Description for a problem studied at the Canadian Math-in-Medicine Study Group Toronto 2009
< http://www.maths-in-medicine.org/canada/2009/hemodialysis/ >

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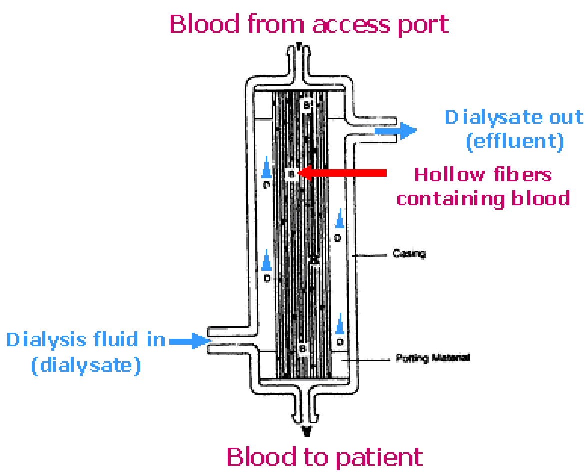
Background



The figure on the left is a schematic of a dialysis cartridge. Blood (red) enters the dialysis filter from the top, and then travels inside of thousands of parallel hollow fibers. Dialysate fluid (blue) bathes the outside of the hollow fibers and is pumped from the bottom to the top. By means of convection and diffusion, plasma water and solutes leave the inside of the hollow fibers and enter the stream of dialysate fluid space (encased by glass) that exits through the bottom left port. The figure on the right is a dialysis cartridge that has been partially opened for demonstration purposes.

One of the major functions of the kidney is the removal from the circulation of toxic compounds and the maintenance of water and salt balance. Kidney function can be replaced in patients with kidney failure by hemodialysis, an extracorporeal procedure in which blood passes through thousands of hollow fibers made of a semipermeable membrane bathed by a balanced electrolyte solution ("dialysate"). Solutes are cleared through the membrane from the blood to the dialysate, and its concentration varies by both diffusion and convection processes. The hemodialysis procedure thereby allows diffusive clearance of solutes as well as convective clearance of water and solutes to extend life in patients with kidney failure.

The most abundant cation in human extracellular fluid is sodium. Plasma volume is closely related to the regulation of sodium balance. Maintenance of plasma osmolarity and [Na^+] within tight boundaries is a hallmark of all terrestrial mammals.[1] [Na^+] affect the three-dimensional conformations of proteins and enzymes, and play a critical role in maintaining electrical gradients across cell membranes, in nerve-impulse transmission, and in muscle excitation.[2]

In patients treated with hemodialysis, daily water and solute balance is controlled entirely by the dialysis procedure, which is done every other day for approximately 4 hours per session. All water and salt ingested in the 44h preceding dialysis must be removed in a 4h dialysis session. To accomplish this, physicians prescribe the following: blood flow rate, dialysate flow rate (which runs counter-current to blood to maximize diffusive clearance), amount of volume to remove (ultrafiltration), and the dialysate composition of sodium, potassium and bicarbonate. Each of these variables affects the sodium flux during hemodialysis. Most physicians utilize a standard dialysis solution containing 140 meq/L of sodium, 2 to 4 meq/L of potassium, and 35 meq/L of bicarbonate. Interestingly, the sodium concentration of dialysate is fixed, irrespective of an individual patient's pre-dialysis sodium concentration and weight. Sodium flux during dialysis is critically important: excessive removal of sodium can lead to life-threatening drops in blood pressure, while insufficient removal of sodium can lead to severe hypertension and post-dialysis thirst.

Sodium flux during hemodialysis is of significant clinical importance and lends itself to quantitative analysis and modeling. The goal of this project is to develop a mathematical simulation of sodium flux during hemodialysis, with the long-term goal of developing a clinical calculator that enables physicians to prescribe individualized sodium dialysate prescriptions in order to improve the safety of the dialysis procedure.

Previous attempts at modeling sodium flux during hemodialysis have not adequately considered the following physiological considerations:

a) The co-occurrence of convection and diffusion of sodium in the blood and the dialysate, and how they interact through the fiber membrane
b) The Gibbs-Donnan effect[3]
c) Dynamic changes in a patient's plasma water sodium concentration due to osmotic shifts and potassium flux across the interstitial fluid, extracellular fluid, and intracellular fluid compartments.

Specfic Goals

- Develop a mathematical model of sodium flux that takes into account convection, diffusion, as well as intercompartmental transfer (extra-, intracellular, and interstitial) of water and salt in the body, such as the Gibbs-Donnan effect
- In a patient with a given pre-dialysis sodium concentration, potassium concentration, and extracellular fluid volume, determine the dialysate sodium concentration and ultrafiltration rate needed to achieve metabolic goals (fluid and salt removal)

References

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4. Kurtz I, Nguyen MK. Evolving concepts in the quantitative analysis of the determinants of the plasma water sodium concentration and the pathophysiology and treatment of the dysnatremias. *Kidney Int.* Nov 2005;68(5):1982-1993.
5. Sternby JP, Nilsson A, Garred LJ. Diffusive-convective mass transfer rates for solutes present on both sides of a dialyzer membrane. *Asaio J.* May-Jun 2005;51(3):246-251.