# FOR THE RECORD

In 1979 I became an innocent victim of the Iranian revolution and incarcerated until 1982. Fortunately for me, during the period of incarceration, I discovered that one to two glasses of water, at the most three in very exceptional case, could relieve the most devastating abdominal pain associated with peptic ulcer disease; not once or twice, but as many times as it was tested in the very stressful setting that had precipitated the disease. During two years and seven months, this abdominal pain relieving and clinically curing property of water emerged as an indisputable fact in well over three thousand old and new cases of clinically diagnosed peptic ulcer disease sufferers. It is now a fact that water has pain relieving properties independent of any medication. It is also an indisputable fact that under the most severe and world-recognised stressful setting of the main political prison of Iran, water by itself removed the clinical symptoms and the signals of a classical disease condition. This pain relieving and symptom removing property of water became so blatantly obvious that even the medically unprofessional and harsh revolutionaries recognized the merits of this discovery, to the extent that they changed their minds and allowed me to live. These statements are recorded historical facts, even reported in the Editorial article of the Journal Of Clinical Gastroenterology, June of 1983 (1).

Professor Howard Spiro in his comments about my report in, "About This Issue," makes two important statements, " ... clinical observations can lead to many new questions and even to new theories." ".... - if drinking a glass of water relieves your heartburn, think about it!" The very questions that unceasingly consumed my mind from those early-on days of my imprisonment.

Since the summary executions did not permit long-term planning for anything, I became eager to write my observations for the record, in case I could not present my findings later on in person. Some of the early cases I treated wrote the account of their own long history of the disease and how the new method of treatment was considered more superior. A very crude presentation, in form of an article, was prepared (given the inherent limitations of space, reference material and equipment) and some of these letters were attached to it. Sure enough, soon my trial time came, when I had to face 32 counts of revolutionary accusations with a sure penalty of no less than death attached to most of these items. Since my trial was being announce on the television several times a day, with the appropriate revolutionary slogans, for quite a number of days before the fateful date, on the face of it, the outcome seemed more than the anticipated conclusion.

At the opening session, I handed the article and the letters to Hajagha Mohammadi Gilani, the supreme religious revolutionary judge - he had passed sentence of death on two of his own (in hiding) sons who preferred a different approach to the revolution - and asked him to have it read and released for publication. I told him that this is one of the most important discoveries in the science of medicine, a discovery that will change the practice of medicine all over the world. I entrusted all the papers into his care, in case I was not able to further the work. The outcome, after medical review of the article and the testimonials, I was *allowed* to defend myself (no lawyers permitted) during nine sessions of court, and live to write these lines. My short

sentence allowed me to stay another year and a half in prison to complete my research into some other aspects of stress and to continue my observations on the water treatment of "dyspeptic" symptoms (including melena and hematemesis) that seemed to clinically fit a thirst situation more appropriately than a classical disease entity.

It became clinically obvious that water metabolism disturbance could also be anxiety- and fear-stress induced and this disturbance would produce a series of signals, of which dyspeptic pain was one such signal, hypertension was another signal, gout, and delayed onset of diabetes seemed to be also associated with stress, as did back (sitting in one position all the time) and some joint pains. Extensive theoretical research into the physiology of pain seems to demonstrate that chronic and recurring pains in the body, until proven otherwise, should be considered as signals of "free water" deficiency-induced multi-systems' disturbance, as such, a thirst signal. The arguments in favor of these views have been presented in the article, *"Pain: A Need For Paradigm Change," Anticancer Research, Vol. 7, 5B, Sept.- Oct., Pages 971-989, 1987 (2).*

Since one thousand years ago, when Avicenna and Razi treated dyspeptic pain with an antacid for the first time, no progress in the research of the significance of this pain signal has taken place. Just because we have developed the means of looking into the stomach and the intestine and have begun to investigate the mucosa, and because we see different states of the mucosal tissue at different stages of a changing steady-state situation, we automatically label these states as separate pathological entities. We prefix "itis" with the anatomical name of the organ and a new "disease" and another scientific enigma is born. We make a more gross mistake; we look at the ulceration in the stomach and the duodenum as if it is the disease entity itself. We ignore the pain signal and treat it with irreverence and disrespect. Until we see the "hole," any approach to the dyspeptic pain will do. We even pour a toxic metal down the "tube" well knowing that the body has no means of metabolizing and/or clearing the portion that is absorbed in the system.

We take advantage of the advancements in science and manipulate the receptors of an important neurotransmitter system with the appropriate blocking agent; when this same blocking agent does not do the job of bringing about pain relief, we supplement the blocking action of this product with the aluminum containing mixtures that can bring relief to the patient. Finding all these procedures unsatisfactory in the long-run, we are now introducing substances that block the action of the $H^+$-$K^+$ pump, our explanation, this substance brings about the "cure" of the "hole" a few days earlier than the receptor blocking agents *(McFarland, RJ, et al., Omeprazole Provides Quicker Symptom Relief and Duodenal Healing Than Ranitidine; Gastroenterology 1990; 98: 278-283)*! When this argument is pushed into the mind of the clinician, he is not told that the same hydrogen pump mechanisms are possibly involved in pH regulation of some tissues that do not employ the bicarbonate buffering system. Since we are tuned to the statistical means of interpretation, when a number of patients (in the short time of the clinical evaluation) develop adverse neurological symptoms, the rest of the patients carry the banner for the product.

Why? Because we do not acknowledge a metabolic process for water, which has to accompany the food that is processed in the same "tube" system; we use the word "hydrolysis" without appreciating that water plays an active role in the chemical reactions of the body. Although the advancement of the different branches of molecular science have demonstrated an expanding role for water in the

body physiology, clinically we are not very well versed with some of these properties of water.

Although the main body water regulating neurotransmitter systems and their subordinate down-stream sub-systems are fully recognized, we still play with these mechanisms pharmaceutically without due respect for the main water regulatory drive and functions of these systems. In short, we are only recognizing the gross physical properties of water and not its primary chemical properties. Just because the solutes in the main body solvent are highly reactive substances, we concentrate on the minute fluctuations of these and disregard the highly reactive hydrolytic property of water itself. We think that the water regulation of the body is entirely coupled to ionic exchange across the cell membrane, whereas, free water has a diffusion rate across the cell membrane independent of that which is coupled to the ion exchange by the various pump proteins (2).

If all the sensor regulators of the body physiology are understood to be different proteins, naturally constructed for a particular function, it is a fact that these proteins function more efficiently in solutions of lower viscosity. If the thirst mechanism is controlled by various protein sensor regulators, then these will function more efficiently when more water is available in their environment. It seems simple logic that it is the water itself that regulates its own efficient intake. Two facts support this statement - one, we become chronically dehydrated with age increase, it seems, as a result of the loss of thirst sensation, to the point that the ratio of the intracellular water to the extracellular water content of the body changes drastically - two, that with voluntary and regular increase in daily water intake, the thirst sensation becomes more acute in people who would not acknowledge thirst before.

Based on these assumptions, it must be acknowledged that *the basic understanding on the ionic regulation of water in the body is incomplete and therefore this paradigm needs to be changed.* When the cell membrane has a free water permeability property - depending on the cholesterol content of the membrane - at an approximate rate of 10-3 cem/sec, and this rate may fluctuate with temperature change, it is an indication that the cells of the body also rely on this route of entry of water for the cytosolic homeostatic balance of water. Therefore, the ion coupled flow of water, that is held as the basis for understanding of water regulation of the body, is an incomplete assumption. That this is an incomplete assumption is fully understood by the physiologists and the research scientists, who have even gone through the trouble of exposing a possible mechanism for the production of "shower head" cluster perforations across some cell membranes established by the water regulatory role of the antidiuretic hormone and its receptor mechanisms.

But the implications of this discrepancy in understanding has not filtered into the mainstream of the practice of medicine and the adopted treatment procedures. Why? Because we are so preoccupied by the desire to dismember the body into the sub-disciplines of the practice of clinical medicine, failing to appreciate that the body is a product of a tightly integrated multi-system system.

For example, if the two initiating components of the histamine-renin-angiotensin ll-angiotensin lll-aldosterone system are acknowledged for their water regulatory roles, the subordinate downstream sub-systems will have to be judged as water regulators too, even if sodium retention is involved; their actions should not be continuously blocked, they should be satisfied by provision of the substance that they seek - namely water - and particularly as the body does

not manufacture it, unless food is being metabolized.

Kinin production by the salivary glands is a sodium deficiency induced mechanism (2). The body goes through this process to promote increased circulation within the salivary glands for their adequate saliva production, a physiological necessity for the acts of mastication and swallowing. If sodium balance in the body regulates the extracellular fluid volume, then kinin production, as a result of a possible decreased fluid balance in the body, will mask the gross body water deficiency by maintaining the total hydration of the salivary glands. It is therefore simple logic that the "dry mouth" is not an early signal of water deficiency in the body, and its presence is an indication of gross fluid imbalance. To rely on this signal for the fine regulation of the water intake of the body would mean that the body is constantly being run on a deficit balance to the optimum body "free water" needs. Exactly what is produced by the use of the different diuretics in the early treatment of hypertensives, resulting in a more determined corrective process, forcing the patient to drink more water, although the intake is not adequate for a long lasting effect.

If the dyspeptic pain of a recognized disease condition, under the stressful setting of a political prison life, becomes relieved with increased regulation of water intake, surely this finding is important enough to merit further research by others interested in the progress of science! Why has this dyspeptic pain relieving property of water not been explored up to now? It has been recognized for some time - in the eighteenth, nineteenth and early twentieth century - attendance at water spas had a main abdominal pain relief attraction for those who could afford it.

Since it was published as recently as 1983, and reported in the media, that normal tap water had a curative property for ulcer pain sufferers, nearly seven years has passed. Why have the universities and practitioners not taken any interest in the subject? Surely, it would serve the interests of the pain suffering patients more than any other method of treatment if these observations and claims could be repeated. I presume the whole subject seems too good to be true, or else it seemed so absurd and crackpotish that it need not have been entertained by those busy with such a highly sophisticated scientific approach to the practice of the present day medicine. To the average suspicious critic, the claims of the efficacy of simple water in peptic ulcer disease treatment must appear as an act of arrogant sensationalism, particularly if the claimant is not a recognized name and the clinical research and observations are not made in a recognized institution. This attitude of blase individualism can delay the application of the progress of science to the treatment procedures in the practice of clinical medicine, but it can not enforce a prolonged emotional disregard of the exposed role of water metabolism disturbance and its signal systems in disease emergence (2).

This Foundation was created to expand on the ramifications of the chronic pain relieving property of water - and to bring about a change in the basic paradigm that has allowed this property of water to remain concealed, even when so much progress has taken place in other fields of science. The following seemingly simple statement during an encounter at a scientific meeting has crystallized our direction and resolve.

I was asked to speak at the gastroenterology meeting in a foreign country. The meeting was organized by the gastroenterology society of the host Capital, but "hosted" by a most famous company that manufactures a brand name of cimetidine. Not knowing who I was and what I was going to talk about, the following discus-

sion took place between the company representative and me before I began my talk. I think we should very seriously ponder the issue - He asked me, "do you use our product?" I said, "no, I do not". He asked, "are you using the product of our competitors?" I said, "no, I do not use the product of your competitors either". With much surprise he asked "then, what do you use to treat your patients?" I told him, "I use water". With much amazement, he said, "what, water alone?" I said, "yes, water alone." Then I began to ask him the two questions that have bothered me for some time. "As researchers into the effect of histamine metabolism and functions in the body physiology, your company must be aware of the primary role of histamine in the water regulation of the body - firstly, why do you insist that its actions should be blocked and, secondly, why do you not explain this water regulatory role of histamine in the body to the clinicians who are being asked to block this action by the use of your product?" In an irritated tone of voice, he replied, "we are not here to educate the doctors, they should discover that for themselves! We are a manufacturing company interested in selling a product!"

With such a firm dependence on the manufacturing and commercial arm of the health-care systems, what hope is there for the natural to emerge as an alternative to the established invasive and drug-dependent treatment procedures in the practice of clinical medicine? If the clinicians begin to recognize and appreciate the natural role of the neurotransmitter systems that regulate the water intake and its distribution in the body have this particular function as their primary objective and responsibility, one half of the battle is won.

To that end, the conceptual research into the neurotransmitter histamine, the abstract of which has been printed in the book of Abstracts of the Third Interscience World Conference in Monte-Carlo, March 1989, has been updated. Slides of the theme models designed to explain some of the recognized and conceptualized regulatory roles of histamine, prepared for the same conference are being presented in the article, "Neurotransmitter Histamine: An Alternative View Point", in this volume. It is hoped that the factual and the conceptual projections on this neurotransmitter will leave no doubt in the minds of the gastroenterologists, and others who deal with this amine in clinical practice, that there is an unquestionable merit in treating the often recurring dyspeptic pain with water in preference to any other medication; that every clinician has a moral responsibility to those who consult with him/her to warn them against the use of aluminum containing antacids for the regulation of a simple thirst pain, when aluminum is being singled out as a potential toxic agent in the production of neurofibrillary tangles in Alzheimer type dementia *(2 & Zatta, P, et al.; Alzheimer Dementia and the Aluminum Hypothesis, Medical Hypothesis 1988; 26, 139-142).* We should explore to see if, by the discontinuance of the use of aluminum containing antacids, we can achieve the same results in prevention of Alzheimer type dementia, as it was achieved in Guam by clearing the drinking water of its aluminum impurity .

Our objective is to show that water metabolism disturbance of the body has more signals than the simple dry mouth or even the chronic joint or dyspeptic pains, even allergies or hypertension, etc.

In our view, the dyspeptic pain, as a cardinal sign of cellular water deficiency, is the most significant signal in the human body, it has far-reaching and long-term implications. To address some aspects of this view, Dr. Jawed Iqbal, an eminent scientist in his own field of research, and who has been looking at some of the implications of our proposed paradigm change, is presenting two of the topics of his research - The Regulatory Role Of Free Water -

and - Tryptophan. We selected these two articles to complement the article on the neurotransmitter histamine. To indicate the vast ramifications of ignoring a thirst signal of the body, when so much damage from the potential malregulation of the metabolism of an essential amino acid and a precursor of so many different neurotransmitter systems can result. The main direction of the content of this issue takes its lead from the article, Pain: A Need For Paradigm Change. We are attempting to expand on the possible ramifications of chronic cellular dehydration that becomes established as a result of insufficient and irregular water intake as we progress in age.

Histamine is the main natural agent that deals with the regulation of water intake of the body, even to the point of regulating the cation exchanges at the cell membranes. This is the primary function of the amine. Because of its omnipresence, it has been studied and wrongly implicated in certain signal producing and abnormal steady-state situations that are classified as disease states of the body. To the best of our ability, and dependent on the available research results, that would allow a different interpretation and exposure of the useful and the indispensable function of histamine in the regulation of local and the general physiology of the body possible, a function that should be very reluctantly blocked with antihistamines, the formation and presentation of an alternative view of this neurotransmitter has been attempted. Assuming that the human body is the product of a highly integrated multi-system system, the main missing link in the understanding of disease emergence was the fact that water metabolism of the body is not a well regulated phenomenon. It can become signal producing when its metabolism is disturbed. Since water is the main substance around which all systems are designed, its position in disease conditions should become clear. It is our view that if the application of scientific knowledge around water metabolism is studied and incorporated into the practice of medicine, the practice of medicine becomes a simple art.

At the moment, the accent is on the manipulation of the signals of water metabolism disturbance with manufactured products, albeit, in different scientific guises and explanations. This approach may stem from an understanding of science of chemistry, but to the nature in the design of the structure of the body it is not scientific. The nature in the design of the body would better understand the manipulation of the signals of water metabolism disturbances with the application of the scientific knowledge of that particular discipline of science. By recognizing the fact that the neurotransmitters, histamine and serotonin, and their subordinate renin-angiotensin system have a primary water intake and regulatory functions - a simpler recognition of the primary function of these agents - the practice of medicine will become a much simpler and patient-serving application of a noble art, instead of its present commercial trends that have disturbed the relationship between the patient and the physician.

The title of this publication reflects our aim for the incorporation of a scientific approach to the signals of water metabolism disturbances that would eventually make the practice of medicine simple. We only need to open our minds to the extent that if we recognize a hunger pain and signal, the body also has a thirst pain and signal. In the same way that we do not try to convince the body that it is not hungry, but should take the colored magical pills that are on the market to deal with a simple natural hunger "signal," we should force a similar attitude in dealing with the thirst signals of the body. In the long run, this approach would reflect the height of advancement in the science of medicine, whereas even with tremendous strides in advancement of science, the present

seemingly science-based practice of medicine leaves much to be desired.

Judging by the rumblings in the policy making stratum of the society, reflected in the various articles written on the subject (The Sounding Board articles of the recent issues of the New England Journal Of Medicine, to name but a few) the transformation of medicine is imminent. According to Professor Uwe E. Reinhardt of Princeton University, "American Health Care At The Cross Roads, 1989," a change in the practice of medicine is an unavoidable event that is in the winds. If that change is going to come, then, taking the simple patient serving direction exposed by the need for the basic paradigm change regarding the water metabolism of the body would serve the physician and the support scientists better than the past tendencies of the invasive and pharmaceutical direction that have confused the application of science to the practice of medicine.

In our Special Issue On AIDS (August 1989), it was announced that we aimed to begin the publication of the Journal Science In Medicine Simplified from the beginning of this year. Timely advice from a close friend of the Foundation made us defer the publication of a regular Journal until our views have been presented to a group of scientists who may then wish to support a regular publication, dealing with the issues raised in our presentations. We have prepared a series of articles addressing the potential and conceptual ramifications of the paradigm change, that will be further polished and presented for discussion in our subsequent issues. It is the sincere hope of this Foundation that, for or against, a dialogue will soon be established and the publications of the Foundation will become the forum for the exposure of ideas that can transform medical practice all over the world.

The readers are cordially invited to contribute to the transformation of medicine that we think a paradigm change will bring about. Based on the pain relieving property of water that demonstrates this substance's primary importance, in presentation of our views, we have assumed that in most multi-factorial disease conditions, it is the primary role of the water regulation for the neurotransmitter regulators that is paramount; if, by the use of directly active medications, without due regard to the main cause of the problem, interference with the function of these regulators are contemplated, the system may become vulnerable to drastic and irreversible change. This becomes particularly applicable to dyspepsia that leads to so many different subordinate and connected problems, although the connections are not apparent at the moment; the same approach applies to the conditions of allergic reactions, to hypertension, and so on.

The beauty of our approach is that it allows a clarification of the relationship of various disease states that at the moment seem totally unconnected; who for example connects dyspepsia of early life to Alzheimer type dementia of later life! Our approach allows for an expansion of preventive medicine, a more desirable way of dealing with health problems of our society.

It is our sincere hope that the dedicated scientists will take pleasure at being in a position to begin and expand on the very limited attempts of this Foundation in trying to shed light on the simple scientific approach to the practice of medicine, knowing full well that the task at hand is more than monumental and needs a vast number of dedicated minds.

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