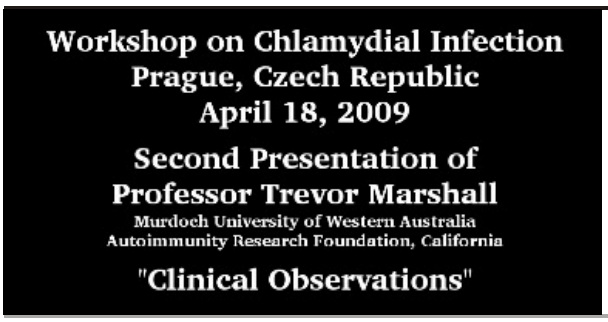


The Marshall Protocol in a Clinical Environment: Observations from the Initial Cohort

PRESENTED BY PROF TREVOR MARSHALL
Director, Autoimmunity Research Foundation

Prague, Czech Republic, Workshop on Chlamydial Infection, April 18, 2009.
Transcript of http://vimeo.com/4293599 video.

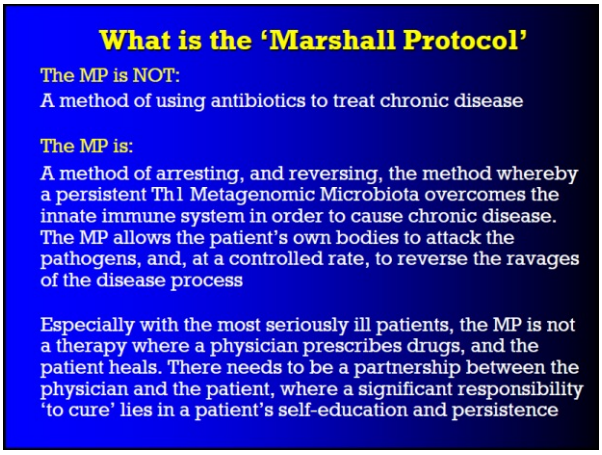
Transcript

Dr. Radek Klubal: I would like to welcome back Dr. Marshall. He is mostly known according to Marshall Protocol, a curative medical treatment for chronic inflammatory disease, based on the Marshall Pathogenesis. And he promised to comment [on] the situation and to say his real view of the problem. So please, you can start.

Slide #1

Thank you very much. I'm going to quickly run through the Marshall Protocol. It is just an overview. What I first want to point out is something that was said by the FDA, the U.S. Food and Drug Administration Commissioner, when he was talking to the U.S. Congress in 2006. And he said that new scientific discoveries are generating an emerging science of safety. This new science combines an understanding of disease and its origins at the molecular level (including adverse events) with new methods of signal detection, data mining, and analysis.

In other words, what the FDA Commissioner has been pushing towards is an understanding of the disease and the exact way the drugs work. That is really what we have been doing with the Marshall Protocol.



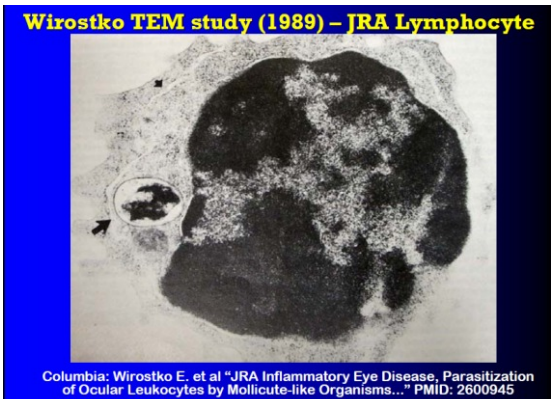
Slide #2

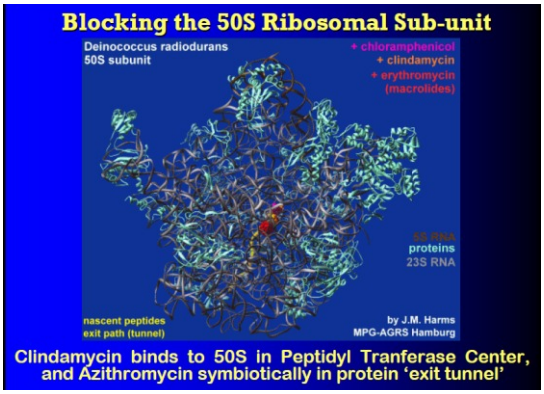
So, I will start off by saying what the Marshall Protocol is not. Firstly, it is not a method of using antibiotics to treat disease. That is first and foremost.

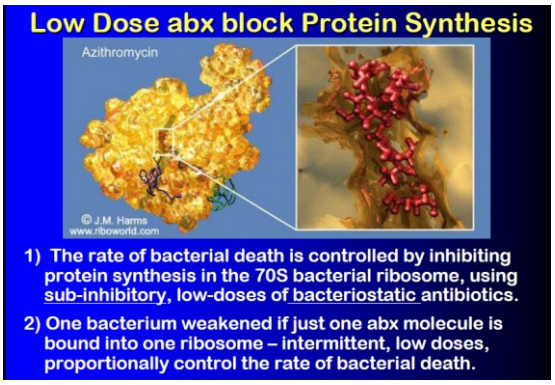
The MP is a method of arresting and reversing the method whereby the persistent Th1 Metagenomic Microbiota, in other words the biofilm of bugs, overcomes the innate immune system in order to cause the chronic disease.

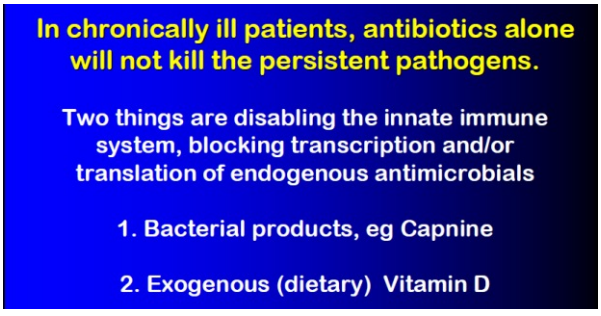
The MP allows the patient's own bodies to attack the pathogens and at a controlled rate, to reverse the ravages of the disease process.

Especially with the most seriously ill patients, the MP is not a therapy where a physician can prescribe drugs and the patient will heal. There needs to be a partnership between the physician and the patient, where a significant responsibility towards cure lies in a patient's own self education, understanding what is happening in their bodies as they heal. And persistence, it is tough.









Slide #3

Now the documents describing the actual protocol are available online here at this URL. And this presentation is going to be very quick and concentrate on those aspects of recovery which will be most helpful to physicians who are seeking to understand the six stages of disease and recovery.

And you can find those six stages in graphical form at that URL [http://AutoimmunityResearch.org/Phase1.pdf]. As I said, a copy of these slides is available if you give us your email address afterwards.

Slide #4

Again, this is a picture of the cytoplasmic inclusions and these are some longer type of bacterial inclusions as well, inside the cell.

Slide #5

OK. so we all know that antibiotics work really well. This is a picture from the Max Planck Institute. And it shows part of the bacterial ribosome which turns RNA into proteins.

And you have various antibiotics, the clindamycin, macrolides, etc, and they sit in there and they stop proteins being made.

Slide #6

And here are some other pictures.

We know that the rate of bacterial death is controlled by inhibiting protein synthesis in the bacterial ribosome. We have to use sub-inhibitory (that is very low) doses of bacteriostatic antibiotics in order to address the bio-films.

One bacterium is weakened if just one antibiotic molecule is bound into one ribosome. So intermittent, low doses, proportionately control the rate of bacterial death.

So we know all that, right? We have read it. Well, it is all wrong.

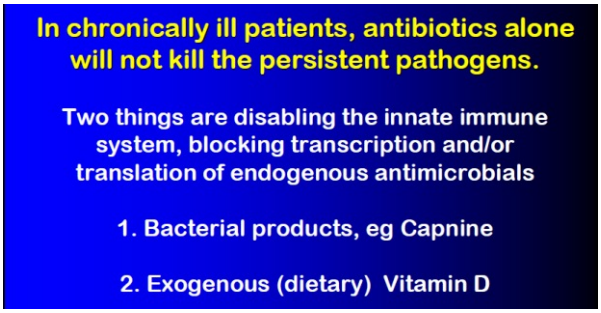
Slide #7

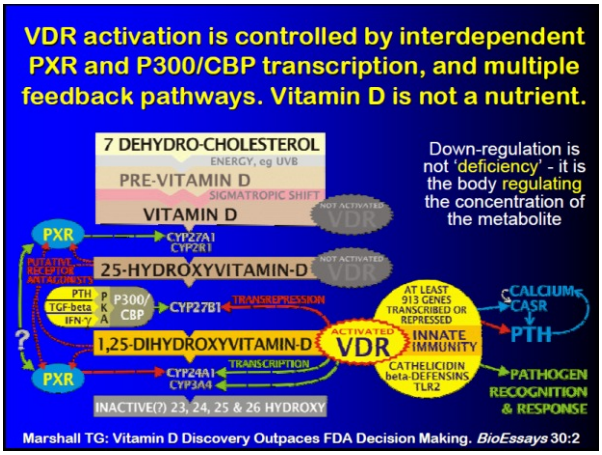
In chronically ill patients, people who are really ill, antibiotics alone will not kill the persistent pathogens.

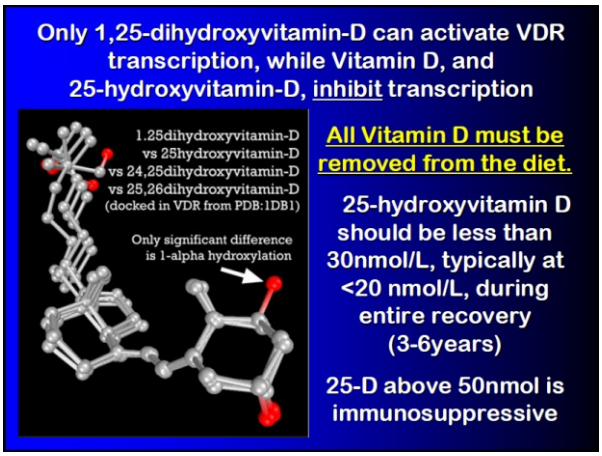
If you get the disease early enough, then the patients will respond to the antibiotic reasonably well. But as the bacteria slowly overcome the patient's immune system and shut down the patient's own immune response, you get to the point where the antibiotics just do not work anymore in vivo.

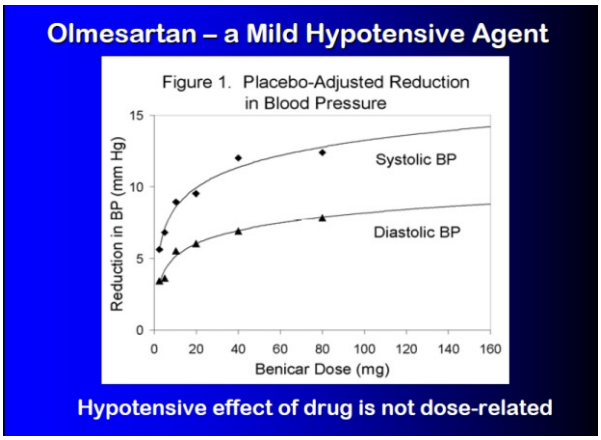
Remember that most antibiotics are actually tested outside the body, in the lab. When they are operating inside the body, it is a totally different environment.

All three major antibiotics that we use, well actually, minocycline and clindamycin and an antibiotic targeted against Tuberculosis — rifampin, they are all part of the VDR metabolism graph that I









showed you earlier on today. They are agonists to the PXR, they behave differently in vivo.

Two things are disabling the innate immune system. One is the bacteria themselves. The bacteria are, in a number of different ways, overcoming the innate immune system and slowly shutting it down, thus allowing the bacteria to persist within the phagocytes.

And then the other thing is exogenous Vitamin D. Because all we are doing when we give Vitamin D supplements to a patient is actually making it easier for the bacteria to shut down the innate immune system.

Slide #8

This graph I showed in my first presentation. I won't go over it again.

To point out, here is the PXR making the key enzymes CYP27A1 and here another key enzyme CYP24A1, CYP24A1 and CYP3A4, actually. And the PXR nuclear receptor is targeted by rifampin, minocycline and clindamycin. So they have effects beyond the effects that they have in the Petri dish.

Slide #9

So the first thing about the Marshall Protocol is in order for the innate immune system to be given its best chance at restarting, all Vitamin D must be removed from the diet.

The 25-hydroxyvitamin D, which is what you will measure in the blood when your Vitamin D that you get back from labs, should be less than about 30nanamolar per liter (nmol/L), about 30nmol/L, typically less than 20nmol/L during the entire period of recovery, which in most chronically ill patients is typically 3 to 6 years.

Now if the 25-hydroxyvitamin D gets above 50nmol/L it is immunosuppressive and it will be very, very difficult indeed for the immune system to restart.

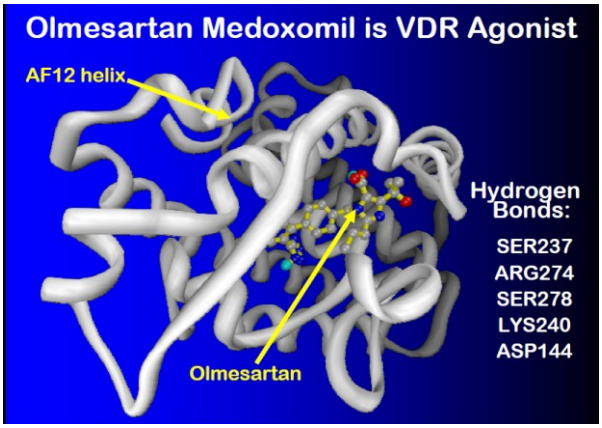
Slide #10

Well, we can use a drug to help the VDR restart. It is a drug called Olmesartan, which was developed for high blood pressure. It is a mild hypertensive agent.

Here you can see the amount of blood pressure reduction in healthy patients. It is not very much, about 12mm of mercury and occurs at very, very low doses of Benicar.

The blood pressure effect is not really dose-related. Blood pressure drops very rapidly and then stays essentially constant as the dosage increase(s).

This is typical of the behavior of a receptor antagonist.



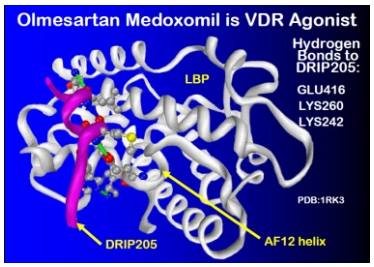
Slide #11

But this particular drug is what is called an agonist, or it switches on the VDR (the Vitamin D Receptor) which is at the heart of the immune system.

So when Olmesartan is put inside the VDR it switches it on. It forms hydrogen bonds with the same amino acids, essentially, as 1,25-Dihydroxyvitamin D, the body's own hormone for switching on the VDR.

But what Olmesartan does not do, is it does not go into thyroid receptors and ruin them. It does not go into the glucocorticoid and mineralcorticoid receptors and mess up the adrenal axis. And if you try and give Vitamin D to people, that is what happens.

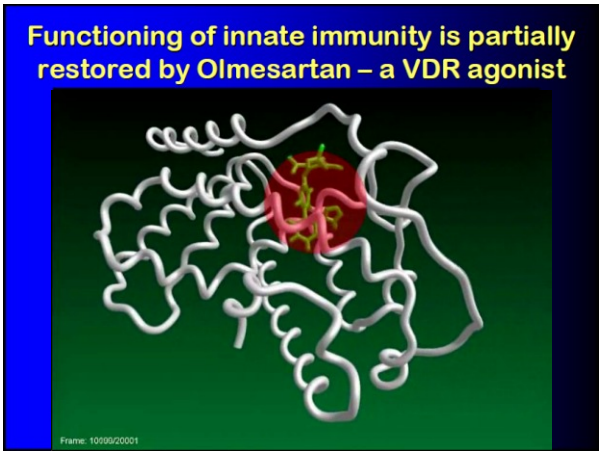
So it is a different way of turning on the Vitamin D receptor and it avoids the flow-on effects to the other nuclear receptors that the Vitamin D metabolites have.



Slide #12

This is another image of how the VDR works.

I am going to skip this one because we are short on time.

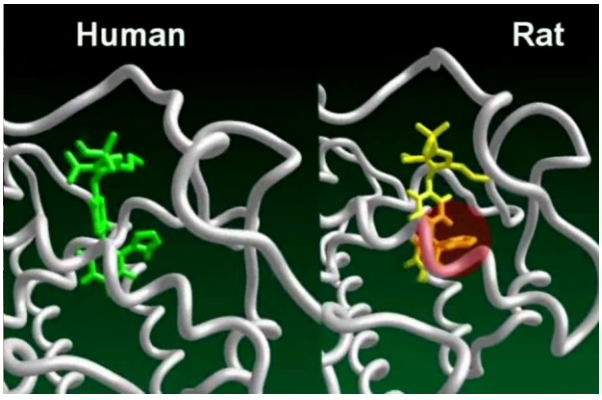


Slide #13

And if you remember, this is the picture we show the emulation of the behavior of the human Vitamin D Receptor with Olmesartan sitting stably in the binding pocket and keeping the helices in the correct location — keeping the molecule in the correct shape so it can transcribe the genes that the VDR has to transcribe, including the body's immune defenses: cathelicidin, beta-defensins, and TLR2.

Slide #14

Here we have the rat VDR. It looks essentially the same but there are some very significant differences.

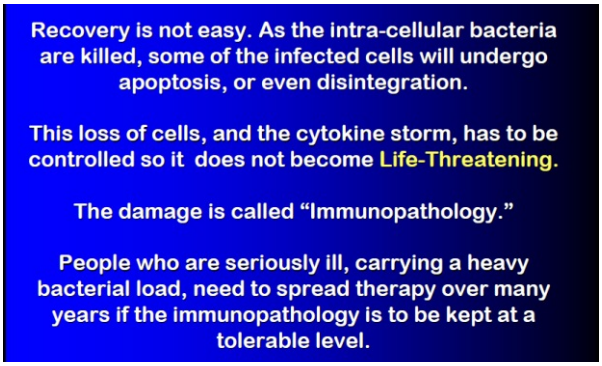


This particular element, the tetrazole, is just not behaving properly.

You can see it sits in a totally different orientation from where it is in *Homo Sapiens*.

It is also wandering around quite a lot. The forces are very weak on it. That is because the receptors are different.

A rat is different from a human being.



Slide #15

So, once we switched on the immune system, of course, then everything is plain sailing from that point, right? You have got your immune system working again — well there is a problem.

When the immune system kicks back in and it recognizes the bacteria, the persistent bacteria, which are in the body and which are causing the problem, then it goes after those bacteria and you get an effect called immunopathology.

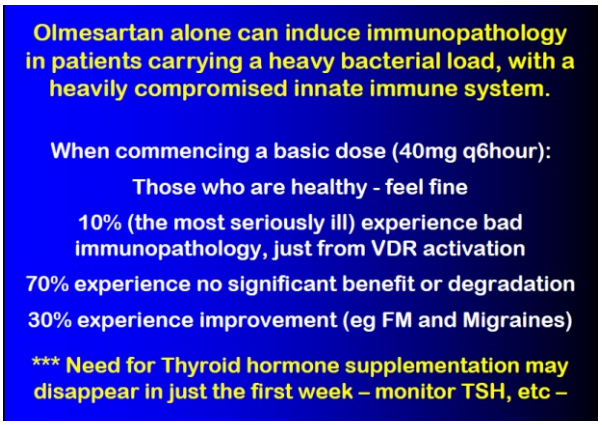
The immune system, as it attacks the intracellular bacteria, then some of the cells that those bacteria are in will undergo apoptosis and some will disintegrate.

In other words, you will loose cells. The loss of cells and the resulting cytokine storm has to be controlled or otherwise it can be life threatening.

The damage is called immunopathology and it means the damage to other parts of the body caused when the immune system is actually doing its job.

People who are seriously ill and carrying a heavy bacterial load need to spread the therapy over many years if the immunopathology is to be kept at a tolerable level.

The symptoms of immunopathology are very similar to the disease symptoms themselves.



Slide #16

Now, Olmesartan alone can induce immunopathology in patients carrying a heavy bacterial load, with a heavily compromised innate immune system.

When you commence the basic dose of the Olmesartan, which is 40mg every 6 hours for recovery from immune disease, then those people who are healthy feel fine. The drug does nothing if the immune system is already working. Then helping the immune system work a little better does not make any difference.

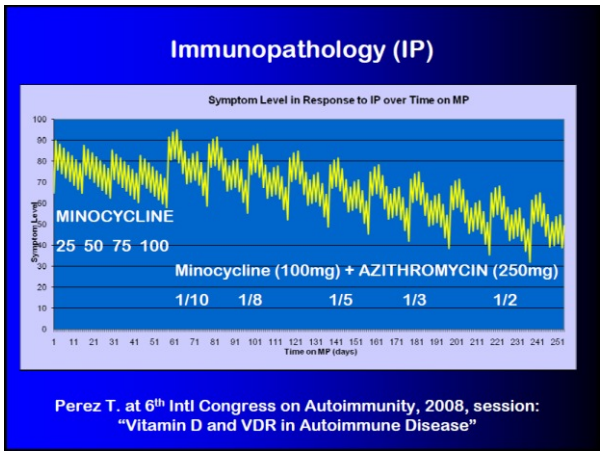
In healthy people it has no effect. The blood pressure is a little depressed a little bit, as we saw in the other graph.

About 10 percent of the patients, the most seriously ill, experience very bad immunopathology just from their VDR activation.

About 70 percent really have no significant benefit or degradation at that point and about 30 percent experience improvement. Especially from fibromyalgia and spinal pain and migraines.

But a physician must be very, very careful. When you get the VDR back in control, the effects on the adrenal axis and the thyroid axis will disappear. And we have found that, in some patients, the need for thyroid hormone supplementation can disappear in just the first week, and certainly within the first few months. So if people are on thyroid medications you need to be very, very, careful and monitor the TSH and other parameters very, very carefully.

There are very profound changes that are going on when the VDR is working again.



Slide #17

This is the graph that we gave at the Autoimmunity Congress in Portugal, and it is basically showing the symptom level or basically the amount of discomfort as a function of time from one day to 250 days on the MP.

Because the immune system in most patients will not actively attack the pathogens, and that is 70 percent of cases. In those cases people use the antibiotics to help the immune system recognize the pathogens, to weaken the pathogens a little, and to get things going.

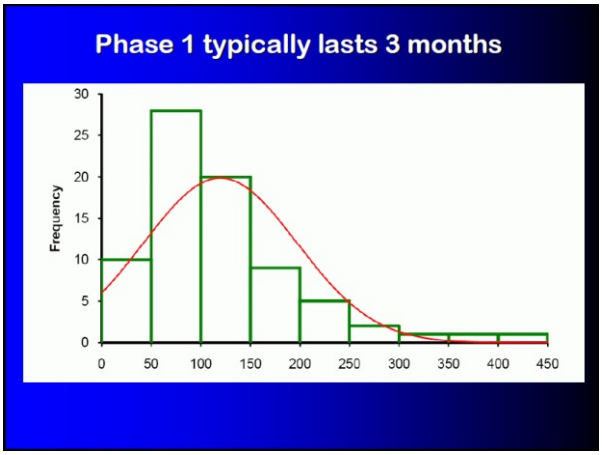
We start off with minocycline initially at a dose of 25mg every 48 hours, increasing to 100mg every 48 hours. Then when the patients have got comfortable with that level, they add a second antibiotic (which is usually azithromycin and this starts at 1/10th of a 250mg tablet).

One tenth of a 250mg tablet.

This is very difficult for physicians. Physicians are used to giving four or five 250mg tablets to handle simple disease. But if you give that to a patient who is taking Benicar, and who has the chronic inflammatory disease, you will find him in the cardiac ward very quickly. You have got to be very, very careful with the antibiotics. You start them at a tenth of a tablet, then gradually work up over a period of about a year to around a half of a tablet every 10 days.

Every ten days. And that is the maximum rate.

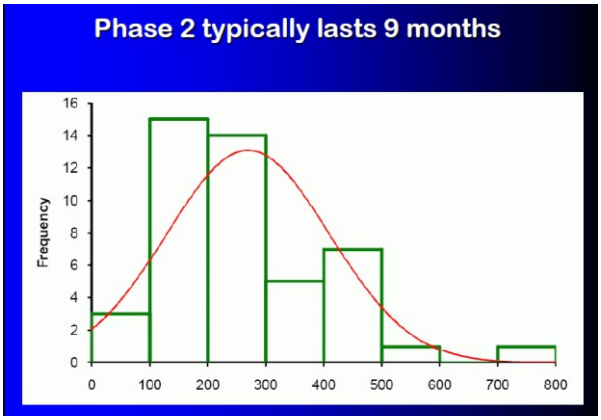
So you can see that you have the symptoms fluctuate on a 48 hour basis. Then when you increase the dosing, the symptoms increase again. And here the symptoms really jump up when you add the tiny fraction of azithromycin and then over that 10 day cycle, you see the 10 days cycles of the azithromycin, the 48 hour cycles from the minocycline superimposed. For more details you can go to the video of this session which is online.

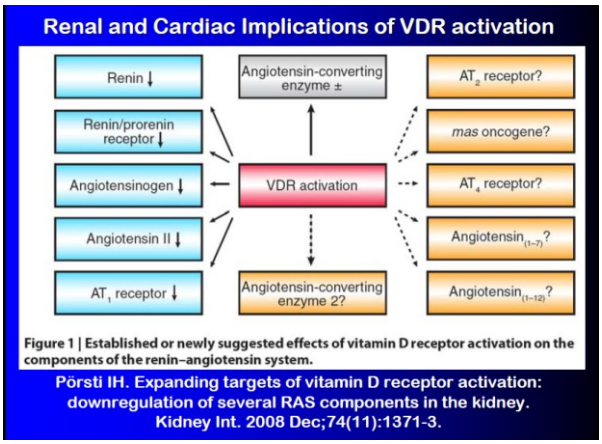


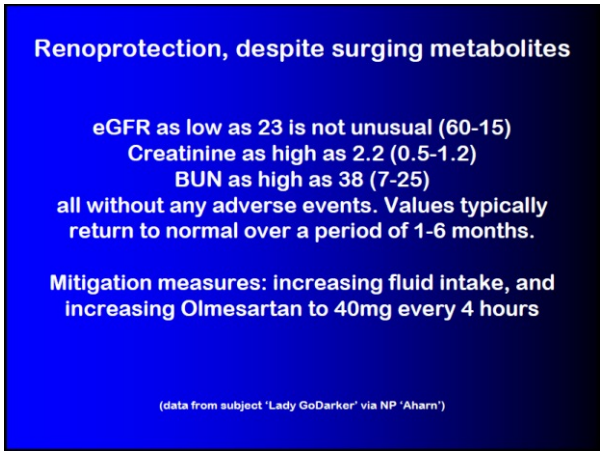
Slide #18

Phase 1, which is minocycline alone [with olmesartan], typically lasts about three months. Here we have periods ranging from 0 days to 450 days with the average being somewhere around 120 and the most frequent period around 90 days — about three months.

So people can build up their dosage from 25 to 50, to 75, to 100mg over about three months. And by that time the patient has got fairly familiar with dealing with their immunopathology.







Slide #19

Phase 2, two antibiotics, typically lasts about nine months.

And here we have data from our initial cohort, or a sampling from our initial cohort, ranging from 0 days to around 800 days.

You can see most people are clumped around the 200 day-mark, about nine months.

Slide #20

When you activate the VDR, it has profound effects on the kidneys and cardiac function of the individual. That is because the VDR activation turns on the renin subsystem, the VDR actually transcribes (actually transrepresses) renin.

It also transcribes the angiotensin and down-regulates and up-regulates the angiotensin converting enzyme, the ACE that I had spotted up on my earlier graph.

It also changes AT1, AT2 receptor.

The physician should look at this paper: "Expanding targets of Vitamin D receptor activation: down-regulation of several RAS components in the kidney." Renin is down-regulated.

Typically, what we see is that, at some point during the recovery, everybody will suffer from very low glomerular filtration rates (GFRs) and usually fairly high creatinine. Because just about everybody has gastrointestinal involvement and some form of renal (kidney) involvement.

Slide #21

The Olmesartan gives protection of the kidneys despite the surge in metabolites.

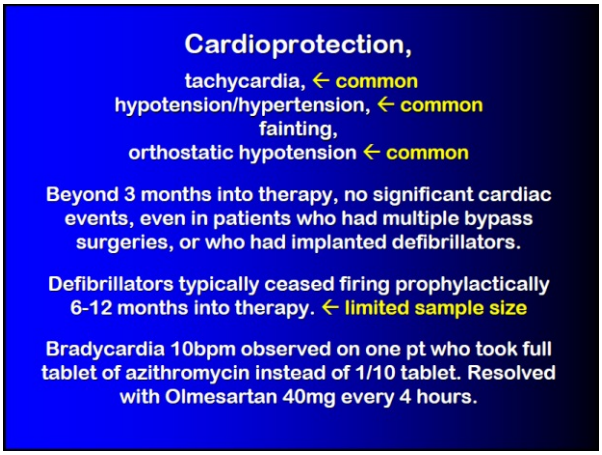
We see GFRs as low as 23 is not unusual (normal GFR is around 60). Creatinine as high as around 2.2 (normal max. 1.2). And a Blood Urea Nitrogen as high as 38 (typically 7-25) and all of those without any adverse events.

The blood work values typically return to normal over a period of about 1-6 months. The mitigation measures are increasing the fluid intake and increasing the olmesartan to 40mg every 4 hours. I stress that — increase.

The olmesartan protects the kidneys.

Yes, giving the patient the olmesartan is going to activate the VDR which causes the GFR to drop. But if you cut the olmesartan back, you are leaving the immune system activated, with nothing to protect the kidneys from the cytokine storm.

You increase the olmesartan.



Slide #22

Cardio-protection: Well, we typically see immunopathology. Tachycardia (fast heartbeat) is very common. Either increased or decreased blood pressure is very common. Not very often see fainting, but orthostatic hypotension, which means fainting when somebody crouches down for a minute or two and then stands up, as they will momentarily loose, become faint is the best way to say it, maybe loose their balance. Orthostatic hypotension is very, very common as people recover.

Beyond three months into therapy we do not really see very many significant cardiac events, except when they take too much azithromycin at the start of Phase 2.

But even in patients who have had multiple bypass surgeries, who have had implanted defibrillators, most of those [cardiac events] disappear after three months.

Defibrillators: Even though it was a limited sample size (just a few patients), defibrillators typically cease firing after about six to twelve months into the therapy, which is a nice objective measure for the cardiologist to put his arm around and say, hey, I understand that.

Bradycardia, which means very slow heart beat, as low as 10 beats per minute, was observed in one patient who took a full tablet of azithromycin — a full tablet, only 250mg — instead of 1/10th of a tablet. That was resolved with Olmesartan 40mg every 4 hours and waiting a day or two.

Slide #23

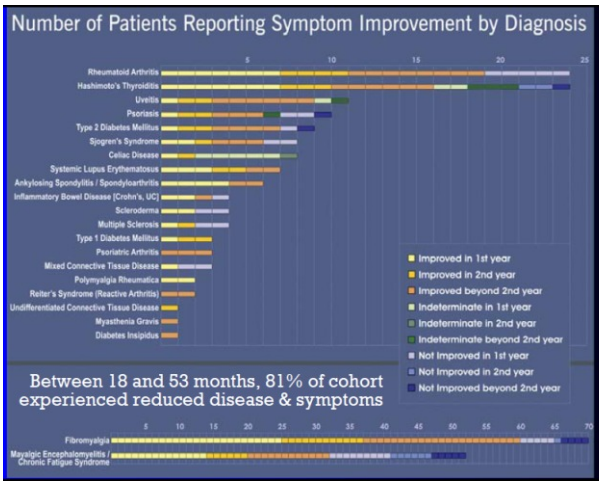
So, for immunopathology, we have seen 10bpm bradycardia, periodontitis, skin eruptions, shortness of breath, suicidal ideation (which is one to keep a close watch on), bipolar disease, obsessive compulsive disorder and even one or two grand mal seizures, caused by immunopathology. People taking too much antibiotic, not being careful, not understanding what they were doing.

Patient education: it is very important for the physician to let the patient know what is happening and to maintain very close contact with the patient.

Now, with our Internet outreach we have tried to take some of that load off the physician's shoulders but we can not do it all.

Chronic pathogens are very nasty indeed, they must be respected. They have to be killed slowly and steadily. And therapy must be guided by an understanding of the disease model.

You have got to understand what you are doing. It is not just good enough to take an antibiotic and see what happens. Once you have activated the innate immune system again, everything happens very quickly.



Slide #24

This is a graph that we gave of a sampling from our cohort. Our currently reporting cohort is around 600. Many of them have been members of the cohort for three or more years. This was a sampling from them with a whole lot of different disease diagnoses. You will be able to read these on the printouts.

Rheumatoid Arthritis, Hashimoto's Thyroiditis, Uveitis, Psoriasis, Type 2 Diabetis, Sjogrens, Celiac, SLE/Lupus, Ankylosing Spondylatis, Inflammatory Bowel Disease (Crohn's), Scleroderma, Multiple Sclerosis… All of these have responded, in time, to the therapy which involves switching on the VDR and letting the body attack the hidden pathogens.

Fibromyalgia is even more effective. We have got 70 patients reporting in this particular group. And Chronic Fatigue Syndrome / Myalgic Encephalomyelitis, there are 52. And in that group, not improved beyond second year, there is probably about ten percent in the CFS and maybe 5 to 10 percent in the Fibro group.

But we find that 81 percent of the cohort who started out experienced reduced disease and symptoms between 18 and 53 months, depending on how sick they were when they started out.

So that is my quick summary of the Marshall Protocol. Thank you.

Questions

Dr. Radek Klubal: Thank you very much. It is very good to open the field. My question is, is there any animal model in that we can see the same effect, because if you have rats, mice with certain genetic predisposition like rheumatic arthritis or something? If you keep them under sterile condition they won't develop the disease and if you keep them under normal conditions they develop the disease. So that would be probably a good model to test how that antibiotics work?

Dr. Marshall: Well, but Professor Bach, who invented the hygiene hypothesis, derived the hygiene hypothesis, I spoke to him quote recently in Portugal. And they found that, in fact, if they injected their NOD mice with some bacterial proteins very close to birth, that they did not develop the Diabetes. So there are a lot of questions about exactly how the NOD mice work at this point. So I do not really want to go into that one.

But look, if I was trying to find an animal model which was similar to humans I would go that animal's genome and I would find out what transcribes cathelicidin, what transcribes beta-defensins, what transcribes TLR2, and start from that point.

Now I do not think you will find them all in one receptor as you do in *Homo sapiens*. I think you will find them spread out over the genome.

Dr. Radek Klubal: Yes. What about the dosage of the medication, because I think every human is elementally different?

Dr. Marshall: Well, there are different types of medication used for medicine, medication... . There is medication which is dose-specific, in other words, in which the effect is dose-specific.

And there are the newer types of medications which are the receptor blockers and the receptor agonists, which tend to have all-or-nothing and tend to be very, very, safe because there is no extra advantage as you increase the dose.

That is what I showed in my second slide. The effect is *not* dose dependent. And, in fact, there was a case in Turkey where a patient tried to commit suicide by taking a whole month's supply of Valsartan (which is somewhat similar to this drug) and it made no difference at all. They were not even sick.

These new class of drugs, the receptor blockers, are very safe. They are *not* dose dependent. *Their effects are not dose dependent*.

We have identified three effects of Benicar. At very low dose, it affects the angiotensin 2 receptor, at a slightly higher dose, it affects the VDR, and at very high dose it gives palliation and protection due to probably the opioid delta, and maybe some other receptors that we have not fully isolated yet.

But you have got discrete steps of activity in the dosing regime. It is not a continuum. And once somebody has got to taking the Olmesartan once every three or four hours there is no benefit from giving a higher dose than that, they get no benefit. It is just the way that these new class of drugs work. Did I explain that?

Dr. Radek Klubal: Is there any race difference. Like black people, white people?

Dr. Marshall: We have not seen any. We have a pretty diverse group from all over the world, actually, and we have not seen any real differences. It is basically the same.

Dr. Radek Klubal: Thank you.

Questioner (Czech MP-doctor): I have just a question to the pulsed dosing of the antibiotics, because one of my friends who was before treated by azithromycin, he took 500mg three times per week or maybe even more. He took, by mistake, 250mg in the beginning of Phase 2 and he got really terrible symptoms. If you could explain us in more detail why this happens.

Dr. Marshall: Well, the reason it happens is because what the Benicar does is turn on the immune system. So when you weaken the bacteria a little bit with the azithromycin or a little bit of minocycline, then the immune system comes in, recognizes the chemical signals from the pathogens and kills them.

You are not trying to directly kill the pathogens with the antibiotics with the Marshall Protocol. *You are just trying to weaken them*. Like I said: one antibiotic molecule lodged in one ribosome disables, *partly disables*, one bacterium.

Questioner (Czech MP-doctor): I forgot to tell that this reaction came at the end of this ten day period.

Dr. Marshall: Azithromycin has got a half life in cells of 45 days. So it stays around an awful long time which is a real problem when people take too much, because they are stuck with too much for a month. We are starting to move now towards using clindamycin instead of azithromycin. Clindamycin is a 48-hour dosing just the same as Minocycline.

But clindamycin goes after the neurological symptoms very quickly.

The problem is that it enhances suicidal ideation, depression, OCD. All of the neurological sequeli are enhanced when you use clindamycin in Phase 2. That is why we have avoided it until recently because in an environment where the physician is not in too close a contact with patient — and we are at great distance because of the Internet — it is very hard to support people that have suicidal ideation.

We had a grand-mal seizure from a patient in Canada who took a 250mg azithromycin at the start of Phase 2. So it is a real problem that the patients become very sensitive to the antibiotics when you turn on the VDR again. It is a real problem.

Questioner (Czech MP-doctor): Thanks for your answer.

Dr. Radek Klubal: What happens after you stop?

Dr. Marshall: Well the problem with stopping, it is a very difficult job to stop. Because when you turn on the immune system it keeps running. Even if you cut the Benicar off, the immune system will keep running for usually for weeks, a couple of weeks. And during that time the body, or the organs, are no longer being protected by the reno-protection, the cardio-protection, and even the eye-protection that is offered by the Benicar. So it is really tough.

You can sometimes use one of the other ARB's to reduce the symptoms and that is what I suggest to some physicians that absolutely have to wean patients off. But it really is problem to get off the Benicar because you need the palliation and the organ protection from the Benicar, at the same time as you may not need quite as much immune activation as you are getting, as much immune stimulation as you are getting.

Dr. Radek Klubal: What happens to your saliva after you are on such a dose of…

Dr. Marshall: We have not done any full genome studies.

Dr. Radek Klubal: Because I would like to see it after one year of such small amounts of antibiotics.

Dr. Marshall: Well, the study with West China Hospital will be doing that. They have got all of the latest sequencing equipment, the pyro equipment. And I am sure they will be keeping a close eye on that. We signed a collaborative deal with West China Hospital back in December and we are just cementing all of the studies now that will be going forward for this year. And they would be doing things very thoroughly because they are a Cochrane Collaboration Unit.

Questioner (Martin78): One of the basic parts of this treatment is avoiding Vitamin D. That is maybe the part of the treatment that most people find most controversial. At least when I am discussing it with others. What do you have to say to researchers that are claiming that taking Vitamin D actually transcribes or increases cathelicidin or other AMP's and that they have studies showing that Vitamin D is good for the immune system.

Dr. Marshall: Well, but they do not have studies showing that. That is the whole point.

There was a Cochrane analysis recently for example, of cancers. Which showed that — no sorry, it was an NIH NCI analysis (National Cancer Institute) — analysis of the benefits claimed for cancer. And they went through all of the studies and they could not find any of the studies where the data supported the conclusion that was being drawn by the clinicians.

The problem is, the data is usually good. It is very difficult when you are given a substance that changes 900 genes — how are you going to measure 900 things in the blood to see what is happening? You can not do that. You can only look at a subset. And so many of these studies did not even look at the subset properly. They did not even look at the active metabolite, the 1,25-Dihydroxyvitamin D that turns on the VDR. They did not look at the VDR transcripts, CYP24 for example, to see if the VDR was working. They were very poorly done.

But even then, if you look at the study results, they do not support the conclusions that were being drawn.

There was one study on cancer — this is covered in detail in the paper that which is in press, right at this moment in the New York Annals, in the Annals of the New York Academy of Sciences — which was written by my colleagues Joyce Waterhouse and Capt. Tom Perez. They went through some of these Vitamin D studies. And what they pointed out was, even the study itself showed that there was a U-shaped curve. That if the patient's Vitamin D was observed low they had a higher risk (Vitamin D along here, risk of cancer along here), they had a higher risk if they had lower Vitamin D. Then it dropped down to about the 25/50 nanomolar region, which I spoke about, and then it increased again as their Vitamin D levels increased because of supplementation.

So if the researchers actually understood what Vitamin D was doing, the data was there telling them what was going on. But they [cancer study researchers] just did not understand what they were doing.

I chaired a session at the International Congress on Autoimmunity in Portugal last September. Some of those presentations are online on Vimeo and you can watch them and find out all about Vitamin-D-related issues. And, as I said, there is a paper which has just been published in Autoimmunity Reviews and that is available online and there is a paper which is in press at the moment at the Annals of New York Academy of Sciences asking and answering that same question: *'how could so many people have made such a big error?'*

Questioner: Dr. Marshall mentioned that it should be a long time, even a life-long treatment, so what about that long time that was mentioned?

Dr. Marshall: Well, "life long", I mean it has been a lifetime building up to this point. You are born with the microbiota, you are born with one. It usually does not give you disease until you reach middle age or, hopefully, old age. But you are born with a microbiota. So, you have been working up to this stage for quite a long time.

Many patients are triggered, “pushed over the edge,” if you like, by an acute infection. In many diseases this happens. In MS it is reported, certainly in CFS it is reported very commonly. So, it has been a lifetime getting here but it does not take a lifetime to get out of there.

Recovery times vary by the patients, and the ones that we have contact with on the Internet, those that we are observing, are probably the sickest of the patients that are out there. Absolutely desperate by the time they try something as 'weird' as the Marshall Protocol.

So, we find that typically after about 18 months the patients see the light at the end of the tunnel. They can sense that they are improving a little bit. We get them to write down logs, frequent logs. There are some forms which they can download and that allows them to keep track of what it used to be like so they can look back in 12 months and say, "well, yes, this has improved," you know. About 18 months they see improvement.

They are going to be photosensitive for about two to three years, gradually getting less photosensitive as the time goes by. And then once they get to about the two to three year mark, they are able to start integrating again with their community, with their family, with jobs, that sort of thing. So, that is the time frame.

Now, the problem is that we have a total time of observation of only about six and a half years, at this point, from when we started. So I can not extrapolate beyond six and a half years. But we have a lot of people who have gotten to the four or five year mark that are back at work, studying again.

One of my colleagues that has presented at Portugal and that is presenting at a conference in Beijing next month, was literally confined to bed four years ago. Could not do anything. So it is not a life-long recovery but the problem is that the recovery is continuous. Because people who are ill, never really knew what it was to be not ill, they had some form of disability from quite young. You know, they had their tonsils out when they were five years old, for example. And therefore, it continues to get better, certainly throughout the first six years.

Will it be life long? I doubt it. By the time you get to for or five years you are not taking antibiotics anymore, you just take the Benicar, it is all that is required. And you are not using the Benicar for immune activation, you are using it for palliation at that point.

Questioner: This treatment with Benicar, will this also cover viral problems?

Dr. Marshall: We have seen viruses disappear because when the immune system is activated again it will go after all the body's pathogens. It will go after funguses, after viruses, and of course the bacteria. You are not weakening the viruses in the same way as you are weakening the bacteria with the antibiotics. But we have had viruses disappear; disappear as the patients recover. And even simple things like warts disappear, for example, as people recover. That is routine.

Questioner: ...Antivirals?

Dr. Marshall: Oh no. You want to stay away from the antivirals. The problem with the antivirals is they profoundly effect the human enzyme system. They are a classic case of something that has worked well in the lab, in the Petri dish, but which does not work inside the body. They are also a classic case of the drug which is very dose-dependent in terms of its side effects.

The antivirals we tell people just to stay away from. In many cases, people feel better after they have taken the antivirals. And that is primarily because it upsets all of the enzymes that are on my chart there of the Vitamin D Metabolism: CYP3's, CYP2's. They are all knocked out by the antivirals. So it gives a palliation effect short-term, but long-term, all it is doing is knocking out the immune system.

Dr. Radek Klubal: Thank you very much.