cases of retroperitoneal fibrosis are secondary to specific causes, namely: drugs, infection, retroperitoneal haemorrhage and malignancy, while the other two-thirds of cases are considered idiopathic, as no specific causes can be identified.

The histological lesions of retroperitoneal fibrosis in patients with and without inflammatory aneurysm are not different and the suggested pathogenesis for the disease does not differentiate between the two forms. In fact, inflammation and autoimmunity have been advocated as the pathogenetic processes leading to idiopathic retroperitoneal fibrosis. Inflammation is well documented by the rise of inflammatory tests and by the presence of inflammatory cells sometimes associated with frank vascular lesions in the fibrotic tissue. The reported association of the disease with other autoimmune disorders suggests that idiopathic retroperitoneal fibrosis could be an immune-mediated disorder with marked inflammatory vascular traits. Parums et al. [1] postulated that the disease may be due to an immune reaction to some components of atherosclerotic plaques, i.e. ceroids, which are a complex of proteins and oxidized LDL. This hypothesis has been partially confirmed by the finding of antibodies directed against ceroid in the sera of patients with retroperitoneal fibrosis. However, the same antibodies have also been detected in the sera of healthy elderly subjects and in patients with atherosclerosis [1]. In fact, no clear differences in the severity of atherosclerosis have been demonstrated between patients with chronic periaortitis and controls [2] and this theory would not explain retroperitoneal fibrosis occurring in children and young people, who have no atheromatous arterial disease. Another possible pathogenetic hypothesis for chronic periaortitis suggests that vasa vasorum of the aortic adventitia could be the primum movens of chronic periaortitis, as demonstrated for other inflammatory aorta disorders and its main branches such as Takayasu arteritis, Behcet’s disease and aortitis associated with spondyloarthropaties [3]. As hypothesized by Numano et al. [4], regarding the above-mentioned diseases, vasa vasorum vasculitis of the aortic adventitia may trigger the recruitment of inflammatory cells in the aortic adventitia and in the retroperitoneum. The inflammatory process may progress from the adventitia to the media and the intima with consequent infiltration of lipids, blood cells and other blood material causing intimal changes similar to typical atherosclerotic lesions or inflammatory aneurysms. Our recent demonstration, that patients with active retroperitoneal fibrosis had a significantly increased number of circulating endothelial cells of microvascular origin with an activated phenotype (as evidenced by the surface expression of E-selectin), in comparison to healthy subjects and patients with diffuse atherosclerosis, would indicate that endothelial injury, as a part of immune-mediated inflammatory vascular damage, may play a key role in the pathogenesis of chronic periaortitis [5] and may support the above-mentioned pathogenetic hypothesis.

In conclusion, in our opinion, the retroperitoneal fibrosis observed in patients with and without inflammatory aneurysm could however be considered idiopathic.

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Association of low-grade urinary albumin excretion with left ventricular hypertrophy in the general population: a reply

Sir,

In their study of the relationship between urine albumin-to-creatinine ratio (UACR) and left ventricular hypertrophy (LVH) in the general population, Dr Lieb and colleagues [1] showed that the prevalence of LVH rose significantly with levels of urinary albumin excretion. While an observational study can only show association and not causation, the authors suggested that elevations in blood pressure may be the pathophysiological link between UACR and LVH.

We believe that the interaction of aldosterone and salt is another, equally plausible, ‘missing link’ in the physiology connecting albuminuria and LVH. Aldosterone plays an essential role in salt and water balance, by acting on epithelial mineralocorticoid receptors. Yet, aldosterone’s effects via mineralocorticoid receptors in non-epithelial tissues may play a more important role in the pathogenesis of chronic heart and kidney disease than its classical, epithelial effects. In animal models, administration of aldosterone with excess salt produces cardiac fibrosis and hypertrophy, independent of blood pressure, reflecting a direct effect of aldosterone on the heart [2,3]. Similarly, unopposed aldosterone in the presence of high salt intake causes increased glomerulosclerosis and severe proteinuria via non-epithelial, pro-fibrotic effects on the kidney [4–6]. These fibrotic effects of aldosterone physiologically explain recent clinical trials in which mineralocorticoid receptor blockers, such as eplerenone and spironolactone, have emerged as effective therapy for chronic heart and kidney disease [7–11]. These effects also may explain the important results of Dr Lieb and colleagues’ study, if albuminuria and LVH are truly linked by a common intermediary mechanism: mineralocorticoid receptor activation in the presence of high sodium cofactor.

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**Reply**

Sir,

We would like to thank Dr Bomback and Dr Klemmer for their interesting comments [1] on our recent paper [2]. Their mechanistic explanation for the association of low-grade albuminuria and LVH observed in a population-based sample, i.e. activation of the renin–angiotensin–aldosterone system with evolving renal damage, is quite plausible. Indeed, aldosterone has both myocardial and renal effects and plays important roles in the pathogenesis of both left ventricular hypertrophy and microalbuminuria. In support of the clinical and experimental data mentioned by Bomback and Klemmer, we recently demonstrated, in a population-based survey, that in particular serum aldosterone concentrations are associated with septal and posterior wall thickness in both women and men [3]. In addition, in women there was a strong association between serum aldosterone concentrations and echocardiographic indices of left ventricular mass, further underscoring the significance of aldosterone-related cardiac effects [3]. In the present independent community-based sample [2] however, serum markers of neurohormonal activity were not measured, and therefore not included in our statistical analyses.

**Conflict of interest statement.** None declared.

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**Lanthanum carbonate, body lanthanum accumulation and potential liver toxicity**

Sir,

We read with interest the article in the *Journal* by Ben-Dov et al. [1] and the accompanying Editorial by Cozzolino and Brancaccio [2], on possible effects of lanthanum carbonate on the liver. Ben-Dov et al. [1] reported that lanthanum (La) carbonate administration to uraemic rats for 4 weeks was not associated with signs of hepatotoxicity using light microscopy, magnetic resonance imaging and serum biochemistry methods. They were unable to confirm our previous finding of reduced liver weight [3]. They provided two different possible explanations for this discrepancy. First, they reasoned that we might have used an incorrect expression of liver weight [3]. They provided different possible explanations for this discrepancy.

First of all, we observed that the mean liver weight of non-uraemic rats given La carbonate for 4 weeks was significantly lower than that of uraemic rats given no La supplementation, the liver weight corrected for femur length or body weight. Second, they speculated that the rats of our study might have been exposed to heavy external La contamination, that is lower body weights in uraemic rats for 4 weeks was significantly lower than that of uraemic rats given no La supplementation, the liver weight corrected for femur length or body weight. They were unable to confirm our previous finding of reduced liver weight [3]. They provided two different possible explanations for this discrepancy. First, they reasoned that we might have used an incorrect expression of liver weight [3]. They provided two different possible explanations for this discrepancy.

We had already answered similar remarks, by other authors, in a previous correspondence in Kidney International [4–6]. Since the aforementioned authors are apparently not aware of our previous Letter-and-Reply exchange, we would like to clarify these points again.

First of all, we observed that the mean liver weight of uraemic rats given La carbonate for 4 weeks was significantly lower than that of uraemic rats given no La supplementation, the liver weight corrected for femur length or body weight. We provided this clarification after having done a reanalysis of our data in response to the comment by Rambeck [7], by proceeding to a formal comparison of liver weight after normalization for total body weight using ANOVA. This analysis showed a significant group effect for body weights, that is lower body weights in uraemic vs non-uraemic groups ($P < 0.001$), and also a significant treatment effect, that is lower body weights in La vs no La treatment ($P < 0.022$), with no interaction. Moreover, ANOVA also showed...