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Challenges facing age-management/longevity medicine

Prior to the discovery of penicillin and production of antibiotics, extrinsic disease was the greatest threat to achieving maximum life potential (longevity). That single event increased life-span several decades for the majority of people living in first world nations. However, protection against lethal infection provided by antibiotics exposed older humans to a wide variety of life-threatening diseases resulting from disintegration of internal order during senescence. These intrinsic diseases including diabetes, stroke, heart attack, cancer, and a multitude of others, resulted in creation of medical subspecialties. Although each specialty focused upon different organs and systems, they all administered treatment in response to disease. In other words, the operative model for modern medicine which deals with intrinsic disease is the same as that which was used for extrinsic disease, ie, a disease occurs and then it is treated. However, unlike therapy for infection which generally cures disease, treatment of intrinsic diseases only provides symptomatic relief, rarely affecting the underlying causes. Also, because it targets specific symptoms, this approach treats the disease condition as an isolated entity, independent of other bodily functions. Thus, the cardiologist, neurologist, allergist, and dermatologist focus their attentions only upon problems occurring within the system(s) limited by their training. Accordingly, they prescribe drugs that were created to specifically suppress or relieve symptoms directly related to the problem(s). Despite the fact that this approach rarely provides a cure, it is effective in extending life, if not necessarily its quality, because many of the symptoms of intrinsic disease such as extremely high blood pressure, severe hyperglycemia, or profound breathing difficulties can lead to fatal complications.

The pharmaceutical industry fits well within the disease model for medical practice. This is because advances in cellular biology and biochemistry allow medicinal chemists to design compounds capable of modulating receptor, enzyme, and other molecular functions that block or attenuate the symptoms of underlying disease. Generally these effects are accompanied by secondary and unintended metabolic consequences. However, if the net result of administering the compound is to relieve primary symptoms then a simple and measurable indicator of efficacy has been achieved and a new drug is born. In other words, the pharmaceutical industry embraces the disease-oriented approach to medical practice because it provides a simple and unambiguous measure of efficacy for their products.

With continuing research into the consequences of aging, it is becoming apparent that medical practice must evolve from this disease-oriented model to one that is health-directed so as to ensure quality of life with longevity. In this alternative approach, patient health and vitality is prolonged and onset of intrinsic disease(s) is delayed or even prevented well into old age. Although this approach is currently being employed by practitioners around the world, it is widely opposed by many in the traditional medical community and especially by the pharmaceutical industry. This is true for several reasons which include the following:

1. To sustain optimal health during aging, integrated functions of interdependent physiological systems must be preserved as much as possible. This is a very difficult task since temporal, quantitative, and qualitative signaling between these functional elements is impossible to simulate perfectly using current technology.

2. A holistic approach to medicine blurs the line between specialties since it requires consideration of the entire body and its interrelated functions rather than single systems in isolation. This requirement tends to diminish a specialists expertise and thus is unacceptable to some, and
3. Effective interventions that delay or prevent consequences of aging are not easily demonstrated because rather than simply reducing the intensity of preexisting symptoms as is required in the disease-oriented model, proof under the health-oriented model requires that efficacy be demonstrated by the absence or delay in onset of symptoms. This is a negative proof that requires large numbers of subjects and extended periods of observation to achieve.

As a result, it is not surprising to find that practitioners committed to their individual specialty approach to patient care are not willing to accept change. Since many of the practitioners of "anti-aging" medicine have little or no classical specialty training, they are often considered unqualified to offer therapies that are the domain of specialists. A relevant example is the dispensing of hormones by those not boarded in endocrinology. Similarly, pharmaceutical companies that see mandates for change in current medical practice as a threat to their "bottom lines" strongly object to these changes.

Another problem facing change to health orientation of medical practice is that it has been sensationalized by the popular media as offering the "fountain of youth". Understandably, this type of publicity, coupled with the activities of unscrupulous entrepreneurs seeking to capitalize upon public demand for longevity, caused the emerging field to be tainted.

Despite these problems, there is a sound basis for seeking interventions in aging that have the potential for successful clinical application. The most relevant of these are studies performed in animals showing that enhancement of neural and endocrine functions increase population life span presumably by reducing the incidence of age-related, intrinsic disease. (Cotzias et al 1974; Walker et al 1988; Besson et al 2003). However, the existence of such support for clinical application of age-management/longevity therapies has not blunted the resolve of those with vested interest in the status quo to block change in medical practice. In fact, their efforts have been strengthened to some degree the actions of several internet and compounding pharmacies that were involved in unprofessional and illegal activities. The owners of those "businesses" were recently indicted for subverting the doctor-patient relationship through illegal sale of steroids and bio-identical hormones purportedly for "anti-aging" purposes. (Leusner et al 2007; O'Keeffe and Quinn 2007).

The primary approach taken by those who wish to block change in medical practice has been to legally challenge the safety of compounded prescriptions used by practitioners of age management/longevity medicine. Their basic argument is that because bio-identical hormones have not passed scrutiny of double-blinded, placebo testing and have not been approved by FDA under a new drug application (NDA), they may be unsafe. The argument is somewhat weak because these products have been used for many years without any indication of public harm. Also, the complainants fail to acknowledge that FDA approval under a NDA does not guarantee safety. In fact, some of the drugs that have been approved for use by the FDA have been reported to have much more severe side effects than any for bio-identical hormones. Some of these include severe heart disease attributed to Vioxx and neurological disorders associated with the use of "statins" and many other FDA-approved drugs (Ray et al 2002; Medications.com 2007).

Furthermore, several FDA-approved drugs have been reported to cause secondary or iatrogenic diseases. Interestingly, these diseases that presumably resulted from side effects of the primary drug have led to development of new drugs to treat their symptoms thereby expanding pharmaceutical sales. For example, Requip is being widely marketed to treat restless leg syndrome which has been associated with the use of Lipitor (www.medications.com). Lipitor is a "statin" drug that inhibits the production of cholesterol which is essential for many bodily functions. By indiscriminately inhibiting cholesterol synthesis in the nervous system, Lipitor may indirectly cause membrane degeneration and contribute to adverse neuromuscular problems. Reports of these relationships have begun appearing in peer-reviewed medical journals, and numerous people have reported similar symptoms at public adverse effect reporting websites such as www.medications.com. These report such problems as "trouble swallowing, trouble talking and enunciating words, feeling constant fatigue, neck aches, motor neuropathy which mimics ALS, blinding headaches, nausea, vertigo, disorientation, memory loss, extremely dry eyes, pain/stiffness in the neck and calf muscles and abdominal pain." Also, as shown in the Women's Health Initiative, synthetic hormones such as medroxyprogesterone that may be more potent than its bio-identical analogue don't necessarily have the same spectrum of actions. As a result, it has the potential to cause side effects through interactions with other hormones that would not otherwise occur with the natural progesterone (Nilsen and Brinton 2003).

These untoward side effects can be explained by the fact that drugs are produced to relieve isolated symptoms

or to produce specific effects. Thus, their actions on other essential aspects of bodily function are largely ignored and at best minimized since they are not part of the disease orientation model.

Finally, a disincentive for pharmaceutical companies to run expensive clinical trials involving products commonly used in prescription compounding for age-management medicine is that they are not patent protected. Thus, no company would expend their resources to meet efficacy and safety standards knowing that their competitors would simply use the same generic product without concern for ownership infringement or violation.

In summary, because recognized training programs for practitioners of longevity medicine do not exist; because of the excessive time, effort and expense required to achieve negative proof for therapeutic interventions in aging, ie, ones in which treatment prevents or delays onset of intrinsic disease; and because protection of investments for proving that bio-identical hormone replacement or similar interventions in aging prolong health and vitality is lacking, the evolution of medical practice from a disease to health orientation will not occur as a smooth transition. Rather, it will slowly struggle for acceptance under the earlier model of common usage. Indeed, there are active assaults against this transition such as the Safe Compounding Drug Act of 2007 proposed by Senators Kennedy (D/MA) Burr (R/NC) and Roberts (R/KS). Under the guise of protecting public safety, the legislation would severely restrict and possibly totally block access of practitioners and their patients to effective compounds for extending health and vitality during aging. While there are organized efforts to prevent these assaults, the burden of facilitating and expediting the process of change in medical practice falls largely upon the practitioners themselves who must report relevant findings to the medical community at large as part of the legitimizing process. Recognizing that many practitioners may not be familiar with the process of writing manuscripts for peer-review in professional journals nor have the time to devote to that task, I suggest a more appropriate alternative. As editor of *Clinical Interventions in Aging*, I urge all practitioners to observe and record outcomes of their treatments. Then these data should be submitted to the Editor as brief descriptions and be included with personal clinical experiences, opinions, outcomes (favorable or adverse), simple case reports, letters, questions, or comments. The contributions will be edited and published in future volumes of the Journal. Although the section in which these reports are to be published will not necessarily meet peer-review criteria, it will serve as a forum for information exchange between practitioners of age management/longevity medicine and perhaps contribute significantly to improving attitudes in support of the changing focus of medical practice from that of disease treatment to health maintenance. In addition, I encourage all who feel that such evolution is important and worth supporting to join the Society for Applied Research in Aging. Become active in its programs for lobbying regulatory agencies to legitimize the field of age-management/longevity medicine so that others may view our professional objectives in a favorable light.

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