ventricular mass index (LVMI)). When VEGF was added to the model, the moderate relationship between serum Ang-1 with total renal volume and LVMI was lost. Importantly, in our study there was no association between serum VEGF level and platelet counts in the autosomal dominant polycystic kidney disease (ADPKD) study subjects. Moreover, there were no significant differences between levels of serum VEGF measured in samples collected at baseline and after 18 months in 10 patients ruling out variable ex vivo platelet activation in our samples. Paired serum and plasma VEGF levels have previously been shown to correlate in control and colorectal cancer subjects. Both plasma and platelet levels of VEGF and Ang-1 are elevated in hypertensive subjects, thus indicating the apparent utility of measurement of both sera and plasma VEGF. Although we concur that our results do not permit us to comment upon the source of angiogenic growth factors, they do impart new information regarding the relationship of VEGF with renal and cardiac structure in ADPKD.


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Chronic renal failure induced by lead

To the Editor: We read with interest the review article by Evans and Elinder,1 who attempted to challenge the well-established fact that lead exposure causes chronic renal failure (CRF). Nevertheless, it seems that the authors missed some important facts when citing our studies.2–4 In the paper,1 the authors commented that the studies2–4 were limited by not measuring glomerular filtration rate (GFR) and not adjusting for confounding factors (acidosis, inflammation, and hyperparathyroidism). Furthermore, there is limited knowledge and lack of validation of ethylenediaminetetraacetic acid (EDTA) test among CRF patients. These interpretations are not entirely correct.

For example, we have reported3 that GFR improved significantly by the end of the 27th month in patients receiving EDTA chelation therapy. The mean change in GFR in the chelation group was 2.1 ± 5.7 ml/min, as compared with −6.0 ± 5.8 ml/min in the controls (P < 0.001). The rate of decline in GFR in the chelation group was also lower than that in the controls during the 24-month period of repeated chelation therapy or placebo. Anyway, we reckon that the studies2–4 were not adjusted for the above-mentioned confounders, but we wonder if the chronic kidney disease stage 3 of the studied population2–4 could cause any considerable acidosis, inflammation, or hyperparathyroidism. In contrast, advanced-stage chronic kidney disease or end-stage renal disease2 might be the exception. Literature data on the validation of the EDTA test among CRF patients are few, but we have demonstrated5 that repeated chelation therapy slowed the progression of renal insufficiency in non-diabetic patients with high normal-body lead burden.


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The Authors Reply: We are pleased that Lin et al.1 have read and commented on our mini review in Kidney International2 in which we challenge the often-repeated, but not very well-founded, view that exposure to lead may cause chronic renal failure (CRF) in adults. The finding of Lin et al. that repeated infusions of ethylenediaminetetraacetic acid (EDTA) in patients with reduced renal function (serum creatinine 1.5–3.9 mg/dl, estimated glomerular filtration rate (GFR) 18–56 ml/min per 1.73 m2) decrease the decline in estimated renal function compared with controls is remarkable, to say the least. We argue, however, that the GFR in these studies was not actually measured, but estimated from the serum creatinine concentration and creatinine clearance.
Serum creatinine is influenced by many factors besides the GFR. Although these studies show a beneficial effect from chelation therapy, it is not clear whether the positive effect is due to the lowering of body lead, chelation of other metals like cadmium with established nephrotoxic properties, or if EDTA merely affects the creatinine metabolism. The EDTA test was developed to detect excessive body lead, but has not been validated as a diagnostic test to establish different levels of body lead among patients with reduced GFR. Among patients with severe CRF, urinary excretion of the EDTA–lead complex is delayed up to 8 days, and the peak of the lead excretion is delayed even more in patients without previous known excessive exposure to lead. Furthermore, Lin et al. have demonstrated that inflammation is associated with blood lead levels among dialysis patients. It may well be that these associations also affect the lead levels in CRF patients, in whom both inflammation and chronic kidney disease-mineral–bone disorder are present early on in the course of the disease. We thus feel that the controlled studies by Lin et al. using EDTA chelation therapy are indeed interesting and should be repeated by others, but do not prove the causality between low-level lead exposure and CRF.


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