Periodontology 2000, Vol. 72, 2016, 13–18
Printed in Singapore. All rights reserved

The aging population: demographics and the biology of aging

Eleni Kanasi*, Srinivas Ayilavarapu* & Judith Jones

The world is aging. Epidemiological studies show that 11% of the world's population is over 60 years of age, with a projected increase, by 2050, to 22% of the population (33). Currently, however, there are large variations among countries and continents. Nearly one-third of Japan's population (32%) is over 60 years of age (Fig. 1), and Japan has the highest life expectancy (of 26 years) at age 60 (Fig. 2). The lowest life expectancy at age 60 is that of Africa, at 17 years (Fig. 2).

In developed countries, the percentage of adults who are over 65 years of age is increasing in absolute numbers. Metrics from the Center for Disease Control's Morbidity and Mortality Weekly Report show a doubling of the population over 65 years of age in a 30-year time span (11). From 2000 to 2030, the percentage of the population who are 65 years of age and older will increase from 12.4% to 19.6% in the USA, from 12.6 to 20.3% in Europe, from 6% to 12% in Asia, from 5.5% to 11.6% in Latin America and the Caribbean and from 2.9% to 3.7% in Africa. This transition comes with previously unseen public health challenges. For example, 80% of elderly individuals have at least one chronic condition and 50% have two (11). Apart from increased morbidity, mortality and health-care costs, these conditions may sometimes lead to severe disability.

Since the establishment of the National Institute of Aging (1974), concerted efforts have expanded epidemiologic studies to include older cohorts (15). The National Center for Health Statistics increased the age of their surveyed population to 75 years. The Framigham Heart Study focused on retention of older participants and has reported only 6% loss to follow-up at 65 years and older. The reason for involving older cohorts in current studies, has been the public health significance, as well as the health issues associated with aging.

The aging population of the developed world will have important consequences for oral health and disease. Oral diseases that are more common with aging include oral cancers, dental caries and periodontal diseases. This article describes the changing global demographic profile and the effects of an aging society on the prevalence and incidence of periodontal diseases. We review the definitions of normal and successful aging, the principles of geriatric medicine and the highlights of biological aging at cellular, tissue and systems levels.

Definitions of aging

Every species has its own characteristic lifespan, which is determined by evolution and is modified by multiple diverse factors, including biological mechanisms. Understanding the underlying biology of epigenetic processes (i.e. those relating to or arising from non-genetic influences on gene expression) in greater detail, and implementing appropriate interventions, could be used to promote a healthy lifespan and healthy aging of humans. (7, 29). Aging, which is, in part, a determinant of the lifespan of a human, can be defined simplistically as the continuing loss of physiological integrity and subsequent impaired function leading to death (29). Centenarians are often the focus of extensive research, showing genetic and epigenetic variation relative to others. For example, a group of Ashkenazi Jewish centenarians exhibit homozygosity for an allele associated with favorable lipoprotein profiles, cardiovascular health, insulin resistance and longevity (6).

*Co-first authors.

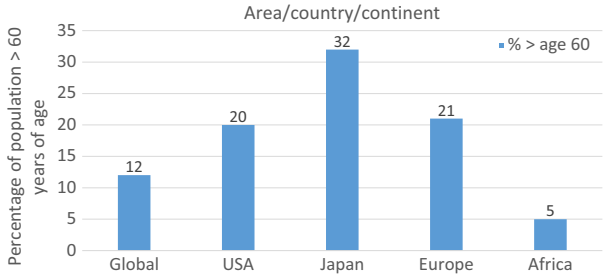

Fig. 1. World Health Organization-derived data showing the percentage of the population older than 60 years of age, in different areas, continents and countries, in 2013 (38).

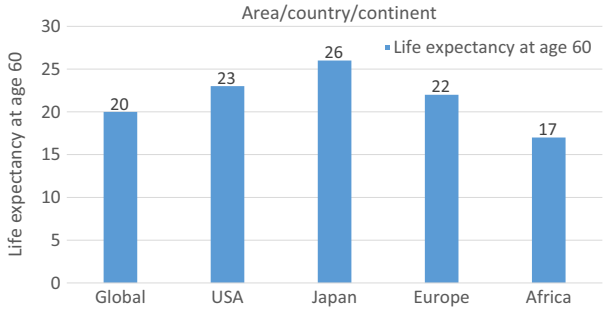

Fig. 2. World Health Organization-derived data showing the life expectancy (in years) at 60 years of age, in different areas, continents and countries, in 2013 (38).

Epidemiology of aging

Population-based mortality data analyses are often used by epidemiologists for initial screening to promote understanding of disease processes and geographic areas of concern. Population cohorts are often followed over time and stratified according to gender or age. The United States Census Bureau and the National Center for Health Statistics stratified data according to gender and showed increased mortality in more recent years that was caused by non-communicable diseases (e.g. lung cancer, chronic obstructive pulmonary disease and diabetes) (14).

More births after World War II and successful interventions against infertility have contributed to an increase in the population of the USA that is older (14). However, the aging population is increasingly burdened by morbidities and comorbidities associated with aging. Comparison of the National Health and Nutrition Examination Survey in 1988–1994 with that from 2009–2010 shows that sedentary lifestyles increased from 9.1% to 51.7% in women and from 11.4% to 43.5% in men, with the body mass index increasing across all ages and ethnicities (25). By 2014, the increase in obesity in the USA had put the US obese adult population at close to 30% and at 10% for diabetes (16).

Together with an aging population comes a responsibility for 'healthy' and 'successful' aging. Currently, most attempts to achieve healthy aging are community based and not well organized. Research is heavily focused on healthy diets (5), physical exercise and cognitive behavior therapy (21). Physical independence is recognized in the Japanese supercentenarian cohort as the main factor for longevity, rather than the ability to predict mortality through biomedical factors (4). A Swedish study reported decreased mortality among people without disabilities and a decline in the prevalence of disability from 1991 to 2010 (3). In China, although hypertension seems to have increased among urban elderly populations, awareness, treatment and control have also increased (39).

Periodontal epidemiology and aging

Oral aging is a current focus of several organizations including the Federation Dentaire Internationale, the World Health Organization and the American and Japanese Dental Associations. In their Tokyo Declaration, the Japanese Association identified the elderly population as one of its main target groups. The goal is for each person to retain more than 20 teeth by age 80 (32). The magnitude of this goal is hard to comprehend, unless evaluated on the basis of the second most prevalent dental disease, namely periodontal disease.

The prevalence estimate of periodontal diseases in the USA and worldwide varies according to disease definition and bias, as a result of differing examination protocols. Worldwide, the prevalence of severe periodontitis is estimated to affect 10.8% of the population, or 743 million people, making it the sixth most prevalent condition affecting humans (34). The number of disability-adjusted life-years as a result of severe periodontitis has increased worldwide and shows increasing trends with age (30). In the USA, after adjusting for bias in partial examination protocols in the National Health and Nutrition Examination Survey III data set, Albandar et al. (1) reported that the prevalence of periodontitis in US adults over 30 years of age was 50%. According to estimates of periodontal diseases in US adults from the National Health and Nutrition Examination Survey for 2009-2010, the prevalence of periodontitis increased with increasing age (12). Although 38.5% of adults under 65 years of age had moderate to

severe periodontitis, almost two-thirds (64%) of those 65 years of age and older had moderate or severe periodontitis. Furthermore, there were important sociodemographic differences, with men having more periodontitis than women, plus inequalities based on race, ethnicity and income. Interestingly, the prevalence of periodontal disease decreased in individuals over 80 years of age, presumably because of loss of teeth with the greatest susceptibility to periodontitis (2).

Successful aging and periodontal diseases

Rowe & Kahn (35), in their seminal paper on successful aging, discussed the differences between normal, pathological and successful aging. Their definition of successful aging included: 'three main components: low probability of disease and disease-related disability, high cognitive and physical functional capacity, and active engagement with life.' Applied to any physiological parameter or set of parameters, such as the periodontium, persons who age successfully will have an intact dentition with limited attachment loss and minimal limitations on function. Rowe & Kahn (35) also plotted age according to the probabilities of disease, disability and death. Extending their concept to the periodontium, disease would be represented by the incidence of mild, moderate or severe disease. Disability would be indicated by disease-related functional decrements in the periodontium, including tooth mobility and sensitivity that impairs function, appearance and social interactions. Rowe & Besdine (circa 1983) discussed the principles of geriatric medicine used to describe the interaction of age and disease (17). They suggested that age could have no relationship to disease, and used the example of anemia. Alternatively, age could be related to a decreased prevalence of disease (e.g. autoimmune diseases) or to an increased incidence and severity of disease. Both the prevalence and the severity of periodontitis increase with increasing age.

Biology of aging

Biologically, aging is defined as a 'time-dependent functional decline that affects most living organisms' (29). This functional decline results in the loss of physiological integrity and, in turn, leads to pathologies including cardiovascular disease, cancer, diabetes and neurological disorders (29). Current molecular and cellular research shows that there are nine hallmarks of aging (Fig. 3): genomic instability; telomere attrition; epigenetic alterations; loss of proteostasis; deregulated nutrient-sensing; mitochondrial dysfunction; cellular senescence; stem cell exhaustion; and altered intercellular communication (29). The same report suggests interventions to improve a human health during aging (29).

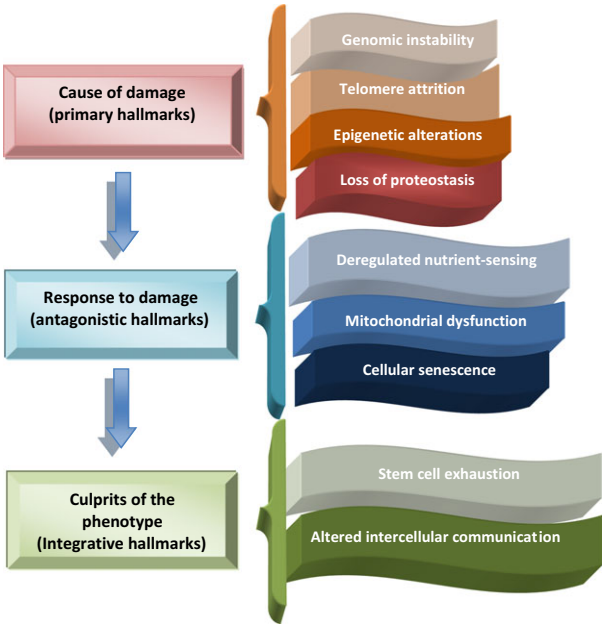

Fig. 3. Nine hallmarks of aging categorized according to the point at which they act and create cellular damage (primary causes, compensatory responses and the end result). adapted with permission from Lopez-Otin et al. (29) .

Genetic and epigenetic alterations

Gradual accumulation of products of cellular and extensive DNA damage contribute to the aging process. Continuous oxidative DNA damage in cells interferes with RNA transcription and is thought to be one of the prominent causes of aging (20). Various exogenous (e.g. chemicals or ultraviolet/infrared radiation) or endogenous (oxidative stress or replicative errors) agents can cause DNA damage or result in insufficient DNA repair and telomere attrition that favor aging (29). Epigenetic alterations are defined as 'changes to the genome that do not involve changes in the DNA sequences' (9). These alterations involve chromatin changes by DNA methylation, histone modifications and changes to coding and noncoding RNA profiles. Additionally, epigenetic alterations can result in changes in gene expression and in genetic architecture (9).

Stem cell exhaustion and cellular senescence

Stem cell exhaustion is an important aspect of aging that affects the regenerative potential of the organism and can lead to immune senescence. Recent experiments on stem cell rejuvenation have shown successful reversal of the aging phenotype (29). Cellular senescence has been defined as 'stable arrest of the cycle associated with stereotype phenotypic changes' (29) and can be attributed to telomeric shortening, nontelomeric DNA damage and depression of the genetic locus cyclin dependent kinase inhibitor 4/ADP-ribosylation factor 4 (INK4/ARF4). Increased cell senescence in aging may be a beneficial compensatory mechanism for reducing oncogenic cells and mechanisms, but this requires an efficient turnover mechanism that seems to be impaired with aging and exhausts the regenerative potential of progenitor cells (29).

Inflammation, immune responses and malnutrition in aging and periodontitis

Aging is thought to be associated with a low-grade inflammatory phenotype in mammals that is called 'inflammaging' and is the product of the autophagic capacity impairing so-called 'housekeeping activities' in cells, resulting in protein aggregation, mitochondrial dysfunction and oxidative stress (36). The systemic inflammation associated with inflammaging has been thought to exacerbate vascular pathology and cause atherosclerosis, increased secretion of cortisol (resulting in insulin resistance in muscles) and bone resorption (36). Aging has been associated with a decline in immune responses, including mucosal IgM levels, cytokines and markers for B- and T-cells (24). However, some studies found no evidence of age-related host immune changes in elderly subjects with periodontitis (31).

Older individuals with periodontitis had higher levels of serum antibodies to *Porphyromonas gingivalis*, and increased numbers of neutrophils were observed in those with severe periodontal disease (31). One animal study showed that older mice developed periodontitis and bone loss as a natural function of age and suggested a novel aging animal model to study the mechanisms of aging and periodontitis (26). Another human study showed that the generation of neutrophil extracellular traps was lower in older individuals. However, the authors concluded that altered formation of neutrophil extracellular traps is not associated with an increased incidence of periodontitis in older people (18). Studies have also linked malnutrition to immune deficiencies in the elderly because protein-calorie malnutrition and zinc deficiency are associated deficiencies in immune cell functions (28). One long-term elderly care study showed that 18% of the population had severe malnutrition (23, 28).

Association of aging and periodontitis

Is age-related tooth loss induced by periodontitis? In the past, it was assumed that aging ultimately results in tooth loss, especially as a result of periodontitis (10). Aging has been associated with periodontitis and tooth loss in various cross-sectional studies, but the data analyzed were mostly aggregated and current research has questioned this association (10). The cellular aspects of the aging process and its association with periodontitis have not been well characterized and warrant further investigation (22). Histologically, there is less fibrous and cellular content in an aged person's periodontium compared with that of a young individual (37). Well-designed studies in older people have shown that periodontitis is a multifactorial disease, and its extent and severity affect only a limited proportion of the aging population (13). A compromised or debilitated medical condition, rather than direct physiological aging, may be an important determinant of periodontitis in many elderly subjects. Additionally, periodontitis in the aged might serve to worsen systemic health (13). The effects of systemic diseases and medications, psychological effects and decreased interest in or ability to perform oral hygiene practices are thought to result in periodontal diseases, and ultimately in tooth loss, in aged individuals (24).

Delayed cell proliferation and wound healing in aging

An important point to consider in relation to periodontal diseases and aging is whether aging causes delays in wound healing. Although Holm-Pederson & Löe (19) described delayed healing in the periodontium of older adults, most studies have failed to show that increased age is detrimental in periodontal treatment of people with moderate-to-advanced forms of

periodontal disease (27). Delayed stem-cell proliferation associated with aging may impact maintenance and survival of a living being, but excessive proliferation could also result in depleted reserves of stem cells (29). Studies are needed to address the association of delayed cell proliferation and wound healing with the onset of periodontal diseases and response to treatment.

Aging, periodontitis and overall health

Aging is associated with an increased prevalence of systemic diseases (notably arthritis, cardiovascular diseases and stroke) (Fig. 4) (8). These conditions, coupled with multiple pathologies and multiple medications, are associated with a decline in physiological function (e.g. lack of manual dexterity, prone to injuries or injury related and reduced salivary flow) that can contribute to the development and progression of oral diseases as a result of the neglect of oral hygiene and the accumulation of bacterial plaque. Aged individuals are also less likely to access dental treatment, and such persons with the highest disease prevalence are the least likely to have access to care. This, in turn, can have periodontal, dental and medical consequences (28). Furthermore, immune senescence in the elderly can contribute to the proliferation of bacteria and can partly explain the role of poor dental health in aspiration pneumonia (28). As dental procedures can cause transient bacteremia, which is associated with cardiovascular disorders from direct bacterial actions or indirect immune-cell-mediated vascular pathology, it may be important to establish (when absent) and to maintain good oral health in older individuals (28).

Conclusions

Aging is a natural phenomenon that leads to a decline in physiological function in older adults and is associated with a predisposition to multiple oral and systemic pathologies. Epidemiologic studies show higher rates of periodontal diseases in elderly populations and additional comorbidities that prevent successful aging. Successful oral aging is the current focus of multiple groups, including the World Health Organization, which has identified the elderly population as one of its main target groups. The goal is for each person to retain more than 20 teeth by age 80. Nonetheless, the prevalence of periodontal disease is continuously rising as the population is aging. Every species has its own characteristic lifespan, which is determined by evolutionary history and is modified by multiple diverse factors, including biological mechanisms. Long-term DNA damage, leading to secondary cellular defects and disparity between reparative and cell-destructive mechanisms, is primarily responsible for the aging phenomenon. There remains a gap in the literature of the molecular mechanisms in the aging process and their causal association with oral diseases such as periodontitis. Disease or not, it is important to establish access to dental care, good oral-health practices and nutrition in the global aging population. Together with an aging population comes a responsibility for 'healthy' and 'successful' aging.

Acknowledgment

We would like to thank Kendrick Smaellie for her support with the preparation of this manuscript.

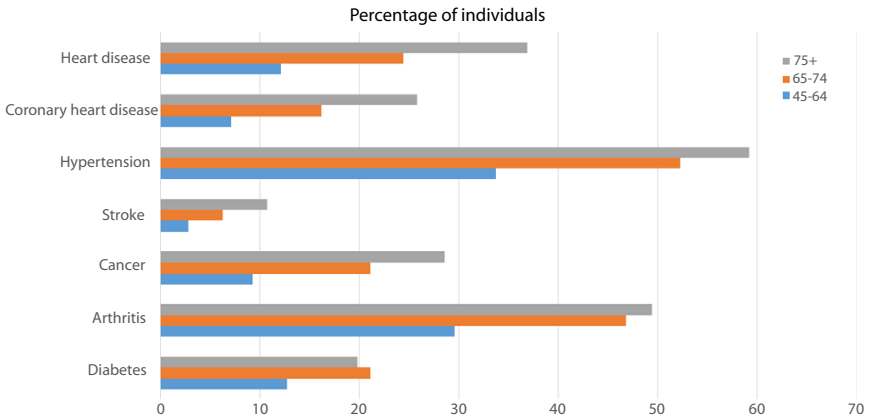

Fig. 4. Percentage of individuals with chronic systemic conditions in the USA, according to age (8).

References

1. Albandar JM. Underestimation of periodontitis in NHANES surveys. *J Periodontol* 2011: **82**: 337–341.
2. Albandar JM, Brunelle JA, Kingman A. Destructive periodontal disease in adults 30 years of age and older in the United States, 1988–1994. *J Periodontol* 1999: **70**: 13–29.
3. Angleman SB, Santoni G, von Strauss E, Fratiglioni L. Temporal trends of functional dependence and survival among older adults from 1991 to 2010 in Sweden: toward a healthier aging. *J Gerontol A Biol Sci Med Sci* 2015: **70**: 746–752.
4. Arai Y, Inagaki H, Takayama M, Abe Y, Saito Y, Takebayashi T, Gondo Y, Hirose N. Physical independence and mortality at the extreme limit of life span: supercentenarians study in Japan. *J Gerontol A Biol Sci Med Sci* 2014: **69**: 486–494.
5. Assmann KE, Lassale C, Andreeva VA, Jeandel C, Hercberg S, Galan P, Kesse-Guyot E. A healthy dietary pattern at midlife, combined with a regulated energy intake, is related to increased odds for healthy aging. *J Nutr* 2015: **145**: 2139–2145.
6. Atzmon G, Rincon M, Schechter CB, Shuldiner AR, Lipton RB, Bergman A, Barzilai N. Lipoprotein genotype and conserved pathway for exceptional longevity in humans. *PLoS Biol* 2006: **4**: e113.
7. Barzilai N, Bartke A. Biological approaches to mechanistically understand the healthy life span extension achieved by calorie restriction and modulation of hormones. *J Gerontol A Biol Sci Med Sci* 2009: **64**: 187–191.
8. Blackwell DL, Lucas JW, Clarke TC. Summary health statistics for U.S. Adults: National Health Interview Survey, 2012. Washington, D.C. Vital Health Stat 2014: 10(260).
9. Brunet A, Berger SL. Epigenetics of aging and aging-related disease. *J Gerontol A Biol Sci Med Sci* 2014: **69**(Suppl 1): S17–S20.
10. Burt BA. Periodontitis and aging: reviewing recent evidence. *J Am Dent Assoc* 1994: **125**: 273–279.
11. Centers for Disease Control and Prevention. Trends in aging – United States and worldwide. *MMWR Morb Mortal Wkly Rep* 2003: **52**: 101–104, 106.
12. Eke PI, Dye BA, Wei L, Thornton-Evans GO, Genco RJ. Prevalence of periodontitis in adults in the United States: 2009 and 2010. *J Dent Res* 2012: **91**: 914–920.
13. Ellen RP. Periodontal disease among older adults: what is the issue? *Periodontol 2000* 1998: **16**: 7–8.
14. Ezzati M, Friedman AB, Kulkarni SC, Murray CJ. The reversal of fortunes: trends in county mortality and cross-county mortality disparities in the United States. *PLoS Med* 2008: **5**: e66.
15. Fried LP. Epidemiology of aging. *Epidemiol Rev* 2000: **22**: 95–106.
16. Friedman SM, Shah K, Hall WJ. Failing to focus on healthy aging: a frailty of our discipline? *J Am Geriatr Soc* 2015: **63**: 1459–1462.
17. Ghezzi EM, Berkey DB, Besdine RW, Jones JA. Clinical Assessment of the Elderly Patient. In: Holm-Pedersen P, Walls A, Ship J, editors. *Geriatric dentistry*. Singapore: Wiley, 2015: 61–80.
18. Hazeldine J, Harris P, Chapple IL, Grant M, Greenwood H, Livesey A, Sapey E, Lord JM. Impaired neutrophil extracellular trap formation: a novel defect in the innate immune system of aged individuals. *Aging Cell* 2014: **13**: 690–698.
19. Holm-Pedersen P, Loe H. Wound healing in the gingiva of young and old individuals. *Scand J Dent Res* 1971: **79**: 40–53.
20. Holmes GE, Bernstein C, Bernstein H. Oxidative and other DNA damages as the basis of aging: a review. *Mutat Res* 1992: **275**: 305–315.
21. Huang TT, Liu CB, Tsai YH, Chin YF, Wong CH. Physical fitness exercise versus cognitive behavior therapy on reducing the depressive symptoms among community-dwelling elderly adults: a randomized controlled trial. *Int J Nurs Stud* 2015: **52**: 1542–1552.
22. Huttner EA, Machado DC, de Oliveira RB, Antunes AG, Hebling E. Effects of human aging on periodontal tissues. *Spec Care Dentist* 2009: **29**: 149–155.
23. Keller HH. Malnutrition in institutionalized elderly: how and why? *J Am Geriatr Soc* 1993: **41**: 1212–1218.
24. Kiyak HA, Persson RE, Persson GR. Influences on the perceptions of and responses to periodontal disease among older adults. *Periodontol 2000* 1998: **16**: 34–43.
25. Ladabaum U, Mannalithara A, Myer PA, Singh G. Obesity, abdominal obesity, physical activity, and caloric intake in US adults: 1988 to 2010. *Am J Med* 2014: **127**: 717–727 e712.
26. Liang S, Hosur KB, Domon H, Hajishengallis G. Periodontal inflammation and bone loss in aged mice. *J Periodontal Res* 2010: **45**: 574–578.
27. Lindhe J, Socransky S, Nyman S, Westfelt E, Haffajee A. Effect of age on healing following periodontal therapy. *J Clin Periodontol* 1985: **12**: 774–787.
28. Loesche WJ, Lopatin DE. Interactions between periodontal disease, medical diseases and immunity in the older individual. *Periodontol 2000* 1998: **16**: 80–105.
29. Lopez-Otin C, Blasco MA, Partridge L, Serrano M, Kroemer G. The hallmarks of aging. *Cell* 2013: **153**: 1194–1217.
30. Marcenes W, Kassebaum NJ, Bernabe E, Flaxman A, Naghavi M, Lopez A, Murray CJ. Global burden of oral conditions in 1990–2010: a systematic analysis. *J Dent Res* 2013: **92**: 592–597.
31. McArthur WP. Effect of aging on immunocompetent and inflammatory cells. *Periodontol 2000* 1998: **16**: 53–79.
32. Muller F, Naharro M, Carlsson GE. What are the prevalence and incidence of tooth loss in the adult and elderly population in Europe? *Clin Oral Implants Res* 2007: **18**(Suppl 3): 2–14.
33. Newgard CB, Sharpless NE. Coming of age: molecular drivers of aging and therapeutic opportunities. *J Clin Invest* 2013: **123**: 946–950.
34. Richards D. Review finds that severe periodontitis affects 11% of the world population. *Evid Based Dent* 2014: **15**: 70–71.
35. Rowe JW, Kahn RL. Successful aging. *The Gerontologist* 1997: **37**: 433–440.
36. Salminen A, Kaarniranta K, Kauppinen A. Inflammaging: disturbed interplay between autophagy and inflammasomes. *Aging (Albany NY)* 2012: **4**: 166–175.
37. Severson JA, Moffett BC, Kokich V, Selipsky H. A histologic study of age changes in the adult human periodontal joint (ligament). *J Periodontol* 1978: **49**: 189–200.
38. WHO World Health Statistics. ISBN 978-92-4-156488-5. Accessed online at http://www.who.int/gho/Publications/world_health_statistics/2015/en/ on 12/3/2015.
39. Wu L, He Y, Jiang B, Sun D, Wang J, Liu M, Yang S, Wang Y. Trends in Prevalence, awareness, treatment and control of hypertension during 2001–2010 in an Urban elderly population of China. *PLoS ONE* 2015: **10**: e0132814.