

GOUT, KIDNEY STONES AND THE KETOGENIC DIET

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By far the biggest concern voiced against the Ideal Protein Program is the notion that a protein-based, ketogenic diet is somehow unhealthy and causes gout and/or kidney stones. This opinion is shared by many medical practitioners as well as lay folks. So pervasive is this belief that many of our competitors only use a ketogenic protocol for a 2 week "induction phase" before adding sufficient carbohydrates to bring the dieter out of ketosis. Other similar programs avoid ketosis completely, giving a hypo-caloric diet with a minimum amount of protein (like us) but keeping enough carbohydrates in the diet so as to preclude ketosis and avoid dealing with the issues of stones and gout. This type of program would be adequate for the "at home, do it yourself dieter", requiring little in the way of patient monitoring. While the patient will lose weight on these programs, they will not experience all the benefits they would get on a true ketogenic protocol. First, it will take them longer to attain their goal weight, a ketogenic diet is the most efficient means to lose fat. More importantly, by maintaining a fair amount of carbohydrates in the diet, the patient has little chance to actually "re-set the pancreas" and give the cells enough time to regain their insulin sensitivity. A true "medical grade protocol", such as the Ideal Protein Diet, should offer ALL of these benefits and patients suffering from the symptoms of Metabolic Syndrome should not accept less.

PROTEIN DIETS CAUSE ELEVATED LEVELS OF URIC ACID

This is a common misconception. It is true that a diet strictly composed of fats and whole food proteins, such as the "classic Atkin's Diet would probably raise uric acid levels, but not all proteins are created equal. Uric acid (in vivo) is produced by the action of the enzyme *xanthine oxidase* on chemical entities called *purines*. Pure proteins do not contain any purines. Pure proteins are protein isolates and albumin (or egg white). Purines are part of the DNA and RNA structure in the cell. Therefore when one consumes a lot of cells, one gets a lot of purines (such as a diet containing strictly whole protein sources). Red meats, organ meats (liver, sweetbreads, brains, tripe), fermented foods (lots of yeast cells) such as cheese, beer, wine contain a rather high level of purines. Caffeine has a structure similar to a purine and, if acted on by xanthine oxidase, can produce some uric acid. An egg on the other hand, being only one cell (if not fertilized) has an extremely low content of purines (actually, being a sex cell, it only has half of the chromosomes, so only half the DNA and therefore half the purine content of a somatic cell). The main protein sources of protein in the Ideal foods are, whey isolates, soy isolates and albumin.....no purines whatsoever!

YEAH, WELL, MY FRIEND WENT ON AN ISOLATE DIET AND GOT STONES...

An elevated blood level of uric acid is a common consequence of "Metabolic Syndrome". That being said, it is entirely possible for a patient, placed on a ketogenic diet, albeit one low in purines, to develop gout or kidney stones. Therefore there must be something else coming into play besides a diet high in purines. During ketosis excessive ketone bodies are excreted primarily in the urine but can also be eliminated via the breath ("acetone breath") and via the feces. This is particularly true in the beginning weeks of a ketogenic protocol when the cells of the body do not have all of the necessary enzymes readily available to fully utilize these ketones as an energy source, hence some are excreted. Ketone bodies are slightly acidic and therefore these would tend to make the urine more acidic. If this condition is not addressed it is possible that renal urate stones may form or a gout attack may be precipitated.

THE 'DISASSOCIATION CONSTANT': pKa

Weak organic acids such as uric acid may exist in two forms. One is called the *unionized form* (think of salt crystals in a salt shaker). The other form is the *ionized or disassociated form* (think of the salt crystals now dissolved in a glass of water). Which form the acid exists as is dependent upon the pH of its environment (here we are speaking of the blood and urine). The pKa is the pH at which the acid exists as half ionized, half unionized. The pKa for uric acid is 5.5, meaning at a pH of 5.5 half of it is like salt crystals and half of it is like the 'dissolved salt'. In the blood stream the bicarbonate buffer (sodium bicarbonate or potassium bicarbonate.....see the section on acid / base balancing in "The Pathogenesis of Syndrome X: The Relationship Between Insulin and Glucagon" in our Clinic Manual) reacts with uric acid and produces "salts" mono-sodium urate and mono-potassium urate.

$\text{KHCO}_3 + \text{R-COOH (uric acid)} \rightarrow \text{R-COOK (mono-potassium urate)} + \text{H}_2\text{CO}_3$ (carbonic acid) which then reacts with the enzyme alpha-carbonic anhydrase (with zinc as a catalyst) and becomes water and carbon dioxide (water is eliminated as urine, CO_2 is of course exhaled. The same reaction occurs if sodium bicarbonate is the buffer (NaHCO_3) and of course the salt mono-sodium urate would be produced.

Now, so not to confuse, remember the body tightly controls the pH of the blood and maintains it between 7.3 and 7.4. This means (because pH numbers are logarithms...powers of ten) uric acid in the blood exists more than 100 fold in the ionized (dissolved form) over the unionized form. At a pH of 5.5, they exist in equal parts, so if we raise the pH to 7.4 (a hundred fold increase) the ionized form is the predominate species. As the environment becomes more alkaline to the pKa (higher pH number) the more of the acid / salt becomes ionized (dissolved) and no crystals will form. However another factor also comes into play, the concentration of the acid / salt. Think of dissolving salt in a glass of water, as you put in the salt it readily dissolves. You keep adding more salt until no more will dissolve. At this point we say the solution is saturated. If you put more salt in, the crystals fall to the bottom of the glass, they *precipitate out of solution*. Should this happen in the blood stream, the precipitated UA crystals may accumulate in a joint and trigger an inflammatory response. This is how gout occurs.

INTO THE KIDNEYS

As blood is filtered by the kidneys (in the glomeruli) urine is produced and uric acid is actively secreted by the distal tubule. Remember it can exist as two forms, the insoluble unionized form or as the urate salt, which is about 20 times more soluble than its unionized partner. If the urinary pH is 5, precipitation occurs when the concentration of uric acid is only 60 mgs per liter of urine. The average human excretes about 400 mgs of uric acid daily, so a urine with a pH of 5 would require over 6 liters of urine output per day to avoid crystallization! At a pH of 6, this doesn't occur until the urine contains 220 mgs of uric acid per liter.¹ The obvious consequence of uric acid precipitation in the renal tubules is stone formation (urolithiasis). The Ideal Protein Diet mandates that a dieter consume, at a minimum, 2 liters of water daily along with the alkaline mineral supplements potassium, calcium and magnesium and four cups of "green vegetables" and two salads. In addition, for every cup of a caffeinated beverage, the dieter will consume an extra cup of water. For the majority of dieters this protocol is sufficient to keep the urine in the pH range of 6 and stone formation will not be an issue.

SPECIAL PATIENT POPULATIONS

According to Resnick and Schaeffer, individuals with a predilection for the formation of uric acid stones may be divided into four board categories. The first is patients with diseases associated with elevated levels of serum uric acid such as primary gout. About one quarter of patients with gout form uric acid stones and approximately one quarter of patients who form stones have had gout at one point. The second category is patients with a propensity to dehydration. These may include those with chronic diarrhea, ulcerative colitis and those with ileostomies. The third category comprises patients with hyperuricosuria without elevated serum uric acid levels. In men this is defined as excreting over 800 mgs. of uric acid daily or 750 mgs of uric acid output in women. Certain medications such as thiazide type diuretics can increase the excretion of uric acid and lead to stone formation. The final category is people who form stones despite normal serum levels of uric acid and do not demonstrate hyper secretion of UA in the urine. These patients usually have persistent acidic urine. The authors call this condition *idiopathic uric acid lithiasis*.

¹Resnick, MJ and Schaeffer, AJ: Urology Pearls. Hanley & Belfus Publishing, First Edition 1999. P.181

MANAGEMENT OF THESE PATIENTS ON THE IDEAL PROTOCOL

The clinician should carefully review the *HEALTH PROFILE* checking for a history of gout or kidney stones or conditions conducive to dehydration (i.e. chronic diarrhea, colitis, or having an ileostomy bag). Adequate hydration must be given to this group and it would be prudent to increase the daily water requirement to at least 3 liters per day. Each clinic should stock a roll of *PHENAPHTHAZINE PAPER* (commonly sold as "NitraTest Paper") which can be obtained at a pharmacy or on-line ('google' NitraTest). Unlike litmus paper, NitraTest determines the pH of the urine in the range of 4.5 to 7.5 and dipping a strip of this paper "mid-stream" will give an accurate reading of the urinary pH. While the majority of dieters will do just fine in the "6" range, the clinician should ensure this group maintains a urinary pH of at least 6.5. The dieter may be tested in the office during the weekly follow-up and be given an eight inch or so strip of paper to take home to monitor their urinary pH daily (they only need about an inch for one test). Results should be brought to the clinician on a weekly basis. It is recommended that the patient test 3 times a day: first urine in morning, midday and before bed. They will follow this procedure until an average urinary pH can be determined by the clinician and then only weekly tests (at the follow-up) will be necessary.

ADJUSTING THE URINARY pH

PRESCRIBERS: (MD's, DO's, NP's and PA's) For the fore-mentioned patient population the following protocol is recommended:

- Test urine pH at the initial consultation (using NitraTest Paper).
- Have patient return to office and re-check pH at day 4 of the Diet.
- If pH of urine is not at least 6.5 institute treatment with potassium citrate.
- Initiate dosage at about 60 mEq's of K-citrate (given in divided doses TID to QID with meals) per day. Urocit-K 10 is convenient (2 tabs at breakfast, 1 tab at lunch, 2 tablets at supper, and 1 tablet with the bedtime snack would be a good starting regimen). For those who have trouble swallowing tablets, liquid forms or packets of crystals are available (Polycitra-K). These are generally available generically and will cost the patient little out-of-pocket. (Polycitra-K comes as a 30mEq packet, so 1/2 packet dissolved in water QID would be perfect).
- Peak levels are reached by Day 3, so re-check urinary pH at the first weekly follow-up. Titrate dosage as necessary to ensure the urinary pH is at least 6.5.
- Approximately 60 mEq's of K-citrate will raise the urine pH by 0.7 units.
- Explain the necessity of adequate hydration! (3 liters per day of water).
- It may be advisable to draw a beginning potassium level and repeat at week 3.
- Potassium sparing diuretics should be discontinued and replaced with a small dose of a loop-diuretic if necessary. Observe other precautions so as not to induce hyperkalemia: (i.e. ACE inhibitors, Rx potassium supplements, etc. may have to be decreased or discontinued while on this therapy).
- Instruct the patient to take the dose with a meal or within 30 minutes of eating.
- As the Urocit-K 10 tabs are large, instruct them not to lie down for 30 minutes after swallowing...take with plenty of water.

NON-PRESCRIBERS: (DC'S, NATUROPATHS, ETC.) The following are non-RX alternatives:

- Follow the first two bullet points listed above.
- If pH of urine is not at least 6.5, institute treatment with Sodium Bicarbonate (baking soda).
- Initiate dosage at 1/2 teaspoonful dissolved in about 4-5 oz. water 3 times a day - between meals. This will provide about 75 mEq's of bicarbonate.
- Re-check urinary pH at the first weekly follow-up. If urine is not 6.5, add 1 -2 more 1/2 tsps doses. NOTE: BECAUSE THIS REGIMEN PROVIDES PLENTY OF SODIUM, THE PATIENT SHOULD NOT USE THE SEA SALT AND USE THE HIGHER SODIUM CONTENT FOODS SPARINGLY! WATCH FOR SIGNS OF FLUID RETENTION - RINGS FITTING TIGHTLY, SWOLLEN ANKLES, SLOW WEIGHT LOSS, ETC.

As an alternative to the above regimen, this protocol may be used:

Give one "Ideal Potassium /Calcium" tablet after each of the 4 meals and add 1/2 tsp. of baking soda (dissolved in water) between breakfast and lunch and another dose of the same between lunch and supper. This will not provide as much sodium (which may be desirable in some cases) and will form more mono-potassium urate, which is *more soluble than the sodium salt!* *If this protocol is used, it is IMPERATIVE the clinic contact Michael P Ciell, Chief Science Officer & Vice President of Clinical Operations prior to initiating the regimen. We want to go over any RX medications and concurrent health concerns (such as a history of arrhythmia) so as to preclude an electrolyte imbalance.*

Finally, remember you can always place these dieters on the "Alternative Protocol" if these extra steps are too 'much' for them to follow or, because of complicated Rx drug interactions with potassium supplementation or any other co-morbidity that would make these measures risky. As the patient improves and meds are discontinued, you may of course place the patient on the regular protocol, following the above guidelines.

Obtaining pH Test Paper

I ordered the 'Nitra-Test' pH paper on line and the cheapest I found was about \$41.00 per roll (with shipping), not exactly cheap! Our friends at www.ourhealthcoop.com have offered Ideal Protein Clinics a special price. Go to their web site and under "Products" click on "Home pH Test Kit Refills" (this is just the roll of pH paper without the booklet). It lists for \$12.99 but for our clinics the price is \$9.99.....which is awesome! If ordering on-line , enter 'idealph' in the coupon code area of the shopping cart checkout. Alternatively you may call Teri Edgell@ 1(800) 667-0781 or (561) 889-6754 and place your order over the phone. They will also send it to Canada for our Canadian Clinics. I recommend that every clinic should have at least one roll on hand.