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New Frontiers in Medicine:

The body as the shadow of the soul

This article will explore some of the simple but often ignored aspects of healthcare and look at the complementarities of some new directions in healthcare research. Particular areas of interest will include lifestyle, neurosciences, genetics and mindfulness-based therapies.

The best things in healthcare are (nearly) free.

Many of the old foes as far as health is concerned, like the risk of infectious diseases, are far less problematic now than they have been historically. Better sanitation, housing and nutrition have been the major contributors to longer life expectancy. Indeed, lifestyle issues are now becoming the most significant threat to health in the community, but this also means that they offer the greatest potential as therapies.

Modern medicine, on the other hand, makes less of a contribution to overall longevity than is sometimes assumed. Advances in medical technology and science certainly make the front pages of newspapers but, despite the promises, they infrequently make for better and more cost-efficient healthcare. This can be illustrated by recent data on cancer.

So simple, an intervention as moderate and regular physical exercise, has been found to make a major contribution to cancer survival as illustrated by three recent studies. A study of 2987 women with breast cancer followed for up to 18 years found that the risk of death from breast cancer for those who engaged in >9 Metabolic Equivalent Task (MET)-hr/wk (roughly the equivalent of walking 3-5 hr/wk) was halved compared to sedentary women? A 14 year study looking at approximately 3000 men over 65 years old with prostate cancer found that if they exercised regularly they had a third the chance of developing aggressive disease.' A study on 526 patients with stage II and III colorectal cancer followed for over 5 years found that the risk of death was halved.'

If these effects arose from a new cancer drug they would have been hailed as the greatest breakthrough in the history of cancer medicine. Similar potential is found in the role of nutrition. For example, "Women in the highest quartile of plasma total carotenoid concentration (marker of intake of vegetables and fruit) had significantly reduced risk for a new breast cancer event (HR 0.57)." (i.e. a 43% reduction in risk of recurrence). This was controlled for other factors influencing

prognosis.⁴ A randomised controlled trial (RCT) on 2437 women with breast cancer found that a low-fat diet was associated with a 24% reduction in recurrence and 19% improvement in survival after 5 years.'

These figures compare very favourably with the 5-year survival benefit of chemotherapy for the 22 major adult malignancies which is estimated to be around 2%. "As the 5-year relative survival rate for cancer in Australia is now over 60%, it is very clear that cytotoxic chemotherapy only makes a minor contribution to cancer survival. To justify the continued funding and availability of drugs used in cytotoxic chemotherapy, a rigorous evaluation of the cost-effectiveness and impact on quality of life is urgently required."⁶ Most drug research, of course, is more about marketing and profit than it is about science or patient wellbeing. The figures for breast cancer, which is one of the 'success stories' are summarised in the following table.

Effect on 5-year	Node positive	Node negative	survival of chemo-therapy
Women 50-65y	2.1%	3.9%	

Even these figures are probably overestimates of the real survival benefit of chemotherapy when one considers the publication bias inherent in the studies on chemotherapy for breast cancer. A review found that studies with pharmaceutical company funding were far more likely to be positive (84% vs 54%; P=.02), compared to studies performed with independent funding, leading the authors to conclude that: "pharmaceutical involvement in published clinical breast cancer research may affect study design, focus, and results."

Fawzy's study on 68 patients with early stage malignant melanoma divided patients into two groups. One received usual cancer care alone and the other received usual care plus 6 weeks of stress management. Immune function was monitored and it showed that, after being originally comparable, the stress management group had significantly improved by 6 months after the intervention. More interesting was the fact that at 6-year follow-up, there was a halving of recurrence and a much lower death rate among the patients who had received the stress management 6 years before.⁸

The first study to look at a holistic lifestyle program for cancer was performed by Dr Dean Ornish.⁹ He had previously shown that his program, based on yoga principles, was associated with the reversal of heart disease. A more recent study of the program was performed on men with early prostate cancer (biopsy positive and raised 'PSA) who chose not to have treatment, (watch and wait), which is a reasonable option, as many early prostate cancers are slow growing.¹⁰ Of the 80 patients, half were randomised to a lifestyle (experimental) group and the other half continued on their usual lifestyle (control group).

The Ornish lifestyle intervention consisted of a vegan diet (high on fruits, vegetables, whole grains, legumes and soy) and low-fat (10% calories from fat). Their diet was supplemented by soy (tofu), fish oil (3gm daily), vitamin E (400IU daily), selenium (200mcg daily) and vitamin C (2gm daily). They were encouraged to exercise by walking for 30 minutes, 6 times weekly. They also had stress management consisting of gentle yoga, meditation, breathing exercises and PMR (progressive muscle relaxation), and they attended a support group for one hour weekly. They found that the lifestyle group had average reversal of their PSA readings and improvements in other cancer markers and none of the 40 men went on to have aggressive cancer over a one year follow-up. Among the 40 men who stayed on their usual lifestyle, the average PSA had gone up, other cancer markers were far worse and 6 men had gone on to have aggressive cancer over the year and needed aggressive medical and surgical treatment. Again, if this were an expensive technological therapy, a lot of noise would have been made about it.

The importance of stress and mental health

In terms of longevity and wellbeing, one issue is looming as increasingly important. Poor mental health has a number of effects on physical health including:

1. direct physiological effects on the body.
2. as an independent risk factor for a range of illnesses.
3. increasing risk-taking behaviour, violence, suicide and accidents.
4. associations with co-morbidities like substance abuse.
5. increasing the likelihood of poor health behaviours like physical inactivity, smoking and poor diet.

The stress of modern life is increasing at an alarming rate. For example, surveys given to similar populations over a 30 year period indicate that there has been a 45% increase in the amount of daily stress that people report over that time.¹¹

Depression "causes the largest amount of non-fatal burden, accounting for almost 12% of all total years lived with disability worldwide."¹² It is predicted that in Australia mental health issues, particularly depression, will be the single biggest burden of disease within the next 20 years; bigger than cardiovascular disease or cancer.¹³ UK government figures suggest that 7-10% of young people in the UK have anorexia or depression at any one time. In Australia, it is thought that, at any one time, 20% of adolescents have one or more mental health problems and that for 10% it is severe enough to warrant the need for professional help.¹⁴ The higher reporting of mental health problems may be due in part to an increased awareness about mental health, but is also an effect of more stressful and busy lives, the quickening pace of life, greater insecurity in employment and home life and lowering resilience.

Stress has affects on neurotransmitters which regulate mood. The most important

of these is serotonin.¹⁵ Approaches to managing depression include the biomedical approach - if the level of a chemical (serotonin) in the brain is low then that is the cause of depression and the solution is to increase that chemical with a drug. From a philosophical perspective however, Plato might say that what happens in the physical world (e.g. the chemical change in the brain) is not the cause of the problem (depression), it is the effect of what happens in mind. The mind (cause) drives the biology (condition).

*"I wonder that they cannot distinguish the cause from the condition which the many, feeling about in the dark, are always mistaking and misnaming."
Plato: Phaedo*

He would therefore advocate examining and changing thought in order to improve not only the state of our neurotransmitters, but also physical health. The major beneficial change we can bring to our thoughts or cognitions is to raise the level of awareness—attention regulation or mindfulness—and thence by conscious examination to bring some sense of reason and order to our thinking—apply reason in order to dispense with false opinion. As such, Plato may be described as Western civilisation's first and greatest 'cognitive therapist' and the psycho-social and psycho-spiritual approaches to managing depression

would find a great level of sympathy with his views. Indeed, Plato's view would not be inconsistent with current evidence.

Despite the heavy marketing, the pharmacological management of depression is not as effective as it is made out to be. Depending on whether one reviews only published data, or also includes unpublished data, the level of placebo effect of anti-depressants can vary from 60% to 80%. Pharmaceutical companies don't tend to publish data which reflects negatively on their products. That pharmaceutical company research is 20 times less likely to report negative findings than independent research has many implications for research, evidence, ethics, funding, clinical decisions, and medico-legal issues.¹⁶ Furthermore, the evidence suggests there is no sound evidence basis for using antidepressants in children and adolescents. Interestingly, brain scans of people who receive active and placebo antidepressants show that the placebo response is biologically similar to that in people who receive the active drug.¹⁷ Put another way, thought drives chemistry.

Psycho-genetics: is this the next frontier?

Genetics are playing an increasingly influential part in shaping modern thought. Undoubtedly, genetics helps to shape just about everything about us. What has been less known, however, is that our genetics are also significantly impacted upon by psychosocial factors. Genetic expression is affected by psychological state which has implications for development and acceleration of various diseases, including addictive behaviours¹⁸ and depression.¹⁹

Mental state effects genetic function. For example, high stress is associated with increased number of genetic mutations.²⁰ The body compensates by increasing DNA repair capacity, but those who do not cope well with stress have impaired

ability to repair DNA which has implications for carcinogenesis and other illnesses.^{21,22,23} Trauma is a major stressor and stress is a pro-oxidative state. Oxidative states, however they are induced, are associated with higher DNA damage.²⁴

A retrospective case-control clinical study compared DNA repair capacity in 33 women with breast cancer and 47 cancer-free women and found that cancer cases (5.6%) had a 36% reduction in DNA repair capacity compared with the control group (8.7%). Younger breast cancer patients had a more significant reduction in DNA repair capacity.²⁵ Furthermore, in healthy pre-menopausal women, psychological stress (both perception and chronicity) is significantly associated with known determinants of cell death and longevity through higher oxidative stress, lower telomerase activity (responsible for repairing the DNA's telomeres) and shorter telomere length. Women with the highest levels of perceived stress compared with low stress women, have telomeres shorter on average by the equivalent of at least one decade (9-17 years) of additional ageing, which has a number of implications for understanding how stress promotes earlier onset of age-related diseases.²⁶

Genes are not as static as once thought. Although the field is relatively new one, I would have to say that the potential is immense in terms of explaining the cause and progression of illness. The therapeutic potential has not been explored yet but is likely to be equally immense.

"The body is the shadow of the soul." Marsilio Ficino

Like a car and its driver, the mind drives the body. This has been known for a very long time. It also seems that it has been known for a long time that the brain is the organ that translates thought into biological activity. Michelangelo, who was steeped in Platonic thought as a young man, can be seen to have expressed his view on the mind-brain-body connection with his painting, "The Creation of Adam".

In the painting he depicts God—perhaps representing consciousness and intelligence—as being enveloped by the brain. Every significant anatomical feature of the brain is mapped out in this painting.²⁷ It is hard to know exactly what Michelangelo had in mind, but it would not be difficult to surmise that he was suggesting that spirit—consciousness and intelligence—regulates and governs what happens in this physical world of matter.

Michelangelo - The Creation of Adam: The Sistine Chapel ceiling

The effect **of the mind on the body**

Psychological states, and emotion in particular, have a major impact upon what goes on in the body. The 'fight or flight' response has an important part to play in helping us to escape from a threat or rise to a challenge. It can, when it is prolonged or activated inappropriately, have a major negative impact upon health. Major catastrophes like earthquakes, for example, produce a large but short-lived

spike on the incidence of fatal heart attacks on the days immediately following the event in those individuals who are already susceptible to having a heart attack.^{2a29} In fact, it is thought that except for the largest earthquakes as many or more people die from heart attacks than from the direct effects of the earthquake itself. Perhaps not surprisingly, major football matches are a significant risk factor for heart attacks in males. "On days when the local professional football team lost at home, mortality attributable to acute myocardial infarction and stroke increased significantly in men (relative risk 1.28). No increase was observed in women."³⁰ Risk of admission for acute myocardial infarction increased by 25% on 30 June 1998 (the day England lost to Argentina in a penalty shoot-out) and the following two days."³¹

Men and women respond to stress differently. Early stress research was performed on men and not women and so the main paradigm was the activation response of 'fight or flight'. This is predominantly mediated through the sympathetic nervous system. Arousal is accentuated by testosterone. Subsequent research on women has revealed that they experience a different response, now called the 'tend and befriend' response.

In women, 'the fight and flight' response is moderated or down-regulated through the release of various female hormones such as oxytocin. These are also secreted at times of bonding, nurturing, breast feeding and during intimacy. Thus women are more coded for 'nurture' in times of stress, which might go part way to explaining why women are more likely to communicate and share feelings, whereas men are more coded for activation. It might help explain why men are less likely to express feelings and can experience a tendency to 'over-activate' or become aggressive.

Prolonged stress leads to greater physiological 'wear-and-tear' on the body which is called "allostatic load". High allostatic load leads to or is associated with:

- Impaired immunity.
- Accelerated atherosclerosis (hardening of the arteries).
- Metabolic syndrome (hypertension, central obesity, hyperlipidemia and type-2 diabetes).
- Bone demineralization (osteoporosis).

It is also associated with atrophy or loss of nerve cells in the brain, particularly in the hippocampal formation, associated with learning and memory, and the prefrontal cortex, associated with working memory and higher executive functions like reasoning. The amygdale, which mediates the fear response, on the other hand grows with increased allostatic load. It is important to note that high allostatic load is not just seen in stress or anxiety but is also seen in chronic depression.

Chronic allostatic load is also associated with a condition called 'vital exhaustion' which is measured by a person's response to the statement, "At the end of the day I am completely exhausted mentally and physically." If a male agrees with the statement consistently over a long period of time and in the absence of anaemia, thyroid problems or some other physical cause, then they have a significantly higher chance of death from a cardiac event. A study on 3365 males followed for

9.5 years found that the risk of cardiac death was nearly 9 times higher over the next 10 months in men with vital exhaustion, and even 3^{1/2} years

later the risk was still more than three times normal independent of other cardiac risk factors³⁴ Even more important to note is that if a person at risk of heart attack helps themselves to improve their ability to cope with stress, they significantly reduce their risk of having recurrences or dying from heart disease. This is illustrated by a review of 23 studies which found an increased risk of 70% for death and 84% for recurrence for those with heart disease who received no psychosocial treatment.³⁵

The production of inflammatory chemicals, like cytokines, is a part of the stress response. Pro-inflammatory cytokines produced by immune cells in response to danger signals also act on the central nervous system³⁶ Prolonged activation can precipitate the development of depression and trigger the 'sickness response' giving a biological explanation for somatisation—the physical expression of psychological states—and many of the symptoms associated with depression such as: lack of motivation, energy and appetite. This brain cytokine system can become sensitized early in life depending on how we learn to cope with challenges.

Interestingly, romantic love is associated with a range of other changes in neurotransmitter receptor changes, principally high dopamine and low serotonin activity. These changes are almost identical to the changes seen with Obsessive Compulsive Disorder^{37,38} Whether this tells us more about romantic love or OCD is an interesting debate.

Psychoneuroimmunology

Psychoneuroimmunology is the study of how our psychological state influences our immune function. This effect is mediated through the nervous and endocrine systems. The central nervous system is constantly communicating with the immune cells, which are like the guardians of the body. Furthermore, the immune cells 'talk' back to the central nervous system, mainly the limbic system which is the part of the brain which regulates emotion. Our mental and emotional states have a significant impact upon both our body's defences against infection and cancer, and also on the conditions where the immune system is inappropriately 'overactive', sometimes called immune dysregulation, such as in inflammatory and autoimmune conditions and allergies. Hence, mental and emotional states can significantly impact upon a variety of health parameters. For example, stress, depression and/or social isolation can:

- Lower immune markers like white cell counts and levels of immunoglobulins.³⁹
- Increase susceptibility to infections if exposed to viruses.⁴⁰
- Increase severity and progression of infections. For example, people with HIV are 2-3 times as likely to progress to AIDS over 5 years if they have greater life stress and low social support."⁴²
- Increase relapse of chronic and latent infections like shingles, cold sores, or

glandular fever.

- Increase activity of inflammatory illnesses like asthma, dermatitis and rheumatoid arthritis.⁴³
- Increase activity of autoimmune conditions where the body's defences have turned against the body as if it were 'foreign' tissue.⁴⁴ MS patients, for example, are twice as likely to have more frequent and severe relapses if they have higher levels of stress.⁴⁵
- Produce a poor response to immunisation so that they are less effective.
- Increase the activity of allergic conditions.
- Impair immune response to some cancers for which the immune system is an important defence, such as malignant melanoma.

Mindfulness and the brain sciences

Attention regulation—our ability to know where our attention is and to direct it consciously—is a topic worthy of a lot more attention among researchers and clinicians. There are a lot of habits our children are being trained into which may be far from healthy in the long term. For example, children who watch higher levels of television by the age of 3 are significantly more likely to display attention problems (e.g. ADHD) at the age of 7.⁴⁶

How one spends one's leisure activities throughout life has a major effect also on the incidence of dementia. Over a 40 year retrospective study, it was found that a person who has less than average diversity in their leisure activities, spends less time on them and has more passive activities (principally watching TV) is nearly four times as likely to develop dementia.⁴⁷ Other studies have suggested similar findings.⁴⁸

The potential predisposing factors for Alzheimer's Disease are being increasingly explored using brain imaging. There are various modes of brain activity. For example in young adults during tasks associated with paying attention, parts of the brain associated with attention and proprioception are activated. In 'default states' - when the mind is inattentive, idle, recalling the past or daydreaming - there is activation of brain regions which correspond with those regions which show amyloid deposition in Alzheimer's Disease adults. It seems that early stages of Alzheimer's Disease show prominent atrophy and metabolic abnormalities in the parts of the brain associated with default states.⁴⁹ Whether default states cause Alzheimer's Disease is uncertain. Do they place wear and tear on brain through too much default activity? Does inattention become wired into our brain circuitry? Is it the result of repeatedly going over stressful events from the past? The therapeutic potential is the really important thing. To what extent can we prevent or even reverse the early stages of Alzheimer's Disease through attention regulation such as in mindfulness-based therapies?

Meditation

Meditation can mean many different things depending upon which aspect is being emphasised: attention regulation, relaxation, presence, concentration, inner peace, acceptance, spirituality. Arguments about what meditation is and

what it is not sometimes resemble the story of the 'blind men and the elephant'.
"Peace. It does not mean to be in a place where there is no noise, trouble or hard work. It means to be in the midst of those things and still be calm in your heart." Author unknown

"When she (the soul) returns into herself and reflects then she passes into the other world, the world of purity, and eternity and immortality and unchangeableness which are her kindred ... and this state of the soul is called wisdom." Plato

"The quickest way to learn speed-reading is to get an unexpected letter from the taxation office." The Cockle Bur

A lot of modern research attention is now being given to a form of meditation called mindfulness. Derived from it are a number of mindfulness-based therapies such as Mindfulness-Based Stress Reduction, Mindfulness-Based Cognitive Therapy and Acceptance-Commitment Therapy. Research on the efficacy of mindfulness is extending into a range of conditions including the management of stress and anxiety, depression, eating disorders such as bulimia, panic disorder and chronic pain management. It has also been found to be helpful for immune modulation by reducing inflammation and enhancing useful immune function. It helps to facilitate healthy behaviour and lifestyle change, improves sleep and coping and can improve performance.

The basic assumptions of mindfulness practice⁵⁰ are that:

1. People generally operate on automatic pilot and are unaware of moment-to-moment experience.
2. We are capable of developing sustained attention.
3. Development of this ability is gradual, progressive and requires practice.
4. Awareness makes life richer and more vivid and replaces unconscious reactivity.
5. Gives rise to veridicality (truthfulness) of perceptions.
6. Awareness enhances perceptiveness, effective action and control.

Meditation generally, and mindfulness in particular, help to remedy these problems. Many will no doubt approach meditation for the centrally important spiritual and philosophical benefits which it confers, but in the health setting most patients are not necessarily interested in this dimension of meditation practice but are more interested in the healthy 'side-effects'. Research on various meditation practices has shown a range of physiological and psychological benefits (see Table 1).

An eleven-year follow-up study by an insurance company involving 600,000 non-meditators compared to 2,000 meditators found significant reductions in various illnesses.⁵¹ There was an overall 63% reduction in health-care costs with 11.4 times less hospital admission for CVD, 3.3 times less cancer and 6.7 times less

mental disorders and substance abuse.⁵²

This particular study did not control for lifestyle and personality factors and so self-selection, healthy lifestyle change and the direct physiological benefits associated with meditation would all have contributed to the findings.

The research on mindfulness which has had most impact has been the research on the prevention of relapse for severe depression. Mindfulness-Based Cognitive Therapy seems to reduce relapse by changing the relationships to negative thoughts rather than by changing belief in thought content as is the case with conventional cognitive therapy. One doesn't have to control thoughts, but equally one doesn't have to be controlled by them, nor does one need to discursively analyse them.⁵³ The results have so far shown that Mindfulness-Based Cognitive Therapy reduced the relapse rate over a 2-year period from 78% to 36% in 55 patients with 3 or more previous episodes.⁵⁴

Even more interesting is the growing evidence that long-term meditation changes the anatomy of the brain and significantly slows its age-related degeneration by reducing the levels of chemicals associated with allostatic load. MRI was used to assess the cortical thickness in 20 long-term mindfulness meditators.

Physiological effects

- decrease in oxygen consumption and metabolic rate.
- lowering of cortisol and catechol receptor sensitivity.
- reduction in blood pressure and heart rate.
- reduction in serum **cholesterol**.
- increase in skin resistance, decrease in blood lactate.
- EEG changes (increase in alpha and theta waves and EEG coherence).
- a reduction in epileptic seizure frequency.
- changes in neurotransmitters including high serotonin and dopamine.
- selective increase in cerebral blood flow.
- **reduction in cortisol levels.**
- **reduced TSH and T3 levels.**
- **improved immune function and reduction of** inflammation.
- reduced calcium **loss (lowered cortisol).**
- adjunct to therapy (CVD, cancer, **chronic** pain, asthma, diabetes ...)

Psychological effects

- improved response time and reflexes.
- improvement in perceptiveness of hearing and other senses.
- decreased anxiety.

- more optimism, decreased depression.
- greater self-awareness, self-actualisation and autonomy.
- **improved** coping capabilities.
- adjunct **to psychotherapy**.
- reduced **addiction, reliance upon drugs or alcohol**.
- improved **sleep; more restful, less insomnia, and in time less** sleep needed.
- reduced aggression **and** criminal **tendency**.
- improved I.Q. and **learning capabilities (various age-** groups).
- greater efficiency and **output and reduced** stress at work.
- better time management **and improved** concentration and memory. *ability to change undesired personality traits.

The brain regions associated with attention, interoception and sensory processing were thicker in meditators than matched controls, including the prefrontal cortex through which reasoning seems to work. The effect was most marked in older participants indicating that meditation might offset age-related cortical thinning: "evidence for experience-dependent cortical plasticity associated with meditation practice."⁵⁵

There is gathering evidence that the long-term application of mindfulness-based practices is associated with neural plasticity and possibly even neurogenesis—the ability for the brain to make new neurons. A term which is now being coined is called "the mindful brain".⁵⁶ These findings have implications for the training of health professionals and mindfulness is now a part of the core curriculum in the training of medical students at Monash University and the Monash program has been piloted at Harvard University.⁵⁷

Meditation has much to teach us about ourselves and much to teach us about happiness. A few salient points are worth mentioning in closing.

Pleasure and happiness are not the same thing.

- Happiness is natural and restores itself given the right conditions.
- For better or for worse, we all tend to meditate on something or other.
- Consciousness powers, or gives life to, thoughts and feelings.
- We almost constantly think our way out of happiness.
- Meditation gently refocuses the attention.
- It is important to learn to be accepting of, and not reactive to, the thoughts and feelings of which we wish to be free.

- Our state of mind is reflected in our body.

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