



APSGN

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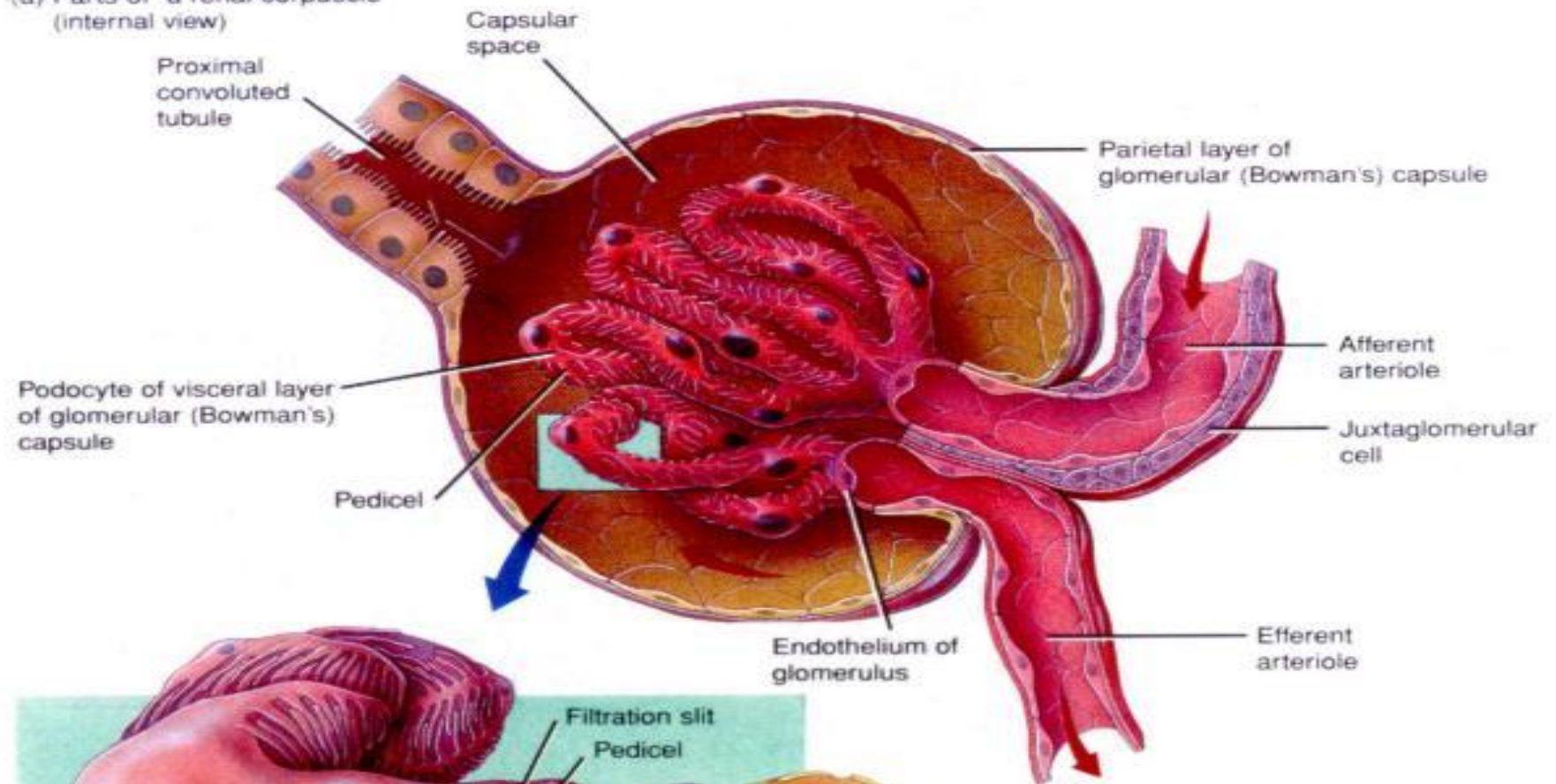
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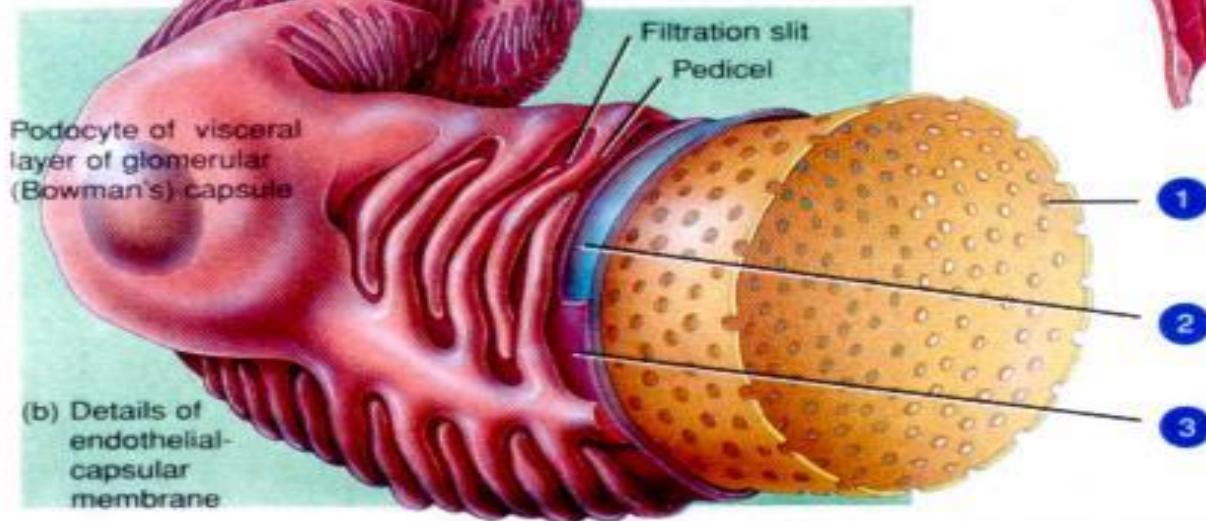
Over view of the PIAGN

(a) Parts of a renal corpuscle
(internal view)



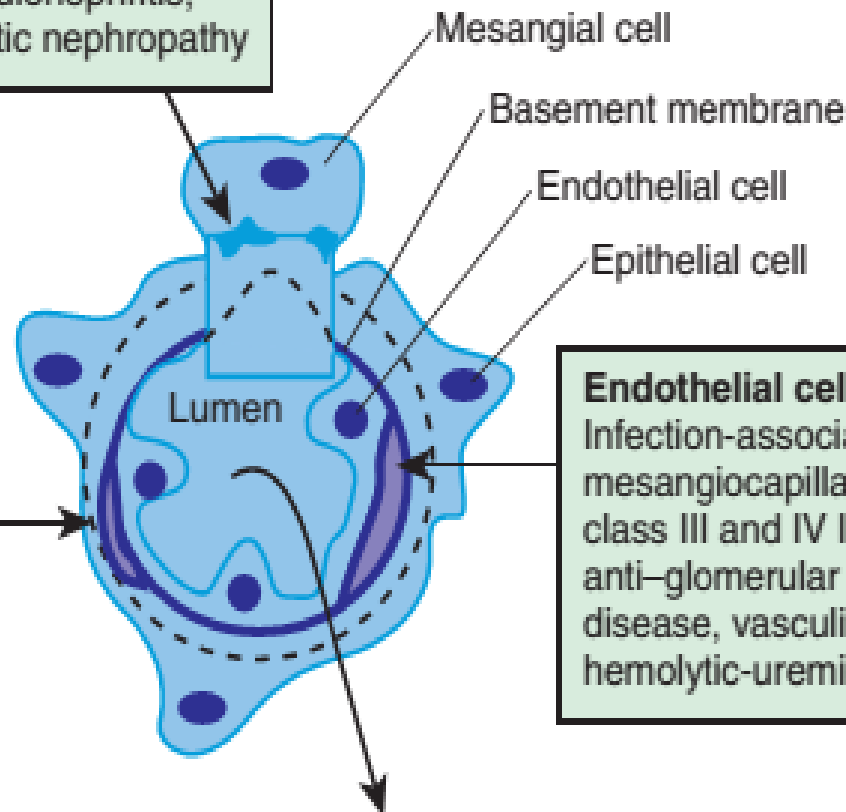
Podocyte of visceral
layer of glomerular
(Bowman's) capsule

(b) Details of
endothelial-
capsular
membrane



Mesangial cell disease

IgA nephropathy, IgM nephropathy, mesangioproliferative glomerulonephritis, class II lupus nephritis, diabetic nephropathy



Epithelial cell injury

Membranous nephropathy, minimal change disease, focal and segmental glomerulosclerosis, class V lupus nephritis, diabetic nephropathy

Endothelial cell injury

Infection-associated glomerulonephritis, mesangiocapillary glomerulonephritis, class III and IV lupus nephritis, anti-glomerular basement membrane disease, vasculitis and cryoglobulinemia, hemolytic-uremic syndrome

In health, solutes are filtered into the urinary space. The presence of abnormal amounts of protein or cells suggests glomerular pathology.

A nephritic or rapidly progressive presentation ensues. (From Chadban SJ, Atkins RC: Glomerulonephritis, Lancet 365:1797–1806, 2005)

Infections That Affect the Kidney (Nonviral)

Bacterial Infections
Tropical Infections
Infection-Related Glomerulonephritis
Parasitic Infections
Malaria
Filaria
Schistosomiasis
Leishmaniasis
Trypanosomiasis
Trichenella
Echinococcosis (Hydatid Disease)
Fungal Infections
Others
Serious Forms of Urinary Tract Infection .

Infection-Related Glomerulonephritis:
IRGN is a term used to describe GN is associated with ongoing infection (syn-infectious) or that which occurs with a latent period following an infection (post-infectious).

❑ **Abstract:**

The pathogenesis of infection-related renal complications includes:

- ✓ *direct invasion of renal parenchyma.*
 - ✓ *stimulation of an immune reaction.*
 - ✓ *injury to the capillary endothelium.*
 - ✓ *induction of a humoral response.*
 - ✓ *nephrotoxicity associated with the therapy of choice.*
-
- *Studies other non-streptococcal bacterial, fungal, and parasitic infections, some of which occur predominantly in tropical and subtropical regions, but which have been increasingly diagnosed in other regions of the globe on account of travel mobility.*

Non-streptococcal bacterial infection associated glomerulonephritis

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graph TD; A[Non-streptococcal bacterial infection associated glomerulonephritis] --> B[Staphylococcus infection related GN [extravascular]]; A --> C[Staphylococcal or other bacterial infection related GN [intravascular]]; B --> D[• Visceral infection]; B --> E[• Skin infection]; B --> F[• Joint infection]; B --> G[• Osteomyelitis]; B --> H[• Pneumonia]; C --> I[• Bacterial endocarditis]; C --> J[• Shunt nephritis]; C --> K[• Central venous catheter];
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Staphylococcus infection related GN [extravascular]

- Visceral infection
- Skin infection
- Joint infection
- Osteomyelitis
- Pneumonia

Staphylococcal or other bacterial infection related GN [intravascular]

- Bacterial endocarditis
- Shunt nephritis
- Central venous catheter

Viruses

Viral Infections and Kidney Diseases

Specific Viral Kidney Diseases

Parvovirus B19 (PVB19)

Herpes Viruses

Cytomegalovirus (CMV)

Adenovirus

BK-Virus (BKV)

Coronavirus

COVID-19

Hepatitis B Virus (HBV)

Hepatitis C Virus (HCV)

Viral Hemorrhagic Fevers

Dengue Virus

Yellow Fever

Ebola Virus

Hantavirus

Viral Infections and the Kidney (VI)

❑ Abstract:

- ✓ *Productive viral replication in the kidney of immuno - compromised hosts are of particular concern for children.*
- ✓ *VI in kidney transplant recipients, HBV, HCV, HIV-1, hantaviruses, and the new coronavirus SARS-CoV-2.*
- ✓ *In children with immunodeficiency states, (herpes viruses, polyomavirus, adenovirus).*
- ✓ *With increasing application of molecular techniques, the understanding of the role of viruses in the pathogenesis of kidney diseases is expected to increase.*
- ✓ *Specific antiviral treatments and vaccines are currently under development and are expected to improve the outcome of viral-mediated kidney diseases in children.*

□ **APSGN:**

➤ **OVERVIEW**

- ✓ *Is the prototype for a postinfectious immune complex mediated GN.*
- ✓ *2-6 weeks after a skin (summer and autumn), 7-10days after URTi (winter and spring).*
- ✓ *Epidemic and sporadic infections have been reported.*
- ✓ *Highest in economically disadvantaged geographic areas.*
- ✓ *Cell surface M virulence proteins and nephritogenic antigens, with activation of the complement pathway playing a key role.*
- ✓ *From asymptomatic microhematuria to a RPGN.*
- ✓ *Peak in school-aged children, (boys as twice affected).*
- ✓ *Gross hematuria and HTN, then oliguria or azotemia (Nephritic syndrome).*

❑ **APSGN:**

➤ **OVERVIEW**

- ✓ *Nephrotic syndrome is less common.*
- ✓ *Depression of C3 complement, positive ASO and anti-DNAse B titers.*
- ✓ *The prevalence varies by geographic, socioeconomic, host, bacterial factors.*
- ✓ *APSGN has decreased in more economically advantaged countries.*

❑ *Epidemiology:*

- ✓ *APSGN may occur as epidemics or in isolated.*
- ✓ *APSGN has been declining, (appropriate medical care).*
- ✓ *In developed countries, the severity of APSGN decreasing.*
- ✓ *Over 470,000 cases of APSGN occur annually, (97% in less developed countries).*

□ *Epidemiology:*

- *APSGN caused by a nephritogenic Ag (group A streptococci Beta hemolytic).*
- *M types 1, 2, 4, 12 associated with epidemic nephritis (URTi).*
- *M types 47, 49, 55 associated with epidemic nephritis (pyoderma).*
- *Nephritis by non-group A streptococcus (group C).*
- *Focus on two streptococcal antigenic fractions as to their nephritogenicity:*
 - ✓ *1- nephritis associated plasmin receptor (NAPlr).*
 - ✓ *2- streptococcal pyrogenic exotoxin (erythrotoxin) B (SPEB) and its zymogen precursor (zSPEB).*

Schematic representation of proposed mechanisms involved in the development of APSGN.

MES: mesangial cell;

END: endothelial cell;

PMN: polymorphonuclear cell;

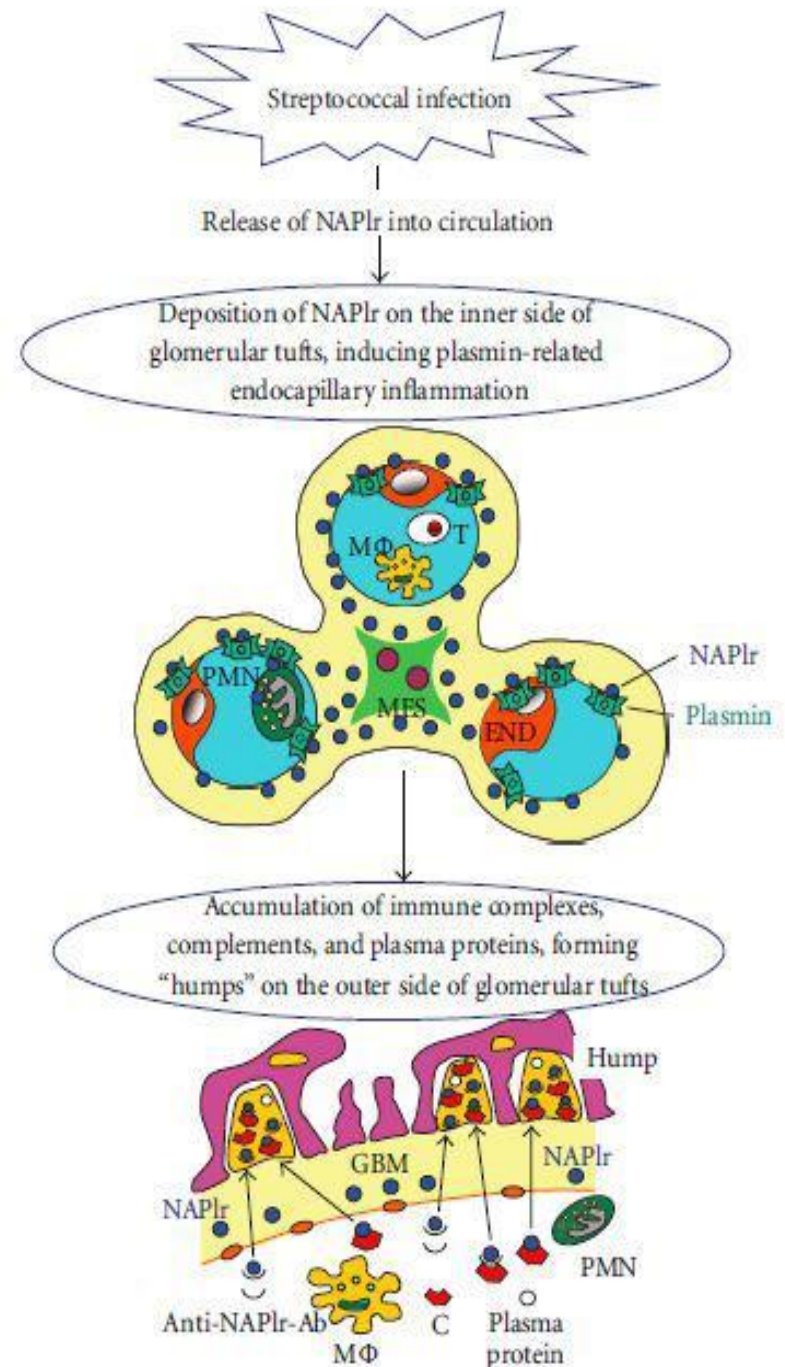
MΦ: macrophage;

T: T lymphocyte;

GMB: glomerular basement membrane;

C: complement; Anti-NAPlr - Ab: Anti-NAPlr-antibody.

Courtesy of open access article, "The Role of Nephritis-Associated Plasmin Receptor (NAPlr) in GN Associated with Streptococcal Infection." Oda T, Yoshizawa N, Yamakami K, et al. Journal of Biomedicine and Biotechnology, 2012; doi: 10.1155/417675



□ *Pathogenesis:*

Table 1 Pathogenetic mechanisms participating in acute post-streptococcal glomerulonephritis

Mechanism	Evidence
Nephritogenic antigens (NAPlr, SPEB, streptokinase, others)	NAPlr and SEPb demonstrated in renal biopsies
Circulating immune complexes	Circulating anti-SPEB and anti-NAPlr antibodies in APSGN patients
In situ Immune complexes (cationic antigens)	SPEB co-localized with complement in glomeruli and demonstrated in the subepithelial electron-dense deposits (“humps”) in APSGN
Autoimmunity (anti-IgG, other) •	Neuraminidase is produced by some nephritogenic streptococci. Serum neuraminidase activity in APSGN patients
Anti-Ig (induced by the loss of sialic acid of the IgG or binding of the Fc fragment of IgG to type II receptors on the surface of group A streptococcus)	Serum anti-IgG titers; Renal anti-IgG deposits
Other autoimmune reactivity	Anti-DNA, anti.C1q, ANCA and anti-cardiolipin antibody demonstrated in serum
Other	
Increased plasmin activity in glomeruli (facilitating immune complex deposition)	Co-localization of plasmin and NAPlr in glomeruli. Increased urinary plasmin activity
Neuraminidase-induced glomerular infiltration of desialised leukocytes	Desialised leukocytes accumulate in the glomeruli of patients with APSGN

❑ *Pathogenesis:*

- ✓ *Role as a nephritogen is related to their plasmin-binding capacity which facilitates immune complex deposition and inflammation (NAP1r, SPEB, streptokinase, enolase).*
- ✓ *APSGN cases exhibit an increase in urinary plasmin-like activity.*
- ✓ *SPEB is the only streptococcal antigen that has been demonstrated within the electron dense subepithelial deposits (humps) that are the hallmark of APSGN.*

❑ *Pathogenesis cont...*

- ✓ *SPEB/ zSPEB induces chemotaxis (increases angiotensin II production by mesangial cells).*
- ✓ *Fc portion of antibodies directed to SPEB binds to the C-terminal domain.*
- ✓ *The attractiveness of a charge-related GBM injury is by histones that are cationic elements as part of the pathogenesis of APSGN.*
- ✓ *Histones Enter the circulation after streptococcal lysis and capable of inducing in situ immune-complex formation.*

❑ *Humoral immune mechanisms:*

- ✓ *Activation of the complement system is a consequence of the glomerular antigen/antibody reactivity.*
- ✓ *The alternative complement pathway is usually most active in APSGN, with depression of C3.*
- ✓ *Protein H (surface streptococcal protein), in combination with IgG may activate the classical complement cascade, some time by the lectin pathway, and in individuals who are genetically unable to activate this pathway.*

❑ *Cellular immune mechanisms:*

- ✓ *Cellular adhesion molecule (ICAM-1, LFA-1) overexpression with infiltration of lymphocyte and macrophages in the glomeruli of these patients.*
- ✓ *Higher numbers of CD4-positive lymphocytes are present in renal biopsies (first 3–4 weeks of disease and decrease in frequency afterwards).*
- ✓ *Increased glomerular expression of IL-8 has been found to correlate with neutrophil infiltration and transforming growth factor- β expression with mesangial expansion.*

❑ *Autoimmune Reactivity:*

- ✓ *Most notably anti-IgG reactivity.*
- ✓ *In the first week of disease, rheumatoid factor cryoglobulins (in about two-thirds of patients).*
- ✓ *Furthermore, anti-IgG glomerular deposits are frequently found on biopsies.*
- ✓ *The anti-IgG reactivity may be the result of autoantigenic modification mediated by Ig desialization caused by streptococcal neuraminidase.*

❑ *Autoimmune Reactivity cont...*

- ✓ *Another potential cause of anti- Ig reactivity is the binding of IgG to type II receptors in the streptococcal wall.*
- ✓ *Anti-DNA and antiC1q antibodies along with anti-neutrophil cytoplasmic antibodies (ANCA).*
- ✓
- ✓ *ANCA has been found in up to 70% of ASPGN patients with azotemia or crescentic GN.*
- ✓ *An autoimmune hemolytic anemia secondary to anticardiolipin antibody has also been reported.*

❑ *Genetic Aspects:*

- ✓ *Higher rate of disease in siblings (more than general population) during epidemics.*
- ✓
- ✓ *APSGN has also been associated with HLA-DR4 and DR-1.*
- ✓ *Genetic mutations in the complement factor H (CFH) gene have been suggested as a cause for inducing dense deposit disease, as well as a chronic glomerulonephritis triggered initially by streptococcal infection.*

Table 2 Differences between PSGN and SAGN. (Adapted from reference [77])

Parameters	PSGN	SAGN
Age	Mainly children	Mainly adults, occasionally children
Infection source	Pharyngitis, pyoderma, otitis media, tonsillitis, infected scabies	Endocarditis, skin abscess, leg ulcers, osteomyelitis, septic arthritis, pneumonia
Infection free latent period	Present	Not present
Clinical features	Hematuria, hypertension, oliguria, mild proteinuria, occasionally renal dysfunction	AKI, microscopic hematuria, nephrotic range proteinuria, occasionally leukocytoclastic vasculitis rash
Laboratory features	Low C3, normal C4	Low C3 in 30–50%, normal C4
Renal histopathology	LM: Diffuse exudative proliferative GN	LM: Mesangial hypercellularity, endocapillary proliferation in some, segmental necrotizing lesions common, acute tubular necrosis frequent
	IF:C3 with or without IgG along capillary loops and mesangium EM: Predominantly subepithelial deposits	IF: IgA dominant or codominant with C3 or exclusive C3, pauci-immune in a few. EM: Predominantly mesangial deposits
Outcomes	Usually complete recovery	Unpredictable