

THE AFIB REPORT

Your Premier Information Resource for Lone Atrial Fibrillation!

NUMBER 28

APRIL 2003

3rd YEAR



In this issue we welcome two guest authors. Fran Ross relates the remarkable story of her full recovery from LAF and several other disorders through dietary changes, and Patrick Chambers, MD begins a three-part series on the all-important role of magnesium, not only in LAF, but in our general health as well. The contributions by Fran and Patrick are much appreciated. Not only do they bring a different perspective to "The AFIB Report", but they also give me a chance to focus more on my research – specifically compiling the results from our recent survey.

I have finally managed to put the responses from approximately 350 participants onto a spreadsheet and, beginning with the May issue, will share my evaluation of the data with you. A preliminary look indicates that we may have discovered several correlations that may throw new light on the mechanism underlying LAF. Stay tuned!

Just a reminder - if you haven't already done so, don't forget to get your copy of my recent book "Lone Atrial Fibrillation: Towards A Cure" at www.afibbers.org/lafbook.htm - it provides a wealth of information on dealing with LAF.

Enjoy!

*Wishing you lots of sinus rhythm,
Hans Larsen*

Table of Contents

Evaluation of Survey Results
My Return From the Abyss by Frances Ross
Magnesium & Potassium in LAF – Part 1 by Patrick Chambers, MD

Evaluation of Survey Results

The 5th lone atrial fibrillation survey (LAFS V) yielded 166 responses. Combining these responses with those from previous surveys results in a total database of 352 afibbers. Thus it is possible to establish the values of common

variables such as present age, age at diagnosis, gender, number of episodes in the last 6 months, etc. with a fair degree of reliability as the means and distribution of these variables are based on a sample size of around 350.

Answers to questions such as "Have you been diagnosed with diabetes", which was only asked in LAFS V and in our very first survey can be answered with a somewhat lesser degree of reliability due to the smaller sample size. The reliability is further reduced when it comes to evaluating the prevalence of diabetes in a subgroup of afibbers (adrenergic, mixed, vagal or permanent). Thus in order to arrive at meaningful conclusions it is essential to use the proper statistical techniques to evaluate the survey responses.

The evaluation of the survey results involves three different approaches:

1. Conclusions drawn from a simple study of averages (means and medians) and range of the variables.
2. Conclusions drawn by comparing the prevalence of a particular condition among afibbers to that found in the general population.
3. Conclusions drawn from performing an analysis of the correlation between 2 sets of variables.

All statistical tests are carried out using the GraphPad InStat program (GraphPad Software Inc., San Diego, USA).

1. Study of averages and ranges

An example of this type of study would be the evaluation of episode duration. A close look at the results for mixed afibbers shows that the average (mean) duration of episodes is 4.7 hours (median 2.5 hours) for women and 11.6 hours (median 6 hours) for men. Also, that the range of episode duration is 0-48 hours for men and 0-21 hours for women. A comparison of the means for men and women shows that the difference in episode duration is statistically significant with a probability (p) value of 0.03. This means that there is less than a 3 in a hundred (3%) chance that the finding that the means are different is due to chance. In this study differences between means will be considered significant if the value of the two-tailed t-test (p) is 0.05 or less.

The comparison of episode severity between different groups of afibbers poses a particular problem.

The number and duration of afib episodes and the total time spent in fibrillation over a 6-month period is our "gold standard" measure of the severity of paroxysmal LAF. It is an essential component in evaluating the effectiveness of drugs, supplements and other interventions. It is, unfortunately, difficult to calculate a meaningful average of these values for a group of afibbers. The problem is that most respondents have fairly low values, but a small majority has greatly elevated values, which essentially makes a normal average (mean) quite meaningless in describing the overall severity for a particular group. For example, the calculated average time spent in afib per month for paroxysmal afibbers is 15 hours despite the fact the 81% of them spend less than 15 hours in afib. The average is skewed because a small group spends between 50 and 120 hours in fibrillation per month. I have, therefore, decided to use median rather than mean (average) values in describing group averages related to episode severity. The median is the value in the middle, i.e. the value above which half of all individual values can be found and below which the remaining 50% can be found. Using the median eliminates the bias introduced by a small group of "heavy hitters".

2. Study of prevalence of condition

Several questions in LAFS V relate to the prevalence of conditions such as diabetes, hypertension, congestive heart failure, etc. The percentage of mixed afibbers diagnosed with diabetes is 1.8% (sample size N=57). The prevalence in the general population (aged 30 to 64 years) is between 3 and 9%. Thus the prevalence of diabetes among mixed afibbers is well below that found in the general population.

3. Correlation analysis

The discovery of correlations between variables is perhaps the most exciting part of the survey data evaluation. Two measures are used in determining whether one set of variables is correlated with another, the correlation coefficient and the probability of significance.

The correlation coefficient (calculated by the GraphPad program) is expressed as a number between minus one and plus one. A minus one indicates a perfect negative correlation, while a plus one indicates a perfect positive correlation. A correlation of zero means there is no relationship between the two variables. When there is a negative correlation between two variables, as the value of one variable increases, the value of the other variable decreases, and vice versa. In other words, for a negative correlation, the variables work opposite each other. When there is a positive correlation between two variables, as the value of one variable increases, the value of the other variable increases. The variables move together.

In the case of mixed afibbers the correlation coefficient between the average duration of episodes experienced over a 6-month period and the number of years since diagnosis is 0.3677 (sample size N=77). The probability of this correlation being due to chance (p) is 0.001; in other words, there is only a one in a thousand probability that the observed correlation is due to chance. We would say that the correlation between years of AF and episode duration is moderate. In other words, the longer you have experienced afib the longer the episodes tend to last.

Generally, a correlation coefficient greater than 0.7 indicates a strong correlation, a value between 0.4 and 0.7 a moderate degree of correlation, and a value between 0.2 and 0.4 a weak one. However, a correlation coefficient of say 0.3500 for a large sample of 50 or more is considered a stronger indicator of correlation than is the same correlation coefficient if observed for a sample of only 15 participants. For the purpose of this survey, no correlation will be considered statistically significant unless p is equal to or less than 0.05.

The correlation coefficient also provides a measure of the percentage of variation of a dependent variable that is due to variation in its associated independent variable. The coefficient of determination (r-squared) is the square of the correlation coefficient. Taking the correlation between years of afib and duration of episodes as an example, the correlation coefficient "r" is 0.3677. The coefficient of determination (r-squared) is thus 0.135 meaning that 13.5% of the variation in episode duration can be explained by the variation in number of years of AF. This finding, of course, is both good news and bad news. The good news is that the number of years of AF is only a minor element in determining the duration of episodes and the bad news is that we still need to discover what lies behind the remaining 86.5% of variation in episode duration.

The presence of a few "heavy hitters" poses a problem when it comes to evaluating possible correlations between episode frequency and duration and other variables. In order to ensure valid correlations the analysis is performed on two sets of data. One containing all data and one with the "heavy hitters" omitted. "Heavy hitters" are defined as follows:

- Episode frequencies greater than the mean plus two standard deviations (of the complete data set).
- Episode durations greater than one week (168 hours)
- Total time spent in afib greater than the mean plus two standard deviations (of the complete data set).

Thus correlations involving episode severity is performed on both the complete data set and the data set with "heavy hitters" omitted. All other correlation analyses are performed on the full data set only.

Correlation is determined by using the Pearson or Spearman correlation coefficients or the Chi Square test as appropriate.

Finally, it should always be kept in mind that a high correlation coefficient is not enough to establish cause and effect. It also has to be scientifically plausible that an association exists. For example, a strong correlation between regular aspirin usage and nighttime leg cramps must have a plausible scientific explanation before it can be considered valid.

The actual results of the survey will be evaluated and published according to these guidelines beginning with the May issue.

My Return From the Abyss **by Frances Ross**

I got AF at 22 years of age. It came out the blue after the birth of my first son. Unfortunately, sometimes when it happened I would pass out. Witnesses said I convulsed. So the diagnosis came as epilepsy. I was put on anticonvulsants. They never worked. In the beginning my AF was maybe twice or three times a week. Always at rest. It was short-lived, well the really fast racing part was short lived. Maybe 2 to 4 hours (in the end it could go on for days then became permanent). Every so often I would go to my GP and complain about it, but he told me

it was just palpitations and I was being over anxious. So I decided they must be panic attacks and gave up with the doctors.

Nine years later, when I was having a prenatal for child number 3 I went into AF sitting in the doctor's waiting room for two hours. I could not think why I was having a panic attack. Nothing was scaring me. But there was a Calor gas heater on and I thought that must be taking the oxygen out of the atmosphere. I have always needed lots of fresh air, especially in AF as I was prone to passing out. When I got to see the doctor he started with blood pressure. He told me something was wrong with my heart (helloooah!!!). Silly me said, oh I'm just having a panic attack. He said that's not a panic attack it's coming from your heart. Was I frightened?! I told him that I had asked him about it before, but they said it was normal and I was just being anxious, so I decided it must be panic attacks. He told me he thought it was AF, but as I had had it such a long time and was pregnant there was nothing they could do until after the baby was born.

After the baby was born I was sent to the cardio. Got the Holter and a few tests. It was AF and they put me on digoxin. Then I got on with my life.

Years later I read about cardioversion and asked why I had never been sent. They told me my AF was too long standing and it wouldn't work. I stayed on the digoxin for ten years. I got worse and worse (what I would have done to know about the long term effects of digoxin then, and also the Mg depletion). Also the digoxin had changed my eating habits. I could not tolerate food in the day. I would maybe have a bag of crisps and a bag of sweets mid afternoon. So just ate a big evening meal to make sure I got nutrition. I always cooked so a lot of what I ate was semi fresh, but not organic and I was known to cut corners and buy ready made meals a lot.

AF became unbearable. I seemed to be in it permanently. I read about ablation and went back to the doctor to ask about getting one. He told me that there was no way as my heart was far too healthy and I could end up with a lot more problems. I felt that things could not get worse. Little did I know!

My GP sent me to a new cardio in 2000. He had a fit and said I should never have been put on digoxin - he must have read the digoxin literature. I was upset because I had obviously been put on the wrong drug. He prescribed me arhythmol. Did more tests, 24-hour urine analysis, treadmill, echo, things I never got the first time round. I asked him if it was possible that my AF and 'epilepsy' were linked as both were electrical faults (my GP always said there was no connection). He said absolutely no. But I did get a referral to a neurologist, something I had never had despite 18 odd years on anticonvulsants.

Around this time, on the digoxin, I started getting terrible pain in my shoulder and back. I went to my GP who told me that because of the tender spots that I had a form of ME (fibromyalgia). He said it was my immune system attacking my muscles, and would be interested to know if my AF got worse when I was fighting a virus (well we all know the answer to that). I even started suspecting I had a form of MS as areas of me would become very painful - felt like patches of skin had been burnt or all the skin grazed off. But there was nothing to see. At other times they were totally numb and I could have burnt myself and not felt a thing. I also had developed terrible startle reactions. When I passed out now it was at night or early morning on waking up. But I never lost full consciousness. I was not aware of what was going on around me, but stayed conscious in a tunnel in my brain (and my husband said I was convulsing). I knew I was fighting for my life. I had near death experiences. When I got back my heart was very, very slow. I could hear it in my head. It would take me ages to be able to move after, hours to recover the feeling in my body, and my brain would not send words to my mouth. The rest of the day was in a confused mess with sound being muffled, distant and loud at the same time.

Just after stopping digoxin I read about MSG and aspartame and also preservatives and sulphites, etc. They were linked with seizures and arrhythmia, so I cut them out. It got difficult reading labels so I decided to cook from scratch. This was difficult as my health was so bad and even standing cooking or doing the dishes made me faint. But I developed a dance to keep my legs moving and kept the door open. It helped and I knew I had to persevere.

The new cardio put me on arhythmol. I didn't get on with arhythmol. So was put on sotalol. This made breathing difficult and a new diagnosis became imminent. I was told that I now had central sleep apnoea. The neurologist

would suss it out. However after long EEGs and other tests I was declared fit. There was absolutely nothing wrong with my nervous system and I never had epilepsy. I started weaning myself of tegretol now.

I was sent on to the respiratorist. I was put on the waiting list for a sleep study, but it would take about a year. Things kept getting worse and the passing out worse. I went back to my GP and said I thought it was the sotalol. He said no, that breathing difficulties were not a side effect of sotalol. GGRRRRRRRR. It was probably that I had narcolepsy. My near death experiences were hypnogogic hallucinations and the fact I could not move after was sleep paralysis. There was a syndrome called sleep epilepsy. It was unfortunate that I experienced them all at the same time. AAAaaaaaaaagggggghhhhhh.

They upped my sotalol and my GP agreed that I was in chronic AF. See if a bigger dosage helps. Breathing got worse, it was as if I had to breathe through water and I kept forgetting. I found AF support groups and was mortified to learn that sotalol should be monitored by ECG before starting and every time the dose was upped. I had never been given one.

Went back to my GP and asked why I was not being monitored. Brought up my concerns about long QT. My GP did an ECG. I asked him about my QT wave. He said it looked slightly long but various factors had to be taken into consideration such as height, weight, age etc. He faxed the ECG to the cardio. He wrote back by fax and that it was just AF and nothing was abnormal and something about the T wave. My dose was to be upped again.

By this time I was more or less an invalid. I was in chronic AF. Life had no quality. All I knew was I had to eat correctly and healthily. It was my only hope to keep myself going. Kept going back to the GP with research on AF. Somehow or other they managed to convince me I just needed a higher dose of sotalol. Up it went again. I was now on 160 mg twice daily!! After about a year of sotalol, I went back with something that showed breathing difficulties to be a side effect. They relented and gave me flecainide. I thought great, as I knew I was vagal and this might just do it. However my GP and cardio would never accept vagal.

The flecainide worked for a couple of days. My breathing became better and my high level of anxiety abated. But on the third day I woke up with tremors all over. Light was pulsating in my eyes. I felt better than on sotalol but did not like my new found really fast heart rate (I had got used to the slower rates on sotalol). It happened to be the day the doctor brings his surgery to where I live. I went up and he took my pulse. He said he was taking me through personally to the Health Centre as he did not like what was happening. He told me in the car that my cardio had told them to keep me on sotalol and not change my meds. I said I would never touch it again and would not take it. By the time we got there my heart rate had dropped and all it showed was sinus tachycardia of 100 and something. I was over the moon. I was in sinus!

However, the GP told me I had an allergic reaction and had to stop the flecainide. He gave me atenolol. He told me to go back and see him the following week and they would up my dose of atenolol. He had only put me on 50 mg. However, I had already decided that I was not going to keep taking tablets. On the atenolol my breathing difficulties came back though not so severe. Also my anxiety level rose again so I took half my dose. When I went back to see the GP it was his partner on duty. I told him I wanted to stop taking tablets. I asked him if he could give me atenolol 25 mg with a score down the middle. He tried to talk me out of it, but I was insistent. He said he shouldn't, but if I insisted I wanted to cut down he would give me a smaller dosage – one with a score through the middle so my dosage could be better monitored. He then told me about one of the first patients he had treated with AF who refused to take his meds and he seemed fine. This is the only GP I have a soft spot for now. All the others had treated me like an anxious girl who could be fobbed off with their medical jargon. And they got scared as they could never back up their claims and theories with the “trust me I'm the expert” scenarios as I had been reading and reading. I had learned to trust myself and listen to my body. Only I knew what was happening. They twisted the way I presented it and even told me I was not suffering anxiety but depression. But I do know the difference. They wanted to put me on SSRIs. I realised that doctors only looked for easy solutions. Give it a diagnosis and then some more pills.

On Dec 28, 2001 I stopped taking my meds. I had been additive-free for about a year. About a week later I was cooking in the kitchen and I realised how happy I was. I was not dizzy or feeling faint. Then I realised my heart was beating normally. Only twice since then have I had AF. Once after eating chicken with MSG by mistake and the other time after taking Mg citrate (go figure). I will not touch supplements or any pills now.

Sometimes I wonder if it is the supplements that keep everyone in AF. Loads of people try diet, but everyone seems to rely on supplements (apart from Erling who is AF free but does take a couple of supplements).

I eventually got my sleep study through last April after stopping meds and getting rid of my AF and side effects. Guess what? No, I didn't have narcolepsy either (although I do have the genetic HLA DR7 typing code on two accounts).

If I come across as anti-doctor it is because of my experience. But I would rather not see one again if I can help it.

I don't know the real reason why. All I know is that, after 20 years of AF, I am free. And this is not the usual story. This is how I did it. Since then I have played more with diet as after curing my AF I became aware of reactive hypoglycemia. And have now got this out of the way too. But of course I have to stick to my diet. But I prefer it this way as all my health is back. I have cured more than just AF and don't have fibromyalgia or burning spots, no headaches, no tremors, no startle reaction, no seizures, no fainting. The only thing I have not cured is low blood pressure, but I can live with that.

Magnesium & Potassium in Lone Atrial Fibrillation – Part I

by Patrick Chambers, MD

Lone Atrial Fibrillation (LAF) is AF without discernible cardiovascular disease, e.g., without congestive heart failure, high blood pressure, prior cardiac surgery, rheumatic heart disease, etc. It has been associated with a number of diseases primarily involving organs other than the heart. These include seemingly widely disparate disorders such as hyperthyroidism, gastroesophageal reflux disease (GERD), dysautonomia (abnormality of autonomic nervous system), impaired glucose tolerance, etc. LAF involves a “defective substrate” and is triggered by an increase in sympathetic tone (adrenergically mediated LAF or AMAF) or an increase in parasympathetic tone (vagally mediated LAF or VMAF). The disorder is chronic in nature and may occur intermittently (paroxysmal) or be a constant companion (permanent).

The phrase “defective substrate” has become integral to any discussion of the cause of LAF. Organ candidates for this “substrate” include the heart, as well as kidney, adrenal gland, pancreas, GI tract and autonomic nervous system (ANS). This defect could involve an enzyme, a hormone or receptor site, a membrane pump, channel or exchanger, to name a few. It could be environmental, genetic or both. Magnesium (Mg) deficiency has emerged as a significant player in the etiology of LAF. This is not completely unexpected, since some 350 different enzymes(1) or about 80% of all enzymatic reactions in the body(2) rely on magnesium. Although much has been written on the role of Mg deficiency in other diseases, little has been devoted to LAF. Much is still unknown, e.g., why one individual with Mg deficiency manifests with insulin resistance and another with insulin hypersensitivity, is not clear. What is clear is that LAF is not caused by a single factor, but by the delicate interplay of many factors. Some of those due to Mg deficiency follow.

ROLE OF MAGNESIUM

Cell Membranes

One of the most important roles of Mg involves maintenance of the intracellular environment. It does this primarily by attaching to phospholipids in membranes (both of the cell and its organelles, such as mitochondria, sarcoplasmic reticulum...) to reduce their permeability and enhance their function (12). It is also a required cofactor in the various membrane ATP (energy requiring) pumps. The most important of these pumps is the Na/K pump. Others include Ca/Mg, K/H and Na/H pumps. In addition there are channels (such as Ca and Na) and exchangers (such as Na-Mg, Na-Ca and Na-H). Neither channels nor exchangers require ATP and are passive (rely on diffusion). Some of these are also adversely affected by Mg deficiency. For example, Mg is a

Ca channel blocker and Mg deficiency leads to increased intracellular Ca via channel (and pump) because heart cells must maintain a Ca gradient of 25,000:1 (difference between extracellular and intracellular concentrations)(71).

Mg deficiency also results in dysfunction of the Na-Mg exchanger(56), leading to increased intracellular Na via exchanger (and pump) due to a Na gradient of 13:1(71). If there is insufficient Mg for adequate ATP, then the primarily extracellular cations sodium (Na) and calcium (Ca) tend to leak into the cells and the primarily intracellular cations potassium (K) and Mg tend to leak out. However, membrane leakiness in magnesium deficiency depends less on ATP related activity and more on the membrane stabilizing effects of magnesium phospholipid complexes(12). This leakiness disrupts proper gradients and cellular function. In addition Mg is an antioxidant and Mg deficiency allows accelerated free radical damage to cell membranes (lipid peroxidation), further compromising cellular cation (positive ion) homeostasis(3,24,32,60,61).

Maintenance of proper cationic (Na, K, Ca, Mg) gradients is especially critical for successful muscle contraction and nerve impulse transmission. In fact the earliest symptoms of magnesium deficiency are neuromuscular symptoms, e.g., muscle twitching (fasciculations), difficulty sleeping, difficulty swallowing. Accordingly, the list of disorders associated with Mg deficiency is top heavy with neuromuscular diseases, e.g., asthma (bronchial smooth muscle), migraines and eclampsia (vascular smooth muscle), leg cramps (skeletal muscle), LAF (cardiac muscle) and even chronic constipation (GI smooth muscle).

Mg and K

Like Mg, K inhibits free radical formation(4). In fact, there are a number of parallels between these two cations. Both are inextricably linked to specific anions (Na for K and Ca for Mg). Hyperkalemia (like hypermagnesemia) does not typically occur in patients with normal renal function. Aldosterone increases the secretion/excretion of both K and Mg(5). Successfully replenishing a K deficiency (like a Mg deficiency) in the presence of low intracellular Mg is difficult and takes months(6). Even in the presence of a normal serum K, reduced dietary K can be problematic, just as for Mg(4). K and Mg both can reduce high blood pressure(7). Fruits and vegetables are great sources for both minerals (mother was right). Both because K is so vital to cardiac function and because Mg is so vital to K utilization(33), any discussion of Mg and LAF is incomplete without inclusion of K.

Absorption and Excretion

In addition to passive diffusion there appears to be an ATP requiring mechanism for Mg absorption from the GI tract(8). Similarly, in the kidney in addition to passive diffusion there appears to be an additional active transport system for the reabsorption of Mg(9,10,12,19). In short, Mg via ATP is required for a portion of its own GI absorption and renal reabsorption(19). Likewise GI absorption of K is decreased and renal reabsorption decreased, if there is a Mg (and therefore ATP) shortage in GI and kidney cells respectively(14,19,56). Both absorption and reabsorption of K (and Mg) worsen with age(11). Some hormones, e.g., glucagon (produced in the pancreas) and calcitonin, stimulate renal reabsorption of Mg via cyclic AMP (cAMP), which requires the Mg dependent enzyme adenylate cyclase(90).

MAGNESIUM AND HORMONES

Homeostasis

Neither Mg nor K has good neurohormonal controls for either GI absorption or renal reabsorption to maintain proper balance (v parathormone, calcitonin and vitamin D for Ca, aldosterone and atrial natriuretic peptide (ANP) for Na)(35). However, insulin, parathormone (PTH) and Vitamin D do play a role in Mg homeostasis by increasing cellular uptake(13). The former is primarily associated with carbohydrates and the latter two with Ca, a Mg antagonist. A variety of other hormones have been implicated in urinary magnesium wasting. These include catecholamines, TSH (thyroid-stimulating hormone or thyrotropin), T3 (triiodothyronine), T4 (thyroxine) and calcitonin (produced in the thyroid gland), glucocorticoids (affect glucose metabolism, especially cortisol) and mineralocorticoids (affect sodium metabolism, especially aldosterone), ADH (antidiuretic hormone from pituitary) and angiotensins (liver and lungs)(14,15,20,57). Catecholamines are produced by both the adrenal medulla (humoral) and sympathetic nerves (neurotransmitter). Corticoids (corticosteroids) are produced by the adrenal cortex. High dietary sodium and calcium may also result in urinary magnesium wasting(16).

Insulin

Insulin causes cellular uptake of Mg(12). Magnesium deficiency results in insulin resistance(13) as well as impaired insulin secretion(17,22,23). Furthermore, the most significant mechanism for urinary magnesium wasting is probably through glycosuria (glucose in the urine) secondary to impaired glucose tolerance(14,21,23,25). Insulin resistance appears to be due to defective tyrosine-kinase activity (requires Mg) at the insulin receptor level and increased intracellular calcium(18). This resistance mandates release of more insulin, causing more Mg (and K) to be transported from blood into cells. Intracellular Mg (and K) must then be maintained against a greater concentration. This gradient is about 40:1 for K and 3:1 for Mg (intracellular v. extracellular)(71). The concomitant urinary Mg wasting aggravates this further causing both additional membrane instability (decreased magnesium phospholipid complexes) and pump dysfunction (defective Ca/Mg ATPase and Na/K ATPase pumps), causing more Mg loss and more insulin resistance (see cAMP/cGMP discussion below).

Parathormone

The parathyroid gland in response to low serum magnesium or calcium releases PTH. PTH then increases GI absorption and renal reabsorption of Mg(12). However, adequate magnesium is required for parathyroid hormone synthesis and secretion(20). So this also is a kind of a hormonal catch 22 (Mg is required for the efficacy of one of its regulating hormones) similar to the electrolyte catch 22 (Mg is required for its own cellular uptake). Mg deficiency also causes end organ PTH resistance (serum Ca does not rise when PTH is increased in Mg deficient patients)(12,48,55,87).

Vitamin D

Intestinal absorption of magnesium and calcium is enhanced by Vitamin D(52). Mg absorption in Vitamin D deficiency is decreased(72). In addition serum concentration of 1,25 dihydroxy cholecalciferol (cholecalciferol = Vitamin D3) is low or low/normal in a magnesium deficient state and does not rise in response to a low calcium diet. This is because the formation of 1,25 dihydroxy cholecalciferol involves a magnesium dependent hydroxylase enzyme(12). Magnesium deficiency also results in end organ resistance to vitamin D and its metabolites(12). This is another hormonal catch 22. Vitamin D increases net absorption of Mg but to a lesser degree than for Ca (34,35). The subsequently elevated blood Ca may result in greater urinary Mg wasting(12).

Glucagon

Insulin and glucagon (and to a lesser extent catecholamines) counter regulate each other in maintaining glucose balance. Glucagon causes glycogenolysis (break down of glycogen) and gluconeogenesis (production of glucose) increasing blood glucose while insulin transports glucose (and K) into the cell decreasing blood glucose. Magnesium deficiency has been strongly associated with chronic fatigue syndrome (CFS)(106). Some have suggested that this may be because Mg is required for six of the nine enzymatic steps in glycolysis (breaking down glucose to produce energy, i.e., the opposite of gluconeogenesis)(91,95). Furthermore, cAMP via adenylate cyclase, a Mg dependent process, mediates glucagon receptor activity(105). Therefore, in order to effectively counterbalance insulin glucagon requires Mg.

Aldosterone and ANP

Mention aldosterone and most think renal Na reabsorption and renal K secretion/excretion. Few realize that aldosterone also causes urinary Mg wasting due to blood volume expansion and consequent greater delivery of sodium, calcium, and magnesium to the distal renal tubules(14). Magnesium deficiency enhances angiotensin-induced aldosterone synthesis (RAAS)(47). Indeed, there have been many articles written touting the antihypertensive qualities of Mg supplementation in those deficient. Magnesium deficiency causes hypertrophy of the juxtaglomerular apparatus (JGA), located in the kidney(36,37). This releases renin, which ultimately increases aldosterone, lowering serum Mg (and K). This, of course, again aggravates membrane permeability and pump function.

Aldosterone levels fluctuate diurnally—highest concentration being at 8 AM, lowest at 11 PM, in parallel to cortisol and ACTH rhythms(64). These levels increase with age. Aldosterone may be a major contributor to LAF, predominantly via the resultant increase in the intracellular Na/K ratio. Unfortunately, the deleterious effects of aldosterone and the RAAS do not end with Na/K. Recent research(41) has shown that the heart and endothelium both contain receptors for aldosterone and that this mineralocorticoid is responsible for left ventricular fibrosis, dilatation, and hypertrophy. Spironolactone, a K sparing diuretic, blocks many of the adverse

effects of aldosterone but has some adverse side effects, including causing development of breasts in males and irregular menses in females. An exciting new diuretic called eplerenone(39) is similarly K sparing and cardioprotective, but without the side effects of spironolactone. Evidence has accumulated in recent years indicating that these K sparing drugs may also exert some Mg-sparing properties(51,52,59).

Atrial natriuretic peptide (ANP) is the hormonal antagonist of aldosterone. It causes renal reabsorption of K and excretion/secretion of Na. Congestive heart failure (CHF) and atrial fibrillation (AF) stimulate release of ANP from atrial cells via atrial muscle cell stretching that occurs at such times. ANP is also secreted during exercise(68). In fact, hypoxia is a potent stimulus for ANP(70). K and ATP (and Mg) mediate the release of ANP. Many believe that ANP is helpful in terminating episodes of AF by favorably rebalancing the intracellular Na/K ratio. It is also a Ca channel blocker(69).

References

1. Magnesium: We Don't Appear to be Getting Enough, [Burton M. Altura](#), Science News Online, August 29, 1998, http://www.sciencenews.org/sn_arc98/8_29_98/food.htm
2. <http://www.mksalaman.com/features/f1095/article2.html>
3. Dietary Magnesium Affects Susceptibility of Lipoproteins and Tissues to Peroxidation in Rats, [Rayssiguier Y, Gueux E, Bussiere L, Durlach J, Mazur A.](#) J Am Coll Nutr 1993 Apr 12(2):133-7.
4. Importance of Potassium in Cardiovascular Disease, [Sica et al.](#), J Clin Hypertens 4(3): 198-206,2002. <http://www.medscape.com/viewarticle/438088>
5. Magnesium, Potassium and Hormones in Urines of Patients with Essential Hypertension, Abstracts of Journal of Japanese Society for Magnesium Research, [J.J.S.Mg R.](#) Vol. 14, No.1 (1995), pp. 35-44. http://www.mgwater.com/jmgr95_1.shtml#REP4
6. Oral Magnesium Supplementation to Patients Receiving Diuretics: Normalization of Magnesium, Potassium and Sodium, and Potassium Pumps in the Skeletal Muscles, [Ugeskr Laeger](#) (Denmark) Jul 4 1994, 156 (27) p4007-10, 4013.
7. Daily Intake of Macro and Trace Elements in the Diet. 4. Sodium, Potassium, Calcium, and Magnesium, [Ann Ig](#) (ITALY) Sep-Oct 1989, 1 (5) p.923-42. http://www.lef.org/prod_hp/abstracts/php-ab236a.html#57
8. Diagnosis of magnesium-induced diarrhoea, [Fine, D.F. et al](#) (1991b) New England Journal of Medicine, 324, 1012-1017. <http://www.foodstandards.gov.uk/multimedia/pdfs/evm-01-13.pdf>
9. Cytosolic Mg²⁺ Modulates Whole Cell K^{*} and CF Currents in Cortical Thick Ascending Limb (TAL) Cells of Rabbit Kidney, [Kelepouris E, Kidney Int](#) 37: 564, 1990. http://www.barttersite.com/hypomagnesemia_Agus.htm
10. Mg(2+)-dependent inward rectification of ROMK1 channels expressed in *Xenopus* oocytes, [Nichols CG, Ho K, Hebert S, J Physiol \(Lond\)](#) 476: 399-409, 1994. http://www.barttersite.com/hypomagnesemia_Agus.htm
11. Body Composition, Health Status, and Urinary Magnesium Excretion Among Elderly People, [Lowik, M.R. et al](#)(1993) Magnesium Research 6, 223-232. <http://www.foodstandards.gov.uk/multimedia/pdfs/evm-01-13.pdf>
12. Magnesium in Clinical Practice, [Jean Durlach](#), Section I, Elements of Magnesium Biology, pp 1-39, John Libbey & Company, 1985. <http://www.mgwater.com/durex01.shtml>
13. Magnesium Deficiency Produces Insulin Resistance and Increased Thromboxane Synthesis, Hypertension (USA), 1993, 21/6 II (1024-1029). <http://www.ionicminerals.com/research/magnesium/arts.html>
14. Disorders of Magnesium Metabolism, [JIFCC](#), v 11 (2), 1999, pp 10-18. http://www.ifcc.org/ejifcc/vol1_1_no2/pdf/Magnesium_Article.pdf
15. Magnesium metabolism, a review, [Ebel, H. and Gunther. T.](#) (1980), Journal of Clinical Chemistry and Clinical Biochemistry, 18, 257-270. <http://www.foodstandards.gov.uk/multimedia/pdfs/evm-01-13.pdf>
16. The Relationship Between Dietary Intake and Urinary Excretion of Sodium, Potassium, Calcium and Magnesium: Belgian Interuniversity Research on Nutrition and Health. [Kesteloot, H. and Joossens, J.V.](#) (1990), J. Hum. Hyperts. 4, 527-533. <http://www.foodstandards.gov.uk/multimedia/pdfs/evm-01-13.pdf>
17. Magnesium and carbohydrate metabolism, [Therapie](#) (France), 1994, 49/1 (1-7) <http://www.ionicminerals.com/research/magnesium/arts.html>
18. Hypertension, Diabetes Mellitus, and Insulin Resistance: the Role of Intracellular Magnesium, [Paolisso G, et al.](#) Am J Hypertens 1997 Mar 10(3): 368-370 <http://www.spectracell.com/diabetesmellius.html>
19. Cell Magnesium Transport and Homeostasis: Role of Intracellular Compartments, [Romani et al](#) (1993), Miner. Electrolyte Metab. 19, 282-289. <http://www.foodstandards.gov.uk/multimedia/pdfs/evm-01-13.pdf>

20. The Role of Magnesium in Clinical Biochemistry: An Overview, Ryan, M.F. (1991), *Am. Clin. Biochem.* 28, 19-26. <http://www.foodstandards.gov.uk/multimedia/pdfs/evm-01-13.pdf>
21. Magnesium Metabolism and Deficiency, Rude, R.K. (1993), *Endocrinol. Metabol. Clin North Am.* 22, 377-395. <http://www.foodstandards.gov.uk/multimedia/pdfs/evm-01-13.pdf>
22. Magnesium and carbohydrate metabolism, Therapie (France), 1994, 49/1
<http://www.ionicminerals.com/research/magnesium/arts.html>
23. Magnesium and Glucose Homeostasis, *Diabetologia* (Germany, Federal Republic of), 1990, 33/9(511-514)
<http://www.ionicminerals.com/research/magnesium/arts.html>
24. Magnesium and the Cardiovascular System: I. New Experimental Data on Magnesium and Lipoproteins, Durlach et al., Chapter 113, in *Molecular Biology of Atherosclerosis*, © John Libbey & Company Ltd, pp. 507-512 <http://www.mgwater.com/dur24.sritml>
25. Renal Hypomagnesemia in Human Diabetes Mellitus: Its Relation to Glucose Homeostasis, McNair P, Christensen, MS, Christiansen C, et al: *Eur J Clin Invest* 1982; 12:81-85.
26. Subclinical hyperthyroidism as a risk factor for atrial fibrillation, Auer J, et al. *Am Heart J* 2001;142:838-42.
<http://www.tsh.org/research/new/utiger1/1>
27. Thyrotoxic Periodic Paralysis: An Overview, *Rev Neurol* 1999 Sep 16-30; 29(6): 510-2.
<http://www.periodicparalysis.org/PPRC/PP/>
28. Combining Structural Genomics and Enzymology: Completing the Picture in Metabolic Pathways and Enzyme Active Sites, Heidi Eriandsen et al., *Current Opinion in Structural Biology* 2000, 10:719-730
29. Catechol-O-Methyl Transferase Activity: Assay, Distribution and Pharmacological Modification, Ilkka Rpenila, Institute of Biomedicine, Department of Pharmacology and Toxicology, University of Helsinki, Finland, 1999. <http://ethesis.helsinki.fi/julkaisut/laa/biola/vk/reenila/catechol.pdf>
30. The Medical Biochemistry Page, Copyright© 1996-2002 Dr. Michael W. King
<http://www.indstate.edu/thcme/mwking/aminoacidderivatives.rtml>
31. The Role and Mechanisms of Angiotensin II in Regulating the Natriuretic Peptide Gene Expression in Response to Cardiac Overload, 2.4. Natriuretic Peptides, Maria Suo, April 2002, Oulu University Library.
<http://herkules.oulu.fi/isbn9514266994/html/x1344.html>
32. Magnesium and the Cardiovascular System: I. New Experimental Data on Magnesium and Lipoproteins, Durlach et al., Chapter 113, in *Molecular Biology of Atherosclerosis*, © John Libbey & Company Ltd, pp. 507-512. <http://www.mgwater.com/dur24.shtml>
33. Cardiovascular Consequences of Magnesium Deficiency and Loss: Pathogenesis, Prevalence and Manifestations. Magnesium and Chloride Loss In Refractory Potassium Repletion, Mildred S. Seelig, M.D., M.P.H., *American Journal of Cardiology* 63:4G-21G, 1989. <http://www.mgwater.com/cardio.shtml>
34. Magnesium, *Clin. Sci.* 57:121, 1979 <http://www.mdschoice.com/elements/elements/major/minerals/magnesium.htm>
35. Cardiovascular Med. 3:637, 1978 <http://www.mdschoice.com/elements/elements/major/minerals/magnesium.htm>
36. Relationship of Juxtaglomerular Apparatus and Adrenal Cortex to Biochemical and Extracellular Fluid Volume Changes in Magnesium Deficiency, Cantin M, *Lab Invest* 22:558-568,1970.
<http://www.mgwater.com/conseq.shtml>
37. Plasma Magnesium Concentration as a Possible Factor in the Control of Aldosterone Secretion, Care AD, McDonald IR, *Biochem J* 87:2P-3P, 1963. http://www.barttersite.com/consequences_of_magnesium_defici.htm
38. Consequences of Magnesium Deficiency on the Enhancement of Stress Reactions; Preventive and Therapeutic Implications (A Review), Mildred S. Seelig, MD, *Journal of the American College of Nutrition*, Vol. 13, No. 5, 429-446 (1994). <http://www.coralcalmag.com/stress.htm>
39. Effects of Prolonged Strenuous Exercise on Plasma Levels of Atrial Natriuretic Peptide and Brain Natriuretic Peptide in Healthy Men, Haruo Ohba, MD et al., *Am Heart J* 141(5): 751-758,2001.
<http://www.medscape.com/viewarticle/409229>
40. Eplerenone: A New Aldosterone Receptor Antagonist - Are the FDA's Restrictions Appropriate? Domenic A. Sica, MD, *J Clin Hypertens* 4(6):441-445, 2002. <http://www.medscape.com/viewarticle/445177>
41. <https://secure.salu.net/eq-i-perl/get.cgi?pub=50136&ext=doc>
42. New Insights Into the Role of Aldosterone in Cardiorenal Disease and the Clinical Implications, Symposium held in Anaheim, California on November 10, 2001, Copyright © 2002 the University of Michigan Medical School. <http://www.medscape.com/viewprogram/1004>
43. The Biochemical Basis of Neuropharmacology, Cooper, J.R., Bloom, F.E., and Roth, R.H. (1996) Seventh Edition, Oxford University Press. <http://artsci-ccwin.concordia.ca/psvchology/psvc358/Lectures/transmit2.htm>
44. Excitotoxins, Blaylock, R. Santa Fe: Health Press, 1997. <http://smart-drugs.net/ias-excitotoxins.htm>
45. Excitatory Amino Acids as a Final Common Pathway for Neurologic Disorders, Lipton, S. & Rosenberg, P., (1994)" *NEJM* 330: 613-22. <http://smart-drugs.net/ias-excitotoxins.htm>

46. Inhibition of Astrocyte Glutamate Uptake by Reactive Oxygen Species: Role of Antioxidant Enzymes, Sorg, O. et al (1997), Mol. Med 7: 431-40. <http://smart-drugs.net/ias-excitotoxins.htm>
47. <http://www.msgrtruth.org/diabetes.htm>
48. Magnesium Deficiency Produces Insulin Resistance and Increased Thromboxane Synthesis, Hypertension (USA), 1993, 21/6 II (1024-1029). <http://www.ionicminerals.com/research/magnesium/arts.html>
49. Functional Hypoparathyroidism and Parathyroid Hormone and Organ Resistance in Human Magnesium Deficiency, Rude RK, Oldham SB, Singer FR, Clin Endocrinol (Oxf) 5: 209-224, 1976. <http://www.barttersite.com/mgburn.htm>
50. Acid Peptic Disorders, Ronald Hsu, MD, FACP, FACC, Director of Endoscopy, Division of Gastroenterology, University of California Davis Medical Center. <http://213.239.53.100/search?q=cache:pga7PNAWQwC:medocs.ucdavis.edu/IMD/420B/esylabus/acidpeptic.htm>
51. Hypomagnesemia, The Bartter Site. <http://www.barttersite.com/hypomagnesemia.htm>
52. Magnesium and Potassium-Sparing Diuretics, Ryan MP, Magnesium 1986;5 (5-6):282-92. <http://www.barttersite.com/mgK.htm>
53. Magnesium in Clinical Practice, Jean Durlach, Section V, Magnesium and Therapeutics, pp. 219-228, John Libbey & Company, 1985. <http://www.mgwater.com/durex03.shtml#fx1.321>
54. An Increase in Plasma Atrial Natriuretic Peptide Concentration During Exercise Predicts a Successful Cardioversion and Maintenance of Sinus Rhythm in Patients with Chronic Atrial Fibrillation, Wozakowska-Kaplon, B, et al., Pacing Clin Electrophysiol, Vol. 23 (Pt 2), November 2000, pp. 1876-79.
55. Metabolic Alkalosis, Sameer Yaseen, MD, August 2, 2002. <http://www.emedicine.com/med/topic1459.htm>
56. Hypomagnesemia, Zalman S. Agus, Journal of the American Society of Nephrology, Vol 10 (7), July, 1999. http://www.barttersite.com/hypomagnesemia_Agus.htm
57. Magnesium: Its Proven and Potential Clinical Significance, Fox et al., South Med J 94(12):1195-1201, 2001. www.medscape.com/viewarticle/423568
58. Magnesium status and health, Dreosti, I.E. (1995), Nutrition reviews53, S23-S27. <http://www.mgwater.com/dur06.shtml>
59. Grass Tetany, Chapter 19, Magnesium and neuro-muscular transmission, Andre Voisin. <http://www.soilandhealth.org/01aglibrarv/010106voisin/010106gtchap19.html>
60. Magnesium in Clinical Practice, Jean Durlach, Section V, Magnesium and Therapeutics, pp.219-228, John Libbey & Company, 1985. <http://www.mgwater.com/durex03.shtml#fx1.321>
61. Consequences of Magnesium Deficiency on the Enhancement of Stress Reactions; Preventive and Therapeutic Implications (A Review), Seelig MS, J Am Coll Nutr, 1994 Oct, 13:5, 429-46. <http://www.mgwater.com/conseq.shtml>
62. Magnesium-Deficient Myocardium Demonstrates an Increased Susceptibility to an In Vivo Oxidative Stress, Freedman AM, Cassidy MM, Weglicki WB: Magnes Res 4:185-189, 1991. <http://www.mgwater.com/dur11.shtml>
63. Magnesium and lipids in cardiovascular disease, Rayssiguier, Y. & Gueux, E. (1986), J. Am. Coll. Nutr. 5, 507-519. <http://www.mgwater.com/dur24.shtml>
64. Magnesium and Lipid Metabolism. In Metal Ions in Biological Systems, Magnesium and Its Role in Biology, Nutrition and Physiology, Rayssiguier, Y. (1990), ed. H. Sigel, Vol. 26, pp. 341-358. New York: Marcel Dekker. <http://www.mgwater.com/dur11.shtml>
65. Endocrine Physiology Lecture 5, Aldosterone by Dale Buchanan Hales, PhD, Department of Physiology & Biophysics. <http://WtVw.uic.edu/classes/phyb/phyb402db/lecture5.ppt>
66. Effect of Exercise in the Heat on Plasma Renin and Aldosterone with Either Water or a K Rich Electrolyte Solution, Francis, K.T. & MacGregor, R. (1978): Aviation Space Environ. Med. 49, 461-465. <http://www.mgwater.com/dur18.shtml>
67. New Experimental and Clinical Data on the Relationship between Magnesium and Sport, Y. Rayssiguier, C. Y. Guezennec, and J. Durlach, Magnesium Research (1990) 3, 2, 93-102. <http://www.mgwater.com/dur18.shtml>
68. Effects of Right Lateral Decubitus Position on Plasma Norepinephrine and Plasma Atrial Natriuretic Peptide Levels in Patients with Chronic Congestive Heart Failure, Miyamoto, S, et al., American Journal of Cardiology, Vol. 89, January 15, 2002, pp. 240-42
69. An Increase In Plasma Atrial Natriuretic Peptide Concentration during Exercise Predicts a Successful Cardioversion and Maintenance of Sinus Rhythm in Patients with Chronic Atrial Fibrillation, Wozakowska-Kaplon, B, et al., Pacing Clin Electrophysiol, Vol. 23 (Pt 2), November 2000, pp. 1876-79
70. Cyclic GMP-Mediated Inhibition of L-type Ca²⁺ Channel Activity by Human Natriuretic Peptide in Rabbit Heart Cells, Tohse N, et al., British Journal of Pharmacology, Vol. 114, No. 5, March. 1995, pp. 1076-82. <http://herkules.oulu.fi/isbn9514252721/html/x549.html>
71. Importance of Magnesium for the Electrolyte Homeostasis - An Overview, Armin Schroll, Deutsches Herzzentrum Munchen, Klinik fur Herz- und GefaBchirurgie, Lothstr. 1 1, D-80335 Munchen, Germany, January 30, 2002. <http://www.mgwater.com/schroll.shtml>

72. Lone Atrial Fibrillation: Towards A Cure, [Larsen, HR.](#), 2003, pp. 63, 64, 96,116. www.afibbers.org
73. Principles and Applications of Bioelectric and Biomagnetic Fields by [Jaakko Malmivuo](#) and [Robert Plonsey](#), Chapter 24, Cardiac Defibrillation in [Bioelectromagnetism](#), Oxford University Press, 1995. <http://butler.cc.tut.fi/~malmivuo/bem/bembook/24/24.htm>
74. Guidelines for the Management of Patients with Atrial Fibrillation, [Fuster et al.](#), ACC/AHA/ESC, J Am Coll Cardiol 2001;38:1266i-1xx http://www.acc.org/clinical/guidelines/atrial_fib/V_pathophysiological.htm
75. Atrial Fibrillation: From Cell to Bedside, [Phillip Sager, MD](#), Co chairs: [Robert Myerburg, MD](#), and [Jasmir Sra, MD](#), [Autonomic Aspects of Atrial Fibrillation](#) by [Philip T. Sager, MD](#), <http://www.medscape.com/viewarticle/422901>
76. Update on Atrial Fibrillation, [EMEX Workshop](#), Friday 29 September 2000 Amsterdam [Electrophysiology of Atrial Fibrillation](#), Prof. [Arthur Wilde, MD](#) Dept. of Clinical [Electrophysiology](#), University Hospital, Amsterdam. http://www.emex.nl/3_uoaf_ab2.html
77. Molecular Adaptations in Human Atrial Fibrillation: Mechanisms of Protein Remodeling, by [Bianca Johanna Josephina Maria Brundel](#), p. 15. <http://www.ub.rug.nl/eldoc/dis/medicine/b.i.j.m.brundel/cl.pdf>
78. Non-pharmacological Treatment of Atrial Fibrillation, by [Ole-Gunnar Anfinnsen, MD, PhD](#), [Indian Pacing and Electrophysiology Journal](#), 2002, 2:4. <http://www.ipei.org/0201/anfinnsen.htm>
79. Apex-to-base dispersion of refractoriness underlies the proarrhythmic effect of hypokalaemia/hypomagnesaemia in the rabbit heart, [J Electrocardiol](#) 2002 Jul;35(3):245-52. <http://www.uic.edu/classes/pcol/pcol425/restricted/Vogel/arr.pdf>
80. Dispersion of Cell-To-Cell Uncoupling Precedes Low K+-Induced Ventricular Fibrillation, [N. Tribulova, M. Manoach, D. Varon, L. Okruhlicova, T. Zinman, A. Shainberg](#), [Physiol. Res.](#) 50:247-259, 2001. <http://www.biomed.cas.cz/physiolres/2001/issue3/tribul.htm>
81. Magnesium Potassium Interactions in Cardiac Arrhythmia. Examples of Ionic Medicine. [Magnes Trace Elem](#) (Switzerland) 92 1991, 10 (2-4) p193-204. http://www.lef.org/prod_hp/abstracts/potassiumabs.html#27
82. OGTT: Indications and Limitations, by [Roger Nelson, MD](#), [Mayo Clin Proc](#) 63:263-269, 1988.
83. [Tietz'](#) Fundamentals of Clinical Chemistry (5th ed.) c. 2001.
84. Transient Atrial Fibrillation Precipitated by Hypoglycemia, [Odeh, Majed, et al.](#), [Annals of Emergency Medicine](#), v 19, May 1990, pp. 565-67.
85. Hypoglycemia - A Rare Cause of Atrial Fibrillation, [Yinnon, A.M., et al.](#), [IsrJ Med Sci](#), v25, 1989, pp. 346-7.
86. Proarrhythmic Effects of Reactive Hypoglycemia, [Rokas S, et al](#), [Pacing Clin Electrophysiol](#) 1992 Apr;15(4 Pt 1):373-6. <http://www.ncbi.nlm.nih.gov/entrez/querf.cgi?cmd=Retrieve&db=PubMed&listuids=1374880&dopt=Abstract>
87. Functional hypoparathyroidism and parathyroid hormone and organ resistance in human magnesium deficiency, [Rude RK, Oldham SB, Singer FR](#), [Clin Endocrinol \(Oxf\)](#) 5: 209-224, 1976. http://www.barttersite.com/hvpomagnesemia_Agus.htm
88. Hypoglycemia. <http://www.allerQvcentre.com.au/id129.htm>
89. Postprandial Reactive Hypoglycemia, [JF Brun, C Fedou, J Mercier](#), [Diabetes & Metabolism \(Paris\)](#) 2000, 26, 337-351. <http://www.alfediam.org/media/pdf/RevueBrunD&M5-2000.pdf>
90. Severe Hypermagnesemia Resulting from Laxative Use in a Patient with Renal Insufficiency, [Zaman et al.](#) http://www.turner-white.com/pdf/hp_mar02_laxative.pdf
91. GP Notebook, A Clinical Encyclopedia on the World Wide Web, [McMorran et al.](#), Oxford Solutions Ltd Press, 2001. <http://www.gpnotebook.co.uk/medwebpage.cfm?ID=993329210>
92. Free Plasma Magnesium Following Glucose Loading in Healthy Humans, [Jacomella et al.](#), [Acta Diabetologica](#), Vol 34 Issue 3 (1997) pp 235-237. <http://link.springer-ny.com/link/service/journals/00592/bibs/7034003/70340235.htm>
93. The Isoprenoid Pathway in Lone Atrial Fibrillation with Embolic Stroke, [Ravikumar and Kurup](#), [Indian Heart J](#) 2001; 53: 184-188.
94. Digoxin: The Medicine from Hell?, [Hans Larsen](#). <http://www.afibbers.org/S/afib15.htm>
95. Summary of Major Nutrients: Functions of Magnesium. [Dr Igor Tabrizian](#) - Nutrition Review Service, 1 August 2001. <http://www.cancersupportwa.org.au/Spotlight/Igor/8IT.htm>
96. [Mattioli, AV](#), et al. Clinical, Echocardiographic, and Hormonal Factors Influencing Spontaneous Conversion of Recent-Onset Atrial Fibrillation to Sinus Rhythm, [Mattioli, AV, et al.](#), [American Journal of Cardiology](#), Vol. 86, August 1, 2000, pp. 351-52. <http://www.vourhealthbase.com/arrhythmias.html>
97. Mini-review: The Glucagon-Like Peptides, [Daniel J. Drucker](#), [Endocrinology](#), Vol. 142, No. 2. <http://www.w.glucagon.com/Glucagon-like%20peptides%202001%20Review.%20pdf.pdf>
98. Increased Nonoxidative Glucose Metabolism In Idiopathic Reactive Hypoglycemia, [Leonetti F, Foniciello M, Iozzo P, Riggio O, Merii M, Giovannetti P, Sbraccia P, Giacari A, Tamburrano G](#). [Metabolism](#), 1996, 45, 606-610. <http://www.alfediam.org/media/pdf/RevueBrunD&M5-2000.pdf>

99. Pancreatic Alpha-Cell Function In Idiopathic Reactive Hypoglycemia. Ahmadpour S, Kabadi UM, Metabolism, 1997, 46, 639-643. <http://w.alfediam.org/media/pdf/RevueBrunD&M5-2000.pdf>
100. Le Syndrome D'hypoglycemie Reactionnelle: Mythe Ou Reatite, Lefebvre PJ, Luyckx AS, Gerard J, Journees Annuelles de Diabetologie de l'Hotel-Dieu, 1983. Flammarion Medecine-Sciences, Paris, 111-118. <http://www.alfediam.org/media/pdf/RevueBrunD&M5-2000.pdf>
101. Life Situations, Emotions and Hyperinsulinism, Sidney A Portis, JAMA, v. 142, April 22, 1950, pp. 1281-86.
102. Neuronal Activation Of Brain Vagal-Regulatory Pathways And Upper Gut Enteric Plexuses By Insulin Hypoglycemia, Yuan PQ, Yang H, Am J Physiol Endocrinol Metab 2002 Sep;283(3):E436-E448.
103. Lone Atrial Fibrillation In Vigorously Exercising Middle Aged Men: Case- Control Study. Karjalainen, Jouko, et al. British Medical Journal, Vol. 316, June 13, 1998, pp. 1784-85. <http://www.afibbers.org/arrhythmias.html>
104. Susceptibility of the right and left canine atria to fibrillation in hyperglycemia and hypoglycemia. Vardas PE, Vemmos K, Sideris DA, Mouloupoulos SD, J Electrocardiol 1993 Apr;26(2):147-53. <http://www2.canisius.edu/~corsot/biochemistrv/gluconeogenesis.htm>
106. Magnesium Deficiency and Its role in CFS, Sarah Myhill, M.D., from her book Diagnosing and Treating Chronic Fatigue Syndrome, 11/14/2000. <http://www.immunesupport.com/library/showarticle.cfm/id/2892>
107. Inactivation of Catecholamines, Frank Vincenzi M.D, University of Washington School of Medicine, Human Biology 543, Principles of Pharmacology. <http://courses.washington.edu/chat543/cvans/catechol.htm>
108. <http://216.239.39-100/search?q=cache:mZJOe-FmXEUC:www.its.caltech.edu/>
109. <http://home.intekom.com/pharm/guatrom/g-dop200.html>
110. <http://www.macses.ucsf.edu/Research/Allostatic/notebook/heart.rate.html>

THE AFIB REPORT is published monthly by:
Hans R. Larsen MSc ChE, 1320 Point Street, Victoria, BC, Canada, V8S 1A5
E-mail: editor@afibbers.org World Wide Web: <http://www.afibbers.org>

Copyright 2003 by Hans R. Larsen

THE AFIB REPORT does not provide medical advice. Do not attempt self-diagnosis or self-medication based on our reports.
Please consult your healthcare provider if you are interested in following up on the information presented.