## Abstract

Cyanobacteria are commonly-occurring contaminants of surface waters worldwide. Microcystins, potent hepatotoxins, are among the best characterized cyanotoxins. During November, 2001, a group of 44 hemodialysis patients were exposed to microcystins via contaminated dialysate. Serum microcystin concentrations were quantified with enzyme-linked immunosorbent assay which measures free serum microcystin LR equivalents (ME). We describe serum ME concentrations and biochemical outcomes among a subset of patients during 8 weeks following exposure. Thirteen patients were included; 6 were males, patients' median age was 45 years (range 16 - 80), one was seropositive for hepatitis B surface antigen. The median serum ME concentration was 0.33 ng/mL (range: <0.16 - 0.96). One hundred thirty nine blood samples were collected following exposure. Patients' biochemical outcomes varied, but overall indicated a mixed liver injury. Linear regression evaluated each patient's weekly mean biochemical outcome with their maximum serum ME concentration; a measure of the extrinsic pathway of clotting function, prothrombin time, was negatively and significantly associated with serum ME concentrations. This group of exposed patients' biochemical outcomes display evidence of a mixed liver injury temporally associated with microcystin exposure. Interpretation of biochemical outcomes are complicated by the study population's underlying chronic disease status. It is clear that dialysis patients are a distinct 'at risk' group for cyanotoxin exposures due to direct intravenous exposure to dialysate prepared from surface drinking water supplies. Careful monitoring and treatment of water supplies used to prepare dialysate is required to prevent future microcystin exposure events.

## Background

Warm, stable, eutrophic conditions favour growth of cyanobacteria in freshwater systems, and cyanobacteria are commonly-occurring contaminants of surface waters worldwide. The effects of climate change and global human population growth with resultant surface water quality degradation directly and indirectly support the increased occurrence of cyanobacteria and their toxins. Microcystins are one of the best characterized groups of cyanotoxins. They are low molecular weight hepatotoxic polypeptides of varying potency; the primary mode of action is as protein phosphatase inhibitors. Microcystins are well documented to cause wildlife and livestock mortality events, but documented human exposures are uncommonly reported.

End stage renal failure (ESRF) leaves affected patients with little or no kidney function. Hemodialysis is one method to partially replace kidney function and has proved to be an effective life prolonging treatment for ESRF patients worldwide. During hemodialysis treatment, a patient's blood is continuously extracted and flows through an extracorporeal dialyzer within which blood flows along a semi-permeable membrane; on the other side of the membrane is a prepared dialysate solution which is maintained at a lower hydrostatic and osmotic pressure. During the hours of hemodialysis treatment, excess intravascular fluid and endogenous toxic waste products such as urea and phosphate are removed from the patient's circulation. Cleansed blood is continuously returned to the patient's circulatory system. The frequency and length of treatment and the specific formulation of dialysate solution is part of a customized treatment regimen developed for each patient's needs (Himmelfarb and Alp Ikizler, 2010). A large volume of dialysate solution is required during each treatment session and is prepared from treated and sanitized fresh water. The semi-permeable membrane, the osmotic and the pressure