

INFECTIONS IN THE ELDERLY

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ABSTRACT

Infections are a leading cause of morbidity and mortality in the elderly. Altered host defences, a senescent immune system, chronic illnesses, and environmental factors all contribute to the aged's predisposition to infection. Infections can present in atypical fashion contributing to diagnostic and therapeutic delays. Awareness of altered antibiotic absorption, metabolism, and excretion in the elderly is essential to correct antibiotic selection and dosing. Additionally, antibiotic interactions with medications commonly used to treat chronic illnesses should be taken into consideration prior to antibiotic prescribing. Prevention of infectious complications in the elderly requires interest, education, vaccination, and early intervention.

Keywords: Physiologic changes, pseudosilent presentation, asymptomatic bacteriuria, E. coli 0157:H7, vaccination

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INTRODUCTION

In developed and developing countries, older adults have witnessed a revolution in the management of the illnesses that ravaged the world of their youth. They survived the infectious diseases that devastated many communities in the pre-vaccination, pre-antibiotic era: polio, influenza, cholera, typhoid, tuberculosis, *Streptococcus pneumoniae*, etc. Despite improvements in community hygiene and public health, the development of potent antimicrobials and invasive medical technology, infections remain a leading cause of death in the aged. Appreciating the pathophysiology of infection in the elderly is essential to prevention and timely intervention. A review of predisposing factors, presentation variations, common clinical syndromes, antimicrobial therapy and the available measures for preventing common infectious diseases in the elderly follows.

REASONS FOR INFECTIONS

Predisposition to infection in the elderly is multifactorial and incompletely understood. Environmental factors, altered mechanical host defences, senescence of the immune system, nutritional deficiencies, and underlying medical illnesses all contribute to the milieu that constitutes a physiologically (not necessarily chronologically) "old" patient⁽¹⁾.

The environment significantly participates in the aged's propensity for infection. Mobile, independent people have different cutaneous and oropharyngeal bacterial flora from

people confined to a bed or a chair. Organisms isolated from a homebound patient differ from those found colonizing an institutionalized patient, which are again different from those colonizing the elderly in an acute-care facility. The more debilitated the patient, the more common it is to find colonization with gram-negative bacilli⁽²⁾. Colonizing pathogens are of clinical significance as subsequent infections often involve opportunistic bacteria previously colonizing the patient⁽³⁾. Once hospitalized, the elderly patient has a two-to-five times increased risk of nosocomial infection with an associated higher mortality when compared to younger patients⁽⁴⁾. Thus, the risk and prognosis of infection are correlated to the environment from which they acquire that infection.

The physiological changes that occur with ageing affect the host-versus-pathogen outcome. The body's natural barriers (ie. skin, mucous membranes) are altered by ageing. Epidermal thinning, decreased glandular secretions, and increased oropharyngeal colonization with virulent pathogens have all been documented to favour microbial invasion. In the urogenital system, the urinary flow rate decreases predisposing to increased bacterial adherence. The presence of prostatic hypertrophy or a permanent indwelling bladder catheter further compromises the patient's ability to resolve bacteriuria. Gastric acid production decreases with age which may result in increasing bacterial colonization of the stomach. The senescent or previously damaged tracheobronchial tree is less able to clear secretions leading to bacterial colonization. Thinning subcutaneous tissue, constant pressure in the bedfast patient, and maceration in the incontinent patient ultimately contribute to skin breakdown and bacterial colonization and invasion⁽⁵⁾.

At the cellular level, age-related changes within the immune system also influence the outcome of host-versus-pathogen interactions. The increased production of phagocytes responsible for intracellular killing of pathogens may be delayed or absent, particularly in the presence of uraemia or carcinomatosis. A normal or low peripheral white cell count can be a poor prognostic finding in an infected aged patient. Ageing appears to have an adverse effect on the production of interleukin I (IL-I) - an intercellular messenger, or cytokine which stimulates T lymphocytes. The suppressor T-cells increase, while the helper T lymphocytes decrease with age. This is correlated with a decreased antibody response to antigen. Although total immunoglobulin does not change, there is less specific antibody made to a particular antigen with more autoantibodies and circulating immune complexes present⁽⁶⁾.

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Interleukin I also normally stimulates the hypothalamus to produce fever in response to infections. With decreasing production of IL-1, the hypothalamus may not be stimulated. Therefore, "apyrexia" does not exclude infection in an elderly patient⁽⁷⁾. Taken together, the ageing immune system is less efficient when responding to pathogens. It would seem likely that waning immunity contributes to the increased mortality and morbidity from infection in the elderly.

Finally, more than 85% of elderly patients have one or more chronic diseases or degenerative processes. Cardiovascular disease, chronic lung disease, hypertension, and diabetes mellitus are epidemiologically related to patients' higher morbidity and mortality when infections occur. Not only can pre-existing illnesses predispose the patient to infection (eg. diabetes mellitus can alter phagocyte and T lymphocyte function), but the drugs taken to treat chronic disease may also predispose the patient to infection (eg. corticosteroids and chemotherapeutic agents)⁽⁸⁾.

PRESENTATION OF INFECTIONS

There are many changes occurring within an ageing individual that diminish or alter the outward symptoms and signs of infection. The possibility of the elderly presenting atypically must be everpresent in the mind of the clinician. Illness may not be recognized as such by the aged individual. The elderly tend to accept deteriorating health without question. Their symptoms may also be so non-specific that they may be dismissed by the non-vigilant medical practitioner. The presentations have been classified in the following way:

- Typical (not age-specific)
- Geriatric
- Silent (ie. missed)
- Pseudosilent (ie. ignored)

Typical: Age changes are not uniform and some individuals even in advanced age show "normal" physiological responses and therefore will present with classic signs and symptoms.

Geriatric: Many body systems lose reserve capacity. Stress imposed on a system can precipitate organ failure. Stress on one system may precipitate failure of several systems. This is demonstrated by the increasing confusion, repeated falls, urinary and/or faecal incontinence, and azotemia that often accompany sepsis in the elderly.

Silent or missed presentation: The clinical presentation does not indicate the site of infection or even the presence of infection. There may be a delay in presentation until the disease is in a very advanced state. This is particularly true of intra-abdominal catastrophes presenting as nonfocal sepsis. Other examples include: Stiff neck thought to be due to cervical osteoarthritis instead of meningitis, or a murmur and hemiplegia thought to be due to a cerebrovascular accident and atherosclerotic valvular disease rather than to endocarditis with an embolic stroke.

Pseudosilent or ignored presentation: The patient may present as a social crisis because of the sudden development of functional decline as previously outlined. The doctor ignores the non-specific functional decline, attributing it to old age. The opportunity to treat a remedial cause is missed⁽⁹⁾.

INFECTION SYNDROMES

Pneumonia

Pneumonia is the leading cause of death from infectious disease in people aged 45 and over, and is among the top five overall causes of death in those over 65 years. Senile emphysema, diabetes mellitus, cerebrovascular accidents, alcoholism, malnutrition, cancer, and hospitalization are particularly pertinent risk factors for pneumonia development. The most common community-acquired organism is the pneumococcus;

Staphylococcus and Gram negative bacilli are frequently hospital-acquired. In nursing and residential home patients, Gram negative bacilli, anaerobes, *Mycobacterium tuberculosis* and *Legionella* have been reported to cause pneumonia more frequently than in the younger population⁽¹⁰⁾.

The clinical presentation may be altered in the aged. The cough may be suppressed, the temperature rise may be less and pleuritic pain may be less acute than typically seen in younger patients. An elevation in respiratory rate and pulse are the most reliable physical signs. The chest roentgenogram is usually helpful. In one-third of elderly patients multiple lobes are involved⁽¹¹⁾.

The course of the illness may vary as well. In some patients, a second pneumonia may occur as soon as the first pneumonia resolves, without an intervening period, due to superinfection or aspiration. The subgroup with multilobar pneumonia has a 33% mortality within four days of presentation. Those with hypotension, hypothermia, a low leukocyte response and concomitant multisystem organ failure have a particularly poor prognosis⁽¹²⁾.

Urinary Tract Infections

Infection of the urinary tract is the second most frequent overall infection, and the leading nosocomial infection in the elderly. One must distinguish simple bacteriuria from true infection.

The incidence of bacteriuria increases with age. True bacteriuria has a prevalence of about 10% in males and about 25% in females over the age of 65 years. In the non-institutionalized patient with bacteriuria, *E. coli* is found in 75%. Once institutionalized, there is a dramatic increase in *Proteus*, *Klebsiella*, and *Pseudomonas aeruginosa*. This is attributed to the changed environment, the presence of an indwelling catheter, and the common use of antibiotics in institutions⁽¹³⁾.

Symptoms must be assessed in light of the ageing genitourinary system. Nocturia is very common in elderly individuals and is not necessarily indicative of infection. Urgency, dysuria, and difficulty passing urine are the most significant symptoms of infection. Acute infection may lead to incontinence, but chronic infection is not a cause of incontinence.

Asymptomatic bacteriuria should not be treated. Treating recurrent asymptomatic bacteriuria results in antibiotic-resistant bacteria and is of no proven benefit to the patient. Recent controlled studies have not found an associated decreased survival in patients with untreated asymptomatic bacteriuria. Treatment is indicated only when the patient is symptomatic. Careful evaluation of the genitourinary system should exclude structural features that will result in recurrent infections if not promptly addressed^(14,15).

Intra-abdominal Infections

A high index of suspicion is required to detect intra-abdominal sepsis. One review found that the abdomen was the most common source of infection in a series of aged patients with pyrexia of unknown origin. There may be no evidence of shock, abdominal rigidity, guarding or distention. Mental confusion, disorientation, and disregard for food may be the only early signs⁽¹⁶⁾.

Biliary tract sepsis is commonly encountered. The gall bladder becomes infected and there may be rapid progression to acute purulent cholecystitis, gangrenous cholecystitis or suppurative cholangitis with minimal clinical findings. The presence of jaundice or peritoneal signs usually indicates extensive infection. Other common intra-abdominal sources include diverticulitis, liver abscess, and a perforated abdominal viscus with peritoneal soiling.

Appendicitis is not confined to the younger age groups. The mortality and complications of appendicitis in the elderly are exceedingly high. This is related to a delay in diagnosis or the presence of other concomitant disease⁽¹⁷⁾.

Bacteremia

The age-specific attack rate for septicemia is high in patients over 60 years, and increases further in individuals over 80 years. Predisposing factors are usually related to problems within the genitourinary, biliary, or respiratory tract, in that order. However, in institutionalized patients, skin and subcutaneous infections follow the urinary tract in frequency as a source of bacteremia⁽¹⁸⁾.

The classic pattern of sepsis may not be present. Fever can be absent in up to 13% of patients and leukocytosis is absent in up to 30%. Mental confusion, respiratory alkalosis, unexplained hypotension, recurrent falls, apathy, or immobility may be the presenting problems. Blood cultures should be considered a routine investigation for an elderly person who is generally unwell. It must be remembered that a negative blood culture does not exclude a diagnosis of septicemia. Bacteremia is often intermittent. A single blood culture is 80-90% sensitive; subsequent culture raises the sensitivity rate to 90-99%. Likewise, recent or concurrent antibacterial use should not dissuade the collection of blood for culture. One study found 40% of afebrile bacteremic patients to have positive blood cultures while receiving antibacterial therapy^(19,20).

With prolonged bacteremia, hypotension and vasoconstriction follow; the patient appears cold, clammy, and peripherally cyanosed. Disseminated intravascular coagulation, renal cortical necrosis, and adult respiratory distress syndrome may dominate the clinical picture.

The mortality of elderly patients with bacteremia is 40-60%. The aged's mortality from nosocomial bacteremia is the same as for community-acquired bacteremia, unlike younger patients where community-acquired bacteremia has a lower mortality⁽²¹⁾.

Bacterial Endocarditis

The availability of antibiotics has changed the incidence of rheumatic heart disease increasing the average age of the patient with bacterial endocarditis to over 50 years old. Presently, patients over the age of 60 comprise 35-45% of patients with endocarditis in many reported series. Predisposing features include sclerotic heart valves, bicuspid valves, prosthetic devices (valve or pacemaker), invasive vascular procedures or intravenous lines, dental procedures, skin lesions, and gastrointestinal lesions. Endocarditis in the elderly can occur on normal valves as well.

In many, endocarditis presents with fever, a cardiac murmur, and anemia. However, 30-70% of aged endocarditis cases present atypically. Fever is present in 80%, but a new or changing murmur is found in only 36%. Confusion is found more frequently than in younger patients with endocarditis. The initial diagnosis was found to be incorrect in 68% of elderly with endocarditis in one series, while younger patients were misdiagnosed in only 24% of cases⁽²²⁾.

The causative bacteria are viridans streptococci, other streptococci (including *Streptococcus bovis*), staphylococci, and Gram negative rods. The use of intravenous catheters accounts for the high incidence of *Staphylococcus* infections. The findings of *Strep. bovis* should prompt an investigation of the colon, as it has been associated with colonic carcinoma and atypical polyps^(23,24).

Complications in the elderly are similar to those in younger patients except there is a higher risk of a major neurologic event. Morbidity and mortality are higher in the elderly due to

a number of factors: less organ reserve, late presentation, and late diagnosis. A recent publication reported permanent disability or death in 43% of patients over 60 years, 32% in those 40-60 years old, and 20% if less than 40 years old^(24,25).

Infectious Diarrhoea

Self-limited infectious diarrhoea in young adults often goes unreported. The elderly are less able to tolerate the fluid and electrolyte shifts. Although the pathogens are similar, they are not infrequently associated with extraintestinal complications. For instance, the elderly with *Salmonella* gastroenteritis have a higher frequency of subsequent *Salmonella* arterial and pulmonary infections. Therefore, unlike younger patients with *Salmonella* gastroenteritis, the elderly should be considered for therapy⁽²⁶⁾.

Another pathogen causing high mortality in the elderly is enterotoxigenic (or enterohemorrhagic) *E. coli* 0157:H7. This pathogen is acquired by ingesting ground beef or raw milk. The resultant bloody diarrhoea has been associated with the hemolytic uremic syndrome and thrombotic thrombocytopenic purpura in the elderly, with the attendant high mortality⁽²⁷⁾.

Additionally, pseudomembranous colitis due to *Clostridium difficile* should be considered in an older patient with bloody diarrhoea and a recent history of antibiotic use.

ANTIBIOTIC THERAPY

Antibiotics should be used discriminately, and only after appropriate cultures have been obtained. A careful assessment of the benefit versus the toxicity of therapy should be made.

Understanding the alteration of drug distribution in the elderly is an important factor is drug selection and dosage. This topic has been discussed extensively in another article published in this issue⁽²⁸⁾. In patients on medication in addition to antibiotics, awareness of possible drug interactions is essential in avoiding complications. For example, trimethoprim-sulfamethoxazole (TMP-SMX), erythromycin, or metronidazole may suddenly increase the anticoagulant effect of warfarin by decreasing the metabolic clearance of warfarin. Erythromycin increases the serum level of theophylline compounds by decreasing their metabolism, thus potentiating theophylline toxicity. TMP/SMX may potentiate the action of chlorpropamide resulting in unexpected hypoglycemia. Rifampicin induces hepatic enzymes to clear warfarin, anticovulsants, (and oral contraceptives) with potentially disastrous results⁽²⁹⁾.

Antibiotics alter intestinal bacterial flora, which may result in diminished Vitamin K production and/or selective bacterial overgrowth. The selective overgrowth of cytotoxin-producing *Clostridium difficile* is responsible for pseudomembranous colitis.

PREVENTION OF INFECTION IN THE ELDERLY

The most efficient method of limiting the morbidity and mortality of infectious diseases in the elderly is by preventing their occurrence. Preventive health measures begin with education of the patient or the patient-guardian regarding nutrition, avoidance of tobacco and ethanol, prevention of bedsores, and the effect of chronic disease on infection risk. A patient or family member aware that subtle changes in general activity or behaviour may be a harbinger of infection will present earlier in the course of that illness, with subsequent improved outcome.

Besides the passive measures to diminish the consequences of infection, there are several active efforts that are available to physicians. Diphtheria, tetanus, influenza, and *Streptococcus pneumoniae* are associated with a higher morbidity and

mortality in the aged. These illnesses strike those whose immunity has waned from distant infection and vaccination. Vaccines are currently available that are of documented benefit. Diphtheria-tetanus (Td) boosters should be given at ten year intervals. Influenza vaccine is reconstructed yearly to represent the prevalent strains. The polyvalent pneumococcus vaccine is given once with a booster in 6-8 years in high risk individuals, it includes >90% of the pneumococcal serotypes isolated in Singapore (1977-86)⁽³⁰⁾. Influenza and pneumococcal vaccine should be offered to those over the age of 65 years or those with chronic medical illnesses^(31,32).

Additionally, antibiotics to prevent bacterial endocarditis should be given to the elderly with underlying cardiac valvular disorders who will undergo any of the following: dental procedures likely to result in gingival bleeding, surgery of instrumentation of the respiratory, gastrointestinal or genitourinary systems.

SUMMARY

Advances in the diagnosis and therapy of infectious diseases have benefited all members of society. Despite our efforts, the elderly too frequently succumb to infection. Many variables contribute to the morbidity of infection in the aged. It remains the physician's responsibility to be aware of subtle presentations of infectious disease in the elderly and assure an accurate diagnosis is obtained. The ultimate outcome of an infectious process depends on the type of invading organism, underlying disease, previous vaccination efforts, status of host defense mechanisms, early recognition, and effective nontoxic treatment of the infection. The atypical presentation of infection may pose diagnostic difficulties, but explains the enthusiastic physician's fascination with the practice of geriatric medicine.

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