key points

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Nephrotic syndrome results from dysfunctional glomerular filtration and consists of three clinical features: severe proteinuria (> 3.5 grams/24 hours); hypoalbuminaemia (serum albumin < 30 g/L); and peripheral oedema. It may occur in people of all ages. Severe proteinuria is the primary mechanism by which nephrotic syndrome arises. The glomerular filtration barrier becomes dysfunctional which leads to pathological filtration of significant amounts of albumin, which is then excreted in the urine. Hypoalbuminaemia occurs and although hepatic albumin synthesis is often upregulated, this does not fully compensate for urinary albumin loss.

The distribution of oedema in nephrotic syndrome may differ from that typically seen in heart failure. Periorbital, facial or genital oedema are commonly reported. Pleural effusions and ascites can occur but pulmonary oedema is less common. Patients with nephrotic syndrome may present with a normal eGFR. Others may have chronic renal impairment at presentation. If the nephrotic syndrome remains uncontrolled even those with normal kidney function at presentation can develop progressive chronic kidney disease. Acute kidney injury (AKI) may occasionally be seen in association with nephrotic syndrome.

Serum concentrations of cholesterol are raised in many patients with nephrotic syndrome. Nephrotic syndrome increases the risk of venous thromboembolism (VTE) which can sometimes be the presenting symptom. Patients with nephrotic syndrome are at increased risk of bacterial infections because of urinary loss of immunoglobulins. Primary causes of nephrotic syndrome include membranous nephropathy, minimal change disease and focal segmental glomerulosclerosis. In children, minimal change disease is the most common cause. Secondary causes relate to glomerular dysfunction secondary to a systemic disease such as diabetes mellitus, systemic lupus erythematosus or amyloidosis.

Initial investigations focus on confirming diagnosis and finding an underlying cause. A renal biopsy is indicated in almost all cases. This will confirm the underlying diagnosis, guide management and give prognostic information. All patients with suspected nephrotic syndrome should be referred urgently to nephrology.

Early initiation of loop diuretics is vital in the management of oedema. Dietary sodium intake should be restricted to < 2 g sodium (< 5 g salt) per day. Regular monitoring of renal function is advisable when commencing or titrating up diuretics to monitor for electrolyte disturbances or AKI. Management of primary glomerular diseases often involves immunosuppressive agents which are initiated and monitored by the nephrology team. In cases where nephrotic syndrome is secondary to a systemic disease, such as diabetes mellitus, treatment involves a combination of the general principles and disease-specific management.