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Immunity: Herbal Medicine and the TH1/TH2 Balance

by Paul Bergner

Abstract: The concept of imbalance between elements of the humoral and cell-mediated immunity (TH1/TH2 imbalance) in allergic, autoimmune, cancer, and other disease conditions is an emerging paradigm that may explain the observed beneficial immuno-modulating effects of some herbal medicines in these conditions. It may also explain observed side effects of immune stimulating herbs in conditions such as systemic lupus erythematosus, rheumatoid arthritis, multiple sclerosis, chronic fatigue syndrome, and allergies. Prescribing of herbal medicines according to this theory, however, has pitfalls. Specific health conditions often do not fit neatly into the TH1/TH2 theory, and herbal medicines often have complex actions on immunity that cannot be defined to consistently affect one side or the other of the equation. The theory and its weaknesses are reviewed here, along with research into herbal medicines that may affect the TH1/TH2 balance. We conclude that in lieu of a lack of definitive research into the nature of TH1/TH2 balance in specific conditions, and more extensive human trials into the effects of herbal medicines on that balance in specific conditions, herbs should be prescribed according to their traditional indications and contraindications in these diseases rather than according to this new theoretical rationale.

The explosion of research into immunity following the onset of the AIDS epidemic in North America in the early 1980s led to a hypothesis on immune balance that arose in 1986. It was known that the T-helper (TH) cell, the host cell for the HIV virus, was the critical activator of the immune response, and that it catalyzed both the cell-mediated immunity, with its chief players being the macrophages and T-Killer cells, and the humoral immunity, involving B-cells, plasma cells, and antibodies. New research, almost exclusively in mice, showed that the TH cells, although ini-

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Case Report: West Nile Fever with Meningitis

by Paul Bergner

See also Bergner, "West Nile: from the Front Lines," *MH* 2003-Fall;13(4): 1, 9-15 for a series of West Nile case studies

Abstract: A clinical description of West Nile infection is presented along with a case study and herbal therapeutics for a case of West Nile Meningitis.

West Nile fever has now spread to most of North America, and recognition of the condition and support for mild to serious cases will soon become as routine a part of the herbalists practice as the treatment for influenza. Unlike influenza, however, West Nile infection can have recurring neurological and other symptoms, such as recurring fatigue, for 18 months or more after the acute symptoms subside. Care begins with recognition of the infection, which is usually mistaken for other low grade problems, such as fatigue due to stress or depression, or simple headache. Lethargy and headache are the chief early symptoms. As the condition develops, a low grade fever and a non-painful, non-itchy rash may appear. The fever may be cyclic, with depressed body temperature early in the day, and mild fever in the afternoon and evening. The main fever usually subsides within the 24 hours after appearance of the rash, although intermittent mild relapses are common. The rash is often overlooked by the patient. Lymphatic involvement appears in some individuals and may occur anywhere in the body. Most patients do not know they have the condition, and do not feel sick enough to miss work or see a doctor. Most patients with mild illness who do see a physician are sent home with Tylenol for their headache. Some key signs for recognizing the illness:

1) It occurs during West Nile season. This may vary slightly from state to state, but is roughly from early June through the first hard freeze.

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TH1/TH2 Balance *from page one*

tially undifferentiated, transformed into two different types – TH1 cells which secrete cytokines that promote the cell-mediated immunity, and TH2 cells with cytokines that promote humoral immunity. It was also discovered that the proportions of these TH cells could become imbalanced, often with TH2 cells predominating and TH1 deficient. An immune system imbalanced in this way may produce many antibodies and pro-inflammatory cytokines, but may fail to produce sufficient macrophages or T-killer cells, which normally clear antigens, virally-infected cells, or cancerous cells. In short, the system may become hyper-reactive to stimuli, but inefficient in clearing the condition causing the stimulus, with chronic disease being the result. Subsequent research into the paradigm has mainly examined this problem of TH2 dominance, which conditions might be characterized by it, how the imbalance emerges, and which agents or strategies might restore the imbalance (Kidd; Patarca-Montero).

Table 1 shows a list of conditions that may be associated with TH2 dominance. A word of caution: Research also shows that some allergic and autoimmune conditions are characterized by TH1 dominance, and others may include either TH1 or TH2 dominance.

TH2 dominance may develop from many factors, including nutritional deficiencies; chronic inflammation; oxidative stress; general immune weakness inclining to chronic infection; some immunizations; exposure to pesticides, heavy metals, or other chemicals; and chronic stress. Several or many of these factors may be necessary to collectively cause the imbalance (Kidd; Patarca-Montero). Once established, however, the TH2 dominance may be aggravated in a vicious-cycle manner. The overactive humoral immunity, for instance, with underactive antigen clearance may make the individual more susceptible to food antigens or to chronic low grade viruses which might not otherwise cause symptoms. The increased inflammation and hypersensitivity to multiple antigens may in turn aggravate the TH2 dominance. Even normal random acute infections may elicit an unbalanced and injurious response. The result is a complicated ecological imbalance requiring multi-factorial interventions.

Stress, corticosteroids, iatrogenic effects

An important contributor to TH2 dominance is chronic stress with elevated cortisol. In the normal daily rhythm of adrenal secretions, cortisol dominates

Some conditions which may be related to TH2 dominance

- Allergic rhinitis
- Asthma
- Atopy
- Autoimmunity (some conditions)
- AIDS
- Cancer (some types)
- Depression-related immune weakness
- Eczema
- Exercise-related immune weakness
- Chronic Fatigue Syndrome
- Gulf War Syndrome
- Mercury-related immune dysregulation
- Pesticide-related immune dysregulation
- Post-immunization adverse effects
- Pregnancy (natural TH2 dominance may protect the fetus)
- Tuberculosis-related immune dysregulation

(Cavallo and Cavallo, Gleicher, Inoue et al, Kidd, Patarca-Montero et al, Wei et al)

during the activity of the day, especially in the morning, and the hormone DHEA dominates at night. Both hormones are derived from a common substrate, and excess cortisol may be produced at the expense of DHEA. Cortisol, although it inhibits TH2 immune responses, promotes the shift of undifferentiated TH cells to TH2 types, whereas DHEA promotes the development of TH1 cells (Hassig et al, Norbiato et al). Corticosteroid drugs, the treatment-of-choice in many TH2 dominant conditions can have the same effect as cortisol. Although these drugs suppress TH2 activity initially, like cortisol, they promote TH2 dominance overall, and create a vicious cycle. Supplementation of DHEA may be a critical intervention in recovery from TH2 conditions while withdrawing steroid medications. Correction of underlying lifestyle factors such as chronic stress, sleep debt, excessive exercise, poor nutrition, chronic dieting, stressful relationships, or post-traumatic-stress-disorder may be necessary. Effective herbal anti-inflammatory treatments which do not themselves unbalance the system may be useful. Of these, glycyrrhiza, which extends the half-life of endogenous cortisol and reduces the demands for production by the adrenal glands may be most useful in

the patient who is not currently taking exogenous cortisol analogues. By reducing net cortisol production it may free substrate for the manufacture of DHEA. Chinese tonic herbs, especially the category of kidney yin tonics, may also be useful.

Immunization as a trigger

Some immunizations can stimulate a TH2 imbalance and heighten hypersensitivity to other antigens. Specifically, pertussis, tetanus, anthrax, typhoid, tetanus, and cholera immunizations stimulate TH2 responses (Patarca-Montero et al). See the accompanying case studies, which each describe auto-immunity or hypersensitivity triggered by immunization. Once the system is imbalanced, unrelated antigens which formerly produced sub-clinical effects may produce active disease. Clearance of latent viruses and food antigens, for instance, may be reduced while reactivity to them may be increased. Either class of antigen may function as auto-antigens against self-tissue. The combination of elevated cortisol from stress and multiple immunization may be especially potent, and has been proposed as part of the etiology of Gulf War Syndrome (Patarca-Montero et al).

Oxidation and glutathione depletion

Glutathione is the an important protective and regulatory antioxidant inside cells. Under oxidative stress and in the absence of the full complement of dietary antioxidants to restore the glutathione, the ratio of normal glutathione to oxidized glutathione decreases. This change in within macrophages effectively switches them to TH2-triggering cells (Patarca-Montero et al). This implies that reduction of oxidative load, increased dietary intake or supplementation with vitamin C and other antioxidants, and including selenium and sulfur-containing foods which promote glutathione production, may be necessary. Milk thistle seed (*Silybum marianum*) is also known to increase glutathione levels in test animals. Oral supplementation with glutathione itself has not been demonstrated to beneficially affect intracellular glutathione levels in humans, and the glutathione precursor N-acetyl-cysteine has also failed to positively effect intracellular glutathione (Bernhard et al; Witschi et al).

Herbs affecting TH1/TH2 balance

Traditionally, herbs such reishi (*Ganoderma*), shiitake (*Lentinus*), maitake (*Grifola*), and astragalus (*Astragalus*) are important herbs for autoimmune and allergic conditions. Research into the effects of these

and herbs on TH1/TH2 balance is at best preliminary. Most such research has been done in vitro or in animal trials. Only a handful of clinical trials in humans have been conducted. To be conclusive, an herb would need to be studied in a healthy population and in a group with a specific condition, and changes in both TH1 and TH2 status measured. Even if the effects of an herb are accurately determined, specific conditions often do not fit neatly into the TH1/TH2 model (See discussion below). Clinical application of information from herbal trials would thus require case-by-case lab assessment of TH1/TH2 status (possible via a skin-prick test) and the changing status monitored. Suggestive research for the effects of some is listed below.

Astragalus

Several trials of astragalus in human subjects show a shifting in the balance of the immune system away from TH2 dominance toward a balance with TH1. The blood of a group of patients with herpes simplex keratitis was examined and found to be TH2 dominant. After treatment with astragalus, however, the imbalance was improved (Mao et al.) In a clinical trial with lung cancer patients, TH2 dominance was first established by comparison to a healthy control group, and then administration of astragalus was found to correct the imbalance (Wei et al). This is, of course, potentially useful in cancer because the TH1 system is primarily responsible for anti-tumor activity.

Ganoderma

Reishi mushroom (*Ganoderma lucidum*) is frequently used in autoimmune and allergic conditions by contemporary North American medical herbalists and by conventional physicians in China and Japan. One trial in mice showed that a reishi product stimulated a TH1 type response without reducing or otherwise affecting TH2 activity (Kohguchi et al.)

Maitake mushroom

Extracted polysaccharides of *Grifola frondosa* mushroom were found to selectively stimulate TH1 responses in mice which are genetically TH2 dominant (Kodama et al.) The authors suggest that the polysaccharide fraction promotes the differentiation of TH cells to the TH1 type. In another trial of mice with TH2 dominance attributed to the presence of tumors, researchers concluded that *Grifola* polysaccharides promoted TH1 activity and inhibited TH2 activity (Inoue). *Grifola* polysaccharide extracts are used for immune system modulation in Japan. For a general review, see Mayell. The nature of the extracts

used is proprietary, but their polysaccharide nature suggest that water-based preparations, as decoctions, or their derivatives should be preferred to alcohol extracts – polysaccharides are insoluble in alcohol.

Salvia and Coriolus

Researchers in China gave 50 mg/kg doses of *Coriolus versicolor*, along with 20 mg/kg doses of *Salvia miltiorrhiza* to a hundred healthy subjects for four months, and compared the results to placebo. The herbal combination significantly stimulated TH1 response, enhancing cell-mediated immunity. Researchers assessed the status of the patients liver and kidney function and found to adverse effects to this long-term administration (Wong et al.)

Schizandra

Schizandra chinensis has not been researched to any extent for its direct effect on TH1/TH2 balance. However it may indirectly affect that system through its adaptogenic or antioxidant effects. Research has shown that it may reduce the cortisol elevation that accompanies intense exercise in athletes (Ponassian et

al), and a number of trials shows that it enhances cellular glutathione levels, especially in the liver (Chiu et al; Ichikama et al; Ko et al; Zhu et al). Reduction of hypercortisolemia or enhancement of glutathione status may in turn support TH1 status in the immune system. Note that the antioxidant effect in research trials has been due to lignans, which are alcohol soluble. These would be present in tinctures or powders. Because the traditional alcohol dose of Schizandra in Chinese medicine is quite high (½-2 ounces per day), the powder form may be most useful.

Panax ginseng

Several trials, not included here, examined the effects of isolated ginseng constituents on immune balance. The clinical application of such research is questionable. A trial of ginseng in human patients specifically evaluating the TH1/TH2 response tested normal subjects and those with immunodeficiency. The blood of both groups showed increased activity of the TH1 system. The trial but did not measure effects on TH2 and offers no information on net immune balance (See et al.) A trial in rats also showed increased TH1 activity, and the authors speculated but did not definitively demonstrate that it also down-regulated TH2 functions (Patarca-Montero et al.) One animal trial showed that alcoholic ginseng extracts injected into mice abdomens stimulated both the TH1 and TH2 systems (Liou et al.). Note that *Panax ginseng*, which in traditional Asian medicine is considered to have a “heating” quality is traditionally contraindicated in conditions with heat signs, especially the “deficiency heat” syndromes commonly associated with autoimmunity and some allergies. On the basis of the scant science above, statements about the effect of normal oral supplementation of ginseng on immune system balance cannot be made positively.

Garlic

A trial of garlic in mice showed stimulation specifically of the TH1 system, and shifting the balance of immunity toward TH1 from TH2 (Ghazanfari et al.) A group of authors also has reviewed literature on garlic and concluded that it may be useful in cancer due to stimulating effects on the TH1 system (Lamm et al.) An in vitro trial showed, on the other hand, that garlic suppressed TH1, and those authors speculated that it may be useful in conditions associated with TH1 dominance (Hodge et al.) Garlic has pronounced constitutional heating effects, and regular or prolonged use would be contraindicated in most autoimmune and allergic conditions for this reason.

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Turmeric

Western herbalists often use *Curcuma longa* or its extracts anti-inflammatory effects in place of non-steroidal anti-inflammatory drugs in autoimmunity and other inflammatory conditions. Several trials of the effect of Curcuma on immunity show that it may promote TH2 dominance over TH1, possibly by suppressing TH1 responses. In one trial of mice suffering from a TH1 dominant experimental neurological illness, curcumin extracted from turmeric effectively reduced the TH1 response due at least in part to reduction of the differentiation of TH cells to the TH1 type (Natarajan.) Curcumin inhibited TH1 cytokine secretion in another mouse trial (Kang et al). The short-term anti-inflammatory effect of turmeric is established, but the mechanism and the long term effects on TH1/TH2 balance has not been examined, and the herb or its extract may perpetuate an immune imbalance if used chronically.

Echinacea

The effect of echinacea products on TH balance may be difficult to predict. Various research studies have established that it increases cell-mediated immunity over time (Currier and Miller; See et al; , but it also increases antibody counts (Freier et al.; Rehman et al.; Schraner et al.) Perhaps most significant in consideration of immediate effects is that echinacea acutely increases lymphocyte production, and may double levels for about 48 hours after administration (Ram). It is possible that giving echinacea to an individual who has a preexisting TH2 dominance could exacerbate autoimmunity or allergy by causing proliferation of the TH2 cell types. This could explain the acute adverse effects that sometimes occur when echinacea is taken by patients with autoimmune conditions. This author has collected fourteen case reports from professional herbalists in North America of echinacea aggravating autoimmune conditions within hours to several days after acute administration.

Another view of TH1 and TH2

Although the model of TH1/TH2 balance provides a new tool for examining immune status, critics of the model say that it is oversimplified. For a complete review, see Kidd whose review article appears in full text online. Most of the current model is based on animal research, and derived from basic research done on mice during the 1980s. Subsequent research, and especially that humans in the last three years, has shown that the early research may be inadequate to predict effects on humans.

Part of the oversimplification has been the labeling of autoimmunity, atopy, allergy, or any specific condition as being automatically due to TH1 or TH2 dominance. It is now known, for instance, that atopic patients may be either TH1 or TH2 dominant (Barth et al.; Smart and Kemp) Some autoimmune conditions are usually due to TH1 dominance, not TH2. These may include type I diabetes, rheumatoid arthritis and psoriasis (Simpson et al.), multiple sclerosis (Natarajan). Other autoimmune conditions, including systemic lupus erythematosus and inflammatory bowel disease, may be either TH1 or TH2 dominant (Hodge; Berrebi et al; Patarca-Montero).

Conclusion

In the absence of more definitive trials on the TH1/TH2 balance in humans, and on the effects of individuals herbs on that balance in patients with particular conditions, herbs are best prescribed according to their indications and contraindications based on traditional medicine rather than on theoretical reductionist science.

Cases: Immunization and TH system imbalance

Case 1

A 42 year-old woman in a health care profession received an influenza immunization. This occurred shortly after the stress of ending a relationship. Within a week she developed severe allergy symptoms, with rhinitis and red inflamed eyes. She had two cats, and had been allergic to cats during her teenage years, but not since then. Accompanying the heat signs in the head and face were cold hands and feet, a pattern she said was long-standing. This pattern may accompany “stuck” liver energy, and is a common presentation with food allergies, and sometimes with birth control pills. A formula of alteratives, liver-cooling, and liver-moving herbs rapidly resolved the acute symptoms and reduced the intensity of the coldness of the hands and feet. The diet was screened for potential food allergens in the hope that reducing their allergic load would allow her to tolerate the cat hair antigens. The strategy worked, along with a powder of Mahonia, Taraxacum, and Schizandra taken in small to moderate doses for three weeks, as the chronic pattern of digestive heat, heat signs in the head, and cold hands and feet was eliminated, and the patient could then tolerate the cat antigens.

Analysis

The woman had chronic but mostly sub-clinical symptoms of allergy to the food and cat hair antigens. The influenza immunization switched her system to TH2 dominance, resulting in strengthened allergic response but reduced ability to clear the antigens. Removal of the antigens and constitutional treatment restored the balance. In this case the Schizandra may have assisted in switching the system toward a balance of TH1/TH2 through its adaptogenic or antioxidant effects (see discussion of Schizandra in the main article).

Case 2

A 54 year-old male received a puncture wound in the foot from a sharp wire impacted with farm-related fecal matter. He received a routine tetanus shot the next day, and for the next four days experienced joint pain in all major joints. There was no indication of infection at the site of the wound. The joint pain gradually subsided over a period of weeks. Six weeks later he had a gastrointestinal infection which the doctor suggested was Norwalk virus. The chief symptoms were fever, abdominal cramping, and diarrhea. On the third day of the infection, his knee became sore, and the pain increased in severity until it would not support him and he had to walk with a cane. He had the knee treated with acupuncture and unspecified Chinese herbs, including *Panax notoginseng* for a period of two weeks, and continued to walk with the cane for another six weeks. He also took a formula of curcuma, glycyrrhiza, and plantago for anti-inflammatory effects. Eventually the knee healed, but only after permanent cartilage damage had occurred.

Analysis

The tetanus immunization initiated a powerful TH2 response resulting in the initial joint inflammation, perhaps by activating previously subclinical auto-antibodies. Although the initial symptoms subsided, the immune system remained in a TH2 imbalance, and the subsequent infection again triggered autoimmunity which attacked the knee. It is possible that the *Panax notoginseng* helped to restore the TH1/TH2 imbalance, but also possible that the curcuma, even though acutely contributing to pain relief, may have aggravated the imbalance. [See discussion in main article]

Case 3

A 35-year old army veteran was diagnosed with systemic lupus erythematosus in 1991. The onset of symptoms was dated to the time she took multiple im-

munizations in preparation for the Gulf War. She did not ultimately leave the states during the war. Symptoms are chronic joint inflammation and pain, especially in knees, elbows, hands, and chronic constant fatigue. Medications: Prednisone, Methotrexate (weekly); Indomethacin; Plaquenil; Vicodin: Narcotic-analgesic (during flares). She could not reduce medications without inducing a flare. Over the course of a ten months, she removed major food allergens from her diet (dairy, glutenous grains), was treated with an herbal formula for leaky gut syndrome. She also took milk thistle seed extract (*Silybum marianum*) for liver support and protection and turmeric (*Curcuma longa*) and bromelain as anti-inflammatories. All symptoms greatly improved, and she did not require periodic hospitalization as before. She was able to reduce her prednisone dose by 20%, and eliminated all other drugs except the methotrexate. Her anti-nuclear antibody results were near-normal and were the lowest since the onset of the disease 6 years previously. Her chronic digestive symptoms were greatly improved and her anxiety level was greatly reduced.

Analysis

The multiple immunizations switched her immune system to TH2 dominance, and her previously-tolerated food antigens began to cause major disease. Most of the progress in the case was due to elimination of those antigens and repair of the chronic inflammation in the gut. The diet was greatly improved with regard to antioxidant balance, with fewer pro-oxidant cooked oils, and more anti-oxidant fruits and vegetables. The healing of the gut may have contributed to a rebalancing of the immune system through reduction of stress. Antigenic food challenges in the leaky gut patient usually result in surges of stress hormones, and these were probably reduced in this patient. The milk thistle seed may have also assisted in immune balance by supporting normal glutathione status.

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West Nile from page one

2) The patient complains of malaise and headache, and the headache is typically frontal, and usually *behind the eyes*. This is an unusual description for a headache, but is the usual volunteered description in West Nile fever. This may progress, with meningeal complications, to a more severe whole-head headache and backache.

The acute complications of West Nile infection may be severe, including meningitis, encephalitis, and permanent neurological damage in a polio-like syndrome. Although these complications make a lot of press, they are probably less frequent in West Nile fever than the serious or fatal complications of influenza in elders – tens of thousands of elderly or immune-compromised patients die of the infection each year. Because the initial symptoms of West Nile can include neurological symptoms and stiff neck, the progression from mild to serious infection is something of a spectrum without an abrupt defining signal.

The aftermath of the condition can be troublesome in many patients. West Nile is characterized as a “shao-yang” disorder in Chinese medicine, characterized by intermittent febrile symptoms, lethargy, and poor appetite. In traditional North American herbalism it would be characterized as remittent or bilious fever, and it may resemble remitting blood infections such as malaria in its presentation. Not only does the fever frequently oscillate during the acute stage, but the entire condition may appear to disappear and then remit. This is more common for the neurological symptoms than for the fever, but may also occur with fever. A number of patients during last year’s season in Colorado had apparently completely recovered from the first symptoms of West Nile, but a period of stress within weeks brought on a relapse and full-blown encephalitis with high fever and hallucination. These and other patients also experienced periodic relapses of fatigue and neurological symptoms over the months following their infection.

A study that followed New York patients for eighteen months after initial West Nile infection found that the majority of patients continued to suffer recurring symptoms in the aftermath of West Nile for a full year (Klee et al.) Cognitive symptoms such as confusion, difficult concentration, and depression were present at much higher rates one year after infection than at baseline, as were other symptoms such as fatigue, insomnia, muscle weakness, and headache. Only 37% of

patients had experienced a full recovery at 12 months. Eighteen months after infection more than 40 percent reported difficulties with walking, muscle weakness, fatigue or insomnia, the researchers report, and 30 percent were still experiencing memory loss, confusion, depression and irritability. Functional ability seemed to reach a plateau, with no improvement after 12 months. Note that most of these patients were elderly, and baseline symptoms scored were obtained on recall, so some of the symptoms reported may be due to normal aging or the common pathologies of the elderly. Notably, full recovery was unrelated to severity of the original infection – patients with simple West Nile fever with headache were as likely to be impaired at 12 months as those with meningitis or encephalitis, although statistically there was a trend for more serious impairment in those with encephalitis. Recognition of the milder symptoms of West Nile Fever may be critical in some patients to prevent complications; supportive measures and encouragement to rest may be important in apparently mild illness, and ongoing support for the 12-18 months afterwards may also be useful.

Case Study

At the height of 2004 West Nile season in Colorado, a thirty-three year old female developed symptoms of fatigue and headache, which she attributed to stress. Within a week, she developed a backache, which a naturopath treated as a musculoskeletal problem, but which was probably the first sign of meningitis. She also had swollen glands. The next day a high fever (104 degrees) developed, and she drove herself to the emergency room. Doctors gave her fluids and prescribed ibuprofen for the head and back pain. She was told she probably had West Nile fever, but that the hospital did not routinely test for it because the test was too expensive. The client’s lack of medical insurance may have contributed to the decision. She was mentally confused the next day, and unable to remember whether or how much ibuprofen she had taken, and found ibuprofen pills sitting around in various places around her apartment. Later in the day, she was bedridden with the fever, and began to hallucinate, with visions of “angels singing opera.” Due to extreme weakness and possible partial paralysis she could not get out of bed, so called 911, fearing that she was dying. The EMT’s examined her and noted a rash on her trunk, a common sign characteristic of West Nile infection. The doctor tested the stiffness of her neck, and told her she had “borderline” meningitis. The nuchal rigidity test has a sensitivity of only 30% for meningi-

tis, being negative in 70% of cases of patients who actually have the disease. He said a definitive diagnosis would require an examination of the spinal fluid, which he declined to perform. She was again given fluids, a dose of a second non-steroidal-anti-inflammatory drug, and sent home.

I saw her the next morning. Her fever was resolved at the time, her skin was cold to the touch, but she still had a significant headache and backache. Her speech slurred occasionally, and she had occasional gait disturbance. Someone was caring for her daughter, and her mother was arriving from out of town the next day to care for them both. I recommended the following two formulas:

A tincture of equal parts of:

<i>Echinacea angustifolia</i>	Echinacea
<i>Ligusticum porteri</i>	Osha
<i>Eupatorium perfoliatum</i>	Boneset
<i>Ceanothus velutinus</i>	Red Root
<i>Glycyrrhiza glabra</i>	Licorice

This was put into an equal volume of a proprietary syrup containing unspecified proportions of:

<i>Echinacea angustifolia</i>	Echinacea
<i>Sambucus nigra</i> flowers	Elder
<i>Eupatorium perfoliatum</i>	Boneset
Thymus vulgaris essential oil	Thyme oil
Syrup	Sugar

To be taken at 1-2 droppers per waking hour for the first day, and per 2 hours afterwards until 2 ounces had been taken.

The rationale for the tincture was for immune support at the level of the lymphatics and the extracellular spaces. A tea was also recommended, with equal parts of:

<i>Mentha piperita</i>	Peppermint
<i>Achillea millefolium</i>	Yarrow
<i>Eupatorium perfoliatum</i>	Boneset
<i>Scutellaria lateriflora</i>	Scullcap
<i>Lavandula officinalis</i>	Lavender

This is a balance of tonic and relaxant diaphoretics, with an emphasis on the relaxant properties (*Eupatorium*, *Scutellaria*, *Lavandula*). The rationale was to relax the extreme tension in her system, and especially to “relax” the membranes, including the

meninges, a concept from Physiomedicalist traditions. In retrospect, *Asclepias tuberosa* (Pleurisy root) the premier “membrane relaxant” in Physiomedicalism, would have been a good addition, but this formula achieved the task. The formula also provides a mixed tonic and relaxant diaphoretic activity appropriate for the intermittent nature of West Nile fever. In her case, as in many, she had low body temperature in the morning, with mild fever in the afternoon and early evening. The chief herb in the above collective treatment is *Eupatorium perfoliatum* (Boneset) which has traditionally been considered a specific for intermittent fevers.

She misunderstood the directions, made a lot of the tea, and took one cup of the tea per hour instead of the tincture. She said the head and back pain started to diffuse within twenty minutes, were completely comfortable within a few hours, and she steadily improved after that over the course of ten days. Fortunately her mother came from another state and nursed her for a week. At three weeks, she still had regular relapses of the fatigue and exhaustion, and as I’ve found is typical with patients, she failed to relate these recurrent symptoms to the West Nile.

On the fortieth day after the original symptoms, the patient had a relapse for two days with a fever peaking between 102-103 degrees. The characteristic West Nile rash was widespread on her torso. She began taking the original herbs in decoction immediately and rested for the two days, and all symptoms resolved.

Commentary

Chronic stress contributed to the severity of the case, as she had experienced the death of her father and a divorce that left her a single mother within the previous half-year, and was experiencing financial stress related to the divorce. West Nile illness of this severity is usually limited to the elderly, or those with medical causes of weakened immunity, although younger people with predisposing weakened host resistance are by no means rare.

Klee AL, Maldin B, Edwin B, Poshni I, et al. *Emerg Infect Dis* 10(8):1405-1411, 2004

Clinical Trials

Recent Echinacea trials

by Paul Bergner

Abstract. Several failed clinical trials of Echinacea for the treatment of the common cold have received widespread press coverage in recent months, but a much more successful trial in February received no mention in the major media. The failed trials used commercial products or their equivalent, according to manufacturers dosing recommendations. The successful trial used a higher dose and higher quality form, and more closely approximated the treatment protocol of professional herbalists in the U.S.

Overview

Two trials of Echinacea in the treatment of the common cold have appeared in the medical literature in the last year (Taylor et al; Yale and Liu). These continue to receive widespread coverage in the media. The first, published in December of 2003, showed the lack of efficacy of an Echinacea product in children (Taylor et al) and the second, in June 2003, in adults (Yale and Liu). A third trial in adults, in February of 2004, showed strong and statistically significant results on both severity and duration of cold symptoms in adults, but has received virtually no media attention (Goel et al.). The first two trials used commercial products at the dose recommended by the manufacturer, while the protocol of the third trial more closely approximated the methods of professional medical herbalists in North America today.

Pediatric trial.

In a trial conducted by M.D.s and N.D.s in the Seattle area, a total of 707 upper respiratory infections in 407 children divided into an Echinacea and a placebo group were treated over a four month period. The Echinacea group received dried pressed juice of *E. purpurea* leaves, found by assay to be equivalent to the fresh juice, a product widely distributed in Germany by the Madaus company. The product was combined with syrup, and given to children aged 2-5 years old in doses of 3.75 ml twice per day, and in children aged 6-11 at 5 ml twice per day. These doses are 50% and 67% of the manufacturer's recommended doses respectively, adjusted for the age of the subjects. There was no difference between the Echinacea and the placebo group in duration, severity, days of fever, peak

Echinacea protocol

A typical protocol of a contemporary North American medical herbalist for the use of Echinacea in the common cold:

- 1) A well-made tincture of the root of *E. angustifolia* or *E. purpurea*.
- 2) The medicine administered at first onset of symptoms.
- 3) A high dose of a teaspoon or more per hour for the first few hours, then tapering to 4 tsp per day on the second day and continuing while symptoms are present.
- 4) Aggressive treatment with Echinacea especially for those with chronic immune weakness rather than those in generally good health who happen to have a minor respiratory infection.

severity, days at peak severity of symptoms. The only trend approaching significance ($p=.09$) was for the Echinacea group to have about a 30% longer period of fever than the placebo group.

Adult trial

In a double-blind trial using a standardized and concentrated extract of *Echinacea purpurea*, there was

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no benefit in the group taking the herb for a common cold over those taking a lactose placebo. The dose was 100 mg, three times a day, of a EchinaFresh, an Echinacea extract made from the leaves and flowering tops of *E. purpurea* and standardized for a content of 2.4% soluble -1,2-D-fructofuranosides, made by Enzymatic Therapy, Green Bay, Wis. It is difficult to compare the strength of the medicine to more traditional forms and doses, but it is the dose recommended by the manufacturer. The standardization to a single constituent does not guarantee activity, because the active constituents in Echinacea have not been reliably defined. No significant difference in symptom resolution between the groups was found, and symptom resolution scores were identical on days 8-9 of the treatments, failing to show even a non-significant trend favoring the Echinacea group (Yale and Liu).

Successful trial

The well-designed trial from February 2004 tested a highly standardized Echinacea product, and found statistically significant effects on both severity and duration of cold symptoms in adults (Goel et al). The product, Echinilin, Natural Factors Nutritional Products, Inc., Vancouver, BC, Canada, contains alkamides, cichoric acid, and polysaccharides at concentrations of 0.25, 2.5, and 25 mg/mL, respectively, prepared from freshly harvested Echinacea purpurea plants. A group of 282 subjects, aged 18-65 years old, with a history of two or more colds in the previous year, but otherwise in apparent good health, were divided into an Echinacea group and a placebo group. All subjects were instructed to start the Echinacea or placebo at the onset of the first symptom related to a cold, and to take ten four ml doses the first day and four four ml doses on subsequent days for seven days. The total daily symptom scores were found to be 23.1% lower in the Echinacea group than in placebo in those who followed all elements of the study protocol, and the results reached statistical significance. This trial was the best designed of the three discussed in this article, based on previous research, because: 1) The product was assayed for strength, using multiple constituents are markers 2) The subjects

Table 1

Improvement in symptom scores and duration in Echinacea group treated for the common cold, compared to placebo.

Symptom	Symptom severity	Symptom duration
Sore throat	-25%	-40%
Nasal discharge	-27%	-29%
Nasal congestion	-22%	-38%
Cough	+25%	+33%
Tiredness	-31%	-31%
Headache	-39%	-33%
Chills	-44%	-57%
(Goel et al)		

selected had evidence of chronic immune weakness. Previous trials have shown that individuals with markers of immune deficiency respond more favorably to Echinacea than those with normal immunity 3) The medicine was administered at the first onset of symptoms 4) It was given in a very high dose the first day (forty ml daily dose) and in relatively high doses on subsequent days (sixteen ml per day) and 5) the dose was repeated frequently. This constitutes a "best case" trial according to the standards of contemporary herbalism. Table 1 shows the results of the trial, in terms of reduced symptom severity and reduced duration compared to placebo. In the Echinacea group, 50% of subjects had a 50% reduction in severity scores by the 4th day, while the same reduction in the placebo group took 5.5 days. Of the symptoms, only cough was greater in severity or duration in the Echinacea group than in the placebo group. Note that a cough is a vital and curative symptom in respiratory infection, and a slightly stronger cough might indicate heightened vitality.

The trials by Taylor et al, and Yale and Liu were well-designed from a scientific point of view, and demonstrated, according to the standards of modern science, that the two products were ineffective in the test groups in the dose recommended by the manufacturer. Goel et al used a different product, and set the dose according to the dose/kg used in rodent trials, larger by a factor of about three than that in Taylor et al. Because of the unspecified strength of the product used by Yale and Liu, no comparison can be made.

Book Reviews

Plant Medicine in Practice: Using the teachings of John Bastyr, by William Mitchell. Philadelphia, Churchill Livingstone, 2003. ISBN: Hardcover. 458 pages. \$66.95

John Bastyr, ND, learned first learned herbalism from his mother, who followed the Kneipp system of herbalism and nature cure. He was eventually licensed as a physician, began practicing medicine in the 1930s, and continued in practice for almost 60 years. For 35 years, he lectured on medical herbalism among other topics to physicians-in training, first at National College of Naturopathic Medicine, and later at Bastyr University, which was named after him. (Note: He had no role in the founding or administration of Bastyr University). By the 1970s, he was possibly the most clinically experienced medical herbalist in North America. His student from that time, William Mitchell, N.D., after practicing twenty-five years himself, confirming and expanding on Bastyr's observations and experience, has offered this textbook of materia medica. Mitchell also draws on the clinical observations of naturopathic colleagues in his own generation. The book reflects without a doubt more accumulated clinical experience than any similar book in print in North America today. Bastyr's methods of herbalism reflect roots in the Eclectic medical tradition, but they are clearly expanded and developed through his decades of experience and teaching. The book is arranged according to the structure of his lecture, by herbal action or organ affinity, with 73 chapters. While his observations make up the foundation of the book, most of the work is actually Mitchell's, and Bastyr's teachings are "spun" somewhat with the addition of some constituent-science. The title is thus misleading, but for the advanced student or professional practitioner, Bastyr's clinical pearls, proven and passed on by Mitchell, are treasures.

Medicinal Plants of the Mountain West: Revised and Expanded Edition, by Michael Moore Sante Fe: Museum of New Mexico Press, 2003 ISBN: 0-89013-454-5 Soft-cover 351 pages. \$24.95

Twenty-five years have passed since Michael Moore's first book on the plants of the Mountain

West was published. The book rapidly became a classic text for the growing movement of medical herbalism in North America, especially in the West. Now an older, wiser, and more experienced Moore has updated the book. Although adding only twelve new herbs, he has doubled the size of the text. Included are comments on the environmental status of many of the plants. Also covered are plant identification, habitat, collecting tips, therapeutic uses, contraindications, how to prepare medicines, and growing information. Most monographs are several pages in length. Even if you have the first book, you'll be glad you got the update.

Botanica Poetica: Herbs in Verse, by Sylvia Seroussi Chatroux, M.D. Ashland, Oregon: Poetica Press, 2004. ISBN:0-9665524-2-3 Hardcover 112 pages. \$18.00

Tired of trying to decipher obscure scientific language in herbal clinical trials? Take a break with some herbal poetry to refresh your spirit. I initially approached this book with some skepticism, but that vanished after reading the first poem, and has not returned after reading twenty more. The style and rhyming is humorous, but the content is quite solid. I've

Continued on page twenty

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never before seen a bibliography in a poetry book, but Chatroux has one, and it includes some of my favorite herbal reference books. She's done her homework on every single herb, and somehow managed to synthesize the key information about each of the 111 herbs into verse. Most include, in addition to primary uses, information on adverse effects, energetics, or species names. The poems amaze my students and make them laugh. Me too. The poems are interspersed with old woodcuts of the plants. This book makes a wonderful gift for your favorite herbalist or student.

A Review in Verse

The rhymes are funny, poignant too
her research thorough, the content's true.
One thing's sure, her poetry
is a lot more fun than chemistry

Chatroux, a Family Practice physician who incorporates natural therapies, had plenty of practice before turning to the subject of herbal materia medica for her poetry. She's previously done volumes on homeopathy (*Materia Poetica: Homeopathy in Verse*) and pathology (*Medica Poetica: Malady in Verse*), each with the same skillful light verse combined with solid content.

Dandelion

Taraxacum officinale

On any lawn, you're apt to find
A weed that grows call Dandelion.
Its roots and leaves are known to cure
To heal the liver, make blood pure
And it is true that Taraxacum
Is also full of potassium
In case you need to diurese
It's powerful and works with ease
It will not leave you all deplete
Of minerals, it is replete
So, should your liver start to ail
The flow of bile begin to fail
If you've a case of flatulence
A loss of appetite perchance?
The bitter herb from root and leaf
Will surely bring you some relief
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Relieve congestion, eliminate
Kidneys, liver, stomach, spleen
This common weed does wonders keen
The bitter cool of root and herb
Will on your system work superb.

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