Pediatric RESEARCH

COMMENT

The two extremes meet: pediatricians, geriatricians and the life-course approach

Matteo Cesari[1,2], Nicola Vanacore[3] and Carlo Agostoni[1,4]

Pediatric Research (2019) 86:432–435; https://doi.org/10.1038/s41390-019-0479-4

Pediatrics and geriatrics have traditionally occupied the two extremes of the spectrum of medical specialties. They are commonly perceived in antithesis and by no means apt to interact. A pragmatic example was described in a geriatric textbook where such dualism was presented by showing how the same manifestations (e.g., crying, incontinence, dependency, communication difficulties, falls…) are seen as frustrating and negative when applied to an older person, but easily acceptable if presented by a baby.[1] Nevertheless, it cannot be ignored that life is a continuous line with a beginning and an end. Every point of life is sequential and helps define the individual's trajectory as well as offering the opportunity to foresee future health outcomes.[2]

In a world that is globally aging, the increased burden of age-related conditions is threatening the sustainability of our societies and healthcare systems.[3] The traditional definition of older age according to a mere chronological criterion (i.e., the number of years the person has lived) is growingly perceived as obsolete and inadequate.[4,5] It is a fact that age per se only partially explains the individual's health status. Moreover, the number of persons aged ≥65 years is today too large and their health status too heterogeneous to accept this cut point as sufficiently robust/informative to define the criterion for referral to geriatric medicine. The threshold might be raised (e.g., to 70, 75, or even 80 years), but such expedient will likely remain arbitrary and surely not resolutive. There is indeed the necessity to modify the approach to aging. It is necessary to give less importance to the rough criterion of chronological age. Decision algorithms centered on parameters more respectful of the individual's biology (i.e., aging dynamics) should be prioritized. Interestingly, if the value given to chronological age will gradually fade, pediatricians and geriatricians may find themselves closer than expected. It will then be possible, for example, to find the potential for more exchanges in the management of the growing number of individuals who are chronologically young but biologically exposed to accelerated and accentuated aging (e.g., persons with Down's syndrome).[6–8] Pediatricians and geriatricians may find a first/immediate field of interaction in these populations (usually considered "too old for the pediatrician" and "too young for the geriatrician") clearly suffering of unmet clinical needs due to the inadequacy of the current healthcare systems. Bridging the two specialties may mean promoting the continuation of specialist's care in persons presenting a particular clinical complexity. Consistently, synergies in the design of interventions for similar health issues might perhaps be envisaged. For example, interventions tackling nutritional deficiencies can be seen as symmetric and responsive to similar challenges at the two extremes of life. Both infants and older persons are exposed to the risk of malnutrition and qualitatively poor diet. The need of favoring accessibility while responding to individual tastes determines an important challenge. In both cases, phobic behaviors against specific foods (i.e., new experience for the infant, unpleasant past experience for the older person) may further cause malnutrition. Furthermore, both populations may need external help for feeding. As a common result, similar nutritional deficiencies (e.g., energy, protein, water, vitamins, minerals) may develop, potentially to be targeted by common interventions characterized by easy-to-assume formulas, enriched with selected micronutrients (e.g., zinc, liposoluble vitamins), specifically focused at promoting the efficiency of the immune system.

Under this scenario, geriatricians have been developing instruments aimed at bypassing the traditional canons of chronological age and diseases. A wide spectrum of geriatric tools is today available for measuring the homeostatic vulnerability of the person and the age-related accumulation of deficits.[9] By paying special attention to the individual's functions and capabilities, geriatric medicine has chosen to favor an approach capable of better reflecting the person's biology with the final aim of promoting the personalization of care.[10]

As described by Kuh and colleagues,[11] during the first years of life, the individual generates his/her capital of biological reserves that will set the starting point of the physiological decline expected during the second part of his/her living. The more reserves the individual will accumulate during his/her young and adulthood (through genetic profile, intrauterine conditions, fetal growth rates, post-natal biological development, healthy lifestyle, education, social network, access to care and preventive campaigns…), the higher will be the amount of resources on which he/she will rely on for his/her second part of life. This means that, although the unavoidable age-related decline of function may still follow a similar pattern across individuals, those with healthier growth at the beginning will benefit from larger biological capital "to spend" before the onset of clinical manifestations at older age. They will, thus, be in a more favorable position for delaying the incidence of disabling conditions that occur in the geriatric population. At the same time, it is also noteworthy how the order in which functions are lost during the age-related disabling process is consistent with the progression of functional development seen in the young child.[12,13] In other

[1]Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy; [2]Geriatric Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [3]National Centre for Disease Prevention and Health Promotion, National Institute of Health, Rome, Italy and [4]Pediatric Intermediate Care Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
Correspondence: Matteo Cesari (macesari@gmail.com)

Received: 12 May 2018 Revised: 19 March 2019 Accepted: 14 June 2019
Published online: 25 June 2019

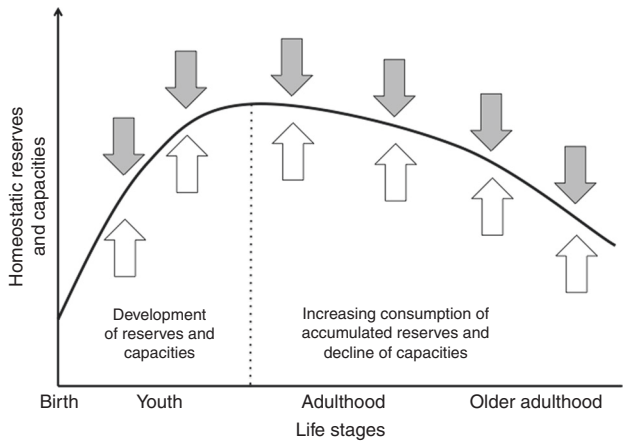

Fig. 1 The life-course approach bridging the two extremes of life. Modified from Kuh et al.[11] and Kuruvilla et al.[14] The black line describes the parabola of the person's homeostatic reserves and capacities from birth to older adulthood. The gray and white arrows, respectively, represent the negative and positive stressors acting over the trajectory, modifying its course across life stages

words, our functional life might be described as a parabola, in which the first years of life determine the height of the vertex and this latter influence the health status experienced during the descending part of the curve[14] (Fig. 1).

Unfortunately, although pediatrics and geriatrics are pushing their boundaries one toward the other, a gap in the middle still divides them. The most known scientific hypothesis possibly filling this gap is represented by the "thrifty phenotype hypothesis," raised by the epidemiologist David Barker and described by the chemical pathologist Nick Hales in the early Nineties. The starting point can be found in the retrospective observations of a cohort of 64-year-old men ($n = 648$) living in the Hertfordshire for whom birth weight records were available. It was demonstrated that the incidence of diabetes was six-fold higher in men with low birth weight compared to those with the highest records.[15] It was then proposed that one of the major long-term consequences of inadequate early nutrition was an impaired development of the endocrine pancreas, thus determining the increased susceptibility to type 2 diabetes and its metabolic complications. It was thus hypothesized that the poor nutrition of the fetus and infant could be the cause of permanent changes of specific organs and tissues.[16] Retrospective observations also considered the unfavorable role of "rapid weight acceleration" through all the pediatric age.[17] Both these hypotheses have generated a plethora of studies over the following 25 years, discussing the role of the maternal nutrition up to the "first 1000 days", from genomics to epigenetics.

Longitudinal studies conducted by pediatricians allow for better insights into how interventions impact the mental development,[18,19] the onset of chronic diseases normally associated with adulthood (e.g., obesity,[20] insulin resistance,[21] hypertension[22]), and future healthcare costs.[23] Accordingly, the former hypotheses have been switched towards a more generic "early life programming".[24] Under this scenario, it is today possible to identify multiple interventions able to modify the future trajectory of the health status when implemented at early life. Among the most promising actions, lifestyle modifications (i.e., physical exercise and nutrition across pregnancy), treatment of maternal mood disorders, and environmental improvement (against prenatal teratogenicity and neurodevelopmental toxicity) are probably those with strongest evidence.[25] At the other end of the spectrum, geriatricians have been trying over the past decades to anticipate the assessment of older persons in order to identify those more prone to decline and put in place preventive strategies before the onset of irreversible age-related conditions.[26,27]

As a matter of fact, most studies still remain confined to the maternal–infant area. At the same time, the management of older persons finds difficulties at systematically being based on the clinical life course of the individual. Even at the level of insurance companies and public health institutions, this type of data is lacking. A simple reason might be found in the fact that studies funded with the original purpose to explore long-term outcomes have been funded only 30–40 years ago. The Special Turku Coronary Risk Factor Intervention Project (STRIP)[28] is a first example in Europe, but it has been limited to the achievement of early adulthood. In the United States, the Bogalusa Heart Study,[29] based on observational data, was started in 1972 and is still ongoing. Nevertheless, we still lack homogeneous observations directly linking the young with the old and vice versa, thus the "tomb in the womb" largely remains a suggestive hypothesis with some supportive suggestions. To make possible the connection of the two worlds, it is necessary to standardize language and methodologies while planning long-term observations of participants enrolled in relevant randomized controlled trials. It is important in this context to put aside paradigms of traditional medicine centered on age and diseases in order to favor new models of research and care based on functions, comprehensive assessment, and analysis of interacting biological phenomena throughout the life span. These initiatives might be methodologically complex to design and conduct, as also demonstrated by some paradigmatic negative experiences (e.g., the National Children's Study).[30] Nevertheless, long-term longitudinal studies potentially following participants from "womb to tomb" may not be impossible, as the ongoing Dunedin Multidisciplinary Health and Development Study[31] might suggest after almost 50 years of activity.

Under a public health perspective, the cultural encounter between pediatricians and geriatricians has not yet generated policies oriented to an evidence-based approach for the life course. However, there is already consistent evidence showing the potential in this field. For example, it has been demonstrated that social isolation and loneliness are associated with worse cardiovascular and mental health outcomes;[31] or that the nutritional status of both women and men before conception has profound implications for the growth, development, and long-term health of their offspring;[32] or that the exposure to green space in early life may support better cognitive function later in life.[33] These data should lead to specific, measurable, and reproducible policy actions, also allowing comparisons across regions and countries.

Interestingly, in a recent article published in the Bulletin of the World Health Organization (WHO),[14] Kuruvilla and colleagues explain the benefits of connecting the first and second halves of life with the aim of improving personalization of care and promote a sustainable development to health. Thus a model of healthy aging based on a life-course approach is not that utopian and may indeed pave the way for exchanges between the two medical disciplines covering the extremes of life. Only this model may actually help filling the gap of knowledge, linking with robust numbers obtained from ad hoc designed studies the two extremes of life. In fact, the pediatrician's knowledge on how biological reserves and resilience can be generated will here perfectly inform and complement a discussion about the complexity of the failing systems that is usually managed by the geriatrician. In other words, it might be possible that experiences from the two backgrounds could be shared in order to synergistically act using their fully complementary knowledge and reshape the individual's biology across his/her life experience. Accordingly, we should endorse an experience-based medicine (extremely relevant even for the creation of innovative "shared" approaches), while waiting for a robust evidence-based approach (probably for still many years).

Under this perspective, it is noteworthy the novel construct of intrinsic capacity recently proposed in the WHO World Report on Ageing and Health.[34] In an innovative framework of healthy

ageing, the WHO defines intrinsic capacity as the composite of all the physical and mental capacities of the individual. By interacting with the surrounding environment, intrinsic capacity concurs at defining the person's functional ability (i.e., the health-related attributes that enable people to be and to do what they have reason to value). The model is inspired by the attempt to promote a different approach toward aging and age-related conditions and accordingly modify our public health, clinical, and research paradigms (largely unresponsive to the needs and capacities of older persons).[35]

This framework is theoretically conceived for being applied to individuals aged above the country-specific median of life expectancy at birth. However, it is still rooted on several well-established and peculiar concepts shared by both the pediatric and geriatric disciplines, such as the need of a holistic approach to the individual while interacting with the other medical specialties, or the consideration for the socio-economical background. Pediatricians and geriatricians well know how the outcome of (chronic) conditions is largely related to socio-economic determinants.[36,37] Within this context, it is thus not surprising the capillarity that these specialties have always been looking for in the community, seeking to bridge hospital and primary care as much as possible. It is indeed in such kind of networking that geriatricians and pediatricians may effectively interact and serve institutional/governmental bodies in the definition of cost-effective interventions characterized by continuity of care.

The aging phenomenon is increasingly perceived and considered both at the population level (where the most negative consequences of it are growingly recognized and feared) as well as within the scientific community. The correct appreciation of the older person's conditions (thus the design of the correct interventions) needs to take into account that those abnormalities and their progression might date back several years (if not decades).[38] Therefore, clinical decisions are not taken on the basis of arbitrarily designed and cut-point-driven algorithms but supported by the analysis of the trajectory that the individual's functions are following. A similar approach is nested in the pediatrician's background as exemplified by the existence of instruments as the pediatric growth charts. The pediatrician uses them to intervene when the monitored trajectory deviates from a normal pattern. In other words, he/she is not focused on the result of a standalone assessment but on the longitudinal evolution of the case. It is noteworthy that the WHO is planning to possibly generate in the future a sort of nomograms for intrinsic capacity in order to obtain an instrument able to monitor the trajectories of the physiological decline in the aging individual and promote pro-active/preventive interventions.[39] In this context, it is not negligible the clear vision for the future implementation of technologies in the definition and monitoring of the individual's functions for both clinical and public health purposes. Today, technologies (e.g., actimeters, voice recognition devices…) are already able to monitor functions and detect eventual changes of clinical relevance.[40] In other words, it is foreseeable that, in the next future, this kind of information will increasingly come to support clinical interventions[41] and public health strategies.[42] This means having the potential for generating novel sources of (clinical and research) information based on the longitudinal monitoring of the individual across his/her life stages.

The reason why pediatricians and geriatricians should be kept separated and unable to communicate is simply illogical given the unity of the life course. Categorizing the life experience into phases may surely make sense from a clinical/practical viewpoint but still represents an old-fashioned way to approach themes concerning the aging process. The integrity of the individual across the continuum of his/her life should be preserved in order to develop personalized and biology-driven care interventions. Ideally, the pediatrician and the geriatrician should aim at stretching their knowledge as much as possible to meet at the edge of their index fingers, like God and Adam in the Michelangelo's masterpiece at the *Cappella Sistina* in Rome, giving origin to a new era in medicine and prevention.

AUTHOR CONTRIBUTIONS

All the authors contributed to the design, development, drafting, and critical revision of the article.

ADDITIONAL INFORMATION

Competing interests: The authors declare no competing interests.

Publisher's note: Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

REFERENCES

1. Senin, U., Cherubini, A. & Mecocci, P. [*Paziente Anziano, Paziente Geriatrico e Medicina Della Complessità. Fondamenti di Gerontologia e Geriatria*] (EdiSES, Naples, 2013).
2. Cesari, M., Vellas, B. & Gambassi, G. The stress of aging. *Exp. Gerontol.* **48**, 451–6 (2013).
3. Tinetti, M. & Fried, T. The end of the disease era. *Am. J. Med.* **116**, 179–85 (2004).
4. Franceschi, C. et al. The continuum of aging and age-related diseases: common mechanisms but different rates. *Front. Med. (Lausanne)* **5**, 61 (2018).
5. Mitnitski, A., Howlett, S. & Rockwood, K. Heterogeneity of human aging and its assessment. *J. Gerontol. A Biol. Sci. Med. Sci.* **73**, 877–84 (2017).
6. Carfì, A. et al. Characteristics of adults with down syndrome: prevalence of age-related conditions. *Front. Med. (Lausanne)* **1**, 51 (2014).
7. Carfì, A., Brandi, V., Zampino, G., Mari, D. & Onder, G. Care of adults with Down syndrome: gaps and needs. *Eur. J. Intern. Med.* **26**, 375–6 (2015).
8. McCabe, L. L., Hickey, F. & McCabe, E. R. B. Down syndrome: addressing the gaps. *J. Pediatr.* **159**, 525–6 (2011).
9. Mitnitski, A., Mogilner, A. & Rockwood, K. Accumulation of deficits as a proxy measure of aging. *ScientificWorldJournal* **1**, 323–36 (2001).
10. Applegate, W., Blass, J. & Williams, T. Instruments for the functional assessment of older patients. *N. Engl. J. Med.* **322**, 1207–14 (1990).
11. Kuh, D. & New Dynamics of Ageing (NDA) Preparatory Network. A life course approach to healthy aging, frailty, and capability. *J. Gerontol. A Biol. Sci. Med. Sci.* **62**, 717–21 (2007).
12. Katz, S. Studies of illness in the aged: the index of ADL: a standardized measure of biological and psychosocial function. *JAMA* **185**, 914 (1963).
13. Katz, S., Downs, T., Cash, H. & Grotz, R. Progress in development of the index of ADL. *Gerontologist* **10**, 20–30 (1970).
14. Kuruvilla, S. et al. A life-course approach to health: synergy with sustainable development goals. *Bull. World Health Organ.* **96**, 42–50 (2018).
15. Hales, C. et al. Fetal and infant growth and impaired glucose tolerance at age 64. *BMJ* **303**, 1019–22 (1991).
16. Hales, C. & Barker, D. Type 2 (non-insulin-dependent) diabetes mellitus: the thrifty phenotype hypothesis. *Diabetologia* **35**, 595–601 (1992).
17. Barker, D., Osmond, C., Forsén, T., Kajantie, E. & Eriksson, J. Trajectories of growth among children who have coronary events as adults. *N. Engl. J. Med.* **353**, 1802–9 (2005).
18. Lucas, A., Morley, R., Cole, T. & Gore, S. A randomised multicentre study of human milk versus formula and later development in preterm infants. *Arch. Dis. Child. Fetal Neonatal Ed.* **70**, F141–6 (1994).
19. Agostoni, C. et al. Developmental quotient at 24 months and fatty acid composition of diet in early infancy: a follow up study. *Arch. Dis. Child.* **76**, 421–4 (1997).
20. Stettler, N. Nature and strength of epidemiological evidence for origins of childhood and adulthood obesity in the first year of life. *Int. J. Obes. (Lond.)* **31**, 1035–43 (2007).
21. Singhal, A., Fewtrell, M., Cole, T. & Lucas, A. Low nutrient intake and early growth for later insulin resistance in adolescents born preterm. *Lancet* **361**, 1089–97 (2003).
22. Forsyth, J. et al. Long chain polyunsaturated fatty acid supplementation in infant formula and blood pressure in later childhood: follow up of a randomised controlled trial. *BMJ* **326**, 953 (2003).
23. Agostoni, C. & Fattore, G. Growth outcome: nutritionist perspective. *World Rev. Nutr. Diet* **106**, 12–8 (2013).
24. Lucas, A. Programming by early nutrition: an experimental approach. *J. Nutr.* **128**, 401S–406S (1998).
25. Langley-Evans, S. Nutrition in early life and the programming of adult disease: a review. *J. Hum. Nutr. Diet* **28**(Suppl 1), 1–14 (2015).
26. Morley, J. et al. Frailty consensus: a call to action. *J. Am. Med. Dir. Assoc.* **14**, 392–7 (2013).

27. Galvin, J. Prevention of Alzheimer's disease: lessons learned and applied. *J. Am. Geriatr. Soc.* **65**, 2128–33 (2017).
28. Nupponen, M. et al. Metabolic syndrome from adolescence to early adulthood: effect of infancy-onset dietary counseling of low saturated fat: the Special Turku Coronary Risk Factor Intervention Project (STRIP). *Circulation* **131**, 605–13 (2015).
29. Yan, Y. et al. Black-White difference in the impact of long-term blood pressure from childhood on adult renal function: the Bogalusa Heart Study. *Am. J. Hypertens.* **31**, 1300–1306 (2018).
30. Landrigan, P. J. & Baker, D. B. The National Children's Study — end or new beginning? *N. Engl. J. Med.* **372**, 1486–7 (2015).
31. Poulton, R., Moffitt, T. E. & Silva, P. A. The Dunedin Multidisciplinary Health and Development Study: overview of the first 40 years, with an eye to the future. *Soc. Psychiatry Psychiatr. Epidemiol.* **50**, 679–93 (2015).
32. Leigh-Hunt, N. et al. An overview of systematic reviews on the public health consequences of social isolation and loneliness. *Public Health* **152**, 157–71 (2017).
33. Barker, M. et al. Intervention strategies to improve nutrition and health behaviours before conception. *Lancet* **391**, 1853–64 (2018).
34. WHO. *World Report on Ageing and Health* (World Health Organization, Geneva, 2015).
35. Beard, J. & Bloom, D. Towards a comprehensive public health response to population ageing. *Lancet* **385**, 658–61 (2015).
36. Sereni, F. et al. Social and economic determinants of pediatric health inequalities: the model of chronic kidney disease. *Pediatr. Res.* **79**, 159–68 (2016).
37. Andrew, M., Mitnitski, A. & Rockwood, K. Social vulnerability, frailty and mortality in elderly people. *PLoS ONE* **3**, e2232 (2008).
38. Cesari, M. & Canevelli, M. Horse-racing effect and clinical trials in older persons. *Front. Aging Neurosci.* **6**, 175 (2014).
39. Beard, J. et al. The World Report on Ageing and Health: a policy framework for healthy ageing. *Lancet* **387**, 2145–54 (2015).
40. Steinhubl, S., Muse, E. & Topol, E. The emerging field of mobile health. *Sci. Transl. Med.* **7**, 283rv3 (2015).
41. Snyder, A., Colvin, B. & Gammack, J. Pedometer use increases daily steps and functional status in older adults. *J. Am. Med. Dir. Assoc.* **12**, 590–4 (2011).
42. Althoff, T. et al. Large-scale physical activity data reveal worldwide activity inequality. *Nature* **547**, 336–9 (2017).