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Expired Breath Oxidant Activity during Haemodialysis

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Dear Sir,

Complement activation during haemodialysis with a cuprophan membrane produces a severe transient neutropenia caused by sequestration of activated neutrophils in the pulmonary microcirculation [1]. Coincident with this hypoxaemia develops, but the relationship of pulmonary leucosequestration to pulmonary dysfunction during haemodialysis is controversial [1]. Animal and in vitro experiments have suggested that pulmonary dysfunction during early haemodialysis is mediated by free radicals released from activated neutrophils within the pulmonary microcirculation [2–5]. However, in contrast to animal models of systemic complement activation [5], we have been unable to demonstrate increased free radical release during haemodialysis by measuring plasma free radical reaction products [6], and were unable to detect any evidence of haemodialysis-induced pulmonary vascular injury in vivo [7]. Hydrogen peroxide is a volatile oxygen species which is released (along with oxygen radicals) by activated neutrophils, and can enter the gas phase at physiological temperatures. Spontaneous chemiluminescence in human breath has been shown to correlate with hydrogen peroxide content [8], and in the adult respiratory distress syndrome (ARDS), a condition in which free radicals released from activated neutrophils are thought to be important in the pathogenesis of pulmonary injury, an increased concentration of hydrogen peroxide in expired breath condensate has been reported [9]. Plasma free radical reaction products are not increased in patients with ARDS [10], suggesting that breath hydrogen peroxide content is a more sensitive index of oxygen radical generation in the lung. We therefore investigated the effect of haemodialysis on expired breath hydrogen peroxide concentration.

Five patients with end-stage renal failure (aged 34–60 years) were studied during a routine haemodialysis session with a cuprophan membrane (Lundia Plate, Gambro, Sweden). Breath condensate was collected before and serially during the first 2 h of haemodialysis, by passing expired breath through an 80-cm plastic tubing (internal diameter 15 mm) submerged in an ice-water bath. Expired air was collected until about 1 ml of breath condensate had pooled in the tubing, which was usually accomplished within 10 min. Hydrogen peroxide was measured in the condensate by the scopoletin/horseradish peroxidase method [11]. Studies in normal subjects demonstrated that hydrogen peroxide concentration in the breath condensate remained constant over a 2-hour period and was not affected by changes in respiratory rate or rhythm. Serial measurements of neutrophil count and arterial oxigen tension during haemodialysis were also performed.

Mean ($\pm$SD) circulating neutrophil count fell from $3.6 \pm 0.9 \times 10^9$ before dialysis to $1.2 \pm 0.9 \times 10^9$ at 15 min ($p < 0.01$), and had recovered by 60 min ($3.9 \pm 1.6 \times 10^9$). Mean arterial pO_2 fell from 100 ± 7 mm Hg at $t = 0$ to 78 ± 12 mm Hg at 30 min of haemodialysis ($p < 0.05$) and hypoxaemia persisted throughout the first 2 h of haemodialysis (arterial pO_2 was 85 ± 16 and 81 ± 18 mm Hg at 60 and 120 min respectively). Despite the development of significant neutropenia and hypoxaemia during haemodialysis, there was no significant change in breath hydrogen peroxide levels during the first 2 h of haemodialysis (at 0 min 0.43 ± 0.26 μmol/l, at 15 min 0.48 ± 0.28 μmol/l, at 60 min 0.49 ± 0.28 μmol/l, at 120 min 0.47 ± 0.33 μmol/l. Hydrogen peroxide concentrations in breath condensate from the dialysis patients were similar to those from normal subjects.

Our results do not suggest an important role for free radical-mediated pulmonary injury in the pathogenesis of haemodialysis-induced hypoxaemia. Although this conclusion appears to be at variance with the results of animal models of systemic complement activation [4, 5], it

is compatible with the results from clinical studies of pulmonary dysfunction during haemodialysis [12]. Activated complement components, rather than free radicals, may produce transient pulmonary hypertension and hypoxaemia during haemodialysis [1]. Indeed, if significant free radical-induced pulmonary injury did occur during haemodialysis, it might be expected that lung disease from repeated pulmonary leucosequestration would be a recognised complication of long-term haemodialysis. However, such an effect has not been documented.

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