NephU™

Improving Awareness & Patient Outcomes

Current Understanding of IgA Nephropathy (IgAN)

April 2023 US.CORP.D.23.00018

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Panelist & Moderators:

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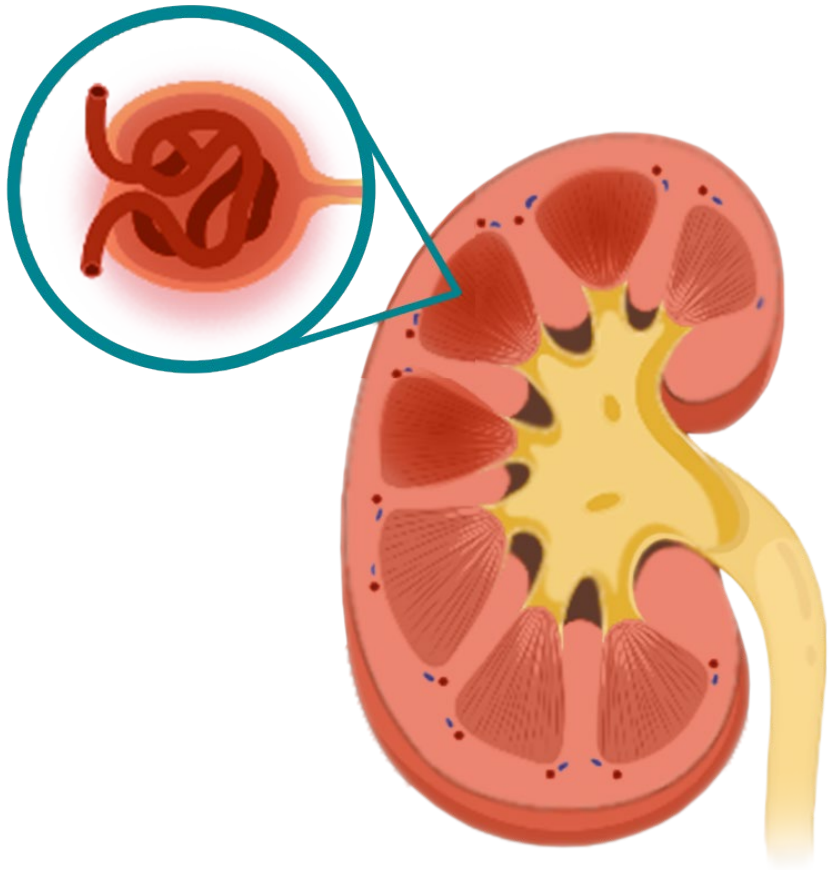
What is IgA Nephropathy (IgAN)?[1,2]



- Also known as Berger's disease, IgAN is the most common glomerulonephritis worldwide[2]
- Autoimmune disease characterized by:[2]
  - Abnormal production of IgA (resulting in formation of Gd-IgA)
  - An immune response characterized by the formation of antibodies against Gd-IgA
  - Deposits of IgA-containing immune complexes in renal glomeruli causing damage
- Etiology of IgAN is multifactorial and is hypothesized to have a multi-hit pathogenic process[2]

Gd-IgA = galactose-deficient immunoglobulin A

1. Image created with BioRender.com
2. Gutiérrez E, et al. Nephron 2020;144:555-571. Accessed December 2021.

Who is Affected by IgAN?

20-40% of affected individuals progress to kidney failure[1]

Incidence of about **2.5/100,000/year** and males are twice as likely to be affected[2,3]

Affects people of all ages but onset is often in **teens and young adults**[3]

Most likely to cause kidney failure in East Asian ancestry > Caucasians > African descent[4]

1. Gesualdo L et al. Semin Immunopathol. 2021;43:657-668. Accessed December 2021.
2. McGrogan A, et al. Nephrol Dial Transplant. 2011;26(2):414-430.
3. https://www.niddk.nih.gov/health-information/kidney-disease/iga-nephropathy/ Accessed December 2021.
4. https://kdigo.org/guidelines/gd/ Accessed January 2022

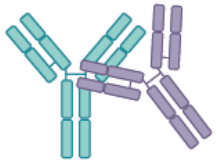
Pathogenesis of IgAN: The Four Hit Hypothesis[1,2]

Hit #1

Production of aberrant, galactose-deficient IgA1 (Gd-IgA1), by plasma cells.

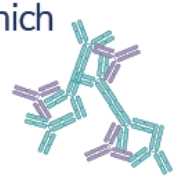
Hit #2

Synthesis of **autoantibodies** directed against the aberrant, Gd-IgA1.



Hit #3

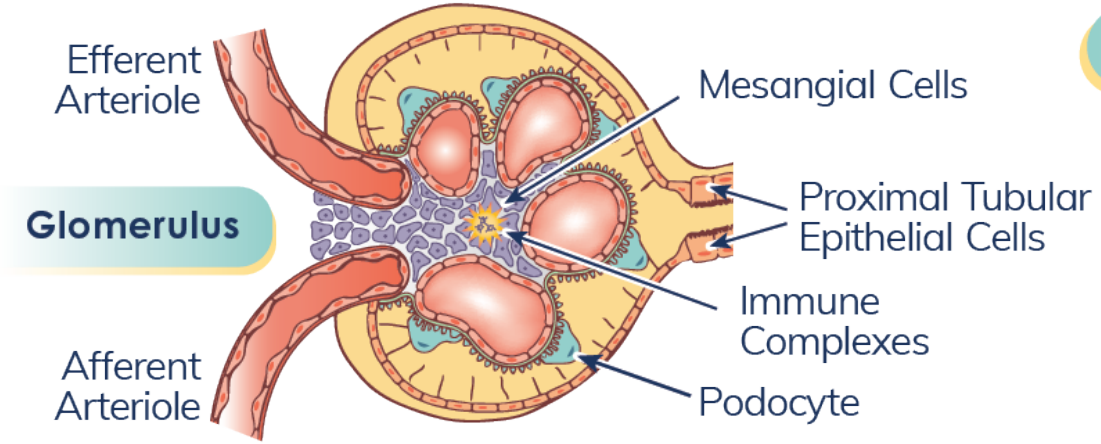
Binding of autoantibodies to the Gd-IgA1 generates **pathogenic immune complexes**, which circulate in the bloodstream.



Hit #4

Circulating immune complexes deposit at the points of filtration (mesangial cells, located between glomerular basement membrane and fenestrated endothelium of the kidney).

Deposition of immune complexes result in local immune activation, inflammation, and glomerular injury.



Outcome Of The Four Hit Pathogenic Process:

- Injury to the podocytes and proximal tubular epithelial cells
- Worsening kidney function progressing to chronic kidney disease.
- Which left unaddressed, can lead to kidney failure and the need for renal replacement therapy, such as transplant or dialysis.

1. Suzuki H et al. J Am Soc Nephrol. 2011;22:1795-1803.
2. Xu L et al. Mod Pathol. 2010;23:1241-1250.

Clinical Presentation and Validation of IgAN

Symptoms

- Can be non-specific, or patients may be asymptomatic for years[1]
- Symptoms can include:
  - Hematuria (microscopic or macroscopic)[1]
  - Protein in the urine[1]
  - High blood pressure[2]
  - In some patients, macroscopic hematuria is often preceded by upper respiratory infection[3]

Diagnosis & Prognosis

- Diagnosed when the patient has a kidney biopsy, and the microscopic examination shows deposits of IgA-containing immune complexes in renal glomeruli[1,2]
- MEST-C histological score for prognosis[4]
  - **M**: mesangial
  - **E**: endocapillary
  - **S**: segmental sclerosis
  - **T**: interstitial fibrosis/tubular atrophy
  - **C**: crescents

1. https://www.niddk.nih.gov/health-information/kidney-disease/iga-nephropathy/ Accessed December 2021.
2. Gutiérrez E, et al. Nephron 2020;144:555-571. Accessed December 2021.
3. Gesualdo L et al. Semin Immunopathol. 2021;43:657-668. Accessed December 2021.
4. Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases. Kidney Int. 2021 Oct;100(4S):S1-S276.

General Management of IgAN[1]

OPTIMIZED SUPPORTIVE CARE

The primary focus of management should be optimized supportive care.

The objective of optimized supportive care is to slow down progression of CKD and reduce cardiovascular risk.

- Assess Cardiovascular Risk
- Controlled Blood Pressure
- Dietary Sodium Restriction
- Smoking Cessation
- Weight Control & Exercise

Patients At High-Risk Despite Maximal Supportive Care

"High-risk" is defined as **proteinuria >0.75–1 g/d** despite 90 days of optimized supportive care.

- Consider the opportunity to participate in a clinical trial
- Consider immunosuppressive therapy with caution

1. https://kdigo.org/guidelines/gd/ Accessed January 2022

For More Information:[1-4]

IGA NEPHROPATHY FOUNDATION
Dedicated to finding a cure.

IgAN.org

NATIONAL KIDNEY FOUNDATION®

kidney.org

KDIGO

2021 Clinical Practice Guidelines for the Management of Glomerular Disease
KDIGO.org/guidelines/gd/

Information on clinical trials
clinicaltrials.gov

1. https://igan.org/ Accessed April 2023
2. https://www.kidney.org/ Accessed April 2023
3. https://kdigo.org/guidelines/gd/ Accessed April 2023
4. https://clinicaltrials.gov/ Accessed April 2023

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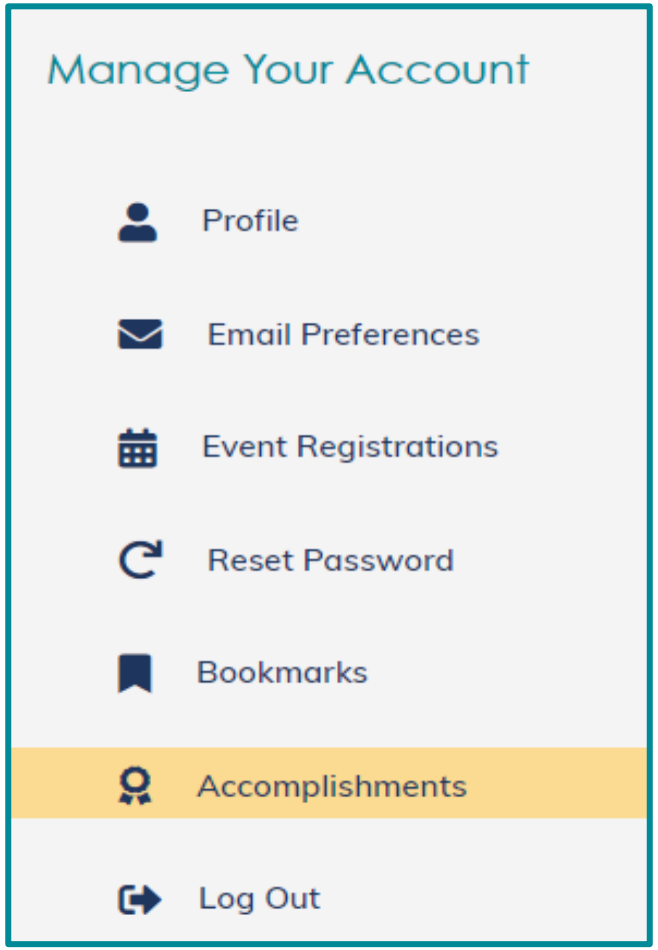

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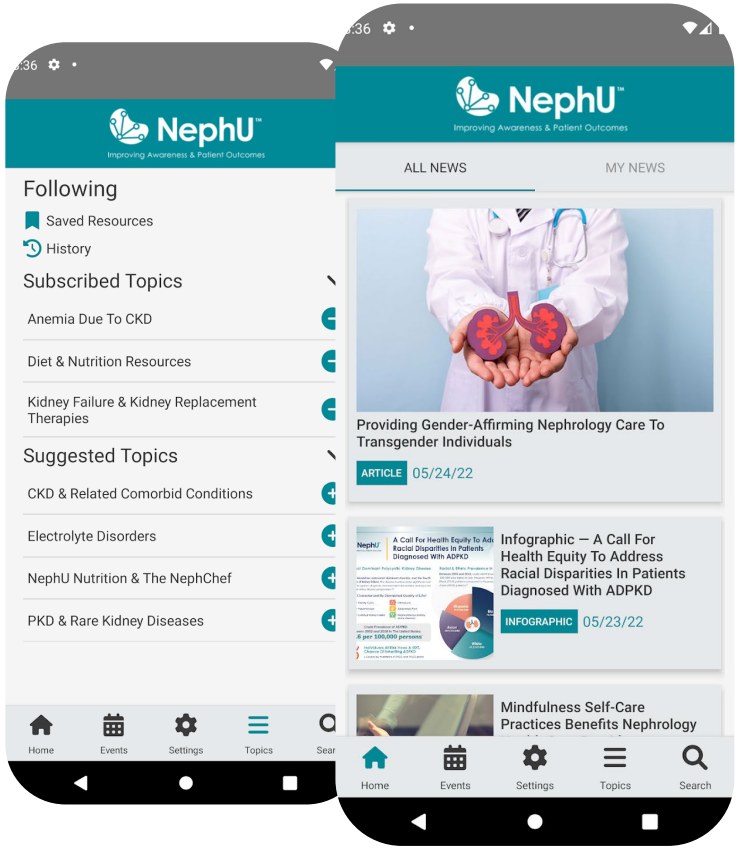

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Current Understanding of IgA Nephropathy (IgAN)

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