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Foodborne Illness in the Elderly†

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ABSTRACT

The elderly (≥65 years of age) are more susceptible to morbidity and mortality from foodborne-induced gastroenteritis than younger individuals. Several factors contribute to the increased susceptibility to foodborne infections as well as other infections in elderly populations. These include an age-associated decrease in humoral and cellular immunity, age-related changes in the gastrointestinal tract (decreased production of gastric acid and decreased intestinal motility), malnutrition, lack of exercise, entry into nursing homes, and excessive use of antibiotics. Data from foodborne outbreaks associated with nursing homes indicate that the elderly are more likely to die from foodborne *Campylobacter, Clostridium perfringens, Escherichia coli* O157:H7, *Salmonella,* and *Staphylococcus aureus* infections than the general population. Infections by *Salmonella* species are the most common cause of illness and death in nursing homes with *Salmonella enteritidis* as the major cause of both morbidity and mortality. While it is impossible to turn back the clock, practicing a healthy life-style with regular exercise, maintaining a balanced diet, receiving regular health care, paying attention to personal hygiene, and monitoring food preparation and handling should lead to a reduced incidence of foodborne and other infections in the elderly.

The frequent occurrence of nursing home foodborne outbreaks indicates that the elderly are particularly susceptible to gastroenteritis-induced mortality *(80, 95).* Surveys reveal that elderly individuals are more vulnerable to gastroenteritis-induced death. Using 1985 hospitalization data from a health system database, Gangarosa et al. *(51)* found that of 87,181 gastroenteritis cases, 17.0% occurred in individuals ≥70 years of age, and 37.9% of the cases were in individuals aged 1 month to 19 years. There were 514 gastroenteritis-related deaths in the database; 67.5% of the deaths occurred in the ≥70-year-old group, whereas only 1.9% of gastroenteritis cases in the younger group ended in death *(51).* Analyzing deaths associated with diarrheal disease in the United States from 1979 to 1987, Lew et al. *(81)* found that deaths in the 1-month to 4-year-old group accounted for approximately 11%, whereas 51% of people >74 years of age who developed diarrhea subsequently died.

In addition to gastroenteritis, the elderly are more susceptible to contracting and/or dying from a large number of other infectious diseases including urinary tract infections, pneumonia, tuberculosis, bacteremias, and meningitis as well as other infections *(12, 40, 41).* Many of these infections are preventable if diagnosis and treatment are not delayed.

Ben-Yehuda and Weksler *(12)* describe the elderly as suffering from age-associated immune deficiency; the weakened immune system may explain, in part, the increased susceptibility of elderly populations to infections, but undoubtedly other factors also play a role. In the present review, the factors that may contribute to increased susceptibility of the elderly (here defined as those individuals ≥65 years of age) to foodborne illness are discussed.

FACTORS THAT MAY CONTRIBUTE TO INCREASED SUSCEPTIBILITY, MORBIDITY, AND MORTALITY TO FOODBORNE PATHOGENS IN THE ELDERLY

The elderly represent a very heterogenous population in terms of health, physiological functions, and susceptibility to disease. For any given physiological function, the distribution and heterogeneity of that function becomes more diverse as the population ages *(114).* A function may decline at a slow rate in one elderly person but at a faster rate in another person of the same age. The age at which disability and increased susceptibility to infections occurs will be dependent upon the rate of decline in various physiological functions *(114).*

Immune system and aging. It would seem logical to consider the immune system of the healthy young (19 to 39 years of age) as the norm; thus, many of the parameters listed in Table 1 indicate that the immune status of the elderly deviates from that norm. Data from healthy individuals were used to develop Table 1; however, it is obvious that there are contradictions within many of the immunological parameters listed in the table. These discrepancies probably reflect the high degree of individual differences seen in the

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TABLE 1. *Comparison of the immune systems of healthy elderly humans (≥65 years of age) and young healthy humans (19 to 39 years of age)*

Immune characteristic	Status in elderly compared to young	References
Number of mature T cells	↔[a]	*(19, 74, 127)*
	↓	*(76, 101)*
Number of immature T cells	↑	*(76)*
Number of helper T cells ($CD4^+$)	↔	*(74, 76, 101, 111, 127)*
Number of cytotoxic/suppressor T cells ($CD8^+$)	↓	*(76, 127)*
	↔	*(74, 101)*
Number of B cells	↔	*(19, 101, 127)*
	↓	*(103)*
Number of natural killer cells	↔	*(19, 127)*
	↑	*(78)*
Number of naive $CD4^+$ T cells	↓	*(19, 64, 74, 101, 111, 125, 127)*
Number of memory $CD4^+$ T cells	↑	*(64, 74, 101, 111, 122, 125, 127)*
	↔	*(19)*
Number of naive $CD8^+$ T cells	↓	*(19, 127)*
Number of memory $CD8^+$ T cells	↔	*(74)*
	↑	*(122, 127)*
	↓	*(19)*
Mitogen-induced T-cell proliferation	↓	*(31, 75, 88, 96, 122, 124, 125)*
Cytotoxic $CD8^+$ T-cell response against influenza virus-infected target cells	↓	*(90)*
Production of IL-1	↑	*(103)*
Production of IL-2	↓	*(22, 75, 91, 103, 104, 105, 106, 122)*
Production of IL-4	↑	*(90, 101)*
	↓	*(3)*
	↔	*(22, 122)*
Production of IL-5	↔	*(22)*
Production of IL-6	↔	*(22)*
	↑	*(103)*
Production of IL-8	↓	*(58)*
Production of IL-10	↑	*(19, 24)*
Production of IFN-γ	↓	*(19, 22, 90, 103)*
	↔	*(122)*
Production of TNF-α	↔	*(22)*
	↑	*(103)*
	↓	*(58)*
Delayed-type hypersensitivity reactions	↓	*(34, 113)*
	↔	*(75)*
Primary vaccination with tetanus toxoid	↓	*(103)*
Boosting with tetanus toxoid	↓	*(5, 103)*
Concentration of serum IgG	↑	*(75, 103)*
	↓	*(29)*
	↔	*(4)*
Concentration of serum IgA	↑	*(4, 75, 103)*
	↔	*(29)*
Concentration of serum IgM	↓	*(4, 29)*
	↔	*(103)*
Concentration of serum IgE	↓	*(3, 103)*
Concentration of salivary IgG	↑	*(4, 29)*
Concentration of salivary IgA	↑	*(4, 29)*
Concentration of salivary IgM	↑	*(4)*
	↔	*(29)*
Salivary sIgA secretion rate	↓	*(29, 93)*
Anti-inflammatory capacity of red blood cells[b]	↓	*(54)*
Natural anti-α-galactosyl (Gal-α[1 → 3]-Gal) IgG antibody	↑	*(20)*
Autoantibodies and circulating immune complexes	↑	*(20, 59, 112)*
Monoclonal antibodies (benign monoclonal)	↑	*(83, 110)*

[a] ↔, Parameter approximately same in both elderly and young; ↑, parameter increased in elderly; ↓, parameter decreased in elderly.

[b] Red blood cells protect the individual against the inflammatory consequences of immune complexes and complement activation in the circulation. The red blood cells acting via the complement receptor, CR1, function as carriers of immune complexes to the liver and spleen and as a cofactor for Factor I in cleavage of C3b resulting in inactivation of complement *(54, 84)*.

elderly population as well as differences in age of the groups studied and their health status. Variation could be introduced due to differences in investigative techniques, as well.

T-cell function declines with aging. Mitogen-induced T-cell proliferative responses, delayed-type hypersensitivity reactions, and T-cell-dependent antibody production (primary and booster vaccination with tetanus toxoid, for example) are decreased (Table 1). Production of interleukin-2 (IL-2) by T cells declines with aging (Table 1), and IL-2 is a key component of these T-cell-mediated responses *(94)*. Generation of high-affinity IL-2 receptors after stimulation by mitogen or antigen also decreases with aging *(94)*.

In the elderly, there is a preponderance of antigen-experienced memory T cells as compared to naive (virgin, i.e., have not yet encountered antigen) T cells (Table 1). The T-cell population in the young resembles the naive T cells that emigrate from the thymus to the peripheral immune system. With aging, however, there is a shift from naive T cells to memory T cells *(94, 104)*. Because there is a decrease in naive, undifferentiated T cells in the elderly, there is a decreased ability to respond to new antigens, as well as to new antigens expressed by mutated infectious agents or to new antigens present in vaccines *(46)*.

Naive T cells preferentially produce IL-2, and the decrease in naive cells with aging is the explanation for decreased levels of IL-2 in the elderly *(104)*. Decreased production of IL-2 and IL-2 receptor may be due to alterations in signal transduction across the T-cell membrane. Defects in signal transduction pathways involving calcium mobilization and protein phosphorylation may explain the failure of IL-2 gene transcription, which leads to decreased T-cell responses in older individuals *(94, 104, 109, 125)*.

Most antigens invoke antibody synthesis by B cells in a T-cell-dependent fashion. Cooperation with naive helper T cells is necessary for naive, undifferentiated B cells to differentiate and mature into antibody-producing cells when they respond to T-cell-dependent antigens *(94, 103)*. IL-2 is involved in B-lymphocyte growth and immunoglobulin secretion *(48)*. Thus, the decrease in naive T-helper cells and IL-2 production suggests that there is decreased response by naive B cells to newly introduced antigens, thereby resulting in decreased humoral immunity. The increase in autoantibodies, circulating immune complexes, natural antibody (anti-α-gal), and monoclonal antibodies seen in elderly populations (Table 1) indicates that aging B cells produce abnormal antibodies, suggesting that there may be some degree of derangement in B-cell activity or regulation. It is not clear, however, if serious consequences result from this perceived derangement of B cells.

That the elderly are more susceptible to gastrointestinal infections suggests that the mucosal immune system may be impaired. Schmucker et al. *(121)* has recently reviewed the impact of aging on gastrointestinal mucosal immunity and concluded that the literature in the field is confusing and contradictory. The age-increased incidence in gastrointestinal diseases indicates that there is increased need to determine the relationship between mucosal immunity and disease in elderly populations *(121)*.

Thus, immunological studies with elderly individuals do indicate that one manifestation of aging is a gradual decrease in the efficiency of B-cell- and T-cell-mediated immune responses. It is probable that the changes in immune functions listed in Table 1 are more exaggerated in ill elderly patients. For example, Lesourd et al. *(76)* demonstrated a 1.6-fold increase in immature T cells in elderly patients who had a history of recent disease as compared to healthy patients of the same age. Also, IL-2 production by peripheral blood mononuclear cells isolated from elderly patients with urinary tract infections was 2.5-fold lower than that from cells isolated from healthy age-matched individuals *(25)*.

Major surgery and immunosuppression. Major surgery can result in a decrease in certain T-cell-mediated immune functions. Using peripheral blood T cells isolated from patients ($n = 69$; age $= 65 \pm 9$ years) before, during, and after major surgery, Hensler et al. *(63)* demonstrated marked decreases in cell proliferation and cytokine production by the T cells. The affected cytokines included IL-2, IL-4, interferon (IFN)-γ, and tumor necrosis factor (TNF)-α. Within 3 to 5 days after the operation, however, the immunological parameters returned to normal levels *(63)*. Thus, major surgery leads to a short period of immunosuppression during which the patient may be at increased risk for infections. Elderly patients who have age-induced immunosuppression will be at additional risk for infections after major surgery as compared to younger patients.

Gastrointestinal tract and aging. Inflammation of the gastric mucosa (gastritis) and atrophy occur in ~50% of the population >50 years of age *(13)*. Inflammation and atrophy escalate with increased age. These alterations of the gastric mucosa lead to hypochlorhydria (decrease in stomach acid) and may even lead to achlorhydria (complete loss of stomach acid) *(12, 35, 99)*. Low gastric acidity may also be due to drugs (antacids, histamine H_2-receptor antagonists, or marijuana), gastrectomy (removal of part or all of the stomach), or malnutrition *(17)*.

Stomach acid production in aged men and women, in the absence of atrophic gastritis, is similar to that of young individuals *(38, 47, 57, 67, 72)*. Interestingly, Goldschmiedt et al. *(57)* reported that aging was associated with increased acid production. The reporting of decreased gastric acid production in the elderly in earlier studies was flawed because of the inclusion of elderly individuals with atrophic gastritis or *Helicobacter pylori* infections *(86)*. The prevalence of both *H. pylori* infection and gastritis with atrophy leading to reduced acid production increases with age; however, in healthy elderly individuals without these pathologies, acid secretion does not decrease with age *(72)*. Thus, aging per se is not responsible for decreased stomach acid secretion.

Because the stomach plays an important role in limiting the number of bacteria that enter the small intestine, a decrease or loss of stomach acidity increases the likelihood of infection if a pathogen is ingested with food or water *(17, 55, 99)*. Patients with hypo- or achlorhydria are more susceptible to cholera, salmonellosis, shigellosis, or giardiasis *(55, 97)*. Natural gastric juice is lethal to *Shigella sonnei* in vitro but there is no lethality when the pH of the juice is ≥3 *(42)*. Volunteer studies indicated that the infecting dose for *Vibrio cholerae* is $\sim 10^8$ organisms for normal individuals; however, neutralization of stomach acid by administration of bicarbonate lowered the dose to $\sim 10^4$ organisms per individual *(23)*. In cholera outbreaks that occurred in Israel and Italy, gastrectomized patients suffered a more serious disease *(56, 119)*.

Stomach ulcers are treated with drugs such as antacids that neutralize gastric acid or histamine H_2-receptor antagonists that block gastric acidity output *(13)*. These drugs lead to healing of ulcerative lesions; however, they do interfere with the antibacterial action of gastric secretions. The use of antacids or histamine H_2-receptor antagonists was directly associated with *Listeria monocytogenes* infections in patients during a listeriosis outbreak in Boston hospitals in 1979 *(65)*. Schlech et al. *(120)* demonstrated that the reduction of gastric acidity in rats by a histamine H_2-receptor antagonist decreased the infective dose of *L. monocytogenes*. Thus, the drug-related decrease in gastric acidity in the Boston hospital listeriosis patients obviously permitted survival of the ingested *Listeria*. It is clear that hypo- or achlorhydria is associated with increased infection by gastroenteritis-causing microorganisms.

Gastrointestinal motility (peristalsis) decreases with aging *(35, 99)*. Because peristalsis provides a mechanical means for removal of ingested pathogens, the strong peristalsis initiated by an enteropathogen (diarrhea) aids in elimination of the organism during intestinal infections *(50)*. The administration of antidiarrheal agents may compound diarrheic infections. Humans with shigellosis, when treated with an antimotility agent, developed a more severe disease with prolonged carriage of the organisms *(44)*. There is an increased risk of *Escherichia coli* O157:H7 infections progressing to hemolytic uremic syndrome (HUS) in children given antimotility agents *(11)*. In infected children who did not develop HUS, administration of an antimotility agent prolonged bloody diarrhea. Tarr *(129)* did not recommend treatment of *E. coli* O157:H7 infections with antimotility agents or narcotics to relieve diarrheic symptoms because the drugs delayed clearance of the pathogen from the intestinal tract with the possibility of increased Shiga-like toxin absorption. Thus, the use of antimotility agents to relieve diarrheic symptoms induced by gastrointestinal pathogens interferes with the cleansing action of peristalsis and may lead to worsening of the disease.

The decrease in gastric acidity and intestinal peristalsis seen in elderly populations makes them more susceptible to gastrointestinal infections. This susceptibility is increased when elderly patients are dispensed medications that decrease stomach acidity or antimotility agents to relieve diarrheic symptoms.

Nutrition and aging. Under certain conditions, the elderly can be host to a number of nutritional problems such as protein-energy undernutrition, vitamin and trace mineral deficiencies, and malabsorption of nutrients *(34)*. There are many reasons why a certain portion of the elderly population is malnourished, and a number of risk factors that can induce malnutrition are listed in Table 2.

Malnutrition, regardless of age, leads to increased incidence of infections, delayed wound healing, and poor clinical outcomes *(14, 30, 99)*. There is a close relationship between nutrition and immunity, and malnutrition can adversely affect a number of immune functions (Table 3). Nutritionally acquired immunodeficiency syndrome (NAIDS) is the term used to describe immune dysfunction associated with malnutrition *(9, 10)*. Because the elderly suffer from age-induced immunodeficiencies (Table 1), NAIDS can impose an additional strain on the aging immune system with resultant increased risk of infections.

It has been estimated that the diets of approximately one third of the elderly are deficient in vitamins and trace

TABLE 2. *Risk factors for decreased nutrient intake in the elderly*[a]

1. Altered taste and smell (decrease in pleasure of eating)
2. Early satiety
3. Medication (loss of appetite, nausea, malabsorption)
4. Changes in emotional state (depression, grief, loneliness)
5. Change in mental state (dementia, paranoia, mania)
6. Digestive disorders (dental problems, dryness of mouth, difficulty in swallowing, hypo- and achlorhydria, gastrointestinal diseases, malabsorption)
7. Chronic illnesses (diabetes, pulmonary diseases, cardiovascular diseases, cancer)
8. Physical disability (difficulty in shopping for and in preparing food)
9. Poverty
10. Living alone; social isolation
11. Cigarette smoking; alcohol abuse

[a] Data taken from a variety of references *(1, 62, 136, 138, 139)*.

TABLE 3. *Immune functions that may be affected by malnutrition*[a]

1. Decrease in cell-mediated immunity
   a. Depression of cutaneous delayed-type hypersensitivity to both recall and new antigens
   b. Suppression of T-cell proliferative response to mitogens and antigens
   c. Reduced antibody synthesis to T-cell-dependent antigens
   d. Delay in skin allograft rejection
   e. Reduced number of mature T cells with concomitant increase in immature T cells
   f. Decrease in number of $CD4^+$ T cells
2. Decrease in humoral immunity
   a. Decreased antibody production
   b. Decreased response of B cells to mitogens and antigens
   c. Reduced secretory IgA level
   d. Decreased B cell numbers
   e. Decrease in vaccine response
3. Impaired complement activation system
   a. Reduction in level of C3 component
   b. Reduction in level of factor B (factor B is a component of alternate complement activation)
4. Reduced macrophage and neutrophil response
5. Atrophy of lymphoid tissue
6. Reduced synthesis and release of IL-2 and γ-IFN

[a] Data taken from a variety of references *(30, 75, 77, 131)*.

elements *(33)*. The supplementation of vitamins and/or minerals to the diet of the elderly has been shown to improve various immunological parameters. For example, when the diet of a population of independently living healthy subjects ≥65 years of age was supplemented with vitamin E, Meydani et al. *(92)* demonstrated enhancement of various cell-mediated immune functions. There was improvement of delayed-type hypersensitivity responses and increased synthesis of antibodies to hepatitis B antigen and tetanus toxoid (both are T-cell-dependent antigens). Vitamin E supplementation had no effect on nonspecific IgG, IgA, or IgM levels and had no effect on T- and B-cell numbers *(92)*. The individuals receiving vitamin E supplementation also reported fewer infections.

There does not appear to be a need for iron supplements in the diet of most segments of the U.S. population including the elderly *(39)*. The elderly do not excrete iron as readily as younger individuals; therefore, iron storage increases with aging *(39, 69)*. Thus, in the absence of clinical signs of iron deficiency, such as anemia, iron supplements are not recommended for the elderly *(39)*.

Elderly subjects (>65 years of age), living independently and who are apparently healthy, showed significant improvement in immune status when given optimum amounts of vitamins and minerals *(32)*. After 12 months of supplementation, there were increases in the number of $CD4^+$ T cells, improvement in lymphocyte response to mitogen stimulation, increase in the levels of IL-2 and IL-2 receptor, and increase in natural killer cell activity. In addition, Chandra *(32)* showed that nutrient-supplemented individuals had fewer infections as compared to those individuals receiving placebo treatment. Similarly, Bogden et al. *(15)*, studying apparently healthy, independently living subjects aged 59 to 85 years, demonstrated that daily micronutrient (vitamins and minerals) supplementation, over a 12-month period, led to a significant improvement in delayed hypersensitivity skin test responses as compared to the group receiving a placebo. It is probable that an elderly population that is obviously malnourished will show improvement of immune status if their diets are properly supplemented.

Even though Bogden et al. *(15),* Chandra *(32),* and Meydani et al. *(92)* demonstrated that nutrient supplementation improved immune status in apparently healthy elderly subjects, it is not clear that these subjects were actually suffering from NAIDS. It is clear, however, that many elderly patients in nursing homes do have NAIDS with concomitant increased medical care expenditures, morbidity, and mortality *(62, 99, 139).* Malnutrition in nursing home elderly may result from the risk factors listed in Table 2; however, the nursing home environment also can lead to malnutrition in these individuals. Loss of privacy, loss of control over food choices, inappropriate meal timing, inappropriate food temperatures, the presence of noisy or psychotic patients during eating, the need for assisted feeding, and unattractive eating surroundings may lead to a decrease in nutrient intake by elderly nursing home patients *(62).*

Thompson et al. *(132)* recommended nutritional therapy for elderly hospitalized and nursing home patients. In addition, the apparently healthy, independently living, but economically straitened elderly should be given protein-calorie, vitamin, and trace element supplements *(132).* In the long run, administration of nutritional therapy to geriatric populations will decrease medical costs and limit morbidity and mortality.

Exercise, immunity, and aging. An acute bout of exercise is immunosuppressive in both the young and elderly. The effect of chronic (long-term) exercise on immune function, however, is less clear because studies in humans have shown conflicting results *(89).* However, it is believed that moderate regular exercise is an important factor in maintaining good health and immune function in the elderly. Exercise benefits the skeletal, muscular, cardiovascular, respiratory, endocrine, and nervous systems of elderly individuals *(35).* Regular exercise also increases several indices of immune function in the elderly. Lymphocyte proliferation upon stimulation by mitogen, natural killer cell activity, and cutaneous delayed hypersensitivity responses are significantly increased in elderly subjects enrolled in a fitness program *(31).* In addition, nutritional supplementation combined with the fitness program had an even greater positive effect on immune responses *(31).* Elderly recreational male runners (mean age 64) showed increased lymphocyte proliferative responses to mitogen and increased cytokine production (IL-2, IL-4, and IFN-γ) as compared to sedentary elderly controls (mean age 66) *(122).* However, other immune parameters did not differ greatly between the two groups.

Long-term regular exercise appears to improve age-related decline in certain T-cell immune functions and is probably necessary for maximum efficiency of the immune system in the elderly *(100).* An excellent review discussing the role of exercise and immunity in aged individuals has recently appeared *(134).*

Nursing homes and foodborne disease in the elderly. Elderly nursing home residents have certain characteristics that make them more susceptible to infectious diseases. Age-related decreases in immune function, NAIDS, underlying illnesses, diminished physiological functions, immobility, decreased gastric acidity, and treatments involving antimicrobial agents make the elderly particularly vulnerable to foodborne infections *(80, 82).* Thus, the nursing home environment is a unique ecological niche in which a large number of susceptible elderly persons live together and share institutionally prepared foods. If a breakdown in food hygiene occurs in the nursing home setting, there is potential for foodborne outbreaks with high morbidities and mortalities *(79).*

Levine et al. *(80)* studied the 115 foodborne outbreaks (4,944 cases and 51 deaths) that occurred in nursing homes for the years 1975 to 1987. The causative pathogens were identified in 52 of the outbreaks and included *Bacillus cereus, Campylobacter jejuni, Clostridium perfringens, E. coli* O157:H7, *Salmonella* species, *Staphylococcus aureus,* and *Giardia lamblia.* Three pathogens accounted for 40.8% of the total cases: *C. perfringens* (10.0%), *Salmonella* species (20.3%), and *S. aureus* (10.5%). Known pathogenic agents accounted for 92.2% of the 51 deaths that were due to foodborne disease in nursing homes. Four pathogens accounted for 90.1% of the deaths: *C. perfringens* (3.9%), *E. coli* O157:H7 (7.8%), *Salmonella* species (74.5%), and *S. aureus* (3.9%) *(80).* In a Canadian nursing home *E. coli* O157:H7 outbreak not reported by Levine et al. *(80),* 55/169 residents were infected *(21).* Twelve of the infected individuals developed hemolytic uremic syndrome with death occurring in 11. Antibiotic treatment was associated with higher case fatality.

Mishu et al. *(95)* analyzing *Salmonella enteritidis* outbreaks in the United States for the period 1985 to 1991, found that 11.2% (1,481 cases) of the 13,168 cases of *S. enteritidis* infections occurred in nursing homes and hospitals. There were 50 deaths attributed to *S. enteritidis,* 45 of which occurred in nursing homes and hospitals. Levine et al. *(80)* found that *S. enteritidis* alone was responsible for 37.3% of the foodborne disease deaths in nursing homes for the period 1975 to 1987. In 1995, five deaths due to *S. enteritidis* were reported, four of those deaths occurred in nursing home residents *(28).* Nursing home residents in the United States, therefore, are at risk for death from foodborne diseases, particularly those due to *Salmonella* and *E. coli* O157:H7.

Incidents in residential homes (95% of which were homes for the elderly) accounted for 282 of the 1,275 outbreaks of infectious intestinal diseases in England and Wales for the period of 1992 to 1994 *(117).* Foodborne transmission accounted for 58/282 (20.6%) of outbreaks; 25/58 (43.1%) of the foodborne outbreaks were due to *Salmonella* infections and 23/58 (39.7%) were due to *C. perfringens.* Unfortunately, Ryan et al. *(117)* do not discuss the number of cases involved in the foodborne outbreaks but did say that 26 deaths resulted from the 282 residential home

TABLE 4. *Deaths from foodborne disease in the United States: comparison between nursing home population and general population*

Pathogen	Deaths per thousand cases	
	General population	Nursing home population[a]
Campylobacter	2.1[b]	11.1
Clostridium perfringens	0.46[b]	4.0
Escherichia coli O157:H7	21.8–26.8[c]	117.6
Salmonella species	1.5[b]	37.8
Staphylococcus aureus	0.0[b]	3.9

[a] Levine et al. *(80)* (data for 1975 to 1987).
[b] Bean et al. *(7, 8)* (data for 1983 to 1992).
[c] Buzby et al. *(18)* (table 10, estimates for 1993).

outbreaks; 18 of the deaths were due to *Salmonella* species. Similarly to reports from the United States, *Salmonella* species caused most of the foodborne outbreaks and deaths in England and Wales residential homes. However, foodborne disease from *C. perfringens* in residential homes appears to be more common in England and Wales than in the United States.

Nursing home residents are more likely to die from foodborne infections than the population at large. The data presented in Table 4 indicate that residence in a nursing home increased the risk of death from infections caused by the foodborne pathogens, *Campylobacter, C. perfringens, E. coli* O157:H7, *Salmonella,* and *S. aureus.*

The use of antibiotics by the elderly. Antimicrobial compounds are among the most frequently prescribed pharmaceuticals in nursing homes and may account for at least 40% of prescribed medication *(99)*. Antibiotic treatment in nursing homes was often initiated in the absence of a physician's examination and microbial culture information *(73, 137)*. Antibiotics were often prescribed for infections in which antibiotics are not considered to be effective. In other cases, a certain antibiotic was prescribed even though a less expensive and more effective one would have been more appropriate *(71, 107, 137)*. The intensity of antibiotic use combined with inappropriate usage leads to the potential for emergence of resistant microorganisms as well as an increase in health care costs.

SUSCEPTIBILITY OF THE ELDERLY TO SPECIFIC FOODBORNE PATHOGENS

C. jejuni. *Campylobacter* is the most common diarrheic bacterial pathogen isolated in the United States. The most frequently isolated species is *C. jejuni (18)*. The majority of cases of *C. jejuni* diarrhea are sporadic. Foodborne outbreaks due to the organism are relatively uncommon with only about 1% of the total foodborne disease outbreaks in the United States being due to campylobacteriosis *(7)*. In the United States and other developed countries, the incidence of campylobacteriosis is highest in the <1-year-old group with the next highest incidence occurring in the 20- to 40-year-old group. The elderly, as a group, do not appear to be particularly susceptible to *C. jejuni* infections *(130)*. Levine et al. *(80)*, in their review of foodborne disease outbreaks in nursing homes, reported that two outbreaks involving 90 individuals and one death were due to foodborne *C. jejuni* during the period 1975 to 1987.

For the period 1985 to 1991, there were 7,366 estimated cases of Guillain-Barré syndrome (GBS) in the United States with 37.7% of the cases occurring in the ≥65 age group *(108)*. During that time period, there were 3,770 estimated deaths attributed to GBS; 66.0% of those deaths occurred in the ≥65 age group. *C. jejuni* infections played an important role in the GBS deaths because ~29% of GBS cases have their origin in *C. jejuni* gastroenteritis *(123)*. Although the elderly do not have increased susceptibility to campylobacteriosis, sequelae of *Campylobacter* infections such as GBS occur at a higher rate in older individuals.

Cryptosporidium. Neonatal rodents, calves, and lambs, in comparison with adult animals, are highly susceptible to oral infections due to *Cryptosporidium.* Similarly, cryptosporidiosis is much more common in young children than in adults *(140)*. The susceptibility of elderly humans to *Cryptosporidium* infection is not clear. However, one report does indicate that the elderly are more susceptible to infections by the parasite. In the waterborne outbreak of *Cryptosporidium* that occurred in Milwaukee in the spring of 1993, the likelihood of infection was increased 2.6-fold in individuals ≥60 years of age as compared to those 0 to 11 years of age and was increased 1.6-fold in comparison to individuals 12 to 59 years of age *(36)*.

Bannister and Mountford *(6)* discussed severe *Cryptosporidium* diarrhea in three elderly subjects (ages 69, 70, and 78) and suggested that the elderly, due to their immune-deficient status, may be at increased risk for cryptosporidial infections, and the disease may be more severe. Hospitalized elderly patients (mean age = 77) with chronic diseases were shown to have a high morbidity for cryptosporidial infection *(98)*. It is known that malnutrition predisposes to a more prolonged and severe cryptosporidiosis *(2)*; thus, elderly patients suffering from NAIDS may be at increased risk for infection by the parasite.

***E. coli* O157:H7 (EHEC).** In the United States, the mean infection rate per 100,000 for EHEC in the age group <5 to 19 years is 4.5 (range 3.1 to 6.1) and 0.9 (range 0.5 to 1.2) for age group 20 to 59 years. The mean infection rate increases to 1.7 (range 1.6 to 1.8) for those >60 years of age *(18)*. In the summaries of notifiable diseases in the United States, 11.4% of the 1,420 cases of EHEC reported in 1994 were in individuals ≥60 years *(26)* and 12.4% of the 2,139 cases of EHEC reported in 1995 occurred in individuals ≥65 years of age *(27)*.

Ryan et al. *(116)* reporting a nursing home outbreak found that 11.8% of 34 EHEC-infected patients (all were >80 years of age) died. Similarly, Carter et al. *(21)* found that 34.8% of 55 EHEC-infected nursing home patients died. The mean age of the nursing home residents in the report of Carter et al. *(21)* was 83.5 ± 10.8 (range 39 to 101). Thus, the elderly, particularly those in nursing homes, are vulnerable to EHEC infections and suffer high mortality.

L. monocytogenes. U.S. data from 1980 to 1982 indicated that listeriosis was more common at the extremes of age. The attack rate for infants <1 month of age was 57/100,000, whereas it was 1/100,000 for individuals >70 *(37)*. Mortality was 17.1% for infants <1 month of age but was more than 30% in the >70 group. Bula et al. *(16)* discussed 57 cases of listeriosis in adult (>18 years of age) nonpregnant patients from Switzerland for 1983 to 1987. Those patients >65 years of age comprised 54.4% (31/57) of the cases. In addition, mortality was highest in the elderly; 45.2% (14/31) of the patients >65 died compared to 15.4% (4/26) in the <65 age group *(16)*. Two hundred and twenty-five cases of listeriosis occurred in nonpregnant French patients in 1992: 4.1%, 24.3%, and 71.6% of cases occurred in the 1 to 29, 30 to 59, and ≥60 age groups, respectively *(60)*. The immunocompromised elderly were particularly at risk. Of the elderly patients discussed by Goulet and Marchetti *(60)*, 84.8% had immunosuppressive risk factors such as dialysis treatment, types I and II diabetes, alcoholism, hepatic failure, malignancies, acquired immune deficiency syndrome (AIDS), organ transplants, immunosuppressive therapy, etc. While the incidence of listeriosis has decreased in the United States *(128)*, it is still necessary to exercise vigilance to protect the elderly from this potentially fatal disease.

***Salmonella* species.** Using 1986 data obtained in United States populations, Hargrett-Bean et al. *(61)* found the rate of *Salmonella* infection was ~15 cases/100,000 in the 15 to 60-year age group but was higher in the ≥65 age group. Data obtained from foodborne outbreaks in nursing homes for the period 1975 to 1987 *(80)* indicated that *Salmonella* species accounted for 23.5% of foodborne outbreaks, 20.3% of the foodborne cases, and 74.5% of the deaths due to foodborne illnesses. The elderly appear to be particularly susceptible to *Salmonella* infections and *Salmonella*-induced death.

Shigella. The mean number of cases/year of shigellosis for the United States for the years 1988 to 1995 was 28,029 (range 23,548 to 32,198). Children <5 years of age accounted for 28.5% of the cases; 23.2% occurred in children aged 5 to 14 years. However, individuals ≥65 years of age, accounted for only 2.0% of cases *(27)*. Thus, it would appear that the elderly may be less susceptible to *Shigella* infections or have lower probability of being exposed.

Toxoplasma gondii. Aged mice are significantly more susceptible to *T. gondii* infection with higher mortality than young mice *(45, 52, 68)*. At similar infective doses, aged mice had a severalfold increase in brain tissue cyst burden when compared to young mice *(53)*. Aged mice studies would indicate that older humans should be more susceptible to *T. gondii* infection and disease but there are no supporting data. However, the prevalence of *T. gondii* seropositivity increases with increasing age in humans *(43, 135)*.

In immunocompromised populations (AIDS, transplant, or cancer patients), toxoplasmosis generally represents reactivation of a prior infection *(49)*. However, there is a paucity of data concerning parasite reactivation in healthy *T. gondii*-seropositive elderly individuals who are merely immunocompromised by age. A recent report by Johnson et al. *(70)* suggests that reactivation of toxoplasmosis may occur in older individuals. Some of the cases of atypical severe toxoplasmic retinochoroiditis that were observed in seven elderly (ages 69 to 82) individuals appeared to have been the result of reactivation of a preexisting infection. Even though there are few supporting data, it is probable that elderly humans are more susceptible to infection by *T. gondii* or to reactivation of latent toxoplasmosis. Many cases may not be detected because symptoms of toxoplasmosis may not be readily recognized by geriatricians.

Yersinia enterocolitica. The largest number of cases and highest incidence of *Yersinia* infection are seen in children <5 years of age *(66, 102, 126)*. Only about 10% of the cases are seen in individuals >60 years of age *(102, 118)*; the incidence of infection in the elderly is similar to that seen in the 20 to 59 age group *(102)*. It would appear that the elderly are no more susceptible to *Yersinia* infections than young adults.

***C. perfringens* and *S. aureus*.** Two foodborne pathogens that appear to be more common in nursing home populations than in the general population are *C. perfringens* and *S. aureus*. For the period 1988 to 1992, *C. perfringens* comprised 1.6% of the outbreaks, 4.9% of cases, and 1.4% of deaths seen in foodborne outbreaks in the United States *(7)*. Levine et al. *(80)* found that in nursing home foodborne disease outbreaks, *C. perfringens* caused 5.2% of the outbreaks, 10.0% of cases, and 3.9% of the deaths. For *S. aureus*, U.S. foodborne disease outbreak data indicated that the organism caused 2.1% of outbreaks, 2.2% of cases, and

TABLE 5. *Factors that play a role in the morbidity and mortality of the elderly to foodborne illnesses*

1. Age-induced decrease in stomach acid production allows ingested pathogens to enter the intestinal tract.
2. Age-induced decrease in cellular and humoral immunity due to decreased T-cell activity decreases resistance to pathogens.
3. Age-induced decrease in peristalsis (as well as use of antimotility drugs) does not allow the speedy elimination of enteric pathogens. The resulting proliferation of pathogens in the gut allows toxin formation and/or attachment and damage to the intestinal wall.
4. Decreased food consumption and poor nutrition leads to nutritionally acquired immunodeficiency syndrome (NAIDS); NAIDS combined with the normal age-related decrease in immune function places an additional strain on the immune system's ability to fight pathogens.
5. The nursing home environment, the morbid condition(s) of nursing home clientele, intense use of antibiotics in nursing homes, and the poor personal hygiene practiced by some nursing home residents facilitates spread of infections.
6. Even though the percentage of ≥65-year-old individuals who are below the poverty level has decreased from 24.6% in 1970 to 11.7% in 1994 *(133)*, there is still a high percentage of elderly who are too poor to have adequate nutrition and medical care.

no deaths *(7)*. However, nursing home foodborne disease outbreak data indicated that *S. aureus* caused 10.4% of outbreaks, 10.5% of cases, and 3.9% of deaths *(80)*. The elderly in nursing homes appear to be at risk for *C. perfringens* and *S. aureus* foodborne illnesses.

While the elderly are considered to be a segment of the immunocompromised population, the invoking of an age-induced decrease in cellular and humoral immunity does not completely explain the increased morbidity and mortality due to foodborne diseases (and other infections) seen in the elderly. Therefore, foodborne infections in aged populations probably are due to a combination of factors acting in concert with age-decreased immune function (Table 5).

PERSPECTIVE

Prevention of infections in the elderly is a matter of adhering to a healthy life-style including regular exercise, a balanced diet, adequate and regular health care, a regular vaccination schedule, and careful attention to personal hygiene. Prevention of foodborne diseases requires, in addition, careful monitoring of foods, e.g., where the food is eaten, which foods are consumed, how foods are prepared and served, etc. However, the elderly who are afflicted with chronic diseases, are functionally impaired, are on medications, and who reside in nursing homes are at risk for foodborne infections as well as other infections because they have less control over their environment and life situation.

The population of the United States is aging: in 1995, individuals ≥65 years of age comprised 12.8% of the United States population, but by 2040, the elderly population is expected to increase to 20.3% *(133)*. In addition, the number of individuals in the ≥85-year age group is expected to increase approximately threefold by 2040 *(133)*. The current trend of aging of the U.S. population suggests that more of the elderly, particularly those in the ≥85-year-old group, will be cared for in nursing homes because many of them will be impaired and less able to care for themselves. For these elderly individuals in nursing homes, health care professionals must be aware of their increased susceptibility to infections and must place greater emphasis on decreasing the incidence of both foodborne and nonfoodborne infections.

It is interesting that chronic disability rates in the U.S. elderly have been declining since 1982. There are approximately 1.4 million fewer disabled individuals in the ≥65 age group today than would be expected on the basis of the health status of the elderly in 1982 *(87, 115)*. This improvement in health status in the elderly will probably continue and will make an important contribution to decreased medical costs. However, with the expected increase in the numbers of ≥85 aged individuals, who are more likely to be frail and disabled, resources such as nursing homes, health care personnel, medical care, infection control programs, and funds needed to care for these individuals should be expanded substantially. Nicolle et al. *(99)* indicate that geriatric care resources will be more restricted in the future than they are currently. Health care professionals who specialize in geriatric care will be faced with the challenge of developing programs that will provide optimal and cost-efficient care to ever-increasing elderly populations while at the same time, the budgets for such care will be decreasing.

The dilemma of dealing with an increase in elderly populations is not limited to the United States and other developed countries because the number of individuals >60 years of age is increasing throughout the entire world. The world's population of individuals >60 will increase from 9.5% today to 20% by the year 2050. By the year 2100, 27% of the world's population will be >60 *(85)*. Therefore, the economic and social implications of a population of increasingly older individuals must be confronted by all countries, whether developed or underdeveloped.

REFERENCES

1. Abrams, W. B., M. H. Beers, and R. Berkow (ed.). 1995. The Merck manual of geriatrics, 2nd ed. Merck & Co., Inc., Whitehouse Station, N.J.
2. Adal, K. A., C. R. Sterling, and R. L. Guerrant. 1995. *Cryptosporidium* and related species, p. 1107–1128. *In* M. J. Blaser, P. D. Smith, J. I. Ravdin, H. B. Greenberg, and R. L. Guerrant (ed.), Infections of the gastrointestinal tract. Raven Press, New York.
3. Al-Rayes, H., W. Pachas, N. Mirza, D. J. Ahern, R. S. Geha, and D. Vercelli. 1992. IgE regulation and lymphokine patterns in aging humans. J. Allergy Clin. Immunol. 90:630–636.
4. Arranz, E., S. O'Mahony, J. R. Barton, and A. Ferguson. 1992. Immunosenescence and mucosal immunity: significant effects of old age on secretory IgA concentrations and intraepithelial lymphocyte counts. Gut 33:882–886.
5. Arreaza, E. E., J. J. Gibbons, G. W. Siskind, and M. E. Weksler. 1993. Lower antibody response to tetanus toxoid associated with higher auto-anti-idiotypic antibody in old compared with young humans. Clin. Exp. Immunol. 92:169–173.
6. Bannister, P., and R. A. Mountford. 1989. *Cryptosporidium* in the elderly: a cause of life-threatening diarrhea. Am. J. Med. 86:507–508.
7. Bean, N. H., J. S. Goulding, C. Lao, and F. J. Angulo. 1996. Surveillance for foodborne-disease outbreaks—United States, 1988–1992. Morb. Mort. Weekly Rep. 45(SS-5):16–20.
8. Bean, N. H., P. M. Griffin, J. S. Goulding, and C. B. Ivey. 1990. Foodborne disease outbreaks, 5-year summary, 1983–1987. Morb. Mort. Weekly Rep. 39(SS-1):25–29.
9. Beisel, W. R. 1995. Herman Award Lecture, 1995: infection-induced malnutrition—from cholera to cytokines. Am. J. Clin. Nutr. 62:813–819.
10. Beisel, W. R. 1996. Nutrition and immune function: overview. J. Nutr. 126:2611S–2615S.
11. Bell, B. P., P. M. Griffin, P. Lozano, D. L. Christie, J. M. Kobayashi, and P. I. Tarr. 1997. Predictors of hemolytic uremic syndrome in children during a large outbreak of *Escherichia coli* O157:H7 infections. Pediatrics 100(1):e12.
12. Ben-Yehuda, A., and M. E. Weksler. 1992. Host resistance and the immune system. Clin. Geriatr. Med. 8:701–712.
13. Berkow, R. (ed.). 1992. The Merck manual of diagnosis and therapy, 16th ed. Merck & Co., Inc., Rahway, N.J.
14. Black, R. E., and C. F. Lanata. 1995. Epidemiology of diarrheal diseases in developing countries, p. 13–36. *In* M. J. Blaser, P. D. Smith, J. I. Ravdin, H. B. Greenberg, and R. L. Guerrant (ed.), Infections of the gastrointestinal tract. Raven Press, New York.
15. Bogden, J. D., A. Bendich, F. W. Kemp, K. S. Bruening, J. H. Skurnick, T. Denny, H. Baker, and D. B. Louria. 1994. Daily micronutrient supplements enhance delayed-hypersensitivity skin test responses in older people. Am. J. Clin. Nutr. 60:437–447.
16. Bula, C. J., J. Bille, and M. P. Glauser. 1995. An epidemic of food-borne listeriosis in western Switzerland: description of 57 cases involving adults. Clin. Infect. Dis. 20:66–72.
17. Butterton, J. R., and S. B. Calderwood. 1995. *Vibrio cholerae* O1, p. 649–670. *In* M. J. Blaser, P. D. Smith, J. I. Ravdin, H. B. Greenberg, and R. L. Guerrant (ed.), Infections of the gastrointestinal tract. Raven Press, New York.

18. Buzby, J. C., T. Roberts, C.-T. J. Lin, and J. M. MacDonald. 1996. Bacterial foodborne disease: medical costs & productivity losses. ERS, USDA. Agricultural Economic Report, No. 741, Washington, D.C.
19. Cakman, I., J. Rohwer, R.-M. Schütz, H. Kirchner, and L. Rink. 1996. Dysregulation between TH_1 and TH_2 T cell subpopulation in the elderly. Mech. Ageing Dev. 87:197–209.
20. Candore, G., G. Di Lorenzo, P. Mansueto, M. Melluso, G. Fradà, M. Li Vecchi, M. E. Pellitteri, A. Drago, A. Di Salvo, and C. Caruso. 1997. Prevalence of organ-specific and non organ-specific autoantibodies in healthy centenarians. Mech. Ageing Dev. 94:183–190.
21. Carter, A. O., A. A. Borczyk, J. A. K. Carlson, B. Harvey, J. C. Hockin, M. A. Karmali, C. Krishinan, D. A. Korn, and H. Lior. 1987. A severe outbreak of *Escherichia coli* O157:H7-associated hemorrhagic colitis in a nursing home. N. Engl. J. Med. 317:1496–1500.
22. Caruso, C., G. Candore, D. Cigna, G. di Lorenzo, G. Sireci, F. Fieli, and A. Salerno. 1996. Cytokine production pathway in the elderly. Immunol. Res. 15:84–90.
23. Cash, R. A., S. I. Music, J. P. Libonati, M. J. Snyder, R. P. Wenzel, and R. B. Hornick. 1974. Response of man to infection with *V. cholerae*. I. Clinical, serologic, and bacteriologic response to a known inoculum. J. Infect. Dis. 129:45–52.
24. Castle, S., K. Uyemura, W. Wong, R. Modlin, and R. Effros. 1997. Evidence of enhanced type 2 immune response and impaired upregulation of a type 1 response in frail elderly nursing home residents. Mech. Ageing Dev. 94:7–16.
25. Catania, A., L. Airaghi, P. Motta, M. G. Manfredi, G. Annoni, C. Pettenati, F. Brambilla, and J. M. Lipton. 1997. Cytokine antagonists in aged subjects and their relation with cellular immunity. J. Gerontol. Ser. A Biol. Sci. 52A:B93–B97.
26. CDC (Centers for Disease Control and Prevention). 1994. Summary of notifiable diseases, United States, 1994. Morb. Mort. Weekly Rep. 43:10.
27. CDC (Centers for Disease Control and Prevention). 1995. Summary of notifiable diseases, United States, 1995. Morb. Mort. Weekly Rep. 44(53):4, 10, 13, 74–75.
28. CDC (Centers for Disease Control and Prevention). 1996. Outbreaks of *Salmonella* serotype enteritidis infection associated with consumption of raw shell eggs—United States, 1994–1995. Morb. Mort. Weekly Rep. 45:737–742.
29. Challacombe, S. J., R. S. Percival, and P. D. Marsh. 1995. Age-related changes in immunoglobulin isotypes in whole and parotid saliva and serum in healthy individuals. Oral Microbiol. Immunol. 10:202–207.
30. Chandra, R. 1995. Nutrition and immunity in the elderly: clinical significance. Nutr. Rev. 53(no. 4, part II):S80–S85.
31. Chandra, R. K. 1989. Nutritional regulation of immunity and risk of infection in old age. Immunology 67:141–147.
32. Chandra, R. K. 1992. Effect of vitamin and trace-element supplementation on immune response and infection in elderly subjects. Lancet 340:1124–1127.
33. Chandra, R. K. 1997. Graying of the immune system. Can nutrient supplements improve immunity in the elderly? J. Am. Med. Assoc. 277:1398–1399.
34. Chandra, R. K. 1997. Nutrition and the immune system: an introduction. Am. J. Clin. Nutr. 66:460S–463S.
35. Christiansen, J. L., and J. M. Grzybowski. 1993. Biology of aging. Mosby, St. Louis, Mo.
36. Cicirello, H. G., K. S. Kehl, D. G. Addiss, M. J. Chusid, R. I. Glassk, J. P. Davis, and P. L. Havens. 1997. Cryptosporidiosis in children during a massive, waterborne outbreak in Milwaukee, Wisconsin: clinical, laboratory and epidemiological findings. Epidemiol. Infect. 119:53–60.
37. Ciesielski, C. A., A. W. Hightower, S. K. Parsons, and C. V. Broome. 1988. Listeriosis in the United States: 1980–1982. Arch. Intern. Med. 148:1416–1419.
38. Collen, M. J., J. D. Abdulian, and Y. K. Chen. 1994. Age does not affect basal gastric acid secretion in normal subjects or in patients with acid-peptic disease. Am. J. Gastroenterol. 89:712–716.
39. Conner, J. R., and J. L. Beard. 1997. Dietary iron supplements in the elderly: to use or not to use. Nutr. Today 32:102–109.
40. Crossley, K. B., and P. K. Peterson. 1996. Infections in the elderly. Clin. Infect. Dis. 22:209–215.
41. Cunha, B. A. (ed.). 1988. Infectious diseases in the elderly. PSG Publishing Co., Inc., Littleton, Mass.
42. Dare, R., J. T. Magee, and G. E. Mathison. 1972. In-vitro studies on the bactericidal properties of natural and synthetic gastric juices. J. Med. Microbiol. 5:395–406.
43. Dubey, J. P., and C. P. Beattie. 1988. Toxoplasmosis of animals and man. CRC Press, Inc., Boca Raton, Fla.
44. DuPont, H. L., and R. B. Hornick. 1973. Adverse effect of Lomotil therapy in shigellosis. J. Am. Med. Assoc. 226:1525–1528.
45. Emmerling, P., H. Hof, and H. Finger. 1979. Age-related defense against infections with intracellular pathogens. Gerontology 25:327–336.
46. Ernst, D. N., W. O. Weigle, and M. V. Hobbs. 1993. Aging and lymphokine produced by T cell subsets. Stem Cells 11:487–498.
47. Feldman, M., B. Cryer, K. E. McArthur, B. A. Huet, and E. Lee. 1996. Effect of aging and gastritis on gastric acid and pepsin secretion in humans: a prospective study. Gastroenterology 110:1043–1052.
48. Fitch, F. W., D. W. Lancki, and T. F. Gajewski. 1993. Cell-mediated immune regulation: help and suppression, p. 733–761. *In* W. E. Paul (ed.), Fundamental immunology, 3rd ed. Raven Press, New York.
49. Frenkel, J. K. 1990. Toxoplasmosis in human beings. J. Am. Vet. Med. Assoc. 196:240–248.
50. Furuta, G. T., and W. A. Walker. 1995. Nonimmune defense mechanisms of the gastrointestinal tract, p. 89–97. *In* M. J. Blaser, P. D. Smith, J. I. Ravdin, H. B. Greenberg, and R. L. Guerrant (ed.), Infections of the gastrointestinal tract. Raven Press, New York.
51. Gangarosa, R., R. I. Glass, J. F. Lew, and J. R. Boring. 1992. Hospitalization involving gastroenteritis in the United States, 1985: the special burden of the disease among the elderly. Am. J. Epidemiol. 135:281–290.
52. Gardner, I. D., and J. S. Remington. 1977. Age-related decline in the resistance of mice to infection with intracellular pathogens. Infect. Immun. 16:593–598.
53. Gardner, I. D., and J. S. Remington. 1978. Aging and the immune response. I. Antibody formation and chronic infection in *Toxoplasma gondii*-infected mice. J. Immunol. 120:939–943.
54. Gershon, H. 1997. The anti-inflammatory role of the erythrocyte impairment in the elderly. Arch. Gerontol. Geriatr. 24:157–165.
55. Giannella, R. A., S. A. Broitman, and N. Zamcheck. 1973. Influence of gastric acidity on bacterial and parasitic enteric infections. Ann. Intern. Med. 78:271–276.
56. Gitelson, S. 1971. Gastrectomy, achlorhydria and cholera. Isr. J. Med. Sci. 7:663–667.
57. Goldschmiedt, M., C. C. Barnett, B. E. Schwartz, W. E. Karnes, J. S. Redfern, and M. Feldman. 1991. Effect of age on gastric acid secretion and serum gastric concentrations in healthy men and women. Gastroenterology 199:977–990.
58. Gon, Y., S. Hashimoto, S. Hayashi, T. Koura, K. Matsumoto, and T. Horie. 1996. Lower serum concentration of cytokines in elderly patients with pneumonia and the impaired production of cytokines by peripheral blood monocytes in the elderly. Clin. Exp. Immunol. 106:120–126.
59. Goodwin, J. S. 1995. Decreased immunity and increased morbidity in the elderly. Nutr. Rev. 53 (no. 4, part II):S41–S46.
60. Goulet, V., and P. Marchetti. 1996. Listeriosis in 225 non-pregnant patients in 1992: clinical aspects and outcome in relation to predisposing conditions. Scand. J. Infect. Dis. 28:367–374.
61. Hargrett-Bean, N. T., A. T. Pavia, and R. V. Tauxe. 1988. *Salmonella* isolates from humans in the United States, 1984–1986. Morb. Mort. Weekly Rep. 37(SS-2):25–31.
62. Henderson, C. T. 1988. Nutrition and malnutrition in the elderly nursing home patient. Clin. Geriatr. Med. 4:527–547.
63. Hensler, T., H. Hecker, K. Heeg, C.-D. Heidecke, H. Bartels, W. Barthelen, H. Wagner, J.-R. Siewert, and B. Holzmann. 1997. Distinct mechanisms of immunosuppression as a consequence of major surgery. Infect. Immun. 65:2283–2291.
64. Hirokawa, K. 1992. Understanding the mechanism of the age-related decline in immune function. Nutr. Rev. 50:361–366.
65. Ho, J. L., K. N. Shanda, G. Friedland, P. Eckind, and D. W. Fraser. 1986. An outbreak of type 4b *Listeria monocytogenes* infection involving patients from eight Boston hospitals. Arch. Intern. Med. 146:520–524.

66. Hoogkamp-Korstanje, J. A. A., and V. M. M. Stolk-Engelaar. 1995. *Yersinia enterocolitica* infection in children. Pediatr. Infect. Dis. J. 14:771–775.
67. Hurwitz, A., D. A. Brady, S. E. Schaal, I. M. Samloff, J. Dedon, and C. E. Ruhl. 1997. Gastric acidity in older adults. J. Am. Med. Assoc. 278:659–662.
68. Johnson, L. L., G. W. Gibson, and P. C. Sayles. 1995. Preimmune resistance to *Toxoplasma gondii* in aged and young adult mice. J. Parasitol. 81:894–899.
69. Johnson, M. A., J. G. Fischer, B. A. Bowman, and E. W. Gunter. 1994. Iron nutrition in elderly individuals. FASEB J. 8:609–621.
70. Johnson, M. W., C. M. Green, G. J. Jaffe, H. Sudhalkar, and A. K. Vine. 1997. Atypical, severe toxoplasmic retinochoroiditis in elderly patients. Ophthalmology 104:48–57.
71. Jones, S. R., D. F. Parker, E. S. Liebow, R. C. Kimbrough, and R. S. Frear. 1987. Appropriateness of antibiotic therapy in long-term care facilities. Am. J. Med. 83:499–502.
72. Katelaris, P., F. Seow, B. P. C. Lin, J. Napoli, M. C. Ngu, and D. B. Jones. 1993. Effect of age, *Helicobacter pylori* infection, and gastritis with atrophy on serum gastrin and gastric acid secretion in healthy men. Gut 34:1032–1037.
73. Katz, D. R., T. R. Beam, F. Brand, and K. Boyce. 1990. Antibiotic use in the nursing home. Physician practice patterns. Arch. Intern. Med. 150:1465–1468.
74. Kudlacek, S., S. Jahandideh-Kazempour, W. Graninger, R. Willvanseder, and P. Pietschmann. 1995. Differential expression of various T cell surface markers in young and elderly subjects. Immunobiology 192:198–204.
75. Lesourd, B. 1995. Protein undernutrition as the major cause of decreased immune function in the elderly: clinical and functional implications. Nutr. Rev. 53(no. 4, part II):S86–S94.
76. Lesourd, B. M., C. Laisney, R. Salvatore, S. Meaume, and R. Moulias. 1994. Decreased maturation of T-cell populations in the healthy elderly: influence of nutritional factors on the appearance of double negative CD4−, CD8−, CD2+ cells. Arch. Gerontol. Geriatr. (suppl. 4):139–154.
77. Lesourd, B. M., and L. Mazari. 1997. Immune responses during recovery from protein-energy malnutrition. Clin. Nutr. 16(suppl. 1):37–46.
78. Lesourd, B. M., and S. Meaume. 1994. Cell mediated immunity changes in aging, relative importance of cell subpopulation switches and of nutritional factors. Immunol. Lett. 40:235–242.
79. Levine, M. M., and O. S. Levine. 1994. Changes in human ecology and behavior in relation to the emergence of diarrheal diseases, including cholera. Proc. Natl. Acad. Sci. USA 91:2390–2394.
80. Levine, W. C., J. F. Smart, D. L. Archer, N. H. Bean, and R. V. Tauxe. 1991. Foodborne disease outbreaks in nursing homes, 1975 through 1987. J. Am. Med. Assoc. 266:2105–2109.
81. Lew, J. F., R. I. Glass, R. E. Gangarosa, I. P. Cohen, C. Bern, and C. L. Moe. 1991. Diarrheal deaths in the United States, 1979 through 1987. A special problem for the elderly. J. Am. Med. Assoc. 265:3280–3284.
82. Li, J., G. S. Birkhead, D. S. Strogatz, and F. B. Coles. 1996. Impact of institution size, staffing patterns, and infection control practices on communicable disease outbreaks in New York State nursing homes. Am. J. Epidemiol. 143:1042–1049.
83. Ligthart, G. J., J. Radl, J. X. Corberand, J. A. van Neuwkoop, G. J. van Staalduinen, D. J. Wesselman van Helmond, and W. Hijmans. 1990. Monoclonal gammapathies in human aging: increased occurrence with age and correlation with health status. Mech. Ageing Dev. 52:235–243.
84. Liszewski, M. K., and J. P. Atkinson. 1993. The complement system, p. 917–939. *In* W. E. Paul (ed.), Fundamental immunology, 3rd ed. Raven Press, New York.
85. Lutz, W., W. Sanderson, and S. Scherbov. 1997. Doubling of the world population unlikely. Nature 387:803–805.
86. Majumdar, A. P. N., R. Jaszewski, and M. A. Dubrick. 1997. Effect of aging on the gastrointestinal tract and the pancreas. Proc. Soc. Exp. Biol. Med. 215:134–144.
87. Manton, K. G., L. Corder, and E. Stallard. 1997. Chronic disability trends in elderly United States populations: 1982–1994. Proc. Natl. Acad. Sci. USA 94:2593–2598.
88. Matour, D., M. Melnicoff, D. Kaye, and D. M. Murasko. 1989. The role of T cell phenotypes in decreased lymphoproliferation of the elderly. Clin. Immunol. Immunopathol. 50:82–99.
89. Mazzeo, R. S. 1996. Exercise, immunity, and aging, p. 199–214. *In* L. Hoffman-Goetz (ed.), Exercise and immune function. CRC Press, Boca Raton, Fla.
90. Mbawuike, I. N., C. L. Acuna, K. C. Walz, R. L. Atmar, S. B. Greenberg, and R. B. Couch. 1997. Cytokines and impaired $CD8^+$ CTL activity among elderly persons and the enhancing effect of IL-12. Mech. Ageing Dev. 94:25–39.
91. McElhaney, J. E., B. L. Beattie, R. Devine, R. Grynoch, E. L. Toth, and R. C. Bleackley. 1990. Age-related decline in interleukin 2 production in response to influenza vaccine. J. Am. Geriatr. Soc. 38:652–658.
92. Meydani, S. N., M. Meydani, J. B. Blumberg, L. S. Leka, G. Siber, P. Loszewski, C. Thompson, M. C. Pedrosa, R. D. Diamond, and B. D. Stollar. 1997. Vitamin E supplementation and in vivo immune response in healthy elderly subjects. A randomized controlled trial. J. Am. Med. Assoc. 277:1380–1386.
93. Miletic, I. D., S. S. Schiffman, V. D. Miletic, and E. A. Sattely-Miller. 1996. Salivary IgA secretion rate in young and elderly persons. Physiol. Behav. 60:243–248.
94. Miller, R. A. 1996. The aging immune system: primer and prospectus. Science 273:70–74.
95. Mishu, M., J. Koehler, L. A. Lee, D. Rodrigue, F. H. Brenner, P. Blake, and R. V. Tauxe. 1994. Outbreaks of *Salmonella enteritidis* infections in the United States, 1985–1991. J. Infect. Dis. 169:547–552.
96. Murasko, D. M., P. Weiner, and D. Kaye. 1987. Decline in mitogen induced proliferation of lymphocytes with increasing age. Clin. Exp. Immunol. 70:440–448.
97. Nalin, D. R., R. J. Levine, M. M. Levine, D. Hoover, E. Bergquist, J. McLaughlin, J. Libonati, J. Alam, and R. B. Hornick. 1978. Cholera, non-vibrio cholera, and stomach acid. Lancet ii:856–859.
98. Neill, M. A., S. K. Rice, N. V. Ahmad, and T. P. Flanigan. 1996. Cryptosporidiosis: an unrecognized cause of diarrhea in elderly hospitalized patients. Clin. Infect. Dis. 22:168–170.
99. Nicolle, L. E., L. J. Strausbaugh, and R. A. Garibaldi. 1996. Infections and antibiotic resistance in nursing homes. Clin. Microbiol. Rev. 9:1–17.
100. Nieman, D. C., and D. A. Henson. 1994. Role of endurance exercise in immune senescence. Med. Sci. Sports Exercise 26:172–181.
101. Nijhuis, E. W. P., E. J. Remarque, B. Hinloopen, T. van der Pouw-Kraan, R. A. W. van Lier, G. J. Ligthart, and L. Nagelkearken. 1994. Age-related increase in the fraction of $CD27^-$ $CD4^+$ T cells and IL-4 production as a feature of $CD4^+$ T cell differentiation *in vivo*. Clin. Exp. Immunol. 96:528–534.
102. Ostroff, S. M., G. Kapperud, J. Lassen, S. Aasen, and R. V. Tauxe. 1992. Clinical features of sporadic *Yersinia enterocolitica* infections in Norway. J. Infect. Dis. 166:812–817.
103. Paganelli, R., E. Scala, I. Quinti, and I. J. Ansotegui. 1994. Humoral immunity in aging. Aging Clin. Exp. Res. 6:143–150.
104. Pahlavani, M. A., and A. Richardson. 1996. The effect of age on the expression of interleukin-2. Mech. Ageing Dev. 89:125–154.
105. Pawelec, G., M. Adibzadeh, H. Pohla, and K. Schaudt. 1995. Immunosenescence: aging of the immune system. Immunol. Today 16:420–427.
106. Payette, H., M. Rola-Pleszczynski, and P. Ghadirian. 1990. Nutrition factors in relation to cellular and regulatory immune variables in a free-living elderly population. Am. J. Clin. Nutr. 52:927–932.
107. Pickering, T.-D., J. H. Gurwitz, D. Zaleznik, J. P. Noonan, and J. Avorn. 1994. The appropriateness of oral fluoroquinolone-prescribing in the long-term care setting. J. Am. Geriatr. Soc. 42:28–32.
108. Prevots, D. R., and R. W. Sutter. 1997. Assessment of Guillain-Barré syndrome mortality and morbidity in the United States: implications for acute flaccid paralysis surveillance. J. Infect. Dis. 175(suppl. 1):151–155.
109. Proust, J. J., R. A. Quadri, A. Arbogast, M.-A. Phelouzat. 1996. Mécanismes moléculaires du dysfonctionnement lymphocytaire lié à l'âge. Pathol. Biol. 44:7290–736.
110. Radl, J. 1990. Age-related monoclonal gammapathies: clinical lessons from the aging C57BL mouse. Immunol. Today 11:234–236.
111. Remarque, E. J., E. W. P. Nijhuis, B. Hinloopen, L. Nagelerken, E. A. van der Velde, and G. J. Ligthart. 1996. Correlation between the

antibody response to influenze vaccine and helper T cell subsets in healthy aging. Vaccine 14:127–130.

112. Richmond, G. W., and B.-H. Yu. 1993. Autoantibodies, autoimmune diseases, and vasculitis in the aged. Immunol. Allergy Clin. N. Am. 13:647–672.
113. Roberts-Thomson, I. C., S. Whittingham, U. Youngchaiyud, and I. R. Mackay. 1974. Aging, immune response, and mortality. Lancet ii:368–370.
114. Rosenberg, I. H. 1997. Nutrition and senescence. Nutr. Rev. 55(no. 1, part II):S69–S73.
115. Rowe, J. W. 1997. The new gerontology. Science 278:367.
116. Ryan, C. A., R. V. Tauxe, G. W. Hosek, J. G. Wells, P. A. Stoesz, H. W. McFadden, P. W. Smith, G. F. Wright, and P. A. Blake. 1986. *Escherichia coli* O157:H7 diarrhea in a nursing home: clinical, epidemiological, and pathological findings. J. Infect. Dis. 154:631–638.
117. Ryan, M. J., P. G. Wall, G. K. Adak, H. S. Evans, and J. M. Cowdan. 1997. Outbreaks of infectious intestinal disease in residential institutions in England and Wales 1992–1994. J. Infect. 34:49–54.
118. Saebø, A., and J. Lassen. 1991. A survey of acute and chronic diseases associated with *Yersinia enterocolitica* infection. Scand. J. Infect. Dis. 23:517–527.
119. Schiraldi, O., V. Benvestito, C. di Bari, R. Moschetta, and G. Pastore. 1974. Gastric abnormalities in cholera: epidemiological and clinical considerations. Bull. W. H. O. 51:349–352.
120. Schlech, W. F., D. P. Chase, and A. Badley. 1993. A model of food-borne *Listeria monocytogenes* infection in the Sprague-Dawley rat using gastric inoculation: development and effect of gastric acidity on infective dose. Int. J. Food Microbiol. 18:15–24.
121. Schmucker, D. L., M. F. Heyworth, R. L. Owen, and C. K. Daniels. 1996. Impact of aging on gastrointestinal mucosal immunity. Digest. Dis. Sci. 41:1183–1193.
122. Shinkai, S., H. Kohno, K. Kimura, T. Komura, H. Asai, R. Inai, K. Oka, Y. Kurokawa, and R. J. Shephard. 1995. Physical activity and immune senescence in men. Med. Sci. Sports Exer. 27:1516–1526.
123. Smith, J. L. 1995. Arthritis, Guillain-Barré syndrome, and other sequelae of *Campylobacter jejuni* enteritis. J. Food Prot. 58:1153–1170.
124. Solana, R., J. L. Villanueva, J. Peña, and M. de la Fuente. 1991. Cell mediated immunity in aging. Comp. Biochem. Physiol. 99A:1–4.
125. Song, L., Y. H. Kim, R. K. Chopra, J. J. Proust, J. E. Nagel, A. A. Nordin, and W. H. Adler. 1993. Age-related effects in T cell activation and proliferation. Exp. Gerontol. 28:313–321.
126. Stolk-Engelaar, V. M. M., and J. A. A. Hoogkamp-Korstanje. 1996. Clinical presentation and diagnosis of gastrointestinal infections by *Yersinia enterocolitica* in 261 Dutch patients. Scand. J. Infect. Dis. 28:571–575.
127. Stulnig, T., C. Maczek, G. Böck, O. Majdic, and G. Wick. 1995. Reference intervals for human peripheral blood lymphocyte subpopulations from 'healthy' young and aged subjects. Int. Arch. Allergy Immunol. 108:205–210.
128. Tappero, J. W., A. Schuchat, K. A. Deaver, L. Mascola, and J. D. Wenger. 1995. Reduction in the incidence of human listeriosis in the United States. Effectiveness of prevention efforts? J. Am. Med. Assoc. 273:1118–1122.
129. Tarr, P. I. 1995. *Escherichia coli* O157:H7: clinical, diagnostic, and epidemiological aspects of human infection. Clin. Infect. Dis. 20:1–10.
130. Tauxe, R. V. 1992. Epidemiology of *Campylobacter jejuni* infections in the United States and other industrialized nations, p. 9–19. *In* I. Nachamkin, M. J. Blaser, and L. S. Tompkins (ed.), *Campylobacter jejuni:* current status and future trends. American Society for Microbiology, Washington, D.C.
131. Terr, A. I., D. P. Dubey, E. J. Yunis, R. G. Slavin, and R. H. Waldman. 1991. Physiologic and environmental influences on the immune system, p. 187–199. *In* D. P. Stites and A. I. Terr (ed.), Basic and clinical immunology, 7th ed. Appleton & Lange, Norwalk, Conn.
132. Thompson, J. S., J. Robbins, and J. K. Cooper. 1987. Nutrition and immune function in the geriatric population. Clin. Geriatr. Med. 3:309–317.
133. U.S. Bureau of the Census. 1996. Statistical abstract of the United States: 1996 (116th ed.). Washington, D.C. (Tables 16, 17, 734).
134. Venkatraman, J. T., and G. Fernandes. 1997. Exercise, immunity and aging. Aging Clin. Exp. Res. 9:42–56.
135. Walker, J., D. J. Nokes, and R. Jennings. 1992. Longitudinal study of toxoplasmosis seroprevalence in South Yorkshire. Epidemiol. Infect. 108:99–106.
136. Wallace, J. I., and R. S. Schwartz. 1994. Involuntary weight loss in the elderly, p. 99–111. *In* R. R. Watson (ed.), Handbook of nutrition in the aged, 2nd ed. CRC Press, Boca Raton, Fla.
137. Warren, J. W., F. B. Palumbo, L. Fitterman, and S. M. Speedie. 1991. Incidence and characteristics of antibiotic use in aged nursing home patients. J. Am. Geriatr. Soc. 39:963–972.
138. Weimer, J. P. 1997. Many elderly at nutritional risk. Food Rev. 20(1):42–48.
139. Whitehead, C., and P. Finucane. 1997. Malnutrition in elderly people. Aust. N. Z. J. Med. 27:68–74.
140. Zu, S.-X., G.-D. Fang, R. Fayer, and R. L. Guerrant. 1992. Cryptosporidiosis: pathogenesis and immunology. Immunol. Today 8:24–27.