

CENTENARIANS IN GOOD HEALTH CONDITIONS

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Italian Multicenter Study on Centenarians (IMUSCE)**

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SUMMARY

The increased survival of the population represents the most relevant demographic phenomenon during the end of the 20th century. Aging of the population is correlated with two factors: (i) reduction of the birth rate, and (ii) decrease of mortality rate. The progressive increase of the advanced age suggested the necessity of analyzing absolutely new aspects and facts, namely the properties of centenarians. The true centenarian subjects are in good clinical conditions, therefore, we can call them healthy centenarians. This is the reason why we can classify the centenarians in 3 groups on the basis of the criteria evaluating the clinical and physical conditions of them (groups A, B, C, being in good, moderate or poor clinical conditions, respectively). The healthy centenarian subject had overcome the negative environmental factors, and therefore, his/her survival is accompanied by a slow and gradual loss of the reserves of functional capacities, i.e., the exhaustion of the factors being the true determinants of the longevity.

Keywords: centenarians, successful aging, healthy centenarians

INTRODUCTION

One of the most important phenomena, especially in the industrialized countries is the increase of the medium life span and the aging of the population. The prolonged aging process is a peculiarity of the human species, and the protected ones (e.g., the domestic animals). The increased life expectancy is not contradicting the basic concepts, namely that the maximum life span is species-specific, and it is genetically determined. It seems to be likely that those limits may be extended in the future.

Nevertheless, aging cannot be considered as a programmed process regulated only by genetic control. On the contrary, we have to admit the polygenic hypothesis of the determination of longevity. The coexistence of other factors is possible, both of genetic basis (e.g., hyperlipoproteinemias, thalassemia, etc.) and of environmental type (like social problems, stress, poorly stimulating environment, missing social relations, nutritional dysba-

lance, tabagism, etc.) being able to interfere with various mechanisms and to reduce life expectancy.

In addition, numerous factors are of a certain importance, being able to cause molecular, cellular or oxidative damages, mitochondrial alterations, somatic mutations. Aging can be considered, therefore, as a network characterized by numerous cellular, molecular and environmental factors, and furthermore, a certain activity and efficiency should also be attributed to the immune system, and to the endocrine factors (Franceschi et al., 1995).

The elderly subjects today are in better conditions than individuals of the same age in the past, as it has been evidenced by numerous longitudinal studies (Olsen et al., 1991; Amaducci et al., 1993; Maggi et al., 1994, 1995; Maxson et al., 1997). In the entire industrialized world, the proportion of elderly is progressively increasing, due to both the increased medium life span, and the decreased birth rate (Figure 1).

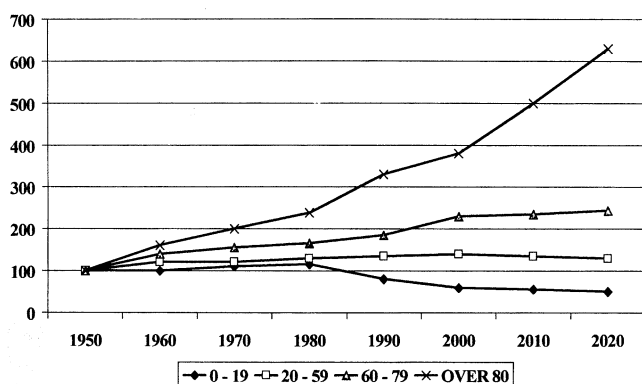


Figure 1. Relative changes in the composition of the Italian population by age-classes since 1950 and forecasts until 2020, taking the values of 1950 as 100 %.

The trend shown by Figure 1 causes inevitably also an increase of the fraction of disabled elderly. Nevertheless, it seems that this tendency has recently decreased due to a progressive improvement of the clinical conditions of the elderly subjects (Kramer, 1980; Golini et al., 1995; Pasqualini and Salvioli, 2000). The increased survival causes particularly the extension of degenerative phenomena, with direct consequences on the elderly subjects. This explains the increased occurrence of causes of death in the advanced age, such as vascular, cerebral and cardiac accidents, renal insufficiency, neoplasias, and the observation of an increased frequency of arteriosclerotic alterations. The increased medium

survival caused also a longer life of the women, compared to men. In our opinion, this phenomenon is connected to the protective effects of estrogens on the vascular complications.

The degenerative processes of arteriosclerotic origin appear after a period of the presence of risk factors. Because the protective effects of the estrogens decrease or disappear during the menopause, the risk factors become of the same significance both in women and men, with the only difference that their full effects appear in women about 30 years later than in men. In addition, the protective action of estrogens in women of advanced age might be responsible for the prolonged survival under deteriorated clinical conditions. The natural consequence of the progressively increasing medium life span is a new phenomenon, which may be defined as “centenaryness”.

For example, in Italy, we had only 49 centenarians in 1921, this number was 1,304 in 1981 (Antonini et al., 1987), growing to almost 5,000 by 1997, and to 8,300 in the projection for 2020 (Figure 2). The maximum human life span was estimated as 120 years. An excessively longevous woman was the French Jeanne Calmant (Guinness dei primati, 1997) who has reached the age of 122 years. The centenarians are characterized by a progressive, slow loss of their reserve functional capacities, i.e., their survival is really determined by genetic factors, influenced by environmental and socio-economic factors.

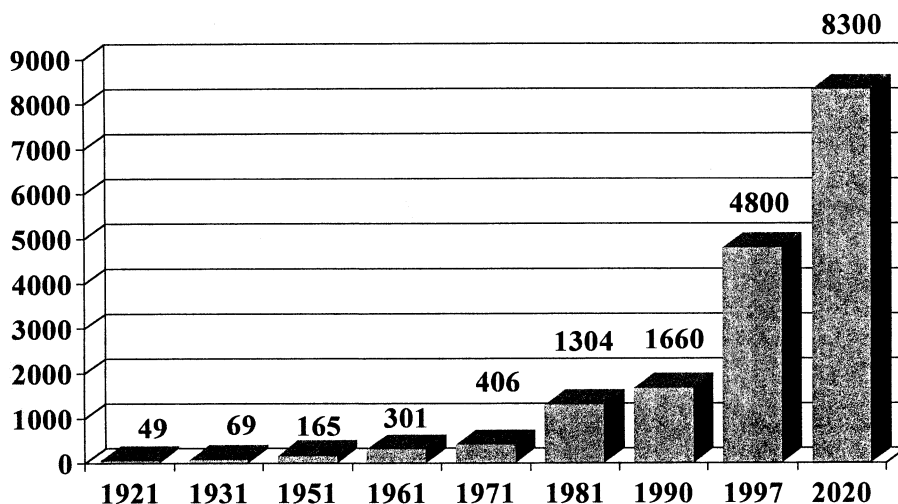


Figure 2. The real numbers of centenarians in Italy since 1921, projected until 2020. (IMUSCE, 1995).

The identification of the genes and the life style, being able to protect us against the most important diseases, like tumors, cardiovascular, metabolic diseases, dementia, could certainly improve our understanding on the biological basis of the longevity. The increasing number of centenarians in the world is correlated with the decrease of numerous negative factors (low hygiene, infectious diseases, nutritional deficiencies, bad socio-environmental situations), and with the increase of positive ones (better socio-sanitary assistance, better hygiene, better nutritional status). The death-causes are often related to accidental external factors, like falls, a sudden catch of cool, which may interrupt a weak equilibrium.

SUBJECTS AND METHODS

Our study pool consisted of 546 centenarians, mean age 101.40 ± 1.65 years representing all the regions of Italy, used also for the studies of IMUSCE (1995). According to our studies, this pool represents more than 10 % of all the actually living centenarians in Italy. This fact renders the sample quite important. Actual age- and sex-distribution in the sample is shown in Table I. Since the beginning of these studies, it was evident that the centenarians display a wide variety of individuals, who may be classified clinically in 3 main groups, A, B, C, being in good, moderate or poor clinical conditions, respectively.

Table I

AGE- AND SEX-DISTRIBUTION OF THE CENTENARIAN STUDY POOL

Years	100	101	102	103	104	105	106	107	108	109
F (n)	162	118	55	46	23	13	7	3	1	3
%	30.1	22.0	10.2	8.6	4.3	2.4	1.3	0.6	0.2	0.6
M (n)	40	35	15	10	3	2	2	-	-	-
%	7.4	6.5	2.8	1.9	0.6	0.4	0.4	-	-	-
Total n	202	153	70	56	26	15	9	3	1	3

Notes: F = females, M = males, n = number

In order to define the inclusion and exclusion criteria, the points of views of evaluations and classifications, we applied a questionnaire with the following contents.

- (i) Personal data: birth date, marital status (checked in relevant documents).
- (ii) Social environmental conditions: scholar years, hobbies, life and family style, habits.

- (iii) Family anamnesis: health status of living parents.
- (iv) Physiological anamnesis: food, alcohol consumption, smoking habits.
- (v) Recent and remote pathologies: identification of symptoms of the principal pathologies, insight into the medical reports.
- (vi) Sensory evaluation: hearing and sight (with lecture of optometric scale).
- (vii) Pharmacological anamnesis.
- (viii) Objective physical examination: head, neck, heart, lung, abdomen, musculo-skeletal and articular apparatus, nervous system.
- (ix) Evaluation scales like mini mental state examination (MMSE) (Folstein et al., 1975); geriatric depression scale (GDS) (Brink et al., 1982); activity of daily living (ADL) (Katz, 1983), and instrumental activity of daily living (IADL) (Lawton and Brody, 1969).

In addition, routine laboratory tests have also been recorded, such as blood counts, serum ferritin, transferrin, rest-nitrogen, alkaline phosphatase (ALP), protein contents, aspartate transaminase (AST), Na, K, thyroid stimulating hormone (TSH), creatinine, glucose, alanine aminotransferase (ALT), and cholesterol levels. A careful, critical evaluation allowed us to divide the centenarians in the following 3 groups based on the listed criteria, applied also by IMUSCE (1995).

Group A (with good health status): Absence of physical disabilities, severe cognitive impairment, clinically severe disease, ictus during the preceding 6 months, severe renal failure, severe anemia, and of any other severe disease.

Group B (with moderate health status): all the subjects who could not be classified as groups A or C.

Group C (with bad health status): Presence of severe cognitive impairment (MMSE < 12), severe physical impairment (ADL = F-G; IADL = 0), cancer, ictus during the preceding 6 months, anemia (hemoglobin < 7 g/dl), severe liver disease, renal failure.

RESULTS AND DISCUSSION

The centenarians had the distribution in groups A-C on the basis of the above criteria, as shown in Table II.

The first observation to be made is that group A represents a minority in the total pool of centenarians. As it could be expected, females are prevailing in our total study pool. Nevertheless, the sex ratio of centenarians is shifted in favor of the males in the group A. This phenomenon may be the natural consequence of the high prevalence of females with disabilities, and chronic, degenerative pathologies in this late age.

Table II

AGE- AND SEX-DISTRIBUTION OF CENTENARIANS IN THE FUNCTIONAL GROUPS

Groups	Number	% of total	Females	Males
Group A	118	21.6	78	40
Group B	184	33.7	145	39
Group C	234	42.9	205	29
Unevaluable	10	1.8	7	3
Total pool	546	100.0	435	111

The centenarian subject, on the one hand, is an individual displaying a delayed aging process, arriving very slowly to the age when more and more severe pathologies will appear, however, this type of aging is the result of an accidental situation. On the other hand, he/she is also characterized by a relatively good clinical status, displaying physiological aging phenomena. From the mixture of various manifestations of this process, various sub-groups come into being displaying more or less severe clinical conditions. The "true centenarian" is who belongs to our group A, having eventually some modest signs of restricted pathologies, localized to some organs or apparatuses (e.g., hypoacusia, locomotor disorders, etc.). These subjects may be called centenarians in good health, representing the ideal, successfully aged individuals (Motta et al., 2000). These subjects have the main characteristics listed in Table III.

Table III

LIST OF MAIN ITEMS IN THE PROFILE OF CENTENARIANS IN GOOD HEALTH

Civil status: widowhood
 Familiar background: comfortable flat, with relatives, or institutionalized
 Residence: prevalently in urban areas
 Good education level
 Long-lived parents
 Intense working activity
 Fair autonomy
 Mediterranean diet
 Risk factors: low occurrence and slighter clinical manifestations, than in the average elderly
 Normal clinical parameters
 Extreme fragility

The existence of at least a group of centenarians in good health gains a particular importance, if considering that several Danish scientists are of the opinion that the centena-

rians have always various chronic complications, therefore, they cannot be considered as healthy in any aspects (Andersen-Romberg et al., 2001). Apparently, there is no doubt that there exists a group of centenarians, which obviously displays the signs of aging, however, without any particular alterations (demonstrated also by autopsies) (IMUSCE, 1995). These subjects are almost completely autonomous, and able to take care of themselves.

On this basis, however, we prefer the usage of the term “centenarians in good health conditions” instead of healthy centenarians. This approach is supported also by our data obtained for the 3 functional groups of the centenarians (Table II). These results show unanimously that it is possible to maintain a relatively good level of autosufficiency and cognitive performance even in the ultralongevous individuals.

In our view, the centenarians in good health conditions remained relatively intact from the negative environmental factors, and their long survival is due to their inherent genetic species-specific characteristics, determining the maximum life span. It is important to stress, however, that even these elderly subjects are characterized by a phenomenon of extreme interest, which is the frailty. It means that the functional reserves of the oldest-old subjects are gradually lost, i.e., the genetic factors involved in the maintenance of longevity are gradually exhausted.

Until now we have been unable to prolong directly the human life span. The improvement of the medium life span in the modern societies is related rather to the elimination of a series of factors influencing negatively the survival. Consequently, one can predict that as soon as we shall be able to reduce further the negative environmental factors, the number of centenarians and also their age may increase, until we can reach the genetically determined maximal human life span. This process implies that the oldest-old age group in the future will consist prevalently of women, however, they will show a high incidence of morbidity and disability in the extreme ages with a progressive loss of autosufficiency and autonomy.

There is an old aphorism saying: “One is born, ages and then dies”. It has ever been a dream of humans to become immortal and young forever. Gerontology is aimed at bringing humans to an old age worth of living. This might be realized by reaching the physiologically aged status, which is devoid of polypathologies, and characterized only by age-specific processes. The actual model of this type of aging is, between dream and reality, the centenarian in good conditions of health.

The suggestions which may derive from the observations of the great olds, are rather simple: we need a good genetic basis, a healthy alimentation, proper physical exercise, to

maintain normal body weight, to consume only a few pharmacas, to think in a positive way and to like to live. Only in this way we can hope to become centenarians of the third millennium.

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APPENDIX

List of participants in the Italian Multicenter Study on Centenarians (IMUSCE) in various cities of Italy. All the participants had equal merits in the realization of this work (Coordinators were: C. Franceschi (Ancona) and L. Motta (Catania)).

Bari: A. Capurso, A.M.Colacicco, V. Solfrizzi
 Bologna 1 : M. Bonafe' , C. Barbi
 Bologna 2 : A. Gaddi, S D'Addato, Z. Sangiorgi
 Brescia : m. Trabucchi, S. Boffelli, R. Rozzini
 Catania 1 : R. Rapisarda, F.B Tomasello, E. Bennati
 Catania 2: L. Ferito, A. Frantone, A. Zoccolo
 Catanzaro : F. Perticone, L. Nardi, M. Berardelli
 Cosenza : G. De Benedictis, E. Falcone, M. De Luca
 Firenze 1 : G. Casotti, D. Monti, E. Petruzzi
 Firenze 2: S. Sorbi, E. Grassi, S. Latorraca
 Genova: S. Bertolini, M. Agretti, P. Costelli
 Messina : V. Nicita Mauro, G. Basile
 Milano 1: D. Mari, F. Duca, P. Terrazzi.
 Milano 2 : E. Bosi, M. Manzoni
 Modena 1 : G. Salvioli, M.V. Baldeli, M. neri
 Modena 2 : A. Cossarizza, L. Troiano, G. Pini
 Napoli : M. Varricchio, A. Gambardella, G. Prolisso
 Palermo : G. Frada', M. Barbagallo, R. Pollina
 Parma: M. Passeri, P. Sansoni, G. Lavagetto
 Pavia : E. Ferrari, C. Battezzatore, G. Molla
 Perugia: U. Senin, A. Cherubini, M.C. Polidori
 Roma : V. Marigliano, C. Bauco, C. Borriello
 Sassari: L. Deiana, C. Carru, G. M. Pes, G. Baggio
 Siena: S. Forconi, S. Boschi, M. Guerrini
 Torino: F. Fabris, G. Cappa, E. Ferrario