

Some Considerations when Undergoing Treatment for Chronic Illnesses and Autoimmune Diseases

Prof. Emeritus Garth L. Nicolson, PhD, MD (H)

The Institute for Molecular Medicine, 16371 Gothard St. H, Huntington Beach, California 92647 USA

Tel: (714) 715-5978 Fax: (714) 596-3791 E-mail: gnicolson@immed.org Website: www.immed.org

There are a number of considerations when undergoing therapy for chronic illnesses, including whether to use traditional as well as integrative and nutraceutical approaches. Some of these are discussed in the following sections, including antibiotic/antiviral/antifungal therapies and herbal and dietary supplements for commonly found infections. The Institute for Molecular Medicine is a nonprofit institution and does not endorse commercial products or treatment approaches. The products and procedures below are only examples of the types of treatment approaches and remedies that could be beneficial to patients with chronic illnesses. Consult your personal practitioner for advice on treatments, dosing and schedules that can vary for each patient.

Antibiotic and Nutraceutical Therapy for Chronic Infections Found in Most Chronic Illnesses

Many patients with fatiguing illnesses, such as Gulf War Illnesses (45%), Fibromyalgia (60-70%), Chronic Fatigue Syndrome, ME (50-60%), autoimmune diseases (such as Rheumatoid Arthritis, Multiple Sclerosis, Lupus (SLE) and others, neurological diseases (such as ALS, Parkinson's, Alzheimer's, etc.) and neurobehavioral diseases (such as Autism Spectrum Disorders, Asperger's, etc.) have chronic infections of *Mycoplasma*, *Chlamydia*, *Borrelia*, *Brucella*, *Bartonella* and other bacterial, viral (HHV-6, CMV, etc.), parasite and fungal infections [1-3]. For patients with intracellular bacterial infections, 6 months [no break] treatment, then 6-week *on* 2-week *off* antibiotic cycles (Doxycycline, Ciprofloxacin, Azithromycin, Minocycline, Clarithromycin or others) work best using oral capsules without starch fillers. Some patients benefit from combinations of antibiotics, such as Doxycycline plus Azithromycin or Ciprofloxacin, especially if there are limited responses to either drug alone. Combinations of antibiotics with different mechanisms of action usually work best. In addition, these infections are intracellular, and Plaquenil has been used to alkalize cellular compartments and improve bacterial killing. Some recommend every-other-day dosing, which presumes that the microorganisms are cycling, which is mostly true, but compliance is important if this approach is used. Oral antibiotics should be taken with a full glass of water with crackers/bread to avoid esophageal irritation (do not lie down for 1 hr). Direct sunlight must be avoided for many antibiotics.

To overcome antibiotic (or others) Herxheimer reactions (generally die-off reactions involving chills, fever, night sweats, muscle aches, joint pain, short term memory loss, fatigue, a general worsening of signs/symptoms likely due to cytokine release or showers) or other adverse responses I.V. antibiotics have been used for a few weeks—then switched to oral. Also, oral Benadryl (diphenhydramine, 50 mg) taken at least 30 min before antibiotics is useful and lemon/olive drink (1 blended lemon, 1 cup fruit juice, 1 tbs olive oil—strain and drink liquid). This period usually passes within a few weeks and differs from allergic reactions that can cause immediate rashes, itching, swelling, dizziness, and trouble breathing—if allergic reactions occur, seek immediate medical attention. Many antibiotics cannot be used during pregnancy or taken by infants. Some practitioners have used cycles of Augmentin in between the 6-week antibiotic cycles or concurrently, if needed, to help to suppress secondary bacterial infections. In addition, some patients have benefited from adding Flagyl (Metronidazole, for bacterial and protozoal infections) to kill cyst forms. For viruses, some add anti-virals for the first few weeks (see next section). Mycoplasmas have been reported to have some characteristics of viruses, so this can be useful, and viral infections are also important in these illnesses. Often patients have multiple bacterial infections along with other co-infections. For more information on how to treat difficult co-infections see Mycoplasma Support <http://www.mycoplasmasupport.org>. For more complex, multiple infections, such as Lyme disease co-infections, more complicated treatment regimens must be employed [4], as is also discussed in Dr. Richard Horowitz's book ("How Can I Get Better," St. Martin's Griffin, ISBN 978-1-250-07054-8).

Nutraceuticals, vitamins, herbs and supplements and other support products can be found in the sections listed below. For patients who cannot take antibiotics, Rain Tree had three herb products that usually cannot replace antibiotics but are a fairly good alternative: Myco+; A-F; and Immune Support, www.rain-tree.com. Although no longer in business, some of these products can be found elsewhere. For patients who cannot take antibiotics, the Cowden protocol of herbals has proved useful for treatment of complex infections like Lyme disease without antibiotics (http://lymediseasresource.com/Dr_Lee_Cowden). Included in this protocol are: Banderol, Burbur-

Pinella, Magnesium Malate, Parsley, Samento, Sealantro, Serrapeptase, Sparga, Stevia, and Takuna. More information on purchasing these formulations can be found on the following websites:

https://www.pureformulas.com/brand/nutramedix.html?utm_source=pureformulas&utm_medium=_&utm_content=_&utm_campaign=nutramedix_searchpg-br_022316 **or** https://www.amazon.com/NutraMedix-Cowden-Support-Program-Month/dp/B07BHXNY43/ref=sr_1_16_a_it?ie=UTF8&qid=1537473789&sr=8-16&keywords=nutramedix

Dr. Mercola's website offers another type of protocol involving Astaxanthin, Grapefruit seed extract, Cilantro, Quercetin, Andrographis, Artemisinin, GABA, melatonin, Curcumin, Whey protein, CoQ10, Resveratrol, Krill oil and probiotics. <https://articles.mercola.com/lyme-disease/treatment.aspx>. These non-drug approaches are also useful for maintenance after antibiotics have been discontinued.

Antiviral Therapy for Chronic Viral Infections

Large subsets of chronic illness and other autoimmune patients have chronic viral infections, such as HHV-6, CMV, among others. For HHV-6 and CMV infections, Ganciclovir is the antiviral of choice. This can be used I.V. (5 mg/Kg I.V. over 1 hr every day) or oral (1000 mg 2X/day) in 3-week cycles. Some patients have benefited from the use of Famvir. This can be used as an oral dose (500 mg 2X/day for 2 weeks. Nutraceutical treatments can be used instead or concurrently, such as Genistein (in soy/red clover) to inhibit viral kinase, Rosemary/lemon balm to reduce complement activation, Selenite (see minerals) to inhibit viral replication, Barley grass and Lauric acid to inhibit lipid metabolism of viruses and *Phyllanthus amarus/niruri* to inhibit viral reverse transcriptase. Immune enhancement is important (see section below).

General Nutritional Considerations

Chronic illness patients are often immunosuppressed and susceptible to opportunistic infections, so proper nutrition is imperative. You should not smoke or drink alcohol or highly caffeinated products. Drink as much fresh fluids as you can; pure water is best. Try to avoid high sugar and trans-fat foods, such as military (MRE) or other fast foods and acid forming, allergen-prone and system stressing foods or high sugar/fat junk foods. Note: decreasing sugar intake is essential--*simple or refined sugars can suppress your immune system*. Increase intake of fresh vegetables, fruits and grains, and decrease intake of trans-fats and sugars. To build your immune system cruciferous vegetables, soluble fiber foods, such as prunes and bran, wheat germ, yogurt, fish and whole grains are useful. In some patients exclusive use of 'organic' foods has been beneficial [5]. Diet and especially reduction in sugar intake is also important to control yeast infections.

Vitamins and Minerals

Chronic illness patients are often depleted in vitamins (especially B complex, C, E, CoQ10) and certain minerals. These illnesses often result in poor absorption. Therefore, high doses of some vitamins are useful; some, such as vitamin B complex, cannot be easily absorbed by the gut (oral dose), so sublingual (under tongue) *natural* B-complex liquid (Total B, Real Life Research, or www.vitainshoppe.com) should be used instead of capsules. General vitamins plus extra C, E, CoQ10, Betacarotene, Folic acid, Bioflavoids and Biotin are best. L-Cysteine, L-Tyrosine, L-Glutamine, L-Carnitine, Malic acid and especially flaxseed or fish oils are reported to be useful. Certain minerals are depleted in chronic illness patients, such as Zinc, Magnesium, Chromium and Selenium. Some recommend up to 300 mcg/day Sodium selenite, followed by lower doses. Vitamins and minerals should not be taken at the same time of day (3-4 hr difference) as antibiotics or antivirals (or oxygen therapy), because they can affect absorption or act against therapy. Some recommend that antioxidant vitamins be taken at least 4 hr before or after oxygen therapy. The suggested doses of vitamins can vary dramatically among patients; consult with your physician or nutritionist for appropriate dosage. Some patients may require analysis of vitamins, minerals and amino acids so that appropriate doses can be recommended: Nu-Life (Sophista-Care, 760-837-1908), Immune-Pak (Care Management Products, 888-845-1467), Prohealth, 800-366-6056, www.immunesupport.com VitaminShoppe, www.vitaminshoppe.com

Membrane Lipid Replacement for Chronic Infections and Restoring Mitochondrial Function

Membrane Lipid Replacement is useful in providing membrane lipids in un-oxidized forms to repair nerve cell and mitochondrial membranes that are damaged by heavy metals, chemicals and infections [6]. We recommend all natural Healthy Aging containing NTFactor or Patented Energy chewable wafers (4 grams/day) (Nutritional Therapeutics, www.NTFactor.com, 800-982-9158). For children, one-half the adult dose is used—tablets should be ground up between two spoons into a course powder that can be added to applesauce. Alternatively, Patented Energy chewable wafers or the colorless, odorless, tasteless powder can be substituted. NTFactor Lipids® itself is tasteless, but children usually like the taste of the chewable wafers. The adult daily dose is usually 8-10 tablets or 4 wafers per day. For children 1 tablet or 1/2 wafer for children up to 2 years-old, 2 tablets/1 wafer for 2-3 years old and 3 tablets or 1-1/2 wafers for 4-6 years-old, and older can take 4 tablets or 2

wafers. Teens take the adult dose. Research has demonstrated no adverse responses with NTFactor Lipids, even many times these doses. Since this formulation is a completely natural membrane lipid mixture, there are no known toxicities and no known toxic dose limits. NTFactor Lipids® also comes in a form with vitamins, minerals and probiotics (Propax, 800-982-9158, www.NTFactor.com). Additional CoQ₁₀, Alpha-lipoic acid, L-Carnitine, unsaturated Fatty acids and NADH are also useful. A combination product, ATP Fuel® contains all of these ingredients in capsules (www.ResearchNutritionals.com).

Biofilm and Chronic Intracellular Infections

One of the reasons that patients fail antibiotic and other therapies for bacterial infections is that bacteria can persist in dormant states or hide inside cells or in biofilms and survive, even when antibiotic concentrations are used that should kill them. Some antibiotics and drugs penetrate into cells and tissues better than others, allowing infections to survive under conditions that should be effective. Also, infections can hide in biofilms, which are extracellular matrix-like meshworks that prevent penetration of antibiotics and drugs. Matrix-busting treatments have been used to break down biofilm, so bacteria and other infections can be treated effectively. Some examples are: enzymes, such as nattokinase, lumbrokinase, serrapeptase, as well as Stevia and monolaurin, have been used to break down biofilm and allow penetration of drugs and antibiotics (see Cowden Nutramedix at the top of page 2).

Oxidative Therapy for Chronic Infections

Oxidative therapy can be useful in suppressing a variety of anaerobic infections: several weeks of Hyperbaric Oxygen (1.5-2 ATM, 60 min) treatments, I.V. ozone or hydrogen peroxide are useful, but must be administered by experienced practitioners to avoid adverse reactions. For personal use, peroxide baths using 2 cups of Epsom salt in a hot bath or Jacuzzi can be employed. After 5 min, add 2-4 bottles 16 oz. of 3% Hydrogen peroxide. Repeat 2-3X per week; no vitamins or antioxidants 4 hr before the bath. The Hydrogen peroxide is added after your pores open. Hydrogen peroxide can also be directly applied to skin after a work-out or hot shower/tub. Leave Hydrogen peroxide on for 5 min, and then wash off. For oral irrigation, mix 1 part 3% Hydrogen peroxide with 2 parts water and use like a mouth wash 3X per day. Most chronic illness patients have periodontal problems, and oral infections and bone cavitation infections are common. These should not be ignored, because these infections can become systemic and spread to other sites.

Testing and Therapy for Heavy Metal Contamination

The Institute for Molecular Medicine has found that many chronic illness patients have heavy metal contamination that must be considered. Most studies have concentrated on Mercury, Lead, Aluminum, Cadmium and other heavy metals. Veterans may have Uranium contamination. Although heavy metal mobilization and removal is a long-term process, sometimes taking over one year, it does not require expensive, invasive, weekly treatments at clinics. Patients should have a heavy metal analysis of hair, stool and urine at a reputable diagnostic laboratory (Doctors' Data, www.doctorsdata.com, 800-323-2784, Great Smokies Diagnostic, www.gsdl.com, 800-522-4762). All results should be evaluated by a practitioner. Such analyses are only of excreted heavy metals; deposits deep in tissues cannot be tested using these procedures. Non-invasive treatments to remove heavy metals include oral dosing, trans-dermal patches and anal suppositories containing chelating agents. The former can be found at www.edtachelation.com and the latter is available from World Health Products (Detoxamin, 877-656-4553). It is very effective and can be used long-term with very few or no side effects. It is claimed that Garlic Plus (Longevity, 800-580-7587, www.longevityplus.net) is useful, but there are no studies to substantiate this claim.

Replacement of Natural Gut Flora and Digestive Enzymes

Patients undergoing treatment with antibiotics risk destruction of normal gut flora. Antibiotic use that depletes normal gut bacteria and can result in over-growth of less desirable bacteria and fungi. To supplement bacteria live cultures of *Lactobacillus acidophilus* and other "friendly" bacteria are strongly recommended. Mixtures of *L. acidophilus*, *L. bifidus*, *B. bifidum*, *L. bulgaricus* and FOS (fructooligosaccharides) to promote growth of these probiotics in the gut are useful (examples, DDS-1, DDS-Plusor, Multi-Flora, UAS Labs, 800-422-3371, www.uaslabs.com); Theralac, 800-926-2961, www.theralac.com, *L. acidophilus* mixtures (>15 billion live organisms) should be taken 3X per day and 2 hr after any antibiotics. For irritable bowel, the nutraceutical Calm Colon (Samra, 310-202-9999) has proven to be very effective in clinical trials. For heavy metal removal, Garlic Plus (Longevity, 800-580-7587, www.longevityplus.net) has been proposed. For help with bowel bacteria and bladder infections, D-mannose (Biotech Co., 800-345-1199) has been used. This natural sugar inhibits binding of bacteria to biological membranes. In addition, to improve digestion and especially absorption enzyme mixtures have proven useful, such as Wobenzym (Health Stores, 800-578-5939, www.healthstores.com or Zooscape, 800-760-8783, www.zooscape.com).

Natural Immunomodulators and Remedies

A number of natural remedies, herbal teas, Lemon/Olive drink, Olive leaf extract (Oleuropein), Wormwood extract (Artemisinin/Artesunate), are often useful, especially during or after antibiotic therapy. More important examples are immune modulators, such as bioactive Whey protein (ImuPlus, 800-310-8311, www.imuplus.com; Immunocal, 800-337-2411, www.immunocal.com), ImmunoPro (Needs, 800-634-1380, www.needs.com or www.immunesupport.com), Transfer Factor (4-Life, 800-852-7700, www.transferfactor-4-life.com), ImmunFactor 2, 8 or 9 (Chisolm Biologicals, 800-664-1333), Immuni-T (Longevity, 800-580-7587, www.longevityplus.net), MGN3 (Lane Labs, 800-526-3005, www.lanelabs.com), ImmunotiX 3-6 (beta-Glucan, Xymogen, 800-647-5100, www.xymogen.com), ImmPower (American Bioscience, 888-884-7770, www.americanbiosciences.com) and Microbojen (Jernigan Nutraceuticals, 316-651-5739, <http://abc.eznettools.net/jernigannutraceuticals>). Some additional remedies are: Olive leaf extract (many sources), NSC-100 (Nutritional Supply, 888-246-7224), Tahitian Noni (Morinda, 800-445-8596, www.tahitiannoni.com), Laktoferrin (Nutricology, 888-563-1506 or www.iherb.com), Echinacea-C (several sources) or Super Defense Plus (BioDefense Nutritionals, 800-669-9205). These products have been used to boost immune systems. Although they appear to help many patients, their clinical effectiveness has not been carefully evaluated. They appear to be useful during therapy to boost the immune system or after antibiotic/antiviral therapy in a maintenance program, but their successful use appears to be for specific patients.

Yeast/Fungal or Bacterial Overgrowth

Yeast overgrowth can occur, especially in females (vaginal infections). Gynecologists recommend Nizoral, Diflucan, Mycelex, or anti-yeast creams. Metronidazole [Flagyl, Prostat] has been used to prevent fungal or parasite overgrowth or other antifungals [Nystatin, Amphotericin B, Fluconazole, Diflucan] have been administered for fungal infections that can occur while on antibiotics. Herbals that have proved effective are: Pau d' arco, 7 capsules/2X/day, Grapefruit seed extract, Oregano complex, Garlic extract, Mycopril (a Fatty acid from coconut), and Artemesia, a Chinese herb that is often used to treat malaria. Some patients have as their principal problem systemic fungal infections that can be seen using dark-field microscopy of blood smears. For superficial fungal infections, such as fungal nail, a topical mixture of Laminsil in 17% DMSO 2X/day is effective. As mentioned above, *L. acidophilus* mixtures (>3 billion live organisms) are used to restore gut flora. Bacterial overgrowth can also occur, for example, in between cycles of antibiotics or after antibiotics/antivirals have been stopped. This can be controlled with 2-week courses of Augmentin (3 X 500 mg/day) in between cycles or concurrent with other antibiotics. Nutraceutical approaches to controlling yeast infections include: Pau d' arco, Grapefruit extract, Olive leaf, Caprylic acid, Garlic extract and Oregano oil.

4

Antidepressants, Narcotics, etc.

Antibiotic uptake and immune responses may be inhibited by some drugs, and antidepressants, such as Sertaline [Zoloft], Fluoxetine [Prozac], Amitriptyline [Elavil], Maprotiline [Ludiomil], Desipramine [Norpramin], Clomipramine [Anafranil], Nortriptyline [Pamelor], Bupropion [Wellbutrin]. Also muscle relaxants (Cyclobenzaprine [Flexeril]), opiate agonists, anti-convulsives or certain analgesics (Oxycodone [Percodan], Carbamazepine [Tegretol], Acetaminophen/ Hydrocodone [Vicodin]), narcotics (Codeine w/Penergan, Propoxyphene [Darvon], Morphine), antacids, anti-diarrheas (among others) should be avoided, if possible, or gradually decreased during therapy. Some drugs (certain antidepressants, analgesics, narcotics, etc.) may inhibit immune responses and interfere with therapy. These should be decreased and gradually eliminated.

Flying, Exercise and Saunas

Flying, excessive exercise and lack of sleep can make signs/symptoms worse. Flying exposes you to lower oxygen tension, and can stimulate borderline anaerobes that grow better at low oxygen (see above). Some exercise is essential, but avoid relapses due to **over-exertion**. Dry saunas help rid the system of chemicals, and saunas should be taken daily or 3 sessions per week--moderate exercise, followed by 15-20 min of dry sauna and tepid shower. Repeat saunas no more than 2X per day. Work up a good sweat, eliminating chemicals without placing too much stress on your system, and replace body fluids and electrolytes during and after each session. During exercise patients should always avoid pollutant and allergen exposures. For recovery after exercise and to decrease muscle soreness, some use a Jacuzzi or hot tub, but only after a sufficient cool-down period. Don't get overheated in the process. *Remember, don't over do it, or you will likely relapse!*

Antibiotics/Antivirals Recommended when Indicated for Treatment of Intracellular Infections in Chronic Illnesses

Prof. Emeritus Garth L. Nicolson, PhD, MD (H)

The Institute for Molecular Medicine, 16371 Gothard St. H, Huntington Beach, California 92647 USA
Tel: (714) 715-5978 Fax: (714) 596-3791 E-mail: gnicolson@immed.org Website: www.immed.org

Doxycycline (aka Vibramycin, Doxychel, Doxy-D, Doryx)

Doxycycline is a broad-spectrum tetracycline with good lipid solubility and ability to penetrate the blood-brain-barrier. This antibiotic acts by inhibiting microorganism protein synthesis; it is readily absorbed by the (normal) gut, and peak blood concentrations are maintained between 2-18 hrs (half-life, 18-22 hrs) after an oral dose of drug. Food, calcium, magnesium, antacids and some drugs reduce absorption, and alcohol, phenytoin [Dilantin] or barbiturates reduce blood half-life or suppress the immune system. **Minocycline** [Minocin] can be substituted, and for some illnesses (RA) it is preferred because it penetrates tissues better (same dose/day). For bacterial infections associated with chronic illnesses, the recommended oral dose is 200-300 mg/day (2-3X 100 mg capsules, 2 in the morning) for 6 months. After 6 months, 6 week cycles are suggested (2-weeks in between). Initially, doxycycline can exacerbate chronic signs and symptoms (Herxheimer reactions or adverse responses, such as transient fever, skin, gut discomfort, etc.) but these are usually reduced within a few weeks (*see first section*). Patients usually start feeling better with alleviation of major signs and symptoms within 12 weeks, but in some patients' major symptoms are not alleviated until after 12 weeks. Severe reactions or prior damage to the gastrointestinal track may require I.V. administration of 100-150 mg/day (rapid I.V. administration must be avoided) for 2-3 weeks, then the remainder of the course should be oral (to avoid thrombophlebitis and other complications that can occur with prolonged I.V. therapy). Some patients react to the *starch filler* in the capsules and must use Doryx, a granular form of pure Doxycycline. Virtually all patients relapse (show the same major signs and symptoms) if they stop therapy before 6 months. In a pilot study, ~85% relapsed after 12 weeks of therapy, so the first 6 months without a break is recommended. Doxycycline has been used successfully *in addition to* other antibiotics in situations where either antibiotic alone had minimal effects (i.e., Doxycycline plus Ciprofloxacin or Doxycycline plus Azithromycin). Doxycycline and Minocycline are primarily bacteriostatic and effective against the following organisms: gram-negative bacteria (*N. gonorrhoeae*, *Haemophilus influenzae*, *Shigella* species, *Yersinia pestis*, *Brucella* species, *Vibrio cholera*); gram-positive bacteria (*Streptococcus pneumoniae*, *Streptococcus pyogenes*); mycoplasmas (*Mycoplasma pneumoniae*, *Mycoplasma fermentans* [inc. incognitis strain], *Mycoplasma penetrans*); others (*Bacillus anthracis* [anthrax], *Clostridium* species, *Chlamydia* species, *Actinomyces* species, *Entamoeba* species, *Treponema pallidum* [syphilis], *Plasmodium falciparum* [malaria] and *Borrelia* [Lyme] species).

Precautions: Avoid direct sunlight and drink fluids liberally, especially with oral capsules. Doxycycline or Minocycline therapy may result in overgrowth of fungi or yeast and non-sensitive microorganisms (*see Considerations, first page*). Patients on anticoagulants may require lower anticoagulant doses. Use during pregnancy or in children under 8 years is not recommended, in the latter case due to tooth discoloration, but lower doses of doxycycline have proven to be very effective in children with GWI/CFS (weight 100 lbs. or less, 1-2 mg/lb. divided into two doses; weight over 100 lbs. use adult dose). Patients with impaired kidney function should not take Doxycycline, and the following drugs should not be taken with Doxycycline: Methoxyflurane [Penthrene], Carbamazepine [Tegretol], digoxin or diuretics. Other drugs can affect uptake or immune systems (see above). For complicating bacterial infections, 2 weeks of Augmentin (3X 500 mg/day) can be taken in between courses of antibiotics. For fungal and yeast complications, please see the instructions above.

Adverse Reactions: In a few patients Doxycycline causes gastrointestinal irritation, anorexia, vomiting, nausea, diarrhea, rashes, mouth dryness, hoarseness and in rare cases hypersensitivity reactions, hemolytic anemia, skin hyper-sensitivity and reduced white blood cell counts. In general, Doxycycline is considered a very safe drug, in that there are few adverse reactions reported in the literature.

Ciprofloxacin (aka Cipro, Cifox, Cifran, Ciloxan, Ciplox)

Ciprofloxacin is a broad-spectrum synthetic fluoroquinolone antibiotic with good absorption characteristics. This drug acts on bacterial DNA gyrase to inhibit bacterial DNA synthesis. Ciprofloxacin is secreted rapidly in

the urine and has a half-life in the blood of ~4 hrs. Food delays the absorption (by ~2 hrs) but doesn't effect total absorption; antacids containing magnesium, aluminum or other salts as well as various drugs reduce absorption and should not be taken at the same time of day. For chronic illness use, the recommended dose is 1,500 mg/day (oral, 3X 500 mg capsules, 2 in morning) for 6 months, then 6-week cycles of therapy. Ciprofloxacin may or may not be taken with meals. Initially, Ciprofloxacin may exacerbate some signs/symptoms (Herxheimer reactions or adverse antibiotic responses) but these are usually gone within a few weeks or so. Patients report that doses of 1000 mg/day or lower are not effective in alleviating symptoms. Patients usually start feeling better with alleviation of major signs/symptoms within 4-6 weeks, but in some patients signs/symptoms are not reduced until after 6 weeks. Ciprofloxacin has been used for patients in which Doxycycline cannot be tolerated or in some patients that no longer respond to Doxycycline. In a few cases Ciprofloxacin has been used simultaneously with Doxycycline. Herxheimer reactions, if present, usually pass within days to a few weeks; prior damage to the gastrointestinal system may require I.V. 400-500 mg X2/day (over one hr per each infusion, rapid I.V. administration is to be avoided) for 2-4 weeks, then the remainder on oral antibiotic (oral doses). Virtually all patients relapse (with major signs/symptoms) if drug is stopped during a 6-12 week course of therapy. Additional antibiotic courses result in milder relapses after the drug is discontinued. Subsequent cycles of antibiotics may require the use of Doxycycline or other antibiotics. Sparfloxacin, a fluoroquinolone with better tissue penetration, can be substituted (oral dose, 400 mg/day), but some patients indicate greatly increased sun sensitivity. Levofloxacin, Ofloxacin, Gatifloxacin are newer fluoroquinolones with better tissue penetration than Ciprofloxacin and can be substituted for Ciprofloxacin. Ciprofloxacin is effective against the following organisms: gram-negative bacteria (*Shigella* species, *Citrobacter diversus*, *Citrobacter freundii*, *Escherichia coli*, *Klebsiella pneumoniae*, *Haemophilus influenzae*, *Enterobacter* species, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Yersinia pestis*, *Vibrio cholera*), *Moraxella catarrhalis*; gram-positive bacteria (*Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Staphylococcus hominis*, *Staphylococcus aureus*, *Staphylococcus saprophyticus*); mycoplasmas, moderately active (*Mycoplasma* species); others (*Clostridium* species, *Chlamydia* species, *Mycobacterium tuberculosis*).

Precautions: Direct sunlight is to be avoided, especially with sparfloxacin, and patients should not take Floxacin and Theophylline concurrently. Ciprofloxacin therapy may result in drug crystals in the urine in rare cases, and patients should be well hydrated to prevent concentration of urine. Pregnant women and children should not use this drug due to reduction in bone and cartilage development.

Adverse Reactions: Adverse antibiotic responses resulted in discontinuing drug in ~3.5% of patients, and such reactions included nausea (5%), diarrhea (2%), vomiting (2%) abdominal pain (1.7%), headache (1.2%) and rash (1.1%). In rare cases ciprofloxacin may cause cardiovascular problems (<1%) and central nervous system (dizziness, insomnia, tremor, confusion, convulsions and other reactions (<1%). Small numbers of patients have experienced hypersensitivity (anaphylactic) reactions that have required immediate emergency treatment. Other drugs may affect absorption and immune systems.

Azithromycin (aka Zithromax)

Azithromycin is a azalide (macrolide) antibiotic with good absorption and a serum half-life of ~68 hrs. This class of drug acts by binding to the 50S ribosomal subunit of susceptible organisms where it interferes with protein synthesis. Food decreases absorption rate, but absorption is unaffected by antacids containing magnesium, aluminum or other salts; other drugs may affect absorption (see above). For GWI/CFS/FMS use, the recommended dose is 500 mg/day (oral, 1-2X 250 mg capsules taken at once) for each 6-week cycle of therapy. Azithromycin should not be taken with meals (1 hr before or 1 hr after). Initially, Azithromycin may exacerbate some symptoms but these are usually gone within a few weeks. Patients usually start feeling better with alleviation of most major signs/symptoms within several weeks, but in some patients major symptoms are not alleviated within months. Azithromycin has been used for patients in which Doxycycline cannot be tolerated or in patients that no longer respond to Doxycycline. Herxheimer reactions usually pass within a few days to weeks. Virtually all patients relapse (show the same major signs/symptoms) after terminating therapy in less than 12 wks. Additional cycles of antibiotic result in milder relapses after drug is discontinued. Azithromycin has been shown to be safe for pediatric use (10 mg/kg/day is recommended for children under 14, but see below). Azithromycin is effective against the following organisms: gram-negative bacteria (*Bordetella pertussis*, *Shigella* species, *Haemophilus influenzae*, *Chlamydia* species, *Yersinia pestis*, *Brucella* species, *Vibrio cholera*); gram-positive bacteria (*Streptococci* group C, F, G); mycoplasmas (*Mycoplasma* species); others (*Clostridium* species, *Treponema pallidum* [syphilis], and *Borrelia* species).

Precautions: Azithromycin is principally absorbed by the liver, and caution should be exercised with patients

with impaired liver function. Antacids containing magnesium, aluminum or other salts should not be taken at the same time of day with azithromycin. Other drugs can also interfere. Macrolides plus Terfenadine [Seldane] or Astemizole [Hismanal] may dangerously elevate plasma antihistamine and cause arrhythmias and increase serum theophylline levels in some patients, particularly those receiving methylated Xanthine causing nausea, vomiting, seizures. Plasma levels of Carbamazepine [Tegretol] can also be elevated, leading to Carbamazepine toxicity and nausea, vomiting, drowsiness and ataxia.

Adverse Reactions: Adverse antibiotic responses were mild to moderate in clinical trials and included diarrhea (5%), nausea (3%), abdominal pain (3%). In rare cases (<1%) azithromycin may cause cardiovascular problems (palpitations, tachycardia, chest pain) and central nervous system (dizziness, headache, vertigo), allergic (rash, photosensitivity, angioderma), fatigue and other reactions (<1%). In pediatric patients >80% of the adverse responses were gastrointestinal. In children, doses above the suggested 10 mg/kg/day have been shown to produce hearing loss in some patients.

Clarithromycin (aka Biaxin)

Clarithromycin is a broad spectrum macrolide antibiotic with good absorption and serum half-life. This drug acts by binding to the 50S ribosomal subunit of susceptible organisms and interfering with protein synthesis. The drug is mostly bacterostatic but high concentrations can be bactericidal. Food decreases absorption rate, but absorption is unaffected by antacids containing magnesium, aluminum or other salts. Some drugs may interfere with absorption or depress immune systems (see above). For chronic illness patients the recommended dose is 500-750 mg/day (oral, 2-3X 250 mg capsules, 2 taken in morning) for 6 months of therapy, then 6-week cycles. Clarithromycin should not be taken with meals (1 hr before or 1 hr after). Initially, clarithromycin may exacerbate some symptoms due to Herxheimer reactions and bacterial death but these are usually gone within wks. Patients usually start feeling better with alleviation of most major signs and symptoms within 1-2 weeks, but in some patients major symptoms are not alleviated until after 12 weeks or so. Clarithromycin has been used for patients that do not respond or cannot tolerate Doxycycline. Herxheimer reactions usually pass within days to weeks. Virtually all patients relapse (show the same major signs/symptoms) when therapy is stopped within 12 weeks. Additional cycles of antibiotic result in milder relapses after drug is discontinued. For children, the recommended dose is 15 mg/kg/day X2; at this dose some children have gastrointestinal problems. Clarithromycin is effective against the following organisms: gram-negative bacteria (*Neisseria gonorrhoeae*, *N. meningitidis*, *Moraxella catarrhalis*, *Campylobacter jejuni*, *Eikenella corrodens*, *Haemophilus ducreyi*, *Bordetella pertussis*, *Shigella* species, *Salmonella* species, *Haemophilus influenzae*, *Chlamydia* species, *Yersinia pestis*, *Brucella* species, *Vibrio cholera*, *Aeromonas* species, *E. coli*, gram-positive bacteria (*Streptococcus pyogenes*, *S. pneumoniae*, anaerobic *Streptococci*, *Enterococcus faecalis*, *Staphylococcus aureus*, *S. epidermidis*, *Bacillus anthracis*, *Corynebacterium diphtheriae*, *C. minutissimum*, *Listeria monocytogenes*, *Actinomyces israelii*); mycoplasmas (*Mycoplasma* species, *M. pneumoniae*, *Ureaplasma urealyticum*); others (*Clostridium* species, *Treponema pallidum* [syphilis], *Legionella pneumophila*, *L. micdadei*, *Mycobacterium avium*, *M. chelonae*, *M. chelonae abscessus*, *M. fortuitum*, *Rickettsia* species and *Borrelia* species). Yeasts, fungi and viruses are resistant.

Precautions: Clarithromycin is principally absorbed by the liver, and caution should be exercised with patients with impaired liver function. Antacids containing magnesium, aluminum or other salts should not be taken at the same of day as azithromycin. Other drugs may also interfere (see above). Macrolides plus Terfenadine [Seldane] or Astemizole [Hismanal] may dangerously elevate plasma antihistamine and cause arrhythmias and increase serum theophylline levels in some patients, particularly those receiving methylated Xanthine causing nausea, vomiting, seizures. Plasma levels of Carbamazepine [Tegretol] can also be elevated, leading to Carbamazepine toxicity and nausea, vomiting, drowsiness and ataxia. Macrolides like Clarithromycin should not be used with Cyclosporin [Sandimmune].

Adverse Reactions: Adverse antibiotic responses were mild to moderate in clinical trials and included diarrhea, nausea, and abdominal pain. In rare cases (<1%) Azithromycin may cause cardiovascular problems (palpitations, tachycardia, chest pain) and central nervous system (dizziness, headache, vertigo), allergic (rash, photosensitivity, angioderma) and fatigue.

Clindamycin (aka Cleocin, Dalacin, Lacin)

Clindamycin is a semisynthetic antibiotic made from Lincomycin and is effective against severe anaerobic infections. It is primarily bacteriostatic against a wide range of Gram-positive and anaerobic pathogens, including some protozoa. It has good absorption and tissue penetration; its half-life is ~3 hrs in adults and ~2 hrs in children. Since clindamycin use can result in severe colitis even weeks after cessation of the drug, it should not be used as primary therapy. Food does not adversely affect absorption rate, but absorption is affected by antacids containing magnesium, aluminum or other salts. Some drugs may interfere with absorption or depress immune systems (see above). The recommended dose is 600-1200 mg/day (oral, 4-8 X 150 mg capsules, in three divided doses) for 6-week cycles of therapy. Herxheimer reactions may exacerbate signs/symptoms but these are usually gone within days-weeks. Patients usually start feeling better with alleviation of most major

signs and symptoms within days-weeks, but in some patients major symptoms are not alleviated until after several weeks or so. For children, the recommended dose is 8-16 mg/kg/day divided into 3-4 doses.

Precautions: Clindamycin should not be used for patients with nonbacterial (viral, fungal) infections. Its use is associated in some patients with colitis and severe, persistent diarrhea and abdominal cramps, and when this occurs the drug should be discontinued. It must not be used with opiates or Diphenoxylate with Atropine [Lomotil]. Cholestyramine or Colestipol resins bind Clindamycin and should not be given simultaneously.

Adverse Reactions: Adverse antibiotic responses were mainly diarrhea in 2-20% of cases, some severe and dangerous (colitis). Pseudomembranous colitis may develop during or several weeks after therapy. This can be serious if ignored. Other gastrointestinal effects of the drug have been reported (nausea, vomiting, esophagitis, abdominal pain or cramps), and hypersensitivity reactions, including skin rashes occur in up to 10% of patients. Mild cases of colitis should be managed promptly with fluid, electrolyte and protein supplementation as indicated. Other effects include transient leucopenia, polyarthritis and abnormal liver function (jaundice and hepatic damage rarely occur). Clindamycin should not be used with Erythromycin. Clindamycin has been shown to have neuromuscular blocking properties that may enhance the action of other neuromuscular drugs. Clindamycin should only be used with caution in patients receiving such drugs.

Ganciclovir (aka Cytovene)

Ganciclovir is a synthetic antiviral made from a guanine derivative that is active against Cytomegalovirus (CMV) and related Herpes simplex viruses, such as HHV-6 viruses. Ganciclovir inhibits replication of Herpes viruses by inhibiting viral DNA replication by its incorporation into viral DNA and by inhibition of viral DNA elongation. The recommended dosage of Ganciclovir [i.v.] is an initial induction dose of 5 mg/Kg I.V. at a constant rate over 1 hr twice on the first day and then once /day for 3 weeks. For oral use Ganciclovir 1000 mg X3/day with food for a 3-week course. The drug reaches a maximum blood dose within 3 hrs after oral administration with food, with a half-life of 4.6 hrs. Ganciclovir has been used mainly for treatment of CMV retinitis, CMV in organ transplant cases, and CMV in AIDS cases. Its use in chronic CMV and HHV-6 infections has not been fully investigated.

Precautions: Ganciclovir should not be used in pregnancy, by nursing mothers or in patients with renal impairment or in patients with an absolute neutrophil count of <25,000 cells/microliter. In elderly patients particular attention must be paid to renal function before and during drug administration. Some patients should have serum creatinine or creatinine clearance values monitored to allow for possible dose adjustments in renally impaired patients. Ganciclovir can be used in children at the dose levels mentioned above with similar results. In addition, Ganciclovir should not be taken with drugs that have the potential to cause neutropenia and anemia. For example, and Ganciclovir and Zidovudine both have the potential to decrease white blood cells and cause anemia. Ganciclovir can change serum clearance rates of Didanosine and other drugs, and Ganciclovir used with drugs that inhibit rapidly growing cell populations may show added toxicity. Therefore, Dapsone, Pentamidine, Flucytosine, Vincristine, Vinblastine, Adriamycin, Amphotericin B, among other drugs should not be used with Ganciclovir.

Adverse Reactions: Adverse drug responses were seen in patients that are hypersensitive to Ganciclovir or Acyclovir. The most common side effects were reductions in white blood cells (6-29%), anemia (9-19%), impairment in fertility, chills (7%), sweating (11%), abdominal pain (15%), vomiting (13%), diarrhea (40%), paresthesias (8%) and retinal detachment (8-11%) as well as less frequently chest pain, headache, malaise, constipation, cough, anxiety, confusion, depression, dizziness, dry mouth, insomnia, tremor and edema. The values were obtained for patients with CMV retinitis, organ transplants and AIDS, and they may not reflect the actual incidence rates in chronic illness patients.

Famciclovir (aka Famvir)

Famciclovir is an orally administered pro-drug of the antiviral agent Penciclovir. It is a synthetic acyclic guanine derivative of Penciclovir that undergoes rapid biotransformation to the active antiviral compound Penciclovir, which has inhibitory activity against Herpes viruses. Famciclovir inhibits viral replication. For Herpes virus infections Famciclovir 500 mg 3X/day for 7-14 days is the standard dose. Following oral administration of Famciclovir, the drug is deacetylated and oxidized to form Penciclovir. The half-life of Penciclovir is 2-3 hrs. Famciclovir is used in patients with Herpes zoster, Herpes simplex, genital Herpes, and Herpes infections in AIDS patients and in sexually transmitted herpes infections.

Precautions: Famciclovir should not be used in pregnancy, by nursing mothers or in patients with renal impairment. Famciclovir should not be used with drugs that are significantly eliminated by active renal tubular secretion. Use in children has not been established.

Adverse Reactions: Adverse drug responses were seen in patients that are hypersensitive to Famciclovir. The most common side effects were headache (22%), nausea (11%), diarrhea (4-7%), vomiting (1-3%), flatulence (<2%), rash (<1%), fatigue (4-6%), reductions in white blood cells (1-3%) and anemia (<1%).

Final Comments/Suggestions

Recovery will be gradual not rapid, and almost all patients with complex, multiple bacterial infections will experience initial Herxheimer reactions that can be quite severe and can last for weeks. You will have to be patient and not abandon therapy prematurely, because few patients who have been sick for years recover in less than one year of therapy [7]. Do not take antibiotics or antivirals at the same time of day as vitamins, minerals, supplements, etc. Vitamins and minerals should be taken 2 hrs before or after antibiotics or antivirals to prevent interference with drug uptake. Stop antibiotics or antivirals if adverse reactions occur. You will experience cycles of relapse when severely physically or mentally stressed, and you should not be alarmed if some signs and symptoms occasionally return or worsen. This is not unusual. Eventually you will be off antibiotics or antivirals, but you will need to continue various supplements to prevent relapse and to maintain your immune system and general nutritional status.

This material has not been evaluated by the FDA. It is general information, for the most part published, and it should not be construed as personal guidance. Thus it is not intended to be direct medical advice or specific advice to prevent, diagnose, treat or cure any illness, condition or disease. It is very important that you make no change in your healthcare plan or health support regimen without researching and discussing it in collaboration with your professional healthcare advisors.

References

1. Nicolson, GL. Chronic infections in neurodegenerative and neurobehavioral diseases. *Laboratory Medicine* 2008; 39(5): 291-299.
http://www.immed.org/infectious%20disease%20reports/infectious%20disease%2011.23.08/Nicolson_LabMedicine0508.pdf
2. Nicolson GL, Haier J. Role of chronic bacterial and viral Infections in neurodegenerative, neurobehavioral, psychiatric, autoimmune and fatiguing illnesses: Part 1. *Brit. J. Med. Practit.* 2009; 2(4): 20-28.
<http://www.immed.org/NeuroDiseases/NeuroDegenPubs03.2010updates/BJMPnicolsonhaier-Part1.pdf>
3. Nicolson GL, Haier J. Role of chronic bacterial and viral Infections in neurodegenerative, neurobehavioral, psychiatric, autoimmune and fatiguing illnesses: Part 2. *Brit. J. Med. Practit.* 2009; 3(1): 301-311.
<http://www.immed.org/NeuroDiseases/NeuroDegenPubs03.2010updates/BJMPnicolsonhaier-Part2.pdf>
4. Burrascano, JJ, Jr. Advanced topics in Lyme disease: diagnostic hints and treatment guidelines for Lyme and other tick-borne illnesses. *Managing Lyme Disease*, 16th Edition, 2008.
http://www.immed.org/treatment%20considerations/2.2.09Updates/Lyme_Burrascano_10_2008.pdf
5. Nicolson, G.L. and Ngwenya, R. Dietary considerations for patients with chronic illnesses and multiple chronic infections. A brief outline of eighteen dietary steps to better health. *Townsend Lett.* 2001; 219: 62-65.
<http://www.immed.org/treatment%20considerations/08.16.2012update/TownsendDietConsid.-01.7.pdf>
6. Nicolson GL, Ash ME. Membrane Lipid Replacement for chronic illnesses, aging and cancer using oral glycerolphospholipid formulations with fructooligosaccharides to restore phospholipid function in cellular membranes, organelles, cells and tissues. *Biochim. Biophys. Acta* 2017; 1859: 1704-1724.
org/10.1016/j.bbamem.2017.04.013
<http://dx.doi.org/10.1016/j.bbamem.2017.04.013>
7. Nicolson GL, Nicolson NL. Diagnosis and treatment of mycoplasmal infections in Persian Gulf War Illness-CFIDS patients. *Intern. J. Occup. Med. Immunol. Tox.* 1996; 5: 69-78.
<http://www.immed.org/GWI%20Research%20docs/06.26.12.update.pdfs.gwi/Nicolson-IJOMIT1996.pdf>