Editorial

Throwing Pots and Commitments for 2008

Luigi Ferrucci

Longitudinal Studies Section, Clinical Research Branch, National Institute on Aging, Baltimore, Maryland.

It’s that time of year again when, in a spurt of optimism, many of us make great promises to ourselves about a fresh start in the New Year, when we will do the right things. Let’s be honest, most of the time those commitments are forgotten after few days.

Well, this year I’m going to do something different! Instead of making commitments that can easily be broken, I want to daydream about a better future for geriatric medicine and aging research. Dear Reader, below I share my musings for 2008 with the hope that you can help me bring them to fruition.

Facing Complexity

Advancing age brings increased derangement of multiple interacting, interrelated complex systems (1,2). In just the last decade, we have come a long way toward the goal of better understanding the complexity of aging. We know so much more about how the aging process creates susceptibility to multiple diseases, affects homeostasis, and promotes compensatory mechanisms. I am confident that when we can translate this knowledge into practice, the results will be astonishing. To accomplish this task, there is still much work to be done. In primis, we need to turn to methodology. Many of the design elements and statistical instruments used in geriatrics and gerontological research were developed during an era when identifying risk factors for chronic conditions such as cardiovascular disease and cancer in longitudinal studies was the primary focus. Most of these approaches assume a lag time between risk factor exposure and development of a disease outcome. It is now becoming clear that this paradigm limits our ability to study aging.

Scientists have proposed that the aging process constitutes a constant change across alternative (quantistic) states of homeostatic equilibrium, which requires the reactive tuning of hundreds if not thousands of signaling and metabolic pathways and implies changes in physiology and behavior (3,4). The best way to capture and analyze these processes is still unclear and needs to be better understood and developed. Only a few courageous scientists have ventured in this direction, and their quest for more knowledge is not painless (5,6). A grant proposal aimed at approaching complexity could be triaged for “lack of focus” and “confusion in the aims.” A strict focus on a narrow and well-defined research topic is a premium for promotion and tenure committees, while pursuing complexity might be viewed as “too broad.” A manuscript that applies the paradigm of complexity may be rejected by reviewers because the “journal readers will not understand and will lose interest.” The curious thing is that most of us would probably agree that these attitudes represent the main obstacles to progress. But—wait a moment—we are the “study sections,” we are the “promotion and tenure committees,” and we also are the “journal reviewers.” Thus, this year, the change should start with us.

Nurturing the New Generation of Geriatricians and Gerontologists

Fostering the development of a new generation of geriatricians and gerontologists is both the most important and most challenging objective we must pursue. Given the financial burdens of caring for an increasingly aged population, there is some emergent (mistaken) thinking that prolonged periods of advanced training are an unnecessary luxury. Nothing could be more false. Progress and innovation by creative people nurtured through intensive training must change the course of anticipated events. If not, the health care and retirement security institutions as we know them will be crushed by the demographic imperative and consequent escalation in public costs, even in countries that have long enjoyed universal coverage (3). We desperately need good geriatricians, critical advances in our understanding of aging, and age-related diseases, new tools for the treatment of chronic diseases and the prevention of disability. We bear an enormous responsibility. Education and research, possibly combined, are our only hope.

Unfortunately, I cannot even begin to think how in these times of scarce resources, we can ensure that the new geriatricians and gerontologists have the opportunity to immerse themselves in the state of the art of knowledge. How can they acquire the skills of geriatric medicine and at the same time develop the mental flexibility and strategies they will need to meet the unknown challenges waiting in the mist of the future? Many exceptionally talented individuals are lost from us along the way. I assure you—if we don’t help them quickly—our field will miss them dearly.

Fostering Translational Research

Because older people need more and better opportunities to free themselves from the burden of disease and disability, I wish to make translational research a priority. Sadly, the expression “translational research” has become a mantra in every scientific meeting, a sound bite whose content is
becoming more and more vague and ambiguous. Beyond the stereotypes, however, there is probably no other area within geriatric research that better illustrates the need for a new equilibrium between assuming more responsibility and willingness to take risks. The area of clinical trials has approached older persons with caution, circumspection, and a small dose of shunning (7). One consequence of this attitude is that the safety and efficacy of most treatments administered to older persons were tested in much younger and healthier individuals. An even more striking result is the paucity of development and testing of interventions and management strategies for the geriatric conditions that are so burdensome for frail older persons. Of course, it is our responsibility to protect frail elderly people from injury and abuse. However, similar to educating children, too much protection can be dangerous. Testing a new treatment implies taking some risks. The biological or physiological parameters that we want to modify are interconnected to myriad other mechanisms in a state of equilibrium that has been refined over millions of years of evolution, and has gone through innumerable adaptations during the life of an older individual. To conceive that such a delicate equilibrium can be altered without consequences is foolish. We can only try to ensure that the negative consequences will be small compared to the advantages. The solution is not to create strict inclusion criteria but, rather, to design trials that enable as many people as possible to be eligible and to participate willingly, while at the same time implementing strategies that foster compliance and safety.

We are witnessing a tension between those who struggle to boost the quality of research and clinical care in older persons and the constraints faced by regulatory and funding agencies toward the peculiar problem posed by aging. Those who care for older persons clearly see that their health and well-being cannot be accurately described using conventional definitions of diseases, which remain central to clinical medicine. Sarcopenia, mobility disability, age-related multiple hormone dysregulation, anorexia, frailty, and failure to thrive constitute new and old terminology that geriatricians have generated to better describe the problems that really matter for their patients and that still lack an “official” stamp or label. Having to work within the boundaries of rules and regulations developed at a time when we knew very little about health in older persons, the U.S. Food and Drug Administration (FDA) is faced with the challenge of evaluating clinical trials for new treatments targeted to these “nondisease” conditions. Not surprisingly, the FDA’s transition to a new set of definitions is difficult and we haven’t done much to help them. In spite of the many publications, meetings, seminars, and discussions, there is still wide disagreement on whether the “geriatric conditions” listed above should be considered true clinical entities and, if so, what the standard diagnostic criteria should be.

Clearly, part of the uncertainty concerns a desire for scientific rigor and perfection, but fighting for ownership and antagonistic attitudes within the field also exist. This could be the year for change. We could start by agreeing on operational definitions for the “geriatric conditions” and bring our scientific societies into the decision-making process, thereby obtaining their endorsement. As we gather more information and compare data and experiences, those definitions may be refined, but, at least for now, they will represent a common platform. There is a lot more that we can do:

- Promote the recognition of the appropriate key words into the MeSH list of Medline and other scientific search engines
- Develop specific International Classification of Diseases codes for geriatric conditions
- Expand the geriatric perspective in the “sacred” texts of modern medicine
- Provide robust validity and reliability to geriatrics outcome measures
- Expand the discussion of the unique design features of clinical trials for frail older persons

LEADING THE PACK

When I discuss geriatrics with my friends and colleagues, I always conclude that the major obstacle to progress is inaction, either because of fear of making mistakes, because decision and action create stress and conflict, or because of a sense of subordination to other specialties or fields of research. On the contrary, I wish that geriatricians and gerontologists would stop following and start leading the pack. Geriatric medicine was the first discipline to grasp the relevance of comorbidity, the interaction between environment and the pathophysiology of diseases, the value of physiological compensation, and the difference between disruption of a specific physiologic element that leads to disease and overall dysregulation of the biological network aimed at maintaining homeostasis and coping with stress (3,8,9). Only recently, other specialties have begun to recognize the complexity of health, primarily because they also have begun to understand that the picture of morbidity has mutated. With the aging of the population and improvements in chronic disease management, more and more patients are presenting with complex clinical pictures that require a comprehensive approach. In no way do I want to claim that understanding diseases has become unimportant. Older persons will inevitably develop diseases and require state-of-the-art traditional medical care. However, studies of comprehensive geriatric assessment have suggested that the geriatrician’s emphasis on complexity of health in old age is more effective, and perhaps even more cost effective than the simple medical treatment of diseases. Interestingly, this approach appears to be most effective when the geriatrician’s contribution is not limited to the design of the care plan but is also extended to direct care, including day-by-day adjustment and long-term monitoring (10,11). Given these results, I am puzzled by the suggestion that geriatricians should act as consultants in the network of services (12). I personally believe that geriatricians should be in direct contact with their patients.

We need to have mechanisms that ensure funding for research on aging and that geriatric curricula are truly focused on “aging,” thus entailing a substantive effort toward understanding the aging process and improving care for
elderly people (3,13). We should make an effort to improve the quality of our publications and the “status” of our journals. As the Editor of the Journal of Gerontology: Medical Sciences, I cannot be completely unbiased on this topic, so take my comments cum grano salis (with a grain of salt). I sincerely believe that we should publish some of our best work relevant to aging in geriatrics journals and extensively cite this work in anything we write. No need to argue, I do understand that this might conflict with the need to improve our personal curricula vitae and I am guilty as anybody else of the same sin: I dream to publish my papers in the New England Journal of Medicine, Science, or Nature. Thus, we are all part of the diffuse, negative attitude about the aging literature. If we want to see the fields of aging and gerontology flourish, if we want to have a couple of aging journals in the top tier, we need to break this vicious cycle. In medio stat virtus, do your best—and remember to cite the Journal of Gerontology: Medical Sciences as much as you can.

**THROWING POTS**

In geriatrics and gerontology, the material we work with is similar to the ultimate, finest porcelain. As someone who enjoys working with clay, I cannot even begin to explain how demanding it is to throw porcelain. The raw material has practically no body or strength and, if not treated properly, will collapse during the throwing and crack during the firing. The path to learning to work with porcelain is thorny and paved with many failures and few ephemeral joys. However, if you can handle porcelain, the results can be almost miraculous and unsurpassed by any other material. In the magisterial words of René Dubos in the book *Mirage of Health* (14):

> While it may be comforting to imagine a life free of stresses and strains in a carefree world, this will remain an idle dream. Since the days of the cave man, the earth has never been a Garden of Eden, but a Valley of Decision, where resilience is essential to survival. The earth is not a resting place. Man has elected to fight, not necessarily for himself, but for a process of emotional, intellectual and ethical growth that goes on forever. To grow in the midst of dangers is the fate of the human race, because it is the law of the spirit."

Whether or not you agree with me, whether or not you share my hopes and dreams, I wish we could engage in an open conversation about the future of geriatrics and gerontology in the pages of the Journal. I will be happy to receive and publish your additional thoughts, alternative thoughts, and, especially, disagreements. As long as we all believe that the health and well-being of our elderly patients is what really matters, no obstacle is insurmountable. Our decision, our choices are the ultimate test of our values. Imagine what may happen if . . .

**CORRESPONDENCE**

Address correspondence to Luigi Ferrucci, MD, PhD, Longitudinal Studies Section, Clinical Research Branch, National Institute on Aging, NIA-ASTRA Unit, Harbor Hospital, 5th Floor, 3001 S. Hanover St., Baltimore, MD 21225. E-mail: ferruccilu@grc.nia.nih.gov

**REFERENCES**