The blood of normal human subjects contains 10 - 20 μg Pb/100 ml (equivalent to 0.5 - 1 μmol/l). The blood levels are higher in Pb poisoning. Haematological and neurological symptoms appear when blood Pb is in the range 5 - 10 μmol/l. (Hernberg, 1980). Nearly all the Pb in the blood is in the red cell fraction: the percentage of Pb in serum rises from about 1% when the blood Pb content is 1 μmol/l. to 2% at 7 μmol/l. (Manton & Cook, 1984). The aim of the present research is to understand the factors that determine the distribution of Pb across the erythrocyte membrane, under physiological and pathological conditions, when the erythrocyte Pb content is in the range 1 - 20 μmol/l.cells, and the serum Pb concentration is in the range 5 - 200 nmol/l.

Earlier studies have shown that there are two main pathways for Pb2+ movement across the erythrocyte membrane (Fig. 1). When erythrocytes are suspended in Pb-buffered media containing 10^-8 to 10^-6 M Pb2+, Pb2+ uptake is HCO3-- and Cl--dependent, and DIDS-sensitive (Simons, 1986a). The anion exchanger is implicated in Pb uptake, and appears to catalyse an exchange of PbCO3Cl- for Cl- (Simons, 1986b). Binding by the erythrocyte membrane is negligible, compared with uptake into the cytoplasm (Simons, 1986a). Pb2+ efflux can occur passively, catalysed by the anion exchanger, but is also brought about by an ATP-dependent and vanadate-sensitive pathway. This pathway has been characterised in experiments with resealed ghosts (Simons, 1988). It was shown that Pb efflux occurs against a concentration gradient for Pb2+, and has a Vmax of 14 mmol/(l.cells x hr) and Km of 5 x 10^-8 M intracellular Pb2+ (Fig. 2). The IC50S for vanadate inhibition of Ca2+ efflux and Pb2+ efflux are the same. Intracellular Ca2+ inhibits Pb2+ efflux, but is
Figure 1 Pb²⁺ can cross the erythrocyte membrane by two pathways. The anion exchanger allows bidirectional movement by exchange of PbCO₃Cl⁻ for Cl⁻ (inwards Pb²⁺ movement shown for convenience). The Ca²⁺ pump catalyzes ATP-dependent extrusion of Pb²⁺, which can occur against an electrochemical gradient.

Figure 2 Variation of lead efflux rate with Pb²⁺ concentration. Each point gives the initial rate of efflux, ± S.D., plotted against the initial Pb²⁺ concentration. The line is a rectangular hyperbola, and corresponds to a Vₘₐₓ of 230 ± 14 µmol/(l.cells.min) and a Kₘ of 47 ± 8 nM Pb²⁺. Taken, with permission, from Simons (1988).