

## Short Communication

# The energy cost of kidney proton dialysis in sickle cell anaemia

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Accepted 10 April, 2018

The acidosis known to be associated with sickle cell anaemia is exploited in this work to estimate its energy cost to the kidney that has to dialyse the excess protons from the blood into urine against a concentration gradient, thereby doing significant extra work. The mean blood and urine pHs measured for the four discrete sickle cell states (42 subjects with approximately equal numbers of males and females per group, to minimise sex bias) are: HbAA =  $7.39 \pm 0.07$  and  $6.54 \pm 0.15$ , HbAS =  $7.35 \pm 0.09$  and  $6.44 \pm 0.15$ , HbSS =  $7.32 \pm 0.08$  and  $5.89 \pm 0.39$ , HbSS-crisis =  $7.15 \pm 0.12$  and  $4.75 \pm 0.46$ , respectively. From these data, the estimated enthalpies of dialysis,  $\Delta H_d$ , for each of the four states are: HbAA =  $1.96RT$  4.94 kJ, HbAS =  $2.10RT$  5.29 kJ, HbSS =  $3.29RT$  8.29 kJ, and HbSS-crisis =  $5.53RT$  13.93 kJ. The estimated entropies of dialysis,  $T\Delta S_d$ , compared to the normal HbAA state are: HbAA =  $0.00RT$  0.00 kJ; HbAS =  $0.14RT$  0.35 kJ, HbSS =  $1.34RT$  3.38 kJ and HbSS-crisis =  $3.57RT$  8.99 kJ ( $R = 8.31J\cdot mol^{-1} K^{-1}$  and  $T = 303K$ ). The conclusion from this work is that sickle cell disease is very energy costly to the kidney as most of the energy for proton dialysis is wasted as a result of high entropy.

**Key words:** Sickle cell, anaemia, energy, kidney, dialysis, proton, and enthalpy

## INTRODUCTION

Evidence exists that for those with sickle cell syndromes “kidney damage starts very early and progresses throughout life” (Rossi-Espagnet et al., 1968; Eckman and Platt, 1991; Saborio and Scheinman, 1999). This statement is consistent with the observed renal insufficiency in those with sickle cell anaemia (Karayakin, 1979). A major function of the kidney is the dialysis of protons or hydrogen ions,  $H^+$ , from the blood into urine. This dialysis is done against a significant concentration gradient from the ordinarily alkaline blood of  $[H^+] = 10^{-7.4} mol\cdot L^{-1}$  (pH = 7.4) into acidic urine of  $[H^+] = 10^{-6.6} mol\cdot L^{-1}$  (pH = 6.6). This implies an “active transport” mechanism and significant energy expenditure (Guyton and Hall, 2000). Those with sickle cell disease (SCD) are known to suffer blood acidosis, particularly lactic acidosis (Neely et al., 1969; Freund et al., 1992; Alphonse et al., 1998). This would change the hydroxyl ( $OH^-$ ) to proton ( $H^+$ ) ratio in blood away from 6:1 at pH 7.4, which is consistent with the known efficient octahedral charge- packing arrangement that has six protons at the vertices of an octahedron and a stabilizing hydroxyl counter-ion at the octahedral hole, which accounts for blood pH stability (Osuagwu, 2004). Any pH shift from blood pH of 7.4 will mean a shift

from most efficient and stable octahedron to some other less efficient and stable arrangement (Fuller, 1975). This implies increased disorder or entropy compared to the normal state. To maintain this ideal structure, the blood behaves in such a way that when blood and body fluids become too acidic or alkaline urine acidity is altered to restore balance (Smith, 1995). This is achieved by increase or decrease in the rate of proton excretion from the blood into the urine. This work notes that protons in blood and urine are maintained in dynamic, steady-state, equilibrium across the semi-permeable kidney membrane system. The relative proton,  $H^+$ , concentrations in blood and urine across the kidney, makes it possible to calculate the enthalpy of dialysis,  $\Delta H_d$ , for the extraction of protons from blood into urine. Using the urine to blood proton ratio,  $K_O$ , in HbAA as normal and, therefore, reference, the entropy change  $T\Delta S_d$  for HbAS, HbSS and HbSS-crisis disease states are calculated. Part of the entropy cost comes from the fact that extraction of energy from ATP decreases as the acidity of the medium moves away from physiological pH, 7.4. Decreasing efficiency of the enzyme ATPase involved in ATP metabolism contributes to this, for instance (Bronk, 1973).

**Table 1.** Blood and urine pHs in sickle cell states.

Genotype/State	n	Blood pH	Urine pH
HbAA = 0	42	7.39 ± 0.07	6.54 ± 0.15
HbAS = 1	42	7.35 ± 0.09	6.44 ± 3.15
HbSS = 2	42	7.32 ± 0.08	5.89 ± 0.39
HbSS-crisis = 3	42	7.15 ± 0.12	4.75 ± 0.46

**Table 2.** Estimates of the energy of proton dialysis in different sickle cell states.

Sickle cell genotype	AA	AS	SS-steady state	SS-crisis
Sickle cell state	0	1	2	3
[H <sup>+</sup> ], urine, mol- L <sup>-1</sup>	10 <sup>-6.54</sup>	10 <sup>-6.44</sup>	10 <sup>-5.89</sup>	10 <sup>-4.75</sup>
[H <sup>+</sup> ], blood, mol-L <sup>-1</sup>	10 <sup>-7.39</sup>	10 <sup>-7.35</sup>	10 <sup>-7.32</sup>	10 <sup>-7.15</sup>
[H <sup>+</sup> ] urine/ [H <sup>+</sup> ] blood, K.	K <sub>0</sub> 7.08	K <sub>1</sub> 8.13	K <sub>2</sub> 26.92	K <sub>3</sub> 251.19
RELATIVE CONCENTRATION GRADIENTS, K <sub>n</sub> /K <sub>0</sub>	1.00	1.15	3.80	35.48
H <sub>d</sub> , RT	1.96	2.10	3.29	5.53
H <sub>d</sub> , kJ	4.94	5.29	8.29	13.93
H <sub>d</sub> , Ratios	1.00	1.07	1.68	2.82
T S <sub>d</sub> , RT	0.00	0.14	1.34	3.57
T S <sub>d</sub> , kJ	0.00	0.35	3.38	8.99
T S <sub>d</sub> , Ratios	-	1.00	9.57	25.50

## MATERIALS AND METHOD

A total of 168 subjects (roughly equal numbers of males and females to minimise sex bias) were involved in this study. The subjects were patients of the Federal Medical Centre (F.M.C) and some private Clinics in Owerri, Imo State, Nigeria and volunteers. There were four groups of 42 subjects each for HbAA, HbAS, HbSS and HbSS-crisis states. The genotype of each subject was confirmed by electrophoresis.

5 cm<sup>3</sup> of venous blood was drawn from each subject with disposable syringe and quickly transferred into a tube with anticoagulant (disodium EDTA). The pH of the blood was determined as quickly as possible with an EI 1182 pH-meter. 5 cm<sup>3</sup> of urine was collected from each subject and the pH determined on the spot, to avoid alterations due to CO<sub>2</sub> evaporation, which would alter the pH of the fluid, overtime.

## RESULTS AND DISCUSSION

Table 1 shows the summary of the results of the pH determinations. For analytical purposes, the HbAA State is assigned an ordinal position of 0, HbAS = 1, HbSS = 2, HbSS crisis = 3, reflecting relative manifestations of the disease.

From Table 2, the relative energy cost, H<sub>d</sub>, of kidney proton dialysis in the different sickle-cell states are shown to be significantly different. The energy cost increases exponentially with the intensity of the sickle cell state / factor (r = 0.9589, p < 0.05). And so does the estimated associated potential disorder in the system, as indicated by the differences in the energy of entropy, T S<sub>d</sub>. This suggests that the better management of acidosis in sickle-cell disease would be of significant benefit to the

kidney of the sufferer. This is because an overworked kidney, that is at the same time exposed to the kind of oxidant stress that the proton, H<sup>+</sup>, can bring about, is likely to become, sooner or later, distressed. Blood alkalanization, particularly through dietary means, should be made part of the management strategy for sickle cell disease. Rou-tine blood and urine pH monitoring should, also, be made part of sickle-cell management regime, particularly with respect to the obviation of crisis, as very low pH is associated with high entropy and the crisis state as seen from the tables above.

This investigation would help explain observed kidney complications and higher than expected kidney failure rate in sicklers. Treatments that systematically reduce acidosis in sicklers would significantly conserve metabolic energy as well as protect the kidney from disruptive over-work and potential failure. Because the proton or hydrogen ion, H<sup>+</sup>, is the ultimate residue of energy nutrient metabolism in the body, this work represents, in an approximate way, a summary of the energetics of sickle cell disease in the kidney.

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