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Re: OSR Information

Subject: Re: OSR Information
From: "andrewhallcutler" <AndyCutler>
Date: Wed, 28 Apr 2010 18:21:38 -0000
Yahoo! Message Number: 279813
Onibasu Link: http://onibasu.com/archives/am/279813.html

Someone kindly pointed out that I didn't read this carefully enough when I made my prior reply. I replied as if it was from Dr. Woeller, this actually is Dr. Haley's response.

> For those of you interested in Dr. Haley's response regarding OSR and its1/2 life. I did receive an email back from Dr. Haley. Here was his response:
>
> *"OSR has a plasma and organ half-life of 6 to 7 hours in test animals (rats).

In a dozen of them, in one experiment, by one investigator who hasn't published the results.

This really is not good enough information to assert a half life in humans.There should be both replication of the rat studies by other investigators, publication of all studies or at least presentation in a form similarly detailed to what one would use in publication, and at least some measurements in actual human beings, e. g. blood concentrations at 2 and 8 hours after oral ingestion in a dozen people.

> It peaks at 2 hours after ingestion in the plasma and all organs we tested(brain, kidney, liver, intestines, bone marrow, epidermal and internal fattissues). At 24 hours after ingestion the plasma and organ levels are downto 4-12% of the peak values at 2 hours.

Simply repeating information provided earlier does not advance the argument. Generally what Dr. Haley is doing here is to avoid the progressive flow of thought that constitutes argument in favor of just repeating informationalready shown to be flawed.

For progress in understanding to be made, those arguing really need to be ethical and respond to each other's reasoning point by point, moving the argument forward until they can reach some points of agreement rather than just continually reiterating the same point so as to avoid the possiblity of conceding anything.

> I have taken OSR three times daily for over a year, early morning, noon and evening based on the 6-7 hour plasma half life. My health analysis is excellent, I have no build up of OSR, no loss of essential minerals (we checked this out long ago), and I feel quite healthy. I have been taking OSR 3 ½ years. My blood glutathione is 1580 whereas the average is 669, so I amin good shape with regards to this oxidative stress marker----and I had nosigns of any other oxidative stress markers at my last physical.

I admire Dr. Haley's fortitude in choosing to be the first human test subject. However there is a long history of horrible catastrophes due to release of drugs where the investigators used themselves as test subjects rather than relying on a large enough group selected to represent the population who actually would use the stuff. E. g. thalidomide, heroin.

Information on a couple of dozen more human subjects, including measurementof OSR blood levels for kinetics, would be very much more convincing.

Also a technical note: OSR is the type of compound that will be an interference in most assays for glutathione. I'd like to know the details of the assay and how they are sure the result truly represents

glutathione, rather than (glutathione + OSR).

> This information has been on our website for quite a long time. I think the comments of Dr. Cutler are quite old and keep being brought up by those that may not want OSR to be used."

This is a nice rhetorical device. Dr. Haley admits the information he is presenting is old (saying it has been on their website for quite a long time)then accuses me of using "old information," as if that was relevant.

It doesn't matter if the information is old or new, accuracy is what counts. I presented accurate information that I believe shows it is not ethical to sell or prescribe or dispense OSR for many reasons, Dr. Haley has not rebutted or even addressed any of it. Dr. Haley in his prior communication stated he had no special expertise regarding chelation (and made it clear that was true). Take it from someone who DOES have special expertise regarding chelation, there is not enough information to have any reasonable likelihood of understanding how to use OSR safely. In my opinion it is not ethical to sell it, prescribe it, dispense it, or encourage people to use it outside the context of a situation where they understand they are taking essentially the same risks as someone in a phase 1 or 2 clinical trial of an experimental new drug.

I understand that ethics involves personal values and opinions may differ on this, but I find it truly shocking they differ so profoundly in this case. But then I also find it truly shocking that most physicians continue to administer mercury laden vaccines to infants even today (e. g. the H1N1 flushot, which the health departments made a special exception for even in states like Washington that legally prohibit the use of mercury preserved vaccines in children).

Obviously, reasoning is not working in conveying my legitimate (and correct) technical concerns to Dr. Haley and DAN! doctors - they aren't taking anyactions to address these concerns, or to control risks from the unknown factors that motivate these concerns. If anyone else has a better idea of how to convince them, please go for it!

Andy

www.noamalgam.com

www.noamalgam.com/hairtestbook.html

www.noamalgam.com/nourishinghope.html

www.noamalgam.com/biologicaltreatments.html

PS, the original interaction between Dr. Haley and myself is reproduced below for your reference.

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A message purported to be Boyd Haley's response to me is circulating on theinternet. I believe it is appropriate for me to respond to it with some further useful information. I have cut my responses into this message, and also appended the message in full at the end of the `discussion' so there can be no question I have not taken it out of context in any way. It is of course possible, given the joys of digital communications, that this messagehas been forwarded many times and may have been modified so that it does not accurately convey Dr. Haley's views, or may not have been intended as anything other than a private message to a single specific recipient (and maythus have been imprecise and not well wordsmithed for completely reasonable reasons). However all I can do is respond to it as is and if there have been any modifications or statements not accurately conveying Dr. Haley's thoughts I hope he will feel free to correct those. I'll be forwarding him a courtesy copy of this privately, and to Dr. Flatabø if I can find a valid email address for him, as well as circulating it publicly.

Anyone who wishes may forward this or repost it provided that the entire message, without any modification is posted and any additional commentary is clearly identified as such and ONLY appears at the beginning of the message.

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Dr. Haley's original message (preceded by > >) with my comments
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> --- In Autism-Biomedical-Europe@yahoogroups.com, Geir Flatabø <geirf> wrote:
>
> Boyd Haleys Response to Andy Cutlers "message"
>
> Geir Flatabø
>
>
> > First, the only claim made for OSR is that it is a lipid soluble,
> > dietary antioxidant that scavenges free radicals and helps
> > maintain a healthy glutathione level.

The response claims that OSR is `an antioxidant.' This is true. So is lipoic acid. So is DMSA. Like lipoic acid and DMSA, OSR is also a chelator, and in fact was held out as one repeatedly before commercial sale of OSR asa nutritional supplement brought the need for FDA compliance into the picture. Free speech is actually quite limited under US law ? for example, Boyd Haley is not legally able to discuss much true information about OSR. Were he to discuss its chelating properties now that it is on the market hemight no longer be able to sell it. This may account for the pretense that it is not a chelator and is not being used as a chelator by most who prescribe or take it.

I understand that Dr. Haley sells OSR as an antioxidant and only intends itto be used to promote normal health. The companies that sell Alpha LipoicAcid as nutritional supplements also sell it as an antioxidant, to supportoptimal health, and seem blithely unaware of the fact it is a chelator. Regardless of verbal statements, intent, or legal theories, OSR is a chemical, just like alpha lipoic acid. What it does is governed by the laws of nature. Since it is a chelator it must be taken on a proper chelation schedule or not at all. It is never prescribed properly in this manner and there was no information available until Dr. Boyd Haley's public disclosure of work in the message I'm responding to from which kinetics can be derived that could even be used to figure out how to do that.

The argument that OSR is an antioxidant and therefore safe when prescribed negligently (ignoring the need to prescribe it on a proper chelation schedule) is similar to the argument that thimerosal doesn't cause autism becauseit is being used as a preservative in vaccines, not as a poison, or that mercury in dental amalgam fillings doesn't cause disease because it is `locked up' in the amalgam. All chemicals do whatever they are going to do whenpeople take them, as dictated by the laws of nature. They do not only do what the doctor intended them to do. If the doctor didn't understand some of the laws of nature that govern what that particular chemical does insidethe patient, the chemical doesn't magically NOT do whatever it is the doctor doesn't know about. OSR is a chelator. It is not safe simply because itis called an antioxidant.

> > Maintaining a healthy glutathione level

Dr. Haley's discussion of glutathione and its role is also fairly misleading, but I don't have the time to provide a primer on glutathione physiology so I'll simply point out that the worst measured blood glutathione levels seen in autistic children are only about 30% below the normal range. Since the glutathione transferase enzymes have kinetics that are no more than first order in glutathione concentration, this means they at worst only excretetoxins 30% slower than some normal children.

> > can possibly help detox
> > the body of any toxin that is carried out
> > of the body as a glutathione complex,
> > and this includes many heavy metals

The 30% or less subnormal level of glutathoine in autistic children (this is also seen in adults with heavy metal problems) is not enough of a difference to be clinically significant. E. g. people with Gilbert's syndrome have dramatically reduced glutathione conjugation rates from conception but are not born autistic, do not turn autistic any more often than other children, and usually grow up to be normal and healthy without any health problemsother than their doctor being confused about their chronic mild bilirubin elevation after their first blood test.

> > as well as toxic
> > organic molecules that are attached to glutathione
> > by the enzyme glutathione-S-transferase
> > after the oxidation by the Phase II P-450 enzymes.

Dr. Haley also provides a wide ranging discussion of ALA that is unrelated to any of the chemistry of ALA. Since it is wide ranging I will only correct a few points here, and refer those who are interested in a more detaileddiscussion to the review by Biewenga et al.
http://www.ncbi.nlm.nih.gov/pubmed/9378235
Lipoic acid (and its amide) are reduced to the dihydro form ? the dithiolwhich is the chelator ? by an enzyme in the mitochondria which is essential for life. If this conversion does not occur with great rapidity in you(or your child), death occurred a long time ago. You don't have to worry about whether it is happening.

This enzymatic conversion is responsible for the antioxidant properties of ALA. ALA itself, in the disulfide form, is not an antioxidant. DihydroALAis the antioxidant. ALA is like a `pro-drug,' a compound the body metabolizes into its active form.

Alpha lipoic acid greatly increases glutathione levels and reduces oxidative stress.

Alpha lipoic acid is well known to cross cell membranes and the blood-brainbarrier.

ALA greatly increases the excretion of glutathione bound mercury by the liver.

While mercury is excreted in the bile bound to glutathione, binding it to glutathione does not remove it from cells generally. Increasing glutathione levels dramtically for long periods of time does not clear any mercury atall from the brain.

> I know of Andy Cutler

We have unfortunately not had the opportunity to meet in person.

> and have read his book and I
> agree that he has proposed a detox scheme
> involving LPA (lipoic acid) that I have found quite
> reasonable as I am also not a fan of using toxic chelators.

Then I don't understand why OSR is on the market. It is a synthetic chelator like DMPS and DMSA, but unlike them has an aromatic ring and is thus almost guaranteed to be toxic to people with chemical sensitivity. Heavy metals induce chemical sensitivity in many people. Laboratory rats don't have it and normal healthy volunteers don't have it ? but a lot of autistic children and adults with heavy metal problems do.

> However, this detox scheme has not effectively reversed
> the oxidative stress (as measured by low reduced glutathione
> levels) in many who have tried it, or so I am told.

It is hard to take the "or so I am told" phrase with a straight face. Hopefully this is just poor choice of words, rather than Dr. Haley actually relying entirely on unsubstantiated gossip to decide which chemicals to give to living people in hopes of helping them.

Dr. Haley claims he has been told ALA detox does not reverse oxidative stress. I challenge him to provide any data supporting this (since there is none I know of and I have sought relevant information quite vigorously). WhatI have often found with statements like this is that people who did other random protocols (e. g. the DAN! protocol, or took ALA daily for a while, or chelated with DMSA for 3 months then gave up when progress stalled as expected and as described in figure 15 of my book Amalgam Illness: Diagnosis and Treatment) claim they did `my protocol' and it `didn't work.' It takes careful questioning to figure out what they really did. Sometimes they are just "Dr. X said Dr. Y told him that he heard a seminar where Dr. Z stated ..."

The entire following section which I have marked with a "+" sign before the> > is incorrect and unrelated to reality. See the paper cited above for accurate information.

+ > > This may be due to the fact that LPA (has a
+ > > disulfide linkage and already in the oxidized
+ > > form and unable to bind any metal in its delivered
+ > > form) can add to the oxidized stress level as

The following snippet is correct but quite misleading, see above for usefulcontext.

> LPA (lipoic acid) has to be reduced to the
> dihydrolipoic acid (dihydro-LPA) form before
> it can bind to any metal. This reduction
> of LPA to dihydro-LPA requires reducing
> potential

And this further information is also wrong.

+ > > and reduces the body's ability to
+ > > produce reduced glutathione

This is well known to be incorrect. Taking lipoic acid greatly increases the level of reduced glutathione by exporting reducing equivalents from the mitochondria, where they are not available to the enzyme that regenerates reduced glutathione from oxidized glutathione, to the cytosol where they are. Also some direct reduction of oxidized glutathione to reduced glutathione occurs by dihydrolipoic acid reacting and turning back into lipoic acid.

> since both the reduction of oxidized LPA and
> oxidized Glutathione (GSSG) are
> biochemical steps that consume reducing
> equivalents in the form of the basic
> molecule(s) NAD(P)H.

The reduction of ALA (or what Dr. Haley calls LPA) occurs in the mitochondria, where reducing equivalents are plentiful and can not be used up.

The reduction of oxidized glutathione occurs outside the mitochondria wherereducing equivalents are limited.

The diffusion of dihydrolipoic acid ? the reduction product of lipoic acid ? from inside the mitochondria to outside greatly increases the reducing equivalents available to reduce oxidized glutathione and greatly elevatesthe levels of reduced glutathione.

> Using a beginning oxidized molecule to treat
> patients who are already under oxidative stress
> is not the best approach in my opinion.

I can highly reccomend Devlin's Textbook of Biochemistry with Clinical Correlations (Wiley) for adequately detailed information on where the oxidizingand reducing equivalents in cells come from and how reducing equivalents are handled.

With somewhat more accurate information Dr. Haley would understand that in fact the reducing equivalents that ALA uses up are freely available in the mitochondria at no energetic cost to the cell, and are UNavailable in thoseportions of the cell that needs them without exogenous (that is, you take it) lipoic acid. ALA is an antioxidant precisely because it makes these reducing equivalents available to the part of the cell outside the mitochondria, where they are needed and are in limited supply, and increases the level of reduced glutathione which is exactly the opposite of what he says happens. Many many technical papers (cited by Biewenga in the review I've provided a link to the abstract of) show that ALA greatly increases glutathionelevels in human subjects. This is very well established by now. It is not something on which educated opinion may reasonably differ.

> One big difference between OSR and LPA is
> one is totally in the reduced form (OSR)
> and one is in the oxidized form (LPA).

For those who are still concerned, dihydroALA is commercially available as a nutritional supplement. You can use it, it is just as good a chelator asALA. They are completely interchangeable.

> Another difference is OSR is without a charge

The acidity constants for thiols ? those sulfhydryl groups we are always talking about as the things that bind mercury, are such that OSR is mostly in the ionized and negatively charged state in solution, contrary to Dr. Haley's claim. Thus OSR will not act very differently than ALA. They will

both exist in the watery part of the body primarily as a negative ion, and will have similar ability to cross cell membranes and the blood-brain barrier.

If Dr. Haley has determined the pKa1 and pKa2 of OSR I'd like to see the data. It's a very straightforward thing to do.

> and LPA has a negatively charged acid
> group on it, this likely could change the
> partitioning in the cell membrane
> and fatty tissues.

The partition coefficient of ALA is well known, and the fact that it gets into and out of cells, and into and out of the brain, are also well known. Again, OSR will behave quite similarly to ALA.

> Further, google "lipoic acid MSDS" and the material
> safety data sheet will give you a LD-50 value, do
> the same with vitamin E. We could not determine
> a LD-50 of OSR and the group that tested its safety
> stated the LD-50 is above 5 grams/kg body weight.
> Just because something is natural does
> not mean it is safe.
>
> Also, Andy makes some comments about me that
> are just not true.

I don't believe so. I've certainly tried to limit my comments to truthful and accurate opinions. If I have in fact done so (factual errors, not Dr. Haley's opinion versus mine as to whether he understands the significance of half order kinetics, the need for proper administration timing of chelators, etc.) then I hope Dr. Haley will point them out to me privately so I can apologize and offer a public retraction. I consider this to be a technical dispute ? a heated argument among scientists as often occurs ? that is not at all personal and is not meant in any way to detract from Dr. Haley's character or past accomplishments.

> I have
> taught graduate level biochemistry/physiology
> courses since 1974, specializing in biochemical
> kinetics/thermodynamics and bioenergetics. My
> area of research expertise for over 30 years was
> to use novel, chemically synthesized compounds to
> unravel problems in energy utilizing enzymes and
> pathways. Without hopefully sounding like a braggart,
> I was quite successful.

I do not dispute any of this, and do agree it is an impressive set of accomplishments.

> I certainly do understand chemical and biochemical
> kinetics/thermodynamics

I don't agree that Dr. Haley understands the specific, esoteric issues relevant to chelation with alpha lipoic acid, DMSA, DMPS or OSR on a protocol most likely to help everyone who uses it. I can't address his broader understanding of other technical issues, but his general background as he presents it here is quite impressive.

This seems like the argument of whether you want a Nobel prize winner to fix your car, or an auto mechanic. You actually want the person with the limited specific knowledge you need to do the job, not the person with the most overall knowledge. This is usually the lowly mechanic.

> and how certain compounds pass through
> the membranes and organs of mammals.
> I have had a huge amount of NIH funds over many
> years to study such phenomenon and sat on NIH
> Study Section Panels for many years helping
> evaluate federal grants. My past training and experience
> has played a major role in my research success.

In the face of his response filled with innacurate information on the topicat hand ? chelation ? as demonstrated above, Dr. Haley presents his education and experience as proof of knowledge. Honestly, it is difficult tofigure out something polite to say in response to that. Yet I do want to be

polite and respectful to Dr. Haley. He has certainly done a great public service promoting knowledge of the health problems mercury can cause. Hehas been very generous with his time ? and worked hard to minimize expenses ? when speaking for things like autism conferences. Many who have contacted him privately also appreciate how helpful he has been. He is reputed to be a very nice and decent man and I in fact look forward to meeting him some day if our paths do cross. However he has provided, and continues to provide, inaccurate information in a field in which he claims to have expertise ? and that wrong information will lead many people to cause greatharm to themselves or their children. Basically I view this as part and parcel of the old saying "the road to Hell is paved with the best of intentions," and view Dr. Haley as just as nice a guy as most of the pediatricianswho turned kids autistic, or the dentists who poisoned adults, while genuinely believing they were helping. They, too, simply assumed they knew what they were doing because they had the right credentials and never went back to check the basics or ask questions.

I don't particularly want to attack Dr, Haley's credentials. I want to modify his behavior, and yours. I don't want people hurting themselves and their kids through inappropriate use of OSR, and I don't want physicians hurting their patients by prescribing it. I don't want Dr. Haley to feel attacked, belittled, or just bad. I simply want him to have a professional attitude and take more personal responsibility to go review the relevant material, brush up on kinetics and pharmacology, and start offering accurate information. Any professional will tell you their career consists of constantlylearning, re-learning and verifying basic information so they can apply itproperly and get good results. Accurate information is what will let people figure out how to use OSR properly, and when to use it.

I could also argue that Dr. Haley makes money selling OSR, I don't make anyselling ALA (and if I thought there was some more effective way to chelate, I could easily change my books to reflect that and probably would be ableto sell a ton of `new editions' to past customers if I did so. Continuing to support chelating with ALA is no more economically beneficial to me thanswitching to something else). However I don't think he's as motivated by making money selling OSR as he is motivated to try to come up with a means to help sick people, and that means happens to be OSR.

While I do view Dr. Haley's accomplishment in getting lots of NIH grants asa difficult and impressive, I don't think I would personally hold that outas evidence of competence given that this is the agency that has funded tidal waves of studies pretending to prove vaccines and mercury don't cause autism, amalgam fillings don't cause any health problems, and has repeatedlybalked at and tried to stop clinical trials of chelating autistic children.

Thus my opinion (based on Dr. Haley's response) is that at present Dr. Haley does not have the relevant knowledge to responsibly discuss mercury chelation, or the appropriate manner in which to use OSR (or any other antioxidant such as alpha lipoic acid that is also a chelator) in people seeking care who actually want to get better as opposed to people in medical experiments where they expect to end up as statistics. Given his stated background it should not be difficult for Dr. Haley to hit the books, brush up on the relevant topics, and be able to do this shortly. I look forward to that.

> No one in medicine totally understands all of
> the intricacies required for heavy metal detox
> or movement of chemicals around the body and
> I am not claiming exceptional knowledge.

I am claiming exceptional knowledge.

If Dr. Haley wishes to bone up as I've suggested here so he understands what ALA and glutathione do, and why a high equilibrium binding constant doesn't indicate whether or not some reaction goes back and forth rapidly then he will share some of this exceptional knowledge.

> I just claim to be a solid, well trained
> scientist that knows how to design and test
> certain compounds to accomplish
> specific goals

An enumeration of these goals would have been quite relevant. Which compounds did Dr. Haley design and for what purpose? Perhaps details are available at his University web page ? can someone provide the reference?

> and how to test them to make sure they are as safe
> as one can possibly predetermine them to be.

> I then know enough to proceed slow and easy with
> the help of other well trained associates doing the
> monitoring until maximum safety and efficiency
> is established or not. What bothers me about
> Andy Cutler's article is that he judges my work
> but does not know what I have done,

I believe I am adequately aware of most of Dr. Haley's work, both public and private, relating to mercury. E. g. his role in certain decisions of theDAN! committees, that he personally was the first human subject to try OSR, the outcomes of court proceedings he was involved in, certain journal papers, etc. I am sure there are also things I am not aware of but the internet seems to be God's gift to gossip and I do hear a lot.

I can only judge things based on what is public or I happen to hear throughthe rumor mill.

> or what I can disclose and cannot disclose and still be of
> immediate help to many.

Information that can't be disclosed isn't available to me to decide what I think, or to anyone else. I'd be a lot more inclined to accept "trust me" as an argument if everything ELSE I heard was right. This long response isto point out that a large amount of what I am hearing is flat out wrong. In the face of that, I don't think it is reasonable for me (or anyone else)to accept `trust me' as an adequate argument.

I understand that the lack of free speech in the United States can really make this difficult for Dr. Haley. I don't believe he is trying to do anything wrong, or does not believe that what he has privately concluded is correct, even if he can't share it with people.

> He is interpreting going slow and doing careful
> work as not having done essential studies and
> this is not the case.

This is not my interpretation.

I am interpreting releasing the compound commercially without publicly available information on its metabolism or kinetics to be shockingly irresponsible.

Many people, both parents with sick children and adults caring for themselves, seek information in great detail on the various internet discussion groups such as this one, the autism mercury list, the adult metal chelation list, the frequent dose chelation list, curezone, etc. They express a very strong desire, both generally, and to me directly, to have as many facts as possible about the interventions they are considering for themeselves or their chidlren. `Trust me' isn't good enough and they make that clear. Goodintentions aren't enough for them any more ? they learned that the hard way. This is the reason I've spent vast amounts of time patiently answering (and repeatedly re-answering) questions, offering explanations, and providing details. The only studies that really matter are the ones that are publicly available for review, discussion, dissection and use by others. Otherwise the argument is "trust me, it is safe," which is the same argument doctors continue to make for vaccines and dentists continue to make for amalgam fillings. This is no longer a legitimate argument in the public scientific discourse about chronic health problems.

> Initially, the compound was not offered to
> anyone except those who were capable of
> testing it slowly and carefully. Andy's concerns
> as mentioned in his missive are those that any
> careful person would test for, and we did,

Providing details of this publicly would allay much concern. I'm curious how Dr. Haley might have gotten a bunch of chemically sensitive people to take OSR, and how he might have determined what it did to them.

> with safety being the highest priority.
> I can also assure you that the DAN doctors couldn't
> have been more cautious in regards to evaluating OSR
> and it is today not a "DAN" approved procedure.

I am glad to hear the DAN! movement has been responsible enough NOT to add OSR to its protocol

even though the informal DAN! network has been used to market OSR.

> We recently just started and much work was
> done before any OSR was provided to anyone.

It is nice of Dr. Haley to share the information below with us. This is the kind of information that needs to be available, in much greater detail than here but this is certainly a good start.

> In the recent past we have obtained pharmacokinetic
> studies on OSR, data on OSR's oxygen radical
> absorbance capacity and identification of the
> metabolites of OSR in human liver homogenates.

I'd love to know the molecular structure of those metabolites.

> We know that OSR peaks in the plasma and all
> tested organs after two hours post ingestion, at 24 hours
> post ingestion the levels are between 4 to 12% of
> the two hour peak values.

One major issue in chelation is that all chelating agents have to be given more or less once a half life (see any standard medical text, e. g. Goodmanand Gilman's Pharmacological Basis of Therapeutics). Since kinetic data on OSR is unavailable in the literature it has not been possible for anyone to prescribe it responsibly. Dr. Haley has been so kind as to provide us with a preview of his unpublished studies, below, that allow some reasonableestimate to be made of half life. Do note that when I say "half life," this presumes first order kinetics which are not necessarily the case. Also the range of values he gives doesn't include the number of individuals in the trial so I can't estimate a 95% confidence interval for the range of values in the population. Thus what I am doing below is making reasonable estimates based on unproven assumptions and inadequately detailed data ? notreally enough to base giving OSR to real human beings, but a lot better than nothing. These estimates are a place to start. Hopefully Dr. Haley's very limited permission (from the FDA I believe) to speak about OSR will permit him to answer some questions by providing more detailed data.

Dr. Haley says that OSR levels in blood fall to 4-12% of 2 hour levels by the time of a 24 hour measurement. 2 hours gives time for the OSR to distribute so that simple calculations based on blood level should be reasonable estimates. I'll show this example here and discuss it.

The half life range is between

-22*ln(2)/ln(0.04) and ?22*ln(2)/ln(0.12)

or 4.74 and 7.19 hours.

Most things taken by mouth do have about a 2 hour absorption period that can be added to the half life, so most people should be OK at least with the chelating performance of OSR if it is taken every 6 hours around the clock,a few will actually tolerate 8 hour dosing. Taking it less frequently WILL cause damage in anyone with a clinically significant level of heavy metals and WILL make them harder to help later.

Clearly, all instructions on the use of OSR to date have been inappropriateand potentially harmful. Knowing the stuff is a chelator (regardless of its FDA status) and not knowing the half life the only responsible instructions for use are every 2-3 hours day and night.

I really don't think it is appropriate to rely on a single set of unpublished measurements and say it is going to be OK to use OSR as a chelator every6 hours, but clearly it is NOT going to be OK for most people to use OSR (for any purpose) and take it less often than every 6 hours by the clock.

I do really appreciate Dr. Haley having gone to the trouble and expense of making these measurements, and of sharing them with us prior to publication!

> OSR was found to enter the cells of all tissues tested, and to be excreted,
> most likely as an oxidized species as indicted by the mass spectrometrydata
> obtained with liver homogenates. This study indicated that the first two
> main products of OSR modification by liver homogenates were those with 2 and

> 3 oxygens attached to the arm with the sulfhydryl attached as would be expected for a free radical scavenger.

It would be nice to know the actual structure of these, or at least how rapidly the OSR is metabolized. E. g. if it is metabolized rapidly it has a shorter effective half life or lifetime in the bloodstream. For example, DMSA needs 4 hour dosing because it is metabolized, DMPS can be used with 8 hour dosing because it is not metabolized.

> OSR did not concentrate in the brain and was effectively excreted from this organ. While I cannot assure one of the mechanism it is well known that most compounds taken into the body are excreted by mechanisms that protect the brain from excess exposure. I think the same is true of OSR, it is obviously being excreted by a mechanism that is designed to removed compounds with oxidized sulfhydryls. Do note the similarity of the sulfhydryl containing arms of OSR to that of reduced glutathione. This was put in the design of OSR on purpose to take advantage of any characteristic that would allow additional safety and utility.

Dr. Haley provides some dribs of information about the metabolism, kineticsand excretion of OSR. Any interested person may note that if they read the Physician's Desk Reference (PDR ? the public library usually has one) or the drug package insert that comes with more or less anything obtained atthe pharmacy, extensive information on metabolism, kinetics and excretion is available. This is because it is important information. Just calling something a nutritional supplement doesn't make this information any less important ? and it is generally pretty well known for the vitamins, minerals, amino acids, etc. typically thought of as supplements.

> Finally, Andy's comments about LPA being a superior binding agent because it forms a six membered ring is seriously flawed, the affinity of binding any specific metal depends a lot on the angle of binding that specific (coordination chemistry) and a six membered ring is only considered themost stable or sterically favored if the angle is that of a carbon atom, notany metal. For example, the most stable bond angle of the two bonds of Hg2+ is 180o, consider that there is no way a 180o bond angle can be formed with Hg2+ in a six membered ring consisting of 5 carbons as found in dihydro-LPA.

Dr. Haley's assertion that mercury II (also referred to as mercuric mercuryor Hg++) only forms linear (180o) complexes surprises me. This is not what one finds find if one checks standard chemistry texts, e. g.

Cotton and Wilkinson, Advanced Inorganic Chemistry: a comprehensive text. Third edition, 1972, John Wiley and Sons.

Accurate information is found on page 519.

"18-15 Mercuric complexes

A number of these have been mentioned above. The Hg++ ion has indeed a strong tendency to complex formation, and the chaacteristic coordination numbers and stereochemical arrangements are two-coordinate, linear, and four-coordinate, tetrahedral. Octahedral coordination is less common, a few three-and five-coordinate complexes are also known."

A tetrahedral complex is one in which the mercury ion is bonded in the samemanner that carbon atoms bond ? the angle that makes 5 and 6 member rings highly stable and preferred. The mercuric ion (which is what is in people, poisoning them, that they need to chelate out) will form all of the typesof complexes that are necessary for DMSA, DMPS, ALA and OSR to chelate it.

For anyone more modern than to like dusty old books, or who doesn't have a bunch of undergraduate chemistry textbooks lying around, this information can also be found on the internet with trivial ease. Searching Google for: mercury coordination chemistry

Yields results, the first page of which contains the following. I've givenURL's and quotes from the page that comes up.
http://www.ncbi.nlm.nih.gov/pubmed/18260625

"The mercury atoms in the latter compound form a tetrahedral network,"
http://pubs.acs.org/doi/abs/10.1021/ic049500%2B

"with tetrahedral mercury(II) centers"
It is both very well known by those who understand chemistry, and also trivially easy to find out either in a library or on the internet, that Hg++ forms tetrahedral complexes. I don't know why Dr. Haley would argue otherwise. The incorrect assertion that ALA doesn't chelate Hg++ because Hg++ onlyforms linear complexes would seem to be an argument that OSR is a REAL chelator and ALA is not. This implicitly contradicts the statement that OSR is only held out as an antioxidant.

One of the things that happens in medicine is that people vary a lot, so ifa doctor does more or less any random thing (including nothing, this is called the placebo effect), some of them get better. The real question is not whether one or a few people whose cases came out well can be found and used for advertizing, but what the statistics are regarding various outcomes,and how the alternatives stack up to the proposed intervention. You've all heard stories about the kids who responded to some or other thing like horseback riding, a super nanny, turning off the television, or being firm and improve magically. This doesn't mean these interventions are very likelyto work for your kid or necessarily be a good idea.

I do not think that a reasonable person who grasps all the relevant facts would truly want to take the risk of using OSR as anything but an experimental new chelating agent. If OSR were the only choice, then the risks of using a chelator with an as yet to be solidly determined half-life (and many other relevant factors remaining unknown, at least publicly) would perhaps make sense, versus the risk of not chelating at all. This isn't the case. ALA is a proven alternative (and Cilantro is an unproven alternative thathas the advantage of being a food people have eaten for millenia) Most certainly some people who experiment will not suffer consequences, but if you or your child does, then the good luck of others is irrelevant. And even if you feel compelled to experiment, you want to reduce the risk as much as possible by understanding kinetics, metabolism, etc. so you can use a proper protocol that gives you the best odds.

Hopefully Dr. Haley's legal situation in selling a nutritional supplement to promote normal healthy levels of glutathione, and as an antioxidant will permit him to provide further accurate information so that it is possible to figure out if OSR is appropriate to use more widely. I am sure this would be of great interest to a wide audience, who like Dr. Haley and myself would like nothing better than for all the autistic children to return to normal neurological development, and for all the chronically ill adults to find something that promoted a normal state of health.

Andy

www.noamalgam.com

www.noamalgam.com/hairtestbook.html

www.noamalgam.com/nourishinghope.html

www.noamalgam.com/biologicaltreatments.html

(Andrew Hall Cutler PhD)

> > Boyd E. Haley, PhD

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Boyd Haley's original message follows as I received it
++

> --- In Autism-Biomedical-Europe@yahoogroups.com, Geir Flatabø <geirf> wrote:
>
> Boyd Haleys Response to Andy Cutlers "message"
>
> Geir Flatabø
>
> > First, the only claim made for OSR is that it is a lipid soluble, dietary
> > antioxidant that scavenges free radicals and helps maintain a healthy

glutathione level. Maintaining a healthy glutathione level can possibly help detox the body of any toxin that is carried out of the body as a glutathione complex, and this includes many heavy metals as well as toxic organic molecules that are attached to glutathione by the enzyme glutathione-S-transferase after the oxidation by the Phase II P-450 enzymes.

I know of Andy Cutler and have read his book and I agree that he has proposed a detox scheme involving LPA (lipoic acid) that I have found quite reasonable as I am also not a fan of using toxic chelators. However, this detox scheme has not effectively reversed the oxidative stress (as measured by low reduced glutathione levels) in many who have tried it, or so I am told. This may be due to the fact that LPA (has a disulfide linkage and already in the oxidized form and unable to bind any metal in its delivered form) can add to the oxidized stress level as LPA (lipoic acid) has to be reduced to the dihydrolipoic acid (dihydro-LPA) form before it can bindto any metal. This reduction of LPA to dihydro-LPA requires reducing potential and reduces the body's ability to produce reduced glutathione since both the reduction of oxidized LPA and oxidized Glutathione (GSSG) are biochemical steps that consume reducing equivalents in the form of the basic molecule(s) NAD(P)H. Using a beginning oxidized molecule to treat patients who are already under oxidative stress is not the best approach in my opinion. One big difference between OSR and LPA is one is totally in the reduced form (OSR) and one is in the oxidized form (LPA). Another difference is OSR is without a charge and LPA has a negatively charged acid group on it, this likely could change the partitioning in the cell membrane and fatty tissues. Further, google "lipoic acid MSDS" and the material safety data sheet will give you a LD-50 value, do the same with vitaminE. We could not determine a LD-50 of OSR and the group that tested its safety stated the LD-50 is above 5 grams/kg body weight. Just because something is natural does not mean it is safe.

Also, Andy makes some comments about me that are just not true. I have taught graduate level biochemistry/physiology courses since 1974, specializing in biochemical kinetics/thermodynamics and bioenergetics. My area of research expertise for over 30 years was to use novel, chemically synthesized compounds to unravel problems in energy utilizing enzymes and pathways. Without hopefully sounding like a braggart, I was quite successful. I certainly do understand chemical and biochemical kinetics/thermodynamics and how certain compounds pass through the membranes and organs of mammals. I have had a huge amount of NIH funds over many years to study such phenomenon and sat on NIH Study Section Panels for many years helping evaluate federal grants. My past training and experience has played a major role in my research success.

No one in medicine totally understands all of the intricacies required for heavy metal detox or movement of chemicals around the body and I am not claiming exceptional knowledge. I just claim to be a solid, well trained scientist that knows how to design and test certain compounds to accomplish specific goals and how to test them to make sure they are as safe as one can possibly predetermine them to be. I then know enough to proceed slow and easy with the help of other well trained associates doing the monitoring until maximum safety and efficiency is established or not. What bothers me about Andy Cutler's article is that he judges my work but does not know what I have done, or what I can disclose and cannot disclose and still be of immediate help to many. He is interpreting going slow and doing careful work as not having done essential studies and this is not the case. Initially, the compound was not offered to anyone except those who were capable of testing it slowly and carefully. Andy's concerns as mentioned in his missive are those that any careful person would test for, and we did, with safety being the highest priority. I can also assure you that the DAN doctors couldn't have been more cautious in regards to evaluating OSR and it is today not a "DAN" approved procedure. We recently just started and much work was done before any OSR was provided to anyone.

> In the recent past we have obtained pharmacokinetic studies on OSR, data on OSR's oxygen radical absorbance capacity and identification of the metabolites of OSR in human liver homogenates. We know that OSR peaks in the plasma and all tested organs after two hours post ingestion, at 24 hours post ingestion the levels are between 4 to 12% of the two hour peak values. OSR was found to enter the cells of all tissues tested, and to be excreted, most likely as an oxidized species as indicted by the mass spectrometrydata obtained with liver homogenates. This study indicated that the first two main products of OSR modification by liver homogenates were those with 2 and 3 oxygens attached to the arm with the sulfhydryl attached as would be expected for a free radical scavenger.
>
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> Boyd E. Haley, PhD

Andy

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Onibasu Link: http://onibasu.com/archives/am/279813.html

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- Re: Question about about lipoic acid "a.carly2008" <a.carly2008>

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