*The Journal of*

# INTEGRATIVE MEDICINE SA


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**Are we first doing harm?**

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1. Stat10Choice TM package insert, Winthrop Pharmaceuticals; Sep 2009

# Editorial

When asked by Reni Rouncivell, owner of MedSpec Publishing, to become Editor of this publication, I was both honoured and pleasantly surprised by the sheer number of research that has been done in the field of CAM over the past 10 years. Having been involved in CAM since 1995, I lost track of current research once I was convinced of the efficacy of CAM to address the burden of disease in South Africa. I didn't need any more proof! I therefore found it useful and very informative, with many tools and applications for future development, to become reacquainted with the wealth of evidenced based research available today. I'm excited to bring this information to colleagues in the field, covering a wide range of high quality, peer reviewed, practical and diverse topics.

On a practical note, let us consider the typical patient profile in primary health care facilities:

1 self-limiting infections (viral, fungal & bacterial)
2 flare-ups of chronic diseases from steady state
3 psychosomatic or mind-body diseases
4 acute diseases, trauma, incidents

Points 1 – 3 make up at least 95% of private practice, where TLC and system support, using an integrative model, CAM and stress management provide tools for management. Point 4 is where the real importance of Western technology, analytical approach & research advances, make a huge difference in saving lives and restoring quality of life. It is clear that as medical students, we are not trained in, or prepared for, the vast majority of the patients we see in private practice!

***The Journal of Integrative Medicine SA*** will have tremendous value as additional resource of practical information for the medical and allied healthcare professional to provide a better service, with a greater scope of healing arsenal and tools. The medical practitioner and medical related fields are not currently catered for in the application of CAM.

My role as Editor, will be to select suitable and interesting articles, and write article summaries, from a range of CAM and related journals, and bring you the selected articles and summaries, with the latest information after evaluating alternative therapies, and how to integrate these into clinical practice. Topics will include functional medicine, botanical medicine, vitamins & supplements, nutrition & diet, mind-body medicine, acupuncture, Ayurveda, indigenous medicine systems, homeopathy, naturopathy, yoga & meditation, manual therapies, energy medicine, spirituality & health. In due course, profiles of successful integrative clinics and integrative approaches for preventing and treating chronic illness will be covered, as well as herbal alternatives to prescription drugs, the biochemistry of natural substances, food as medicine, and mind-body approaches to disease management.

This will be a quarterly publication distributed freely to medical practitioners and allied health professionals, with a representative selection of relevant articles and article summaries, to satisfy an audience with varied interests on different CAM topics.

There is the possibility of an alliance with the University of Stellenbosch, specifically the Certification Course in Functional and Integrative Medicine, in the foreseeable future. Local content from evidenced based article contributions on CAM, suitable case studies, letters to the editor, comments and specific topic requests, will also be included in future issues.

In this issue, we cover an interesting cornucopia of topics, ranging from positive psychology and the use of positive activity interventions, mindfulness meditation and psychological wellbeing, the use of lavender oil in coping with stress and pain, the antimicrobial activity of tea tree oil, the use of CAM in fertility challenges, definition and lifestyle factors in metabolic syndrome, and many more!

I invite you to join me on this exciting journey of learning, discovering and utilising so many options to improve health, manage disease (health challenges) and providing an excellent service to our patients and clients! Enjoy the reading and please send some positive feedback!

Yours in health and wellness.

Arien


Biography:

Dr Arien van der Merwe is a medical doctor, public speaker and trainer, internationally published author, of more than 17 books on health and wellness, and specialist corporate health and wellness service provider, with 16 years' experience in integrative medicine, workplace wellness, stress management and health promotion. She is the Medical Specialist, Health and Wellbeing, for EOH Health and the appointed Editor for the recently launched Integrative Medical Journal SA, that is distributed by Medspec Publishing to medical and other health care practitioners. Dr Arien writes for, and consults regularly, to many magazines in South Africa. She is an elected Fellow of the Royal Society of Public Health in the UK, for the work she does in South Africa to promote public health and wellness through education, training and communication. She is also a Member of the International Stress Management Association, UK branch. Arien believes in a holistic, integrative approach to optimise health and wellbeing. For more information, please visit www.HealthStressWellness.com.

# Publishers Note

I am delighted to be able to bring this launch issue of ***The Journal of Integrative Medicine SA*** to you. As publishers of specialised medical journals over the last eleven years in South Africa this is a new and very exciting venture for us! Our company philosophy has always been to bring the local medical practitioner the very best and latest international research in your respective therapeutic fields and this new journal is no different!

Our research showed that there is a shortage of information for General Practitioners and allied health professionals when it comes to the field of complementary and alternative medicine (CAM) and the integration of some of these products and modalities into what is considered the more conventional western medical treatment options. We do not see the two modalities as opposing each other at all as new thinking seems to support a more holistic approach to patient treatment.

Today it seems many patients are taking more responsibility for their own health and are more educated due to a myriad of factors, the internet being the main source of information. Retail pharmacies are packed with new 'natural' and neutraceutical brands extolling the benefits of 'self treatment'. Medical aid or more aptly a lack of medical aid funds are also driving patients to self-medicate. All of these factors are leading you to see a more questioning and demanding patient. This journal will hopefully assist you in dealing with many of these new demands and questions.

We have been very fortunate in securing a license agreement from Mary Ann Liebert Publishers Inc, out of New York in the USA. Entering their 31st year, Mary Ann Liebert, Inc. is a leading company in the scientific, technical, and medical knowledge and information industry. They are known for authoritative international publications in cutting-edge basic and translational biomedical research. Their flagship publication, ***Genetic Engineering and Biotechnology News*** (GEN) was the first trade magazine in what was then a fledgling industry. Today GEN is the most widely read publication in its field worldwide, and their company is acknowledged as the leading publisher in biotechnology.

Therefore we are very fortunate in that we will be bringing you a selection of articles out of the following journals in their stable:

- ***Alternative and Complementary Therapies***
- ***Journal of Alternative and Complementary Medicine***
- ***The Journal of Medicinal Food***
- ***Medical Acupuncture***
- ***Rejuvenation Research***

Our editor Dr Arien van der Merwe will be selecting relevant articles as well as including some local 'flavour' with her editorial, commentaries and certain articles where and when relevant.

I welcome your feedback and input on this publication and please send us any comments regarding the content, I know this is an ever changing and dynamic therapeutic field and as such we hope we can stimulate some healthy and robust interaction and discussion. Our promise to you as we enter our 11th year is that we will continue to do our very best to meet the needs of members of the medical fraternity and allied sectors!

Enjoy and may I wish you all a very peaceful and restful holiday season!

Reni Rouncivell
Publisher
MedSpec Publishing

MedSpec Publishing has been providing high quality international information to the South African medical profession for many years, representing the following international publications/publishers in South Africa:

- New England Journal of Medicine (NEJM)
- Oxford University Press
- Goodwin Group International
- Dove Press
- American Society of Clinical Oncology (ASCO)
- Journal of PAINSA

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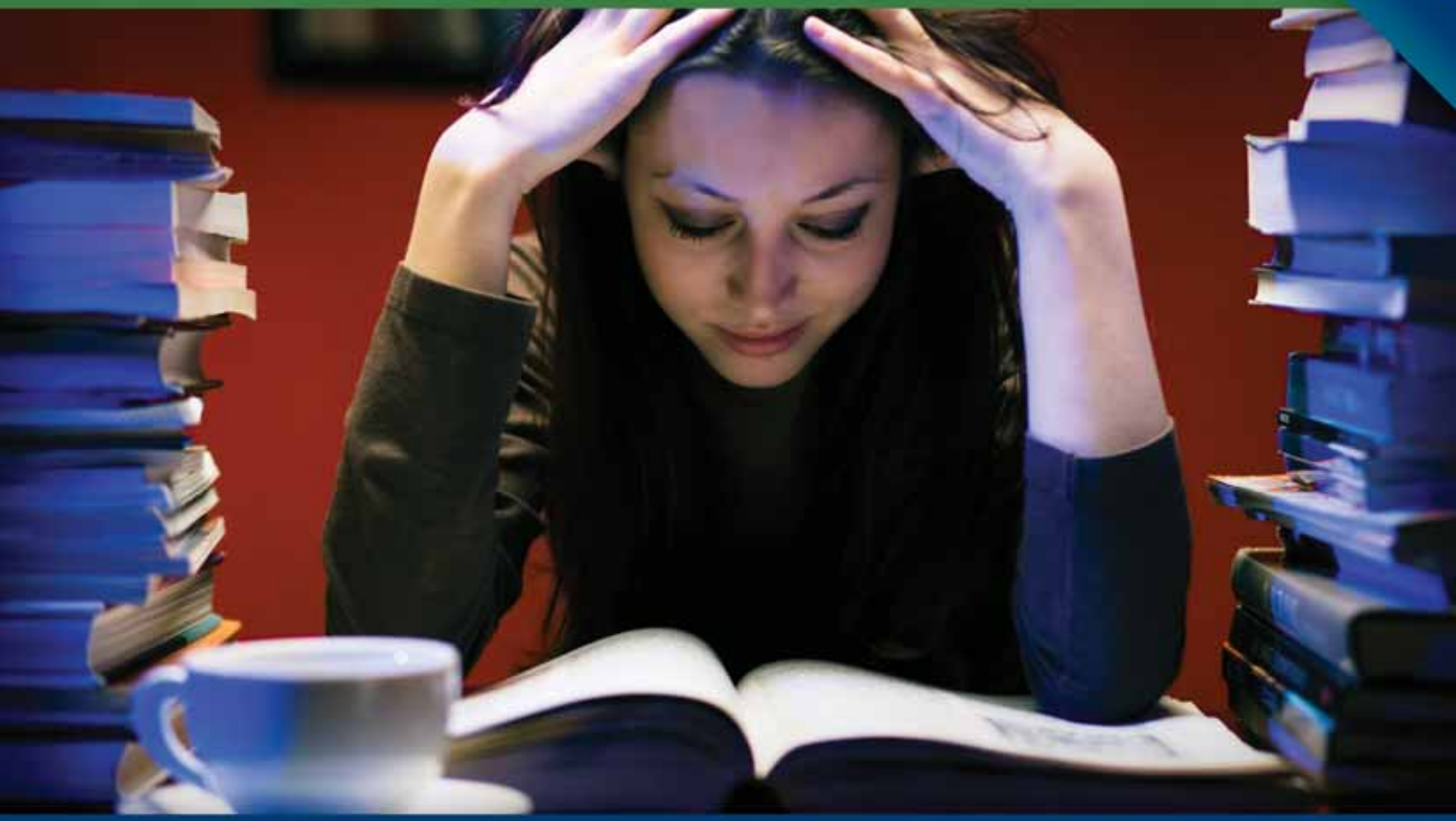

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*References*
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*2. Roodenrys et al. Neuropsychopharmacology. 2002; 27 (2):279-281*
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PUBLISHER / MEDSPEC PUBLISHING
Reni Rouncivell: Tel: (012) 661 3294 Fax: 086 561 5122, Cell: 082 441 6904, e-mail: reni@medspec.co.za, Private Bag X1036, Lyttelton, South Africa 0140

ADVERTISING & RATES
Lelani Adendorff: Tel: (012) 661 3294 Fax: 086 561 5122, Cell: 079 512 6990, e-mail: lelani@medspec.co.za, Private Bag X1036, Lyttelton, South Africa 0140

SUBSCRIPTIONS & ACCOUNTS: Elizabeth Versteeg, Tel: 072 189 8499, e-mail: accounts@medspec.co.za

FOR ADDRESS CHANGES PLEASE CONTACT: CALLY LAMPRECHT, cally@medspec.co.za

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# Delivering happiness: Translating positive psychology intervention research for treating major and minor depressive disorders

## Introduction

Despite the availability of many treatment options, depressive disorders remain a global public health problem. Even in affluent nations, 70% of reported cases either do not receive the recommended level of treatment or do not get treated at all, and this percentage does not reflect cases of depression that go unreported due to lack of access to health care, stigma, or other reasons. In developing countries, the World Health Organization estimates that <10% receive proper depression care due to poverty, stigma, and lack of governmental mental health resources and providers.

Current treatments do not work for everyone, and even people who achieve remission face a high risk of recurrence and residual disability. The development of low-cost effective interventions that can serve either as initial therapy for mild symptoms or as adjunctive therapy for partial responders to medication is an immense unmet need. Positive activity interventions (PAI's) teach individuals ways to increase their positive thinking, positive affect, and positive behaviours. The majority of such interventions, have been conducted with individuals who were not depressed, but two randomised controlled studies in patients with mild clinical depression have reported promising initial findings.

This is a summary of a review of the relevant literature on the effectiveness of various types of PAI's, drawing on social psychology, affective neuroscience and psycho-pharmacology research, to propose neural models for how PAI's might relieve depression, and discuss the steps needed to translate the potential promise of PAI's as clinical treatments for individuals with major and minor depressive disorders.

## Background information

Depression affects more than 100 million people worldwide, and in 2000, was the second leading cause of disability among individuals aged 15–44. The World Health Organisation (WHO) projects that by 2020 depression will be second only to ischemic heart disease as the leading cause of disability for all ages and both genders. In the United States 8.2% of the U.S. population over 18, suffer from either major depressive or dysthymic disorder. In the United Kingdom, depression is the third most common reason for a primary care consultation. Worldwide, about 850 000 lives are lost each year due to suicide. Studies show that approximately 1 in 8 adolescents may be suffering from depression. Even more upsetting is that only about 30% of these children who are suffering motional/mental turmoil, are receiving any treatment for it.

South African statistics on depression are scarce, but one study published in the SAMJ, May 2009, by M Tomlinson, Dan Stein et al, where 4 351 adult South Africans of all racial groups were assessed, reported on the prevalence of major depressive disorder as being 9.7% of the general population. The study did not evaluate mild to moderate depression or dysthymia.

Data from a study from 52 countries, published in a 2004 issue of The Lancet, showed that those who had a first

heart attack, reported high general stress and depression 55% more frequently than people of the same age and gender who had not had a heart attack. It is well known that depression is found in those with heart disease and diabetes as a triad of symptoms, increasing the risk of death from heart disease.

Even more alarming are the current rates of treatment. From 2001 to 2003, only 30% of adults in the United States reporting mood, anxiety, or impulse control disorders received 'minimally adequate treatment'. This means that, even in affluent nations, 70% of reported cases either do not receive the recommended level of treatment or do not get treated at all, and this percentage does not reflect cases of depression that go unreported due to lack of access to health care, stigma, or other reasons. In developing countries, the WHO estimates that less than 10% receive proper depression care due to poverty, stigma, and lack of governmental mental health resources and providers.

## High cost of depression treatment

Therapeutic interventions are costly, due to the need for a trained or licensed therapist to direct therapy. Treatment costs for depression can range from R1800 for three psychotherapy sessions to over R20 000 for the American Psychological Association's recommended course of treatment of 10 psychotherapy sessions combined with antidepressant medication for optimal care of moderate to severe depression. In addition, individuals at relatively high risk of developing depressive disorders, such as those with low education or financial duress, may be the least able to afford treatment. Even in developing countries where generic antidepressants are widely available, their cost remains high relative to per capita income.

## Evaluation of drug therapy

Depression is a heterogeneous condition with molecular and biochemical origins that are still not fully understood. Hence, it is not surprising that current drug therapy is suboptimal. Response rates to a single antidepressant are generally considered to be 60%–70%, with over 80% of the drug effect accounted for by placebo effects. Even with this relatively high percentage of 'responders' to drug treatment, initial pharmacotherapy produces remission in only 30%–40% of the depressed population. Furthermore, a substantial delay exists in onset of treatment action, leading both patients and clinicians to wait several weeks before determining whether augmentation or modification is needed. Practice guidelines suggest that when either drugs or therapy are not yielding symptomatic relief within 4–8 weeks, clinicians should switch or add a complementary treatment (i.e., add drugs to therapy or therapy to drugs). Unfortunately, however, the response rates diminish with additional strategies, and about one third will not remit even after two to four pharmacotherapy treatment trials. Finally, although drugs can be very helpful for many patients, they can be associated with adverse effects that patients often must endure to obtain the benefits.

Even when successful, drug therapy has been criticised for not arming patients with personalised tools they can use to prevent relapse and remission. Many studies have shown that patients treated to remission with behavioural activation or cognitive therapies are less likely to relapse after treatment termination than patients treated to remission with medication. Cognitive and behavioural approaches to treating depression have limitations, but at least appear to teach patients strategies that enable them to avoid falling back into negative thought patterns and behaviours.

## Moving beyond a focus on symptom reduction

Cognitive, behavioural, and interpersonal approaches to treating depression are effective in reducing acute distress in depressed patients, and compare favourably to medication among all but the most depressed individuals. In theory and in practice, all of these approaches, including cognitive therapy, behavioural activation, and interpersonal therapy, focus on alleviating the symptoms of depression. Although all of these approaches to treating depression have met with success, no technique works for everyone. Accordingly, the use of positive activity interventions (PAI's) is proposed to complement current drug and psychotherapeutic treatment.

## The benefits of PAI's

Researchers in the area of positive psychology believe we can now learn even more about the human condition by studying what is right in optimally healthy individuals. The body of work already compiled not only advances our understanding of why some people are happy, grateful, and optimistic, but also suggests how people can learn to practice intentional activities to increase their levels of these positive attributes. These ideas have broad relevance to the treatment of depression, as a singular focus on ameliorating depressive symptoms, compared to the thrust of most therapeutic and drug approaches to depression treatment, leaving patients in a languishing state in which they do not suffer from depression, but still have a low sense of well-being. It is argued that PAI's, which aim to help patients experience positive thoughts, affect, and behaviours, can galvanise them to move past the point of simply not feeling depressed to the point of optimal wellbeing.

Common positive exercises that have been tested in randomised controlled interventions include writing letters of gratitude, counting one's blessings, practicing optimism, performing acts of kindness, meditating on positive feelings toward others, and emphasising and encouraging signature strengths. Because PAI's teach patients ways to increase their positive cognitions, emotions, and behaviours without professional help, they may serve as vital tools to prevent relapse in response to potential depression triggers, like stress. Because they are cost-effective and convenient to deliver, PAI's can also help lessen the gap between the treated and untreated in the depressed population. Finally, because PAI's are self-administered, patients will attribute

***"The World Health Organisation (WHO) projects that by 2020 depression will be second only to ischemic heart disease as the leading cause of disability for all ages and both genders."***

improvements in their moods and symptoms to their own doing, and not to an external agent (i.e., an antidepressant or a therapist).

Patient empowerment is especially important, considering that autonomy is a core psychological need, and an internal locus of control positively affect depression symptoms. Although the number of empirically validated PAI's may seem small, scientists know a great deal about the general psychological mechanisms that make PAI's effective, including boosting positive emotions and facilitating experiences that meet people's core needs for autonomy, relatedness, and connectedness. PAI treatments should therefore strive to cultivate an individual's well-being, as well as other areas of his or her life (e.g., work, relationships, health), rather than only ameliorating depressive symptoms.

## The value of positive emotions

Positive emotions, the hallmark of wellbeing, do not just make people feel good - they have been found to foster successful outcomes in numerous life domains, including superior job performance, higher creativity, greater marital satisfaction, enhanced social relationships, and better physical health. The benefits of positive emotions are especially relevant to those suffering from depression, as positive emotions have been shown to accelerate recovery from the cardiovascular effects of negative emotions, improve broad-minded coping skills, and buffer against relapses.

Even momentary positive feelings can produce durable resources (e.g., new ideas, new relationships), as positive emotions have been shown to broaden thinking and attention. Broadened mindsets bring about novel ideas and actions (e.g., the urge to play and explore) and lead to the building of long-term social, psychological, intellectual, and physical skills and reserves. For example, if a person gets 15 minutes of positive emotions from counting her blessings, she may muster the energy to attend the art class she always considered attending, and, while in class, might meet a friend who becomes a companion and confidant for years to come. Among individuals with depression, higher levels of approach-oriented motivation are associated with less severe depression and a greater likelihood of recovery. In contrast to the narrowing of attention and behavioural inhibition characteristic of negative states, positive emotions trigger upward spirals toward greater resilience, and psychological wellbeing.

## Examples of PAI's

Positive activities such as the regular practice of gratitude, optimism, kindness, and meditation are similar in that they are all relatively brief, self-administered exercises that promote positive feelings, positive thoughts, and/or positive behaviours, rather than directly aiming to fix negative or pathological feelings, thoughts, and behaviours. Randomised controlled longitudinal experiments have validated the effectiveness of these intentional activities in raising wellbeing and reducing depressive symptoms.

## Research and the psychological mechanisms underlying the effectiveness of PAI's

Previous studies by Lyubomirsky and colleagues, have found evidence that the relation between a positive cognitive intervention and subsequent decreases in depressive symptoms, is mediated by increases in positive affect. Similarly, a study with Anglo-Americans and Asian-Americans found positive experiences, as well as feelings of control and connectedness, to mediate the relationship between the PAI and subsequent increases in wellbeing. It is believed that assessing potential mediating variables, such as positive thoughts, positive behaviours and positive feelings will advance our understanding of the psychological mechanisms underlying why PAI's work, thus helping refine current positive interventions and design new ones.

PAI's are effective for enhancing wellbeing and ameliorating depressive symptoms. Depressed individuals are relatively eager to feel better and may put more effort into the positive activities. Greater incentives and effort have been shown to increase the positive effect of treatment in past studies.

***"...low levels of happiness are highly correlated with depression scores"***

PAI's have a lower resistance to entry for those lacking motivation, energy or enthusiasm. A depressed person should be much more likely to complete a positive activity at home than locate a therapist, arrange an appointment, and drive to a therapist's office. Finally, although happiness and depression are theoretically distinct constructs, low levels of happiness are highly correlated with depression scores, thus further supporting the prediction that PAI's shown to increase wellbeing, will serve to decrease depressive symptoms in clinically depressed individuals.

Seligman and colleagues conducted an online experiment in which they randomly assigned 411 mildly depressed volunteers, with a mean score of 14.1 on the Center for Epidemiologic Studies Depression scale (CES-D), to engage for 1 week in one of five well-being–enhancing activities (involving practicing gratitude, positive thinking, and one's strengths), versus a placebo control activity (involving writing one's early experiences). Participants in the placebo condition experienced a short-term boost, but returned to their baseline after a week. By contrast, those who completed the positive exercises experienced a boost in wellbeing and a decline in depressive symptoms, and these benefits were maintained after the intervention ended. Two of the activities, writing about three good things in one's life and using one's signature strengths in a new way, resulted in lasting improvements in depression and wellbeing for 6 months!

It is noteworthy that every treatment group in the abovementioned study showed significant decreases in depressive symptoms after just 1 week or less of participation. These results indicate that not only can PAI's be effective in reducing depressive symptoms, but that they can also work quickly. In another study, Seligman instructed severely depressed individuals (CES-D mean of 33.9) to engage in the 'three good things' PAI every day. Within 15 days, participants' CES-D scores decreased by 16.7 points (from severe to mild-to-moderate depression) and 94% experienced relief. Thus, although the development, research, and implementation of positive psychology interventions are in their early stages, such interventions show promise for improving the lives of many, and doing so at a relatively rapid pace and a low cost. JIM SA

# BodyTalk

Overview: BodyTalk is an astonishingly simple and effective holistic therapy that allows the body's energy systems to be re-synchronized so they can operate as nature intended. Each system, cell, and atom is in constant communication with each other at all times. Through exposure to the stresses of day-to-day life, however, these lines of communication can become compromised or disconnected, which then leads to a decline in physical, emotional and/or mental well-being. Reconnecting these lines of communication enables the body's internal mechanisms to function at optimal levels, thus repairing and preventing disease while rapidly accelerating the healing process. In this way, BodyTalk stimulates the body's innate ability to balance and heal itself on all levels.

When stress occurs the body becomes less efficient at healing itself. This causes illness and disease on all levels - mind, body and spirit. We can find out where the body is functioning inefficiently due to stress using a gentle muscle-checking technique. Using gentle balancing techniques, the body's internal awareness is redirected to focus on these areas and facilitate the body's return to balance.

Clinical results have shown that this method of healing helps the nervous system to focus better on all systems within the body. As the body becomes aware of the areas that have previously been ignored, balance is re-established.

The body is then capable of improving its function on all levels with lasting results.

## What It Helps

ADD/ADHD, Allergies, Arthritis, Asthma, Autoimmune Issues, Back Pain, Behavior problems, Chronic fatigue, Depression, Digestive disorders, Emotional disorders, Endocrine issues, Fears and phobias, Fibromyalgia, Infertility, Infections, Insomnia, Headaches, High cholesterol, High blood pressure.

## How It Works

### Location

The practitioner finds the priority areas in the body that need to be addressed. This may be a physical area: an organ or an area of the spine, a scar from an accident or surgery, an allergen, a bacteria, or a virus or toxin that is slowing down the immune system. There could be a mental emotional factor causing stress, such as a memory of emotional or physical trauma, or a limiting belief system. Other areas of focus could include an environmental factor or a blockage in the acupuncture meridian system. Any number of these issues will impact the ability of the body to function at optimal levels.

### Change

The practitioner holds the areas that have been highlighted and gently taps over the brain and over the heart. Tapping over the brain helps the whole nervous system to become aware of what it needs to do to balance itself in relation to the areas that are being held. The brain then improves communication between the targeted systems. This will increase nerve function, blood supply, and lymph flow in those areas. In the case of a memory or emotion the whole mind body system will reduce the charge around that issue. Tapping on the heart ensures the new information is stored throughout the whole body, by encoding the changes in the heart's electrical field, allowing lasting improvements in function.

### Healing

As the body becomes aware of areas of imbalance, it naturally redirects resources to those areas. The body's systems move from fight or flight (stress) mode to parasympathetic (healing) mode. There is a return to normal balance and wellness on all levels - physical, mental, and emotional.

**For further info visit our website at www.bodytalksystem.co.za**

# Potential neural mechanisms underlying the effectiveness of PAI's as treatment for depression

## Introduction

The question arises, that if PAI's can successfully alleviate subjective reports of depressive symptoms, how might they impact mood-relevant or reward-relevant neural circuits? Two decades of research into the cognitive and affective neuroscience of mood disorders were examined for answers. Functional neuro-imaging studies have led to a hypothetical neural model in which major depressive disorder (MDD), is a result of a lack of coordination between the dorsal attention–cognitive control system and ventral limbic–affective systems in the brain.

Evidence using positron emission tomography, has shown decreased dorsal cortical activity and increased ventral limbic activity associated with negative mood. Although the results have not always been consistent due to differences in tasks or patients' clinical profiles, fMRI studies have also revealed a hypo-functioning dorsal cognitive control system and hyper-functioning emotional system. Case–control studies in depressed patients without medication, have found elevated activation in response to negative stimuli in the amygdala, as well as either decreased, or increased activation in the dorsolateral–prefrontal cortex (dlPFC) and dorsal anterior cingulate cortex, depending on task load.

Pilot studies of patients on antidepressants have found a reversal of this pattern as a result of mood improvement. Whereas antidepressants have been hypothesised to target the amygdala and other limbic regions directly and affect a bottom-up pathway, cognitive behavioural therapy (CBT) has been proposed to operate on the dorsal cognitive control system and to affect a top-down control pathway. Antidepressants appear to increase the activity of the dlPFC, whereas CBT may decrease dlPFC activity and increase activity in the hippocampus and the dorsal cingulate.

The inability to experience pleasure from activities usually found enjoyable, e.g. hobbies, exercise, social interaction or sexual activity (anhedonia), is a core symptom of depression, and a number of functional magnetic resonance imaging (fMRI) studies have shown reduced activation in the reward system in patients with MDD. This reduced activation has been correlated with self-reported low positive affect, suggesting that the activation of the reward circuit detected by fMRI is related to current emotional experience. The regions traditionally implicated in reward-related processing, such as the expectation of reward and the experience of pleasure and social rewards, include the ventromedial PFC, caudate, nucleus accumbens, and the midbrain (such as the ventral tegmental area). Studies using positive stimuli have revealed decreased activation in MDD versus normal subjects in the ventral striatum. Research has also indicated that activation in the left frontal region is associated with greater levels of positive, approach-related emotions, while activation in the right frontal region is associated with negative, withdraw-related emotions.

## Possible brain mechanisms underlying PAI's

Because non-responders to pharmacotherapy continue to exhibit increased amygdala activation, it can be postulated that improvement of core mood symptoms and anhedonia with PAI's in such individuals, might be linked to down regulation of the hyperactivated amygdala response, and up regulation of the reward system. If participants are able to improve their cognitive strategies (e.g., feelings of control or connectedness) through PAI's, then such effects might be linked to beneficial neural changes in the top-down dorsal cognitive control pathway.

## Need for further studies of PAI's in depressive disorders

Much work needs to be done to directly test the efficacy of PAI's as a treatment for major and minor depressive disorders, and investigate both the psychological and neural mechanisms underlying their effectiveness. PAI's might be suitable as monotherapy for mild depressive or adjustment disorders, as well as adjunctive therapy for partial responders to medication. In both settings, the need exists for 8- to 12-week randomised controlled trials, to test the efficacy of PAI's as acute therapy to examine response and remission rates in comparison to usual care. Given the attractiveness of PAI's for vulnerable populations such as children, teenagers, the elderly, and medically ill, trials will need to be representative of such populations. Longer term studies (e.g., 6–12 months) to study the efficacy of PAI's for maintaining sustained remission and preventing recurrences will also be needed. Studies to better understand the mechanisms underlying potential benefits of PAI's could yield significant insights. However, given the potentially high benefit–risk ratio of PAI's in improving depression outcomes and the relatively low cost involved, even though such studies should be a priority for funding agencies focusing on alternative therapies, these could, in the meantime, be implemented as part of a general regime for the management of depression.

## Self-administered treatment

Self-administered or self-help interventions, which can be delivered outside of a clinic, have several key advantages over solely clinical treatments. Self-administered treatments cost significantly less than therapeutic interventions and are more convenient to deliver. For example, for a relatively trivial per capita cost, interventions can be delivered via the Internet, CD's, DVDs, workbooks and mobile phone applications. Once implemented, a self-administered treatment can service a large number of patients, without the need to add more trained personnel. With the advent of social media, computer based treatments do not have to be solitary activities, but can also facilitate interpersonal support from peers and therapists.

The meta-analysis of PAI's found that individually delivered positive psychology interventions show the greatest benefits, followed by group-administered interventions. This finding makes practical sense, as some populations may not benefit from self-administered treatment. For example, self-administered activities would not be ideal for those suffering from severe depression or for individuals with a bias against self-help, who may perceive positive activities as fake attempts at coercing them into improvement. Nevertheless, the meta-analysis showed that, in addition to individual and group therapies, participating in self-administered positive activities also significantly enhanced wellbeing.

A recent publication analysing 81 randomised, double blind clinical trials, with 21 611 evaluable patients, only 53% of all the MDD trials in the last 25 years were found to be successful, implying that 47% failed to separate from placebo. The data showed that over the last 25 years, treatment effect size clearly diminished at a similar rate for both U.S. and non-U.S. trials, despite a marked increase in the sample size of the trials, and that placebo rates slightly increased. Such findings are consistent with the widely accepted notion that current antidepressant medication treatments are not successful for a sizeable proportion of patients, incur a heavy financial burden, frequently take weeks to be effective, may be stigmatising for some, and hold a risk of both minor and serious side effects. Compared to this, PAI's as new category of depression interventions, either as a therapy on its own, or in conjunction with other therapies, have the potential to benefit depressed individuals not responding to pharmacotherapy, or not able or willing to obtain treatment, is less expensive to administer, less time-consuming, promise to yield rapid improvement of mood symptoms, can reach unlimited numbers of people with depression, hold little to no stigma and carry no side-effects.

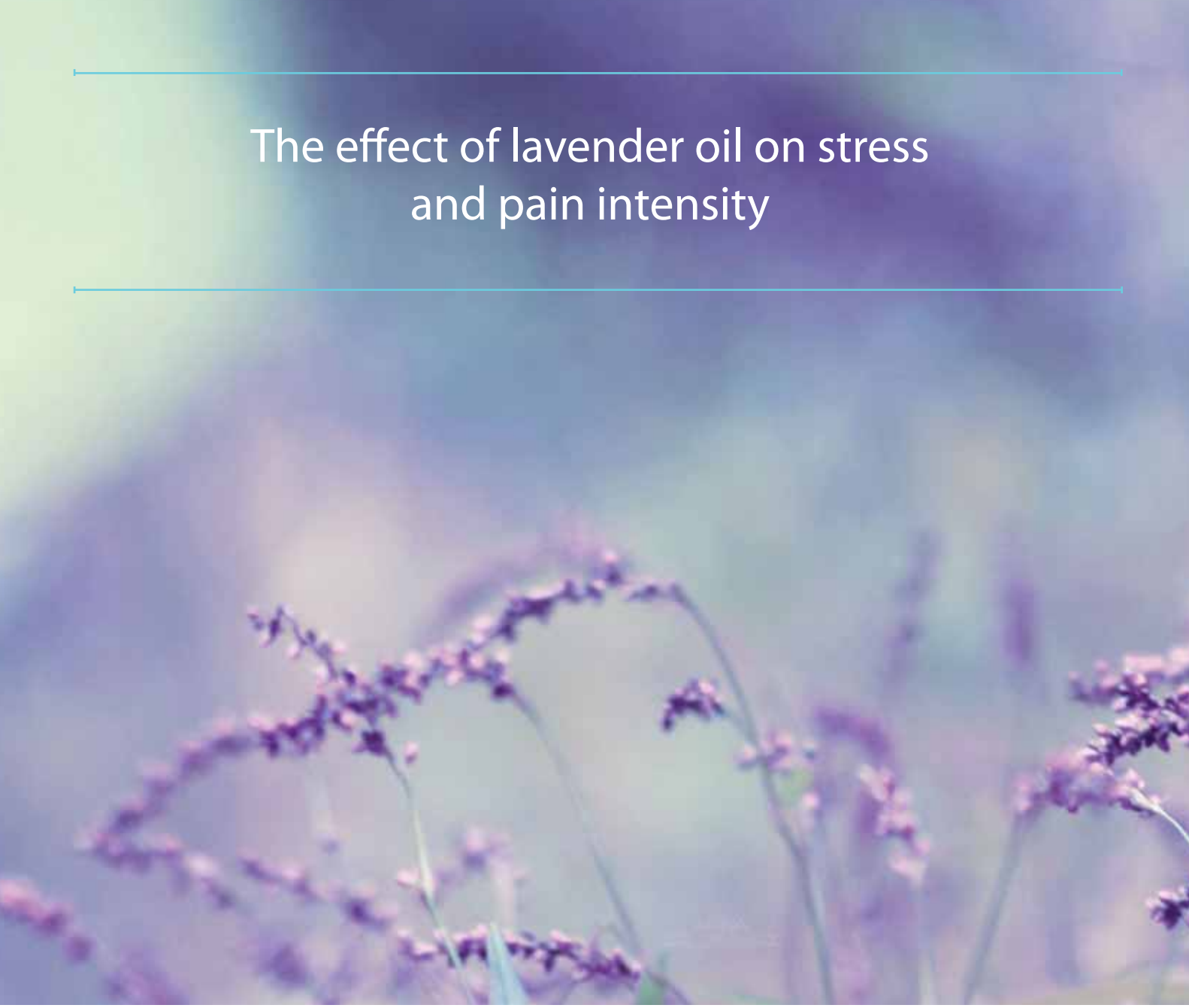
Although positive psychological science is only about a decade old, positive interventions have already gained considerable theoretical and practical support in the literature. Future research on PAI's in clinical settings would further the treatment of depression by cultivating positive thoughts, feelings, and experiences, rather than aiming solely to ameliorate depressive symptoms, PAI's represent a unique approach that may appeal to people who are not optimally served by cognitive–behavioural or interpersonal therapies, as well as patients who are already taking antidepressant medication, but have shown a small to moderate response. The self-help nature of PAI's allows for potentially extensive and cost effective distribution of the treatment. JIM SA

***Summarised from an article written by Kristin Layous, Joseph Chancellor, Sonja Lyubomirsky, Lihong Wang and P. Murali Doraiswamy and published in The Journal of Alternative and Complementary Medicine. August 2011, 17(8): 675-683.***

***Complete referenced article is available on request***

***"The self-help nature of PAI's allows for potentially extensive and cost effective distribution of the treatment."***

# The effect of lavender oil on stress and pain intensity



The purpose of this study was to investigate whether lavender oil aromatherapy can reduce the levels of stress and pain intensity in 30 healthy, randomly allocated volunteers. The experimental group received oxygen with a face mask coated with lavender oil for 5 minutes, and the control group received oxygen through a face mask with no lavender oil for 5 minutes. The stress level (0=no stress, 10=maximum stress) and pain intensity of needle insertion (0=no pain, 10=worst pain imaginable) were measured.

There were no significant differences in age, sex, height and weight between the two groups. Stress level and pain intensity of needle insertion before aromatherapy were similar between the two groups. However, the stress values after aromatherapy were significantly reduced compared to the control. In addition, the pain intensity of needle insertion was significantly decreased after aromatherapy compared to the control.

High baseline anxiety and stress are found to increase intra-operative anaesthesia requirements and affect the smoothness of recovery from anaesthesia. Anxiolytic and sedative drugs such as benzodiazepines or opioids in ambulatory patients may delay discharge from the hospital.

Alternative methods such as aromatherapy using lavender oil have been used to manage pain, as well as to control postoperative nausea and vomiting.

The study results demonstrate that lavender inhalation significantly reduced the stress levels in volunteers. In addition, aromatherapy reduced the pain intensity of needle insertion.

Preoperative anxiety may increase anaesthesia requirements, thereby adversely affecting its administration and patients' recovery, and also decrease patients' satisfaction with their peri-operative experience. In addition, anxiety can result in a high incidence of postoperative pain, increased analgesic use, and prolonged hospital stay. Sedatives and opioids are often used to reduce the preoperative anxiety. However, they are associated with undesirable effects, especially for ambulatory surgery. Benzodiazepines, the most common premedication administered to alleviate pre-operative anxiety and stress, may interact with hypnotics and analgesics and prolong patient discharge. In addition, opioids contribute to postoperative nausea and vomiting. Non-pharmacological techniques to prevent or treat pain and emesis during

surgery, will not prolong sedation after surgery, or increase the incidence of vomiting. These techniques are also cost effective. The advantages of aromatherapy include being non-invasive and easy to apply. The use of essential oils offers a simple, low risk, cost effective nursing intervention that has the power to improve patient outcome and increase patient satisfaction. Lavender oil is one of the safest essential oils with wide therapeutic action and few reported sensitivities or irritations. The exact mechanisms by which aromatherapy produces relaxation are unknown. Essential oils exert both physiologic and psychological effects. Lavender oil is reported to have an effect on the glutaminergic system and to potentiate the responses of γ–aminobutyric acid receptors.

This study's positive findings are similar to those of other investigations, which showed that the inhalation of essential oils (usually lavender, but also orange in one study) reduced anxiety in healthy student volunteers, as well as in patients. It has also been reported that 2% lavender oil inhalation decreased opioid consumption after surgery without adverse effects. In this study, volunteers who inhaled 2% lavender oil inhalation reported a lower intensity of needle pain compared with the control. The effect lasted for 20 minutes. Jojoba oil was used in this study to dilute the essential oil of lavender. It is odourless and non-allergenic, and has no influence on pre-operative anxiety in surgical patients.

Lavender inhalation was associated with significantly reduced stress levels, and pain intensity of needle insertion. These findings may prove to be important in controlling preoperative fear and stress, particularly in an ambulatory setting. Further studies are required to establish the value of aromatherapy before surgery. JIM SA

***Summarised from article written by Sioh Kim, Hyun-Jae Kim, Jin-Seok Yeo, Sung-Jung Hong, Ji-Min Lee and Younghoon Jeon. The Journal of Alternative and Complementary Medicine. September 2011, 17(9): 823-826.***

***Complete referenced article is available on request***

# Metabolic syndrome: Towards a global definition

Statistics: Demonstrating the essential need and urgency to define and address this prevalent health challenge

Based on the ATP III (The Adult Treatment Panel III) guidelines published in the National Health Statistics Report, May 2009, approximately 34% (more than one third) of the adults in the United States could be diagnosed as having metabolic syndrome.

This is congruent with findings from a study published in the South African Medical Journal, vol. 99, no. 5, May 2009, where the frequency of metabolic syndrome, overweight, obesity and risk of developing metabolic syndrome in workers at Kanye Seventh-day Adventist Hospital, Kanye, Botswana, were examined, and it was found that 34% of the hospital's workers had metabolic syndrome, the same percentage were at high risk of developing metabolic syndrome, 28.7% were obese, and 27.3% were overweight. Female gender was found to be strongly associated with obesity and metabolic syndrome. The age group of 35 - 54 years was most affected.

Another study by J Ker et al, published in the

Cardiovascular Journal of SA in 2007, where the frequency of the metabolic syndrome in screened South African corporate executives were measured using the ATP III criteria, has recognised the importance of the metabolic syndrome as a clinical entity. A group of 1 410 corporate executives, belonging to a specialist health and fitness company in South Africa were tested, using three criteria as specified by the ATP III panel. Results showed that 31% of this group of corporate executives fulfilled the criteria for the diagnosis of metabolic syndrome. In a small subset of black executives, a similar finding was obtained. Another third of the executives had two criteria of the metabolic syndrome.

## Background

The metabolic syndrome has existed in various forms and definitions, as a cluster of metabolic abnormalities with insulin resistance as the underlying major characteristic, has been known by several names since 1923.

Metabolic syndrome (Syndrome X; insulin-resistance syndrome) consists of a constellation of metabolic abnormalities that confer increased risk of cardiovascular disease and diabetes mellitus.

During the last five years, there has been controversy surrounding the definition of metabolic syndrome and the significance of the syndrome. This controversy has led to a lack of clarity about its role and value in clinical practice as opposed to its role in research.

Does metabolic syndrome predict cardiovascular disease risk better than the individual components? The relative value of metabolic syndrome in predicting type 2 diabetes mellitus remains uncertain. This controversy drove the need for a universally accepted single definition.

## Problem with definition

There are approximately six different definitions of metabolic syndrome, with the difference being the addition of one or more different components. Even the waist circumference as an obligatory component or just one of the criteria of the syndrome has added to the confusion.

## Definition

A unified definition was finalised after a collaboration between the International Diabetes Federation, American Heart Association/National Heart, Lung and Blood Institute, the World Heart Federation, International Atherosclerosis Society and the International Association for the Study of Obesity. This new published definition involves the following factors:

- Increased waist circumference: Population - specific and country specific cut-off points to be used. Usually abdominal circumference more than 102 cm in men, and more than 88 cm in women
- Increased triglycerides (or drug treatment for it):1.7mmol/1 or above.
- Reduced HDL (or drug treatment for it) : < 1.0 mmol/l for men; < 1.3 mmol/l for women.
- Elevated blood pressure (or antihypertensive drugs used): 130 mmHg systolic; 85mmHg diastolic or above.
- Increased fasting glucose (drug treatment for increased glucose) >5.5 mmol/1.

## Comments

The challenge is that the definition for an expanded waist circumference remains unsettled. Insulin resistance explains most of the symptoms of metabolic syndrome. Evidence now indicates that metabolic syndrome begins with excess central adiposity, but genetic predisposition is a contributing factor. Recently a polymorphism in the multi-PDZ domain-containing adaptor protein (PDZ-K1) regulating HDL receptor scavenger receptor type B Class 1 was found to associated with metabolic syndrome.

Shift work, sleep deprivation and bright light exposure at night also relate to increased adiposity and metabolic syndrome. Recently, vitamin D deficiency was linked to the risk of cardiovascular disease and low vitamin D was strongly associated with overweight and metabolic syndrome, according to Prof James Ker, Dean Dept Medicine UP.

In conclusion, the inclusion of glucose intolerance and/or insulin resistance as obligatory criteria in the definition of metabolic syndrome, seems to be important for the ability to predict all-cause mortality and cardiovascular morbidity.

***Summary based on following articles:***


1. Ingrid Larsson, Annakarin Lindroos, Theodore C. Lystig, Ingmar Näslund and Dr. Lars Sjöström. Metabolic Syndrome and Related Disorders. Summer 2005, 3(2): 102-112.
2. SA Medical Chronicle, April 2010, based on an article published in the Cardiovascular Journal of SA in 2007.


***Complete referenced article available on request***

***"This controversy has led to a lack of clarity about its role and value in clinical practice as opposed to its role in research. "***

# An integrative approach to effectively manage metabolic syndrome

Addressing metabolic syndrome in an integrative medicine approach, that can be applied to private practice, local clinics, community primary care facilities and in the workplace, has to become a top priority to address the burden of this disease (health challenge) in South Africa. By 2010, 150 million people have been diagnosed with metabolic syndrome, using the diagnostic criteria as per the previous article summary. We know that only about 20% are actually diagnosed, hence the utmost importance of regular health and wellness screenings, one of the main reason for promoting workplace wellness interventions. It is predicted that this figure will increase to 300 million by the year 2030. Compare this figure to the 35 million positive HIV people globally, with 22 million of those in Africa, and it is clear that metabolic syndrome is an even bigger health challenge to for which to find integrative medical and wellness solutions.

An integrative medicine approach, including the use of functional medicine, nutriceuticals (nutri- from nutrition and *–ceutical* from pharmaceutical), the usual lifestyle options, a realistic exercise program combined with nutritional guidance, advice on dealing with carbohydrate addiction, stress management and relaxation training, combined with a support network, will go a long way in providing solutions to address this most prevalent health challenge. Add to this the search for cause, by looking at the deeper mental-emotional blocks, the psycho-spiritual connection, where physical disease is regarded as a manifestation of a deeper subconscious pattern that has to become conscious, and the journey into healing can begin. Regarding dis-ease as a teacher rather than a curse or punishment, gives patients hope and many tools to use in managing their illness. This allows for an attitude of self responsibility and learning, rather than becoming a victim of the disease.

## To summarise:

- Behaviour modification, including a change in eating patterns to a healthy, varied and tasty diet that includes a variety of seasonally available fruit and vegetables, nuts, seeds, low glycemic index carbohydrates, healthy fats (essential fatty acids as in extra virgin olive oil, grapeseed and avocado oils) and portion controlled protein from fish, poultry and lean meat, with increased intake of fibre rich food.
- Regular, gentle, enjoyable exercise matched to the individual fitness level
- The use of specific nutriceuticals and nutritional factors specifically designed for managing metabolic syndrome: e.g. beta-glucan from oats, antioxidants from berries, alpha-lipoic acid (ALA), chromium, biotin, vanadium, phaseolamin (Phase 2) and the vitamins that will reduce blood homocysteine levels, such as folic acid and vitamins E and B12.
- Addressing insulin resistance: betaglucan in oat soluble fiber may lower blood glucose levels after sugar intake, chromium polynicotinate, vanadium, molibdenum and alpha lipoic may assist insulin function through improved performance of glucose tolerance factor. Gymnema sylvestre, fenugreek and cinnamon are herbs that increase insulin receptor sensitivity and glucose metabolism.
- Beta-glucan and Omega 3 fatty acids as found in cold water fish oil may reduce blood levels of low-density lipoprotein (LDL) cholesterol, and triglycerides, and may variably increase high-density lipoprotein (HDL) cholesterol.
- Antioxidants and chromium with biotin may exert positive effects on blood cholesterol.
- Beta-glucan may produce a sensation of satiety when taken before meals, and thereby assist in controlling calorie intake.
- Reduction in blood pressure result from weight control and lifestyle changes.
- The oxidative stress and advanced glycation end products may be reduced by bioflavonoids, proanthocyanidins, alpha lipoic acid and other antioxidants. High dosages of B-complex vitamins improve glucose metabolism.
- Of the utmost importance: address subconscious emotional blockages and long forgotten memories that play an important role as causal factor in the specific symptoms of metabolic syndrome. In short, struggling with metabolic syndrome is not due to lack of will power - there are more factors involved in this health challenge found in more than one third of the general population!

## Integrative Wellness Solutions in a Nutshell

- healthy eating habits with unre¬fined, low glycemic index (GI) carbohydrates (e.g. wholewheat, oats, muesli, legumes, cold potatoes, legumes), high fibre intake, reduced saturated fat intake, fresh vegetables and limited fruit (three a day), enough high quality proteins (e.g. lean meat, fish, eggs), and limited amounts of unsaturated fats
- no alcohol, smoking cessation
- suitable food supplements and herbal remedies
- regular moderate exercise
- stress management and daily relaxation time

- digging for subconscious emotional issues

More information on the specific useful nutrients for metabolic syndrome

- **Chromium** is probably the most important mineral for maintaining constant blood sugar levels. It is used for the treatment of high (hyper-) and low blood sugar levels (hypoglycaemia). Chromium forms part of the glucose tolerance factor (GTF), an important molecule in the man-agement of carbohydrate metabolism, as it improves the functioning of insulin. GTF (and hence chromium) improves the absorption of glu¬cose in the cells so that it can be used for generating energy. GTF binds to insulin and the cell receptors to improve the absorption of glucose, thereby reducing blood sugar levels. GTF consists of one chromium molecule, two niacin molecules (vitamin B3) and three amino acids (glycine, cysteine and glutamic acid).

- **Vitamin E** reduces cell damage and prevents the oxidative damage to endothelial tissue, associated with hypercholesterolaemia and high triglycerides. Vitamin E can also reduce the insulin requirements of insulin dependant diabet¬ics. Type 1 diabetics must start with 80mg of vitamin E a day and their insulin dosage must be monitored carefully. The insulin can systemati-cally be reduced as the vitamin E dose is increased to 320mg a day, the recommended maintenance dosage for type 2 diabetics.

- **Vitamin C** improves glucose tolerance and liver function. The transport of vitamin C into the cells is facilitated by insulin. Those with insulin resistance, therefore often don't have enough intracellular vitamin C.

- **Co-enzyme QI0** is important in the metabolism of oxygen and the production of the energy molecule ATP (adenosine triphosphate). It improves oxygen consumption at cellular level.

- **Manganese** is an essential mineral involved in various enzyme systems which control the metabolism of glucose and proteins, bone formation, synthesis of L-dopamine (a neu-rotransmitter), cholesterol and mucopolysaccharides. Marginal defi¬ciencies are common because of soil depletion, which leads to reduced manganese in nuts and wholegrain products.

- **Flavonoids** such as **quercetin, proanthocyanidin** (from the extract of grape seeds or pine bark and ***Ginkgo biloba*** are strongly recommended. These prevent damage from the free radicals caused by abnormal glucose/energy metabolism, reduce the damage to peripheral blood vessels, prevent loss of sight and protect all the organs (such as the brain) from increased blood sugar levels. Alpha-lipoic acid exerts antioxidative effects and improves insulin resistance and blood glucose levels.

- **Magnesium** can stimulate insulin activity. Low magnesium levels are common in insulin resistance, hypertension and hypercholesterolaemia.

- **Pyridoxine** (vitamin B6) can improve the peripheral damage to the extremities caused by poor blood circulation. Vitamin B6 also improves the oxygen supply to tissue and helps to prevent atherosclerosis. As well as other B-group vitamins: B3, 5, I2; folic acid, biotin, inositol

- **Zinc** and **vanadium** to improve insulin sensitivity and as co-factor of glucose tolerance factor

- **Medicinal herbs** to produce favourable changes in insulin sensitivity and blood glucose levels:

- *Gymnema sylvestre*

- Cinnamon

- Ginkgo biloba

- Blueberry (bilberry or *Vaccium myrtillus*)

- Milk thistle (silymarine)

- Fenugreek (Greek hay or *Trigonellafoenum-graecum*)

- Garlic & onions

Finally, and probably most important of all, the subconscious emotional and psycho-spiritual issues have to be addressed for a return to the original state of perfect health.

***As James Hillman said in his book 'A Blue Fire':***

***'The right reaction to a symptom may as well be a welcoming rather than laments and demands for remedies, for the symptom is the first herald of an awakening psyche which will not tolerate any more abuse. Through the symptom the psyche demands attention. Attention means attending to, tending, a certain tender care of, as well as waiting, pausing, listening. It takes a span of time and a tension of patience. Precisely what each symptom needs is time and tender care and attention. Just this same attitude is what the soul needs in order to be felt and heard.'*** JIM SA

***"...healthy eating habits with unrefined, low glycemic index (GI) carbohydrates (e.g. wholewheat, oats, muesli, legumes, cold potatoes, legumes), high fibre intake, reduced saturated fat intake, fresh vegetables and limited fruit (three a day), enough high quality proteins (e.g. lean meat, fish, eggs), and limited amounts of unsaturated fats"***

# 'Mindfulness and psychological wellbeing: Are they related to type of meditation technique practiced?'

This study examined whether practitioners of two meditation types differ on self-reported mindfulness skills and psychological well-being. This cross-sectional study comparing two convenience meditation groups drawn from local meditation centers, one group practicing mindfulness meditation (MM), and the other practicing transcendental meditation (TM). The study was conducted at several meditation centers in southern Netherlands. Thirty-five (35) participants practiced MM (69% women) and 20 practiced TM (42% women).

Participants completed questionnaires on mindfulness skills (Mindful Attention Awareness Scale and two subscales from Kentucky Inventory of Mindfulness Skills), psychological wellbeing (perceived stress, global mood, and quality of life), and meditation duration and frequency.

All self-reported mindfulness facets correlated with almost all measures of wellbeing across groups, but no differences were evident between meditation types regarding mindfulness or wellbeing. Days per week spent on meditation was the only multivariable predictor of both higher mindfulness and lower perceived stress.

The results suggest that self-reported mindfulness and psychological wellbeing may be associated with meditation frequency rather than any potential differences when comparing MM and TM in this study. Substantial differences between MM and TM groups were present on basic demographics, which were controlled statistically.

It is important to note that psychological wellbeing measured as perceived stress, global mood and quality of life improved for all participants in both groups. The conclusion therefore is also that daily meditation practice, regardless the specific technique being used, can be of potential benefit to every one of us.

## In a nutshell

### Definition of Transcendental Meditation (TM)

Transcendental Meditation (TM) refers to the Transcendental Meditation technique, a specific form of mantra meditation (*Ed. – a mantra is a given sentence or word repeated, as a tool to quiet the mind in order to stop the mental chatter of the active left brain hemisphere*), introduced in India in the mid-1950s by Maharishi Mahesh Yogi (1914–2008). It had reached global proportions by the 1960s (*Ed. - mostly because of The Beatles being its primary advocates*). TM is one of the most widely practiced, and widely researched meditation techniques.

### Definition of Mindfulness Meditation (MM)

The first component of mindfulness involves the self-regulation of attention, so that it is maintained on

immediate experience, thereby allowing for increased recognition of mental events in the present moment. The second component involves adopting a particular orientation toward one's experiences in the present moment, an orientation that is characterized by curiosity, openness, and acceptance. In this two-component model, self-regulated attention (the first component) involves conscious awareness of one's current thoughts, feelings, and surroundings, which can result in metacognitive skills for controlling concentration. Orientation to experience (the second component) involves accepting one's mindstream, maintaining open and curious attitudes, and thinking in alternative categories. Training in mindfulness and mindfulness-based practices, oftentimes as part of a quiet meditation session, results in the development of a Beginner's mind, or looking at experiences as if for the first time. JIM SA

***Summary from article 'Mindfulness and Psychological Well-Being: Are They Related to Type of Meditation Technique Practiced?', by D Schoormans and Ivan Nyklíček; The Journal of Alternative and Complementary Medicine. July 2011, 17(7): 629-634***

***Definition of meditation techniques sourced from Wikipedia, the Free Encyclopaedia (en.wikipedia.org/wiki/Dictionary)***

***"...mindfulness and psychological wellbeing may be associated with meditation frequency rather than any potential differences when comparing MM and TM"***

# Survey of the antimicrobial activity of commercially available

## Australian Tea Tree (Melaleuca alternifolia) Essential Oil Products In Vitro

The aim of this study was to investigate the antimicrobial activity of a range of commercially available tea tree oil (TTO) products and to evaluate whether formulation plays a significant part in their antiseptic activity.

The antimicrobial activity of the purchased products and control TTO solutions was assessed against *Escherichia coli, Staphylococcus aureus, Salmonella typhimurium, Pseudomonas aeruginosa,* and *Candida albicans* using well diffusion, broth microdilution and broth macrodilution assays.

Zone sizes obtained by the agar well diffusion assay ranged from 0 to 49.8 mm, with the more viscous and lipophilic products producing the smallest zones. Micro- and macrodilution methods showed that eight products had minimum inhibitory concentrations that were lower than the nonformulated TTO control. The remaining three products showed activity equivalent to the TTO control.

The oil of *Melaleuca alternifolia* also known as tea tree oil (TTO), has been used as an antiseptic remedy for decades. Although there is no published documentation of specific medicinal applications of the *M. alternifolia* plant or oil by Aboriginals prior to white colonization of Australia, the Bundjalung Aboriginals of New South Wales used the plant for medicinal purposes and told of the wound healing properties of the water from a lake into which *M. alternifolia* leaves had fallen. Extensive medicinal use of TTO did not begin until its antiseptic and disinfectant properties were reported in the 1920s by Penfold and Grant. It has been claimed that TTO was used by Australian munitions factories during World War II. Also during the war, maintaining production of TTO was considered so vital that bush cutters of *M. alternifolia* were exempt from national service.

Good quality, locally grown and manufactured TTO products are easily available in South Africa.

Until the beginning of the 1960s, when Peña successfully treated trichomonal vaginitis and other vaginal infections with TTO, the oil was not mentioned further in the scientific literature. After this, TTO use remained uncommon until a natural product renaissance occurred in the early 1980s. A study in 1990 examining the effect of a 5% TTO product versus 5% benzoylperoxide for the treatment of acne revealed that TTO and benzoylperoxide were equally effective in reducing acne lesions, although TTO use resulted in fewer side-effects. Since then, a wide variety of TTO products have been formulated, and further studies on the effects of TTO against a broad range of micro-organisms and superficial clinical conditions have been conducted. One such study has demonstrated that hand washes containing 5% TTO are more effective at removing contaminating bacteria from hands than regular non medicated soap.

Despite the popularity of TTO and TTO products, only very few studies of the appropriateness and *in vitro* efficacy of commercial TTO formulations that claim to have antiseptic activity have been undertaken.

In two of these studies, the release of terpinen-4-ol from several different topical formulations was found to depend on both the formulation of the preparation and the concentration of TTO. This is particularly important since terpinen-4-ol has been claimed to be one of the main components responsible for the antimicrobial activity of TTO. Other natural products that have shown antimicrobial activity, such as propolis, have been tested for synergism with topical antimicrobials or compared to standard treatments with good outcomes.

When antiseptic TTO products are formulated, the activity of the preparations should be attributed to the active ingredient, namely, the TTO. Having a product with optimal TTO solubility in the base and optimal delivery of TTO to the affected skin area in appropriate concentrations must be considered paramount for marketing a successful antiseptic TTO preparation. The potential exists for poorly formulated products, where the antiseptic activity of TTO has been supplemented by the presence of preservatives such as parabens, or co-solvents such as alcohols that have antimicrobial activity themselves.

This study provided a quantitative evaluation of the antimicrobial activity of a range of commercially available antiseptic TTO products. Values obtained for the non formulated TTO, which was used in all assays and served as a positive control, corresponded well to literature values for all tested microorganisms. However, any discussion of the relative activity of each of the products must be considered in terms of the method used to assess activity because the method undoubtedly influences the results obtained.

Results indicated that the commercially available antiseptic TTO products showed antimicrobial activity that was equivalent to, or greater than the non-formulated TTO control. This suggests that the TTO within these products has retained its antimicrobial activity. Furthermore, the enhanced activity of the products may be attributed to other antimicrobial excipients within the products such as preservatives, or to synergistic antimicrobial interactions between the TTO and other product excipients. The observation that the commercially available antiseptic TTO products tested in this study retained adequate antimicrobial activity emphasizes the importance of considering how product bases and excipients may interact with the active compound during formulation to ensure efficacy of the final product. Finally, the current data suggest that these TTO products may also be active in vivo. This can, however, only be determined through further studies and in clinical trials. JIM SA

***Summary of article by Per S. Thomsen et al, 'Survey of the Antimicrobial Activity of Commercially Available Australian Tea Tree (Melaleuca alternifolia) Essential Oil Products In Vitro', published in The Journal of Alternative and Complementary Medicine; September 2011, 17(9) pg 835-841.***

# Women's use of complementary and alternative medicine (CAM) for Fertility Enhancement: A Literature Review

The use of complementary and alternative medicine (CAM) has increased in Western countries, with women identified as the primary users. Women's use of CAM in reproductive health is well documented; however, little is known about the use of CAM to enhance fertility, despite anecdotal evidence that this is a growing trend in reproductive medicine. The objective of this review was to examine the literature on women's use of CAM to enhance fertility, focusing on prevalence, motivations for use, and how information is sourced.

A systematic search of multiple databases was conducted using key words and selection criteria.

A total of eight articles that met the selection criteria, published between 1990 and 2010, were found and included in the review. The articles were analysed under five key themes:

1. User prevalence
2. User profile
3. Motivation for use
4. Expectations and satisfaction
5. Referral and information sources

This review demonstrates important gaps in the evidence regarding women's use of CAM for fertility enhancement. There are no population-based studies with representative samples, no commonly accepted definitions of CAM research, and few studies describing women's motivations for and experiences of using CAM for fertility enhancement. Importantly, little is known about women's sources of information about CAM in this context.

## Background

Complementary and alternative (CAM) includes a broad spectrum of modalities and therapies outside the domain of conventional medicine. There has been a rise in the use of, and expenditure on CAM as a health care option in Western countries over the past 2 decades, although the prevalence of use varies between and within countries and according to the definition of CAM used. CAM use has steadily increased in the United States from 39% in 1990 to 50% in 2007; in Australia from 50% in 1993 to 69% in 2006; and in Germany from 52% in 1970 to 73% in 2002. Out-of-pocket expenses for CAM use in the United States were estimated to be $US27 billion in 2007, with $US12.2 billion spent on visits to CAM practitioners. In Australia, expenditure on CAM in 2005 was $AUD4.13 billion, with $AUD85 million spent on visits to naturopaths and herbalists (excluding the costs of medicines) in 2004.

The situation in South Africa is similar, based on information published on the Health Products Association of SA (HPASA) web-site, www.hpasa.co.za, where preliminary results from a business survey commissioned by the HPA, point to an increase in financial growth for the CAMS industry from R2,3 billion in 2003 to R4 billion in 2007 and to a growth among participating companies of 27% for 2006/2007.

In line with international trends, the Australian literature shows that CAM users are more likely to be women, well educated, employed with higher than average incomes,

and with private health insurance. CAM use by Australian women includes consultations with practitioners (38%) and self-medication with over-the-counter (OTC) CAM supplements (66%) or non-prescription medications (50%). In 2006, 75% of Australian women of reproductive age used some form of CAM, and in line with the international evidence, Australian women use CAM during pregnancy.

In 2006, 1 in 6 Australian women of reproductive age who tried to conceive or had been pregnant, reported infertility. Of these 72% sought medical advice and 50% used assisted reproductive technologies (ART). The increased availability of diagnostic and treatment modalities and trends in women's older age at first birth, suggest that more couples may now be using fertility treatments to achieve parenthood than previously. The increased demand for fertility treatment in Australia is evidenced by both a 54% rise in the number of ART cycles, the growing proportion of births attributed to ART over the past decade, and the escalating number of claims for rebates for these services among women aged 35–44 years. The costs associated with achieving a live birth with ART increase substantially with advancing maternal age; however, the success of ART declines. Despite differences in the funding arrangements for ART, the international evidence is similar to the Australian experience with regard to maternal age and increased prevalence of use. These facts, coupled with the reported negative experiences of ART associated with discontinuation of these regimens, may provide some understanding of women's increasing use of CAM for fertility enhancement.

This evidence points to important gaps in knowledge about women's use of CAM for fertility enhancement. The objective of the current literature review was to identify existing studies in this area and is intended to provide the basis for identifying gaps in the evidence pointing to areas for future research. The social pressures and psychological stress associated with involuntary childlessness that encourages women to "try anything" must also be acknowledged. However, little is known about the use of CAM for fertility enhancement, in particular the prevalence of use, the profile of users and their motivation, expectations and satisfaction, or the information sources consulted. There is also some concern about women's use of CAM by medical specialists because of the limited evidence of the safety and efficacy of many CAM regimens.

## Prevalence of CAM use for fertility enhancement/care

All eight studies reviewed provided details on the prevalence of CAM use for fertility enhancement. The proportion of women or couples using CAM for fertility enhancement varied considerably from 29% to 91%. The most common CAM used in fertility enhancement were herbal medicines, which was reported in all articles, along with acupuncture and nutritional advice including the use of supplements. More unusual types interventions reported as CAM were the use of religious interventions and spiritual healing, the wearing of fertility accessories and changes in attire and sexual practices.

## CAM user profile

Users of CAM for fertility enhancement are typically women who are older (median age 35 years - range 26.7 years–40 years), with high educational attainment, working as professionals and earning high incomes. While some studies did not report directly on income, the inclusion of private health insurance status can be seen as a proxy for income, reflecting ability to pay. Additional associations with CAM use for fertility enhancement included the number of years trying to conceive and concurrent or past use of conventional medical technologies. Women who used CAM had been trying to conceive for a longer period of time and were concurrently using or had previously used ART without success.

## Motivations for use

Four studies reported on motivations for using CAM for fertility enhancement and one raised motivations in the discussion. Women who use CAM for fertility enhancement have often been unsuccessful in achieving a pregnancy with ART and have a positive attitude to the benefits of CAM use. It was reported that women used CAM in conjunction with ART to maximize their chances of becoming pregnant, often after unsuccessful use of or dissatisfaction with ART. Other motivations reported included the improved quality of life and better health and wellbeing associated with CAM use; the positive relationship with CAM practitioners; and the supplemental use of CAM with conventional treatments. Previous CAM use was reported as a possible proxy for motivation, and women also reported using CAM to regain control over their bodies.

## Expectations of and satisfaction with CAM use for fertility enhancement

Australian women reported that their decisions to use CAM for fertility enhancement had proved to be empowering and that specific treatments were beneficial in improving their health, ***but it was the relationships with CAM practitioners that were the most satisfying and affirming, especially when compared to the often difficult relationships with conventional medical fertility specialists.*** English study participants were sceptical about the benefit of CAM for fertility enhancement, although most thought it had been helpful psychologically and for relaxation.

## Referral and information source

Study participants reported having discussed the use of CAM with their general practitioners (31%) and/or fertility specialists (26%), with family members (22%), friends (16%), and CAM providers (14%), who were also reported as being influential in the decision to use CAM. The Internet, television (5%) and magazines (6%) were also reported as sources of information.

The literature reviewed is valuable as it indicates that there are similarities between CAM use in the general health literature and its use for fertility enhancement. This is particularly the case with studies reporting on motivations for CAM use and user profiles. However, much more knowledge is needed. Fertility enhancement occurs on a continuum from trying to optimize the conditions to achieve pregnancy to a desperate attempt to achieve and maintain pregnancy when all other options are failing. It is

***"The most common CAM used in fertility enhancement were herbal medicines..."***

this continuum that needs to be more fully understood, and which is likely to provide patterns of CAM use not seen in the general literature.

The diversity of modalities and practices reported in the studies reviewed point to the fact there is no clear or common definition of CAM. This raises the question of what should be included as CAM in reproductive health research to further our knowledge in this area. Should a definition of CAM in reproductive health research be limited to the ingestion of biologic substances or the use of modalities that can potentially harm women or their fetuses and for which a strong evidence base is needed? Accepting a wider definition, which includes all practices and modalities irrespective of potential harm, could serve different research purposes, such as developing an understanding of women's desperation to achieve parenthood or the impact of relaxation, reassurance, and attention on achieving and maintaining a pregnancy.

The field of fertility enhancement with the use of CAM is a rapidly growing one, and this article is an important first step because it highlights the gaps in our knowledge. Understanding the characteristics of users of CAM for fertility enhancement, their motivations, factors impacting on their choices, and the information sources contributing to decision-making is therefore important. There is an urgent need for a research agenda that includes broader sampling, strict definitions of CAM, and greater consistency across studies, in order to rigorously develop knowledge that can inform women, CAM and medical practitioners, and policy decision-makers alike. In the first instance, there is a need for well-designed national population-based studies that can answer the questions that are raised in the literature reviewed in this article. Such studies will make important contributions to the growing body of information about the benefits, harms, and costs of using different CAM interventions for fertility enhancement, as well as the resource implications of this use. JIM SA

***This summary is based on an article by Jo-Anne Rayner, Karen Willis and Rebekah Burgess. The Journal of Alternative and Complementary Medicine. August 2011, 17(8): 685-690***

***Complete referenced article available on request***

# Nutritional supplementation improves symptoms in autism-spectrum disorder: A case study

Autism spectrum disorder presents with impairments in communication and social interaction, repetitive, restrictive patterns of behaviour, and abnormalities in cognitive function, attention, learning and sensory processing. Traditional management is variable and includes applied behaviour analysis, speech and language therapy, social skills training, occupational and physical therapy, and medication. Recent evidence suggests that nutrition and nutritional supplementation may also play an important role in the management of these disorders. In particular vitamin B6, magnesium and dimethylglycine (DMG) have been associated with improved language, better eye contact and decreased behavioural problems in children on the autism spectrum. DMG is an amino acid, closely linked to vitamin B12, that facilitates the conversion of methionine from homocysteine.

Dr Rebecca Xia from the Department of Physical Therapy at Creighton University in Omaha describes a patient in whom nutritional supplementation with dimethylglycine and a combination of high dose vitamin B6 (pyridoxal HCL) and magnesium was associated with significantly improved symptom scores. The patient was a 9-year-old boy with a diagnosis of pervasive developmental disorder – not otherwise specified, whose symptoms included language delay, inability in social interaction, low eye contact and behavioural difficulties. To measure outcomes of treatment, the Autism Treatment Evaluation Checklist (ATEC) was administered by both his grandfather and his grandmother before nutritional supplementation and 5 months after starting supplements. The ATEC rating scale assigns a score in 4 categories, rating Speech/Language Communication, Sociability, Sensory/Cognitive Awareness and Health/Physical/Behaviour, and from that also derives a total score. Both grandparents lived with the boy and his mother and were aware of the interventions. Improvements in score were observed on all subscales of ATEC by both grandparents, with high correlation in scores between the two assessors (correlation coefficient = 0.988). Improvements in total score were 47.6% and 53.1% recorded by the grandfather and grandmother, respectively. In particular an increased ability to communicate with more verbal and eye contact was noted on the ATEC scores and also observed by his mother and at school. Improvements were also noted in his attentiveness, ability to follow directions, calmer behaviour with less tendency to tantrums, falling asleep in the evening and better sleeping at night. He became more flexible with respect to his daily routine and the mother reported a significant improvement in the quality of their lives.

Improvements in behaviour have been retained for almost 2 years since the patient began nutritional supplementation and no adverse effects of supplementation have been observed.

Although these findings may not necessarily be generalisable to other patients, they provide useful data for accumulating evidence to support providing nutritional supplementation to patients with autism spectrum disorder.

***Reference Xia RR. Effectiveness of nutritional supplements for reducing symptoms in autism-spectrum disorder: A case report. J Altern Complement Med 2011; 17(3): 271-274.***

# Celiac Disease: Current Perspectives

## Introduction

Celiac disease is an autoimmune disease, also known by various other names, including celiac sprue, nontropical sprue, gluten intolerance and gluten-sensitive enteropathy. It primarily involves the small bowel, but also manifests with various extraintestinal effects. Patients are intolerant to gluten in wheat and related proteins in barley and rye, and sometimes also to proteins in oats. Because symptoms and immunologic features overlap with those of other digestive disorders, diagnosis may be difficult and management requires lifelong adherence to a diet that excludes these grains.

## Epidemiology

In Western populations, the Middle East and North Africa, the prevalence of celiac disease is estimated at >0.5%. In the United Sates, based on analysis of blood samples, the estimated prevalence in apparently healthy individuals is 1 in 133 and in symptomatic individuals, 1 in 56. However, although 30% to 40% of the population carry the genetic biomarkers for celiac disease, only 2% to 3% develop symptoms and malabsorption. The prevalence is increasing dramatically and the incidence rate is estimated to have doubled over the time period of 1974 to 1989. Other studies suggest that the current prevalence is some 4.5 times that of 50 to 60 years ago.

## Gluten intolerance

In patients who are genetically predisposed to celiac disease, the body produces an inappropriate autoimmune response to gliadin, a storage protein (prolamin) found in wheat. Other prolamins found in barley (hordeins), rye (secalins) and, in a small percentage of people, oats (avanins) may also elicit an antibody response. Because oats are often contaminated with prolamins from wheat or other grains, some suggest that it should, anyway, be excluded from the diet of patients with celiac disease. The T cell-mediated immune response to these proteins produces antigliadin immunoglobulins A (IgA) and G (IgG) direct towards tissue transglutaminase (tTG), an enzyme normally present in the small intestine. The autoantibodies cause atrophy of the duodenal and jejunal mucosa, resulting in leakage of tTG, inflammation of enterocytes and reduction of the mucosal surface available for absorption of nutrients. These pathologies may remain for several years even after removal of gluten from the diet. Associated symptoms include abdominal pain, chronic diarrhoea and malabsorption of nutrients.

Another component that may play a role in the development of celiac disease, especially in older individuals who have previously been able to tolerate gluten, is an abnormally permeable intestinal wall. In this respect, celiac disease may share a common pathology with irritable bowel syndrome (IBS). Indeed, studies suggest that individuals with IBS may be up to four times more likely than controls to develop biopsy-confirmed celiac disease. Conversely, some have speculated that the mucosal inflammation occurring in patients with celiac disease may predispose patients with the disease to IBS.

## Extraintestinal symptoms

In addition to the symptoms related directly to small bowel inflammation, celiac disease and resultant malabsorption syndromes may be associated with significant extraintestinal morbidity. Symptoms include anemia, tooth enamel defects, disorders of the central and peripheral nervous systems, pancreatic disease,

gynaecologic disorders (including infertility), chronic fatigue, short stature in children, joint pain and dermatitis herpetiformis. Celiac disease may also be associated with other autoimmune diseases, such as type 1 diabetes and thyroiditis; intestinal T-cell lymphoma and increased risk of mortality.

Furthermore, adherence to a strict gluten-free diet that excludes whole grain foods containing wheat, barley or rye may pose its own challenges to adequate nutrient intake, as these diets are often deficient in B vitamins, iron and fiber. Gluten-free products may also be higher in calories, fat and carbohydrate and can be expensive.

## Diagnosis

Because symptoms are vague, often atypical and overlap with other gastrointestinal disorders, diagnosis based purely on symptom presentation is difficult. Furthermore, celiac disease is relatively uncommon and most patients presenting with gastrointestinal symptoms will have other causes.

Standard diagnostic tests include detection and quantification of IgA antibodies against tTG enzyme. Detection of IgA antibodies directed against tTG and endomysial have high sensitivity and specificity for diagnosis of celiac disease. IgG screening is not specific for celiac disease, but may be an important alternative to anti-tTG IgA in patients who are IgA deficient. Screening for IgA and IgG antibodies directed against diamidated gliadin peptide (anti-DGP) is a newer accurate test for initial screening. However, because antibodies may occur in people without celiac disease, diagnosis must be confirmed with biopsy of the small intestine.

In genetically predisposed individuals, genotyping may also be useful for diagnosis. Ninety five percent will have the DQ2 or DG8 form of histocompatibility leukocyte antigens (HLAs).

Current recommendations are that a diagnosis of celiac disease requires 4 out of 5 of the following criteria:

1. Presence of typical symptoms
2. Positive serum celiac disease IgA autoantibodies at a high titre
3. A DQ2 or HLA-DQ8 genotype
4. Celiac enteropathy seen on small bowel biopsy
5. Positive response to a gluten-free diet

## Dietary treatment, supplements and emerging therapies

The mainstay of management for patients with celiac disease is a gluten-free diet that needs to be maintained for life. However, despite even strict adherence to such a diet, symptoms may remain in 2% to 5% of patients.

Two thirds of patients with celiac disease and approximately 50% of those on a gluten-free diet will be nutrient deficient and consequently, require dietary supplementation.

Recommended nutrient supplements include vitamin B12 for anemia and neurologic complications, folic acid, iron and vitamin D.

In patients following a gluten-free diet, pancreatic insufficiencies are thought to contribute to persistent diarrhoea, and oral supplementation with pancreatic enzymes has been shown to significantly reduce diarrhoea frequency. Although the evidence for clinical application is still lacking, both lipase (enteric-coated formulations) and amylase have been proposed for use as treatment modalities for celiac disease. Trials are underway to investigate whether supplementation with enzymes to degrade gluten and other prolamins prior to digestion may help to reduce autoantibody production and increase the tolerability to gluten-containing foods in patients with celiac disease.

Probiotics alter the composition of the gut flora and fermentation-derived metabolites and thereby regulate epithelial cell barrier function and modulate the immune response. Some studies suggest that they may help to reduce mucosal damage and markers of inflammation in celiac disease.

One novel treatment approach that has been proposed for investigation is the use of parasitic helminths (e.g. *Trichuris suis* and *Nector americanus*) that have been found to have anti-inflammatory properties after colonising the gut. These organisms may modulate the immune system that is overactive in patients with autoimmune and allergic disorders. A clinical study is underway to investigate disease activity, immunity and gluten sensitivity in patients with celiac disease who have been inoculated with hookworm (*N. americanus*).

## Primary prevention

Previous studies have suggested that earlier introduction of gluten to an infant's diet in genetically predisposed individuals may increase the risk for development of autoimmunity, and studies are ongoing to investigate whether the timing of introduction of gluten-containing foods may affect the probability of developing early-onset celiac disease. Investigators are comparing gluten introduction at age 6-9 months with introduction at 9-12 months of age and a gluten-free diet.

Breast feeding also appears to be important. A longer duration of breast feeding and continuation after the introduction of gluten has been associated with a delay in the onset of the disease, but not with any effect on severity.

## Ongoing research

Other topics of ongoing research include studies to determine the upper tolerable intake of gluten, interventions with which to reverse intestinal permeability and using celiac disease as a model with which to better understand the autoimmune process.

## Conclusions

There is growing awareness of celiac disease, leading to an increase in diagnosis. In this regard, new diagnostic techniques are required to avoid the necessity for invasive biopsy procedures. Additional studies are required to investigate the role of nutrient supplementation and the use of probiotics, prebiotics and their combined use (synbiotics) in the management of symptoms. Furthermore, future research may lead to novel approaches that may reduce the necessity for strict dietary restriction in patients with celiac disease. JIM SA

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# BCIM calls for an international think tank to discuss the way forward for teaching integrative medicine

In March 2012, the first cohort of doctors and nurses trained at the newly established British College of Integrative Medicine (BCIM) will graduate with a diploma in the Study of Integrative Medicine (DipSIM). Britain has not offered post-graduate degree qualifications in integrative medicine (IM) before. The DipSIM is a part-time 2-year course. The college was established to specifically address the need for training and education in IM, which aims to provide low-cost, effective therapeutic and self-help approaches to health.

It is increasingly becoming evident that the conventional drug-based approach to health care is costly and unsustainable both socially and economically. IM integrates approaches to health from allopathic medicine, complimentary, alternative, psychologic, spiritual, environmental, nutritional and self-help sources with the objective to provide healthcare that addresses the 'whole person'. The aim of IM is to help patients to identify and understand the cause and meaning of their own illness, identifying the physical, emotional, spiritual, social and environmental factors that contribute to illness and its treatment, so that they can participate in a self-healing process to achieve the best outcomes from therapeutic interventions. Diagnosis and treatment modalities depend on a multidisciplinary team guided by the patient's own values, needs and choices. They draw from allopathic, functional and environmental medicine and complementary and alternative therapies; psychologic therapy, support groups and spiritual healing; and nutritional therapy, emphasising healthy eating. IM professionals are required to continually learn and update their knowledge, audit outcomes and reflect on experiences with patients, with assistance from ongoing professional supervision. They are encouraged to concentrate not only on nurturing their patients' health and well-being, but to improve their own self-care as well.

Society is expected to benefit from IM in that both communities and business need to be involved in generation of health and wellbeing. Environmental toxicity needs to be identified and eliminated and green policies need to be implemented. The hope is that IM can result in sustainable healthcare and significant cost savings through primary and secondary prevention of illness and, in particular, lifestyle-related illnesses. Already various programs based on healthy eating and exercise have proven to prolong survival in cancer patients and significantly reduce costs associated with care of patients with cardiovascular disease.

However, the benefits of IM are not just based around cost-savings. They should also have a substantial impact on physical and psychological wellbeing for both patients and practitioners.

IM is already well established in America and Australia, and as the international interest grows, so do requirements for consensus among educational leaders on the terms, standards and competencies required for the practice of IM. Consequently, the BCIM is calling for dialogue and the establishment of an international IM body, the "Integrative Medicine International" (IMI) to focus on securing international agreement on professional training and standards. Furthermore, the second DipSIM, which begins in October 2011 has been opened to all medical graduates, including, in addition to doctors and nurses, psychologists, occupational therapists, dentists, pharmacologists, dieticians, and physiotherapists. The integration of IM into so many medical disciplines will pave the way for an innovative multidisciplinary approach to medicine in the future. JIM SA

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# How do you treat stress in your practice? Part 1

Neuro Emotional Technique

Hans Selye, MD, PhD, DSc (1907–1982), one of the first scientists to study stress, defined stress as: "the non-specific response of the body to any demand for change."[1] Dr. Selye found that the same physiologic and behavioral reactions occur, regardless of the cause of the stress—which can be physical, mental/emotional, or chemical in nature. Furthermore, stress can be the result of both real and imagined threats.[2] Regardless of the reality of a threat, the physiologic and behavioral responses are identical. These reactions, which include autonomic, endocrine, and behavioral responses, if prolonged, may prove to be harmful, even deadly.[3]

With these facts in mind, I liken our ability to cope with stress to a cup of water—with the water representing stress (see Figure 1). Everyone's cup is unique, just as is an individual's ability to cope with varying amounts of stress. When one's cup is only half full, one is fairly resilient. But when one's cup is nearing maximum capacity, bodily systems start to break down and illness results. When this occurs, we have two choices: (1) reduce the amount of stress; or (2) get a "bigger cup."

I take a multipronged approach toward treating stress—and, by the way, I treat all my patients for stress. I work with people first to identify the causes of the stress in their lives, whether these causes are physical, mental/emotional, chemical, or other sources. Then we work to either reduce the amount of stress or to lessen its destructive impact, while, at the same time, helping patients become more resilient, giving them a "bigger cup."

However, there is one significant hurdle to overcome when considering stress—many of us do not realize its cause. Phobias are good examples of this: Patients with phobias commonly have no recollection of any events that might have caused their phobias.[4] The same may be said about anxiety or depression. People often do not really know why they are feeling this way. What is worse is that people may think they know what is causing their feelings, but, in actuality are frequently wide of the mark. This may be because a stress reaction can be a nonconscious learned automatic behavior.5 If one does not know its cause, then remedying it is nearly impossible.

One of the techniques I use to treat stress is the Neuro Emotional Technique® (NET), which has been shown to be effective for reducing stress and its sequelae.[4,6–11] The beauty of techniques such as NET, and other similar techniques e.g., PSYCH-K®), is that the cause of the stress can be identified through kinesiology-style manual muscle testing.[12,13] If the stress has mental/emotional roots originating from painful events that occurred earlier in life and are long-forgotten, then, by using muscle testing, these events can be explored and resolved in a safe, therapeutic environment.[14] This is done by recalling the specific event and fully feeling the emotion or emotions associated with the event until resolution is reached. Following a clearing, the urge to perform the automatic behavior is lessened, allowing patients to make better, more-conscious choices. I have

used this approach for many years, and with it, I have seen countless patients gain relief, reclaim control, and return to good health and well-being.


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*—Anne M. Jensen, DC, ICSSD, MSc, D.Phil(Cand)*
*Evidence-Based Health Care Programme*
*Departments of Primary Care and Continuing Professional Development*
*University of Oxford Oxford, United Kingdom*


## Sleep, Exercise, and Diet

Stress cannot always be avoided in modern life. Therefore, it is critical to give the body the ability to mount an effective and efficient defense against stress. The most important defensive prescription that I recommend is sleep, exercise, and eating raw fruits and vegetables.

Sleep allows the organs to regroup and refresh. It provides the body with a period of time when there are few external energy demands and the cells of each organ are able to return to homeostasis, a state at which the physiologic and biochemical reactions of the body are at rest and are not striving to correct imbalances.

Exercise induces several groups of cells to perform a primary purpose for each group—that is, the pumping of blood from the heart to the organs and muscles, the delivery of oxygen along with the transport of waste to the lungs, the movement of air in and out of the lungs, and the contraction and movement of muscle fibers. Exercise helps the body retain memory of what the critical processes are, and, with regular exercise the body will be able to defend itself better against the influences of stress-related hormones and cellular destruction.

Finally, raw fruits and vegetables offer some of the most powerful defenses against stress in the form of vital vitamins, antioxidants, and other nutrients. Raw foods are natural sources of energy and sustenance and can therefore be assimilated better. Better assimilation leads to more-effective utilization for the multitude of biologic events necessary for a successful defense against stress.


*—Ilene S. Ruhoy, MD, PhD*
*Institute for Environmental Medicine*
*Touro University, Henderson, Nevada*
*and Department of Pediatric Neurology*
*Seattle Children's Hospital, Seattle, WA*


## Building Resilience

Our approach to Hans Selye's (MD, PhD, DSc; 1907– 1982) coined term *stress*[1] affirms the multidimensional layers/impact of stress on the human body and psyche. Patients coming to the OSU Center for Integrative Medicine (CIM) present for a variety of reasons, including consultation or treatment utilizing integrative approaches to mental illness, medical conditions, primary care, and proactive strategies for health. Patients may manifest a primary stress disorder somatically, while others may recognize stress as secondary to a medical condition.[2]

Physicians and complementary providers at the CIM are knowledgeable in recognizing primary and concomitant stress disorders, and in determining integrative strategies that address stress, based upon etiology and as part of a comprehensive whole-person treatment plan. Recommendations include: relaxing before sleep; a hot bath with lavender oil or magnesium salts; inhaling the aroma of essential lavender oil[3]; melatonin for inducing sleep onset; and valerian root, lemon balm, and passion flower to improve latency of sleep. Patients under extreme stress are advised to take a supplement with a well-balanced form of vitamin B-complex.[4]

In an attempt to meet patients' need for low-cost, community- based stress reduction, physicians and providers are now able to refer patients to receive a low-dose (a less–time-intensive) adaptation of mindfulness-based stress reduction (MBSR-ld), called Mindfulness in Motion. It was designed for busy working adults, and has been shown to reduce perceived stress significantly ($P = 0.0025$) and increase mindfulness ($P = 0.01$).[5] In beginning to offer group stress reduction, the impact on community health is affirmed. Individual need, provider expertise, and patient preference all factor into recommended interventions for addressing stress and building resilience.


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*—Maryanna D. Klatt, PhD, RYT*
*Laura Kunze, MBA, MAET, ATR-BC*
*Ruslana Kurpita, MD, DABHM*
*The Ohio State University*
*Center for Integrative Medicine*
*Columbus, OH*

## Patient-Centered Perspective

Stress is an inherent component of our collective human experience. It is becoming apparent that we can manage stress effectively, which is of great importance in clinical care.[1,2]

Our initial approach in treating stress is to help the patient understand how stress is translated physiologically in the body. Biofeedback, guided breathing exercises, and meditation are powerful tools for this purpose. Biofeedback gives the patient objective data to compare with his or her subjective state, while abdominal breathing and meditation allow a patient to be present in a state of relaxation.[3,4]

Once a patient understands how stress is affecting the body and is committed to stress management, the next step is to create a care plan to achieve this goal. Gaining mindfulness into individualized stressors and the stress responses provides an opening for insight into how to develop meaningful coping skills.

Furthermore, we often evaluate the need for exercise and fitness, integrative nutrition, and targeted supplementation. Fitness is widely recognized to be effective for its impact on mental health and general well-being.[5] A personalized program increases adherence, and is a necessity. We often refer patients to an exercise physiologist and physical therapist to ensure an individualized focus. Integrative nutrition involves evaluating and addressing systemic inflammation, nutrient absorption, omega-3 fatty-acid imbalance, food sensitivities, and the need for supplementation.

Human beings are incredibly robust. Just as stress is to be expected in life, resilience is equally as inherent. Discovering the power of mindfulness, minimizing our reactions to stress, and evaluating lifestyle are all paramount for how we manage generalized stress in a clinical setting.

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*—Amber Fyfe-Johnson, ND*
*Gary Carlson, MD*
*Henry Emmons, MD*
*Gregory Plotnikoff, MD, MTS, FACP*
*Jeffery Dusek, PhD*
*Integrative Health Research Center*
*Penny George Institute for Health and Healing*
*Abbott Northwestern Hospital*
*Minneapolis, MN*

## Integrative Approach

While I treat musculoskeletal disorders and pain, many of my patients have concurrent emotional stress, and occasionally distress. I use a combination of acupuncture techniques along with two programs within the institution with which I am affiliated—relaxation training and a *t'ai chi chuan* program. I found that the following combination of acupuncture points is most effective for treating stress:

- Auricular Vitality (193.F)
- Auricular External Nose (57.C)
- Auricular Tranquilizer (7.0)
- Auricular *Shen Men* (1.C)
- GV 20
- *Yin Tang*
- Seven Internal Dragons (CV 14, ST 25 B/L, ST 32 B/L, ST 41 B/L).

Our MindBody Program provides patients and staff with mind–body healing strategies and education, encouraging the incorporation of these strategies into patient care, and fosters a caring and healing environment throughout our institution. Some of the techniques used include breathing techniques, meditation, hypnosis, mindfulness, imagery, and healing touch.

Our *t'ai chi chuan* program is conducted by physical therapists who practice and teach *t'ai chi chuan*. The program is unique in being able to accommodate patients with various levels of disability, by adapting the program to individual persons' limitations.

*—Alex Moroz, MD, FACP*
*Integrative Musculoskeletal Program*
*Rusk Institute of Rehabilitation Medicine*
*New York, NY*

## Mind–Body Medicine

Stress is a ubiquitous problem that has a negative impact on both physical and mental health.[1,2] Mind–body medicine is highly effective for reducing stress in a wide variety of patient populations.[3]

Mind–body medicine includes such techniques as relaxation exercises, meditation, breath work, imagery, biofeedback, art, physical movement, autogenics, and self-hypnosis, among others. To help my patients overcome stress, I offer a variety of these techniques, and invite each patient to participate in designing an appropriate individualized treatment program.

My most frequent recommendations for stress reduction are breathing exercises and physical activity. Breathing, which lies at the boundary between the somatic and visceral nervous systems, is the one of the most direct ways to affect various body functions positively. Breathing exercises can be taught easily and effectively during a brief clinic visit. I also recommend physical activity for its ability to mitigate the damaging effects of stress on the body, both mental and physical.

The most important part of helping patients manage their stress is to lead by example. Our own self-care practice lends credibility to the advice we give our patients, improving both adherence and outcomes.[4,5]


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*—Chanel Marie Helgason, MD*
*Department of Psychiatry*
*University of Nebraska, College of Medicine*
*and Synergenius Telepresence*
*Omaha, NE*


## Patient Education and Self-Responsibility

At Integrative Health, the Complementary and Alternative Medicine services at Beebe Medical Center, I consider patient education and self-responsibility essential for managing stress. Consultation sessions and self-help classes are offered to help individuals recognize, assess and manage their stress levels. The relationship between stress and illness is examined and a personalized multifaceted plan is developed.

Evaluation sessions help patients identify key stressors in their lives. Using the GSR2™ [galvanic skin response] biofeedback system, these patients gain an understanding of their stressful thoughts and physiologic reactions. Patients learn to assess their own stress levels using the subjective units of discomfort scale (SUD) from 0 to 10 before and after a session. Patients are encouraged to keep a log and follow a stress-reduction plan to monitor their progress. Then patients are guided to experiment with different kinds of techniques to discover what they enjoy and what is most effective for them.

A variety of stress management techniques are offered to hospital inpatients, outpatients, and staff members. These methods include guided imagery,[1] mindfulness-based stress reduction (MBSR),[2] relaxation techniques,[3] aromatherapy, [4] acupressure,[5] Therapeutic Touch,[6] Reiki,[7] Hawaiian *Laulima*,[8] biofeedback,[9] laughter yoga,[10] *t'ai chi chuan*,[11] *qigong*,[11] herb information,[12] mandala meditation,[13] and sound healing.[14] Sound healing includes audio programs, nature sounds and music, a zither and keyboard for patients to play, hand drumming meditation, and singing bowl meditation. Massage, acupuncture and chiropractic therapies are also available.


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*—Cheyenne Luzader, MS*
*Complementary and Alternative Medicine*
*Beebe Medical Center*
*Lewes, DE*


## Holistic Care for Chronic Psychosocial Stress in Women

I commonly see women (ages 18 to > 70) in the Women's Clinic, where I work, who have significant levels of psychosocial stress. Chronic stress over time may be associated with significant health issues, such as cardiovascular disease, some types of cancer, depression, and anxiety. Therefore, a critical component of the Clinic's holistic health care has been to help patients find effective, feasible methods of dealing with chronic psychosocial stress.

Several methods that I have used over the past decade to reduce the stress of my patients have yielded good results. The first step is to engage in therapeutic listening. I explore with patients their perceived or potential sources of stress, and help these patients to determine what course(s) of action might be most beneficial. Based on this approach, many CAM therapies such as yoga, exercise, journaling, and social support have been identified and used successfully. However, the most consistent strategy that has yielded success is referring patients to the mindfulness-based stress reduction (MSBR) program led by two physicians and a physical therapist at the Clinic site. This program incorporates techniques, such as walking meditation, creating a life map, yoga, and listening to tapes of guided imagery. The response of the many women who have attended this course has been positive, life changing, and they report success in controlling the response to stress in their lives.


*—Melissa H. Frisvold, PhD, CNM, RN*
*Nurse Midwifery Program*
*Undergraduate & Graduate Studies*
*Child & Family Health Co-op Unit*
*School of Nursing, University of Minnesota*
*Minneapolis, MN*


## Breath Psychology

Breath psychology is an ancient applied science, which is most effective for managing stress. The kind of treatment flourishes in economically less-developed countries of the world, in such forms as *pranayama* or *chi-gung*, and remains a foundation for modern public health care in general and psychotherapy in particular.[1]

While the general public may learn readily to breathe properly through regular practice, owing to the typically stressful lifestyles of contemporary society, healthy breathing exercises are best learned in breath workshops run by an experienced breath practitioner. This allows participants to explore positive and negative aspects of arousal and stress; the intimately interrelated nature of breath and stress; how stress is typically associated with shallow or inhibited breathing; the benefits of relaxed diaphragmatic breathing; and the stimulating effects of longer inhalations and relaxing effects of longer exhalations. If further practice is needed, conscious four-stage breathing may be practiced for energy and concentration. Breath control effects can be amplified through imagery, actuality, and spiritual practices.

There are various means of assessing stress and breath patterns in a workshop. A participant may rate perceived stress level on a quantifiable scale and measure inhalations and exhalations by using a watch or following his or her heartbeat. For example, stress is reduced readily by inhaling to the count of three heartbeats and exhaling to the count of six heartbeats.


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*—Stephen David Edwards, PhD, DEd, DTE*
*Psychology Department*
*University of Zululand*
*Umhlanga Rocks, South Africa*


## Homeopathy

The modern-day lifestyle is filled with many stressors, which, over time, can cause disturbances in human mental, emotional, and physical well-being.[1] In fact, stress-related illnesses account for a large number work absences[2] and have been linked to cardiovascular disease, depression, insomnia, and a variety of other illnesses.[3] Individual personality traits (hereditary and childhood environmental factors) influence the response to, and recovery, from stress,[4] and people vary greatly in their presenting symptoms and illnesses.

Homeopathy is a healing modality that aims to treat the individual person who has characteristic presenting symptoms, with the remedy that matches that patient's symptom picture most closely. Each homeopathic remedy has a unique mental/ emotional and physical symptom picture. For instance, *Nux vomica* is well-suited to a patient who has a "type A" personality and typically responds to stress with anger and irritability. *Natrum muriaticum* is good for patients who very often become introverted and depressed in response to stress. *Kalium carbonicum* can help patients who somatize their stress and usually develop peptic ulcer disease. *Ignatia amara* is a remedy for patients who respond to stress by becoming overly emotional, with tearfulness, sobbing, sighing, and rapid alternations of moods being most characteristic. *Gelsemium* and *Argentum nitricum* are remedies indicated for anticipatory anxiety, such as nervousness before an examination.

In complex homeopathic prescribing, the synergistic effect of many homeopathic remedies is obtained by selecting those remedies that address the symptom picture of anxiety and stress broadly. Our aim in practice, therefore, when treating patients homeopathically, is to look at a person's constitution holistically. It is our experience that homeopathic remedies, whether prescribed singularly or in complex combinations, may reestablish homeostasis and prevent the development of pathology. Further clinical research is needed to explore these applications and prove their benefits.


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*—Janice Pellow, MTech (Hom)*
*Radmila Razlog, MTech (Hom)*
*Faculty of Health Science*
*Department of Homeopathy*
*University of Johannesburg*
*Johannesburg, South Africa*


## Naturopathy and Patient-Centered Care

The clinical presentation of stress is common, and one of the first steps is to try to understand the patient and see: (1) how he or she defines "stress" (physical pain, insomnia, fatigue, difficulty with concentrating, etc.); and (2) what the individual attributes the stress to. Then, taking a more detailed history can reveal the patient's determining factors of health and how healthy the patient is (is he or she getting enough sleep, nutritional support, social support, etc.?). I also want to discern whether a patient sees his or her own reactions to circumstances as something that the individual can change. Or does the patient feel helpless (which will add to the stress response)?

Most patients benefit from relaxation techniques,[1] as well as learning how to refocus on doing things to promote health, even if circumstances (such as financial ones) cannot be changed immediately. A chronic stress response will make a patient exhausted, if he or she does not begin to self-nourish and self-nurture. I advise my stressed patients to reduce their caffeine intake gradually, as, typically, they are depending on the stimulation of such beverages as coffee. It takes time to substitute better sources of energy, such as improved nutrition and sleep. In naturopathic medicine, we often work to support the function of organ systems that are engaged (and overworked) in any given condition. When patients are stressed, some adrenal- gland support makes sense, even though it is not the complete solution. Pantothenic acid (vitamin $B_5$) is a cofactor in the production of cathecholamines. Vitamin C is also necessary for the conversion of tyrosine to epinephrine, and there is a crucial role for ascorbic acid in catecholamine and steroidal-hormone synthesis.[1,2]


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*— Fraser Smith, ND*
*National University of Health Sciences*
*Lombard, IL*

## T'ai Chi Chuan

There is no doubt that, by definition, stress is ubiquitous. It has been so since the beginning of time and will continue to be so until the end of time. While some stressors can be life-threatening, most modern stressors are not.

Centuries ago, our ancestors responded to the stress of a violent attack by developing forms of martial arts, such as *t'ai chi chaun*. Today we are more at risk from the distress associated with the lack of physical activity and how we respond to the minor and not-so-minor challenges of life. Yet the ancient practice of *t'ai chi chuan* can still be used to address stress.[1–3] I have been teaching the "*Tai chi* for *Arthritis*" (TCA) form[4–5] promoted by arthritis foundations[6] as an effective intervention for helping individuals deal with both external stressors (such as traffic) and internal stressors (such as the physical or emotional pain from chronic disorders).

The gentle *qigong* movements of the TCA form, combined with a focus on breath, induce the relaxation response in many individuals. For example, in a seated position the *qigong* movements can be used with breath control to minimize the stress response to sitting in stationary traffic ("FIRST place the car in park; the person behind you will honk when it is time to move"); or to taking school examinations. I have taught the ancient art of *t'ai chi chuan* successfully for stress reduction to patients who have survived cancer, those with diabetes or fibromyalgia, elementary through college-age students, and educators at all levels.


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*—Roy W. Geib, PhD*
*Department of Microbiology and Immunology*
*Indiana University School of Medicine–Terre Haute*
*and Center for the Study of Health, Religion, and Spirituality*
*at Indiana State University*
*Terre Haute, IN*


## T'ai Chi Chuan for a Traveling Medical Team

After a 36-hour journey by airplane and bus, a medical mission team I worked with arrived at the Ilula District Hospital in Tanzania. This interdisciplinary team of health care professionals traveled to this hospital in a village in Tanzania because of the passion in our hearts—a passion to help improve the ability of the health care providers in this village to deliver care to the people of Ilula and the surrounding communities.

However, in Tanzania, one does not not start a visit with activities, one begins by building relationships. We first had to renew friendships with our colleagues in Ilula and build relationships with people we had not yet met. Yet, we were tired, jet lagged, stressed, and rattled by the last 10-hour bus ride over narrow mountain roads.

One person in our group recalled that I practice *t'ai chi chuan* at home in Minnesota and asked that I teach some simple movements to our group. Out on the porch of the guesthouse looking over the Tanzanian highlands, we practiced a simple form—the Yang style Eight Movement—by lifting our hands and settling into a *Wu Chi* posture. The tension in our backs, necks and legs gave way to concentration on the movements and graceful completion of each movement. I felt my *qi* gathering and renewing within me. To my surprise, this group of travel-weary medical providers all reported the same feelings. The use of *t'ai chi chuan* for stress reduction while we traveled allowed us to have a successful start to our mission.


*—Kathryn Waud White, DNP, CRNA, RN*
*University of Minnesota School of Nursing*
*Minneapolis, MN*


## Relaxation and Biofeedback Techniques

Patients with psychiatric problems often have their own perceived stress and are much more sensitive to stress than people in the general population. Many forms of mental disorders have their origins in biology.[1] Stress has the potential to trigger underlying biologic changes or vulnerabilities in patients with psychiatric disorders, places these patients at increased risk for stress, and, eventually, may culminate in relapse of mental illness.

In addition, stress can disrupt symptom control in patients with mental disorders indirectly through effects on psychologic functions. However, attempts get over this hurdle and overcome stress actually induces more stress in these patients. Thus, finding good stress-management modalities to suit such patients well, and practicing these techniques on a regular basis is a worthwhile goal.

We applied relaxation and biofeedback techniques for stressed patients with psychiatric problems. Our focus was on modifying breathing rate, relaxing the muscles throughout the body, overcoming negative thinking, and calming disruptive thoughts,[2,3] to reduce stress and anxiety.[4,5]

Biofeedback, a type of mind–body complementary therapy, is based on the theory that mental and emotional factors can affect health. The modalities we applied for biofeedback included monitoring heart rate, respiration rate and depth, heart rate variability (HRV), skin-surface temperature, and electrodermal responses to measure, process, and provide feedback to patients regarding their neuromuscular and autonomic nervous system activity.[2,3]

Biofeedback in our practice is combined with relaxation techniques. The relaxation and biofeedback program includes ten consecutive sessions daily, or at least 3 times per week, depending on the severity of mental and physical conditions. A single session can last ~ 40–50 minutes.

Biofeedback is effective for helping people learn to manage stress or emotional distress.[6] Patients gain the ability to participate in the program, learn certain skills adapted to their particular needs, and benefit from their experiences. Patients also report improvements in outlook, reductions in psychologic distress, and increases in perceived support from mental health professionals. These patients feel at ease and relaxed, which supports the utility

of relaxation and biofeedback techniques for stress patients who have psychiatric disorders.

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*—Mei-Chi Hsu, PhD, RN[1]*
*Chun-Hsien Tu, MD[2]*
*Chiung-Yu Huang, PhD, RN[1]*
*1Department of Nursing, I-Shou University*
*Jiaosu Village, Yanchao District, Kaohsiung City*
*Taiwan, Republic of China*
*2Psychiatry Department, E-Da Hospital*
*Kaohsiung City, Taiwan, Republic of China*

## Acupuncture for PTSD in War Veterans

Incorporating the 5-point auricular protocol used to treat stress, pain, and addiction, the acupuncture interns at the National University of Heath Sciences, in Lombard, Illinois, have been recently treating veterans diagnosed with post-traumatic stress disorder (PTSD). These veterans have served in Vietnam, Korea, and Iraq and are treated in the University's "At Ease" Post Traumatic Stress Disorder Clinic.

Points needled include *Shen Men* (Neurogate); Sympathetic; Kidney; Liver; and Lung, bilaterally, and retained for 20–40 minutes. Patients are treated in private and in group settings once per week. Treatment duration is dependent on multiplicity and severity of symptoms. Of note is the decrease in heightened startle reflex, one of the byproducts of hypervigilence. This appears to reduce the fight-or-flight response normally triggered by stressful situations, whether these situations are real or imagined.

In some instances *qigong* relaxation exercises have been specifically used to treat anxiety, and *t'uina* acupressure has been included to relieve localized pain. In one such case, a veteran with severe shoulder pain and immobility had a significant lessening of pain (which was reduced from 9 to 3, with 10 being the highest number, based on a visual analogue scale) and restored use of his arm.

Veterans with common complaints, such as insomnia, anxiety, depression, fatigue, or drug dependence, have also gained significant relief after several sessions. One example is a Vietnam veteran who, after years attempting sleep in his recliner while surrounded by weapons, was able to return to his bed for a full night's sleep, without dependence on the antianxiety and anti-insomnia medications he had been taking.

Suicide is a major issue for recent veterans, with a *DAV Magazine* article reporting 18 veterans per day taking their own lives.[1] Constructive Living Counseling, an adaptation by David K. Reynolds, PhD, of Japanese behaviorial-based Morita Therapy, is also being incorporated into treatment for patients with PTSD who have serious symptoms of depression. Recently, a request was made by a local veterans facility for the clinic at the University to offer acupuncture therapy in the near future to amputees who experience phantom pain.

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*—Frank Yurasek, PhD, MS, LAc*
*Acupuncture & Oriental Medicine Program*
*National University of Health Sciences*
*200 East Roosevelt Road*
*Lombard, IL*

# Medical decision making in Integrative Medicine: Safety, efficacy and patient preference


Scott Shannon, MD, Andrew Weil, MD, and Bonnie J. Kaplan, PhD

The essence of providing patient care revolves around the process of medical decision making (MDM). For most health care providers, this process flows smoothly from diagnosis to treatment planning. Practitioners typically become aware of this complex process only when questions arise. Occasionally, a health care provider will seek some secondary source of information, a book, a colleague, or a website to reach clarity. Only very occasionally, will the patient come into this inner sanctum of health care practitioners: treatment planning. It is hoped that all will routinely engage the patient in a discussion to arrive at informed consent, so that treatment may begin.

This process of MDM is at the core of what makes up health care. In the last 20 years, evidence-based medicine (EBM) has made huge inroads into medical training in an effort to instill sound reasoning about efficacy and effectiveness in all medical graduates. In this article, the terms *efficacy* (demonstration of benefit under ideal conditions, typically in randomized controlled trials [RCTs]) and *effectiveness* (demonstration of benefit in real-life conditions) are used very carefully, and not interchangeably.

The value of efficacy lies mainly in its ability to indicate potential for effectiveness accurately. Sadly, in the drive to emphasize the importance of delineating clearly sound measures of clinical effectiveness, modern medicine has come to equate RCTs as the final arbitrators of clinical decision making. As discussed below, RCTs are but one tool to sort out these complex questions. In integrative medicine (IM), particularly, with its emphasis on patient variables and practitioner participation, evaluation of efficacy is not sufficient.

For some time, IM has functioned like a stepchild to conventional care in MDM as the research base and number of large RCTs remains imbalanced. Almost all decision

making based on the primacy of large RCTs creates a strong preference for the conventional care options, given the primacy of pharmaceutical funding, which drives the vast majority of large RCTs. In fact, overdependence on RCTs has been fostered by the need for conventional pharmaceuticals to meet Food and Drug Administration (FDA) requirements for marketing. Gradually, the influence of EBM has been misinterpreted to embrace RCTs as the only form of evidence considered to be valid. It is also important to note that some of the assumptions upon which RCTs gained favored status over observational data have now been shown to be without merit.[1]

This article describes the process of MDM from the perspective of IM. First, the article reviews why RCTs are but one approach to sorting out the issue of efficacy and effectiveness.

This article proposes an amended scale of effectiveness that includes alternative criteria. Second, the article examines why treatment benefit is but one of the two crucial questions that we need to ask about every treatment that we consider. Maizes et al.[2] and others in IM have argued that risk issues must be an increasing part of the discussion about treatments plans. This article proposes a scale for risk concerns aimed to create a needed dialectic process to balance every discussion of effectiveness. Finally, the importance of patient variables is discussed in the context of IM.

## Medical History and the Emergence of the Safety–Efficacy Split

The tension between safety and efficacy has historical roots going back thousands of years. Soon after the time of Hippocrates, medical thought progressively split into two generally opposing camps: the rationalists and the empiricists.[3] Rationalists tend to be driven by theory and broad principles. Empiricists tend to be driven by sensory impressions and observed detail.

This dichotomy played out in the American medicine of the early nineteenth century. The rationalist camp was mainly composed of the Solidist tradition that followed the principles of the Scottish doctors William Cullen, FRS, FRSE, FRCPE (1712–1790), and John Brown, DM (1735–1788), as well as the prominent American, Benjamin Rush, MD (1746–1813). The vast majority of American physicians practiced the principles of conventional medical doctrine expounded by these three physicians who used reason and logical analysis based upon emerging principles in mechanics, hydraulics, and chemistry.

The conventional treatments of preference at that time were bloodletting and purging (typically accomplished via the use of calomel, a mercury-containing compound). The basic approach was built on the foundation of fighting disease. The empiricist camp at that time was composed of a mix of herbalists, Eclectics, Thompsonians, and homeopaths, all with a strong preference for safe and gentle approaches that caused less direct morbidity. The most critical philosophical distinction was that practitioners in the empiricist camp applied a philosophy that centered on using the body's own innate powers of healing.

Since that time, American medicine has followed similar divergent lines of philosophy: the allopaths (a name given to MDs by Samuel Hahnemann, MD, that means "against disease") prefer potent, external interventions that fight disease; and the complementary and alternative medicine (CAM) community prefers safe, natural approaches that leverage the body's ability to heal. That dialectic of efficacy versus safety continues to this day. Allopathic, conventional medicine continues to apply a premise of fighting illness without a model of the body's healing power. Safety appears to fall secondary to efficacy in the treatment selection hierarchy for allopathy. As evidence, deaths secondary to correctly prescribed medication reactions now constitute the fifth leading cause of death in the United States, while all iatrogenic deaths amount to 225,000 per year and rank as the third leading cause of death in the United States.4

In contrast, most of IM is built around treatment approaches (mind–body medicine, lifestyle changes, dietary adjustments, etc.) that have minimal risk of harm. The use of herbs and supplements constitutes the most risky area of IM. Since 2008, the federal government has mandated that all supplement manufacturers list toll-free numbers on their product labels and requires these manufactures to relay to the FDA all serious side-effect reports. This new adverse events reporting system (AERS) forms a mirror complement to the mechanism that exists for pharmaceutical medications and uses the same definitions for "serious events." In 2008, only 1013 events were reported for natural products versus more than 500,000 for pharmaceuticals. Eight patient deaths were reported from these unregulated products5 versus more than 100,000 documented in the Starfield report above.

Public concern over this preference for safety has contributed to a growing interest in CAM and IM, as documented by a rapid increase in rates of utilization over the last 20 years.6 CAM and IM tend to prefer natural or lifestyle approaches to treating illness. They recognize a healing power within the body, and this carries with it a high priority on avoiding unneeded risks in the provision of care.

Ultimately, the authors of this article hope to create a starting point for discussion on how the foundation of MDM must reflect the priorities of IM. It is our belief that (1) amended measures of efficacy, (2) a much stronger emphasis on risk concerns, and (3) a considered exploration of specific patient issues will create a more fully elaborated foundation for MDM in IM.

## Rethinking Medical Decision Making

### A Example of How It Could Work

A 50-year-old woman comes to see her primary care provider (PCP) with a chief complaint of fatigue and sleep issues. She has had issues with chronic back pain for years, has gained significant weight, and her marriage of 24 years is struggling. Currently, her 19-year-old son is failing classes at his community college and she suspects marijuana abuse. She ruminates about this and has lost interest in her usual activities. After reviewing her laboratory results (thyroid-stimulating hormone, complete blood count, and comprehensive metabolic panel) her PCP tells her that she thinks that this woman is depressed.

The physician tells her that exercise and weight loss would help her feel better, but the patient responds with rejoinders about her back pain and how it has limited her ability to engage in any vigorous activity. Her PCP then offers

a prescription for a selective serotonin reuptake inhibitor (SSRI) antidepressant, saying that it is well-tolerated with minimal side-effects, and it should help her recover. After learning that it might cause a headache or rarely fatigue, the woman provides her informed consent.

This scenario plays out in very similar ways thousands of times each day in offices all over the United States. The concern here is not with the diagnosis, but rather with the limited treatment plan and lack of real informed consent. This woman has not been apprised of some of the real risks involved with SSRI treatment and has not been informed of alternative treatment options. Never mentioned were the increased risks of gastrointestinal bleeding, sexual side-effects, and suicidal thinking, among other concerns. Also, the physician never mentioned St. John's wort or S-adenosylmethionine (SAMe) as reasonable treatment options with safer side-effect profiles. The article by Linde and Bernier in the Cochrane Review notes that St. John's wort was found to be as effective as conventional antidepressants for treating major depression.* The Agency for Healthcare Research and Quality (AHRQ) in the Department of Health and Human Services sponsored a major meta-analysis on SAMe in the treatment of major depression in 2003.† This review of 47 studies found no differences between SAMe and conventional antidepressants in the treatment of major depression. Both SAMe and St. John's wort share a more favorable side-effect profile than SSRI antidepressants.

Using the concepts presented in this article, the treatment encounter with this middle-age woman would proceed differently. After a discussion of the value of exercise and weight loss, the physician would let this woman know that her choices should include three agents that reach level one in grading of efficacy: St. John's wort; SAMe; and a conventional antidepressant (a number in this class have multiple positive RCTs).

Then the provider would share that St. John's wort has a safety rating of *Excellent Safety* (Level 2) with only minor issues reported: headache; sun-related rash, nausea, and no known fatalities for St. John's wort alone. (However, given the risk of drug–drug interactions resulting from cytochrome p450 effects, the rating would have to be lowered to *Moderate Safety* (Level 3) if the woman is using other medications.) SSRIs could obtain a safety rating of *Unsafe* (Level 5), as there have been multiple reported fatalities with SSRIs alone from serotonin syndrome (10 in 2008 of 98,898 exposures).‡ However, as these issues have only occurred with overdoses, the rating would be more appropriately set at *Poor Safety* (Level 4) given the increased risk of GI bleeding. SAMe would obtain a safety rating of *Moderate Safety* (Level 3) based on its ability to trigger manic cycling.

At this point, the PCP would share these safety ratings with the patient and explore questions or concerns. The patient might have a preference among these three choices and this preference (and belief system) would improve the probability of a positive response to the treatment chosen, thus creating some separation in terms of efficacy from the other treatment choices. This new approach would create a level and accurate playing field that would make true informed consent possible as all efficacious treatments are considered in the light of new safety ratings.

As becomes evident, a revised approach to safety ratings would change the character of our patient interactions, as we are forced to share a much more severe look at safety issues. Clearly, a review of safety ratings that embrace this rather harsh level of scrutiny would steer patients away from some commonly accepted treatments, but, as practitioners we could regain the patient respect that has been lost over the last 20 years as more and more safety violations from previously respected medications arise in the lay press. The public would dearly appreciate this enhanced level of caution on safety issues as well as a broader review of treatment options.

*Ref. 22.

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## Efficacy and Effectiveness

RCTs have dominated decision making about efficacy in health care for almost 50 years. Many researchers have explored the difficulty of subjecting IM treatment approaches to RCTs. There are some characteristics of IM interventions that make RCTs particularly difficult to carry out, and perhaps even less relevant, than for conventional allopathic medicine. As Fønnebø pointed out,[7] the gap between published studies of integrative approaches on the one hand, and the clinical reports by practitioners on the other hand, may partially result from the fact that placebo-controlled RCTs are designed to evaluate pharmaceutical interventions.

Certainly, there is strong evidence that RCTs lack external (or ecologic) validity.[8] This issue has been addressed quite often over the last decade, but nowhere has it been more strongly demonstrated than in the recent STAR*D evaluation that showed that only 22% of the STAR*D participants would have passed screening criteria to be entered into a conventional RCT.

There are other criticisms of RCTs worth noting. For instance, the emphasis on RCTs is based on the premise, now known to be false,1 that all other forms of evidence provide biased information on treatment effects. In addition, RCTs are too expensive, which can result in pressure to bury negative results that will block market approval and decrease corporate income. The high cost of RCTs has resulted in pressure to make them shorter and shorter, so that, currently, physicians are in the untenable position of making treatment recommendations for medication use that may continue for decades on the basis of data derived from 6 weeks of exposure to an agent. In other words, clinicians are making guesses about long-term effectiveness based on efficacy data collected over a period of 6 weeks.

## Alternative Sources of Valid Information

There are reasonable alternatives to the overdependence on the RCT as *the* measure of the potential impact of a treatment. First, recall that history has taught us that fact in science is never determined by a single study, but rather, by the weight of the evidence. It is right that medicine rests upon a foundation that begins with good clinical observations, case reports, and careful interpretations. Replication across scientists, which is the true hallmark

of valid science, establishes whether those clinical observations are important and perhaps generalizable.

For interventional treatments, multiple experimental designs can then be used to test hypotheses of efficacy: case-control studies; within-subject crossover designs; blinded comparisons to other treatments; and (when appropriate) placebo controls. Walach and colleagues have written a critique of the hierarchical approach to medical research (which places RCTs at the top) as it has been applied to CAM interventions.[9] Their alternative to the hierarchical approach, which they refer to as a *circular model*, is consistent with the ideas just presented regarding multiple methodologies with replications resulting in a proper evaluation of the weight of the evidence, especially for complex interventions.

Recently, clinical scientists have been rediscovering a particularly useful set of criteria for defining causality. Sir Austin Bradford-Hill, FRS (1897–1991), was a British statistician and epidemiologist who promoted the use of randomization for clinical trials used to test health care interventions, a position he took prior to World War II.[10] In 1965, Bradford- Hill, in his presidential address to the Section of Occupational Medicine of the Royal Society of Medicine, proposed a set of criteria to be used for drawing conclusions about causality in terms of disease etiology.[11] However, his criteria have also proven valuable for evaluating treatments. As he pointed out, not all criteria are appropriate for all issues being analyzed, but he listed nine in total from which appropriate ones should be selected for any given situation:

(1) *Strength* - referring to the robustness of the association between the causative agent and the outcome

(2) *Consistency* - meaning being able to obtain similar results across different research sites and methodologies (i.e., replication)

(3) *Specificity* - by which Bradford-Hill meant one disease having one specific outcome, which may not be relevant to complex disorders (e.g., psychiatric problems)

(4) *Temporality* - referring to the commonsense notion that the cause always precedes the outcome

(5) *Biologic gradient* - which is best described as a dose– response curve: increased treatment would presumably result in a proportionate increase in the effect (again, not relevant in all disorders)

(6) *Plausibility* - referring to whether the results are biologically sound

(7) *Coherence* - which refers to the agreement of a study's findings with what is already known (hence, not relevant in situations of truly novel interventions)

(8) *Experiment* - the situation in which randomly introducing the causative agent results in the outcome

(9) *Analogy* - which is the idea that a similar cause results in a similar outcome.

It is particularly interesting to note that the Bradford-Hill criteria, specified by the individual who influenced the methodology we now accept for RCTs massively, lists *experiment* with randomization methods as only one of nine criteria for establishing causality.

## Unique Features of IM Research

In addition to issues such as ecologic validity (mentioned above), there are several other methodological issues that clearly distinguish IM research from the environment of classic pharmaceutical RCTs. Two of these relate to patient variables (discussed further below). For instance, the healing relationship of a doctor and patient is generally excluded or "controlled for" in conventional RCTs, whereas some researchers would argue that unconditional positive regard forms the underpinnings of the healing relationship between two people.[12]

The enhanced focus on the healing relationship is thus another factor delineating IM from conventional health care models. A second example is the concept of individualized care, which is rarely included in RCTs (perhaps the MTA study in childhood ADHD is a notable exception[13]). The notion that each patient is unique and quite different permeates IM.

However, classic RCT research design requires patients to be broken out into groups with a similar diagnosis, which impairs the ability to evaluate an individualized treatment system, such as classical homeopathy, Traditional Chinese Medicine, or Ayurveda. In each of these systems, the patient must be individualized into a quite unique pattern that does not lend itself to a more broad disease generalization such as that found in conventional allopathic medicine. Curiously, the cutting edge of modern medicine anticipates that customized and individualized care looms as a result of advances in single nucleotide polymorphisms (SNPs) and the ability to create a specific genetic fingerprint for each individual.

A third methodological issue that distinguishes IM from the environment of pharmaceutical RCTs involves systems thinking. With its roots in holistic, natural, and aboriginal medicine, IM has always embraced a more systems-based orientation to patient care than conventional care. It should come as no surprise that a narrow modality for evaluating treatment effectiveness would become increasingly limiting to IM research.

The movement toward increasingly narrow scientific evaluations may create an artificial and arbitrary view of human health, medicine, and treatment effectiveness. Fritjof Capra, PhD, the well-known physicist, indicated that the great surprise of twentieth century science was that complex systems cannot be understood by analysis.[14,15] Ecology and epigenetics are examples of the strong movement toward systems thinking in modern biology.

In spite of these issues, the IM community has acknowledged the importance of RCTs in the EBM pantheon. In 1982, only 11% of the CAM studies published were RCTs. By the 2000s, this number had increased to > 80%.[16] In spite of the rising number of RCTs, many of the studies published in IM struggle with small size and/or poor methodology. This information, added to the weaknesses of efficacy-based RCTs suggests the importance of reevaluating our methods of evaluating research results.

## Commercial Funding and the Distortion of Data

The previous discussion ignores the fact that the dependence on efficacy-based RCTs for MDM rests on the premise that the available database exists without compromise. Sadly, a spate of recent publications have documented that this is not the case. In psychiatry, the recent article by Turner[17] highlights the commercial distortion of the existing evidence. That article documents the massive publication bias found across antidepressant trials (50% of negative studies published versus 91% of positive studies) and the consistently upward "adjustment" of effect size (ranging from 11% to 69%; averaging 33%) by the commercially funded authors.

Psychiatry ranks as the number-one specialty for payments by the pharmaceutical industry to clinical practitioners not engaged in research.[18] Psychiatry also generates a disproportionate amount of pharmaceutical revenues with two of the top four drug categories (antipsychotics, #1 and antidepressants, #4) in total sales. With its more ambiguous diagnostic criteria, psychiatry also stands as a prime target for this commercial distortion of evidence and applied external influence. However, similar data continue to accrue from a variety of different specialties supporting a skeptical view of commercial neutrality in modern pharmaceutical research.[19]

In psychiatry, three massive noncommercially funded studies published in the last 7 years (CATIE, STEP-BD and STAR*D) share a few common traits besides the lack of commercial funding: more naturalistic designs; longer length of study; and a humbling negative reappraisal of the value of psychiatric medications. Their results reinforce the need for more independence in the funding of medical research. In a step toward protecting the sanctity of the body of evidence in medicine, perhaps all financial support should be routed through an independent funding body that will assign payments based on value to the field. Such a system would in effect create a third tier of blinding: patient; practitioner; and payment.

## The Issue of Blinding in IM

Bradford-Hill was a strong proponent of the value of blinding in studies of external medical interventions, but many IM treatments (such as acupuncture, manipulation, and Reiki) make it nearly impossible to blind a study, as the person delivering the treatment knows whether it is being done correctly. Interpretation of results in IM settings with the challenge of having a placebo control is another area of concern. Recently, a number of large studies in acupuncture have been published that demonstrate both sham acupuncture and true acupuncture produce significantly better outcomes than conventional care.[20,21] Some scientists interpret these results as a demonstration that acupuncture is no better than the control. Others argue that the results show that all forms of acupuncture (true or sham) appear to be more effective than conventional care. Linde's recent study documents a significant nonspecific effect for sham acupuncture (2010).[22] This controversy highlights the inherent difficulties in IM research design.

## Proposed Scale for Grading Treatment Value in IM

Clearly, all levels of evidence have strengths and weaknesses; no level is without value or completely useful. Our job as clinicians is to sort out the evidence base in MDM, not wait for large RCTs as they typically have limited value for most complex cases. In IM, our job is more complex and heightens the need to be comfortable in this process of sorting evidence. A new scale for grading treatment efficacy and effectiveness might look like this:

- *Level one—Very strong indicators of efficacy:* large RCTs that were not commercially funded; multiple (three or more) commercially funded RCTs without evidence of publication bias or negative studies; the weight of evidence across multiple designs, replicated by multiple sites
- *Level Two—Strong indicators of efficacy:* one or two commercially funded RCTs without any negative studies within treatment class or type; open randomized clinical trials; multiple large observational studies with strong support from the Hill criteria; replication from multiple sites
- *Level Three—Moderate indicators of effectiveness:* multiple RCTs with conflicting RCTs for same treatment type or class; at least one large observational study (cohort study); multiple small studies with strong support from the Hill criteria and replication across sites
- *Level Four—Weak indicators of uncertain value:* poorly designed studies without strong support from the Hill criteria; small observational studies
- *Level Five—Very weak indicators of efficacy or effectiveness:* expert opinion of effectiveness; case series; multiple anecdotal reports.

## Proposed Scale for Grading Treatment Safety in IM

Health care professionals typically agree on the relative ordering of treatments based on the level of evidence when there are no concerns about safety. However, there is less agreement when safety issues are present, which is almost the norm. Following the historical divide, IM typically prefers treatments that have a high level of safety and enhance patient autonomy, while, in conventional allopathic medicine, the relative emphasis is on efficacy. For example, conventional care may prefer a statin medication for preventing heart disease while IM practitioners will prefer diet, exercise, and supplements. IM practitioners will say their treatments are safer, make more sense, and help the patient become healthier. Conventional allopathic practitioners will say their approach is more practical, facilitates compliance, and is more scientific.

Thought leaders in EBM have proposed a few different grids for integrating safety and efficacy information for MDM. These grids (effective, not effective, safe, not safe) form a useful foundation for this process. Other statistical tools such as number needed to harm and number needed to treat also add to this discussion. However, the paradigm of safety does not yet have the clarity and sophistication that can be found in considerations of efficacy. How do we define harm? What does risk mean?

Our position is that, much as EBM has led the way for guiding MDM based on rigorous efficacy evaluations, so must IM establish criteria that lead the way to MDM based on evaluations of effectiveness that address the risks to patient safety more rigorously. IM has already begun

to set the standards for surveillance of the safety issues within health care, and for evaluation of effectiveness that accommodates safety concerns.

As with EBM, the criteria must be rigorous and beyond reproach as we seek to reinstill one of the most time-honored tenets of medicine: *primum non nocere* (first, do no harm). A new safety scale would look like this:

- *Level One—Absolute safety:* no indications of significant risk; no fatalities or severe chronic debility; evidence that treatment supports health; if invasive: multiple noncommercial long-term studies (over 2 years in length) documenting this safety; no risks evident for developing youth and, if suspect, they are ruled out by negative studies; must be in active use as a treatment for > 5 years
- *Level Two—Excellent safety:* minor concerns about safety are present; time-limited issues (e.g., nausea, headaches) may be present; must be in active use for > 5 years
- *Level Three—Moderate Safety:* some concerns noted with severe health risks, but uncommon (under 1/1000); no fatalities noted; must be in active use > 3 years
- *Level Four—Poor safety:* suspected issues with more common (1/1000–1/100) major health risks; one report of suspected fatal outcome
- *Level Five—Unsafe:* tied to multiple fatalities or frequently related to the onset of severe chronic illness (1/100 or more).

## Patient Factors

From the perspective of IM, the belief systems of both patient and practitioner play a central role in all MDM. Jerome D. Frank, MD (1909–2005), the famous psychotherapy researcher and psychiatrist, co-wrote the book *Persuasion and Healing: A Comparative Study of Psychotherapy*,[23] almost 50 years ago, in which he and his coauthor outlined many factors that alter and drive the healing relationship. These considerations of set, setting, meaning, and context can be thought of as the foundation of the psychologic and emotional factors that drive the placebo response. More broadly, it can be seen as an outline of the nonbiologic elements of healing itself.

Weil has argued that many modern medical treatments function as active placebos having both physiologic and psychologic facets,[24] suggesting that practitioners should try to maximize the placebo response as it elicits the healing power of the body without risk. Perhaps the commercialization of MDM is merely a process to engender belief in new commercial products. If antidepressants carry weak inherent biologic effectiveness, the confidence of the prescribing physician may enhance their impact. As many physicians have been quoted as saying: "One should use a new treatment as much as possible while it still has the power to heal." Based on recent data,[25] that window for our current antidepressants may be closing as we are now witnessing a steady decline in the perception of antidepressant potency as more scientific questions arise about their efficacy.

Given the history and philosophical preferences of allopathic medicine, it should come as no surprise that the factors defining the healing response become minimized or ignored in current practice. This failing must be remedied, as these factors account for a huge component of how humans heal and recover. The healing relationship has taken a much larger role in IM as practitioners in nearly all CAM modalities place a much higher emphasis on it. The importance of these issues can be demonstrated most clearly in psychiatry research, where the placebo response plays a huge role accounting for as much as 40%–% 90+ of the total response.[26]

Significant placebo and expectancy responses inhabit other areas of medical practice, such as dealing with pain and even life expectancy in patients with terminal cancer. Clearly, patient factors must compose a significant part of all treatment selection processes. Ideally, every treatment should be matched to the individual's belief system to reach the highest level of response possible.

## An Ecologic Model of Evaluation

A larger, broad framework of patient factors must drive the treatment selection process in health care. Otherwise many relevant concerns drop from view. This is the case currently in much of modern health care. The bio-psycho-social model has potential as a template. Patient-centered care (PCC) approached this issue from another angle. PCC focuses more on the specifics of the doctor–patient relationship, [27] while the bio-psycho-social model uses a broad net for evaluation.[28] However, both are only an approximation of the more-inclusive ecologic model that, by definition, incorporates all elements of the patient's life in consideration. The ecologic model also carries an appreciation of sustainability as a core element for all biologic interventions. Within the ecologic framework, various structures for consideration are feasible. One helpful structure would set up six tiers or niches. These would be environmental, physical, emotional, mental, social, and spiritual.

Using this model, the practitioner assesses the effect of a considered treatment upon each niche. The details of this evaluation are beyond the scope of this article but have been outlined elsewhere.[29] However, the environmental niche deserves emphasis as it has yet to fully enter our consideration. This is a two-way evaluation. First, does a treatment damage or alter the environment for other people? Of what benefit is a helpful treatment for 1 patient if it damages the health of 10 others?

Technically, this aspect is not about a particular practitioner's patient but about the effect of a treatment (and its associated cascade of events) on all other living creatures. However, if this concern about sustainability is ignored, it will ultimately decay the health of every patient. It most likely already has. For example, medicine has recently acknowledged the complexities of indiscriminant antibiotic use in creating resistant strains of bacteria. Second, does the environment alter the patient's health? Increasingly, our failure to protect our environment has translated into widespread health risks. Soon, we will all understand that to protect our health we must protect the environment. Any line separating the two is illusionary. In addition, the overharvesting of wild botanicals threatens species viability and access for other patients in need.

## Patient Preference, Cost, and Access Issues

At times, other issues will drive the MDM process. Most public-sector patients in the United States have no access to the use of evidence-based nutritional supplements, as there is little likelihood of overcoming the FDA hurdle for an indication without commercial funding. Given this reality, it is extremely improbable that any nutritional product will be available for low-income populations who are not able to pay out-of-pocket for a safe, effective treatment that matches their belief systems. Given the current financial stresses and the extreme limitations of our insurance model, these issues are relevant for many middle-class Americans as well. Thus, access and cost constitute a huge issue in MDM.

Also, patients will, at times, make choices that are based more on practicalities than on belief systems. For example, a holistically oriented patient who develops severe back pain in the face of intense life stress may acknowledge all of the needed inner work and lifestyle changes needed to come back to balance and address the pain. That patient may also have some real-life urgencies (job, child care, etc.) that push him or her toward the perceived speed of pain medications and surgery even though that patient has some deep hesitations about that approach.

## Informed Consent

The current model of informed consent must be called into question as we acknowledge the bifurcated nature of modern health care (CAM versus conventional). As an example, conventional practitioners typically do not have familiarity with integrative techniques, given the training system that often artificially divides treatment modalities by issues other than science. Even as far back as the early 1990s, Eisenberg's two large studies,30,31 documented that conventional practitioners and patients practiced a health care version of "don't ask, don't tell" about CAM approaches. The converse situation is quite likely true as well, but has not been documented in the same manner.

## What practitioner can accurately obtain informed consent?

Most practitioners know well and prefer only one side of this philosophical fence. Thus, what patient ever receives a full and balanced overview of all possible treatment choices? IM providers may have to play a role in the recognition and resolution of this deficiency. As one of the few providers in the health care arena educated specifically on both sides of the conventional/CAM dichotomy, the IM community may be the only group able to appreciate the limits of our current system of informed consent. As such, we must begin a dialogue to highlight, address and resolve this rather massive medicolegal shortcoming.

The ideal process in MDM would remodel the process of informed consent. The actively engaged patient would be offered a quick overview of appropriate treatments (both CAM and conventional) with an unbiased reflection of both safety and effectiveness. The patient would then declare a preference for one over the other(s). Once a practitioner ascertains the basic worldview of a patient (natural versus conventional; safety versus effectiveness) many simple elements of MDM would flow quickly in the future.

## Conclusion

Three elements form the irreducible basis for appropriate MDM: safety; efficacy; and patient factors. Practitioners must eliminate the significant, artificial, and philosophically driven divide between CAM and conventional care as reflected in the full appreciation of the safety and effectiveness of possible treatments. Any treatment choice should reflect the needs and desires of the individual patient.

The evidence base in medicine reflects enormous complexity. The search for causality in possible treatments filters many divergent concerns. RCTs represent one of many tools in treatment selection and the ranking of efficacy. Other tools such as the Bradford-Hill criteria can deliver a more balanced consideration of evidence. Commercial bias in funding of research distorts the evidence base needed for MDM and must be acknowledged. Our vigilance for the safety of treatments should be heightened. Rankings of effectiveness for medical treatments form but one corner of the triangle of MDM.

The protection of health forms a crucial foundation for all MDM. Is a treatment valuable if it cures the illness at hand but damages the health of a patient in some other manner? IM can support the creation of a needed dialectic between effectiveness and safety in the examination of any possible treatment. The rankings of safety should be severe and honest, and take a public health orientation that guards the sanctity of each individual's well-being. Risk must be acknowledged in all forms.

Patient belief and other patient-centered factors should drive much more that occurs in MDM. The individual patient forms the apex of the triangle in MDM. Every treatment may have rankings of safety and effectiveness but there is no right or wrong in MDM without considering the specific needs of the individual patient. The individual's belief system will affect the value of a treatment significantly and cannot be ignored. A comprehensive consideration of the patient's ecosystem as it relates to MDM will offer the best filter for treatment selection. Other patient factors such as cost and access may drive MDM. Finally, a deep reevaluation of the informed consent process will bring MDM closer to an ideal that is rarely met today.

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*Scott Shannon, MD, is an assistant clinical professor of psychiatry at the University of Colorado, in Denver, Colorado. Andrew Weil, MD, is the founder and director of the Program in Integrative Medicine, a professor of medicine and public health, and the Jones-Lovell endowed chair in integrative rheumatology at the University of Arizona, in Tucson, Arizona.*

*Bonnie J. Kaplan, PhD, is a professor in the department of paediatrics and community health sciences at the University of Calgary, in Calgary, Alberta, Canada.* 

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# The medicalization of life. Are we first doing harm?

Q: Describe what you mean by the term "medicalization of life."

**Tieraona Low Dog:** Numerous individuals and organizations have attempted to define this term. Medicalization basically refers to when we, as a society, transform behaviors or bodily functions from their natural state into a disease state. For instance, when I was a child, there were "shy" kids. We seldom talk about shy kids anymore—instead they are all labeled as having "social anxiety." All of us will inevitably age. Yet, now, there are antiaging groups, as if we could, or should, somehow stop the process. Aging has always been viewed as a normal life stage. So when I am talking about medicalization, I am really talking about the risk that we face when we turn everyday experiences into diseases.

I would say, in fairness, that I think there is such a thing as constructive medicalization. For instance, a person with epilepsy 100 years ago might have been stigmatized as being "possessed" or "damaged." Today, an individual can understand what causes seizures and receive appropriate treatment, instead of living under the weight of the belief that seizures are caused by some demonic or angelic curse. However, in general, I think there is a grave risk of over-medicalizing, and we are now in an era of excessive treatment and interventions for things that could be viewed more normally as a part of life. I am deeply concerned that the medical communities, conventional and complementary and alternative medicine [CAM], are continuing to narrow the definition of who and what is normal.

Q: Can you give us further specific examples of how our culture has medicalized life?

**TLD:** There are statistics suggesting that between 1 in 5, or 1 in 8, children have a mental health diagnosis. I am sorry, I simply do not believe that 1 in 5, or 1 in 8, children—depending upon whose statistics one considers—has a mental health problem.

We now are diagnosing attention deficit hyperactivity

disorder [ADHD] in more and more people, young and old. We are diagnosing bipolar spectrum in children 5, 6, and 9 years old. Labeling moods and behaviors, and defining more and more narrowly those traits we consider desirable or normal, incurs the risk of giving large numbers of individuals a diagnosis, an ICD-9 [International Classification of Diseases–9] number and, ultimately, a drug.

The rise in psychoactive medication being prescribed to children under the age of 18 is one of the fastest-growing areas in the pharmaceutical industry—a fact that is deeply disturbing to me. I am concerned that the boy who fidgets in fifth grade or the 12-year-old girl who daydreams during class is at risk of being labeled as having ADHD. Or that every teenager who is impulsive or acting out suffers from "disruptive attitude disorder."

Could it be that many of our classrooms are not inspiring places for young minds to learn and develop? Could it be that part of growing up means challenging the status quo and searching for one's own identity? I am not saying that there are not children, or adults, who would benefit from medication, but I do believe we should be much more cautious in prescribing drugs that can have long-term adverse effects on health.

Of course, from an integrative medicine perspective, we could argue the importance of diet and physical activity, discuss the possible need for certain key nutritional supplements, and focus on the impact of differing parenting styles on child development, as well as reducing exposures to environmental toxicants that can wreak havoc with our neurologic health—but I am worried that, even here, we run the risk of "giving the diagnosis" and simply choosing a different, albeit friendlier, route of "treatment."

Depression is another area where I believe we are overmedicalizing people's lives and emotions. There are times when we go through rough patches, we lose jobs, suffer divorce, or feel alone and lost. This is an inevitable part of being human.

If one looks at data published in the *Journal of the American Medical Association [JAMA]* and *The New England Journal of Medicine [NEJM]*, the benefit of antidepressant medications appears to be much less than many clinicians currently believe. People with severe depression experience the greatest benefit from antidepressants, but the benefit appears to be minimal or nonexistent for people with mild-to-moderate depression. Yet, we keep prescribing these drugs to many patients who are not likely to experience any real therapeutic benefit.

I believe that we are overprescribing antidepressants to people who do not need them, and creating an atmosphere in which we are teaching people that they must seek professional treatment if they are sad, stressed, or not sleeping 8 hours per night. I am concerned that we are convincing a generation of people—maybe many generations—that they need medications in order to function. Imagine investing a fraction of the time, money, and energy spent on pharmacologic treatment, to teaching people skills that they can use to weather life's storms with resiliency and strength.

Let's move from mental health to heart health. Clinicians, researchers and the Food and Drug Administration [FDA] have continued to broaden the number of people that should be taking statin medications. The guidelines for what is considered a "healthy cholesterol level" keeps getting lower. And with the JUPITER [Justification for the Use of Statins in Primary Prevention: An Intervention Trial Evaluating Rosuvastatin] trial,1 there is now FDA approval for rosuvastatin to be prescribed for people who have "normal cholesterol but high C-reactive protein." I do not question that inflammation is a critical part of heart disease, or most chronic disease for that matter, but there are many strategies for reducing inflammation that do not involve taking a prescription drug!

The everyday consumer living in the United States is bombarded every day with advertisements for a wide array of pharmaceutical products, including those that lower cholesterol. The advertisements tell consumers that lovastatin reduces the risk of heart attack by 36%. Who wouldn't want to reduce their risk of heart attack by 36%? However, read the fine print. Three percent of subjects in the placebo group had a heart attack compared to 2% of people taking the drug. The absolute risk reduction was 1%. Most people do not really understand statistics, so, while it sounds dramatic when we say "36% risk reduction," an absolute risk reduction of 1% really isn't that exciting clinically speaking.

At what point do we ask "why are we recommending all these medications when studies investigating the Mediterranean diet or physical exercise have shown similar benefit"?

Q: Why do you believe that this trend of viewing natural life or bodily processes as medical problems has occurred? What has contributed to this shift?

**TLD:** I think pharmaceutical companies are primarily driving the trend as well as the fact that the media often perpetuates the message of fear. Part of the problem is that we can now effectively prevent or treat many of the acute diseases that used to take so many lives. Now we are trying to manage chronic disease and, by definition, many of the medications we develop only truly apply to a relatively small number of individuals. A pharmaceutical company needs to have a broad base of customers, so it is to its advantage to convince as many people as possible that they need medication.

The shift toward medicalization is also driven by fear. There is a growing sense that we need to fear things, such as disease or infirmity. The news media cycle is now available 24/7 on television and internet. People are weathering an information storm that leads many to believe something is wrong with them. Headlines tell us that 1 in 3 women will experience an osteoporotic fracture and that a 50-year old woman has a 2.8% risk of death related to hip fracture during her remaining lifetime, equivalent to her risk of death from breast cancer.

It sounds like, once a woman hits 50, her bones will become brittle and break. Yet, the risk that a 50-year-old woman will fracture her hip by the time she is 60 is just 0.4%. The average age of hip fracture in women is roughly 80 years. But consumers are told: "Don't worry," and, on the television set, a beloved actress in a beautiful setting tells them that taking a once-monthly medication reversed her bone loss and might be right for them, too.

While the bisphosphonates have clearly shown benefit

in elder, or high risk patients with documented osteoporosis, there are no clear data that these agents reduce the risk of fracture in patients with osteopenia, even though such agents are routinely prescribed for women in their 50s who have a minor loss in bone density. I believe it is an absolute mistake to allow direct-to-consumer advertising on television for medical products, as these advertisements are often misleading even they are though technically "true."

Q: What is the risk of an increasingly medicalized society?

**TLD:** Overuse of medication is certainly one risk. People will be prescribed medications that may not be medically necessary and that may cause harm. Statins, antidepressants, and bisphosphonates are not benign drugs. The reason they are not available over the counter is because there are risks, as well as benefits. We, as clinicians, must be mindful of this.

Another risk is that people will become obsessed with their health. While I am primarily concerned with the overuse of prescription medications, I am not uncritical about the overmedicalization that occurs within the field of CAM. It seems as though everyone has a food allergy or leaky gut, is environmentally toxic, has adrenal fatigue, is iodine-deficient, or is suffering from "aging."

There is no end to the "problems" that each of us has. Is the human species really this fragile? This is not to say we should not be fighting for a cleaner environment and healthier food or that food allergies and intestinal permeability do not occur. However, the dominant message today is that, when it comes to health, something is wrong with everybody, and it must be fixed with a supplement, special diet, colon cleanse, medication, or surgery. Even if there is nothing wrong with a person, some company or practitioner can offer that consumer something that will make him or her better. Just look at all the multilevel marketing products out there, the wonder fruits and juices that claim to consumers they will "keep you young."

Q: Do you think that women's lives or any other subgroups of the population are particularly at risk for being medicalized by the system?

**TLD:** All people are at risk of being medicalized—women, elders, children, and men—though I believe many aspects of being female have been medicalized for generations. I would say that we have medicalized birth to an extent that it is almost unrecognizable. Fewer and fewer women experience a "natural" birth. There is no question that a rise in early elective inductions has contributed to the 32% cesearean-section rate we now have in the United States. Inducing a woman without a favorable cervix before the forty-first week of pregnancy is generally not a good idea unless the baby is at risk. With induction, the woman will be placed on a fetal monitor, stuck in bed with limited movement, and her labor will be longer and more painful, requiring analgesia—a cascading chain of events that often will result in a cesarean.

Midwife-led care has been shown to have better outcomes in low-risk women than physician-led care. With fewer caesarean sections and less analgesia, women are more likely to breastfeed, have greater satisfaction with the birthing experience, et cetera, et cetera. I am delighted that, with the new health care bill, midwives will now be compensated at the same rate as physicians for vaginal births.

Menopause has also been medicalized to an unimaginable degree. It makes one wonder what in the world women did when they turned 50 a hundred years ago. And don't tell me women didn't live to be 80 years old—they did. If a woman made it past her childhood and childbearing years, she had a strong chance of living into her 80s during the eighteenth and nineteenth centuries.

Q: What can clinicians and consumers do to break away from the trend that there is a pill for every problem?

**TLD:** Clinicians need to listen generously so that they can really hear what is going on with their patients and mindfully assess each patient's situation. We need to reassure patients and physicians that not every sniffle or ache suggests a serious disease. A fear-based approach to medicine causes physicians to order many unnecessary tests and it often leads to overprescribing medications.

A 2-year-old child with a 101ºF fever, who is running around and playing, probably does not need a trip to the doctor (or NP or PA) but many such children end up there, and, more often than not, the child is given an antibiotic to alleviate the parent's anxiety. It would be so much better if the clinician could take a few minutes to sit and reassure the mother or father by saying: "Your baby is strong and healthy and will be able to fight off this viral infection. Now if her fever goes above 103ºF or she stops drinking fluids, then I want you to call me." However, unfortunately, we do what is expedient—we prescribe.

Clinicians need to remind themselves and their patients that the body is designed for self-healing. If given the right food, plenty of physical activity, and a dose of common sense—the body is fairly resilient and able to ward off many acute and chronic illnesses. We have existed on this planet for a very long time, and our bodies have become highly adept at weathering the storms of illness and injuries. Let's rejoice that, at least in the United States, we have good sanitation, antibiotics, emergency rooms, and surgical suites—and let us guard against feeding the frenzy of "unwellness" no matter what our specialty may be.

It is O.K. to have occasional aches and pains and sometimes experience the doldrums. It is O.K.—or at least normal from a medical perspective—for teenagers to act out and for 8-yearolds to fidget. Birth and aging and death are all part of the human experience. Optimal health and well-being does not mean that one will never be hurt or be sick or suffer loss. I would argue that optimal health is having resiliency and strength to ride the ups and downs of life with courage, grace, and a small dose of humor.

*"The miracle is not to fly in the air, or to walk on the water, but to walk on the earth."* —Chinese Proverb

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*Tieraona Low Dog, MD, is the director of the fellowship in integrative medicine at the Arizona Center for Integrative Medicine, University of Arizona Health Sciences Center, in Tucson, and a clinical associate professor in the department of medicine at the Center.* JIM SA

# Oral Consumption of Cranberry Juice Cocktail Inhibits Molecular-Scale Adhesion of Clinical Uropathogenic *Escherichia coli*

ABSTRACT Cranberry juice cocktail (CJC) has been shown to inhibit the formation of biofilm by uropathogenic *Escherichia coli*. In order to investigate whether the anti-adhesive components could reach the urinary tract after oral consumption of CJC, a volunteer was given 16 oz of either water or CJC. Urine samples were collected at 0, 2, 4, 6, and 8 hours after consumption of a single dose. The ability of compounds in the urine to influence bacterial adhesion was tested for six clinical uropathogenic *E. coli* strains, including four P-fimbriated strains (B37, CFT073, BF1023, and J96) and two strains not expressing P-fimbriae but exhibiting mannose-resistant hemagglutination (B73 and B78). A non-fimbriated strain, HB101, was used as a control. Atomic force microscopy (AFM) was used to measure the adhesion force between a silicon nitride probe and bacteria treated with urine samples. Within 2 hours after CJC consumption, bacteria of the clinical strains treated with the corresponding urine sample demonstrated lower adhesion forces than those treated with urine collected before CJC consumption. The adhesion forces continued decreasing with time after CJC consumption over the 8-hour measurement period. The adhesion forces of bacteria after exposure to urine collected following water consumption did not change. HB101 showed low adhesion forces following both water and CJC consumption, and these did not change over time. The AFM adhesion force measurements were consistent with the results of a hemagglutination assay, confirming that oral consumption of CJC could act against adhesion of uropathogenic *E. coli*.

KEY WORDS: anti-adhesion urinary tract infections Vaccinium macrocarpon

## INTRODUCTION

Urinary tract infections (UTIs) are the most common community-required infections affecting the human body,1 with yearly costs estimated to be $1.6 billion in the United States.[1,2] The main UTI pathogen is Escherichia coli, which causes 90% of community-acquired UTIs and 30% of nosocomial UTIs.[3,4] Infections are initiated when pathogenic bacteria attach to uroepithelial cells via the binding of bacterial adhesins to the receptors on the host cell membrane.[5] Typical adhesins of uropathogenic *E. coli* include type 1 fimbriae, P fimbriae, and X adhesins.[5] Type 1 fimbriae-mediated adherence can be blocked by d-mannose, a-methylmannoside, and many other mannose analogs, and therefore this mechanism is termed mannose-sensitive adhesion.[6] The binding of P fimbriae and X adhesins to uroepithelial cells cannot be blocked by mannose or its analogs, and thus this mechanism is termed mannose-resistant adhesion.[7,8]

UTIs are conventionally treated with antibiotics, but there are concerns due to the development of antibiotic resistance and the problem of recurrent UTIs that affect some patients. Therefore, alternative therapies are drawing increasing interest among researchers. The American cranberry (*Vaccinium macrocarpon*) was shown to prevent UTIs in some studies,[9–11] but the underlying mechanisms have not been fully explored. A family of phytochemicals in cranberry, Atype proanthocyanidins (A-PACs), were identified as the anti-adhesive components.[12] The nondialyzable material in cranberries, containing mainly A-PACs and some unidentified molecules, has been used in some studies and had antiadhesive activity.[13] Incubation

of P-fimbriated *E. coli* with 60 µg=mL A-PACs significantly decreased mannoseresistant human red blood cell (HRBC) hemagglutination, and similar effects were observed when A-PAC solution was replaced with urine that was collected from volunteers who drank cranberry juice cocktail (CJC).[14] In our previous study using atomic force microscopy (AFM) to measure adhesion forces between P-fimbriated *E. coli* and a silicon nitride probe, the average adhesion forces decreased after 12 cultures in the presence of light CJC (from 1.60 ± 0.71 nN to 0.56 ± 0.3 nN) or PACs (from 1.60 ± 0.71 nN to 0.42 ± 0.2 nN), and the frequency distribution of adhesion forces shifted to lower values as the concentration of cranberry juice in the culture medium increased.[15,16]

Previous studies have not addressed whether cranberry juice compounds have molecular-scale anti-adhesive activity after passing through the digestive system. Therefore, we investigated CJC's effects on adhesion forces of clinical E.coli strains, including antibiotic-resistant strains that were isolated from patients with cystitis or acute pyelonephritis. Using direct adhesion force measurements with AFM, the effects of cranberry components or metabolites remaining in urine on the adhesion of *E. coli* were investigated. The adhesion forces measured with AFM were correlated to the results of a macroscopic assay, namely, the agglutination of red blood cells (RBCs) exposed to specific *E. coli* agglutinins. To our knowledge, this is the first molecular-scale study to confirm the existence of anti-adhesive molecules in urine after oral consumption of CJC.

## MATERIALS AND METHODS

### Urine samples

Urine samples had been collected for other Institutional Review Board–approved research studies at IRB through Rutgers University, Cook College, New Brunswick, NJ, USA. The samples sent to Worcester Polytechnic Institute (Worcester, MA, USA) were de-identified, and no personal information was provided. A random, crossover design was applied, with a single volunteer. The volunteer was a healthy white male, 42 years old. He drank 16 oz (473mL) of commercial CJC or water. After he consumed the single dose, urine was collected at intervals of 0, 2, 4, 6, and 8 hours. Samples were immediately frozen and shipped to Worcester Polytechnic Institute, where they were stored at -20ºC. Urine samples were later thawed and filtered through polyethersulfone syringe filters with 0.8-µm (Pall Corp., East Hills, NY, USA) and 0.2-µm (VWR International™, West Chester, PA, USA) pores, sequentially.

### Bacterial cultures

Six *E. coli* clinical strains that cause acute pyelonephritis or cystitis were selected, and a laboratory strain with no fimbriae was used as a control. The clinical strains possess various surface properties, adhesin types, and antibiotic sensitivities (Table 1). To study different types of adhesins we chose two strains from each of the most common subgroups: (1) strains that demonstrate mannose-resistant hemagglutination (MRHA) but no P-fimbriae (B73 and B78); (2) strains that express P-fimbriae from class II (B37 and CFT073); and (3) strains that express P-fimbriae from class III (BF1023 and J96).

Bacteria were cultured at 37ºC in colonizing factor antigen medium, composed of 1% (wt/vol) casamino acids (Bacto™, Sparks, MD, USA), 0.078% (wt/vol) yeast extract (Bacto), 0.4m*M* $MgSO_4$ (Sigma-Aldrich, St. Louis, MO, USA), and 0.04m*M* $MnCl_2$ (Sigma-Aldrich) in ultrapure water, and the pH was adjusted to 7.4 using sodium hydroxide (Sigma-Aldrich). For culture plates, 2% agar (Bacto) was added to the medium. Bacteria were grown overnight and harvested at late exponential phase, when the absorbance of the culture was 0.9–1.1 at a wavelength of 600 nm, measured with a spectrophotometer (Thermo Spectronic, Rochester, NY, USA). Bacteria were washed three times with ultrapure water by centrifuging the solution at 2,000 *g* and removing the supernatant.

### AFM adhesion force measurements

Bacteria were attached to glass slides before AFM experiments.[21,22] Glass slides were treated with 3:1 (vol/vol) $HCl/HNO_3$ solution (Fisher Chemical, Fair Lawn, NJ, SA) for 45 minutes and rinsed with ultrapure water. Slides were soaked with 7:3 (vol/vol) $H_2SO_4/H_2O_2$ solution (Fisher Chemical) and rinsed with ultrapure water. The acid cleaned glass slides were stored at 4ºC in ultrapure water until use. Glass slides were functionalized with an amine group to facilitate bacterial attachment. Glass slides were treated with ethanol (Sigma-Aldrich) and methanol (Sigma- Aldrich) and then immersed in a solution of 35% 3-aminopropyltrimethoxysilane (Sigma-Aldrich) in methanol for 15 minutes, followed by rinsing with ultrapure water. A 300-µL solution of 100m*M* 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (Pierce, Rockford, IL, USA) was added to the washed *E. coli* cells and incubated at 37ºC for 10 minutes with rotation at 18 rpm, followed by addition of a 600-µL solution of 40mM N-hydroxysulfosuccinimide (Pierce) solution and incubation at 37ºC for 10 minutes with rotation at 18 rpm. Bacterial solution incubated with 1-ethyl-3-(3- dimethylaminopropyl) carbodiimide and N-hydroxysulfosuccinimide was added to the 3-aminopropyltrimethoxysilane- treated glass slides and agitated at 70 rpm for 4 hours to allow bacteria to bind onto the slides. Viability and morphology of bacteria cells were maintained during the binding process.[21]

AFM adhesion force measurements were performed using a Dimension 3100 instrument with a Nanoscope IIIa controller (Veeco Metrology, Santa Barbara, CA, USA). Silicon nitride cantilevers with spring constants of 0.12 ± 0.02N=m (DNPS, Veeco Metrology) were used to acquire images and force data. Before experiments, the cantilevers were cleaned by immersion in ethanol and exposure to ultraviolet light. All the measurements were done with the slides and cantilevers immersed in the same urine sample with which the slides were treated, in order to mimic the physiological environment. From each slide, five bacteria were probed, and 10 force measurements were made in the center of each bacterium. Force data were exported in ASCII format and analyzed as described previously[23] to acquire adhesion force–separation distance data. During the portion of the force profile where the AFM tip retracts from the bacterial surface, adhesion peaks are often observed. On each retraction curve the peaks represent the moment when the AFM probe pulls off from the cell surface, and the values of the forces at the peaks are defined as adhesion forces between the probe and the cell surface.

### Statistical analysis

SigmaStat® version 2.03 (Systat Software, San Jose, CA, USA) was used to analyze force data. A two-way analysis of variance test was used to compare the two groups that

were treated with urine samples collected after water or CJC consumption. Background (bacteria treated with urine samples that were collected before drinking water or CJC) adhesion forces were also compared with adhesion forces measured for the bacteria treated with urine samples that were collected after consumption of water or CJC.

### HRBC agglutination assay

Whole blood (type O positive) acquired from a volunteer was stored with EDTA at 4ºC. Before the agglutination experiment, the RBCs were separated from whole blood by centrifugation at 200 *g* for 10 minutes, in order to remove the platelets and plasma. The resulting RBCs were suspended in phosphate-buffered saline and washed three times. After each wash the supernatant was removed, and the remaining cells were resuspended in phosphate-buffered saline. The concentration of RBCs in the suspension was measured using a hemacytometer (Hausser Scientific, Horsham, PA, USA). The suspension was diluted with urine to a concentration of $10^7$ RBCs/mL. The urine samples used in the HRBC agglutination assay were those collected at intervals of 0–2 hours or 6–8 hours after water or CJC consumption, as described above.

*E. coli* bacteria harvested at late exponential phase were diluted in urine to $10^9$ cells/mL. RBCs and bacteria were incubated separately in urine at 37ºC for 3 hours. Then, the two were co-incubated for 90 minutes to allow agglutination. The number of bacteria that attached to RBCs was counted under a light microscope (Eclipse E400, Nikon, Tokyo, Japan). For each urine sample, the number of attached *E. coli* bacteria was counted on 20 RBCs.

## RESULTS

### Adhesion force measurements and analysis

When the clinical *E. coli* strains were incubated with the background urine sample (urine collected just before water or CJC consumption), this resulted typically in adhesion forces above 1 nN, which varied somewhat depending on the strain (Table 2). *E. coli* BF1023 had the highest background adhesion force of 1.68 ± 1.01 nN, whereas B73, B37, B78, CFT073, and J96 had background adhesion forces between 1.00 and 1.30 nN. HB101, the laboratory strain that has no fimbriae, showed the lowest background adhesion force of 0.40 ± 0.26 nN.

When cultured with urine samples collected at different time intervals following CJC consumption, all the clinical *E. coli* strains demonstrated decreasing adhesion forces with time after initial CJC consumption (Fig. 1). The adhesion forces of clinical bacteria cultured with urine collected 0–2 hours after drinking CJC decreased to below 1 nN for all the clinical strains. Adhesion forces continued to decrease for 8 hours, becoming as low as 0.20–0.50 nN. The control strain, HB101, did not show significant changes in the adhesion forces during the 8 hours following CJC consumption.

Water consumption did not affect the adhesion forces of the clinical and laboratory strains, with the exception of B37 (Table 2). Following water consumption, B37 showed an adhesion force of 0.84 ± 0.49 nN at 0–2 hours and 0.75 ± 0.40 nN at 2–4 hours, which were significantly different from the background, but those adhesion forces were still higher than adhesion forces measured after CJC consumption at the same time intervals. For B73, B78, CFT073, BF1023, and J96, the adhesion forces stayed above 1 nN or slightly below 1 nN with no significant differences from the background measurement. The adhesion forces of HB101 remained between 0.30 and 0.50 nN with no significant differences from the background.

Analysis of variance tests showed that for all the clinical strains, adhesion forces after CJC consumption were significantly lower than the background adhesion force (Table 2). The adhesion forces measured after CJC consumption also were lower compared with those measured at the same time intervals after water consumption. B37 showed higher adhesion forces with treatment of urine collected after water consumption, but within 4 hours after consumption, the adhesion forces after water consumption were only slightly higher than those after CJC consumption, and the difference between the two was not statistically different. After 4 hours the adhesion forces after water consumption increased and became significantly higher than the CJC group. For the majority of clinical strains, namely, B73, B78, CFT073, BF1023, and J96, the difference of adhesion forces between CJC and water was statistically significant at each time interval, with adhesion forces after water consumption higher than those after CJC consumption.

### HRBC agglutination assay

Coculturing clinical strains with urine samples collected 6–8 hours after CJC consumption resulted in a high degree of retention of bacteria on RBCs (Fig. 2). The mean number of attached E. coli cells per RBC was > 6, with two strains having especially high retention (11.35 bacteria/RBC for CFT073 and 11.85 bacteria/RBC for BF1023). The retention after culturing with CJC collected at 6–8 hours was significantly lower, being typically below 2 bacteria/RBC. The control strain HB101 demonstrated low retention to RBCs after culturing in urine collected 6–8 hours after consumption of either water (0.15 bacteria/RBC) or CJC (0.35 bacteria/RBC), and there was no statistically significant difference between water and CJC.

## DISCUSSION

### Adhesion forces of E. coli

Antibiotic resistance has been a major problem in the treatment of bacterial infections. CJC is a promising preventive therapy for UTIs because it works as an anti-adhesive instead of a bactericide and thus does not induce the development of antibiotic resistance. In this study, three antibiotic-resistant strains isolated from female patients with cystitis were selected to investigate CJC's effects on these bacteria (Table 1). All of the antibiotic-resistant strains showed little change in adhesion forces after water consumption compared with a significant decrease after CJC consumption, indicating that cranberry juice is effective in preventing nonspecific adhesion of these antibiotic-resistant *E. coli* strains.

For many years, it has been recognized that uropathogenic *E. coli* strains typically demonstrate mannose-resistant adhesion in MRHA experiments.[7,8,24] Many phytochemicals in other fruits can inhibit mannose-sensitive adhesion, but cranberry is one of the only fruits found to inhibit mannose-resistant adhesion.[25,26] Therefore, it is important to investigate the adhesive properties of uropathogenic *E. coli* strains that demonstrate MRHA,

especially how oral consumption of cranberry juice affects the adhesion of these strains in a simulated physiological environment (urine collected from a volunteer after CJC consumption). Therefore, strains used in this study are from two MRHA-positive subcategories: B37, CFT073, BF1023, and J96 have P-fimbriae, whereas strains B73 and B78 do not have P-fimbriae but exhibit MRHA.

P-fimbriae are considered the dominant virulence factors in upper UTIs.[27] They were named after the P blood group antigens [a family of oligosaccharides with the Galα(1→4) Galβ moiety] to which they bind. Although Galα(1→4)Galβ containing receptors are not abundant in the membrane of shed human epithelial cells,[28] they are dominant in human renal cell membranes.[29] P-fimbriae adhere to epithelial cells in multiple tissues in upper urinary tract,[30] explaining the high probability of P-fimbriae-mediated upper UTIs, such as acute pyelonephritis. P-fimbriae also adhere to the epithelial and muscular layers of the bladder,[31] indicating their involvement in lower UTIs. In addition, human polymorphonuclear leukocytes in blood only have trace amounts of glycolipids containing Galα(1→4)Galβ,[32,33] rendering a poor binding of human polymorphonuclear leukocytes with pathogenic P-fimbriated bacteria and thus the killing of these bacteria. We showed a significant decrease in adhesion of P-fimbriated strains (B37, CFT073, BF1023, and J96) after incubation with urine samples that were collected after CJC consumption compared with the non-fimbriated strain HB101, which demonstrated low adhesion forces throughout the 8 hours after CJC consumption. These results indicated that the anti-adhesive components or metabolites of CJC remaining in urine have an inhibitive effect on uropathogenic *E. coli* adhesion.

The adhesins of the other two MRHA-positive strains, B73 and B78, have not been clearly identified yet; they may be Dr adhesins, which belong to the X adhesin family. The X adhesin family consists of Dr adhesins, S fimbriae, F1C fimbriae, M adhesins, G fimbriae, and other unidentified X adhesins.[5] The Dr adhesins differ from fimbriae because they are not distinct filaments. They can exist as a fine mesh, a coil-like structure, or a filamentous capsular coating.[34] The receptors for Dr adhesins are the Dr blood group antigens located on the decay-accelerating factor, a group of cell membrane proteins regulating the complement cascade.[35] The binding site of Dr adhesins in the urinary tract include the renal interstitium, Bowman's capsule, tubular basement membrane, ureteral transitional epithelial cells, and exfoliated cells in urine.[35]

B73 and B78 were isolated from cystitis patients, and the Dr adhesin family constitutes 78% of X adhesin strains among isolates from cystitis patients.[34] Therefore, it is likely that B73 and B78 have Dr adhesins. Our results showed that, similar to P-fimbriated strains, B73 and B78 showed decreased adhesion forces after being treated with urine from the volunteer who consumed CJC. Although the molecular binding mechanisms of Dr adhesin and P-fimbriae are different in the urinary tract, CJC can inhibit the adhesion of both, which could be a result of decreased nonspecific adhesion induced by CJC metabolites remaining in urine. Using contact angle measurements, a previous study36 showed that cranberry juice could induce a decrease in nonspecific adhesion between P-fimbriated *E. coli* and uroepithelial cells. Because nonspecific adhesive interactions, including van der Waals forces, electrostatic forces, and hydrophobic interactions, do not involve the specific adhesin–receptor binding, it is likely that CJC metabolites influence the strains without P-fimbriae similar to the way they affect P-fimbriated strains by diminishing nonspecific interactions.[37,38] It is also possible that CJC metabolites can change the amount and conformation of *E. coli* surface macromolecules and thus the adhesion activity.[15,39] We showed previously that cranberry juice reduced the equilibrium length of *E. coli* P-fimbriae from -148 nm to -148 nm,15 suggesting the compressing of surface macromolecules on *E. coli* could be a mechanism of decreased adhesion, which could explain the nonspecific adhesion decrease after CJC consumption in both P-fimbriated and non–P-fimbriated *E. coli* strains.

### RBC agglutination assay

Although the adhesion forces measured with a silicon nitride AFM probe represent the nonspecific adhesion of *E. coli* cell surfaces, including van der Waals forces and electrostatic and hydrophobic interactions, biological interactions also include specific types of adhesion, such as receptor ligand bonds. AFM adhesion force measurements represent nonspecific adhesion between the silicon nitride AFM probe and the bacterial surfaces, whereas the RBC agglutination assay represents overall interaction between bacterial cells and human cells, which contains both nonspecific and specific adhesion.

Compared with the control strain HB101, all the clinical strains demonstrated high retention to RBCs after coculturing with the urine sample collected 6-8 hours after water consumption (Fig. 2), which can be explained by the fact that HB101 does not have any adhesins. When cocultured with the urine sample collected 6–8 hours after CJC consumption, the retention of HB101 did not change compared with urine collected 6–8 hours after water consumption. These results suggest that CJC metabolites remaining in urine can inhibit overall adhesion of uropathogenic *E. coli*.

In conclusion, by incubating uropathogenic *E. coli* with urine collected after water or CJC consumption and measuring the resulting change of adhesion force between *E. coli* cell surface and an AFM probe, we were able to demonstrate that the anti-adhesive components in CJC could reach the urinary tract and that these components were active in preventing nonspecific adhesion. We also confirmed that CJC components remaining in urine played a role in inhibiting specific adhesion of *E. coli* by means of the HRBC agglutination assay. In order to further investigate the effects of CJC for longer periods after consumption and the variance between individuals, we are currently working on a study involving 11 volunteers, and the urine samples will be collected over a 48-hour period after CJC or placebo consumption.

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AUTHOR DISCLOSURE STATEMENT

No competing financial interests exist.

# The Use of Probiotics in Irritable Bowel Syndrome

Penny Locke
Nutraceutical Specialist, sanofi-aventis
BSc Dietetics, Post Grad Dip Dietetics, PDBA

## Irritable Bowel Syndrome

Irritable bowel syndrome (IBS) is a common disorder characterized by abdominal pain and altered bowel habit for at least 3 months. IBS is one of the most common disorders managed by physicians and gastroenterologists[1].

IBS can not be cured but the goal of treatment is to relieve symptoms. The aetiology is poorly understood which makes finding suitable treatment options difficult. The pathophysiology is multifactorial and most hypotheses generally include altered intraluminal milieu, immune activation, enteric neuromuscular dysfunction, and brain-gut axis dysregulation.[2,3]

## Probiotics and IBS: the rationale[2,3]

*Alterations in the intraluminal milieu*

It has been suggested that patients with IBS have altered colonic microflora. An alteration in gut flora may result in an increased production of species that produce more gas and short chain fatty acids and are more fervent in the deconjugation of bile acids. It has also recently been suggested that patients with IBS have altered small intestine microflora - that is they have developed small intestinal bacterial overgrowth (SIBO). This has been associated with abnormalities in small intestine motor function. Probiotics may help restore the balance of the intestinal flora in such conditions.

There is evidence to support post-infectious IBS. Certain probiotics possess antibacterial and antiviral properties; which may help in preventing an incident of IBS that may follow bacterial gastroenteritis.

*Immune activation*

Evidence suggests an association between IBS and immune activation and potential colonic mucosa inflammation. Some research suggests that certain probiotics may posses' anti-inflammatory properties which may help with mucosal inflammation. It has been suggested that specifically the *Bifidobacterium* species may possess immune-modulating activity.

*Enteric neuromuscular dysfunction*

Probiotics may also have a role to play in both dysmotility and visceral hypersensitivity. Some data on post-infectious IBS show probiotics to be effective in preventing and reversing dysmotility. Probiotics may also have an effect on visceral hypersentivity through their anti-inflammatory, barrier enhancing and neuromodulatory actions.

*Brain-gut axis dysregulation*

There is evidence which suggests that pro-inflammatory cytokines may play a role in brain axis dysregulation. Probiotics have been shown to help with inflammatory process far from the bowel - it follows that probiotics with anti-inflammatory action may have a role in brain axis regulation. This is an area that needs to be explored further.

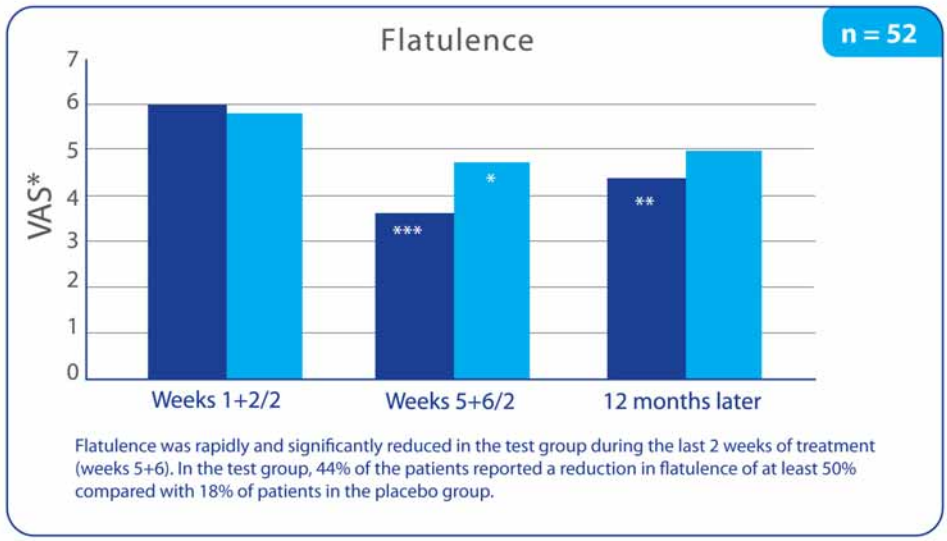
## Probiotics in IBS: The evidence[4]

### Alteration of Intestinal Microflora is Associated with Reduction in Abdominal Bloating and Pain in Patients with IBS.

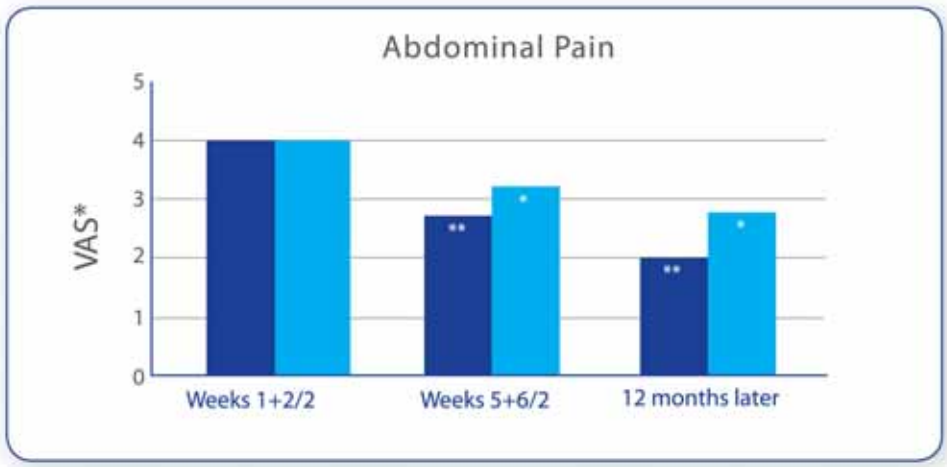
The study comprised of 52 patients with IBS and was performed as a double-blind placebo controlled trial. Patients were randomized into two groups, one receiving 400ml per day of a rose-hip drink containing 5 x $10^7$ CFU*/ml of *Lactobacillus plantarum* and 0.009 g/ml oat flour, and the other group receiving a plain rose-hip drink.

The administration lasted for four weeks. Patients recorded their own Gastrointestinal (GI) function two weeks before the study (weeks 1+2) and throughout the study (weeks 3-6). At a 12 month follow up patients also completed the same questionnaire on GI function as at the start of the study.

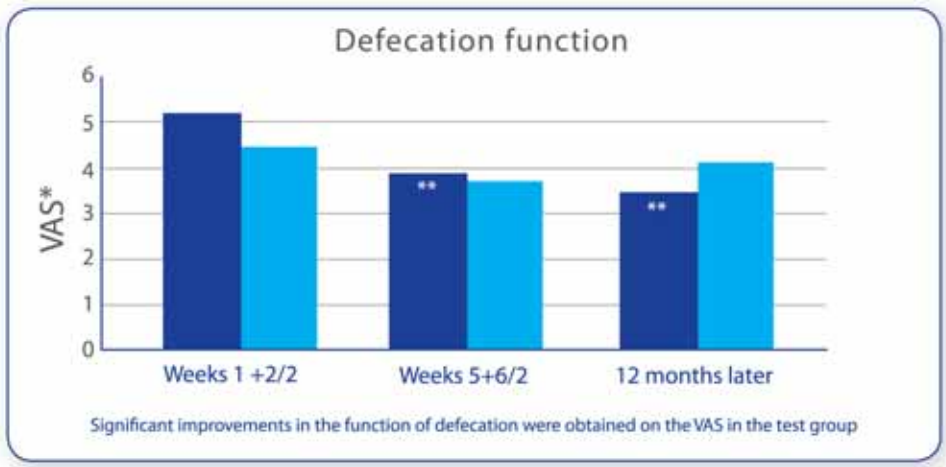
## Results:




Degree of flatulence reported once a week on a VAS (evaluated from 0 to 10 [no flatulence-worst possible flatulence]). The mean degree of symptoms is reported ± SEM. Weeks 1 and 2 precede administration. Statistically significant changes are noted as *p < 0.05, **p < 0.01 and ***p < 0.001. Comparison with weeks 1 and 2; comparison with weeks 1+2/2. No differences were seen between the test group and the placebo group during weeks 1+2/2 using the Mann Whitney U test and Student's t test. ■ = treatment arm (n = 25); ■ = placebo arm (n = 27).




Abdominal pain reported once a week on a VAS (evaluated from 0 to 10 [no pain-worst possible pain]). The mean degree of symptoms is reported ± SEM. Significant changes are noted as *p < 0.05, **p < 0.01, and ***p < 0.001. Comparison with weeks 1+2; comparison with week 1. No differences were seen between the test group and the placebo group during weeks 1+2/2 using the Mann Whitney U test and Student's t test. ■ = treatment arm (n = 25); ■ = placebo arm (n = 27).




Defecation function reported once a week on a VAS (evaluated from 0 to 10 [perfect function-worst possible function]). The mean degree of symptoms is reported ± SEM. Statistically significant changes are noted as *p < 0.05, **p < 0.01, and ***p < 0.001. Comparison with weeks 1 and 2; comparison with weeks 1 + 2/2; comparison with week 1; comparison with week 2. No difference was seen between the test group and the placebo group during weeks 1 + 2/2 using the Mann Whitney U test and Student's t test. ■ = treatment arm (n = 25); ■ = placebo arm (n = 27).

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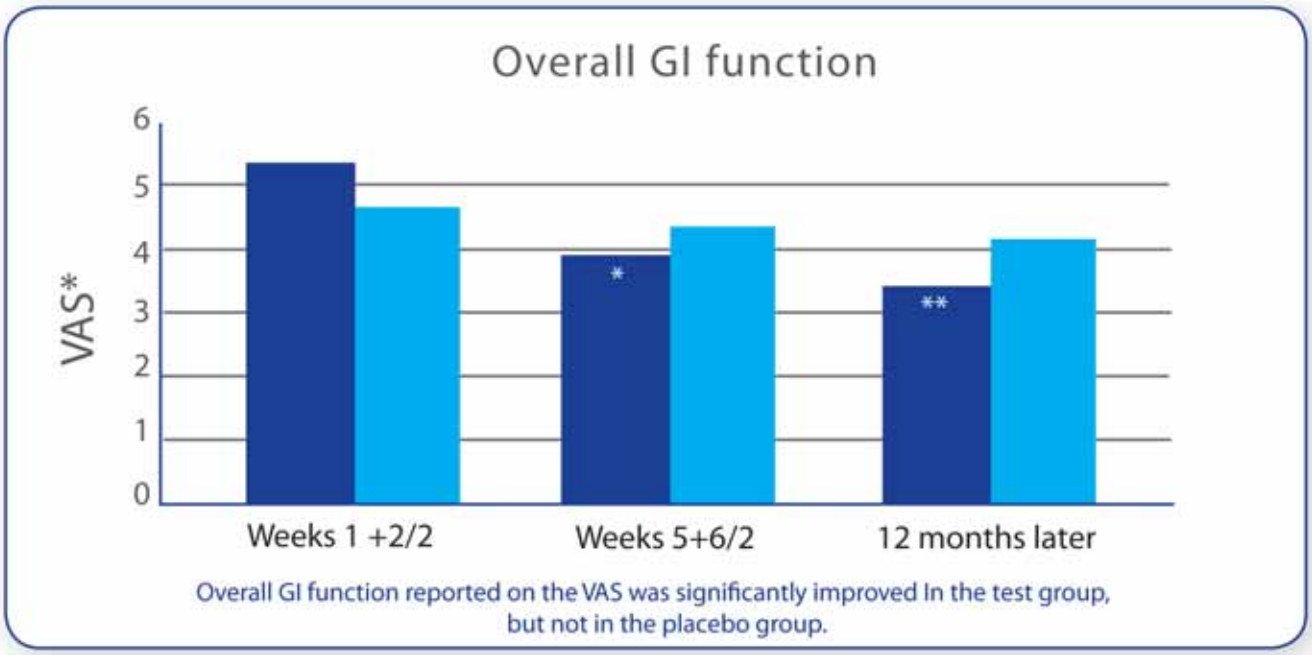


Overall GI function reported once a week on a VAS (evaluated from 0 to 10 [perfect function-worst possible function]). The mean degree of symptoms is reported ± SEM. Significance and comparisons as above. No significant difference was seen between the test group and the placebo group during weeks 1 + 2/2 using the Mann Whitney U test and Student's t test. ■ = treatment arm (n = 25); ■ = placebo arm (n = 27).

***VAS** = Visual Analog Scales

**CONCLUSION:** The results of the study indicate that the administration of *Lactobacillus plantarum* [5 x10$^{7}$ CFU*/ml (400ml) = 20 billion CFU's*/400 ml] with known probiotic properties; decreased pain and flatulence in patients with IBS.

## Supplementation

GastroChoice™ IBS contains a combination of probiotics, prebiotics, digestive enzymes and glutamine to aid in relieving symptoms of abdominal discomfort, pain and intestinal spasms associated with digestive problems[5]

GastroChoice™ IBS contains a high concentration of probiotics - 25.5 billion CFU*/ capsule at the time of manufacture and is available in a convenient once a day dosage. It contains four strains including *Lactobacillus acidophilus*, *Bifidobacterium lactis*, *Lactobacillus plantarum*, *Lactobacillus rhamnosus* to help in alleviating symptoms of IBS.[5]


***CFU** = Colony Forming Units

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# A little something that means the world to the heart

## What can you do – today – to promote heart health?

It's only recently that we have come to understand, the impact of stress on our bodies, or the physical havoc that emotional trauma can wreak. We're still finding out what price we pay – though we know it's a heavy one – for some of our unnatural everyday lifestyle issues like working night shifts, or spending all day doing computer work. There are aspects of our own bodies that we only vaguely understand, and that's part of what makes us so miraculous.

The functioning of the heart is something we're still exploring. On a purely physical level, we understand the mechanism perfectly well. We understand a lot about how lifestyle can impact on the heart. But there is still much we do not understand. It was only in 1978, for instance, that the nutrient and antioxidant Coenzyme Q10 (CoQ10) took its rightful place in our understanding of heart health when Peter Mitchell, a research scientist, was awarded the Nobel Prize for his work on the body's energy pathways and role of CoQ10.[1]

### What is CoQ10?

Coenzymes are nutrients upon which enzymes depend for their function. They are present in certain foods and are sometimes also synthesised in the body. CoQ10, also sometimes referred to as ubiquinone or ubidecarenone, is one of these coenzymes, and is necessary for the work of at least three mitochondrial enzymes which are the source of all the body's energy. Specifically, CoQ10 is necessary to trigger the conversion of glucose into adenosine triphosphate (ATP), upon which all cellular functions depend.[2]

### CoQ10, works in several important ways:

1. Energy booster. When energy production lags, and cells stop functioning optimally, energy-hungry organs like the heart also function sub-optimally. That's why CoQ10 is considered to be a prime cardiotonic, and is highly recommended for people who live busy, demanding lives, or who perform regular high-intensity exercise. CoQ10 also supports post-exercise recovery.[3]

2. Antioxidant. CoQ10 is also a powerful antioxidant [2], protecting cell structures from free radicals, and repairing free radical damage. This is a particular benefit to strenuous exercisers, as free radical activity is sometimes generated by aerobic exercise. It regenerates vitamins C and E when they become inactive due to free radical damage. [4]

3. Cholesterol-fighter. CoQ10 inhibits the oxidation of bad cholesterol – LDL – which is what builds up in artery walls, and creates the problems; and it helps maintains healthy cholesterol levels in people who're not yet experiencing cholesterol imbalances.[5] It is particularly helpful for people on the statin class of anti-cholesterol medications as these block the key enzyme, HMG-CoA reductase which is required for making CoQ10 in your body.[6]

Beyond this, CoQ10 is also helpful as it relieves the muscle pain sometimes caused by statins.[7]

> "The heart has reasons that reason does not understand"
>
> - French theologian Jacques Benigne Bossuel.

### What happens if CoQ10 levels drop?

CoQ10 expert Dr Peter Langsjoen points out that along with the heart; skeletal muscle, the brain, liver and gum tissue are also big energy consumers which "require optimal amounts of CoQ10 for optimal energy production for optimal health."[8] If CoQ10 body levels begin to drop, therefore, so does our general health.

Finally, there is also an apparent connection between CoQ10 and migraine: in some people, it seems to reduce the frequency and duration of migraines.[9]

### Who is at risk?

As we get older, bioproduction of CoQ10 slows, so people who are middle-aged or older should look to supplementation.[10] Also:

- if your diet is lacking in protein, B- or

C-vitamins and magnesium, since these vitamins are necessary for bioproduction of CoQ10;
- if you are on a low-fat diet, since fats need to be present in the digestive tract in order to absorb CoQ10 from foods;
- if you have an increased risk for heart disease or already have cardiovascular disease; or
- if you have a chronic illness, as poor energy production in the cells can be an underlying factor of chronic illness.

Dietary sources include oily fish, organ meats such as liver, whole grains and some seeds and nuts.[11] Supplements should be taken with a meal, preferably accompanying food containing essential fatty acids, such as fish, or along with an omega 3 supplement to enhance absorption.[7]

**Possible sidebar**

## CHOLESTEROL AND CoQ10

High blood cholesterol levels are a big problem for South Africans. Statistics from the Heart and Stroke Foundation SA suggest that 4% of men and 5% of women, aged 30 years and older die because of the impact of high blood cholesterol; and that premature deaths caused by heart and blood vessel diseases (CVD) in people of working age (35-64 years) will increase by 41% between 2000 and 2030.[12]

For some people, unhealthy cholesterol can be resolved through lifestyle adjustments. Others will have to rely on cholesterol drugs, such as the statins, which are highly effective. Yet up to 50% of statin-dependent patients discontinue cholesterol-lowering medication within the first year of their first script.[13]

Statins are known to deplete the body of CoQ10, which is what leads to statin-induced myopathy, a condition in which a person experiences muscle pain.[14] Leading cardiologist Dr Peter Langsjoen describes how statins block cells' ability to make the molecule mevalonate which is the essential precursor to both cholesterol and CoQ10 production.[15]

Supplementing with CoQ10 is therefore highly recommended for people on statins, partly to boost the body's resources of the nutrient, and partly to decrease muscle pain associated with statin treatment. Studies have in fact shown reversal of skeletal muscle pain and weakness by adding supplemental CoQ10 to statin drug therapy.[15]


Source: www.coq10facts.com.au SLIDE 2
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# INTERNATIONAL CONGRESS CALENDAR

**JANUARY 19-22, 2012: 9th ANNUAL NATURAL SUPPLEMENTS:** An Evidence-Based Update @ Hilton San Diego Bayfront in San Diego, California. Renowned faculty will present a concise, clinically relevant overview of the latest information on natural supplements and nutritional medicine with an emphasis on disease states. http://www.scripps.org/conferenceservices; med.edu@scrippshealth.org

**FEBRUARY 24-26, 2012: INSTITUTE FOR FUNCTIONAL MEDICINE** presents THE HORMONE ADVANCED PRACTICE MODULE© in New Orleans, Louisiana. http://functionalmedicine.org/

**MARCH 1-3, 2012: THE ANNIE APPLESEED PROJECT** presents its 5TH EVIDENCE-BASED COMPLEMENTARY/ALTERNATIVE CANCER THERAPY CONFERENCE @ the Embassy Suites in West Palm Beach, Florida. CONTACT: http://www.annieappleseedproject.org/5th/evcocath.html

**MARCH 26-28, 2012: BIT presents its 4TH INTERNATIONAL CONFERENCE OF ANTIBODIES** – Winning the Race for Antibody R & D in Beijing, China. http://www.bitlifesciences.com/ica2012.

**MARCH 28-APRIL 1, 2012: INTERNATIONAL COLLEGE OF INTEGRATIVE MEDICINE CONFERENCE** – "The Gut" in Lexington, Kentucky. Program Chair, John Parks Trowbridge, DO. CONTACT: 866-464-5226; http://www.icimed.com

**APRIL 20-22, 2012: 7TH JOINT AMERICAN HOMEOPATHIC CONFERENCE** – Raising the Bar: The Art & Science of Homeopathic Medicine @ Hyatt Regency Reston in Reston, Virginia (near Washington Dulles Airport). Speakers: Rajan Sankaran, André Saine, Miranda Castro, Amy Rothenberg, Russell Malcolm, Iris Bell, Karen Allen and more. CONTACT: 877-624-0613; http://www.nationalcenterforhomeopathy.org

**APRIL 20-22, 2012: ADVANCES IN CANCER STRATEGIES:** Improving Outcomes and Quality of Life @ Stamford Plaza Hotel and Conference Center in Stamford, Connecticut (near New York City). Focus on cancer treatment, prevention, and cancer aftercare. Keynote speaker: Bernie Siegel, MD. http://www.healthymedicineacademy.com

**MAY 15–18, 2012: International Research Congress: Integrative Medicine & Health**
Location: Portland, Oregon On May 15–18, 2012, the Consortium of Academic Health Centers for Integrative Medicine will host the third International Research Congress on Integrative Medicine and Health at the Portland Marriott Downtown Waterfront. This Congress will showcase original scientific research through eight keynote and plenary sessions, oral and poster presentations, and innovative sessions. Areas of integrative medicine and health research presented and discussed at the Congress will include basic science, clinical trials, lifestyle and prevention, methodology, health services, cost effectiveness, and education. The Consortium is committed to making this meeting an international focal point for this wealth of talent and resources.

**MAY 13-15, 2012: INTERNATIONAL CONFERENCE ON INTEGRATIVE MEDICINE** @ the Jerusalem International Convention Center in Jerusalem, Israel. Held simultaneously in English, French, and German. rlevy@paragon-conventions.com http://www.mediconvention.com/


# Helps prevent eyes from ageing.

**A blurry field of vision develops as one result of ageing, but it is in our power to influence health in old age to the good. AMD is a widespread eye disease and the most frequent cause of blindness.**

## The risk factors of AMD:

**Age**
At 50 the risk of getting AMD is estimated at 2%. It rises to 30% by age 75.

**Heredity**
Those with direct family members diagnosed with AMD are at a greater risk.

**Macular pigment level**
Thinner pigment cannot protect the macula effectively.

**Gender**
Women may be at greater risk of getting AMD than men.

**Smoking**
Smoking increases the risk of getting AMD.

**Nutrition**
Malnutrition weaken the protection against free radicals.

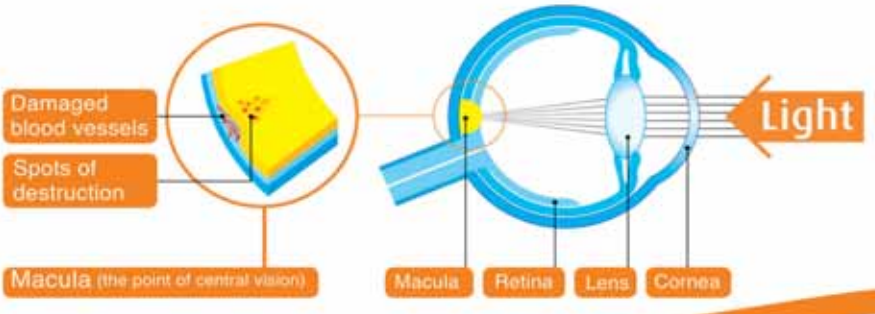
**Sun**
Significant cumulative light exposure increases the risk of getting AMD.

## What is AMD?

### Age-related macular degeneration is a breakdown of the macula. AMD is the leading cause of irreversible vision loss.

In Europe every second person over 65 years of age already has degenerative signs in their eyes!* Every year *new* patients come for treatment. This number is increasing annually as this disease becomes increasingly widespread.

* Euroeye study





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Pharmacist and mother of twins,
Kloof Road Dispensary,
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