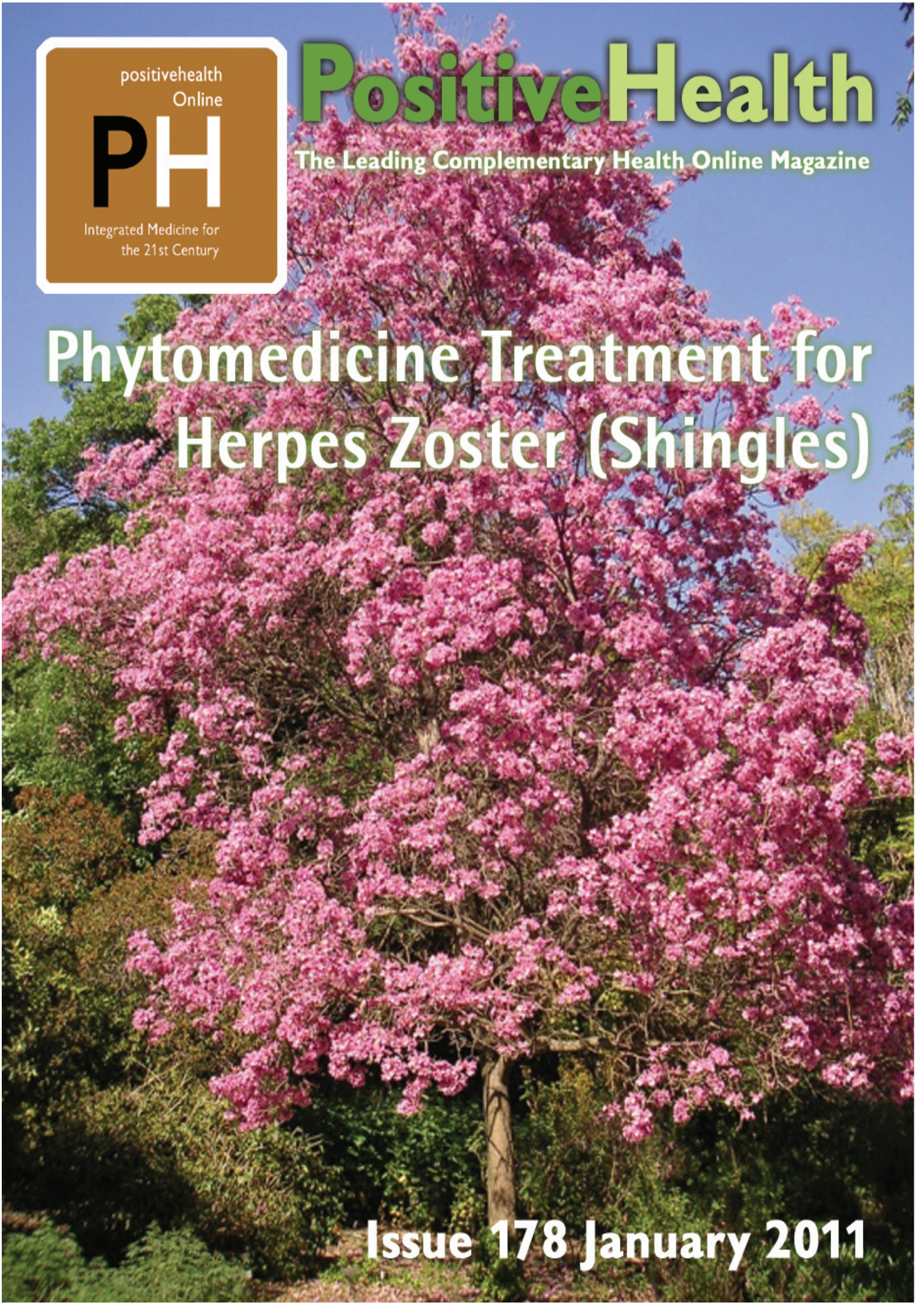
positivehealth
Online
PH
Integrated Medicine for
the 21st Century
PositiveHealth
The Leading Complementary Health Online Magazine
Phytomedicine Treatment for
Herpes Zoster (Shingles)
Issue 178 January 2011

Chronic Fatigue Syndrome and Immune Modulation with *Coriolus Versicolor*†

by Dr Jean Monro MB BS MRCS LRCP FAAEM DipABEM

Chronic fatigue, also referred to as myalgic encephalomyelitis, chronic viral syndrome and post viral fatigue syndrome, is a complex clinical syndrome. It is characterized by incapacitating fatigue, neurological problems and a constellation of symptoms that can resemble many other illnesses.

Definition and Clinical Evaluation of Prolonged Fatigue[1]

Prolonged fatigue is defined as self-reported, persistent fatigue of one month or longer. Chronic fatigue is defined as self-reported persistent or relapsing fatigue of six or more consecutive months.

The Symptoms and Signs of Chronic Fatigue Syndrome (CFS)

The symptoms include:

- Muscle pain;
- Multi-joint pain without joint swelling or redness;
- Sore throat;
- Self-reported impairment in short-term memory or concentration severe enough to cause substantial reduction in previous levels of occupational, educational, social or personal activities;
- Changes in mood;
- Headaches of a new type, pattern or severity;
- Unrefreshing sleep;
- Tachycardia;
- Coldness of the extremities;
- Sweating;
- Pallor and sluggish pupils;
- Post-exertional malaise lasting more than 24 hours.

The signs include:

- Low-grade fever;
- Non-exudative pharyngitis;
- Palpable or tender lymph nodes.

Causes of this Syndrome

Amongst the causes are post-viral disruptions of immune functions (PVS). A variety of viruses have been implicated in the development of CFS, including herpes viruses (EBV, CMV, herpes simplex and human herpes 6: HHV6), polio, Coxsackie, adenoviruses and retroviruses. Other causes may include chemical and metal exposure (e.g. pesticides and organic solvents exposure).

In patients with CFS/myalgic encephalomyelitis, the major complaint is rapid fatigability, which some doctors have linked to mitochondrial failure in CFS patients who have associated heart impairment. This is related to weak heart muscle function; thus it is possible to monitor and measure the level of CFS via an autonomic function test to check heart rate variability (HRV).

Coriolus Versicolor – a Continuing Solution

Coriolus versicolor is a mushroom from the Amastigomycota group of mushrooms. This group of mushrooms is a large and diverse group that does not produce a motile stage and is not adapted to an aquatic environment. It contains all edible and medicinal fungi.

There are four subdivisions:

Coriolus

Coriolus

Coriolus

- Zygomycotina;
- Ascomycotina;
- Basidiomycotina;
- Deuteromycotina.

Coriolus is from the family of Polyporaceae from the Basidiomycetes group. It contains a polysaccharopeptide (PSP) which has been non-specifically used in a number of conditions to alleviate symptoms and prevent a decline in immune status.[2] The fungus *Coriolus versicolor* is found almost worldwide with variation due to habitat. To eliminate these variations, strain CV-OH1 was established some 20 years ago by Gourmet Mushrooms Inc, in California, USA.

Therapeutic Properties

Coriolus versicolor can enhance superoxide dismutase (SOD) activity.[3] It is thought to protect macrophages from the damage induced by reactive oxygen species by enhancing antioxidant

capacity.[4] Activation of peritoneal macrophages by PSP has been shown and an immunomodulatory effect on the defensive cells was demonstrated.[5] In view of these findings, Coriolus was used for its effects on host defence potentiation.

Usage/Potency Properties

- Long term stability;
- Complies with British Pharmacopoeia (BP);
- Sterile conditions;
- No pesticides;
- No heavy metal.

This study is specifically looking at the CV-OH1 strain which demonstrates rapid and aggressive colonization and far outmatches other isolates in bioactivity and vigour. A mother culture of strain CV-OH1 has been developed and maintained since isolation and this is used to produce the spawn. In-house checks confirm that the mother culture does not move from the original isolate. The production process involves the inoculation of sterile organic edible grain with the spawn from the mother culture.

The fungus is allowed to completely colonize the growth medium aseptically and at the correct stage of development, at maximum bioavailability, the living biomass is aseptically air-dried and granulated before being tested microbiologically. This technique produces a raw material which is sterile and contains no pesticides, heavy metals, is free from foreign matter and is totally reproducible.

The material is shipped to a UK Good Medical Practice (GMP) pharmaceutical facility where it is manufactured into 500 mg tablets with the addition of cellulose, silica, a granulating agent and a tablet press lubricant. The finished tablet Coriolus MRL†† complies with the BP requirements for tablets and long-term stability is being established using TVC and PCR. This tablet was suitable to be given to CFS patients to determine the immune enhancing properties of *Coriolus versicolor*. A PCR/electrophoresis method is being established to determine the DNA of this product as an additional method of quality control.

In this study, CFS patients were tested with *Coriolus versicolor* (CV-OH1 strain 500 mg tablet) to check if the tablet would have similar immune-enhancing properties. In order to determine the therapeutic response, patients were examined for dysautonomia pre- and post-treatment.

Previous studies have reported beneficial immune-enhancing properties *in vivo* and *in vitro*, as well as preventative properties associated with antioxidant properties. These findings allow the use of *Coriolus versicolor* in chronic fatigue patients who all have marked autonomic dysfunction.

Natural Killer Cells[6]

We know that natural killer (NK) cells are the first line of defence against newly arising malignant cells and cells infected with viruses, bacteria and protozoa. They form a distinct group of lymphocytes with no immunological memory and are independent of the adaptive immune system.

Natural killer cells constitute 5% to 16% of the total lymphocyte population. Their specific function is to kill infected and cancerous cells. Viruses lack the apparatus for self-renewal, so it is essential for them to penetrate the cells of the infected host in order to take over its replicative machinery. It is clearly in the interest of the host to find a way to kill such infected cells before the virus has had a chance to reproduce.

NK cells appear to do just that when studied *in vitro*. They are large granular lymphocytes with a characteristic morphology. They are thought to recognize structures on high molecular weight glycoproteins which appear on the surface of virally infected cells, and which allow them to be differentiated from normal cells. This recognition probably occurs through lectin-like (i.e. carbohydrate-binding) receptors on the NK cell surface, which bring killer and target into close opposition.

Activation of the NK cell ensues and leads to polarization of granules between nucleus and target within minutes, and extra-cellular release of their contents into the space between the two cells, often utilizing the cytolysin [antibodies that cause the dissolution of various cells of an organism or bacterium] perforin [protein in killer cells and natural killer cells that causes lysis of target cells on contact]. NK cells kill by activating apoptosis. In addition to perforin, the granules contain tumour necrosis factor ß and a family of serine proteases termed granzymes, one of which, granzyme B, can function as an NK cytotoxic factor. Fully ionised ATP can cause apoptosis in many different cell types; the effectors themselves are resistant probably due to a lack of ATP receptors on their surface.

These factors sequentially induce NK-mediated lysis. Virally infected cells can be killed by cytotoxic T cells and ADCC [antibody-dependent cell-mediated cytotoxicity].[7]

Sample for the Study

Patients were examined and a number of the abnormal findings were recorded in patients with chronic fatigue syndrome, such as lymphadenopathy and pharyngitis. There was also disturbance of autonomic function in all patients evaluated by HRV.

The HRV test confirmed dysautonomia [malfunction of the autonomic nervous system] (statistics compiled by Dr Alexey Tarnakin). Symptoms of dysautonomia are numerous and vary widely from person to person. Dysautonomia is a full-body condition; a large number of symptoms are present that can greatly alter a person's quality of life. Each patient with dysautonomia is different: some are affected only mildly while others are left completely bedridden and disabled.

All 36 patients had HRV examination before treatment (31 standing as some were too weak for sustained standing). The results are presented in Table 1. The age range is between 17 to 83 years, with a female to male ratio of 2:1.

Summary:

The Total Power (TP) of Heart Rate Variability (HRV) was slightly decreased with a mild increase on standing.

The Low Frequency component (LF) of TP HRV and the High Frequency component (HF) of TP HRV were moderately decreased.

The LF/HF Ratio was within normal range.

On standing, there was a mild increase of LF and a mild decrease of HF with subsequent increase of LF/HF Ratio.

The individual analyses of HRV before Coriolus treatment are presented in Table 2.

Summary:

10 out of 36 patients had a decrease in the

Table 1 Heart Rate Variability Before Treatment

	Lying 36 patients	Standing 31 patients
Mean RR	868±156	774+110
Minimum RR	562	524
Maximum RR	1058	1048
SDNN	45.9	47.7
RMSSD	54.9	39.3
SDSD	54.9	39.3
NN50	46.9	47.8
pNN50	10.5	8.62
Total Power of HRV 3466±1018	2593±954	2706±1420
VLF	374	427
LF 1170±416	247±214	364±686
HF 975±203	220±266	188±255
LF/HF Ratio 1.5 – 2.0	1.76±1.25	3.11±2.67

Key:

SDNN: Standard deviation of the normal-to-normal interval
RMSSD: Square root of the mean squared differences of successive NN intervals
SDSD: Standard deviation of differences between adjacent NN intervals
NN50: Number of interval differences of successive NN intervals greater than 50 ms
pNN50: NN50 count divided by the total number of all NN intervals
VLF: Very low frequency

TP of HRV, 22 out of 36 patients had normal TP of HRV and 4 out of 36 patients had an increase of the TP of HRV.

LF and HF components were decreased in 33 out of 36 patients with LF/HF Ratio less than 1.5 (predominance of vagal tone) in 19 out of 36 patients and with LF/HF Ratio more than 2.00 (sympathetic predominance).

On standing, 9 out of 31 patients had a decrease of the TP of HRV, 20 out of 31 patients had normal TP of HRV and 2 out of 31 patients had an increase of the TP of HRV.

LF component was decreased in 28 out of 31 patients with LF/HF Ratio less than 1.5 (predominance of vagal tone) in 8 out of 31 patients and with LF/HF Ratio more than 2.00 (sympathetic predominance) in 17 out of 36 patients.

HF component was decreased in 30 out of 31 patients.

These results suggest a decrease of the total activity of the autonomic nervous system with altered sympathetic tone.

Tests Performed

- T-lymphocyte subsets;
- Natural killer cells : CD3-CD16+CD56+;
- Epstein-Barr virus (EBV) Viral Capsid Antibody IgG and IgM;
- EBV Early Antigen Diffuse Antibody IgG;
- EBV Nuclear Antigen Antibody;
- EBV Nuclear Antigen IgM;
- Human Herpes Virus 6 IgG;
- Cytomegalovirus IgG and IgM.

Test Results

All patients were found to have combinations of high antibody levels to Epstein-Barr virus in the groups mentioned and/or human herpes virus 6 and/or cytomegalovirus.

- T cells (%CD3+CD26) showed increased activation in two thirds of the patients before and after review;
- Depression in 22% of patients and 11% remained static;
- T cells (CD3+HLA-DR+) showed activation in 77% and decreased activation in 11%;
- T helper suppressor cells were variable in their original presentation;
- The normal range of natural killer cells is 5 – 20% and the cell count is 75-1800 cmm;
- Natural killer cells were found to be low in our patients before treatment, the average being 129.64 cmm;
- An increase in natural killer cells following treatment with Coriolus was demonstrated – average being 175 cmm, which is an increase of 45%.

Discussion

The results show that *Coriolus versicolor* has improved natural killer cell numbers in CFS patients. Levels of T cells levels were elevated and are responsible for the adaptive immune responses which may help clear infections. The T helper suppressor cells were also moderately elevated. These cells help maintain and regulate immune responses so that the body does not exaggerate antigen production.

The study has demonstrated, in a group of 36 patients who have defined chronic fatigue syndrome/autonomic dysfunction, that two months' treatment with Coriolus MRL†† has had a reasonable immunotherapeutic effect. These findings suggest that *Coriolus versicolor* is capable of inducing both the innate and adaptive stages of an immune response.

Table 2 Heart Rate Variability before Coriolus Treatment

Lying 36 patients			Standing 31 patients		
RR less 0.67sec	RR 0.67 – 1.0 sec	RR more 1.0 sec	RR less 0.67sec	RR 0.67 – 1.0 sec	RR more 1.0 sec
2	28	6	4	25	2
Total Power of HRV less 2000	Total Power of HRV 2000 – 4000	Total Power of HRV more 4000	Total Power of HRV less 2000	Total Power of HRV 2000 – 4000	Total Power of HRV more 4000
10	22	4	9	20	2
LF less 600	LF 600 – 1600	LF more 1600	LF less 600	LF 600 – 1600	LF more 1600
33	3	0	28	2	1
HF less 700	HF 700 – 1200	HF more 1200	HF less 700	HF 700 – 1200	HF more 1200
33	3	0	30	1	0
LF/HF Ratio less 1.5	LF/HF Ratio 1.5 – 2.0	LF/HF Ratio more 2.00	LF/HF Ratio less 1.5	LF/HF Ratio 1.5 – 2.0	LF/HF Ratio more 2.0
19	4	13	8	6	17

References

1. Fukuda K, *et al*. The Chronic Fatigue Syndrome: A Comprehensive Approach to its Definition and Study. *Ann Intern Med*. 1994;**121:**953-9.
2. Ng TB. A Review of Research on the Protein-Bound Polysaccharide (Polysaccharopeptide, PSP) from the Mushroom *Coriolus versicolor*. (Basidiomycetes Polyporaceae). *Gen Pharmacol*. 1998; **30:**1-4.
3. Kobayashi Y, Kariya K, Saigenji K, Nakamura K. Suppressive Effects on Cancer Cell Proliferation of the Enhancement of Superoxide Dismutase (SOD) Activity Associated with the Protein-Bound Polysaccharide of *Coriolus Versicolor* QUEL. *Cancer Biother*. 1994; **9:**171-8.
4. Jun L, Mei Z, Yuan C. Reversal of Inhibition of Reactive Oxygen Species on Respiratory Burst of Macrophages by Polysaccharide from Coriolus versicolor. *Int J Immunopharmacol*. 1993; **15:**429-33.
5. Liu WK, Ng TB, Sze SF, Tsui KW. Activation of Peritoneal Macrophages by Polysaccharopeptide from the Mushroom, *Coriolus versicolor*. *Immunopharmacology*. 1993; **26:**139-46.
6. Roitt IM. *Roitt's Essential Immunology*. 9th ed Oxford: Blackwell Science; p 18-20.
7. ibid. p 33-5. 1997.

Notes

† A part of this article appeared in the *Journal of Integrative Medicine*; 8:101-8. 2004.

†† Mycology Research Laboratories Ltd, Windsor House, 9-15 Adelaide Street, Luton, Beds, LU1 5BJ, UK. Tel: +44 (0)1582 485 209; info@mycologyresearch.com www.mycologyresearch.com

Reprint Acknowledgement Citation

Reprinted with permission from *Positive Health* PH Online Issue 178 January 2011: www.positivehealth.com/article-view.php?articleid=2941

Other PH Articles about Coriolus MRL

Coriolus versicolor for HPV Patients with Cervical Lesions (LSIL)[1,2] by J Silva Couto and D Pereira da Silva, Published in *Positive Health* PH Online Issue 147 May 2008:

www.positivehealth.com/article-view.php?articleid=2381