PRIMEVIEW

IgA NEPHROPATHY

nature REVIEWS DISEASE PRIMERS

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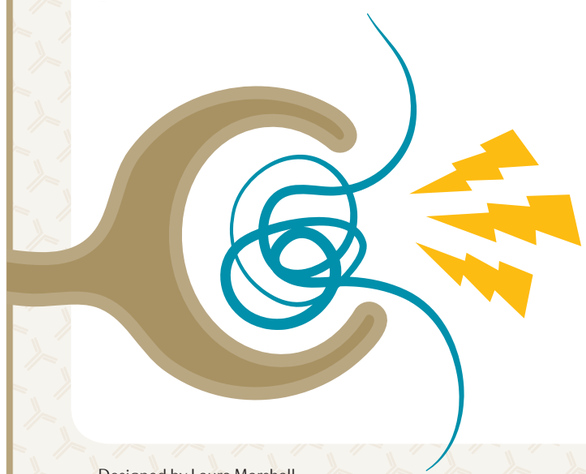
Globally, IgA nephropathy (IgAN) is the most common type of glomerulonephritis in which inflammation of the glomeruli and the blood vessels in the kidney occur. The disease is probably triggered by the aberrant glycosylation of IgA1, which is recognized as an autoantigen. The subsequent immune reaction leads to deposition of immune complexes in the glomeruli, activation of mesangial cells and a gradual decline in renal function.

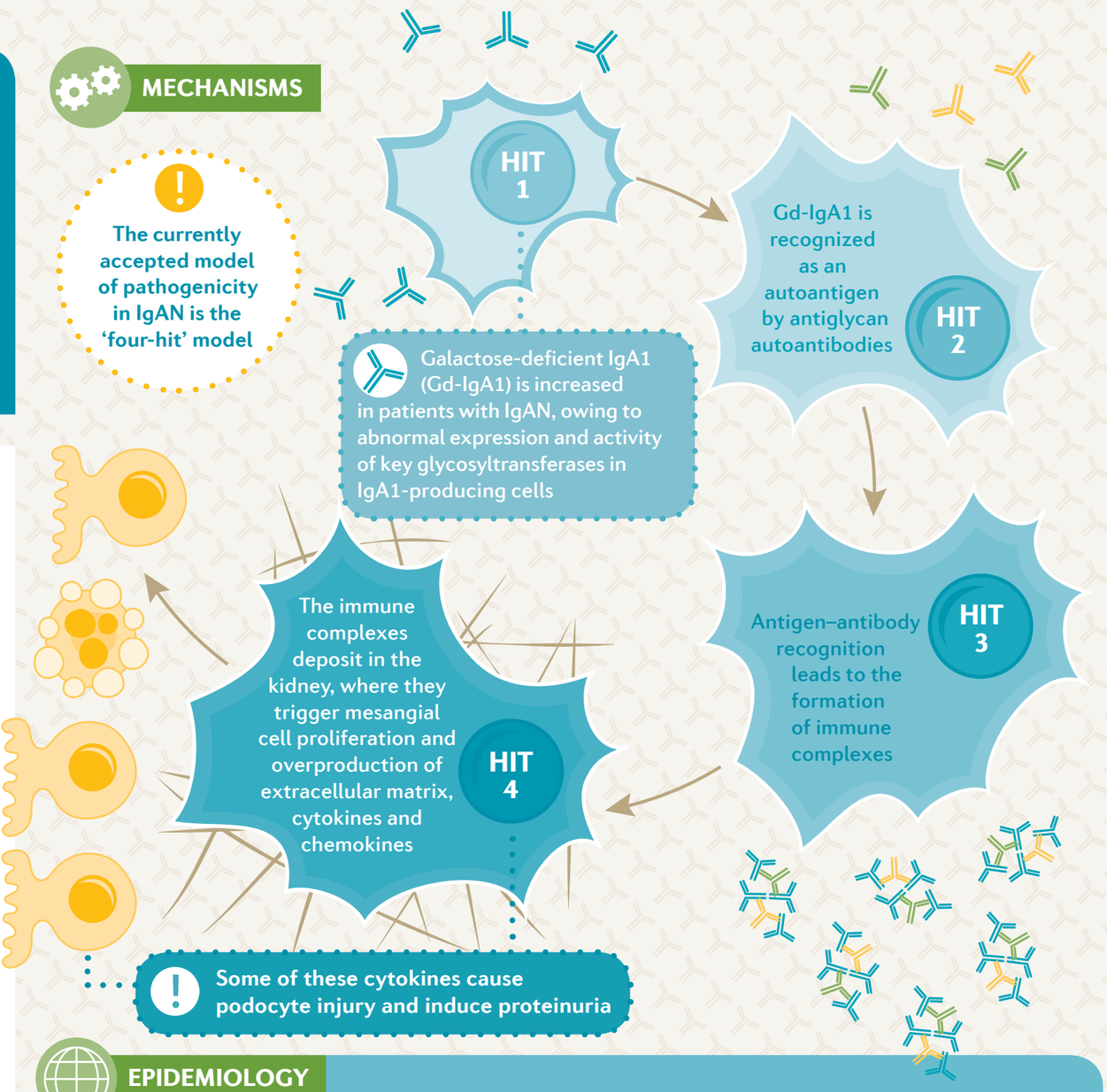
DIAGNOSIS

Patients can present with microscopic haematuria (blood in the urine) or macroscopic haematuria (visible), frequently with hypertension. Laboratory tests and renal biopsy are needed to confirm a diagnosis. Laboratory analyses include determination of the presence of glomerular red blood cells and red blood cell casts in the urine (indicative of glomerular bleeding), assessment of renal function, including the level of protein in the urine and the estimated glomerular filtration rate, and the blood levels of IgA and various cytokines implicated in the disease. In IgAN, biopsy shows IgA-containing immune deposits and mesangial cell proliferation, and might reveal crescentic glomerular lesions.



MECHANISMS

The currently accepted model of pathogenicity in IgAN is the 'four-hit' model



Some of these cytokines cause podocyte injury and induce proteinuria

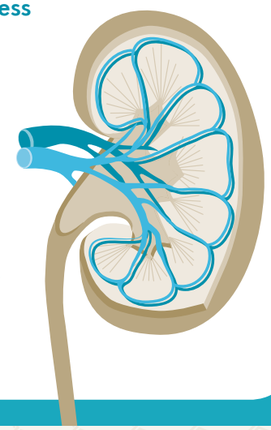
EPIDEMIOLOGY

As IgAN can only be confirmed with renal biopsy, the prevalence and incidence statistics are reliant on biopsy policies in various regions of the world. When policies change to widen the criteria for biopsy, the prevalence has been shown to increase. Risk factors for IgAN include low socioeconomic status and genetic background (individuals of East Asian origin have a higher background genetic risk than those from Africa). The nephropathy is more common in younger patients (children and young adults <30 years of age) than older adults.

MANAGEMENT

As long as the patient has minor haematuria, normal blood pressure and normal glomerular filtration, only periodic monitoring is required. For patients with high blood pressure, medical blockade of the renin–angiotensin system is often a first-line treatment. Dietary restriction of sodium, lipid-lowering techniques and smoking cessation are general and often-recommended approaches. For patients who have moderate-to-severe and persistent proteinuria, corticosteroids are given, although the long-term effects on renal survival are unclear. Chinese patients with IgAN seem to benefit from immunosuppression therapy with mycophenolate mofetil.

Patients who progress to chronic kidney disease might eventually require renal replacement therapy (transplantation or dialysis). Given the systemic nature of the disease, kidney transplantation does not prevent recurrence.



OUTLOOK

Research in IgAN is focusing on non-invasive diagnostic techniques that would reduce the need for biopsy. To that end, urinary and serum biomarkers are being actively sought. A plausible approach would be a panel of biomarkers, including levels of Gd-IgA1 and autoantibodies, and measurement of the expression of microRNAs related to glycosyltransferases.

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