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

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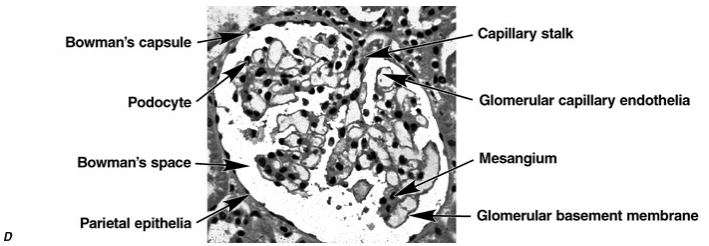


Glomerular architecture. *A.* The glomerular capillaries form from a branching network of renal arteries, arterioles, leading to an afferent arteriole, glomerular capillary bed (tuft), and a draining efferent arteriole (modified from Hypertension 5:8–16, 1983). ***B.*** Scanning electron micrograph of 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[1] and Mark Haas, MD, PhD[2]

Created: February 10, 2016.

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/

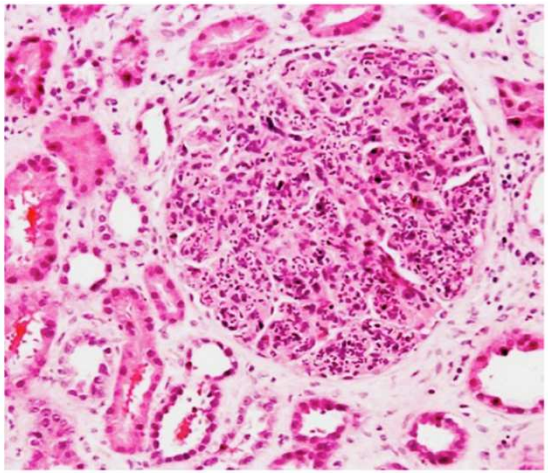


Figure 1. Acute post-streptococcal glomerulonephritis (GN) with severe proliferative and exudative GN. The glomerulus is enlarged and markedly hypercellular with a large number of neutrophils. Note the red blood cells in some tubular lumens. Hematoxylin and eosin (H & E) stain, original magnification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

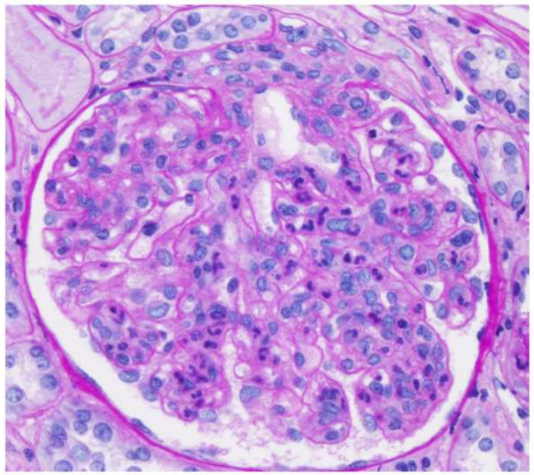
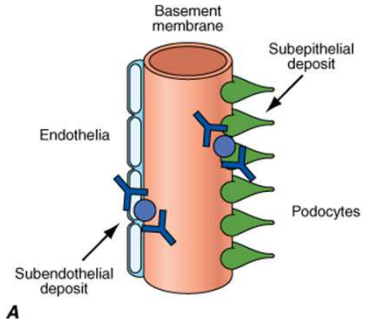


Figure 2. Acute post-streptococcal GN with proliferative and exudative GN. The glomerulus shows endocapillary hypercellularity with multiple neutrophils, although far fewer than the glomerulus in Figure 1. Periodic acid-Schiff (PAS) stain, original magnification x400.



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.

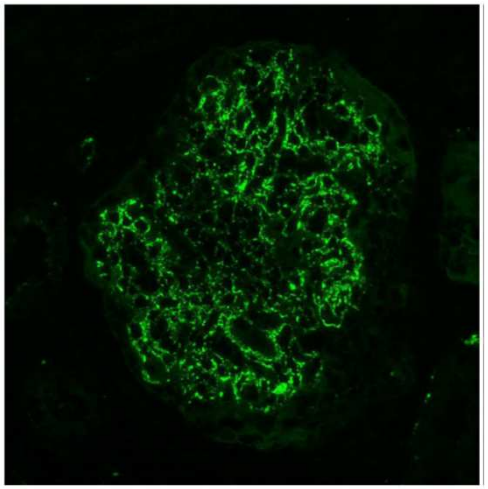
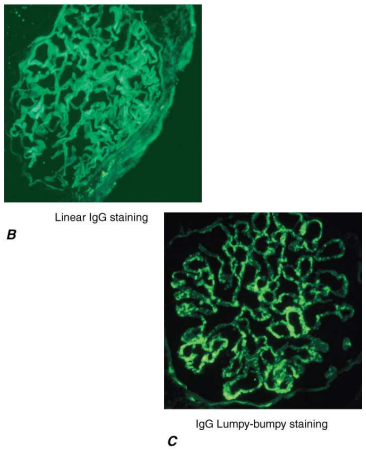


Figure 3. Immunofluorescence staining for C3 in acute post-streptococcal GN. There is granular staining in the glomerular capillary walls and mesangium, in a "starry-sky" pattern. Fluorescein isothiocyanate (FITC) conjugated anti-human C3, original magnification x400.



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.

Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: http://www.accessmedicine.com

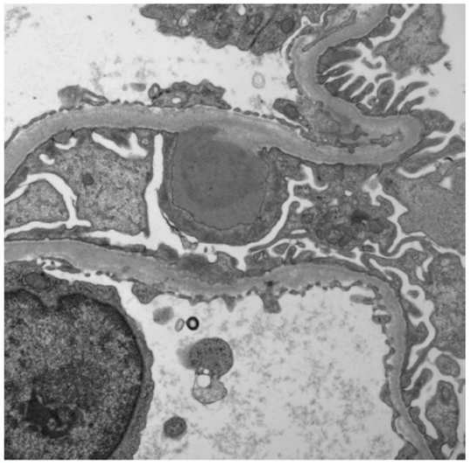


Figure 4. Electron-microscopy in acute post-streptococcal GN. Note the large, "hump"-like subepithelial deposit. The periphery of this deposit is slightly less electron-dense than its center, indicating very early resorption. The glomerular capillary with the subepithelial "hump" also contains a small subendothelial 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

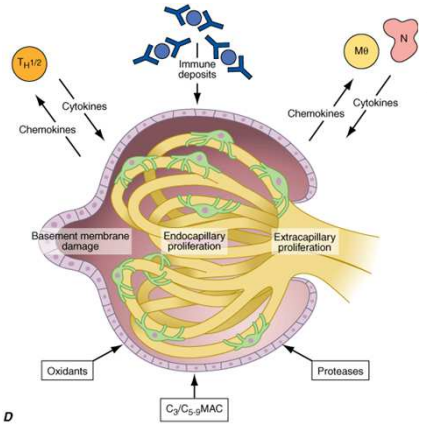
Mechanism	Evidence	Reference
Nephritogenic antigens (NAPlr, SPEB, streptokinase, others)	NAPlr and SEPB demonstrated in renal biopsies	(Oda, et al., 2010; Poon-King, Bannan, Viteri, Cu, & Zabriskie, 1993; Nordstrand, McShan, Ferretti, Holm, & Norgren, 2000)
Circulating immune complexes	Circulating anti-SPEB and anti-NAPlr antibodies in APSGN patients	(Yoshizawa, et al., 2004; Parra, et al., 1998)
In situ 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, & Rodríguez-Iturbe, 2005)
Autoimmunity (*anti-IgG, other*)	Neuraminidase is produced by some nephritogenic streptococci. Serum neuraminidase activity in APSGN patients	(Mosquera & Rodríguez-Iturbe, 1984; Rodríguez-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

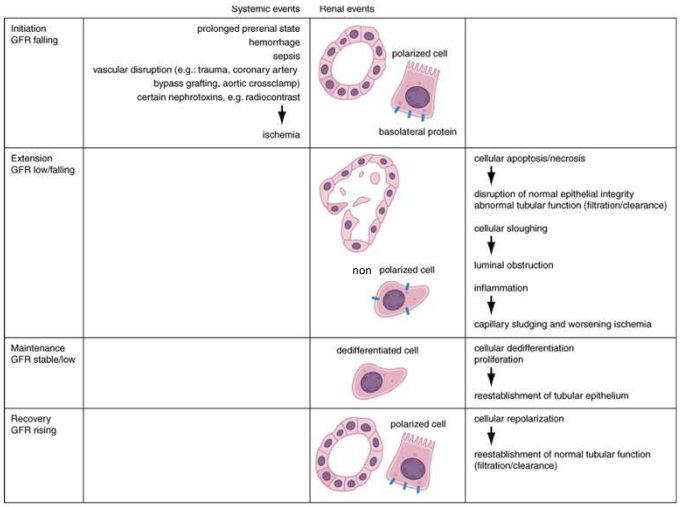
Mechanism	Evidence	Reference
Anti-Ig (induced by the loss of sialic acid of the IgG or binding of the Fc fragment of IgG to type II receptors on the surface of group A streptococcus)	Serum anti-IgG titers Renal anti-IgG deposits	(Rodríguez-Iturbe B. , 1984; Parra, et al., 1998; Rodríguez-Iturbe, Rabideau, García, & 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)
Other		
Increased plasmin activity in glomeruli (facilitating immune complex deposition	Co-localization of plasmin and NAPlr 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 & Rodríguez-Iturbe, 1986; Marín, Mosquera, & Rodríguez-Iturbe, 1995)

ANCAs antineutrophil-cytoplasmic autoantibodies



Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: http://www.accessmedicine.com

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.



Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: http://www.accessmedicine.com

Insufficienza renale acuta

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

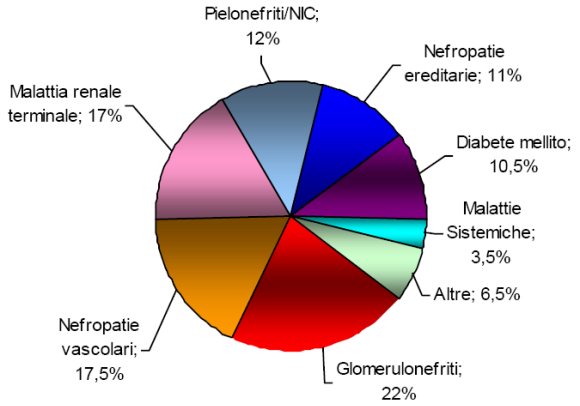
Malattia renale cronica

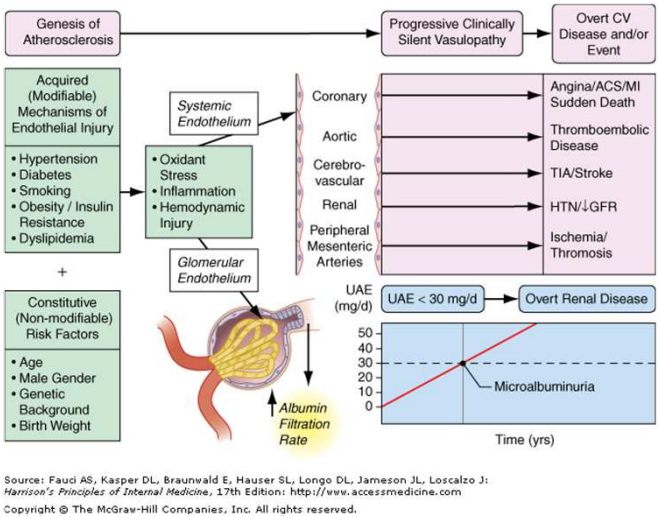
Condizione patologica caratterizzata da fenomeni infiammatori e riparativi renali che nel tempo possono causare una riduzione della funzione renale con tendenza progressiva verso l'insufficienza renale cronica

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

The Journal of Clinical Investigation COMMENTARY

A generic crystallopathic model for chronic kidney disease progression

Orson W. Moe

J Clin Invest. 2021;131(16):e151858 https://doi.org/10.1172/JCI151858

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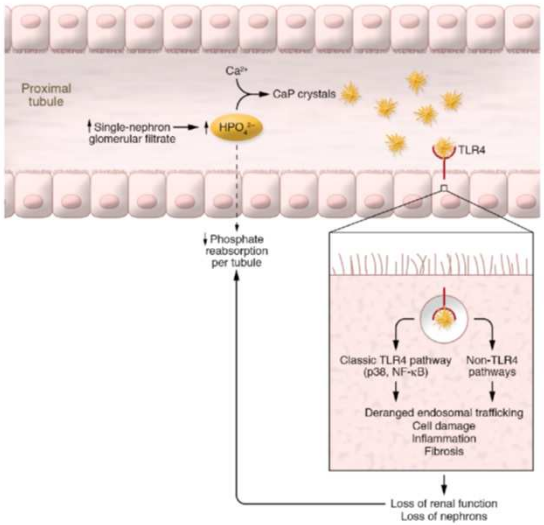
Chronic kidney disease (CKD) has reached epidemic proportions globally. The natural course of chronic kidney disease is almost uniformly progressive, albeit at different rates in different individuals. The downhill course appears to pervade kidney diseases of all etiologies and seems to spiral down a self-perpetuating vortex, even if the original insult is ameliorated or controlled. In this issue of the *JCI*, Shiizaki, Tsubouchi, and colleagues proposed a model of renal tubule luminal calcium phosphate crystallopathy that accounts for renal function demise. Calcium phosphate crystals attached to TLR4 and underwent endocytosis at the brush border, triggering inflammation and fibrosis. This mechanism might operate in different kinds of kidney disease, with a theoretical phosphate concentration threshold in the proximal tubular lumen, beyond which is triggered undesirable downstream effects that eventuate in loss of renal function. If this model parallels human CKD, clinicians may focus efforts on determining phosphate exposure in the proximal tubular lumen.



The Journal of Clinical Investigation RESEARCH ARTICLE

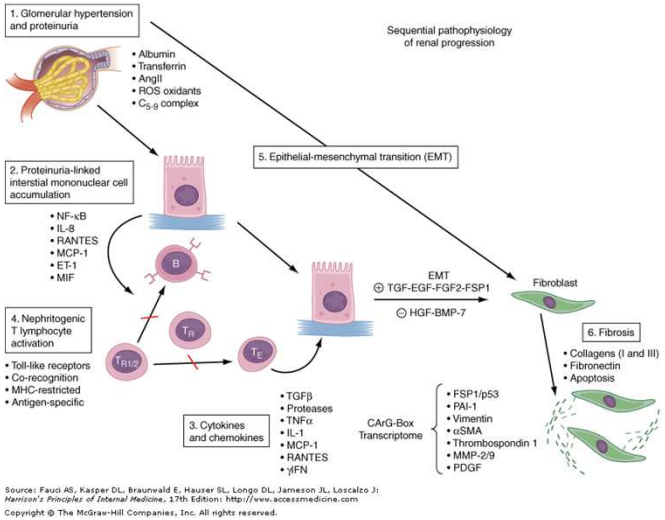
Calcium phosphate microcrystals in the renal tubular fluid accelerate chronic kidney disease progression

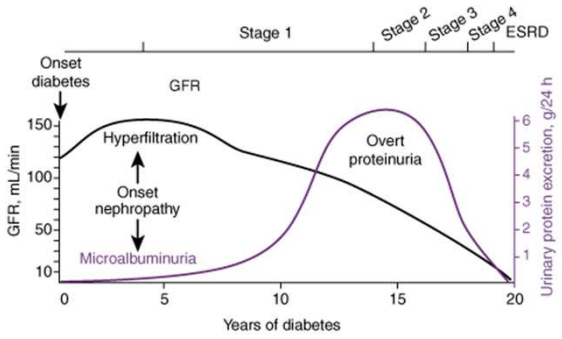
Kazuhiro Shiizaki,[1,2] Asako Tsubouchi,[3] Yutaka Miura,[1] Kinya Seo,[4] Takahiro Kuchimaru,[5] Hirosaka Hayashi,[1] Yoshitaka Iwazu,[1,6,7] Marina Miura,[1,6] Batpurev Battulga,[8] Nobuhiko Ohno,[8,9] Toru Hara,[10] Rina Kunishige,[3] Mamiko Masutani,[11] Keita Negishi,[12] Kazuomi Kario,[12] Kazuhiko Kotani,[7] Toshiyuki Yamada,[7] Daisuke Nagata,[6] Issei Komuro,[13] Hiroshi Itoh,[14] Hiroshi Kurosu,[1] Masayuki Murata,[3] and Makoto Kuro-o[1]

The Western pattern diet is rich not only in fat and calories but also in phosphate. The negative effects of excessive fat and calorie intake on health are widely known, but the potential harms of excessive phosphate intake are poorly recognized. Here, we show the mechanism by which dietary phosphate damages the kidney. When phosphate intake was excessive relative to the number of functioning nephrons, circulating levels of FGF23, a hormone that increases the excretion of phosphate per nephron, were increased to maintain phosphate homeostasis. FGF23 suppressed phosphate reabsorption in renal tubules and thus raised the phosphate concentration in the tubule fluid. Once it exceeded a threshold, microscopic particles containing calcium phosphate crystals appeared in the tubule lumen, which damaged tubule cells through binding to the TLR4 expressed on them. Persistent tubule damage induced interstitial fibrosis, reduced the number of nephrons, and further boosted FGF23 to trigger a deterioration spiral leading to progressive nephron loss. In humans, the progression of chronic kidney disease (CKD) ensued when serum FGF23 levels exceeded 53 pg/mL. The present study identified calcium phosphate particles in the renal tubular fluid as an effective therapeutic target to decelerate nephron loss during the course of aging and CKD progression.

Reference information: *J Clin Invest*. 2021;131(16):e145693. https://doi.org/10.1172/JCI145693.

Figure 1. Model of renal tubular crystallopathy and CKD progression proposed by Shiizaki, Tsubouchi, and coworkers. In CKD of any etiology, high filtration in intact nephrons and reduced phosphate reabsorption driven by high parathyroid hormone and FGF23, and CKD itself, increase luminal phosphate concentrations. When calcium phosphate reaches a certain threshold in the end of the proximal tubule, crystals form and bind to brush border TLR4, which secures the crystals on the cell surface, internalizes the crystals, and activates a series of cascades. Subsequent damage of the tubules sets off inflammation and fibrosis in the tubulointerstitium, engendering further loss of renal function. The process reiterates in a vicious cycle.





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

Vedi

1. Equilibrio idrosalino
2. Equilibrio acido-base
3. Equilibrio fosfo-calcico
4. Ossigeno ed eritropoiesi