THE DEFINITIVE GUIDE FOR INTRAVENOUS THERAPY with NUTRIENTS

including

Complete Instructions for Sterile Compounding of Preservative-free Nutrients *and* Allergens

REVISED JANUARY 2015

BY

W. A. SHRADER, JR., MD

Fellow, American Academy of Environmental Medicine

Board Certified in Environmental Medicine

Fellow, American Academy of Environmental Medicine

Certified Chelation Therapist

Dr. W. A. Shrader, Jr. is a Past President and Fellow of the American Academy of Environmental Medicine (AAEM), and is Board certified in Environmental Medicine. He is a past CME Director of AAEM and is the Secretary of the Board of Governors for Environmental Medicine.

Dr. Shrader has been a member of the American College for the Advancement of Medicine (ACAM) since 1990, and is on the Board of Directors and Treasurer. He currently teaches IV therapy for both AAEM and ACAM. This book is a reflection of all of that, and we hope you enjoy it!

This Guide includes subject matter that may be considered investigational by the FDA, and many nutrients are considered by the FDA as "unapproved new drugs". The FDA has rendered no opinion as to the content of this Guide, except for annotated comments specifically quoted within.

Some material in this Guide was originally published in the *Environmental Physician Newsletter* of the American Academy of Environmental Medicine from 1992 through 1995.

Table of Contents

The Use of IV Therapy with Nutrients for Physicians

Introduction

This is a guide for physicians, D.O.s, naturopaths and other qualified personnel to teach how to administer intravenous therapy with nutrients to patients. This can be done in the physician's office, but is also suitable for use in the hospital. IV therapy with nutrients is inexpensive and can be dramatically effective. It is unfortunate that IV therapy with nutrients is currently performed almost exclusively in physicians' offices; it is drastically needed in most hospital settings. Magnesium, when used for eclampsia and premature labor, is so far the only nutrient that is regularly used in the hospital environment. NAC also has been used in hospital settings to treat the acetaminophen overdose (one of the most frequent causes for emergency room visits in the USA today), but is still mostly used orally. I have no doubt the day will come when we see many IV nutrients used routinely on hospitalized patients who so desperately need them. It's just a matter of time.

Since I started using nutrient IV therapy around 1980, I have seen it go from almost totally taboo and obscure to something now quite commonly used by physicians who practice integrative medicine around the country. No, it is still not employed by "mainstream" medicine, but certainly the time for use of nutrient IV therapy in the fields of integrative and alternative medicine has come. I teach nutrient IV therapy for the American Academy of Environmental Medicine (AAEM) and the American College for the Advancement of Medicine (ACAM), and I hope my teaching is adding to the numbers of physicians who employ it. The results of IV therapy with nutrients are very often remarkable, and - perhaps most importantly - IV therapy with micro- and macronutrients is generally one of the safest office procedures you can perform.

Prior to 1998, there were only about 47 decent references in the literature regarding IV therapy with nutrients, mostly discussing magnesium and its use for acute asthma. Since then, studies of nutrients administered intravenously have increased practically logarithmically. There are now hundreds of new papers every year. Each year I pick what I think are the most important publications and update the reference material in this Guide.

Although IV therapy may be new to you, I'm certainly not going to try to teach you something that's difficult, dangerous or will not be significantly beneficial to your patients. I'm a firm believer in solid clinical medicine. That's what this Guide is about. The Guide should make it comfortable and easy for you to begin to use IV therapy in you office almost immediately and with confidence.

I know the mention of "IV therapy" brings unpleasant thoughts to many of you. Most of you remember our days as interns and residents, administering powerful IV drugs - often in the middle of the night - to seriously ill patients. We remember those 2:00 AM calls to rush and re-start Mrs. so-and-so's IV (which had generally infiltrated at least 2 hours previously). Inevitably, Mrs. so-and-so's only viable vein left for us to use was her vena cava.

You also may have heard about some terrible reaction to an intravenous injection of some supposedly harmless substance - even a vitamin.

In short, most of you have less than fond memories of IV therapy, and you may be a bit hesitant to use it in your offices.

Well, it's time for you to put all those memories and anecdotes in the closet - forever. Intravenous therapy with nutrients has no relationship to potentially dangerous IV therapy with powerful pharmacological agents. (Please note that whenever I use the term "IV therapy" in this Guide, it will refer to IV nutrients only, not drugs, etc.) Additionally, nutritional products for intravenous use have been extensively refined over the last several years, and have become easily available without preservatives.

Why IV Therapy?

There are many answers to that question, and most of you know most of them, so I'll just touch upon the obvious. We all treat patients with nutrient deficiencies. In fact, I'd go so far to say that the considerable majority of patients who are ill have significant nutritional deficiencies, especially as they get older. There are many reasons for this, but probably one of the most significant in these modern times is food sensitization. A patient with food intolerances (I hesitate to use the term "allergy," but it fits here, too) has considerable intestinal irritation on at least a microscopic (cellular) level. When we see a patient with eczema or urticaria, for example, we have to realize that a similar pathology is occurring at the mucosal level in the patient's intestine also; we just can't see it. That means there will usually be something wrong with that patient's mucosal uptake or transport of nutrients.

I don't know about most of you, but since I see patients with allergy, I'd say the considerable majority - well, what the heck, let’s say 80% - of my patients have food intolerances. To me, this means they have malabsorption secondary to gut irritation at some level. This generally results in a compromised patient, simply because nutrient deficiencies always compound our patients' problems. Almost without exception, the older the patient, the more severe will be the nutrient deficiencies. I would venture to say that magnesium deficiency is the most rampant in civilized societies. Where it used to be primarily a deficiency of older people, now it’s not uncommon for people under 30 with a poor diet.

We now have the problem of the almost ubiquitous use of H-2 receptor blocking drugs, such as Tagamet, Prilosec and others. When these first came out, those of us who even vaguely understood nutrition knew there was going to be a major problem with these drugs down the road. This is because they are quite effective in totally blocking the production of hydrochloric acid in the stomach.

The problem here of course is that we *need* hydrochloric acid to leach essential minerals from our foods so we can absorb them, including calcium and magnesium. Needless to say, articles have been appearing in the past few years demonstrating the bad effects of depletion of these minerals, including a higher instance of osteoporosis in patients taking these drugs chronically. The frightening thing is that the multitude of trace minerals we require are completedy ignored because they are not well understood in the causation of human disease, but they they are not absorbed for the same reason as calcium and magnesium.

I recently saw a 28 year old patient admitted by the ER physician to the hospital because of a severely stiff neck, and the provisional diagnosis was meningitis. Her serum magnesium was 1.4, with a normal range of 1.7 to 2.2. It’s important to note here that serum

magnesium levels are very innacurate; by the time serum magnesium levels become low, patients are *severely* magnesium deficient, and cellular levels are critically low. No wonder she had a stiff neck! Luckily, somebody finally had the intelligence to check her magnesium level, and the situation was corrected, but not until several days had passed on antibiotics with a negative spinal tap after four failed attempts (#5 was negative).

When we give an oral supplement to such a patient, it is often incompletely or minimally absorbed. On the other hand, if we give a nutrient to such a patient intravenously, we pretty much know it's going where we want it. It just makes sense that the odds are a great deal more on our side with the intravenous route.

Interestingly, magnesium is a paradox. If a patient is magnesium deficient, he or she will absorb less and less magnesium from the diet, the worse the deficiency becomes. This is because magnesium is a nutrient that is absolutely required by almost all of the enzymes our cells need to function and perform, including those responsible for mineral (and other nutrient) absorbtion. So the lower magnesium gets, the worse off you are.

On the other hand, once a patient is given a few doses of IV magnesium, absorbtion will improve, and the patient can then usually be maintained on oral magnesium. I have seen this clinically over and over, especially with patients who have dysphagia or trouble swallowing. Once the deficit is replenished, oral magnesium seems adequate, and if patients are diligent in taking their magnesium, they most often do not require IV supplementation.

IV therapy is sometimes the *only* way to begin some patients on the road to recovery. Many patients who are severely nutrient deficient are unable to absorb through the intestine the very nutrients they lack (magnesium is a good example), simply because those nutrients are critical in one or more of the enzymatic pathways that regulate absorption! The result is - of course - they get sicker. Often oral supplements will make them ill, or they simply won't tolerate them. The very patients who have the most severe deficiencies are the ones who are often unable to take oral supplements without having problems. And even if they can, they likely won't absorb them because of severe food intolerance and intestinal mucosal injury.

Lastly, IV therapy often works almost instantaneously. We still must rely upon consistent oral therapy for most all of our patients, but that always takes time to work – often a minimum of three weeks to sometimes up to 3 months or so. IV treatment with the same nutrients works much more quickly, and that’s often a major reason I do it.

Chapter 1: In the Medical Literature: Specific Reported Actions and Benefits of Nutrients Given Intravenously

As I mentioned, the use of intravenous nutrients has steadily increased over the years, and has been reported in the medical literature that all physicians can easily access. The following information has all appeared in the references available on PubMed (Medline). So if you are ever challenged about using nutrients intravenously, here you can stifle the criticism. Please be aware that to conserve space I have included only selected references from the entire body of published articles that appear every year in the references at the end of this Guide. There have generally been *many* more published than the ones I included in this Guide; most of the studies I did not include were repeats of similar studies. Recent references which repeat previously published information will usually not be cited here.

Alpha Lipoic Acid (ALA)

Alpha lipoic acid, though I don't use it in my office, has shown dramatic benefits when give IV to patients. It has been used to reduce the symptoms of peripheral neuropathy in Type-II diabetics (63-68, 71-73), to effectively treat neuropathic pain in these patients (63), improve endothelium-dependent vasodilatation in patients with type 2 diabetes (66, 63), in the effective treatment of pancreatic cancer with liver metastasis (69), and for the treatment of hepatitis C (70).

When given intravenously at a dosage of 600 mg/day over a period of 3 weeks, alpha lipoic acid has been shown to lead to a significant and clinically relevant reduction in neuropathic pain (63).

The safest and likely most effective form of ALA comes from Europe, and it is available in this country from selected compounding pharmacies. Specifically, I know that McGuff is a reliable source of ALA.

Vitamin A

Vitamin A is an oil soluble vitamin that is available from several compounding pharmacies. I don't use it because I had some questionable reactions when I used it several years ago. However, one notable study found improvement in morbidity and mortality when it was given intravenously to high-risk, low birth weight infants (74).

Vitamin B_6 (pyridoxine) and Folate

It has been long known that long-term use of theophylline can cause pyridoxine deficiency, so articles have appeared proving the use of IV pyridoxine has been successfully employed for the treatment of associated complications (75). Articles have also appeared demonstrating IV pyridoxine and P-5-P have been successfully used for the treatment of (sometimes otherwise intractable) seizures (83, 86, 88, 92), hyperemesis gravidarum (79, 75), acute mushroom poisoning (81), ginkgo nut intoxication (82), isoniazid toxicity (87**Error! Reference source not found.**), and elevated homocysteine levels (84, 89, 96). IV *folate or folinic acid (and B_{12})* have been associated with correction of elevated homocysteine levels as well (85, 89, 91, 93, 94, 96, 103).

Vitamin B_{12} (cyanocobalamin, hydroxocobalamine, methylcobalamin)

Vitamin B_{12} (cyanocobalamin, hydroxocobalamine, methylcobalamin)

Intravenous B_{12} has been used perhaps most successfully for the treatment of acute cyanide poisoning (OK, American physicians may not know this!) (101, 104, 112, 113). As indicated above, it has been used to reduce homocysteine and nephropathy in end-stage renal disease (103, 105, 106, 110), and it has been shown to lower homocysteine levels cause by anesthesia from nitrous oxide (97). It has been reported to benefit uremic and diabetic neuropathy in dialysis patients (108). IV B_{12} has been used successfully to treat Alzheimer-like dementia (114) and has been used to completely cure fecal and urinary incontinence in a patient with post-gastrectomy megaloblastic anemia (115).

High dose methylcobalamine has been used to successfully treat peripheral neuropathy and chronic axonal degeneration (108).

Dr. Jonathan Wright observed way back in 1989 (20) that *IM injections* of B_{12} stopped the wheezing response in children with asthma, so it's very likely, when given IV, it can play a role in the treatment of chronic asthma (236).

Vitamin C (ascorbate, ascorbic acid)

Certainly it seems that Vitamin C and magnesium are the two most important nutrients we study and employ. The published literature pertaining to Vitamin C is prolific, as is that of magnesium. I will comment in this Guide only about the most important references for vitamin C.

As you probably know, Vitamin C has been used frequently in the areas of "detox", infectious diseases and for the treatment of cancer. Several articles have discussed the mechanism of action as to why Vitamin C works well to kill cancerous cells and spare healthy ones (131, 132, 145, 153, 162, 167, 178, 182).

It is known that Vitamin C induces the formation of peroxide in human cells. Peroxide is highly toxic to all cells, but normal cells have a large supply of the enzyme, *catalase*, which converts potentially harmful peroxide to hydrogen and water. Cancer cells have 10 to 100 times less catalase then do healthy cells. Hence, the peroxide produced by IV or even oral Vitamin C cannot be detoxified by those cells. The result: death of the cancer cell. Although other mechanisms have been discussed, I feel this is likely the most important.

Another article indicates that reduction of cellular ATP may also be a mechanism of the action of IV Vitamin C (116). It has been found that high dose intravenous ascorbate treatments may reduce inflammation in cancer patients (116).

Numerous articles have appeared establishing that Vitamin C may significantly mitigate several types of cancer (116, 134, 135, 139, 142, 149, 150, 156). Dr. Hugh Riorden (now deseased) certainly deserves much credit for his pioneering cancer research with Vitamin C, and several of his articles appear in those cited here.

Dr Jeanne Drisco's article (ref. 156 above) details the survival of two patients with far advanced ovarian cancer, and is a must read. Drisco and others have more recently found that IV Vitamin C in combination with glutathione is of no further benefit in the treatment of cancer than intravenous Vitamin C alone (126).

I have used Vitamin C for the treatment of various types of cancer in my office for 25 years. I have to say that I have not been very impressed that it generally performs miracles for patients with cancer, and I have personally seen few amazing "cures". However, Vitamin C seems to significantly improve the quality of life, physical function, and toxicities associated with chemotherapy, including fatigue, nausea, insomnia, constipation and depression for many of these patients, and there have been articles published that definitely verify this (123, 183).

There has also been a great deal published about the anti-inflammatory and antioxidant beneficial effects of Vitamin C, especially pertaining to the endothelium of arteries in coronary artery disease, heart failure and the myocardium (133, 137, 155, 158, 160 163, 168, 171-175, 177). It is known now that patients undergoing PCI (percutaneous intervention) treatment for coronary disease, pre-procedure intravenous Vitamin C is associated with less myocardial injury (116).

We all have heard of the dangers of the cardiac pump during cardiac bypass. One article demonstrates that Vitamin C prophylaxis promotes oxidative lipid damage during surgical ischemia-reperfusion and could possibly prevent many of these complications (143). The conclusion is that all patients with arterial disease of *any type* would be wise to use Vitamin C, as a minimum in the oral form.

Articles have also appeared showing the positive effects of Vitamin C for the compromised endothelial function in the arteries of patients with Kawasaki's disease (165, 169) and for patients with postural tachycardia (127).

Other various trials with Vitamin C have been published, including two on the positive effects on patients with inclusion body myositis (166, 181, 166, 181), as a successful treatment for acute pancreatitis (154), and as a successful treatment for jellyfish stings (148). Articles suggest that IV Vitamin C is effective in the treatment of shingles (122) and may mitigate the development of post-herpetic neuralgia (128). It has also been found that it may be possible to improve microvascular function in sepsis by using intravenous vitamin C as an adjunct therapy (116, 118).

Vitamin C may reduce blood loss in abdominal myomectomy (uterine fibroidectomy) (125). Intravenous vitamin C can significantly decrease phosphorus level in hemodialysis patients (123).

Physicians have used intravenous Vitamin C successfully for many maladies, including treatment of acute and chronic viral infections, chronic fatigue syndrome, removal of toxins from the body and other reasons, We must wait for valid studies to appear in the literature regarding the absolute effectiveness for these conditions; however, a 2013 article indicates Vitamin C can lower Ebstein Barr Viral EA IgG and EBV VCA IgM antibody levels over time (117).

In 2011, the FDA issued an order to McGuff Pharmaceuticals that they were no longer permitted to manufacture and sell injectable Vitamin C, which they had done for several years with a valid license. There was a long list of "deficiencies" in McGuff's manufacturing process that the FDA cited to stop their legal manufacture and sale, and the reasons appear to be quite concocted. I think there is little question that this action could be the beginning of a broader attack on injectable Vitamin C, since it is being used in the

treatment of cancer as I mentioned above, and as most of you know, the politics of the treatment of cancer are primarily and absolutely governed by Big Pharma and $$$. Two other manufacturers of Vitamin C remain. We'll have to wait and see what the FDA does to them, but it may well be the same thing. In the meantime, McGuff does have a legal *compounding* division, and they now compound their Vitamin C. It will just require a prescription and is more expensive. Let's hear it for the FDA! After all, we know they just want to *protect* us!

L-Carnitine

Although we have not used this in our office, l-carnitine has been reported to reduce the adverse metabolic effects of certain illnesses (200), especially for patients on long-term dialysis (185, 187, 191, 192, 195, 197, 199). One study indicates intravenous l-carnitine is of benefit for Type-II diabetic patients with periforal vascular disease (198).

Coenzyme Q10

We know that CoQ10 is necessary for patients taking lipid-lowering agents and is beneficial for patients with congestive heart failure. A published study of intravenous CoQ10 indicates it may protect the myocardium during cardiac valve replacement (201). Oddly, this study was done in 1999 and hasn't been repeated. Guess nobody cares?

Glutathione (GSH)

Glutathione (GSH) is a potent endogenous antioxidant that protects major organs from oxidant injury and is frequently associated with organic antioxidant protective systems (217, 218, 223). It has been clearly demonstrated in the medical literature that in *many* disease states, tissues are very low in GSH (numerous references, not included here). It's considered the most potent detoxification agent made by the body, and can be synthesized in the body from the amino acids L-cysteine, L-glutamic acid and glycine. GSH is a free radical scavenger and has activity similar to Vitamin C. Oral glutathione has a maximum and limited absorbtion, so it's no wonder that the potential of IV glutathione is remarkable, since very high tissue levels can be achieved.

IV GSH can reduce or eliminate tissue damage in patients with liver disease and toxicity (213, 214, 216, 206).

IV GSH has proven to be beneficial when used to reduce the toxicity of chemotherapeutic agents to normal cells (202, 207, 210, 215). It also has been used as a preventative and treatment agent for patients with chemotherapy induced peripheral neuropathy (202).

Additionally, intravenous GSH has been shown to improve pain-free walking distance in patients with peripheral obstructive arterial disease (208), reduce lipoperoxidative damage in patients with early septic shock (209), reverse some adverse effects of diabetes (211 below, 219, 222), improve anemia in patients with chronic renal failure (220), and aid mercury removal in patients with high levels mercury (205).

GSH has been shown to markedly improve the outcome of the treatment of cadmium toxicity with EDTA (203).

Importantly, as I'll discuss later, GSH has been shown it can be dramatically helpful for the treatment of many patients with Parkinson's disease (212).

There is ample evidence in the literature to support frequent use of intravenous glutathione for a host of medical conditions, many yet to be investigated. In my opinion, it should be employed routinely in many hospital settings, yet it is not at this time.

Many studies have been published demonstrating the value of glutathione as a detoxification and a protective agent. It amazes me that it is not used routinely in hospitals around the world as an additive to the therapy for a myriad of medical problems. However, this is another example of studies being done, proving a point, but not making inroads into "standard" medical treatment. This is because the money is not there to promote it, and studies are not repeated because of the same problem. Like other nutrients, thought slightly more expensive than some, it is readily available from many sources – but not from Big Pharma, where the Big Money is. Hence, most physicians have no clue as to its potential value. It cannot be patented in its most useable form, and so there's no big money in producing it commercially.

Vitamin K-1

This is another nutrient for which we have no call to use IV in my office. The published studies are what you'd expect: intravenous Vitamin K-1 is effective to treat excessive anticoagulation (224, 226, 227).

Magnesium

Here we have a greater abundance of literature advocating IV use than for any other nutrient. When I first began IV therapy with magnesium for the treatment of asthma in my office circa 1986, no articles had yet appeared in the literature discussing the use of intravenous magnesium for the treatment of acute asthma. I had heard about the potential benefits from a few colleagues, because magnesium seemed to be a bronchodilator when given intravenously, but there was nothing in the literature to go by. Okayama's article in 1987, published in JAMA, was the groundbreaker (14). From 1988 through 1997, several more important articles appeared, the most important of which I've cited here (16, 18, 23, 24, 32, 37, 42-52, 56, 57).

After 1998, the medical literature began to overflow with articles about the treatment of asthma with intravenous magnesium, so I won't cite them all individually here, but some are listed by category in the reference section. The references I cited for the years since 1998 were selective - there are *many* more not cited in this Guide. There is no question that intravenous magnesium can be a critically important adjunct, or stand-alone treatment, for acute asthma and/or status asthmaticus.

In recent years the numbers of these articles have slowly diminished. I guess authors figured out that *everyone* should now know that intravenous magnesium is often critical in the treatment of acute asthma and status asthmaticus, and they are using it. Unfortunately, this is nowhere near the case.

If you want to prove that point, simply visit your local emergency room and ask whether they use intravenous magnesium routinely to treat acute asthmatics when they appear there.

This illustrates a point that is very important in the ongoing evaluation of the benefits of nutritional medicine. Magnesium sulfate, the nutrient usually used in the studies of IV treatment of asthma, is available everywhere, and it's *cheap*. Major drug companies do not produce this and do not own a patent on it, as it's been on the market, available to anyone, for *many* years. There is little "money" in it to prove that intravenous magnesium can be as effective as expensive bronchodilators for asthma, has far fewer side effects, and is much cheaper.

Since magnesium sulfate is available from scores of suppliers, why should any one company want to keep proving how beneficial it is when it can be purchased almost anywhere for almost nothing? *Big Pharma* would *never* be interested because it is concerned primarily with *Big Money*. Suppliers who produce magnesium sulfate simply don't have the money to support large studies to promote it. Even if they did, why spend money to promote something when people may then go anywhere and buy it?

This remains the major dilemma in getting the word out as to the effectiveness of nutrients for the treatment of disease. There's no big money in it because most all nutrients are available most anywhere. Nobody "owns them" (except for patented neutracuetical formulations). And then of course there's the FDA, but that's another story. Don't get me started.

The magnesium story is interesting and illustrates the serendipity that often seems to be present in the field of medicine. I'm sure many of you who are older (okay, I guess that's me) remember using intramuscular injections of magnesium sulfate for patients with eclampsia to lower blood pressure that was often frighteningly high. I finished that part of my training in 1969, still using IM injections.

In 1975, somebody figured that if you dared to give the stuff intravenously, it might work even better. Well, that's exactly what happened. The *very first three articles* published about the use of intravenous magnesium described excellent treatment results with eclampsia and toxemia of pregnancy over that of treatment with IM injections (1-3). Since that time, as is common, there began an increasing stream of articles describing the use of magnesium for this purpose, and several are still published each year, though with slightly diminishing frequency. It was also probably noted that in some cases magnesium given intravenously decelerated labor (it's a muscle relaxant and can act as a tocolytic), so an article was published (12), and many have followed.

We know that during toxemia and eclampsia, patients not infrequently have tachyarrhythmias, ventricular arrhythmias and other problems, and it's my bet that somebody noticed when intravenous magnesium was given for toxemia, it helped arrhythmias as well, so we began seeing articles addressing those issues (4,5,6). Serendipity. And those principles blossomed.

As I mentioned, from 1998, the magnesium references I cite are listed by category, so you can look them up easily without specific reference numbers. I will, however, cite a few of these articles here to bring your attention to the importance intravenous magnesium has gained over the years for the treatment of many conditions.

Anesthesiologists have found that intravenous magnesium can reduce the amount of anesthetic given to patients (228, 233, 234), reduce post operative requirements for

analgesics (231, 232) and may be used to produce hypotension when necessary during operative procedures (235). It has been found to facilitate endotracheal intubation (228).

Intravenous magnesium has been life saving in the treatment of ventricular and atrial cardiac arrythmias in many types of situations (262, 264, 265, 269, 275, 279, 285, 288, 289, 293, 295, 300), for ventricular arrythmias associated with open-heart surgery (298) and for atrial fibrillation associated with cardiac procedures (263, 264, 267, 270, 271, 272, 274, 283, 284, 258). IV magnesium has been proven to decrease the incidence of death for patients with acute myocardial infarction (268, 273, 276, 277, 282, 286, 287, 292, 299). I feel that it should be *routinely* given to all cardiac patients entering the hospital with any type of chest pain, but it usually isn't.

Magnesium has been extensively used in the field of neurology and neurosurgery. It has been shown to reduce vasospasm in patients with subarachnoid hemorrhage (303, 314, 315, 316, 319, 320, 321, 322, 324, 328, 329, 332), beneficial for patients with idiopathic sudden sensorineural hearing loss (331), be an effective treatment for patients with migraine headache (334, 336, 338, 340), and effective for patients with neuropathic pain poorly responsive to strong opioid analgesics in patients with cancer and other types of pain (330, 333, 341). It has been shown to be highly effective in the treatment of chronic low back pain (Magnesium has also been found to play a role in the treatment of peripheral neuropathy secondary to chemotherapy (303) and in the treatment of status epilepticus (307). Other studies abound.

IV magnesium has also been valuable in postoperative pain management for patients undergoing thoracotomy (357), and it is safe for moderate, persistent pulmonary hypertension of the newborn (358).

Variously, IV magnesium has been shown to be helpful for the treatment of patients with tetany in severe tetnus (360) and reduce the morbidity for patients with sickle cell pain crisis (364). It has been shown that it can relieve the intractable pain of trigeminal neuralgia when given IV with lidocaine for an hour, once weekly for three weeks (305).

The use of intravenous magnesium in the field of obstetrics and gynecology has become legion. It has been used IM since before I was in med school (1969) to lower blood pressure in women with eclampsia and toxemia, and is now used commonly IV (344- 354).

In addition, intravenous magnesium is now used commonly used to slow or stop premature labor (347, 350, 351).

I use IV magnesium chloride (1-3 grams) most commonly in my office for patients with low magnesium, most who present with difficulty swallowing. It used to be a problem seen in patients over 60, but now I'm seeing it much more commonly in much younger patients, many under age 40. An article from 2014 points to the danger of giving magnesium to elderly patients with myasthenia gravis (303). So we must all be acutely aware of this problem before we give it to a patient with dysphagia.

The bottom line: intravenous magnesium has been proven to be effective for scores of conditions and likely will continue to appear frequently in the medical literature for the treatment of many others.

I don't use magnesium sulfate in my office, but instead use magnesium *chloride*. This is because magnesium sulfate not uncommonly causes patients to have a headache. This is likely because some patients don't detoxify sulphate as well as they do chloride, and especially environmentally ill patients. When we used to use the sulfate form in our IV workshops, it soon became apparent that some participants complained of a headache after the workshops. So for many years I've used the chloride form instead – still very inexpensive. The standard concentration of MgCl is 200 mg./ml as opposed to 500 mg./ml in the sulfated form.

If you decide to use the chloride for this reason, please remember that you shouldn't give it intramuscularly (IM) because it stings and burns significantly. For IM use, I'd advise the sulfate.

Molybdenum

Molybdenum has a primary function in the enzyme, sulfite oxidase, and converts sulfite to sulfate. Many asthmatics are sensitive to sulfites. Dr. Jonathan Wright, in 1989, published an article describing the benefit of intravenous molybdenum to treat chronic asthmatics (19). In my own published article describing the treatment of acute and chronic asthma, I felt molybdenum played a significant role in the positive results we achieved with the use of intravenous molybdenum as part of my protocol for chronic asthmatics (236).

N-Acetyl Cysteine (NAC)

NAC has been shown to prevent and reverse hepatic damage, and articles are becoming more common. It is perhaps best known for its life-saving properties in the treatment of acetaminophen overdosage, now the most common pharmaceutical poisoning in the U.S. (375, 389, 390, 402, 406, 408, 412, 375, 379, 380). It has also been shown to be hepatoprotective and effective to treat ischemic hepatitis (394, 410, 413), and preventative for liver ischemia in hepatic surgery (381). It has been shown to be effective in treating aluminum phosphide (used as a fumigant) poisoning (375).

NAC has been shown to benefit patients with alcoholic hepatitis and used to treat and prevent contrast induced nephropathy (414).

NAC has been shown to be effective in treatment of a case liver failure associated with Dengue fever, most important since this mosquito-borne disease is being reported with increasing frequency in the souther USA (375). It also has been used for treatment of severe Amanita phalloides (mushroom) poisoning in a child (375).

NAC has also been shown to lower total plasma homocysteine in patients undergoing cardiac procedures and has a strong reno-protective effect (391, 392, 396, 397, 403). It has shown to be useful in the treatment of patients with end stage renal disease (393).

Many patients have adverse or fatal reactions to contrast media injected for many common precedures done for various reasons in the USA. Perhaps one of the most extraordinary uses of NAC has demonstrated that it can be used both as a preventative and in the treatment of otherwise fatal nephropathy caused by contrast media (400, 404, 405, 407, 411, 382).

NAC has been shown to improve pulmonary function in patients during off-pump coronary bypass surgery (383).

Phosphatidyl Choline

Although only one clinical reference has been published (445), phosphatidyl choline (Lipostabil®) has been somewhat beneficial for patients with multiple sclerosis in my practice, and other physicians have had success with ALS and other neurological diseases.

Interestingly, Lipostabil is now being used for "body contouring" – it allegedly dissolves fat when delivered subcutaneously – and a case was reported in 2011 of acute renal failure and liver dysfunction after injection of 3.5 gms. (70 cc) in both gluteal regions (442).

Sodium Bicarbonate (Bicarb)

Every physician is familiar with the administration of Bicarb during cardiac resuscitation to ameliorate acidosis. Those references are numerous in the medical literature, and are not included in this Guide.

On the other hand, sodium bicarbonate has other significant benefits, and has been used successfully to treat many types of poisoning and toxicity (primarily acidosis), including those due to amitriptyline and other tricyclic antidepressant overdoses (415, 426, 436), poisoning due to indoxacarb (an insecticide) poisoning (417), Metformin-associated lactic acidosis (422, 432), salicylate toxicity (423, 415), diabetic ketoacidosis in children (429), citalopram-induced junctional bradycardia (433), life-threatening asthma in children (436), acute strychnine poisoning (437), diphenhydramine-induced wide complex dysrhythmia (441), contrast-induced nephropathy (416), treatment of refractory cancer pain, (418) and many other conditions.

Thiamine

IV Thiamine has been used, of course, for the treatment of Beriberi (rare today) (446). There have also been several reports of the use of intravenous thiamine for the treatment of Wernicke's encephalopathy, usually associated with chronic alcoholism (450, 453, 455).

There has been a case report of treatment with IV thiamin for severe lactic acidosis and thiamine deficiency during total parenteral nutrition (456).

We do not use thiamine in my office at higher concentrations than found in the available B-complex (100 mg./ml), as there are reports of anaphylactic-type reactions with higher and even very low doses of thiamine (446). After review, it appears some of these reported incidences could be related rather to a preservative in the early reported cases.

In summary, there are growing multitudes of reliable studies in the medical literature concerning the use of intravenous nutrients that all physicians can read. It never ceases to amaze me how few "conventional" physicians are aware – and make use – of any of these studies.

As I stated before, the primary reason that intravenous therapy with nutrients is not "mainstream", is that there is really no money in it. Physicians don't receive visits from representatives selling intravenous nutrients, but rather by representatives from the drug industry. This industry runs much of the country now. Just watch the evening news.

Chapter 2: IV Therapy with Nutrients – Dosages, Safety, Precautions, Contraindications, Treatment of Adverse Reactions

Dosages of Nutrients to Use for IV Therapy

When I employ IV nutritional therapy in my office, I often use doses of nutrients simply in the "normal" (or RDA) suggested oral range. A normal oral dosage, but given IV, goes much further than it would if given orally. On the other hand, frequently it's important or necessary to use *pharmacological* doses of nutrients, especially for catastrophically or seriously ill patients. Ascorbate (Vitamin C) is a good example. For an acutely ill patient, we will often use dosages of ascorbate in the 50- to 100-gram range. For magnesium, the dose can range from 1 to 4 grams (or even more) intravenously.

For many of the nutrients we use, we often don't really know how or why exactly such large doses work. We do know, for example, that a high cellular concentration of ascorbate can be viral-toxic, hence there's a good reason it can work for acute mononucleosis and other acute viral illnesses. I'm usually strictly a clinician, so although I'll include up-to-date references, much of what you will read in this Guide is clinical common sense advice and instruction resulting from many years of experience, complete with formulas and sources. Unfortunately, there's still very little literature about the effect of IV therapy with *mixed* nutrients, which often likely act in concert with one another.

Safety of IV Therapy

Any time one uses IV techniques of any kind, there are certain caveats. Theoretically, and actually in real life, giving a patient an absolutely pure, isotonic, intravenous injection of any essential water soluble nutrient - except perhaps an incredibly massive dosage - could not possibly do any harm. These are, after all, essential nutrients; without them we would die. An injection of a pure essential nutrient, all other things aside, could not possibly be harmful. The only problems that arise from IV therapy generally stem from preservatives in the solution or from the osmolarity. In actuality, however, when these agents are used correctly, and this Guide is followed closely, problems from these factors are extremely rare.

Many of you have not used nutrient IV therapy yet because it is not accepted as the "standard of care." However, this is changing, and the references in the medical literature continue to grow yearly. At last estimate, I've given somewhere over 20,000 IV nutrient injections in my office. Actual reactions to IV therapy in my office are now essentially nonexistent, and the few true adverse reactions I've seen have been exclusively due to preservatives rather than any nutrient itself. More about that later.

I remember how nervous I was when we gave our first IVs in the office. But after I personally gave 4 or 5, I calmed down a bit. After about the 20th, patients finally stopped asking me why I looked so "pale." Now my office staff handles most of the IVs. As I said, we have recognized that IV nutrient therapy is one of the safest things we can do in our office. You will find this, too – all you have to do is get on with it.

I've spoken on several occasions with Dr. Jonathan Wright, and I've heard Dr. Alan Gaby state numerous times that neither physician has seen a severe reaction when using their IV protocols, some of which I'll mention. At the present time, physician members and Fellows of the American Academy of Environmental Medicine (AAEM) and the American

College for the Advancement of Medicine (ACAM) are by far the largest groups using intravenous therapy with nutrients in the country.

Use Preservative-free nutrients

I did encounter some problems that concerned me when I first started using IV therapy with nutrients, and these appeared to be true "allergic" reactions during administration of the IV itself. This occurred twice in our office in the early days, and both of the patients were asthmatic. Both reacted with typical allergy-type symptoms: sneezing, watery/itchy eyes, some facial edema (mild), redness, itching of the throat, and – in one case – mild urticaria. These reactions were of sudden onset, and were unquestionably from the IV materials. Neither patient needed emergency care, and we're all trained to handle that, should they have needed it. On the other hand, neither of these patients had an overwhelming desire to continue with further parenteral therapy.

Both IVs involved employed nutrients containing a *preservative,* and both were likely due to benzoyl alcohol. At that point in my experience, I didn't know whether preservatives were important or not, so I talked with Dr. William Rea, a colleague of mine who I knew at that time used IV therapy. Bill set me straight and said he *never* used IVs with preservatives for exactly the reasons I observed. On the other hand, delayed reactions with increased symptoms after an IV are not totally uncommon, but it's likely a "detox" reaction and I'll discuss this later.

A simple moral has come out of this story: **use only preservative-free nutrients**. Although the reactions I observed with preservatives were not life threatening, they certainly could have been. I had been gravitating to mostly preservative-free nutrients, anyway, but these experiences drove the point home. You can obtain any preservative-free nutrient from qualified compounding pharmacists, and a few manufactured nutrients – usually in single dose vials – come without preservatives.

I have also found – also via other IV users beginning to use our protocols – that some patients are intolerant to the discomfort some solutions cause during administration. This usually pertains to hypertonic solutions, but not necessarily so. I have adjusted the pH of all of my protocols with sodium bicarbonate to a level most patients tolerate well (pH 6.8). These appear in the IV protocol list.

We've also found that $MgSO_4$ occasionally causes headaches in sensitive patients when used in any of the protocols here. Magnesium chloride doesn't appear to do this. Hence, I now use magnesium chloride rather than magnesium sulfate (500 mg./ml) in all of my IVs. I compound my own MgCl in my office at 500 mg./cc. You can, however, obtain MgCl in a standard concentration of 200 mg./cc from several sources, and compounding pharmacies generally stock this as their "standard" dose. If you use MgCl (200), it requires a larger volume to obtain the same dose as $MgSO_4$ (500). In other words, if you want to administer 2 grams of magnesium chloride at 500 mg. per cc, you'd use 4 ccs. If you want to give the same dose using magnesium chloride at 200 mg. per cc, obviously you use 10 ccs.

Magnesium chloride does not appear to cause more discomfort than the sulfate when given IV, *but it certainly causes more discomfort when given IM*. Advice: *don't give the chloride IM*.

Now that I've touched upon the "worrisome" parts, let me give you some of the good news.

IV Therapy Makes Patients Love You

In this Guide I'm going to give you IVs for "all occasions". Perhaps the most gratifying thing you will find with IV therapy is that you will now be able to have a new patient, seeing you for the first time, leave your office feeling much better than when he or she came in. It's nice to have happy patients who think their physician can perform miracles. They tend to tell their friends. (They tend also to tell their other physician, who invariably attributes the results to coincidence. But I suppose we can't all be smart).

On the other hand, those of you who have a working relationship with the other physicians in your area will be able to develop some coordinated investigation. For example, I have a patient who had had an angioplasty, was still having intractable angina, and was all set up to go for a bypass. With his physician's permission (not his cardiologist's), I placed the patient on a combination of IV and oral nutrient therapy. His angina improved immediately and disappeared completely within 4 weeks, after which time I began chelation, and his physician reported me to the Board. No, just kidding here. But as I mentioned, IV therapy works quickly – often immediately – and that impresses patients no end. If only I could impress my traditional colleagues as quickly as I do my patients – but I'm sure none of you has that problem, do you?

Laboratory Testing for Nutrients

We have all heard about sophisticated tests available to evaluate a patient's status of micro- and macronutrients espoused at our meetings, and certainly some may be valid. The sad truth is that many are not, and insurance companies do not cover most of these tests. It's my personal feeling that "loading" or "challenge" tests are the best, but I don't feel that when I perform any *in vitro* test for, say, molybdenum, that I'm getting a true picture of a patient's status.

Insurance companies do pay, for example, for *serum* magnesium testing. The problem is that, once a patient's serum magnesium is found to be low, the patient is already in dire straits and at very high risk for a cardiogenic event. Serum magnesium does not fall below the normal range until a patient is very seriously magnesium depleted. Believe me when I say that most of the patients we see are magnesium deficient, and if you doubt that, you can always do a magnesium loading test.

It's not my intention to pooh-pooh the available tests for nutritional status, as they're all we have (aside from electro-diagnostic methods), and some may be valuable. I'm just saying that it's a new frontier, we have a lot to learn, and – most importantly – "normal" for one person could be verhy bad for another. Certainly, if several tests indicate a nutrient is low, it's likely low. So where does this leave us in regards to IV therapy?

Use of IV therapy will not be generally dictated to you by a patient's compromised nutritional status as determined by a laboratory analysis, but instead will be based on your clinical expertise and experience. Many patients who benefit from IV therapy would test in the "normal" range for many or even most nutrients. Here again it's the pharmacological dosage that seems to bring about the benefit, rather than a physiological dosage. For those patients who are deficient, however, some tests may prove valuable to monitor therapy.

This Guide will give you practical, step-by-step instructions to augment your practice with IV nutrient therapy so you may further help your patients. I will include lists of materials required, sources for all your needs, and idiot-proof instructions, so you can train your laboratory monkey to do all this, if you don't have a nurse or technician. My patients get a bit disturbed when my chimp (Oscar) starts their IV, but they get used to him – eventually. I am kidding here, but it's almost that easy.

Contraindications to IV therapy

- Absolute
  - Allergy or sensitivity to a nutrient. This is *extremely* rare (so much so that I doubt it exists) since true "allergy" to a pure nutrient itself is physiologically impossible, no matter what your chemically-sensitive patients might tell you. Most all IV nutrients are synthetic; however, commonly available (IV) vitamin C is produced from fructose. Since fructose may have traces of corn or other allergens, it's remotely possible a rare patient may be unable to tolerate it. Corn-free Vitamin C (beet, tapioca, artichoke, other) is available (non-sago) from several suppliers, but is more expensive when compared to "regular" Vitamin C. I have used corn-based vitamin C for many, many years without incident.
  - High dosages of certain nutrients. Unpleasant or severe reactions are common from higher than physiological doses of certain vitamins. Niacin and thiamine are good examples, and anaphylaxis to high-dose thiamin has been reported. I would not advise administering dosages of nutrients higher than those discussed in this Guide.
- Relative: mostly danger from *hypo*tonic solutions
  - *Severe* red cell fragility disorders
    - Thalessemia Major (the most possible)
    - enzyme disorders of the red cell (glucose-6 phosphate deficiency, others (possible)
    - spherocytosis (possible)
    - sickle cell anemia (doubtful)
  - *Severe* environmental illness: these patients often must be started on IV therapy very slowly, and be built up to higher dosages slowly. These types of patients, when they react adversely, have the most problems with the "B" vitamins. Surprisingly, most patients with severe problems may be started immediately on the "SuperImmuno" Protocol, as it appears to have enough detoxification ability to prevent significant adverse reactions (the glutathione protocol is usually tolerated by similar patients as well).

Possible Reactions to IV Infusions

The most common adverse reactions to an IV of any type are vasovagal ("fainting"). This usually will occur with an IV "push" (more rapid infusion) containing magnesium, which can cause a rapid fall in blood pressure. This is quite easy to distinguish from an anaphylactic response.

Vasovagal reactions and a patient's blood pressure plummeting with a rapid infusion of **magnesium** is characterized by:

- Pallor
- Cold, clammy feel and look
- ***Slow***, faint pulse with corresponding drop in BP

Anaphylactic reactions, on the other hand, are characterized by:

- *Redness of the eyes* and often the skin
- Anxiety, sometimes with flushing
- ***Rapid*** pulse with falling blood pressure

Treatment of Adverse Reactions

- For *true anaphylaxis*, give 5,000 to 10,000 U of aqueous heparin rapidly IV and institute standard emergency procedures. Heparin interrupts the complement cascade and has the ability to stop anaphylaxis rapidly. Give adrenaline if heparin fails. The chances you will ever see this from IV nutrient therapy, if you follow the guidelines in this syllabus, are *extremely remote*.
- Elevate the feet/legs (IVs are best given in a lounge-type chair for this reason)
- Smelling Salts – should always be on hand in any office where needles are used.
- Administer O_2, 3-6 L/min.
- Slow the IV until the patient has recovered. Since virtually all reactions are vasovagal and secondary to an over-enthusiastic (too rapid) infusion of magnesium, the push or infusion may be re-instituted once the patient feels well again (obviously you must be certain this problem is vasovagal and not of the more severe type before you do this). This may take 15-30 minutes (or sometimes more).
- **Note**: this is not necessarily true with *alpha lipoic acid*; side effects and reactions to this nutrient are not uncommon, and I do not employ it in my office.

The Safety Record for IV Nutritional Therapy

- True anaphylaxis has never been documented with *preservative-free* nutrients, other than thiamine (high dose).
- I have given well over 20,000 IV treatments in my offices, and I have never seen anaphylaxis. The few allergic reactions we have seen have *always* been traced to preservatives, either before we stopped using them, or accidentally given when a manufacturer changed a nutrient.
- Other physicians using IV therapy with nutrients have had similar experiences.

Again, DO NOT USE *ANY* NUTRIENT WITH A PRESERVATIVE. If you use a commercial amino acid mixture, such as Travesol® and FreAmine® (which have a preservative), it's wise to use it with a protocol that has a *significant ability to detoxify*, such as the example "SuperImmuno" in this syllabus. Compounded amino acids without preservatives are available from compounding pharmacies, but are more expensive.

In the next chapter, I'll go over some general rules, enumerate a list of general and specific supplies to have on hand, and give you the protocol I use most often in my office. Now I know most of you use other time-tested methods that often can accomplish the same objective. However, you will discover very quickly that the addition of IV therapy to your

traditional techniques will give you a tool that will repeatedly go beyond most you have learned in the past.

By the way, some insurance companies will cover IV therapy with parenteral nutrients, and I'll give the specifics for how to bill for this procedure. I will cover such topics as the IV treatment of acute viral infections of all varieties, CFIDS, severely immunologically compromised patients, cardiovascular disease, eczema, urticaria, arthritis, "E.I." and other problems we all see on a regular basis.

In conclusion, there's no question that office IV nutritional therapy is simple and it's safe. It won't interfere with anything you already do. It can allow you to treat patients who are now on your "hopeless" list (it certainly has for me!). It will enable you to treat problems that no other physician is able to treat – with or without powerful drugs. Finally, it can often be a useful tool to allow your patients who are doing "well" to do even better. No physician who practices integrated medicine should be without it, and if I can help it, you won't!

Chapter 3: Calculation of Osmolarity

Before we get into the protocols to be covered here, which you will be able to alter at will (and I hope you do), I need to cover the important issue of osmolarity. Whenever you give an IV of any kind, you need to understand the basics of this issue. The principal is really quite simple. IV solutions should, whenever possible, have the same osmolarity as plasma (isosmolar or isotonic). This prevents pain, venous irritation and avoids exacerbating illnesses where red cell fragility is an issue.

In this chapter, I'll give you the protocol I use for "migraine" headaches, but which works well for "tension" headaches also, or as an old German friend of mine used to say, "your basic" headache.

Osmolarity

IV solutions should optimally be in the range of that of plasma, which is typically between 280 and 310 milliosmoles per liter (mOsm/L), or .280 to .310 milliosmoles per milliliter or cc (mOsm/ml). Solutions more dilute than this should be avoided because significantly hypo-osmolar solutions can be dangerous or even fatal if administered. I like to keep all of the solutions I use above .31 mOsm/L. Hyper-osmolar solutions are tolerated by most patients, but the higher the osmolarity, the more slowly a solution needs to be given, the larger the vein for infusion must be, and the more likely it is that your patient won't be a happy camper because of discomfort. We try to keep many of our solutions in the isotonic range, but we don't worry much when they are slightly to moderately hyperosmolar, primarily when considering convenience for all concerned. Here are the limits for IV administration:

Safe upper limits of osmolarity *for IV solutions (approximate)*

	Large vein	Medium vein	Any vein
IV Push (mOsm/L)	**1400**	**950**	**400**
IV Infusion (mOsm/L)	**1200**	**600**	**400**

Most patients tolerate solutions of 400 mOsm/L or less easily in any vein, even when given rapidly, so we try to stay below this range for several of our protocols. Remember, the stronger the solution, the more likely that it will cause pain or even sclerosis of the vein (hypotonic solutions can cause sclerosis, too). My protocols for cancer are generally higher than this, but it may be that the large doses of Vitamin C don’t harm veins as much as other solutions.

I've found that there are certain nutrients that might cause discomfort for patients even when the solution is isotonic, especially when used alone, but also when mixed with other agents. These are pyridoxine HCl (B-6), B-Complex, thiamine, dimethylglycine (DMG) and KCl (always use *extreme* caution when using this agent).

One thing to do when a patient complains of pain from an IV you know is isotonic -- after you've checked needle position -- is to add a quantity of .9% NaCl or sodium bicarb. This will usually relieve the problem.

Calculating Osmolarity

When figuring osmolarity of specific nutrients, one must take into account the diluent, solute, solvent, dissociation constant and the physical structure of the nutrient itself. So unless you're a nuclear physicist who's into frustration and biochemistry, I don't think you should try to calculate the osmolarity of *nutrients* at home - use the table that follows to calculate the osmolarity of your *solutions*. Feel free to copy the table to use for osmolarity calculation, or call my office and I'll e-mail it to you.

If you get your supplies from McGuff, they'll be happy to send you a list of the osmolarity of their supplies, which includes most of what we use. They also have a program available for a fee that will calculate the osmolarity of your solutions

Some of the osmolarities on Table 1 are approximate. In these cases, this was the best we could do, and these values were obtained from the supplier, manufacturer or laboratory. I'm sure these values are very close to the actual values, and we've had no problems using these numbers in our calculations on a large number of patients.

The values in Table 1 are for nutrients commonly available. Some are available from several companies and may contain preservative. Be sure to check that before you order any pre-packaged nutrients (we use very few pre-packaged nutrients because of the preservative issue, with the exception of Vitamin C, sodium bicarb, calcium gluconate and potassium chloride, which do not contain any harmful preservatives). If you are using *specially prepared agents* - from a compounding pharmacy, for example - you should ask them if they would supply you with the osmolarity of the items.

We actually use this table often in our office, since certain patients need variations of one of our "standard" protocols, and there are constantly new things we would like to try for a particular disorder or a particular patient. I'd advise you that when you make a copy of the table, revise it for your needs, include the formula below the table, and leave an area on the bottom of the paper for you or your nurses to calculate the amount of solution necessary to add (almost always Sterile Water for Injection). In other words, make it into an office form like we did.

Of course, you may enter the calculations in an Excel spreadsheet, so that when you fill in the amount of each nutrient you want to administer, it automatically calculates the amount of water to add. If you'd like a copy of mine, I'll be happy to e-mail it to you (wshradermd@aol.com).

Table 1: Osmolarity Calculation Worksheet for Commonly Used Nutrients

IV Additives	mOsm/mL	(multiply times:)	nutrient added (mLs)		Total mOsm
Amino Acids (FreAmine III 8.5%)	0.81	X	cc	=	
Ascorbic Acid 500 mg/mL	5.80	X	cc	=	
B-6 (Pyridoxine) 100 mg/mL	1.11	X	cc	=	
B-12 (hydroxocobalamine) 1000 mcg.*	0.31	X	cc	=	
B-Complex 100 mg/mL	2.14	X	cc	=	
Sodium Bicarbonate 8.4%	2.00	X	cc	=	
Calcium Gluconate 10% 100 mg./mL	0.72	X	cc	=	
Sodium EDTA 150 mg./mL	1.34	X	cc	=	
Folic Acid 10 mg./mL	0.20	X	cc	=	
Germanium 100 mg./mL **	0.25	X	cc	=	
Glutathione 100 mg./mL ***	0.38	X	cc	=	
Heparin 5,000 U/mL	0.46	X	cc	=	
HCl (hydrochloric acid) 2 mg./mL)	0.11	X	cc	=	
Lactated Ringer's	.28	X	cc	=	
Magnesium Sulfate 500 mg./mL	4.06	X	cc	=	
Magnesium Chloride 200 mg./mL	2.95	X	cc	=	
Mineral Mix (Dr. Shrader's)**	0.57	X	cc	=	
Molybdenum 500 mcg./mL **	0.80	X	cc	=	
Pantothenic acid 250 mg./mL	0.85	X	cc	=	
Potassium chloride 2 mEq/mL **	4.00	X	cc	=	
Selenium 200 mcg./mL **	0.09	X	cc	=	
Taurine 50 mg./mL.	0.50	X	cc	=	
Zinc 10 mg./mL **	0.50	X	cc	=	
TOTALS FOR ADDITIVES:			**cc**	=	

* Do not mix with copper (becomes deactivated)

** Do not ever give IV push

*** Do not mix with vitamin C. Not very effective if given by infusion. Give IV Push for appropriate effect.

DESIRED OSMOLARITY RANGE = 280 to 310 mOsm/L (.280 - .310 mOsm/mL)

Osmolarity of common additives:

DILUENTS	mOsm/mL
Water, sterile	0.00
NaCl (.9%)	.31
Lactated Ringer's	.28

Osmolarity Calculation Formula

To figure the number of ccs of Sterile Water to add to create a desired osmolarity of .310 mOsm/mL (upper range of plasma) (explanation to follow):

$$\frac{\text{Total mOsm of Additives}}{.310} - (\text{Total ccs of additives}) = \text{ccs of water to add}$$

*A *negative* number for the answer indicates a *hypo*-osmolar (hypotonic) solution. To figure the number of ccs of NSS (.9% NaCl) to add to bring the hypotonic solution to the desired osmolarity, *divide* this *absolute* number by .031, and add that amount of NSS. If NSS is used as the IV solution, you must calculate the NSS as you would **an additive,** and "**ccs of water to add" as 0 (zero).** Do the same if you were to use Lactated Ringer's.

Calculating Osmolarity (with examples)

Let's assume we have a patient to whom we would like to give the protocol below, which is my headache protocol:

Headache Protocol

Nutrient	**Amount to add**
Magnesium chloride, 2 grams (200 mg/ml)	10 cc
B-6 (pyridoxine), 500 mg (100 mg/ml)	5 cc
Calcium gluconate, 200 mg (100 mg/ml)	2 cc

This protocol often works well for "classic" migraine, but also often works for "garden variety" and "tension" headaches. To help learn to calculate osmolarity of IV solutions, we'll calculate how much water you need to add to this protocol to make it isotonic. Note: most magnesium infusions that you want to be acutely therapeutic should be given rapidly enough to cause some moderate "flushing" symptoms. So these must be given IV *push*.

The formula, expressed in words, is: Total mOsm of all the nutrients you put in, *divided* by .310 (mOsm/ml, which is the upper end of "normal' plasma osmolarity) *minus* the total ccs of all the nutrients you put in (mOsm cancels out) *equals* the total ccs of sterile Water for Injection that needs to be added to the syringe or the IV with the nutrients you've added. Refer to the bottom of Table 1 for the formula to use for calculation of water to add. *We use water because the osmolarity of water is zero; normal saline usually will produce about twice the osmolarity as water does*.

In the example above, place the number "10" (cc) in the **nutrient added (mLs)** column, in the magnesium chloride (200 mg/ml) row. Multiply this by 2.95 (the mOsm/ml of 200 mg/cc magnesium chloride), giving a value in the "mOsm" column of 29.5. Repeat this with 5 cc of B-6; you multiply it by 1.11, which gives 5.55 in the "mOsm" column. You're using 2 cc of calcium gluconate, and you multiply that by .72, which gives you 1.44 in the "mOsm" column. Not Einsteinien so far.

So, you add up the columns, and here is what you should have in the "Totals for Additives" row at the bottom of the table:

Total quantity of ccs of additives: **17**

Total **mOsm** of additives (29.5 + 5.55 + 1.44): **36.49**

Applying the formula, you divide 36.49 by .310, getting a preliminary result (I hope) of **117.7**.

You then subtract the total ccs of your additives (**17**), and this gives you **100.7, which is the number of ccs of Sterile Water to add to your nutrients to make the solution isotonic** (you can round this to the next higher or lower number). Now you could draw up your 17 ccs of additives into a 60 cc syringe. But wait – where then would the 100.7 ccs of water go? There's not enough room in the syringe.

So we must fudge. Since seems logical to put this in a 60 cc syringe, we'll do that. But first we have to make sure the solution is not too hypertonic. To do this, we use the same formula, but instead of calculating the amount of water to add to make this push isotonic (osmolarity of .310), we need to calculate the resultant *osmolarity* if we only put this in a 60 cc syringe. So the osmolarity is the unknown.

To do that, let's figure how much water we would *actually* add by using a 60 cc syringe. That will be 43 ccs, because 60 minus 17 equals 43 cc. Now plug this into the formula. Instead of dividing 36.49 by .310, you have to divide it by "X". Using the formula again:

Total mOsm of Additives – (Total ccs of additives) = ccs of water to add
.310

$\frac{36.49}{X} - (17) = 43$ (since we now know this number)

So, 43 X = 36.49 – 17 (you have to cross-multiply), or

and 43 X = 19.49, so

$X = \frac{19.49}{43}$

and X = .451

Since we know that an IV push with an osmolarity of about 400 is within safe limits of tolerance to inject in any vein, we find that it's certainly OK to do this in a medium vein.

As you'll see if you look on the protocol table later in this Guide, we *actually* use a 30 cc (holds 35 cc) syringe and three grams of magnesium rather than two. So the osmolarity is much higher and this protocol should be given in a large vein. If you try to give this in a 60 cc syringe, it simply takes too long to cause significant vasodilation.

This push must be given in only 10-15 minutes, and some flushing must occur. If you don't see flushing, it won't work.

Let me stress here: do **not** use NSS, half-normal saline or Ringer's Lactate as your diluent! This would make your solution too hypertonic. Rarely if your patient were to complain of significant discomfort with a lower osmolarity IV, you could try to add some NSS or half normal saline. For reasons unknown, I've found this to work once in a while.

In the example above, if you wanted to give a smaller volume (if you have a "tolerant" patient, for example), remember you sometimes may increase the osmolarity of a solution further if you have a *larger vein* with which to work.

So you can also mix and match this formula again, probably like you hated to do in high school, and calculate different answers (or ask different questions). Let's say you wanted to give this IVP in a *30 cc syringe* (which actually measures to 35 cc). You simply make the osmolarity your unknown value (X) again, rather than the quantity of water to add. For the example above:

$\frac{36.49}{X} - (17) = 17$ (since we know this number)

So, 17 X = 36.49 – 17 (you have to cross-multiply),

and 17 X = 19.49, so

$$X = \frac{19.49}{17}$$

therefore, X = 1.14 (1140 mOsm/L)

Since the safe upper limit is 950 of a medium vein and 1400 for a large vein (antecubital), you can give this push in a 30 (35) cc syringe in a *large vein*. OK?

You can also answer questions such as, "What's the most ascorbate (500 mg/ml) I could give in 250 cc of Sterile Water for Injection without exceeding an osmolarity of, say, .310 mOsm/ml? You get the answer as follows: (5.80(X)/.310) - X = 250, where X is the number of ccs of ascorbate you're going to add. So (18.71X) - X = 250, so 17.71X = 250, and X = 250/17.71, which is 14.12 cc, or about 7 grams of Vitamin C (if your ascorbate is 5.8 mOsm/ml -- which it probably is). This translates to about 28 grams per liter for your solution to be isotonic. As you'll see, many of our IV protocols use considerably more ascorbate than this, even up to 100 grams per liter (50 grams/L gives an osmolarity of .57 mOsm/ml). Interestingly, many patients tolerate this solution when it is run in quite quickly (1-1-1/2 hours), but when you add some of the "irritating" agents mentioned previously, the infusion rate must often be reduced considerably.

Again, you computer whizzes out there might want to plug these values into Microsoft Excel or another spread sheet. Your staff could just plug in the ccs being used, and you could come up with the water to add with the stroke of a key. We've done this in our office, and it makes work easier. We'll e-mail this Excel program to you, if you wish.

The protocols in this Guide, no matter which you choose, should always be complimented with a high quality daily multivitamin and mineral supplement. In our offices, in addition to our daily multivitamin/mineral supplement, I tend to add 15-50 mg. of zinc picolinate, Unique E ® (a special brand of vitamin E with mixed tocapherol), ARG's CoQ10 with tocotrienol, both 2-3 times a day, 3000-5000 units of vitamin D3, and 1000 mg. of Tyler Encapsulations' Eskimo 3® (EPA) or Nordic Naturals ProEPA®.

Chapter 4: General Instructions and the Meyer Protocol

The express purpose of this chapter is to give you a protocol to start using in your office right away that will make you comfortable using IV nutrient therapy. Many of your patients desperately need it, and if you know exactly what to do and when to do it, you'll be able to provide relief for a significant number of patients whom no other physician has been able to help. That's one of the things that makes "alternative" medicine so much fun, isn't it? Well, nutrient IV therapy is a tool that will give you that extra edge.

This chapter will go over the basics you will be using for all of your IV therapy, and in the next chapter I'll specifically give you the protocols we've been using to treat our patients with acute and chronic asthma since the 1986 (236). The first is an IV "push" (IVP) protocol, and the second is an augmentation of the same protocol, given as an IV "drip" or infusion.

The Two Fundamental Rules for IV Therapy

1. **Rule #1**: You should have on hand all emergency equipment necessary to treat a patient who might have an anaphylactic reaction in your office. This would include oxygen, Ambu bag, airways, heparin, adrenaline, and the other necessities we all hope we will never have to use. The emergency equipment you need is no different than you should have for any emergency that could arise in a physician's office.

   If you and your staff are not familiar with the emergency procedures used to treat a possible anaphylactic reaction, you should not be testing with allergens, treating with allergens, administering injections of any kind, or giving IV therapy of any kind. Your CPR training should be current, as should that of your staff.

2. **Rule #2**: That being said, if you ever have to use any of your emergency training or equipment for an emergency, it will be much more likely to be for a patient you are testing or giving an allergy shot than for one to whom you are administering an IV. Many of the IV materials we will discuss can actually serve as an augmentation to the emergency equipment you already should have. So, the first amendment to Rule #2 is that you will not likely have to utilize Rule #1.

IV therapy with essential nutrients, when done properly, is one of the safest things you can do in your office, not to mention one of the most powerful. Once you begin with even the basic protocol included in this chapter, I promise you'll wonder how in the world you ever did without it. The results of nutrient IV therapy can't really be compared to oral therapy. Nutrients simply act differently when you are able to produce serum concentrations dozens to hundreds of times what you could achieve with oral administration. It opens up a whole New World.

Basic Supplies

Your basic supplies for administering all of your IV pushes and infusions in the office are as follows:

1. Syringes: 60 cc, 30 cc, 10 cc for withdrawing solutions from vials and bottles, and for administration. We use B-D or Terumo syringes with luer-lock tips and 18 gauge No-Kor needles for drawing up solutions, but there are certainly many other choices. For the IV discussed in this chapter, you'll need just a 30 cc syringe.
2. Winged infusion sets, 23 and 25-gauge ("butterflies"). Patients get very uneasy if they see you coming at them with a 30 cc syringe (not to mention the difficulty holding the syringe if it were to have just a needle attached during a 10 minute push), but a winged infusion set seems to be easily accepted. The 23 or 25-gauge sets are used for adults, and the 25 gauge sets are used for kids, "difficult" veins, and small volume delivery (< 35 cc). If you are giving a 60 cc injection, you won't be very happy using a 25-gauge needle. Also, don't purchase the short 6" infusion sets – you'll need the longer ones to give you more room to work. The butterflies are also used for most drip infusions. We sometimes use a 24-gauge intracath, but this is not necessary for an IV push. The butterfly-type intracaths are also very nice, and may be used for IV infusions (which can take several hours), but they're more expensive. However, for short IVP protocols, a butterfly is adequate for your patient.
3. 60" IV administration sets. You should use "vented" administration sets with the simple chamber.
4. Needles: All you need are 18 gauge No-Kor 1-1/2" needles. Regular needles are much more damaging to rubber stoppers. 18 gauge "No-Kor" needles work best, and will never "core" out a piece of rubber from a stopper that could get into the bottle or the patient.
5. Cotton swabs, alcohol, tourniquet, and 2" x 2" gauze, hypoallergenic tape, and maybe an arm board.
6. IV Solution. This is almost always Sterile Water for injection. We keep on hand 250 cc, 500 cc and 1000 cc bags. We used to say that glass bottles were essential, primarily because the polymer from a plastic bag will always leach into the solution to some degree. In 2012, glass bottles became unavailable. There was just not enough demand for glass to warrant that the manufacturer continue producing glass bottles. We fought this on many fronts, but now apparently we seem to have lost.

   For IV pushes, we keep a 250 cc bag of sterile water in the refrigerator and draw the water we need for each push IV out of that. It will last several weeks in the fridge, as long as you use sterile technique with alcohol wiping each time you draw the water out.

   Type of plastic we use

   We use Sterile Water for Injection because I like to administer IVs as close to isotonic as is feasible, as has been explained.

   The bags carry the following warning label: "Warning: Hypotonic and hemolytic. Do not inject until made approximately isotonic by addition of appropriate solute." In other words, never use plain sterile water alone. I'm sure this is common sense to all of you,

but your nurses and technicians need to know that this *plain water is for dilution purposes only*. Do not keep it with your emergency supplies! You also will need Normal Saline (.9%, 250 cc) for some uses.

7. IV stands (poles). These tend to be expensive, so we only have only two in our office (essentially for use when a patient feels like he or she needs to walk around or go to the bathroom). You may also purchase "disposable" IV poles from several suppliers. These are actually re-usable. For much less expense, just go to your local hardware store, get some strong hooks, and screw them into the wall wherever you're going to perform your infusions (hopefully you'll be doing this soon – not just IV pushes). Be sure to put them about 6-7 feet high.
8. Somebody who knows how to start an IV.

A Word about Osmolarity

Many of the injections we administer are slightly or moderately hypertonic. There are reasons for this that will become obvious. In a perfect world, every injection you give should be somewhere around 310 milliosmoles per liter (mOsm/L), but for most IVs, that's usually not possible. And moderately hyperosmolar solutions generally aren't a problem. There are various limits, however, and this was covered. Most patients seem to tolerate moderately hyperosmolar solutions without pain or danger of venous irritation, as long as they are given properly (which can mean slowly, in a large vein).

None of the solutions included here are hypotonic, as those can be bad news because they can cause red cell lysis in certain patients, as was mentioned. Don't experiment unless you calculate osmolarity first.

Methods of Administration

The first protocol we're going to start with is given IV push (IVP). This means you, your nurse or assistant - or even the patient - administers the injection via syringe, rather than hanging an IV bottle. This will get you started with IV therapy. Once you can do this "push", you'll be able to give many of the protocols that appear in this Guide. Once you've started with these, you'll be ready to go on to other IV protocols, administered via a hanging bottle.

In reality, though IV push sounds easier, we've found that for all but the smallest of formulas, it can be a hassle. You or your nurse has to sit there for up to 20 minutes, and time is too valuable for most of us to do that all day. Once a patient has done several IV pushes, he or she can push the IV himself or herself. Many patients actually prefer this because they know how quickly they like the infusion to be given.

Many of our IVs are given by drip infusion. For now, start with a few pushes - until you feel confident - then you can go to the infusion protocols. Generally speaking, IV pushes work more rapidly than drip infusions, so on average we administer more pushes in our office and we do infusions.

One final word before we get into the actual protocols: whenever you give anything IV for the *first time* to any particular patient, you need to give the first cc or two very slowly. Then stop and wait a moment to be certain the patient is not going to have an adverse

reaction. If all is OK - and it's *extremely* rare that it won't be OK - then you may push or drip the solution as tolerated, and you may give successive IVs to that patient without doing this.

Meyer Protocol

This is a protocol that a Baltimore physician, Dr. John Meyer, developed many years ago. Alan Gaby, (who took over Dr. Meyer's practice) has taught us about this at his meetings and ours. He's been known to call it "Scurvy with a Syringe on Top". He feels it's one of the most valuable IV treatments he uses, and so do I. Both of my protocols for asthma are actually variations of this.

The protocol can be used for asthma, urticaria, CFIDS and a good number of other illnesses. *This is the protocol I use most often in my office*. It's generally given IVP in a 30 cc (actually holds 35 cc) syringe, and most patients seem to tolerate it well). I like to use both higher concentrations and slightly higher dosages of magnesium and ascorbate than Meyer's original protocol for a number of reasons.

I often give this IV as the first IV anybody gets, and I often use it on the first visit. It's the IV I use for patients who "just don't feel well", which certainly applies to most of our patients.

Meyer Protocol – given IV Push (35 cc syringe)

Nutrient	**Amount**
Vitamin C (ascorbate) 500 mg/cc	4 cc
B-6 (pyridoxine hydrochloride) 100 mg./cc	1 cc
B-12 (hydroxo- or methylcobalamine 1000 mcg./cc	2 cc
B-Complex 100 mg./cc	1 cc
Calcium gluconate 10% 100 mg./cc	2 cc
Magnesium chloride 200 mg/cc	5 cc
Pantothenic acid (pantothene, 250 mg./cc)	1 cc
Sterile distilled water	19 cc
Total volume	**35 cc**

All of the nutrients are drawn up in the 30 cc syringe and given in a large vein over about 10-15 minutes. If you are unfamiliar with this procedure, please refer to the "Push" instructions in the next chapter to get the step-by-step details.

We *almost always use this IV as our "primer,"* or first IV that a patient is given. The reason this is used as a "primer" is that when we've tried to use most of the other protocols without first employing a "priming dose" of nutrients, patients have often appeared to experience detox-type reactions, such as acute asthma, etc. We have caused 3 patients with asthma to need a visit to the emergency room the evening of the day of an *infusion* IV protocol because we didn't first use one of the primer IVs.

So use a "primer" before you give most of the infusions in this Guide.

It is also the most effective IV for the price – with the exception of the glutathione protocol, discussed later – one can give for most patients' symptoms. It is effective for

fatigue, asthma, and many other symptoms. When we use this protocol for urticaria, we then add 5,000 units of heparin (heparin is used for anaphylaxis, and works quite quell for urticaria, although the "Meyer" protocol really works quite well on its own).

Frequency: 1-3 X/week. After used once or twice, it can be followed by a more comprehensive protocol, or it can be stretched out to PRN. A significant number of patients with varying illnesses seem to benefit from this protocol when it's given on a long-term basis, and it usually can be "stretched" to longer intervals, which can be monthly to every 2 months or so. Again, this is the most common IV used in my office, and we have a number of patients who come in every so often just to receive this protocol.

Case Example:

W.E., a 73 year old male, was referred on Sept. 15, 1997, by a dietitian in Florida, for intravenous therapy for his diabetic gangrene of the left foot. He was too ill to travel to New Mexico, so I never actually saw the patient. Instead, I had numerous conversations with the patient and his wife and my nurse and myself gave directions, by telephone and by fax, as to exact treatment protocols.

Essentially this gentleman was in very grave danger of losing his left foot secondary to diabetic gangrene. When he was referred, his physician had recommended amputation, as there was virtually no circulation in the small distal vessels of the left foot (see arteriogram).

I first recommended the "Super Immuno" protocol, but it was too difficult and cumbersome for Home Health and the patient's wife to handle. So instead of using that protocol one to three times a week as I recommended, they essentially used *one* bottle weekly for three weeks. He did improve slightly at that time. When we next spoke, however, I advised that they began the Meyer protocol instead. His wife and the Home Health nurse was able to handle this easily and he received the protocol about twice a week for six weeks.

At the end of that time, his foot had returned to its normal color and to the amazement of his physician, the patient no longer required the amputation.

After several more weeks, however, the patient began EDTA chelation therapy (good "adjunctive" advice, not mine) and the family was relying very heavily on chelation treatments to reverse the arteriosclerosis. After several months (by midsummer of 1998) it became evident to the patient's wife that the Meyer protocol had worked considerably better than chelation, as by this time the patient actually had progressed to gangrene. She began using the Meyer again, and once again it helped considerably; however, the patient received the protocol only very irregularly and in Sept. 1998, ended up receiving an amputation of the fourth and fifth toes of the left foot.

My most recent conversation with Mrs. E. was 12/2/98. At that time the patient was having many other problems, but since the Meyer protocol was being used occasionally, his diabetic arteriosclerosis was under good control. We've seen many, many similar examples since then.

Chapter 5: Basic Asthma Protocols and Step-by-Step Preparation & Administration of the Push and the Infusion Protocols in your Office

IV Protocols for Acute and Chronic Asthma

These protocols, especially when combined with immunotherapy, can keep our asthmatics medication free, and usually has succeeded in getting steroid-dependent asthmatics off their steroids[Error! Reference source not found.] (236). I'll tell you about the push first, and then the infusion, and I will give you the exact details for drawing up both.

Acute Asthma Protocol - Given IV Push (60 cc syringe) with a 23 gauge needle

Nutrient	**Amount**
Vitamin C (ascorbate) 500 mg/cc	3 cc
B-6 (pyridoxine hydrochloride) 100 mg./cc	3 cc
B-12 (hydroxo- or methylcobalamine 1000 mcg./cc	5 cc
B-Complex 100 mg./cc	2 cc
Sodium bicarbonate 8.4%	6 cc
Calcium gluconate 10% 100 mg./cc	2 cc
Magnesium chloride 200 mg/cc *****	10-15 cc
Pantothenic acid (pantothene, 250 mg./cc)	2 cc
Sterile distilled water	27-22 cc
Total volume	**60 cc**

*** Do not start with 3 grams (15 ccs) of magnesium (chloride) in a patient's first IV push**. You should probably start with 2 grams (10 cc). We typically give 2 grams in the 1st push, and will then go to 3 grams in the next push or drip infusion, providing the patient has tolerated the first treatment well. Optimal dosage will vary from patient to patient, according to weight and response. Obviously, 3 grams IV push could be too much to tolerate for a tiny patient, or a patient with low blood pressure.

Chronic Asthma Protocol - Given by IV infusion (250 cc bottle)

Vitamin C (ascorbate) 500 mg/cc	12 cc
B-6 (pyridoxine hydrochloride) 100 mg./cc	5 cc
B-12 (hydroxo- or methylcobalamine 1000 mcg./cc	5 cc (******* IV Push)
B-Complex 100 mg./cc	2 cc
(Sodium) bicarbonate	17 cc
Calcium gluconate 10% 100 mg./cc	2 cc
Magnesium chloride 200 mg/cc	15 cc
Mineral Mix (Shrader's) *******	1 cc
Molybdenum 500 mg./cc	1
Pantothenic acid (pantothene, 250 mg./cc)	2 cc
N acetyl cysteine (250 mg./cc) – optional	(5-8 cc)
Sterile distilled water	250 cc
Total volume	**310 cc**

Footnotes to the preceding IV Protocols:

Note: From time to time I make revisions in my protocols. These up-to-date revisions are usually done in January, so books ordered after that are usually up-to-date.

******* B-12 and the Mineral Mix: We make this mineral mix in the office, but it is now available from College Pharmacy and other compounding pharmacies. Just ask them for Dr. Shrader's Mineral Mix. This is a mixture of most of the IV trace minerals available for IV use and contains *boron* 1 mg./ml., *zinc* 5 mg./ml., *copper* 1 mg./ml, *molybdenum* 250 mcg./ml., *selenium* 200 mcg./ml., *chromium* 100 mcg./ml., *manganese* 100 mcg./ml., *vanadium* 100 mcg./ml., *lithium* 5 mg./ml., and *strontium* 1 mg./ml. This mixture contains copper, and copper appears to inactivate B-12 when they are mixed together, so you must give the B-12 (hydroxo- or methylcobalamine) IV push at the *end* of the infusion (or you may even give it IM). If you don't have any copper in the IV, the B-12 may be mixed in the IV itself and need not be given IV push.

You may also add 3 cc of NAC (n-acetyl cysteine, 250 mg./cc) to the push, and 5-8 cc to the infusion protocols. This seems to help a great many asthmatics, and we have made it "routine" now.

Before I go further, I should mention the status of many nutrients with the FDA. The FDA "approves" a few IV nutrients, and most of those are for Total Parenteral Nutritional therapy or conditions causing severe nutritional depletion, and even that approval is unclear. In fact, when you talk to the FDA about this, there does not seem to be a generally accepted policy - at least that I've been able to find.

On the other hand, there is no question that the FDA allows physicians to give any substance to a patient via any route they choose, whether or not it is FDA-"approved" as long as: 1) it is not an illegal substance, 2) it is not procured from a "non-FDA-approved" manufacturer inside or outside the U.S., 3) it is not sold by the physician retail, and 4) it is given to a "named" patient (not given to someone for use somewhere else on "unknown" parties).

Officials from the FDA have advised me explicitly that physicians are allowed to mix most any "concoction" in their office and give it to a patient. Since the FDA very much dislikes compounding pharmacies, they will offer little or no comment about compounded products. Even though this has gone as far as the Supreme Court, and the compounding pharmacies have won the right to compound, the FDA immediately thereafter issued a warning that all compounded products had to contain FDA approved substances. Ridiculous? You bet, but remember the FDA can say anything it wants until the next time in it is challenged.

It is important that patients be advised that anything not FDA-approved is "investigational, and you may want to write a disclaimer and have patients sign a consent form. I didn't used to do this, but I do now.

There is also the question of using FDA-approved substances for non-FDA-approved uses. This is not illegal as far as the FDA is concerned, but could always be questioned by state medical review boards, and it is almost always questioned by insurance carriers.

As physicians, our first duty to our patients is to do no harm. As Environmental, Alternative and Complimentary physicians, most of us feel our second duty is to give our patients the best care humanly possible, using every method we have available, as long as what we do is safe. In our zeal to do this, most of us at some point find we must give our patients more than just drugs. The majority of the patients we see are, after all, often so sensitive or allergic to many or most drugs, we are forced to look for other avenues of treatment. Hence we turn to nutrients, which we have learned our patients not only tolerate but often desperately require. But to do this, we often tread on the edge of "traditional" medicine. I guess I'm old-fashioned, but I trust "the powers that be" will take this into account when they look into what I do for my patients. Well, at least they have in the past.

Realistically, they may not always be that way, even if our intentions are solid gold.

I've rambled a bit here, but there's a point to all of this. You need to know that there are, for reasons I still can't comprehend, physicians and "authorities" out there who feel nutrient therapy is "unscientific" (especially IV nutrients!), and unproven, at best. They are wrong of course, but everyone's entitled to an opinion. It is the US of A, after all.

The bottom line is that if you're planning to use IV therapy with nutrients, you must be prepared to be challenged by those groups who have some special interest - for whatever reason - to demand that "traditional" medicine be practiced by all. I can't tell you how angry this makes me, but I've learned to live with this attitude. Considering all this, it may be a good idea to check with your state Medical Board as to the status of this kind of therapy. There are a great many physicians who use IV nutrient therapy out there, and those of us who do know how well it can work. But it still must be considered a New Frontier, and that fact alone could make your life a bit more exciting than you might want.

That's the end of the philosophy. Just remember you're out there to give your very best to your patients. If you do it carefully and well, you'll be rewarded in many ways. I feel very strongly that the people who look askance at these methods will change, once they know you're simply trying to help patients the best way you can. Am I being naive? I hope not.

Exactly How to Do It

For those of you who are experts, please try to bear with this blow-by-blow account (experts can skim this). I thought it would be best to lead those of you who are just beginning (or your nurse/technician) through the "drawing up" process once. This way, there should be no later confusion in the mechanics of this otherwise exciting stuff. We'll do this both for the IVP and the drip protocol - they vary a bit from each other - and once you've got it, the same principal will apply for all IVs in this guide.

There are probably "ideal" ways to draw up and prepare an IV solution that contains multiple substances. On top of that list is that each nutrient could be drawn up separately and mixed in a sterile mixing container, re-drawn from there and given to the patient (or given directly from the container for an infusion). This would prevent minute cross mixing of any of your nutrients and might theoretically decrease the likelihood of bacterial contamination. The same goes for an IV drip protocol: each nutrient could be drawn using a separate syringe and injected into the IV bottle.

We started doing IV therapy this way. It was time-consuming. It created an incredible amount of waste (syringes). It was *expensive*. Generally it was nice and proper,

and a very large pain in the neck. I advise all of you who want to find this out to do it this way – once.

If, however, you are a reasonable, cautious, responsible doctor, and/or have an IV therapist who is likewise, there is an easier way: for an IVP, draw each nutrient, in turn, into a large syringe and inject it into the patient (uh, don't forget to use that butterfly!). For an IV drip infusion via an IV bottle, you could use *one syringe* to draw up the materials. In either case, minute cross-mixing will occur, but it is unimportant. Sterility should never be an issue when you are using non-preserved or refrigerated nutrients and use reasonable caution, and it's easier on your nurses and the environment to use one syringe.

I know, I know. This is not a technique that would be condoned by the National Perfection Society. On the other hand, we've given over 20,000 IVs using this approach, and I have never seen a problem with bacterial contamination, nor has any patient reacted to the trace amounts of nutrients - introduced into a vial by using this technique - that they weren't "supposed" to get. Further, I've spoken with many physicians who have given as many or more IVs than I have, and the majority do it this way.

The major precaution I would admonish you to take would be to be sure your nurse is in the habit of putting the nutrients back in the fridge as soon as each IV is mixed. The only calls I've had from physicians over the years having to do with contaminated solutions have to do with this issue. If you give a solution with bacteria in it you will get what you'd expect: chills, shaking and even a slight fever shortly after – or during – the administration. In one case a physician was being sued. You've been forewarned.

The only exception to this multiple-nutrients-in-the-same-syringe approach is *folic acid* (folate), as it precipitates (temporarily) in acid solutions, so you may have to add bicarb. *Sodium bicarbonate* will sometimes "fizz out" of the syringe if you try to give it in an IV push solution, so we generally don't give bicarb with our pushes. All other nutrients we use are "mixable" without precipitation, etc.

Drawing up Nutrients: Asthma IV Push Protocol

First place the vials of nutrients on the counter in the order you are going to draw them up. *Although we don't do it necessarily in the examples here, nutrients that have a "color" to them (B-complex and B-12) ideally should be drawn up after those without color, since – if you don't – any cross contamination of vials will* really *show.*

We will be using a 60 cc syringe to draw up the nutrients for this IV. All nutrients will be drawn into the same syringe.

BEFORE you begin IV therapy with this protocol, there are a few precautions to note:

- Rapid infusion of magnesium (though more difficult to do with this protocol because of the large size of the syringe), could cause your patient to become "flushed," with a sensation of "heat," often in the face, skin, trunk or groin, followed by hypotension and even fainting. Once the first "warm" sensations are noted, *the push should be slowed until the sensation is less intense, mild, or stops.* (Note: if you're treating acute asthma or a headache, it is desirable to create *some* flushing, as those IVs are given to produce vasodilatation or bronchodilatation.)
- A vitamin "taste" from the B-vitamins will be rapidly noted by most.

- Since this solution is hypertonic, your patients may note an "aching" sensation proximal or even distal to the IV site. Rubbing the area of discomfort with your hands, slowing the infusion, or both, will usually relieve this.
- Be sure to watch carefully as you give the push, and pull back on the syringe frequently to make sure the blood is free flowing and that the needle placement remains correct. You *really* want to avoid extravasation into the soft tissue, as it will produce an *intense* burning sensation that may last an hour or longer. One way to avoid this is to insert the needle *well* into the vein when you start the IV.
- The most severe systemic reaction possible could be a feeling of light-headedness or faintness caused by the magnesium. However, unless the IV is slowed at this point, the patient may become nauseated, or possibly may even faint.
- **If there is an intense "burning" sensation at the needle site when performing an IV push with any combination of nutrients, *stop the IV immediately and examine the site*, as it could indicate infiltration due to improper placement of the needle.**

Preparation Instructions for this "Push": Drawing up the Nutrients

1. Remove the foil stickers (if any) from the tops of the vials from which you will draw the nutrients, and line them up in front of you *left to right*, in the same order they appear in the protocol. You will use some sterile water at the end. In my office, we draw out of the same 250 cc bottle of sterile water generally until it's almost gone; however, it *must* be stored in the refrigerator between uses.

   The order of vials: Vitamin C, B-6, B-12, B-complex, sodium bicarbonate, calcium gluconate, magnesium chloride, and pantothene, followed by the sterile water.
2. Wipe the tops of all vials with an alcohol swab.
3. Equalize the pressure in all of the vials with a small sterile needle (stick the needle briefly through tops of all vials), since new vials of nutrients may occasionally be over-pressurized. If you've already drawn from the vials, they should be at neutral pressure before you start.
4. Attach an 18 gauge No-Kor needle to the **60 cc syringe**

Vitamin C

5. Draw back the plunger of the 60 cc syringe to the 3 *cc mark*.
6. Invert the vial of ***Vitamin C*** (you draw up all of the following nutrients with each nutrient vial inverted), insert the needle of the syringe into the vial of **Vitamin C**.
7. Inject 3 ccs of air into the vial as was done previously for the infusion protocol.
8. Withdraw 3 ccs of **Vitamin C** into the syringe.

Important: with a "push", once you've drawn up the first ingredient (the Vitamin C here), push the plunger slightly forward in the syringe past the 3 cc mark and expel a few drops of solution. Then pull it back again to *exactly* the 3 cc mark. This will leave a *small bubble of air* in the *very top* of the syringe, just below the hub of the needle. You will have very slightly less than 3 ccs of Vitamin C in your syringe, but the bubble is primarily to prevent major cross-contamination of your nutrients, since you're going to be drawing up several nutrients with one syringe.

Basically, you want very close to 3 ccs of Vitamin C in the syringe, but a small air bubble at the top, no matter how you want to make it happen.

With an IV "push", you draw up all nutrients into the same syringe. In your office you will likely be using multi-dose vials from which to draw, because if you do a significant number of IVs daily in your office, you will use larger vials of individual nutrients than you might use for a single dose. This is fine, as long as you plan to draw up the nutrients from multi-dose vials in a single day or so and the remainder is refrigerated.

Since all of the nutrients are going to go into one syringe, I will give you all of the specific measurements so you get the proper amounts of each nutrient. It may be a little confusing at first, since you're not just using one syringe and immediately injecting each nutrient someplace right after you draw it up, as you do for an infusion protocol. You'll get the hang of this after the first two nutrients or so.

NOTE: That same bubble should always be present in the syringe after you draw up each nutrient.

9. Remove the needle from the **Vitamin C** and *push the vial of **Vitamin C** back*, so you know you've used it. You should now have 3 ccs of **Vitamin C** in your syringe with a tiny air bubble at the very top of the syringe.

B-6

10. Pull back the plunger of the 60 cc syringe to the 6 *cc mark* (you're going to use 3 ccs of this nutrient, and there are already 3 ccs of Vitamin C in the syringe; you will add 3 ccs of the vitamin B-6 to this, so the total in the syringe will be 6 ccs. This will be cumulatively true with each successive step here.
11. Insert the needle into the vial of **B-6** (pyridoxine).
12. Inject 3 ccs of air into the vial of **B-6** *without injecting any of the Vitamin C already in the syringe into the vial of **B-6***. In doing this, the plunger should be pushed back up to the 3 *cc mark* but you should *keep that air bubble there* throughout this and all of the following steps).
13. Withdraw 3 ccs of **B-6** into the syringe. In doing this, the plunger should be pulled back to the 6 *cc mark again*.
14. Remove the needle from the vial of **B-6**, and *push the vial of **B-6** back*.

If you ever "miss" a bit, it's not a major problem, *but leave it the way it is*. IF YOU "OVER-DRAW, TO 7 ccs, FOR EXAMPLE, DO NOT INJECT ANY MATERIAL BACK INTO THE VIAL OF B-6, if you do this here YOU WILL PRODUCE A CROSS-CONTAMINATION. If this should happen, just go on with life. But if you do it, either squirt any excess into a towel or remember to add whatever amount of nutrient you've overdrawn to the measurements here. If you ever decided to work for the government, it would be close enough.

B-12

15. Draw back the plunger to the *11 cc mark* of the syringe (you're going to draw up 5 ccs of this nutrient).

16. Insert the needle into the vial of **B-12**
17. Inject the air into the vial by pushing the plunger forward to the 6 *cc mark*.
18. Withdraw 5 ccs of **B-12**, to the 11 *cc mark* of the syringe
19. Remove the needle from the vial, and push the vial back.

B-Complex – 2 cc vial

20. Draw back the plunger to the *13 cc mark* of the syringe (you're going to draw up 2 ccs of this nutrient).
21. Insert the needle into the vial of **B-Complex**
22. Inject the air into the vial by pushing the plunger back to the *11 cc mark*.
23. Withdraw 2 ccs of **B-Complex**, back to the *13 cc mark* of the syringe
24. Remove the needle from the vial, and *push the vial back*.

Sodium bicarbonate

25. Draw back the plunger of the 60 cc syringe to the *19 cc mark* of the syringe (you're going to draw up 6 ccs of this nutrient). The purpose of the bicarbonate in all of the IVs in this *Guide* is to adjust the pH to about 6.8. We have calculated these amounts with a pH meter over the years, so you won't have to recalculate it.
26. Insert the needle into the vial of **sodium bicarbonate**.
27. Again inject the air into the **sodium bicarbonate** *without injecting any of the contents of the syringe* into the vial of **sodium bicarbonate**. In doing this, the plunger should be pushed forward again to the *13 cc mark* – just remember to leave that air!
28. Withdraw 6 ccs of **sodium bicarbonate** back to the *19 cc mark* on the syringe.
29. Remove the needle from the vial of **sodium bicarbonate**, and *push the vial back*. The bicarb may foam a bit, and if it does, pull the plunger back so as not to allow nutrients to foam out of the syringe until nutrients are mixed and the foaming stops.

Calcium gluconate

30. Draw back the plunger of the 60 cc syringe to the *21 cc mark* of the syringe (you're going to use 2 ccs of this nutrient)
31. Insert the needle into the vial of **calcium gluconate**.
32. Again inject the air into the **calcium gluconate** *without injecting any of the contents of the syringe* into the vial of **calcium gluconate**. In doing this, the plunger should be pushed forward again to the *19 cc mark* – just remember to leave that air!
33. Withdraw 2 ccs of **calcium gluconate** back to the *21 cc mark* on the syringe.
34. Remove the needle from the vial of **calcium gluconate**, and *push the vial back*.

Magnesium chloride

35. You're going to draw up 10 ccs of this nutrient but you won't likely be able to inject all of the air at once, so it would be best to insert a small, sterile needle through the top of the **magnesium chloride** first (leave it there until you've drawn up the solution), so you can simply draw the 10 ccs of solution out without pressurizing the vial.

36. Insert the needle of the syringe into the vial of **magnesium chloride**.
37. Withdraw 10 ccs of **magnesium chloride**, to the *31 cc mark* of the syringe. If you're using more than 10 cc, obviously you must adjust the following directions accordingly.
38. Remove the needle from the vial, and *push the vial back*.

Pantothenic acid (B-5, pantothene) – 2 cc vial

39. Draw back the plunger to the *33 cc mark* of the syringe, (you're going to draw up 2 ccs of this nutrient).
40. Insert the needle into the 2 cc vial of **Vitamin B-5** (pantothene)
41. Inject the air into the vial by pushing the plunger forward again to the *31 cc mark*.
42. Withdraw 2 ccs of **Vitamin B-5**, back to the *33 cc mark* of the syringe.
43. Remove the needle from the vial, and *push the vial back*.

Okay, you're done drawing up the nutrients!

Preparation of the IV

The nutrients you have drawn into the 60 cc syringe will be given IV "push," using only a butterfly set. However, before the IV can be given, ***sterile water must be added to the nutrients in the 60 cc syringe to dilute them to a reasonable osmolarity***.

1. Wipe the port on the bag of sterile water with alcohol.
2. Place the the 250 cc bag on the counter and insert the 18-gauge needle of the **syringe containing your nutrients** into the center of the port for injection.
3. Draw 27 ccs of water into the syringe to fill the syringe to the 60 cc mark.
4. Right before the syringe is full, draw a few ccs of air into the syringe and tilt it back and forth a few times to completely mix the contents. Flick to syringe several times to get the air bubbles out and finish drawing up the water.
5. Remove the needle from the syringe and attach a **winged infusion set**. **DO NOT REMOVE THE NEEDLE GUARD YET.**
6. **Fill the tubing of the winged infusion set with the IV solution until the solution comes out of the needle, into the needle guard, and any large air bubbles are out of the tubing. Leave the needle guard on.**
7. You would normally take your patient's vital signs before administering this or any other IV.
8. Tear off a 3-4" piece of tape and have it handy to tape the needle to the skin (1" 3M Micropore tape) and to use once the needle is removed.
9. Put on the tourniquet.
10. If your patient's veins are the least bit reasonable, use a *larger* butterfly (21-23 gauge). Only use a small (25 gauge) butterfly if your patient has *very* difficult veins. Remember, the *push takes significantly more effort and time with a 25-gauge needle*. Pushes in a 30 cc syringe are done with a 25 gauge butterfly.

    Insert the butterfly needle, bevel up (seems to be the easiest), *all the way (or almost all the way) into a large vein*, preferably in the antecubital space (crook of the arm) of your ~~victim~~ patient, and preferably in one, swift motion, so that the needle is inserted

almost *up to the flexible plastic butterfly part of the needle*. As soon as the needle enters the vein, you will note a small amount of a back-flow of blood appear in the butterfly tubing. Put a piece of tape over the flexible plastic butterfly where it enters the skin, covering it and the spot where the needle enters the skin.

11. **Release the tourniquet**.
12. *Slowly* inject about 1-2 ccs of the solution, then *stop* for about 30 seconds to be certain your patient is experiencing no adverse reaction. Watch the tubing and the site *carefully* as you do this to be certain the solution goes into the patient's vein and not the subcutaneous tissue!
13. Be sure to watch carefully as you give the push, and pull back on the plunger of the syringe frequently to make sure the blood is free-flowing. Remember, **stop immediately** if your patient has **any** sensation of *severe burning, pain or discomfort, or if you recognize there is any infiltration*.
14. Once all appears to be OK, continue the IV injection.
15. You may proceed with the injection at a speed your patient will tolerate. If he or she experiences any of the symptoms as noted previously, *stop the push for a moment*. As the symptoms abate, you may resume. This IV may be given to most patients over a period of 10-15 minutes without problems.
16. Once the IV is finished, fold a 2" X 2" gauze pad in quarters. *Carefully* peel back the tape covering the needle where it enters the arm, while holding down the plastic butterfly portion. Press the 2" X 2" *lightly* to the skin where the needle is inserted and at the same time remove the needle with a quick, smooth motion. As the needle is removed, *increase* the pressure on the gauze pad about a minute and then apply the piece of tape you used previously tightly over the gauze. The patient may remove the tape and gauze in about 10-15 minutes.

Abrams, College and **McGuff's Pharmacies** have most of the formulas we routinely use in our office *pre-mixed*, and at reasonable prices. These can be ordered "as is" if you don't want to get into mixing IVs in your office, and they will send them to patients' homes, etc. You can possibly find these also at other compounding pharmacies as well, and you can certainly ask your local compounding pharmacy if they would make up these protocols (except ask that they keep the Vitamin C separate) for you to use in your office or if they would send them to patients.

Since it is labile, Vitamin C needs to be kept refrigerated, stored in the dark and added to any of the pre-mixed protocols available from compounding pharmacies immediately before the IV is given.

Mixing: IV Drip Infusion for Chronic Asthma

Position and prepare the vials you will be using as appear in the **Chronic Asthma Protocol**. It's always important that you put a vial aside when you're finished with it, as this prevents the question, "Now, did I mix this in yet?" It also helps to check each nutrient off as you add it.

Note About the IV Bag

IV bottles of sterile water are no longer available, so as I mentioned, we now have to be content with IV bags. They are not nearly as bad as they used to be, and the water in these bags simply tastes "stale" and no longer has a "plastic" taste. Certainly the water must contain some plasticizers, and hopefully the amounts are small enough to be relatively harmless. We may never know. We still use vented administration sets.

Drawing up the Nutrients

IV infusion protocols are generally drawn up using a single syringe for all of the nutrients. It saves money. We have done this in our office since 1986, and have not seen a problem. Use of multiple syringes – one for each nutrient – is quite costly and unnecessary. When one syringe is used, e.g. 10 cc, a minimal but measurable amount of "cross-contamination" between vials of nutrients is bound to occur. However, the effects of this are negligible if the procedure is done carefully and as directed. The exceptions are folic acid and sodium bicarb. If sodium bicarb is drawn up first, it doesn't seem to be a problem. Folic acid should be drawn up in a *separate 3 cc syringe and added to the infusion, unless you've just drawn up bicarb as the last nutrient*.

Cross-contamination of nutrient vials is noticeable if a small amount of a "colored" nutrient (such as $\mathbf{B_{12}}$) is inadvertently introduced into a vial of a "clear" nutrient, such as magnesium sulfate. *Therefore, I usually draw up the clear or non-colored nutrients first, followed by the nutrients that have any color.* This will not be true here for instructional purposes to follow the order of this protocol (it's alphabetized), but you should get in the habit of doing it in your office.

Chronic Asthma Protocol

Nutrient	Osmolarity	Ccs
Ascorbic Acid 500 mg/mL	5.80	12
B-6 (Pyridoxine) 100 mg/mL	1.11	5
B_{12} (hydroxocobalamine) 1000 mcg.	0.31	5 **
B-Complex 100 mg/mL	2.14	2
Bicarbonate Sodium 8.4%	2.00	17
Calcium Gluconate 10% 100 mg./mL	0.72	2
Folic Acid 10 mg./mL	0.20	1
Magnesium Chloride 200 mg./mL	2.95	10
Mineral Mix	0.57	1
Molybdenum 500 mcg./mL	0.80	1
Pantothenic acid 250 mg./mL	0.85	2
Potassium chloride 2 mEq/mL	4.00	1
Additives		54
mOsm Additives		*151.6*
Sterile Water		250
Osmolarity (mOsm/L)		**499**

** Given IV Push at the end

Drawing up the IV

Select a 10 cc syringe and an 18 gauge No-Kor needle.

1. Remove the foil stickers from the tops of each vial (if there are any) and line up the vials in front of you (cross-wise from *left to right*) from which you will draw the nutrients, in the same order they appear down the list in the protocol: Vitamin C (ascorbate), B-6 (pyridoxine), (the **B_{12}** does not appear here because it is given IV push at the end of the infusion), B-complex, sodium bicarbonate, calcium gluconate, folic acid, magnesium chloride, Mineral Mix, molybdenum, pantothenic acid, Potassium chloride and the 250 cc bag of sterile water.
2. For each IV nutrient to be added, pull the plunger of the syringe down, filling it with the same amount of air as the volume of the solution you're going to use. Some prefer to insert a small (25 ga.) sterile needle into the top of the nutrient vial first, draw up the nutrient, leave it there until you've finished drawing up the nutrient, then transfer it to the next vial, so you can simply draw the amount of solution out without depressurizing the vial. The small needle will draw in air to depressurize the bottle as you remove volume.
3. Wipe the tops of all vials with an alcohol swab.
4. *Equalize the pressure in all of the vials* with a small sterile needle (stick the needle briefly through tops of all vials). You don't need to do this if you put a 25 ga. needle into the vial while you are withdrawing the nutrients.
5. Attach the 18 gauge No-Kor needle to the 10 cc syringe.

Vitamin C – usually comes in a 50 cc vial

6. Pull back plunger of syringe to the *12 cc mark* (a 10 cc syringe actually measures to 12 cc)
7. Insert the needle of the syringe into the vial of **Vitamin C** and **invert the vial** (you will do this with all of the vials of nutrients as you use them). You can also insert a an additional 25 gauge needle into the top of the vial, rather than use it to equalize all vial pressures before starting, to equalize pressure in each vial as you draw up each nutrient, in which case you do not need to inject the air and you don't need to equalize pressures in the vials before starting.
8. Inject the 12 ccs of air into the Vitamin C vial. Note: the full volume of air may not all go in *at once*, so release pressure on the syringe and allow some bicarb to flow into the syringe, push in some more air, back and forth, and so on. Remember, if you have inserted another (25 ga.) needle into your vial to continually equalize the pressure as you draw up the nutrient, if you inject air the nutrient will be forced out of that needle. So don't inject the air if you use this technique
9. Withdraw 12 ccs of **Vitamin C** from the vial into the syringe and remove the needle from the vial of Vitamin C.
10. **Push the vial of Vitamin C *back*.** This may sound silly, but when you're using 10-20 nutrients, especially if some are multi-dose vials, it can become quite confusing if you forget to push a vial you've used out of the way, should you get interrupted during the process.
11. Inject the Vitamin C into the IV bag through the tan rubber injection port.

Vitamin B-6 – usually comes in a 2 to 10 cc vial

12. Pull back the plunger of the 10 cc syringe to the *3 cc mark*.
13. Insert the needle into the vial of **B-6** (pyridoxine).
14. Inject the 3 ccs of air into the vial of **B-6**.
15. Withdraw 3 ccs of the **B-6.**
16. Remove the needle from the vial of B-6, and *push the vial of **B-6** back*.
17. Inject the **B-** into the IV bag through the rubber injection port.

B-Complex – usually comes in a 2 to 10 cc vial

6. Draw back the plunger to the *2 cc mark* of the syringe.
7. Insert the needle into the vial of **B-Complex**
8. Inject the air into the vial of **B-Complex**.
9. Withdraw 2 ccs of **B-Complex**
10. Remove the needle from the vial, and *push the vial back*.
11. Inject the contents of the syringe into the IV bag through the rubber injection port.

Sodium bicarbonate – usually comes in a 50 cc vial

12. Pull back the plunger of the 10 cc syringe to the *10 cc mark* of the syringe
13. Insert the needle into the vial of **sodium bicarbonate**
14. Inject the air into the **sodium bicarbonate**.
15. Withdraw 10 ccs of **sodium bicarbonate.**

16. Repeat these steps with 7 more ccs of **sodium bicarbonate**, since you need a total of 17 cc.
17. Remove the needle from the vial of **sodium bicarbonate**, and *push the vial back* **so you know you've used it.**
18. Inject the contents of the syringe into the IV bag through the rubber injection port.

Calcium gluconate – usually comes in a 5 to 50 cc vial

19. Pull back the plunger of the 10 cc syringe to the *2 cc mark* of the syringe
20. Insert the needle into the vial of **calcium gluconate**.
21. Inject the air into the **calcium gluconate**.
22. Withdraw 2 ccs of **calcium gluconate.**
23. Remove the needle from the vial of **calcium gluconate**, and *push the vial back*.
24. Inject the contents of the syringe into the IV bag through the rubber injection port.

Folic acid – usually comes in a 5 to 10 cc vial

25. Pull back the plunger of a separate 3 cc syringe to the *1 cc mark* of the syringe. Note: if you move this step to right after you draw up the bicarb, you can use the same 10 cc syringe you've been using. Once again, this step is here because the nutrients are alphabetized.
26. Insert the needle into the vial of **folic acid**
27. Inject the air into the **folic acid**
28. Withdraw 1 cc of **folic acid**
29. Remove the needle from the vial of **folic acid**, and *push the vial back*.
30. Inject the contents of the syringe into the IV bag through the rubber injection port.

Magnesium chloride (200 mg./ml) – usually comes in a 10 to 50 cc vial

31. Pull back the plunger to the 10 *cc mark* of the syringe.
32. Insert the needle into the vial of **magnesium chloride**.
33. Inject the air into the vial of **magnesium chloride**.
34. Withdraw 10 ccs of **magnesium chloride**. Inject the contents of the syringe into the IV bag through the rubber injection port.
35. Repeat these steps with 5 more ccs of **magnesium chloride**, since you need a total of 15 cc., or just do the whole 15 at once if you have a large enough vial.
36. Remove the needle from the vial of **magnesium chloride**, and *push the vial back*.

Mineral mix – usually comes in a 2 to 10 cc vial

37. Draw back the plunger to the 1 *cc mark* of the syringe.
38. Insert the needle into the vial of **mineral mix**.
39. Inject the air into the vial of **mineral mix**.
40. Withdraw 1 cc of **mineral mix**.
41. Remove the needle from the vial, and *push the vial back*
42. Inject the contents of the syringe into the IV bag through the rubber injection port.

Molybdenum – usually comes in a 2 to 10 cc vial

43. Draw back the plunger to the 1 *cc mark* of the syringe.

44. Insert the needle into the vial of **molybdenum**.
45. Inject the air into the vial of **molybdenum**.
46. Withdraw 1 cc of **molybdenum**.
47. Remove the needle from the vial, and *push the vial back*
48. Inject the contents of the syringe into the IV bag through the rubber injection port.

Pantothene (vitamin B-5) – usually comes in a 2 to 10 cc vial

49. Draw back the plunger to the *2 cc mark* of the syringe.
50. Insert the needle into the 2 cc vial of **pantothenic acid** (pantothene).
51. Inject the air into the vial of **pantothenic acid**.
52. Withdraw 2 ccs of **pantothenic acid**.
53. Remove the needle from the vial, and *push the vial back*.
54. Inject the contents of the syringe into the IV bag through the rubber injection port.

You're now done drawing up the nutrients. You won't draw up the B-12 until the end of the IV to give IV push. Don't throw the 10 cc syringe away – you'll need it for the B-12.

Setting up the IV

Note: Your patients should have eaten something prior to receiving this IV. When you administer IV therapy at your office, advise patients to *eat before they come in*, whenever possible. Most patients do much better with IVs of any kind if they've eaten *beforehand*.

1. Pull apart the "Bubble Pak" containing the vented IV administration set, and remove the tubing.
2. **Move the wheel clamp on the IV tubing distally to about 2 feet from the distal end (the end opposite the "spiked" end, which will be the end closest to the patient) and *close the wheel clamp tightly***.
3. Remove sterile cap from the "spiked" end of the IV tubing (administration set).
4. Remove the protective cover from the port in the IV bag and Insert the spiked end of the IV tubing firmly into the IV bag through the administration set port.
5. *Be sure the wheel clamp is closed tightly*! Hang the IV bag on the IV pole (stand). In our office, we use a hook attached to the cabinet near the sink. This is so any IV solution can go into the sink while the IV line is flushed. The IV is then moved to wherever the patient is.
6. *(Be sure the wheel clamp is closed tightly*!) Squeeze the drip chamber a few times to get the IV solution to fill the reservoir about *half full*.

   NOTE: The administration set will have a "vent" valve near or on the reservoir. *THE VENT IS ALREADY OPEN – just leave it alone*.
7. Open the winged infusion set, (we use *Terumo Sur-Flo*®, 23 gauge X ¾" infusion sets, McGuff cat. # 1837 for this IV), unscrew the cap and connect it to the administration tubing (you have to also remove the cap from the end of the administration tubing). *Leave the needle guard on the butterfly in place* (you should also have 25 gauge butterfly sets for "difficult" or small veins, and 21 gauge sets for IVs you want to go in more quickly. If you prefer, you can use a 24 ga. intracath for infusions).

8. Slowly open the clamp and slowly let the solution run through the tubing of the administration set *until it comes out of the needle*, *into the needle guard*. Most of the air bubbles will come out of the tubing as you let the solution flow through it (small bubbles won't do any harm to the patient, anyway).
9. Once this is done, again close the wheel clamp tightly.
10. You then take the patient's vital signs -- blood pressure and pulse, before you begin *any* IV therapy on *any* patient.
11. Tear off three 3" pieces of hypoallergenic tape (we use 3M Micropore hypoallergenic surgical tape), and stick them just by their ends somewhere within easy reach (the IV pole is usually convenient), so you can reach up and grab them when you need to.
12. Apply the tourniquet to your patient's arm.
13. If your patient's veins are the least bit reasonable, use a 23-gauge butterfly for this IV, since you want it to run in about a hour or so. Only use a 25-gauge butterfly if your patient has *very* difficult veins. Insert the butterfly needle, **bevel up,** *at least half way into a vein*, and preferably in one, swift motion, so that the needle is inserted at least half way up to the flexible plastic butterfly part of the needle. (This may be hard for you to do the first time around, so just practice.) As soon as the needle enters the vein, you will note a small amount of a back-flow of blood appear in the butterfly tubing. You may advance the needle further once it's in the vein.
14. **Release the tourniquet**. Immediately put a piece of tape over the flexible plastic butterfly tab, covering it. This solution is tolerated by most people in a more peripheral vein, but large veins will avoid problems if you're not yet uses to starting IVs.
15. Tape the butterfly tubing again *proximally* to the skin with another piece of tape, and with the third piece of tape, tape the *administration tubing* to the patient's *clothing* (shirt or dress sleeve).
16. Open the wheel clamp, very gradually at first, to be certain your patient has no adverse response to the solution, and to best prevent the vein from "blowing out." Watch the tubing and the site carefully as you do this to be certain the solution is running into the patient's *vein* and not the *subcutaneous tissue* (it burns)!
17. Set the drip rate at about 10-15 drops per minute (count them) for the first 2-3 minutes. **Watch the site, watch the patient, and** s**top the IV** if your patient has *any* sensation of *severe burning, pain or discomfort* (some "aching" of the upper arm could occur – the patient can massage it – but this is not infiltration: infiltration burns at the needle site).
18. Once several ccs have been administered and if your patient has no discomfort or other unusual symptoms, you may then speed the rate up to *as rapidly as he or she will tolerate*. A "wide open" flow, using a 21-gauge needle, is tolerated by those patients who experience no discomfort and 250 cc will go run about 45 minutes wide open.
19. The IV may be allowed to run as ***completely*** *out* as possible before it is disconnected, and you could tell your patients to let your nurse know when the IV is almost gone. Air will *not* flow into a patient's vein – the IV stops flowing soon after the fluid flows out of the reservoir – and you give the $\mathbf{B_{12}}$ right before that, at the end of the IV.

Vitamin B_{12}– usually comes in a 2 to 10 cc vial

20. Pull back the plunger of the 10 cc syringe to the *5 cc mark* of the syringe
21. Insert the needle into the vial of **B_{12}**.
22. Inject the air into the **B_{12}**.
23. Withdraw 5 ccs of **B_{12}.**

24. Administration sets have a port for injection of IV materials. You will inject the B-12 here at the end of the IV. Wipe the port with alcohol and tightly pinch the administration tubing closed (with your fingers) just above the port and inject the B-12 into the port. Release the tubing and let the rest of the IV solution flush the B-12.

25. Once the IV is finished, fold a 2" X 2" gauze pad in quarters. *Carefully* peel back the tape covering the needle where it enters the arm, while holding down the plastic butterfly portion. Press the 2" X 2" *lightly* to the skin where the needle is inserted and at the same time remove the needle with a quick, smooth action. As the needle is removed, *increase* the pressure on the gauze pad for about a minute and then apply the last piece of tape tightly over the gauze. The patient may remove the tape and gauze in about 10-15 minutes.

NOTE: For infusions of 500 to 1000 ccs, we often prefer to use an in-dwelling catheter, such as Angiocath® by B.D. (we generally use 24 gauge teflon). This allows patients to bend their arms. These come in various sizes, and they are slightly more technically difficult to insert than a butterfly. Once you get used to them, however, you won't use anything else.

When the IV is done, remove the needle, apply slight pressure to the IV site with a 2" X 2" gauze, folded in quarters, and tape it down.

How Do these IVs Work?

When I first started with IV therapy, I cited very few references about nutritional IV therapy because there just *weren't* any. Now there are many more (see *References* at the end of this Guide). Unfortunately, except for TPN, my article is the only one yet published about nutrient *mixtures*, so there are not many definitive mechanisms I can cite for protocols containing more than one nutrient. No doubt this protocol works so well for a very large number of reasons that you and I could theorize for many pages, based on hundreds upon hundreds of studies done on humans and animals which demonstrate, at least partially, how and why certain nutrients work. I'll just mention a few reasons here.

As most of you are aware by now, magnesium is a potent bronchodilator (for asthmatics), vasodilator (used to treat the hypertensive crisis in toxemia of pregnancy) and muscle relaxant (it is used to stop labor during premature labor). There have now been a large number of studies demonstrating this, and I've cited the important ones. If you were ever questioned by anyone as to why this IV has a bronchodilating effect, these articles (and the references they cite) would be worthwhile to have on hand. Articles appeared in 2005 citing experimentation with inhaled magnesium sulfate as a bronchodilator.

We know pyridoxine participates with magnesium almost everywhere in the body, and that these both act on c-AMP in the bronchioles.

B_{12} has a considerable effect on the wheezing response. B_{12} has been used alone (by daily injection) with success to treat childhood asthma by Dr. Jonathan Wright [20], since B-12 improves the response asthmatics have related to their sulfite sensitivity.**Error! Reference source not found.**

Vitamin C likely has several direct and indirect mechanisms of action in this protocol. To cite just one, ascorbate has been shown to acutely decrease airway responsiveness to inhaled histamine in subjects with hay fever.[22]

Interestingly, magnesium sulfate works when used alone, but in our experience, not nearly as well as the combination of nutrients, nor is the effect as long lasting. This is, of course, a problem. Once you start mixing up nutrients, it automatically becomes much more difficult to scientifically explain the effects because of the complex interactions involved. Hence, we don't try very much. I must repeat at this point that there is very little published literature regarding the use of mixed IV nutrients, so it's understandable why this type of treatment could come under attack.

More on the Push

With this particular IV, the magnesium is usually the limiting factor in how fast you can give it. Magnesium is a potent vasodilator and should be given at a speed that causes the patient to feel "warm" or slightly "flushed" for the best effect for acute asthma. Oddly, male patients get a very warm feeling in the anal area, while females experience it in the vaginal area. Many women would probably say this is a good overall indication as to what the difference is between men and women: men are generally ---holes. Oh, well.

If the push is given too quickly, the patient could become very light-headed and even faint. This has happened to us a few times, but has no lasting adverse effects on the patient. If this should happen, simply pause the infusion, slide the patient to the floor (or give the IV with the patient in a reclining chair in the first place) and raise his or her legs if necessary. As soon as the patient feels well enough to sit again, resume the infusion, but more slowly. The warning sign is that the patient usually will complain that the flushing is extreme, they feel dizzy and/or nauseated, and will look lethargic, pale and perhaps "sweaty". That's the time to pause a few minutes, before you drop the bottom out of their BP.

If the patient doesn't get significant relief with the first IVP, it may be repeated in 20 to 30 minutes. I have seen this fail only twice - much less, percentage-wise, than adrenaline or Susphrine. Should this not work for your patient, you may give any of the medications you would usually give for acute asthma. The IV will not interfere with the action of any of the agents you would be likely to use for this purpose. It may be wise to start the push with 1.5 grams of MgCl and see how it works. Usually two grams seems to work well, but some patients need three grams to get enough bronchodilitation.

This is an IVP protocol you're going to find valuable. It generally has a lasting effect for 1 to 3 days initially, and this may increase significantly with time. However, once the patient has been given one to three of these, we will often go to the longer drip infusion protocol.

If you have a spirometer, it might be a good idea to measure pulmonary function before and after the IV. This would impress anyone who would question the efficacy of what you're doing.

The Drip Infusion Protocol for Chronic Asthma

This is my creation, but came partly – as always – from some exciting trials by other physicians. Dr. Jonathan Wright, for example, has investigated the role of molybdenum given IV to his patients with asthma for several years now.[19] There's little question that it can be of significant value for many patients with decreased sulfite oxidase activity, and asthmatics often tend to fall in this group. If your asthmatic patient has a urine sulfite of 20 PPM or greater, you can bet that molybdenum will help.

If you would like to have it compounded, 10% HCl can add a great deal to this protocol, and you would use about 10 cc. The HCl was a discovery by one of my nurses in this protocol, but it is well known, though not used much anymore. It's known that IV HCl is a useful tool for infection, and asthmatics with a chronic "bronchitis" component of their asthma seem to often benefit from its addition, as do some other patients. I had one asthmatic patient using this IV on whom we'd done sequential PFT's over a period of 2 years. If the HCl was left out, her PFT would reflect a worsening. Her FVC doubled using this protocol about once a month - alone). So, especially if your asthmatic patient has frequent URIs, consider trying HCl in this IV.

I feel the trace minerals are important to create a lasting response, but only if you use the protocols for at least 2-3 mos.[236]

N-acetyl cysteine may be of benefit because it "rescues" glutathione, **Error! Reference source not found.** the most potent antioxidant and detox agent we produce in the body.

Long Term Effects

Both of these protocols have cumulative, long-term effects for asthma, but the infusion has impressive overall "staying power". You'll find that, at first, the IVP protocol will need to be used about twice weekly for the best results, though some patients immediately seem to do well for longer periods. Once you've got the IVP dose of magnesium to 2.5 grams, it would probably be best to go to the longer drip protocol. However, the long protocol does not appear to work well for patients with *acute* asthma, probably due to the dilution factor, since it does not produce an acute bronchodilation. Again, some patients require over 3 grams IVP (cautiously).

Generally, after you've given a few IVs and have switched over to the drip protocol, you'll find the patient gets longer and longer relief as time goes on. You should tell your patients that everybody's different, and to have patience. It may first take a few months of once- or twice-a-week treatments, but the time between IVs should stretch out to monthly or every six weeks at some point. If you use adjunctive care, as you always should (immunotherapy, avoidance of allergens, food rotation or food immunotherapy and so forth) the need for IVs lessens or disappears. I feel that your patients on IV therapy should **always** be on oral supplements, as should all of your patients for optimal results in whatever you're doing. If your patients with asthma live in a city, they might do well with an extra half milligram of oral molybdenum daily.

We have deliberately treated a few patients without adjunctive care, and they have done well simply using the above IV drip protocol. In fact, we've had a few patients discontinue their immunotherapy in favor of IV treatment because they felt it worked as well and was more convenient than taking weekly shots (when we were doing that).

I wanted to comment about *pediatric dosage* to use when you employ IV therapy. The answer is that there are none. I have used our adult protocols frequently down to age 5, and not so frequently for asthma down to about age 8, both without difficulty. However, IV "pushes" done for asthma with kids should be as close to isotonic as you can get (usually by reducing the magnesium and ascorbate) to allow volumes of between 30 and 60 cc. to be given. The major problem with kids is mechanical - the size of their veins - so extreme care must be used to employ solutions that are non-sclerosing. Fortunately, the children we see with asthma generally respond well to the integrative treatment with which we're all familiar: avoidance, dietary therapy and immunotherapy.

Billing Codes

You must check these codes yearly, as they tend to change. No matter what you do, some insurance companies pay and some do not**.** If a company does not pay, I'd advise you don't push them – generally they will not cave in, and they will tend to give you more problems justifying IV therapy than it's worth. There is a fear now that insurance carriers can charge you with "fraud" if you use – and they have paid for – "unproven" things.

I would *strongly* urge you not to bill Medicare for IV therapy, and NEVER bill Medicaid for it, unless you can prove beyond a shadow of a doubt that the therapy you gave was necessary and indicated, not to mention accepted.

1. 99211 – Minimal office visit, and
2. 90784 – for the IV for a patient with asthma – if you want to justify you've given magnesium for acute asthma, refer to multiple references in the literature and included here [most insurance companies no longer pay for this code].
3. 90780 – used for any other IV (you may have to justify the IV for insurance), and you may add:
4. 90781 – for each extra hour, per hour (unit)
5. 90799 – "unlisted" therapeutic or diagnostic injection (asking for trouble, likely)

I would advise that you not specify that the substances you are using are nutrients unless you're asked. The FDA considers nutrients given parentally to be drugs, and so should you (for these purposes), but insurance companies often don't.

Waiver Forms for IV and other "non-conventional" therapy

Whenever you are using other than what is termed "standard of practice" methodology in your office, you should advise your patients. We do this in writing, and have patients sign forms. At the end of this guide, I've included most of our standard forms we use in my office. Please feel free to use them if you wish.

Variations

All of the treatment protocols you've seen here will enhance your patient care tremendously. If you treat asthmatics, you're going to wonder, as I did, how you did it without this powerful extra tool. You'll find, as you get comfortable with IV treatment, that patients vary in their response, and that they vary in their *requirements*. Hence you're going to want to experiment with different dosages, additions or subtractions from the above. My staff is superb, and I basically let them do most of this on their own. As I mentioned before, they often come up with incredible combinations. In fact, some of the protocols you see here

were "discovered" by my staff. Believe me when I tell you that your nurse or technician is going to get better at this than you are, if she (or he) does your IV therapy.

One word of caution, however. The magic word with IV therapy is *osmolarity. Do not alter the above protocols substantially unless you understand how to calculate osmolarity*. You can certainly make small changes without much of a problem, and hyperosmolar solutions are often well tolerated, but use reasonable prudence (see next chapter).

Protocols for Migraine and Headaches

FDA Regulations

Well, as most of you know by now, the FDA has held "search and seizure" – for lack of a better term – "raids" of physician's offices and several vitamin manufacturers/distributors. Jonathan Wright's For Your Health Pharmacy was a casualty of one of these raids several years back. The FDA seized $100,000 worth of materials and equipment from them, and the seizure was indeed "justified" (according to the FDA regulations, anyway), because Dr. Wright was using a preservative-free B vitamin from Germany – not FDA approved. Legal issues and constitutional rights aside, however, we have learned something from all this.

ACE was seized, but it is still available from some suppliers who have handled it previously. Glycyrrhizin was seized, but is available from College Pharmacy, albeit with a preservative. Remember one important fact: many of the seizures over the years seem without justification, but all have been justified, at least according to the letter of the law of the FDA.

One of the FDA's primary concerns is the use of nutrients, devices or other substances *not manufactured in the U.S.,* and the manufacture and distribution of non-FDA-approved strengths of nutrients. The FDA still tells me that it is legal for a physician to use any substance available on his or her patient, provided the patient is informed the treatment is not necessarily condoned by the FDA, and provided the substance is produced in the U.S., and certainly if it is manufactured by an FDA-approved company. However, and this is a BIG however, some substances remain in the gray area.

You may order, by prescription (which may be faxed) from compounding pharmacies, most any special nutrient not easily available elsewhere, such as preservative-free nutrients. *You should put "for office use only" on your prescriptions. Be certain that you don't give any of these specially-ordered materials to patients for use at home (they have to order those directly from the pharmacy under your guidance) and that you do not sell or give them to other physicians (or non-physicians) for use!* Were you to do this, you could be considered a "distributor" by the FDA. Several states seem to be adopting the rule that you cannot order compounded products "for office use" and this could be a problem in the future.

Another thing you should know about Medicaid and Medicare patients. If you see one of these patients for an office visit, administer an "established" treatment, but during the same visit administer any treatment Medicaid or Medicare considers not "standard of care," and if you bill them for this, they may disallow the entire claim. Potentially more disastrous, they can interpret this as fraud, if they so desire. Most other insurance carriers will pay for an office visit, even if what you do during that visit is considered by them to be "non-standard" - they just could refuse to pay for the procedure, not the office visit. However, now some companies are acting like Medicare and Medicaid, and can accuse you of fraud if you bill for a procedure that is "non-standard". I hope this is clear to you all, as it affects most of us because of what we do, and I am certain of the accuracy of the above statements. Medicaid or Medicare can now confiscate the assets of your entire practice -- and even your

home and assets -- if you are accused of fraud, so you should probably read this last paragraph again.

The moral of this story is that it would be wise for you not to participate with *any* insurance carrier if you are using "unconventional" treatment, or at least not bill them for it. I am really not talking necessarily about IV therapy here at all, but any treatments you might employ that are considered not "standard" or any "non-traditional" procedure you can imagine. So, once again, even though our ultimate goal is to always give our patients the best, most cost-effective care available, we must remember to be careful out there, no matter what we're doing. *It appears few insurance companies wants to go so far as to accuse you of fraud – they simply refuse to pay. But Medicaid and Medicare do – and they* will *if they want to get you. Bottom line? I strongly advise you to use caution with all insurance carriers, but do not treat Medicaid or Medicare patients under any circumstances except by exclusive, individual contract outside the system.*

One severe financial issue is this: if any insurance carrier finds you have been billing for something they don't like – even if they have paid you for a long period of time – once they make the determination, they can go after you for money they have *already paid you* for the procedure. I know a number of physicians who have had to return over $100,000 to Medicare for this very reason.

I do not feel IV therapy with nutrients is -- or should be considered -- investigational at all – there's a very long track record here, among those who use it. I mean of course that – in my opinion - many nsurance companies might view it is investigational, and that you should probably consider this if you are going to use it. Here is where the references at the end of this Guide are so important. Use them to defend IV therapy if you need to.

You *may* want to talk to your State Board as to their stance on nutrients discussed in this column. Further, you might want to get their OK for every nutrient or agent that does not have an established "grandfather" FDA standing. This obviously depends on your Board. If it is "unfriendly, such as that of California at the present time, stay away. All "standard" vitamins and minerals have been "tolerated" by the FDA – so far – by "default," simply because of their long-standing use for TPN. Some other agents have a classification that is not clear yet, even within the FDA. My advice is to always cover your bases and check with any sources available to you. Always remember -- most of what is done in general medicine is not "approved" by the FDA; techniques are not within their jurisdiction. Just don't use any "illegal" substances, and you should be OK.

I can tell you at this point that dimethylglycine (DMG or vitamin "B-15") is considered a very questionable substance by the FDA, and we have removed it from our shelves. The same goes for glycyrrhizin (licorice extract) and Adrenal Cortical Extract (ACE). Also there is some question about Germanium.

I submitted our list of IV agents to my own State Board of Medical Examiners many years back in Hawaii, and they were never questioned. I also submitted the same list of IV agents to our State Malpractice Agency (owned and operated by physicians) – when I still carried malpractice – and they said it was OK.

I heard from the FDA in 1992, and got the "official" word as to what IV nutrients they approved. But before I talk about that, I wanted to fill you in about a few things that

have come up in conversations with a considerable number of FDA officials over the past years.

One thing I've found during several hours of conversation with various FDA officials is that views vary widely, depending on the official, his or her mood, and probably the day of the week. Most of the FDA agents and officials with whom I have talked were supportive, honest and "real" people. Many clearly expressed the view that the FDA should stay completely clear of the way physicians practice medicine in the privacy of their own offices. For example, Dr. Peter Rheinstein, who was Director of Medical Staff for the Office of Health Affairs/FDA told me that, "a physician's private practice, where you don't advertise or sell products [non-FDA approved agents, as long as they are not illegal substances], is not generally violated by the FDA."

I heard the following "policy" statement regarding any IV nutrients or other IV agents that we might use repeated enough times that it bears mentioning here. Mrs. Cole, of the Texas Regional Office of the FDA, said the FDA requires products we use to be "purchased from 'reliable' regionally approved manufacturers [in the U.S.]," or from "companies found to be operating under `good manufacturing standards' [by the FDA]." Mrs. Verly Walker, of the Denver Regional Office of the FDA (which is responsible for my state, New Mexico), stated we could use products from suppliers who have "undergone establishment inspection" and the products "are produced under good manufacturing practices, as defined in the code of FDA Regulation" (sorry, I don't happen to have that code handy just now, and couldn't find out what it was, either, but I'm sure there is one .... somewhere).

I asked a number of officials about Jonathan Wright's case when it happened, but most knew nothing about it, and this was during the time it was very high profile in the news, etc. Others couldn't comment much because the matter was under litigation. One agent, who asked not to be identified, did tell me that the FDA would never have come into the picture if it had not been from pressure by the Washington State Board of Medical Examiners. In fact, Mr. Hamilton, of the Prescription Drug Dept. of the Office of Compliance at FDA Headquarters, commented that the FDA "does not regulate the practice of medicine," and also that the FDA "usually takes action only with the advice of the local Medical Board."

This is why I have repeatedly stressed that you maintain a running dialog with your State Board of Medical Examiners. I always have felt that you should tell them what you're doing and why you're doing it, and ask that they immediately advise you of complaints or problems. I've felt that if one were to cooperate from the start, and let them know one respects their views and concerns, that one might be on more solid footing if it ever came to a complaint. I know some of you feel you simply can't do this because of the "climate" in your particular state, and for good reason. For example, I spoke to Mrs. Rosario Vior of the regional California FDA office, and her comments regarding the practice of medicine in California made me feel quite relieved I don't practice there [and this was in 1994!]. So when it comes to interaction with your State Board, it's quite important that you "test the waters" before you jump in, first by making inquires of your colleagues as to the attitude of your Board. Different States have Boards with radically different attitudes. New York and California seem to be the most fearsome. (NY now has an "alternative medicine" bill that offers some measure of protection for physicians.)

After much talking and reading between the lines, it became quite apparent that the FDA is generally not at all much interested in what a private physician does for individual patients in the privacy of his or her office. We are allowed to use products from "FDA-approved" companies or pharmacies, but there's a hitch. The FDA does not give its blessing to a small distributor until that distributor or manufacturer has been investigated and/or inspected by the FDA. Some of the sources I mention in this Guide have met FDA requirements, but others may not have, as they may have not have been "investigated."

On the other hand, these agents (such as ACE) are available elsewhere, and until they are "officially" declared illegal from that company, it is possible you could obtain and use them, as long as you don't sell, promote or advertise them to patients or other physicians. And remember, those disclaimers are a good idea -- your patients do have the right to know that what you are doing is not necessarily condoned or approved by the FDA or anyone else. As long as you trust the source from which you obtain these agents, all may be OK, unless or until you are told by someone in authority to stop. If you were to harm a patient with an agent that is not FDA-approved, or an agent with which your State Board disapproves, you could be in Big Trouble. My motto, as always: let's be careful out there.

The FDA Speaks

Now on to the "official" version. You may remember that we have a somewhat reluctant Big Brother who has been appointed to watch over some (lots?) of what we do. The FDA, as I've told you, does not really care to interfere in the way a physician practices medicine. The FDA feels they have the responsibility to monitor products available on the market for safety, and I think rightly so; after all, somebody has to. I guess we could try the novel idea of leaving the responsibility of monitoring safety of the parenteral nutrients we use up to the companies who produce these products, but that's just not how it works anymore. There's an argument for both sides of this issue. In any case, the FDA is stuck with responsibility for the ultimate safety of many products used on people, and certainly for that of parenteral nutrients. These are considered prescription drugs, and if the FDA were not so busy doing other things, regulation enforcement might be even tighter than it is at the present time.

Mr. Frank R. Fazzari, who was Chief of the Prescription Branch (HFD-313), Division of Drug Labeling Compliance, Office of Compliance, Center for Drug Evaluation and Research, FDA, was kind enough to reply to my inquiry as to the legal "status" of our entire list of available IV nutrients (I think the reason it took him so long to reply was that he had to type out his title in his letter to me). The reason I say "available" nutrients is because these are available for purchase from a number of sources in the U.S., but we don't actually use them all. When you see something in quotes, it is taken verbatim from his letter to me, dated Feb. 5, 1992.

Let me make a few general comments before I get specific here.

The FDA operates under several guidelines when it comes to various substances. Specific substances have specific rules. The rules for nutrients are largely stated in the FDA's Compliance Policy Guide 7132c.02. Injectable nutrients are considered prescription drugs, no matter what they are, or how simple they are. As such, the same rules that apply to any other drugs apply to parenteral nutrients. These substances are supposed to go through the same approval process as are any drugs, before they are used on people.

In 1938, the Food, Drug and Cosmetic Act was enacted, which established a pre-market review procedure for new drugs. This act required companies to obtain an effective new drug application (NDA) to demonstrate safety before marketing a new drug. The act exempted certain drugs marketed under the 1906 Food and Drugs Act -- sort of a "grandfather" situation. The FDA was made so busy by this new ruling that many drugs were grand-fathered into use without total scrutiny. Consequently, many products were introduced to the market without effective NDA's because the FDA advised the manufacturers that many products were generally recognized as safe -- GRAS -- (i.e. not new drugs). Such advice was often based on a determination that the products were identical, similar or related to one or more drug products with effective NDA's. Many other products were introduced because the manufacturers concluded, without FDA advice, that the products were generally recognized as safe or that they were covered by the grandfather exemptions. These last 2 statements are quite important when it comes to our parenteral nutrients.

This (and other things) prompted the 1962 amendments to the 1938 act. The amendments did several things, and added the further pre-requisite that new drugs had to be not only safe, but proven effective. This is where Investigational New Drug studies, or IND's came to be. The 1962 amendments required that the FDA evaluate all drugs that had passed muster under the rules in effect between 1938 and 1962. This became known as the Drug Efficiency Study Implementation, or DESI for short. DESI removed a great number of products from the marketplace or changed labeling to reflect that effectiveness for certain conditions was not proven -- most of you will remember when all that happened (gosh, seems like yesterday -- or a thousand years ago).

With respect to new drug products first marketed after 1962 and not identical, similar or related to a pre-1962 drug products, the FDA has required approved NDA's prior to marketing. The FDA has initiated immediate enforcement action against products marketed without approved NDA's, and also against unapproved products that are identical or related to products approved on the basis of safety and efficacy after 1962 (products without NDA's). The hook here seemed to be that any product exactly the same or similar to a pre-1962 product was OK, even if the regulatory status of that drug had not been resolved.

The FDA has now seemingly abandoned this policy in favor of stricter control of most all products on the market, whether or not they are related to pre-1962 products. In 1984, new exceptions were added to what is now known as the "compliance" policy. There's a whole list of these, but what might apply to the parenteral nutrients in question are the following: 1) The FDA may take action against any drug product marketed after Nov. 13, 1984, or 2) it may take action against any new product that is of a different dosage or route of administration than pre-1984 drugs.

I apologize for cluttering you brain with the preceding few paragraphs, but some of the background is important. The reason some of the above may not be extremely clear is that I took it verbatim from the Federal Register, Vol. 49, No. 189, kindly sent to me by Mr. Fazzari; it seems that Governmental Publications are not necessarily distinguished for their clarity.

Now to the crux of this whole issue: what about that list of nutrients I sent Mr. Fazzari? The list is essentially the list of agents you see in Table 2 (our protocols), minus a

few (our protocols no longer use some of the agents I asked about, and one agent has been added -- germanium -- which I'll mention again). Mr. Fazzari's comments are as follows:

"1. There are approved NDA's for specified firms covering the following drugs in your list:

Amino Acids (Travesol 8.5%)
c-AMP (adenosine monophosphate)
B-1 (thiamine)
B-6 (pyridoxine)
B-12 (hydroxocobalamine)
Folic Acid (5 mg./ml)
Magnesium Sulfate (500 mg./ml)
Manganese (0.1 mg./ml)
MVC + 3 (Multivitamin Mix)
Potassium Chloride
Zinc (10 mg./ml)"

"2. The following drugs included in your list are unapproved new drugs and can only be marketed under the terms of the FDA's Compliance Guide (7132c.02) - Marketed New Drugs Without NDA's or ANDA's (copy enclosed) [I'll go over this all after Mr. Fazzari's comments]. That is, firms proposing to market drug products under this CPG must submit appropriate documentation for FDA review prior to marketing:

Ascorbic Acid 222 mg./ml
Ascorbic Acid 500 mg./ml
B-Complex
Bio-Trace/4R (multi trace minerals)
Calcium Gluconate
Calcium Glycerophosphate
Selenium (200 mcg./ml)"

"3. The FDA has determined that the following are unapproved new drugs and require FDA approval at this time.

ACE (Adrenal corticoid extract)
B-15 Pangamic Acid
Folic Acid (10 mg./ml)
Glutathione (60 mg./ml)
glycyrrhizin
HCl (Hydrochloric acid for injection)
Magnesium Chloride (200 mg./ml)
Molybdenum (100 mcg./ml)
Vanadium"

[Compounding pharmacies have most of the above available, with the exceptions of ACE, Ca glycerophosphate and Bio-Trace/4R.]

If you missed the quotes, the above is verbatim from Mr. Fazzari's letter. Mr. Fazzari then went on to say:

"Please note that the above determinations are for marketed drug products and the FDA generally does not limit the manner which practitioners use approved drugs, or marketed drugs without FDA approval meeting the conditions of the Compliance Policy Guide (CPG 7132c.02 (copy enclosed) within the practice of medicine. However, the FDA may proceed with regulatory action if it is determined that a licensed practitioner promotes and/or advertises such drugs for uses outside their approved or labeled uses."

Well, it looks to me that the parenteral agents in the first group above are OK. It also looks as if the second group could possibly be considered "exempt" or OK because those agents might have been grand-fathered, as they could be similar to agents tacitly approved by the FDA before 1984. The third group -- the one I have been most concerned about all along -- is clearly not approved. Parenteral germanium would undoubtedly belong to this last group. You'll note that magnesium and folic acid are approved only in certain dosages, a reflection of the change in FDA policy since 1984.

The CPC guide 7132c.02 that Mr. Fazzari sent is really almost indecipherable to me. It covered the points I mentioned above. But what we need, of course, are specifics. We need to know which agents we are using might be considered to be grand-fathered in, pre-1984 or pre-1962. I am only guessing that it might include all of the agents in the second group above. So when we use any agent from that second or third group of nutrients, we must trust that any manufacturer whose product we are using has submitted an NDA to the FDA. I think it's a safe bet that this is not the case for some of the agents in the second group, and many -- or even most -- in the third.

If one were administering IV therapy with "unapproved" agents, what would happen in a "worst case" scenario of FDA disapproval? I've asked several FDA officials this question, and the response was very similar: likely not much of anything, unless you had complaints pending or your State Board has had problems with you in the past. The FDA would likely give you a warning that your materials are not FDA approved, and that you should stop using them. If they received further complaints, it is possible that they would confiscate your materials. Would you get in trouble? Again, not likely, unless you have other problems pending or previous actions had been taken against you. Unless you are promoting (or stand to profit from distributing) unapproved materials to physicians or patients and/or advertising such unapproved materials, the FDA is really not much interested. It's much more likely you would have a problem with your State Board or other physicians than you would with the FDA (however, if you've sued the FDA for any reason, all bets are definitely off).

On the other hand -- at least currently -- the FDA is less likely to interfere in the area of pharmaceutical compounding. You will recall that the FDA has given guidelines to one of our suppliers, College Pharmacy, and Tom Bader feels he is complying above and beyond these guidelines. If you fear threatened from somewhere about any IV therapy you are using, it might be best to inquire whether a licensed pharmacist could compound any agents you are using. I think this could be overkill for most of the agents you might use, especially if you keep a low profile and don't sell or advertise these agents, but some of you may feel you need

to do this with some or all of the nutrients you use which were included in the second and third categories from Mr. Fazzari's letter.

It also appears that the FDA would be not be likely to bother you if you were to compound your own materials, especially if you were to perform routine sterility tests (cultures) on any materials you would make, and you didn't "sell" them to any person(s). This is not as difficult as it sounds, and I'll tell you how to do this in the second part of this Guide. Physicians are legally able to compound for their own patients at the present time.

Here's a more recent and more disturbing development. On January 1, 2004, the first version of **USP Chapter 797**, "Pharmaceutical Compounding: Sterile Preparations" became official, This details the procedures and requirements for compounding sterile preparations and sets standards that are applicable to all practice settings in which sterile preparations are compounded. Since the standards became official, they have been widely adopted, are enforced by many state boards of pharmacy, and may be surveyable by accreditation organizations. On June 1, 2008, the revisions to USP Chapter 797 will become the official standard and will be published in the Second Supplement to USP 31-NF 26 and in the Pharmacists' Pharmacopeia.

The laws defining each *state's* sterile compounding regulations can be categorized according to three status levels: no reference, indirect, and direct (See Table 1). No reference status indicates states without laws or regulations that reference sterile compounding or parenteral nutrition practices in any way. The indirect status level indicates that the laws and regulations of those states do not specifically cite 797, but regulations are in place addressing sterile compounding or parenteral nutrition. States with direct status either require compliance with 797 or have harmonized their laws and regulations with the chapter. Table 1 summarizes that status of the states in 2011: there were five no reference, 29 indirect, and 17 direct states.

Table 1. 2011 Regulatory Status Levels

No Reference	Indirect			Direct	
Michigan	Alaska	Alabama	Arkansas	Colorado	Connecticut
Nebraska	Arizona	California	D. of Columbia	Florida	Georgia
New York	Delaware	Idaho	Illinois	Iowa	Indiana
Pennsylvania	Kansas	Kentucky	Louisiana	Maryland	Massachusetts
Hawaii	Maine	Missouri	Mississippi	Minnesota	New Mexico
	Montana	North Carolina	North Dakota	Oklahoma	South Carolina
	New Hampshire	New Jersey	Nevada	South Dakota	Texas
	Ohio	Oregon	Rhode Island	Utah	Virginia
	Tennessee	Vermont	Washington	West Virginia	
	Wisconsin	Wyoming*			

*As of January 2012, Wyoming has adopted regulations that move it into the Direct category

The law was enacted to assure that hospitals and compounding pharmacies whowere making sterile preparations did it properly. But this effectively means that all physicians who make up sterile preparations in their offices – an IV, for example – need a class 10 clean room – or thereabouts – to do it. This means positive pressure, a sterile hood, sterility testing and the list goes on and on. No physician could possibly afford to do it, and in fact, most compounding pharmacies avoid *compounding steril products for injection* because of the

cost of compliance caused by USP 797. Most docs who do IVs are affected by this law, and even allergists who draw up and "package" allergens for their patients would have to do this.

So what does this all mean to us? Well, not a great deal at present. The problem with USP 797 is one of enforcement: this is not easily enforced in a physician's office without a zillion regulators on the job. If you have come to the attention of your State Board, on the other hand, and your state is supposed to be in any kind of compliance with USP 797 (table above), you could theoretically be investigated.

Food for thought. Update to follow . . . . . .

Chapter 6: Advanced IV Nutrient Protocols

A summary of all of the major parenteral protocols I've been using over the past several years appears at the end of this Guide, including the Vitamin C protocols for cancer. The advanced protocols in this chapter may be used for most of the problems you might see in your office.

- **Glutathione Protocol**: David Perlmutter, MD, who practices in Florida, gets the original credit for this protocol for Parkinson's. You can get the details for his use on his website, www.brainrecovery.com. He employed this for use for patients with Parkinson's disease, and he and others have also used this IV for other neurological conditions. This protocol is often effective for patients with Parkinson's and lessens tremors, spasticity and rigor. As for MS, ALS, and other more severe neurological problems – well, we'll see.

  Since glutathione is the major enzyme of detoxification in the body, it made sense to me to try it on chemically sensitive patients, or patients who were attempting to recover from one or more chemical exposures. After all, we've used IV glutathione for 20 years in my office in IV infusion protocols, primarily because it "should" help. In reality, I'd never observed that it was singularly beneficial, since it was always given with other nutrients and in very small doses.

  However, we were giving it by infusion – over 1-3 hours – and I was using dosages from 200 to 500 mg. at most. Dr. Perlmutter found that glutathione did not work for Parkinson's patients if it was given by infusion; tissue levels apparently did not get high enough with a "slow" administration. Additionally, he found that the effective dose for Parkinson's was 1300 – 1400 mg. or more, three times per week.

  So we tried this dose, but on chemically ill patients and patients with several other problems, such as "migraine" headaches and allergic reactions to foreign substances, such as bonding in a tooth. To my surprise, it has worked marvelously well. In fact, it has been dramatic for almost everything we've used it on. Many chemically ill patients swear by it! I have since increased the dose up to 2500 mg. when the lesser amount fails - it may work better for some. Usually it seems that doses higher than 1400 mg. do not offer additional benefit

  I'd advise you to start with 600 – 800 mg, and work up by 200-300 mg. per IV from there. If you use it to treat Parkinson's, also work up slowly, and start with 400 mg. for any patient who has (or has had) lots of mercury fillings. If you start with the full dose, you may cause Parkinson's symptoms to become acutely aggravated, since most appear to have heavy metal issues (mostly mercury), and glutathione appears to unbind significant mercury to the circulation.

  - ◊ **Frequency**: this IV must be given 1-3 times weekly for all patients to begin with, given over about 10 minutes. Parkinson's patients generally require continual use of this protocol 2-3 times weekly. Other patients need it less often. Do not give up on this one until you've evaluated patients with the 2500 mg. dose. Although glutathione is fairly isotonic, it feels "uncomfortable" for some patients, so we add some sterile water or NSS to

the syringe. We now add the diluent (50% of NSS and 50% sterile water) equal to the amount of glutathione and any other nutrient in the IV.

For many of our patients, including some of those few we have with Parkinson's, I have found that an IV push of 600 - 1000 mg. of glutathione with 1 cc (1000 mcg.) of B-12, 2 cc of N-acetyl cysteine, 1 cc of B-complex and 500 - 1000 mg. of MgCl as an alternative to a larger dose of glutathione, often seems to work as well as higher doses of glutathione alone. In fact, this is now one of the most common protocols we use in my office.

The implications for this protocol for mercury detox are significant. It may be theoretically superior to DMPS or DMSA, but I have seen no comparisons yet.

NOTE: It would be interesting if you would try this protocol on various conditions and send us feedback as to how it seems to work (fax: 505-820-7315). I think the possibilities for this protocol are significant, and it is not expensive.

Wellness Pharmacy (see "Suppliers", before "References" at the end of this chapter) has a proprietary form of glutathione that they feel is superior to other types. It comes at 200 mg./cc, and costs about $2.00/cc. We have used it, but I can't say whether it's better than others available.

Super-Immuno Protocol

This protocol is by far one of the most valuable we use in our office, though certainly not the most common. I use this protocol sometimes for acute chemical exposure/sensitization, though I tend to use the Glutathione protocol more these days. I use the Super-Immuno for severely ill patients and for most illnesses we could possibly see in our office. I make no claims for it, but if you would care to try it, we have never seen it cause an acute adverse reaction of any kind. Oddly enough, this IV has never been noted to cause the "detox" reactions we have seen with some of our other IV protocols. Most patients treated with this protocol have noted immediate improvement in their symptoms, almost no matter what they are. That seems surely to be an incredible claim. Much more study is needed, certainly, but my results have been most encouraging, to put it mildly. This protocol does have one disadvantage: it is expensive.

Please note that the FDA considers several agents in the protocol as "unapproved". This protocol has been used in our office on individual patients as often as 2-4 times weekly for up to about 2 weeks, and then generally once weekly until the patient needs no further treatment, there seems to be tolerance, failure or any adverse reaction. If these phenomena do not appear, the IV may be used on a decreasing frequency basis until the patient no longer needs it. I have seen one patient (who had MS) who seemed to become moderately intolerant to the protocol, and it had to be discontinued after 8 infusions (weekly), even though her initial response was positive.

Macular Degeneration Protocol

This protocol is a modification of Dr. Jonathan Wright's original, and has an

interesting story behind it. Dr. Wright had been treating an elderly lady with macular degeneration whose husband was an accountant. As such, her husband had recorded every nutrient she had ever taken for her condition, and Dr. Wright noted that although she had been taking plenty of zinc and selenium orally for her problem, there had been no improvement in her vision. Since Dr. Wright often feels "IV is best," he thought he'd try an IV protocol of the same nutrients for her condition. Well, to make a long story short, it worked, and her vision improved significantly. Dr. Wright has since modified his original protocol and has treated a number of patients, a number with success and some without. There have been articles published regarding oral nutritional therapy of macular degeneration with most all of the nutrients in this protocol.

The protocol we use now (included in Table 2) was created by Dr. Kalpana Patel. Dr. Patel is the Past President of the American Board of Environmental Medicine and a longstanding IV therapist and Fellow of the AAEM. Dr. Patel has presented the use of this protocol at past AAEM Nutritional courses. She has worked with her husband, an ophthalmologist, *and absolute, positive changes were well documented by retinal scanning* in a considerable number of patients.

Treatment with this protocol is begun 3 times weekly, decreased after 3-4 weeks to twice weekly, and then given as needed. A total of 20-30 treatments are required. The second month, in one of the two IVs weekly the dose of selenium is increased to 800 mcg. and the dose of zinc is increased to 20 mg.

Dr. Patel also suggests a daily *oral supplementation* with the following: a good multivitamin, 4 grams of Vitamin C, 1200 U of vitamin E (we prefer Unique E®), 15 mg. of manganese, a good B-Complex, zinc 50-100 mg. and selenium 400 mcg. Thank you, Kalpana!

Our success rate on a very limited number of patients has been the same -- sometimes it has worked and sometimes it has not. The odds do appear in favor, however. Your patients should notice a subjective improvement in vision within 6 weeks, or there's a good chance it isn't going to work (in my experience).

Ideally, you should administer this IV in cooperation with an ophthalmologist, so vision could be checked every 3 to 6 months. In our limited experience, the improvement is generally subjective and not anatomically objective without more sophisticated testing. In other words, the patient and the ophthalmologist should notice a considerable improvement of vision over time, lasting longer and longer between IVs. However, the ophthalmologist may likely not notice a visible change in the pathological appearance of the retina, unless he/she uses special diagnostic tools.

This is an important point. We had a patient in Hawaii who noted a definite improvement in her vision, but her ophthalmologist (who was extremely skeptical), told her – in no uncertain terms – the IV "wasn't helping" because he could find no change in the retinal pathology. Because of his comments, she stopped treatment, even though she felt it had been helping.

Another short story about this protocol, and I'll go on. I was forced to cancel my malpractice insurance as a direct result of using it.

In Hawaii, I was insured by a California company, Medical Insurance Exchange of California (MIEC). One of my "colleagues" reported to the insurance company that I was using this protocol. MIEC notified me that they felt the treatment was generally inappropriate (at that time we had 3 patients out of 3 who had benefited), that I must present all my "credentials" to them and that I would have to appear before a medical review board in Hawaii, basically – I felt – to try to prove I wasn't a "quack." If the review board would exonerate me, MIEC would consider continuing my insurance; otherwise they would cancel my policy. Needless to say, I didn't need that kind of grief in my life, nor did I feel MIEC was the kind of company I would really feel comfortable representing me in times of adversity. So I told them they could stuff their insurance policy in their ear and quickly switched insurance companies. Propriety is not without cost, however.

The moral here is – as always – clear things up first with "the powers that be" before you jump into something. Had I been to my Medical Board beforehand, I might have had the support I needed (in Hawaii that wouldn't have been likely, though). It was a great idea with New Mexico, however. This little story may give you some insight as to why I keep repeating this. You'll be very happy in the end if you are able to cover your bases, I promise you. If your Board of Medical Examiners is known to be receptive, it's my feeling you should tell them what you'd like to do. If not, be conservative and help your patients the best way you know how. As time goes on, I will try very hard to substantiate some of the protocols I've mentioned with much more support from the literature that I've given you to date. The more ammunition you have, the better off you'll be.

All of these IV protocols are from my individual experience (except the Myers), but are now endorsed by the AAEM, as we teach IV therapy in Part IV of the AAEM courses for Category I ACCME credit. Since we get Category I credit from the ACCME, IV therapy with nutrients is tacitly approved by the AMA, via their ACCME. So if you're ever challenged by anyone (State Board, etc.), be certain you dwell on this. For "preventative measures", I recommend highly that you attend the IV course given by the AAEM (or ACAM if they offer Category I credit for it), if you haven't already.

Protocol for Acute Viral Illness

This protocol is also one of the most useful I have found in my practice. Dr. John Myers in Baltimore, MD, originally developed it, and I've modified it somewhat by adding a few more nutrients, but it's quite similar to the original. The anti-viral properties that it appears to have been generally attributed to the very high dose of ascorbate (a number of papers in the literature have clearly demonstrated the viro-toxic/antioxidant properties of ascorbate, both administered orally and in vitro).

I've used this IV in my office since 1986, often for acute viral illnesses, and in my experience, it is quite consistently effective. I've found this IV can be of significant benefit to a patient who is acutely ill with what appears to be a viral illness and simply can't "afford" to get sick. This would include movie actors, rock stars and lawyers who sue doctors for a living. The protocol may be used daily as needed, but I have found – for acute viral illness – it generally needs to be used only once, twice – or rarely – three times.

It's best to infuse this into a large (preferably antecubital) vein. The infusion should take between 1-1/2 to 2 hours. Again, this protocol may be repeated daily or every other day for as long as it takes for your patient to feel well again, but should generally not have to be

given more than 3 times. If the patient has not had a response by the 2nd infusion, it's probably not going to work, or you'll need to try a higher dose of Vitamin C in a shorter period of time (an hour).

You may change this protocol as you see fit. If you add more ascorbate, be sure to add about a gram of calcium gluconate to this IV for each additional 10 grams of ascorbate (ascorbate has a "chelating" effect and can cause a drop in serum calcium, with resultant tremors). You should keep the osmolarity below aproximately 700 mOsm/L. If you wish to give more ascorbate (which would make this IV exceed this range of osmolarity), I'd advise giving it slowly enough so there is no discomfort to the patient. The problem is that it has to be given *fast enough* to get high plasma levels of ascorbate.

The higher the dose of Vitamin C, usually the more thirsty patients get, and you should provide plenty of water. Vitamin C also has a diuretic effect on some patients at high dosages. The maximal amount of ascorbate physically can't exceed about 100 grams, and you'd need to delete some of the additives in this IV if you go in that direction, and you'll almost certainly run into venous irritation or sclerosis at some point. We've given up to 100 grams of ascorbate in a day for a viral illness with determined patients (see also the IV protocols for cancer), though I've heard from at least one physician who says he has given 200 grams a day in two sittings. I can't really recommend that yet, as I've had no experience with over 100 grams IV daily.

Chronic Illness Protocol

This protocol is essentially one we use in my office for the majority of patients who don't have any of the other specific conditions treatable with our other protocols, and for those who cannot afford the "Super-Immuno". I often modify this protocol significantly, depending on the condition with which I'm dealing. For my severely chemically sensitive patients, if I am not using the Super-Immuno, I will sometimes modify this protocol by adding more glutathione and/or ascorbate. This is also generally the protocol I use when I'm not really sure which protocol to use. If you do use this, you should feel free to vary the quantities of nutrients for your patients in order to see what works best for each patient. Remember to adjust the osmolarity accordingly.

You'll note the "mineral mix" in Table 2 is a rather complicated formula, and is not generally available. If you would like to use this or any other formula of your own design, get it from a compounding pharmacy. This particular mixture is available from College (or you can compound it yourself – see chapter on compounding your own nutrients).

Alzheimer's Protocol

This protocol should be considered investigational, since I have not used it in my office. The protocol comes as a courtesy of Dr. Daniel Clarke and Dr. Rubin Oganesov. They feel it works well, but I've only spoken to them on the telephone. I thought it was important to include it here, but it is not yet included on the list of our "standard" protocols. If any of you employ it with success, please let us know!

The list of nutrients is as follows:

S.O.D. (superoxide dismutase, 16 mg./mL)	5 cc
Glutathione (50 mg./mL)	5 cc

N-acetyl-Cysteine (100 mg./mL)	10 cc
Taurine (50 mg./mL)	5 cc
Co-enzyme Q10 (20 mg./mL)	3 cc
Acetyl-L-Carnitine (100 mg./mL)	5 cc
Vitamin C (50 mg./mL)	10 cc

This is given in 250 cc NSS and infused over approximately 1½ hours. It is moderately hypertonic. I have not used S.O.D., Acetyl-L-Carnitine or Co-enzyme Q10 intravenously, and since this is the case, I would advise that this protocol be used, at least at first, with caution. I would greatly appreciate any feedback you could give us if you try this protocol.

Adjunctive IV Treatment for Cancer with IV Vitamin C

Many physicians use IV nutritional protocols to treat patients with cancer, and we've done it for many years. Since cancer is a politically sensitive issue, I don't talk about it much, no do most of the other physicians who use it. This will undoubtedly change.

Previous articles on cancer treatment have appeared in the "non-peer reviewed" literature in past years, but finally my journal review in Dec. 2003 turned up *two major articles* in the "accepted" medical literature – Medline (PubMed) (149,156). So now you can refer potential detractors to the literature *they* read! This is critically important right now. Hopefully it will cease to be in the future. I very strongly urge you to order these articles, read them, and keep them on hand if you plan to use this approach.

These two articles discuss the treatment of cancer with intravenous vitamin C, and Drisco's article is very persuasive. I've modified the protocols used to include bicarb and Calcium, which I think are important, and the formulations appears in Table 3. The authors suggest starting with 15 grams of vitamin C to be sure of tolerance, then going to 60 grams twice weekly. Both papers determined dosages of vitamin C by measuring pre- and post-infusion serum ascorbate levels; the patients treated with ovarian cancer were maintained at 200 mg./dl, and treatment was concomitant (same day) with chemotherapy. Infusions are suggested 2-3 times weekly, but were given once daily (at 60 grams) for a week for one patient. The authors also suggest checking patients who will receive this IV for G6PD deficiency. Riorden suggested that alpha lipoic acid, 300 mg., p.o. b.i.d. increased the effectiveness of IVC.

This solution is moderately hypertonic for an infusion, and of course the more Vitamin C, the more hypertonic, but patients seem to tolerate it. It should be given in a large vein, no faster than 1 gram of vitamin C per minute, and patients seem to tolerate .5 grams per minute without problems. We have used this protocol in our office and have gone as high as 100 grams of IV Vitamin C. The solution needs to be given in 1 to 1-1/2 hours, so the preferred route is via a 24-gauge intracath in the antecubital vein. Some patients on chemo have a chemotherapy port that certainly simplifies administration.

The general approach in our office is to give this IV – usually 60 grams over a period of 1-1/2 hours – three times weekly until a positive change is noted in one of the patient's cancer markers (CA-125, etc.), x-rays or some specific parameter the patient's oncologist is monitoring. If there is a positive change, the frequency may be reduced at that point to 1-2 times weekly.

Some physicians alter this protocol with hydrogen peroxide every other treatment, though I don't really want to go into that in this syllabus. After reading the articles I read about phosphatidyl choline (published in 2005 – see references) it may be prudent to add PlaquEX or LipoStabil to your cancer regimen. Stay tuned.

Chelation Therapy

This is our chelation protocol:

Nutrient	**mOsm/cc**	**Amount (cc)**	**Total mOsm**
EDTA – 150 mg./cc - *dose determined by creatinine!*	1.34	*20* *	26.80
Vitamin C (500 mg./cc)	5.80	14	92.80
Vitamin B-12 (1000 mcg./cc)	0.31	1	0.31
B-complex (100 mg./cc)	2.14	2	4.28
Sodium bicarb (8.4%)	1.79	20	35.80
Heparin (5000 U/cc)	.46	0.5	0.23
MgCl (500 mg./cc)	5.90	3	17.70
Pantothene (250 mg./cc)	0.85	1	0.85
Pyridoxine (100 mg./cc)	1.11	1	1.11
Potassium chloride 2 mEq./cc	4.00	1	4.00
additives		65.5	
mOsm additives			183.88
Sterile water		500	
Osmolarity (mOsm/L)			317

* *it is mandatory to calculate the patient's dose, dependent on creatinine (see the following)*

It is not the purpose of this Guide to give you a fully detailed description of chelation therapy. However, I do use chelation routinely in my office, primarily for treatment of cardiovascular patients, and the effects can be dramatic, enable patients to bypass dangerous surgery, and increase quality of life and longevity. So I would be remiss not to talk about it here.

Chelation therapy uses EDTA (ethylene-diamine-tetraacetic acid) in one of a few forms, in order to reduce oxidative stress on various organs in the body. It was once thought that chelation directly removed plaque from arteries, but this is not really the case, although it likely eventually occurs in some circumstances. For cardiovascular disease, EDTA acts primarily as a potent antioxidant to reduce and ablate oxidative damage to medium, small and very small blood vessels that we all have accumulated. I use disodium magnesium EDTA.

If you plan to use chelation in your office, I would *strongly* encourage you to join ACAM (the American College for Advancement in Medicine), as I have, and attend their training course and other courses. They not only teach you a great deal, but you are also placed on their chelation referral list, and they will indeed give your name to prospective patients.

ACAM offeres a certification examination that may be taken once you complete their chelation course, and if you pass it, you can become a Certified Chelation Technician. Their number is: 800-532-3688, or visit www.acam.org.

The TACT trial results are now available (double blind chelation study) and shows a benefit for patients who receive chelation therapy for cardiovascular disease, though modest. Since chelation is such a political issue, you can bet that this study will be torn to pieces by the establishment, but at least it's a start!

My chelation protocol is very close to the "standard" ACAM chelation protocol that most ACAM members use (though there is no "official" standard). I would advise you to use *exactly* this protocol, as doctors who perform chelation would be much more likely to support you, if you have any legal problems resulting from chelation, if you are using this protocol.

The major potential problem with chelation therapy has to do with renal function. There have been a few complications reported in the past that have been primarily associated with patients with compromised renal function who received very high doses of EDTA (far higher than those recommended now). *For this reason, the dose of EDTA is limited, and is always calculated from the creatinine, or creatinine clearance*.

The maximum amount of EDTA you can give is 3 grams.

Calculation of creatinine clearance

To calculate creatinine clearance (CrCl), you must take into account the patient's creatinine, sex, age, height and *lean body weight* (LBW).

LBW for males = 50 kg + 2.3 kg/inch over 5 feet

LBW for females = 48.5 kg + 2.3 kg/inch over 5 feet, and you

Use the patient's *actual weight* if it is less than their LBW

The formula to use is: $\mathbf{CrCl} = \frac{\mathbf{(140 - age)\ times\ LBW}}{\mathbf{Age\ times\ creatinine}}$

To calculate the dose of EDTA, the formula is:

$$\mathbf{EDTA\ dose} = \mathbf{50\ mg./kg\ of\ LBW} \times \frac{\mathbf{CrCl}}{\mathbf{100}}$$

For example, say you have a male who is 65 years old, is 5 feet 7 and weighs 175 lbs, and his creatinine is 1.0

For his **LBW**, it's: 50 + 16.1 = **66.1**

So, his **CrCl** is $\frac{(140 - 65)\ (66.1)}{(65)\ (1.0)}$ or $\frac{(75)\ (66.1)}{65}$ or $\frac{4957.5}{65}$ or **76.27**

So his EDTA dose is (50 mg./kg.) (66.1) X $\frac{76.27}{100}$

or (3305 mg.) X 0.7627, which equals 4333 mg., or **4.8 grams**

Since that is way over the maximum of three grams, you would just give 3 grams (20 cc) in his IV. You know he *could* get more than that, if the max dose weren't 3 grams, but it is. Obviously, this formulation is primarily to calculate dosages for patients who have an abnormal creatinine, to make sure you're giving a safe dose of EDTA. In any case, you never give over 3 grams of EDTA, and do the calculation for all patients.

This IV is generally given over a period of 3 hours (about 1 drop per second), once weekly for 20-40 treatments. I then give it once every two weeks awhile, depending on a patient's symptoms, and then monthly. Most patients with significant cardiovascular disease and risk factors continue to do this indefinitely, some going to every 2-4 months. It can be a remarkable treatment for some patients.

Plaquex

This is phosphatidyl choline, made for IV use. It increases HDL and the action of HDL, and there are several other very strong mechanisms for its action. I've used it in my practice, and it may be effective if used *according to the manufacturer's instructions*. The problem is that it's very expensive to use with the frequency they suggest, and few patients can afford it.

Plaquex also has a common side effect in that it can cause *significant* irritation of the vein into which it is infused. The vein can become firm and slightly painful, and although the inflammation appears to spontaneously resolve over a period of time, it may worsen if it is repeatedly injected, especially into the same vein. For this reason – and because it is so expensive – I stopped using this product.

Plaquex can only be obtained from the manufacturer, it is not FDA approved, and is ordered by way of patient personal importation. If you think you'd like to use this material, the best way is to go to their Website: www.plaquex.ch. There you can download information for physicians and order it. I must say it appears interesting.

Suppliers for Materials

My lists of suppliers for all materials for IV administration and compounding nutrients and tables of my current IV Protocols follow.

Miscellaneous standard supplies:

Moore Drug Exchange: 1-800-678-8678, Darby Drug Co., Inc.: 1-800-247-4768

IV Nutrients (Current Suppliers as of 1/25/2015)

Abrams Royal Pharmacy (compounding)
8220 Abrams Rd.
Dallas, TX 75231
800-458-0804, 214-341-7966
Website: www.abramsroyalpharmacy.com

Alk Abello (sterile vials)
800-325-3010

Allergy Laboratories (sterile vials)
800-654-3971

Antigen Laboratories (sterile vials)
800-821-7013

Apothecure (compounding)
13720 Midway Rd., Suite 109
Dallas, TX 75244
800-969-6601, 214-960-6601
www.apothecure.com

College Pharmacy (compounding)
3505 Austin Bluffs Parkway
Colorado Springs, CO 80918
800-888-9358, Fax: 800-556-5893
719-262-0022, Fax: 719-262-0035
www.collegepharmacy.com

Millipore (filters, pumps, filtration apparatus, lab equipment)
800-645-5476
Website: www.millipore.com

McGuff Co. (IV supplies)
3524 West Lake Center Dr.
Santa Ana, CA 92704
800-854-7220, Fax: 714-540-5614
E-mail: answers@mcguff.com
Website: www.mcguff.com

McGuff Compounding Pharmacy
2921 W. MacArthur Blvd
Suite 142
Santa Ana, CA 92704
877-444-1133, Fax: 877-444-1155
714-438-0536, Fax: 714-438-0520
E-mail: pharmacyanswers@mcguff.com
Website: www.mcguff.com

Merit Pharmaceuticals
2611 San Fernando Rd.
Los Angeles, CA 90065
800-421-9657
Website: www.meritpharm.com

Save on Scales (digital scales)

Website: www.saveonscales.com

Sigma-Aldrich (lab supplies)
800-325-3010
Website: www.sigmaaldrich.com

Spectrum (raw USP nutrients), now changed to LetCo
800.239.5288
Website: www.letcomedical.com

Table II – Dr. Shrader's Office IV Protocols (selected) – 2009

⇓ IV Push Protocols ⇓ ⇐ All IV Infusion protocols ⇒

Protocols ⇨ / Nutrients ⇩	mOsm per mL	Meyer (rev.)	Acute Asthma	Headache Migraine, muscle spasm	Glutathione Protocol	Chronic Asthma	Chronic Illness CFIDS, etc.	Acute Viral Illness	Super - Immuno	Macular Degeneration	Chelation
Amino Acids (FreAmine III 8.5%) *	0.81						50				
Ascorbic Acid 500 mg/mL	5.80	4	3			12	20	200	50	10	15
B-6 (Pyridoxine) 100 mg/mL	1.11	1	3	4		5	2	1	2	1	1
B-12 (hydroxocobalamine) 1000 mcg. **	0.31	2	5		1	5 **	5 **	1	15 **	5 **	1
B-Complex 100 mg/mL	2.14	1	2		1	2	2	1	2	2	2
Bicarbonate Sodium 8.4%	2.00					17	15	60	20		20
EDTA (magnesium/disodium) 150 mg./mL	1.34										20 ❦
Calcium Gluconate 10% 100 mg./mL	0.72	2	2			2	2	40	20		
Folic Acid 10 mg./mL †^	0.20					1 ^	1 ^	1 ^	1 ^		1
Germanium 50 mg./mL †	0.25								10		
Glutathione 100 mg./mL **†	0.38				6 to 25						
Heparin 5,000 U/mL	0.46	Optional									
Magnesium Chloride 200 mg./mL	2.95	5	10-15	15	5	10	5	5	5	5	5
Mineral Mix *** †	0.57					1	2		2	1	
Molybdenum 500 mcg./mL †	0.80					1					
N-acetyl cysteine 100 mg./mL	1.91				2						
Pantothenic acid 250 mg./mL	0.85	1	2			2	3	3	3		1
Potassium chloride 2 mEq/mL	4.00	**NO**	**NO**	**NO**	**NO**	1	1	1	1		1
Selenium 200 mcg./mL	0.09									2-4	
Taurine 50 mg./mL. †	0.50						6		10	3 to 30	
Zinc sulfate (5 mg./mL)	0.11								1	2-4	
Additives		16	26-32	19	15 to 34	54	109	313	125	26 to 57	66
mOsm Additives		*44.1*	*59.2-73.9*	*48.7*	*23.3 to 30.5*	*151.6*	*219.8*	*1334*	*377*	*81 to 95*	*177*
Sterile Water	0	17	27	16	15	250	500	800 Ÿ	450 º		500
Normal Saline, .9%	.31									250	
Syringe or IV bottle, in mL		35	60	35	35-60	250	500.0	1000	500	250	500
Osmolarity (mOsm/L)		**1336**	**1095-1253**	**1391**	**776 to 623**	**499**	**361**	**1198**	**655**	**573 to 566**	**313**

* Caution: contains preservative (may be compounded preservative-free)

** Given IV push at end of infusion (not counted in volume or osmolarity calculations).

† Not FDA-approved nutrients/mixtures

*** "Shrader's Mineral Mix": the formulation is *boron* 1 mg./mL., *zinc* 5 mg./mL., *copper* 1 mg./mL, *molybdenum* 250 mcg./mL., *selenium* 200 mcg./mL., *chromium* 100 mcg./mL., *manganese* 100 mcg./mL., *vanadium* 100 mcg./mL., *lithium* 5 mg./mL. and *strontium* 1 mg./mL. (College has this formula, and other pharmacies may have this and different formulations available also)

Ÿ Remove 200 mL of water from the IV bottle before adding additives

º Remove 50 mL of water from IV bottle before adding additives

❦ EDTA dose must be calculated before this solution is given! (see text)

^ Add folic acid *last* to all protocols – use a separate syringe

Protocols developed by W.A. Shrader, Jr., MD, except "Meyer", macular degeneration, and original glutathione protocol. All have received extensive therapeutic use.

Table 3: Vitamin C Protocols for the Adjunctive Treatment of Cancer

	Vitamin C						
	15 grams	**30 grams**	**45 grams**	**50 grams**	**60 grams***	**60 grams**	**100 grams**
	500 cc bottle					1000 cc bottle	
	Amounts to add (cc)						
Ascorbic Acid 500 mg/ml	30	60	90	100	120	120	200
Sodium Bicarbonate 8.4%	18	18	28	45	50	50	60
Calcium Gluconate 10% 100 mg./ml	10	10	15	25	40	40	40
Magnesium Chloride 200 mg./ml	5	5	5	5	5	5	5
Additives	63	93	138	175	215	216	305
Milliosmoles of additives	253	427	625	724	839	861	1345
Sterile Water (bottle size)	250	500	500	500	500	1000	1000
Remove:			**40**	**80**	**100**	**300**	**200**
Total Volume	313	553	598	595	615	915	1105
Osmolarity (mOsm/L)	**385**	**722**	**1044**	**1179**	**1365**	**940**	**1217**
Infusion rate (drops/min.):	*120*	*130*	*130*	*130*	*130*	*180*	*185*

** This solution is quite hypertonic, and some patients may not tolerate it in anything other than a very large vein*

Chapter 7: Preparation and Use of Preservative-free Nutrients

Nearly the same method is used to compound IV nutrients as is that used to compound preservative-free allergens (see next chapter). The only major difference is that for nutrients, you use sterile water rather than Coca's solution, you don't need a larger particulate filter, and there are fewer steps required. Since most of you purchased this Guide to learn IV therapy, I'll teach you how to make IV nutrients first. Making IV nutrients is much easier than making allergens.

Raw powdered nutrients may be obtained from a pharmaceutical supply company (e.g. Letco) in at least pharmaceutical grade (USP, > 98% pure), a compounding pharmacy (more expensive) or a vitamin manufacturer if you have connections. I'll talk about these things shortly. First let's talk about the major differences between preserved and preservative-free nutrients.

Preserved Nutrients: The Good, the Bad (and the Ugly)

The Good

Preserved nutrients do not need to be refrigerated. They have the advantage of being inexpensive because they usually come in larger, multi-dose vials. They are easily available.

The Bad and Ugly

As I've already said, preserved nutrients can be dangerous, and the danger with preserved nutrients is higher than that of preserved allergens. After all, you're giving this stuff IV. Reactions to preservatives in this case are potentially fatal. Don't use them.

Preservative-Free Nutrients (PFN)

The Good

You will not see reactions to PFN. If a patient reacts to an IV containing only PFNs, you will know they are generally reacting to what the nutrient *is causing in the body* – often a "detox" reaction. You also will be able to sleep at night with the knowledge that you are not "pickling" your patients. The exception is that B-complex sometimes is not tolerated by rare patients

If you compound nutrients yourself in your office, they are quite inexpensive when compared to those you would purchase from a compounding pharmacy, or even with preserved nutrients you would buy from a manufacturer or distributor.

The Bad

PFNs from compounding pharmacies are not as convenient to use as are nutrients with preservatives. They usually must be prescribed for individual patients, which means you have to write a prescription here and there. They come as single dose units for individual patients, and as such a compounding pharmacy must distribute them in smaller "single use" vials, or the largest amount in a vial they can get away with. So they are also more expensive than preserved nutrients.

PFNs must be refrigerated between each use, if you do happen to get more than one dose out of any single vial. (Of course, if you compound them yourself, you can put them in larger vials, which I do. This is quite safe as long as you use sterile technique.) Although compounding pharmacies often understand you are using their single dose vials on more than

one patient, it simply is not their responsibility. The FDA, on the other hand, could take exception to this issue, although I have never heard of this happening to a physician.

If you compound yourself, you or your staff must find the time to do it and time is money.

The Ugly

The FDA still has the job to see that patients are "protected". Currently, it is not illegal for physicians to compound their own preservative-free extracts or nutrients. It would be illegal were a physician to sell them to other physicians, pharmacies, etc. So don't plan to go into business doing this. USP 797, discussed previously, adds a layer of risk, though at the moment I perceive it to be very slight, if you compound IV materials yourself.

Theoretically, the FDA could come to your office and check to see that you are using reasonable precautions when you do this. Occasional sterility testing would help convince the FDA — or any investigator from any agency — you were doing this properly. You could do this by performing aerobic and anaerobic cultures in your office on some type of random selection and schedule. Office incubators cost from about $125 to $200, and need not be much bigger than a breadbox. You would simply be looking for the growth of any organism, so theoretically you could perform your own readings. Alternatively you could send them to a local lab for culture.

The only incident – and there is only one – I have heard was an occasion when a State Medical Board told a physician he couldn't do this. He could likely have fought it and won, but he just didn't want to get into a fight. This was, however, before USP 797.

Materials You Will Need

The following is a list of materials you'll need to set up preservative-free nutrient preparation, along with some approximate costs. The catalog numbers listed are those from IBI and Millipore.

1. A digital gram scale. This does not have to be fancy, but must measure accurately down to at least 0.1 gram. Any good lab supplier carries these, and it does not have to be expensive. I got mine from Saveonscales.com)
2. Vacuum pump - This may be a hand-operated pump (Millipore hand vacuum pump), or an electric pump. *I would suggest the electric pump if you're going to be compounding nutrients – but you might want to start with a hand pump.* **(**We use an electric pump, Barnant Model 400-1901, Barnant Co., Barrington, IL, 60010, which costs about $200 (www.fishersci.com). Different models of Barnant pumps are available on www.pgcscientifics.com, and their model 475-3010 looks fine, and is $182.40).
3. Rubber Tubing – Included with your pump. However, for the electric pump, the tubing tends to be too soft, and will collapse with the more difficult extractions. You will probably need to get sturdier tubing (clear polyethylene) at your local hardware store, as we did.
4. 250 ml Erlenmeyer flasks (Pyrex, Sigma-Aldrich), probably two (if you break one).
5. 500 ml beaker (Pyrex, Sigma-Aldrich), probably two (if you break one).
6. No. 6 Green neoprene stopper ($.75 ea.), one for each flask you get, plus a few extra.

7. Millipore filter system, Millipore Sterifil Aseptic filter system, from Millipore, $79). This is a gizmo that holds the filters you will use for extraction – details below. (Note: if you are planning to make any of your own allergens for testing or treatment, you should plan to use separate filter holder for this.)
8. .65 micrometer filters (Durapore membrane filters, DVPP04700 from Millipore, $124/100filters).
9. Filter forceps – to place these in the filter system – OK, you really don't need these if you're careful.
10. Millex Sterile filtration units, SLGV025 LS, 0.22 micrometer from Millipore, $125/50. These are for the final filtration step.
11. 30 ml Luer-Lok plastic syringes.
12. 1000 ml Erlenmeyer flask (for making trace minerals, from Sigma-Aldrich).
13. Graduated cylinder, 100 ml (Pyrex, from Sigma-Aldrich, $26.70).
14. 18 gauge needles, No-Kor 1½ ", and short 25 gauge needles.
15. You'll need 30 and 50 cc sterile vials (we get ours from Alk-Abello).

Diluent: You should use sterile water for irrigation, since that's what compounding pharmacies use. This comes in soft plastic bottles, but there is no "plastic" taste to the water.

Weighing: You should purchase disposable wighing dishes from Sigma-Aldrich that can be used over and over, very inexpensive

Always "zero" your mechanical scale with the dish you'll use to hold the powder you measure on your scale. Digital scales have a "zero" button. Just push the button with the paper on the scale, after it registers that it is ready. Nothing needs to be sterile at the time of weighing. Put the weighing dish on the platform of the scale, *adjust the scale to zero balance*, and you're ready to go.

Solution Process

The process of extraction of nutrients takes place in only 2 stages:

1. Solution and
2. Filtration

Solution

The solution process is accomplished in a 250 cc Erlenmeyer flask for more difficult-to-dissolve materials such as B-5 and glutathione, since it helps to shake the container ro dissolve some nutrients, and in a 500 cc beaker for most all other nutrients. The mineral mix (Shrader's) – if you choose to make it – is made in a 1000 cc Erlenmeyer flask. In this step, the nutrient is mixed with sterile water to be dissolved in *solution*.

In this process, how much water you use, and how much nutrient, depends on the strength (mg./mL) of the final product you want, and of course the quantity of nutrient. The vial size you put it in is up to you, but as a rule, you should not make up vials of nutrient you won't use in about 6 months or less, unless you freeze it, in which case you can store most nutrients for several years. *See the table at the end of this chapter for the specific amounts of nutrients and water you will need to use for each nutrient you compound*. We don't freeze

our nutrients. The exceptions to this "freezing" rule are glutathione and vitamin C – these should never be frozen. I purchase all of the Vitamin C we use from Merit or McGuff, and preservative-free magnesium sulfate and chloride, sodium bicarbonate, potassium chloride and calcium gluconate are inexpensive enough that you probably will not want to compound them yourself.

For the example below we're going to compound pyridoxine (vitamin B-6).

In most cases, you *cannot make a nutrient stronger* than what I have listed in this Guide. The nutrients simply won't go into solution at concentrations higher than these.

1. Measure the proper amount of sterile water with the graduated cylinder or a 250 cc Erlenmeyer flask (in this case, you measure 200 cc). You can do this with the flask directly by using the graduations. Then add the proper amount of nutrient, in this case (refer to Table 4), 20 grams of pyridoxine HCL to 200 cc of sterile water in a 500 cc beaker to make the concentration 100 mg./cc. Depending upon the nutrient, you're going to end up with slightly *more* solution than you think you would because nutrients go into solution and expand the volume. Organic nutrients, and high concentration nutrients expand the volume slightly more than inorganic ones. *For MgCl at 500 mg./cc, for example, you use 200 cc of water, and it will make four very full 50 cc vials of product, with an extra vial of 30 cc*. In the case of B-6, you'll make four vials of 50 cc, and they will be full.
2. With nutrients harder to dissolve (e.g. glutathione, B-complex), you'll need to shake them in a 250 cc Erlenmeyer flask. In that case, you need to cap the flask with a rubber stopper and shake the solution until it is dissolved as much as possible. This will be quickly with many nutrients, and a bit more slowly with others. Sometimes letting it stand for a while helps. In a worst-case scenario, only a tiny amount will not dissolve. Don't worry about that – it just means your solution is as concentrated as it will go. Once the nutrient is dissolved in the water, you can filter it.
3. Set up the filtration equipment. This consists of the vacuum pump, the three-part Millipore filter and the tubing (the top cover for the upper part of the filtration unit is for storing a solution in the fridge if you ever need to, and is not used here). Attach the tubing (you should have about two feet) to the suction port of the vacuum pump. Push the small plastic fitting that attaches to the filter unit into the distal end of the tubing. This attaches the tubing to the lower part of the Millipore filtration unit. You can leave the tubing with the distal plastic fitting attached to the pump permanently.
4. Place the middle part of the filtration unit – the filter holder – on the top of the reservoir or bottom part. Do not force the filter holder too tightly into the bottom part of the filter unit (there is no screwing involved with this connection - the filter holder simply fits snugly to the bottom part). The suction applied by the pump alone does this well enough. If you push them together too firmly, they will be very hard to separate!
5. Place a .45 or .65 micron filter (depending upon your preference, really) in the filter holder with the filter forceps. Be careful to center the filter
6. Carefully screw the top part of the filter unit to the filter holder, without wrinkling

the filter. If it is not tight and even, it will leak at that junction.

7. Pour the pyridoxine solution into the upper part of the filter holder. Plug in the pump, or pull on the manual pump syringe. In most cases, the nutrient solution will immediately begin to come through the filter into the bottom of the container. If it does not, check to be sure you did not leave one of the blue paper separators in with the filter!
8. Do not try to swirl the solution once filtration is in process. If you do, some of the solution can be sucked into the pump tubing. If this happens, you will have to take the pump apart and clean the pump diaphragm, since a nutrient solution can dry "sticky" and this will interfere with the suction mechanism of the diaphragm.

Once all of the solution is in the bottom of the apparatus, you can detach the tubing from the filter apparatus and detach the top unit (filter holder and top reservoir). The suction seals this pretty well, so you'll need to get used to doing this gingerly by twisting and without spilling your solution. Now you're ready to go to the final filtration.

Up until now, you should have been taking care to use reasonable precautions so as not to significantly contaminate your nutrient. Now you must get serious and use sterile technique for the final process: filtration/purification. Any bacteria getting into the mix from this point will contaminate your solution.

Filtration

You should choose and label the correct number of vials in which you will be putting your nutrient, depending upon how much volume you're compounding (I usually do this as the first step). The nutrient labels are created with MS Word, so you, or someone in your office, need to be computer-literate with labels to do this. You can do it by hand, but let's face it, that's tacky. You will likely be using 30 or 50 cc. empty sterile vials. I use 100 cc vials for glutathione and EDTA, since we use a considerable quantity of those. Regardless of vial size, the process is the same. The smaller the syringe you use, the less pressure you will have to apply to expel the nutrient through the final filter, but the more often you will have to fill the syringe. I usually use a 30 cc syringe, though it requires more pressure than a smaller one to filter the nutrient.

1. Cleanse the top of the first empty, labeled vial with alcohol and insert a sterile 25 gauge needle into one side of the rubber top. The purpose of this is to let air escape from the vial as you are injecting the nutrient with the syringe (with the next filter attached) into the vial.
2. Remove the top part of the filtering apparatus, discard the filter and draw up the volume of your nutrient to fill the barrel of the syringe. Expel any air from the syringe. Do not attach anything to your syringe yet. Dip the distal end of the syringe into the nutrient solution and draw up the nutrient.
3. Carefully open a Milex-GV Millipore filter unit and attach it to your Luer-Lok syringe containing the nutrient extract. Place an 18-gauge No-Kor needle on the distal end on the Milex syringe filter. Remove, but do not discard the needle cap.
4. Insert the needle into the center of the rubber top of your empty nutrient vial, into which you will be putting your nutrient.

5. Apply steady, even pressure to the plunger, and the nutrient will flow quickly through the filter at first. You'll notice that the flow will sometimes diminish slightly as you continue to filter more of the solution. With a few nutrients (pantothenic acid, usually), you may have to use a second or third filter, in which case you must use your needle cap to re-cap the needle as you are changing filters.
6. When you have expelled the nutrient in the syringe, remove the needle from nutrient vial (leaving the needle and filter stuck in the top of the vial), and draw up more (or the rest) of the nutrient. Re-attach the syringe to the filter and needle in the vial and continue filling the vial, or begin filling the next empty vial.
7. Repeat this with as many vials as you're going to fill with the amount of solution you've made.

At this point you need to rinse your equipment thoroughly with plain water and put it on paper towels to dry. You can then proceed to your next nutrient. Put the compounded vials of nutrients in the refrigerator immediately, and keep them there all the time, except when making up your IVs.

Once you've found out how much time the processing of one nutrient takes, you'll be able to gauge how many you (or your staff) are able to do in a given time. It's wise to do this yourself for the first few nutrients, and then teach someone in your office to do it. Your lab monkey can also do this one. Nutrient compounding takes far less time than the allergen extraction in the last chapter.

Some specifics about nutrients

Be sure your staff pays attention to the characteristics and color of your nutrients. If your nutrients ever appear discolored or cloudy at room temperature, you could have a problem with contamination, and *you must discard it and compound again*.

Vitamin B-12

Since the concentration of B-12 is only 1 mg. (1000 mcg.) per cc, it doesn't take much B-12 powder to make a whole lot of IV B-12: 1 gram will make 1000 cc. This being the case, I buy 1 gram of B-12 and make up make 100 ccs, so at a concentration of *10 mg./cc*. I store that as *concentrate* and you must dilute it by a factor of 10 into 50 cc vials when necessary.

Folic acid

Folic acid is the only nutrient I make that acts "oddly" if mixed in the concentrated form with several other nutrients. It precipitates unless the solution is alkaline. Hence, if you make and use folic acid, you must always add it by way of a separate syringe and as the last ingredient you put in an IV, and you need to use a gram of bicarbonate when you compound it (otherwise it won't dissolve – see footnote, Table 4).

Sodium Bicarbonate

Sodium bicarb precipitates with some nutrients because some don't stay in solution as well if the solution is alkaline. A few drops of bicarb won't do this, so we get around this problem by drawing bicarb up first to put in IV infusion solutions and still using the same syringe to draw up the other nutrients.

Trace Minerals

The trace minerals may be mixed as a trace mineral "mix", or can be added to IVs individually. The formulation for the mineral mix I use appears in Table 5. To make the mix (or any mix) you just add them all to the same 1000 ccs of sterile water for injection.

The trace minerals are slightly different from the other nutrients we use. When you make up a trace mineral, you want to achieve a certain concentration of the trace mineral per cc in the solution you make. To do that, you must add more of the salt containing the mineral than you would think. To explain this, I'll use boron as an example.

You want a solution of boron that contains 1 milligram of boron per milliliter (1 mg./ml.). To make a liter of boron solution, you'd simply need 1 gram of boron (1 mg. X 1000). However, pure "boron" does not exist outside of the laboratory. We must use a *salt* of boron, in this case, boric acid.

The formula for boric acid is H_3BO_3. To calculate the percentage by weight of boron in boric acid, you need to know the molecular weights of the elements in boric acid (you get those from a periodic table). The molecular weight of boron is 10.8, hydrogen is 1.0, and oxygen is 16. The total molecular weight of boric acid is 10.8 + (3) x 1 + (3) x 16, or 61.8. So there is only 17.475, or about 17 % boron (10.8/61.8 x 100) in boric acid.

To calculate the amount of boric acid you need to get 1 mg./ml of boron, you use the following formula (B = boric acid):

17 % of B = 1 mg.; or .17475 (B) = 1

so B = 1 / .17475, and B = 5.722 mg. per cc

To make 1000 ccs of IV solution of boron, you'd need 5722 mg., or about 5.7 grams of boric acid.

To simplify this, in Table 5 at the end of this chapter I have given you the exact amounts of the various salts you must use to make the common IV trace minerals. So you won't have to do the calculations above unless you want to add another trace mineral to your regimen.

You'll notice the amounts of mineral salt you need to add are sometimes small. Don't forget to zero your scale with the container or piece of paper you're going to use to hold the nutrient!

Chapter 8: Preparation and Use of Preservative-free Allergens

Many of you reading this do not do allergy testing, and some of you do. Remember, even if you don't currently do allergy testing or treatment, you can always make your own allergens with which to test any substance you can think of, if it's available. This can open many new doors for treatment. You can also make allergens with autologous (from the patient) body fluids, such as urine and stool, if you're adventurous. The principals you read here can be applied very well to all autologous substances.

For more years than I'd like to admit, I'd been testing my patients with allergen extracts that contained preservative, usually in the form of phenol, 0.4%, not to mention glycerin. If I were going to test a patient who knew he or she had had severe or significant problems when they were tested to preserved allergens in the past, I would generally 'neutralize" the patients before testing with phenol and glycerin. This of course meant provocation to phenol and glycerin before any testing was done in order to obtain the correct neutralizing dose. We appeared to get away with that for most patients for years.

When I was practicing in Hawaii, I saw patients who were predominantly allergic". In contrast with my large allergy (mostly foods and inhalants) practice, I saw relatively few patients with severe, disabling problems such as chemical sensitivity and/or severe adverse reactions to chemicals. However, since moving back to civilization (forgive me, Hawaii), there was a turn of events. I see a growing number of patients with far more serious problems. Many of these patients neutralize poorly or react extremely to neutralization with any agent containing preservative or glycerin.

I quickly found, as my practice grew in New Mexico, that I had a growing number of patients I really couldn't test without making them severely ill, or worse, that I couldn't test at all. Patients were having more and more reactions in the office. My phone got into the terrible habit of ringing at home after midnight more nights than I could stand. Very unhappy patients on the other end of the line were telling me things like, "You told me that neutralization stuff would make the testing OK. Well, let me tell you what happened after I got home...." So I did the only logical thing: I cut my phone lines.

No, that's not true, and to this day my home phone number is still listed in the phone book. What I did do, however, after I'd had my fill of complaints, was switch to preservative-free allergens (PFA) for testing. I will give you enough information here so that you can make a choice of the type of materials you use to test and treat your patients.

This discussion will cover some of the more pertinent pros and cons of preserved and PFA and detailed instructions, suppliers and costs of all the things you would need to make your own PFA to use for testing in your office, and for preservative-free nutrients. The instructions should be explicit for you. You will even be able to teach your lab monkey to make them (unfortunately, it will take approximately 34 years to do this — so be sure to get yourself a young monkey). Realistically — monkeys excluded – as I've found with many things in life, all you need is somebody to tell you exactly how to do something, and you'll be off and running. And yes, this is possible even with brain surgery.

Preserved Allergens: The Good, the Bad and the Ugly

When I talk about preserved allergen extracts, I will generally be referring to extracts containing phenol, and to some degree, glycerin. Glycerin is really more of a "stabilizer"

than a "real" preservative. There are other preservatives out there (thiomerasol, benzyl alcohol, etc.), but they're not commonly used. They're also probably no better than phenol.

Allergen manufacturers are required by the FDA to put glycerin in all allergens they sell. Allergen extracts routinely come in 50% glycerin to maintain potency and stability (glycerin acts as a preservative at higher concentrations). Aqueous solutions of allergens, which do not contain glycerin, are available from several manufacturers. These allergens are not considered as stable as those which contain glycerin, but are "legal". They are still required, however, to contain a preservative of some sort.

All diluent available from manufacturers in pre-measured vials contain 0.4% phenol as well. *You can't buy pre-measured diluent* (usually 4, 8 or 9 cc) *for allergens without phenol*. In an attempt to circumvent the phenol problem, some physicians use plain normal saline as their diluent. This must be measured "by hand" and placed in empty diluent vials. Some of these physicians thus claim they use "preservative-free" extracts. I guess you'd have to say that this might be technically correct, but the diluents all will contain some amount of *glycerin*, as the concentrates used to make these allergens all contain 50% glycerin. If aqueous extracts are used, then there would still be one or another type of preservative at some concentration at all dilutions.

Certainly, the concentration of glycerin or preservative becomes less, the more diluted an extract is (the higher the dilution number, the less preservative or glycerin). The fact remains that extracts from any manufacturer contain either glycerin or a preservative. If these extracts are then used to make dilutions — no matter what the diluent — the dilutions contain these agents as well. They may be said to be "preservative-free" if saline is used as the diluent, but the glycerin is still there in measurable amounts.

Basically, one either gets glycerin or preservative (usually 0.4% phenol) in any commercially-available allergen or diluent. If you buy from a commercial supplier, you can't get around this fact of life.

The Good

Allergen extracts containing preservatives are easily and readily available from a number of reputable companies. They're easy to use right out of the bottle. Some companies who manufacture preserved allergens may also offer actual patient treatment sets. These companies will not make preservative-free extracts or treatment sets for you — they are prohibited by the FDA.

Allergens manufactured with preservative will remain sterile for very long periods of time. *Concentrates* containing preservatives or glycerin will invariably last (if kept in the refrigerator) for many years – long past the stated expiration date — without becoming contaminated with bacteria.

Glycerin (50%), present in the concentrates purchased from allergen manufacturers, enhances the stability and longevity of most protein extracts. The shelf life of extracts containing glycerin is further enhanced with phenol or another preservative, which prevents bacterial overgrowth. The phenol essentially "pickles" the invaders.

When preserved allergen testing sets are left out of the refrigerator during the actual testing of patients (often all day), one may be relatively certain they will not grow bacteria. This is true for dilute allergens as well as concentrated ones, since standard available diluent also contains 0.4% phenol.

Considering the above, preserved allergen testing sets need not be re-mixed on an extremely frequent basis. This will vary according to physician preference and is partly determined by the volume of testing done in a specific office. Many physicians re-mix preserved allergen testing sets every 3 months, more to maintain potency rather than to risk possible bacterial or viral contamination. That being said, I know of physicians who only re-mix testing sets containing phenol once a year or so and certainly seem to have no problem with sterility (now potency might be another issue!).

Preserved or glycerinated allergens are manufactured under well-controlled standards, and potencies and purity of most commercially available concentrates are fairly reliable. Some preserved extracts are not "standardized" (although the "standard" used is rather debatable, should you ask me).

Most patients – genenerally speaking, now – don't have problems being tested with preserved allergens, or those containing glycerin. This certainly appeared to be true of my patient population in Hawaii. Similarly, *most* patients don't have problems being treated — even long term – with preserved extracts.

Patients with mild to moderate intolerance to phenol or glycerin can indeed be successfully neutralized to these agents, using the Miller technique. Neutralizing doses of these agents may be effective when given immediately before testing or treatment with allergens containing them. These patients frequently react less adversely to sublingual (transmucosal) administration of these extracts, so some of these patients will tolerate treatment using this route of administration.

Lastly, preserved allergens are affordably priced. Prices don't vary extremely between manufacturers, so one is likely to see similar prices for the same items from different companies, often determined by volume ordered.

The Bad

As I mentioned, patients with moderately severe to very severe problems — and certainly not just those who have problems with chemicals — will often not tolerate being tested with extracts containing phenol or glycerin in any amount. Should you do so, these patients will frequently become quite ill for several days after testing, and they won't appreciate it one bit. Many or most will refuse to be tested or treated further. These same patients usually will not neutralize well to either phenol or glycerin, so you would also often not be able to mask them with a neutralizing dose prior to testing. If you are treating a patient population generally severely environmentally ill, you've either long ago switched to preservative-free extracts, or you've probably often wished you had them available.

Phenol and glycerin may tend to "cancel" if used for SET (serial endpoint titration) in patients who are not extremely ill, at least at the time of testing. However, these preservatives often interfere severely with the observed local and systemic response to provocation testing, especially to foods. Also, delayed symptoms, likely due to "unbinding" of phenol or glycerin, are common and usually unpleasant with both SET and provocation.

Right before we switched to preservative-free extracts, I recall very vividly wondering more and more whether a patient's symptoms were from the phenol or glycerin, rather than the substance being tested. And most of the times I wondered about it, it was likely that that certainly was what was happening (an obvious tip-off was when a patient had the same — or very similar — symptoms to the first several items tested).

If you're testing with allergens preserved with phenol and/or containing glycerin, you're doubtlessly treating with them as well. These agents, even in patients who do not appear to have severe general problems, can cause sensitization. After frequent treatments, it's not uncommon to see sensitization — or even what appears to be true "allergy" — develop (although It appears to be more common when therapy is given by injection than when given transmucosally). This most often manifests as increasing swelling or reactivity at the injection site, often to the point where dosage must be reduced or stopped altogether. Or the adverse reaction to these agents may well cause systemic symptoms that undo whatever benefits a patient might be receiving from the allergens injected, and desensitization or neutralization will appear to begin to fail. Adverse reactions to sublingual treatment are subtler, and usually manifest as one sort of symptom or another being produced after treatment, often worsening as treatment progresses.

Phenol and glycerin — in my opinion — 'contaminate" the response to provocation. In looking back, I feel very clearly that the symptoms brought about by preservative-free extracts are much clearer and often more specific than with preserved allergens. I think a considerable number of patients are intolerant enough to phenol or glycerin to "cloud" their responses. As most of you know, phenol or glycerin when tested alone will very often produce a positive wheal and flare, especially with dilution #2, and virtually always with dilution #1. If they are provoked alone, they will very often cause symptoms.

Even in the patient who is not extremely ill, extracts containing preservatives are just often more difficult to neutralize. Think about it: you're really trying to "neutralize" two or three things at once! We've all had the experience of being unable to completely neutralize the occasional patient. There's little doubt in my mind that this doesn't happen nearly as often with preservative-free extracts.

The Ugly

Have you ever mixed your own allergens in diluent preserved with phenol? If you have, you've no doubt noticed that very peculiar, irritating, antiseptic smell the phenolated saline has when you happen to squirt some out of the bottle. That, as most all of you know, is phenol; only 0.4%, but it goes a long way! Phenol is, as advertised, a preservative. Do you really want to Pickle your Patients?

Phenol is also known to be toxic at higher levels, as studies have shown again and again. If something is dangerous at high levels, isn't it a bit strange to assume it's harmless at low levels? Phenol also now appears likely to be carcinogenic. Do you really want to be injecting a potentially dangerous substance repeatedly into your patients? Would you like to have this done repeatedly on yourself? Think about it.

Preservative-Free Allergens (PFA): The Good, the Bad and the Ugly

The Good

PFA extracts don't contain any preservatives (or 'stabilizers", such as glycerin) at all ('Well duh, now" as my kids might say). This means:

- Patients who are severely ill will likely react adversely much less often to testing or treatment allergens because of the absence of phenol or glycerin. Accordingly, one would expect to be able to test more patients than one would using preserved allergens, without risking an adverse response. You might be surprised to see that your patient load would increase, once the "word" got around that you have begun

using PFA. If you doubt your patients are reacting to phenol or glycerin, start doing provocation with these agents as a control (I would guess that some of you do this anyway). If not, I think you'll be surprised at the results.

- There will be no "interference" in either skin response or symptoms induced by provocation from the preservative or glycerin present in your testing material. If a patient has a skin response or systemic response to PFA, one can be fairly sure it's from the specific substance to which one is testing, and not to what really amounts to be "contaminants" in one's testing solutions.
- Sensitization to phenol or glycerin obviously could not develop during treatment.
- There is no need to neutralize patients to phenol and/or glycerin before proceeding with testing, or as often is the case, before each and every treatment injection. Similarly, there is no need to use phenol and glycerin controls when testing.
- You need not worry about "pickling" your patients with phenol, or injecting your patients with a substance that could be potentially harmful over the long term.

Preservative-Free Allergens

The Bad

PFA are not available from allergen manufacturers. The only way to obtain them is to ask a pharmacist to compound them for you, or to do it yourself. Compounding pharmacists who will compound allergens usually do not have an office down the street, and will are more expensive than "standard" allergens containing preservative. You usually must go out of town to a large compounding pharmacy, or you must compound these allergens in your office. Since compounding, care and maintenance may take more time than you may have personally, one of your staff usually must be trained to do it.

Since making your own PFA does require more time than simply ordering them from a manufacturer, this means slightly more money. In reality, if you do it properly, it may not cost much more to make your own. But it is more trouble, certainly.

PFA must be handled more carefully than preserved allergens, as they will grow bacteria if contaminated (I'll talk about this later). It's also a fact that you can't get saline diluent without preservative in pre-measured vials (say, 4 or 8 cc) from manufacturers. This being the case, you must use empty sterile vials and pre-fill them with normal saline solution taken from an IV bottle to make diluent for your testing sets. This is cheap to do, but requires that extra time again.

PFA *concentrates* do appear to last for fairly long periods of time in the refrigerator. As long as they are not contaminated, they are fine, and may last up to a year. The absence of glycerin will contribute to a shorter shelf life and earlier loss of potency. But I feel very strongly that the advantages of PFA far outweigh this possible disadvantage.

Theoretically, allergens sitting out all day without preservative will likely grow bacteria, sooner or later. Therefore, it is important to put the allergens back in the refrigerator as often as you could during the day. We try to do this, and have not seen overt problems with contamination. Some of my colleagues even go so far as to freeze allergens for *treatment sets* in between uses. I can't really comment on the necessity of freezing testing sets, but it has never been necessary for us if proper safeguards are followed. Freezing may indeed be a great idea for your concentrates, and will likely extend the shelf

life from one year to about 2 years.

One would surmise correctly that PFA testing sets need to be re-mixed more often than do allergens with preservative. We re-mix our dilute (anything more dilute than a number 2) antigens approximately monthly, because they lose potency quickly. More concentrated allergens may last longer. We have not seen any issue with bacterial growth or contamination, or of skin infection or abscess in any patient.

Certainly, cultures on random extracts should be performed occasionally. If you treat with preservative-free allergen extracts as well as test with them, it might be wise to have two sets, testing and treatment, mixed from the same concentrates at the same time. The treatment set could be kept frozen, to be thawed when you mix treatment vials. Should you do this, you should give a pretreatment test dose, intradermally, of the beginning treatment dose for any particular patient.

The Ugly

The FDA still has the job to see that patients are "protected". Currently, it is not illegal for physicians to compound their own preservative-free extracts or nutrients. It would be illegal were a physician to sell them to other physicians, pharmacies, etc. So don't plan to go into business doing this: the FDA would consider you to be a "manufacturer".

Theoretically, the FDA could come to your office and check to see that you are using reasonable precautions when you do this. Occasional sterility testing would help convince the FDA — or any investigator from any agency — you were doing this properly. You could do this by performing aerobic and anaerobic cultures in your office on some type of random selection and schedule. Office incubators cost from about $125 to $200, and need not be bigger than a breadbox. You would simply be looking for the growth of any organism, so theoretically you could perform your own readings. Alternatively you could send them to a local lab for culture.

The only incident – and there is only one – I have heard was an occasion when a State Medical Board told a physician he couldn't do this, and it had to do with nutrients, not allergens. He could likely have fought it and won, but he just didn't want to get into a fight.

Pros and Cons: Summary

It all comes down to a personal decision for all of you as to what type of materials you want to use for testing and treatment. If you hadn't noticed, I very strongly prefer preservative-free everything.

If the current scenario in the world persists, you and I are going to see more and more patients with more and more serious problems. More and more of them are not going to tolerate being tested with materials containing potent, quite ubiquitous agents such as phenol or glycerin. More and more of them are going to ask not to be tested and/or treated with these chemicals. As physicians who practice Integrative Medicine, I feel we have a moral obligation to use the purest agents possible to test and treat our patients. But that's not all.

I'm almost certain you would find making the change to PFA is almost painless, when compared to the probable benefits. Imagine how nice It would be to know with absolute certainty your patient is not reacting to the phenol or to the glycerin you've just given them, but is truly reacting to the allergen, and to be certain you won't kill them with an IV preservative. If you use escalating dose schedules in your immunotherapy to inhalants, I

think you'll be amazed to find that, in many cases, the dose limitation you thought was due to the strength of allergens was actually due to the patient's reaction to the glycerin – especially in the more concentrated mixes, or to phenol. Escalating dose therapy is effective, but one must generally get to very high doses of allergen to accomplish optimal response. With glycerin and phenol, you often just can't get there.

Don't you think it would really be nice to get that phenol, glycerin and other preservatives out of your office?

I have discussed the pros and cons of preservative-free allergens for testing and treatment of our patients, and for preservative-free nutrients. I strongly favor the use of allergens without preservative, primarily because the more patients I see, the more sensitive the patients I see are. Probably 40% of my patients would not tolerate being tested to or treated with preserved allergens. As I mentioned, you need to make your own choice whether you want to use allergens with or without preservative. Should you choose to use allergens without preservative, the complete instructions follow. Please keep in mind that the AAEM and other allergy societies currently teach only the use of preserved allergens. This is a medical-legal issue, and the AAEM cannot officially advocate the use of preservative-free allergens at the present time (if you didn't get it, this is a disclaimer).

If you are going to use allergens without preservative, first you need supplies. For that you need a supplier, and I was going to mention only one. This particular supplier happened to supply large users of allergens without preservative, such as Dr. Bill Rea, EHC-Dallas. Any friend of Bill's is a friend of mine, and I'd gotten raw materials from them for years. This was a "mom and pop" outfit, and they offered particularly excellent and personal service. They would also try to find any allergen you might need that they didn't stock (they stocked over 700 allergens).

Unfortunately, they retired in 2012, and the only suppliers I know currently with allergen powder are Greer and Hollister Steir. You can easily find them on the Internet.

Materials You Will Need

The following is a list of materials you'll need to set up preservative-free allergen preparation, along with approximate costs. The catalog numbers listed are those from IBI and Millipore. Please note that prices will likely be higher than noted herem as they change yearly.

1. A digital gram scale, the same as you need for nutrients. This does not have to be fancy, but must measure accurately down to 0.1 gram. Any good lab supplier carries these, and it does not have to be expensive. I got mine from www.saveonscales.com.
2. Vacuum pump - This may be a hand-operated pump (Millipore hand vacuum pump), or an electric pump. *I would suggest the electric pump if you're going to be doing large numbers of nutrients – but you might want to start with a hand pump.* **(**We use an electric pump, Barnant Model 400-1901, Barnant Co., Barrington, IL, 60010, which costs about $200 (www.fishersci.com). Different models of Barnant pumps are available on www.bestlabdeals.com, and their model 475-3010 looks fine, and is $182.40).
3. Rubber Tubing – Included with your pump. However, for the electric pump, the tubing tends to be too soft, and will collapse with the more difficult extractions. You will probably need to get sturdier tubing (clear polyethylene) at your local hardware store, as we did.

4. 250 ml Erlenmeyer flask (Pyrex, Sigma-Aldrich)
5. No. 6 Green neoprene stopper ($.75 ea.), one for each flask you get, plus a few extra.
6. .5 to 1 micron pre-filter (Whatman GFJB: $60. 10/100) or Millipore AP25. We use the Millipore .5 micron pre-filters (Millipore cat #AP25 047 00: $36.00/100). Both are satisfactory.
7. Millipore filter system, Millipore Sterifil Aseptic filter system, from Millipore, $79). This is a gizmo that holds the filters you will use for extraction – details below. It's the same one I mentioned for nutrients. (Note: if you are planning to make any of your own IV nutrients, you should plan to use separate filter holder for this.)
8. .65 micrometer filters (Durapore membrane filters, DVPP04700 from Millipore, $102/100filters)
9. Filter forceps – to place these in the filter system – OK, you really don't need these if you're careful
10. Millex Sterile filtration units, SLGV025 LS, 0.22 micrometer from Millipore, $115/50. These are for the final filtration step.
11. 20 ml Luer-Lok plastic syringes
12. 1000 ml Erlenmeyer flask (for making Coca's solution)
13. Graduated cylinder, 100 ml (Pyrex, from Sigma-Aldrich, $26.70).
14. 18 gauge needles, No-Kor 1½ ", and short 25-30 gauge needles for venting.
15. You'll need 20, 30, and 50 cc sterile vials (we get ours from Alk-Abello).

Diluent

The diluent used for the extraction of allergens is Coca's Solution:

NaCl	5.00	grams
$NaHCO_3$	2.75	grams
Pure water	1000	ml

You may obtain the materials to make diluent from a compounding pharmacy, or direct from a supplier, such as Spectrum (see Suppliers). You may weigh these materials for yourself or ask a pharmacist to weight this out for you. The water may be purchased most anywhere; we use reverse-osmosis/de-ionized water that we get from our local health food store at 35 cents a gallon (can't beat that!). You may use Sterile Water for Irrigation, mentioned earlier.

The extracting solution need not be mixed under sterile conditions, but it should be kept refrigerated once it has been mixed. The amount of solution mixed need not be 1000 ccs. Your particular needs may be less. Coca's is so inexpensive it doesn't matter if you discard overages if you make too much.

Allergens

Allergens for extraction are available in great variety. Pollens, danders, dusts, molds and others are obtainable from IBI and elsewhere. These are generally the "real thing", and their potency is virtually 1:1, or 100% as the dry substance. Allergens for testing and

treatmetn start at 1:20 (5%) in our office. In other words, this means 1 gram of allergen per 20 ml of extracting solution. In reality, it would be unlikely for you to obtain a perfect 1:20 solution, but it really doesn't matter. As long as you are using the same solution for testing as you are for treatment, a few percentage points either way won't matter. It's relative.

The costs of allergens vary with their "rarity". Grasses, for example, run from about $2.50/gram to $15, the average being about $6-$7. Foods are generally $2-$3/gram and molds run $10-$15/gram. Rinkel mold mixes ("A", "B" and "C") are about $15.00/gram, as is T.O.E. On the other hand, dust mite is $150/gram. Fortunately, dust mite is generally tested and treated at 1:100, so it is less expensive than it would appear (1 gram makes 100 ccs).

The amount of allergen you will prepare will depend upon your needs. As I mentioned, concentrated allergen will remain stable for a considerable time if kept refrigerated, and longer if kept frozen. In fact, there is evidence that frozen "allergoids" will remain stable almost indefinitely. The amount you would make would depend strictly upon the volume of patients you test and treat. Your nurses or technicians will probably have a better idea than you do as to the amount of allergen you use monthly in general.

We use our allergens for testing only, and we re-mix testing sets about every 3 months. Dilutions less than #2 are mixed at least monthly, and weekly in allergy season (March) when we treat from the extracts. Our usual treatment method is LDA immuno-therapy, which *does not use the allergens we extract for testing* – call me to learn more about this method).

I make up 20 mls of solution at a time, using *1 gram of allergen and 20 ccs of Coca's solution*. In reality, depending upon the powdered allergen you are extracting, you will end up with less solution than you start with because the pollens, foods, etc (and the filters) absorb some water. An allergen like milk may need to be made slightly more dilute, is it forms a slurry when you add sterile water. A conservative approach would be to estimate you're going to "lose" as much as 20% of the volume of the solution you intended to make during the extraction process. I'll explain why in a moment. This amount of concentrate lasts my office a year or more.

Extraction Process

The process of extraction of allergens takes place in 4 stages

1. Extraction
2. Clarification
3. Filtration (purification)
4. Dilution.

This means essentially getting the allergen in solution/suspension, purifying it, and making your dilutions for testing and/or treatment. Dilutions for testing and treatment are the usual 1:5 dilutions we are taught to use at the AAEM, Pan Am and elsewhere, so I won't be going into this at all. If you don't know how to make 1:5 dilutions, go directly to jail, and do not collect $200; go to the AAEM Instructional courses.

The extraction process may tend to disperse some airborne allergen. For this reason, it would be optimal if you had a separate room in which to perform the process. More ideally, one would want a laminar flow hood to provide absolute sterility during the mixing

process. I checked on the price of the least expensive "portable" laminar flow unit, and it was somewhere in the range of $1500-$2000. Needless to say, we don't have a hood or a dedicated room.

Should this be your situation, it would be wise to have an air filtration unit running in the area during the procedure. Patients should not be present in the room at the time when allergen could become airborne, and the door to the room should be kept closed if patients are in the office. Anyone mixing the allergens would be wise to wear a pollen filtration mask, as we've had one technician and an office manager go into sneezing fits before we learned these lessons. In fact, I generally extract potent allergens (pollens, danders - especially cat - mites and molds), on a day of the week we don't have many (or any) patients in the office.

Before you let this intimidate you, remember one thing; once you've figured how much allergen you want to mix up - say, a year's supply or so - you won't be doing this very often.

Extraction

During this step, allergen is mixed with diluent and the active protein component is "extracted" into the solution. This is what the Erlenmeyer flasks are for.

1. Mix up the Coca's solution by adding the salt and bicarbonate in the proper proportions to non-sterile, purified water as noted above, or to sterile water for irrigation. If you're making 1000 ccs - which I'd recommend because it's easiest and cheap, and you've got the 1000 cc Erlenmeyer flask – just add 1000 ccs of water and dump the proper amount of salt and bicarb into the flask and swirl it until it's mixed (you might want to start with less than a full flask of water so it won't slosh out, then add the additional water after the solutes are in solution). You must use pharmaceutical grade salt and bicarb; if you obtain the material from Spectrum, get the "reagent grade" or USP (See the table at the end of this section).

2. Measure the proper amount of extracting solution in the graduated cylinder and add it to one of the 250 cc Erlenmeyer flasks. Then add the proper amount of allergen. The correct proportion is *1 gram of allergen to 19 ccs of extracting fluid* for a 5% (1:20) solution. Remember, depending upon the allergen, you're going to end up with less solution than you think you will. I gave the figure of 20% less, but that will vary and will almost never be greater than 20% less. The reason is that some of the mixtures, such as milk, some other foods and some of the molds make pretty thick - almost congealed - slurry when they're mixed. This tends to absorb more allergen that won't get through the filters easily.

   For example, if you are planning to make 50 ccs of allergen, you would use 2.5 grams of allergen and 50 ccs of diluent, and plan to lose about 10 ccs. This means you'll probably end up with 40-45 ccs. For 100 ccs of allergen, you'd use 5 grams of allergen and 100 ccs of diluent. I would suggest you never make less than 10 ccs of allergen. Milk is definitely the worst and creates a"slurry". You may even find you need 39 ccs of Coca's (and make a 1:40 dilution) so you get enough allergen.

   Take into account the fact that you will probably be re-mixing the higher (more dilute) dilutions in your testing sets about every month - perhaps more often if you're

more fastidious or use more material. We test about 2-5 new patients per week, and use 5 cc testing vials in our testing sets. I make up 20 ccs of concentrated antigen, which means we end up at worst with about 16 ccs of concentrate when we do extractions. Accordingly, assuming we may use 1 cc of concentrate every 2-3 months (using 1:5 dilutions), that should make our concentrates last quite a long time. I freeze all concentrates I make. If you plan on freezing your concentrates, be sure you leave enough room in your bottles for the ice to expand or they will break.

The immunotherapy I use is the "American" version of EPD (which was developed in England), that I developed in 2002, so I do not use the testing antigens I make for treatment – just for testing. If you're treating with your allergens, you need to consult with whoever does the ordering in your office to find out exactly how much allergen you're using and plan to extract accordingly.

3. Add the allergen to the diluent (Coca's) in a 250 cc Erlenmeyer flask and cap with a rubber stopper. Swirl the mixture around until it's "mixed". These allergens won't dissolve in the diluent because they're pollens, cornmeal, and the like. You should start with about 3 separate allergens in 3 separate flasks, just to see what your time factor is in preparation. Later you might want to do more or less at one sitting.
4. Put the mixtures in the refrigerator for about 4-8 hours, and try to go and swirl the mixtures around every hour or so. You may leave the mixtures longer than 4 hours, but the longer you leave them, the more chance there will be for bacterial or mold growth. If you leave them too long, you might get enough bacterial growth and actually be testing your patients to bacterial "antigens". We've left them over night without noticeable adverse results (however, once I accidentally left the mixture in the fridge for about 2 weeks, and grew the nastiest mold creature I've ever seen).
5. Remove each antigen from the fridge as you plan to extract it**.**

An additional word here about the care you should take in preparation. Equipment needs to be rinsed a few times during an extraction and washed lightly between the extractions of different allergens. I use a mild, "unscented" soap which can be purchased at a health food store or elsewhere. The soap needs to be dilute. Rinse your equipment as you proceed with tap water.

You may wash your glassware as the final step with purified water if you wish. You can accomplish the latter by setting a 2-gallon container of the water on top of the cabinet above the extraction counter with a length of IV tubing extended down to the work area. Leave the IV flow adjuster attached to the tubing, so the flow of pure water can be turned on and off. This makes it simple to rinse various items with pure water during the clarification/purification procedure.

Clarification

The clarification/purification process is the most complex part of all of this, but really quite simple after you've done it once or twice. (Remember "see one, do one, teach one", from medical school? Same thing here.) Here's where most of the equipment mentioned above comes into play.

One would think that sterile procedure would need to be used throughout, but in reality that is not very important until the *last step*, which removes bacteria. Just take

reasonable care to keep things clean as you go, and don't touch the "inside" part of anything with your fingers.

1. Set up the filtration equipment, which consists of the vacuum pump, the Millipore filter holder and the tubing. Our vacuum pump turns on when it's plugged in. Plug it in first and check which port on the pump is "suction" and which port is "exhaust". If you have a hand pump, you just use that here, but I wouldn't recommend it. Hook the suction port of the pump to the tubing (about two feet of tubing), and hook the tubing to the lower part of the Millipore filtration unit. The Millipore unit basically comes in 4 parts: a cover or top, an upper part (where you will pour the allergens – holds about 200 cc comfortably), a threaded middle part which holds the filter in place and also connects the bottom part, which is where the filtered allergens end up (the whole unit has sort of an hourglass shape). There may be 4 little ports on the top cover of the upper part, which allow air to enter the mechanism. These may come with several very tiny (course) filters of their own. Simply plug 3 of the 4 ports with the rubber caps provided, and fit the 4th port with one of the tiny filter mechanisms provided, with a filter in it (this can be used over and over, as long as it's not contaminated or gotten wet.) If you have no filters for these holes, don't worry about it. I don't use the top unless I'm storing allergen in the fridge for some reason.

Note: I substituted the soft rubber tubing the company provided with a firm, clear silicon tubing, since the soft rubber tubing tends to collapse with significant suction from the electric pump.

2. Once the unit is all hooked up and ready to go, carefully place a .5 micron or a 1 micron pre-filter (#6 under "materials" above) in the Millipore filtration unit. This is done by unscrewing the upper part from the middle part, picking up a filter with forceps or fingers, placing the filter on top of the white middle part, and carefully screwing the upper part to the middle part. Screw the unit together tightly, or it will leak. Once this is done and the filter is in place, do not force the upper part of the assembly tightly into the bottom part of the filter unit (there is no screwing involved with this connection - the assembled upper part simply fits snugly to the bottom part). If you push them together too firmly, they will be very hard to separate! (The suction alone applied by the pump does this well enough.)
3. Open the flask of allergen you have taken out of the fridge after extraction and swirl it around to get it into suspension one last time. Remove the stopper and remove the top cover from the upper part of the filter holder, and pour the unfiltered allergen mixture into the upper part of the filter holder. Don't rinse the Erlenmeyer flask yet – you may be using it again soon. Plug in the pump. In most cases, the allergen extract will immediately begin to come through the filter into the bottom of the container (actually a plastic flask of sorts).

Some very thick mixtures will not get filtered completely with one filter, depending upon the volume you have made, and the filter must be changed *in the middle of clarification process* (this is also the "rule" with the finer filters used for continued clarification, discussed in a moment). You'll realize this when the pump starts to labor, and very little material is going through the filter. You will then also see lots of "bubbling" of the material coming through the filter. You must watch carefully at this point, as you don't

want the extract "bubbles" to be sucked into the vacuum hose and get sucked into the pump.

To change the filter in the middle of an extraction, unplug or otherwise turn off the pump. Remove the whole upper assembly from the bottom part. *Do not unscrew the white part from the upper part of the unit*, or your unfiltered solution will slop all over your table. I know - I've done it.

Remove the top cover of the upper part of the unit. Pour the remaining unfiltered extract back into the original Erlenmeyer flask. You may then unscrew the upper part of the unit from the middle part and discard the plugged-up filter. Replace the filter with a new one, and repeat Step #3. This may have to be done more than once, or you may get away with using only one filter, depending upon the viscosity of your solution, which depends on the allergen you're making. After you've poured unfiltered mixture from the Erlenmeyer flask into the upper part of the filter unit, turn the pump back on. Repeat these steps until the whole mixture has been filtered. You usually won't have to do this for the larger-pore filters, really, unless you are filtering large amounts of allergen, since the coarse pre-filters don't plug up very easily. You are now ready to go to a smaller-pore filter.

4. Rinse the Erlenmeyer flask at this point with pure water (don't wash, just rinse). Pour the clarified allergen mixture you've filtered in the bottom of the filter apparatus back into the rinsed Erlenmeyer flask again. Rinse (don't wash, just rinse) the filtering apparatus. (not the top cover - just remove that if you use it) with pure water. Or, if you did contaminate the top and need to rinse it, remove the tiny filter from the top first.
5. Place a .45 or .65 micron filter (depending upon your preference, really) in the filter holder with the filter forceps or fingers. Be careful to center the filter, and then tighten the apparatus without wrinkling the filter.
6. Connect the upper plus the middle part back again to the bottom part of the filter apparatus. Pour the partly clarified allergen into the upper part of the filter, connect the tubing and turn on the pump.
7. This part can be the most time-consuming, depending on the viscosity of the clarified mixture. You usually have to change filters during this further clarification process. My average is about 2-3 filters per 20 cc. extract. Once the pump starts laboring, and the bubbles appear in force, you must give in and change the filter, as per step #6 above. Do this until you've completed the clarification process - until all your allergen is filtered.

Up until now, you should have been taking care to use reasonable precautions so as not to contaminate your extract or clarification extract. Now you must get serious and use sterile technique for the final process: filtration/purification. Any bacteria getting into the mix from this point will contaminate your allergens.

Filtration/Purification

Up to this point, you should have chosen and labeled the size vial in which you will be putting your extract concentrate, depending upon how much you've made. You will be using a 20, 30 cc. or a 50 cc. empty sterile vial, probably. Some of you high volume folks may want to use a 100 cc. vial. Regardless of size, the process is the same.

1. Cleanse the top of the empty, labeled vial with alcohol and insert a sterile 25-30 gauge needle into one side of the rubber top. The purpose of this is to let air escape from the vial as you are injecting allergen with the syringe (with the next filter attached) into the vial.
2. The size of the syringe you use for this final stage of the filtration will be determined by how much allergen you've made. I like to use a 20 cc syringe (holds 25 cc) to get optimal "leverage" (I'll explain that below). 10 cc is probably optimal, but too small. Remove the top part of the filtering apparatus and draw up some of your clarified allergen into the barrel of the syringe – without the needle attached. This maneuver should be done carefully by dipping the distal end of the syringe into the allergen.
3. Carefully open a Milex-GV Millipore filter unit and attach it to your Luer-Lok syringe containing the allergen extract. Place an 18-gauge needle on the distal end on the Milex syringe filter, and expel any air from the syringe (Note: do not discard the cap.)
4. Once the air is out of the syringe (or mostly out, as the case may be), remove the protective needle cap, and insert the needle into the rubber cap of your empty concentrate allergen vial, into which you will be putting your allergen.
5. Apply steady, even pressure to the plunger, and the allergen will flow quickly through the filter at first. However, you'll notice the flow will sometimes diminish as the filter becomes progressively plugged. Here you're faced with the same situation as above: you must change filters as you go.
6. When you have forced as much allergen as you can through the filter into the vial, you must change the filter. To do this, *carefully* re-cap the 18-gauge needle and remove the needle from the filter and place it on the counter, then draw up more (or the rest) of the allergen, attach a new filter to the syringe, re-attach the needle to the filter and repeat step # 5. I use 1-3 filters per 200 cc on average.

And that's all there is to it! You're done. At this point you need to wash your equipment with a mild soap solution, rinse thoroughly with tap water and put it on paper towels to dry. If you think any allergen has gotten into the rubber tubing, you need to wash that as well. You are then ready to proceed to the clarification of the next allergen. Obviously, you want the equipment clean, as cross-contamination of allergen would be a problem. Put the extracted allergen in the refrigerator immediately, and keep it there until you are ready to make your dilutions for your testing or treatment sets. If it will be there longer than a few days before you make dilutions or treatment sets, freeze it.

Once you've found out how much time the processing of one allergen takes, you'll be able to gauge how many extractions you (or your staff) are able to do in a day. It's wise to do this yourself for the first few allergens, and then teach someone in your office to do it. Remember your lab monkey can do this, but you'll need to have lots of patience (2-10 years) and so be sure to get a young monkey.

More About The Fine Points

If you are using your allergens for testing, all this is quite simple. As I mentioned, I remix our dilute (#4 and more dilute) allergens in our testing trays about every month, and keep them in the refrigerator as much during the day as possible.

If you are concerned about a visit from the FDA or your State Medical Board (extremely unlikely unless they are watching you for some reason) you should have a small incubator. Contact your local lab as to their source. You may want to do cultures once every month, give or take, but only *after* somebody tells you to.

Be sure your staff pay attention to the characteristics and color of your allergens. If your allergens ever appear discolored or cloudy, you know you've got a problem with contamination, and you must usually totally re-extract.

We've noted that the concentrates of some of the food allergens, especially milk, last considerably less time without contamination than others if they are out of the refrigerator a lot. If you are unsure, culture any suspicious allergen right away, or simply toss it and re-mix (probably cheaper in the long run to toss it). If you don't want to do cultures in your office, your local lab would probably be happy to do it for you. You actually would need both aerobic cultures, which you could do in your office, and anaerobic cultures, which must be done at your local hospital lab.

Allergens Used For Treatment

Injected Foods or Inhalants

If you are using allergens for treatment, you have an additional responsibility, especially if patients are taking their shots at home. If you distribute small vials (1-2 cc.), you're probably OK, as long as your patients are aware of the "risks" of preservative-free allergens. Have these patients sign a waiver, and advise patients that the allergens must be kept refrigerated or preferably frozen. I would never give more than a months' supply for refrigeration only. Frozen allergens can be used almost indefinitely.

If you are giving allergen to patients in your office or at home kept in larger vials (for treatment for more than a month at a time), or if you want to be extremely cautious, the vials of extract for treatment should always be kept frozen in between use. I know several physicians follow this policy. I would still have patients sign a waiver delineating the possible risks (infection at the injection site, etc.).

Whether repeated freezing and thawing has an effect on the allergens - your guess is a good as mine. I've spoken to several physicians who do this, and they feel that freezing doesn't change the potency of allergens significantly. I have seen no problems over the years.

Food, Chemical or Inhalant "Drops" (sublingual)

Here, you've got no problem. These should be kept refrigerated, but contamination is not a factor unless the allergen happens to "grow" something to which your patient is sensitized. I would say up to a month's supply (possibly more) would be reasonable for drops used sublingually, as long as they are kept refrigerated most of the time. Remember, however, that patients tend to carry their food and/or chemical drops around with them, so smaller volumes would be more prudent.

Conclusion:

Preservative-free allergens are in this clinician's opinion, the only way to go. If you use preservative-free allergens, you are very unlikely to harm your patients. In fact, you will almost certainly have less problems than if you were using glycerin or phenol. If you are using glycerinated concentrates, but diluting them with plain normal saline, don't kid yourself or anyone else: you're still using a sensitizing agent to which many, many patients become sensitive.

If you use glycerinated concentrates, you are not really using "preservative-free" allergens, and you shouldn't tell your patients that you are. The reason? If any of these patients become sensitized to glycerin and then go see another physician, they will say they were being treated with "preservative-free extracts" and didn't do well. I have seen this more times than I can count. These patients do quite well being tested (and treated) with *real* preservative-free extracts, but it's often very difficult to convince them they'll do "just fine" with testing (aside from side effects not due to preservatives) because they've reacted in the past to "preservative-free" extracts that actually contained glycerin.

If the FDA or your state board comes to pay you a visit because they've heard your using preservative-free extracts, you will go to jail for the rest of your life - sorry about that. Just kidding! The FDA permits you to do this. If anyone ever visits your office and you can show that you are taking "reasonable" precautions, they will leave you alone and go on their way. If you are not taking precautions, there is no evidence they won't do the same thing – except report you to your State Board, who then may come to check whether you are culturing your allergens on some regular basis. The Federal regulations do not yet state how you – as a physician – must culture the preservative-free materials you make yourself. The FDA considers this "practice of medicine" and will not interfere unless there is a considerable special circumstance.

In fact, I am not aware of any case of the FDA interfering in this manner unless your preservative-free materials are being illegally imported from a foreign country, or you are selling them to other physicians. I don't know of a foreign country that supplies preservative-free allergens, however – only nutrients.

It all comes down to a personal decision for all of you as to what type of materials you want to use for testing and treatment. If you hadn't noticed, I very strongly prefer preservative-free everything.

If the current scenario in the world persists, you and I are going to see more and more patients with more and more serious problems. More and more of them are not going to tolerate being tested with materials containing potent, quite ubiquitous agents such as phenol or glycerin. More and more of them are going to ask not to be tested and/or treated with

these chemicals. As physicians who practice Integrative Medicine, I feel we have a moral obligation to use the purest agents possible to test and treat our patients. But that's not all.

I'm almost certain you would find making the change to PFA is almost painless, when compared to the probable benefits. Imagine how nice It would be to know with absolute certainty your patient is not reacting to the phenol or to the glycerin you've just given them, but is truly reacting to the allergen, and to be certain you won't kill them with an IV preservative. If you use escalating dose schedules in your immunotherapy to inhalants, I think you'll be amazed to find that, in many cases, the dose limitation you thought was due to the strength of allergens was actually due to the patient's reaction to the glycerin – especially in the more concentrated mixes, or to phenol. Escalating dose therapy is effective, but one must generally get to very high doses of allergen to accomplish optimal response. With glycerin and phenol, you often just can't get there.

Don't you think it would really be nice to get that phenol, glycerin and other preservatives out of your office?

I hope this Guide has been of great help to you, and that you have fun with this. If you have any questions, comments or suggestions, please write or fax my office. Be sure to include your fax number or your e-mail address so I can get back to you.

Table 4: Nutrient Formulations for Compounding Preservative-free Nutrients

Nutrient	**Spectrum cat. #** (800-791-3210)	**Final concentration in mg./ml (cc)**	**Amount in grams to add**	**Diluent: sterile water in ml. (cc)**
B-6 (pyridoxine)	P-4722	100	20	200
B-12 (hydroxycobalamine)	H-1129P	1	0.1	100
B-Complex *				
B1 (thiamine HCL)	T-4562	*100*	*20*	*200*
B2 (riboflavin)	R-7774	*2*	*0.4*	*200*
B3 (niacinamide)	N-5535	*100*	*20*	*200*
B5 Pantothene; calcium pantothenate)	CA-159P	*2*	*0.4*	*200*
B6 (pyridoxine HCL)	P-4722	*2*	*0.4*	*200*
Calcium gluconate	C-8231	100	20	200
Calcium pantothenate (vitamin B-5)	CA-159P	250	50	200
EDTA (magnesium disodium)		150	30	200
Folic acid	Fo-105P	10	1	100 **
Glutathione	G-4521	100	20	200 ***
Magnesium chloride	M-7304	500	100	200
Magnesium sulfate	M-7929	500	100	200
Molybdenum	A-1675P	0.5	0.6	1000
N-acetyl cysteine		200	20	100 ****
Pantothenic acid	CA-159P	250	25	100
Sodium bicarbonate	S-1554	8.4 %	17	200

* all nutrients in B-Complex added to the same 200 cc.

** You must add 1 gram of sodium bicarbonate to make this nutrient.

*** diluent is NSS. This must be stored in a dark container in the fridge or it will oxidize (turn yellow and/or become less active) quickly

**** You must add 6 grams of sodium bicarbonate to make this nutrient.

Table 5: Nutrient Formulations for Compounding Preservative-free Nutrients – Trace Minerals

Nutrient	Spectrum cat. #	Final Concentration in *mcg*./ml (cc)	Amount in grams	Sterile Water in ml. (cc)
Shrader's mineral mix (or minerals can be used individually if you put each in 1000 cc)				
Boron (boric acid)	B-7660*	100	5.7	1000
Chromium chloride (Cl_3)	C-1896	100	0.3	1000
Copper chloride (Cl_2)	C-6641	100	2.7	1000
Lithium chloride (Cl)	L-4408	5000 (5 mg.)	30	1000
Manganese Chloride (Cl_2)	M-3634	100	0.36	1000
Molybdenum (ammonium molybdate)	A-1675P	250	.3	1000
Selenium dioxide (O_2)	S-1122	200	0.3	1000
Strontium chloride (Cl_2)	S-0390	100	3	1000
Vanadium (vanadyl sulfite)	V-1020P		0.5	1000
Zinc sulfate	Z-4750	5000 (5 mg.)	25	1000

* Although they ARE cheap, the quantities of minerals available from Spectrum are more than most of us could use in many, many years (50-100 grams or more). Therefore you may wish to obtain these from a compounding pharmacy in much smaller quantities.

Waiver Forms

Consent for Non-conventional Treatment

1. I, _____, hereby authorize the following procedure: use of _____ a testing modality for diagnosis of _____, or _____ treatment, a treatment for _____ _____.
2. I understand that the procedure will involve _____ _____, possibly combined with diet and lifestyle modifications.
3. I understand that _____ is not a currently medically accepted procedure for testing or treating _____ and, thus, that its use for this purpose may be considered by some insurance companies to be "medically unnecessary" or "experimental". The procedure has some risks. Dr. _____ has explained to me verbally the short and long-term risks, which may include temporary worsening of my current symptoms or headache, tachycardia (increased heart rate), syncope (fainting), visual difficulties, shortness of breath, joint pains, red eyes, itchy eyes, nasal congestion, numbness, gastrointestinal disturbances and a very rare but serious reaction called anaphylaxis. Also, further side-effects or complications could be: _____
4. By signing this form, I accept those risks. Moreover, I understand and accept that because this procedure may be considered "medically unnecessary" or "experimental", it may not mitigate, alleviate, or cure my condition (s). Its possible benefits may not be apparent immediately. The possible benefits include mitigation or improvement of my current symptoms, improvement of respiratory function, decreased skin reactions, increased stamina, improved metabolism, decrease in frequency or severity of headaches, improved concentration, and others.
5. I understand the nature of the treatment, which has been explained to me by Dr. _____.
6. I understand that the currently "standard" medically indicated treatment(s) for my condition is/are _____ _____. I understand that the risks of those treatments include: no improvement or worsening of my condition; headache, tachycardia (increased heart rate), syncope (fainting), visual difficulties, shortness of breath, joint pains, red eyes, itchy eyes, nasal congestion, numbness, gastrointestinal disturbances and a very rare but serious reaction called anaphylaxis and others.
7. Based on the risks and potential benefits of the currently medically indicated treatment(s) and of the proposed treatment, I have elected to forego or supplement the indicated treatment(s) and receive the proposed treatment from Dr. _____.
8. I further understand and agree to adhere to the treatment schedule and attend the follow-up visitations set by Dr. _____ to permit observation and study of my progress. I also agree to comply with the recommended lifestyle modifications in order to provide optimum opportunities for the beneficial effects of chelation therapy.
9. I understand that I may suspend or terminate my treatment at anytime by informing Dr. _____
10. I assume full liability for any adverse effects that may result from the non-negligent administration of the proposed treatment. I waive any claim in law or equity for redress of any grievance that I may have concerning or resulting from the procedure, except as that claim pertains to negligent administration of this procedure.
11. I hereby confirm that the nature and purpose of the aforementioned treatment may be considered medically unnecessary or experimental and not currently indicated treatments. The risks involved and the possibilities of complications have been explained to me. I fully understand that the treatment to be provided may be considered experimental and unproven by scientific testing and peer-reviewed publication.

Signature of Patient _____ DATE:_____ TIME:_____

Signature of Witness _____

Agreement by Medicare Beneficiary for Medical Services by Physician Opted Out of Medicare

Date: _____ Time: _____

_____ , a patient and Medicare Part B beneficiary ("Patient"), and _____, M.D. (Physician"), a physician licensed to practice medicine in _____ enter into this agreement for the provision of medical services specified herein ("Services") in accordance with the provisions of Section 4507 of the Balanced Budget Act of 1997. Wherefore, in exchange for consideration, the receipt and sufficiency of which the Parties hereby acknowledge, Patient and Physician agree as follows:

1. Patient acknowledges and agrees that this Agreement has been entered into, and that Patient has received a copy of this Agreement, before Physician has provided the services specified herein to Patient.

2. Patient acknowledges and agrees that this Agreement has not been entered into at a time when Patient is facing an emergency or urgent health care situation.

3. The services to be provided Patient are: _____
_____
_____
_____ (collectively referred to hereinafter as "Services")

4. Patient agrees not to submit a claim (or request that Physician submit a claim on Patient's behalf) under the Social Security Act, as amended (42 U.S.C. § 1395a), for the Services, even if such Services are otherwise covered under Medicare Part B.

5. Patient agrees to be personally responsible, whether through private insurance or otherwise, for the payment of Services.

6. Patient acknowledges that Medicare will not provide reimbursement for the Services and that no Medicare fee limits (including those specified in 42 U.S.C. §§ 1395a; 1848(g)) will apply to the amount Physician charges for Services.

7. Patient acknowledges that Medigap plans under 42 U.S.C. § 1882 do not, and other supplemental insurance plans may not, make payments for the Services.

8. Patient acknowledges that, as a Medicare beneficiary, Patient has the right to have the Services provided by other physicians or practitioners for whom payment would be made under Medicare, 42 U.S.C. § 1395a.

9. Physician has informed Patient that Physician is not excluded from participating in Medicare Part B under 42 U.S.C. § 1128.

10. By signing this contract Patient understands that Patient is forgoing his or her right to receive Medicare benefits for the Services from Physician, but that Patient is not forfeiting all Medicare benefits for other services from other Medicare providers.

11. Physician filed an affidavit with Medicare effective on _____. That affidavit expires on _____. This Agreement expires on _____.

Signature of Patient _____ Date: _____

Witness: _____

Signature of Physician: _____ Date:_____

Witness: _____

Notice in Advance of Service to Patient that Service May Not Be Covered by Medicare

PHYSICIAN NOTICE:

Your insurance plan will only pay for services that it determines to be "reasonable and necessary" under its coverage policy. If your insurance plan determines that a particular service, although it would otherwise be covered, is "not reasonable and necessary" under its coverage policy standards, the plan will deny payment for that service. I believe that, in your case, your insurance may deny payment for EPD immunotherapy because it is not considered the "standard of care" in the USA and possibly because it is not FDFA-approved.

BENEFICIARY AGREEMENT:

I have been notified by _____ that he/she believes that, in my case, my insurance may deny payment for the service identified above, for the reasons stated. I agree to be personally and fully responsible for payment.

Signed,

_____ _____
Beneficiary (or Representative) Signature *Date*

_____ _____
Witness *Date*

NOTICE IN ADVANCE OF SERVICE TO PATIENT THAT
SERVICE MAY NOT BE COVERED BY MEDICARE

NOTICE TO MY PATIENTS:

Medicare will only pay for services that it determines to be "reasonable and necessary" under Section 1862 (a)(1) of the Medicare law. If Medicare determines that a particular service, although it would otherwise be covered, is "not reasonable and necessary" under Medicare program standards, Medicare will deny payment for that service. I believe that, in your case, Medicare is likely to deny payment for _____ for the following reasons:

_____
_____
_____

BENEFICIARY AGREEMENT:

I have been notified by my physician that he or she believes that, in my case, Medicare is likely to deny payment for the services identified above, for the reasons stated. If Medicare denies payment, *I agree to be personally and fully responsible for payment*.

Signed,

_____ _____
Beneficiary (or Representative) Signature *Date*

_____ _____
Witness *Date*

IV Therapy for Asthma/Other Health Problems -- Signature Form

Dr. _____ treats a number of illnesses using IV therapy (parenteral therapy) with various nutrients. This is because, for most patients with significant health problems, IV therapy has been shown in his practice to be effective in the long term, and because Dr. _____ feels it is far safer than giving you powerful and potentially dangerous drugs which often have significant adverse side effects.

Parenteral therapy with nutrients is not yet considered to be "traditional" therapy in this country. More and more physicians are finding the benefits from this approach, but it will take quite some time before it is considered the "standard" of care. For this reason -- because it is a non-traditional approach -- Dr. _____ wants you to understand the risk verses benefit ratio of this important approach to helping solve your health problems.

IV therapy with nutrients must be considered "investigational" in this country and *does not benefit all patients*. Some of the IV nutrients in the form or dosage used by this office are not yet approved by the FDA. If you have asthma or another serious illness, *IV therapy could even make you considerably worse after the first (or even the first few) treatment(s)*, so you must be aware of this eventuality. We generally ask our patients to commit to 3 treatments at a minimum, as it sometimes takes 3 treatments to see a significant effect. However, if satisfactory subjective or clinical results are not noted by the time the first 3 treatments are complete, we generally discontinue therapy and move on to another approach.

IV therapy is generally administered once or even twice weekly until you are able to go longer between treatments without loss of benefit. Generally speaking, should you note an improvement with IV therapy, you should find that the periods of improvement last longer and longer as time goes on. IV therapy with nutrients is often combined with other treatment modalities in this office, and it is hoped and somewhat expected that IV therapy can be discontinued without loss of benefit when the other treatment modalities take effect.

The general risks of IV therapy include, with decreasing frequency: worsening of symptoms after the first 1-3 treatments (lessening with each, if it happens); failure to achieve a substantial benefit; discomfort during the infusion; irritation of the vein, causing eventual closure of the vein; inflammation at the site of an IV (phlebitis); death. All except the first 3 are extremely rare, and there has never been a reported death from IV therapy with any of the nutrients used in our office (I include it here because it must be included in any disclaimer form).

By signing this form, you acknowledge that you understand all of the above information, and that you are consenting to parenteral therapy with nutrients with such knowledge.

Thanks very much.

Signed: _____ Dated: _____

[note: this is my form, not from J. Emord]

References

Please note: There references are *important to you*.

You can use them to justify your IV therapy with nutrients if you are challenged by *anyone*. Each year I take considerable time to update them to include the most important articles published over the past year. This latest update is complete through December 31, 2010.

IV References, not categorized (pre-1998 – sequential, by date)

Note: intravenous vitamin references did not began appearing in the medical literature until about 1975, except for some general references of multivitamins used in TPN. The references that appeared between 1975 and 1998 – about 61 of them – were the "ground-breakers", so I've listed them separately here. After about 1992, IV vitamin references increased steadily. My article (2004) is the only one (so far) justifying the use of multiple nutrients (236).

These references are all indexed in PubMed and Medline. Other general references are not indexed here, though there are many.

1. Pritchard JA, Pritchard SA. Standardized treatment of 154 consecutive cases of eclampsia. Am J Obstet Gynecol. 1975 Nov 1;123(5):543-52.
2. Librizzi RJ. Management of preeclampsia and eclampsia: an intravenous approach with magnesium sulfate. J Am Osteopath Assoc. 1976 Oct;76(2):135-8. No abstract available.
3. Young BK, Weinstein HM. Effects of magnesium sulfate on toxemic patients in labor. Obstet Gynecol. 1977 Jun;49(6):681-5.
4. Fisher J, Abrams J. Life-threatening ventricular tachyarrhythmias in delirium tremens. Arch Intern Med. 1977 Sep;137(9):1238-41.
5. Dyckner T, Wester PO. Ventricular extrasystoles and intracellular electrolytes before and after potassium and magnesium infusions in patients on diuretic treatment. Am Heart J. 1979 Jan;97(1):12-8.
6. Kumar A, Hasan M, Ahuja RC, Gupta NN, Bajpai PC, Seth TD. Intravenous magnesium in tachyarrhythmias. Indian Heart J. 1979 Sep-Oct;31(5):268-73. No abstract available.
7. Sibai BM, Lipshitz J, Anderson GD, Dilts PV Jr. Reassessment of intravenous MgSO4 therapy in preeclampsia-eclampsia. Obstet Gynecol. 1981 Feb;57(2):199-202.
8. Cohen L, Kitzes R. Magnesium sulfate and digitalis-toxic arrhythmias. JAMA. 1983 May 27;249(20):2808-10.
9. Morton BC, Nair RC, Smith FM, McKibbon TG, Poznanski WJ. Magnesium therapy in acute myocardial infarction--a double-blind study. Magnesium. 1984;3(4-6):346-52.
10. Clinton CW, Braude BM, James MF. Painful muscle spasm reversed by magnesium sulphate. A case report. S Afr Med J. 1985 Aug 31;68(5):332-3.
11. Rasmussen HS, McNair P, Norregard P, Backer V, Lindeneg O, Balslev S. Intravenous magnesium in acute myocardial infarction. Lancet. 1986 Feb 1;1(8475):234-6.
12. Wilkins IA, Goldberg JD, Phillips RN, Bacall CJ, Chervenak FA, Berkowitz RL. Long-term use of magnesium sulfate as a tocolytic agent. Obstet Gynecol. 1986 Mar;67(3 Suppl):38S-40S.
13. Reisdorff EJ, Clark MR, Walters BL. Acute digitalis poisoning: the role of intravenous magnesium sulfate. J Emerg Med. 1986;4(6):463-9. Review.
14. Okayama H, Aikawa T, Okayama M, Sasaki H, Mue S, Takishima T. Bronchodilating effect of intravenous magnesium sulfate in bronchial asthma. JAMA. 1987 Feb 27;257(8):1076-8.
15. Tzivoni D, Banai S, Schuger C, Benhorin J, Keren A, Gottlieb S, Stern S. Treatment of torsade de pointes with magnesium sulfate. Circulation. 1988 Feb;77(2):392-7.
16. Rolla G, Bucca C, Caria E, Arossa W, Bugiani M, Cesano L, Caropreso A. Acute effect of intravenous magnesium sulfate on airway obstruction of asthmatic patients. Ann Allergy. 1988 Nov;61(5):388-91.

17. Freeland-Graves J. Manganese: An essential nutrient for humans *Nutrition Today* 13-19, 1988 Nov/Dec.
18. McNamara R. Spivey W. Skobeloff E. Jacubowitz S. Intravenous magnesium sulfate in the management of acute respiratory failure complicating asthma. *Ann. Emerg. Med*. 18(2): 197-9, 1989 Feb.
19. Wright J. Littleton K. Defects in sulfur metabolism. *Internatl. Clin. Nut. Rev.* 9 (3): 118-19, 1989 Jul.
20. Wright J. *Vitamin B-12:* Powerful protection against childhood asthma. *Internatl. Clin. Nutr. Rev*. 9(4): 185-8, 1989.
21. Noppen M. Vanmaele L. Impens N. Schandevyl W. Bronchodilating effect of intravenous magnesium sulfate in acute severe bronchial asthma [see comments]. Comment in: *Chest* 1991 Feb, 99(2): 525-6; *Chest*. 97(2): 373-6, 1990 Feb.
22. Bucca C. et al. Effect of vitamin C on histamine bronchial responsiveness of patients with allergic rhinitis. *Ann. of Allergy*. 65:311-14, 1990 Oct.
23. Bone R. Burch S. Management of status asthmaticus. *Ann. Allerg*. 67(5): 461-9, 1991 Nov.
24. Kuitert L. Kletchko S. Intravenous magnesium sulfate in acute, life-threatening asthma [published erratum appears in *Ann. Emerg. Med*. 1992 Oct, 21(10): 1272]. *Ann. Emerg. Med*. 20(11): 1243-5, 1991 Nov.
25. Kanazawa H. The role of free radicals in airway obstruction in asthmatic patients. Chest 100: 1319-22, 1991 Nov.
26. Ruffman R. Wendel A. GSH rescued by N-acetyl cysteine, *Klin. Wochenschr* 69:857-62, 1991.
27. McClain, C. et al. Trace minerals in liver disease [zinc, selenium, copper, chromium and iron]. *Seminars in Liver Disease* 11(4): 321-37, 1991.
28. Bucca C. et al. Effect of Vitamin C on transient increase of bronchial responsiveness in conditions affecting the upper respiratory airways. Beyond Deficiency: New Views on the Function and Health Effects of Vitamins, *New York Academy of Sciences*. Abstract 16, 1992 Feb 9-12.
29. Anibarro B. Asthma with sulfite intolerance in children: a blocking study with cyanocobalamin. *J. Aller. Clin. Immunol*. 90: 103-9, 1992 Jul.
30. Stephen JM, Grant R, Yeh CS. Anaphylaxis from administration of intravenous thiamine. Am J Emerg Med. 1992 Jan;10(1):61-3.
31. McClain C. et al. Minerals and inflammatory response. *J. Amer. Coll. Nutr*. 11(5): 598 Abstract 4, 1992 Oct.
32. Green S. Rothrock S. Intravenous magnesium for acute asthma: failure to decrease emergency treatment duration orneed for hospitalization [see comments]. Comment in: Ann. Emerg. Med. 1993 Mar 22(3): 616-17, discussion 618-19, Comment in: *Ann. Emerg. Med*. 1993 Mar 22(3): 617, discussion 618-19, Comment in: *Ann. Emerg. Med*. 1993 Mar, 22(3): 617-8, discussion 618-9, Comment in: *Ann. Emerg. Med.* 1993 Mar 22(3): 618; discussion 618-19; *Ann. Emerg. Med*. 21(3): 260-5, 1992 Mar.
33. Prasad A. Zinc and lymphocyte immune function. *J. Am. Coll. Nutr*. 11(5): 597 Abstract 3, 1992, Oct.
34. Campbell M. Low levels of manganese in bronchial biopsies from asthmatic subjects. *J. Aller. Clin. Immunol*. 89: (1, Part II): 332/749, 1992 Jan.
35. Odeh M. The role of zinc in acquired immunodeficiency syndrome. *J. Int. Med*. 231: 463-69, 1992.
36. Bernstein W. Khastgir T. Khastgir A. Hernandez E. Miller J. Schonfeld S. Nissim J. Chernow B. Lack of effectiveness of magnesium in chronic stable asthma. A prospective, randomized, double-blind, placebo-controlled, crossover trial in normal subjects and in patients with chronic stable asthma. *Arch. Int. Med*. 155(3): 271-6, 1995 Feb 13.
37. Keen J. Intravenous magnesium sulfate for acute asthma. *J. Emer. Nursing* 21(1): 44-6, 1995 Feb.
38. Johnson K. Klingman E. Preventative nutrition: disease-specific dietary interventions for older adults. *Geriatrics* 47: 39-49, 1992 Oct.

39. Zidenberg-Cherr S. Essential trace elements in antioxidant processes. *Trace Elements, Micronutrients and Free Radicals* 107-27, 1992.
40. Johnston C. Antihistamine effect of supplemental ascorbic acid in neutrophil chemotaxis. *J. Amer. Coll. Nutr*. 11(2): 172-4, 1992.
41. Turnlund J. Vitamin B6 depletion followed by repletion with animal or plant source calcium and magnesium in young women. *Amer. J. Clin. Nutr*. 56: 905-10, 1992.
42. Sydow M. Crozier T. Zielmann S. Radke J. Burchardi H. High-dose intravenous magnesium sulfate in the management of life-threatening status asthmaticus [see comments]. Comment in: *Intensive Care Med*. 1995, Jan 21(1): 94-5; *Intensive Care Med*. 19(8): 467-71, 1993.
43. Tiffany B. Berk W. Todd I. White S. Magnesium bolus or infusion fails to improve expiratory flow in acute asthma exacerbations. *Chest* 104(3): 831-4, 1993 Sep.
44. Rolla G. Bucca C. Brussino L. Colagrande P. Effect of intravenous magnesium infusion on salbutamol-induced bronchodilatation in patients with asthma. *Magnesium Research*. 7(2): 129-33, 1994 Jun.
45. Schiermeyer R. Finkelstein J. Rapid infusion of magnesium sulfate obviates need for intubation in status asthmaticus. *Amer. J. Emer. Med*. 12(2): 164-6, 1994 Mar.
46. Lemesle F. High-dose intravenous magnesium sulfate in the management of life-threatening status asthmaticus [letter; comment]. Comment on: *Intensive Care Med*. 1993, 19(8): 467-71; *Intensive Care Med*. 21(1): 94-5, 1995 Jan.
47. Bloch H. Silverman R. Mancherje N. Grant S. Jagminas L. Scharf S. Intravenous magnesium sulfate as an adjunct in the treatment of acute asthma [see comments]. Comment in: *Chest* 1996 May, 109(5): 1411-2; *Chest* 107(6): 1576-81, 1995 Jun.
48. Moan M. Fanta C. Bronchodilator therapy in the management of acute asthma. *Comprehensive Ther*. 21(8):421-7, 1995 Aug.
49. Downey P. Cox R. Update on the management of status asthmaticus. *Cur. Opin. Ped.* 8(3): 226-33, 1996 Jan.
50. Hill J. Britton J. Effect of intravenous magnesium sulpfate on airway calibre and airway reactivity to histamine in asthmatic subjects. *Br. J. Clin. Pharmacol*. 42(5): 629-31, 1996 Nov.
51. Ciarallo L. Sauer A. Shannon M. Intravenous magnesium therapy for moderate to severe pediatric asthma: results of a randomized, placebo-controlled trial [see comments]. Comment in: *J. Ped*. 129(6): 783-51996 Dec; *J. Ped*. 129(6): 809-14, 1996 Dec.
52. Frakes M. Richardson L 2nd. Magnesium sulfate therapy in certain emergency conditions. *Amer. J. of Emer. Med*. 15(2): 182-7, 1997 Mar.
53. Lang D. Trends in US asthma mortality: good news and bad news [editorial; comment]. Comment on: *Ann. Aller. Asthma Immunol*. 1997 Apr: 78(4): 347-54 *Ann. Aller. Asthma Immunol*. 78(4): 333-7, 1997 Apr.
54. Sly R. O'Donnell R. Stabilization of asthma mortality [See comment]. Comment in *Ann. Aller. Asthma Immunol.* 78 (4): 333-7, 1997, Apr. *Ann. Aller. Asthma & Immunol.* 78 (4): 347-54, 1997.
55. Lieberman J. Kane G. Asthma mortality: the worldwide response. *J. Royal Soc. Med.* 90(5): 265-7, 1997 May.
56. Devi P. Kumar L. Singhi S. Prasad R. Singh M. Intravenous magnesium sulfate in acute severe asthma not responding to conventional therapy. *Indian Ped*. 34(5): 389-97, 1997 May.
57. Mills R. Leadbeater M. Ravalia A. Intravenous magnesium sulphate in the management of refractory bronchospasm in a ventilated asthmatic. *Anaesthesia* 52(8): 782-5, 1997 Aug.
58. Nakazawsa T. Kawakami Y. Sudo M. Kobayashi S. Suetsugu S. Nakajima S. Yamakido M. Nagano H. [Trends of asthma death among adults in Japan 1992-1994. Analysis of 313 cases reported questionnaires sent to hospitals with more than 100 beds]. *Arerugi – Jap. J. Allergology* 47(1): 41-7, 1998 Jan.

59. Keistinen T. Saynajakangas O. Tuuponen T. Kivela S. Ostro B. Chestnut L. Assessing the health benefits of reducing particulate matter air pollution in the United States. *Environ. Research* 76(2): 94-106, 1998 Feb.
60. Mannino D. Homa D. Pertowski C. Ashizawa A. Nixon L. Johnson C. Ball L. Jack E. Kang D. Surveillance for asthma--United States 1960-1995. *MMWR CDC Surveillance Summaries* 47(1): 1-27, 1998 Apr 24.
61. Beasley R. Nishima S. Pearce N. Crane J. Beta-agonist therapy and asthma mortality in Japan [letter]. Lancet. 351(9113): 1406-7, 1998 May 9.
62. Ertle A. London M. Insights into asthma prevalence in Oregon. *J. Asthma*. 35(3): 281-9, 1998.

IV References, categorized by nutrient, most recent to older (Dec. 31 1998 - present)

Alpha Lipoic Acid

63. Mijnhout GS, Kollen BJ, Alkhalaf A, Kleefstra N, Bilo HJ. Alpha lipoic Acid for symptomatic peripheral neuropathy in patients with diabetes: a meta-analysis of randomized controlled trials. Int J Endocrinol. 2012;2012:456279. doi: 10.1155/2012/456279. Epub 2012 Jan 26
64. Xiang G, Pu J, Yue L, Hou J, Sun H. α-lipoic acid can improve endothelial dysfunction in subjects with impaired fasting glucose. Metabolism. 2011 Apr;60(4):480-5. Epub 2011 Jan 20.
65. Mijnhout GS, Alkhalaf A, Kleefstra N, Bilo HJ. Alpha lipoic acid: a new treatment for neuropathic pain in patients with diabetes? Neth J Med. 2010 Apr;68(4):158-62.'
66. Heinisch BB, Francesconi M, Mittermayer F, Schaller G, Gouya G, Wolzt M, Pleiner J. Alpha-lipoic acid improves vascular endothelial function in patients with type 2 diabetes: a placebo-controlled randomized trial. Eur J Clin Invest. 2010 Feb;40(2):148-54. Epub 2009 Dec 27.
67. Liu F, Zhang Y, Yang M, Liu B, Shen YD, Jia WP, Xiang KS. [Curative effect of alpha-lipoic acid on peripheral neuropathy in type 2 diabetes: a clinical study] Zhonghua Yi Xue Za Zhi. 2007 Oct 16;87(38):2706-9. Chinese.
68. Jin HY, Joung SJ, Park JH, Baek HS, Park TS. The effect of alpha-lipoic acid on symptoms and skin blood flow in diabetic neuropathy. Diabet Med. 2007 Sep;24(9):1034-8. Epub 2007 May 8.
69. Berkson BM, Rubin DM, Berkson AJ. The long-term survival of a patient with pancreatic cancer with metastases to the liver after treatment with the intravenous alpha-lipoic acid/low-dose Naltrexone protocol. Integr Cancer Ther. 2006 Mar;5(1):83-9.
70. Melhem A, Stern M, Shibolet O, Israeli E, Ackerman Z, Pappo O, Hemed N, Rowe M, Ohana H, Zabrecky G, Cohen R, Ilan Y. Treatment of chronic hepatitis C virus infection via antioxidants: results of a phase I clinical trial. J Clin Gastroenterol. 2005 Sep;39(8):737-42.
71. Ziegler D. Thioctic acid for patients with symptomatic diabetic polyneuropathy: a critical review. Treat Endocrinol. 2004;3(3):173-89. Review.
72. Tankova T, Cherninkova S, Koev D. Treatment for diabetic ononeuropathy with alpha-lipoic acid. Int J Clin Pract. 2005 Jun;59(6):645-50.
73. Bruckner I, Bustan C, Adamescu E, Dobjanschi C. Diabetic neuropathy--choices of treatment. Rom J Intern Med. 2002;40(1-4):53-60.

Vitamin A

74. Darlow BA, Graham PJ.. Vitamin A supplementation for preventing morbidity and mortality in very low birthweight infants. Cochrane Database Syst Rev 2000;(2):CD000501

Vitamin B-6 and folate

75. Uzman S(1), Uludağ Yanaral T, Toptaş M, Koç A, Taş A, Bican G. Tuberk Toraks. Acute isoniazid intoxication: an uncommon cause of convulsion, coma and acidosis. 2013;61(1):50-3.
76. Jewell D, Young G. WITHDRAWN: Interventions for nausea and vomiting in early pregnancy. Cochrane Database Syst Rev. 2010 Sep 8;(9):CD000145.

77. Kuwahara H, Noguchi Y, Inaba A, Mizusawa H. [Case of an 81-year-old woman with theophylline-associated seizures followed by partial seizures due to vitamin B6 deficiency] Rinsho Shinkeigaku. 2008 Feb;48(2):125-9. Japanese.
78. Sym SJ, Ryu MH, Lee JL, Chang HM, Kim TW, Lee SS, Lee JS, Kang YK. Salvage chemotherapy with biweekly irinotecan, plus 5-fluorouracil and leucovorin in patients with advanced gastric cancer previously treated with fluoropyrimidine, platinum, and taxane. Am J Clin Oncol. 2008 Apr;31(2):151-6.
79. Sheehan P. Hyperemesis gravidarum--assessment and management. Aust Fam Physician. 2007 Sep;36(9):698-701. Review.
80. Teune LK, vd Hoeven JH, Maurits NM, Bos AF, Alffenaar JW, Reijngoud DJ, Brouwer OF, Sival DA. Pyridoxine induces non-specific EEG alterations in infants with therapy resistant seizures. Seizure. 2007 Jul;16(5):459-64. Epub 2007 Apr 3.
81. Leathem AM, Dorran TJ. Poisoning due to raw Gyromitra esculenta (false morels) west of the Rockies. CJEM. 2007 Mar;9(2):127-30.
82. Hasegawa S, Oda Y, Ichiyama T, Hori Y, Furukawa S. Ginkgo nut intoxication in a 2-year-old male. Pediatr Neurol. 2006 Oct;35(4):275-6.
83. Wang HS, Kuo MF, Chou ML, Hung PC, Lin KL, Hsieh MY, Chang MY. Pyridoxal phosphate is better than pyridoxine for controlling idiopathic intractable epilepsy. Arch Dis Child. 2005 May;90(5):512-5.
84. Gonella M, Calabrese G, Mengozzi A, Aleo AG, Vagelli G, Mazzotta A, Deambrogio P. The achievement of normal homocysteinemia in regular extracorporeal dialysis patients. J. Nephrol. 2004 May-Jun;17(3):411-3.
85. de Gomez Dumm NT, Giammona AM, Touceda LA. Variations in the lipid profile of patients with chronic renal failure, treated with folic acid. Int J Vitam Nutr Res. 2003 May;73(3):215-20.
86. Kuo MF, Wang HS. Pyridoxal phosphate-responsive epilepsy with resistance to pyridoxine. Pediatr Neurol 2002 Feb;26(2):146-7.
87. Citak A, Kaya O, Ucsel R, Karabocuoglu M, Uzel N. Acute isoniazid neurotoxicity in childhood. Turk J Pediatr 2002 Jan-Mar;44(1):54-7.
88. Gupta VK, Mishra D, Mathur I, Singh KK. Pyridoxine-dependent seizures: a case report and a critical review of the literature. J Paediatr Child Health 2001 Dec;37(6):592-6.
89. Henning BF, Zidek W, Riezler R, Graefe U, Tepel M. Homocyst(e)ine metabolism in hemodialysis patients treated with vitamins B6, B12 and folate. Res Exp Med (Berl) 2001 Mar;200(3):155-68.
90. Tremblay R, Bonnardeaux A, Geadah D, Busque L, Lebrun M, Ouimet D, Leblanc M. Hyperhomocysteinemia in hemodialysis patients: effects of 12-month supplementation with hydrosoluble vitamins. *Kidney Int* 2000 Aug;58(2):851-8.
91. Touam M, Zingraff J, Jungers P, Chadefaux-Vekemans B, Drueke T, Massy ZA. Effective correction of hyperhomocysteinemia in hemodialysis patients by intravenous folinic acid and pyridoxine therapy. Kidney Int 1999 Dec;56(6):2292-6.
92. Goto T, Matsuo N, Takahashi T. CSF glutamate/GABA concentrations in pyridoxine-dependent seizures: etiology of pyridoxine-dependent seizures and the mechanisms of pyridoxine action in seizure control. Brain Dev 2001 Mar;23(1):24-9.
93. Hauser AC, Hagen W, Rehak PH, Buchmayer H, Fodinger M, Papagiannopoulos M, Bieglmayer C, Apsner R, Koller E, Ignatescu M, Horl WH, Sunder-Plassmann G. Efficacy of folinic versus folic acid for the correction of hyperhomocysteinemia in hemodialysis patients. *Am J Kidney Dis* 2001 Apr;37(4):758-65.
94. Henning BF, Zidek W, Riezler R, Graefe U, Tepel M. Homocyst(e)ine metabolism in hemodialysis patients treated with vitamins B6, B12 and folate. *Res Exp Med* (Berl) 2001 Mar;200(3):155-68
95. Tremblay R, Bonnardeaux A, Geadah D, Busque L, Lebrun M, Ouimet D, Leblanc M. Hyperhomocysteinemia in hemodialysis patients: effects of 12-month supplementation with hydrosoluble vitamins. *Kidney Int* 2000 Aug;58(2):851-8

96. Touam M, Zingraff J, Jungers P, Chadefaux-Vekemans B, Drueke T, Massy ZA. Effective correction of hyperhomocysteinemia in hemodialysis patients by intravenous folinic acid and pyridoxine therapy. Kidney Int 1999 Dec;56(6):2292-6.

Vitamin B-12

97. Kiasari AZ(1), Firouzian A(1), Baradari AG(1), Nia HS(2), Kiasari SH(3). The Effect of Vitamin B12 Infusion on Prevention of Nitrous Oxide-induced Homocysteine Increase: A Double-blind Randomized Controlled Trial. Oman Med J. 2014 May;29(3):194-7.

98. Shibuya K(1), Misawa S, Nasu S, Sekiguchi Y, Beppu M, Iwai Y, Mitsuma S, Isose S, Arimura K, Kaji R, Kuwabara S. Safety and efficacy of intravenous ultra-high dose methylcobalamin treatment for peripheral neuropathy: a phase I/II open label clinical trial. Intern Med. 2014;53(17):1927-31. Epub 2014 Sep 1.

99. Fortin JL, Judic-Peureux V, Desmettre T, Manzon C, Grimon D, Hostalek U, Fétro C, Capellier G. Hydrogen cyanide poisoning in a prison environment: a case report. J Correct Health Care. 2011 Jan;17(1):29-33.

100. Shepherd G, Velez LI. Role of hydroxocobalamin in acute cyanide poisoning. Ann Pharmacother. 2008 May;42(5):661-9. Epub 2008 Apr 8. Review.

101. Borron SW, Baud FJ, Barriot P, Imbert M, Bismuth C. Prospective study of hydroxocobalamin for acute cyanide poisoning in smoke inhalation. Ann Emerg Med. 2007 Jun;49(6):794-801, 801.e1-2. Epub 2007 May 4.

102. Uhl W, Nolting A, Golor G, Rost KL, Kovar A. Safety of hydroxocobalamin in healthy volunteers in a randomized, placebo-controlled study.Clin Toxicol (Phila). 2006;44 Suppl 1:17-28.

103. Hoffer LJ, Saboohi F, Golden M, Barre PE. Cobalamin dose regimen for maximum homocysteine reduction in end-stage renal disease. Metabolism. 2005 Jun; 54(6):835-40.

104. Bugarin Gonzalez R, Portela Romero M, Martinez Varela F, Galego Feal P. [Intravenous administration of vitamin B12a in cases of cyanide poisoning] Aten Primaria. 2005 Apr 30; 35(7):382-3. Spanish.

105. Tremblay R, Bonnardeaux A, Geadah D, Busque L, Lebrun M, Ouimet D, Leblanc M. Hyperhomocysteinemia in hemodialysis patients: effects of 12-month supplementation with hydrosoluble vitamins. *Kidney Int* 2000 Aug;58(2):851-8.

106. Henning BF, Zidek W, Riezler R, Graefe U, Tepel M. Homocyst(e)ine metabolism in hemodialysis patients treated with vitamins B6, B12 and folate. *Res Exp Med* (Berl) 2001 Mar;200(3):155-68.

107. Collins DA, Hogenkamp HP, O'Connor MK, Naylor S, Benson LM, Hardyman TJ, Thorson LM. Biodistribution of radiolabeled adenosylcobalamin in patients diagnosed with various malignancies. *Mayo Clin Proc* 2000 Jun;75(6):568-80.

108. Kuwabara S, Nakazawa R, Azuma N, Suzuki M, Miyajima K, Fukutake T, Hattori T. Intravenous methylcobalamin treatment for uremic and diabetic neuropathy in chronic hemodialysis patients. Intern Med 1999 Jun;38(6):472-5.

109. Herzlich BC, Schiano TD. Reversal of apparent AIDS dementia complex following treatment with vitamin B12. J Intern Med 1993 Jun;233(6):495-7.

110. Dierkes J, Domrose U, Ambrosch A, Schneede J, Guttormsen AB, Neumann KH, Luley C. Supplementation with vitamin B12 decreases homocysteine and methylmalonic acid but also serum folate in patients with end-stage renal disease. Metabolism 1999 May;48(5):631-5.

111. Houeto P, Borron SW, Sandouk P, Imbert M, Levillain P, Baud FJ. Pharmacokinetics of hydroxocobalamin in smoke inhalation victims. Toxicol Clin Toxicol 1996;34(4):397-404.

112. Houeto P, Hoffman JR, Imbert M, Levillain P, Baud FJ. Relation of blood cyanide to plasma cyanocobalamin concentration after a fixed dose of hydroxocobalamin in cyanide poisoning. Lancet 1995 Sep 2;346(8975):605-8. Comment in: Lancet. 1995 Dec 23-30;346(8991-8992):1706-7

113. Forsyth JC, Mueller PD, Becker CE, Osterloh J, Benowitz NL, Rumack BH, Hall AH. Hydroxocobalamin as a cyanide antidote: safety, efficacy and pharmacokinetics in heavily smoking normal volunteers. J Toxicol Clin Toxicol 1993;31(2):277-94.

114. Ikeda T, Yamamoto K, Takahashi K, Kaku Y, Uchiyama M, Sugiyama K, Yamada M. Treatment of Alzheimer-type dementia with intravenous mecobalamin. Clin Ther 1992 May-Jun;14(3):426-37.
115. Kurabayashi H, Kubota K, Kawada E, Tamura K, Tamura J, Shirakura T. Complete cure of urinary and faecal incontinence after intravenous vitamin B12 therapy in a patient with post-gastrectomy megaloblastic anaemia. J Intern Med 1992 Mar;231(3):313-5.

Vitamin C

116. Wang ZJ(1), Hu WK(1), Liu YY(1), Shi DM(1), Cheng WJ(1), Guo YH(1), Yang Q(1), Zhao YX(2), Zhou YJ(1). The effect of intravenous vitamin C infusion on periprocedural myocardial injury for patients undergoing elective percutaneous coronary intervention. Can J Cardiol. 2014 Jan;30(1):96-101. doi: 10.1016/j.cjca.2013.08.018. Comment in Can J Cardiol. 2014 Jan;30(1):3-5.
117. Mikirova N(1), Hunninghake R(1). Effect of high dose vitamin C on Epstein-Barr viral infection. Med Sci Monit. 2014 May 3;20:725-32. doi: 10.12659/MSM.890423.
118. Wilson JX, Wu F. Vitamin C in sepsis. Subcell Biochem. 2012;56:67-83. doi: 10.1007/978-94-007-2199-9_5.
119. Fritz H, Flower G, Weeks L, Cooley K, Callachan M, McGowan J, Skidmore B, Kirchner L, Seely D. Intravenous Vitamin C and Cancer: A Systematic Review. Integr Cancer Ther. 2014 May 26;13(4):280-300. [Epub ahead of print]
120. Mikirova N, Casciari J, Rogers A, Taylor P. Effect of high-dose intravenous vitamin C on inflammation in cancer patients. J Transl Med. 2012 Sep 11;10:189. doi: 10.1186/1479-5876-10-189.
121. Chen P, Yu J, Chalmers B, Drisko J, Yang J, Li B, Chen Q. Anticancer Drugs. 2012 Apr;23(4):437-44. doi: 10.1097/CAD.0b013e32834fd01f. Pharmacological ascorbate induces cytotoxicity in prostate cancer cells through ATP depletion and induction of autophagy.
122. Schencking M, Vollbracht C, Weiss G, Lebert J, Biller A, Goyvaerts B, Kraft K. Intravenous vitamin C in the treatment of shingles: results of a multicenter prospective cohort study. Med Sci Monit. 2012 Apr;18(4):CR215-24.
123. Takahashi, Hidenori, Mizuno, Haruyoshi, Yanagisawa, Atsuo. High-dose intravenous vitamin C improves quality of life in cancer patients. Personalized Medicine Universe 1 (2012) 49-53.
124. Gholipour Baradari A, Emami Zeydi A, Espahbodi F, Aarabi M. The effect of intravenous vitamin C on the phosphorus level reduction in hemodialysis patients: a double blind randomized clinical trial. Med Glas Ljek komore Zenicko-doboj kantona. 2012 Feb;9(1):37-41.
125. Einerson B, Nathorn C, Kitiyakara C, Sirada M, Thamlikitkul V. The administration of ascorbic acid (vitamin C) in abdominal myomectomy could reduce the blood loss during the procedure, operation J Med Assoc Thai. 2011 Feb;94 Suppl 1:S134-46.
126. Chen P, Stone J, Sullivan G, Drisko JA, Chen Q. Anti-cancer effect of pharmacologic ascorbate and its interaction with supplementary parenteral glutathione in preclinical cancer models. Free Radic Biol Med. 2011 Aug 1;51(3):681-7. Epub 2011 May 30.
127. Stewart JM, Ocon AJ, Medow MS. Ascorbate improves circulation in postural tachycardia syndrome. Am J Physiol Heart Circ Physiol. 2011 Sep;301(3):H1033-42. Epub 2011 May 27
128. Schencking M, Sandholzer H, Frese T. Intravenous administration of vitamin C in the treatment of herpetic neuralgia: two case reports. Med Sci Monit. 2010 Apr 28;16(5):CS58-61.
129. Chen Q, Espey MG, Sun AY, Pooput C, Kirk KL, Krishna MC, Khosh DB, Drisko J, Levine M. Pharmacologic doses of ascorbate act as a prooxidant and decrease growth of aggressive tumor xenografts in mice. Proc Natl Acad Sci U S A. 2008 Aug 12;105(32):11105-9. Epub 2008 Aug 4.
130. Kodama M, Oyama A, Takagi H. Control of interstitial pneumonia by drip infusion of megadose vitamin C, dehydroepiandrosterone and cortisol. A short review of our experience. In Vivo. 2008 Mar-Apr;22(2):263-7. Review.
131. Duconge J, Miranda-Massari JR, Gonzalez MJ, Jackson JA, Warnock W, Riordan NH. Pharmacokinetics of vitamin C: insights into the oral and intravenous administration of ascorbate. P R Health Sci J. 2008 Mar;27(1):7-19. Review.
132. Ferretti G, Bacchetti T, Masciangelo S, Pallotta G. Lipid peroxidation in hemodialysis patients: effect of vitamin C supplementation. Clin Biochem. 2008 Apr;41(6):381-6. Epub 2007 Dec 27.
133. Shinke T, Shite J, Takaoka H, Hata K, Inoue N, Yoshikawa R, Matsumoto H, Masai H, Watanabe S, Ozawa T, Otake H, Matsumoto D, Hirata K, Yokoyama M. Vitamin C restores the contractile response

to dobutamine and improves myocardial efficiency in patients with heart failure after anterior myocardial infarction. Am Heart J. 2007 Oct;154(4):645.e1-8.

134. Stephenson CM, Levin RD, Lis CG. Phase 1 trial of high-dose intravenous vitamin C treatment for patients with cancer. J Am Osteopath Assoc. 2007 Jun;107(6):212-3. No abstract available.

135. McCarty MF, Barroso-Aranda J, Contreras F. A two-phase strategy for treatment of oxidant-dependent cancers. Med Hypotheses. 2007;69(3):489-96. Epub 2007 May 14.

136. Briguori C, Airoldi F, D'Andrea D, Bonizzoni E, Morici N, Focaccio A, Michev I, Montorfano M, Carlino M, Cosgrave J, Ricciardelli B, Colombo A. Renal Insufficiency Following Contrast Media Administration Trial (REMEDIAL): a randomized comparison of 3 preventive strategies. Circulation. 2007 Mar 13;115(10):1211-7. Epub 2007 Feb 19.

137. McNulty PH, Robertson BJ, Tulli MA, Hess J, Harach LA, Scott S, Sinoway LI. Effect of hyperoxia and vitamin C on coronary blood flow in patients with ischemic heart disease. J Appl Physiol. 2007 May;102(5):2040-5. Epub 2007 Feb 15.

138. Moreau KL, DePaulis AR, Gavin KM, Seals DR. Oxidative stress contributes to chronic leg vasoconstriction in estrogen-deficient postmenopausal women. J Appl Physiol. 2007 Mar;102(3):890-5. Epub 2006 Nov 16.

139. Yeom CH, Jung GC, Song KJ. Changes of terminal cancer patients' health-related quality of life after high dose vitamin C administration. J Korean Med Sci. 2007 Feb;22(1):7-11.

140. Muran PJ. Mercury elimination with oral DMPS, DMSA, vitamin C, and glutathione: an observational clinical review. Altern Ther Health Med. 2006 May-Jun; 12(3):70-5.

141. Kodama M, Kodama T. Four problems with the clinical control of interstitial pneumonia, or chronic fatigue syndrome, using the megadose vitamin C infusion system with dehydroepiandrosterone-cortisol annex. In Vivo. 2006 Mar-Apr;20(2):285-91.

142. Padayatty SJ, Riordan HD, Hewitt SM, Katz A, Hoffer LJ, Levine M. Intravenously administered vitamin C as cancer therapy: three cases. CMAJ. 2006 Mar 28;174(7):937-42. Comment in: CMAJ. 2006 Mar 28;174(7):956-7.

143. Bailey DM, Raman S, McEneny J, Young IS, Parham KL, Hullin DA, Davies B, McKeeman G, McCord JM, Lewis MH. Vitamin C prophylaxis promotes oxidative lipid damage during surgical ischemia-reperfusion. Free Radic Biol Med. 2006 Feb 15;40(4):591-600.

144. Grebe M, Eisele HJ, Weissmann N, Schaefer C, Tillmanns H, Seeger W, Schulz R. Antioxidant vitamin C improves endothelial function in obstructive sleep apnea. Am J Respir Crit Care Med. 2006 Apr 15;173(8):897-901. Epub 2006 Jan 26.

145. Gonzalez MJ, Miranda-Massari JR, Mora EM, Guzman A, Riordan NH, Riordan HD, Casciari JJ, Jackson JA, Roman-Franco A. Orthomolecular oncology review: ascorbic acid and cancer 25 years later. Integr Cancer Ther. 2005 Mar;4(1):32-44. Review.

146. Sturm B, Laggner H, Ternes N, Goldenberg H, Scheiber-Mojdehkar B. Intravenous iron preparations and ascorbic acid: effects on chelatable and bioavailable iron. Kidney Int. 2005 Mar;67(3):1161-70.

147. Kodama M, Kodama T. The clinical course of interstitial pneumonia alias chronic fatigue syndrome under the control of megadose vitamin C infusion system with dehydroepiandrosterone-cortisol annex. Int J Mol Med. 2005 Jan;15(1):109-16.

148. Kumar S, Miranda-Massari JR, Gonzalez MJ, Riordan HD. Intravenous ascorbic acid as a treatment for severe jellyfish stings. P R Health Sci J. 2004 Jun;23(2):125-6.

149. Riordan HD, Riordan NH, Jackson JA, Casciari JJ, Hunninghake R, Gonzalez MJ, Mora EM, Miranda-Massari JR, Rosario N, Rivera A. Intravenous vitamin C as a chemotherapy agent: a report on clinical cases. P R Health Sci J. 2004 Jun;23(2):115-8.

150. Riordan HD, Hunninghake RB, Riordan NH, Jackson JJ, Meng X, Taylor P, Casciari JJ, Gonzalez MJ, Miranda-Massari JR, Mora EM, Rosario N, Rivera A. Intravenous ascorbic acid: protocol for its application and use. P R Health Sci J. 2003 Sep;22(3):287-90.

151. Taji Y, Morimoto T, Okada K, Fukuhara S, Fukui T, Kuwahara T. Effects of intravenous ascorbic acid on erythropoiesis and quality of life in unselected hemodialysis patients. J Nephrol. 2004 Jul-Aug;17(4):537-43.

152. Tarng DC, Liu TY, Huang TP. Protective effect of vitamin C on 8-hydroxy-2'-deoxyguanosine level in peripheral blood lymphocytes of chronic hemodialysis patients. Kidney Int. 2004 Aug;66(2):820-31.

153. Padayatty SJ, Sun H, Wang Y, Riordan HD, Hewitt SM, Katz A, Wesley RA, Levine M. Vitamin C pharmacokinetics: implications for oral and intravenous use. Ann Intern Med. 2004 Apr 6;140(7):533-7.Comment in: Ann Intern Med. 2004 Apr 6;140(7):I61.

154. Du WD, Yuan ZR, Sun J, Tang JX, Cheng AQ, Shen DM, Huang CJ, Song XH, Yu XF, Zheng SB. Therapeutic efficacy of high-dose vitamin C on acute pancreatitis and its potential mechanisms. World J Gastroenterol. 2003 Nov;9(11):2565-9.

155. Schindler TH, Nitzsche EU, Munzel T, Olschewski M, Brink I, Jeserich M, Mix M, Buser PT, Pfisterer M, Solzbach U, Just H. Coronary vasoregulation in patients with various risk factors in response to cold pressor testing: contrasting myocardial blood flow responses to short- and long-term vitamin C administration. J Am Coll Cardiol. 2003 Sep 3;42(5):814-22.

156. Drisko JA, Chapman J, Hunter VJ. The use of antioxidants with first-line chemotherapy in two cases of ovarian cancer. J Am Coll Nutr. 2003 Apr;22(2):118-23.

157. Lin CL, Hsu PY, Yang HY, Huang CC. Low dose intravenous ascorbic acid for erythropoietin-hyporesponsive anemia in diabetic hemodialysis patients with iron overload. Ren Fail. 2003 May;25(3):445-53.

158. Nightingale AK, Blackman DJ, Field R, Glover NJ, Pegge N, Mumford C, Schmitt M, Ellis GR, Morris-Thurgood JA, Frenneaux MP. Role of nitric oxide and oxidative stress in baroreceptor dysfunction in patients with chronic heart failure. Clin Sci (Lond). 2003 May;104(5):529-35.

159. Deng YB, Li TL, Xiang HJ, Chang Q, Li CL. Impaired endothelial function in the brachial artery after Kawasaki disease and the effects of intravenous administration of vitamin C. Pediatr Infect Dis J. 2003 Jan;22(1):34-9.

160. Tomiyama H, Watanabe G, Yoshida H, Doba N, Yamashina A. Reduction of oxidative stress augments natriuretic effect of furosemide in moderate heart failure. Am Heart J. 2003 Jan;145(1):E2.

161. Schindler TH, Lewandowski E, Olschewski M, Hasler K, Solzbach U, Just H. [Effect of vitamin C on platelet aggregation in smokers and nonsmokers] [Article in German] Med Klin (Munich). 2002 May 15;97(5):263-9. German.

162. Gonzalez MJ, Miranda-Massari JR, Mora EM, Jimenez IZ, Matos MI, Riordan HD, Casciari JJ, Riordan NH, Rodriguez M, Guzman A. Orthomolecular oncology: a mechanistic view of intravenous ascorbate's chemotherapeutic activity. P R Health Sci J 2002 Mar;21(1):39-41.

163. Richartz BM, Werner GS, Ferrari M, Figulla HR. Reversibility of coronary endothelial vasomotor dysfunction in idiopathic dilated cardiomyopathy: acute effects of vitamin C. Am J Cardiol 2001 Nov 1;88(9):1001-5.

164. Rossig L, Hoffmann J, Hugel B, Mallat Z, Haase A, Freyssinet JM, Tedgui A, Aicher A, Zeiher AM, Dimmeler S. Vitamin C inhibits endothelial cell apoptosis in congestive heart failure. Circulation 2001 Oct 30;104(18):2182-7.

165. Shen CT, Wang NK. Antioxidants may mitigate the deterioration of coronary arteritis in patients with Kawasaki disease unresponsive to high-dose intravenous gamma-globulin. Pediatr Cardiol 2001 Sep-Oct;22(5):419-22.

166. Yamada T, Minohara M, Imaiso Y, Sakae N, Hara H, Tanaka K, Yamamoto T, Taniwaki T, Furuya H, Kira J. High-dose vitamin C therapy for inclusion body myositis. Artif Organs 2001 Jun;25(6):430-6. Fukuoka Igaku Zasshi 2001 Apr;92(4):99-104.

167. Casciari JJ, Riordan NH, Schmidt TL, Meng XL, Jackson JA, Riordan HD. Cytotoxicity of ascorbate, lipoic acid, and other antioxidants in hollow fibre in vitro tumours. Br J Cancer 2001 Jun 1;84(11):1544-50.

168. Hamabe A, Takase B, Uehata A, Kurita A, Ohsuzu F, Tamai S. Impaired endothelium-dependent vasodilation in the brachial artery in variant angina pectoris and the effect of intravenous administration of vitamin C. Am J Cardiol 2001 May 15;87(10):1154-9.

169. Ellis GR, Anderson RA, Chirkov YY, Morris-Thurgood J, Jackson SK, Lewis MJ, Horowitz JD, Frenneaux MP. Acute effects of vitamin C on platelet responsiveness to nitric oxide donors and

endothelial function in patients with chronic heart failure. J Cardiovasc Pharmacol 2001 May;37(5):564-70.

170. Grossmann M, Dobrev D, Himmel HM, Ravens U, Kirch W. Ascorbic acid-induced modulation of venous tone in humans. Hypertension 2001 Mar;37(3):949-54.

171. Chambers JC, Haskard DO, Kooner JS. Vascular endothelial function and oxidative stress mechanisms in patients with Behcet's syndrome. J Am Coll Cardiol 2001 Feb;37(2):517-20.

172. Mak S, Newton GE. Vitamin C augments the inotropic response to dobutamine in humans with normal left ventricular function. Circulation 2001 Feb 13;103(6):826-30. Comment in: Circulation. 2001 Feb 13;103(6):782-3. UI: 21112918.

173. Hamabe A, Takase B, Uehata A, Kurita A, Ohsuzu F, Tamai S. Impaired endothelium-dependent vasodilation in the brachial artery in variant angina pectoris and the effect of intravenous administration of vitamin C. Am J Cardiol 2001 May 15;87(10):1154-9.

174. Mak S, Newton GE. Vitamin C augments the inotropic response to dobutamine in humans with normal left ventricular function. Circulation 2001 Feb 13;103(6):826-30. Comment in: Circulation. 2001 Feb 13;103(6):782-3.

175. Chambers JC, Haskard DO, Kooner JS. Vascular endothelial function and oxidative stress mechanisms in patients with Behcet's syndrome J Am Coll Cardiol 2001 Feb;37(2):517-20

176. Halimi JM, Mimran A. Systemic and renal effect of nicotine in non-smokers: influence of vitamin C. J Hypertens 2000 Nov;18(11):1665-9.

177. Ellis GR, Anderson RA, Lang D, Blackman DJ, Morris RH, Morris-Thurgood J, McDowell IF, Jackson SK, Lewis MJ, Frenneaux MP. Neutrophil superoxide anion--generating capacity, endothelial function and oxidative stress in chronic heart failure: effects of short- and long-term vitamin C therapy. J Am Coll Cardiol 2000 Nov 1;36(5):1474-82.

178. Sakagami H, Satoh K, Hakeda Y, Kumegawa M. Apoptosis-inducing activity of vitamin C and vitamin K. Cell Mol Biol (Noisy-le-grand) 2000 Feb;46(1):129-43.

179. Volchegorskii IA, Vasil'kov AY. Effects of ascorbic acid on lipid peroxidation and functional state of neutrophils at the early period after transurethral resection of the prostate. Bull Exp Biol Med 2000 Nov;130(11):1055-7.

180. Giancaspro V, Nuzziello M, Pallotta G, Sacchetti A, Petrarulo F. Intravenous ascorbic acid in hemodialysis patients with functional iron deficiency: a clinical trial. J Nephrol 2000 Nov-Dec;13(6):444-9.

181. Yamada T, Minohara M, Imaiso Y, Sakae N, Hara H, Tanaka K, Yamamoto T, Taniwaki T, Furuya H, Kira J. High-dose vitamin C therapy for inclusion body myositis. Fukuoka Igaku Zasshi 2001 Apr;92(4):99-104.

182. Casciari JJ, Riordan NH, Schmidt TL, Meng XL, Jackson JA, Riordan HD. Cytotoxicity of ascorbate, lipoic acid, and other antioxidants in hollow fibre in vitro tumours. Br J Cancer 2001 Jun 1;84(11):1544-50.

183. Takahashi, Hidenori, Mizuno, Haruyoshi, Yanagisawa, Atsuo. High-dose intravenous vitamin C improves quality of life in cancer patients. Personalized Medicine Universe 1 (2012) 49-53.

L-Carnitine

184. Chan YC, Tse ML, Lau FL. Two cases of valproic acid poisoning treated with L-carnitine. Hum Exp Toxicol. 2007 Dec;26(12):967-9.

185. Biolo G, Stulle M, Bianco F, Mengozzi G, Barazzoni R, Vasile A, Panzetta G, Guarnieri G. Insulin action on glucose and protein metabolism during L-carnitine supplementation in maintenance haemodialysis patients. Nephrol Dial Transplant. 2008 Mar;23(3):991-7. Epub 2007 Nov 28.'

186. Chan YC, Tse ML, Lau FL. Two cases of valproic acid poisoning treated with L-carnitine. Hum Exp Toxicol. 2007 Dec;26(12):967-9.

187. Biolo G, Stulle M, Bianco F, Mengozzi G, Barazzoni R, Vasile A, Panzetta G, Guarnieri G. Insulin action on glucose and protein metabolism during L-carnitine supplementation in maintenance haemodialysis patients. Nephrol Dial Transplant. 2008 Mar;23(3):991-7. Epub 2007 Nov 28.'

188. Makino Y, Sugiura T, Ito T, Sugiyama N, Koyama N. Carnitine-associated encephalopathy caused by long-term treatment with an antibiotic containing pivalic acid. Pediatrics. 2007 Sep;120(3):e739-41. Epub 2007 Aug 27.

189. Russell S. Carnitine as an antidote for acute valproate toxicity in children. Curr Opin Pediatr. 2007 Apr;19(2):206-10. Review.

190. Loffredo L, Pignatelli P, Cangemi R, Andreozzi P, Panico MA, Meloni V, Violi F. Imbalance between nitric oxide generation and oxidative stress in patients with peripheral arterial disease: effect of an antioxidant treatment. J Vasc Surg. 2006 Sep;44(3):525-30.

191. Signorelli SS, Fatuzzo P, Rapisarda F, Neri S, Ferrante M, Oliveri Conti G,Fallico R, Di Pino L, Pennisi G, Celotta G, Anzaldi M. Propionyl-L-carnitine therapy: effects on endothelin-1 and homocysteine levels in patients with peripheral arterial disease and end-stage renal disease. Kidney Blood Press Res. 2006;29(2):100-7. Epub 2006 Jun 30.

192. Rathod R, Baig MS, Khandelwal PN, Kulkarni SG, Gade PR, Siddiqui S. Results of a single blind, randomized, placebo-controlled clinical trial to study the effect of intravenous L-carnitine supplementation on health-related quality of life in Indian patients on maintenance hemodialysis. Indian J Med Sci. 2006 Apr;60(4):143-53.

193. Silvestro A, Schiano V, Bucur R, Brevetti G, Scopacasa F, Chiariello M. Effect of propionylcarnitine on changes in endothelial function and plasma levels of adhesion molecules induced by acute exercise in patients with intermittent claudication.Angiology. 2006 Mar-Apr;57(2):145-54.

194. Siciliano M, Annicchiarico BE, Lucchese F, Bombardieri G. Effects of a single, short intravenous dose of acetyl-L-carnitine on pattern-reversal visual-evoked potentials in cirrhotic patients with hepatic encephalopathy. Clin Exp Pharmacol Physiol. 2006 Jan-Feb;33(1-2):76-80.

195. Vernez L, Dickenmann M, Steiger J, Wenk M, Krahenbuhl S. Effect of L-carnitine on the kinetics of carnitine, acylcarnitines and butyrobetaine in long-term haemodialysis. Nephrol Dial Transplant. 2006 Feb;21(2):450-8. Epub 2005 Nov 11. Erratum in: Nephrol Dial Transplant. 2006 Apr;21(4):1141.

196. Ferrari R, Merli E, Cicchitelli G, Mele D, Fucili A, Ceconi C. Ann N Y. Therapeutic Effects of l-Carnitine and Propionyl-l-carnitine on Cardiovascular Diseases: A Review. Ann N Y Acad Sci. 2004 Nov;1033:79-91.

197. Calvani M, Benatti P, Mancinelli A, D'Iddio S, Giordano V, Koverech A, Amato A, Brass EP. Carnitine replacement in end-stage renal disease and hemodialysis. Acad Sci. 2004 Nov;1033:52-66.

198. Ragozzino G, Mattera E, Madrid E, Salomone P, Fasano C, Gioia F, Acerra G, del Guercio R, Federico P. Effects of propionyl-carnitine in patients with type 2 diabetes and peripheral vascular disease: results of a pilot trial. Drugs R D. 2004;5(4):185-90.

199. Brass EP, Adler S, Sietsema KE, Hiatt WR, Orlando AM, Amato A. Intravenous L-carnitine increases plasma carnitine, reduces fatigue, and may preserve exercise capacity in hemodialysis patients. Am J Kidney Dis 2001 May;37(5):1018-28.

200. Winter S, Birek L, Walker T, Phalin-Roque J, Chandler MJ, Field C, Zorn E. Therapy of metabolic disorders with intravenous (IV) access ports and long term intravenous L-carnitine therapy. Southeast Asian J Trop Med Public Health 1999;30 Suppl 2:152-3.

Coenzyme Q10

201. Zhou M, Zhi Q, Tang Y, Yu D, Han J. Effects of coenzyme Q10 on myocardial protection during cardiac valve replacement and scavenging free radical activity in vitro. J Cardiovasc Surg (Torino) 1999 Jun;40(3):355-61.

Glutathione

202. Pachman DR, Barton DL, Watson JC, Loprinzi CL. Chemotherapy-induced peripheral neuropathy: prevention and treatment. Clin Pharmacol Ther. 2011 Sep;90(3):377-87. doi: 10.1038/clpt.2011.115.

203. Gil HW, Kang EJ, Lee KH, Yang JO, Lee EY, Hong SY. Effect of glutathione on the cadmium chelation of EDTA in a patient with cadmium intoxication. Hum Exp Toxicol. 2011 Jan;30(1):79-83.

204. Wolf S, Barton D, Kottschade L, Grothey A, Loprinzi C. Chemotherapy-induced peripheral neuropathy: prevention and treatment strategies. Eur J Cancer. 2008 Jul;44(11):1507-15. Epub 2008 Jun 18. Review.

205. Muran PJ. Mercury elimination with oral DMPS, DMSA, vitamin C, and glutathione: an observational clinical review. Altern Ther Health Med. 2006 May-Jun;12(3):70-5.

206. Melhem A, Stern M, Shibolet O, Israeli E, Ackerman Z, Pappo O, Hemed N, Rowe M, Ohana H, Zabrecky G, Cohen R, Ilan Y. Treatment of chronic hepatitis C virus infection via antioxidants: results of a phase I clinical trial. J Clin Gastroenterol. 2005 Sep;39(8):737-42.

207. Zhu BD, Li X, Zhao QC, Huang XL. [Enhancement of antioxidant capability of cancer patients during chemotherapy by reduced glutathione] Ai Zheng. 2004 Apr;23(4):452-5. Chinese.

208. Arosio E, De Marchi S, Zannoni M, Prior M, Lechi A. Effect of glutathione infusion on leg arterial circulation, cutaneous microcirculation, and pain-free walking distance in patients with peripheral obstructive arterial disease: a randomized, double-blind, placebo-controlled trial. Mayo Clin Proc. 2002 Aug;77(8):754-9.

209. Ortolani O, Conti A, De Gaudio AR, Moraldi E, Cantini Q, Novelli G. The effect of glutathione and N-acetylcysteine on lipoperoxidative damage in patients with early septic shock. Am J Respir Crit Care Med. 2000 Jun;161(6):1907-11.

210. Böhm S, Oriana S, Spatti G, Di Re F, Breasciani G, Pirovano C, Grosso I, Martini C, Caraceni A, Pilotti S, Zunino F. Dose intensification of platinum compounds with glutathione protection as induction chemotherapy for advanced ovarian carcinoma. Oncology. 1999;57(2):115-20.

211. Ciuchi E, Odetti P, Prando R. The effect of acute glutathione treatment on sorbitol level in erythrocytes from diabetic patients. Diabetes Metab. 1997 Feb;23(1):58-60.

212. Sechi G, Deledda MG, Bua G, Satta WM, Deiana GA, Pes GM, Rosati G. Reduced intravenous glutathione in the treatment of early Parkinson's disease. Prog Neuropsychopharmacol Biol Psychiatry. 1996 Oct;20(7):1159-70.

213. Loguercio C, Piscopo P, Guerriero C, De Girolamo V, Disalvo D, Del Vecchio Blanco C. Effect of alcohol abuse and glutathione administration on the circulating levels of glutathione and on antipyrine metabolism in patients with alcoholic liver cirrhosis. Scand J Clin Lab Invest. 1996 Aug;56(5):441-7.

214. Dentico P, Volpe A, Buongiorno R, Grattagliano I, Altomare E, Tantimonaco G, Scotto G, Sacco R, Schiraldi O. [Glutathione in the treatment of chronic fatty liver diseases] Recenti Prog Med. 1995 Jul-Aug;86(7-8):290-3. Italian.

215. Plaxe S, Freddo J, Kim S, Kirmani S, McClay E, Christen R, Braly P, Howell S. Phase I trial of cisplatin in combination with glutathione. Gynecol Oncol. 1994 Oct;55(1):82-6.

216. Trevisani F, Tamé MR, Bernardi M, Tovoli C, Gasbarrini A, Panarelli M, Gasbarrini G. Severe hepatic failure occurring with T61 ingestion in an attempted suicide. Early recovery with the use of intravenous infusion of reduced glutathione. Dig Dis Sci. 1993 Apr;38(4):752-6.

217. Robinson MK, Ahn MS, Rounds JD, Cook JA, Jacobs DO, Wilmore DW. Parenteral glutathione monoester enhances tissue antioxidant stores. JPEN J Parenter Enteral Nutr. 1992 Sep- Oct;16(5):413-8.

218. Ortolani O, Gratino F, Leone D, Russo F, Tufano R. [Usefulness of the prevention of oxygen radical damage in the critical patient using the parenteral administration of reduced glutathione in high doses] Boll Soc Ital Biol Sper. 1992 Apr;68(4):239-44. Italian.

219. Paolisso G, Giugliano D, Pizza G, Gambardella A, Tesauro P, Varricchio M, D'Onofrio F. Glutathione infusion potentiates glucose-induced insulin secretion in aged patients with impaired glucose tolerance. Diabetes Care. 1992 Jan;15(1):1-7.

220. Costagliola C, Romano L, Scibelli G, de Vincentiis A, Sorice P, Di Benedetto A. Anemia and chronic renal failure: a therapeutical approach by reduced glutathione parenteral administration. Nephron. 1992;61(4):404-8.

221. Coppola L, Grassia A, Giunta R, Verrazzo G, Cava B, Tirelli A, D'Onofrio F. Glutathione (GSH) improved haemostatic and haemorheological parameters in atherosclerotic subjects. Drugs Exp Clin Res. 1992;18(11-12):493-8.

222. Ceriello A, Giugliano D, Quatraro A, Lefebvre PJ. Anti-oxidants show an anti-hypertensive effect in diabetic and hypertensive subjects. Clin Sci (Lond). 1991 Dec;81(6):739-42.

223. Aebi S, Assereto R, Lauterburg BH. High-dose intravenous glutathione in man. harmacokinetics and effects on cyst(e)ine in plasma and urine. Eur J Clin Invest. 1991 Feb;21(1):103-10.

Vitamin K-1

224. Dezee KJ, Shimeall WT, Douglas KM, Shumway NM, O'malley PG Treatment of excessive anticoagulation with phytonadione (vitamin K): a meta-analysis. Arch Intern Med. 2006 Feb 27;166(4):391-7.

225. Chambrier C, Bannier E, Lauverjat M, Drai J, Bryssine S, Bouletreau P. Replacement of long-chain triglyceride with medium-chain triglyceride/long-chain triglyceride lipid emulsion in patients receiving long-term parenteral nutrition: effects on essential fatty acid status and plasma vitamin K1 levels. JPEN J Parenter Enteral Nutr. 2004 Jan-Feb;28(1):7-12.

226. Shields RC, McBane RD, Kuiper JD, Li H, Heit JA.. Efficacy and safety of intravenous phytonadione (vitamin K1) in patients on long-term oral anticoagulant therapy. Mayo Clin Proc 2001 Mar;76(3):260-6.

227. MacLaren R, Wilson SJ, Campbell A, Anderson D, Rocker G. Evaluation and survey of intravenous vitamin K1 for treatment of coagulopathy in critically ill patients. Pharmacotherapy 2001 Feb;21(2):175-82.

Magnesium References

Magnesium: Anesthesia

228. Aissaoui Y, Qamous Y, Serghini I, Zoubir M, Salim JL, Boughalem M. Magnesium sulphate: an adjuvant to tracheal intubation without muscle relaxation--a randomised study. Eur J Anaesthesiol. 2012 Aug;29(8):391-7. doi: 10.1097/EJA.0b013e328355cf35.

229. Gozdemir M, Usta B, Demircioglu RI, Muslu B, Sert H, Karatas OF. Magnesium sulfate infusion prevents shivering during transurethral prostatectomy with spinal anesthesia: a randomized, double-blinded, controlled study. J Clin Anesth. 2010 May;22(3):184-9.

230. Ryu JH, Kang MH, Park KS, Do SH. Effects of magnesium sulphate on intraoperative anaesthetic requirements and postoperative analgesia in gynaecology patients receiving total intravenous anaesthesia. Br J Anaesth. 2008 Mar;100(3):397-403.

231. Arcioni R, Palmisani S, Tigano S, Santorsola C, Sauli V, Romanò S, Mercieri. Combined intrathecal and epidural magnesium sulfate supplementation of spinal anesthesia to reduce post-operative analgesic requirements: a prospective, randomized, double-blind, controlled trial in patients undergoing major orthopedic surgery. Acta Anaesthesiol Scand. 2007 Apr;51(4):482-9.

232. M, Masciangelo R, De Blasi RA, Pinto G. Combined intrathecal and epidural magnesium sulfate supplementation of spinal anesthesia to reduce post-operative analgesic requirements: a prospective, randomized, double-blind, controlled trial in patients undergoing major orthopedic surgery. Acta Anaesthesiol Scand. 2007 Apr;51(4):482-9.

233. Cizmeci P, Ozkose Z. Magnesium sulphate as an adjuvant to total intravenous anesthesia in septorhinoplasty: a randomized controlled study. Aesthetic Plast Surg. 2007 Mar-Apr;31(2):167-73.

234. Gupta K, Vohra V, Sood J. The role of magnesium as an adjuvant during general anaesthesia. Anaesthesia. 2006 Nov;61(11):1058-63.

235. Elsharnouby NM, Elsharnouby MM. Magnesium sulphate as a technique of hypotensive anaesthesia. Br J Anaesth. 2006 Jun;96(6):727-31. Epub 2006 May 2.

Magnesium: Asthma (with *multiple nutrients*)

236. Shrader, W.A. Jr. Short and long term treatment of asthma with intravenous nutrients. Nutr J. 2004 May 14; 3(1): 6.

Magnesium: Asthma

237. Rowe BH, Camargo CA Jr. The role of magnesium sulfate in the acute and chronic management of asthma. Curr Opin Pulm Med. 2008 Jan;14(1):70-6. Review.

238. Creagh-Brown BC, Ball J. An under-recognized complication of treatment of acute severe asthma. Am J Emerg Med. 2008 May;26(4):514.e1-3.

239. Rowe BH, Camargo CA Jr. The role of magnesium sulfate in the acute and chronic management of asthma. Curr Opin Pulm Med. 2008 Jan;14(1):70-6. Review.

240. Mohammed S, Goodacre S. Intravenous and nebulised magnesium sulphate for acute asthma: systematic review and meta-analysis. Emerg Med J. 2007 Dec;24(12):823-30. Review.

241. Mannix R, Bachur R. Status asthmaticus in children. Curr Opin Pediatr. 2007 Jun;19(3):281-7. Review.

242. Beasley R, Aldington S. Magnesium in the treatment of asthma. Curr Opin Allergy Clin Immunol. 2007 Feb;7(1):107-10. Review.

243. Behbehani N, Fitzgerald JM. The assessment and management of patients with acute asthma *Int J Tuberc Lung Dis*. 2006 Apr;10(4):356-64. Comment in: *Int J Tuberc Lung Dis*. 2006 Oct;10(10):1182-3.

244. Cheuk DK, Chau TC, Lee SL. A meta-analysis on intravenous magnesium sulphate for treating acute asthma. Arch Dis Child. 2005 Jan;90(1):74-7. Review.

245. Blitz M, Blitz S, Beasely R, Diner BM, Hughes R, Knopp JA, Rowe BH. Inhaled magnesium sulfate in the treatment of acute asthma. Cochrane Database Syst Rev. 2005 Jul 20;(3): CD003898. Review.

246. Sellers WF. Intravenous magnesium sulphate and salbutamol for asthma. Anaesthesia. 2004 Feb;59(2):198.

247. Silverman RA, Osborn H, Runge J, Gallagher EJ, Chiang W, Feldman J, Gaeta T, Freeman K, Levin B, Mancherje N, Scharf S; Acute Asthma/Magnesium Study Group. IV magnesium sulfate in the treatment of acute severe asthma: a multicenter randomized controlled trial. Chest 2002 Aug;122(2):489-97. Erratum in: Chest 2002 Nov;122(5):1870. Comment in: Chest. 2002 Aug;122(2):396-8.

248. Singh M. Management of acute asthma. Indian J Pediatr 2001 Sep;68 Suppl 4:S23-30.

249. Rowe BH, Edmonds ML, Spooner CH, Camargo CA. Evidence-based treatments for acute asthma. Respir Care 2001 Dec;46(12):1380-90; discussion 1390-1.

250. Schenk P, Vonbank K, Schnack B, Haber P, Lehr S, Smetana R. Intravenous magnesium sulfate for bronchial hyperreactivity: a randomized, controlled, double-blind study. Clin Pharmacol Ther 2001 May;69(5):365-71.

251. Rowe BH, Edmonds ML, Spooner CH, Camargo CA. Evidence-based treatments for acute asthma. Respir Care 2001 Dec; 46(12): 1380-91

252. Schenk P, Vonbank K, Schnack B, Haber P, Lehr S, Smetana R. Intravenous magnesium sulfate for bronchial hyperreactivity: a randomized, controlled, double-blind study. Clin Pharmacol Ther 2001 May;69(5):365-71.

253. Rowe BH, Bretzlaff JA, Bourdon C, Bota GW, Camargo CA Jr. Magnesium sulfate for treating exacerbations of acute asthma in the emergency department. Cochrane Database Syst Rev 2000;(2):CD001490.

254. Alter HJ, Koepsell TD, Hilty WM. Intravenous magnesium as an adjuvant in acute bronchospasm: a meta-analysis. Ann Emerg Med 2000 Sep;36(3):191-7. Comment in: Ann Emerg Med. 2000 Sep;36(3):234-6.

255. Ciarallo L, Brousseau D, Reinert S. Higher-dose intravenous magnesium therapy for children with moderate to severe acute asthma. Arch Pediatr Adolesc Med 2000 Oct;154(10):979-83.

256. Gurkan F, Haspolat K, Bosnak M, Dikici B, Derman O, Ece A. Intravenous magnesium sulphate in the management of moderate to severe acute asthmatic children non-responding to conventional therapy. Eur J Emerg Med 1999 Sep;6(3):201-5.

257. Swain R, Kaplan-Machlis B. Magnesium for the next millennium. South Med J 1999 Nov;92(11):1040-7.

Magnesium: Cardiovascular

258. Gu WJ, Wu ZJ, Wang PF, Aung LH, Yin RX. Intravenous magnesium prevents atrial fibrillation after coronary artery bypass grafting: a meta-analysis of 7 double-blind, placebo-controlled, randomized clinical trials. Trials. 2012 Apr 20;13:41. doi: 10.1186/1745-6215-13-41.

259. Dabbagh A, Rajaei S, Shamsolahrar MH. The effect of intravenous magnesium sulfate on acute postoperative bleeding in elective coronary artery bypass surgery. J Perianesth Nurs. 2010 Oct;25(5):290-5.

260. Patsilinakos S, Christou A, Kafkas N, Nikolaou N, Antonatos D, Katsanos S, Spanodimos S, Babalis D. Effect of high doses of magnesium on converting ibutilide to a safe and more effective agent. Am J Cardiol. 2010 Sep 1;106(5):673-6. Epub 2010 Jul 23.

261. Shah SA, Clyne CA, Henyan N, Migeed M, Yarlagadda R, Silver BB, Kluger J, White CM. Impact of magnesium sulfate on serum magnesium concentrations and intracellular electrolyte concentrations among patients undergoing radio frequency catheter ablation. Conn Med. 2008 May;72(5):261-5.

262. Ho KM. Intravenous magnesium for cardiac arrhythmias: jack of all trades. Magnes Res. 2008 Mar;21(1):65-8. Review.

263. Shepherd J, Jones J, Frampton GK, Tanajewski L, Turner D, Price A. Intravenous magnesium sulphate and sotalol for prevention of atrial fibrillation after coronary artery bypass surgery: a systematic review and economic evaluation. Health Technol Assess. 2008 Jun;12(28):iii-iv, ix-95. Review.

264. Chung KJ, Wang YC, Liu BM, Supernaw RB. Management of ventricular dysrhythmia secondary to trazodone overdose. J Emerg Med. 2008 Aug;35(2):171-4. Epub 2007 Jul 20.

265. Stiles MK, Sanders P, Disney P, Brooks A, John B, Lau DH, Shashidhar, Wilson L, Mackenzie L, Young GD. Differential effects of intravenous magnesium on atrioventricular node conduction in supraventricular tachycardia. Am J Cardiol. 2007 Oct 15;100(8):1249-53. Epub 2007 Aug 6.

266. Onalan O, Crystal E, Daoulah A, Lau C, Crystal A, Lashevsky I. Meta-analysis of magnesium therapy for the acute management of rapid atrial fibrillation. Am J Cardiol. 2007 Jun 15;99(12):1726-32. Epub 2007 Apr 26.

267. Ho KM, Sheridan DJ, Paterson T. Use of intravenous magnesium to treat acute onset atrial fibrillation: a meta-analysis. Heart. 2007 Nov;93(11):1433-40. Epub 2007 Apr 20. Review.

268. Li J, Zhang Q, Zhang M, Egger M. Intravenous magnesium for acute myocardial infarction. Cochrane Database Syst Rev. 2007 Apr 18;(2):CD002755. Review.

269. Hoshino K, Ogawa K, Hishitani T, Isobe T, Etoh Y. Successful uses of magnesium sulfate for torsades de pointes in children with long QT syndrome Pediatr Int. 2006 Apr;48(2):112-7..

270. Brackbill ML, Moberg L. Magnesium sulfate for prevention of postoperative atrial fibrillation in patients undergoing coronary artery bypass grafting. Am J Health Syst Pharm. 2005 Feb 15;62(4):397-9.

271. Kohno H, Koyanagi T, Kasegawa H, Miyazaki M. Three-day magnesium administration prevents atrial fibrillation after coronary artery bypass grafting. Ann Thorac Surg. 2005 Jan;79(1):117-26. Review.

272. Henyan NN, Gillespie EL, White CM, Kluger J, Coleman CI. Impact of intravenous magnesium on post-cardiothoracic surgery atrial fibrillation and length of hospital stay: a meta-analysis. Ann Thorac Surg. 2005 Dec;80(6):2402-6.

273. Nakashima H, Katayama T, Honda Y, Suzuki S, Yano K. Cardioprotective effects of magnesium sulfate in patients undergoing primary coronary angioplasty for acute myocardial infarction. Circ J. 2004 Jan;68(1):23-8.

274. Coleman CI, Kalus JS, White CM, Spencer AP, Tsikouris JP, Chung JO, Kenyon KW, Ziska M, Kluger J, Reddy P. Cost effectiveness of ibutilide with prophylactic magnesium in the treatment of atrial fibrillation. Pharmacoeconomics. 2004;22(13):877-83.

275. Rukshin V, Santos R, Gheorghiu M, Shah PK, Kar S, Padmanabhan S, Azarbal B, Tsang VT, Makkar R, Samuels B, Lepor N, Geft I, Tabak S, Khorsandhi M, Buchbinder N, Eigler N, Cercek B, Hodgson K, Kaul S. A prospective, nonrandomized, open-labeled pilot study investigating the use of magnesium

in patients undergoing nonacute percutaneous coronary intervention with stent implantation. J Cardiovasc Pharmacol Ther. 2003 Sep;8(3):193-200.

276. Shechter M, Hod H, Rabinowitz B, Boyko V, Chouraqui P. Long-term outcome of intravenous magnesium therapy in thrombolysis-ineligible acute myocardial infarction patients. Cardiology. 2003;99(4):205-10.

277. Smetana R, Stuhlinger HG, Kiss K, Glogar DH. Intravenous magnesium sulphate in acute myocardial infarction--is the answer "MAGIC"? Magnes Res. 2003 Mar;16(1):65-9.

278. Caron MF, Kluger J, Tsikouris JP, Ritvo A, Kalus JS Effects of intravenous magnesium sulfate on the QT interval in patients receiving ibutilide. Pharmacotherapy. 2003 Mar;23(3):296-300.

279. Nel L, Hatherill M, Davies J, Andronikou S, Stirling J, Reynolds L, Argent. Organophosphate poisoning complicated by a tachyarrhythmia and acute respiratory distress syndrome in a child. J Paediatr Child Health 2002 Oct;38(5):530-2.

280. Hoshino K, Ogawa K, Hishitani T, Kitazawa R. Studies of magnesium in congenital long QT syndrome. Pediatr Cardiol 2002 Jan-Feb;23(1):41-8.

281. Ohtsuka S, Oyake Y, Seo Y, Eda K, Yamaguchi I. Magnesium sulphate infusion suppresses the cardiac release of noradrenaline during a handgrip stress test. Can J Cardiol 2002 Feb;18(2):133-40.

282. Chang KH, Uchikoba K, Obara M, Chinzei M, Sumida T, Arita E, Hanaoka K. [Marked reduction of life-threatening ventricular tachyarrhythmias in a critically ill patient by intravenous administration of magnesium sulfate] [Article in Japanese]. Masui 2002 Jan;51(1):56-60.

283. Toraman F, Karabulut EH, Alhan HC, Dagdelen S, Tarcan S. Magnesium infusion dramatically decreases the incidence of atrial fibrillation after coronary artery bypass grafting. Ann Thorac Surg 2001 Oct; 72(4):1256-61; discussion 1261-2.

284. Chiladakis JA, Stathopoulos C, Davlouros P, Manolis AS. Intravenous magnesium sulfate versus diltiazem in paroxysmal atrial fibrillation. Int J Cardiol 2001 Jul;79(2-3):287-91.

285. Christiansen EH, Frost L, Andreasen F, Mortensen P, Thomsen PE, Pedersen AK. Dose-related cardiac electrophysiological effects of intravenous magnesium. A double-blind placebo-controlled dose-response study in patients with paroxysmal supraventricular tachycardia. Europace 2000 Oct; 2(4):320-6.

286. Thiele R, Protze F, Winnefeld K, Pfeifer R, Pleissner J, Gassel M. Effect of intravenous magnesium on ventricular tachyarrhythmias associated with acute myocardial infarction. Magnes Res 2000 Jun;13(2):111-22.

287. GyamLani G, Parikh C, Kulkarni AG. Benefits of magnesium in acute myocardial infarction: timing is crucial. Am Heart J 2000 Apr;139(4):703.

288. Dorman BH, Sade RM, Burnette JS, Wiles HB, Pinosky ML, Reeves ST, Bond BR, Spinale FG. Magnesium supplementation in the prevention of arrhythmias in pediatric patients undergoing surgery for congenital heart defects. Am Heart J 2000 Mar; 139(3): 522-8.

289. Ceremuzynski L, Gebalska J, Wolk R, Makowska E. Hypomagnesemia in heart failure with ventricular arrhythmias. Beneficial effects of magnesium supplementation. J Intern Med 2000 Jan;247(1):78-86.

290. Shechter M. The role of magnesium as antithrombotic therapy. Wien Med Wochenschr 2000;150(15-16):343-7.

291. Ravn HB, Lassen JF, Bergenhem N, Kristensen AT. Intravenous magnesium does not influence the activity of the coagulation cascade. Blood Coagul Fibrinolysis 2001 Jun;12(4):223-8.

292. Raghu C, Peddeswara Rao P, Seshagiri Rao D.Protective effect of intravenous magnesium in acute myocardial infarction following thrombolytic therapy. Int J Cardiol 1999 Dec 1;71(3):209-15. Comment in: Int J Cardiol. 1999 Dec 1;71(3):217-8.

293. O'Brien JM, Rockwood RP, Suh KI. Haloperidol-induced torsade de pointes. Ann Pharmacother 1999 Oct; 33(10): 1046-50.

294. Falck G, Lundgaard H, Jareld T, Skarra S, Arbo I, Gunnes S, Jynge P. Effect of magnesium infusion on bleeding time in healthy male volunteers. Scand J Clin Lab Invest 1999 Oct;59(6):425-30.

295. Kobusiak-Prokopowicz M, Mysiak A. Katedry i Kliniki Kardiologii AM we Wroclawiu. [The effect of intravenous magnesium on the arrhythmias in patients after electrical cardioversion] [Article in Polish]. Pol Merkuriusz Lek 1999 Aug;7(38):51-3.

296. Shibata M, Ueshima K, Harada M, Nakamura M, Hiramori K, Endo S, Sato N, Mukaida H, Suzuki T, Suzuki T, Inada K. Effect of magnesium sulfate pretreatment and significance of matrix metalloproteinase-1 and interleukin-6 levels in coronary reperfusion therapy for patients with acute myocardial infarction. Angiology 1999 Jul;50(7):573-82.

297. Datta S, Nasr NF, Khorasani A, Datta R. Current concepts in cardiopulmonary resuscitation in adults. J Indian Med Assoc 1999 Jul;97(7):259-64, 270.

298. Parikka H, Toivonen L, Verkkala K, Jarvinen A, Nieminen MS. Ventricular Arrhythmia Suppression by Magnesium Treatment after Coronary Artery Bypass Surgery. International Journal of angiology 1999 Jun;8(3):165-170.

299. Ravn HB, Moeldrup U, Brookes CI, Ilkjaer LB, White P, Chew M, Jensen L, Johnsen S, Birk-Soerensen L, Hjortdal VE. Intravenous magnesium reduces infarct size after ischemia/reperfusion injury combined with a thrombogenic lesion in the left anterior descending artery. Arterioscler Thromb Vasc Biol 1999 Mar;19(3):569-74.

300. Parikka HJ, Toivonen LK. Acute effects of intravenous magnesium on ventricular refractoriness and monophasic action potential duration in humans. Scand Cardiovasc J 1999;33(5):300-5.

Magnesium: Cardiac resuscitation

301. de Caen AR, Reis A, Bhutta A. Vascular access and drug therapy in pediatric resuscitation. Pediatr Clin North Am. 2008 Aug;55(4):909-27, x. Review.

302. Shadnia S, Mehrpour O, Abdollahi M. Unintentional poisoning by phosphine released from aluminum phosphide. Hum Exp Toxicol. 2008 Jan;27(1):87-9.

Magnesium: Neurology/Neurosurgery

303. Klair JS(1), Rochlani YM, Meena NK. Myasthenia gravis masquerading as dysphagia: unveiled by magnesium infusion. BMJ Case Rep. 2014 Apr 17;2014. pii: bcr2014204163. doi: 10.1136/bcr-2014-204163.

304. Yousef AA, Al-deeb AE. A double-blinded randomised controlled study of the value of sequential intravenous and oral magnesium therapy in patients with chronic low back pain with a neuropathic component. Anaesthesia. 2013 Mar;68(3):260-6. doi: 10.1111/anae.12107. Epub 2012 Dec 17.

305. Arai YC(1), Hatakeyama N, Nishihara M, Ikeuchi M, Kurisuno M, Ikemoto T. Intravenous lidocaine and magnesium for management of intractable trigeminal neuralgia: a case series of nine patients. J Anesth. 2013 Dec;27(6):960-2. doi: 10.1007/s00540-013-1641-5. Epub 2013 May 28.

306. Pachman DR, Barton DL, Watson JC, Loprinzi CL. Chemotherapy-induced peripheral neuropathy: prevention and treatment. Clin Pharmacol Ther. 2011 Sep;90(3):377-87. doi: 10.1038/clpt.2011.115. Epub 2011 Aug 3. Review.

307. Visser NA, Braun KP, Leijten FS, van Nieuwenhuizen O, Wokke JH, van den Bergh WM. Magnesium treatment for patients with refractory status epilepticus due to POLG1-mutations. J Neurol. 2011 Feb;258(2):218-22.

308. Tuhta GA, Tuhta A, Erdogan M. Gitelman syndrome with mental retardation: a case report. J Nephrol. 2010 Sep-Oct;23(5):617-8.

309. Hwang JY, Na HS, Jeon YT, Ro YJ, Kim CS, Do SH. I.V. infusion of magnesium sulphate during spinal anaesthesia improves postoperative analgesia. Br J Anaesth. 2010 Jan;104(1):89-93.

310. ‘Dorhout Mees SM, Bertens D, van der Worp HB, Rinkel GJ, van den Bergh WM. Magnesium and headache after aneurysmal subarachnoid haemorrhage. J Neurol Neurosurg Psychiatry. 2010 May;81(5):490-3. Epub 2009 Oct 13.

311. Ma L, Liu WG, Zhang JM, Chen G, Fan J, Sheng HS. Magnesium sulphate in the management of patients with aneurysmal subarachnoid haemorrhage: a meta-analysis of prospective controlled trials. Brain Inj. 2010;24(5):730-5.

312. Rinkel GJ. Medical management of patients with aneurysmal subarachnoid haemorrhage. Int J Stroke. 2008 Aug;3(3):193-204. Review.

313. 4: Wolf S, Barton D, Kottschade L, Grothey A, Loprinzi C. Chemotherapy-induced peripheral neuropathy: prevention and treatment strategies. Eur J Cancer. 2008 Jul;44(11):1507-15. Epub 2008 Jun 18. Review.

314. Muroi C, Terzic A, Fortunati M, Yonekawa Y, Keller E. Magnesium sulfate in the management of patients with aneurysmal subarachnoid hemorrhage: a randomized, placebo-controlled, dose-adapted trial. Surg Neurol. 2008 Jan;69(1):33-9; discussion 39.

315. Dorhout Mees SM, Rinkel GJ, Feigin VL, Algra A, van den Bergh WM, Vermeulen M, van Gijn J. Calcium antagonists for aneurysmal subarachnoid haemorrhage. Cochrane Database Syst Rev. 2007 Jul 18;(3):CD000277. Review.

316. Wong GK, Poon WS, Chan MT, Boet R, Gin T, Lam CW. The effect of intravenous magnesium sulfate infusion on serum levels of sodium and potassium in patients with aneurysmal subarachnoid hemorrhage. Magnes Res. 2007 Mar;20(1):37-42.

317. Aslanyan S, Weir CJ, Muir KW, Lees KR; IMAGES Study Investigators. Magnesium for treatment of acute lacunar stroke syndromes: further analysis of the IMAGES trial. Stroke. 2007 Apr;38(4):1269-73. Epub 2007 Mar 8.

318. Natale JE, Guerguerian AM, Joseph JG, McCarter R, Shao C, Slomine B, Christensen J, Johnston MV, Shaffner DH. Pilot study to determine the hemodynamic safety and feasibility of magnesium sulfate infusion in children with severe traumatic brain injury. Pediatr Crit Care Med. 2007 Jan;8(1):1-9.

319. Stippler M, Crago E, Levy EI, Kerr ME, Yonas H, Horowitz MB, Kassam A. Magnesium infusion for vasospasm prophylaxis after subarachnoid hemorrhage. J Neurosurg. 2006 Nov;105(5):723-9. Lancet. 2006 Oct 21;368(9545):1436-43.

320. Wong GK, Chan MT, Boet R, Poon WS, Gin T. Intravenous magnesium sulfate after aneurysmal subarachnoid hemorrhage: a prospective randomized pilot study Neurosurg Anesthesiol. 2006 Apr;18(2):142-8.

321. Wong GK, Chan MT, Poon WS, Boet R, Gin T. Magnesium therapy within 48 hours of an aneurysmal subarachnoid hemorrhage: neuro-panacea Neurol Res. 2006 Jun;28(4):431-5.

322. Schmid-Elsaesser R, Kunz M, Zausinger S, Prueckner S, Briegel J, Steiger HJ. Intravenous magnesium versus nimodipine in the treatment of patients with aneurysmal subarachnoid hemorrhage: a randomized study. Neurosurgery. 2006 Jun;58(6):1054-65; discussion 1054-65.

323. Turan A, Memis D, Karamanlioglu B, Guler T, Pamukcu Z. Intravenous regional anesthesia using idocaine and magnesium. Anesth Analg. 2005 Apr;100(4):1189-92.

324. van Norden AG, van den Bergh WM, Rinkel GJ. Dose evaluation for long-term magnesium treatment in aneurysmal subarachnoid haemorrhage. J Clin Pharm Ther. 2005 Oct;30(5):439-42.

325. Saver JL, Kidwell C, Eckstein M, Starkman S; FAST-MAG Pilot Trial Investigators. Prehospital neuroprotective therapy for acute stroke: results of the Field Administration of Stroke Therapy-Magnesium (FAST-MAG) pilot trial. Stroke. 2004 May;35(5):e106-8. Epub 2004 Mar 11.

326. Muir KW, Lees KR, Ford I, Davis S. Magnesium for acute stroke (Intravenous Magnesium Efficacy in Stroke trial): randomised controlled trial. Lancet. 2004 Feb 7;363(9407):439-45. Comment in: Lancet. 2004 Feb 7;363(9407):414-5.

327. Enya M, Kanoh Y, Mune T, Ishizawa M, Sarui H, Yamamoto M, Takeda N, Yasuda K, Yasujima M, Tsutaya S, Takeda J. Depressive state and paresthesia dramatically improved by intravenous MgSO4 in Gitelman's syndrome. Intern Med. 2004 May;43(5):410-4. Comment in: Intern Med. 2004 May;43(5):351-2.

328. Barile M, van De Wyngaert F, Mbia JJ, Jativa M, Grandin C, Rooijakkers H, Hantson P. Intravenous magnesium sulfate administration in a patient with refractory vasospasm following subarachnoid hemorrhage. Intensive Care Med. 2003 Jul;29(7):1182-5. Epub 2003 Apr 16.

329. van den Bergh WM, Albrecht KW, Berkelbach van der Sprenkel JW, Rinkel GJ. Magnesium therapy after aneurysmal subarachnoid haemorrhage a dose-finding study for long term treatment. Acta Neurochir (Wien). 2003 Mar;145(3):195-9; discussion 199.

330. Brill S, Sedgwick PM, Hamann W, Di Vadi PP. Efficacy of intravenous magnesium in neuropathic pain. Br J Anaesth 2002 Nov;89(5):711-4.

331. Gordin A, Goldenberg D, Golz A, Netzer A, Joachims HZ. Magnesium: a new therapy for idiopathic sudden sensorineural hearing loss. Otol Neurotol 2002 Jul;23(4):447-51.

332. Chia RY, Hughes RS, Morgan MK. Magnesium: a useful adjunct in the prevention of cerebral vasospasm following aneurysmal subarachnoid haemorrhage. J Clin Neurosci 2002 May;9(3):279-81.

333. Sahin N, Ulusan V, Aydogdu T. Magnesium infusion reduces perioperative pain. Kara H, Eur J Anaesthesiol 2002 Jan;19(1):52-6.

334. Demirkaya S, Vural O, Dora B, Topcuoglu MA. Efficacy of intravenous magnesium sulfate in the treatment of acute migraine attacks. Headache 2001 Feb;41(2):171-7.

335. Ko SH, Lim HR, Kim DC, Han YJ, Choe H, Song HS. Magnesium sulfate does not reduce postoperative analgesic requirements. Anesthesiology 2001 Sep; 95(3):640-6.

336. Corbo J, Esses D, Bijur PE, Iannaccone R, Gallagher EJ. Randomized clinical trial of intravenous magnesium sulfate as an adjunctive medication for emergency department treatment of migraine headache. Ann Emerg Med 2001 Dec;38(6):621-7.

337. Heath DL, Vink R. Subdural hematoma following traumatic brain injury causes a secondary decline in brain free magnesium concentration. J Neurotrauma 2001 Apr;18(4):465-9.

338. Demirkaya S, Vural O, Dora B, Topcuoglu MA. Efficacy of intravenous magnesium sulfate in the treatment of acute migraine attacks. Headache 2001 Feb;41(2):171-7.

339. Lampl Y, Gilad R, Geva D, Eshel Y, Sadeh M. Intravenous administration of magnesium sulfate in acute stroke: a randomized double-blind study. Clin Neuropharmacol 2001 Jan-Feb;24(1):11-5.

340. Ginder S, Oatman B, Pollack M. A prospective study of i.v. magnesium and i.v. prochlorperazine in the treatment of headaches. J Emerg Med 2000 Apr;18(3):311-5.

341. Crosby V, Wilcock A, Corcoran R. The safety and efficacy of a single dose (500 mg or 1 g) of intravenous magnesium sulfate in neuropathic pain poorly responsive to strong opioid analgesics in patients with cancer. J Pain Symptom Manage 2000 Jan; 19 (1):35-9.

342. Heiden A, Frey R, Presslich O, Blasbichler T, Smetana R, Kasper S. Treatment of severe mania with intravenous magnesium sulphate as a supplementary therapy. Psychiatry Res 1999 Dec 27;89(3):239-46.

343. Sanders GM, Sim KM. Is it feasible to use magnesium sulphate as a hypotensive agent in oral and maxillofacial surgery? Ann Acad Med Singapore 1998 Nov;27(6):780-5.

Magnesium: Obstetrics

344. Duley L, Henderson-Smart DJ, Chou D. Magnesium sulphate versus phenytoin for eclampsia. Cochrane Database Syst Rev. 2010 Oct 6;(10):CD000128.

345. Duley L, Gülmezoglu AM, Chou D. Magnesium sulphate versus lytic cocktail for eclampsia. Cochrane Database Syst Rev. 2010 Sep 8;(9):CD002960.

346. Omu AE, Al-Harmi J, Vedi HL, Mlechkova L, Sayed AF, Al-Ragum NS. Magnesium sulphate therapy in women with pre-eclampsia and eclampsia in Kuwait. Med Princ Pract. 2008;17(3):227-32. Epub 2008 Apr 10.

347. Lyell DJ, Pullen K, Campbell L, Ching S, Druzin ML, Chitkara U, Burrs D, Caughey AB, El-Sayed YY. Magnesium sulfate compared with nifedipine for acute tocolysis of preterm labor: a randomized controlled trial. Obstet Gynecol. 2007 Jul;110(1):61-7.

348. Marret S, Marpeau L, Zupan-Simunek V, Eurin D, Lévêque C, Hellot MF, Bénichou J; PREMAG trial group. Magnesium sulphate given before very-preterm birth to protect infant brain: the randomised controlled PREMAG trial*. BJOG. 2007 Mar;114(3):310-8. Epub 2006 Dec 4.

349. Schauf B, Becker S, Abele H, Klever T, Wallwiener D, Aydeniz B. Effect of magnesium on red blood cell deformability in pregnancy. Hypertens Pregnancy. 2005;24(1):17-27.

350. Zygmunt M, Heilmann L, Berg C, Wallwiener D, Grischke E, Munstedt K, Spindler A, Lang U. Local and systemic tolerability of magnesium sulphate for tocolysis. Eur J Obstet Gynecol Reprod Biol. 2003 Apr 25;107(2):168-75.

351. Amon E, Midkiff C, Winn H, Holcomb W, Shumway J, Artal R. Tocolysis with advanced cervical dilatation. Obstet Gynecol 2000 Mar;95(3):358-62.

352. Yamaguchi K, Fukuuchi Y, Nogawa S, Dembo T, Tomita Y, Tanaka K. Recovery of decreased local cerebral blood flow detected by the xenon/CT CBF method in a patient with eclampsia. Keio J Med 2000 Feb;49 Suppl 1:A71-4.

353. Duley L, Henderson-Smart D. Magnesium sulphate versus phenytoin for eclampsia. Cochrane Database Syst Rev 2000;(2):CD000128.

354. Duley L, Henderson-Smart D. Magnesium sulphate versus diazepam for eclampsia. Cochrane Database Syst Rev 2000;(2):CD000127.

355. Vigil-De Gracia P, Simiti E, Lora Y. Intrapartum fetal distress and magnesium sulfate. Int J Gynaecol Obstet 2000 Jan;68(1):3-6.

356. El-Sayed YY, Riley ET, Holbrook RH Jr, Cohen SE, Chitkara U, Druzin ML. Randomized comparison of intravenous nitroglycerin and magnesium sulfate for treatment of preterm labor. Obstet Gynecol 1999 Jan;93(1):79-83.

Magnesium: Pulmonary, other than asthma

357. Ozcan PE, Tugrul S, Senturk NM, Uludag E, Cakar N, Telci L, Esen F. Role of magnesium sulfate in postoperative pain management for patients undergoing thoracotomy. J Cardiothorac Vasc Anesth. 2007 Dec;21(6):827-31. Epub 2007 Feb 7.

358. Raimondi F, Migliaro F, Capasso L, Ausanio G, Bisceglia M, Giliberti P, cocaine call Wayne Messina F, Salvia G, Paludetto R. Intravenous magnesium sulphate vs. inhaled nitric oxide for moderate, persistent pulmonary hypertension of the newborn. A Multicentre, retrospective study. J Trop Pediatr. 2008 Jun;54(3):196-9. Epub 2007 Nov 29.

Magnesium, general

359. Bonny O, Rubin A, Huang CL, Frawley WH, Pak CY, Moe OW. Mechanism of urinary calcium regulation by urinary magnesium and pH. J Am Soc Nephrol. 2008 Aug;19(8):1530-7. Epub 2008 Apr 30.

360. Thwaites CL, Yen LM, Loan HT, Thuy TT, Thwaites GE, Stepniewska K, Soni N, White NJ, Farrar JJ. Magnesium sulphate for treatment of severe tetanus: a randomised controlled trial. Comment in: Lancet. 2006 Oct 21; 368(9545):1398-9.

361. Gathwala G, Khera A, Singh I. Magnesium therapy in birth asphyxia. Indian J Pediatr. 2006 Mar;73(3):209-12.

362. Guler A, Satilmis T, Akinci SB, Celebioglu B, Kanbak M. Magnesium sulfate pretreatment reduces myoclonus after etomidate. Anesth Analg. 2005 Sep;101(3):705-9, table of contents.

363. Canavese C, Petrarulo M, Massarenti P, Berutti S, Fenoglio R, Pauletto D,Lanfranco G, Bergamo D, Sandri L, Marangella M. Long-term, low-dose, intravenous vitamin C leads to plasma calcium oxalate supersaturation in hemodialysis patients. Am J Kidney Dis. 2005 Mar;45(3):540-9.

364. Brousseau DC, Scott JP, Hillery CA, Panepinto JA. The effect of magnesium on length of stay for pediatric sickle cell pain crisis. Acad Emerg Med. 2004 Sep;11(9):968-72.

365. Bhatia A, Kashyap L, Pawar DK, Trikha A. Effect of intraoperative magnesium infusion on perioperative analgesia in open cholecystectomy. J Clin Anesth. 2004 Jun;16(4):262-5.

366. Dumont L, Lysakowski C, Tramer MR, Junod JD, Mardirosoff C, Tassonyi E, Kayser B. Magnesium for the prevention and treatment of acute mountain sickness. Clin Sci (Lond). 2004 Mar;106(3):269-77.

367. Gulhas N, Durmus M, Demirbilek S, Togal T, Ozturk E, Ersoy MO. The use of magnesium to prevent laryngospasm after tonsillectomy and adenoidectomy: a preliminary study. Paediatr Anaesth. 2003 Jan;13(1):43-7.

368. Gourgoulianis KI, Chatziparasidis G, Chatziefthimiou A, Molyvdas PA. Magnesium as a relaxing factor of airway smooth muscles. J Aerosol Med 2001 Fall; 14(3):301-7.

369. Papazachariou IM, Martinez-Isla A, Efthimiou E, Williamson RC, Girgis SI. Magnesium deficiency in patients with chronic pancreatitis identified by an intravenous loading test. Clin Chim Acta 2000 Dec;302(1-2):145-54.

370. Saris NE, Mervaala E, Karppanen H, Khawaja JA, Lewenstam A. Magnesium: An update on physiological, clinical and analytical aspects. Clin Chim Acta 2000 Apr;294(1-2):1-26.

371. Po SS, Wang DW, Yang IC, Johnson JP Jr, Nie L, Bennett PB. Modulation of HERG potassium channels by extracellular magnesium and quinidine. Cardiovasc Pharmacol 1999 Feb;33(2):181-5.

Molybdenum

372. Novotny JA, Turnlund JR. Molybdenum intake influences molybdenum kinetics in men. J Nutr. 2007 Jan;137(1):37-42.

373. Werner E, Roth P, Heinrichs U, Giussani A, Cantone MC, Zilker TH, Felgenhauer N, Greim H. Internal biokinetic behaviour of molybdenum in humans studied with stable isotopes as tracers. Isotopes Environ Health Stud 2000;36(2):123-32.

374. Friel JK, MacDonald AC, Mercer CN, Belkhode SL, Downton G, Kwa PG, Aziz K, Andrews WL. Molybdenum requirements in low-birth-weight infants receiving parenteral and enteral nutrition. JPEN J Parenter Enteral Nutr 1999 May-Jun;23(3):155-9.

N-acetyl cysteine

375. Grabhorn E(1), Nielsen D, Hillebrand G, Brinkert F, Herden U, Fischer L, Ganschow R. Successful outcome of severe Amanita phalloides poisoning in children. Pediatr Transplant. 2013 Sep;17(6):550-5. doi: 10.1111/petr.12108. Epub 2013 May 31.

376. Lim G, Lee JH. N-acetylcysteine in children with dengue-associated liver failure: a case report. J Trop Pediatr. 2012 Oct;58(5):409-13. doi: 10.1093/tropej/fmr108. Epub 2011 Dec 23.

377. Tehrani H, Halvaie Z, Shadnia S, Soltaninejad K, Abdollahi M. Protective effects of N-acetylcysteine on aluminum phosphide-induced oxidative stress in acute human poisoning. Clin Toxicol (Phila). 2013 Jan;51(1):23-8. doi: 10.3109/15563650.2012.743029. Epub 2012 Nov

378. Shen F, Coulter CV, Isbister GK, Duffull SB. A dosing regimen for immediate N-acetylcysteine treatment for acute paracetamol overdose. Clin Toxicol (Phila). 2011 Aug;49(7):643-7.

379. Johnson MT, McCammon CA, Mullins ME, Halcomb SE. Evaluation of a simplified N-acetylcysteine dosing regimen for the treatment of acetaminophen toxicity. Ann Pharmacother. 2011 Jun;45(6):713-20.

380. Mehrpour O, Shadnia S, Sanaei-Zadeh H. Late extensive intravenous administration of N-acetylcysteine can reverse hepatic failure in acetaminophen overdose. Hum Exp Toxicol. 2011 Jan;30(1):51-4.

381. Jegatheeswaran S, Siriwardena AK. Experimental and clinical evidence for modification of hepatic ischaemia-reperfusion injury by N-acetylcysteine during major liver surgery. HPB (Oxford). 2011 Feb;13(2):71-8. doi:

382. Anderson SM, Park ZH, Patel RV. Intravenous N-acetylcysteine in the prevention of contrast media-induced nephropathy. Ann Pharmacother. 2011 Jan;45(1):101-7. Epub 2011 Jan 4. Review.

383. Kim JC, Hong SW, Shim JK, Yoo KJ, Chun DH, Kwak YL. Effect of N-acetylcysteine on pulmonary function in patients undergoing off-pump coronary artery bypass surgery. Acta Anaesthesiol Scand. 2011 Apr;55(4):452-9. doi: 10.1111/j.1399-6576.2011.02407.x

384. Swarnalatha G, Ram R, Neela P, Naidu MU, Dakshina Murty KV. Oxidative stress in hemodialysis patients receiving intravenous iron therapy and the role of N-acetylcysteine in preventing oxidative stress. Saudi J Kidney Dis Transpl. 2010 Sep;21(5):852-8.

385. Galbes O, Bourret A, Nouette-Gaulain K, Pillard F, Matecki S, Py G, Mercier J, Capdevila X, Philips A. N-acetylcysteine protects against bupivacaine-induced myotoxicity caused by oxidative and sarcoplasmic reticulum stress in human skeletal myotubes. Anesthesiology. 2010 Sep;113(3):560-9.

386. Dell'Aglio DM, Sutter ME, Schwartz MD, Koch DD, Algren DA, Morgan BW. Acute chloroform ingestion successfully treated with intravenously administered N-acetylcysteine. J Med Toxicol. 2010 Jun;6(2):143-6.

387. Zyoud SH, Awang R, Syed Sulaiman SA, Sweileh WM, Al-Jabi SW. Incidence of adverse drug reactions induced by N-acetylcysteine in patients with acetaminophen overdose. Hum Exp Toxicol. 2010 Mar;29(3):153-60. Epub 2010 Jan 13.

388. Saviuc P, Danel V. (Acute acetaminophen overdose] Rev Prat. 2008 Apr 30;58(8):861-5. French.

389. Smith SW, Howland MA, Hoffman RS, Nelson LS. Acetaminophen overdose with altered acetaminophen pharmacokinetics and hepatotoxicity associated with premature cessation of intravenous N-acetylcysteine therapy. Ann Pharmacother. 2008 Sep;42(9):1333-9. Epub 2008 Jul 15.

390. Crowell C, Lyew RV, Givens M, Deering SH. Caring for the mother, concentrating on the fetus: intravenous N-acetylcysteine in pregnancy. Am J Emerg Med. 2008 Jul;26(6):735.e1-2.

391. Wang JH, Subeq YM, Tsai WC, Lee RP, Hsu BG. Intravenous N-cetylcysteine with saline hydration improves renal function and ameliorates plasma total homocysteine in patients undergoing cardiac angiography. Ren Fail. 2008;30(5):527-33.

392. Barr LF, Kolodner K. N-acetylcysteine and fenoldopam protect the renal function of patients with chronic renal insufficiency undergoing cardiac surgery. Crit Care Med. 2008 May;36(5):1427-35.

393. Thaha M, Widodo, Pranawa W, Yogiantoro M, Tomino Y. Intravenous N-acetylcysteine during hemodialysis reduces asymmetric dimethylarginine level in end-stage renal disease patients. Clin Nephrol. 2008 Jan;69(1):24-32.

394. Kortsalioudaki C, Taylor RM, Cheeseman P, Bansal S, Mieli-Vergani G, Dhawan A. Safety and efficacy of N-acetylcysteine in children with non-acetaminophen-induced acute liver failure. Liver Transpl. 2008 Jan;14(1):25-30.

395. Crowell C, Lyew RV, Givens M, Deering SH. Caring for the mother, concentrating on the fetus: intravenous N-acetylcysteine in pregnancy. Am J Emerg Med. 2008 Jul;26(6):735.e1-2.

396. Wang JH, Subeq YM, Tsai WC, Lee RP, Hsu BG. Intravenous N-cetylcysteine with saline hydration improves renal function and ameliorates plasma total homocysteine in patients undergoing cardiac angiography. Ren Fail. 2008;30(5):527-33.

397. Barr LF, Kolodner K. N-acetylcysteine and fenoldopam protect the renal function of patients with chronic renal insufficiency undergoing cardiac surgery. Crit Care Med. 2008 May;36(5):1427-35.

398. Poletti PA, Saudan P, Platon A, Mermillod B, Sautter AM, Vermeulen B, Sarasin FP, Becker CD, Martin PY.AJR Am J Roentgenol. IV N- acetylcysteine and emergency CT: use of serum creatinine and cystatin C as markers of radiocontrast nephrotoxicity.2007 Sep;189(3):687-92. Comment in:AJR Am J Roentgenol. 2008 Mar;190(3):W224; author reply W225.

399. FP, Becker CD, Martin PY. I.v. N-acetylcysteine and emergency CT: use of serum creatinine and cystatin C as markers of radiocontrast nephrotoxicity. AJR Am J Roentgenol. 2007 Sep;189(3):687-92.

400. Lawlor DK, Moist L, DeRose G, Harris KA, Lovell MB, Kribs SW, Elliot J, Forbes TL. Prevention of contrast-induced nephropathy in vascular surgery patients. Ann Vasc Surg. 2007 Sep;21(5):593-7.

401. Schaller G, Pleiner J, Mittermayer F, Posch M, Kapiotis S, Wolzt M. Effects of N-acetylcysteine against systemic and renal hemodynamic effects of endotoxin in healthy humans. Crit Care Med. 2007 Aug;35(8):1869-75.

402. Godber IM, Jarvis SJ, Maguire D. Hypokalaemia following paracetamol overdose in two teenage girls. Ann Clin Biochem. 2007 Jul;44(Pt 4):403-5.

403. Recio-Mayoral A, Chaparro M, Prado B, Cózar R, Méndez I, Banerjee D, Kaski JC, Cubero J, Cruz JM. The reno-protective effect of hydration with sodium bicarbonate plus N-acetylcysteine in patients undergoing emergency percutaneous coronary intervention: the RENO Study. J Am Coll Cardiol. 2007 Mar 27;49(12):1283-8. Epub 2007 Mar 12.

404. Briguori C, Airoldi F, D'Andrea D, Bonizzoni E, Morici N, Focaccio A, Michev I, Montorfano M, Carlino M, Cosgrave J, Ricciardelli B, Colombo A. Renal Insufficiency Following Contrast Media Administration Trial (REMEDIAL): a randomized comparison of 3 preventive strategies. Circulation. 2007 Mar 13;115(10):1211-7. Epub 2007 Feb 19. Comment in: Circulation. 2007 Aug 21;116(8):e310; author reply e311. Nat Clin Pract Cardiovasc Med. 2007 Sep;4(9):474-5.

405. I, Montorfano M, Carlino M, Cosgrave J, Ricciardelli B, Colombo A. Renal Insufficiency Following Contrast Media Administration Trial (REMEDIAL): a randomized comparison of 3 preventive strategies. Circulation. 2007 Mar 13;115(10):1211-7. Epub 2007 Feb 19.

406. White ML, Liebelt EL. Update on antidotes for pediatric poisoning. Pediatr Emerg Care. 2006 Nov;22(11):740-6; quiz 747-9. Review.

407. Schultz MJ, Baas MC, van der Sluijs HP, Stamkot GA, Smit W. N-acetylcysteine and other preventive measures for contrast-induced nephropathy in the intensive care unit. Curr Med Chem. 2006;13(21):2565-70. Review.

408. Kanter MZ. Comparison of oral and i.v. acetylcysteine in the treatment of acetaminophen poisoning. Am J Health Syst Pharm. 2006 Oct 1;63(19):1821-7. Review.

409. Calello DP, Osterhoudt KC, Henretig FM. New and novel antidotes in pediatrics. Pediatr Emerg Care. 2006 Jul;22(7):523-30. Review.

410. Moling O, Cairon E, Rimenti G, Rizza F, Pristera R, Mian P. Severe hepatotoxicity after therapeutic doses of acetaminophen.Clin Ther. 2006 May;28(5):755-60.

411. Marenzi G, Assanelli E, Marana I, Lauri G, Campodonico J, Grazi M, De Metrio M, Galli S, Fabbiocchi F, Montorsi P, Veglia F, Bartorelli AL. N-acetylcysteine and contrast-induced nephropathy in primary angioplasty. N Engl J Med. 2006 Jun 29;354(26):2773-82.

412. Leow, Melvin [corrected to Leow, Melvin Khee-Shing]. Sule AA, Tai DY, Tze CC, Deepa B, Leow MK. Potentially fatal paracetamol overdose and successful treatment with 3 days of intravenous N-acetylcysteine regime--a case report. Ann Acad Med Singapore. 2006 Feb;35(2):108-11. Erratum in: Ann Acad Med Singapore. 2006 Jun;35(6):446.

413. Desai A, Kadleck D, Hufford L, Leikin JB. N-acetylcysteine use in ischemic hepatitis. Am J Ther. 2006 Jan-Feb;13(1):80-3.

414. Bass S, Zook N. Intravenous acetylcysteine for indications other than acetaminophen overdose. Am J Health Syst Pharm. 2013 Sep 1;70(17):1496-501. doi: 10.2146/ajhp120645.

Sodium bicarbonate

415. Glisson JK, Vesa TS, Bowling MR. Current management of salicylate-induced pulmonary edema. South Med J. 2011 Mar;104(3):225-32. Review.

416. Ueda H, Yamada T, Masuda M, Okuyama Y, Morita T, Furukawa Y, Koji T, Iwasaki Y, Okada T, Kawasaki M, Kuramoto Y, Naito T, Fujimoto T, Komuro I, Fukunami M.Prevention of contrast-induced nephropathy by bolus injection of sodium bicarbonate in patients with chronic kidney disease undergoing emergent coronary procedures. Am J Cardiol. 2011 Apr 15;107(8):1163-7.

417. Park JS, Kim H, Lee SW, Min JH. Successful treatment of methemoglobinemia and acute renal failure after indoxacarb poisoning. Clin Toxicol (Phila). 2011 Oct;49(8):744-6.

418. Hoang BX, Tran DM, Tran HQ, Nguyen PT, Pham TD, Dang HV, Ha TV, Tran HD, Hoang C, Luong KN, Shaw DG. Dimethyl sulfoxide and sodium bicarbonate in the treatment of refractory cancer pain. J Pain Palliat Care Pharmacother. 2011;25(1):19-24.

419. Yeung A, Shanks D, Parwana H, Gin K. Acute propafenone toxicity after two exposures at standard dosing. Can J Cardiol. 2010 Jun;26(6):209-10.

420. Hoste EA, De Waele JJ, Gevaert SA, Uchino S, Kellum JA. Sodium bicarbonate for prevention of contrast-induced acute kidney injury: a systematic review and meta-analysis. Nephrol Dial Transplant. 2010 Mar;25(3):747-58. Epub 2009 Aug 23. Comment in: Nephrol Dial Transplant. 2010 Mar;25(3):650-4.

421. Chan HY, Chan YC, Lau FL. Reversal of Brugada electrocardiographic pattern with sodium bicarbonate solution after amitriptyline overdose. Clin Toxicol (Phila). 2008 Nov;46(9):892-6.

422. Hong YC, O'Boyle CP, Chen IC, Hsiao CT, Kuan JT. Metformin-associated lactic acidosis in a pregnant patient. Gynecol Obstet Invest. 2008;66(2):138-41. Epub 2008 May 16.

423. Kent K, Ganetsky M, Cohen J, Bird S. Non-fatal ventricular dysrhythmias associated with severe salicylate toxicity. Clin Toxicol (Phila). 2008 Apr;46(4):297-9.

424. Patel NP, Pugh ME, Goldberg S, Eiger G. Hyperinsulinemic euglycemia therapy for verapamil poisoning: case report. Am J Crit Care. 2007 Sep;16(5):520, 518-9.

425. Wetzels JF. Letter by Wetzels regarding article, "Renal Insufficiency Following Contrast Media Administration Trial (REMEDIAL): a randomized comparison of 3 preventive strategies". Circulation. 2007 Aug 21;116(8):e310; author reply e311. No abstract available.

426. Woolf AD, Erdman AR, Nelson LS, Caravati EM, Cobaugh DJ, Booze LL, Wax PM, Manoguerra AS, Scharman EJ, Olson KR, Chyka PA, Christianson G, Troutman WG. Tricyclic antidepressant poisoning: an evidence-based consensus guideline for out-of-hospital management. Clin Toxicol (Phila). 2007;45(3):203-33.

427. Recio-Mayoral A, Chaparro M, Prado B, Cózar R, Méndez I, Banerjee D, Kaski JC, Cubero J, Cruz JM. The reno-protective effect of hydration with sodium bicarbonate plus N-acetylcysteine in patients undergoing emergency percutaneous coronary intervention: the RENO Study. J Am Coll Cardiol. 2007 Mar 27;49(12):1283-8. Epub 2007 Mar 12.

428. Schultz MJ, Baas MC, van der Sluijs HP, Stamkot GA, Smit W. N-acetylcysteine and other preventive measures for contrast-induced nephropathy in the intensive care unit. Curr Med Chem. 2006;13(21):2565-70. Review.

429. Ganesh R, Suresh N, Ramesh J. Diabetic ketoacidosis in children.Natl Med J India. 2006 May-Jun;19(3):155-8. Review.

430. Rojas Vega S, Struder HK, Wahrmann BV, Bloch W, Hollmann W. Bicarbonate reduces serum prolactin increase induced by exercise to exhaustion. Med Sci Sports Exerc. 2006 Apr;38(4):675-80.

431. Mueller C. . Prevention of contrast-induced nephropathy with volume supplementation. .Kidney Int Suppl. 2006 Apr;(100):S16-9. Review

432. DePalo VA, Mailer K, Yoburn D, Crausman RS. Lactic acidosis. Lactic acidosis associated with metformin use in treatment of type 2 diabetes mellitus. Geriatrics. 2005 Nov;60(11):36, 39-41.

433. Brucculeri M, Kaplan J, Lande L. Reversal of citalopram-induced junctional bradycardia with intravenous sodium bicarbonate. Pharmacotherapy. 2005 Jan;25(1):119-22.

434. Buysse CM, de Jongste JC, de Hoog M. Life-threatening asthma in children: treatment with sodium bicarbonate reduces PCO2. Chest. 2005 Mar;127(3):866-70.

435. Agarwal P, Agrawal PK, Sharma D, Baghel KD. Intravenous infusion for the treatment of diabetic and ischaemic non-healing pedal ulcers. J Eur Acad Dermatol Venereol. 2005 Mar;19(2):158-62.

436. Donmez O, Cetinkaya M, Canbek R. Hemoperfusion in a child with amitriptyline intoxication.Pediatr Nephrol. 2005 Jan;20(1):105-7. Epub 2004 Oct 26.

437. Shadnia S, Moiensadat M, Abdollahi M. A case of acute strychnine poisoning. Vet Hum Toxicol. 2004 Apr;46(2):76-9.

438. Odegard KC, Schure A, Saiki Y, Hansen DD, Jonas RA, Laussen PC. Anesthetic considerations during caval inflow occlusion in children with congenital heart disease. J Cardiothorac Vasc Anesth. 2004 Apr;18(2):144-7.

439. Yanagawa Y, Kiyozumi T, Hatanaka K, Itoh T, Sakamoto T, Okada Y. Reversible blindness associated with alcoholic ketoacidosis. Am J Ophthalmol. 2004 Apr;137(4):775-7.

440. Sarin B, Chugh PK, Kaushal D, Soni NL, Sawroop K, Mondal A, Bhatnagar A. Sodium bicarbonate-augmented stress thallium myocardial scintigraphy. Eur J Nucl Med Mol Imaging. 2004 Apr;31(4):475-81. Epub 2003 Dec 12.

441. Sharma AN, Hexdall AH, Chang EK, Nelson LS, Hoffman RS. Diphenhydramine-induced wide complex dysrhythmia responds to treatment with sodium bicarbonate. Am J Emerg Med. 2003 May;21(3):212-5.

Phosphatidyl Choline

442. Rey JW, Schreiner O, Barreiros AP, Heise M, Krupp M, Schuchmann M, Otto G, Galle PR, Teufel A. Acute renal failure and liver dysfunction after subcutaneous injection of 3-sn-phosphatidylcholine (Lipostabil®)-case report. Z Gastroenterol. 2011 Mar;49(3):340-3. Epub 2011 Mar 9.

443. Keil C, Zeisig R, Fichtner I. Effect of surface modified liposomes on the aggregation of platelets and tumor cells. Thromb Haemost. 2005 Aug; 94 (2):404-11.
444. Pownall HJ, Ehnholm C. Enhancing reverse cholesterol transport: the case for phosphatidylcholine therapy. Curr Opin Lipidol. 2005 Jun; 16 (3):265-8.
445. Grynderup V, Mikkelsen B. [Treatment of multiple sclerosis with phosphatidyl choline Lipostabil] Ugeskr Laeger. 1968 Apr 4;130(14):594-6. Danish.

Thiamine

446. Juel J(1), Pareek M, Langfrits CS, Jensen SE. Anaphylactic shock and cardiac arrest caused by thiamine infusion. BMJ Case Rep. 2013 Jul 12;2013. pii: bcr2013009648. doi: 10.1136/bcr-2013-009648.
447. Sasaki T, Yukizane T, Atsuta H, Ishikawa H, Yoshiike T, Takeuchi T, Oshima K, Yamamoto N, Kurumaji A, Nishikawa T. [A case of thiamine deficiency with psychotic symptoms--blood concentration of thiamine and response to therapy]. Seishin Shinkeigaku Zasshi. 2010;112(2):97-110.
448. Liu YL, Tsai SH, Chang FW, Yu MH. Ifosfamide-induced encephalopathy in patients with uterine sarcoma. Taiwan J Obstet Gynecol. 2010 Mar;49(1):77-80.
449. Moonen M, Lancellotti P, Betz R, Lambermont B, Piérard L. [Beriberi] Rev Med Liege. 2007 Jul-Aug;62(7-8):523-30. French.
450. Ueda K, Takada D, Mii A, Tsuzuku Y, Saito SK, Kaneko T, Utsumi K, Iino Y, Katayama Y. Severe thiamine deficiency resulted in Wernicke's encephalopathy in a chronic dialysis patient. Clin Exp Nephrol. 2006 Dec;10(4):290-3. Epub 2006 Dec 20.
451. Wilson RK, Kuncl RW, Corse AM. Wernicke's encephalopathy: beyond alcoholism. Nat Clin Pract Neurol. 2006 Jan;2(1):54-8; quiz 58. Harrison RA, Vu T, Hunter AJ. Wernicke's encephalopathy in a patient with schizophrenia J Gen Intern Med. 2006 Dec;21(12):C8-C11. Epub 2006 Aug 22.
452. Harrison RA, Vu T, Hunter AJ. Wernicke's encephalopathy in a patient with schizophrenia J Gen Intern Med. 2006 Dec;21(12):C8-C11. Epub 2006 Aug 22.
453. Chotmongkol V, Limpawattana P. Wernicke's encephalopathy: report of a case. J Med Assoc Thai. 2005 Jun;88(6):855-8.
454. Cho YP, Kim K, Han MS, Jang HJ, Kim JS, Kim YH, Lee SG. Severe lactic acidosis and thiamine deficiency during total parenteral nutrition--case report. Hepatogastroenterology. 2004 Jan-Feb;51(55):253-5.
455. Diltoer MW, Troubleyn J, Lauwers R, De Wijngaard S, Vercammen MJ, Hubloue I, Huyghens LP. Ketosis and cardiac failure: common signs of a single condition. Eur J Emerg Med. 2004 Jun;11(3):172-5
456. Ishimaru T, Yata T, Hatanaka-Ikeno S. Hemodynamic response of the frontal cortex elicited by intravenous thiamine propyldisulphide administration. Chem Senses. 2004 Mar;29(3):247-51.

General IV Vitamin references (1980-present):

457. Kirkemo AK, Burt ME, Brennan MF. Serum vitamin level maintenance in cancer patients on total parenteral nutrition. Am J Clin Nutr 1982 May;35(5):1003-9.
458. Inculet RI, Norton JA, Nichoalds GE, Maher MM, White DE, Brennan MF. Water-soluble vitamins in cancer patients on parenteral nutrition: a prospective study. JPEN J Parenter Enteral Nutr 1987 May-Jun;11(3):243-9.
459. Silvers KM, Sluis KB, Darlow BA, McGill F, Stocker R, Winterbourn CC. Limiting light-induced lipid peroxidation and vitamin loss in infant parenteral nutrition by adding multivitamin preparations to Intralipid. Acta Paediatr 2001 Mar;90(3):242-9.