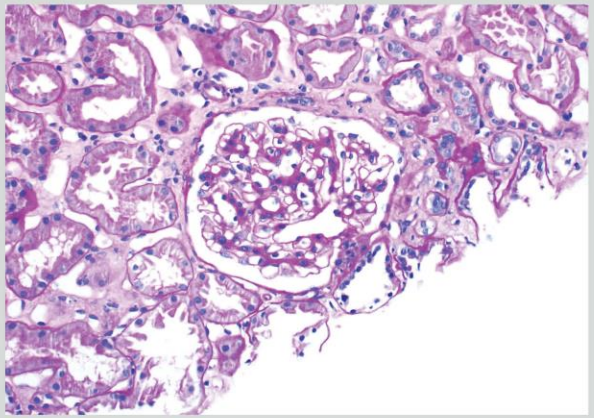
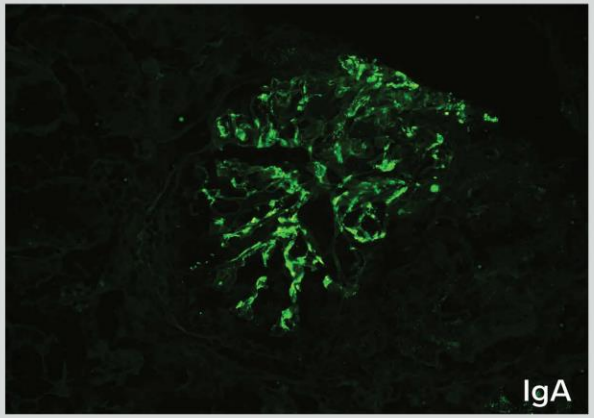
IgA

Secondary IgA Nephropathy?
KDIGO Comments





KDIGO comment on the initial evaluation of IgAN patients:

Assess all patients with biopsy-proven IgAN for secondary causes of IgA glomerular deposits.

IgA deposition has been associated with many conditions, including the following:

- Various infections, including HIV
- Cirrhosis and other hepatobiliary diseases
- Gluten sensitive enteropathy and other gastrointestinal disorders
- Rheumatologic diseases
- Various neoplasms and myeloproliferative diseases

KDIGO Clinical practice guideline for glomerulonephritis. *Kidney International Supplement* Vol. 2, Issue 2, June 2012 p. 209.
Heptinstall's Pathology of the Kidney, 7th edition, 2015; pp. 463-523.

Arkana Laboratories

Henoch Schonlein Purpura (HSP)

- **Most common systemic vasculitis in children**
  - 90% of cases occur in the pediatric group
- Etiology: Unknown
- Pathogenesis: End organ IgA immune complex (IC) deposition
- Complications: Renal

Etiology

- **Unknown etiology!**
- Precipitating antigen may be infectious
  - Many cases follow upper respiratory infection (URI)
- Example: identical twins following adenovirus infection:
  - HSP in one, IgA nephropathy in other

Renal Disease

- Occurs in 20-54 % of children (more prevalent in adults)
  - 2 days to 4 weeks after onset of systemic symptoms
- **Hematuria is most common presentation**
  - With or without red blood cell (RBC) casts
- Nephrotic range proteinuria, ↑ creatinine and or hypertension → ↑ risk of progressive disease (adults)

Renal Disease

- % of glomeruli with crescents has prognostic significance
  - > 50%
  - 37% progressed to end stage renal disease (ESRD)
  - 18% with chronic renal insufficiency (CRI)
- Differential diagnosis:
  - Berger's Disease

Renal Disease

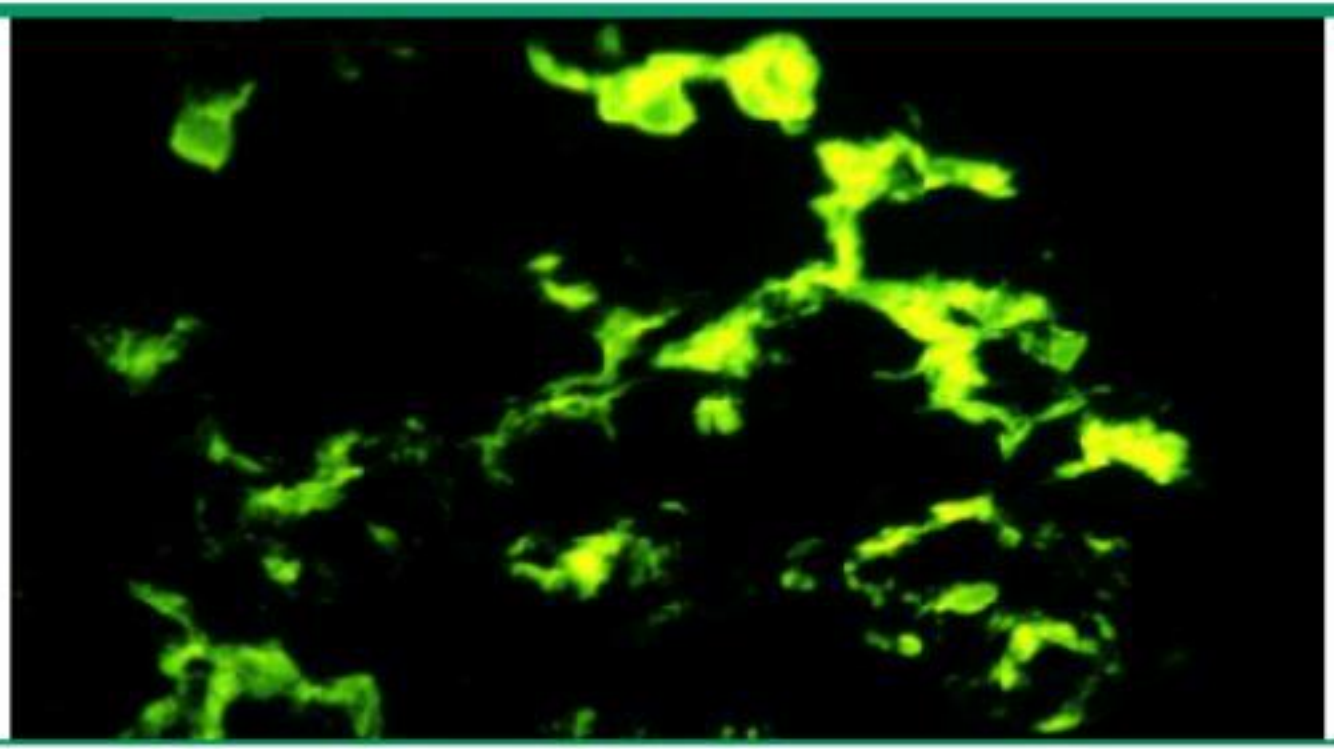
- Correlation between disease severity and biopsy findings
  - Asymptomatic hematuria: focal mesangial proliferation
  - Proteinuria: cellular proliferation
  - Nephrotic range proteinuria: crescents

J Am Soc Nephrol 1999 Dec;10(12):2637-44

Renal Biopsy

- Obtain in severe renal involvement or uncertain diagnosis
- Characterized by IgA deposition in mesangium
  - Immunoflorence studies → IgG, fibrin, C3
- Mesangial proliferation to crescentic glomerulonephritis (GN)
  - Biopsy generally parallels clinical disease severity

Mesangial IgA deposits



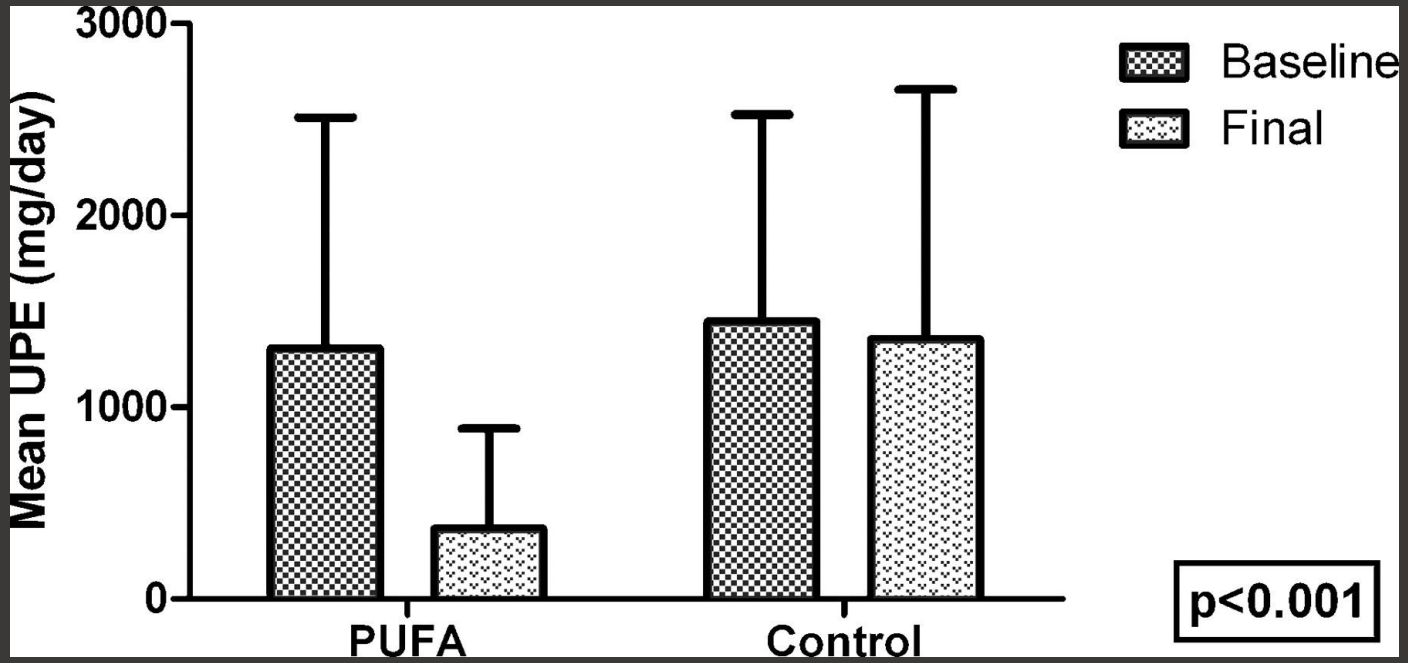
Immunofluorescence microscopy demonstrating large, globular mesangial IgA deposits that are diagnostic of IgA nephropathy or Henoch-Schönlein purpura. Note that the capillary walls are not outlined, since the deposits are primarily limited to the mesangium.

Courtesy of Helmut Rennke, MD.

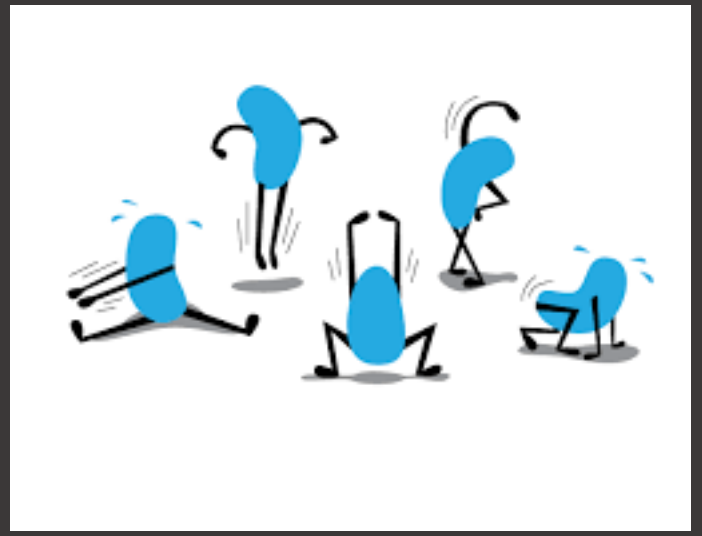
Specific Therapy: Renal disease

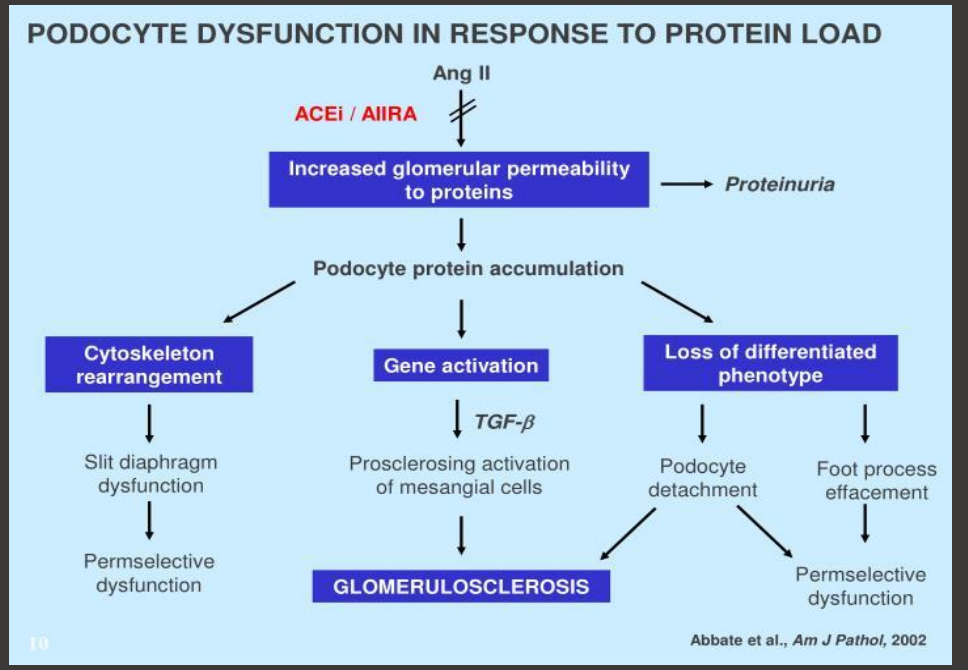
- Should only be considered in patients with:
  - Marked proteinuria and/or impaired renal function
- Therapies for cresentic nephritis:
  - High dose methylprednisolone → oral prednisone for 3 months has shown benefit
  - Azathioprine and corticosteroids
  - Cyclophosphamide

Combined treatment with renin–angiotensin system blockers and **polyunsaturated fatty acids** in proteinuric IgA nephropathy: a randomized controlled trial; Ferraro, P. M. et al. Nephrol. Dial. Transplant. 2009 24:156-160



Proteinuria at 6 months




PODOCYTE DYSFUNCTION IN RESPONSE TO PROTEIN LOAD
Ang II
ACEi / AIIRA
Increased glomerular permeability to proteins
Proteinuria
Podocyte protein accumulation
Cytoskeleton rearrangement
Gene activation
Loss of differentiated phenotype
Slit diaphragm dysfunction
TGF-β
Prosclerosing activation of mesangial cells
Podocyte detachment
Foot process effacement
Permselective dysfunction
GLOMERULOSCLEROSIS
Permselective dysfunction
Abbate et al., Am J Pathol, 2002


S T O P


Weekly
Optional Daily
Daily