



Andrea Mantegna, c. 1459  
Oil on panel Kunsthistorisches  
Museum, Vienna



## Insufficienza renale acuta

Brusca (entro 48 h) riduzione della funzione renale con oliguria (< 35 ml/h per > 6 h) ed aumento di azotemia (> 50 mg/dl) e creatininemia (> 0.3 mg/dl o del 50%) plasmatiche

1. Prerenale
2. Intrinseca
3. Ostruttiva

### 1. Prerenale

- Ipovolemia
- Shock
- Vascolare renale
  - stenosi arteria renale
  - ipertensione maligna

### 2. Intrinseca

- **Necrosi tubulare acuta:**
  - sepsi, mezzo di contrasto, farmaci, tossine
- Glomerulonefrite acuta
- (Pielo)nefrite interstiziale acuta
- Nefropatia vascolare

### 3. Ostruttiva

- calcolosi renale
- neoplasie
- ipertrofia/CR prostatico

- **Farmaci**
  - Antimicrobici (aminoglicosidi, cefalosporine, vancomicina, sulfamidici, amfotericina, aciclovir, foscarnet)
  - Anestetici fluorurati
  - Antiulcerosi
  - Chemioterapici (cis-platino, metotrexate, streptozocina)
  - Immunosoppressori (Ciclosporina A, Tacrolimus)
- **Solventi organici**
  - Glicole etilenico
  - Tetracloruro di carbonio
- **Metalli pesanti**
  - Piombo, cadmio, uranio, mercurio, arsenico, bismuto

- **Tossici endogeni**
  - Mioglobina
  - Emoglobina (emolisi intravascolare massiva)
  - Acido urico (gravi iperuricemie)
  - Calcio (ipercalcemie)
  - Ossalato di calcio
  - Catene leggere

### 1. Prerenale

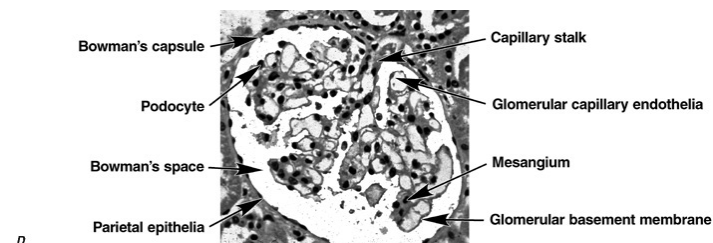
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**Glomerular architecture.** **A.** The glomerular capillaries form from a branching network of renal arteries, arterioles, leading to an afferent arteriole, glomerular capillary bed (tuft), and a draining efferent arteriole (modified from Hypertension 5:8–16, 1983). **B.** Scanning electron micrograph of podocytes that line the outer surface of the glomerular capillaries (arrow shows foot process). **C.** Scanning electron micrograph of the fenestrated endothelia lining the glomerular capillary. **D.** The various normal regions of the glomerulus on light microscopy (A–C, courtesy of Dr. Vincent Gattone, Indiana University; with permission).

## Post-Streptococcal Glomerulonephritis

Bernardo Rodriguez-Iturbe, MD<sup>1</sup> and Mark Haas, MD, PhD<sup>2</sup>

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Acute glomerulonephritis that results from streptococcal infections is the best-studied immune complex-mediated glomerulonephritis. Initially described in the convalescence of scarlet fever, the incidence of acute post streptococcal glomerulonephritis (APSGN) has decreased worldwide, particularly in developed countries where it is now rare and is limited to adult patients who have debilitating conditions. In developing countries, the annual burden of APSGN remains at a level of least 9 cases per 100,000 inhabitants. Two antigenic fractions of the streptococcus (streptococcal GAPDH/nephritis-associated plasmin receptor, and streptococcal pyrogenic exotoxin B and its zymogen precursor) are currently under scrutiny as putative nephritogens. Glomerulonephritis results from the glomerular deposition of circulating immune complexes and by the *in situ* formation of immune complexes. In-situ formation of immune complexes is a characteristic associated with cationic antigens that have a charge-facilitated penetration through the polyanionic glomerular basement membrane. The plasmin-binding capacity of streptococcal antigens favors immune complex deposition and inflammation. The typical pathological changes are endocapillary proliferation with varying degrees of leukocyte infiltration, and C3, IgG, and IgM immune deposits. Electron microscopy shows the hallmark lesion of subepithelial electron dense deposits ("humps"). The immediate prognosis is excellent in children, but adults have a significant early mortality, which partially results from cardiovascular disease. The long-term development of end-stage renal disease is exceptional in children. However, studies in aboriginal communities indicate that patients

Rodriguez-Iturbe B, Haas M. Post-Streptococcal Glomerulonephritis. 2016 Feb 10. In: Ferretti JJ, Stevens DL, Fischetti VA, editors. *Streptococcus pyogenes: Basic Biology to Clinical Manifestations* [Internet]. Oklahoma City (OK): University of Oklahoma Health Sciences Center; 2016-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK333429/>

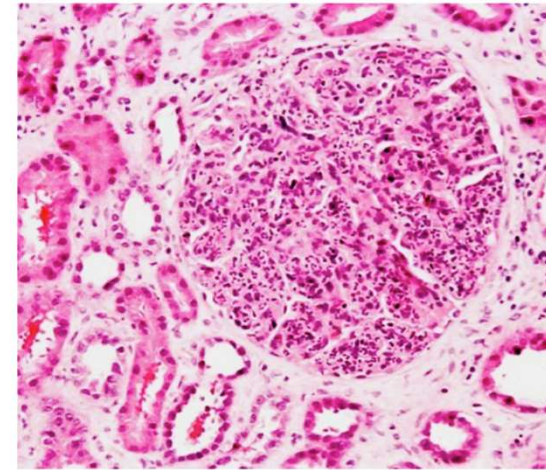


Figure 1. Acute post-streptococcal glomerulonephritis (GN) with severe proliferative and exudative GN. The glomerulus is enlarged and markedly hypercellular with a large number of neutrophils. Note the red blood cells in some tubular lumens. Hematoxylin and eosin (H & E) stain, original magnification x200.

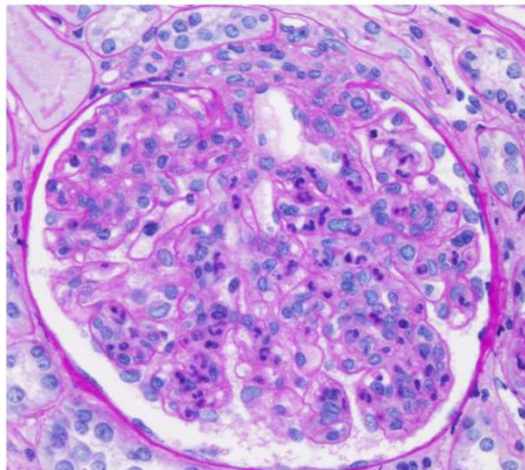
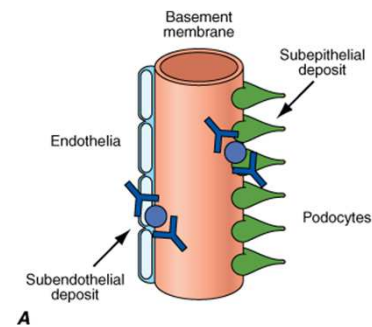


Figure 2. Acute post-streptococcal GN with proliferative and exudative GN. The glomerulus shows endocapillary hypercellularity with multiple neutrophils, although far fewer than the glomerulus in Figure 1. Periodic acid-Schiff (PAS) stain, original magnification x400.



**The glomerulus is injured by a variety of mechanisms. A.** Preformed immune deposits can precipitate from the circulation and collect along the glomerular basement membrane (GBM) in the subendothelial space or can form *in situ* along the subepithelial space.

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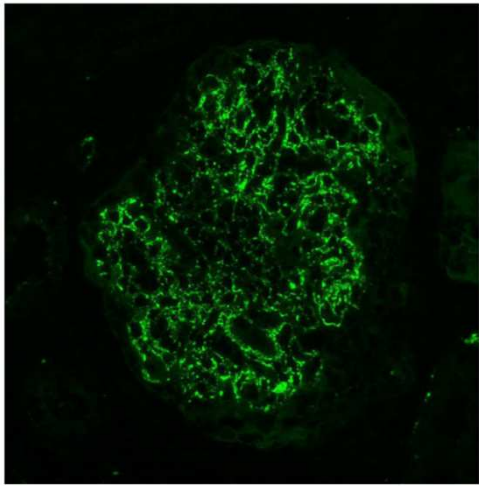
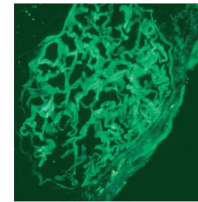
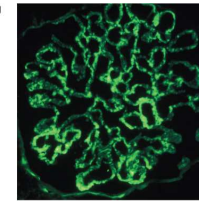


Figure 3. Immunofluorescence staining for C3 in acute post-streptococcal GN. There is granular staining in the glomerular capillary walls and mesangium, in a "starry-sky" pattern. Fluorescein isothiocyanate (FITC) conjugated anti-human C3, original magnification x400.



Linear IgG staining

B



IgG Lumpy-bumpy staining

C

**The glomerulus is injured by a variety of mechanisms. B.**

Immunofluorescent staining of glomeruli with labeled anti-IgG demonstrating linear staining from a patient with anti-GBM disease or immune deposits from a patient with membranous glomerulonephritis. **C.** The mechanisms of glomerular injury have a complicated pathogenesis. Immune deposits and complement deposition classically draw macrophages and neutrophils into the glomerulus. T lymphocytes may follow to participate in the injury pattern as well.

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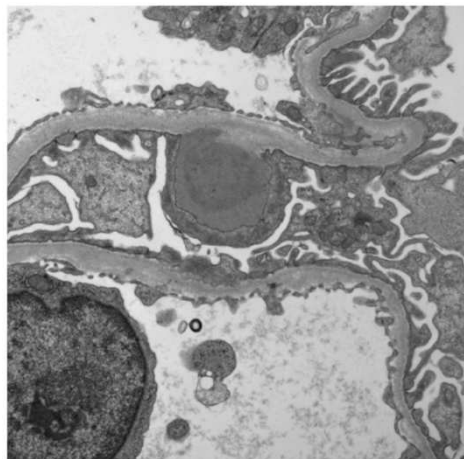


Figure 4. Electron-microscopy in acute post-streptococcal GN. Note the large, "hump"-like subepithelial deposit. The periphery of this deposit is slightly less electron-dense than its center, indicating very early resorption. The glomerular capillary with the subepithelial "hump" also contains a small sub-endothelial deposit. The glomerular basement membranes themselves are unremarkable and the podocyte foot processes are partially effaced. Uranyl acetate and lead citrate stain, original magnification x7500.

**Table 1.** Pathogenetic mechanisms participating in acute poststreptococcal glomerulonephritis APSGN

Mechanism	Evidence	Reference
<b>Nephritogenic antigens</b> (NAPlr, SPEB, streptokinase, others)	NAPlr and SEPB demonstrated in renal biopsies	(Oda, et al., 2010; Poon-King, Bannan, Viteri, Cu, & Zabriskie, 1993; Nordstrand, McShan, Ferretti, Holm, & Norgren, 2000)
Circulating immune complexes	Circulating anti-SPEB and anti-NAPlr antibodies in APSGN patients	(Yoshizawa, et al., 2004; Parra, et al., 1998)
<i>In situ</i> Immune complexes (cationic antigens)	SPEB co-localized with complement in glomeruli and demonstrated in the subepithelial electron-dense deposits ("humps") in APSGN	(Batsford, Mezzano, Mihatsch, Schlitz, & Rodriguez-Iturbe, 2005)
<b>Autoimmunity</b> (anti-IgG, other)	Neuraminidase is produced by some nephritogenic streptococci. Serum neuraminidase activity in APSGN patients	(Mosquera & Rodriguez-Iturbe, 1984; Rodriguez-Iturbe, Katiyar, & Coello, 1981; Asami, Tanaka, Gunji, & Sakai, 1985)

(NAPlr) nephritis associated plasmin receptor

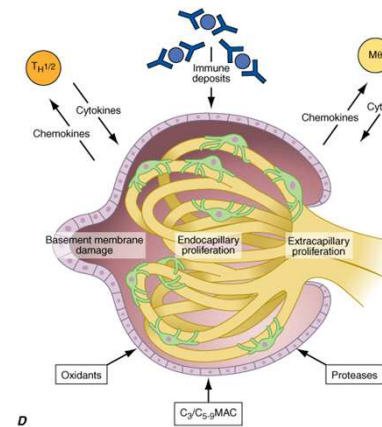
(SPEB) streptococcal pyrogenic exotoxin (erythrotoxin) B



Table 1. Pathogenetic mechanisms participating in acute poststreptococcal glomerulonephritis

Mechanism	Evidence	Reference
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	(Rodriguez-Iturbe B. , 1984; Parra, et al., 1998; Rodriguez-Iturbe, Rabideau, Garcia, & McIntosh, 1980; Burova, et al., 2012)
Other autoimmune reactivity	Anti-DNA, anti.C1q, ANCA demonstrated in serum	(Kozyro, et al., 2006; Ardiles, Valderrama, Moya, & Mezzano, 1997)
<b>Other</b>		
Increased plasmin activity in glomeruli (facilitating immune complex deposition)	Co-localization of plasmin and NAP1r in glomeruli. Increased urinary plasmin activity	(Yoshizawa, et al., 2004; Oda, et al., 2010; Oda, et al., 2008)
Neuraminidase-induced glomerular infiltration of desialised leukocytes	Desialised leukocytes accumulate in the glomeruli of patients with APSGN	(Mosquera & Rodriguez-Iturbe, 1986; Marin, Mosquera, & Rodriguez-Iturbe, 1995)

ANCA antineutrophil-cytoplasmic autoantibodies



The glomerulus is injured by a variety of mechanisms. D. Amplification mediators as locally derived oxidants and proteases expand this inflammation, and, depending on the location of the target antigen and the genetic polymorphisms of the host, basement membranes are damaged with either endocapillary or extracapillary proliferation.

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	Systemic events	Renal events	
Initiation GFR falling	prolonged prerenal state hemorrhage sepsis vascular disruption (e.g.: trauma, coronary artery bypass grafting, aortic crossclamp) certain nephrotoxins, e.g. radiocontrast ↓ ischemia	polarized cell basolateral protein	
Extension GFR low/falling		non polarized cell	cellular apoptosis/necrosis ↓ disruption of normal epithelial integrity abnormal tubular function (filtration/clearance) cellular sloughing ↓ luminal obstruction inflammation ↓ capillary studging and worsening ischemia
Maintenance GFR stable/low		dedifferentiated cell	cellular dedifferentiation proliferation ↓ reestablishment of tubular epithelium
Recovery GFR rising		polarized cell	cellular repolarization ↓ reestablishment of normal tubular function (filtration/clearance)

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## Insufficienza renale acuta

- Oliguria - Anuria
- Ritenzione idrosalina
- Ipervolemia
- Insufficienza cardiaca sinistra (dispnea, edema polmonare acuto)
- Acidosi metabolica
- Nausea e vomito
- Iperpotassiemia
- Iperfosfatemia, Ipermagnesiemia
- Ipcalcemia

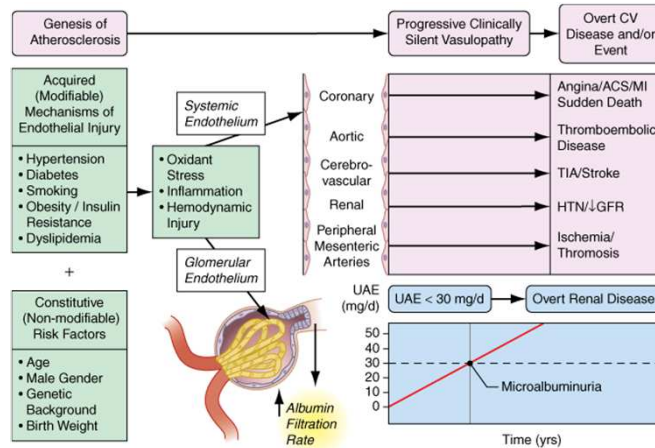
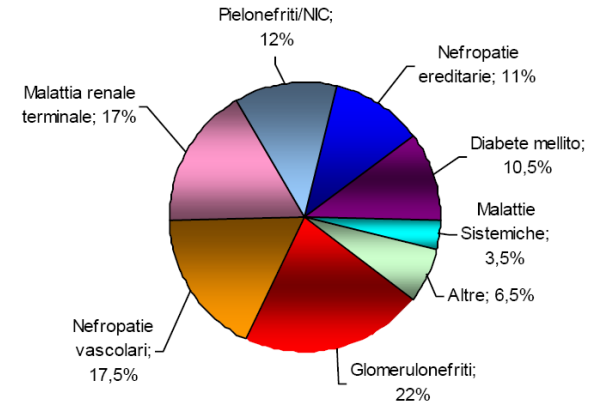
## Malattia renale cronica

Condizione patologica caratterizzata da fenomeni infiammatori e riparativi renali che nel tempo possono causare una riduzione della funzione renale con tendenza progressiva verso l'insufficienza renale cronica

## Insufficienza renale cronica

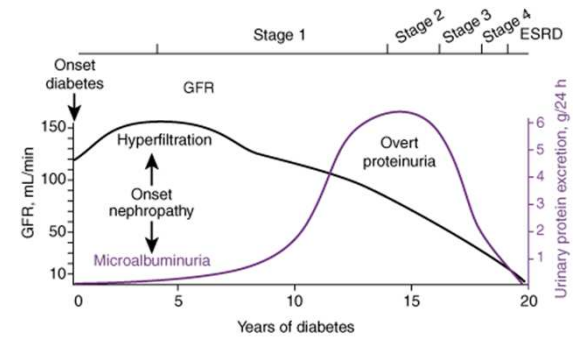
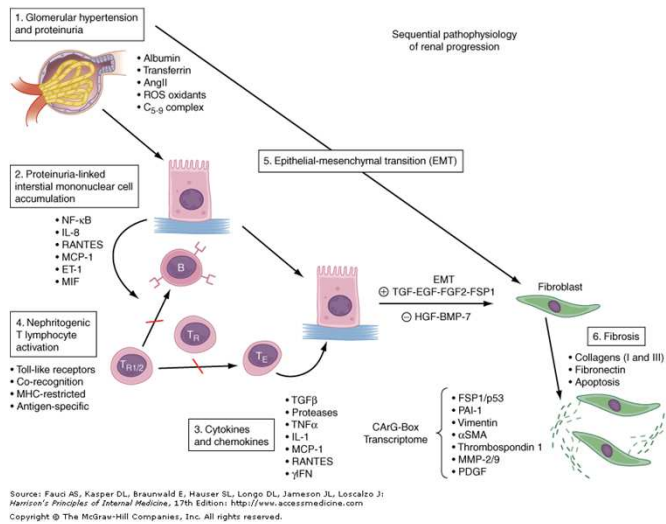
Condizione patologica caratterizzata dalla perdita irreversibile della funzione renale che richiede trattamento (dialisi o dal trapianto di rene)

## Cause di malattia renale cronica



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**Comparative pathophysiology and clinical consequences of atherosclerosis-associated endothelial cell injury in systemic versus renal circulations.** In contrast to the systemic endothelial bed in which early atherosclerotic injury is undetectable, the high volume of fluid filtered across the glomerular endothelium (140–180 L/day) markedly amplifies the functional consequence (increased albumin filtration) of early endothelial (and podocyte) injury in the glomerulus. The emergence of microalbuminuria thus unmasks systemic endothelial injury likely occurring simultaneously in other vascular beds, progressing silently to overt disease years later. CV, cardiovascular; ACS, acute coronary syndrome; MI, myocardial infarction; TIA, transient ischemic attack; HTN, hypertension; GFR, glomerular filtration rate; UAE, urinary albumin excretion



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**Progression of chronic renal injury.** Although various types of renal injury have their own unique rates of progression, one of the best understood is that associated with type I diabetic nephropathy. Notice the early increase in glomerular filtration rate (GFR), followed by inexorable decline associated with increasing proteinuria. Also indicated is the National Kidney Foundation K/DOQI classification of the stages of chronic kidney disease. ESRD, end-stage renal disease

## Insufficienza renale cronica

1. Equilibrio idrosalino
2. Equilibrio acido-base
3. Equilibrio fosfo-calcico
4. Eritropoesi



