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Welcome to the eighth issue of Mycology News, a newsletter for health care professionals dedicated to the dissemination of information on the clinical use of mushroom nutrition. In this edition, we examine the use of Ganoderma lucidium (Reishi) in the management of histamine-mediated allergic responses and the role of Epstein-Bar Virus (EBV) in cancer growth. Dr. Rajendra Sharma details how practitioners could use EBV diagnostic tests to detect the EBV virus and we review the use of Coriolus versicolor (in italics) supplementation in Chronic Fatigue Syndrome.

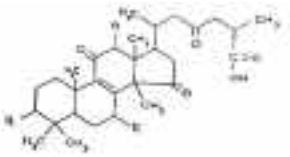
The Use of Ganoderma lucidium (Reishi)

in the Management of Histamine-Mediated Allergic Responses

The following presentation was given by Martin Powell (BSc.Hons., Dip.Ac, Dip.CHM, MRCHM - Natural Health Centre, Luton, United Kingdom) at the 5th International Symposium on Mushroom Nutrition entitled Mushroom Nutrition: A New Class of Clinical Nutrition, held at Westminster University on June 15th, 2003.

Background:
The mushroom Ganoderma lucidum (Reishi) has been used for many centuries in the traditional herbal medicine of China and Japan for its immuno-modulatory and adaptogenic properties. [1]

As well as its general health enhancing action, Ganoderma lucidum has been shown to have specific anti-inflammatory properties and this traditional usage has to been linked to the isolation from the herb of a family of ganoderic acids [2], triperpene compounds with a basic lanostane structure which exhibit anti-inflammatory properties:



The compound Ganoderic Acid C, isolated by careful fractionation of a non-polar solvent extract of Ganoderma lucidum was found to account for most of the anti-inflammatory activity from the herb as determined by in-vitro tests such as histamine release from mast cells [3].

An ethyl acetate extract rich in ganoderic acids was later found by another group of researchers to exhibit both systemic and topical anti-inflammatory activity in standard animal models such as the croton oil induced mouse ear inflammation test. [4]

The currently used topical and systemic anti-inflammatory drugs have serious drawbacks; for example corticosteroids can suppress pituitary–adrenal function, dangerously unbalance fluids/electrolytes and cause undesirable changes in skin texture [5], whilst the salicylic acid derived prostaglandin inhibitors result in severe gastric irritation. [6]

Consequently, the potential use of Ganoderma lucidium (Reishi) supplementation could offer a safe and effective alternative for the reduction of histamine-mediated immune responses.

Case Studies: Hayfever Patients
To assess the efficacy of non-fractionalized Ganoderma lucidium supplementation in two hayfever patients. The principal parameters being symptom allevation*.

Study Design
Open label study in United Kingdom in [2] patients. Patients were interviewed during the Ganoderma supplementation period, in order to assess changes in perceived quality of life, with reference to general hayfever symptoms.

Supplementation Scheduling
Supplementation commenced at 3 grams (6 tablets x 500 mg) per day and was maintained at this until the symptoms abated, at which point it was reduced to a maintenance dose of 1.5 grams (3 tablets x 500 mg) per day until the end of the hayfever season.

RESULTS

PATIENT 1

39 year old male. Chronic hayfever sufferer since childhood with little relief from conventional herbal medication. After 3-4 days supplementation at 3.0 grams (6 tablets x 500 mg) per day of Ganoderma lucidum there was a marked decrease in drowsiness, itchiness and sneezing. After 10 days the patient was able to mow the grass without significant discomfort. Continued alleviation throughout the season. Repeated benefit the following year.

PATIENT 2:

5 year old male. Developed hayfever age 4. Unable to go outside for much of early Summer. Supplementation started at 2 tablets x 500 mg a day, 1 a.m. and 1 p.m. After 1 week 90% reduction in symptoms. No red/sore eyes or sore throat. Only occasional sneezing. Able to play football outside again. Dosage maintained at 2 tablets a day until the end of the season.

DISCUSSION

In both cases there was a rapid and significant alleviation of symptoms on commencement of supplementation with *Ganoderma lucidum* indicating that Ganoderma supplementation may have a role to play in the management of histamine mediated immune responses.

CONCLUSION

Taking into account the limitations of such a small sample size, we have a curiosity and further research is required to confirm the potential of *Ganoderma lucidum* in controlling host-mediated allergic responses

NOTES

1) G.T.Liu in "Mushroom Biology and Mushroom Products", Eds S.T.Chang et al, The Chinese University Press, Hong Kong, 267 (1993).

2) T.Kubota et al, Hely Chim Acta, 65,611 (1982)

3) H.Khoda et al, Chem Pharm, Bull, 33 1367-1374 (1985)

4) W.B. Stavinoha, "Proc 6th Int Symp Ganoderma Ludium", p3- (1995)

5) PJ Roderick et al, Br.J.Clin. Pharmacol. 35, 219-226 (1993)

6) "Martingdale:The Extra Pharmacopoeia", 31st Edition, Pub. The Royal Pharmacuetical Society, London. P 1018-1020 (1996)

Adult - Chronic Hayfever

Week	Tablets/Day	Tablets per Week*
1	6	42
2	6	42
3	6	42
4	6	42
5	6	42
6	6	42
7	6	42
8	6	42
9	6	42
10	6	42
11	6	42
12	6	42

A. Adult

3 tablets Ganoderma in a.m. and 3 tablets p.m. before meals

Child (4years) - Chronic Hayfever

Week	Tablets/Day	Tablets per Week*
1	2	14
2	2	14
3	2	14
4	2	14
5	2	14
6	2	14
7	2	14
8	2	14
9	2	14
10	2	14
11	2	14
12	2	14

B. Child

1 tablet Ganoderma p.m. and 1 tablet a.m.

* Ganoderma lucidum (Reishi) provided by Mycology Research Laboratories Ltd under tradename Reishi-MRL with 500 mg per tablet. (http://www.mycologyresearch.com).

TALKS

Martin Powell will be giving two seminars this year at ***The Natural Trade Show - Brighton*** *on the 14th and 15th March.The first seminar will be on the use of Ganoderma lucidum (Reishi) in the management of histamine mediated allergic responses and the second on the use of mushroom nutrition as immuno-nutrition in cancer care.*

Further details and contact information are given on page 8.

The Role of Epstein Barr Virus (EBV) in Cancer Cell Growth

As discussed in the fourth edition of Mycology News (found in the R&D section of **http://www.mycologyresearch.com)**, since 1999 viral pathogens have been postulated to be indirect triggers for certain cancers. Several examples involving the Epstein-Barr Virus are given below:

Virus	**Cancer**
Epstein-Barr virus (EBV)	Nasopharyngeal carcinoma
	Burkett´s lymphoma
	Hodgkin´s diseases
	Breast cancer

Breast cancer, a multiple-step disease which is the number one cause of cancer related deaths in women has been linked to the Epstein-Barr Virus [1,2,3]. In some countries, an overlap between regions with high incidences of EBV-associated lymphomas and a high frequency of male breast cancer has been reported [2][4]. Furthermore, EBV associated lymphomas have been reported to be localised in the breast [5][6].

In two polymerase chain reaction (PCR) studies, EBV was observed in 20%-40% of breast cancer tumors assessed. Labreacque et al. identified EBV encoded small RNA1 (EBER-1) in a fraction of malignant cells in six different breast tumours while Bonnett et al demonstrated the presence of EBV genome in a large subset of breast cancers[2][7]. The virus was restricted to tumour cells and was more frequently associated with the most aggressive tumours [8].

While the relationship between Epstein-Barr Virus (EBV) and cancer has been established for several years, only recently have researchers at the Manchester-based, Paterson Institute, established that the (EBV) virus removes a key safeguard against the p16 gene (9). The p16 gene acts as a break on both cellular growth and cell division and is one of the body´s main defences against cancer.

The researchers found that the Epstein-Barr Virus (EBV) produces a molecule called LMP1 which has two roles:

a) LMP1 acts as a 'bouncer', banishing one of the key molecules that helps switch on the p16 gene to the outskirts of the infected cell. When the molecule is excluded, the p16 gene is switched off, leaving cells prone to uncontrolled division [9].

b) LMP1 sabotages the breaking system, so that even when p16 is switched on and attempting to stop cell division, infected cells can continue growing and dividing [9][10].

Although we now better understand the role of EBV in promoting cancer growth we still need to understand what it is that triggers such behaviour in a small minority of patients when 90% of adults are infected with the EBV virus and the possible role of adjunct nutrition in addressing these issues.

References:

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2. Labrecque LG, Barnes DM, Fentiman IS, Griffin BE. Epstein-Bar virus in Epithelial Cell Tumors: A Breast Cancer Study. Cancer Research 1995;55:39-45-D-F.

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10 Secrets of a Cancer Virus Revealed-Cancer Research UK website (http://www.cancerresearchuk.org/news/pressreleases/jul21_secrets_virus)

The Use of Diagnostics in Patients with Epstein-Barr Virus (EBV)

Dr. Rajendra Sharma *(MB, BCh, BAO, LRCP+S(I), MFHom) Age 44, Qualified as a doctor in 1984. After a short time in the NHS, he joined his late father in general practice using complementary medicine and orthodox medicine. Dr. Sharma has practised integrated medicine and studied in Europe, India and the USA. He was until recently Medical Director of The Hale Clinic. Dr. Sharma´s published work includes The Family Encyclopedia of Health and co-authorship of Your Child - Asthma. Dr. Sharma co-founded The Diagnostic Clinic in 2002 and is it's Medical Director.*

The Epstein-Barr virus (EBV) is frequently and correctly associated with recurrent illness, persistent tiredness and is considered as one of the main culprits for Chronic Fatigue Syndrome, In addition, the New England Journal of Medicine has cited the possibility of EBV being associated with Multiple Sclerosis (MS) and certainly there is evidence for the virus being associated with unexplained hepatitis. If one reviews the plethora of articles the virus may be the cause of manifold illnesses.

Paul-Bunnel Test

To date the Paul-Bunnel test has been the main stay of orthodox diagnosis. It measures an antibody reaction within an individual's blood sample to sheep red blood cells (RBC). There is a "molecular-mimicry" between sheep's RBCs and the EBV which makes the Paul-Bunnel Test a non-specific test indicating current or past infection without allowing a range of measurements - simply positive or negative and the Paul-Bunnel Test cannot differentiate between current or past infection.

Antigen Testing

E-B nuclear antigen IgG / E-B early antigen IgG / E-B early antigen IgM

The need to establish levels is paramount when monitoring treatment, especially in conditions such as Chronic Fatigue Syndrome where Epstein-Barr Virus may be present and yet may not be the only causative factor.

This is now best done by measuring 3 antigens (parts of the virus molecule)

E-B nuclear antigen IgG
E-B early antigen IgG
E-B early antigen IgM

A clear advantage of repeated antigen testing is that these clear and definitive range of tests allow a practitioner to monitor the effectiveness of treatment. For example, with evidence of the success of several naturopathic treatments against EBV, including the use of *Coriolus versicolor* supplementation, a practitioner can monitor effectiveness as well as adjust supplementation levels for the patient through a simple blood test.

Interpretation of Antigen Testing

The diagnostic interpretation of serological reaction patterns is complicated. Most doctors and complementary medical practitioners would have to be reminded of their basic biochemistry.

Using the following abbreviations the complexity of accurate diagnosis can be explained:

E-B nuclear antigen IgG	**EBNA–IgG**
E-B early antigen IgG	**EA–IgG**
E-B early antigen IgM	**EA–IgM•**

A typical course of reactions in an Epstein-Barr Virus infection can show the following pattern within a considerably variable amount of time:

N/N/N N/N/P N/P/P N/P/N P/P/N P/N/N

The IgM antibody is the earliest marker but the EBNA-IgG can take anywhere from two to eight months to change and indicates active replication. So, a suspected acute case of EBV may show a rise in IgM but many cases appear to practitioners only late in the day in which case the EBNA-IgG is of more benefit in diagnosis.

Normal levels for the key EBV markers are:

		Normal	
E-B nuclear antigen IgG	**EBNA-IgG**	**Less than 0.09**	**ISR**
E-B early antigen IgG	**EA-IgG**	**Less than 0.90**	**ISR**
E-B early antigen IgM	**EA-IgM.**	**Less than 0.09**	**ISR**

The chances of catching all three antigen levels at a high level is slim as it only occurs transiently.

The most relevant factor is that the EBNA-IgG can rise continuously for one to two years so testing for this serially and then finding the levels dropping can be a very useful method of measuring treatment benefit or success.

For practitioner service agreements please contact Ms Danielle Braender at the Diagnostic Clinic.

* Dr. Rajendra Sharma*
The Diagnostic Clinic
50 New Cavendish Street
London W1G 8TL
Tel:44-207-009-4650
info@thediagnosticclinic.com

• N=negative P=positive

EBV Testing Services Available to Practitioners at The Diagnostic Clinic

The Diagnostic Clinic offers EBV diagnostic screening services and interpretation to complementary medical practitioners in the United Kingdom and Europe. The cost for EBV related diagnostic tests are:

TEST	COST	TURN-AROUND TIME
a) EBV (Paul Bunnel Test)	£ 20.00	48 hours
b) Antigen Testing (EBNA-IgG EA-IgG EA-IgM)	£ 80.00	48 hours

Practitioner discounts available and practitioners can either refer patients for EBV testing, receive kits or send samples for EBV testing. Blood samples sent to The Diagnostic Clinic should conform to GCP standards and be stored in appropriate containers. TDC can arrange collection.

The contact to discuss billing and practitioner service agreements is:

Ms Danielle Braender, Clinic Manager, The Diagnostic Clinic, 50 New Cavendish Street, London W1G 8TL, Tel:44-207-009-4650

info@thediagnosticclinic.com

The Use of Coriolus versicolor Supplementation in Chronic Fatigue Syndrome (CFS) Patients.

The clinical correlation of CFS with high EBV titres is routinely seen and raises the question of possible common factors behind EBV proliferation in cancer and CFS patients. Specifically a TH1-TH2 immune shift may play a part in EBV proliferation and ultimately in cancer growth and CFS development.

The following article is reprinted from Mycology News 4 and outlines research by Dr Jean Monro highlighting the potential of mushroom nutrition for helping reverse a TH1-TH2 immune shift.

** Dr.Jean Monro (MB,BS, MRCS,LRCP,FAAEM,DIBEM,MACOEM) is the founder of Breakspear Hospital, a Hempel Hemstead-based outpatient clinic devoted to immuno-compromisd patients. (Dr. Monro is Consultant Physician to Fachkrankenhaus, Nordfriesland-Bredstedt, Germany) Tel:44-1442-261-333/ Fax 44-1442-266-388).*

Cytokine TH1 Immune Response vs Cytokine TH2 Immune Response

The following is based on a presentation by Dr. Jean Monro[1] (Breakspear Hospital) at the 3rd International Symposium on Mushroom Nutrition in Milan, Italy on March 10th, 2001 (complete copies are available on request from Mycology Research Laboratoires Ltd. e-mail: info@aneid.pt).

Maintaining the correct balance between the cellular and humoral immune responses is fundamental to the body's ability to mount an effective immune response to viral and other challenges.

Several distinct sub-populations of T cells have roles as the effectors and regulators of the immune system. Of these the most important are two subsets of CD4+ T cells known as TH1 and TH2 (T-Helper Cell 1 and T-Helper Cell 2), so called because they both exhibit helper functions for B cells and other T cells.

The TH1 and TH2 patterns of cytokine response are mutually inhibitory and between them are responsible for maintaining the balance between the humoral and cell-mediated immune responses.

Peak production of the pro-inflammatory cytokines (TH2) occurs during the night and early morning, at a time when plasma cortisol is lowest (this explains why immuno-inflammatory disorders, such as rheumatoid arthritis and asthma, often exhibit night-time or early morning exacerbation). TH1 immune response peaks from mid-morning to early evening. (fig.1)

TH2 immune response is dominant in chronic viral conditions such as HIV and Hepatitis C and levels of TH1 cytokines and NK cells are decreased in these conditions. TH2 cells secrete Tumour Necrosis Factor as well as pro-inflammatory cytokines, including Interleukin-4, Interleukin-6, Interleukin-10 and Interleukin-11.

TH1 immune response promotes the transformation of CD8 suppressor cells into NK (natural killer) cytotoxic cells which have a vital role in the inactivation of virally infected and mutagenic cells.

TH1 Cytokines include:

IL-2 - The major growth factor for both CD4+ and CD8+ cells, which have anti-tumour, anti-bacterial and anti-viral effects, as well as a role in combating parasitic infections and in auto-immune responses.

Interleukin 12 - Activates NK cells, works synergistically with IL-2 in the induction of NK cells, augments the allogenic CTL response and enhances IL-2 induced proliferation of resting peripheral blood cells.

Interferon Gamma (γINF)– produced by T-lymphocytes (T-Hi subtype) and (NK) cells.

The body is considered to be in a "balanced" immune state when there is a dynamic equilibrium between TH1 and TH2 immune states over a 24 hour period. However, if the body moves to a TH2 immune state and subsequently fails to return to a TH1 state, then a TH1 to TH2 shift has occurred. With a TH1 to TH2 shift the pattern of cytokines becomes locked in an inflammatory repairing pattern, with a concomitant lowering of NK cell levels and perpetuation of infectious diseases.

In particular, a TH1 to TH2 shift creates favourable conditions for the continued proliferation of TH2 conditions such as asthma and rheumatoid arthritis, as well as for the continuation of chronic viral conditions, including CFIDS (ME), HIV and Hepatitis C.

continues…

1 Dr.Jean Monro (MB,BS, MRCS,LRCP,FAAEM,DIBEM,MACOEM) is the founder of Breakspear Hospital, a Hemel Hempstead based outpatient clinic devoted to immuno-compromised patients. Tel:44-1442-261-333/ Fax 44-1442-266-388). Dr. Monro is also Consultant Physician to Fachkrankenhaus, Nordfriesland-Bredstedt, Germany.

TH1 vs. TH2 Immune responses

Cytokine TH1 Immune Response		Cytokine TH2 Immune Response
Cellular Imune response	**Type**	**Humoral Imune response**
10:00 to 20:00	**Timing**	20:00 to 10:00
Anti-Viral Anti Bacterial Anti-Parasitic	**Function**	Pro-inflammatory
Interleukine 2 (IL2) Interleukine 12 (IL12) Interferon Gamma (γNF)	**Cytokines**	Interleukine 4 (IL4) Interleukine 6 (IL6) Interleukine 10 (IL10)
Low	**Cortisol Levels**	High
High	**Natural Killer Cell Activity**	Low

FACTORS PROMOTING A TH1 – TH2 SHIFT

Multiple vaccinations.

Exposure to carbamate and organophosphate insecticides. These inhibit Interleukin-2 driven events that are essential for TH1 function.

Intake of steroids, **such as Cortisol.** Cortisol-induced development of a TH2 cytokine profle from naive cells has been demonstrated.

Stress, both psychological and physical. Stress activates the hypothalamopituitary-adrenal axis and leads to increased production of Cortisol. Excessive exercise and deprivation of food or sleep also result in a falling ratio of DHEA to Cortisol and an increase in a TH1 to TH2 shift. It is known that Epstein Barr Virus antibody titres rise amongst students facing examinations. This virus is usually controlled by a TH1 response. Stress causes loss of control resulting in increased viral replication and hence antibody production.

Cancer. Many of the risk factors for cancer, such as carcinogenic chemicals or tobacco smoke also cause long-term inflammation and lower TH1 levels. In particular, patients with colon cancer have been found to have unusually low levels of TH1. The reduction in TH1 levels impairs the body's ability to effectively combat tumour cells and in addition the enhanced TH2 (pro-inflammatory) responses engendered are responsible for creating new blood vessels around damaged tissues, which can allow the tumour to grow and spread.

MUSHROOM NUTRITION AND THE REVERSAL OF A TH1 TO TH2 SHIFT IN CHRONIC FATIGUE SYNDROME PATIENTS

Measurement of NK cell activity provides a valuable indication of the balance between TH1 and TH2 immune states. In a TH1 immune state, NK cell activity is high, while in a TH2 immune state, NK cell activity is low. NK cell activity is thus a key determinant in evaluating potential reversal agents for a TH1 to TH2 shift.

In her preliminary results with 15 Mylagic Encephaloyelomyelitis (ME) /Chronic Fatigue Immune Dysfunction Syndrome (CFIDS) patients (Mycology News issue 4), Dr. Jean Monro of the Breakspear Hospital found an increase in NK cell cytotoxic activity from an average of 13 CMM at the start of the trial to an average of 31 CMM after 60 days with Coriolus-MRL supplementation (fig.2). NK cell cytotoxic activity in healthy individuals averages 41 CMM. (fig.3)

The above findings support the use of Coriolus-MRL as a reversal agent for a TH1 to TH2 shift. This is also suggested by the anecdotal evidence from Dr Monro's patients and from other researchers of CFIDS patients reporting increased energy levels after a supplementation schedule of Coriolus-MRL.

Dr. Monro is currently completing research on the use of Coriolus-MRL (500 mg tablets of non-extracted Coriolus versicolor) as a mediator to reverse TH2 to TH1 cytokine activity in sixty (60) patients.

WEEK	TABLETS/DAY	TOTAL TABLETS PER WEEK	90 TABLET BOTTLES
1	6	42	
2	6	42	
3	3	21	
4	3	21	
5	3	21	
6	3	21	
7	3	21	
8	3	21	3

fig 2. **Dr. Monro - Supplementation Protocol - Coriolus-MRL**

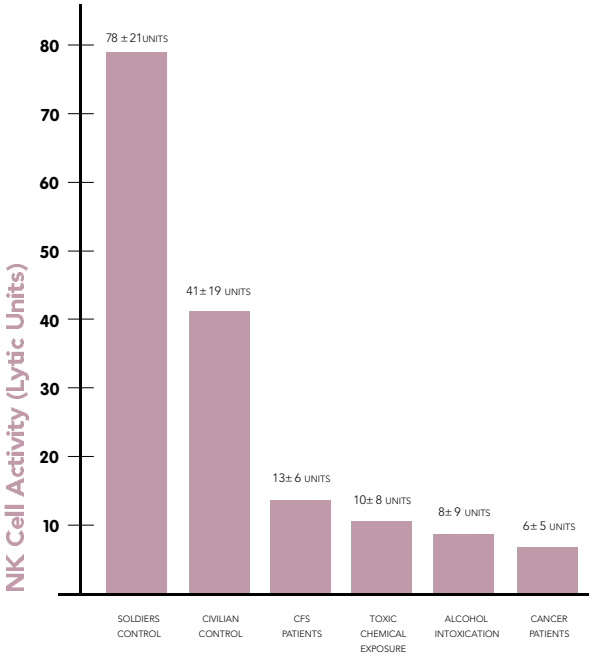

CHART SUPPLIEDBY IMMUNOSCIENCESLABORATORY INC.

1. Holmes GP, et. al. Chronic Fatigue Syndrome: a working case definition Ann Int Med 1988 108 ghj387-389.

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Dove Clinic to Initiate Coriolus versicolor study on patients with Ductal Carcinoma in Situ (DCIS).

Breast cancer is classified by the kind of tissue in which it starts and by the extent of its spread. Cancer may start in the milk glands, milk ducts, fatty tissue, or connective tissue. Different types of breast cancers progress differently [1].

In situ carcinoma, which means cancer in place, is an early cancer that has not invaded or spread beyond point of origin. In situ carcinoma accounts for more than 15 percent of all breast cancers diagnosed in the United States [2].

About 90 percent of all breast cancers start in the milk ducts or milk glands. Ductal carcinoma in situ starts in the walls of milk ducts. It can develop before or after menopause. This type of cancer occasionally can be felt as a lump and may appear as tiny specks of calcium deposits (microcalcifications) on mammograms. Ductal carcinoma in situ, is often detected by mammography before it is large enough to be felt. It is usually confined to a specific area of the breast and can be totally removed by surgery [3].

Based on the favourable results from the use of Coriolus versicolor supplementation in Stage III and Stage IV cancer patients (see Mycology News 7-http://www.mycologyresearch.com), Dr. Julian Kenyon would like to use Coriolus versicolor supplementation (12 grams per day) in twenty (20) patients. The study will involve measuring the following immune parameters at times "0", "3 months" and "6 months":

-Interferon Gama

-Interleukin 4

-Pyruvate Kinase

-Vascular Endothelial Growth Factor

The study would not involve the substitution of any normal procedures, such as surgery. However, there is prior evidence that Coriolus versicolor does support the immune system in immuno-compromised patients. Medical doctors with ductal carcinoma in situ patients who wish to work with Dr. Kenyon in this trial are encouraged to contact Dr. Kenyon at Dove Clinic for Integrated Medicine at Tel: +44-1962-718000. (www.doveclinic.com).

The trial will be designed by the Dr. Kenyon and supported by Mycology Research Laboratories Ltd. Protocol submission to the MCA is expected in the first quarter of 2004.

1) "Breast Disorder" page 1096-1097, The Merck Manual – Home Edition-1997.
2) Ibid, page 1097
3) Ibid, page 1098

Mushroom Nutrition Seminars at Natural Trade Show-Brighton

MARCH 14 & 15TH, 2004

Mr.Martin Powell will be presenting the following two seminars at the Natural Trade Show Brighton on March 14th and March 15th, 2004

1) The Use of Ganoderma lucidium (Reishi) in the Management of Histamine-Mediated Allergic Responses.-March 14th, 2004

In this presentation, Martin Powell (BSc. Biochemistry. L.Ac.) outlines the historical use of Ganoderma lucidium as having both immuno-modulatory and adaptogenic properties. In this presentation he provides clinical examples and theoretical support that justifies the use of Ganoderma lucidum as a safe and effective alternative for the reduction of histamine-mediated immune responses.

2) Mushroom Nutrition as Immunonutrition in Cancer Care-March 15th, 2004.

The potential to modulate the activity of the immune system by interventions with specific nutrients is termed immunonutrition. In this presentation Martin Powell (BSc. Biochemistry. L.Ac.) outlines the biological and enzyme properties that make Coriolus versicolor an important non-specific immunomodulator in cancer care. Specific clinical cases are discussed in the presentation.

To reserve a seat, practitioners are recommended to contact

Sarah Funston – Event Executive

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