



S.I.L.A. NEWSLETTER 22 WINTER/SPRING 2008



Dear SILA Supporter,

The start of 2008 is a good time to look back at the Old Year and see what has been accomplished. I have been involved in putting SILA and sarcoidosis on the airwaves. On June 13th 2007, I attended a workshop at Peckham Library entitled *Your Group on Radio* run by PVSF (Peckham Voluntary Sector Forum). Skills that I was helped to acquire were voice production, microphone technique and making a short feature for radio. The individual recording I made about SILA and sarcoidosis can be heard on www.radiopeckham.org/community. This training was helpful when I was contacted by REM (Radio Europe Mediterraneo www.rem.fm) on 17th October, 2007 to do a telephone interview. This was a good opportunity for letting the radio audience (Spain's largest English speaking radio network) learn about SILA and sarcoidosis, with a doctor.

On 12th December, 2007 I attended the launch of PVSF's New Capacity Building Programme at Peckham Library. At the launch we had taster workshops on how to make the best use of Microsoft Office Packages.

On November 17th 2007 Graham and Claire David held a Charity Ball at the Penarth Masonic Hall in aid of SILA. The Charity Ball with the County Youth Band and disco raised over £3,000 for SILA. Congratulations to all who worked so hard and who contributed to make the Charity Ball such a great success.

The SILA AGM was held on 4th October 2007 at King's College Hospital. Heather Walker was elected Secretary, Paul Sinclair, Treasurer, Desmond Wigglesworth, Assistant Treasurer.

After the Research Project by the University of Edinburgh was mentioned in the last SILA newsletter, Tara Keilmann emailed to say that she was able to recruit and speak to very interesting people and gain insight into sarcoidosis. Tara is no longer recruiting applicants. SILA will be sent the report, when finalised.

Sarcoidosis patients who are interested in athletics may want to read an article in the national magazine *Running Fitness*, January 2008 edition, and read about Robert Chittock, a sarcoidosis patient who visited a company called Sportstest www.sportstest.co.uk and underwent a physiological fitness assessment, an account of which is written up in the magazine.

SILA is in need of more volunteers, especially Trustees so that SILA can keep up and running during the coming year and beyond. Any member who is interested in becoming a Trustee or who wants to help in any other way, please get in touch with the Secretary, at the KCH address on the back page.

Thanks are again due to all members who renew their subscriptions promptly and also those who add donations.

All good wishes for the coming Year.

Heather Walker, Editor, email heather@silas.org.uk
Andrew Ferguson, Assistant Editor.



Contents and introduction

- 3 *Rosemary's Story Part 1.*
- 7 *Quercetin, its Relevance to Sarcoidosis and Viral and Bacterial Infections, and the Value of Small Scale Trials.*
- 10 *Treatment of sarcoidosis – from a basic science point of view.*
- 14 *A Brief Introduction to the Marshall Protocol.*
- 16 *A Guide to Guidance For Physicians: The Marshall Protocol - Phase One.*
- 23 *Using the Sarcoidosis Social Network.*

We lead off with a *Patient's Story*, this time from Rosemary. Some of the story is still to happen, but what has transpired so far is well worth studying, especially when taken in the context of these words in the Introduction to the last issue:

With *chronic* pulmonary sarcoidosis the use of a corticosteroid becomes almost unavoidable (although there are some other medical drugs, they are normally used only when people cannot tolerate steroids). Yet steroids are almost certain to cause some ill effects alongside improving breathing, Di's experience of her skin becoming extremely thin and dry and suffering some weight gain being fairly typical. .

But so far Rosemary, like me, has avoided the use of steroids or other medical drugs for treating her sarcoidosis. Yet there is certainly room for further improvement in her lung function, which is currently less than half of what is probably normal.

There is another strand in Rosemary's Story. She has always been prone to chest infections, which may or may not be associated with her sarcoidosis. Anyhow this winter she has been trying a natural substance, found mainly in apples, called Quercetin. That is a subject in itself, and pages 7-9 take a look at Quercetin, and then go on to give consideration to the general subject of Small Scale Trials.

The impression is sometimes given that there is little available to treat sarcoidosis besides corticosteroids and the immunodepressant methotrexate. Pages 10-13 provide a four page summary of a paper by Dr David Moller which makes it clear that there is a range of options — although most of them are associated with unfortunate side effects.

One treatment not mentioned by Dr Moller, and indeed it is not mentioned by any of the mainstream sites associated with the treatment of sarcoidosis, is the Marshall Protocol (MP). The general situation with regard to the MP is that without doubt there are people who have recovered by using the MP, but for a variety of reasons the treatment protocol is difficult to follow, and the way the MP trial is being conducted means that great difficulties are likely to be encountered in finding a doctor who will prescribe the antibiotics which are a major part of the treatment. Another part of the treatment involves using a particular Angiotensin Receptor Blocker (ARB) in doses which are about four times as large as those used to lower blood pressure. That is a cue for me to acknowledge that I allowed an error to slip into *Di's Story*, which appeared in the last issue of the SILA newsletter. She referred to statins as being part of the MP treatment. What she should have referred to was ARBs. Statins do not relate to the MP at all.

On pages 14-15 I give a brief introduction to the Marshall Protocol and pages 16-22 are devoted to showing the substantial amount of background knowledge that those running the Marshall Protocol site state that doctors need to be familiar with. Altogether this may seem an excessive amount of space to devote to the Marshall Protocol, but it does arouse interest, and probably deserves to be covered thoroughly at least once, despite the fact that it is not a generally accepted method of treatment.

Page 23 gives some tips on using the Sarcoidosis Social Network.

Rosemary's Story, Part 1

Rosemary's Story, Part 1

The reason that this account needs to be in two parts is that the story is perhaps only half way through. However there is something of interest to relate at this stage. In May 2006, I started an experiment which is still ongoing. It was to see if I could avoid going on to steroids (which appeared to be imminent) by the use of cetyl myristoleate (CMO), which had been written about extensively in the last two issues of the SILA newsletter. First I will relate how things were before I started on the CMO (i.e. I leave the text as it was written prior to starting the CMO experiment); then in the next sections I go on to relate the changes that occurred after starting to use CMO intermittently.

Until recent years, as an adult I have always been fit and healthy: no weight problems, no smoking or drinking, plenty of exercise and a healthy diet.

However because lung problems have been a major symptom of my sarcoidosis, I should mention that as a child, born in 1943, I was plagued by winters of chest infections, bronchial attacks, even pneumonia was mentioned at one time. Looking back, it seems a blur of lung related conditions which led to me being away from school on such a regular basis each year that my parents were allowed to teach me at home.

At 17 I underwent a tonsillectomy, which caused a dramatic improvement in my health. These facts are worth mentioning, although it must be a matter for speculation as to whether these early experiences — or the fact that my son experienced similar chest/lung related illnesses (although not my daughter) — are in any way relevant to my sarcoidosis.

Returning to recent times, I suffered what may have been sarcoidosis symptoms for some years before it was finally diagnosed in April 2002. For several winters before that date, I had recurring bouts of 'bronchial' chest infections which my GP would treat with antibiotics. At first the antibiotics worked, but in the winter of 2001/02 I had three bouts of infection, and my breathing became severely impaired.

Fortunately a locum GP saw me, and realised there was an underlying problem. He picked it up through the stethoscope, listening to my lower back lung area. He immediately organised x-rays and blood tests which came back as sarcoidosis. Finally a CT scan confirmed this.

Since then I have seen a consultant every three months, and have lung function tests and x-rays to monitor my condition. I was also given a peak flow monitor on which a healthy woman of my age should register around 400. I found that I was only able to reach 250-270.

For me, the worst aspects of this condition are the breathlessness and tiredness. Accompanying these are dry eyes, various aches and pains, thinning hair and perhaps a little short term memory loss. Of course apart from the 'dry eyes', I realise that the other symptoms could just be part of the aging process.

To expand on my symptoms, the breathlessness is hard to accept; it limits my lifestyle considerably. I find I can only carry lightweight items; shopping has to be undertaken in two or three trips rather than one. I cannot walk and talk at the same time even on level

ground. Gardening is almost out of the question now, even Hoovering can leave me gasping.

Weather conditions play a part: if it is damp or foggy my breathing is impaired even more.

Then there is the extreme tiredness — this is almost a feeling of total exhaustion and can only be alleviated by sleep; resting does no good. I am too tired to concentrate on TV, reading, or listening to music — all things which normally would relax me.

Lots of days the only thing that would carry me through would be the knowledge that as soon as I got home I could go to bed and sleep, possibly for one and a half or two hours. This would happen on a regular basis, around 3–4 pm most days.

This winter, 2006/07, has been the worst: bouts of pleurisy on two occasions, antibiotics which really did little to help, culminating in the consultant saying steroids would most likely be the only answer, and that I had better anticipate having to start at my next consultation — in mid-June 2006.

The cetyl myristoleate (CMO) experiment

Then I read the current SILA newsletter, Winter/Spring 2007, containing the article on CMO, and decided that I had nothing to lose, and hopefully a lot to gain by giving it a try. I started using Myristin Topical Cream (CMO) on 16th May 2007, and almost immediately felt relief — breathing became easier and the tiredness lifted. At the start my steps per respiration cycle were down to 4, but within a couple of weeks I was up to 6. At 6 it is possible to both walk and talk on the level without difficulty, so that was a significant change, and I was able to do many things, such as gardening, I could not have contemplated a short time previously.

After the first week, the lingering cough which I had been suffering from for most of the winter had cleared (unlike other sarcoidosis patients, my cough isn't dry; it is a loose mucus-laden cough which always seems to be related to the rhinitis of my childhood. My lungs always have seemed to be very mucus productive).

My appointment with the consultant was for 14th June 2007. Prior to that I had completed applying two pots of CMO cream, and my steps per respiration cycle were still up at 6. The improvement in my condition was sufficient that the consultant realised that I had no need of steroids for the time being, and said that he would see me in three months time to review the situation. I did not tell him about the CMO cream: I felt it was too soon. I did ask him if he felt that the improvement was due to spontaneous remission. He said that it wouldn't happen so quickly; it is a gradual process.

Another matter of interest is that he brought out from my medical records an old 1994 chest x-ray — taken because it was thought I had broken ribs. He pointed out to me that it was clear that sarcoidosis was present in my lungs then. As I had no manifest indications of sarcoidosis at the time, one wonders how long it had lain dormant.

After just over a week had passed since the last cream was used, I was feeling that I was slowly going 'downhill'. The tiredness was returning and my breathing was becoming shorter. By 21st June, I was down to 5 steps per respiration cycle, and by 27th June down to where I had started, 4 steps per respiration cycle.

On 4th July I started to take 2 Myristin Softgels per day. That would be a daily dose about 2.5 times as large as that obtained by using Myristin Topical Cream. However this experiment immediately gave rise to problems. I happen to one of those people who do not digest the fatty acids contained in CMO, so they gave rise to feelings of being bloated and slightly nauseous; after a few days I stopped taking them. A few days later I resumed taking them, but now accompanied by the digestive enzyme betaine hydrochloride (it was later suggested by the firm EHP Products, from whom these capsules are bought, that lecithin might have been a better digestive enzyme to use). Taking the capsules in conjunction with the digestive enzyme did remove the adverse effects, but unfortunately the capsules seemed to be doing nothing for me. Possibly that is because, although it is only speculation, breakdown in the stomach causes the cetyl myristoleate to lose its efficacy as compared to delivery by injection or by transpiration through the skin.

In fact by 22nd July I was down to 3.5 steps per respiration cycle, lower than my starting point of 4, and with little change in the level of fatigue, but a few days before completing the capsules and digestive enzymes — on 29th July to be precise — I was up to 4 steps per respiration cycle.

By 19th August I was up to 4.5. On 12th September I started applying Myristin Topical Cream again, but did not notice any improvement before I started a cold on 20th September, which of course made it impossible to judge what effect the CMO cream was having, and so I stopped applying the cream on 23rd September.

In fact the cold only lasted about a couple of weeks and was not a particularly bad one, latterly just a slight nuisance. Of course when it had cleared up, the question arose whether I should resume using the Myristin Topical Cream, because my steps per respiration cycle were holding steady at about 4.5, but we decided against that on the grounds that from then on colds were likely to interfere with the experiment. Moreover from 15th October some further improvement started; over the next couple of weeks I reached 5. It was at that level when I saw my consultant again, on 25th October 2007. The consultation included a lung function test: as expected from my steps per respiration cycle measurements it confirmed that there had been a slight improvement since a year previously.

When deciding not to resume using Myristin Topical Cream, Andrew and I also decided to embark on another experiment to see if we could combat my great tendency to succumb to virus infections during the winter. In fact Andrew was interested to see if he could combat his own tendency to succumb to at least one cold each winter, so we settled on a new experiment to see if we could both get through the winter without a virus infection by taking a substance called Quercetin. This calls for some explanation.

Recently some good evidence has shown that Quercetin does have a marked effect on reducing the rate of chest infections. I need say no more on that score because Andrew reports on it elsewhere in this issue. Suffice it to say that we used a substance easily available from health shops (costing about £15 for 50 capsules) called Quercetin Complex. We decided on taking one capsule per day, making the daily dose 250 mg of Quercetin and 250 mg of vitamin C. This was only about a quarter of the dose of Quercetin that was used in the experiment that Andrew reports on (taken from *New Scientist*), but the 1 gram dosage that was used in that experiment was quite likely excessive, since the experimenters

stated that the next step was to find out how much the dose could be lowered and remain effective. Anyhow 250 mg of Quercetin a day is what both Andrew and I have settled for. For my part, although I have been in frequent contact with children with colds, I have remained free from infection. But as the date is now 2nd January, the risky winter period is by no means at an end, so it is still fingers crossed!

The current situation and the benefits of joining SILA

The cetyl myristoleate experiment is somewhat in abeyance at present, as I need to wait until the winter is well behind me. After that, further experiments with cetyl myristoleate will be possible without their being interfered with by chest infections. So far this winter, although I have been daily surrounded by coughs, colds, etc., from all my friends and family, I have escaped myself. If this holds out until the end of March, I shall be able to conclude, with some assurance, that the 250 mg of quercetin and 250 mg of vitamin C that I have been taking daily has had a beneficial effect.

One point of interest is whether medical measurements adequately reflect the improvement in lung function that is apparent from the change in steps per respiration cycle, namely a 25% improvement. Many years ago, when it was apparent that I might have to go onto steroids, I was given a peak flow meter to take home and use from time to time to see what was happening to my breathing. For some years I could achieve a reading of only 250-270. Now, with my breathing steady for the last few months at 5 steps per respiration cycle, I can achieve 280-300. [AF. This reflects my own experience of medical measurements, but in my case with the different device that is used at my clinic, a spirometer, which measures chiefly vital lung capacity. Improvements in vital capacity were clearly evident, but it was also evident that the improvements in vital capacity were insufficient to fully account for the improvements in lung function. The same appears to be the case with Rosemary, since her peak flow meter readings show an approximate 12% improvement while the actual improvement has been 25%.]

Although the improvement in lung function has been a vitally needed improvement, and has so far stopped me having to use steroids, another question is whether I can report any change in the various aspects that I listed previously as: "I find I can only carry lightweight items; shopping has to be undertaken in two or three trips rather than one. I cannot walk and talk at the same time even on level ground. Gardening is almost out of the question now, even Hoovering can leave me gasping." In general fatigue is still a problem. In fact that does not seem to have changed much. With regard to the other problems listed, I can only say that there has been the marginal improvement that might be expected from the small improvement in my lung function. [AF. This is not surprising. It was at 5 steps per respiration cycle that it became apparent to me that I had to do something.]

However, one thing I can say is that five years ago, in 2002 when I was diagnosed with sarcoidosis, I felt that my future was looking bleak. Now, at the age of 65, I look at my situation with far more optimism, helped of course by the slight improvement in lung function and the fact that so far this winter I have not succumbed to a chest infection, but also because after joining SILA I learnt how others were coping with similar problems, and

gained the support of the group, all of which has made a huge difference to my outlook and understanding of sarcoidosis.

QUERCETIN, ITS RELEVANCE TO SARCOIDOSIS AND VIRAL AND BACTERIAL INFECTIONS, AND THE VALUE OF SMALL SCALE TRIALS

by Andrew R.B. Ferguson

In *New Scientist*, on 15 Sept, a trial was reported in which 40 male cyclists were divided into two groups, one being given 1 gram of quercetin a day — equivalent to eating 100 apples — with the other being given a placebo. This resulted in only one in 20 of the quercetin group getting chest infections, whereas 9 out of 20 in the placebo group got chest infections (chest infections are a scourge of extreme mental or physical stress, and is a problem in the army, which is why this study was carried out). The report went on to say:

Tests show that the cyclists taking the supplement had high levels of quercetin in their blood. Lab studies have previously shown that quercetin can bind to viruses and bacteria and stop them replicating; this is what Nieman believes was happening in the cyclists to stop them getting sick.

Nieman also found the cyclists had reduced levels of IL-8, a chemical that helps mediate the immune response to antigens, suggesting that quercetin may also be influencing the immune system in some way.

It is well known that sarcoidosis patients are particularly susceptible to infection. I have heard quercetin being mentioned in the context of sarcoidosis treatment, so it is worth thinking about these results, especially if you are a sarcoidosis sufferer who is particularly prone to suffer from chest infections.

The report also states that, “The average American typically eats around 107 milligrams of flavonoids — which are polyphenols — per day. There are no apparent side effects of boosting the intake, says Nieman.”

Indeed the *Reader's Digest Guide to Vitamins, Minerals, and Supplements* suggests that to treat asthma an even higher dose of quercetin may be used than was used in this trial. For some relevant quotations about quercetin, taken from this Guide, see Appendix A.

I have been asked whether I am suggesting that sarcoidosis patients should try quercetin. The answer is no. I am merely informing them of something that seems to be of potential benefit. When my sarcoidosis was florid (it would be precocious to say “when I had sarcoidosis”!), getting a viral infection was my major worry, since it inevitably developed into a ferocious cough, and I could at times feel that I was about to expire because I could not draw in air. My doctor told me that if I were to actually pass out, my muscles would relax, and I would again draw in air, but I did not want to try the experiment!

During this winter of 2007/2008, although I am no longer so fearful of viral infections, I thought I would join Rosemary (see her Patient's Story in the previous article) to see whether Quercetin could stop me from getting my usual winter cold(s). So far, I feel that it may have been doing that, because often I have felt a cold ‘coming on’, with a lot of sneezing and nose blowing, but it has never developed into a cold. Still it is only January!

Quercetin is not something that the drug industry is going to get interested in, since there is nothing they could patent. We have seen that in the case of cetyl myristoleate, despite it being supported by an excellent laboratory study showing its effectiveness in preventing arthritis in rats. In the case of Quercetin, it was lucky that the U.S. army thought it was

worth financing a trial. But the main trials of Quercetin for alleviating the symptoms of sarcoidosis sufferers will be up to you and me. Those of you who have access to the internet will be able to join in tests which should eventually expand our knowledge of the substance. There is a Group titled *Testing non-drug palliatives*, the address of which is <http://sarcoidosis.ning.com/group/testingnondrugpalliatives>, on the Sarcoidosis Social Network site, which allows you to record the fact that you are about to engage in a trial. I cannot stress strongly enough that if you do not record that you are going to engage in the trial before you do so, then any subsequent report is of little value, because it is impossible to tell whether ten or a hundred people tried the substance and thus whether you are one of ten or one of a hundred.

If you are not already a member of the Social Network then you will have to sign in, but that is a straightforward procedure. If you contribute, you will be participating in a Small Scale Trial, so another word on that subject is in order.

Small Scale Trials

The experiment described in *New Scientist* is a good example of a small scale trial with a harmless substance. If quercetin was a “drug” with unknown side effects, it would be necessary to try it out on a thousand patients or so to see if one in a hundred, say, suffered dire side effects. Those side effects might be anything unexpected, such as was the case with thalidomide. But without that side effect problem, the results from 40 people can be tremendously significant. Indeed most people will intuitively see the results as given above to be significant, but let us look at the statistical situation.

When on placebo, nine people suffered chest infections. Placebos sometimes produce a 30% improvement, so we might suppose that without the placebo effect more people would have suffered infection, but so as not to be too favourable to quercetin, let us keep to the fact that 9 out of 20 got chest infections when quercetin was not used.

Within the quercetin group, only one person suffered a chest infection. Thus on these assumptions, the effect of the quercetin was to reduce the infection rate from 9 people who were likely to get chest infections without treatment, to just one. Or to put it the other way around, it prevented 8 people out of the 9 who might have been expected to get a chest infection, from actually getting a chest infection.

We can now ask whether this result could have come about merely by chance if quercetin was actually capable of preventing every other person getting a chest infection. The answer is that it could, but the chances against that are 60 to one against. In other words, these results show that it is highly likely that one in two people who would have got a chest infection will be prevented from doing so by the chosen dose of quercetin. Most people, I think, would be happy to accept a fifty-fifty chance of prevention provided there is no risk of side effects. This subject of probabilities within small scale trials was covered in some detail on pages 18-22 of the SILA Newsletter, Summer/Autumn 2007.

Those who have access to the internet might like to try this URL, stemming from an evidently reliable source, <http://www.phytochemicals.info/phytochemicals/quercetin.php>. It appears to confirm the report in *New Scientist*, in suggesting that quercetin has

remarkable properties which are relevant to some cases of sarcoidosis. For an extract see Appendix B.

Appendix A

Extracts from Reader's Digest Guide to Vitamins, Minerals, and Supplements

p. 152. [Under the heading Phytochemicals] "More than 4,000 flavonoids have been identified so far, and many of them have been intensively investigated by laboratory and animal studies. Except for one major flavonoid — quercetin — few have been the subject of human studies.

p. 215. [Under the heading Asthma] "The flavonoid quercetin has two main effects: it inhibits the release of histamine and, as an antioxidant, it neutralises unstable oxygen molecules which can cause bronchial inflammation." Dosage recommended is 500 mg 3 times a day. Additional advice is "Take 20 minutes before food; often sold with vitamin C."

p. 323. [Under the heading Mouth ulcers] "Onions contain sulphur compounds with antiseptic properties, and they are also a leading source of the flavonoid quercetin, which stops the body releasing inflammatory substances in response to allergens."

Appendix B

Action of Quercetin:

Quercetin has many health promoting effects, including improvement of cardiovascular health, reducing risk for cancer. Quercetin has anti-inflammatory and anti-allergic effects. All these activities are caused by the strong antioxidant action of quercetin. It will help to combat free radicals molecules, which can damage cells.

As many other flavonoids, quercetin prevents the oxidation of LDL (bad) cholesterol.

The anti-inflammatory action of quercetin is caused by the inhibition of enzymes, such as lipoxygenase, and the inhibition of inflammatory mediators. Quercetin also inhibits the release of histamine, which causes congestion, by basophils and mast cells.

Studies have shown that quercetin reduces the cancer risk of prostate, ovary, breast, gastric and colon cells.

Quercetin also seems to reduce the production of uric acid, by inhibiting the xanthine oxidase, thereby easing gout symptoms.

Studies have shown an improved lung function and lower risk of certain respiratory diseases (asthma and bronchitis) for people with high apple (rich in quercetin) intake.

TREATMENT OF SARCOIDOSIS – FROM A BASIC SCIENCE POINT OF VIEW

This is a four page condensation of D.R. Moller's highly technical paper, titled as above, of ten pages in smaller print. The original paper, published in the *Journal of Internal Medicine*, is dated 2003, and it is available in full, for printing out too, via the following address: <http://tinyurl.com/2uzuwd> Note that references are comprehensive in the original, but have been omitted from the quotations below.

David R. Moller, from Johns Hopkins University, appears to be one of the leading researchers into sarcoidosis. His 2003 paper is highly technical. Below I select some points that I hope are likely to be of interest to a general audience of sarcoidosis sufferers.

Current research, he says, supports the idea that sarcoidosis involves an immune reaction to things which the body recognizes as foreign (antigens). The identifying feature of sarcoidosis, and also the feature which is at the root of some symptoms, is the formulation of nodules known as granulomas. While the next paragraph is somewhat technical, the description of the many forms of treatment which may be used to interfere with the formation of granulomas is instructive and it provides an overview of what follows later (in less forbidding language):

Conventional treatment is focused on attenuating granuloma formation with antimalarial drugs that inhibit antigen presentation or with nonspecific anti-inflammatory agents such as glucocorticosteroids, methotrexate, or azathioprine. Anti-tumour necrosis factor (TNF) agents such as pentoxifylline, thalidomide, etanercept and remicade, have recently shown some successes in sarcoidosis.

What is particularly relevant to the patient is the downside of the various treatments, but before proceeding to that, let us look at a few other points noted by Moller. He makes a number of points, most of which I think are widely accepted. He says that only “a minority of patients have persistent granulomatous inflammation for many years.” However, he says that when this does occur, the usual consequence is progressive fibrosis (formation of scar tissue). He also says that “suppression of granuloma formation results in preservation of organ function and minimizes long-term fibrotic outcomes.” Furthermore he states that, “corticosteroids are effective in suppressing granuloma formation in most patients with sarcoidosis – certainly over the short-term, and likely over the long-term as well.” I have to say that the latter does not accord with another clinical symposium I have read about, held by the US Chest Physicians which can be accessed at <http://tinyurl.com/2uczvx>, which appeared to suggest that there is considerable doubt about whether steroids have a *long-term* beneficial effect. The ACCESS study also seemed doubtful on that score. The difficulty of ever knowing the truth is great in view of the fact that remission may or may not occur of its own accord.

The following observation seems to me to be of considerable interest: “There is usually a threshold level of drug effect for most patients, below which there is progression and above which there is suppression of granuloma formation with stabilization of organ

function.” Interesting, but one wonders whether it is possible to monitor the state of progression accurately, so as to be sure that the optimum dose is being administered. Is, for example, suppression adequately indicated in the case of pulmonary sarcoidosis by improving lung function, for that is far easier to measure than granuloma formation.

He also observes that the rates of “granuloma formation are variable for an individual patient, with some patients progressing very slowly and others with a rapid progression in inflammation and organ dysfunction.” Of course that is only what one would expect, with some cases being acute and others chronic.

Drug treatments

He says that one treatment does not fit all cases because, “different tissues involved with sarcoidosis inflammation respond differently to different drugs. For example, the antimalarial drugs are often more effective in treating skin and mucosal disease (nasal sinus, upper respiratory tract) than pulmonary disease.”

Antibiotics. One way to reduce the formation of granulomas is to reduce the number of bodies (antigens) that cause them to form. It may be for this reason that antibiotic therapy is effective in certain cases. Moller observes:

Reducing antigen deposition may be approached by antibiotic therapy if: (1) microbes are triggers of sarcoidosis and (2) microbes are still present in viable form when patients initially present with their disease. Although still controversial, mycobacterial and propionibacterial organisms have been the microbes most convincingly linked to sarcoidosis. In this context, it is of interest that doxycycline and minocycline that are effective against *Propionibacterium acnes*, and dapsone and clofazimine which have antimycobacterial effects, are beneficial in a subset of sarcoidosis patients. However, these agents have purported anti-inflammatory effects independent of their antimicrobial effects that might also explain their benefit in sarcoidosis. As these drugs are known to be effective in only a few anecdotal cases, one implication of the general lack of response to antibiotic therapy is that viable microbial agents may no longer be present in tissues at time of disease presentation, assuming a microbial trigger operates in sarcoidosis.

Moller seems to me slightly misleading in referring to “only a few anecdotal cases” since over two years Bachelez et al conducted a clinical trial on cases of skin sarcoidosis (which in fact Moller references), and found that doxycycline and minocycline treatment were highly effective in 10 out of 12 cases. The five page paper is available on the web at this URL: <http://archderm.ama-assn.org/cgi/content/abstract/137/1/69>

By way of confirmation of one point Moller made there, I have seen it stated in the Journal of the American Medical Association that minocycline *may* have anti-inflammatory action, and that this makes it impossible to be sure if these tetracyclines are effective (against at least a subset of sarcoidosis cases) *because of their antibiotic action*.

Antimalarial drugs. Moller says that the antimalarial drugs chloroquine and hydroxychloroquine are established first-line drugs for skin and mucosal sarcoidosis if treatment is indicated and corticosteroids are not needed. No particular side-effects are mentioned.

Corticosteroids. Moller observes that these drugs have broad-spectrum anti-inflammatory effects on multiple cells. I have come across various references to corticosteroids as being immunosuppressant, but Moller does not mention that, although he goes on to put the next two drugs in the immunosuppressant category.

Azathioprine. About this Moller says that:

Several studies have documented the benefit of azathioprine as a steroid sparing agent in sarcoidosis. However, given its considerable toxicities which include bone marrow suppression, gastrointestinal effects, hepatitis [liver inflammation], and possibly, oncogenic [cancer causing] effects, the use of the drug in sarcoidosis is reserved for progressive, organ-threatening disease that is not responsive to safer alternatives including low-dose corticosteroid therapy.

Methotrexate. About this Moller says that:

Methotrexate has found utility in the treatment of sarcoidosis, although its overall effectiveness as a steroid-replacing or steroid-sparing drug has not been subject to rigorous multicentre studies. The potential for hepatic [liver], bone marrow and pulmonary toxicity relegates the use of this drug to maintenance treatment of serious organ-threatening disease. The major mechanism(s) of action that are critical in suppressing granuloma formation in sarcoidosis remain uncertain.

Cyclosporin. This is not an immunosuppressant but rather another class of drugs called immunophilins. Moller says that there are good theoretical reasons why cyclosporin should help to slow down granuloma growth, but also comments that:

Several studies have shown cyclosporin is not effective in pulmonary or systemic sarcoidosis. In fact, cyclosporin has shown only limited benefit in small numbers of cases including a handful of severe, steroid-resistant cases of neurosarcoidosis. ... As cyclosporin may cause considerable renal [pertaining to the kidneys] toxicity and carries an increased risk of malignancy, use of the drug should be restricted to the most serious cases of sarcoidosis failing other more standard therapies.

TNF inhibition in sarcoidosis. We now move on to consider four anti-TNF drugs. Moller says that the premise that TNF inhibition may be beneficial in sarcoidosis is an attractive and scientifically sound concept. One such treatment is pentoxifylline. Moller says:

Although pentoxifylline has been shown to be beneficial in early pulmonary sarcoidosis in one study, further clinical experiences have suggested that the drug may have only limited utility in mild disease. Possibly, this is due to the fact that it is difficult to achieve therapeutic doses *in vivo* [in people]... due to frequent gastrointestinal effects.

Thalidomide. Moller says that, "Decades ago, the drug was empirically found to be beneficial in erythema nodosum leprosum. Thalidomide has been shown to inhibit TNF production by mononuclear cells. ... In sarcoidosis, thalidomide has anecdotal benefit in skin and mucosal sarcoidosis including severe lupus pernio, but not pulmonary sarcoidosis. ... The drug has notable toxicities including teratogenicity [birth malformation], peripheral neuropathy [AF. Numbness of the extremities.] and sedation that currently relegates its

use to second or third line therapy for disfiguring skin sarcoidosis.”

Etanercept. This is another anti-TNF drug, but not promising for sarcoidosis. Moller says:

The effectiveness of the drug in sarcoidosis is unknown, but early preliminary reports suggest that, like in Crohn’s disease, the drug may not be effective in sarcoidosis. Toxicities include an increase in infection risk and concerns of possible lupus syndrome or demyelinating disease.

Infliximab. This is the final anti-TNF drug that Moller considers. Again it has a lot against it, mainly that it generates:

Antibody immune reactions that often limits therapy or require concomitant methotrexate to help suppress this humoral [pertaining to body fluids] response. The drug carries an increased risk of infections such as recrudescent tuberculosis and possible allergic reactions to the chimeric antibody [i.e. infliximab itself]. A few anecdotal reports in sarcoidosis suggest that the drug may be effective in sarcoidosis, including steroid-recalcitrant disease.

Different strategies for different stages of sarcoidosis. In this section, Moller suggests that slightly different treatments might be appropriate to acute and chronic sarcoidosis:

As disease remissions in sarcoidosis usually occur within the first several years, minimizing immunosuppression early in the disease may be a reasonable therapeutic goal. ... As the probability of remission in chronic sarcoidosis is low and the cumulative effects of ongoing inflammation considerable, treatment strategies that focus on minimizing the immunopathological effects of granulomatous inflammation may be paramount to consider in these patients.

It would be interesting to know if he would include *not* using corticosteroids as a way of “minimizing immunosuppression,” and hence advisable to avoid them until their use becomes virtually unavoidable due to the severity of the symptoms. I would think that is a wise policy in both acute and chronic cases, but deciding on the appropriate severity is a hard call.

Treatment of progressive pulmonary fibrosis in sarcoidosis. On this Moller says:

Progressive organ damage and pulmonary fibrosis represent major causes of morbidity and mortality in sarcoidosis. Although unproven by rigorous controlled trials, most clinicians view sarcoidosis as a treatable disorder. There is little doubt that corticosteroid therapy or other medications outlined above can improve symptoms and organ function over weeks to months and often years in most patients with sarcoidosis. ... For now, nonspecific anti-inflammatory drug therapy that suppresses granuloma formation is the strategy most likely to prevent or retard progressive fibrosis in sarcoidosis.

Moller concludes with the observation:

The overall goal in chronic sarcoidosis remains clear: suppress granuloma formation and limit tissue injury and fibrosis in those patients that demonstrate progressive organ dysfunction. END

For several months on the Sarcoidosis Social Network there was a Discussion titled *Debating the Marshall Protocol*. It was fairly useful, but it caused a certain amount of aggravation, because those who have benefited from the Marshall Protocol tend to be somewhat evangelistic, which I find understandable, but it tends to irriate others. In fact the aggravation became such that the Discussion was closed, and further debate about the Marshall Protocol banned from the site. Nevertheless the closed Discussion can be accessed for viewing via the Social Network Site, or directly at this address: <http://sarcoidosis.ning.com/forum/topic/show?id=769148%3ATopic%3A2234>, by anyone who wants to get an idea of why the Marshall Protocol is more of a field of debate rather than an available treatment for sarcoidosis.

The debate was useful both for the information it provided and because it enabled me to get into contact with Wayne Hunter, a regular and very knowledgeable contributor to the site. He gave me enough background to enable me to write what follows, which is also incorporated into the latest draft of *The Fundamentals of Sarcoidosis* (the article on the SILA website that attempts to look at the whole picture).

A BRIEF INTRODUCTION TO THE MARSHALL PROTOCOL

Many people will have heard of the Marshall Protocol, but some background knowledge of the subject may be helpful. Much is still in dispute, but these are the essential points that are agreed by impartial observers.

Professor Trevor Marshall PhD, a molecular biologist, cured himself of sarcoidosis and feels convinced that he has a true theory about not only sarcoidosis, but several other similar diseases, and how to cure them. His first attempt at proving it was to organize a trial on the internet using volunteers who are given further guidance via the internet (although they need the cooperation of their doctor).

The treatment consists of getting the levels of vitamin D in the body measured (both the active and inactive forms, and that is specialized task), and then, at least in most cases, taking fairly drastic action to keep down the level of vitamin D (e.g. avoiding certain foods, keeping out of the sun and wearing dark glasses). Treatment also involves taking doses of one specific type of a drug known as an Angiotensin Receptor Blocker (ARB), in doses which are about four times as large as those normally used to reduce blood pressure, while at the same time embarking on a long (several years) course of treatment with several classes of antibiotics, starting with two tetracyclines, initially minocycline (and then as guided by those running the internet trial).

These antibiotics, which are broad spectrum antibiotics, are taken in unusually small doses, and patients are warned to expect to feel worse on many occasions, sometimes far worse, during the whole period of treatment. The generic term for such adverse reactions within the medical profession is "Herxheimer reactions" (also JHRs and Herxes). Outside the Marshall Protocol itself, it is not agreed whether these Herxheimer reactions are a necessary part of the curative process, or something that could be avoided with a differently designed treatment regime. Marshall prefers the term Immuno Pathological Reaction (IPR). But the interesting question is whether these Herxes are unavoidable.

Throwing some light on that question is a 12-person trial which was carried out by

Bachelez et al. on patients with skin sarcoidosis, using minocycline and doxycycline, but none of the other trappings of the Marshall Protocol. 10 patients recovered rapidly (although minocycline at 200 mg/day was usually continued for about a year to try to ensure no remission). These cases did not experience Herxheimer reactions during the curative process. That may be due to the higher dose of minocycline, but the reason has not been fully investigated.

The evidence from the early Marshall Protocol trials was purely anecdotal, since there was no attempt to keep track of those who dropped out. Nevertheless there is no doubt that some people who have followed the procedure are exceedingly pleased with the results. At the present time, the Food and Drug Administration (FDA) are supervising a five year trial in which record is kept of those who have no or adverse reactions to treatment. Thus there is hope, once these trials are complete (it is now about half way through), that clear evidence will emerge of both the possible advantages and disadvantages of following the Marshall Protocol.

From a practical point of view, apart from possible cost as you are not too likely to get the treatment under insurance or National Health care, the chief difficulty is in finding a sympathetic doctor, because it would take a couple of months of study to master the voluminous literature that is recommended as necessary reading by those conducting the internet trial, and even if doctors can find the time to do that, only a few doctors are willing to help their patients try something which may be harmful (and very likely is in some cases), which has not yet been shown to produce positive results based on properly conducted clinical trials.

There will doubtless be some people who want to learn more about this evolving treatment, and Heather Walker has a 36 page *Patient's Story* by New Zealander Guss Wilkinson, which tells of his experiences during his long treatment of sarcoidosis using the Marshall Protocol. It is to some extent illuminating, but since I prepared that and got it printed out to give Heather some copies, I have come to realize that not only will every person react differently to the Marshall Protocol, but also that Guss was a rather special case, being a super-fit karate expert. Extreme exercise is one thing that can upset the immune system so he is not a typical subject.

Of relevance to those who are contemplating embarking on the Marshall Protocol is how difficult it is to actually do. Because it involves the use of antibiotics, it would certainly be impossible to follow it without a supportive GP. One thing that has always disturbed me is that the Marshall Protocol site, at www.marshallprotocol.com, appears to have failed to write a simple exposition of the basic facts that a doctor would need to know before guiding a patient through the Marshall Protocol. In the next few pages I show the results of my early efforts to find out what doctors need to know — according to those guiding the Marshall Protocol — before undertaking the task of guiding their patients. It seemed to me a forbidding task, and I thought that there must actually be a better guide, but one thing to emerge from *Debating the Marshall Protocol* is that there is not.

A Guide to Guidance For Physicians: The Marshall Protocol - Phase One

The first task for prospective Marshall Protocol candidates is to spend a few months ‘doing battle’ with the two Marshall Protocol websites, www.sarcinfo.com and <http://www.marshallprotocol.com>. The latter is labyrinthine, as I shall describe later. Something easier must be offered to the doctor whom one is hoping to persuade to supervise the treatment. The patient is supposed to know at least as much about the Marshall Protocol (MP) as the supervising doctor, so the patient should not only offer the doctor the nine page paper written by the Autoimmunity Research Foundation, available from the web address, <http://autoimmunityresearch.org/phase1.pdf>, but should also be able to understand it and convey to the doctor the nature of the task involved in supervising it. The paper is a coherent route into understanding the Marshall Protocol so is a suitable path to follow. However, an average reader, wondering whether to try out the Marshall Protocol, may be best served by a preliminary layman’s overview, which gives just a rough idea of what the Marshall Protocol actually is. Refining detail can come later.

Rough idea of the MP

The MP is based on the hypothesis that a minute form of bacteria, Cell Wall Deficient (CWD) bacteria, infiltrate immune system cells, where they become fairly safe against the body’s normal defence mechanism. Incidentally that defence system mainly consists of those very immune cells which the CWD bacteria are thought to be detrimentally inhabiting. The Marshall Protocol aims at getting rid of the CWD bacteria, believing them to be the cause of many chronic diseases including sarcoidosis. To do so, it utilises the following procedure (known as a protocol).

Vitamin D is cut out of the diet to reduce the amount of it in the body, and sunlight is avoided to reduce vitamin D synthesis in the skin. Vitamin D, and its breakdown products (metabolites), inhibit the body’s immune system, thus the action of cutting out vitamin D may start the process of killing off the CWD bacteria. When these bacteria die, they release toxins. This may produce an adverse reaction, mimicking, or even exceeding with florid variations, the symptoms of the original disease. These reactions are known as Herx reactions, and are an inescapable part of the cure. Incidentally the body produces enough vitamin D of its own accord so there is no need to fear becoming vitamin D deficient.

One Herx reaction may be photosensitivity, with a risk of damage to the eyes, thus the patient needs to be prepared with special shades (amber sunglasses) to use in case this becomes a problem. These are not expensive.

A drug called an Angiotensin Receptor Blocker (ARB) is then introduced. This drug is normally used, in smaller amounts, for reducing blood pressure (of which more details later). The ARB has two somewhat contradictory effects. It too may cause the immunity system to kill off the CWD bacteria, and hence precipitate a Herx reaction. However the ARB is also an anti-inflammatory, and thus if a little of the ARB causes an intolerable Herx, the first, and perhaps counterintuitive, step is to *increase* the intake of the ARB.

What might be called the third prong of Phase 1 of the Marshall Protocol is to take the antibiotic Minocycline. This also has two somewhat contradictory effects. The normal Marshall Protocol dose is 25mg (mg is a milligram) every 48 hours. This dosage protocol, at least as a starting point, is the best way of getting the immune system to kill off some CWD bacteria. However, when Minocycline is used more frequently, and thus in larger quantities, the anti-inflammatory properties of Minocycline come to the fore. Thus if an intolerable Herx reaction cannot be dealt with by increasing the ARB dosage as per the last paragraph, the next step, again perhaps counterintuitively, is to start using Minocycline if

one has not yet started, or, if one is already using it, then after cutting out Minocycline briefly to see what that does, to *increase* the Minocycline dosage.

The rest of Phase One consists of increasing the curative dose of Minocycline from 25mg every 48 hours to 100mg every 48 hours. Phases Two and Three consist of using several other antibiotics in combination. During Phases Two and Three one still has to deal with Herx reactions, because if there is no Herx reaction, then the disease has been overcome. I should just mention that Herx reactions have recently been given the alternative name Immuno Pathological Reactions (IPRs). That is all you need to know before embarking on this Guide to *Guidance For Physicians: The Marshall Protocol Phase One*. You will benefit, of course, by having the nine pages of the *Guidance* document to hand. The task now is to consider just what the doctor is faced with when he too has this *Guidance* paper to hand, for as with many papers, especially those with links to internet sites, what is said therein is only the tip of the iceberg. The majority of the task of gaining a full understanding lies in other papers that are merely referred to. Also the *Guidance* paper may itself raise questions to which no answer is given, and yet it not apparent where one should go to find the answer. Such points will be raised in the rest of this *Guide to the "Guidance For Physicians"* paper.

Note that the number of pages of text (when printed) shown in the right-hand column does not indicate that reading of those particular pages, or watching of the video where minutes are shown, is necessarily essential. Doctor's view of what they consider necessary will be considered later. It may be taken as read that there is an operative link to the paper (i.e. only a need to click on the link) unless I comment to the contrary.

<u>Paragraph reference numbers down the left side allocated for purposes of this document only</u>	<u>Printed pages or minutes (m)</u>
↓	↓
0.0 The 9 page paper Guidance For Physicians: The Marshall Protocol - Phase One	9 ↓
0.1 "Ref." refers to a reference that is contained in this 9 page paper.	
0.2 "Photosensitivity During Recovery from Th1 Disease" This is twice referred to as being on the Marshall Protocol website, but oddly no link is given. I traced it down to the web address http://www.marshallprotocol.com/forum2/7756.html .	4
0.3 Ref. 1. "Antibiotics in Sarcoidosis - Reflections on the First Year."	12
0.4 Ref. 2. "Antibacterial Therapy Induces Remission in Sarcoidosis - Implications for Autoimmune Disease."	7
0.5 Ref. 3. "High levels of active 1,25 - dihydroxyvitamin D despite low levels of the 25-hydroxyvitamin D precursor - Implications of dysregulated vitamin D for diagnosis and treatment of Chronic Disease." Following the link given tells one that the paper is available at the publisher's website, but without any indication of how to find that, hence "not available" (n/a).n/a	
0.6 Ref. 4. "Putative Antibacterial Mechanisms for Angiotensin Receptor Blockers."	9
0.7 Ref. 5. "Minocycline, doxycycline effective treatments for sarcoidosis." Trying to follow the link which is given, to http://tinyurl.com/2oglm , returns only "Link does not exist. I tried to Google for the title, but without success.	n/a
0.8 Ref. 6. "Common angiotensin receptor blockers may directly modulate the immune system via VDR, PPAR and CCR2b."	19
0.8 Ref. 7. "Molecular genomics offers new insight into the exact mechanism of action of common drugs - ARBs, Statins, and Corticosteroids." This leads to a 62 minute video, hence 62m.	62m
0.10 Ref. 8. "VDR Nuclear Receptor Competence is the Key to Recovery from Chronic Inflammatory and Autoimmune Disease."	3
0.11 Ref. 9. "A review - Vitamin D and Calcium in Sarcoidosis."	3

- 0.12 Ref. 10. "Observations of Jarisch-Herxheimer Reaction in Sarcoidosis Patients." 13
Subtotal so far **79 pages + 62 minutes video**

1.0 STEP ONE

- 1.1 Step one is to measure the level of two of the breakdown products (metabolites) of vitamin D. The short name for those two metabolites is 25-D and 1,25-D. The sentence that I am about to quote gives rise to some difficulties which we will then go on to consider. Before quoting it I must clarify some abbreviations that are used:

- (a) pg/ml stands for picograms per millilitre; a picogram is a million millionth of a gram;
 (b) ng stands for nanogram, which is a billionth of a gram;
 (c) Th1 stands for a certain type of immune cell, namely those which exist in abnormal quantities in the diseases which the MP aspires to cure, and which are therefore called Th1 diseases.

If the level of 1,25-D is elevated (above 45pg/ml) and/or the 25-D depressed (below 20 ng/ml), a Th1 infection should be suspected. Remember, however, that as the level of 25-D rises above 20 ng/ml (usually due to artificial supplementation) it is providing an immunosuppressive action. High levels of 1,25-D are often not evident until the 25-D drops to a therapeutic level (under 15 ng/ml). If D- metabolites tests do not indicate Th1 inflammation but clinical observations suggests Th1 inflammation the MP may be used as a therapeutic probe.

The logic of all that is unlikely to be immediately apparent, so perhaps it is best to think of the possible combinations, which are these:

Case	Level of 1,25 D pg/ml	Level of 25-D ng/ml	Appropriate action
i	>45	>20	Suspect Th1 disease (an OR logic case).
ii	>45	<20	Suspect Th1 disease.(an AND logic case).
iii	<45	<20	Suspect Th1 disease.(an OR logic case).
iv	<45	>20	Lower 25-D until <15 ng/ml then repeat test.
iva	>45	<15	Suspect Th1 disease. (an AND logic case).
ivb	<45	<15	Do not suspect Th1 unless clinical indications suggest otherwise.

When seen in this light, it becomes apparent that only one combination might suggest that it was not a Th1 disease and that would only be arrived at after at least two D-metabolite tests; even then the conclusion might be contradicted by the clinical indications. Since my information is that a D-metabolite test may cost anything between £150 - £300 (US\$285 - US\$570), it would seem that opting for a therapeutic probe may be the better choice, except that, as we shall see, D-metabolite tests are required later anyhow, and it would certainly be interesting to see what the starting Vitamin D values were. A therapeutic probe consists of trying the Marshall Protocol and seeing if anything up to the point of taking minocycline makes the patient feel worse. If the MP is correct, an adverse reaction (a Herx reaction) indicates that a cure via the MP is possible.

2.0 STEP TWO

- 2.1 Step two is short and calls for comment, so it is best to quote it in full:

Restrict dietary intake of Vitamin D by eliminating all supplements and foods high in Vitamin D. The goal is to reduce 25-D to a therapeutic 15 ng/ml or less. Retest 25-D every few months to make sure it is dropping toward the lower end of the therapeutic range. Many in the Phase II study cohort keep their 25-D below 5 ng/ml, without adverse effect.

As mentioned, it seems that even if one economizes by avoiding the cost of initial D-metabolites test(s) in Step One, and utilizes a therapeutic probe instead, there remains a need for several D-metabolite tests to ensure that the level of 25-D is kept in the "therapeutic range" of 15 ng/ml or less.

3. STEP THREE

- 3.1 Step three is essentially about avoiding sunlight and bright lights by staying indoors. Photosensitivity can develop suddenly, so it is wise to be prepared with shades (sunglasses) that fall into the category: “Most NoIR, some Bolle 100, and some Zeiss models.” To find out which models are suitable, one is advised to see “the study website.” I tracked the address to <http://www.marshallprotocol.com/forum2/4.html>. Although there are 18 pages (when printed) I reckon the doctor would only need to read a couple of them, hence the figure of 2 on the right. Incidentally here is a typical case where the patient has to do the work, and not the doctor. While it is not stated in the guidance document under consideration, on the MP website I have seen it recommended that indoor and outdoor shades are needed. The cost of a pair of these glasses low. 2
- 3.2 It is suggested that Ketoconazole 2% cream, applied to unavoidably exposed skin, may provide some protection against the production of 1,25-D, so the doctor may need to know something about Ketoconazole cream. At the end, there is a link to a three page document on that. 3
- 3.3 It is also suggested, in this Step Three, that one should see the document, “Photosensitivity During Recovery from Th1 Disease.” As mentioned in paragraph 0.2, oddly no link is given, but I traced it down to the web address <http://www.marshallprotocol.com/forum2/7756.html>

4.0 STEP FOUR

- 4.1 It appears that this Guidance paper does not provide the supervising doctor with a full briefing on the matter of D-metabolites analysis, because Step Four suggests that there is a need for expert help with D-metabolites analysis, and that the actual numbers of the 25-D and 1,25-D levels should be reported either in the “Preliminary Tests” forum or in the “Private Section for Health Professionals” at the MP website. I tracked down the the “Preliminary Tests” forum to <http://www.marshallprotocol.com/forum22/>. It consists of three links to information from the moderators of the MP site and about fifty other links to individual reports by MP members. The first of these three links is “What to include in your preliminary test results report” and is 3 pages, the second link is “Normal lab ranges” (<http://www.marshallprotocol.com/forum22/4447.html>) and is 2 pages, the third is “Beginning MP information” and is 3 pages. Of course one could go on to read all the material in the other links, but counting these three alone amounts to 8 pages. 8
- 4.2 In this Step it says that “D-metabolites within lab ranges may still indicate disease.” But we have dealt with that, since the previous paragraph mentions the link to a couple of pages explaining normal lab ranges. The general point being made appears to be that in the special case of the MP, expert knowledge is required to interpret the D-metabolites results, since what is accepted as normal by most medics does not apply to the MP. The conclusion seems to be that a supervising doctor must regard this as a co-operative enterprise with the MP modulators.

5.0 STEP FIVE

- 5.1 This step is about the possibility of combining other protocols with the Marshall Protocol (which in general is not advisable). Thus, for instance, starting the MP may involve weaning the patient off steroids. In that case, the doctor may need to locate “Weaning from Steroids” on the MP website. I tracked it down to <http://www.marshallprotocol.com/forum2/1917.html>. There is also a forum with currently twenty postings on the subject at <http://www.marshallprotocol.com/forum38/> but that is probably a task to be left to the patient. 8
- 5.2 If patients are taking medications that are not dealt with individually in the present nine page guidance sheet, then the doctor will need to use the link to a “Complete list of MEDICATIONS TO AVOID.” There is a link to this. 7

6.0 STEP SIX

- 6.1 Step Six involves taking an ARB every six to eight hours. There are many ARBs, but the MP specifies that the only ARB to use is the one with the generic name of olmesartan medoxomil, usually just called olmesartan. Brand names are Benicar (in the US), Olmetec (in the UK), and Votum (in Germany). Ingestion of the ARB has to continue throughout the MP treatment, and is fairly expensive. I have been told that one can obtain Votum from Germany at almost half the price one might have to pay elsewhere. Even then it costs about £720 (US\$1370) a year, which amounts to £2900 (US\$5500) over a four year treatment period.
- Step Six instructions start with:

Begin Benicar 40 mg every six to eight hours (six hours is preferable) to interrupt the inflammatory cycle and reduce the severity of potential Herx reactions. (For example: 6am, 2pm, 10pm **or** 6am, noon, 8pm, midnight.) Benicar comes in 20mg and 40mg tablets.

Stress is given to the fact that Benicar may cause hormonal changes which are unpleasant; also it may improve the immune response and cause bacteria dieoff, and hence a Herxheimer reaction. Trying to look at that from a doctor's viewpoint, he might think that in order to get used to Benicar, that is before antibiotics are introduced, it would be best to start with a lower dose of Benicar. That might have some advantages in reducing the rate of hormonal changes that the body has to make, but as Benicar may itself improve the immune response and so cause a Herx reaction, it would then be necessary to be prepared, if there are any signs of a Herx reaction starting, to switch to at least 40 mg every 8 hours, since whether it causes a Herx or not, Benicar serves as an anti-inflammatory and hence protects organs that might get damaged by an inflammatory reaction. In short an appropriate Benicar "blockade" – reaching 40mg every 4 hours if the Herx becomes bad – must be mounted if there is a Herx reaction while acclimatising to Benicar. Also a normal Benicar blockade of at least 40 mg every 8 hours must be established before using minocycline. Whether my interpretation of starting on Benicar is true remains to be investigated, but as far as I can see the doctor is not given any advice as to whether this course of action would be advisable. This is something the supervising doctor would have to sort out with the aid of the Marshall Protocolists.

6.2 Step Six goes on to give more details of how to deal with bad Herx reactions. It says:

Some patients experience a Herx reaction with Benicar alone because Benicar allows the immune system to begin to function normally and kill the pathogenic bacteria. Occasionally these symptoms are intolerable. The first option to reduce the intolerable Herx is to take Benicar every 4 hours until the Herx subsides before returning to normal Benicar dosing. Additional Benicar should be kept on hand for this reason.

Because frequent low-dose Minocycline has an anti-inflammatory effect, it may also be used to dampen these symptoms. Therefore, doctors are encouraged to *prescribe Minocycline when they write the prescription for Benicar* so the patient will have it on hand if needed. Taking 25 mg of Minocycline every six or 12 hours often relieves symptoms that are intolerable.

While all that makes sense, there is some difficulty unless one has already read Stage Seven, involving the use of Minocycline, so I think that something more lucid is required in lieu of the second paragraph quoted above, perhaps on these lines:

While taking the normal starting dose of Minocycline, at the rate of 25mg every 48 hours, is liable to lead to severe Herx reactions, frequent low-doses of Minocycline have the opposite effect as the anti-inflammatory effect of Minocycline then outweighs the longer term effect of encouraging bacteria to be killed off. So if the use of 40mg of Benicar every 4 hours fails to sufficiently abate the Herx reaction, 25mg of Minocycline may be taken every 12 hours (or if that does not suffice 25mg every six hours) to relieve symptoms that are intolerable.

7.0 **STEP SEVEN**

7.1 It usually take a week or two for the effects of taking the olmesartan to settle down. After that, Step Seven starts with a 25 mg dose of minocycline every 48 hours. This is a stage at which Herx reactions are likely to become a real problem (they may have shown up with olmesartan alone). The guidance states in bold print that patients with severe cardiac symptoms may require immediate intervention, so if the patient has any suspicion of heart problems the doctor will need to follow the link to "[Anticipating, Identifying and Treating Cardiac Symptoms While on the Marshall Protocol.](#)" 3

8.0 **STEP EIGHT**

8.1 Step Eight involves increasing the minocycline dose until it no longer produces Herx reactions. Then the patient is ready to move on to Phase 2 and Phase 3. Only when patients have completed Phase 1 are they allowed to see Phase 2 and Phase 3 (these Phases consist essentially of taking combinations of different antibiotics), but of course the doctor can learn from the Professional part of the MP website exactly what Phase 2 and 3 entail. The reason for this is that the Marshall Protocolists are concerned that patients will 'rush ahead' if they know too much. While this may be the result of bitter experience, it obviously makes it more difficult to persuade your doctor that you are yourself taking responsibility for treatment, which is what you are told you should be

trying to assure your doctor, according to the MP website. That assurance is less than convincing if you have to admit that you are not trusted to know the full details of what the Marshall Protocol entails.

- 8.2 Considerable space is given in this step to dealing with intolerable Herx symptoms. Here is the first part of the main paragraph on that:

If intolerable Herx symptoms continue with increased Benicar and cessation of 25mg of Minocycline, taking Minocycline more often (25mg every six hours or 12 hours or 24 hours) may dampen the Herx reaction because the 12-hour dosing of Minocycline maintains a level of antibiotic which is not as effective at killing the intra-phagocytic bacteria as a full 48 hour immune-enabling pulse.

- 8.3 In Step Eight of the Guidance text, the doctor is informed that more details can be found at the study site, i.e. the Marshall Protocol site. Exactly which of the many links the doctor would consider it advisable to look at is obviously an open question. The file provided for the *Guidance For Physicians Marshall Protocol Phase I*, here being discussed, is available for printing out, as mentioned in the introductory paragraph. When accessing it on the net, it is mainly possible to make use of the links provided to get to the subsidiary files. The various links that are on offer in this last page of the *Guidance For Physicians* (a few already mentioned above) are grouped under headings, and are as follows (provided here without the links but with an indication of how long they are. But let us just pause for subtotals so far.

1st subtotal so far	79 pages + 62 minutes video
2nd subtotal	28 pages
Total so far	107 pages + 62 minutes video

:

Benicar (olmesartan medoxomil, Votum, ARB)

8.3	<i>Why shouldn't we ramp up the dose of Benicar?</i>	2
8.4	<i>The need for a Benicar blockade.</i>	21
8.5	<i>How does Benicar work? Why is it superior to other ARBs?</i>	5
8.6	<i>I just started Benicar. Why do I feel worse?</i>	3
8.7	<i>Does Benicar cause dizziness?</i>	2
8.8	<i>My blood pressure is already low. Can I take Benicar.</i>	5
8.9	<i>How long should I stay on Benicar? Why don't I feel better? When should I start Minocycline?</i>	3
8.10	<i>What is a therapeutic probe?</i>	2

Folates, Food, Light, Lifestyle, Vitamin D

8.11	<i>D-Metabolites Tests.</i>	14
8.12	<i>Vitamin-D Tutorial.</i>	13
8.13	<i>The Importance of Avoiding Vitamin D and Folic Acid.</i>	6
8.13	<i>Foods to Avoid.</i>	7
8.14	<i>The Effect of Sunlight/Daylight and Bright Lights.</i>	6
8.15	<i>The Effect of Light on the Brain (amygdala)</i>	6
8.16	<i>Protecting Your Eyes</i>	26

Hormones

8.17	<i>Adrenal Function Tests.</i>	8
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8.18	<i>Hormonal-interaction Chart</i>	1
Jarisch-Herxheimer Reaction (JHR, Herx)		
8.19	<i>Herx... What is it?</i>	8
8.20	<i>What is cardiac Herx?</i>	7
8.21	<i>My Herxheimer reaction is too strong. What should I do?</i>	11
8.22	<i>How can I control my anxiety and depression?</i>	4
8.23	<i>I have insomnia and fatigue. What should I do?</i>	3
K-cream		
8.24	<i>How does ketoconazole cream work?</i>	3
Minocycline		
8.25	<i>Can I use doxycycline instead of Minocycline?</i>	3
8.26	<i>I'm allergic to an antibiotic on the protocol. Is there a substitute?</i>	3
8.27	<i>Why do you NOT recommend tiny doses of Minocycline? How does a low dose Minocycline work?</i>	3
Non-MP Medication Supplements		
8.28	<i>Medications to avoid when on the Marshall Protocol.I</i>	7
8.29	<i>Weaning from Steroids.</i>	8
8.30	<i>Is it safe to take anticoagulants while on the MP?</i>	2
8.31	<i>Why do I have to stop taking supplements?</i>	8
8.32	<i>Don't I need to take a calcium supplement?</i>	5
3rd subtotal		203
1st subtotal		79 pages + 62 minutes video
2nd subtotal		28 pages
3rd subtotal		203 pages
Total		310 pages + 62 minutes video

This total only gives a rough idea of the material involved, because just as the 9 pages turned into 310 pages when the links are followed, one can expect the 310 pages to turn into many more when the links they contain are followed. However the above serves to give doctors some idea of what they may need to study if they are to supervise the Marshall Protocol.

Costs

One thing that is not easy to get information about is the total cost of following the Marshall Protocol. I can claim only a hazy idea, but any idea is probably better than none, so here is my guide to likely cost, based on the best information I have been able to obtain from those who have followed the Marshall Protocol. The Marshall Protocol is said to take between 3 and 5 years, so I choose an intermediate time of 4 years. The US dollar cost is arrived at by converting at a rate of 1 GBP = US\$1.90

	£	US\$	Notes
NOIR amber shades (2 pairs, indoors and out)			
Vitamin D tests (say 5 at £225 each)	1125	2137	

Olmesartan, using the cheapest variety Votum (4 years at £960 per year)	3840	7296
Antibiotics	?	?
Consultations with doctors (say 4 a year for 4 years at £40 a time)	640	1216

Conclusion

While there is clearly a great deal that can be learnt about the Marshall Protocol, it seems to me that what a doctor needs to know, *to safely administer it*, could be condensed into a much smaller space, perhaps 24 pages, with links to be used only as necessary for patients with special problems.

Using the Sarcoidosis Social Network (at <http://sarcoidosis.ning.com>)

As announced on page 23 of the last SILA newsletter, this Social Network was started by our very own Henry Shelford, who looks after the SILA website, and incidentally has his own site at www.sarcoid.co.uk. Six months after opening, the Network already has over 600 members. I would advise anyone with access to the internet to make use of it. It is fairly easy to use, but perhaps a few tips will be useful.

Signing on as a member is easy. You need to choose a password to use to get you into the site. When signing on you are free to use your own name or a pseudonym.

The network gives an opportunity for people to mutually agree to become "Friends." It took us some time to suss out what that entails, but we think we have now found out that the *only* effect is to allow you to exchange private messages via the facility offered by the site (click on "Send a message" below the picture of your Friend). By the way, Julia is the person to contact for first hand advice on the Marshall Protocol. Debate about the MP has been banned, but the now closed Discussion is still available to read at <http://sarcoidosis.ning.com/forum/topic/show?id=769148%3ATopic%3A2234>

When you join a fairly large site like this, it can be daunting to know where to post your message. You can always go to the main forum and start a new Discussion, but of course it's often better to find a Discussion which is related to your current interest, for instance that may be "fatigue." In that case it is useful to read what other people have said about "fatigue" before posting your question. This is what to do.

Near the top of the page, running across the screen, there are these section options:

Main My page Members Forum Groups Invite

If you choose **Main**, you will notice that there are Groups listed down the left-hand side. Near the top you will find one that is titled "Alphabetical List of Discussions (ALOD)." If you first click on that to open the Group, and then click right to open the first Discussion in the Group, i.e. the one whose title starts "Alphabetical List of Discussions (ALOD)," you can then choose to open that Discussion in a new window. From that point on, you will always have one window open on the ALOD page, which constitutes first a Subject Index, and then a list of Discussions. In fact the list of Discussions is not comprehensive, but efforts are made to keep the Subject Index up to date to the extent that any Discussion that contains a fair amount of potentially useful information is indexed.

You will soon locate a Discussion to Reply to. To add a Reply, go to the end of all the Replies in that Discussion (there may be several pages) and then add your Reply.

The other facility which is somewhat useful for locating things is the Search slot at the top right of the screen. The essential thing to know about it is that all the words you put into the slot have an implicit OR between them. Thus if you use a phrase like "Chronic Fatigue Syndrome" the search will find all Discussions, in any Group, that contain any one of those three words. That would appear to be pretty useless, but the search has one saving grace. It puts at the top of the list of hits those that have *all* the words you entered (though not necessarily in the order you entered them).

One current endeavour on the Sarcoidosis site, or more precisely in the Discussion "Monitoring drug-free recovery from acute sarcoidosis," is to find people who have made a drug-free recovery. It seems incredibly hard to find such a person, even though the medical profession say that about 75% of people recover without treatment. If you can find such a person, then please try to encourage them to join the Sarcoidosis site, locate the Discussion "Monitoring drug-free recovery from acute sarcoidosis" and then add the relevant details about their drug-free recovery. Such a report will be met with jubilation, because so far we have only had one such report.

For all **Correspondence** which includes **leaflet requests**, please enclose a large self-addressed envelope together with four separate “large letter” first-class stamps to:

The Secretary, SILA
c/o The Chest Clinic Office
Kings College Hospital
Denmark Hill
London SE5 9RS



Support Meetings are held at King's College Hospital on the first Thursday of each month with the exception of August when there is no meeting. Enquire at the KCH Help Desk for the location of the meeting. Meetings are held between 7 pm and 9 pm. A map with details of how to reach KCH is on SILA's web-site.

SILA West Midlands Branch This branch is run by SILA member Mrs. Carol Bashford, 38 Yew Croft Avenue, Harborne, Birmingham B17 9TR. Contact Carol: 0121 427 5462 or email carol_bashford@hotmail.com for information on future support meetings, help and information.

The Irish Sarcoidosis Support Group ISARC is at www.isarc.ie email info@sarc.ie Mary Walters is Chair of ISARC, telephone number 1903 87216. The Marian Geraghty Sarcoidosis Trust Fund 10k Run/Walk is an annual event.

Information received: Travel Insurance For People Living With Pre-Existing Medical Conditions

Freedom Insurance Services Ltd.,
Richmond House
16-20 Regent Street,
Cambridge CB2 1DB

Telephone 0870 774 3760/01223 454 290 Monday to Friday 8.30 am - 5.30pm
Saturday 9.00 am - 12 noon. FAX 01233 720 277

www.freedominsure.co.uk email: information@freedominsure.co.uk

Electronic version of the SILA newsletter: The SILA newsletter is placed on the Social Network site (<http://sarcoidosis.ning.com>), in Word format — in the Topic in Main Forum titled *Publication of the SILA Newsletter* — before being sent out as hardcopy. To access this, you need to join the Social Network. But at about the same time, an easily accessed pdf copy will be put on the SILA website (along with other backnumbers). This may reduce paper use, since some people are perfectly happy with an electronic version; please let me, Heather Walker, know if you do not wish to receive the hardcopy version.

Our web address. A SILA member drew our attention to the fact that the old SILA web address, www.sarcoidosis.org.uk – which is no longer owned by SILA – is now pushing a variety of products which have nothing to do with SILA. In fact the address is offered for sale, but we don't want to buy it back. Instead we have tried to contact all websites linking to our old address. Please let us know if you find any we have missed. SILA's sole web site is now www.sila.org.uk, and is paid for and managed for SILA by Henry Shelford.

Annual Subscription to SILA is still £12 per annum. SILA welcomes comments and contributions to the SILA newsletter; also fundraising ideas or initiatives.

Our website can be found at www.sila.org.uk; the email address is heather@sil.org.uk

