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PART I

Epidemiology

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Epidemiology of aging

Lodovico Balducci, William B. Ershler

Descriptive epidemiology

In the Western world the older population has undergone a progressive and accelerated expansion during the past 50 years, and the increment in the number of individuals 65 and older (Fig. 1.1) has been associated with a progressive prolongation of average life expectancy, which in the USA in 2000

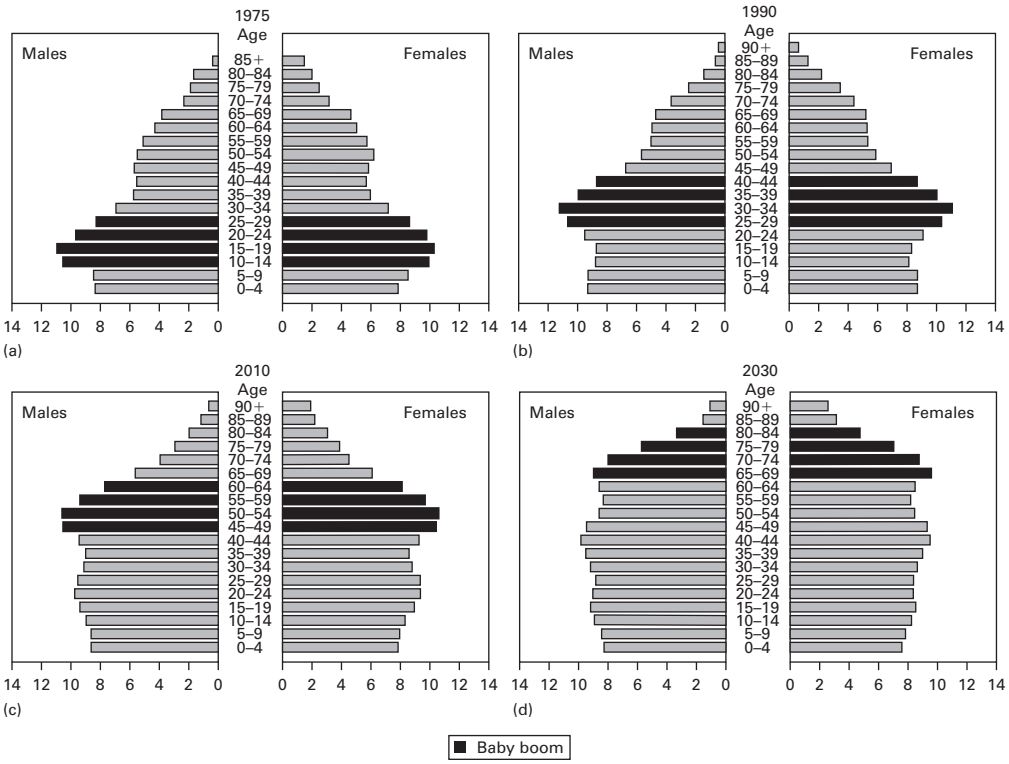

Figure 1.1 The squaring of the pyramid. The shape of the figure representing different age layers of a population is becoming closer and closer to a square, due to a reduction in the younger population and an increment in the older one. From Yancik & Ries, 2004 [1], with permission.

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was 80 for women and 76 for men [1]. A progressive decline in birth rate has occurred, due to more effective birth control and family planning. At the same time, the mortality rate has also decreased, due to improved health and hygiene, the conquering of most infectious diseases, and the absence of worldwide conflicts and epidemics. Reduced natality and mortality rates have produced the so-called "squaring of the pyramid," which refers to the change in the shape of the figure describing the population subdivided in different age layers (Fig. 1.1). In 1975, this figure looked like a pyramid with a large base of young people, becoming narrower and narrower with increasing age. By the year 2030 the figure will become closer to a square, with a smaller basis of younger people and a larger representation of the older population [1]. In some countries, such as Italy and Japan, one may start seeing an "inversion of the pyramid," as the population over 65 already outnumbers that below 20 [2,3].

The aging of the population has been associated with social changes that may influence the care and the welfare of the elderly. Most noticeable are the increased mobility of the population, which makes lasting relationships more difficult and social support less predictable, the reduction in the number of young children available to take care of their aging parents, the massive entrance of women into the workforce, which led to a thinning pool of traditional home caregivers, and overall the dissolution of the extended family, which has deprived the elders both of their traditional source of support and of their traditional social roles [4].

The medical and social implications of the aging of the population are only partially understood. In part, this is due to the fact that the older population is very diverse in terms of health and function and it is difficult to predict on the basis of aging alone what is a person's life expectancy, ability to live independently, and susceptibility to diseases [5,6]. When the life expectancy of different cohorts of older individuals is subdivided into quartiles, one notices a marked discrepancy among the upper, intermediate, and lower quartiles (Fig. 1.2) [7]. Germane to this discussion, the upper life-expectancy quartile of the 85+ cohort is longer than the lower quartile of the 70–75 cohort, underlying how aging refers to a highly diverse physiological event rather than to a chronologic one. Also, to some extent aging is a moving target: we cannot assume that the aging population today presents the same characteristics as that of only a few decades ago. To this point, the case of social security is paradigmatic. In the USA, the age at which a person can draw social security has increased from 65 to 67 as more and more individuals keep working beyond age 65, which represents a substantial change from the time when social security was instituted. One may conclude that the functional status of the elders has improved as their life expectancy has become more prolonged. The older population of today and that of the recent past may also differ on the basis of cultural changes, with important influences on medical care. While even in the recent past older individuals were likely to accept their physicians' recommendations without argument [8], this is rapidly changing. In part this is due to easier access to the media, and in particular to the Internet illustrating medical advances in a timely fashion and proposing alternative forms of medical treatment. In addition, we are witnessing the aging of the so-called generation of "preboomers" and "boomers," who are used to taking primary responsibility for their own health care, an attitude they are not likely to relinquish with aging.

The recognition that the aging population is rapidly increasing and is highly diverse raises the question of whether one may identify common aging trends – in physiological, functional, medical, and social terms – that may define this group of individuals.

There is general agreement that age is associated with a progressive decline in the functional reserve of multiple organs and systems [9], and increased prevalence of chronic diseases [10], including conditions that are typical of aging, albeit not unique, called "geriatric syndromes" [11] (Table 1.1). The consequences of these changes include reduced life expectancy and tolerance of stress, and increased risk of disease and functional dependence. Functional dependence implies that a person may not

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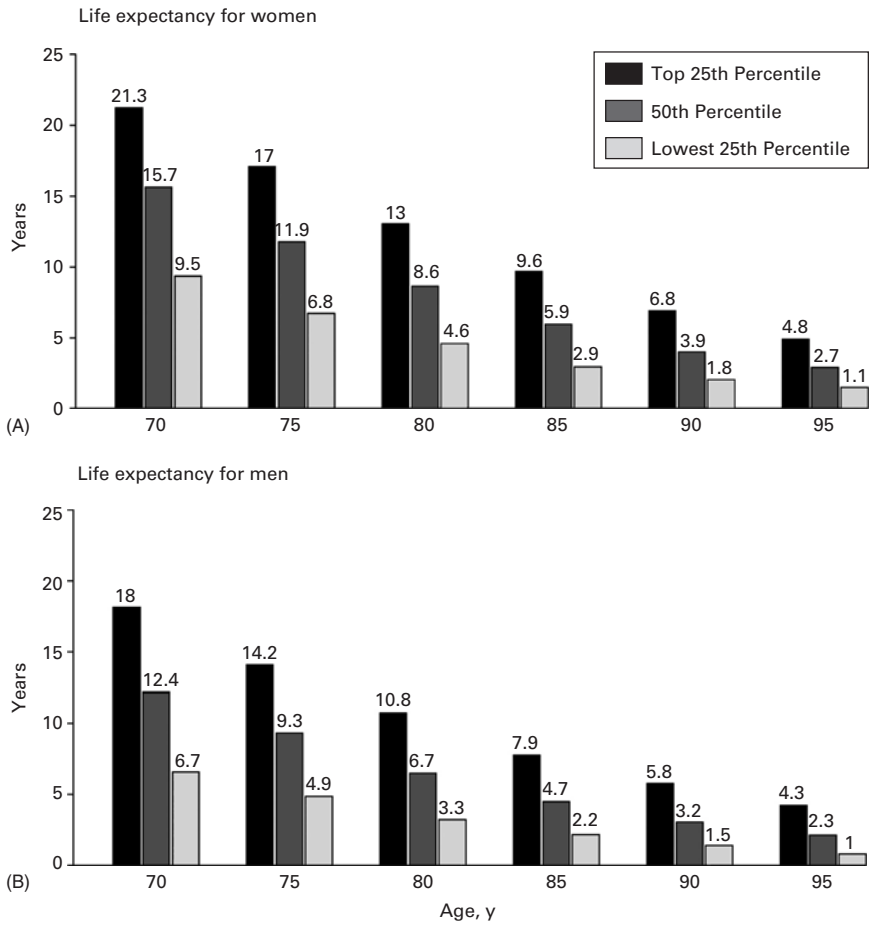

Figure 1.2 Life expectancy divided into quartiles: upper, middle, and lower quartiles for women (A) and men (B) at selected ages. From Walter & Covinsky, 2001 [7], with permission.

Table 1.1. Examples of geriatric syndromes.

Dementia
Severe depression
Delirium, caused by conditions that do not affect the central nervous system (medications, infections, pain, myocardial infarction, etc.)
Osteoporosis with spontaneous bone fractures
Falls
Dizziness
Failure to thrive
Neglect and abuse

be safe when living alone. Functional dependence is a broad term that encompasses different degrees of functional needs, such as the inability to carry on the activities necessary for independent living (instrumental activities of daily living, IADLs) [12] as well as basic activities of daily living (ADLs) [13] (Table 1.2). Clearly, loss of ADLs involves a higher degree of functional dependence than loss of IADLs, and may require a live-in caregiver or admission to a nursing home. Loss of IADLs may be compensated by a visiting caregiver or may be taken care of in an assisted living facility.

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Table 1.2. Activities of daily living.

(A) Instrumental activities of daily living (IADLs)
Use of transportation
Shopping
Taking medication
Providing one's own meals
Using the telephone
Managing money
(B) Activities of daily living (ADLs)
Transferring
Bathing
Going to the bathroom
Grooming
Dressing
Eating

Functional dependence should be distinguished from disability, which also becomes more common with age [14], and which may or may not lead to functional dependence. Disability refers to the inability to perform a certain activity due to a particular functional loss. For example, loss of strength of the lower extremities (*loss of function*) may impede one's ability to climb stairs (*disability*). By itself this disability does not lead to functional dependence as long as an elevator or a wheelchair ramp allows the disabled person to transfer to the upper floors. In the absence of an elevator the disability becomes a *handicap* and leads to functional dependence (inability to transfer). Together with disease and functional decline, disability is a cause of functional dependence, but is not by itself functional dependence.

As an introduction to the themes of this book, we will examine medical and social implications of aging.

Medical implications of aging

The aging of the population has led to shifts in the paradigm of medical diagnosis and medical treatment. The most important medical implications of aging include increased prevalence of chronic conditions, increased mortality from acute conditions, and change in the goals of treatment, from cure to avoidance of disease progression.

Increased prevalence of chronic conditions

The prevalence and the incidence of chronic diseases increase with age. Some of these conditions, including congestive heart failure, cancer, and chronic renal insufficiency, shorten a person's life expectancy [15]. Other conditions, such as arthritis or peripheral neuropathy, may not threaten a person's life, but may reduce functional capacity and cause disability and functional dependence. The consequences of increased prevalence of chronic diseases include:

- Changes in disease manifestations [16,17]. Some of these changes have been well described: these include delayed diagnosis due to *masking*, as is the case when bone pain due to metastatic cancer is mistakenly ascribed to worsening arthritis; or development of unusual symptoms, such as delirium in the presence of a urinary tract infection or myocardial ischemia that may be due to a *summation* of factors, including increased levels of circulating inflammatory cytokines, reduced number and function of cerebral neurons, and reduced oxygen supply to the brain due to coexistent anemia. Comorbidity may also alter the intensity of symptoms. For example, hypertension is associated with reduced and depression with enhanced perception of pain [18].
- Polypharmacy. The risk of drug complications and interactions increases progressively with the ongoing emergence of new drugs [19]. Older individuals are the most vulnerable to adverse events of polypharmacy, due to reduced functional reserve and coexistent diseases. One should not forget, however, that sometimes common drugs may also have positive effects. For example chronic use of non-steroidals has led to a reduction in cancer of the large bowel [20], while the use of statins may be associated with reduced risk of cancer of the large bowel, the breast, and the prostate [21].
- Estimate of life expectancy and disease prognosis. The presence of multiple comorbid conditions in

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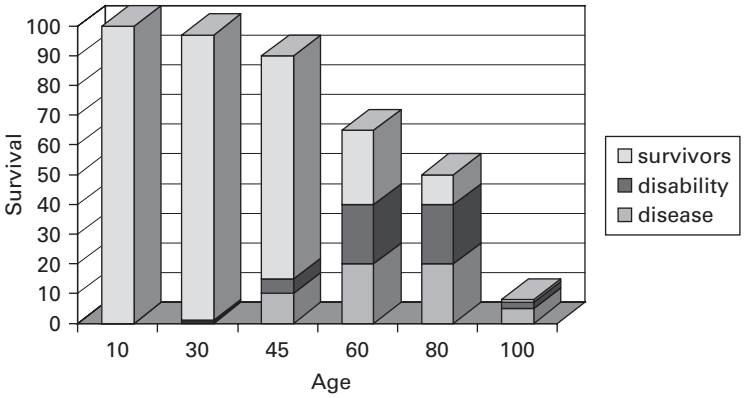

Figure 1.3 The percentage of people surviving at different ages, and the percentage affected by disease and disability. Compression of morbidity refers to bringing these curves closer together, to close the gap between death, disease, and functional impairment.

the same person may complicate the estimate of that person's prognosis and life expectancy. In the presence of conditions associated with rapid mortality, such as acute myeloid leukemia, metastatic cancer, or massive cerebrovascular accident, the influence of other conditions on life expectancy becomes negligible. More commonly, however, one has to account for the combined influence on life expectancy of conditions such as hypertension, well-controlled diabetes, arthritis, chronic lymphocytic leukemia, or low-grade lymphoma, none of which represent an immediate threat to a person's life. Furthermore, different forms of comorbidity may interact with each other. For example, it has become clear that in the presence of the so-called "metabolic syndrome" the risk of recurrence of colorectal cancer after surgery increases [22], and that cancer may enhance the risk of dementia [23].

Increased morbidity and mortality from acute conditions

It is not surprising that the stress represented by an acute illness might overwhelm the limited functional reserve of older individuals. Age is a risk factor for increased mortality following emergency surgery [24], increased risk of complications and hospitalization from elective surgery [24], increased risk for mortality and more prolonged hospitalization for infections [25,26], and increased risk of complications of cytotoxic chemotherapy, including myelodepression, mucositis, peripheral neuropathy, and cardiotoxicity [11].

Goals of medical treatment

While human life expectancy is in continuous expansion, human lifespan seemingly cannot be modified. Lifespan refers to the time one is allowed to live in the absence of disease and trauma, if death was due to the wearing out of one's functional reserve. This consideration, combined with the fact that the majority of chronic conditions affecting older individuals are incurable, may shift the goals of treatment in older individuals from cure toward preservation of function and quality of life. Notwithstanding acute and/or reversible conditions, such as pneumonia or localized cancer, the major goal of medical intervention in older individuals is compression of morbidity rather than elimination of diseases. Compression of morbidity (Fig. 1.3) refers to the delay of disability, functional dependence, and geriatric syndromes to the latest stage of life, and may be achieved with disease prevention, rehabilitation, and management of chronic diseases [27]. Reversal of anemia, even mild anemia, may play an important role in compression of morbidity, as anemia is an independent risk factor for functional decline [28].

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Social implications of aging

The aging of the population involves a number of social implications that are only partly understood. Of particular concern is the dissolution of the traditional sources of support for the elderly at the very same time that the number of elderly is increasing. There is general agreement that the aging of the population will lead to a substantial cost in health care for at least three reasons:

- Increased incidence and prevalence of diseases.
- Increased cost of managing an individual's diseases. As already mentioned, infectious diseases may require a more prolonged hospitalization in older than in younger patients, and age is a risk factor for a wide array of treatment complications. Functional dependence, one of the most expensive aspects of aging, is also a common complication of prolonged hospitalization.
- Emergence of new and expensive treatments, beneficial in diseases such as cancer, hypertension, or diabetes that affect preferentially older individuals.

In addition, one should consider a basic economic difference between the management of younger and older individuals. The restoration of health to a younger patient may be considered an investment toward that person's gaining capacity. The restoration of health to an older individual is associated with little if any economic gain, and predisposes this individual to more diseases and more health-related expenses. Clearly, we are not proposing that older individuals should not receive the best medical care in the name of economic considerations. We are simply highlighting the need to minimize the cost of care by choosing the most effective care delivery. This may include adoption of a healthy lifestyle, interventions aimed at the prevention of disability and functional dependence, chemoprevention of and screening and early detection for common diseases, and avoidance of polypharmacy. For the purposes of this book it is important to underline how mild anemia, which is both a sign of underlying disease and a risk factor for mortality and functional dependence, is largely under-diagnosed in older individuals [28,29]. Most causes of anemia in older individuals are reversible, and this simple intervention by itself may restore and preserve the function and the health of a large number of elderly people.

The delivery of cost-effective health care to older individuals is hampered by the scarcity of practitioners, especially primary care physicians, experienced in the assessment and management of these individuals, and also by the complexity of the current medical system, which imposes multiple visits to different specialists and may require older people to negotiate the hazards of urban traffic and the complex organization of large medical centers, not to mention the maze of rules governing Medicare and health insurance. Clearly, coordination of care and user-friendly healthcare delivery are the foundation of medical treatment of older individuals.

Conclusions

The world population is aging, and this process is particularly accelerated in the Western world. The aging of the population is associated with increased prevalence of disability, functional dependence, and chronic diseases, as well as increased risk of morbidity and mortality from acute conditions. While prevention of deaths and of chronic complications is always a goal of medical treatment, in older individuals compression of morbidity should be the focus of this treatment. Compression of morbidity may be achieved through a number of interventions, including the institution of a healthy lifestyle, the prevention of mobility and balance disorders, the chemoprevention and early detection of common diseases, and the avoidance of polypharmacy.

Coordination of care, and healthcare delivery in an elder-friendly environment, represent the major challenges to cost-effective care of the elderly.

The hematopoietic and blood coagulation systems represent a crossroads of multiple pathologic events involving different organs and systems. The

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study and the management of blood disorders in the elderly may thus have an important role in the preservation of the health and function of older individuals.

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Epidemiology of anemia in older adults

Kushang V. Patel, Jack M. Guralnik

Introduction

The US Census Bureau enumerated 35.0 million adults aged 65 years and older in the 2000 decennial census [1]. Older adults comprised 12.4% of the total US population. By 2050, this segment is projected to grow to 86.7 million, and one out of every five persons will be elderly [2]. Further, the oldest old (those 85 years and older) will grow approximately 400% and represent the fastest-growing age group in the USA. However, the USA is not alone in experiencing population aging, and in fact it is now ranked the 38th oldest country [3]. While population aging is occurring in all regions of the world, rapid declines in fertility rates have generated faster growth rates in the proportion of older adults in developing countries than in developed ones. In view of global population aging and the multiple morbidities associated with aging, the prevention and treatment of conditions that impair functional capacity and quality of life is a major priority of geriatric medicine.

Anemia is a common hematologic condition among older adults, with prevalence estimates increasing as a function of age. Contrary to widely held beliefs that anemia is an innocuous condition of old age, recent evidence suggests that anemia does not reflect a normal aging process, but rather is a marker of underlying pathology and/or a cause of further physiological dysregulation. For instance, in a study of adults aged 85 and older, anemia as defined by the World Health Organization (WHO) was associated with a two fold 5-year mortality risk, independent of age, sex, and medical conditions [4]. Among older adults hospitalized for acute myocardial infarction, lower hematocrit on admission was associated with poorer 30-day survival, while transfusion in those with hematocrit less than 34% was associated with better 30-day survival [5]. In addition to the independent effects anemia has on cardiovascular outcomes [6,7], a number of studies have also shown that lower hemoglobin levels independently predict poor physical function in older adults (see Chapter 15). Given that anemia is not a benign condition in old age, greater attention to the diagnosis and management of anemia in the elderly population is needed. This chapter reviews the distribution and types of anemia among older adults.

Prevalence of anemia in older adults

A number of studies have estimated the prevalence of anemia using the WHO definition of hemoglobin concentration less than 12 g/dL in women and 13 g/dL in men. However, these estimates vary substantially because of biased source populations (e.g., clinic/referral populations) and restricted age ranges. Population-based studies of older adults have provided more stable and consistent prevalence estimates. For example, 15.2% of male and 12.6% of female participants (>70 years) in the Established Populations for Epidemiologic Studies of the Elderly were classified as anemic [8]. Similarly, the InCHIANTI study showed that 11.1% of men and 11.5% of women aged 65 years and older living in two communities in Tuscany, Italy, had anemia [9]. Most recently, Guralnik

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