Group A *Streptococcus* bacteria, most commonly *S. pyogenes*, typically cause superficial infections of the throat (pharyngitis) or skin (impetigo). Bacteraemia is usually resolved within a few days, however, renal complications may develop a few weeks later as a result of humoral immune responses to bloodborne bacterial proteins previously deposited in the kidneys (nephritogenic antigens).
An important factor in the development of kidney dysfunction following a Streptococcal infection is the generation of antibodies that target the secreted bacterial antigens. These antibodies are produced during initial immune responses to bacterial infection when immune cells such as macrophages, neutrophils, CD4+ helper T cells and B cells are recruited to the site of infection.
When antibodies have been produced in abundance by plasma cells, antibody-antigen complexes can form in the bloodstream and become deposited in the kidneys, or unbound antibodies can detect antigen in the kidney and from “in situ” immune complexes.
The normal filtering of waste products from the blood is performed by thousands of nephron structures located in the kidney where renal corpuscles are responsible for allowing small molecules to diffuse out of the capillaries.
The renal corpuscle consists of a fine network of capillaries that are permeable to small molecules. The filtering of small molecules is further facilitated by a basement membrane. In the Bowman's space where filtered blood products are solubilised in the glomerular filtrate has specialised cells called podocytes that maintain capillary function and mesangial cells that play a role in phagocytosis.
Two "nephritogenic" proteins have thus far been identified in Streptococcal infections and include SpeB, a bacterial serine protease enzyme, and NAPIr, a secreted bacterial protein known as "nephritis-associated plasmin receptor". It is thought that these proteins when present in the kidney precipitate enzymatic damage to the basement membrane and endothelial cell integrity thus allowing plasma proteins, erythrocytes and immune complexes to cross into the bowman’s space. The bacterial antigens bind and activate plasmin or plasminogen which in turn activates collagenase and matrix metalloproteinases that degrade the basement membrane. Disrupted membrane function allows bacterial antigens to be deposited inside the Bowman’s space.
Immune complexes can be formed inside the Bowman’s space when free IgG antibodies cross the disrupted basement membrane and contact “planted” bacterial antigens already present, or alternatively, immune complexes that have formed in the bloodstream can be trapped directly in the Bowman’s space.
The deposition of immune complexes in the Bowman’s space activates the classical complement system by recruitment of C1 proteins from plasma. A loss of plasma C3 levels correlates with complement activation and deposits of C3 proteins in the Bowman's space.
Due to complement activation an increased influx of immune cells such as macrophages and neutrophils. Deposits of C3, antibody and bacterial antigens accumulate at the basement membrane, known as “humps”, and these accumulate near podocyte foot processes. Kidney function is severely hampered by influx of immune cells that can block capillaries. There is also marked cell proliferation of mesangial and endothelial cells.
Kidney function is compromised by the breakdown of the filtering function of the basement membrane and the influx of numerous immune cells due to complement activation. This results in plasma protein and erythrocyte leakage onto the urine and a decrease in urine volume. In most cases, mild damage to the kidneys is sustained, but ongoing inflammation can result in complete and irreversible kidney damage which requires dialysis and ultimately a transplant of a functional kidney.