SOUTHAMPTON Children's Hospital

Postinfectious Glomerulonephritis

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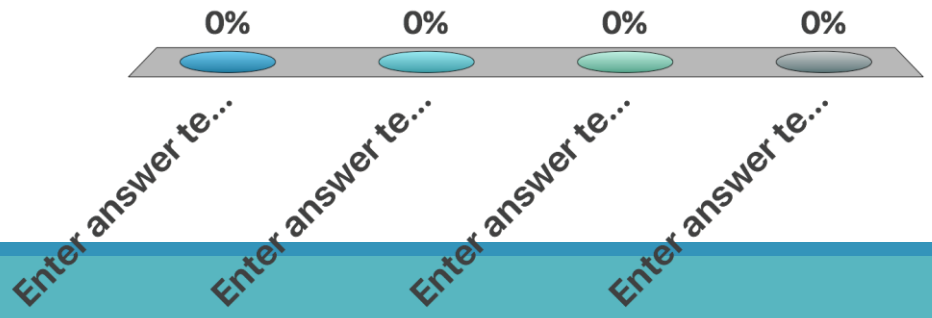
Post streptococcal glomerulonephritis mainly affects:

A. Adults > 60 years old
B. Children between 5 -12 years old
C. Children < 2 years old
D. Both A & B above



Introduction

“Immune mediated glomerular injury that occurs as a result of host response to an extra-renal infection”

Post streptococcal GN, one of the oldest renal diseases – “the dropsy that follows scarlet fever”

The risk of PSGN is increased in older patients (greater than 60 years of age) and in children between 5 and 12 years of age .

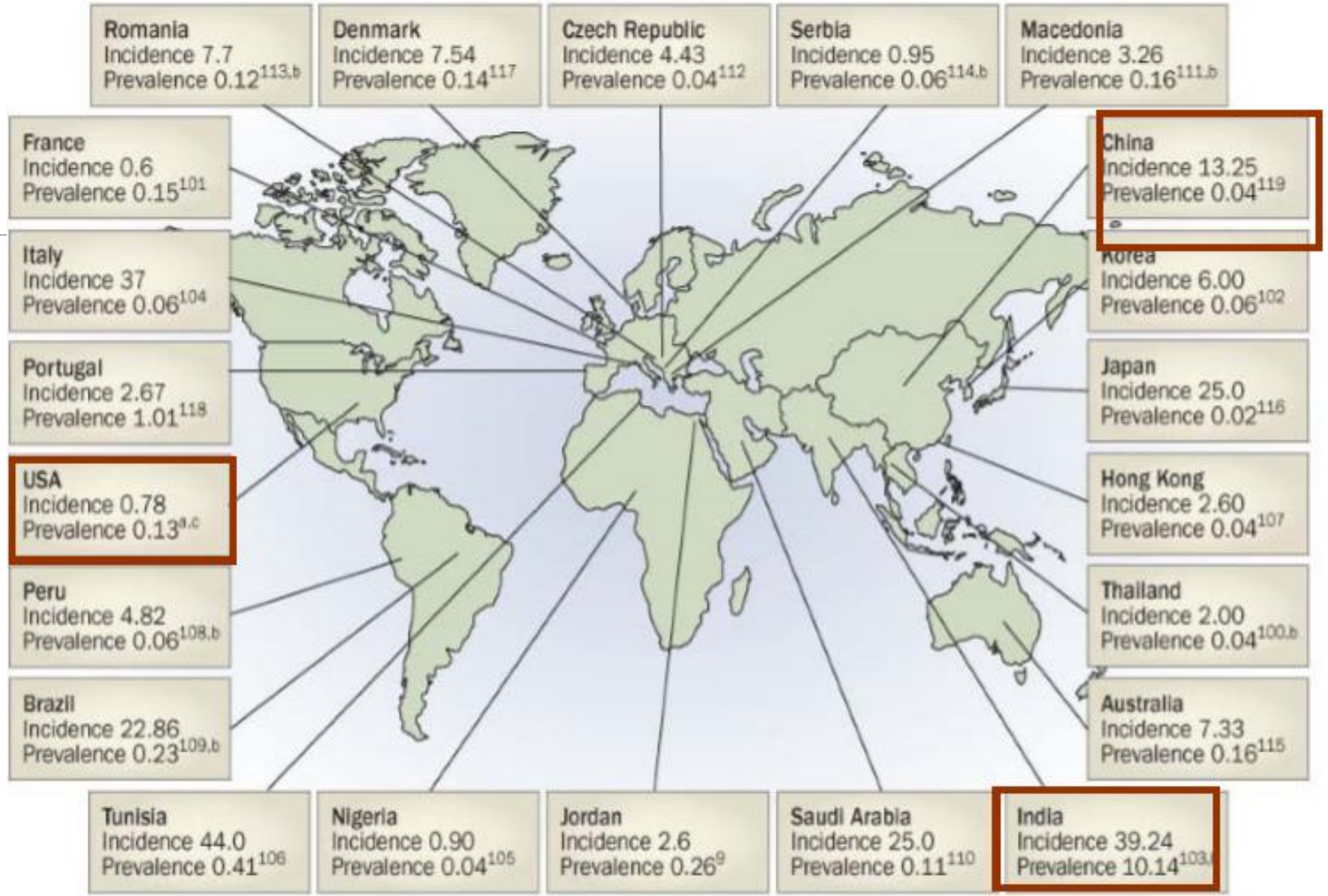
PSGN is uncommon in children less than three years of age.

PSGN is twice as frequent in males as in females .

The changing epidemiology

- Overall reducing incidence over the last 4 decades
- Estimated global incidence 472,000 cases per year

  16000 from developed countries
- Italian registry data – 0.3 cases per 100,000 patient years
- much higher in LMIC countries - >200 cases/mill pop /yr
- AKI related to PIGN 5-30%
- Much wider spectrum of infectious agents



Nature Rev Neph:2009

Changing Trends

Before	Current
Acute poststreptococcal glomerulonephritis (APSGN)	Post Infectious glomerulonephritis (PIGN)
Pathogeneic agents mainly group A streptococcus	Pathogeneic agent : includes staph and gram negative bacteria
Age group - pediatric	Age group – older
Prognosis- complete recovery >95% of patients	Prognosis- complete recovery in 50-60% of patients

Etiology

Bacterial	Viral	Fungal	Parasites
Streptococcus groups A, C, G Streptococcus viridans Staphylococcus (aureus, epidermidis) Pneumococcus Neisseria meningitidis Mycobacteria Salmonella typhi Klebsiella pneumoniae Escherchia coli Yersinia enterocolitica Legionella Brucella melitensis Treponema pallidum Corynebacterium bovis Actinobacilli Bartonella henselae Orientia tsutsugamushi (scrub typus)	Coxsackie virus Echovirus Cytomegalovirus Epstein–Barr virus Hepatitis B, C HIV Rubella Measles Varicella Vaccinia Parvovirus Influenza Adenovirus	Coccidioides immitis	Plasmodium malariae Plasmodium falciparum Schistosoma mansoni Schistosoma haematobium Toxoplasma gondii Filariasis Trichinosis Trypanosomes

PSGN >95%

Pathogenesis of PSGN

“Nephritogenic strains”

M Proteins

Nephritis associated plasmin receptor (NAPlr)

- 92% of patients in convalescence of PSGN
- Glomerular deposition of NAPlr

Streptococcal Pyrogenic exotoxin B (SPeB)

- America and Europe

Nephritogenic streptococcus GAPDH (NAPlr)

↓

Mesangial and GBM binding

↓

Plasmin entrapment and

sustained activity
Inflammatory reactivity

↓

Immune complex penetration through

Damaged GBM formation

↓

Nephritogenic streptococcus GAPDH (SpeB)

↓

Anti-SpeB antibodies

↓

SpeB and Anti-SpeB binding

↓

Circulating SpeB-antiSpeB deposition
In situ SpeB-anti-SpeB

↓

Immune Complex-Mediated Glomerulonephritis

PSGN and Complements

- Mannose binding lectin (MBL) recognises Strep cell wall polysaccharides
- Predominantly alternate pathway activation
- Initially some classical pathway activation – Low C1q, C4
- Crescentic GN association with normal complement levels

Clinical Features

Subclinical form – 4-5 times more common than GN

24% of streptococcal sore throat

1-2 weeks post throat infection, 3-4 weeks post pyoderma

Acute nephritic syndrome “classical presentation”

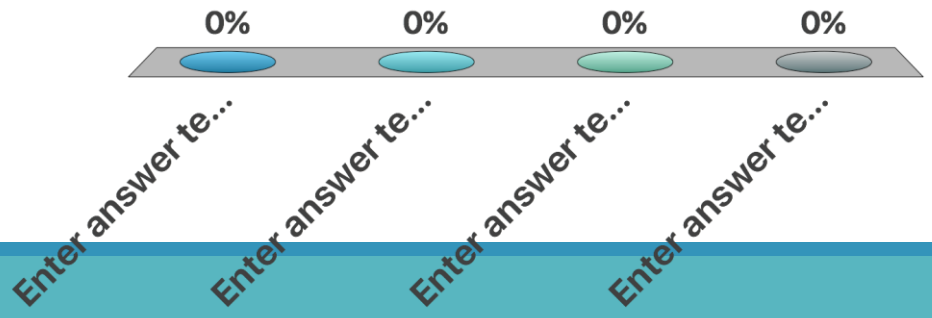
- macroscopic haematuria (30-40%)
- hypertension (60-80%)
- oedema (80%)
- oliguria (>50%)

Nephrotic syndrome – 2 to 4%

HSP like rash

ASO titres for the diagnosis of Post streptococcal glomerulonephritis

A. Highly sensitive
B. Highly specific
C. Both A & B
D. None of the above.



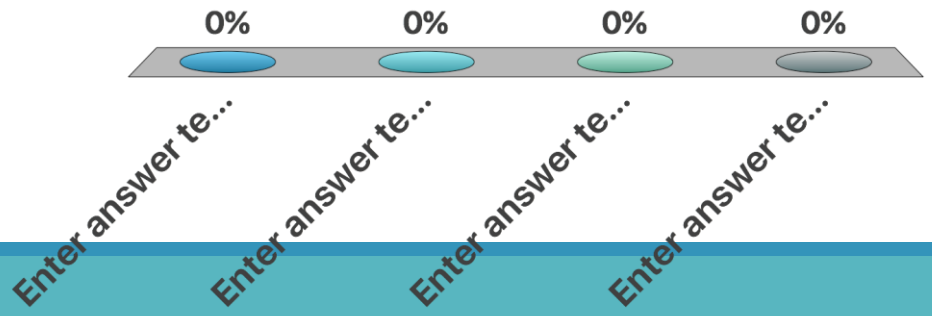
If complement levels are persistently low after an episode post streptococcal glomerulonephritis, the following conditions need to be considered EXCEPT

A. Lupus

B. Membranous nephropathy

C. Membranous glomerulonephritis

D. IgA nephropathy



ASOT

- Highly sensitive >97% but specificity 80%
- Titres higher in sore throat Vs pyoderma
- Peak at 3 weeks after presentation

Consider alternative diagnosis

- Normal complement level: rule out IgA nephropathy
- Low complement level after 1–2 months: consider SLE, MPGN
- Nephrotic-range proteinuria
- Rising proteinuria, RPGN
- Age <2 years
- Extra-renal manifestations

Pathology

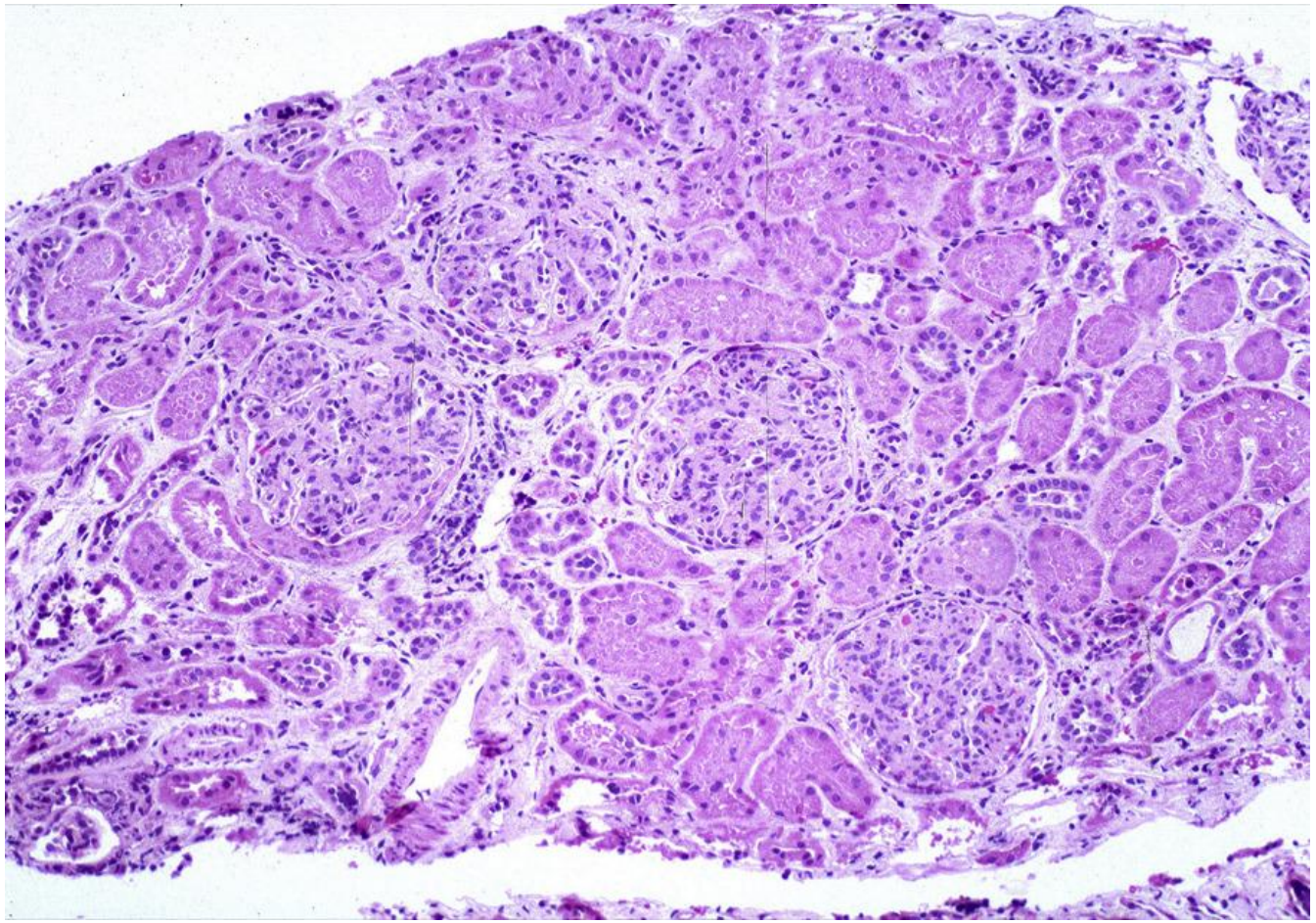
Indications for Biopsy

Early stage phase

- Rapid progressive course
- Hypertension >2 weeks
- Depressed GFR† >2 weeks
- Normal complement levels
- Non-significant titres of antistreptococcal antibodies
- Extra-renal manifestations
- Nephrotic syndrome

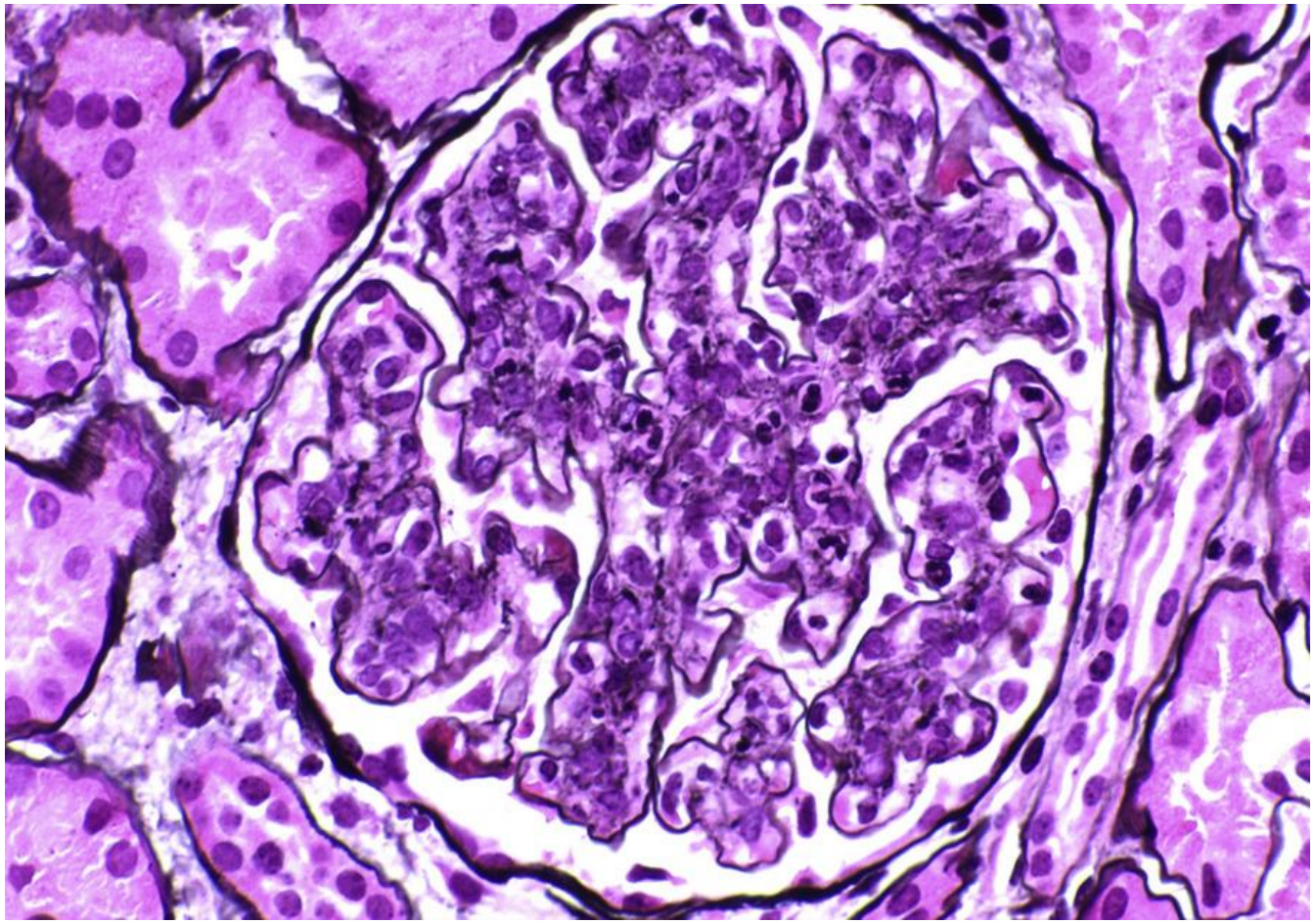
In recovery

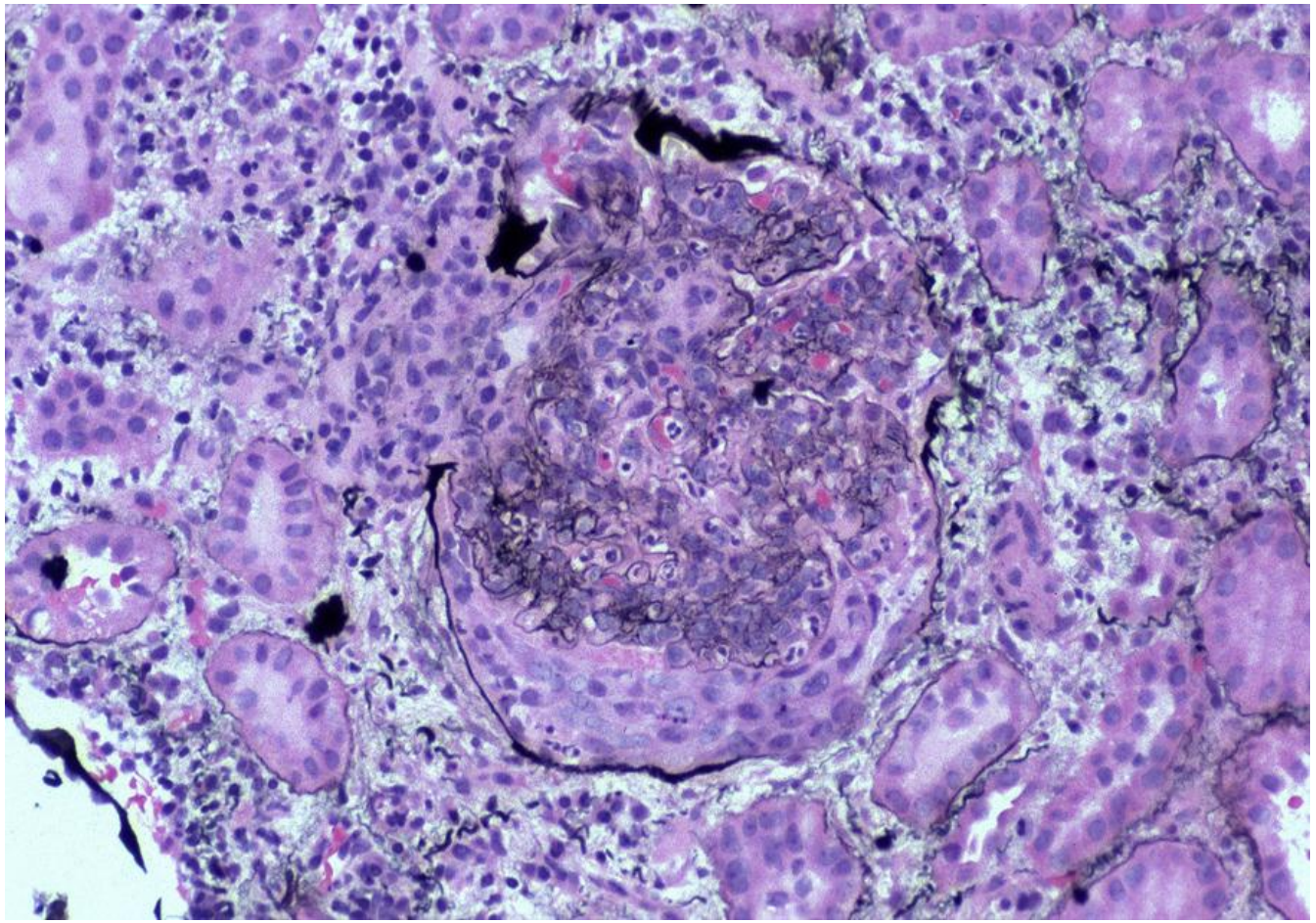
- Depressed GFR >4 weeks
- Hypocomplementaemia >12 weeks
- Persistent proteinuria >6 months
- Persistent microscopic haematuria >18 months

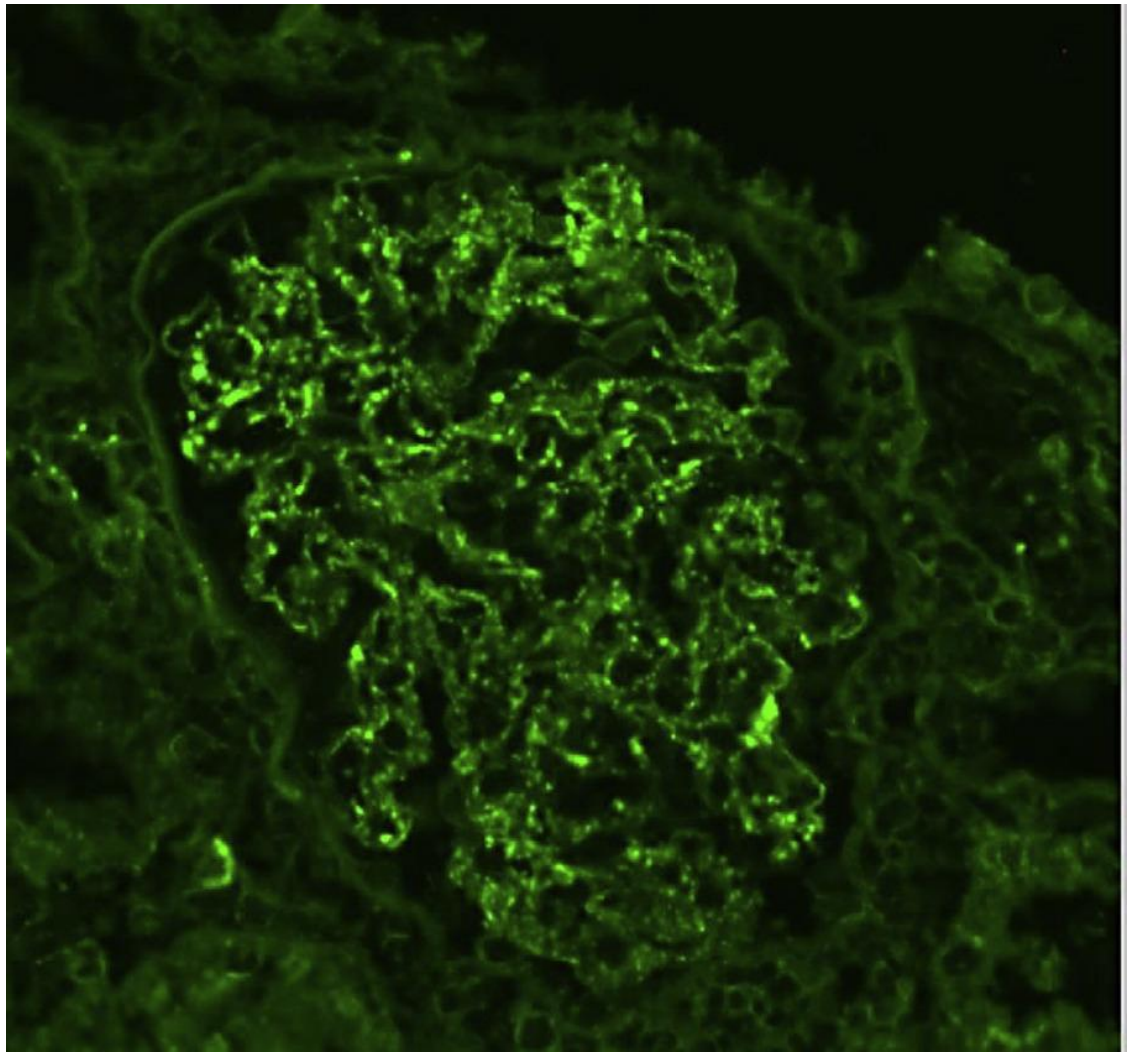


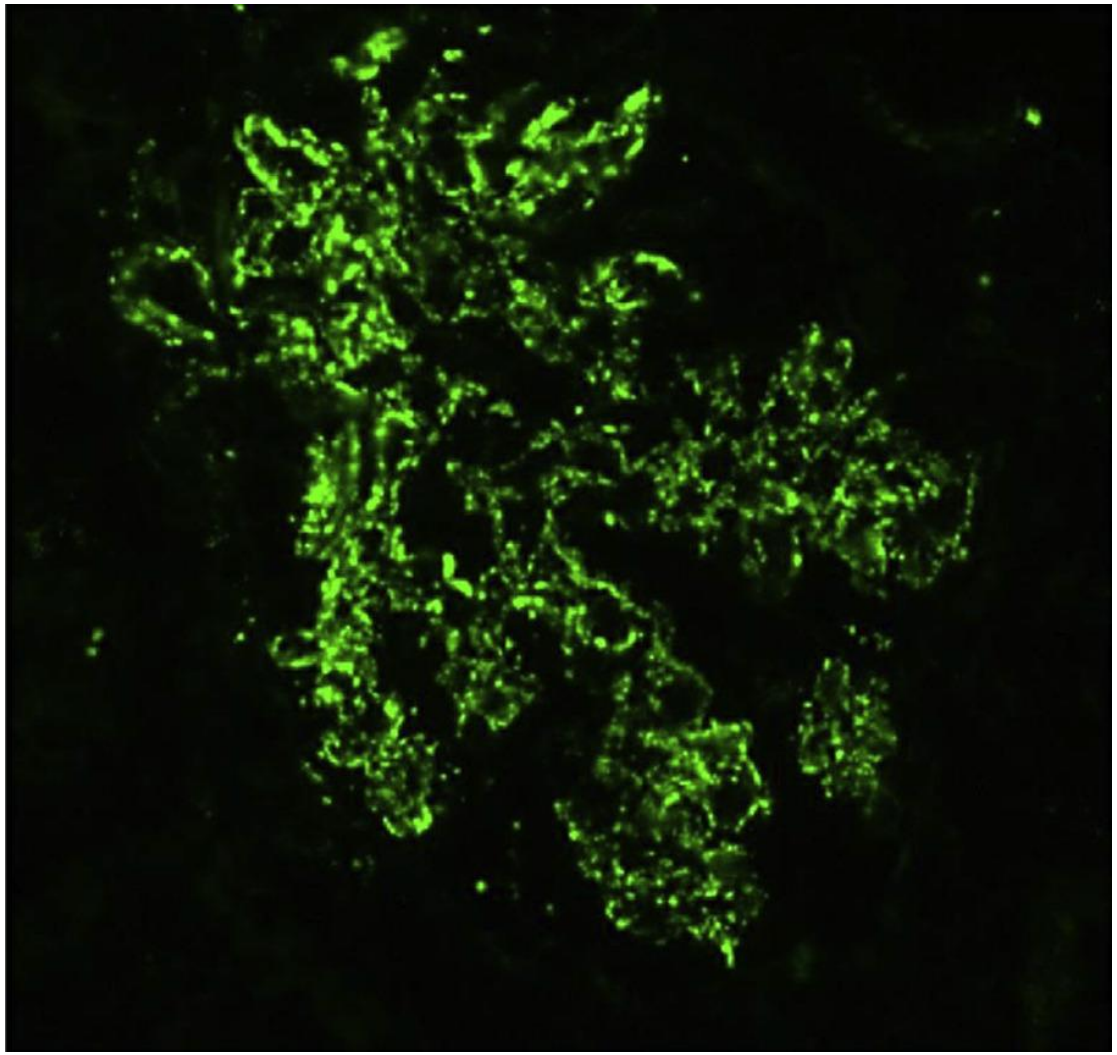
diffuse mesangial and endocapillary hypercellularity, and a large number of polymorphonuclear neutrophils (hematoxylin and eosin stain).

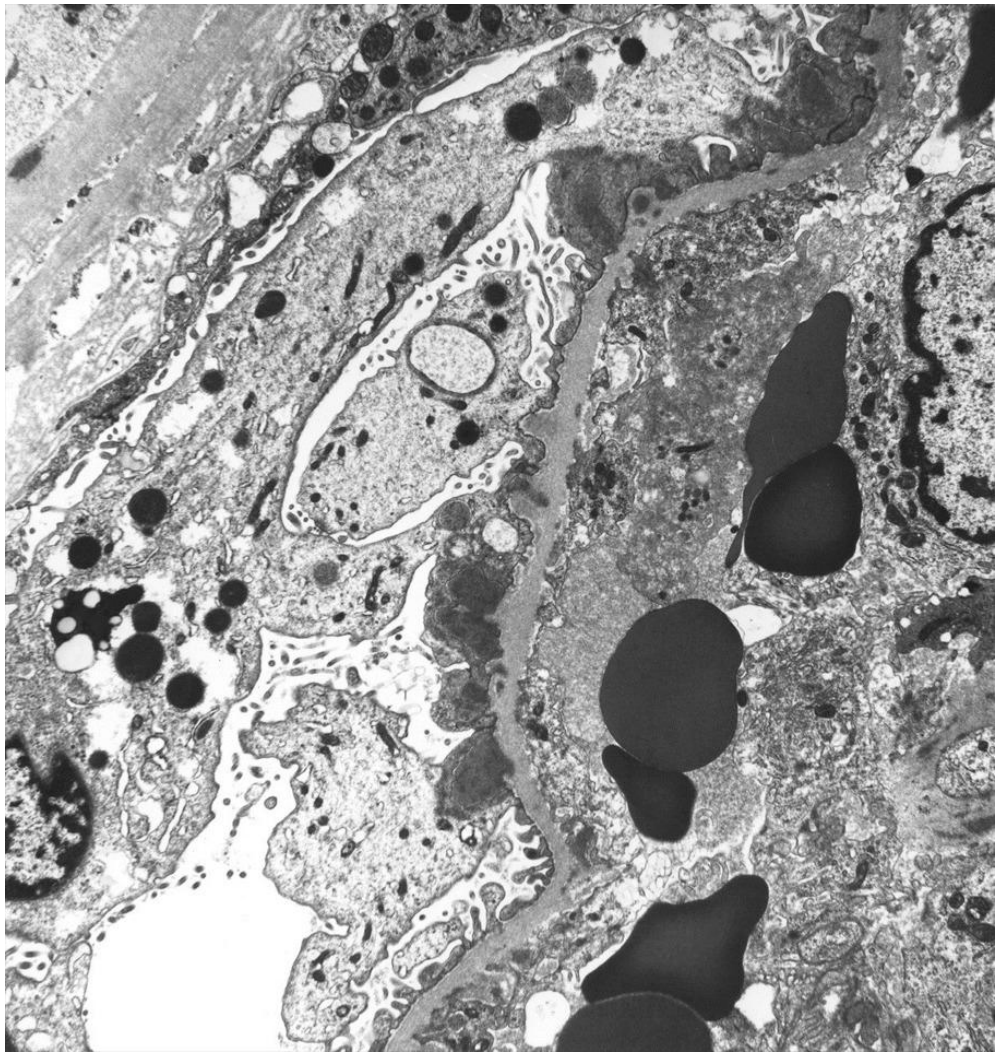
American Journal of Kidney Diseases 2015 66, e31-e32DOI: (10.1053/j.ajkd.2015.08.005)











Treatment

- Antibiotics for treatment
- Fluid and supportive management
- Antibiotics for prophylaxis of PSGN
- Antihypertensive agents
- Immunosuppressants

Antibiotics in PSGN

- Treatment to reduce antigen load – Penicillin / Erythromycin
- Antibiotics for prevention
- No global agreement on treatment on Group A streptococcal pharyngitis

Supportive care

- Fluids – aim for euvolemia
- Salt restriction
- Diuretics
- Antihypertensives

Immunosuppressants

- **Corticosteroids are suggested for severe crescentic GN based on anecdotal evidence only**

Crescentic glomerulonephritis with more than 30% of the glomeruli involved

short course of intravenous pulse steroid therapy is recommended (500 mg to 1 g/1.73 m^2 of methylprednisolone od for 3-5 d).

Special subtypes of PIGN

Endocarditis associated GN

-Previously seen with sub-acute infection with Strep viridans

-Now restricted to adult IV drug users

-Limited data in children

IgA dominant PIGN

-Variant of PIGN – staph

-Consider IgA and HSP

Shunt nephritis

-Associated with VA shunt

-Immunological reaction with activation of classical com pathway

Prognosis

- No hypertension or renal impairment. Proteinuria 3.1% Microhaematuria 6.3%

Sepahi MA, Shajari A, Shakiba M, et al. Acute glomerulonephritis: a 7 years follow up of children in center of Iran. Acta Med Iran. 2011;49:375–378

- Hypertension twice more prevalent than in controls. No significant difference in renal function, haematuria or proteinuria.

Pinto SW, Mastroianni-Kirsztajn G, Sesso R. Ten-year follow-up of patients with epidemic post infectious glomerulonephritis. PLoS ONE. 2015;10:e0125313.

- Children in LMIC – much worse prognosis
- Long term outcome studies scarce
- Excellent long term prognosis

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Summary

- PIGN still a major cause of acute GN
- Infection associated GN a better term ?
- Changing epidemiology
- Multiple streptococcal antigens identified and immune complex deposition most accepted mechanism
- Evidence base for treatment poor
- Excellent long term outcome

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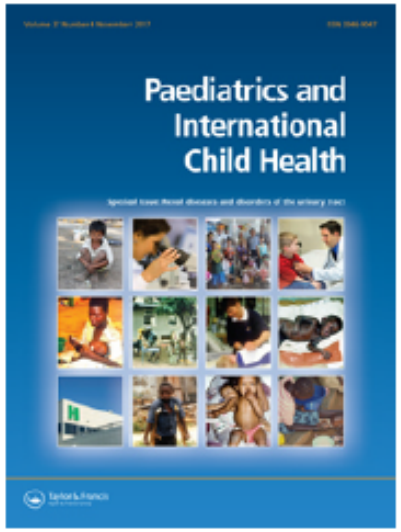

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Paediatrics and International Child Health

ISSN: 2046-9047 (Print) 2046-9055 (Online) Journal homepage: http://www.tandfonline.com/loi/ypch20

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To cite this article: Ramnath Balasubramanian & Stephen D. Marks (2017) Post-infectious glomerulonephritis, Paediatrics and International Child Health, 37:4, 240-247, DOI: 10.1080/20469047.2017.1369642

To link to this article: https://doi.org/10.1080/20469047.2017.1369642