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The Challenge of Inducing Vaccine Protection in the Elderly

Dietmar Herndler-Brandstetter, Angelika Schwanninger, and Beatrix Grubeck-Loebenstein
Immunology Division, Institute for Biomedical Aging Research, Austrian Academy of Sciences, Innsbruck, Austria

INTRODUCTION

In the last century, the morbidity and mortality caused by infectious diseases was dramatically reduced in developed countries because of improved standards of living and public health measures together with medical advances such as antibiotics and immunizations. This led to an unprecedented growth of the human population and to a rapid increase in average life expectancy, for instance from 49.2 years (1900) to 75.3 years (2000) in the United States. However, at the beginning of this century the demographic evolution in many developed countries arrived at a turning point, leading to population stagnation, because of low birth rates, and rapid aging (Fig. 1). This change in the population's age structure, with an increase of the population aged 65 years and over from 21% in 2000 to 30% in 2050 (European Union), will pose an enormous medical and socioeconomic challenge on our future society.

Aging is a multifactorial process characterized by the loss of function at the molecular, cellular, and organism level. A wide range of age-related alterations in immune system function have been described and are collectively referred to as immunosenescence. Clinically relevant is the higher prevalence, the more severe disease course, and the poorer prognosis of certain infectious diseases in the elderly population and the low efficacy of vaccinations. But also the development and progression of other age-related diseases, such as certain cancers, atherosclerosis, dementia, osteoporosis, and rheumatoid arthritis have been associated with impaired immune function in old age (1,2). Infectious diseases with a higher prevalence in elderly persons include respiratory tract infections (influenza and pneumonia are ranked among the ten major causes of deaths in the United States in persons aged 65 years and older), urinary tract infections, skin and soft tissue infections, Herpes zoster, tuberculosis, pneumococcal meningitis, and viral gastroenteritis (3). Furthermore, the increased global mobility of elderly persons may also enhance their risk of encountering newly emerging and reemerging infectious diseases.

Although much progress has been achieved over the past decades in understanding the age-related changes of the immune system, the exact molecular mechanisms are not completely understood yet. Moreover, the development of vaccines that demonstrate a more favorable efficacy profile in elderly persons is still in its infancy. The goal of this chapter is to provide a comprehensive overview about age-related changes of the immune system influencing the outcome of vaccinations and will outline strategies to improve vaccine efficacy in elderly persons.

VACCINE EFFICACY IN THE ELDERLY

The implementation of large-scale vaccination strategies led to the eradication of smallpox in 1980 and to a drastic reduction of poliomyelitis, diphtheria, tetanus, pertussis, measles, mumps, rubella, and *Haemophilus influenzae* infections. More than 25 different infectious diseases can be prevented by vaccinations these days and vaccinations are considered the most cost-effective medical procedure for preventing morbidity and mortality caused by infectious diseases. However, the problem of decreased vaccine efficacy in the elderly, due to an age-related decline in immune system functions, has been recognized only recently. Especially the induction of protective antibody levels as well as functional and long-lived memory T-cell numbers in the case of vaccinations with new antigens remain a major problem in old age (Fig. 2). The situation of elderly persons is further aggravated by a different clinical presentation of infectious diseases, the failure to respond sufficiently to therapy, the frequent occurrence of opportunistic or recurrent infections and the reactivation of latent diseases, for instance those caused by varicella-zoster virus (VZV) and *Mycobacterium tuberculosis*.

Community-Acquired Infections

Influenza is a contagious respiratory illness caused by the influenza virus strains A and B and is ranked among the 10 major causes of deaths among persons older than 65 years in the United States and other developed countries. Especially elderly persons and those with chronic conditions or otherwise immunocompromised persons have an increased risk of serious complications and death (4). The recurrent influenza epidemics are the consequence of point mutations (antigenic drift) of the viral surface proteins hemagglutinin and neuraminidase wherefore influenza vaccines need to be modified and applied annually. Although influenza vaccination coverage among elderly persons (65 years) increased from 15% to 20% (1980) to 65% (2001) in the United States, vaccine acceptance is lower in many other developed countries. Despite the availability of different types of influenza vaccines, the seroconversion after influenza vaccination is still disappointingly low among elderly persons (50% in persons aged 60 to 70 years, 31% for those aged 70 to 80 years, and only 11% for those above the age of 80; Table 1) (5), although reduced rates of hospitalizations and deaths have been attributed to influenza vaccination (6). The reduced vaccine efficacy correlates with lower levels of immunoglobulin A (IgA) and IgG antibodies, delayed antibody titers, and shortened maintenance of titers after vaccination.