

INFECTIOUS

DISEASES

IN THE

ELDERLY

Edited by

Burke A. Cunha

INFECTIOUS DISEASES IN THE ELDERLY

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NOT FOR RESALE



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This book is dedicated to:

Marie, just Marie! *

For her unfailing love, inspiration, support, encouragement, and the faith to keep going against all odds.

With love and appreciation,

BAC

*And to all those in medicine providing competent and loving care to those patients in their twilight years.

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PREFACE

The study of infectious diseases of the elderly has almost become a discipline in itself by the late 1980s. With each passing decade, a larger portion of the population becomes older with a resultant increase in multisystem diseases that accompany the aging process. The host defenses wane with advancing years and are further diminished by diseases or medications making the elderly person a special kind of compromised host. Infectious diseases in the older population warrant a special attention because infections in the aged differ in kind, severity, and presentation from younger adults. Many infectious diseases in the elderly individual are not unlike those in younger adults, but they tend to be more severe or prolonged and may have varied or atypical manifestations. Therapy is a special challenge in the elderly because host defenses are suboptimal. Special attention should be given to antibiotic dosing in the elderly because the majority of these patients will have some degree of hepatic renal insufficiency.

The rationale for a book like this is to make the clinician who cares for geriatric patients with infections more aware of their special problems. The aim of this book is to provide the clinician with a practical guide to the most important infectious disease problems in the elderly.

*Burke A. Cunha, MD
Mineola, NY
1988*

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SECTION I GENERAL CONCEPTS

1

Infectious Diseases in the Elderly — An Overview

Louis Weinstein

That the elderly have an increased susceptibility to infections appears to be well established. This is primarily a quantitative phenomenon that reflects the augmented risk of the development of a variety of infectious disorders and the increased fatality rates associated with them. There is, however, another aspect of the problem in older individuals that has received much less attention than the matter of a general increase in susceptibility. This involves the remarkable changes that have occurred in the natural history and clinical features of some infectious diseases, especially subacute infective endocarditis, pulmonary tuberculosis, and pneumonia caused by *Mycoplasma pneumoniae*, in older individuals. In addition to these qualitative differences, there is also ample evidence to support the fact that these diseases have increased in frequency in the elderly.

The prevalence of bacteremia is higher in elderly than in young persons, and is associated with a decrease in longevity.^{1,2} Ten percent of older men and 20% of aging women experience episodes of bacteremia. Comparative figures in young persons are 0.1% and 5%, respectively. The attack rate of herpes zoster has been reported to range from 2.3 per 1000 patients 30 to 39 years of age, to 6.8 per 1000 in those 60 to 69 years old and 10 per 1000 in persons between the ages of 60 and 79 years.³ Elderly patients are particularly susceptible to the development of pneumococcal pneumonia, and are at much higher risk of complications such as meningitis and endocarditis, when compared to young persons.^{4,5} Pneumococcal bacteremia has been observed in 30% of the elderly and in 10% to 20% of the young; the associated fatality rates are 40% to 60%

and 10% to 20%, respectively.^{4,5} Infection produced by gram-negative organisms such as *Escherichia coli*, *Enterobacter* and *Klebsiella pneumoniae* are involved in the pathogenesis of pneumonia much more commonly in the older age group than in the younger one. An important factor that predisposes the elderly to invasion by these organisms is the risk of aspiration of oropharyngeal contents associated with an altered state of consciousness, diminished gag and cough reflexes, esophageal dysfunction, and the presence of nasogastric or tracheostomy tubes.

A number of studies designed to examine the role of abnormalities of immune mechanisms that might be responsible for the increased susceptibility of the elderly to infection have not yielded promising results. Although it has been shown that the function of T cells is impaired in older individuals,⁶⁻¹⁰ the data are open to question because they were derived from hospitalized and chronically institutionalized patients in whom the influence of factors such as underlying major illness and the nutritional status were not taken into consideration. Studies of the chemotactic and phagocytic activity of polymorphonuclear leukocytes, and the activity of the classic and alternate complement pathways have demonstrated no age differences.^{11,12-14} It is clear that, at this moment, observation of immune mechanisms has not indicated that they play a critical role in altering the susceptibility of the elderly to infection.

A very important aspect of the problem of infection in the elderly is essentially qualitative in nature, and is related to changes in the clinical presentation and natural history of some infectious diseases in which increasing age appears to play a major role. Most striking, in this regard, are subacute infective endocarditis, pulmonary tuberculosis, and pneumonia caused by *M pneumoniae*. In addition to the qualitative changes, it is clear that there are also some quantitative ones.

There is no question that the incidence of subacute infective endocarditis is increasing in older individuals. It has become apparent that, among the patients with this disease, the mean age in the 1960s had already risen to 50 to 54 years. It is presently occurring commonly in those 60 to 80 years old. The ratio of men to women is now 9:1.¹⁵ The most common type of underlying cardiac disorder is atherosclerotic valvular or annular disease; the aortic valve is most often involved. Because of the progressive decrease in the temperature of the body with increasing age, older patients are often considered to be afebrile when their oral temperature does not exceed 98.6°F when, in fact, this represents fever. Cultures of the blood appear to be sterile more often in older than in young patients. This may be related to delay in obtaining these because the patient has no "fever."

Although pulmonary tuberculosis is considered to be decreasing in incidence, a serious question may be raised as to whether, in fact, this is true. The writer's experience with this disease over the past 40 years has

made it clear that a number of changes in the clinical behavior of this disease have confused the diagnosis when it is based on old descriptions of its presentation. One striking feature is a remarkable change in the age and sex distribution. In the past, tuberculosis of the lung was most common in women between the ages of 16 to 30 years. Presently, it occurs most often in men over 50 years old; its presence has been detected in not a small number of patients in their seventies and eighties. Two other features of pulmonary tuberculosis appear to be more frequent in elderly than in young persons. One involves the location of the lesion in the lung. Although the classic presentation in the posterior basilar segment of an upper lobe is still the most common, the writer has been impressed by the increasing frequency with which the lower lobes or even the right middle lobe are involved. Very striking has been his experience with an increasing incidence of negative tuberculin reactions in elderly patients from whose gastric aspirates *Mycobacterium tuberculosis* was recovered. These patients fell into two groups. Most were tuberculin-negative, but responded positively to intradermal injection of *Candida*, streptokinase-streptodornase (SK-SD), and mumps. A small number failed to react to all antigens. The fact that the suppression of reactivity to tuberculin was related to active infection was proved by demonstration of a strongly positive reaction 3 to 4 months after specific therapy was instituted.

An infection that has undergone most remarkable changes in its natural history that appear to be associated with aging is the pneumonia produced by *M pneumoniae*. As first described in the early 1940s when it was called "atypical viral pneumonia," the disease was reported to have the following characteristic clinical features. It occurred primarily in young persons and involved older ones very infrequently. The classic pulmonary lesion was present in the right middle lobe ("right middle lobe syndrome"). The temperature was only moderately elevated in most cases. There were no complications or recurrences, and no deaths. Treatment was not recommended unless the temperature was 102°F or higher; antimicrobial agents were given primarily to make patients "feel better," and not to alter the course of what was considered a benign disorder.

Over the years since it was first recognized, the changes in the clinical behavior of this common pulmonary disease have been most striking. First, and probably most important, has been the rapidly increasing incidence of this pneumonia in the elderly in whom it now appears to be very common. The clinical picture in older persons is, for the most part, very different from that which characterizes the disease in young persons. The level of fever is usually higher. There is no preferred site of the lesion in the lungs; it may be present in the upper or lower lobes or in the left lingula, and be nodular or diffuse. Complications involving the nervous system — mononeuritis, polyneuritis, Guillain-Barré syndrome, meningi-

tis and encephalitis — although rare, occur most often in the elderly, and are not due to active infection, but are probably the result of presently undefined immunologic reactions. The writer has noted recurrence of pneumonia only in old people. One patient studied by him had four such episodes over a period of about 8 months. Each was characterized by a single "coin" lesion located in different areas of the lungs. The diagnosis was established during the last three infections by isolation of *M pneumoniae* from sputum and by serial serologic studies. Although rare, death has occurred in older persons. It is now clear that all older individuals with infection of the lung by *M pneumoniae* must be treated with an appropriate antimicrobial agent.

That aging is associated with an overall increase in susceptibility to a number of bacterial infections, many of which have a fatal outcome, is well established. Although a number of investigations directed to evaluation of the relation of immunologic competency to this have been carried out, none of the data obtained from these studies explain the basis for the increase in susceptibility. The results of some of these have been confused by failure to take into consideration the role played by extraneous factors such as the presence of illness other than infection and the nutritional status of patients.

It is interesting that, in most instances, immunologic studies in the elderly have been performed when the subjects are relatively well and not infected. An important question can be raised concerning the time at which such studies need to be carried out. In my opinion, an ideal approach to this problem involves examination of the level of immunocompetence of older individuals when they are well and again when they develop an infection. Such studies may disclose that while immunologic function is relatively normal during a healthy period, the stress of an acute infectious process decreases its effectiveness. Such investigations require the establishment of a cohort of elderly individuals who are studied longitudinally. A base of data concerning the adequacy of immunologic activity prior to infection will serve to define any important aberrations that may be induced after it develops.

The reasons for the striking changes in the natural history of tuberculosis, subacute infective endocarditis, and pneumonia caused by *M pneumoniae*, as indicated not only by an increase in their incidence but also in their clinical presentation, cannot be explained at this time. That this may also be the case in other infections in older persons is a possibility that needs to be examined. Ideal studies of this phenomenon would involve evaluation of specific factors such as the level of immunocompetence from youth to old age.¹⁶ This is obviously not feasible. However, the first step in investigation of this phenomenon involves careful clinical study of patients throughout their lifetimes, an approach available to all internists and family physicians who often care for patients over extended

periods. While this may not identify the reasons for the unusual behavior of some infections in the elderly, it would be most helpful in determining whether or not such changes in clinical behavior are peculiar to the infections listed above or whether they represent a general response to aging. Such information would be very valuable because it would prevent major diagnostic errors. The experience of the writer underscores the importance of this. He has learned that, were he to use the criteria on which diagnosis of subacute infective endocarditis was made 40 years ago, when the vast majority of patients were relatively young, the presence of the disease would be overlooked in over 90% of patients seen today.

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Host Defenses in the Elderly

John P. Phair

Clinicians have long accepted that infections in the elderly occur with increased frequency, often present obscurely, and cause high mortality and morbidity.¹ The scientific basis for these assumptions is not firm, partially because of a lack of a suitable definition of senescence. There are no physiologic and metabolic parameters analogous to the changes that delineate childhood from puberty. Cross-sectional investigations of host defenses in the elderly have used chronologic age to define the study population, a technique which can result in a survey of survivors, potentially a physiologically younger population. In addition, these investigations have excluded individuals with age-associated diseases such as cancer or diabetes, conditions known to alter host defenses and often complicated by infection.

The evidence that infections impose a risk for the elderly individual is based upon clinical and epidemiologic studies. An increased frequency of nosocomial infections, tuberculosis, herpes zoster, and an augmented morbidity and mortality in acute endocarditis in aged patients has been reported. Nosocomial urinary tract infections and bacteremia are 5 times more common in patients over 60 as compared to those 20 to 40 years of age. Hospital-acquired pneumonia occurs 3 times and wound infections 2 times as frequently in this older population.² These increases may reflect failure of resistance in the aged, or the increased time in hospitals of the elderly for complicated diseases. Invasive techniques of diagnosis and management including urinary instrumentation, intravascular devices, surgery plus the use of antibiotics, corticosteroids, and cytotoxic agents all may contribute to hospital-acquired infections in such patients.³ The increasing frequency and mortality of infective endocarditis in the elderly contrast with results in younger patients; survival among the latter group

is improved with penicillinase-resistant penicillin when compared to the pre- and early antibiotic era.⁴ In the elderly with acute endocarditis the cause of the increased prevalence of metastatic infection which contributes to morbidity and mortality is not understood but may relate to ill-defined alterations in host resistance. Currently tuberculosis is a disease of the elderly.⁵ This may represent a clinical manifestation of the well-studied changes in cell-mediated immunity in this age group. However, an alternative explanation is possible. Individuals 60 years of age and over are the major population exposed as children to this infection. Therefore they represent the major group who develop reactivation disease and who are exposed to infected patients. The localization of tuberculosis to this age group therefore may reflect successful public health measures introduced 50 to 70 years ago, not alteration in resistance of older individuals. In contrast, reactivation of herpes zoster infection is associated with waning of virus-specific immunity.⁶ Shingles, however, is not limited to the old or very old. It is seen in young or middle-aged adults in the absence of an obvious immunologic defect.

HOST DEFENSES

Clinical infection implies that the skin or mucosal barriers have been breached by sufficient numbers of virulent microorganisms to overwhelm local defenses and must be differentiated from colonization. Colonization requires adherence of bacteria to body surfaces such as mucosa and is dependent on the interaction of cellular receptors, bacterial adhesions, and local barriers such as fibronectin and secretory IgA.⁷⁻⁹ In addition, mechanical factors such as filtering of air by the nasal passages, the mucociliary elevator of the bronchial mucosa, cough reflexes, or urinary flow act to limit colonization and subsequent infection.

Once invasion has occurred the ability to resist infection is based on a complex set of cellular interactions which constitute the immune and inflammatory response. For clarity of presentation, cell-mediated immunity, antibody-dependent responses, and nonspecific resistance based on polymorphonuclear leukocytes (PMNs) and serum opsonins are discussed separately. It should be kept in mind, however, that the immune and inflammatory systems respond concurrently and are interrelated. Table 2-1 lists components of host defense and the common infections associated with specific deficiencies.

The immune response, both cell-mediated and antibody-dependent, requires processing and presentation of antigen by macrophages to responsive lymphocytes.¹⁰ Macrophage processing of microorganisms, probably by enzymatic degradation, results in presentation of antigen in association with the class II major histocompatible complex (MHC) to responsive lymphocytes which have differentiated under the influence of