

# Geriatrics: Gateway to Next Medicine<sup>§</sup>

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**Abstract:** As Current Medicine faces the mandate for massive reformulation geriatrics provides the template. In it are found the critical new basic science that underlies life-long health, and the time honored tradition of “caring.”

**Keywords:** Aging, death, disuse syndrome, epigenesis, frailty, geriatrics, hypokinetic disease, medication, sedentary death syndrome.

## EVERY PROJECTION CONCLUDES THAT THE GRAY DAWN OF MEDICINE IS HERE.

Demographic and economic data confirm the reality that the medical system faces transformative challenges. There are now 40.3 million Americans over the age of 65 (16% of total population) the health care of whom costs one trillion dollars per year (36% of total cost). These numbers will soar. Meanwhile geriatric medicine exhibits structural lag stuck in the acute care model in an era where needs are categorically different. The article “Geriatrics: the Fruition of the Clinician” was published in 1974 by Steel and Williams [1]. Rereading it evokes a different era. The Steel, Williams article reflected the lowly status of geriatrics within the general medical curriculum at that time. They suggested that the prejudice of ageism infected both the academic and political realms thereby stigmatizing the whole reach of geriatrics. Steel and Williams referred to geriatrics as the “step-child” of medicine, but asserted that the extended scope of geriatrics, its “caring” imperative, should represent the fruition rather than a step-child relationship. A major part of the diminished prestige of geriatric medicine four decades ago was the lack of a sturdy conceptual platform. The entire area of aging related issues was a backwater of scientific pursuit.

## DIFFERENTIATING AGING

The recent decades have generated immense advances in biology. The dominant strategy of scientific inquiry is reductionism that seeks a deeper understanding by focusing on progressively smaller parts of the whole. The culmination of the reductive strategy of big science was the pursuit of the human genome project. Within it was promised the ultimate comprehension of the Holy Grail of Life. The resultant genocentrism transfixed the biological sciences, including geriatrics. Billions of dollars and decades of research effort were spent in the reductive search for a grand unifying theory, “The Theory of Everything.” [2]. The principal

research strategy involved attempts to relate a specific gene to a disease. Notably, identification of “the aging” gene has proven to be futile. Martin estimates that 6000 genes are involved in human aging [3]. It, like virtually all human ailments, is polygenic. Reductionism reached its limit. Insistence on the genome as the object of study failed leaving an intellectual vacuum [4]. Abandonment of the gene focus changed attention to the organism as a whole, the phenotype. The organism is ordained not only by its genotype but is importantly influenced by environment, the Nature/ Nurture interface. The nexus of the organism with its environment is the new platform for study.

## EPIGENESIS

Feinberg locates epigenetics at the “epicenter of modern medicine.” [5]. This change of emphasis from genotype to phenotype is critical as inherent in it is the inclusion of time in the basic formulation. Meanwhile a separate analytic paradigm emerged seeking to establish a new conceptual framework for aging and its accompanying health correlates. An article published in JAGS 20 years ago “Redefining Human Aging” suggested a generic formulation of the determinative health agencies of older people [6]. Three separate and distinct mechanisms were proposed to distinguish the fundamental processes that underlie the heterogeneity of clinical patterns of older persons. “A grandfather’s clock stops running. Either it is worn out, it is broken, or it needs to be wound up.” It is vividly clear that these three diagnostic categories, age, disease, and disuse are casually conflated leading to major errors in resource allocation. A 1987 editorial in JAMA by Wetle was titled “Age as a Risk Factor for Inadequate Treatment” [7]. Suitability for surgery, ICU admission, transplant appropriateness, dialysis are common circumstances in which an age exponential is invoked in decision making. The differential between these three agencies is imprecise and evolving. In the past tuberculosis was labeled as part of the aging process. More recently arteriosclerosis (“a person is as old as his or her arteries”) was labeled as being temporally caused. Currently Alzheimer’s disease, other neurologic conditions, and diabetes are often casually cited to be results of aging.

## DEFINING AGING

In 2007 Hayflick published a paper in the Annals of the New York Academy of Sciences “Biologic Aging is no

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<sup>§</sup>Presented at Annual Meeting, American College of Physicians, Philadelphia 2009, USA.

Longer an Unsolved Problem” [8]. In it he posits a definitive causation of the fundamental basis of aging, an inexorable result of thermophysical decay, codified in the Second Law that Schrodinger invoked in his magisterial statement “What is Life?” [9]. This universal canon underlies all living and inanimate change. It is the source of the physical principles that govern evolution and development. The widespread scaling relationships inherent in Nature are direct resultants of the mathematics that describe the interplay of time, matter, and energy [10]. Aging is the effect of energy flow on matter over time. Such an inclusive definition of aging positions it within the organism, and thereby not contingent on extrinsic agency. In his article Hayflick makes an emphatic differentiation of disease processes from aging with which it is frequently misrepresented resulting in confused strategies and resource allocation. The nearly exclusive dominance of the Disease Model of Medicine distorts research, education, and practice priorities. A different paradigm is required for the illnesses of older persons. Like the dysfunctional grandfather’s clock all 3 agencies must be considered. Insistence on a categorical separation of aging from disease is critical, but insufficient.

## DISUSE

The third major contributor to geropathology is disuse that is almost unrecognized. Such neglect is now front and center. Just as Hayflick identifies the conflation of categorical disease with aging, important too is the distinction between disuse and aging [11]. Disuse represents the prototype of phenotypic plasticity. It is not genetic, it is not disease, and it is not aging. Disuse represents “needing to be wound up”. One of biology’s identifying characteristics is its plasticity [12]. Plants and animals change constantly. Plants become where they live. Animals become what they do. Anabolic and catabolic processes duel to assure the organism sufficient adaptive capacity necessary to cope with the wide range of environmental challenges. There is no stasis in life. Nature abhors stagnation such bodily responsiveness displays diverse time scales according to the different prompts. The turnover of a body is profound. It is ever changing. Estimates are that the atoms of a human body turn over completely 98% per year The Krebs cycle TCA turns over  $2.6 \times 10$  to the 23<sup>rd</sup> times per minute. 50 grams of protein are synthesized and lost daily. We lose 1 million cells per day. Such replacement rates scale according to energetic processes specified by Yates’s term “homeodynamics” [13]. Old cells still divide. Old people still heal. The adjacent issue to this plasticity is the presence of safety factors. A wide survey of bodily structures and functions reveals a range of safety factors which testify to the evolutionary demand for reserve to cope with environmental perturbations. Such survey reveals that there is a 70% safety margin between base line values and evidence of symptomatic loss. Function below 30% of baseline becomes symptomatic and represents the tipping point where most medical encounters occur. The current epidemic of chronic disease confirms the importance of time in pathologic and developmental mechanisms.

## FRAILITY

The looming condition of frailty dominates late life health patterns, and is the leading cause of disability. Frailty

is not aging, and it is not a disease. What is frailty then? Neither old people are frail, nor all frail people old. Fried’s group has done most to explore the emergent common state of frailty [14]. It is defined as a specific phenotypic pattern the predictable result of insufficient energetic input to the organism as nutrient or physical activity. It is the iconic example of phenotypic plasticity [12], as such frailty is not secondary to single component compromise but instead is a reflection of system wide catabolism, the result of down expression of multi-gene networks. A different paradigm is required [15]. The implication is that aging is inevitable but its components are plastic. We cannot change our nature, but our nurture is eminently approachable. This is the job description of geriatric medicine. Perhaps we need a frailtyologist. The entire field of phenotypic plasticity is new. It emphasizes the reality that heredity is not destiny. The study of Fraga in which the gene pattern of twins is virtually identical at birth but by age 50 is widely divergent is an expression of how genes are altered by their differentiated expression over time [16]. Feldman’s work on niche construction emphasizes how the phenotype builds its own environment [17]. It creates its world as it goes. Most chronic diseases display a large phenotypic plasticity component although they lack recognition. Increasing attention is being paid to the biochemical and cellular steps such as chromatin alteration, change in redox potential, and ATP availability which translate energetic stimulus to genetic expression, and subsequent structural and functional potential.

## A NEGLECTED PATHOLOGY

Phenotypic plasticity has only recently been identified as a substantial topic in biological research. But clinical medicine has been almost oblivious to its functional and structural effects on the human life course. The rubrics of “the Disuse Syndrome” [18], “Sedentary Death Syndrome” [19], and Hypokinetic Disease” [20] draw attention to the fact that physical inactivity constitutes a major environmental stimulus particularly as we age. Vascular remodeling, sarcopenia and osteoporosis, the plasticity of the central nervous system are revealed as being intimately tied to physical activity. Blair’s critical paper “Physical Exercise and All Cause Mortality” demonstrates that before age 60 V02 Max differences are not predictive of mortality, but after age 60 V02 Max becomes highly predictive [21], the survival of the fittest. So too does the bed rest study of Levine constitute an ongoing demonstration of structural and functional changes subsequent to bed rest [22]. Bed rest is dangerous and up regulates a cascade of catabolic features. Space medicine data confirm the negative contribution of disuse [23]. In effect fitness corresponds to a 30 year age differential. Furthermore phenotypic plasticity is not age coded, and it is often reversible. Fiatarone’s classic study of the change subsequent to physical conditioning in 90 year-olds is emphatic [24]. Geriatric medicine represents the summation of a lifetime of environmental challenges, positive and negative. Human aging presents a natural experiment to examine the effects of time on the structure and function of the organism. By and large environmental effects have been held to be circumscribed in their effects on the organism. Gerontologists have not tuned in to the

different time scales of an organism and tacitly regarded the effects of behavior as a minor contributor. Development has largely been held to be an autonomous process with negligible participation by temporal effects thereby omitting differential cuing of the phenotype by different behavior types, i.e. disuse. Many of the late life health syndromes are subject to active correction by a physical activity prescription. Such an advance in conceptual formatting critically asserts that aging is not a disease and thereby requires an entirely different paradigm. Life is not a set of separate episodes, but instead is a time integrated process that is separate from the standard disease model of medicine. Rather than most illness being the bodily expression of extrinsic agents on the organism, singly or in combination, in older people it derives from an inappropriate intrinsic interfacing of nature and nurture. Central to the change in focus from genotype to prototype is the dimension of time. Geriatrics by definition is the effect of time in medicine. Aside from pediatrics the remainder of clinical medicine lacks a specific time component. It is never too late to start but always too soon to stop.

### **INSERTING A GERIATRIC MANDATE INTO NEXT MEDICINE [25]**

As we encounter a broad consensus that America's health care system is severely dysfunctional, I nominate geriatrics as an insightful text in the current health care debate. Widely recognized is the need for a reformulation. Geriatrics appears as an appropriate rehab model. As such geriatrics provides a replacement paradigm for Next Medicine. The conditions perfectly fit. "Real life medicine" is at least as much a social science as a laboratory science. Geriatrics is a prime exhibit of this duality. Behavioral determinants dominate technologic features. Health is Choice not Fate. Within its framework geriatric medicine reflects the very essence of medical "caring". The assurance of caring at life's terminus is a central strut of humanity. Its address is a noble calling, and evokes the highest tenets of professionalism. The "art" of medicine finds full display within geriatrics. The diffuse demands of geriatrics require a different competency and compassion. The "caring" aspect of geriatrics is more central to its creed than the more traditional emphasis on "curing". It is characterized by an emphasis on the person as a whole, rather than a mere assemblage of parts. And further the insistence of geriatrics on continuity of caring imprints the centrality of process over episode that characterizes the standard disease model of medicine. It emphasizes health rather than disease, and provides the primary focus of prevention over repair. Adoption of the geriatric formulary and workbook involves a shift in personnel, training, research, and venue. Rather than the ICU and laboratory being the workplace, it becomes the home, school, and office. Behavior becomes the dominant focus of research rather than the gene. Geriatrics stresses the largely unaddressed feature of phenotypic plasticity in which the dynamics inherent in personal lifelong development prevail. The choice newly elaborated by the new science of health, is our obligation to abandon the failed geno-centric model of fate. Geriatrics is optimistic and importantly, it offers the fulfillment of the human potential, which in my view is the very mission of medicine.

Geriatrics has as its prime focus the maintenance of function over time. Geriatrics stresses health preservation over repair. The predominant focus of current medicine is on disease and its subsequent repair strategy. Procedures and pills are its main tools, however the chronic disease arena which features the huge impacts of phylogenetic plasticity does not respond adequately to procedures or pills. Instead, lifelong lifestyle reorientations are mandated. The important statements of Schroeder [26], McGinnis, and Foege [27] are central to this argument.

Emerging are reports of clinical procedures that augment natural reserves [28-30]. No longer is a decreased structural and functional course the obligate modal course of the aging organism. Old dogs and people can still learn new tricks. The innate competence of the aging organism to offset common deteriorative findings particularly with regard to the cardiovascular system is notable [29].

With the compelling demographic and economic forces assuming center stage in healthcare, the lessons inherent in geriatrics are critical as discussed extensively in the recent book *Next Medicine* [30, 31].

A series of articles published about geriatrics includes one that asked "Is Geriatric Medicine Terminally ill?" [32]. My perspective is, as it always has been, that geriatric medicine should not become a narrow circumscribed subspecialty, but broaden into an integrated component of the multiple aspects of the fully lived life. Now that geriatrics has gained a sturdy science to accompany its caring birthright it achieves nobility that earns universal respect and imitation. Geriatric medicine represents a forceful template for the reorganization of medical care with focus on health and prevention rather than the current fixation on disease and repair. Geriatric medicine inherits the mandate to carry this message.

### **CONFLICT OF INTEREST**

The authors confirm that this article content has no conflict of interest.

### **ACKNOWLEDGEMENTS**

Declared none.

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Received: December 24, 2013

Revised: March 28, 2014

Accepted: May 7, 2014

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