RPSG & KDARs Collaborative

The RPSG

The Renal Patient Support Group

IgA Nephropathy (IgAN)

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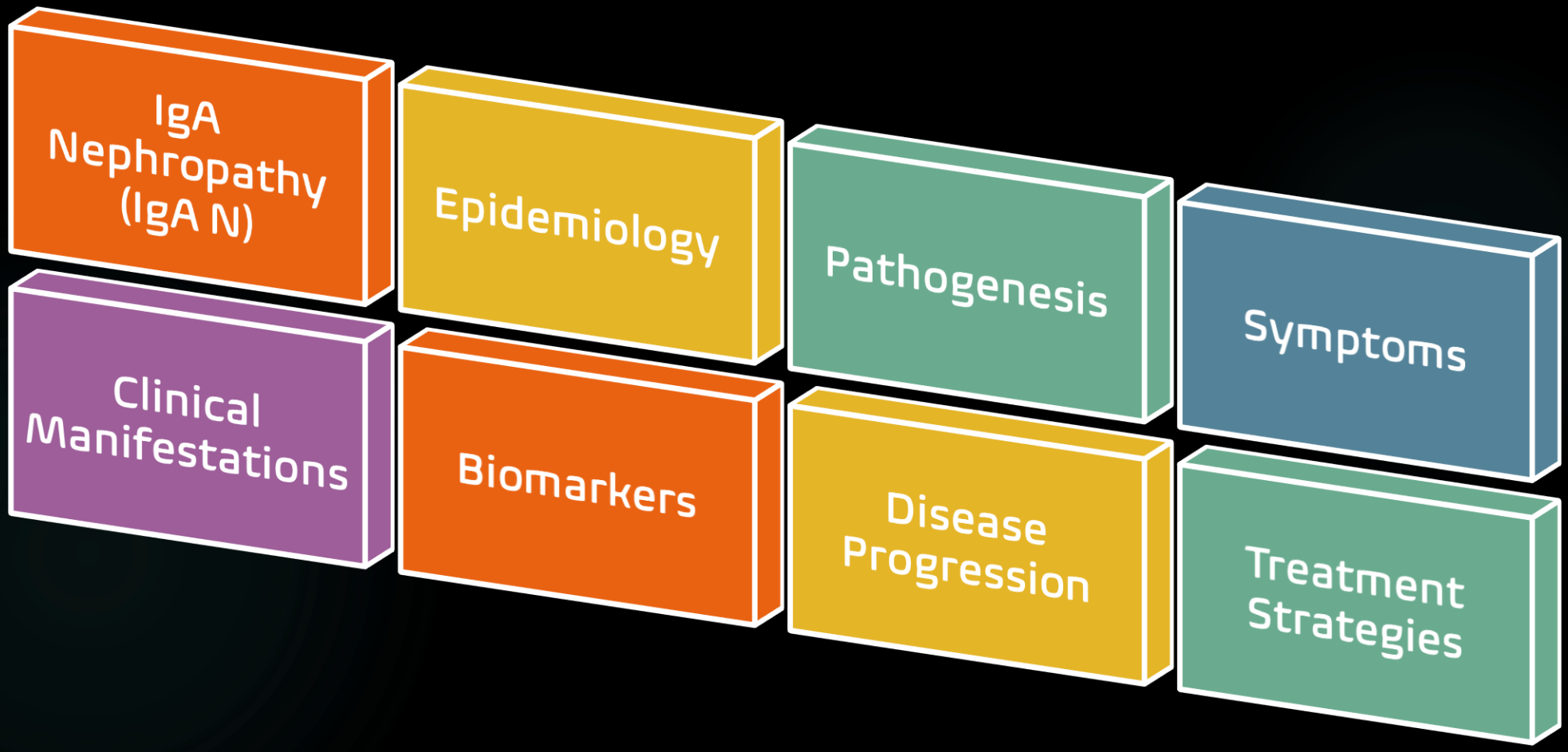
IgA Nephropathy (IgA N)
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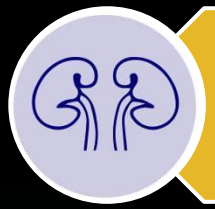
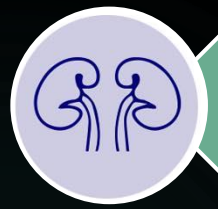
IgA Nephropathy

Also known as Berger's disease



Recipients can present with a range of signs and symptoms, from asymptomatic microscopic haematuria to macroscopic haematuria and/ or proteinuria.



It is the most common form of glomerular disease/ glomerulonephritis worldwide, associated with a poor prognosis and resulting in End-Stage (ESRD).

IgA deposits are also associated with other systemic disease, such as Henoch-Schönlein purpura (HSP)

Susceptibility to IgAN and risk of disease progression are influenced by a confluence of genetic and environmental factors.

Epidemiology

- Prevalence varies geographically, and estimated of disease burden vary according to using biopsy registry data or dialysis registries.
- It is a common cause of CKD, with an overall incidence of at 2.5 per 100, 000 individuals.
- Epidemiological studies have demonstrated that the incidence is increased in individuals of Pacific Asian origin.
- In up to 50% of IgAN recipients, this disease progresses to the end-stage renal disease within 20 to 25 years.
- IgAN more frequently occurs in males than in females and usually affects 16-35 year-olds, which account for approximately 80% of total recipients.

Pathogenesis

- This disease occurs when immunoglobulin A (IgA) deposits in the kidneys lead to the development of local inflammation and renal injury.
- Considered as an autoimmune disease, with a multi-hit hypothesis proposed.
- First hit: the production of galactose-deficient IgA1 and it plays an important role in the formation of immune complexes.
- Second hit: production of IgG autoantibodies, which target the O-glycans in the hinge region, also leading to the formation of immune complexes.
- These complexes induce local inflammatory responses and they are deposited in kidneys. This leads to the activation and mesangial cell damage.
- Antibodies involved in the IgAN pathogenesis: Gd-IgA1, antiglycan autoantibody and C3

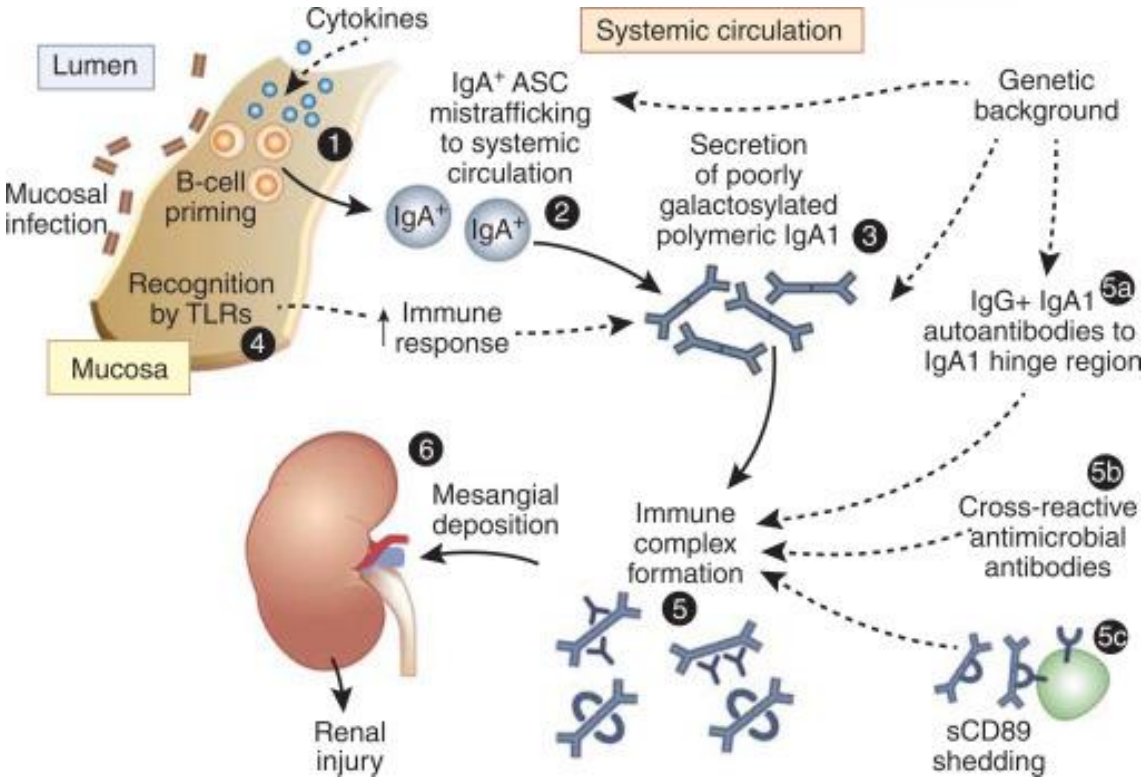


Figure adapted from (Boyd et al. 2012)

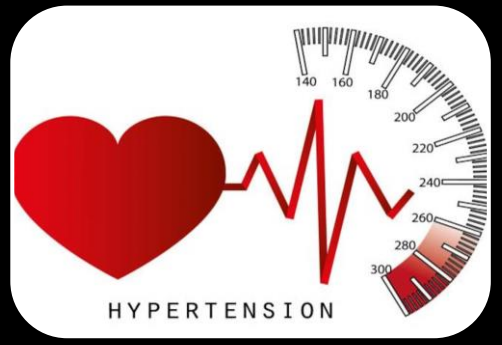
IgA Nephropathy

Protein in the Urine

Pain in the Abdomen

Acute Kidney Failure

Blood in the Urine



Hypertension

Clinical Manifestations

The range of clinical manifestations of IgAN is broad, from asymptomatic microscopic haematuria to rapidly progressive GN.

Common Phenotypes: the two most common clinical presentations are asymptomatic haematuria and progressive kidney disease.

Asymptomatic haematuria with minimal proteinuria (<0.5g/d) may be detected through screening programs.

Isolated microscopic haematuria with minimal proteinuria is regarded as having a favourable prognosis.

Renal survive ranges according to biopsy timing.

Factors associated with poor prognosis include hypertension, proteinuria, and decrease eGFR at diagnosis.

Race/ Ethnicity has been an important determinant of outcome.

Synpharyngitic microscopic haematuria is a classic clinical syndrome associated with first presentation of IgAN.

Persistent proteinuria is associated with progressive disease.

Biomarkers

Renal biopsy is the gold standard for diagnosis and assessment of disease activity and prognosis.

Gd-IgA 1 is increased in the blood and urine of recipients with IgAN.

Gd-IgA 1 in the serum of recipients with IgAN have been found within immune complexes bound to IgG or IgA1 antibodies.

Serum levels of Gd-IgA1-specific IgG autoantibodies are correlated with disease severity.

Increased serum Gd-IgA1 levels are associated with proteinuria and a greater risk of deterioration of renal function in IgAN.

Combination of high serum Gd-IgA1 levels and levels of advanced oxidation protein products is correlated with a more rapid decline in eGFR.

Slowing Renal Damage

Corticosteroids and Immunosuppressive drugs: calm immune system and stop it from attacking glomeruli

ACE inhibitors and ARBs: blood pressure medications used to reduce protein loss and control blood pressure

Treatment Strategies

Conservative Therapy: reduce proteinuria and slow the rate of renal function

Corticosteroids: The aim is to reduce proteinuria in IgAN. The studies suggest that exposure to corticosteroids for a 6 month period may have a "legacy effect", with sustained reduction in the risk of progressive renal dysfunction.

Mycophenolate: data regarding the efficacy of mycophenolate are mixed, current clinical guidelines have recommend against use of this agent in IgAN.

Rituximab: In several studies non effects on proteinuria or renal function were seen.

Combination Therapy is generally reserved for recipients with progressive disease. In treatment on IgAN recipients have demonstrated improvement in renal prognisis after 2-years receiving this type of therapy.

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