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Lecture Series

Evidence-based Research in Complementary and Alternative Medicine I: History

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Contemporary Western medicine has witnessed a fragmentation of our conceptualization of the medical endeavor into 'traditional medicine' and 'non-traditional medicine'. The former is meant to refer to the Western medical tradition, the latter encompasses both 'complementary' and 'alternative' medical practices. Complementary medicine complements conventional medical treatments, and alternative modes of medical interventions are meant to replace traditional Western medicine. Evidence-based research must be directed at establishing the best available evidence in complementary and alternative medicine. This paper is the first of a set of four 'lectures' that reviews the process of evidence-based research, and discusses its implications and applications for the early decades of the 21st century. The purpose of this paper is to introduce the series by examining some of the historical and philosophical foundations of this research endeavor.

Keywords: Evidence-based research – complementary and alternative medicine – mind-body interactions

Naming is Defining

The Land of Media

Ancient Greek mythology tells of Medea, a devotee of the goddess Hecate, and a renowned sorceress in the 7th century BC. Medea was the daughter of King Aeetes of Colchis and the granddaughter of Helios, the sun god. King Aeetes' most valuable possession was a golden ram's fleece. Jason and his crew of the Argo, the Argonauts, sailed to Colchis in pursuit of the Golden Fleece, but Aeetes was unwilling to relinquish it. Jason was the son of Aeson whose great-grandmother was Helen, the grandchild of Prometheus. Prometheus was a direct descendant of Iapetos, regarded by the Greeks as the ancestor of the prediluvian human race (1). The king set Jason on a series of arduous tasks with the promise that, if he completed them, the Golden Fleece would be his. Medea fell in love with Jason and used her magic to help him. In return, Jason promised to marry her. Jason gained the Golden Fleece.

The king, irate by this betrayal, forced Jason to run away with Medea. Jason and Medea took with them her younger brother, Absyrtis. They later killed him and scattered his dismembered body parts in the sea in order to delay King Aeetes' angry pursuit. As the king's men gave proper burial to the king's son, Jason and Medea escaped and reached Iolcus safely, Jason's home. In Iolcus, Medea used her magic potion to restore the health of Jason's father, Aeson. She offered to do the same for Pelias, the king of Iolcus, but she tricked Pelias' daughters into killing the king. The insurrection that ensued forced Jason and Medea to flee again.

The couple reached Corinth, where they settled, and Medea bore Jason two children. Jason meanwhile fell in love with the daughter of Creon, the king of Corinth. Medea, overtaken by jealousy, took revenge by killing Jason's children, and poisoning the robe and crown of Jason's lover. Thus, Creon's daughter perished in agony, in her father's arms. Creon's flesh was burned as well, and he too died in agonizing pain. Medea was forced by Jason out of Corinth.

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She fled with the bodies of the children and found refuge in Athens with King Aegeus. There, she used her magic to enable the elderly king to have a son and she bore him Medus. When Aegeus' first son, Theseus, now a young man, returned to Athens, Medea attempted to poison him. Her malefic plan was exposed and she was forced out of Athens in disgrace with Medus. They settled inland in a region that would become part of Persia, which she named Media after its first King Medus (2).

From Media to Rome

The land of Media was rich in plants endowed with the property of restoring health or of acting as poison. These herbs from Media came to be called the Median herbs, *herba medica*, by the Romans. Soon, a *medicamentum* came to signify an ointment that could be used either for poisoning or for healing (e.g. *medicamento sagittas tingere*, to dip the arrows in poison, Plinius. 27, 11, 76, section 101; *ars medicamenti*, the art of healing). By further transliteration, the term *medicatus* came to mean either at one extreme 'treated for healing', as in our current use of the term 'medicated', or at the other extreme 'poisoned'. The action verb, *medicare*, was formed to designate the action to bring about this state, and its past participle *medicatus* (having medicated) meant either 'having brought about healing' or 'having poisoned'. Its passive form, *medicari* referred to being at the receiving end of the medicating (or poisoning) process, as it were, and held the same past participle, *medicatus* (having been medicated). He who brought about the medicating (or poisoning) was the *medicus*, which interestingly was the identical term that was used to refer to the inhabitant of Media. The *medicus* performed the science of healing (*medicina*); that is to say, he exercised medicine (*medicinam exercere*) in the place appropriate for this task, the *medicabulum*, after having studied the field of medicine (*medicinam excolere*).

In a parallel etymological process, which also originated from the legend of Medea and the healing/poisoning properties of the plants in the land of Media, the phrase *alicui mederi contra* (healing someone from) arose (e.g. *alicui contra serpentium ictus mederi*, healing somebody against snake bites, Plinius 9,31). Whence the maxim arose: *si assuetis mederi possis nova non sunt tentanda* [if you can find comfort in (a certain mode of) healing, new ones should not be attempted]. The art of medicating, *ars medicamenti*, paralleled the art of healing (*ars medendi*), but was not identical to it: the tasks of the *medicus* were specifically to medicate (or to poison), and did not pertain to healing *per se*. The genitive form of the past participle (*medentis*) of the action verb came to refer to he who brought about healing [e.g. *Democrates, e primis medentium*, Democrates, one of the first (one of the top) healers].

The Influence of Rome

These terms and their distinctive meaning—medicating versus healing—dominated Western medicine as originally laid out by Hippocrates (ca. 460–380 BC) and expanded by Claudius Galen (ca. AD 129–200), and remained common terminology until the Middle Ages and beyond, when Latin was the common language. For instance, we find the famous citation by St Bonaventure: *. . .Deus . . . in Sacramentis suis medicinam praeparavit . . . impossibile est, mederi Deum sine gratia iustificante: ergo in omnibus Sacramentis est gratia iustificans* . . . [God prepared a medication (*medicina*) in His own Sacraments . . . it is impossible, that God heal (*mederi*) without justifying grace; therefore, in all the Sacraments there is justifying grace . . .] [Bonaventure of Bagnoregio, *Commentaria in Quatuor Libros Sententiarum Magistri Petri Lombardi, Episc. Parisiensis*, *Quaestio V* (Commentaries on the Four Books of Sentences of Master Peter Lombard, Archbishop of Paris, Question 5)].

As Latin became vulgate, i.e. as the classic language of the Romans became increasingly adulterated by regional linguistic forces and dialects (e.g. Barbarian influences), the clear distinction between he who medicates (*medicus*) and he who heals (*medentis*) was lost. The sciences of medicating (*medicina*) and of healing (*mederi*) overlapped and coalesced into the overarching term medicine, which is used today.

The Four Humors

Hippocrates had originally proposed that the body must be treated as a whole and not just a series of parts, and that it was endowed with an ability of natural healing, which depended on rest, a good diet, fresh air and cleanliness. He noted that there were individual differences in the severity of disease symptoms, and in the individuals' ability to cope with their disease and to heal. Hippocrates thus laid the foundations of the modern theory that thoughts, ideas and feelings, which he proposed to originate in the brain, can influence health and the process of disease (3).

In Hippocrates' view, the process of healing and the purpose of medicating held one and the same goal: to assist the patient in regaining harmonious balance of the tendencies within him/herself and the external forces. He formulated a set of principles that helped to define the tendencies (i.e. temperaments) of each patient, and he defended that the root of one's temperament derived from the four humors dominant in the body. The temperaments revealed the pattern of response to environmental forces (e.g. wind, earth, water and fire) (Fig. 1).

- blood (*sanguine*, warm and pleasant),
- black bile from the liver (*choleric*, hot-tempered),
- phlegm (*phlegmatic*, apathetic) and
- yellow bile from the kidneys (*melancholic*, depressed and sad).

The Hippocratic school soon recognized that fundamental differences among the four basic temperaments included the time-delay and the nature of response to a given challenge stimulus, which is akin to what today is described as the allostatic response (4,5).

Figure 1. The temperaments.

The sanguine temperament typically was said to show quick, impulsive and relatively brief reactions. The phlegmatic temperament was characterized by a longer response-delay, but the response was also short-lived. The choleric temperament manifested a short response time-delay, but the response was sustained for a relatively long time. The melancholic temperament exhibited a long response time-delay, and the response was sustained at length, if not, seemingly, permanently (3,6,7).

According to the Hippocratic model, these patterns of response translated into the ability/inability to ward off diseases and infections, as well as emotions, fears and depression. From pre-Christian Rome to the Middle Ages, and beyond until the 19th century, Western medicine was dominated by the temperaments paradigm, which was taught in all Western medical schools from Salerno to Paris and Oxford.

In brief, it was the purview of *medicare* (to medicate) as well as of *mederi* (to heal) to identify correctly the temperament of the patient from his/her humors (8), and to intervene so as to restore the correct balance among the humors. This concept of temperament persists to some extent in Western medicine

Table 1. Evolution of the concept of temperaments

	Schizothymic (social detachment)		Cyclothymic (social integration)	
	Melancholic	Choleric	Phlegmatic	Sanguine
Hippocrates 400 BC	Philosopher	Scientist	Guardian	Artisan
Plato 340 BC	Ethical	Dialectical	Proprietary	Hedonic
Aristotle 325 BC	Melancholic	Choleric	Phlegmatic	Sanguine
Galen 200	Dogmatic	Agnostic	Traditional	Innovative
Adickes 1907	Religious	Theoretical	Economic	Esthetic
Spränger 1914	Hyperesthetic	Anesthetic	Depressive	Hypomanic
Kretschmer 1921	Hoarding	Marketing	Receptive	Exploiting
Fromm 1947	Feelingful	Thoughtful	Judicious	Perceptive
Myers 1955	Apollonian	Promethean	Epimethean	Dionysian
Keirsey 1978	Idealists	Rationals	Guardians	Artisans
Keirsey 1987				
Personality types				
2001	Idealist	Rationalist	Traditionalist	Hedonist
2004	Hyperesthetic	Anesthetic	Depressive	Hypomanic

even today, but it is principally retained and explored in terms of psychological constructs and psychosocial interactions (Table 1) (6,7).

Traditional Versus Complementary and Alternative Medicine

'Traditional' and 'Non-traditional' Western Medicine

Whereas the West engaged in this perspective of medicine that was based on formulating categories of peoples and of ailments following the Hippocratic tradition, the East followed a medical enterprise that was based on observation and inquiry. One of its founder, Abu Bakr Muhammad bin Zakaria al-Razi (Rhazes, ca. AD 860–930) is still recognized today as possibly the greatest representative of Islamic medicine. Many of his works were translated in Latin in the 13–15th century, and therefore had profound influence on the development of today's Western medicine, based on the scientific method as we commonly embrace it today in medical research (see also Saad, this issue).

Contemporary Western medicine subsequently witnessed a fragmentation of the conceptualization of the medical endeavor into 'traditional medicine' and 'non-traditional medicine'. The former corresponds to the Western medical tradition, from the Sumerian (today's Southern Iraq) text dated ca. 5000 BC, which implicated, for example, 'tooth worms' as the cause of tooth decay, to Imhotep, the 'father of medicine' according to Sir W. Osler (ca. 2600 BC), to the Ebers papyrus of Ancient Egypt [ca. 1700 BC; (9)], to Aesculapius (ca. 1300 BC), to Hippocrates, to Galen (ca. AD 150), to Andreas Vesalius (1514–64), to Ambroise Paré (1517–90), to Harvey (1578–1657), to Mesmer (1734–1815), to Jenner (1749–1823), to Pasteur (1822–95), to Bufalini (1785–1875), to Pacini (1812–83), to Koch (1843–1910), to Cannon (1871–1945), to Barnard (1922–2001) and to the present day exploits of Western medicine. By contrast, the term 'non-traditional' medicine encompasses both 'complementary' and 'alternative' medical practices [complementary and alternative medicine (CAM)]. Complementary medicine complements conventional medical treatments and is used in association with traditional Western medicine. Alternative modes of medical interventions are meant to replace and to be used instead of traditional Western medicine.

Mind–Body Connection

Since the pre-Platonic period, as in contrast to the propositions of Hippocrates (as noted above), the philosophical trends proposed, as for instance Democritus' philosophical system of atoms (ca. 460–370 BC), that the worlds of ideas and of reality, of the mind and of physical processes must be distinct. This perspective was further elaborated in the philosophical systems of Plato and Aristotle, and was formally introduced in modern thought by René Descartes (1596–1650). To a large extent, it has permeated through our modern and contemporary views of Scientism, Modernism and Post-Modernism. The resulting dichotomy between the world of the psyche and the domain of physiological processes is in part responsible for the current fragmentation of academic disciplines in the health sciences (e.g. psychiatry and physiology) (10).

Increasingly, however, research in neurobiology has described the processes by which the brain directs, regulates and coalesces mental and physical processes. It is now clear that the mind and the body interact, influence and regulate each other. The perception of stress can lead to production of 'stress hormones', as well as products of the immune system. These 'stress hormones' act in a feedback mechanism to regulate their own production and the production of certain immune products. These immune products act on the brain to modify behavior and ability to perceive and to respond to stressful challenges by inducing lethargy, fever and nausea (i.e. 'sickness behavior'). These phenomena are evident and documented by scientific research data from fish, to rodents, to humans (10–12). An emerging body of fundamental research in mind–body interactions is now finding its way into translational and clinical research, and 'mind–body medicine' is rising in acceptance. Indeed, we have returned to the classic view of *mens sana in corpore sano* (a healthy mind in a healthy body).

Mind–body medicine can be considered as a complementary or an alternative mode to traditional Western medicine, and a variety of other modes of interventions that are presently used in a CAM paradigm, may act in large part via the mind–body connection. For example, they include biofield therapy (use and affect biological energy fields), bioelectromagnetic-based therapy (involve pulse fields, magnetic fields or alternating currents), aromatherapy (utilization of essential oils from herbs), touch-massage therapy (derived from the ancient laying-down of hands) and music therapy (use of sounds and music to calm and to soothe the mind and to heal the body). Alternative modes of mind–body-mediated CAM interventions may also focus on the relationship between musculoskeletal structures (i.e. chiropractic, osteopathic), between the organisms in its natural habitat and environment (naturotherapy) or between health and nutrition (i.e. dietary supplement and vitamin therapy).

The 'Non-Western' CAM Tradition

Non-Western CAM paradigms have a long and varied tradition, culture and history. They include: *Ayùr Veda* (i.e. knowledge of aging and longevity), a medical system that originated in India close to 5000 years ago, that is based on diet and mind–body–spirit balance (13). It defends that health depends on the harmonious balance among three forces: *vàyo* (air, wind, breath), *pittam* (sun, bile) and *kapham* (moon, phlegm). *Reiki* is an ancient Japanese mode of medical intervention that rests on the concept of universal life energy: the *Reiki* practitioner acts as a channel of this energy to heal the patient's spirit, which directs and controls the healing of the body.

Ancient Aztec medicine defended that health at any given time depended on the relative proportion of the interaction of three principal forces (or souls): *tonali*, located in the head; *teyolia* in the heart; and *ihiyotl* in the liver. Traditional Chinese medicine and its component *Qi gong*, which are possibly among the most common CAM paradigms, are based on the *I Ching*, attributed to Huang Ti, the Yellow Emperor of China (2698–2598 BC). In this medical paradigm, health is reflected by the balance and harmony between two forces:

- *Yin* refers to the earth and the moon, cold and wet, and the absence of light; and
- *Yang* refers to the sun and the sky, heat and dry, and the presence of light.

Thus ensue the polarities of light–dark, heat–cold, wet–dry (i.e. *Yin-Yang*).

Disease results from and in the loss of balance between these forces in the *Yin* (i.e. liver, heart, spleen, lungs and kidneys) and the *Yang* organs (gall bladder, small intestine, stomach, large intestine and bladder), and along certain pathways (i.e. meridians). Sickness—i.e. the derangement of *Yin-Yang* harmonious balance—is brought about by the intertwining effect of external influences (e.g. environment: wood, fire, earth, metal and water; seasons: spring, summer, later summer, autumn and winter; winds: east, south, center, west and north) and by internal influences (e.g. humors: tears, sweat, saliva, sputum and urine). Health is regained by reestablishing *Yin-Yang* balance by treating specific points (i.e. acupuncture points) along the meridians, and by the use of certain herbs (e.g. Ginseng) and organic extracts (e.g. shark fin) (14).

Evidence-based Research in CAM in the Next Decades

It is common practice in contemporary medicine to follow stringently the scientific method in the process of validating the efficacy and the effectiveness of new or improved modes of treatment intervention. It follows that the complementary or alternative interventions succinctly outlined above, as well as those not cited, must be validated by stringent research before they can be reliably integrated into traditional Western medicine. The next decades will witness an increasing number of evidence-based research directed at establishing the best available evidence in CAM (15,16).

Evidence-based medicine was first conceived by Archibald Cochrane (1909–88) as a new perspective on medical intervention that must not to be confused with medicine based on research evidence. Evidence-based research is a research movement in the medical sciences that is based upon the application of the scientific method for the conscientious, explicit and judicious use of current best evidence, evaluated by a systematic process, in making decisions about the care of individual patients. By contrast, medicine based on the evidence is the traditional approach to medical treatment, which rests on long-established existing medical traditions, supplemented by individual pieces of research, which may or may not have undergone adequate or sufficient scientific scrutiny.

The second paper in this series of lectures will describe in detail the fundamental elements that constitute evidence-based research, and its applications and implications to the practice of medicine in our times. Suffice to say at this point that clinical and translational CAM research in the 21st century will rely upon an evidence-based model of systematic evaluation of the research evidence. We will propose that progress in evidence-based CAM will actualize along several dimensions. For example, the field of evidence-based research will need to refine and finalize its tools and protocols. The critical process of evidence-based research in CAM rests on the reliability of the process of evaluation of the research methodology, design, and data analysis. The stringency of the tools utilized to evaluate the scientific literature determines the validity of this systematic evaluation. The process of dissemination of evidence-based evaluative outcomes of CAM research will also need to be improved. The integration of CAM into traditional Western medicine depends as much on the fundamental research that demonstrates its clinical effectiveness as on the practical, contextual and intelligible nature of its dissemination. The integration of CAM in every-day medical decision-making and treatment will require a concerted effort to expand and to deepen education about CAM as well as about the systematic and critical process of evidence-based research.

These and other concerns of evidence-based research will be discussed in depth in future papers of this series, as they pertain to CAM.

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