Hypertension and the kidney: pathogenesis Renin–angiotensin–aldosterone system activation and hypertension The renin–angiotensin–aldosterone system regulates both blood pressure and fluid status via vasoconstriction and the tubular reabsorption of sodium.This may increase their risk of cardiovascular morbidity.Treating those with IgA nephropathy with an angiotensin–receptor blocker reduced urinary angiotensinogen and angiotensin II levels, highlighting the role of the intrarenal renin–angiotensin–aldosterone system in the disease pathophysiology (Nishiyama et al, 2011).Angiotensin II binds to its receptor on vascular smooth muscle and proximal tubular cells leading to vasoconstriction and sodium reabsorption, which in turn leads to increased osmolality of the blood with consequent volume expansion and hence hypertension.In human cases of IgA nephropathy, studies have demonstrated that levels of urinary angiotensinogen and angiotensin II immunoreactivity are significantly higher in those with IgA in comparison to those with minor glomerular pathology (such as minimal change disease or persistent proteinuria).A Cochrane review of 21 studies of people with chronic kidney disease, which included seven dialysis studies and two studies in patients who had had kidney transplants, estimated that reducing salt intake by 4.2 g per day reduced systolic and diastolic blood pressure by −6.91 and −3.91 mmHg (95% confidence interval −8.82 to −4.99, and −4.80 to −3.02) (McMahon et al, 2021).Interestingly, in studies carried out in 501 people in the earlier stages of chronic kidney disease who were not yet undergoing dialysis, mean albuminuria (a recognised risk factor for progression of chronic kidney disease) was 36% lower in those with lower salt intake (95% confidence interval 26–44%) (McMahon et al, 2021).Nagai et al (2005) demonstrated that the renal injury seen in animal models of type 2 diabetes was associated with an increase in intrarenal levels of angiotensin II. The study also demonstrated that renal plasma levels of angiotensin II were already raised in animal models before the manifestations of type 2 diabetes.Reducing angiotensin II levels via treatment with either an angiotensin–converting enzyme inhibitor or angiotensin–receptor blocker during the prediabetic phase decreased the risk of diabetic kidney disease later in an animal's life, independent of its effects on blood pressure.Those with higher salt sensitivity have a higher incidence of hypertension (87.5% vs 50%) than those with low salt sensitivity (P=0.02), and also a higher glomerular filtration rate, suggesting altered tubular excretion of sodium (Barba et al, 2007).Although these were short-term data with a median study duration of 7 weeks, a significant reduction in the risk of progression of chronic kidney disease and associated cardiovascular events would be anticipated if these reductions could be maintained long term.Angiotensin II also increases sodium reabsorption in the distal nephron through the effect of aldosterone production from the adrenal gland.A meta-analysis including 34 trials involving 3230 participants showed that a modest reduction of salt (4.4 g/day) for four or more weeks leads to a significant fall in blood pressure in both hypertensive and normotensive participants.There is a higher prevalence of end organ damage such as left ventricular hypertrophy, concentric hypertrophy and hypertensive retinopathy in those with salt sensitivity in essential hypertension.Several studies have highlighted the role of activation of the renin–angiotensin–aldosterone system in the progression of underlying chronic kidney disease.The World Health Organisation recommendation is to limit sodium intake to 2 g/day (