as End Points

	Creatinine Level Doubling					Dialysis Therapy				
				95% CI for RR					95% CI for RR	
	B	*P*	RR	Lower	Upper	B	*P*	RR	Lower	Upper
Variables included in model										
Age (adults *v* children)	1.273	0.024	3.57	1.18	10.79	2.700	0.014	14.89	1.72	129.07
Sex (female *v* male)	1.741	0.006	5.71	1.67	19.55	3.259	0.005	26.03	2.64	256.73
Mean proteinuria during follow-up (g/d)	0.571	<0.001	1.77	1.35	2.32	0.546	0.005	1.73	1.18	2.52

International Consensus on clinico-pathological Classification of IgAN: Oxford Classification

Kidney International (2009) 76, 546–556- Kidney International (2009) 76, 534–545

Mesangial hypercellularity
Endocapillary hypercellularity
Segmental glomerular sclerosis
Tubular atrophy/interstitial fibrosis
+
Crescents

Yun et al. BMC Nephrology (2020) 21:33
https://doi.org/10.1186/s12882-020-1691-5

BMC Nephrology

RESEARCH ARTICLE Open Access

MEST-C pathological score and long-term outcomes of child and adult patients with Henoch-Schönlein purpura nephritis

Donghwan Yun[1,2], Dong Ki Kim[1], Kook-Hwan Oh[1], Kwon Wook Joo[1], Kyung Chul Moon[3], Yon Su Kim[1,2], Kyoungbun Lee[3*] and Seung Seok Han[1*]

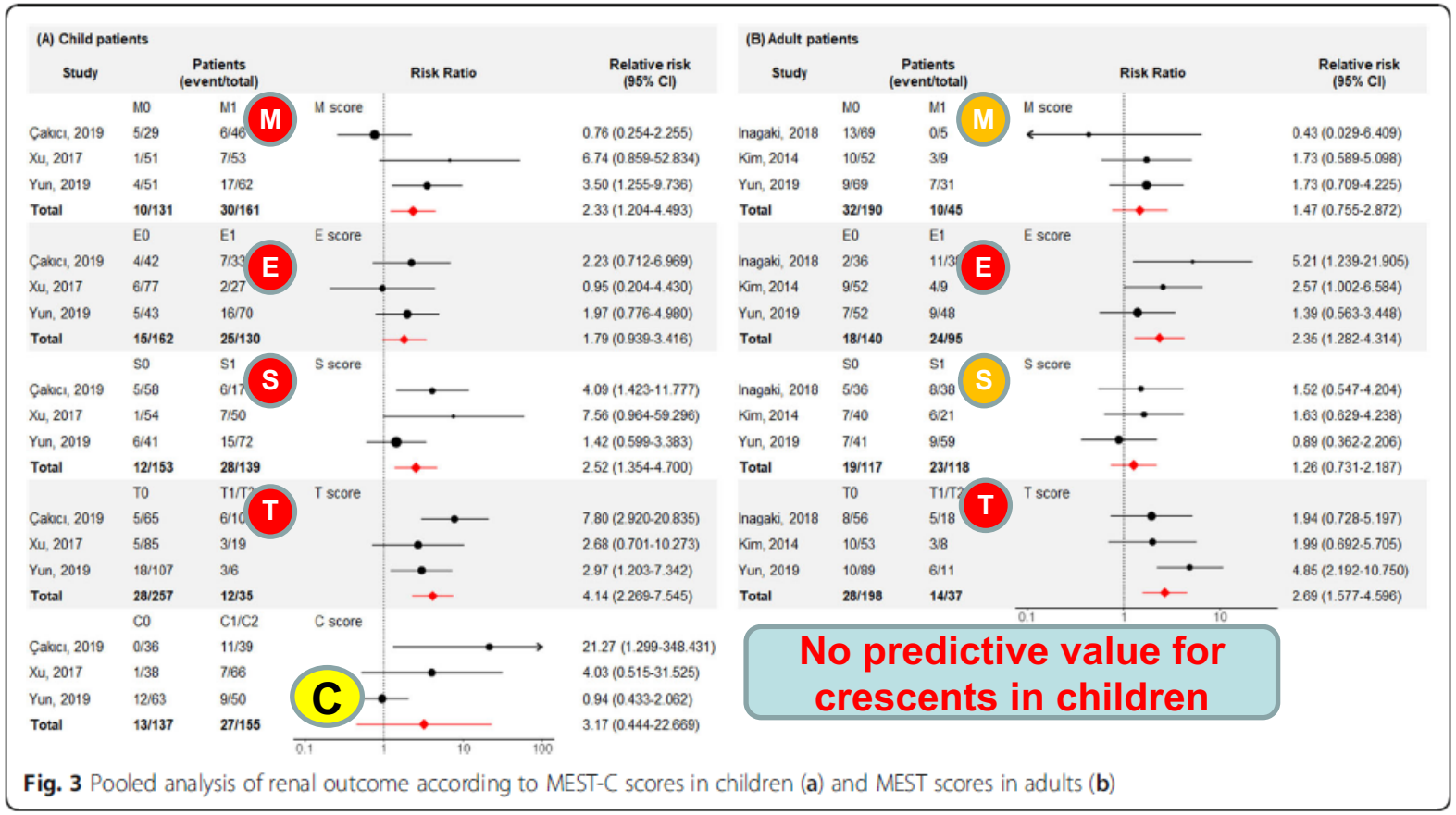


Fig. 3 Pooled analysis of renal outcome according to MEST-C scores in children (**a**) and MEST scores in adults (**b**)

Pediatr Nephrol (2015) 30:189–192
DOI 10.1007/s00467-014-2954-9

EDITORIAL COMMENTARY

The difficulty in considering modifiable pathology risk factors in children with IgA nephropathy: crescents and timing of renal biopsy

Rosanna Coppo · Jean-Claude Davin

Crescents are found when biopsy is prompt

Crescents may be coincident with acute onset and then disappear

Crescents may regress or evolve into sclerotic lesions

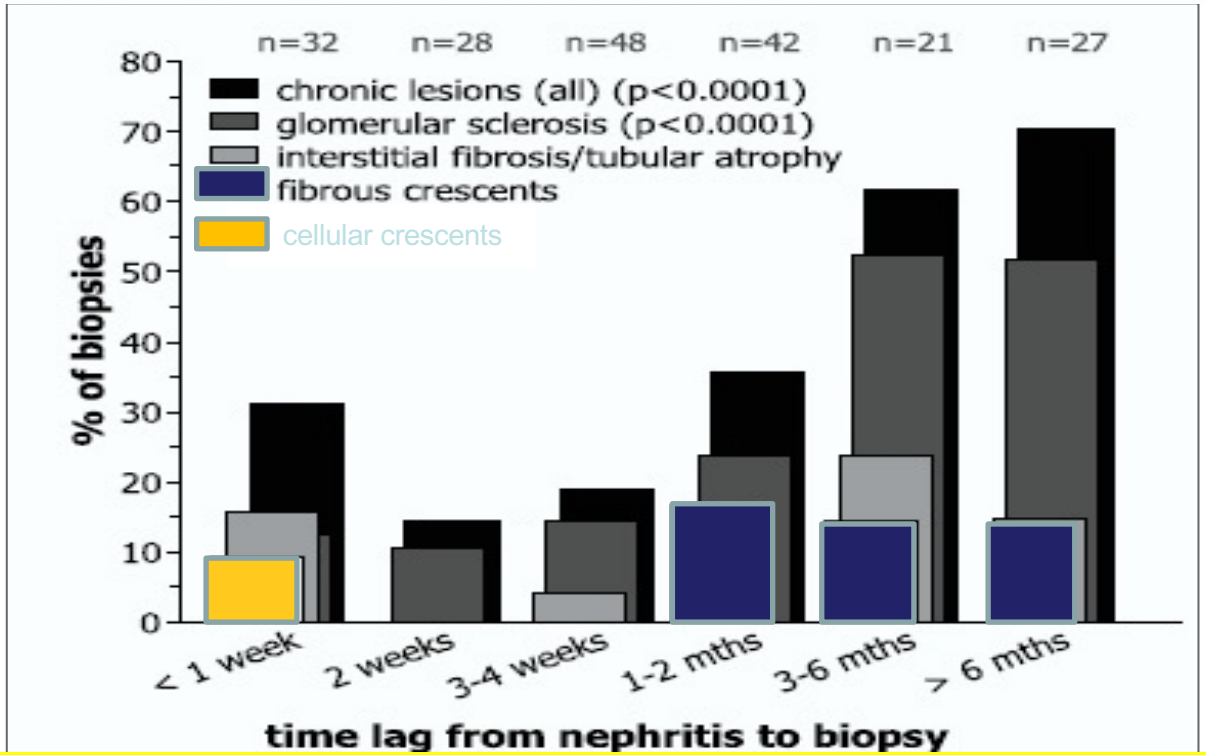
Timing of renal biopsy

Pediatr Nephrol (2018) 33:277–286
DOI 10.1007/s00467-017-3794-1

ORIGINAL ARTICLE

Presentation of pediatric Henoch–Schönlein purpura nephritis changes with age and renal histology depends on biopsy timing

Imke Hennies[1] · Charlotte Gimpel[2] · Jutta Gellermann[3] · Kristina Möller[4] · Brigitte Mayer[5] · Katalin Dittrich[6] · Anja K. Büscher[7] · Matthias Hansen[8] · Wiebke Aulbert[9] · Elke Wühl[10] · Richard Nissel[11] · Gessa Schalk[12] · Lutz T. Weber[13] · Michael Pohl[14] · Simone Wygoda[15] · Rolf Beetz[16] · Günter Klaus[17] · Henry Fehrenbach[18] · Sabine König[19] · Hagen Staude[20] · Ortraud Beringer[21] · Martin Bald[22] · Ulrike Walden[23] · Christian von Schnakenburg[24] · Gunhard Bertram[25] · Michael Wallot[26] · Karsten Häffner[2] · Thorsten Wiech[27] · Peter F. Hoyer[7] · Martin Pohl[2] · for the German Society of Pediatric Nephrology



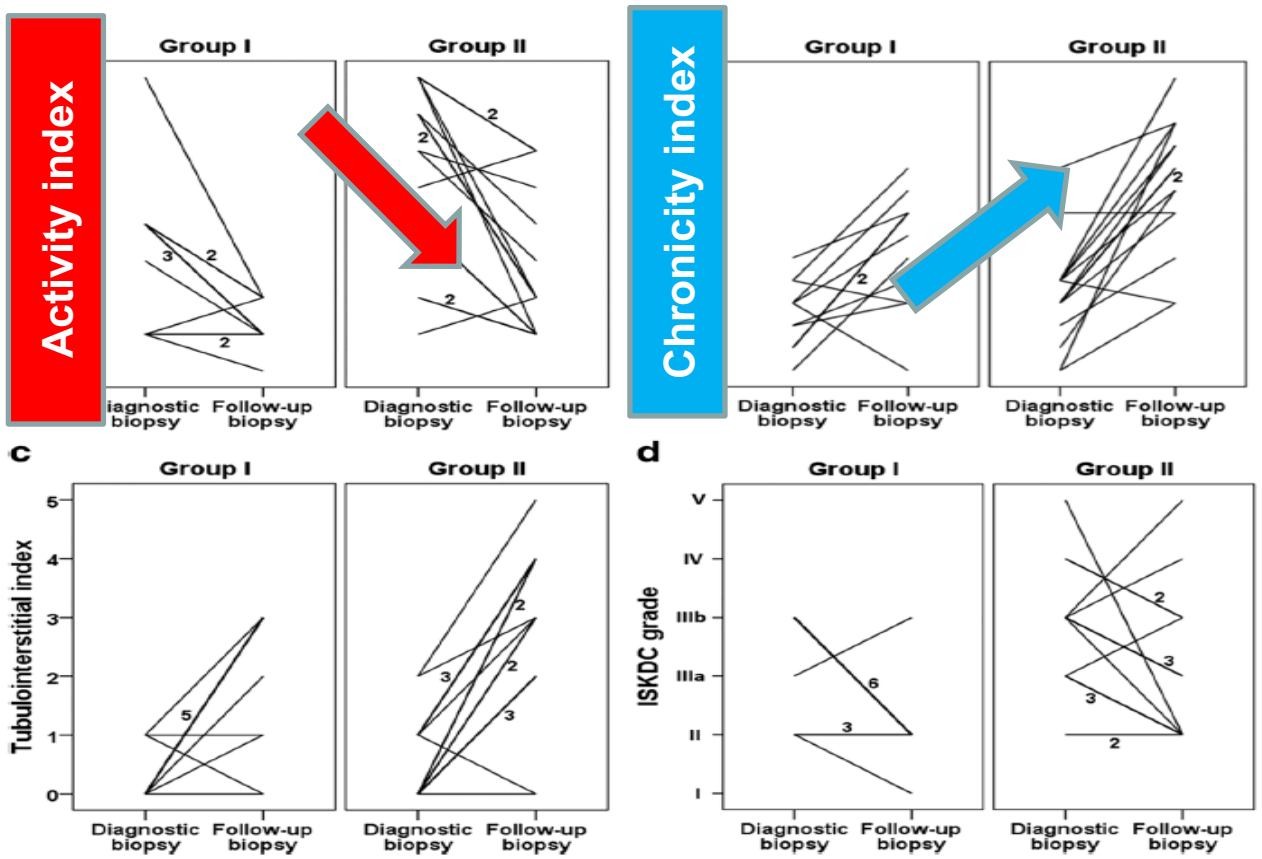
- Cellular or fibrous crescents depend on timing of biopsy
- Chronicity indexes influence negative outcome
- Smoldering low grade proteinuria correlates with chronic lesions

Pediatric Nephrology (2020) 35:659–668
https://doi.org/10.1007/s00467-019-04415-3

ORIGINAL ARTICLE

Prediction of renal outcome in Henoch–Schönlein nephritis based on biopsy findings

Mikael Koskela[1,2] · Elisa Ylinen[2] · Helena Autio-Harmainen[3] · Heikki Tokola[3] · Päivi Heikkilä[4] · Jouko Lohi[4] · Hannu Jalanko[2] · Matti Nuutinen[5,6] · Timo Jahnukainen[2]



IgAVN is a vasculitis
(endocapillary hypercellularity and crescents)

- IgAVN has a acute onset, rapid development and possible regression

- After the acute onset, IgAVN can proceed like primary IgAN, with a slowly progressive course sometimes with new poussées of activity

Need for a prediction model for IgAVN.
Study in progress M.Haas, R.Coppo S.Barbour

Question n 3

- **Would you treat a child with HSP (IgAV) with prednisone to avoid the development of nephritis?**

KDIGO 2012 GN

11.3: Prevention of HSP nephritis in children

11.3.1: We recommend not using corticosteroids to prevent HSP nephritis. (*1B*)

11.4: HSP nephritis in adults

11.4.1: We suggest that HSP nephritis in adults be treated the same as in children. (*2D*)

2.7. Treatment

KDIGO 2020 GN

Recommendation 2.7.1.1. We recommend not using corticosteroids to prevent nephritis in patients with isolated extrarenal IgAV *(1B)*.

RHEUMATOLOGY

Rheumatology 2019;58:1607–1616
doi:10.1093/rheumatology/kez041
Advance Access publication 16 March 2019

Original article

European consensus-based recommendations for diagnosis and treatment of immunoglobulin A vasculitis—the SHARE initiative

Seza Ozen[1], Stephen D. Marks[2], Paul Brogan[2], Noortje Groot[3,4,5], Nienke de Graeff[3], Tadej Avcin[6], Brigitte Bader-Meunier[7], Pavla Dolezalova[8], Brian M. Feldman[9], Isabelle Kone-Paut[10], Pekka Lahdenne[11], Liza McCann[5], Clarissa Pilkington[2], Angelo Ravelli[12], Annet van Royen[3], Yosef Uziel[13], Bas Vastert[3], Nico Wulffraat[3], Sylvia Kamphuis[4] and Michael W. Beresford[5,14]

TABLE 2 Definitions of severity of IgAV nephritis

Severity of IgAV nephritis	Definition
Mild	Normal GFR[a] and mild[b] or moderate[c] proteinuria
Moderate	<50% crescents on renal biopsy and impaired GFR[d] or severe persistent proteinuria[e] [44]
Severe	>50% crescents on renal biopsy and impaired GFR[e] or severe persistent proteinuria[e] [44]
Persistent proteinuria [43]	• UP:UC ratio >250 mg/mmol for 4 weeks[e] [44] • UP:UC ratio >100 mg/mmol for 3 months • UP:UC ratio >50 mg/mmol for 6 months

UP<250 mg/mmol

Practice Point 2.8.1.1. Indications for management of IgAVN in children have recently been published as the result of a European consortium initiative.[20] Briefly:

- **Children above 10 years of age more often present with non-nephrotic range proteinuria, impaired kidney function, and may suffer more chronic histological lesions with delay in biopsy and treatment longer than 30 days.[30]**

Delay in biopsy and treatment > 30 days is harmful

consulted.

KDIGO CLINICAL PRACTICE GUIDELINE
ON GLOMERULAR DISEASES

Practice Point 2.8.1.1. Indications for management of IgAVN in children have recently been published as the result of a European consortium initiative.[20] Briefly:

Expert opinion based indications

The lower threshold of proteinuria for treatment is not indicated

- **Oral prednisone/prednisolone or pulsed intravenous methylprednisolone should be used in children with mild or moderate IgAVN.**

Children with mild or moderate IgAVN CS oral or i.v.

Treatment options for IgAVN

Colchicine

Dapsone

Anti-leukotriene agents

Corticosteroids

Azathioprine

Mycophenolate mofetil

Cyclosporin A

Cyclophosphamide

Plasma exchange

Rituximab

Complement inhibitors

Thank you for your attention
Q&A

Next Webinars

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