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An understanding of trace metal physiology as an aid to interpretation of clearance studies by artificial organs

Sir,
I would like to congratulate Dr Churchwell et al. for their efforts to improve our understanding of trace metal clearance by the Optiflux F-160 and CA-HP 170 artificial kidneys [1]. Their work adds significant data to this subject; however, allow me to add a cautionary note that an understanding of the physiology of these elements is essential to a true analysis of the meaning of their findings. Due to space limitations, I will confine my remarks to selenium which has been an area of interest of our group over the last 30 years [2–3], especially in renal failure [4–9]. While the transport mechanisms for selenium are similar to sulfur, once in the blood, selenium is thought to be usually initially bound electrostatically to albumin, before it becomes incorporated into globular protein [2,7]. Normally, the major excretion routes are either through the kidneys as trimethylselenonium or through the lungs as dimethylselenide. In haemodialysis patients, we have found that the α-2 globulin fraction is a major carrier and is often drawn into the clot [4], thus yielding lower serum values than plasma or whole blood, which investigators often mistakenly use interchangeably. Except for what I assume to be a typographical error where Dr Churchwell notes, ‘Plasma serum levels of trace elements likely differ...’ on page 2975, I find that she has admirably dealt with the discussion of her plasma samples. Unfortunately, she has not accounted for the different levels of binding proteins. Typically, patients in the intensive care unit are catabolic. If she re-examines her data, she would probably find that many of her study patients have low serum albumin and protein values, which would consequently result in a higher fraction of unbound selenium available for clearance through the kidneys at the time of her study. Since she notes that at least one of her patients was receiving MTE-5, that supplementation with less binding protein available would be at great risk for falsely elevating her loss into the dialysate. Selenium loss into the dialysate has not been observed with low-flux kidneys [9], and since protein loss is unmeasurable in unprocessed high-flux kidneys [10], one might hypothesize that the clearance found by Dr Churchwell is falsely elevated as a result of the supplementation of free unbound elements in the absence of a protein carrier.

Conflict of interest statement. None declared.

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Reply

Sir,
We thank Dr. Diskin for his kind remarks and are in agreement with his comments regarding our paper on trace element removal during continuous haemodialysis [1]. Reduction in plasma selenium concentrations due to tissue selenium redistribution may occur in critically ill patients, probably as a result of the systemic inflammatory response syndrome (SIRS) [2,3]. Furthermore, exposure of a renal failure patient’s blood to the dialysis membrane is another source of oxidative stress, potentially resulting in low serum selenium concentrations and reduced glutathione peroxidase activity [4].

As pointed out by Dr. Diskin, selenium concentrations in blood, plasma and serum are different, notwithstanding a typographical error on page 2975 of our paper, in the second paragraph of the Discussion section. The statement ‘Plasma serum concentrations of trace elements’ should read ‘Plasma concentrations of trace elements’. We measured plasma selenium concentrations in our study because these concentrations correlate with short-term selenium

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7. Diskin CJ. Does trace metal metabolism contribute to dialysis patient morbidity? Semin Dial 12; 18–20
8. Diskin CJ. Selenium binding proteins, renal failure, graft rejection and intimal hyperplasia: which are causes and which are effects? Am J Transplant 2005; 5: 2592

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