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# Dermodialysis – Could sweating treatments for chronic renal failure substantially and feasibly improve outcomes in developing and even developed world contexts?

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## ABSTRACT

**In end-stage kidney disease, in the absence of renal replacement therapies such as hemodialysis and continuous peritoneal dialysis, there are high enough amounts of urea and other molecules transferred from the bloodstream into perspiration/sweat for them to crystalize out and deposit on the skin as 'uremic frost'.**

**The use of sweating as the vehicle for removing from the body molecules normally removed in the urine was identified some decades ago, with successes such as reducing blood urea concentrations from 105 to 75 mg/dl over 7 days with little suggestion of a plateau having been reached at the end of the experiment then, eliminating uremic pruritis, and achieving compliance with fluid intake restrictions and the resultant optimization of blood pressure. However, the evolution of hemodialysis and peritoneal dialysis displaced interest in exploring sweating methods properly.**

**There are large fractions of the population of the Developing World that do not have access to hemodialysis or peritoneal dialysis, and where even diagnosed chronic renal failure goes untreated until the concomitant early death results.**

**The hypothesis of this paper is that the use of dermodialytic methodologies involving the use of personal environmental control of temperature and humidity (and incorporating special clothing and/or chambers) in conjunction with low-intensity moderate-duration physical exercise, to stimulate sweating and remove that sweat, would clearly be substantially beneficial to not only the many chronic renal failure patients in the Developing World who would otherwise have no treatment at all, but also to those in the Developed World by way of delaying or reducing the need for hemodialysis or peritoneal dialysis, or even merely by improving the inherent shortcomings of these treatments. The dermodialytic clothing and chambers required are described in some preliminary detail and could be provided at relatively very low and very affordable financial cost, and be suitably sustainable regards maintenance in even very technologically and logistically challenged demographic situations.**

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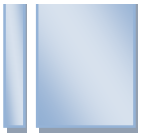
## GENERAL CONCEPT AND GLOBAL APPLICABILITY OF DERMODIALYSIS

### Uremic frost

In end-stage kidney disease, in the absence of renal replacement therapies such as hemodialysis and continuous peritoneal dialysis, there is high enough urea (and other molecules) transferred from the bloodstream into perspiration/sweat for it to crystalize out and deposit visibly ('uremic frost') on the skin when the water of the perspiration/sweat evaporates off.[1] This raises the question of to what clinically useful extent, in what stages of renal failure,



in what populations, use could be made of removing molecules normally removed from the body via the urine, via the skin, in the treatment of chronic renal failure (CRF).

**Sweat, dermodialysis, the Developing and Developed World**

The general concept of using sweat as the vehicle for removing from the body molecules normally removed in the urine was identified some decades ago,[2, 3], but the evolution of hemodialysis (HD) and peritoneal dialysis (PD) displaced interest in exploring it properly – it is proposed here that it remains a very suitable concept for exploration towards developing dermodialysis (DD) treatments as valuable preludes to and replacement for earlier-stage CRF HD and PD, and as an adjunct therapy for reducing the frequency of requirement for HD or PD, or for improving outcomes even where HD or PD frequency is not reduced, in later-stage CRF. However, the potential applicability is greatest in the Developing World where economic, logistical and technical support barriers to the provision of HD or PD are such that commonly more than half of those requiring renal replacement therapies for CRF are not able to access/afford them and are instead left to die of their condition.[4 – 12]

Due to combinations of endemic infectious and toxicological causes and greatly increased and increasing prevalence of type 2 diabetes due to overeating and under-exercise probably in interaction with epigenetic effects from earlier undernutrition.[6, 7, 8, 9, 12, 13] The prevalence of chronic renal failure in the Developing World has in many populations overtaken the prevalence in countries of the Developed World.[9, 13] However, the application also has substantial potential usefulness in the Developed World.

## COMPOSITION OF NORMAL HUMAN URINE

Normal urine contains many solutes (totaling some 42,000 mg/L),[14, 15] destined for removal therein from the body, including both frank wastes/toxins and other things normally kept in some balance in the body by that removal, and other things the removal of which is of unknown benefit. The recently orthodox lore that molecules of molecular weight (MW) less than 7,000 are freely filtered through the glomerulus and into the lumen of Bowman's capsule, whereas larger molecules (e.g. myoglobin at MW 17,000) are filtered less and less freely up to a molecular weight of 70,000 (e.g. albumin) where filtration is effectively nil[16] must be modified in the light of more recent work in urinary proteomics showing that normal urine contains hundreds of different proteins (or parts thereof) in the range of molecular weight 50,000 – 150,000[17] and 2,500 proteins or polypeptides in all.[18]

Table I below is a summary of major groups of urine solutes with their approximate concentration (in mg/L) in normal urine[14] with their molecular weight (rounded off) given also.

**Table 1 Composition of Normal Human Urine, Adapted from Putnam (1971)[14]**

| Molecule | Molecular Weight | mg per Litre |
|---|---|---|
| UREA | 60 | 13,000 |
| INORGANIC SALTS | - | 14,000 total |
| Sodium Chloride | 58 | 8,000 |
| Potassium Chloride | 75 | 1,600 |
| Potassium Sulfate | 170 | 2,600 |
| Magnesium Sulfate | 120 | 780 |
| Magnesium Carbonate | 84 | 140 |
| Potassium Bicarbonate | 100 | 660 |
| Potassium Phosphate | 210 | 230 |
| Calcium Phosphate | 310 | 60 |
| ORGANIC AMMONIUM SALTS | | 4,100 total |

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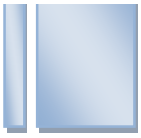


| | | |
|---|---|---|
| Ammonium Hippoate | 200 | 1,200 |
| Ammonium Citrate | 230 | 760 |
| Ammonium Glucuronate | 210 | 660 |
| Ammonium Urate | 190 | 520 |
| Ammonium Lactate | 130 | 390 |
| Ammonium L-Glutamate | 160 | 250 |
| Ammonium Aspartate | 150 | 130 |
| Ammonium Formate | 60 | 90 |
| Ammonium Pyruvate | 90 | 44 |
| Ammonium oxalate | 120 | 37 |
| ORGANIC COMPOUNDS | - | 5,400 total |
| Creatinine | 110 | 1,500 |
| Uropepsin (10-100 times the conc. in serum) | 35,000 | 380 |
| Creatine | 150 | 370 |
| Glycine | 75 | 320 |
| Phenol | 95 | 290 |
| Histidine | 160 | 230 |
| Androsterone | 290 | 170 |
| 1-Methylhistidine | 170 | 170 |
| Imidazole | 70 | 140 |
| Glucose | 390 | 160 |
| Taurine | 130 | 140 |
| Cystine | 240 | 100 |
| Citrulline | 180 | 90 |
| Aminoisobutyric acid | 100 | 85 |
| Threonine | 120 | 85 |
| Lysine | 150 | 75 |
| Indoxylsulfuric acid | 230 | 75 |
| m-hydroxyhippuric acid | 200 | 70 |
| p-hydroxyphenyl-hydrocrylic acid | 180 | 70 |
| Inositol | 180 | 70 |
| Urobilin | 590 | 65 |
| Tyrosine | 180 | 55 |
| Asparagine | 130 | 55 |
| PROTEINS (more than 2,000 different proteins) | Up to 200,000D | 5,000 (roughly) |
| TOTAL SOLUTES | | 42,000 (roughly) |

Which of the normal urine proteins are actually needed to be removed from the blood at the rate that they are (or at all) for an acceptably normal physiology and biochemistry to be had, is not yet fully known, but beta-2-microglobulin (molecular weight 11,600) accumulation over 5-7 years of hemodialysis treatment (particularly with earlier, smaller-pore, equipment that would not filter the molecule from the blood) has been found to be associated with various pathologies including: carpal tunnel syndrome, bone cysts and spondyloarthropathy of joints via deposition of this amyloid protein therein.[19] Of particular relevance to the topic of the possible usefulness of dermodialysis in the treatment of CRF are the potential limitations of molecular size (particularly regards proteins, but also other molecules), in conjunction with molecular shape, electrical charge, and ligand status, in the transfer of blood solutes into sweat.

## COMPOSITION AND LOCALIZATION OF NORMAL HUMAN SWEAT

Now, the composition of "normal" sweat (which almost certainly varies substantially as a function of diet) has been reported to include sodium chloride (which may increase fourfold in concentration with continued sweating), potassium chloride (the increase in concentration with continued sweating not being sustained for as long as that of sodium chloride), hydrogen ions (pH very roughly 6.5), urea (which bacteria break down over time into ammonia(ium), both these having a roughly six-fold variation in concentration), uric acid, lactic acid, glucose, and amino acids (as such and also as polypeptides including proteins).[20]

### Sweating, nitrogen loss and nitrogen balance

Of interest in this regard is the reported increase in nitrogen loss from the body due to sweating, which is substantial enough to require accounting for in nitrogen balance studies. Young men in a vigorous physical conditioning program lost in sweat 1.7 g of N (commensurate with 10.5 g protein) per day on a protein intake of 1.4 g/kg body weight (~100 g protein/d for a 70 kg man), and 2.7 g of N (commensurate with 17 g protein) per day on a protein intake of 2.8 g/kg body weight (~200 g protein/d for a 70 kg man).[21] Both experimental protein intakes were excessive of physiological requirements. This report is consistent with earlier work and reviewing of work, where figures for normal sweat nitrogen ranged from 21 to 130 mg/ 100 ml of sweat,[22 – 24] which figures are commensurate with 0.7 to 4 g of protein for 500 ml of sweat.

### Sweat minerals

More than half a century ago it was reported as being established that normal sweat contained all of the minerals found in the blood, though consensus in quantifications, and on factors affecting variability in these, was lacking. In an experiment with male adult subjects exposed to controlled conditions ('comfortable': 27-28C, relative humidity 43-45%; 'hot, humid': 37-39C, relative humidity 65-73%), loss in body weight attributable to loss of water via the skin was very variable, but averages were 117 g/h under comfortable conditions and 720 g/h under hot humid conditions, the subjects being at rest under all conditions.[25]

Scaling up their earlier results for the hot, humid condition to apply them to 500 ml of sweat (roughly of a potentially clinically relevant magnitude) gives averages of losses in that volume of sweat of: copper, 30 ug, ~1/30 of Recommended Dietary Intake (RDI); manganese, 30 ug, ~1/75 of RDI; magnesium, 0.5 mg, ~0.1% of RDI; calcium, 10 mg, ~1% of RDI; phosphorus, 0.12 mg, ~.01% of RDI.[25] Some of their later results for the hot, humid environment, likewise scaled up for 500 ml of sweat, include losses in that volume of sweat of: calcium, 20 mg, ~2% of RDI (and that the concentration decreased to very roughly 1/4 and less of that after the first 700 ml of sweat had been shed in the first hour); phosphorus, 0.3 mg, ~ .03% of RDI.[25] Other of their later results include that iron (though the subjects received a 25 mg supplement of iron chloride, roughly twice the RDI) was lost in sweat at 10 mg (~5/6 of RDI) over a 7.5 h hot, humid (sedentary) environmental treatment period.[25]

### Sweat protein and nitrogen

It is not known what proportion of the protein composition of normal sweat is due to protein molecules diffusing from the plasma into sweat, nor what proportion is due to active secretion by either sweat glands or sebaceous glands (such as surfactant and antimicrobial proteins), as distinct to what protein (and other) molecules are present in sweat simply from the break-up of the outermost layer of the dermis. In lieu of data for proteins or polypeptides removed from the body in sweat we have only the data for amino acids, which might include proteins and polypeptides.

More than half a century ago it was reported that normal sweat had averages (scaled up here for 500 ml of sweat from the original data for 100 ml of sweat) of: 27 mg of ammonia-nitrogen, 100 mg of urea-nitrogen, 29 mg of amino acid-nitrogen (all together commensurate with only 1 g of protein, physical exercise therefore apparently not having been applied here), 80 mg of glucose, and 1.6 g of NaCl.[20] It was noted that 30 g of urea are eliminated in the urine in 24 h, and that without physical exercise and

attendant sweating only 0.1 g of urea would be eliminated by the skin, and about 1 g of urea eliminated in the case of substantial physical exercise being applied.[20] Obviously these figures for sweat urea are not consistent with those given by Mitchel and Hamilton above[25] in their later and more focally comprehensive work, and also, the amount of nitrogenous waste produced in the body will be greatly dependent on dietary protein consumption.

The sweat of horses is noted to include two main polypeptides of MW 33,000 and 49,000[26] and normal human sweat includes proteins active in immunological defense and others with surfactant activity.[27]

**Sweat and illicit drugs**

Sweat has been used in police work as a source of identifiable and assayable molecules of interest, including amphetamines (MW ~ 135), and opioids, cocaine and cannabinoids and their metabolites (MW ~ 300), and the stratum corneum has been noted to be a temporary reservoir for these molecules, where their concentrations may exceed their concentrations in urine, the molecules coming through into the sweat via diffusion and secretion after as little time as several hours from a dose being given.[28, 29]

Sweating as a function of physical exercise, environmental climate, and altitude

The amount of urea removed in the sweat resulting from vigorous physical exercise is reported to be roughly 10 times that amount removed in the basal insensible loss of 600-700 ml of sweat in 24 hours.[20] There have been differences reported in the composition of sweat resulting from running exercise and thermal exposure: higher NaCl, and lower urea and creatinine in running sweat, whereas sweat potassium did not differ between conditions.[30] At 30 C and 50% relative humidity, changes in air pressure and air oxygen concentration such as occur between elevations of near-sea-level and 3,200 m did not result in changes in sweat rates due to physical exercise, though cutaneous vasodilation was reduced at the higher altitude.[31]

**Skin body region and sweating rates**

In male athletes in an environment at 25C and 50% relative humidity, at exercise intensities of 55% and 75% $VO_2$ max, the highest sweat rates were observed on the central and lower back, though this area does not have the highest regional skin temperature nor the highest regional sweat gland density.[32]

## PROPORTIONS OF NORMAL ELIMINATION VIA SWEAT, URINE AND FECES

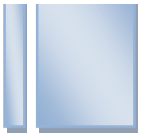
It needs be kept in mind that loss in the feces is a major route of elimination of these and other elements/molecules, and the following data are important here.

During the 7.5 h of hot, humid (sedentary) treatment periods calcium was excreted 30% in sweat, 12% in urine, and 58% in feces; and during the whole days of comfortable treatment periods calcium was excreted 14% in sweat, 21% in urine, and 65% in feces; during the 7.5 h hot, humid (sedentary) treatment periods iron was excreted 37% in sweat, 1% in urine, and 62% in feces; and during the whole days of comfortable treatment periods iron was excreted 13% in sweat, 2% in urine, and 84% in feces.[25]

The loss of nitrogen in sweat in the 7.5 h of hot, humid (sedentary, moderately high protein diet, ~100 g/d) condition was reported as 150 mg/h (3.6 g/d, commensurate with 22 g protein, consistent with being 22% of total output as reported), 68% being excreted in urine and 9% being excreted in feces; and during the whole days of comfortable treatment periods nitrogen was excreted 3% in sweat, 85% in urine, and 12% in feces.[25] The ambiguity or deficiency in the data or the labelling of it, evident on calculation of the protein commensuracy just above, regards whether the hot humid condition data includes or does not the rest of the day other than the 7.5 treatment condition hours, may be somewhat resolved regards overall meaning by considering the data for the whole days of comfortable treatment condition alongside.

## SWEAT COMPOSITION AND RATE IN CHRONIC RENAL FAILURE

In 1978 a study[33] of 21 patients on hemodialysis three times per week for 4 hours on a 1.5 m2 coil dialyser



with the dialysate being delivered by a RSP II Travenol machine, and ten controls matched for age and sex, collecting sweat acquired by stimulation with pilocarpine solution delivered through the skin by iontophoresis, immediately before and after HD, found little if any difference in the HD group before and after HD, presumably because the interstitial fluid had not had enough time or muscular activity to fully equilibrate with the newly-dialysed blood, so I will reproduce (appropriately rounded off) just the pre-dialysis figures here in comparison with the control figures:

**Table 2 Skin Conductances and Sweat Rate and Composition, Adapted from Prompt, Clinton & Kleeman, 1978[33]**

| | Controls (n = 10) | Predialysis (n = 22) |
|---|---|---|
| Sweat rate x $10^{-4}$ mg.$min^{-1}$.$cm^{-2}$ | 6.4 +/- 3.5 | 4.25 +/-2.25 |
| Skin conductance x $10^{-2}$ $Ohm^{-1}$.$cm^{-2}$ | 2.4 +/- 1.25 | 1.6 +/- 0.8 |
| Na/mM | 46 +/- 24 | 34 +/- 17 |
| K/mM | 11.5 +/- 4.7 | 14.9 +/- 6.6 |
| Cl/mM | 46 +/- 25 | 34 +/- 17 |
| Mg/mM | 0.10 +/- .09 | 0.31 +/- 0.11 * |
| Ca/mM | 0.45 +/- .08 | 0.90 +/- 0.39 * |
| Phosphate/$10^{-2}$ mM | 5.7 +/- 3.3 | 8.0 +/- 3.0 * |
| Urea/mM | 14 +/- 6.0 | 66 +/- 31 * |
| | Mean +/- SD | (*) indicates p < .05 |

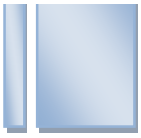
A relevancy of the context here is that the CRF patients were indeed under full HD treatment, and as such would not be expected to have excess blood (and therefore sweat) solute levels as high as a person with CRF who was not receiving at least substantially successful treatment. However, if daily dermodialysis treatment was efficacious enough to warrant its use in some patient and demographic context, in considering the likelihood of its being so efficacious, the following points are potentially meaningful.

That there seems (notwithstanding the lack of statistical significance here – note the low sample sizes) to be some substantial difference between the skin conditions (e.g. sweat rate and conductance) of the CRF (though dialyzed) patients and the healthy controls (strongly consistent with the literature on skin pathologies in CRF being almost universal, see section below), and that this could well be due to chemicals usually eliminated in the urine, building up in concentration notwithstanding the HD, in particular as the inter-dialysis period proceeds, such as to be relocated to the skin in an attempt to eliminate them via sweat (sweat that may or may not happen, depending on the climatic environment and predilections and management of the particular case) – the buildup of these chemicals in the skin, particularly in the absence of sweating, is potentially of great importance in the etiology of the manifold and serious skin pathologies attendant CRF.

That the discrepancies in the directions of difference between Na and Cl, on the one hand, and K, Mg, Ca and phosphate, on the other hand, are curious, as these chemicals are all small ions, such as might be expected to behave in dialysis with some similarity – differences in body/cellular storage or sequestration sites is a possibility suggested, and this would be a potentially important factor in the efficacy of any dermodialysis treatment of CRF.

The authors note that the sweat glands have both secretory and reabsorptive parts, which is in some analogy to the kidneys.

Whether pilocarpine iontophoresis is a comprehensively appropriate method for assaying the characteristics of sweat as resulting from environmental temperature and humidity and



physical exercise is unknown. Certainly the sweats resulting are not exactly equivalent.[34]

In 1986 a study,[35] of 11 end-stage renal failure patients hemodialyzed 3 times per week using either cellulose acetate or cuprophan membranes attached to a Drake-Willock machine with a single-pass system, and 16, 22 or 26 healthy fasting controls 18 – 43 years of age, assaying serum biochemicals at the start and finish of dialysis, and sweat biochemicals in the first and last 45 minutes of dialysis, collecting sweat by stimulation with pilocarpine solution delivered through the skin by iontophoresis, reported results as tabled (rounded off appropriately) here below.

**Table 3 Serum and Sweat Analyses in Controls and Dialysis Patients, Adapted from Cole and Boucher, 1986[35]**

| | Controls (n 16, 22, 26) | CRF pre-dialysis | CRF post-dialysis |
|---|---|---|---|
| Serum creatinine/ uM | 72 +/- 3 * p < .001 | 1,150 +/- 110 | 550 =/- 30 |
| Serum Cl/ mM | 103 +/- 1 * p < .004 | 98 +/- 1 | 97 +/- 1 |
| Serum Sulphate/ uM | 300 +/- 10 * p < .001 | 2,000 +/- 150 | 700 +/- 20 |
| Sweat rate/ mg/cm²/min | 0.29 +/- .01 nss | 0.24 +/- .06 | 0.17 +/- .03 |
| Sweat Cl/ mM | 27 +/- 2 nss | 23 +/- 4 | 22 +/- .04 |
| Sweat Sulphate/ uM | 105 +/- 6 * p < .001 | 400 +/- 40 | 280 +/- 60 |
| | Mean +/- SE | n = 11 | n = 11 |

Potentially meaningful to the question of the efficacy of dermodialysis for chronic renal failure are the following aspects of this data, that serum creatinine after dialysis was still 7-fold the control value. That serum (and sweat) chloride in the dialysis patients was lower both pre- and post-dialysis than in the controls requires explanation – were the controls eating a high-salt diet and the CRF patients eating a low-salt diet? If not, is increased elimination via the feces occurring? That serum sulphate after dialysis was still more than 2-fold the control value, and that sweat sulphate levels are consistent with a biological attempt to compensate for reduced renal excretion with increased excretion in sweat.

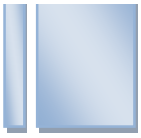
Again, whether pilocarpine iontophoresis is a comprehensively appropriate method for assaying the characteristics of sweat as resulting from environmental temperature and humidity and physical exercise is unknown.

In 1994 a study,[36] of 40 patients with advanced renal failure (24 on maintenance HD, 8 on continuous ambulatory PD, and 8 not on any dialysis treatment) and 40 healthy controls matched for age and sex, collecting sweat acquired over 1 hour by stimulation with pilocarpine solution delivered through the skin by iontophoresis, 2 – 3 hours before hemodialysis, found (astoundingly) no difference in sweat electrolyte concentrations amongst CRF patients on HD, PD, or no dialysis treatment (the exact data was not provided). Other results include the summary results reproduced here below:

**Table 4 Sweat Rates and Electrolytes in CRF Patients and Controls, Adapted from Yosipovitch et.al, 1994[36]**

| | Renal Failure (n = 40) | Healthy Controls (n = 40) |
|---|---|---|
| Weight of sweat/mg | 161 +/- 16 | 262 +/- 14 * p < .0001 |
| Na (meq/L) | 43 +/- 3 | 41 =/- 2 |
| K (meq/L) | 12.4 +/- 0.8 | 8.4 +/- 0.4 * p < .0001 |
| Cl (meq/L) | 21.6 +/- 0.2 | 18.9 +/- 1.4 |

In general, the results are in accord with those of Prompt, Quinton and Kleeman[33] noted just above, and no additional meaning is able to be derived. Unfortunately it was not reported why those CRF patients who were not on any dialysis treatment were not on any dialysis, and whether or not their characteristics differed from those CRF patients who



were on dialysis treatment, nor were any data given for the non-treated CRF patients.

Again, whether pilocarpine iontophoresis is a comprehensively appropriate method for assaying the characteristics of sweat as resulting from environmental temperature and humidity and physical exercise is unknown.

Human body odour in CRF can be differentiated from that of healthy controls, and the large majority of end-stage CRF cases can be differentiated from earlier-stage CRF cases, by electronic assay and the application of principal component analysis and quadratic discriminant analysis.[37] The particular chemicals involved in the odours would be of interest regards their individual quantifications.

## SKIN PATHOLOGIES IN CHRONIC RENAL FAILURE TREATED WITH HEMODIALYSIS

A study[38] of 100 CRF patients on hemodialysis in India in 2006, found that 82 patients complained of some skin problem, and that on examination all 100 patients had at least one skin pathology due to CRF. Prevalances of particular skin pathologies due to CRF included: xerosis (79%), pallor (60%), pruritus (53%) and cutaneous pigmentation (43%); Kyrle's disease (21%); fungal (30%), bacterial (13%) and viral (12%) infections; purpura (9%); the nail pathologies half and half nail (21%), koilonychia (18%), onychomycosis (19%), subungual hyperkeratosis (12%), onycholysis (10%), splinter hemorrhages (5%), Mees' lines (7%), Muehrcke's lines (5%) and Beau's lines (2%); the oral pathologies macroglossia with teeth markings (35%), xerostomia (31%), ulcerative stomatitis (29%), and angular cheilitis (12%); and the hair changes sparse body hair (30%), sparse scalp hair (11%) and brittle and lusterless hair (16%). Also reported were dermatitis (2%), uremic frost (3%), gynecomastia (1%), uremic breath (8%), and pseudo-Kaposi's sarcoma (as rare).

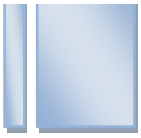
Furthermore, notwithstanding whatever imperfections in HD as practised in the India of the authors in 2006 may not apply to best practice in the most developed countries of the world in the present of 2016, it was stated that the prolongation of life in CRF patients by HD had actually allowed these skin pathologies to develop to more clinical levels of pathology, implying that HD here far from perfectly remedies the loss of renal function in CRF.

## STUDIES OF SWEATING TREATMENTS IN CHRONIC RENAL FAILURE

In 1966 a study[2] was made of 8 patients receiving HD and 4 medical staff healthy controls, undergoing sauna treatment of two 15 min periods at 75C and by implication 10% humidity separated by 10 min out of the sauna, daily except for the days of HD. It was reported that an average of 780 ml of sweat was shed per treatment, and that there was a very strong linear relationship between sweat urea nitrogen and blood urea nitrogen (BUN) (patients and controls all in one group) of 2.97 +/- 0.28 (ratio, regression line slope), from less than 100:40 mg% to 650:220 mg%, the average sweat urea nitrogen being 270 mg% in the CRF patients and 25 mg % in the controls. There was no difference found in sweat Na, K, or Cl, between CRF patients and controls. Calcium in sweat ranged from 2 – 9 mg%, no differentiation of controls from CRF patients being given.

BUNs were reported as ranging from 6 mg% in controls to 196 mg% in CRF patients. The average urea clearance in the sweat was reported as 76 ml/min, therefore 4.2 g of urea being eliminated in the sweat during each sauna treatment – now, 76 ml/min x 30 min = 2,280 ml, and it is not possible that 2 litres of urea was eliminated per treatment. Blood levels of BUN and creatinine were reported as being not different before and after each sauna treatment, though it should be kept in mind that these measurements may not have been such as to account for the time taken for equilibration of urea between various body pools, and therefore any implication here that the amount of urea eliminated via the sweat here is too little to be of much use in the treatment of CRF in any context should be seen as far from conclusive, particularly given the data on symptomatology detailed next.

Four of the eight CRF patients reported improvement in their uremic pruritis during the sauna treatments and 6 reported a pruritis-free period after each treatment lasting initially 4 – 6 hours and increasing by the 5$^{th}$ or 6$^{th}$ treatment to complete relief of



pruritis. Visible skin pathologies were also reported to be improved in these patients. Due to the ability to increase the allowance of fluid intake, the treatment facilitated CRF patients to properly control their body fluid volume, the usual restrictions on fluid intake in the absence of sweating treatment being experienced by CRF patients as onerous enough to substantially reduce their quality of life, and being far from perfectly complied with, this later imperfection quite commonly leading to high blood pressure and resultant (in conjunction with blood chemical derangements) vascular pathologies.

In a 1978 study[3] sweating was induced in three uremic end-stage CRF patients, on controlled and quantified diets, in a bathtub of water at 39 - 43C for three 1 hour periods per day. Sweat was estimated to be lost at the rate of 0.5 – 1 liter/hour, and this replaced by a formulated electrolyte solution. Unfortunately it was not stated in the paper whether or not dialysis treatment was also in use for these patients – it was stated the patients received measured 50 or 60 gram-protein diets, and that their BUNs had stabilized by the time (5 – 8 days) the sweating treatments were implemented, implying that dialysis treatment was ongoing. Blood urea concentrations fell in 2 patients, from roughly 105 mg/dl to 75 mg/dl (the third patient was noted to have had a cardiac condition and to have therefore been subjected to an unreported lesser bath temperature, and cannot be said to have had a statistically significant drop in blood urea), this drop far from certainly having reached a final plateau by the finish of the treatments on the $6^{th}$ and $8^{th}$ days. The two CRF patients given the higher temperature bath treatments had improvement in their uremic symptoms.

Clearances of urea by a forearm collection technique in 2 patients were reported as 20.9 +/- 3.7 and 11.6 +/- 3.9 ml/min – now, 16.5 ml/min x 60 min ~ 1,000 ml, and it is not possible that 1 liter of urea was eliminated during each 1 hour treatment. Average sweat rates were 810 +/- 60 and 570 +/- 160 ml/h. In comparison, work by Komives et al. (1966) was stated to have reported similar urea clearance figures using units of ml/min/1.73 $m^2$, 1.73 $m^2$ being the average skin area, units given without it therefore having the same meaning. Sweat sodium concentrations were 52 +/- 47 and 76 +/- 12 mEq/l, in two of the patients.

The authors posited that the observed removal of urea, water and salt suggested that sweating could be used to treat uremia in conjunction with charcoal hemoperfusion, in patients awaiting vascular access, or during the interdialytic interval in patients with problems with overhydration. Crucially to the proposition of using dermodialysis to treat CRF sufferers, it remains to be established exactly what elimination of particular chemicals can be achieved by specific dermodialysis treatment protocols, in particular contexts of treatment or non-treatment of CRF with HD or PD, in particular stages of CRF, and even the very basics of these seem as yet undetermined other than to the extent of making it certain that further investigation is very much warranted.

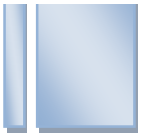
## DERMODIALYTIC METHODOLOGIES AND EQUIPMENT, AND TESTING THEREOF

### Criteria for and aims of proposed dermodialytic methods and equipment

Proposed methodologies for the application of dermodialysis to CRF are envisaged to include those applicable in even situations of greatest economic disadvantage and the least feasible of logistical and technical support. Underpinning all methods suggested here is the use of at least low-intensity moderate-duration exercise, with micro-environmental control such that body core temperatures will be high enough to cause sufficient sweating over some feasible period of time, the sweat being removed along with the metabolic toxins (i.e., urea) it contains by a water rinse, spray or mist. Dietary optimization is envisaged to be a very important part of such treatments, as it is in HD and PD. The aim of dermodialysis treatment is to delay the requirement for, and reduce the frequency of requirement for, HD or PD, and to also prolong and increase the quality of the lives of CRF sufferers who are not able to in the absence of HD and PD.

### Dermodialytic clothing (jacket and pants)

The dermodialysis jacket (DDJ) would be constructed with an outer shell of durable waterproof material, with an inner layer of durable mesh sewn off in



contiguous pockets of such a size(s) as to make each pocket conveniently loadable with a toweling (or other material if unavoidable) wad of a suitable thickness such that the toweling wad would retain its shape when wet and not sag down into the bottom of the pocket. Better material for the wadding may be available or developable, the aim being to optimize the concentration gradient between skin and the DDJ regards removal of waste and excess chemicals from the body, and whatever trade-offs there would be with hygiene, weight, feel and ability to be washed. Material and glue would be supplied for minor repairs of the DDJ.

The DDJ would have plastic tubing (with small holes regularly placed) running horizontally at least across the top of the front and back of the shoulders, and maybe also across the middle of the top of the shoulders, and midway down the torso, and also incorporate small manually adjustable valves for directing the flushing water appropriately regarding the position of the CRF patient during the treatment (e.g. upright, as in walking or some styles of cycling or types of work; bent over as in some styles of cycling and types of work). The DDJ would incorporate a small detachable reservoir of flushing water, heated to and/or maintained at body temperature by the patient's own body heat (and a simple hand-squeeze pump for delivering the flushing water), and another small detachable reservoir for waste water and sweat collected (even if unavoidably imperfectly) along the bottom margin of the jacket (This bottom margin of the jacket would require careful configuring to maximize collecting function and the likely commensurate acceptability to users) (another small hand-pump would take the waste water to the waste reservoir).

The DDJ would need to be roughly the right size for the CRF patient but would incorporate strategically placed Velcro or other fasteners enabling fairly fine modifications of fit to suit the individual body. The DDJ would be able to have layers of other clothing worn over it for temperature control or concealment. The DDJ would have detachable arms without dermodialytic function, such as to be usable for modification of the patient's micro-environment with a view to optimizing sweating.

It would be possible that pants of a similar construction to the DDJ would be both of substantial extra benefit when used in conjunction with the DDJ, being sufficiently acceptable to some CRF sufferers in some circumstances, to be also made available to such CRF sufferers. Such pants may prove to be ultimately necessary in addition to the DDJ for maximally successful treatment of some CRF sufferers, but due to the fact that the back of the torso is the site of most sweating, then the rest of the torso (notwithstanding that this includes the loins), and not so much the legs in many contexts, and the potential factor of acceptability of the treatment for CRF sufferers, and the possibility of using a wet towel rinse for some areas of the body other than covered by the DDJ, it may be appropriate to have well in mind the possible use of the DDJ alone for some CRF patients in some contexts.

It may also be that for some CRF sufferers, in some optimal climates or seasons, a regular schedule of wet towel rinses in conjunction with some sufficient level of physical exercise if necessary to provoke sufficient sweating at suitable times, without use of a DDJ, may be sufficient (and indeed optimal, considering quality of life) treatment in the context of what treatments are available to them.

Dermodialysis chamber

The dermodialysis chamber (DDC) or tent would be constructed with the frame and outer covering made of material suitable to the context of the user(s), and would incorporate some combination of (e.g. three) different physical exercise machineries into one machine inside the one chamber/tent: a treadmill for walking, a cycling machine for stationary bicycling, and levers for use of the arms in physical exercise (in some configurations maybe the stationary skiing machinery incorporating both legs and arms might be feasible); thus there would be the ability to change muscle groups and so allow CRF patients of even low physical exercise capacity to continue low-intensity physical exercise for long enough for successful enough treatment. The energy generated by the use of the exercise equipment would be captured as electricity and used to heat and/or maintain the temperature of the air and rinsing water of the DDC,

or stored in batteries for use in pre-heating the DDC air and rinsing water for subsequent treatments.

It would be appropriate to use the DDJ in conjunction with (inside) the DDC in some environments for some CRF patients, otherwise the DDC would incorporate some halter or vest with the tubing placed such as to deliver the flushing water appropriately by a hand-pump used by the patient, who could also in some environmental contexts use a rinsing towel to wipe sweat off some skin areas while applying fresh water at the suitable temperature. The possibility of having as much as possible of the DDC equipment manufactured as locally as possible, with a view to enhancing local ownership and maintenance, should be investigated, notwithstanding any need for some components to be supplied already manufactured or assembled.

Different versions of DDC, up to and including whole rooms and swimming pools, would be feasible, and may be more efficient than more personalized equipment, in some demographic locations in some seasons. DDC mechanical and other equipment should be constructed sufficiently robustly to reduce the need for maintenance to a level suited to the location of use.

**Testing of dermodialytic methodologies and equipment, and thereby, the hypothesis**

Initial studies to further examine the potential of dermodialysis for treatment of CRF would be inherently relatively inexpensive, low-tech, feasible and efficient, and would involve the appropriately scheduled collection and analyses of blood and sweat chemicals of importance, as result from various protocols of assessed feasibility and likelihood of compliance, and appropriate comparisons amongst these, as well as assessments of subjective quality of life. Likewise would be the appropriate considerations of basic diet for use in conjunction with dermodialysis, where much is already fairly well known from the HD and PD contexts. These further initial studies having further positive results, it would then remain to determine what would be the most appropriate equipment and protocols for specific patients, in their specific climatic and socio-demographic situations.

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