Toward a Unified Field of Study: Longevity, Regeneration, and Protection of Health through Meditation and Related Practices

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The orientation of this volume and the Longevity and Optimal Health: Integrating Eastern and Western Perspectives conference is that there is abundant evidence in the scientific and medical literatures that the diligent practice of certain yoga-meditational regimens can lead to a spectrum of health enhancements, ranging from modest to profound, and that these can be investigated in a scientifically rigorous fashion. This overview will summarize these possibilities regarding improved human longevity, regeneration, and protection of health and serve to introduce the perspectives of conference participants from all of the traditions represented.

The orientation of this volume and the conference from which it derives, Longevity and Optimal Health: Integrating Eastern and Western Perspectives, is meant to be at once bold and scientifically rigorous. Bold, because the Eastern perspectives—specifically the extensive, long-standing, and highly developed yoga systems of Asia, including India and Tibet—claim that there is evidence that the diligent practice of certain yoga-meditational regimens can lead to a spectrum of health enhancements, ranging from modest to profound. Scientifically rigorous because any important claims must be subjected to the highest standards of assessment of truth. The latter principle is a basic—if not always observed—foundational principle of the history of Western, or more accurately, in socio-historical terms, *cosmopolitan* science, as it also is, in its own form of empirical-experimental-logical criteria, within the Eastern scientific systems of mind-body practice known as yoga.

Many of us have come to feel that this principle of commitment to the truth is embodied in His Holiness the Dalai Lama of Tibet, as exemplified in key, seminal statements such as this one: "My confidence in venturing into ("Western") science lies in my basic belief that as in science so in Buddhism, understanding the nature of reality is pursued by means of critical investigation: if scientific analysis were conclusively to demonstrate certain claims in Buddhism to be false, then we must accept the findings of science and abandon those claims."[1] Let us take this position to be our foundation in what follows in this volume and in the enterprises that have arisen and will arise from this and other seminal conferences and initiatives, and examine the claims of the yoga meditation traditions in an open yet rigorous spirit and program of future research.

The stage of these endeavors in which we now find ourselves is new; even if claims may seem to be dramatic, we (the authors of this overview) believe that there already exists, at least, a critical minimum of evidence that is supportive enough to warrant a critical review, as well as further investigation. Of course, at the same time, the more radical the claims are, the more rigorous must be the scrutiny they receive. The claims of these traditions, at least for

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the potential that may be realized by advanced *virtuoso* practitioners of these regimens, are in fact radical, and from the present scientific perspective potentially revolutionary.

Some of the scientists represented in the stellar group that met with H.H. the Dalai Lama at this conference, are currently pursuing follow up research in response to questions and issues raised at the conference. The work of many of this group already possesses potentially revolutionary implications in the life sciences, specifically with regard to the potential for the enhancement of human health and functioning, as will be seen below. Also to be seen below, is a description of the potential common ground of these two perspectives, the Eastern (or, more accurately *multicultural*) and Western (or *cosmopolitan*).

We will now survey some of the key recent Western scientific developments represented by the work of these scientists and others in order to sketch out the background for consideration of the claims of the Eastern yogic traditions. The same organizational framework of the subject matter used in the conference is adapted for the volume, keeping in mind that these categories, of course, overlap in ways that will be discussed below. This framework was developed for the conceptual organization of the conference and this associated volume and was meant to offer an heuristic foundation for communication, integration, and understanding of the broad range of relevant and significant concepts. The primary categories of this framework are longevity, regeneration, protection, and optimization of health and functioning, as well as general issues of methodology. Optimization is considered separately in the concluding paper of this volume, and issues of methodology are considered throughout the introductory and concluding papers, as well as most if not all the papers of this volume.

The work of keeping up with developments in any one single field in medical science is becoming increasingly daunting, and the difficulty is amplified in any attempt at achieving a meaningful multidisciplinary perspective. Recent statistics in bioinformation science reveal that approximately 10,000 new citations are generated in the official medical database of the National Institutes of Health every week (see concluding paper of this volume). When considering not only a multidisciplinary perspective, but a cross-traditional, i.e., an "East-West" perspective along with that multidisciplinary perspective, there is of course even further amplification of the challenges. Yet even a moderately informed investigation of commonalities, common ground, of these traditions proves fruitful, as pioneering publications of H.H. the Dalai Lama with the Mind and Life group (see www.mindandlife.org for list of publications), with Professor Robert Thurman,[2] and with others, attest. Moreover, I believe that, as will also be seen below, even in the existing literatures of East and West there is, to quote in this special context the pioneering bioinformatics researcher, D.R. Swanson, "a vast mosaic of undiscovered connections," a wealth of existing, but as yet "undiscovered public knowledge," waiting to be mined.[3] We intend this framework for the following discussion of the existing but largely unconnected data and knowledge to be regarded in a manner similar to the use of the term "framework" by Francis Crick and Christof Koch in their recent seminal article, "A framework for consciousness":

> A framework is not a detailed hypothesis or set of hypotheses; rather it is a suggested point of view for an attack on a scientific problem, often suggesting testable hypotheses. . .. A good framework is one that sounds reasonably plausible relative to available scientific data and that turns out to be largely correct. It is unlikely to be correct in all the details. A framework often contains unstated (and often unrecognized) assumptions, but this is unavoidable.[4]

Although humility will fortunately prevent us from asserting that our framework is "largely correct," we hope that a powerful motivation for the pursuit of such an extraordinarily important set of subjects will propel us in the direction of accuracy, and at the same time

away from unstated and unrecognized assumptions.

Longevity and Regeneration

As several papers in this volume discuss, the Indo-Tibetan yoga meditation regimen appears to include a form of yogic diet which corresponds to the classic "caloric restriction" (CR) diet, a diet which has been found in hundreds of studies in experimental animals to prevent or delay age-related degenerative changes, prevent or delay increases in age-related disease, and to increase the mean and maximum life span.[5,6] The CR diet reduces the normal total caloric intake by one- to two-thirds while maintaining nutritional balance (protein, vitamins, minerals, etc.), and has been found to be the most robust and validated anti-aging intervention yet tested. Quite significantly, as discussed in these papers and elsewhere,[7,8] the yogic diet in the Indo-Tibetan (and other yogic) traditions appears to substantially correspond to the CR diet, suggesting one form of practice which would produce significant life span- and health span-enhancing effects. Also discussed in Bushell, this volume are the potential anti-aging effects of meditational and yogic practices which lower psychological stress, metabolism, and inflammation, and yogic practices which correspond to Western forms of aerobic exercise.[6] We now focus on yoga meditational practices which are specifically identified as longevity yoga practices in the Tibetan tradition.

In longevity meditation, the practitioner attempts, while in a state of focused absorption akin to the highly suggestible state of hypnosis, to deeply and convincingly imagine himself or herself becoming "transformed" into one of the longevity "deities." There are several different techniques to be applied, in which the practitioner seeks to be "overtaken" or "possessed" by the longevity deity, visualizations in which the *essence* of the deity or many such deities "flows" into the practitioner from the top of the "skull," permeating his or her entire body, being. The longevity deity represents a being that has conquered, in fact even reversed aging, on all levels, including the physiological, which is explicitly described in the longevity meditation texts in terms of rejuvenated tissues throughout the practitioner's body.[9,10]

According to the integrative model being developed by our group, this form of meditation possesses a number of health-benefiting, including longevity-enhancing properties, and here we focus on two. In the first place, we propose that the longevity meditation functions as a powerful means of inculcating in the practitioner a highly positive sense of oneself *in terms of* aging or, more accurately, *longevity*. The practitioner is to continue imagining himself or herself personally taking on progressively more of the properties of the longevity deity. This process of imaginative self-transformation may actually be understood, on one level, in terms of a body of research in Western psychology on "self-stereotypes" and "possible selves" or "hoped-for selves."[11–13] Originally emerging from the research on the detrimental impact of negative stereotypes (racial, gender, etc.) on psychological and physiological health, aging self-stereotype research was originally developed in large part by Becca Levy at Yale and (initially) Ellen Langer at Harvard and focuses not only on the effects of *negative* self-stereotypes, but *positive* ones as well: i.e., on how an "internalized" stereotype, profile, or sense of oneself influences mind and body.

A recent rigorous epidemiological study by Levy and colleagues at Yale turned up unexpectedly positive results in terms of the effects of self-stereotypes on longevity in a large sample of 660 subjects (age > 50) from the Ohio Longitudinal Study of Aging and Retirement.[14] When comparing the effects of the subjects' self-stereotypes of aging as determined by standardized interview instruments, it was found that those with *positive* values lived *over 7.5 years longer than those with negative values*. The effect of the positive sense of self in terms of longevity (the longevity self-stereotypes) in fact

had a greater effect on outcome with respect to life span than many of the major classic predictors:

> The increased life span of 7.5 years in our study is considerable, especially when we compare our findings with those of other longevity studies. The effect of more positive self-perceptions of aging on survival is *greater than the physiological measures of low systolic blood pressure and cholesterol*, each of which is associated with a longer life span of 4 years or less.[15] The survival advantage of more positive self-perceptions of aging is also *greater than the independent contribution of lower body mass index, no history of smoking, and a tendency to exercise*; each of these factors has been found to contribute between 1 and 3 years of added life[16] [our italics].

Additional research by Levy's group and other groups found that positive self-stereotypes of aging, when compared to negative ones, were associated with, among other outcomes, enhanced memory, motor skill (handwriting and gait), cardiovascular functioning, the will to live, *and even recovery from acute myocardial infarction*.[17] Other investigators have determined that a positive personal attitudinal/emotional orientation to aging can similarly positively contribute to health with respect to the life span (and health span), behaviorally and physiologically.[11,12,19–21]

Full discussion of the possible biological mediators of these enhancements associated with internalized psychological (self) stereotypes or identities is complex and outside the scope of this paper, so we will focus on a particular constellation of mediators centered on the substance melatonin. Melatonin is an extremely important pleiotropic substance, with a broad range of health-enhancing and anti-aging properties produced by the body (the pineal gland, the bone marrow, circulating immune cells, and other sources),[22,23] and its production is increased by several forms of meditation, including mindfulness and concentrative forms that are found in the Indo-Tibetan tradition.[24–26] Moreover, we suggest that these longevity meditations associated with the Dalai Lamas and other major figures in the Indo-Tibetan tradition may produce additional melatonin-enhancing effects through specific pineal-activating properties of the particular visualization incorporated in the longevity meditation.

In this part of the meditation, as described in Mullin's translation[27] and other sources,[10] the practitioner intensively and vividly visualizes a powerful activating energy at the top center of the skull where the light energy and/or flowing liquid of the longevity "nectar" enters the practitioner from above the head. This activating energy is directed to the anatomical area in which the pineal gland, the primary producer of melatonin, is located. Elsewhere one of us (Bushell) has reviewed the small but nevertheless significant body of psychophysiological studies which demonstrate that dynamic mental imagery of *activation* can, with practice, produce localized increases in blood flow, temperature, and metabolic activity in particular tissues, including internal organs, and including in cranial and brain tissue.[28–33] Moreover, recent studies of a similar form of meditation, published in *Human Brain Mapping* and the *Proceedings of the Institute of Electrical and Electronic Engineers,* demonstrate that visualization meditation of activating energy directed to the pineal gland location specifically did in fact result in measurable increases in metabolic activity in the pineal gland as assessed by functional magnetic resonance imagery.[34,35] Such increases in pineal metabolic activity are likely to represent increased melatonin synthesis and/or secretion.[36]

By now there is a large and still rapidly growing body of research revealing the substantial life span- and health span-enhancing effects of melatonin across species, including humans,[37–42] and in fact Roth and colleagues found evidence that CR may exert its anti-aging effects in large part through preserving more youthful levels of melatonin production and/or secretion.[5,43,44] A number of the specific anti-aging mechanisms of melatonin have been identified. The molecule

possesses powerful effects which are at once anti-inflammatory and immune-stimulating properties that can reverse the deleterious immune remodeling associated with aging, which results in chronic and widespread inflammatory damage to the host simultaneously with lowered immune defenses against infectious and neoplastic challenges (see below). Melatonin also has a wide range of antitoxic and chelating properties,[45–48] enabling it to assist in counteracting "the toxic endobiotic and xenobiotic metabolites. . .[which] may be the major determinants of the molecular damage that causes aging."[49]

Melatonin is also one of the most powerful antioxidants and free radical scavengers produced by the body, and, in turn, stimulates the other major antioxidant and scavenging enzymes of the body, including superoxide dismutase, catalase, and glutathione peroxidase,[50–52] which further supports its key anti-aging role according to the predominant oxidative stress theory of aging.[53–55] This substance has also recently been found to stimulate the sirtuin gene proteins,[56] whose powerful anti-aging properties were described at the conference by their discoverer, Leonard Guarente of MIT (paper not included in volume).[57]

When released into the circulation, from the pineal and other sources, melatonin distributes these anti-aging, immune-enhancing, tissue-protective, and regeneration-enhancing effects throughout the body, as it is capable of crossing all morphophysiological boundaries and entering all cells and subcellular compartments, including nuclei and mitochondria, where it exerts crucial antioxidant,[52,58,59] radical scavenging,[50,51] and DNA-repair effects.[60–61]

There is a striking, if presently inexplicable, correspondence between this profile of melatonin and its anti-aging, general health-promoting, regenerative actions, and the fluid substance described in the longevity meditations of the Dalai Lamas and other major figures in Tibetan Buddhism. Starting from the location in the top center of the cranial/cerebral region, as mentioned above (although the *initiation* of the flow of this fluid is conceived as being due to the actions of a "deity"—or a "meditation principle" according to the translator), this substance flows down from that location, and as described in the recitation accompanying the visualization, it "fills my body. . . restoring any degeneration . . . in the body fluids, such as blood, lymph. . . flesh tissue, bone tissue. . . and [thereby] lifespan is increased."[27]

This description corresponds in some significant, compelling ways to the potential cascades of regenerative processes that may be facilitated or initiated by melatonin throughout the tissues of the body. According to this neuroendocrine model, melatonin may counteract the tendency of stem cells to become senescent and/or malignant by providing protection for them from oxidative stress and other factors, and may also directly stimulate stem cells, as recently emerging studies have been demonstrating. Building on a landmark study in which it was found that serum from youthful mice could rejuvenate senescent stem cells in other mice because of unknown factor(s) in the youthful serum,[62,63] Bushell recently proposed that melatonin would fit the requirements established by that study for a substance found in the circulation, and potentially capable of facilitating reversal of senescence of progenitor and/or stem cells through cytoprotective and/or direct stimulatory means.[64] The stem or progenitor cells can be both tissue-specific (muscle and liver in the landmark study of Conboy et al.[65]) and/or may originate in the bone marrow or other tissue.[66–67] Intriguingly, the regenerative potential of the bone marrow has been asserted by yoga traditions for centuries.[6,68]

Recent research has focused on the key role of circadian genes in aging and longevity,[69,70] and melatonin is the primary molecular regulator of circadian rhythms.[71] And although melatonin is one of the most powerful antioxidants and free radical scavengers produced in the body, it is also vulnerable to damage by oxidative stress, as are the tissues, organs, and genes responsible for its production, regulation, and functioning.[72] Hence, it appears that aging

may result from the gradual "tipping" of the antioxidant–oxidative stress dynamic in the direction of the latter. In fact, other research indicates that replenishment or substitution of declining melatonin levels may reverse signs and symptoms of aging, including even in certain organisms, such as the zebrafish, which possesses the unusual capacity of "continuous growth," regeneration, and "slow aging" or "negligible senescence."[73,74] In mammals such as laboratory mice, for example, dramatic effects were found when youthful pineal glands were transplanted into old mice, or even with prolonged daily administration of melatonin in the drinking water. In these studies in lab mice, enhanced levels of melatonin "exerted extraordinary positive actions on their performance and reversed or delayed the symptoms of age-related debility, disease, and cosmetic decline in dramatic fashion," producing a "striking difference in vigor, fur quality, motility and weight," "astonishing difference in the fur and in the general conditions (vigor, activity, posture)," as well as life span.[75–79] Elsewhere, Bushell has reviewed the research focused on melatonin's *specific* effects on factors that determine the appearance, deportment, posture, movement, behavior, and *functioning* of animals and humans, with respect to a "youthful" versus "aged" profile, ranging from bone to muscle to skin to nervous system tissue to motor control and cognition, and the overall conclusion from this research is that there is a significant and ubiquitous cytoprotective, aging-retarding action of melatonin throughout the human organism.[64,76] In those articles the ubiquitous anti-cancer actions of melatonin throughout the tissues of the body are also reviewed, with obvious significance for the subject of longevity, as cancer is now the second leading cause of death in humans according to recent statistics.

It was recently determined that at least a major part of melatonin's oncostatic effect is due to its down-regulation of telomerase,[80–82] the extremely important enzyme discovered by Lasker Award winner and conference participant Elizabeth Blackburn.[83] Telomerase can *immortalize* cells by maintaining the integrity of chromosomes, which otherwise decline over the course of the life span, apparently due to some form of programmatic replicative senescence, oxidative stress, and/or other factors. However, this immortalization is another "double-edged sword," as telomerase is, at least in large part, responsible for the immortalization of cancer cells as well as (nonmalignant) stem cells. Intriguingly, a large review of melatonin determined that it is *selectively*, *differentially* protective of cancerous and healthy cells, with a powerful tendency to destroy the former and protect the latter.[84] The evidence is incomplete but nevertheless consistent with the idea that melatonin may differentially up-regulate telomerase in healthy stem cells and down-regulate telomerase in malignant cells.[64] Recent research by Guarente and colleagues found evidence that the anti-aging *SIRT1* gene not only is important for functioning of circadian genes, but also produces effects which are simultaneously regenerative and oncostatic, and melatonin activates this gene.[85,86]

To summarize the hypothetical model outlined here, the total antioxidant status of human serum is to an important extent based directly on melatonin levels.[87] When the latter decline due to an eventual tipping of the balance between pro- and anti-oxidant factors, the decline of tissues and organs of the body becomes initiated and then accelerated, beginning with melatonin itself, and continuing through the tissues responsible for melatonin production—from the circadian genes to the retinohypothalamic tract to the pineal gland—and then onward to the other remaining tissues and organs of the body. Recent research indicates that exogenous melatonin sources appear to be capable of significantly counteracting this ubiquitous and pernicious process.[88] Meditation and related practices, presumably if initiated before the process reaches a clinical point of irreversible damage, could potentially hold off this process, as indicated by the above evidence.

Protection of Health

It is difficult to overestimate the importance of the recent discovery that the vagal nerve complex plays a crucial role in modulating the body's inflammatory response to infectious disease, other forms of physical insult, and psychosocial stress.[89–92] Recently emerging evidence shows that the inflammatory response, along with its role in defeating and/or limiting infectious and other challenges, itself plays a major pathogenetic role in acute diseases and injuries, chronic illness, and diseases of aging. Conversely, Tracey and colleagues have demonstrated that the vagal nerve complex possesses major inflammation-dampening properties, the implications of which are enormous for the entire spectrum of disease and health. Moreover, the implications for the practices of meditation and yoga are likewise of enormous potential importance, because these practices modulate vagal nerve activity.[93]

For example, with respect to infectious diseases, it is only in the last several years that evidence from a range of sources has been brought together for evaluation of an integrated hypothesis regarding inflammation and its relationship to tissue injury/repair.[96,99–102] The resulting inflammatory or "cytokine theory" of disease is based on a large body of accumulated evidence and states that infectious and other physical challenges elicit an inflammatory response mediated by blood borne inflammatory molecules (e.g., cytokines, chemokines) that are intended to destroy infectious pathogens, but which frequently do as much or more harm to the host tissue than the original infecting agents.

This pathophysiological trajectory encompasses a targeted inflammatory response progressing to a system-wide hyperinflammatory state in which these mediators flood the circulation and tissues throughout the body, the so-called "cytokine storm," potentially leading to extensive tissue damage, with bleeding and/or clotting, septic shock, and death, or some combination of these outcomes as discussed by Tracey,[89,90,92] Clark,[94–97] and Bushell.[93,98,99]

Focusing in particular on malaria—arguably the pathogen that causes the most human suffering, affecting approximately 500,000,000 people worldwide—infectious disease researcher Ian A. Clark has explained:

> Malaria causes an acute systemic disease that bears many similarities, both clinically and mechanistically, to those caused by bacteria, rickettsia, and viruses. Over the past few decades a literature has emerged that argues for most of the pathology seen in all of these infectious diseases being explained by activation of the inflammatory system, with the balance between the pro- and anti-inflammatory cytokines being tipped towards the onset of systemic inflammation [and that] *Falciparum malaria primarily is an inflammatory cytokine-driven disease* [our italics].[94]

When Tracey discovered the existence of an innate pathway or reflex that appears to dampen inflammation, the vagal/cholinergic anti-inflammatory system, this discovery opened the door to the theory that meditation and yoga could in turn be relevant for any form of "inflammatory cytokine-driven disease." Dr. Tracey has called attention to the already existing evidence that meditation and related practices possessed both vagal-activating and anti-inflammatory effects, and called as well for further research into these practices for the treatment of inflammatory disease.[90]

Similarly, the work of Dr. Dean Ornish demonstrating that atherosclerotic cardiovascular disease, now also recognized as, in large part, an inflammation-mediated disease involving cytokine-mediated injury, is amenable to interruption and even substantial resolution with meditation and yogic practices.[100]

In 2001, Bushell also called attention to the potential for meditation and yoga as therapeutic modalities for "inflammatory cytokine-driven disease," including infectious diseases, even particularly virulent ones.[99] Basing his model on the work of Philip Hanna and others on the inflammatory crisis produced by anthrax,[102–104] and that of Tracey and colleagues, he recommended that meditative

practices and other vagal stimulatory modalities should be investigated in this context.[99] Bushell added another, neuroendocrine dimension to this model, since meditation enhances two neuroendocrine substances, namely melatonin and dehydroepiandrosterone (DHEA),[95–110] that possess vagal stimulatory, anti-inflammatory, antioxidant, and antimicrobial properties (reviewed in Bushell[6,93,98,99]).

With regard to anthrax, melatonin and DHEA can act in concert to down-regulate the production of inflammatory cytokines generated by anthrax-infected macrophages, a primary mechanism of anthrax-associated morbidity and death.[111] In the case of melatonin, the molecule's actions may be selectively, bimodally determined by the salient inflammatory milieu, both locally and systemically, its net antimicrobial immunostimulatory properties activated by pathogens, its inflammation "resolving" properties activated by pathogen clearance.[112]

With regard to malaria, endogenous DHEA levels predict malaria parasite density, disease susceptibility, and other critical factors in infected individuals.[113,114] Endogenous levels of DHEA peak at puberty and then decline, so interventions that optimize these levels should provide protection. Indeed, meditation increases DHEA levels[107,109,110] and the regular practice of meditation even reverses its typical, age-related decline by an average of 5 to 10 years, to youthful levels leading to an increase of circulating levels into the optimal range for resistance against malaria.[109]

Another critically important finding by Clark is that "infection with *falciparum* malaria is often fatal because mitochondria are unable to generate enough ATP to maintain normal cellular function." Melatonin, serum levels of which are increased by meditation, powerfully enhances mitochondrial ATP-generating functions. Indeed, melatonin specifically and substantially protects liver mitochondria during experimental malarial infection.[115]

Hence, this research, when integrated, strongly implies that meditation may actually produce, through vagal stimulation and increases in particularly potent circulating signaling molecules, *significant* anti-inflammatory, anti-oxidant, cytoprotective, and antimicrobial effects, even—hypothetically, though plausibly—with respect to deadly infectious diseases such as malaria and possibly anthrax. Indeed, many of the most virulent, deadly infectious diseases worldwide appear to be, like malaria and anthrax, in many key respects primarily "inflammatory cytokine-driven diseases" in which inflammatory processes act as a major cause of morbidity and mortality. This list also includes HIV/AIDS, tuberculosis, smallpox, plague, swine flu, schistosomiasis, viral hemorrhagic diseases such as Ebola, dengue, Hantavirus, and others.[93,95] Moreover, the vagally mediated anti-inflammatory effects of meditation and related practices may be complemented by the previously unsuspected and apparently significant antimicrobial, anti-infectious properties of melatonin and DHEA, with respect to many diseases, including HIV/AIDS,[116,128] tuberculosis,[119] schistosomiasis,[115,120] *Staphylococcus aureus*,[121] SARS,[122] *Trypanosoma cruzi*,[123,124] *Candida*,[125] leishmaniasis,[126] viral hemorrhagic disease,[127] and others.[148]

Moreover, meditation-associated protective mechanisms may be of great significance for protection against other forms of physical insult, including mechanical (penetrating, blunt, crush, etc.), thermal (burns), chemical (toxins, pollution, envenomation, etc.), and radiological forms of insult.[93–106] A key general principle is that in many cases, tissue damage resulting from a physical insult or trauma frequently consists largely of "secondary damage" or a "second hit," caused by inflammation and related forms of oxidative and nitrostative stress in response to production of oxygen free radicals, which may produce as much as 90% of local and remote tissue damage related to the inciting trauma.[128] The research further

indicates that by intervening in the insult-induced inflammatory cascade, prevention or reduction of secondary damage may be achieved. One example: lessening inflammation in spinal cord injury may lead to profoundly reduced tissue damage and may even be decisive regarding whether the individual recovers or remains paralyzed.[129–131]

And perhaps most impressively, is the potential for prevention or minimization of tissue damage in response to what is a veritable symbol of tissue-destructive potential: the overwhelmingly corrosive, burning, chemical warfare agent, sulfur mustard or "mustard gas." This substance has been used in war to produce terrible damage to skin, eyes, and lungs—to any exposed tissue—resulting in blindness; suffocating lung damage; and blistering, burned, exfoliated skin. Recent research, however, finds that relatively simple anti-inflammatory and antioxidant treatment alone can actually prevent approximately three-fourths of the tissue damage associated with exposure.[132]

Significantly, the anti-inflammatory-neuroendocrine model may also apply to the spectrum of physical trauma as well as infectious disease discussed above. Both melatonin and DHEA (and their metabolites) possess protective effects with respect to the spectrum of physical trauma, including mechanical, caloric, chemical, and radiological, and specifically with regard to both spinal cord injury and mustard-induced injury and/or burns.[133–136]

Thus, disparate medical studies, including direct and indirect experimental (animal, physiological, molecular biological, neuroendocrine, and genomic) investigations as well as some limited amount of clinical data, when marshaled in an integrated framework, provide surprisingly compelling preliminary evidence of powerful, latent "mind/body" capacities for tissue protection in the entire range of acute physical challenge from infectious to various physico-mechanical forms of tissue trauma. The further development of "mind/body" medicine through well designed clinical studies becomes the, so far too delayed, imperative.

The background research, as noted, includes detailed anthropological studies in the field, as exemplified by the paper in this volume by Jean Jackson, of M.I.T.[137] Such data reveals widespread, cross cultural practices in which individuals enter trance or meditative states and experience (and publicly demonstrate) what appear to be manifestations of such latent, endogenous protective capacities.

One practice reported in cultures throughout the world involves self-inflicted, acute, penetrating traumas with sharp instruments, while the individual maintains such a trance-like or meditative state. According to numerous accounts, documented in photographs, film, video, and in a limited number of clinical and experimental reports by Western physicians and physiologists,[66,137–141] such individuals either do not feel or stoically withstand enormous physical pain and stress—most often there appears to be significant triggering of endogenous analgesia systems—with inhibition of bleeding, reduction/prevention of expected tissue damage and scar formation, and acceleration of healing at the sites of penetrative trauma. Similar, though somewhat less dramatic findings are reported in the medical hypnosis literature (reviewed in Bushell).[138,139]

When all the evidence is considered together, it would appear that individuals actually are potentially capable of significantly, even profoundly limiting the deleterious physiological and psychological effects of physical trauma, echoing assertions of diverse cultural traditions, including the Indo-Tibetan yogic tradition on which much of this volume is based. This tradition—including the present and past Dalai Lamas—has clearly articulated the recognition that meditation and related practices such as yoga possess not only basic longevity-enhancing and tissue-regenerative properties as discussed above, but also specifically powerful disease-countering properties as well, through the activation of endogenous

protective and curative potentials of the body.[9,10,140] We are now in a position to make evidence-based hypotheses regarding the physiology underlying such claims and to make rigorous scientific studies of such practices in the laboratory and in the field.

With regard to chronic and degenerative diseases—ranging from cardiovascular disease, stroke, cancer, Alzheimer's and Parkinson's disease, diabetes, etc., to other major forms of disorder—a growing body of research demonstrates the key roles played by inflammation and neuroendocrine changes, and many now consider aging itself as a cumulative "disease" arising from disordered inflammation and/or neuroendocrine physiology.[37,89,141–144] One may consider many degenerative or aging changes to be a result of "remodeling" of immunomodularity mechanisms leading to heightened baseline inflammation in diverse tissues, as well as simultaneously diminished adaptive antimicrobial (clonotypic) immunity, so called "immunosenescence." Franceschi and Bonafe describe this succinctly:

> Human inmunosenescence represents a complex remodeling, whereby clonotypical immunity deteriorates, while ancestral, innate immunity is largely preserved. Continuous exposure to antigens causes a lifelong, chronic antigenic stress, which is responsible, together with the involution of the thymus, for the accumulation of memory/effector T cells and the exhaustion of naïve T cells. Aging is characterized by a peculiar chronic inflammatory status that we. . . call "inflammaging." Inflammaging is considered the common and most important driving force of age-related pathologies, such as neurodegeneration, atherosclerosis, diabetes, and sarcopenia [i.e., degeneration of muscle tissue] among others, *all of which share an inflammatory pathogenesis* [our italics].[142]

We may add cancer to this list as well.[89]

It is not clear what initiates the deleterious cascades that lead to the state of "inflammaging" and senescence, the "smouldering inflammatory"[145] milieu that promotes widespread oxidative stress, tissue damage, as well as the potential for neoplastic transformation, susceptibility to infection, and the development of these kinds of diseases. Such physiologic derangements may relate to vagus-mediated immunomodulatory effects described and therefore be amenable to intervening meditative and yogic practices as described above. A number of investigators have pointed to the potentially key role of "endocrinosenescence,"[146] particularly with respect, again, to declining levels of melatonin and DHEA.[5,6,37] In this regard, the work of Bruce McEwen on homeostatic mechanisms (the allostatic load model) regulating immune trafficking and inflammation, as well as neuroendocrine activity, especially DHEA and glucocorticoids, appears to be a particularly prescient and productive model for reconciling the "double-edged sword" effects of immune/inflammatory and neuroendocrine functions—at once necessary for survival, but potentially quite deleterious for it.[147] Further interdisciplinary, inter-traditional research to investigate this potential is necessary and is currently in the early stages of pursuit.[148]

Conflicts of Interest

The authors declare no conflicts of interest.

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