Introduction

The articles in this special issue of Nephrology Dialysis Transplantation were presented at a roundtable on risks related to metal absorption in patients with renal disease, held immediately after the ASN/ISN World Nephrology convention in San Francisco, California, October 17, 2001. The goal of this meeting was to present the state of the art on the causes and clinical consequences of exposure to various metals from environmental and medical (iatrogenic) sources. Some of the metals discussed are mainly toxic for the kidney, whereas others are toxic for other organs as well. Normally, the gastrointestinal tract is an effective barrier against the entry of toxic metals from the gut lumen into the organism, as is the skin against entry from the outside. However, in several disease states such as chronic renal failure or Alzheimer’s disease, this barrier may become more permeable, opening the way for potentially threatening states of metal overload.

The dramatic effects of enhanced gastrointestinal aluminium absorption, together with massive aluminium transfer from the dialysate to the bloodstream during the haemodialysis procedure, are still present in the memory of nephrologists who were caring for uraemic patients in the 1970s and 1980s. Although the possibility of aluminium intoxication had been evoked as early as 1970 [1], the toxicological proof for the involvement of this trace metal was provided 6 years later by the pioneering work of Alfrey et al. [2], well after the clinical description of dialysis-associated encephalopathy, osteomalacia and microcytic anaemia. Contaminated dialysis water was the major route of aluminium overload. However, serious intoxations have also been observed via the intestinal route, namely in uraemic patients not yet on dialysis and in dialysis patients treated with a dialysate with extremely low aluminium levels. The intestinal pathway was enhanced by the greater permeability of the gut to aluminium, and especially by the administration of massive oral doses of aluminium-containing phosphate binders given to uraemic patients for extremely long time periods.

Aluminium is not the only metal that may increase in plasma and tissues of uraemic patients or patients with Alzheimer’s disease, due either to enhanced entry via the gastrointestinal tract, transfer via the dialysis procedure, reduced elimination by the kidneys or a combination of these. Such metals include arsenic, cobalt, caesium, chromium, mercury, molybdenum, silicon and strontium, which all tend to increase in chronic renal failure. In contrast, other metals tend to decrease in chronic renal failure, including bromium, rubidium, selenium and zinc. To what extent long-term metal overload or deficiency may result in disease states of clinical significance, however, is not established with certainty in all instances.

Increased environmental exposure to other metals such as cadmium or lead may induce renal disease via direct or indirect toxic effects on the kidney. Yet other metals such as iron may not only be responsible for various pathological states subsequent to either iron overload or deficiency, but may also enhance or attenuate the toxicity of trace elements such as aluminium.

Massive exposure of end-stage renal disease patients to metals may occur inadvertently, as for instance via contaminated dialysis fluid, or due to increased permeability of the intestinal wall in conjunction with the intake of physiological amounts of a given metal. However, it may also occur due to the medical prescription of pharmacological doses, for example with aluminium-containing phosphate binders or intravenously administered iron.

The latter examples should incite us to exercise great caution whenever the administration of large amounts of novel metal-containing compounds is considered for therapeutic purposes. The long time spent between initial suspicion and final proof of the toxicity of pharmacological doses, as exemplified by the aluminium drama, should remain a permanent lesson to all those involved in the development of new metal compounds destined to be administered to uraemic patients in massive doses and over prolonged periods of time.

Tilman B. Drüke
Paris

References