

1 Introduction

Perry, et al, (1982) noted almost twenty years ago that there was a deficiency of the amino acid L-Glutathione in the brains of deceased Parkinsons patients. They, and several other researchers (Sechi, et al, 1996), have pointed out that this deficit can be exploited to improve the lot of Parkinsons patients. In particular, delivery of the L-Glutathione intravenously produced a therapeutic result for a period of one to five days after the IV. Perlmutter (1999, 2001), in particular, has VCR's (videos) of Parkinsons patients before and after the IV L-Glutathione treatment, and the improvement in the symptoms of the Parkinsons patient's is marked. The patient experiences a

1. reduction of rigidity,
2. increase in mobility,
3. improved ability to speak,
4. less depression and
5. reduction in tremor.

Note that with this therapy there is little, if any, reduction in the dosage of Sinemet needed by patients using Sinemet for Parkinsons therapy. Note too, that there is a persistence of the good effects of of the L-Glutathione therapy if it is stopped, say, after three months.

A drawback to this system of therapy for Parkinsons Disease is that the healing effect is severely limited in duration, so that the patients face a regime of weekly to daily injections if they are to have continuous symptomatic relief. Clearly the delivery of the L-Glutathione by mouth in pill form would be desirable, but both Perlmutter(2001) and dddd () state that this is not possible.

The purpose of this note is to show that a scheme for oral delivery of the L-Glutathione is possible, and the scheme can be extended to utilize other amino acids for possible therapeutic purposes against Parkinsons Disease, i.e., to ameliorate the symptoms of Parkinsons Disease. The scheme works on a resolution of the conflict between a need for Vitamin B6 in the brain to interact with and metabolize L-Glutathione in the brain, and an oft but vaguely repeated assertion that the presence of Vitamin B6 in the brain blocks the transport of Sinemet, the most widely used Parkinsons medicine, and of L-Glutathione across the blood brain barrier. These assertions are true but inadequately related to other cofactors in the milieu in which the

interaction is taking place; *in fact if the Vitamin B6 is accompanied by Vitamin B12 and Folic Acid, there is little or no apparent blocking of the Sinemet or L-Glutathione to a Parkinsons patients brain.* From this one can derive a scheme which will deliver quantities of these supplements to the patients brain at a constant rate, the rate being high enough to sustain all neural functions which are necessary to give the patient relief from the symptoms of Parkinsons Disease.

2 The Patients Parkinsonian history

The results described here were obtained on one patient, the author Peter Lewis, and using his responses and judgements to evaluate the efficacy of the therapy schemes for Parkinsons patient's. One-sample results are of course abhorred by statisticians and scientists, but the therapeutic effects obtained with the orally delivered L-Glutathione therapy are marked enough to leave little doubt as to their validity across a broad spectrum of patients. Further, more formal studies of the subtleties and validity of therapeutic improvements with the schemes can then be undertaken.

Details of the patients Parkinsonian and other health related history is given in Appendix A. A short summary is given here so as to motivate the procedures discussed.

Parkinsons Disease first appeared in the patient as a tremor in his right arm in 1987. This was treated mainly with Sinemet up until 1997. Early in 1998 the patient started freezing and experiencing explosive dyskinesia, apparently because he was consuming 20 Sinemet 50/250 pills per day to try to control these Parkinsonian symptoms. Following Freeman (see Fowkes, 1994) a rigorous program of supplements, mostly minerals and vitamins and fatty acids, brought the pill count to about 12 Sinemet 25/100 per day, plus 3 200gm Tasmar tablets. This reduction in medications controlled the dyskinesia. However, after at most an hour without a Sinemet, the patient would experience severe and very painful dystonia in his hands and feet, and rigidity elsewhere.

Subsequently, teeth removal, removal of mercury tattoos in the patients gums and jawbones, and other neural therapy heavy metal detox methods have, except for one circumstance discuss later, vastly improved the overall tone and quality of the patients Parkinsonian condition. Thus in a relaxed and peaceful milieu he can lie in bed for up to eight hours without Sinemet and feel just a slow onset of rigidity in his toes and feet. At that point, even before he takes his dose of Sinemet, he can usually get up slowly and walk!

However, if stress appears while he is in this relaxed state, he is immediately beset by tremor and/or rigidity.

The direction and intensity of the rigidity in the patients toes and feet became the feedback system for evaluating the effects of treatments during this experiment.

An exception to the patients good health (or perhaps a stasis in poor health) started about two years ago and consisted of the onset of chronic sinus/rhinitis/asthma, which left him barely able to breath and certainly incapable of anything else. Relief was found only in a neural therapy procedure, administered by his (biological) dentist, Dr. Kostadino Paulo, from Victoria, B.C.. A central part of this neural therapy procedure is a washing out of the sinus's with a prochine mixture; this on its own, even without the acupuncture-like part of the therapy, gave the patient some relief. We will refer to this subsequently as the chronic sinus mode of the patients Parkinsons Disease.

At present the patient uses about twelve Sinemet 25/100 per day. Note, however, that in the chronic sinus mode, no amount of Sinemet seems to induce a transition to normal states. Nor does the recently introduced (during the sinus attack) Sinemet have any effect on the following 'normal' Parkinson state.

3 The supposed Vitamin B6 block of Sinemet.

There is a well known belief that if Vitamin B6 is available in the patients blood as well as the orally introduced Sinemet, then the Sinemet will be blocked by the Vitamin B6 from crossing the blood-brain barrier. The manifestations of this blockage is quite stark in its effect and, in particular, might force backed up Sinemet into the vomit center in the brain. Most patients have experienced this phenomenon. *It is for this reason that Parkinsons patients are kept away from medication containing Vitamin B6, and from supplemental Vitamin B6.*

This induced shortage of supplementary Vitamin B6 is disturbing from a medical viewpoint since one is constantly reminded in texts that Vitamin B6 is necessary for many normal brain functions to work, and for ingested supplements to function in the brain.

Fortunately the statement of the blocking effect is at best misleading without further qualification as to co-factors which may be present in the milieu. In fact, it appears that Vitamin B6 does not block Sinemet if there is, in addition to the Vitamin B6, some Vitamin B12 and Folic Acid in the

milieu. A similar situation exists with Sinemet and L-Glutathione; severe blocking of the Sinemet by the L-Glutathione can occur , but not in the presence of Vitamin B12, Vitamin B6 and Folic Acid. This fact will be used to introduce L-Glutathione into the brain for therapeutic purposes and in particular to introduce L-Glutathione and other amino acids into the brain to alleviate the symptoms of Parkinsons Disease.

4 Patients results with orally administered L-Glutathione therapy.

4.1 Introduction.

One of the authors, Dr. Klinghardt, tried IV L-Glutathione therapy on the patient two years ago, injecting 600 mg. of L-Glutathione into the patients vein, as prescribed by Perlmutter(2001). Details of the procedure are given in Perlmutter(2001), but the therapeutic effects obtained by Perlmutter did not occur for the patient. The therapy was repeated several times on the patient by Dr. G. Wyker in Carmel and still did not give any observable therapeutic benefit from Parkinsons Disease for the patient.

Early in the morning of December 14, 2002, the IV L-Glutathione therapy was repeated on the patient, this time using 2400 mg of reduced L-Glutathione, and by bedtime it was obvious that the patient was more energetic and lively than he had been for many years. The elevating effect lasted for two days and the influence of the L-Glutathione took about four days to have completely dissipated.

Why did the response change with the higher dose of L-Glutathione? It is conjectured that this was due first to the prescribed absence of supplemental Vitamin B6 in the patient because he was using Sinemet, so that the L-Glutathione was blocked by the Sinemet. And secondly, it was due to the possible presence of the Vitamin B12, Vitamin B6 and Folic Acid in Perlmutter's patients from a possible regular use of Perlmutter's Brain Sustain in their treatment. This would have made it impossible for the Sinemet to block the L-Glutathione.

The need for repeated IV's in treating Parkinsons patient's with this L-Glutathione therapy, even though there is a residual effect when the therapy is discontinued, makes its use qualified. Both Perlmutter(2001) and jjjj () tried oral L-Glutathione therapy and declared, without much detail, that it would not work. Perlmutter(2001) did conjecture that the problem was that L-Glutathione is readily digested in the stomach into its constituent

amino acids. Our results show that this cannot be entirely true. Enough L-Glutathione must be getting through the blood-brain barrier under the milieu we create to achieve a valuable therapy.

We give here several schemes (protocols) which use orally administered L-Glutathione to obtain useful therapeutic effects on Parkinsons patients symptoms.

4.2 Crude method for oral L-Glutathione therapy.

The simplest, rather crude method for the orally administered L-Glutathione therapy is the following.

Suppose that it has been decided to give the patient 500mg of L-Glutathione at three hour intervals, starting say at 6:00am and continuing until midnight, and repeated on successive days. (If one prefers to start later, say 8.00am, then all time points in what follows are shifted up by 2 hours.)

At each time of the seven time points (ingestion points) do the following procedure.

Crude L-Glutathione procedure

1. Place a sublingual B12 tablet under the patients tongue; in our experiments this tablet was a Twinlab B-12 Dot with 500 mcg strength.
2. Three minutes later, swallow a 400 mg Folic Acid tablet or capsule.
3. Three minutes later, swallow a 50 mg Vitamin B6 tablet or capsule.
4. Four minutes later take, one after the other if called for at that time point, the desired strength L-Glutathione capsule, then a Sinemet tablet and then (again, if called for) a Tasmar tablet.
5. The above steps assumes that Sinemet is taken seven times a day, seperated by three hours, this being dictated by the L-Glutathione therapy It might actually be that no Sinemet is needed, or less than seven, and these ingestions of Sinemet can be spread over the seven ingestion times for L-Glutathione. Again the needed number of Sinemet's may be more than seven. Details can be worked out, but *it must be kept in mind that Sinemet ingestion at time points when the way is not prepared with the three B-Vitamins, may result in Sinemet blockage.* And in particular taking the Sinemet just before the Vitamin ingestion points will almost certainly give blockage. Similarly, not waiting for the delay times between taking the B-Vitamins will give Sinemet blocking.

The following notes hopefully explain details of the above procedure completely:

1. The source of (manufacturer of) supplemental Vitamin B6 and the source of the supplemental Vitamin B12 and Folic Acid was quite critical for the suggested procedure to work. More than half the tablet sources did not work at all *and only capsules should be used in the procedure*. Twin Lab and Solgar products were completely reliable; there must be many other capsules from well known companies which can be used, but this should *never* be taken for granted.
2. The size of the Vitamin B6 capsule used – 50 mg. – was fixed by the common stricture in the medical literature that daily Vitamin B6 intake be less than 300 to 400 mg. (The crude protocol gives a daily total from the seven 50 mg pills of 350mg of Vitamin B6. If anything experience has shown that using 100mg of Vitamin B6 at each ingestion point is better in the sense that the therapeutic effect on the patient is greater. Similarly an 800mg capsule of Folic Acid would be preferable. (The P5P form of Vitamin B6 was tried in tablet and capsule packaging, but did not work well with this crude insertion procedure.) Of course one also has to take into account that these pills may be poorly absorbed, especially by older people, making the ingested quantities much smaller than the nominal amount. (The patient on whom the testing was done was 69 years old when the testing was done.)
3. For the patient, 1 gram of L-Glutathione— rather than the 500mg discussed above — at three hour intervals was adequate and seemed safe. This set the total daily dose of L-Glutathione at 7 grams, which is three times the IV L-Glutathione therapy dosage which worked on the patient. A small increase in daily total of L-Glutathione made no discernable difference in the therapy.
4. Justification of the three hour interval between L-Glutathione inputs is much simpler, in that this dosage gave the five benefits claimed above for IV L-Glutathione therapy and also held in check the chronic sinusitis which the patient experienced over the last two years. Changing the timing by changing the interval to four hours allowed the sinusitis to return about three and a half hours after the introduction of L-Glutathione. Note that this high a dose of L-Glutathione should be approached gradually over a two week period. Note too that there is

usually a transient effect in the efficacy of the therapy for up to three weeks after the initiation of therapy. Clearly one would also want to try to decrease the dosage from seven grams after the response to the treatment settles down.

5. Like the IV L-Glutathione therapy, the oral L-Glutathione therapy builds up and accumulates. Thus the timing of the L-Glutathione therapy becomes less critical, in that the times between ingestion of the L-Glutathione pills may change or some scheduled ingestions may be missed out. And, once the therapy has built up, if it is stopped the benefits of the therapy will continue for several weeks. (Further data is needed on this point.)
6. A surprising effect is that the ingestion of the L-Glutathione and the blockage free ingestion of Sinemet depend quite critically on the supplementation of the patients environment with vitamins, minerals and and other supplements. Thus on a few occasions during the application of the L-Glutathione therapy by the patient, almost all ingested Sinemet was, unexpectedly, blocked; it was then realized that on these occasions the patient had accidentally not taken many supplements, and in one case had missed taking them for two days.

More study of this phenomenon is needed to fill in the details. What is clear from the patients experience, as noted above, is that the milieu must contain, in addition to Vitamin B12, Vitamin B6 and Folic Acid, some supplementary Niacin (Vitamin B3) and a lot of Vitamin C. (We return to this addition to the supplementation later in the note.)

This **crude** scheme for oral L-Glutathione therapy is usable even by people not skilled in medical procedures, but the ingestion countdown is easily interrupted by outside events during the five to ten minute ingestion points. Thus a simpler and more robust scheme was sought; it is described in the next subsection.

4.3 A better L-Glutathione therapy delivery scheme using smoothing of slow release encapsulation.

The ideal system of delivery for the background vitamins would be one in which the supply of the triple of Vitamin B6, Vitamin B12 and Folic Acid is at a constant rate, with the rate being high enough to supply the needs of the patients brain for these Vitamins at any time. In other words, no bottoming out of any brain functions should occur. *And, in particular, this means*

that, in contrast to the crude protocol, the ingestion of supplements such as L-Glutathione and medicines such as Sinemet could be easily done at any time of day and not just at the seven ingestion points for L-Glutathione.

A simple smoothing scheme to implement this constant rate brain supplementation with vitamins and medicines of is as follows.

- Have a compounding pharmacy create 12-hour sustained release capsules containing the requisite quantities of Vitamin B12, Vitamin B6 and Folic Acid. This is created with the formula

PYRIDOX/FA/B12 50/5/5

- It would be preferable to have a time release of the three supplements at a constant rate over the 12 hours, but since this is physically impossible, the actual time release product releases at an approximately linearly increasing rate for six hours, and then releases at a linearly decreasing rate which goes to zero at 12 hours. The totals of the three quantities released over the twelve hour period are 50mg of Vitamin B6, 5mg of Folic Acid and 5mg of Vitamin B12.
- Now, to implement a constant rate smoothing scheme, ingest one of these time release pills every six hours, and it is easily shown that this procedure produces a constant supply of $(50/6)$ mg of PYRODOXINE, $(5/6)$ mg of Folic Acid and $(5/6)$ mg of Vitamin B12 per hour. *Typical usage would be to ingest one combined pill at each of the time points 6a.m, 12 noon, 6p.m. and midnight.*

Given the constant rate supplementation background, one can ingest prerequisite L-Glutathione at any time. A convenient set of times for 3 hour separation of L-Glutathione capsules is 6am, 9am, 12noon, 3pm, 6p.m., 9p.m. and midnight. Other pills can be taken on top of (at the same time as) the L-Glutathione, so as to ease the patients pill management task, or at any other convenient or requisite time point.

The patient has found that Sinimet and Tasmar can be taken at the same time point with no blocking with this constant rate supplementation scheme.

It should be noted that the patient and other people who have used just the smoothed Vitamin B12, Vitamin B6 and Folic Acid scheme to get Vitamin B12, Vitamin B6 and Folic Acid supplementation, get a strong

feeling of well-being from its use. This is because it is essentially implementing the common suggestion by doctors that (older) patients, because of absorption problems, take more Vitamin B12 and Folic Acid and Vitamin B12, preferably intravenously or sublingually. Thus Dr. Jonathon V. Wright, discussing the use of a natural blend of eight amino acids to treat depression in his March 2002 Nutrition and Healing Newsletter, says "for best results, use extra quantities of vitamin B12 (1,000 micrograms daily when injected, 5,000 micrograms daily if taken orally) in conjunction with the amino acids. Also be sure to take extra folic acid at the same time as the Vitamin B12 (5 to 10 milligrams daily when taken orally".)

The L-Glutathione therapy using this smoothing scheme seemed uniformly better, to the patient, than the original crude scheme but this may well have been a subjective nuance resulting from the greater ease of doing the therapy. One sure result is that the Tasmar did not cause the blocking which sometimes appeared with the first crude scheme.

4.4 Notes on the orally administered L-Glutathione therapy.

1. The second scheme for oral Glutamine therapy depended on the generation of a constant collar of Vitamin B12, Vitamin B6 and Folic Acid in the milieu. This can be accomplished using a time release capsule, but since this needs to be made by a compounding pharmacy, the cost is high. This cost would be even higher if one attempted to package (No Flush) Niacin, and Vitamin C, into the time release capsule with the Vitamin B12, Vitamin B6 and Folic Acid.

A solution is to look for a commercially available, high quality package containing the five supplements in a combined time released package. No such capsule is likely to be available. An approximation is as follows.

Cheap, sophisticated L-Glutathione therapy protocol.

- (a) There is one time release product available for Vitamin B - Complex, namely Solray Two-Stage, Timed Release B-Complex 75 which releases half the capsule immediately, and half with a 6 - 8 hour delay. *Use one of these capsules at each of the ingestion points 6.00am, 9.00am, noon, 3.00pm, 6.00pm, 9.00pm*

and midnight This gives, for example for Vitamin B6, a total of approximately 525mg of Vitamin B6 per day.

- (b) The Vitamin B3 in the B-Complex 75 capsule is Niacinamide, where we require Vitamin B3 in the form of (No Flush) Niacin, i.e., Hexanicotinate. No commercially available (No Flush) Niacin timed release has been found; thus an approximation to the smoothed, time delay scheme is produced by *taking 250mg capsules of (No Flush) Niacin at each ingestion point.*
- (c) In addition *a time release Vitamin C capsule (Soloray Buffered Super Bio C) is used at the ingestion points 6.00am, 9.00am, noon, 3.00pm, 6.00pm, 9.00pm and midnight, along with the time release B-Complex capsule.*

2. The amount of Vitamin B6 in this last scheme seems to be high, but it implements a result (Lenno, 2002) that excess Vitamin B6 helps to reduce the effects of dyskinesia in Parkinsons patients. The use of 500mg of Vitamin B6 was determined to be optimal for the patient by Dr. Klinghardt using autonomic response testing. Note that the insight exploited in this note, that the presence of Vitamin B6 does not necessarily inhibit ingestion of Sinimet, makes possible the use of this new therapy for dyskinesia for Parkinsons patients. The dyskinesia therapy has been tested on the patient and very positive results were obtained.

Note too that it would probably be preferable to use the P5P form of Vitamin B6, if only to get around possible nerve damage from the use of too much Vitamin B6. However, not off – the – shelf product containing the metabolized form of Vitamin B6 has been found to be available.

3. Encouraged by the above results, an attempt was made to incorporate into the therapy other amino acids. This is discussed below, but the main point for now is that it illustrated quite conclusively that the schemes developed here are fragile, and become ever more fragile as additional amino acids are introduced.
4. Another important point is that the schemes quickly become unworkable in the presence of allergies!

Thus the patient has many allergies, in particular to sugar and wheat, and close exam of the log of the experiments showed that almost all

breakdowns in the ingestion of L-Glutathione occurred after eating of half a Danish with coffee, something which the patient had convinced himself was harmless to him. In fact it is not clear that the fragility was not just due to sugar alone. The patient in fact has always had a sugar addiction, and a sensitivity to sugar's presence in his blood and he normally uses nothing but Stevia for sweetening.

In short, skipping ingested sugar makes the above schemes reliable and productive for him. In fact he attains a sense of well being and a physical stability and balance which he has seldom experienced.

5 Parkinson's therapy using other amino acids

It has been established conclusively that, singly, several amino acids besides L-Dopa and L-Glutathione will benefit Parkinson's patients. These include L-Tyrosine, D-Phenylalanine, DL-Phenylalanine, L-Methionine and L-Tryptophan. (See the Chapter entitled "Parkinson's Disease" in Werbach, 1999, for summaries of these test results.) A reason for possibly preferring to use one of these amino acids in place of L-Glutathione is the high cost of L-Glutathione in capsule form. And again, if one or more of the above amino acids were to be used in the therapy in addition to L-Glutathione, could a more stable therapy for Parkinson's patients than what is available now be obtained? (Note that Wallach and Lan, 1996, advocate this approach to therapy for Parkinson's patients, but give few details.)

An outstanding candidate to examine in this context would be the amino acid dl-Phenylalanine. It is known to be a precursor to dopamine in the brain, and is also a strong anti-depressant. Furthermore, its use will raise levels of testosterone in patients without increasing estrogen, thereby achieving the goal of this kind of therapy to increase libido and energy.

The use of DL-Phenylalanine for Parkinson's therapy has been established for the patient and the results will be detailed elsewhere.

The most important point for here is that the therapy's stability and efficacy depends critically on absence of allergies, or perhaps merely on absence of raw sugar, in the patient. In addition, a state of full supplementation with minerals and vitamins is assumed.

6 Bibliography

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