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 autoimmune phenomena 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 vasculitic 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 Takayas arteritis, Behcet’s disease and aortitis 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.

Conflict of interest statement. None declared.
Cardiac effects in the present independent community- and echocardiographic indices of left ventricular mass, strong association between serum aldosterone concentrations both women and men [3]. In addition, in women there was a association with septal and posterior wall thickness in a population-based survey, that in particular serum aldosterone concentrations are 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 a more sensitive expression of liver weight, namely corrected for femur length. Second, they speculated that the rats of our study might have been exposed to heavy external La contamination. 

First of all, we observed that the mean liver weight of uraemic rats given La carbonate for 4 weeks was apparently not aware of our previous Letter-and-Reply 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, be 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 rats given La carbonate for 4 weeks was significantly lower than that of uraemic rats given no La supplementation, be 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].

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, namely corrected for femur length. Second, they speculated that the rats of our study might have been exposed to heavy external La contamination. Cozzolino and Brancaccio [2] echoed these hypotheses in their Editorial.

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, be 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