

CAM Approaches to Psoriasis: A review of traditional and alternative treatments for the Chiropractic Physician

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Senior Research Project: Literature Review

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October 15, 2012

ABSTRACT

Psoriasis is a common skin disease or condition that causes the skin to present with erythema and irritation and affects people of all ages, but especially those aged fifteen to thirty five. The erythema is caused by hyperemia of the capillaries in the lower layers of the skin. Most people with psoriasis have thick, red skin with flaky, silver-white patches called scales. Although psoriasis is not contagious it plays a critical role in self-esteem of the individual suffering from the condition. The etiology of psoriasis is unknown at the present time but many doctors and scientists believe the condition to be the result of an autoimmune attack of healthy skin cells. Traditional approaches to treat psoriatic lesions have included the following: topical therapy, phototherapy, and systemic therapy, some of which lie outside the scope of the practicing chiropractor. This paper will review and reflect the efficacy of traditional treatments of psoriasis, with its attendant shortcomings and then end with a discussion on techniques and strategies that encompass the scope of Chiropractic and enlist the skill set of the trained Chiropractic physician such as nutritional counseling, stress management, and chiropractic adjustments.

Introduction

Psoriasis is a common skin disease or condition that causes the skin to present with erythema and irritation. The erythema is caused by hyperemia of the capillaries in the lower layers of the skin. Most people with psoriasis have thick, red skin with flaky, silver-white patches called scale that develop on the extensor surfaces of the elbow and knees and the scalp. (1) Psoriasis is most common between the ages of ages fifteen and thirty five. Although psoriasis is not contagious it plays a critical role in self-esteem of the individual suffering from the condition. (2) The etiology of psoriasis is unknown at the present time but many doctors and scientists believe the condition to be the result of an autoimmune attack of healthy skin cells. There appears to be a hereditary component to the etiology of the disease as members of families tend to develop the disease. (3) When a single disease has multiple alternative modes of therapy it is obvious that its etiology is unknown and that no one form of therapy is ideal. This is especially true of psoriasis, for which multiple alternative treatments have been used and suggested. Among these include traditional approaches involving topical therapy, phototherapy, and systemic therapy. These forms of therapy have their benefits, as well as their drawbacks. No single treatment is ideal and it is rare for a patient not to be treated with several alternative treatments during their lifetime. There are many factors that influence the choice of therapy for psoriasis. It is a disease that can begin at any age and have continuous relapses throughout life. Often times treatment is selected based on its ability to clear the psoriatic lesions, or at least reduce a portion of those lesions. (3) This paper will reflect and review the efficacy of traditional approaches of psoriatic treatment and then end with a review of the literature relative to mechanisms of treatment that a CAM practitioner or chiropractor might employ to treat psoriasis along with their relative consequences and success. The article will review the literature that employs techniques and strategies that encompass the

scope of Chiropractic and enlists the skill set of the trained Chiropractic physician. It is not intended to review, in detail, theories relative to the pathogenesis of the disease but rather to provide a resource to the chiropractic student and physician relative to important therapies available for their patients who are suffering under the siege of psoriasis.

Traditional Approaches

Traditional approaches to the treatment of psoriasis include topical therapy, phototherapy, and systemic therapy. The selection of any one treatment over another might seem a daunting task especially when a disease, such as psoriasis, has an unknown etiology. Anne Shannon Monroe reminds us that “when a thing is understood, the cure is half accomplished.” (4) Traditional thinking would identify the causative agent and/or event and then speedily remove the offenders to promote satisfactory healing. Treating psoriasis is much more complex than merely wiping the skin lesions with an antibiotic wipe and calling it a day. There are so many factors that must be taken into account to provide substantial relief, both physiological and psychological. The described forms of therapy below have their benefits, as well as their drawbacks, so we must remember that no single treatment is ideal and it is rare for a patient not to be treated with several alternative treatments during their lifetime. (3)

Topical Therapy

Topical therapies for the treatment of various skin lesions, especially psoriasis, are perhaps the most difficult approaches to exact patient compliance. Any treatment regimen that requires multiple applications throughout the day will probably end in patient non-compliance, which is why many practitioners favor a higher dosage with fewer applications. Among the plethora of

creams, emollients, and ointments prescribed by dermatologists; topical steroids and tars lead the way in effectiveness and are, therefore, more popular among practitioners and patients alike.

Topical Steroids

The action of topical steroids is believed to induce vasoconstriction thereby reducing the attendant erythema, a hallmark presentation of psoriasis, reduce cell proliferation and turn-over, and having an anti-inflammatory effect on the area being treated. (3) One of the major drawbacks to excessive corticosteroid use is developing resistance to the treatment agent thereby reducing its effectiveness of the above described mechanism of action of the agent. As with all medications, whether oral or topical, there may remain potential side effects for continued use and the recognition and acknowledgment of these side effects is important in the development of any effective and safe treatment plan that make both practitioner and patient happy. Prolonged steroid use of at least three weeks could lead to striae and atrophy of the area of application. Striae or stretch marks are a form of scarring on the skin with an off-color hue. They are caused by a tearing of the dermis, which over time may diminish, but will not disappear completely. The tearing of the dermis is due to thinning of the dermal and epidermal skin layers and could be permanent, leading to easy bruising, lacerations, and scarring. (20, 22)

In addition to topical side effects, excessive corticosteroid use over a large area can lead to systemic side effects including pituitary adrenal axis suppression and a reduction in plasma cortisol. (21) Due to the serious complications mentioned above, corticosteroid use is best utilized when no other treatment is available or others have failed. (23) Patients prescribed corticosteroids for treatment of their psoriasis should follow the prescribing directions in exactness and communicate openly and frequently with their doctor regarding treatment so as to avoid any side effects discussed above.

Coal Tar

In the past, coal tar treatments were used to treat many various skin lesions, including psoriasis. However, because of the intensity of the daily treatment regimen for nearly four weeks many physicians have abandoned the practice of using tar to treat psoriasis. The reason for the abandonment is not due to the ineffectiveness of the treatment but rather the time demands of it and some potential adverse side effects that include smell, clothing stains, surface burning, and folliculitis. (3, 24) Also as newer treatment options have become available, physicians and patients have turned away from the tried and true regimen of coal tar applications to much simpler treatments that involve taking a daily systemic or biologic pill. It is much more convenient this way but not without a price. Despite the turning to newer treatment options many still utilize the tried and true tar regime, although finding a practitioner willing to commit to the treatment is getting more difficult to find in the United States. (24) The main objective in the utilization of coal is to overwhelm the skin cell proliferation process by altering the epidermal skin DNA synthesis patterns. (3) Perhaps one reason for the extensive treatment time and commitment is due to the fact that a coal tar treatment alone doesn't affect the psoriatic lesion very quickly but when coupled with another treatment such as UV photo therapy there tends to be an appreciable difference. (5)

Phototherapy

The use of phototherapy has proven to be another effective treatment regimen for the treatment of psoriasis. Phototherapy refers to the use of non-ionizing electromagnetic radiation. (13) This paper reflects on the utilization of ultraviolet radiation (UVR) in the treatment of psoriasis. UVR is part of the wide spectrum of electromagnetic radiation that ranges from radio waves to cosmic rays. The ultraviolet spectrum utilized to treat psoriasis comprises the wavelengths from 200nm to 400nm, with the energy contained in the wavelength being inversely proportional to the wavelength. The lower or smaller the wavelength the greater the impact that wavelength will

have on biological tissues. (13) In fact, the wavelengths that are nearing the 200nm threshold approximate the low range of x-rays. It is hypothesized that photons of higher energy radiation such as x-rays may cure psoriasis but not without the cost of unwarranted physiological effects. Due to the nature of the varying of physiological effects of the different wavelengths within the ultraviolet portion, this portion of the spectrum has been further subdivided into three categories according to their wavelengths. The subcategories are UVC, UVB, and UVA, with the following wavelengths (200-290nm), (290-320nm), and (320-400nm) respectively. (13) A natural source of UVC is from the sun, which approximates x-ray, is entirely absorbed by the atmosphere. Optimal wavelengths are between 300 to 320nm. Any wavelength below 300nm can often result in excessive erythema (13). In order to harness a certain wavelength artificial UV radiation has been designed. Although the mechanism of action for the treatment of psoriatic lesions with UV is not fully understood, the therapeutic results of its use suggest that UVR causes a decrease in DNA synthesis in the proliferating cells of the epidermal and dermal layers of the skin. Obviously each patient will respond differently to the various wavelengths and so emphasis should be placed on taking an adequate health history to determine a patient's sensitivity to UV and also any contraindications that may exist in regards to medications that they may currently be taking. UVB is chosen most often for individuals that appear to have photo-sensitive skin, or fair skin (Type I or II). (28, 29) As mentioned previously, coal tar used in conjunction with UVB has proven to be effective in treating psoriasis. The combined process, called the Goeckerman regimen, involves an application of tar prior to the administering the UV therapy. The combined therapies affect the skin DNA by reducing the hyper-proliferation of epidermal skin cells and reducing the apparent erythema in the area being treated. The combination of tar and UV as utilized in the Goeckerman regimen may require lower doses of UVR to achieve similar results

to UVR treatment in higher dosages alone. (26, 27) The use of UVR in the treatment will typically show dramatic results after 20-40 treatment sessions but a very high cumulative dose may be required to achieve complete remission. (13). A potential side effect to be considered when considering UVR therapy is that of skin cancer. This risk of UVR being regarded as a serious long term hazard has remained unsettled (13), however, epidemiologic and laboratory investigations continue to emphasize the potential carcinogenicity of UVR (13). Since the early 1970's to 1986, there has only been one clinical study that demonstrated any significant increase in malignancies in patients receiving UVR therapy.

Systemic Therapy

Systemic therapy is defined as any treatment that utilizes substances that travel through the bloodstream, reaching and affecting cells all over the body. One traditional substance that has been used to treat psoriasis is methotrexate.

Methotrexate

Methotrexate is used to treat severe psoriasis when other treatments have failed. Methotrexate, as a folic acid antagonist, has a systemic effect on hyper-proliferation of cells by attacking at the cellular level by reducing the impact of folic acid on cell division.

Folate is important for cells and tissues that rapidly divide. (30) Cancer cells divide rapidly, and drugs that interfere with folate metabolism are used to treat cancer. Similarly, epidermal and dermal cells divide and proliferate rapidly in psoriasis and similar drugs are used to treat this condition. The antifolate methotrexate is a drug often used to treat psoriasis because it inhibits the production of the active form of tetrahydrofolate (THF), from the inactive dihydrofolate (DHF). There are, however, side effects to using methotrexate which can be toxic. Some of these

side effects include gastrointestinal inflammation, reduction in bone marrow production, kidney failure, and liver complications and failure. (31, 32, 33) Despite the complications and risks involved in the treatment with methotrexate, a systematic review by Jones et al in 2007 revealed that patients taking 7.5-15mg of methotrexate weekly for psoriasis showed significant reduction in the surface area comprised of the psoriatic lesion in just twelve weeks when compared to placebo. The amount of psoriatic lesion reduction was 114cm², whereas, the psoriatic lesion reduction with placebo was 0cm². (35, 36) In long term use, another systematic review found that twenty eight percent of people taking long term methotrexate developed liver fibrosis, five percent developing advanced liver disease. (37) Patients that are prescribed methotrexate for their psoriasis need to have their liver monitored closely (34) and when treatment was stopped forty five percent of the patients experienced a full relapse within six months.

CAM APPROACHES

The Association of Chiropractic Colleges (ACC) stated in 1996 that chiropractic is a health care discipline which emphasizes the inherent recuperative powers of the body to heal itself without the use of drugs or surgery. The practice of chiropractic focuses on the relationship between structure (primarily of the spine) and function (as coordinated by the nervous system) and how that relationship affects the preservation and restoration of health. (25) Health is the natural state of individuals, and any departure from this state (homeostasis) represents a failure of the individual to adapt to the internal and external environment or is the result of adverse adaptation. The innate or natural tendency of the body is to restore and maintain health by compensating mechanisms, reparative processes, and adaptive responses to genetic and acquired limitations. (25)

Simply put, matter has limitations and when brought to those limits, accommodations must be made. In the case of psoriasis, the etiology is unknown at the present time but many doctors and scientists believe the condition to be the result of an autoimmune attack of healthy skin cells and still others believe there to be a biopsychosocial aspect of the condition. The chiropractic physician can aid the body with the homeostatic drive by helping psoriatic patients reduce stress in their lives, counsel them on nutrition, and provide the facilitation the body needs through the chiropractic adjustment.

Stress Reduction/ BioPsychoSocial Aspect

Somatically psoriasis is mostly a harmless affection of the skin, but the psychological damage which it causes can be great because the psoriatic patient is distinguished by an external mark. (13) It now is generally accepted that many diseases are affected by psychological factors, such

as stomach ulcers and asthma. Emotional factors, also known as stress, can precede the onset or a relapse of psoriasis. (13)

RH Seville investigated the relationship between the onset of psoriasis and stress in 1977, 1978, and 1983. He discovered that of 132 patients, 39% remembered a psychic trauma within one month's time previous to the onset of psoriasis. Patients described the psychic trauma as such things as serious family fights, death or hospitalization of a loved one, testing situations, etc. Seville was able to identify a correlation between traumatic events and the onset of the disease as compared to the other two control groups of the study. (14, 15, 16) Seville further recognized a significant pattern of healing wherein the patients that had the skin disease and were exposed to stress prior to onset, had considerably better prognosis compared to the non-stress patients. Furthermore, after a patient discovers they have psoriasis, most of the time they are not limited by physical function but rather they are immobilized by their perception of themselves and the world around them. So much emphasis is placed on our looks and beauty in society today and when patients become plagued with noticeable skin lesions, mental stress persists, compounding the stress related condition. The quality of our external appearance also contributes to the quality of our self-concept. (13)

Physicians have the wonderful opportunity and responsibility to influence the patient psyche for the better and help modify the negative self-concept.

Jane E Brody commented in the New York Times in 1983 that "the brain influences all sorts of physiological processes that were once thought not to be centrally regulated. The studies also show that the traditional concept of "stress" as a demanding life event is too imprecise to use as a measurement of how stress affects health. What is distressing to one person may be stimulating

to another. Rather, the researchers are finding it is *how* a person responds to life events, not the events themselves that influences susceptibility to disease. The studies indicate that failure to cope well with stress can impair a person's ability to fight off illness, whereas, adequate coping with a high stress life may reflect "psychological hardiness" that is actually protective." (17)

There are a variety of stress reduction techniques at the disposal of stressed out patients and their physicians such as self-help groups, hypnosis, and general relaxation techniques. (18)

The ability to align oneself to a group of people that have similar difficulties offers patients an opportunity to learn coping mechanisms to stressors in their life and how others have success in managing their disease, both physiologically and emotionally. This group setting allows a discussion of the numerous treatment options and their efficacy. Relaxation techniques can correct stress patterns by releasing calming hormones, help modulate the immune system, change breathing patterns, and influence blood pressure, heart rate, and overall muscle tension.(21)

Visualization techniques, like hypnosis, allow a person to develop a better mental image of their surroundings and of themselves by allowing a trained hypnotist to help an individual to focus on positive thoughts and events, thus reducing sympathetic demand. (21) The above mentioned stress reduction techniques have little evidence, when used alone, to support significant improvement or complete remission, but may be helpful when used in conjunction with other treatment regimens.(21)

Henry Ford is attributed with saying, "Whether you think you can or can't, you're right". (19) If a person thinks something is not possible or out of their reach, they will probably not commit much energy and resources to accomplishing that goal. Self-help groups, relaxation techniques, hypnosis and exercise help the patient to better understand the biopsychosocial aspect of their

condition and provide an avenue for relief. The wise physician will match the type of treatment to the patient's individual coping ability and willingness to participate in their own well-being.

Nutrition

John Pagano, in his book, entitled *Healing Psoriasis*, wrote relative to the impact of diet and nutrition on psoriatic flare up. Dr Pagano had great success with psoriatic regression with many patients that modified their dietary intake and underwent various cleansing processes. Dr Pagano advocates a more alkaline diet as composed to the highly acidic diet that plagues many Americans today. The tendency toward a relatively stable equilibrium between the elements that comprise the human body is maintained by varied physiological processes and is termed homeostasis. The time honored adage of "you are what you eat" is exactly that. Our remarkable bodies do the best they can with the elements that we provide it. American diets tend to be highly acidic, whereas homeostasis tends to desire the body in a more alkaline state. Dr. Pagano advocates an alkaline diet that includes such things as fresh fruits and vegetables or most food stuff that have high water contents in them. These food types are easily digestible and can be assimilated faster and quicker in the human system. Acidic food sources such as fats and oils, proteins, sugars, and starches tend to tip the homeostatic scale to the acidic side and accumulations develop rendering the entire system acidic and in an inflamed state. The inflammatory effects of certain foods has been greatly identified by Dr David Seaman. On his website he discusses dietary de-flaming in an attempt to help people reduce their "pro-inflammatory state" that has developed overtime within the body. He notes that poor nutrition, as a lifestyle, could generate chronic inflammation and referred to this as the diet-induced pro-inflammatory state. He indicates that every meal will either promote or inhibit inflammation. Patients need to be taught how to eat properly. A prolonged "pro-inflammatory state," acts as the

fertilizer needed to grow a chronic disease such as heart disease, or something less life-threatening like psoriatic flare ups as suggested by Dr Pagano and Dr Seaman alike. (38)

Chiropractic Adjustment

According to the Association of Chiropractic Colleges, chiropractic is a health care discipline that emphasizes the inherent recuperative powers of the body to heal itself without the use of drugs or surgery. Chiropractors focus on the relationship between the structures of the spine and function as it is coordinated through the nervous system and how that relationship affects the preservation and restoration of health. (25) Interference of neural transmission can be hindered by what the chiropractic profession terms a “subluxation”. A subluxation is a complex of functional, structural, and/or pathological articular changes that compromise neural integrity and may influence organ system function and general health. (25). A subluxation is evaluated, diagnosed, and managed through the use of chiropractic procedures based on the best available rational and empirical evidence. The preservation and restoration of health is enhanced through the correction of the subluxation by the chiropractic adjustment. (25) Dr. Ashley Cleveland further elucidates the role of chiropractors in health; wherein she says that chiropractors, along with other non-allopathic practitioners, emphasize the value of care at the pre-symptomatic stage, when the patient is experiencing “stress” to the body-mind system. Intervention at this point seeks to prevent pre-symptomatic abnormalities from developing into disease. At this stage, the chiropractor acts largely as a health coach, advising the patient about conservative self-care strategies such as diet, exercise, and stress management techniques. The chiropractor checks or inspects the patient’s spine for subluxations and provides the appropriate adjustments to address spinal biomechanics to foster optimal functioning of the nervous system, and thus maintain health. (25) The structural and neural components of the integumentary system can be greatly

impacted by the chiropractic adjustment by promoting an environment where the nervous system is functioning at full capacity.

Conclusion

Psoriasis is a common skin disease or condition that causes the skin to present with erythema and irritation. The etiology of psoriasis is unknown at the present time but many doctors and scientists believe the condition to be the result of an autoimmune attack of healthy skin cells.

When a single disease has multiple alternative modes of therapy it is obvious that its etiology is unknown and that no one form of therapy is ideal. This is especially true of psoriasis, for which multiple alternative treatments have been used and suggested. Among these include traditional approaches involving topical therapy, phototherapy, and systemic therapy. These forms of therapy have their benefits, as well as their drawbacks. No single treatment is ideal and it is rare for a patient not to be treated with several alternative treatments during their lifetime. There are many factors that influence the choice of therapy for psoriasis. Often times treatment is selected based on its ability to clear psoriatic lesions, or at least reduce a portion of those lesions. (3) This article reflected on the efficacy of traditional allopathic methods of treating psoriasis with their inherent complications of merely treating the unsightly skins lesions or rather the symptoms of perhaps a relatively unstable body system. The latter half of this article reflected on treatments or techniques that a CAM practitioner or chiropractor might employ to treat psoriasis along with their relative consequences and success. The article limited the techniques and treatments to stress reduction, nutritional counseling, and the chiropractic adjustment; all of which encompass the scope of Chiropractic and enlists the skill set of the trained chiropractic physician. The psoriatic patient would benefit greatly by starting conservatively and seek to understand the etiology of his or her condition and apply some of the CAM approaches to dealing with

psoriasis, as discussed, first before attempting to treat psoriasis completely from an allopathic standard.

References

1. Habif, Thomas P. 2005. *Skin Disease: Diagnosis and Treatment* 2nd edition. Elsevier Mosby, St Louis, MO. 106-115.
2. Sampogna, F, Chren, MM, Melchi, CF, Pasquini, P, Tabolli, S, Abeni, D. February 2006. Age, Gender, Quality of Life and Psychological Distress in Patients Hospitalized with Psoriasis. *British Journal of Dermatology*. 154 (2): 325–31. PMID 16433804.
3. Lowe, Nicholas J. 1986. *Practical Psoriasis Therapy*. Year Book Medical Publishers, Chicago IL,
4. Pagano, John O.A. 2009. *Healing Psoriasis: The Natural Alternative. The Drug Free Program that Really Works*. John Wiley & Sons, Hoboken, New Jersey.
5. Weinstein, G.D., White, G.M. 1993. An Approach to the Treatment of Moderate to Severe Psoriasis with Rotational Therapy. *Journal of the American Academy of Dermatology*. 28 (3): 454-458.
6. Trozak, J. 1999. Topical Corticosteroid Therapy in Psoriasis Vulgaris: Update and New Strategies. *Cutis* 64: 315-318.
7. Farber, E.M., Nall, L. Childhood Psoriasis. *Cutis* 1999; 64: 309-314.
8. Abel, E.A. Phototherapy: UVB and PUVA. *Cutis* 1999; 64: 339-341.
9. Klaber, M.R. Ultra-violet Light for Psoriasis. *Physiotherapy*. 1980. 66(2): 36-38.
10. Bright, R.D. Methotrexate in the Treatment of Psoriasis. *Cutis* 1999. 64: 332-334.
11. McCullough, J.L., Weinstein, G.D. *Cell Proliferation*. Edinburgh, Churchill Livingstone. 1983.
12. Roenigk H.H., Maibach H.I. *Psoriasis* Marcel Dekker, Inc., New York 1985.
13. Mier, Paul D. *Textbook of Psoriasis*. Churchill Livingstone, New York, 1986. 84-95.
14. Seville, RH. 1977. Psoriasis and Stress. *British Journal of Dermatology*. 97: 297-302.
15. Seville, RH. 1978. Psoriasis and Stress II. *British Journal of Dermatology*. 98: 151
16. Seville, RH. 1983. Psoriasis, Stress. Insight and Prognosis. *Seminars in Dermatology*. 2: 213-216.
17. Brody, Jane E. Emotions to Influence Nearly Every Human Ailment. *New York Times*. May 24, 1983.
18. Kantor S.D. Stress and Psoriasis. *Cutis* 1990; 46: 321-322.
19. Quote World Website, Accessed 7/26/2012. <http://www.quoteworld.org/quotes/483417>
20. Stevanovic D.V. 1972. Cortico-steroid induced atrophy of the skin with telangiectasia. *British Journal of Dermatology*. 87:548-556.
21. Scoggins RB, Kliman B. 1965. Percutaneous absorption of corticosteroids. *New England Journal of Medicine*. 273:832-840.
22. Wilson L, Williams DI, Marsh SD. 1973. Plasma corticosteroid levels in outpatients treated with topical steroids. *British Journal of Dermatology*. 88:373-380
23. Berth Jones, John. March 1994. Prescribing in Psoriasis. *The Practitioner*. 238:231-234.

24. Durocher HJ. (Summer 2011). National Psoriasis Foundation: Psoriasis Advance. Volume 9: Number 3. In To treat or not to treat... with coal tar. Retrieved 10/13/2012, from <http://psoriasis.org/publications/advance/2011/summer/goeckerman>.
25. Cleveland A, Phillips R, Clum G, (2003). The Chiropractic Paradigm. In Redwood D, Cleveland C., Fundamentals of Chiropractic. (pp. 15-27). St Louis, MO: Mosby
26. Anderson TF, Waldinger TP, Voorhees JJ. 1984. UV-B phototherapy, an overview. Archives of Dermatology. 120:1502-1507.
27. Stern RS, Zierler S, Parrish JA. 1980. Skin, carcinoma in patients with psoriasis treated with topical tar and artificial ultraviolet radiation. Lancet. 1:732-735
28. Weinstein GD, White GM. 1993. An approach to the treatment of moderate to severe psoriasis with rotational therapy. Journal of the American Academy of Dermatology. 28 (3):454-458.
29. Abel EA. 1999. Photo therapy: UVB and PUVA. Cutis. 64:339-341.
30. Kamen B. 1997. Folate and antifolate pharmacology. Seminars in Oncology. 24 (5 Suppl 18): S18-30-9. PMID 9420019.
31. Rubio IT, Cao Y, Hutchins LF, Westbrook KC, Klimberg VS. 1998. Effect of glutamine on methotrexate efficacy and toxicity. Annals of Surgery 227(5): 772–8. PMC 1191365. PMID 9605669.
32. Wolff JE, Hauch H, Kuhl J, Egeler RM, Jurgens H. 1998. Dexamethasone increases hepatotoxicity of MTX in children with brain tumors. Anticancer Research 18 (4B): 2895–9. PMID 9713483.
33. Kepka L, De Lassence A, Ribrag V, Gachot B, Blot F, Theodore C, Bonnay M, Korenbaum C, Nitenberg G. 1998. Successful rescue in a patient with high dose methotrexate-induced nephrotoxicity and acute renal failure. Leukemia & Lymphoma 29 (1–2): 205–9. PMID 9638991.
34. Griffiths CEM, Clark CM, Chalmers RJG, et al. 2000. A systematic review of treatments for severe psoriasis. Health Technol Assess 2000. 4:1-125 Search date 1999.
35. Jones G, Crotty M, Brooks P. 2007. Interventions for treating psoriatic arthritis. An overview of therapy and toxicity. The Cochrane Library. Issue 3:2007. Chichester, UK: John Wiley & Sons Ltd. Search date 2000.
36. Wilkens RF, Williams HJ, Ward JR, et al. 1984. Randomized, double-blind, placebo controlled trial of low dose pulse methotrexate in psoriatic arthritis. Arthritis Rheum. 27:376-381.
37. Whiting O'Keefe QE, Fye KH, Sack KD. 1991. Methotrexate and histologic hepatic abnormalities. Am J Med. 90:711-716.
38. Seaman, DR. (October 17, 2012). Deflaming. In Deflaming in Perspective. Retrieved October 17, 2012, from <http://deflame.com/deflaming/>.