Volume 15, Issue 1, Winter/Spring 2008

VitaLink

The professional journal of the Canadian Association of Naturopathic Doctors

Autoimmune Disorders

Canadian Association of Naturopathic Doctors

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Vital Link

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The Vital Link is the professional journal of the Canadian Association of Naturopathic Doctors (CAND). It is published primarily for CAND members and features peer-to-peer research-based articles, relevant naturopathic information and news and events that affect CAND members and the naturopathic profession in Canada. The Vital Link has an outreach to other health care professions and promotes licensed naturopathic doctors to corporations, insurance companies and the Canadian government.

Circulation
The Vital Link is published three times per year and is distributed to more than 1050 licensed Canadian NDs; over 600 students of CNME accredited naturopathic programs in Canada and the U.S., and the CAND supplier members. The Vital Link is also distributed in the CAND's media kit.

Advertising
Professional vendors that provide NHPD-compliant products or other services to NDs are encouraged to advertise in the Vital Link. The CAND's advertising partners enjoy unequalled exposure to licensed Canadian naturopathic doctors.

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Cover designed by Jesse Edwards

Upcoming Themes:
Summer 2008 – Environmental Medicine
Fall 2008 – First Aid/Acute Care

Submissions
When writing for the Vital Link, keep in mind its broad readership and outreach to other professions. Your contribution to the Vital Link will benefit the naturopathic profession as a whole and provide you with personal professional exposure. Previously unpublished material is preferred. Please contact the editor for submission guidelines.

PRESIDENT'S CORNER

Dr. Iva Lloyd, BScH, RPP, ND, CAND Chair

The CAND continues to focus on increasing the awareness and visibility of naturopathic medicine. In addition to the initiatives that the CAND does on an ongoing basis to support its members, there are a number of new initiatives for 2008 that I trust you will find interesting and beneficial.

- **Commercial**. The CAND commercial has been a valuable marketing aid for the profession. This year we will be updating the commercial by introducing new voices and expanding its air time..
- **Naturopathic Medicine Week** has been a national awareness initiative for the past six years. This year the CAND will be increasing its investment in the promotion of Naturopathic Medicine Week and providing all members with posters and handouts to make it easier to participate. A national campaign with strong participation will benefit us all.
- **Bequest Program.** The CAND recently launched a bequest program. The bequest program promises to provide our profession with the needed resources to engage in further awareness initiatives and support regulatory and research initiatives. We encourage you to have the bequest brochures available in your clinic for patients to pick up. The brochures are free of charge and are available through Heather at the CAND office. For more details about the CAND bequest program please turn to page 14 or see the letter enclosed in this issue of the Vital Link.
- **History Book**. By the end of 2008, the history of the naturopathic profession in Canada will be compiled and ready for printing. During the year we will be contacting many of the early graduates, and we will be looking for stories, write-ups and pictures about the profession. This is a one-time initiative and we hope that you take the opportunity to participate. The History Book will be launched at Health Fusion 2009 in Montreal.
- **Research Tab**. In the spring of 2008 we will be adding a research tab to the public side of the CAND website. This section will provide other health care professionals with short abstracts and current research on key aspects of naturopathic medicine. The aim of this section is to support Naturopathic Doctors in building strong professional alliances with other health care professionals.

There is always a lot going on at the CAND. We encourage you to read the monthly E-Link, the quarterly Vital Link and to check the members section of the CAND website on a regular basis in order to stay informed.

We welcome your questions and your feedback. Please contact either myself or Shawn O'Reilly at i.Lloyd@naturopathicfoundations.ca or soreilly@cand.ca

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WINTER 2008

GOVERNMENT RELATIONS REPORT

Shawn O'Reilly, CAND Executive Director, Director of Government Relations

December was a busy month for Government Relations as the government rushed to finish its 2007 initiatives before it recessed for the holiday break. We responded to eight health related proposals, consultations and requests for comment. The pace has continued into the New Year with submissions on Extraordinary Use New Drugs, The Special Access Program, including nomination of Dr. Paul Saunders PhD, ND, DHANP to the Expert Advisory Panel, and the New Food and Consumer Safety Action Plan. On January 28th we are participating in a consultation on the framework for health claims for food here in Toronto. These consultations will be held across the country this winter and we encourage the provincial associations to participate if invited. Participation helps to raise awareness of naturopathic medicine and the value of the information NDs can provide for consultations focused on health care.

In the last Government Relations report we advised that we had nominated Dr. Saunders PhD, ND, DHANP for the Expert Advisory Committee on the Vigilance of Health Products. While Paul's nomination was not accepted, we are pleased to report that the profession will be represented as Dugald Seely ND was accepted and will be sitting as a member of the EAC – VHP.

With the recent announcement of the New Food and Consumer Safety Action Plan, Prime Minister Harper has turned his attention on healthcare. The CAND is already actively involved in the consultative process around the Action Plan and is pleased to see that health care is finally becoming a focus of the Harper Government. We do wonder what, if any, impact the Plan will have on natural health products and the ongoing concerns around access to higher risk products and the product license backlog at the NHPD.

In December the CAND NAPRA Sub-Committee presented to the National Drug Scheduling Advisory Committee (NDSAC) of the National Association of Pharmacy Regulatory Authorities (NAPRA). Our presentation focused on the training and education of NDs and provided the Committee members with specifics on the education and training required for and the practice of Parenteral Therapy by NDs. The presentation was very well received and we are now engaged with the NDSAC in reviewing federal and provincial schedules to isolate any use of the term "parenteral" with the goal of developing appropriate definitions that do not restrict the ability of NDs to access substances they use in Parenteral Therapy. Submissions will be made at the upcoming March meeting.

During the last CNCC meeting representatives discussed the importance of having a well defined National Scope to assist all provinces in effectively lobbying their respective Health Ministries. As a result a National Scope Committee has been formed and will be chaired by Dr. Lorne Swetlikoff ND. We are currently gathering representation from each jurisdiction and will report further in upcoming reports.

If you have any questions or would like further information on the work of the CAND Government Relations Committee please contact Shawn O'Reilly at the CAND office, 1.800.551.4381, 416.496.8633 or email soreilly@cand.ca.

Tax Receipts for 2007 Dues

Please be advised that receipts for 2007 CAND membership dues will be issued by request only.

Members who pay dues by credit card might opt to use their monthly statement in lieu of a receipt. By requesting an electronic receipt (emailed/faxed) you are demonstrating environmental consideration by helping the CAND to eliminate unnecessary paper waste and reduce mailing costs.

To request a receipt for your 2007 CAND membership dues send an email to elink@cand.ca specifying whether you would like to receive a hard or soft (electronic) copy.

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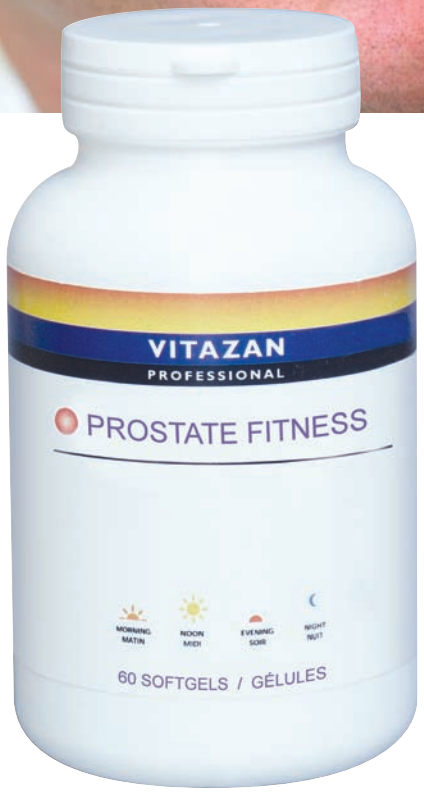

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Call for Mentors

Based on feedback we've received from new practitioners about the challenges of setting up a successful practice, the CAND has developed the Naturopathic Doctors Mentorship Program. Our goal for the mentorship program is to help ease the transition between graduation and practice by fulfilling the informational needs of new NDs and to create a connection and sense of community between new and experienced NDs.

Mentoring is a great way of giving back to your profession and is an exciting way to welcome new NDs into your community.

We are currently seeking NDs from each province and territory willing to volunteer as a point of contact for new NDs entering their community. Mentors' names and contact information will be made available to the graduating classes of CCNM and BINM and will also be posted on the "New Grad" page on the CAND website.

Your role as a Mentor may vary, but could include: meeting with new NDs for an hour or two and answering questions/providing tips on practicing in your area, or, providing points of contact for the local services integral to setting up and running a practice, for example, lawyer, accountant or medical supply company.

The "New Grad" resource page on the CAND website is a living, breathing collection of information and we welcome our Mentors' suggestions for improvement. The page will soon include a flow chart on the process for licensure, career profiles as featured in forthcoming issues of the Vital Link and much more.

In spring and fall 2008 we will hold "A Day With The CAND" at BINM and CCNM respectively. These events will include an assembly with members of the CAND board of directors and staff and will allow students the opportunity to ask questions and obtain information directly from the source.

Help us make a difference. Get involved with the ND Mentorship Program.

For more information or to become a CAND Mentor Contact CAND marketing director Alex McKenna at amckenna@cand.ca or 416.496.8633 or visit the New Grad page at www.cand.ca.

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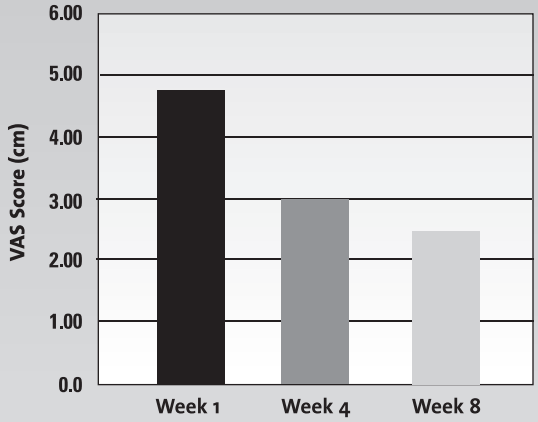

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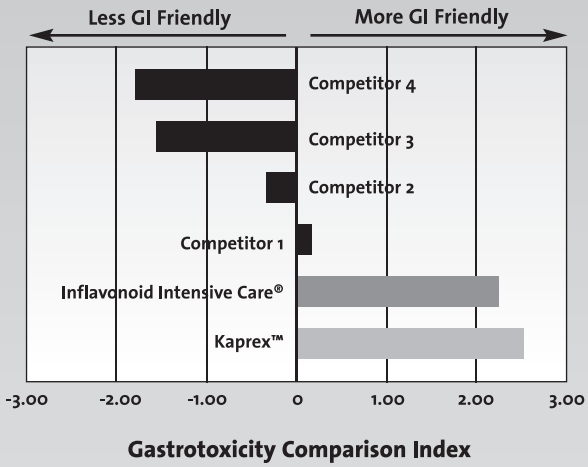

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BUSINESS TIPS

CREATING A PROFESSIONAL IDENTITY

Dr. Daria P. Love, DC, ND

Whether you set up practice in an urban or rural area, have a number of naturopathic doctors to compete with or are the only practitioner for miles, it is important to establish a unique professional identity. While the professional associations have developed good and succinct definitions of naturopathic medicine and our roles as doctors, they do not specifically describe you. The term 'branding' comes to mind, as it creates easy identification and some understanding of 'the product'. Essentially, in building and maintaining a practice, you are selling a product, namely you.

As a naturopathic doctor for almost 27 years, I have tried a number of practice building approaches. I have given talks to groups, done newspaper, radio and television interviews, written articles, worked with other health professionals, but I absolutely believe that the best patient referrals come from patients themselves. A satisfied patient is your advertisement for who you are, what you do and how you do it. Obviously, patient referral becomes more consistent after several years in practice when a solid foundation of patients has been built, but it is not unobtainable for the new practitioner. The creation of a definition of yourself in clear and simple terms, the ten second sound bite, that is easy, not only for you but for others to communicate to potential patients and other health care professionals, is an important beginning of your professional identity.

This identity can be developed around your practice skills, interests, professional and personal goals. It may emphasize a therapeutic focus or specialty such as homeopathic medicine, diet and nutrition, parenteral therapies; or an assessment modality such as electroacupunture assessment, biological terrain assessment, live cell microscopy; or interest based such as cancer, women's health issues, sports medicine; but may also be based on therapeutic style such as integrative, defined therapeutic lifestyle programs, acute or chronic care based. One's personal style of office protocols and patient communication are also very important components of a professional identity.

For instance, 'I am a new practitioner with a general practice and have time to focus on integrating naturopathic health care strategies and assessment methods with consideration to conventional medical approaches for the individual needs of the patient.'

Or, 'My practice focuses on treatment for cancer and chronic illnesses, and I utilize a number of naturopathic therapies, including intravenous administration of vitamins, minerals and homeopathic medicines for both acute and long term care, including pain management and palliative care.'

These 'sound bites' help others decide whether they are interested in consulting you or initiating further dialogue to explore what you can uniquely offer for their personal health care, the health care of their family and friends or professional referral.

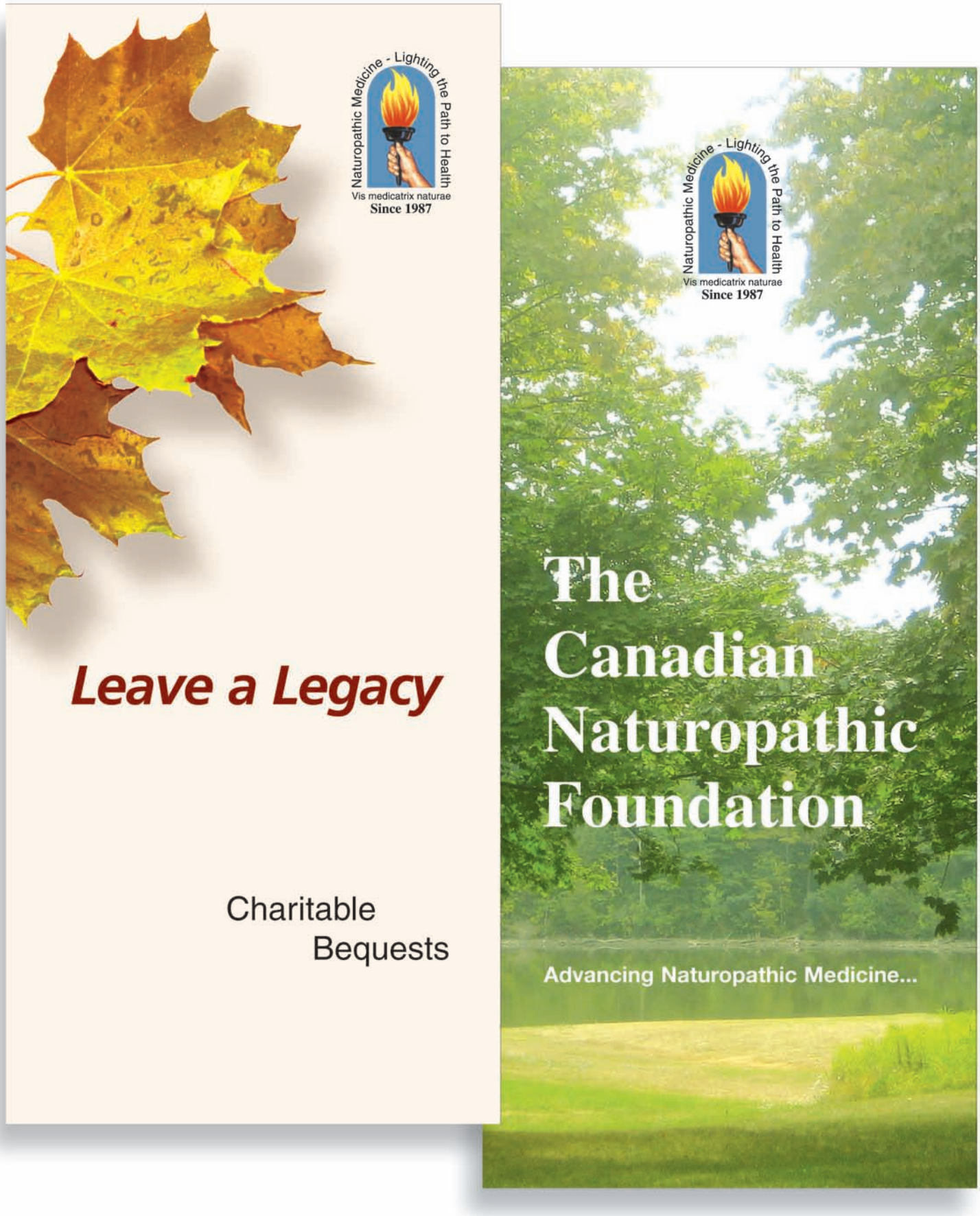
Your professional identity is also invariably linked to your relationship with other health care professionals. While it may be easier to develop an identity within a multidisciplinary setting where the clinic is structured to focus and integrate the skills and modalities of one doctor with those of the other practitioners, the solo practitioner can build this identity through networking, personal contact and patient reference. This may also provide the newer doctor with an insight into the needs and gaps of health care within a community, around which to develop an identity and practice style. The appropriate referral of patients to other practitioners, including other naturopathic doctors, is not only an incredible practice building tool, but will add to your identity as a responsible health care professional in your community. Build a team of other health care professionals to complement your style and abilities in practice. You do not lose a patient by referring; you gain their respect and trust. And a satisfied patient tells others.

Your professional identity is the image others will have of you. Build it to reflect the doctor you are now, and develop it to encompass the doctor you will grow to be in the future.

Dr. Daria Love is a naturopathic doctor and now retired chiropractor. Her professional career has included academic positions with CMCC, OCNM and CCNM as well as a variety of practice situations. Dr. Love is Vice-Chair for the Board of Governors for CCNM. She maintains a private practice in downtown Toronto, and is currently pursuing artistic interests in jewelry. Dr. Love may be contacted at dlove@axxent.ca.

CAND Bequest Program

For more information on the CAND Bequest program or the CNF, please visit www.cand.ca.



Insurance 101: Have We Got You Covered?

Hal Huff Sr., Managing Partner, Partners Indemnity Insurance Brokers Inc.

In the summer 2007 edition of the Vital Link we reviewed what insurance coverage you should be considering as a practicing ND, either as a sole practitioner or operating with others in an office/clinic environment. We have prepared the following insurance chart to assist you in your decision on how best to protect your financial interests as a practicing naturopathic doctor.

Type of Practice	Malpractice Professional Errors & Omissions Liability	Malpractice Additional Name Insured Professional Errors & Omissions Liability	Clinic Malpractice Professional Errors & Omissions Liability	Commercial General Legal Liability	Sole Practitioner Business Package (includes Commercial General Liability)	Office Clinic Business Package (includes Commercial General legal Liability)
ND Regulated Insurance	√					
Additional Insured Name	√	√				
Working For Somebody Else*	√			√		
Working on your own in several locations	√				√	
Own & Operate Office on Your Own	√	√				√
Operate a Clinic with other Professionals	√		√			√

* Working for Somebody Else – could mean as a direct employee or under an independent contractual agreement. The reason we recommend Commercial General Liability in this instance is that if you operating under an independent contractual agreement the employer's insurance policy may not always extend to include you.

Malpractice Professional Errors & Omissions Liability Insurance

All regulated NDs in Canada are required to carry a minimum of $2,000,000 malpractice (E&O liability) insurance. An optional limit of $3,000,000 is available. You may wish to consider the optional limit if you are providing parenteral or chelation therapy for patients.

Additional Named Insured under Malpractice Professional Errors & Omissions Liability Insurance

If you operate your practice under a corporate name this name should be added to your personal Malpractice policy.

Clinic Malpractice Professional Errors & Omissions Liability Insurance

When operating an office or clinic with several practitioners it is important to secure the business against a malpractice claim. It is not unusual for the

continued on next page

patient to claim against both the practitioner and the business name.

Commercial General Legal Liability Insurance

Commercial General Liability insures you for slip and fall claims. For example, if your patient should happen to hurt themselves coming onto your premises or falls while getting on or off the examining table. This would be beyond your Professional Liability Policy Malpractice Insurance. It is important to note that this policy provides insurance for products liability. In most instances this is insured under your Malpractice liability policy, but if your clinic offers services non-related to the practice of an ND you may be at risk. We have found that business office/clinic policies purchased by NDs outside of the CAND program exclude this coverage.

Sole Practitioner Business Package including Commercial General Legal Liability Insurance

As well as Commercial General Legal Liability this policy includes property and crime insurance. The insurance is completely portable. Property includes physical loss or damage including theft to your dispensary, equipment, computer, etc. wherever you are working and while you are in transit between clinics. It also includes your extra expenses required to operate due to a loss to your equipment. Please note that your personal homeowner's insurance policy does not normally extend to insure your home office.

Office/Clinic Business Package Including Commercial General Legal Liability Insurance

This provides insurance for the practitioner who operates their own office or business clinic and requires more extensive insurance coverage. It includes Commercial General Legal Liability, Property and Crime Insurance. This policy covers you for loss of income due to a property claim. 'Crime' would extend to include theft by an employee. This insurance would be required if your property limits exceed $20,000 or if you have an employee or other practitioners working in your office.

If you have any questions please do not hesitate to contact Jenifer Fox at Partners Indemnity at 1-877.427.8683, 416.366.5243 or jfox@partnersindimnity.com

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Naturopathic Association and Academic Updates

The passing of Mrs. Penny Farnsworth

It is with sadness that we report Dr. Gerald Farnsworth ND's wife, Penny, has passed away. A celebration of Penny's life was held January 19 in Kamloops, BC.

Penny's obituary read that she met Gerry, while living in Toronto. They moved to Kamloops, after marrying in Grenfell in 1951. Penny was the glue that held her growing family together as Gerry was frequently away, spear-heading the growth of naturopathic medicine in the Pacific Northwest.

The family wishes that any expressions of sympathy take the form of donations to:

Canadian Naturopathic Foundation
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British Columbia Naturopathic Association (BCNA) – www.bcna.ca

The BCNA Board of Directors is focused on our upcoming annual general meeting, April 3, immediately preceding the 52nd annual Northwest Naturopathic Physicians Convention. A focus for directors over the last quarter has been to complete revisions to the BCNA bylaws, which haven't been updated or modified since 1993. We hope to have the revisions available to members for a vote in April. In addition, directors are individually engaged in various outreach projects, including improvements to the naturopathic medicine listings in the BC Health Guide, liaising with the newly-appointed Health Living Alliance, and a series of advocacy letters to various provincial cabinet members. We have been collectively involved with the provincial Conversation on Health over the last year, which has included many meetings, letters and patient outreach. The final report was released in December; the commentary on complementary medicine was extremely favourable, most of it directly supporting naturopathic medicine. This February's Throne Speech has reconfirmed the current government's commitment to improving health care in BC, drawing heavily from the Conversation. After many years of consultation on defining scope of practice for NDs, the Speech outlined two key elements of the BCNA's Four Point Plan: Prescribing rights and lab access. More information can be found at www.bcna.ca

The Northwest Convention returns to Vancouver on April 4-6, 2008 at the Hyatt Regency. We are very pleased to be the host association for this year's event. Keynote speakers include world renown energetic healer Adam Dreamhealer; senior US botanist and researcher James Duke; Harvard professor and author of Overdosed America Dr. John Abramson; and a long list of much-requested speakers including Drs. Walter Crinnion, Rita Bettenburg, Clyde Jensen, Jonathan Wright and David Lescheid. A special focus on physical medicine will include lectures on detoxification and drainage, manipulation and hydrotherapy. A strong contingent of experienced BC NDs round out the conference, including Drs. Hal Brown, Cathy Carlson-Rink, Paula Fainstat, and Brian Martin. Social events on Friday and Saturday evening are scheduled as well as a tour with James Duke of the VanDusen Botanical Garden, Sunday afternoon. Link to www.nwnpc.com or www.bcna.ca for delegate info, hotel reservations or a full schedule.

Saskatchewan Association of Naturopathic Practitioners (SANP) – www.sanp.ca

SANP is a rapidly growing association. We are the regulatory body as well as the provincial association for naturopathic doctors in Saskatchewan. The number of naturopathic doctors licensed and practicing in the province is growing and we recently introduced the option of Student Membership to naturopathic medical students. Student members will receive two publications yearly describing SANP activities. Student members are also welcome to attend our AGMs, held in May of each year, during Naturopathic Medicine Week. Associate and part-time memberships are also available.

Saskatchewan is a province that holds significant potential. Our economic future is bright; our CFL football team – the Saskatchewan Roughriders – became the 2007 Grey Cup champions this year, which infused an enormous positive energy into our province. The population is growing and the demand for NDs huge. Many of our NDs have new patient wait lists of months to years. Recently two of our members, naturopathic doctors Jonathan Bablad and Julie Zepp Rutledge, have been scheduled to appear on several episodes of Living Saskatchewan www.cbc.ca/livingsaskatchewan. It is a daytime program that features information on everything you would ever want to know about surviving 'the daily grind'.

Due to enormous public interest, we will again be participating in Naturopathic Medicine Week. Last year we had a number of very well attended events – groups from 20 to 70 came out to listen to our members discuss various topics related to Naturopathic Medicine.

Manitoba Naturopathic Association (MNA) www.mbnd.ca

The MNA held its Annual General Meeting on November 2, 2007. We were pleased to welcome Ms. Marni Waggoner as a new public member to the Board. The Manitoba Naturopathic Association also held a successful fundraiser at the IMAX theatre in November.

We are thrilled to announce the December launch of our first cookbook – not only is it a great fundraiser, but it is a wonderful tool for our patients. We have also welcomed two new members to the Association: Dr. Dara Morden, ND and Dr. Lori Mae Janzen, ND. We now have 19 NDs registered to practice in Manitoba. We continue to participate with representatives from Manitoba Health and the regulated health professions regarding a new umbrella act.

Ontario Association of Naturopathic Doctors (OAND) – www.oand.org

Naturopathy Act Update

The transition process established by Ontario's new Naturopathy Act is expected to get underway in the coming months, with the process for selecting members of the Transition Council. The first meeting of the Transition Council is expected by this fall, and the process is expected to take a year or more.

The primary role of the Transition Council is to establish the new College of Naturopaths of Ontario to replace the current regulator, the Board of Directors of Drugless Therapists. This includes creating core regulations, policies and by-laws, business processes and infrastructure necessary for the College to operate and fulfill its mandate to protect the public interest. All major decisions relating to the establishment of the new College will require approval by the provincial government.

The OAND will be actively engaged in the transition process by providing the perspective of the profession on regulations, standards and policies which will be addressed by the Transition Council.

Continuing Education

The OAND has planned a full calendar of CE for 2008, including an enhancement of CE events across the province. The OAND Cardiology Conference on April 19 and 20 at Ryerson University in Toronto features Aggie Casey on Mind-Body Medicine and Mary Wu on TCM Approaches in Cardiology.

Virginia Osborne ND will be presenting a PT Updates session on March 27 and a new regulator mandated PT Emergency Procedures course on March 28 in Toronto and March 29 in Burlington.

The OAND and CCNM will be co-presenting the Primary Care Series 2008, with 5 sessions between February and June.

The OAND Unity Summit and Convention will be from October 17 to 19 in Niagara Falls. The Unity Summit is being held to prepare the profession in Ontario for regulation under the RHPA, to provide a forum for discussion on the breadth and depth of the profession and to define our branding to the public as we prepare to come under a new regulatory framework.

Naturopathic Students' Association (NSA-CCNM) – www.nsa-ccnm.com

The January class of 2011 have moved into the classroom and halls of CCNM. They currently are the largest January intake CCNM has seen, with about 60 new incoming students. A large majority of the new students took part in the January Unity Summit, held in Caledon, ON. The students used the Summit to bond and develop a sense of cohesiveness within the class.

A group of 4th year interns took part in an externship to Vietnam this past summer. This has been part of many different individual programs that have been set up for upper year CCNM students to partake in externships around the globe. Students through various organizations have been traveling to places such as Vietnam, Nicaragua and India, to gain clinical and educational experience outside of the Robert Schad Clinic at CCNM.

CCNM hosted its annual Supplier Show this January, which was a huge success. Students, suppliers and faculty all commented that it was the largest supplier show seen at CCNM. The show is an opportunity for the students to be introduced to the suppliers. The show annually raises money for the Naturopathic Students' Association.

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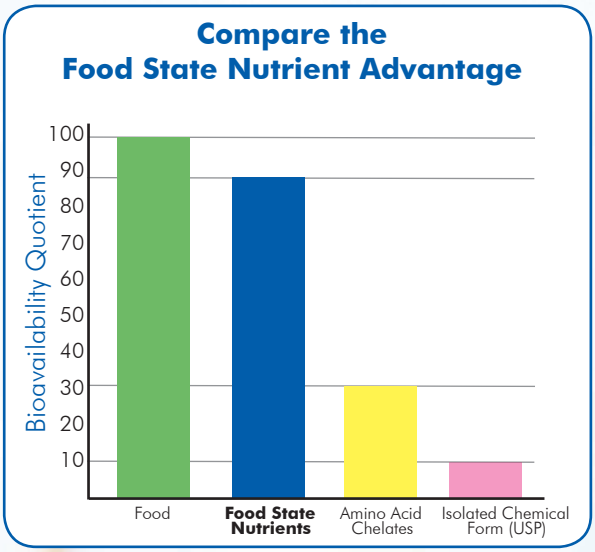

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The role of vitamin D3 in autoimmune disorders

Dr. David Lescheid, BSc, PhD, ND

Abstract:

There has been a substantial increase in our knowledge of the effectiveness of vitamin D3 in the prevention of chronic diseases. We also have learned that vitamin D3 has many other important functions in addition to its well recognized role in calcium and phosphate physiology. This paper will discuss the role of vitamin D3 as an immune balancing hormone that might be able to prevent and treat autoimmune diseases like multiple sclerosis and type I diabetes.

Epidemiological support for the role of Vitamin D in the immune system:

A deficiency in vitamin D3 will affect the balance and function of the immune system and therefore, increase the risk of certain diseases. For example, a number of infectious diseases, including tuberculosis, influenza, pneumonia, chronic hepatitis B, HIV/AIDS and malaria, occur more often in persons with impaired vitamin D3 status. Cancer, a disease associated with impaired immune surveillance, occurs more often in persons with a deficiency of vitamin D3. Finally, dysregulated vitamin D3 metabolism is present in autoimmune disorders such as multiple sclerosis, type I diabetes, rheumatoid arthritis, ankylosing spondylitis, irritable bowel disease (Crohn's disease and ulcerative colitis), sarcoiditis, Grave's disease and Hashimoto's thyroiditis.

The role of Vitamin D3 in specific autoimmune diseases

1) Multiple sclerosis and experimental autoimmune myeloencephalitis (EAE):

The etiology of multiple sclerosis, MS, is complex and currently unknown. Genetics, chronic low grade viral diseases like Epstein Barr virus, higher socioeconomic influences, gender and unknown environmental factors are all recognized contributors to development of the disease[1]. Reduced sun exposure is an environmental factor that is clearly correlated with MS. For example, there is a significant positive relationship between the incidence of MS and a person's place of residence north or south of the equator. Furthermore, persons with common ancestry increase their risk of developing MS if they move to more northern or southern latitudes[1]. Finally, mortality from MS is lowest in individuals with the highest recreational or occupational exposure to sunlight[2].

The maximal protective effect of sunlight occurs if there is at least an average of 2-3 hours of exposure per day in the summer during weekends and holidays between the ages of 6-15[1]. In monozygotic twins, there is a 25% decrease in the incidence of MS for every unit increase in sunlight exposure during childhood[3], suggesting that the protective role of sunlight might be even more important than genetic susceptibility. Other factors, like melatonin synthesis, might contribute to this protective effect but the major difference in persons exposed to more sunlight is increased endogenous synthesis of Vit D3. Regularly exposing bare skin to short periods of UVB light of at least 18kJ/cm is the safest, most effective way to optimize levels of Vit D3. At least 10,000 to 20,000 IU of vitamin D3 is synthesized during the time that it takes to produce slight erythema in Caucasians[4].

Maintaining higher levels of 25(OH) D3 in the blood, via endogenous synthesis or supplementation, is protective. In military personnel, white persons with high circulating levels of serum 25(OH) D3 (>99nmol/L) had significantly lower incidence of MS compared to controls matched for age, sex, ethnicity, dates of sample collection, branch of military service and latitude of residence at the time of entry into the military. This protective effect was substantial, with a 41% decrease in MS risk for every 50 nmol/L increase in 25(OH) D3[1].

Persons with the highest disability from MS are much more likely to be Vit D3 deficient, defined as serum 25(OH) D3 levels < 40nmol/l, than persons with higher levels of serum 25(OH) D3[5]. They also are more likely to have darker skin types[6, 7], which would influence their ability to synthesize adequate amounts of Vitamin D3 from sunlight[8]. Furthermore, periods of increased disease activity are associated with lower serum 25(OH) D3 levels compared to periods of disease remission[9]. It is important to note that the clinical signs and symptoms of MS were present in this study despite most patients maintaining serum 25(OH) D3 levels considered adequate for bone metabolism, >37nmol/l, throughout the year. The month of birth predicts the risk of developing MS in northern countries, like Canada, Scotland, Denmark and Sweden, suggesting that Vit D3 status of pregnant mothers affects the risk of MS in their children. Significantly fewer (8.5%) persons with MS are

born in November compared to May (9.1%). It is postulated that maternal blood deficiency of Vit D3, especially during the 2nd and 3rd trimester, would increase the risk of the child developing MS[10]. We can store about two months supply of Vit D3 and serum 25(OH) D3 levels in women change substantially during different seasons[11].

Experimental autoimmune myeloencephalitis (EAE) is a mouse model of MS that can be prevented by full body exposure to UVB light or by feeding animals diets that are supplemented with 1, 25(OH)2 D3. In contrast, mice fed 1, 25(OH)2 D3 deficient diets had more clinical and pathological signs of EAE[12]. It is interesting to note that when mice were fed diets supplemented with 25(OH) D3, the precursor to 1, 25(OH)2 D3, there was a protective effect in female mice but not in male mice or ovarectomized mice or castrated mice. It was proposed that estrogen from ovarian tissue interferes with the breakdown of 1, 25(OH)2 D3 into its inactive metabolite, calcitroic acid, by CYP24A1, the enzyme termed 24-hydroxylase. This mechanism would allow more 1, 25(OH)2 D3 to accumulate in the spinal cord of female mice than male mice and therefore, have a more pronounced anti-inflammatory and immune balancing effect. If this same effect occurs in humans, it would help explain why reduced sun exposure has a greater impact on the incidence of MS in women compared to men[13]. Clinical severity also can be reversed by feeding the animals diets supplemented with 1, 25(OH)2 D3. This reversal of an MS-like disease was rapid, within 3 days, and suggests that Vit D3 might be a natural inhibitor of MS[12].

The potential mechanisms of Vit D3's effects on EAE or MS are summarized in Table I.

2) Type I diabetes:

Some of the risk factors associated with the development of type I diabetes include genetics, microbial infections, gluten sensitivity, early exposure to cow's milk beta-lactoglobulins, a significant stressful event and other unknown environmental factors20. A deficiency in Vit D3 also increases a person's risk of Type I and Type II diabetes[21].

The associations between Vitamin D3 and blood sugar regulation are listed in Table 2.

The non-obese diabetic, NOD, mouse is an animal model of type I diabetes. NOD mice that are Vit D3 deficient are much more likely to develop symptoms of diabetes than mice that have adequate Vit D3 stores[26, 27]. Supplementing NOD mice with high doses of 1, 25(OH)2 D3 or its analogs delays the progression of insulitis and development of Type I diabetes[27, 28, 29, 30]. The dose of Vit D3 used to prevent diabetes in some of these animal studies was 5 mg/kg (200IU/kg) every other day and caused hypercalcemia. It is important to note that Vit D3 was delivered intraperitoneally in these mice and therefore, it is not known whether equivalent oral doses would have the same effect. Early and long term supplementation with Vit D3 had the most protective effect, with a 30% reduc-

Table I: Potential mechanisms of Vitamin D3 for treating EAE or MS

Mechanism	**Pathological relevance**
Increased levels of TGF-β	Increased TGF-β is associated with decreased disease severity [1,14,15]
Increased number and activity of regulatory T cells	Regulatory T cells are decreased in persons with active MS [1]
Increased level and activity of IL-10	Regulatory T cells suppress EAE via an IL-10 dependent mechanism; severity of EAE decreases with increased levels of IL-10 in mouse spinal cord cells; mice with EAE and genetically engineered defects in the IL-10 pathway will not respond to 1, 25(OH)2 D3 [16]
Decreased chemokine, iNOS activity and CD11b+ monocyte recruitment	Attenuated inflammatory and immune response [17]
Reduce pro-inflammatory macrophages to baseline levels in the CNS	Attenuated inflammatory and immune response [18]
Selective apoptosis of activated encephalitogenic CD4+ T cells	Reduction of the demyelinating process [17, 19]

Table 2: Associations between Vit D3 and blood sugar regulation

Association
Vitamin D receptors are found in pancreatic β cells [22]
Normal levels of 1, 25(OH)2 D3 are required for the synthesis and release of insulin [21]
There is increased risk of insulin resistance and pancreatic β cell dysfunction in insulin sensitive persons with hypovitaminosis D [23]
Increasing serum 25(OH) D3 in persons with insulin resistance and hypovitaminosis D from 25nmol/L to 75 nmol/l increased their insulin sensitivity by 60% [23]
Calbindin D28K, a Vit D3 dependent binding protein and an important component of intracellular calcium signaling and insulin release, is found in pancreatic β cells [24]
Calbindin D28K helps protect pancreatic β cells from the destructive inflammatory cytokines associated with autoimmunity [25]

tion in the relative risk of Type I diabetes[22]. This evidence suggests that the maximal protective benefits of vitamin D occur if supplementation begins early on in development before insulitis and diabetes has already been established.

A deficiency in Vit D3 during pregnancy increases the incidence of autoimmune diseases, such as type 1 diabetes, in genetically predisposed individuals[30], suggesting that the protective effects of vitamin D occur early in development. The protective effect is dose dependent, with no reduction in risk if 10mg (400IU) or less vitamin D3 is given daily to pregnant mothers but daily doses of 50 mg (2000 IU) or more having a strong protective effect[31]. Another large, well-designed study followed children for 4 years after birth and found a significant decrease in islet cell autoimmunity with increased maternal intake of dietary sources of vitamin D. Islet cell autoimmunity, the presence of antibodies directed against the islet cells, is a preclinical stage of type I diabetes and is a good predictor of future disease development. This protective effect of Vit D3 was independent of known genetic risk factors (HLA genotype), family history of type 1 diabetes, presence of gestational diabetes mellitus, and ethnicity[32].

The protective effect of Vit D3 supplementation extends to children. A large, multicenter, case control study in Europe found that the risk of type 1 diabetes in children decreased by about 1/3 when they were supplemented with Vit D3[33]. Infants in Finland supplemented with Vit D3 had a 78% reduction in the risk of Type I diabetes[34]. Finland, because of its Northern latitude, does not have significantly high intensity of UVB light throughout many months of the year to support endogenous synthesis of Vit D3 and therefore, supplementation might have greater effects in this population compared to populations living closer to the equator.

In Norway, supplementing infants with cod liver oil, but not Vit D3, during their first year of life protected them from developing type I diabetes later on in life. A typical 5 ml daily dose of cod liver oil contains 10ug (400IU) Vit D3, 0.6 g DHA, 0.4g EPA and 875-1,950 IU of vitamin A. It was proposed that the anti-inflammatory effects of the long chain n-3 fatty acids, DHA or EPA, in cod liver oil played a more important role than Vit D3 in decreasing the risk of diabetes. Alternately, synergistic activity between Vit D3 and other components in cod liver oil might provide the optimal protective effect[35]. This study did not identify the amount of Vit D3 supplemented or the serum levels of 25(OH) D3. The amount of Vit D3 commonly found in supplements, 200-400IU, might have been too low to have any therapeutic value[31]. Furthermore, the danger of vitamin A toxicity is much less if oil-based formulations of retinol are used[36] and therefore, cod liver oil remains a safe, effective source of Vit D3.

Potential mechanisms for Vitamin D3 in the treatment of type 1 diabetes are listed in Table 3.

The present evidence suggests that maintaining optimal Vit D3 metabolism may be a safe, effective way to prevent the onset of type I diabetes in genetically susceptible persons and/or reduce the further destruction of pancreatic β cells in persons with recently diagnosed diabetes. Additional studies are needed to determine the dose and delivery method of Vit D3 required for maximal prevention without side-effects.

Mechanisms whereby Vitamin D could influence autoimmune processes

There are many places where a defect in the complex biochemical pathway of Vit D3 could contribute to autoimmunity. For example, VDRs exist on the surface of many different immune cells

Table 3: Potential mechanisms for Vitamin D3 in preventing or treating type I diabetes.

Mechanism	Physiological relevance
Attenuate Th1 cytokines, regulate dendritic cell activity and increase regulatory T cell activity	Helps balance the immune system so that it no longer attacks pancreatic β cells [30]
Modulate the expression and release of pro-inflammatory chemokines and cytokines from immune cells and pancreatic β cells	Reduces the likelihood that immune cells will be recruited that cause inflammation and destruction of pancreatic β cells [22, 37]
Increase the expression of inhibitory Kappa B alpha in pancreatic islet cells *a synthetic analog of 1, 25(OH)2 D3 was used in this study	Decreases the transport of nuclear factor Kappa B to the nucleus and therefore, decreases the transcription of many pro-inflammatory cytokines associated with chronic diseases like type I diabetes [38, 39]
Human and rat pancreatic islet cells express toll-like receptors (TLRs) that bind pathogen associated molecular patterns (PAMPs)	Activating TLRs in some cells increases the conversion of 25(OH) D3 to 1, 25(OH)2 D3 Increased 1, 25(OH)2 D3 modulates the acquired immune system and increases the synthesis and release of antimicrobial peptides (AMPs) from the innate immune system cells AMPs can eliminate the microbes potentially associated with type I diabetes as well as help balance the immune system [38, 40, 41]

including the mononuclear phagocyte system cells, dendritic cells, antigen-presenting cells, activated T cells, microglia and astrocytes[42]. The expression of VDRs on B lymphocytes is substantially less than on T lymphocytes. This suggests that 1,25(OH)2 D3 might be more important for immunoregulation in autoimmune disorders involving a Th1 imbalance, like type I diabetes, MS and IBD, than in those involving a Th2 imbalance, like Grave's disease[43]. Cells of the bone marrow and thymus gland also express VDRs, suggesting that Vit D3 plays a role in the early development of immunocompetent T cells[44]. In animal studies, Vit D3 helps ensure that T cells developing in the thymus gland properly recognize self antigens and react appropriately against non-self or dangerous antigens[45].

Many cells of the immune system express the enzyme (termed CYP27B1 or 1α-OH hydroxylase) needed to convert 25(OH) D3 to its hormonally active 1, 25(OH)2 D3 form. Genetic polymorphisms in the promoter sequence of the gene encoding CYP27B1 occur more often in persons with type I diabetes, Hashimoto's thyroiditis, Grave's disease and Addison's disease compared to healthy controls[46]. These individuals might not produce the amount of 1, 25(OH)2 D3 needed to control local cell growth and immunity. Genetic polymorphisms in different segments of this gene occur in Hashimoto's thyroiditis but not in the other autoimmune diseases studied[46], suggesting a unique contribution of Vit D3 to the etiology of autoimmune disease in different endocrine systems.

In the adaptive immune system, Vit D3 is an immunosuppressive hormone, preventing an overactive immune response. A deficiency in Vit D3 or VDRs results in an immune system response that is skewed towards the Th1 phenotype (cell-mediated immunity). Prolonged Th1 responses are associated with autoimmune diseases like type I diabetes, multiple sclerosis, rheumatoid arthritis, Crohn's disease and ulcerative colitis. Adding Vit D3 to cell cultures deficient in vitamin D decreases the proliferation of Th1 dominant cells directly, as well as indirectly by reducing levels of cytokines, such as IFN-γ and IL-2, which usually promote Th1 cell dominance. The production of IL-4 and IL-5, cytokines that promote the development of the Th2 phenotype (humoral immunity), also are increased by Vit D3[47] but the role of 1, 25(OH)2 D3 in Th2 dominant diseases is not yet known. The cytokines involved in Vit D3's regulation of autoimmune diseases are listed in Table 4.

Dendritic cells, DCs, are antigen presenting cells that are activated when they bind microbes or receive distress signals from damaged or infected cells. The primary role of DCs is to process and present antigens to naive T cells and therefore, link the innate immune system to the adaptive immune system. During their development, DCs synthesize, release and recruit cytokines and costimulatory molecules that assist naïve T cells in developing

Table 4: The cytokines involved in Vit D3's regulation of autoimmune diseases

Mechanism	Physiological relevance
Decreases synthesis of IL-12	IL-12 promotes Th1 dominance [48]
Increases synthesis of IL-10	IL-10 is an important immunoregulator that: • down-regulates expression of Th1 cytokines, MHC class II antigens and co-stimulatory molecules • blocks the activity of NF-kB • enhances B lymphocyte survival, proliferation and antibody production [48, 49]
Promotes recruitment, development and function of regulatory T cells	Regulatory T cells secrete cytokines, like TGF-β and IL-10, that have immunoregulatory roles [48]
Decreases production of IL-2, TNF-α, IFN-γ and cell cycle progression of CD4+ cells	Decreases the signals for and the development of pro-inflammatory CD4+ T cells [50]

appropriate immunoreactive or immunosuppressive responses. DCs express VDRs to bind Vit D3 as well as CYP27B1, to convert 25(OH) D3 to 1, 25(OH)2 D3. 1, 25(OH)2 D3 helps keep DCs in a developmental state that fosters the development of tolerigenic T cells[51, 52]. The ability of Vit D3 to promote tolerance occurs in myeloid but not plasmocytoid dendritic cells and is related to selective inhibition of NF-κB activity in these cells[50].

Vit D3 also inhibits human leukocyte antigen (HLA) class II expression on endocrine cells. The surface glycoproteins synthesized when HLA class II is expressed helps the immune system differentiate foreign, potentially harmful cells from innate cells. Endocrine cells, such as thyrocytes and pancreatic β cells, that inappropriately express HLA glycoproteins, are targeted for destruction by autoimmune mechanisms. There is a genetic association between variations in HLA expression and susceptibility to autoimmune diseases like type 1 diabetes, Grave's disease, Hashimoto's thyroiditis and Addison's disease[46].

The suppressive effect of vit D3 on inflammatory immune responses occurs not only in the gastrointestinal tract but also in the epidermis. Excessive UV light will cause epidermal damage and, therefore, an inflammatory response. Macrophages and lymphocytes at the site of the tissue inflammation have VDRs and can metabolize 25OH D3 to 1, 25(OH)2 D3. Once activated, 1, 25(OH)2 D3, modulates excess inflammation by suppressing the adaptive immune response. It is important to note that suppression of the adaptive immune system by 1, 25(OH)2 D3 does not increase host vulnerability to opportunistic infections because it also bolsters the defenses of the innate immune system by triggering the synthesis and release of antimicrobial peptides[53, 54]. The immunosuppressive actions of Vit D3 on the adaptive immune system are balanced by its immunosupportive actions on the innate immune system.

Optimal dosing

There are many different factors that contribute to the incidence of vitamin D deficiency in Canadians of all ages[4, 8]. For example, wearing a sunscreen with an SPF of 8 or more reduces the ability of skin to produce adequate vitamin D by 95%[4, 55, 56]. Geography plays a considerable role in ensuring adequate UVB exposure and, therefore, quantity of vitamin D synthesized. It is impossible to synthesize adequate amounts of vitamin D from sunlight exposure during the months between November and March in latitudes north of 37 ^{0}N[55]. It is estimated that only between 5-15 minutes per day of sunlight (between 10 a.m. and 3 p.m.) to unprotected arms and legs or hands, face and arms 2-3 times per week is sufficient to produce adequate amounts of vitamin D during summer, spring and fall months[56]. Aging decreases the ability to efficiently metabolize previtamin D3 from sunlight. A 70-year-old person will only produce about 25% as much previtamin D3 from the same duration and intensity of sunlight exposure as a healthy young adult[56]. Obesity also significantly decreases the bioavailability of vitamin D by irreversibly sequestering the fat soluble vitamin deep into fat stores where it is unavailable for conversion to 1, 25(OH)2 D3. Obese individuals can only produce about 50% as much serum Vit D3 from the same sun exposure as leaner individuals[56]. This link between obesity and vitamin D deficiency has profound implications when you consider the

incidence of obesity in the adults and children of developed nations. Ethnicity and skin type, particularly the level of melanin pigmentation, also needs to be considered for optimal dosing. Melanin levels in the skin have a profound influence on the endogenous synthesis of vitamin D. Persons with dark skin require 5-6X the length of UVB exposure to synthesize similar levels of Vitamin D3 compared to persons with lighter skin[8]. Finally, because Vit D3 is a fat soluble vitamin, anything that impairs fat digestion and absorption like pancreatic and bile insufficiency, Whipple's disease, sprue and celiac disease will also impair the absorption of Vit D3[4, 8].

The dose and duration of Vit D3 supplementation needed to prevent and reverse the signs and symptoms of autoimmune disorders is not yet known. The current tolerable upper daily limit of Vit D3 intake from all sources is set at 2000IU by Health Canada primarily because of theoretical concerns of hypercalciuria and hypercalcemia with higher levels. Most current scientific evidence suggests that this upper limit is much too low and has hindered research into the benefits of preventing and treating disease with Vit D3[4, 8]. A recent study in 12 persons with active MS showed that supplementation with up to 40,000IU of Vit D3 for 28 weeks did not cause hypercalcemia or hypercalciuria or affect other markers like liver enzymes, serum creatinine, electrolytes, serum protein, and parathyroid hormone. Vitamin D3 supplementation at this dose increased the mean 25(OH) D3 from 78 +/- 35 nmol/L to 386 +/- 157 nmol/L ($P < 0.001$) without any observed side effects[57]. A recent summary concludes that supplementing with Vit D3 would help prevent the development of MS and therefore, be a useful addition to therapy. However, larger, more carefully controlled studies are needed to confirm the dose and duration of Vit D3 therapy needed to produce this protective effect[58].

Maintaining higher levels of Vit D3 during pregnancy also lowers the lifetime risk of the children developing MS suggesting that "prevention of MS by modifying an important environmental factor (sunlight exposure and vitamin D level) offers a practical and cost-effective way to reduce the burden of the disease in the future generations"[59]. Finally, because the protective effect of 25(OH) D3 on the incidence of MS is more pronounced in persons less than 20 years of age[1], it is proposed that the commonly accepted health care policy of liberally covering children and adolescents with sunscreen prior to going out in the sun needs to be revisited.

The epidemiological evidence is strong that an environmental factor contributes to the pathogenesis of autoimmune diseases. This paper has outlined the support for decreased exposure to sunlight and therefore, reduced levels of serum 25(OH) D3, in the development of MS and type I diabetes. There also is substantial support demonstrating that 1, 25(OH)2 D3 can reduce the risk of autoimmune disorders by a number of different mechanisms including the reduction of activity and number of auto-reactive Th1 cells and the promotion of self-tolerance. Although further clinical trials are needed, the current evidence outlined in this paper warrants screening patients, and relatives of patients, with autoimmune diseases for a deficiency in Vit D3 and supplementing when necessary.

About the Author

Dr. David Lescheid graduated with honors from the Canadian College of Naturopathic Medicine (CCNM) in 2002. His education includes a Ph.D. in Molecular Biology and Protein Chemistry from the University of Victoria as well as a B.Sc. in Biology and a Diploma in Health and Fitness studies from Simon Fraser University. He also has additional training in IV therapies, homeopathy and different forms of body work.

Dr. Lescheid was a professor for 5 years at the CCNM where he taught Physiology and Microbiology. As a nationally recognized expert in naturopathic medicine, he is frequently an invited speaker to professional events and has published extensively on complementary and alternative medicine. He enjoys teaching and often holds seminars in his clinic, including courses for continuing education credits for other medical professionals.

In 2006, Dr. Lescheid was appointed to the Expert Advisory Committee (EAC), an advisory board to Health Canada. He also is a member of the Council for Naturopathic Medical Education (CNME), which is an international board that regulates the quality of naturopathic medical education. He also is a member of the Canadian Association of Naturopathic doctors (CAND) government and media relations subcommittees.

Dr. Lescheid currently practices full-time in a large multidisciplinary health clinic in the Ottawa area. Although his practice extends over a broad range of health concerns, he takes a special interest in the immune system and infectious diseases. He also works with men's health issues, overweight and obesity concerns and sports medicine.

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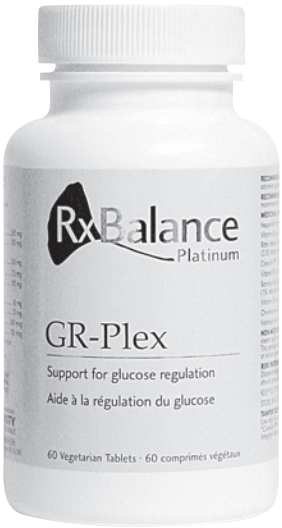

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Autoimmune disease heterogeneity: decoding pathogenesis to better guide treatment

Dr. Tawnya Ward, BSc, ND

A firm grasp of autoimmune disease (AD) pathophysiology is imperative for most naturopathic doctors, irrespective of their focus. AD in its clearest form is prevalent in general practice. Additionally, autism, cardiovascular disease, neurological disorders and apparent hormone imbalances can involve AD. A good understanding of immune homeostasis (or the lack thereof) may improve patient outcome. The problem is that researching immunology today is not a simple task. Within the morass of literature, models of immune regulation are in a state of flux. Conflicting evidence abounds, likely attributable to the plethora of in vitro and animal studies with questionable applicability. By nature, AD are phenotypically diverse with many overlapping features.[1] As doctors and scientists, we attempt to categorize autoimmune diseases into organ-specific or organ nonspecific (systemic), Th1 dominant or Th2 dominant. Such myopic classifications ignore a great deal of inherent overlap, making us lose sight of important similarities that guide appropriate treatment. The goal of this article is to cover the latest data on autoimmune pathogenesis, to compare and contrast various prototypical AD, while giving weight to human models and treatment-oriented concepts.

AD can be divided into either organ specific (OS) or organ nonspecific (ONS). Furthermore, AD may be characterized as Th1 dominant, Th2 dominant or mixed. Many OS AD appear to be Th1 dominant (e.g. Celiac disease, Hashimoto's thyroiditis, Multiple Sclerosis, type 1 Diabetes, Rheumatoid arthritis (RA), Crohn's disease). A number of OS and most ONS AD appear to have some degree Th2 dominance during their course (e.g. Sjogren's, systemic lupus erythamatosus [SLE], RA). Additionally, prolactin (PRL) exacerbates a number of autoimmune diseases including autoimmune Addison's disease, Celiac disease, type 2 diabetes, Hashimoto's thyroiditis, RA and lupus. These classifications according to current literature are outlined in the table below.

Organ specific[2]	**Organ Nonspecific[3]**
Acute rheumatic fever[2] (likely more Th1)[3]	Antiphospholipid syndrome (Th1 or Th2)[20]
Autoimmune Addison's disease (AAD)(PRL)[4]	Rheumatoid arthritis (Th1/Th1 & Th2)(PRL)[4]
Autoimmune alopecia (Th1)[5, 6]	Sjogren's syndrome (Th2 & Th1)[21,22]
Autoimmune hemolytic anemia (Th2)[7]	Systemic lupus erythematosus (Th1 & Th2)(PRL)[4]
Autoimmune polyglandular syndrome	Systemic necrotizing vasculitis
Autoimmune thrombocytopenic purpura (Th1)[8, 9]	Wegener's granulomatosis (Th1/localized, Th2/ generalized)[23]
Celiac disease (Th1)(PRL)[4]	
Dermatitis herpetiformis (likely Th2)[11,12]	
Goodpasture's syndrome (likely Th1/Th2)[13, 14]	
Grave's disease (Th1) (Murine)[15]	
Guillian-barré syndrome	
Hashimoto's thyroiditis (HT)(Th1)(PRL)[4]	
Immune-mediated infertility	
Insulin-resistant diabetes mellitus (Th1)(PRL)[4]	
Myasthenia gravis (mostly Th1, also Th2)[16]	
Multiple sclerosis (Th1)	
Stiff-man syndrome (likely Th1 & Th2)[17]	
Sympathetic ophthalmia	
Type 1 diabetes mellitus (DM-1)(Th1)	
Pemphigus foliaceus, Pemphigus vulgaris, Pernicious anemia	
Vitiligo (Th1 and/or Th2)[19]	

Loss of Homeostasis

Numerous mechanisms can lead to the loss of immune homeostasis. Exogenous mechanisms include molecular mimicry (e.g. DM-1, RA, MS) and superantigenic stimulation (e.g. Staphylococcal protein A and enterotoxins). Endogenous mechanisms include altered antigen presentation, increased T cell costimulation, increased B cell function, apoptotic defects (e.g. SLE), cytokine imbalance and altered immunoregulation.[2] Age, gender (e.g. female), infectious agents and environmental exposures (e.g. aromatic hydrocarbons) may be risk factors.[2] Innate mechanisms for immune homeostasis include self-antigen sequestration, tolerance, central deletion of autoreactive lymphocytes, peripheral anergy, receptor replacement by autoreactive lymphocytes and regulatory mechanisms.[2]

Th1 versus Th2 Cytokine Imbalance

Cytokine imbalance can alter immune cell proliferation, differentiation and activity. Naïve T cells (Th0) can differentiate into Th1 cells (stimulated by interferon gamma), Th2 (stimulated by IL-4) cells or regulatory T cells (TGF-b). Th2 cytokines (IL-4, IL-5) have regulatory, antibody-mediated and anti-parasitic functions. Th1 cytokines (IFN-g, IL-2, IL-12) stimulate macrophage activation and cell-mediated immunity. Th1 cellular responses are generally considered more aggressive, resulting in more inflammation and collateral damage than Th2 responses. Macrophages, dendritic cells and other antigen presenting cells secrete many of the same cytokines as Th1 and Th2 cells, demonstrating their importance in immune homeostasis.[24] Th1 and Th2 immune responses are intricately connected. Th2 cytokines (IL-4, IL-6, IL-10) can down-regulate Th1 cells.[24] Th1 cells (via IFN-g) can block Th2 proliferation. Treatments that inhibit cell-mediated immunity (e.g. vitamin D3) tend to calm Th1 dominant autoimmune conditions.[24]

Regulatory T cells (Treg) help maintain self tolerance. Type 1 Treg cells secrete Th2 cytokines (mostly IL-10 and small amount of transforming growth factor beta [TGF-beta]). Th3 cells secrete IL-10 and TGF-beta.[25] Th3 and Tr1 T cell suppression rely on cytokine induction rather than cell to cell contact.[26] CD4+CD25+ Treg cells inhibit proliferation and cytokine production of CD4+ and CD8+ T cells by means of cell to cell contact.[27, 28, 29] The local environment regulates CD4+CD25+ Treg function with three major classes of molecules including, co-stimulatory molecules, cytokines (IL-2,[30] IL-4,[31] IL-7,[32] IL-15) and danger signals mediated by toll-like receptors.[33] Antigen presenting cells (APC) can produce IL-1, IL-6 and IL-12, increasing Treg activation by IL-12.[34] Optimal TGF-b levels (not low) have been associated with preventing autoimmune DM,[35, 36] autoimmune thyroiditis[37] and the generation of oral tolerance (Th3).[38]

Specific Cytokine Patterns

Rheumatoid Arthritis (RA) pathogenesis involves T cells, B cells and soluble molecules (Th1 & Th2).[39] Early RA cytokines are primarily Th2 (IL-4). IFN-g (Th1), IL-1, IL-2 (Th1), IL-6 (Th2), IL-17 (Th1), TNF-alpha, and GM-CSF are elevated in RA. Pregnancy (elevated Th2; suppressed Th1) often reduces RA disease activity (~75% patients), lending additional evidence to the hypothesis that RA is characterized of Th1 dominance.[24]

Celiac disease (CD) is a Th1 dominant autoimmune disease against IgA connective tissue antibodies (antireticulin and antiendomysial)[40] and tissue transglutaminase (IgA tissue transglutaminase),[41] resulting in inflammation of upper intestine (duodenum), immune infiltration (lamina propria, epithe-

Th1 Dominant	Mixed Th2 /Th1	Th2 Dominant
Acute rheumatic fever [3]	Antiphospholipid syndrome (Th1 or Th2) [20]	Autoimmune hemolytic anemia [7]
Autoimmune alopecia [5, 6]	Goodpasture's syndrome [13, 14]	Dermatitis herpetiformis (likely)[11,12]
Autoimmune thrombocytopenic purpura [8, 9]	Myasthenia gravis(Th1 less Th2)[16]	
Celiac Disease	Rheumatoid Arthritis (RA)	
Graves Disease [15]	SLE (Th2 →Th1)	
Hashimoto's thyroiditis	Sjogren's syndrome [21, 22]	
Insulin Resistent Diabetes	Stiff-man syndrome (Th1 & Th2)[17]	
Multiple Sclerosis	Vitiligo [18, 19]	
Type 1 diabetes mellitus	Wegener's granulomatosis [23]	

lium) and villous atrophy.[40] Innate (IL-15; cytotoxic T cells) and adaptive immunity (IFN-g/Th1; gliadin-reactive CD4+ T cells) are involved.

Systemic Lupus Erythematosus (SLE), the prototype of ONS AD, potentially affects the kidneys, joints, skin, serosal surfaces, blood vessels, central nervous system. Etiological influences appear to be genetic (apoptotic cell clearance)[42, 43], environmental (e.g. UV light)[44] and hormonal (e.g. estrogen). There is a generalized upregulation of Th2 cytokines, excessive antibody production (B-cells) and polyclonal hypergammaglobinemia (with immune complex deposition).[2] Phagocytosis and immune complex removal may be impaired in SLE, promoting excessive tissue damage.[2] Both Th1 (IL-2, IFN-gamma) and Th2 (IL-4) dominance may be present.[45] SLE arthritis is associated with higher IFN-gamma (Th1), older age, female gender, fever and alopecia (when compared to in non-arthritis SLE patients).[42] SLE nephritis patients also tend to have elevated Th1 cytokines.[46] Serositis and central nervous system involvement tends to have elevated IL-4 (Th2) production.[47]

Serological Markers

- **Autoimmune Addison's disease** markers include adrenal cortex autoantibodies.[48]
- **Autoimmune thyroid disease** is most sensitively tested for using thyroid peroxidase (TPO), although false negatives can occur (e.g. juvenile autoimmune thyroiditis).[1, 49] A positive TPO in primary hypothyroidism signifies chronic lymphocytic infiltration of the thyroid.[50] **Graves disease** markers include TPO antibodies and TSH-receptor antibodies.[50]
- **Celiac disease** markers include tissue transglutaminase (IgA)[41] Antigliadin antibodies are not sensitive enough for the diagnosis of CD, with the exception of children 18 months or younger.[50] CD patients can have hypoproteinemia, hypocalcemia, and elevated liver enzymes.[52] Liver enzymes tend to normalize after six months of strict gluten elimination.[53, 54] Prolonged gluten exposure appears to be associated with an increased risk of developing other autoantibodies.[55] Gluten ataxia can be associated with widespread IgA deposition (against type 2 tissue transglutaminase) in the cerebral vasculture and in jejunal tissue.[56]
- **Type 1 Diabetes Mellitus (DM-1)** autoantibodies include those to glutamic acid decarboxylase, pancreatic islet cells, insulin and tyrosine phosphatase-like molecules.[57] Autoantibodies can be present for years before the onset of hypoglycemia.[58] Testing predisposed individuals (e.g. family history of AD) for DM-1 associated autoantibodies and early intervention (e.g. dairy-free wheat-free diet, immune balancing treatments, oral tolerance) may preclude disease onset.
- **Primary biliary cirrhosis** associated autoantibodies include ANA, smooth-muscle, anti-liver kidney cytoplasmic antigens, anti-mitochondrial (>1:40 is most specific hematological marker of primary biliary cirrhosis) and neutrophil cytoplasmic antigens.[1]
- **SLE** is screened for using ANA and ESR. CNS involvement can be associated with thrombocytopenia and antiphospholipid antibodies.[42, 59]
- **Vitiligo** associated autoantibodies are to melanocyte proteins.[1] Interestingly, tyrosinase, the enzyme directed associated with melanin synthesis, is the main target of autoantibodies in both vitiligo and metastatic melanoma.[60] Immune stimulation such as cytokine therapy[61] and auto-vaccinations[62, 63] for metastatic melanoma can often trigger vitiligo.

It should be noted that patients with one OS AD are more likely to have elevated titers of other non-cross-reacting autoantibodies, without associated organ pathology (e.g. **Myasthenia gravis** patients with positive ANA, antithyroid antobodies, rheumatoid factor, anti-lymphocyte antibodies, polyclonal hypergammaglobulemia). **Celiac disease** is associated with an increased incidence of **DM-1**,[64] **autoimmune thyroiditis**,[65] **Addison's disease**,[66, 67, 10] positive ANA and anti-gastric parietal cell antibodies.[66, 67] Concurrent diagnoses of **SLE, RA** and/or limited **systemic sclerosis** are common.[68] A region on chromosome 16 codes for genes associated with **SLE, RA, psoriatic arthritis** & **Crohn's disease**.[2] Gene proximity may be associated with the frequent coexistence of these conditions.

Environmental Factors

- **Silica** (miners), **polyvinyl chloride**, **epoxy resins**, **benzene**, **toluene**, and **trichloroethylene** have been associated with scleroderma.[2] Consider the relevance of silica in supplements, such as chewable vitamin C, which may be partially aspirated as well as dust from kitty litter and dusty arid environments. African dust blowing into the Eastern United States and Canada has been a hot topic, carrying very fine particulate matter (more dangerous pulmonary

consequences than larger particulate matter), radioactive isotopes, heavy metals and infectious microbes.[69] Silica exposure has been associated with autoimmune vasculitis.[70] Silicone breast implants have been speculated to be associated with scleroderma and other connective tissue disorders, although published evidence is conflicting.[71] **Platinum**, a metal associated with autoantibody development,[72] has been found in increased levels in the tissue around silicone breast implants.[73] Saline breast implants usually have a silicone exterior. It is well known that localized fibrosis may occur around the silicone breast implant.[2]

- **Foreign body syndrome** should be considered in the context of autoimmune diseases (e.g. knee, hip, and dental implants, screws, glues used in knee implants, cosmetic implants).[74] Although reactivity to foreign bodies may be controlled (e.g. ozone minor autohemotherapy, neutralization, immune balancing botanicals, probiotics), it is an uphill battle until the foreign body is surgically removed.
- **Pentazocaine** and other medications have been associated with iatrogenic sclerosis. **Aniline** tainted rapeseed oil in Spain (1981) resulted in 20,000 cases of a multisystem disorder resembling scleroderma. **L-canavanine** containing alfalfa seeds (1994) have been associated with SLE development (L-canavanine competes with arginine, may inhibit pyridoxal phosphate pathways). [75]
- **Heavy Metals** can have a profound affect on autoimmune disease. Blood mercury can assess acute exposure of mercury (e.g. leaking amalgams; no seafood consumed within 1 week). Low lactate dehydrogenase (LD) levels are often associated with blood mercury levels elevated above the reference range (as per clinical experience). Optimal blood mercury is less than the bottom 1/6th of the reference range. Lead has been associated with suppressed humoral responsiveness (decreased IgM and IgG titers).[76] Mercury has been associated with MS, Parkinson's disease and autism. It results in elevated Th2 cytokines (IL-4) serum IgE titers. Glutathione depletion due to mercury can cause mast cells to degranulate and potentiate IL-4 (Th2) production.[77] Animal studies have demonstrated that mercury can induce and worsen autoimmune disease in susceptible animals.[78, 79, 80] Mercury can induce increased ANA titers and T cell reactivity in murine models[78, 81] Chelation of heavy metals and if necessary, removal of leaking amalgams can help to remove exacerbating factors in the development and progression of autoimmunity.
- **Petroleum** products may increase autoimmune disease development risk (e.g. lupus related autoantibodies in murine model; n-hexadecane jet fuel and diesel exhaust)[82]. Calgary oil sands communities have an increased prevalence of autoantibodies.[83] Mineral oil has been associated with anti-Ro antibody development, increased LFTs, hypoalbuminemia and cellular immunodeficiency (human case study; subcutaneous administration).[84] Although most of this research details intradermal, subcutaneous and intraperitoneal petroleum influences of autoimmunity, considering the lipophilic nature of petroleum products, there may be a negative effect of topical applications (e.g. most skin care creams are petroleum based). Subcutaneous and intradermal exposure of petroleum compounds occur with the widespread practice of applying petroleum based antibacterial products to cuts and petroleum based creams to damaged skin (e.g. eczema, dermatitis).
- **Vaccine adjuvents**[85], **pristane** (2,6,10,14-tetramethyl-pentadecane), **Bayol F** (Incomplete Freund's adjuvant) and **squalene** injected intraperitoneally can induce autoantibodies (murine model; IL-12, IL-6, TNF-alpha induced)[86], SLE symptoms (murine)[87] and RA-like arthritis (rat models).[88] **Mineral oil** and pristine (intraperitoneal) are associated with lipogranuloma formation (lymphoid neogenesis; increased B-cells, CD4(+)T cells, dendritic cells).[89]

Dysbiosis & Stealth Infections

Rheumatoid Arthritis and HLA-B27 associated autoimmune diseases such as **anklyosing spondylitis** (AS)[90] may develop due to molecular mimicry (e.g. Klebsiella pneumonia[90], proteus mirabilis[91]). **Scleroderma** may be associated with a previous streptococcal infection.[2] Klebsiella pneumonia antibody titers are higher in **AS, Crohn's Disease** and **Ulcerative Colitis** patients than in healthy controls (despite no elevation to E. coli or 10 other obligate anaerobes in any test group).[92] "**B27 disease**" is a new autoimmune disease, occurring in patients with AS or uveitis (HLA-B27 positive),that is associated with molecular mimicry between Klebsiella and spinal collagens types I, III, and IV.[93] Intestinal dysbiosis can be assessed using a stool microbiology and

sensitivity panel. Clearing chronic intestinal and urinary infections may be paramount to controlling these diseases. Most dysbiotic bacteria (including Klebsiella) and yeast appear to be are sensitive to caprylic acid, with the exception of pseudomonas (rare), which usually requires citrus seed extract (contains benzalkonium chloride, active ingredient in Lysol) or alcohol extraction of Uva ursi.

Chronic infections such as hepatitis C virus, Epstein Barr virus, Herpes 6 and 8 viruses, can amplify B cell polyclonal expansion (anti-apoptotic signals), leading to longer survival of B cell subsets.[94] **Sjogren's syndrome** and **RA** (e.g. mycoplasma, EBV, CMV, parvovirus, rubella) may be associated with these viruses.[2] **Systemic sclerosis** may be associated with latent Cytomegalovirus (CMV) infection (via vascular injury, molecular mimicry) and parvovirus B19.[2] Some infections may stimulate auto-reactive immune responses, promoting loss of self-tolerance (e.g. Epstein-Barr virus).[2] Hepatitis C infection has been associated with **SLE** and cryoglobinemia[95] and increases prevalence of autoimmune liver involvement three fold in Sjogrens syndrome.[96] Silymarin may be considered in these patients to limit liver damage, and potentially prevent autoimmune hepatic involvement (additionally silymarin decreases Th1 & increases Th2 cytokines[146]). Assessing for chronic infections (e.g. ASO titer, hs-CRP, Epstein Barr virus and Cytomegalovirus reactivity), followed by appropriate treatment (e.g. ozone major autohemotherapy (MAH), ultraviolet blood irradiation, IV 50-75g vitamin C, IV 0.03% H2O2), and immune system balancing (e.g. vitamin D, ozone minor autohemotherapy (MnAH), normalization of gut flora, allergies treatment, detoxification protocols) may help to these AD. High dose vitamin D3 may modulate numerous forms of autoimmunity.[97] To the contrary, Marshal Protocol advises against the use of vitamin D in RA, SLE, Parkinsons disease and sarcoidosis.[98] It should be noted that although Marshall Protocol advises against immunotherapy such as vitamin D, it does advocate the use long term low dose antibiotics to clear 'cell wall deficient bacteria' (analogous to the stealth infections (e.g. C. pneumonia, EBV, CMV) cleared by UBI, MAH, high dose vitamin C and IV low dose peroxide).

Dental Health

Hippocrates said 2000 years ago "show me the health of a man's mouth and I will show you the health of his body".[99] Chronic infections, leaking amalgams, galvanic charges and surgical implants (especially upper jaw) can all be detrimental to health. Elevated hs-CRP can be evidence of dental infections (e.g. failed root canal(s)). Although composite (white) dental fillings are usually preferable to mercury amalgams and gold fillings (galvanic charge), there is no perfect material. Composite fillings may contain bisphenol A.[100] Upper maxillary dental implants can cause significant autonomic nervous system effects, severely affecting cognition, energy, mood, as well as immune regulation. Gold fillings adjacent to other metals such as amalgam (mercury alloy) or zinc oxide (root canals) can cause a galvanic charge, with the potential to profoundly affect the autonomic nervous system (ANS).[101]

In response to an elevated blood mercury (no seafood 1 week prior), amalgam degradation or excessive chelation challenge results, consideration should be given to proper amalgam removal. Priority should be given to older amalgams, especially those with visible chips, cracks, and striations (e.g. bruxism). IV Ca-EDTA, vitamin C and glutathione, as well as oral NAC should be administered the day of amalgam removal. A downloadable handout on the proper removal of dental amalgams is available through the International Association of Oral Medicine and Toxicology (IAOMT) website. The IAOMT has a licensing program for biological dentists, as well as having a wealth of information available for other health care professionals.

Autoimmunity: it just may be ubiquitous

Atherosclerosis, various pulmonary, skin and kidney diseases have mononuclear infiltration and adaptive immune responses key to their pathology.[102] **Sleep Apnea** has been proposed as a risk factor for the development of cell-mediated autoimmune diseases, by recurrent cell injury from transient episode of hypoxia.[103] Obesity, with its higher endogenous estrogen production and increased risk of sleep apnea, may be a risk factor for the development of autoimmune disease (e.g. SLE, systemic sclerosis, scleroderma). Weight loss may be prudent in such cases.

Autism spectrum disorder has been associated with neuroanatomical alternations involving the cerebellum and limbic system.[104] Abnormalities have also been observed in the cerebral cortex, corpus callosum, brain stem, and basal ganglia.[100, 105, 106, 107] IgG autoantibodies to thalamus and hypothalamus of autistic patients have been reported (in vivo).[108] Elevated lymphocytes and antibodies in the CNS may be associated with a compromised BBB.[109] Elevated brain autoantibodies include those to

serotonin receptors,[110] myelin basic protein,[111] glial fibrillary acid protein,[112] neuron-specific antigens,[113] antibrain endothelial cell proteins and neurotrophic factors[114] and nerve growth factor[115]. A healthy blood brain barrier (BBB) does not **necessarily** preclude this, as B cell tracking across the BBB can promote intrathecal antibody synthesis.[116] Autistic children often have increased gut permeability (urinary lactulose:mannitol test), concurrent with increased food antibody and autoantibody production.

Mercury and chemical detoxification, normalization of the gastrointestional flora and permeability, and treatment of food and environmental allergens should be considered in Autism.

The pathogenesis of **Schizophrenia**, **Parkinson's disease** and **post-partum depression**[117] have been postulated to be linked to immune system responses. Elevated levels of autoantibodies to heat shock protein and brain autoantibodies (CSF and serum) have been reported in Schizophrenia.[118] Parkinson's disease has been proposed to be an autoimmune disorder, involving IFN-gamma (Th1), protective cytokines being IL-10 (Th2).[119]

TREATMENT

Glutathione

Glutathione depletion may shift Th1 to Th2 dominance (mercury depletes glutathione).[24] Low APC levels of glutathione (in vivo) can result in lowered Th1 activity and higher Th2 activity.[121] Repleting glutathione levels appears to augment Th1 activity and balance Th2 activity.[dq] Augmenting glutathione levels may work best for Th2 dominant autoimmune diseases, such as SLE (watch for Th1 SLE symptoms such as arthritis), autism, Parkinson's disease, and early scleroderma/systemic sclerosis. IV glutathione and oral NAC can be used to augment glutathione levels. MAH can be used to augment other antioxidant enzymes such as catalase, glutathione peroxidase and superoxide dismutase.

Intestinal Health

Parasites can deplete glutathione, increasing Th2.[112] When the parasitic load is too low to generate a T regulatory response,[123, 124] this has the potential to exacerbate Th2 mediated autoimmune diseases[125] (e.g. antiphospholipid syndrome, Goodpasture's syndrome, Myasthenia gravis, Rheumatoid Arthritis,[126] early SLE, Sjogren's syndrome, Stiff-man syndrome, Vitiligo, Wegener's granulomatosis, Autoimmune hemolytic anemia, Dermatitis herpetiformis). Chronic helminth infections have the potential to downregulate T and B cell responses by inducing regulatory T cells, IL-10 and TGF-beta.[127 121]

A sudden change in **human intestinal flora**, due to industrialization, surgical childbirth, pasteurized foods, cleaner homes, and indiscriminate use of antibiotics, may have attributed to the sudden rise in AD incidence over the last 50 years.[128] Normalization of the intestinal flora is important for Th2 dominant AD (e.g. autism, Parkinson's disease, SLE, early scleroderma/systemic sclerosis). Although lactobacilli appear to augment Th1 immunity,[129] there is evidence that they may balance Th1 immune responses (may be species and strain specific).[130]

Diet/Nutrition

Arthritis: Avoiding solanine (toxin) containing nightshades (potatoes, tomatoes, peppers, eggplant) may help reduce inflammation in autoimmune arthritis patients (e.g. RA). New potatoes without the skin have far less solanine than old potatoes with the skin (majority of the solanine in the skin). There are anecdotal reports that red skinned potatoes have less solanine, although this lacks supporting published evidence.

Celiac Disease: Eliminating all gluten containing food from a Celiac patient's diet can reduce the probability of developing concurrent autoimmune thyroiditis or DM1 (all Th1 dominant).[55] Breast feeding appears to reduce the incidence of CD.[131] Gluten introduction prior to 4 months of age,[132] and rotaviral infections during infancy[133] appear to increase the risk of developing CD. The overlap of breast-feeding with the introduction of gluten containing food may be an important preventive factor in minimizing CD risk.[134] Iron and B12 deficiency and osteoporosis are common in CD. Ensuring proper absorption (intestinal health, gluten-free diet) as well as adequate supplementation (iron, calcium, B12, glutamine, probiotics) can help replete deficiency.

Diabetes Mellitus: In murine models, diets rich in vitamin A and polyphenols (grape powder) reduced incidence of DM development (Th1), reduced histological evidence of autoimmune DM as well as reduced TNF-alpha production in response to LPS.[135] DM-1 incidence is higher in children who drink cow's milk, likely due to molecular mimicry between milk beta-lactalglobulin, wheat proteins and islet cell proteins.[136] Dairy and wheat avoidance in DM-1 predisposed children is prudent (e.g. family history of celiac disease, autoimmune thyroiditis, autoimmune Addison's disease; elevated glutamic acid

decarboxylase, pancreatic islet cell antibodies, tyrosine phosphatase-like antibodies). **EPA** may be beneficial to decrease downstream inflammation caused by autoimmune disease (e.g. Celiac disease, RA)

Thyroid Disease: Excessive iodine supplementation may be associated with the autoimmune thyroid disease (Th1) development[137] and exacerbation[138]. Iodine supplementation should be monitored in relation to thyroid autoantibodies on a case by case basis.

Th2 Dominant Autoimmune Disease: Dietary flavonoids have been associated with supression of Th2 upregulation[139], which may be of virtue in Th2 dominant autoimmune diseases. Juicing flavonoid rich fruits and vegetables, dietary berries and flavonoid supplementation may be considered in these patients. Additionally, a hypoallergenic diet may be important for patients with Th2 associated autoimmune diseases (e.g. SLE, Sjogrens, RA). Testing (e.g. elimination/rechallenge diet [only 5 days needed for elimination period[140]]; provocation neutralization food allergy testing; food IgG4/IgE panel although often false negative for corn, soy and yeast) and avoiding positive food allergens (e.g. dairy, wheat, egg, corn, soy, yeast) may help to reduce ambient Th2 cytokines. Digestive enzymes and betaine HCl can help to improve digestion and lower allergenic potential. 1 tsp of trisalts (sodium bicarbonate, calcium carbonate, sodium citrate), baking soda or Eno (sodium citrate) in water after consumption of allergic foods consumption or provocation of allergy symptoms can help to alleviate symptoms. These salts help to alkalinize the tissues, precipitating histamine out of solution, rendering it inactive.[140]

Hormones

Estrogen promotes dendritic cell differentiation and APC proliferation.[141] Estradiol binds T and B cell receptors, increasing cell activation and survival.[2] Lymphocyte mediated autoimmune diseases such as MS, RA, Graves' disease, SLE and Hashimoto's thyroiditis are more prevalent in females than males.[141] 90% of women with are in their reproductive years and the two fold increased prevalence of SLE in women taking estrogen (contraception or HRT). In general, women have higher estrogen and prolactin levels, and lower DHEA levels than men.

DHEA appears to enhance IL-2 production and subsequent proliferation of Th1 cells, decreasing ANA titers (murine model). This may be best suited for Th2 associated autoimmune diseases such as SLE (watch for Th1 side effects). Harrison's Textbook of Internal Medicine (16th ed.) lists DHEA 200 mg per day as a treatment for SLE.[2]

Prolactin is immunostimulatory and promotes autoimmunity. It impairs autoreactive B cell destruction, has an anti-apoptotic effect,[142] enhances immune cell numbers and enhances antibody production.[143, 4] SLE, RA, Sjogren's syndrome, Hashimoto's thyroiditis and MS have all been associated with hyperprolactemia.[143] Stress and breastfeeding stimulate prolactin secretion. Highest daily prolactin production is at 2 AM. It should be noted that there is no clear correlation between prolactin level and autoimmune disease activity.[143]

Botanical Medicine

As previously noted by Kevin Spelman et al.[144], numerous botanicals likely exert a significant effect on cytokines. Unfortunately, all of this research was conducted in either animal models or in vitro, which is apparent by the level of contradictory results evident. Human studies may give greater insight in reference to the immunomodulatory effect of botanicals. As noted by Kevin Spelman et al, historical use in conjunction with current data may give us the greatest insight until human data is available. Intestestingly, **Panax ginseng** may help to increase apoptosis in autoimmune disease (Ginsenoside Rh2.)[145]

A number of herbs appear to affect T regulatory function. **Silibinin** (major pharmacologically active component of Silymarin) has demonstrated dose-dependent immunosupressive (downregulation of Th1 cytokines; inhibition of NF-kappaB) and immunomodulatory (upregulation of Th2 cytokines) effects in experimental autoimmune encephalomyelitis, reducing histological evidence of demyelination and inflammation.[146] It has been extrapolated from these results that silibinin may be effective in the treatment of MS. **Astilbin** has been demonstrated to increase IL-10.[147] **Epigallocatechin gallate** (in green tea) has been demonstrated to decrease T cell mediated inflammation and induce monocyte apoptosis.[148, 149] It has been proposed that **Wobenzym** may help to reduce inflammation in chronic glomerulonephritis, thus reducing risk of autoimmune renal disease.[150]

Resveratrol has been demonstrated to inhibit production of IFN-g/IL-2 (Th1) (murine splenic lymphocytes) and TNF-a/IL-12 (Th1) (murine peritoneal macrophages). Resveratrol blocked transcription factor NF-kB activation (inhibiting cell proliferation, cell-mediated cytotoxicity, cytokine production).[151]

If these results are applicable to human models of autoimmunity, the use of resveratrol may help prevent the onset of Th1 dominant autoimmune diseases (e.g. Celiac, Hashimoto's, DM-1, MS), and slow the progression of mixed Th2/Th1 diseases (e.g. SLE, RA). Considering the immune/macrophage role in atherosclerotic plaque development, the Th1 calming effect of resveratrol may be partially attributable to the French Paradox (e.g. red wine; low cardiovascular disease risk despite high fat diet).

Conclusion

Although AD pathophysiology may seem impenetrable at first glance, culminating the morass of literature into simple language can be of great benefit to both doctor and patient. With a firm understanding of the basic immune homeostasis and immunoregulation, the most suiting treatments should be easily gleaned. Although the current groupings of autoimmune diseases (e.g. Th1, Th2 dominant or mixed Th1/Th2; organ specific or systemic) may aid in the diagnosis and understanding of these diseases, one must comprehend the limits of these groupings. Due consideration should be given to human research and treatments demonstrated efficacious in human models. Historical use of botanical medicine may help us cull the conflicting cytokine effects demonstrated in vitro and animal models. My hope is that this article has enlightened you, and sparked a keen interest in the constant evolution of our knowledge of immunopathology. What has been presented here is merely the tip of the iceberg.

About the Author

Tawnya Ward received her ND from the Canadian College of Naturopathic Medicine and a BSc in biology from Dalhousie University. She has been trained by the American College for advancement in Medicine (ACAM/ISCT) for chelation therapy and by International Oxidative Medicine Association for ozone, ultraviolet and peroxide therapies. She has been trained in bio-identical hormones and anti-aging by the International Hormone Society. She has been trained by the American Academy of Environmental Medicine, a specialist organization for allergy, detoxification, and environmental sensitivity. She is licensed through CNPBC in chelation therapy, oxidative medicine and acupuncture. She is Chief Inspector for the Inquiry Committee with CNPBC. Dr. Ward runs her practice at the Pangaea Clinic of Naturopathic Medicine in Richmond, BC.

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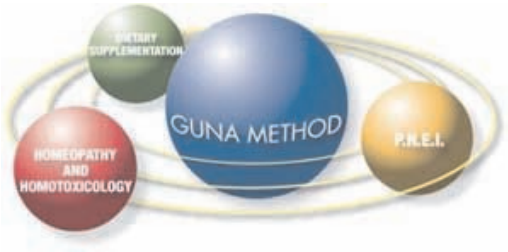
<u>The GUNA Method</u> (From GUNA Italy & *Vibrant Health)*



Physiological Regulating Medicine (The ***GUNA Method***) represents the most up-to-date integration of conventional medicine and homeopathic medicine. The **GUNA Method** includes the most recent knowledge about homeopathy, homotoxicology, **P**sycho-**N**euro-**E**ndocrine-**I**mmunology and nutrition. **GUNA Method**'s innovative approach combines the essential elements of allopathy and homeopathy; integrating the allopathic element related to diagnostic technology and modern physiology, whereas evidence based homeopathy provides the therapeutic effects. **Physiological Regulating Medicine** adds to classical homeopathy a new therapeutic concept of **restoring physiology** through communicating molecules such as *hormones, neuropeptides, interleukins, and growth factors* prepared in homeopathic dilutions, which are at the same physiological concentration as the biological milieu. The homeopathic preparation method of "dilution-dynamization" makes these communicating molecules even more effective, providing a **biofeedback** mechanism capable of restoring the body's homeostatic balance.

Therapeutic Structure of the GUNA Method

Considering the above mentioned assumptions, it is easy to understand the formulation of **GUNA** medications. Although each product has specific fields of application, each composition shows a common structure to ensure a holistic medical approach to acute and chronic diseases.

GUNA homeopathic medications are unique, due both to the ingredients and to the respective dilutions. These medications are designed with a standard common philosophy, which is that "*the etiopathogenesis of a disease can be reflected in its homeopharmacological structure*". The ingredients in each GUNA formulation are assembled and balanced in combinations that result in a powerful **THERAPEUTIC UNIT,** where all components act in concert to restore the body's balance and to correct the diseased state. GUNA medicines represent an integrative therapy, which is effective on both the **inherent causality** and **symptomatic treatments**.

GUNA ingredients act on 5 different levels:

- **DETOXIFICATION:** A detoxified and drained **extra-cellular matrix** absorbs oxygen and nutrients adequately, allowing cellular receptors to be activated by the "therapeutic molecules", thus enabling cells to perform their metabolic function. The **organs of elimination**, activated by specific detoxification ingredients, will be strengthened in their physiological excretory and toxin-release function.
- **P.N.E.I. RE-BALANCE: Modulating the Psycho-Neuro-Endocrine-Immune axis** in both directions, (psychosomatic and somatopsychic), is the essence of **Physiological Regulating Therapy**. In support of sophisticated biological mechanisms, *homeopathic micro doses of: cytokines, hormones, neurotransmitters and selected homeopathic ingredients* (herbal, mineral, or animal origin), reduce, modulate, and stimulate the reactivity of the three main biologic systems (nervous, immune and endocrine), to rebalance their physiological functioning.
- **CELL METABOLIC SUPPORT**: The action of the hormones, cytokines, or any homeopathic remedy on the cell membrane receptors would not be effective if the cell were not in the proper **"energetic" condition** to respond. Therefore, cell metabolic stimulation is a necessary step to assure therapeutic success. *Vitamins, minerals, oligonutrients*, and most importantly, *homeopathic micro doses of Krebs Cycle salts and quinones*, activate the mitochondria as energy reservoirs to restore the **highest ATP synthesis capacity**.
- **CELL NUTRITIONAL SUPPORT:** Nutrients (*proteins, carbohydrates, lipids*) can have an essential role in maintaining or restoring health. The most advanced research studies in nutrition have defined the typology, metabolic routes, and most importantly, the *optimal amounts* of each nutrient necessary for cellular nutrition. GUNA Products contain these **small** *(oligos)***and balanced** *(orto)* **amounts of amino acids**, and **vitamins necessary for proper cell nutrition.** In addition, **oligo nutrients** are incorporated to protect biological structures from free radicals, which are harmful in chronic and degenerative diseases, as well as in the aging process.
- **SYMPTOM CONTROL**: The novel **GUNA** therapeutic concept results from scientific studies in the field of **molecular biology, coupled with homeopathic tradition**. **GUNA**'s nano-pharmacology technology is a process that utilizes homeopathic micro-doses of molecules at the same concentration as in the physiological milieu. These molecular micro-doses are capable of reactivating the appropriate biological immune response. *Interleukins, neurotransmitters, homeopathic hormones, as well as classical homeopathic ingredients,* work in synergistic coordination to reverse inflammatory processes and their resultant physiologic effects. The specific ingredients for each evolutionary phase of the inflammatory process (***calor, dolor, rubor, tumor)*** are uniquely formulated to restore homeostatic balance with a considerable reduction in recovery time.

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An Overview of the Research

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Zyflamend®-Mediated Inhibition of Human Prostate Cancer PC3 Cell Proliferation: Effects on 12-LOX and Rb Protein Phosphorylation. Peiying Yang, Carrie Cartwright, Diana Chan, Mary Vijjeswarapu, Jibin Ding and Robert A. Newman Cancer Biol Ther. 2007 Feb 25;6(2). PMID: 17218785

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Cleveland Clinic

Response of Glioblastoma Cells to a Mixture of Standardized Extracts from Common Herbs and Spices. Mladen Golubic, Judy Bondar, Patrick Leahy, John E.B Fox and Gene Garnett Status: Presented at 3rd Annual Society for Integrative Oncology Meeting, Nov 11-13, 2006, Boston, MA.

Beth Israel Deaconess Medical Center

Rheumatoid Arthritis Research Evaluation of the Effects of Zyflamend, a Unique Herbal Preparation for anti-inflammatory treatment in Rheumatoid Arthritis Patients; A Six month Pilot Study Monitoring Health-Related Quality of Life and Clinical Efficacy Endpoints (Study is currently enrolling). Roberta Lee, MD, Medical Director, The Continuum Center for Health and Healing, Beth Israel Medical Center.

MUSC MEDICAL UNIVERSITY OF SOUTH CAROLINA

Efficacy Study of the Cancer Chemopreventative Potential of Zyflamend for Colon Cancer. Michael J. Wargovich, PhD, FACN, Director of Chemoprevention Research .

COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK

PubMed A service of the National Library of Medicine and the National Institutes of Health www.pubmed.gov

Zyflamend, a unique herbal preparation with nonselective COX inhibitory activity, induces apoptosis of prostate cancer cells that lack COX-2 expression. Bemis DL, Capodice JL, Anastasiadis AG, Katz AE and Buttyan R. Nutr Cancer. 2005;52(2): 202-12. PMID: 16201851.

COLUMBIA UNIVERSITY CENTER FOR HOLISTIC UROLOY

Men in the Columbia University Center for Holistic Urology PIN study are given a specific protocol of dietary supplements from NewChapter, that they are told to take daily to help maintain healthy inflammation levels, while providing antioxidant and nutritional support. Because of the early interest in our study, I have detailed the complete daily nutritional supplement protocol.

Aaron Katz, M.D., Director,
Center for Holistic Urology, Columbia University

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SUPPLEMENTS

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- Supercritical DHA100™
- Supercritical Holy Basil™
- Turmericforce™
- Baikal Skullcap
- Green & White Tea Extract
- Anti-Aging Probiotics™
- Every Man® One Daily Multivitamin

Zyflamend PIN Study
(Prostatic Intraepithelial Neoplasia)

- No drug interactions documented
- 2 patients taking blood thinners (Coumadin, Plavix)
- All patients are 100% compliant
- No alterations in blood chemistry values, EKGs, coagulation profiles or testosterone levels have been found
- 91% have a biopsy negative for prostate cancer
- 65% of biopsies show a return back to normal prostate tissue

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Considering multiple sclerosis, psychoneuroimmunology, and mind-body medicine

Dr. Teri Jaklin, ND

MS represents chronic pain and anxiety for some, poor digestion to many, frequent and urgent bladder commonly, chronic sleep deprivation almost always, deep sensations of cold, weakness and depressed affect to others. Tremendous feelings of fear and anxiety accompanying a diagnosis, uncertainty of exacerbation and a hopelessness associated with the possibility of disability further complicate the patient picture. People feel they have no control and often put off normal life decisions for fear of what the future may bring.

Both conventional neurology and naturopathic medicine have come to understand a number of critical pathophysiological activities that are hallmarks of MS. Functional neurologists like Jay Lombard and David Pearlmutter have clearly outlined the roles of: neuroinflammation, the result of a misdirected immune response; oxidative stress causing neurodegeneration by such aggressive reactive oxygen species (ROS) as hydrogen peroxide, superoxide, nitric oxide, and peroxynitrite [1] as well as direct neuronal damage from excitoxicity caused by an imbalance of excitatory neurotransmitter activity.[2]

Despite this knowledge, there can still be great disparity between the histopathological changes of MS and the neurological deficits from person to person. The acute onset and remission of symptoms is often difficult to comprehend based only on the concept of demyelination. It is often observed that severe neurological deficits may be associated with minor pathological changes in some while, despite extensive demyelination, neurological function is normal in others.

Having worked with people with MS for about twenty years the benefits of a fundamental wholistic treatment plan are clear. Beyond that, the reach of therapy, depending on the patient and the breadth and depth of our own therapeutic style and experience, can be vast. Guyton once described the body as "a social order of about 75 trillion cells organized into different functional structures…each cell benefits from homeostasis and in turn each cell contributes its share towards the maintenance of homeostasis."[12] This being said, there are many components to building a successful treatment plan.

There are number of effective therapeutic approaches which have been exhaustively researched. They include but are not limited to:

Basic support in the form of fish oil for its anti-inflammatory, neuroprotective and neurorestorative properties; methylcobalamin supporting neuronal detoxification and protection; antioxidants and nutrients that cross the blood-brain-barrier and quench excessive ROS activity; and Vitamin D and probiotics for immune regulation.

Nutrition has become a non-negotiable factor of comprehensive MS treatment plans. We now understand the threats of excitotoxicity and how excessive activation of glutamate receptors leads to neuron death.[2] Gluten sensitivity has been shown to induce a state of heightened immunological responsiveness (which frequently occurs with no bowel involvement and is at times exclusively a neurological disease).[3] The work of Dr. Roy Swank MD has shown the inflammatory effects of saturated fats. The autoagression caused by molecular mimics in dairy, gluten and legumes is evidenced in the detailed research of Dr. Ashton Embry PhD. Most recently the widely publicized work of Dr. T. Colin Campbell PhD *(The China Study)* demonstrated the detrimental impact of animal proteins on chronic disease including multiple sclerosis. The basics of good nutrition are essential in the management of inflammation, the promotion of healthy detoxification and the maximization of normal metabolic function. Diet alone can have a tremendous impact on the state of health of many MS patients.

Self care becomes important in removing the focus from solely the brain and the immune system, normalizing the organism as a whole. Circadian rhythm, lymphatic, metabolic and immune regulation and support, can be greatly improved through the use of traditional naturopathic practices like sleep hygiene, castor oil packs, dry skin brushing and hydrotherapy.

Lifestyle modification. As early as 1868 Charcot connected psychological stress to the pathogenesis of MS. There is a consistent association between stressful life events and subsequent onset or exacerbation of multiple sclerosis. While many triggers

have been proposed (including bacterial/viral infection that cause T cells to "mistake" myelin proteins for these antigens, bacterial "super antigens," physical injury or stressful life events), Charcot speculated that grief, vexation, and adverse changes in social circumstance were related to the onset and exacerbation of MS.[4] Since stress is unavoidable in modern life, stress management has become a valuable therapeutic tactic.

An individual's mental/emotional states including physical and mental stressors play an extremely important role in recovery from multiple sclerosis. ***Mens sana in corpore sano*** – a healthy mind in a healthy body – the concept has been around for centuries with little understanding of the mechanisms. In fact, historically Greek and Cartesian dualism held that a man's soul was of an entirely different essence than his body and that these dual entities had no interaction with one another - there existed a dichotomy of soul and body, an absolute split.[5] Both of these concepts cast away any responsibility on the part of the mind for the circumstances of the body. Until very recently this school of thought was deeply entrenched in modern medicine.

While mind-body medicine is not a new concept to naturopathic doctors, it has not been accepted until recently. In the past 30 years, the development of psychoneuroimmunology (PNI) has put a mechanism behind the union of the mind and the body, and indirectly validated the mind-body approach to healing.

Why does the disparity in people with MS exist? Is it possible that this precious tool, the mind-body, is underutilized in our healing plans? Is it possible that even as naturopathic doctors the dogma of the current medical paradigm has influenced our thinking on this essential link in the healing chain? Understanding the mind-body connection in autoimmune is vital.

Discussing and teaching activities such as diaphragmatic breathing, visualization, and guided meditation or encouraging self development thorough resources like Louise Hay's *You can heal your life* (for other titles patients may find helpful visit www.soundstrue.com) are all valuable therapeutic tools. Recommending lifestyle balancing practices like yoga, qi-gong, tai-chi; providing support in often overwhelming lifestyle change; or simply lending a supportive ear if the "treatment" of the day is simply to listen.

Employing such practices combined with decreasing inflammation, removing immune irritants, reducing oxidative damage, encouraging lifestyle and nutritional change will absolutely change the trajectory of the course of disease for people with MS. Remember, "each cell benefits from homeostasis and in turn each cell contributes its share towards the maintenance of homeostasis,"[12] or homeostasis comes one cell at a time, and every step in that direction is part of a greater outcome.

Understanding Psychoneuroimmunology

In multiple sclerosis an excessive inflammatory process is believed to disrupt normal CNS and immune system cross-talk. The theory of HPA axis disruption is supported by patients, who take basic supportive measures mentioned above, but otherwise show the most dramatic improvement with therapeutic interventions specific to the HPA axis and the endocrine system. This area of MS is as fascinating as it is complex. Although much research has been completed in this area a significant amount remains still to be undertaken.

PNI and MS

It is a challenge to simplify the highlights of PNI as it relates to MS. However, the following should be considered:

- ANS dependent neurotransmitters such as norepinephrine, epinephrine as well as glucocorticoids exert suppressive *as well as* enhancing effects on the immune system[6]
- ANS neuropeptides, next to catecholamines also seem to play a complex role in neuro-immune regulation and while acute exposure to elevated levels of catecholamines seems to be adaptive, chronically elevated levels seem to have the opposite effect.[6]
- Blood born cytokines influence central cites such as the hypothalamus where the incidence of patients with lesions is 95% of which the majority (60%) were active.
- The more active lesions in the hypothalamus, the shorter the life expectancy. Data show suppression of the CRH neurons by active hypothalamic lesions, which causes an unfavourable disease course via inadequate cortisol response during relapses of MS.
- Both HPA axis hypo *and* hyperresponsiveness are noted in MS.

- In one study the extent of activation or the HPA axis in MS patients is up to 2.5 fold greater than in normal controls.[16]
- Recent data indicate a decreased GC receptor sensitivity in MS patients and a trend toward clinical worsening in association with increasing GC resistance.[7]
- Anatomical findings indicate dense sympathetic nerve endings within various lymphoid organs[9-11]
- Strong support for the association between stressful life events and disease progression comes from a meta-analysis, indicating an increased risk for MS exacerbation after stressful life events.[8]
- The state of sympathetic dominance is status quo.

The central message from this is ***dysregulation***. The multifaceted nature of the neuro-immune interaction, consistent with the resulting complexities of the MS patient presentation, leave abundant room for the incorporation of practices that will support and regulate the body in its adaptation and coping mechanisms.

Mind-Body Medicine

The mind-body connection occupies a powerful role in the history of many healing traditions, naturopathic medicine being no exception. Many studies now support the fact that emotions affect health. Despite historical resistance, today the science of mind-body medicine is entrenched in some of the most esteemed medical colleges, most notably, Herbert Benson's research on the *relaxation response* and Candice Pert's work confirming the presence of neuropeptides and neurotransmitters on immune cells.[13] Thankfully time and science have marched on in sound validation of mind-body medicine as quite possibly the therapeutic flipside of the pshychoneuroimmunology coin.

As a forefather to mind-body medicine, the placebo effect has proven the impact of psychology on physiology. Herbert Benson, the Harvard father of mind-body medicine reminds us that placebo effect (which he feels should be renamed "remembered wellness") yields clinical benefit in 60–90% of diseases. This must have been high-octane fuel for the advancement of mind-body medicine. Though the placebo effect was often viewed negatively, the question becomes how do we harness the power of the placebo effect and translate it into a therapeutic mind-body effect?

Mind-body medicine is an umbrella term that includes healing traditions that capture the essence of the powerful placebo effect and build on it to provide practices that have been scientifically proven to improve health. These practices include but are not limited to: mindfulness meditation, yoga, qi-gong, tai-chi, breathwork, creative arts, prayer, visualization, guided imagery and cognitive behavioural therapy. While each of these modalities work with our bodies to enhance the vital force, strengthen the flow of qi and regulate physiological systems, we will look, by way of example, at the most popular.

Meditation

With a history of thousands of years, a good body of study now exists supportive of the use of mindful based stress reduction through mindfulness meditation. This is one of the most common mind-body interventions and is a conscious mental process that induces a set of physiological changes known as the *relaxation response*. Research has connected the relaxation response to concentration and control of the ANS to improve mood, clear depression, reduce anxiety and improve overall well being. Physiological responses by way of an improved immune system have also been demonstrated.[14] Meditation is a state of 'bare-attention', focusing on being present in the here and now by managing external distraction. The benefits of meditation have been demonstrated to bring about dramatic effects in as little as 10 minutes of practice, but also to reach far beyond the period of practice with improving coping mechanisms in general.[15] While formalized training is considered most effective, benefit can still be gained from books and CDs.

It is understood that the HPA axis/ANS response are dysfunctional in MS and that the modern lifestyle often includes a state of chronic stress, which aggravates that dysfunction. If we consider the HPA axis as the fulcrum of homeostasis, then even as the exact role of the mind in the body of an MS patient still eludes many medical professions, this too will be validated by science in time. What we do know is that the progress or state of MS is dependant on HPA axis and autonomic regulation. It can, therefore, be speculated that promoting regulation both through traditional practices and the science of mind-body medicine can help ANS balance, and via the vagus nerve, potentially calm the many connected physiological processes that challenge the average MS patient.

Using mind-body techniques for overcoming the fear, teaching trust in the body's innate ability to heal, and continuing to plan, aspire and live despite the diagnosis are all essential psychological parts of the healing journey.

The more naturopathic medicine advances as a science, the more it is called back to its roots. Homeostasis, while at times a lofty goal, hinges on the ability to balance the mechanistic part of our therapeutic approach, for example: nutritional modifications, botanicals, supplements or parenteral therapies with the vitalistic part of a person's healing experience, such as: drainage, self-care, homeopathy or mind-body. The ability of an individual to heal is fascinating. Equally awe inspiring is how the ability to create ownership of the healing process is often directly augmented or reduced by the state of an individual's mind-body, and their desire and ability to make changes.

About the Author

Dr. Teri Jaklin ND is a 2002 graduate of CCNM with a passionate commitment to the foundational principles of naturopathic medicine. She co-founded the Waterdown Clinic of Naturopathic Medicine in 2002 where she holds a private practice. She is Director, Organizational Wellness for an organizational development firm and lectures extensively within the profession, and in many venues for the general public.

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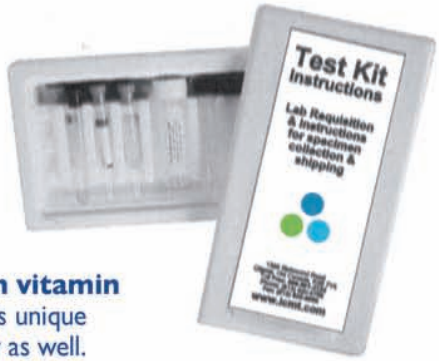

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