Sensitive populations: who is at the greatest risk?

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Abstract

The purpose of this article was to review the existing literature to define those groups of individuals who would be at the greatest risk of serious illness and mortality from water and foodborne enteric microorganisms. This group was found to include the very young, the elderly, pregnant women, and the immunocompromised. This segment of the population currently represents almost 20% of the population in the United States and is expected to increase significantly by the beginning of the next century, because of increases in life-span and the number of immunocompromised individuals. More than half of documented deaths from gastroenteritis and hepatitis A illness occur in the elderly in developed countries. The overall case fatality ratio for foodborne bacterial gastroenteritis outbreaks in nursing homes is 10 times greater than the general population. Pregnant mothers suffer from a case fatality ratio from hepatitis E infections ten times greater than the general population during waterborne disease outbreaks. Enteric diseases are most common and devastating among the immunocompromised. *Cryptosporidium* is a serious problem among patients with acquired immuno-deficiency syndrome (AIDS). Cancer patients undergoing chemotherapy and transplant patients, are also at significantly greater risk of dying from enteric viral infections than the general population. This review indicates the need for consideration of enhanced protection for certain segments of the population who will suffer the most from food and waterborne pathogens.

Keywords: Sensitive populations; Immunocompromised; Elderly; Enteric viruses; Foodborne; Waterborne; Risk assessment

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1. Introduction

In assessing the potential impact of food and waterborne disease, it is important to recognize that certain individuals may be at greater risk of serious illness than the general population. Individuals who are at increased risk of developing more severe outcomes from microorganisms are the very young, the elderly, pregnant individuals, and the immunocompromised (organ transplants, cancer patients, AIDS patients). This group represents almost 20% of the current population in the United States (Table 1). The elderly and the immunocompromised are an ever increasing segment of the population whose numbers are expected to increase in the years ahead. This article presents an assessment of the increased risk for segments of the population from enteric pathogens which may be either water or food borne. A list of the major enteric viruses, bacteria and protozoan parasites considered in this review are shown in Table 2.

The microorganisms associated with half of all water and food borne outbreaks in the United States go unidentified. When an agent can be identified bacteria are most often associated with foodborne illness while protozoa and viruses are most commonly associated with waterborne illness (Centers for Disease Control, 1990). The enteric bacteria most commonly associated with food and waterborne infections are *Salmonella*, *Campylobacter*, *Shigella*, and *Escherichia coli*. Although more commonly associated with waterborne outbreaks both *Giardia* and *Cryptosporidium* have been the cause of food related infections (Peterson et al., 1988; Millard et al., 1994). Norwalk virus is the human enteric virus most often identified in food and waterborne outbreaks of viral gastroenteritis (Craun, 1991; Herwaldt et al., 1994). Hepatitis A and E have also been associated with both water and foodborne infections (Vrati et al., 1992; Caredda et al., 1986). Hepatitis E outbreaks appear to only be associated with gross contamination limited to the developing world. The other enteric viruses have largely been associated with waterborne disease outbreaks (Table 2) (Hawley et al., 1973; Craun, 1991). Rotavirus has been associated with a number of waterborne disease outbreaks (Lycke et al., 1978; Hopkins et al., 1984; Solodovnikov et al., 1989). Although commonly isolated from feces and sewage contaminated waters, enteroviruses are less commonly documented as water or

Table 1
Sensitive populations in the United States

Population	Individuals	Year
Pregnancies	5 657 900	1989
Neonates	4 002 000	1989
Elderly (over 65)	29 400 000	1989
Residences in nursing homes or related care facilities	1 553 000	1986
Cancer patients (non-hospitalized)	2 411 000	1986
Transplant organ patients (1981–1989)	110 270	1981–1989
AIDS patients	142 000	1981–1990

Department of Commerce, 1991.

Table 2
Enteric microorganisms documented to cause waterborne outbreaks

Viruses
Polio
Coxsackie B
Echo
Norwalk
Astro
Rota
Hepatitis A
Hepatitis E
Adeno*
Bacteria
Salmonella
Shigella
Campylobacter jejuni
Yersina enterocolytica
Escherichia coli 0157:H7
Protozoan parasites
Giardia lamblia
Cryptosporidium

*Outbreaks associated with swimming.

foodborne. Outbreaks of Coxsackie virus have been associated with lake water (Hawley et al., 1973) and sharing of water bottles (Moore et al., 1993; Alexander et al., 1993). An echovirus has been reported to be associated with a foodborne outbreak (Beckers, 1986).

2. Outcomes of microbial infection

The outcome of exposure to infectious microorganisms depends on a number of host factors including preexisting immunity, nutrition, age, ability to elicit an immune response, and nonspecific host factors. The type and strain of the microorganism will also affect the outcome. Infection occurs when replication of the organisms within the host takes place. Infection, however, does not mean that the host will develop clinical illness. Some viruses of low virulence appear to rarely produce clinical illness (Henigst et al., 1961), but most enteric pathogens will produce clinically observable illness in 50% or more of the infected individuals (Blazer and Newman, 1982; Gerba and Rose, 1993). With enteric viruses, age plays a major role in the probability of developing clinical illness. In the case of children, clinical illness can vary from 5% in children less than 5 years of age to 75% in adults (Hung et al., 1984; Ledner et al., 1985). With rotavirus, children are more likely to develop gastroenteric disease than adults (Hrdy, 1987). If the illness becomes serious enough, mortality can result. The case fatality ratio for normal healthy adults is low for most enteric pathogens (0.1% or less). Table 3 summarizes data for selected enteric pathogens for the likelihood of clinical illness and case: fatality in the general population.

3. Pregnancy, neonates, and young children

Women during pregnancy may be at an increased risk from enteric viruses and may also act as a source of infection for neonates. During the past decade at least 30 outbreaks of hepatitis E have been documented in 17 countries due to contaminated water (Craske, 1992) and foodborne outbreaks have been suspected (Caredda et al., 1986). Although outbreaks of hepatitis E have not been reported in the United States, cases do occur among tourists returning from developing countries. Waterborne outbreaks have at times involved thousands of individuals. Overall, case fatality ratios have ranged from 1–2% during outbreaks, which is significantly higher than that for hepatitis A virus. However, for pregnant women, the ratio is generally between 10 and 20%, but can be as high as 40% (Gust and Purcell, 1987; Craske, 1992).

Infection during pregnancy may also result in the transmission of infection from the mother to the child in utero, during birth, or shortly thereafter. This appears to be a common mode of transmission of coxsackie- and echo-viruses. Neonates are uniquely susceptible to enterovirus infections. This group of viruses are capable of causing severe disease and death when infection occurs within the first 10–14 days of life. Acquisition of coxsackie B infections early in life is the most significant risk factor leading to fatal disease. Most fatal cases caused by this virus are probably transmitted transplacentally at term (Kaplan et al., 1983). Among 41 documented cases of fatal infection in infants, 24 of their mothers had symptomatic illness consisting of fever, symptoms of upper respiratory tract involvement, pleurodynia, or meningitis. Symptomatic infection occurred between 10 days antepartum and 5 days postpartum. The observed case fatality rate for coxsackievirus in a New England county in the United States was almost 13%, with a morbidity rate of 50.2 per 100 000 live births. Stillbirth late in pregnancy has been reported for the

Table 3
Ratio of clinical to subclinical infections and case fatality rates for enteric microorganisms

Microorganism	Frequency of clinical illness (%)	Case:fatality Rate %
Viruses		
Hepatitis (adults)	75	0.6
Rotavirus	25–60	0.01
Astrovirus (adults)	12.5	–
Coxsackie A16	50	0.12
Coxsackie B	5–96	0.59–0.94
Bacteria		
Salmonella	41	0.1
Shigella	46	0.2
Protozoan parasites		–
Giardia	50–67	–
Cryptosporidium	71	

Rose et al., 1991; Gerba and Rose, 1993; Rose et al., 1995; Evans and Brachman, 1991; Addiss et al., 1995.

echoviruses and coxsackie B viruses (Modlin and Kinney, 1987). More recently coxsackie B viruses have been implicated as a potential important causative agent in spontaneous abortions (Frisk and Diderholm, 1992). Anomalies (urogenital system, heart defects, digestive malformation) in children born to infected mothers coxsackie B viruses have been suggestive in several studies (Modlin and Kinney, 1987).

Echoviruses can also be transmitted from the mother to the unborn child or shortly after birth with a potentially serious outcome (Modlin, 1986). An average case fatality of 3.4% was observed in 16 documented outbreaks of echovirus in newborn nurseries. In two outbreaks of coxsackie B virus in nurseries, the infant mortality rate from myocarditis ranged from 50 to 60% (Modlin and Kinney, 1987).

4. The elderly

The American population is aging. It is projected that from 1980 to 2020, the number of individuals over 65 will double from 25 to 50 million (Sammons, 1986). The fastest growing segment of the population will be the over-85 age group, which is projected to increase from 2.3 to 7.3 million. Infectious diseases are a major problem in the elderly because the immune function declines with age, antibiotic treatment is less effective because of a decrease in physiological function, and malnutrition is more common (Meyers, 1989). As a result outbreaks of gastroenteritis can be devastating in nursing homes resulting in a significantly higher mortality than the general population (Meyers, 1989).

Mortality from diarrhea shows a binomial curve with the greatest risk of mortality occurring among the very young and very old. A majority of diarrheal deaths that occur in the United States are among the elderly (Lew et al., 1991). The bulk of diarrheal deaths occur among the older than 74 years of age (51%), followed by adults 55 to 74 years of age (27%), and those younger than 5 years (11%). These deaths have a distinct clear winter peak that suggests a rotavirus etiology.

Most epidemiological studies concerning a specific agent in the elderly are focused around nursing homes since the impact can be more easily observed as a confined group of individuals. Case fatality rates for specific enteric pathogens are 10 to 100 times greater in this group than the general population (Table 4). One documented outbreak of rotavirus in a nursing home was characterized by high attack rates (66%), with few if any asymptomatic cases (Halvorsrud and Orstavik, 1980). While the number of days of illness was within the range observed for other age groups (1–5 days), the convalescence was prolonged for some individuals. The mortality rate was 1%. Gordon et al. (1990) reported a mortality rate of 1.3% among a retirement community during a foodborne outbreak of the Snow Mountain Agent, a calicivirus. They pointed out that several of the residents sustained serious injuries from falling because of near-syncopal episodes due to dehydration from the gastroenteritis. The elderly would be expected to be more prone to such injuries, because of greater illness severity, than younger adults. Outbreaks of

Table 4
Case fatality observed for enteric pathogens in nursing homes vs. general population

Organism	Case fatality (%) in general population	Case fatality (%) in nursing homes
Campylobacter jejuni	0.1	1.1
Escherichia coli 0157:H7	0.2	11.8
Salmonella	0.1	3.8
Shigella	0.1	–
Rotavirus	0.01	1.0
Snow Mountain agent	*	1.3

From: Levine et al., 1991; Gordon et al., 1990; Halvorsrud and Orstavik, 1980; Bennett et al., 1987; Ryan et al., 1986.
*Only documented deaths have been in the elderly in nursing homes.

Norwalk-like viruses, and enteric adenoviruses have been reported in nursing homes, and geriatric wards in hospitals (Kaplan et al., 1982; Reid et al., 1990). While no mortality was observed during these outbreaks, higher attack rates occurred among the residents, as well as a more severe, or protracted illness when compared to the staff (Oshiro et al., 1981; Pether and Caul, 1983). Interestingly no increase in illness severity or attack rates has been observed among the elderly during outbreaks of Norwalk virus (Kaplan et al., 1982).

Hepatitis A virus usually causes a mild and often asymptomatic infection in children. However, in adults the illness typically produces clinical illness that can lead to death (Ledner et al., 1985). Waterborne outbreaks are often characterized by high attack rates with all or most of the infected individuals exhibiting clinical illness (Bowen and McCarthy, 1980). The case fatality ratio of hepatitis A increases significantly with age. In a recent eight-year review of hepatitis A cases from England, Wales, and Ireland, the case fatality rate of hepatitis A for patients of less than 55 years of age was 0.02–0.03%, 0.9% at 55–64 years of age, and 1.5% for older patients. The median age of those dying from hepatitis A is over 60 in the United Kingdom (Gust, 1990).

The elderly also experience higher mortality rates from enteric bacterial gastroenteritis (Table 4). The overall case fatality ratio for foodborne outbreaks in nursing homes 1975 to 1987 was 1.0%, compared to 0.1% for outbreaks at other locations (Levine et al., 1991). For domestically acquired cases of typhoid, the case fatality rate is higher among individuals 55 years or older (Ryan et al., 1989). In a developing country the highest risk of complications and death were children from birth through one year of age and adults greater than 31 years of age (Butler et al., 1991).

5. Immunocompromised

Infections in the immunocompromised host constitute a relatively new and severe problem magnified by the current AIDS epidemic and by the escalation in organ and tissue transplantations. Enteric pathogens are among the many agents that take advantage of their impaired or destroyed immune system to set up persistent and generalized infections in the immunocompromised host. Such infections are difficult to treat, tend to be long term, add to the burden of the debilitation in the patient, and can result in a significant higher mortality than immunocompetent persons.

The impact of acquired immuno-deficiency syndrome (AIDS) epidemic has increased the number of diarrheal deaths in the 25 to 54 year-old age group (Lew et al., 1991). Enteric diseases are among the most common and devastating problems that affect persons with AIDS. The majority of AIDS patients (50–90%) suffer from chronic diarrheal illnesses, the effects which can be fatal (Janoff and Smith, 1988). Many studies have shown that the rates of diarrheal disease among HIV-infected persons in developing countries are higher than rates in developed countries, probably reflecting more frequent exposure to enteric pathogens by contaminated food and water (Janoff and Smith, 1988). Adenoviruses and rotavirus are the most common enteric viruses isolated in the stools of AIDS infected persons (Cunningham et al., 1988). A comprehensive study of Australian men showed that 54% of diarrheal illnesses in AIDS patients were caused by viruses and that 37% of the viral diarrheas were adenovirus-related (Cunningham et al., 1988). Overall, it is estimated that 12% of the AIDS patients with clinical symptoms suffer from adenovirus infections and that 45% of these cases result in death within two months (Hierholzer, 1992). The other enteric viruses do not appear to be a significant problem in AIDS-associated gastroenteritis (Gorbach et al., 1992).

Enteric bacterial infections are more severe in AIDS patients. For example, patients with *Salmonella, Shigella, and Campylobacter* often develop bacteremia (Baine et al., 1982; Gorbach et al., 1992). Although patients with AIDS may not have more severe illness with *Giardia*, they do exhibit impaired immune response to the parasite (Mandell et al., 1990).

Cryptosporidium is a serious problem among AIDS patients. A severe and protracted diarrhea results with fluid losses of several liters per day in some cases. Symptoms may persist for months, resulting in severe weight loss and mortality. Mortality rates of 50% have been reported for this organism (Clifford et al., 1990).

Cancer patients undergo intensive chemotherapy with cytotoxic and immunosuppressive drugs and often radiation treatment in attempts to destroy the neoplastic growth. These measures also attack the immune system, leaving the patient with little defense against opportunistic pathogens. For example, in cancer immunosuppressed patients the fatality rate for adenovirus infection is 53% (Hierholzer, 1992).

Bone-marrow transplantation is an effective therapy in patients with servere aplastic anemia or acute leukemia. However, because of a very weakened immune system they are very susceptible to infection. The mortality rate among bone-marrow transplants with enteric viral (rotavirus, coxsackie, adeno) infection was observed to be 59% in one study (Yolken et al., 1982). Of eight patients with

rotavirus infections five of eight individuals died. The case fatality rates for adenoviruses for bone-marrow patients ranges from 53 to 69% depending on subgenus (Hierholzer, 1992). Coxsackie A1, which seldom appears to cause diarrhea in healthy individuals, resulted in the deaths of six of seven bone marrow patients in one outbreak (Townsend et al., 1982).

Hypogammaglobulinemic patients are at increased risk of chronic meningoencephalitis from enteroviruses (Rubin and Young, 1988). Chronic meningoencephalitis is most frequently associated with echovirus infection but it has occasionally been reported in association with Coxsackie B infection.

In contrast to many of the other enteric viruses, Norwalk virus nor hepatitis A virus do not appear to be associated with a greater severity or chronic illness in the immunocompromised (Rubin and Young, 1988).

6. Exposure

Another factor potentially enhancing the risk of acquiring a serious infection from water is the degree of exposure. It has been reported that daily intake of tapwater increases significantly with age (Roseberry and Burmaster, 1992), with persons over 65 ingesting more than twice that of children. The mean intake of tapwater during pregnancy is not significantly greater, while in lactating women it slightly higher (Ershow et al., 1991). However, the percentage of individuals ingesting greater than 2 liters per day was greater among pregnant women (10% of the controls and 15% of the pregnant women).

7. Conclusions

It is apparent from this review that certain segments of our population are at increased risk of serious illness and mortality from microbial food and waterborne disease. These include the young, elderly, immunocompromised, and the pregnant. Risks of increased severity and mortality are greater for many of these water and foodborne disease microorganisms. This group of individuals currently represents almost 20% (Table 1) of the population of the United States, and is expected to increase significantly in the years ahead. Infectious diseases are a major problem in the elderly because the immune function declines with age, antibiotic treatment is less effective because of decrease in physiological function, and malnutrition is more common (Meyers, 1989). As a result outbreaks of gastroenteritis can be devastating in nursing homes resulting in a significantly higher mortality (10 to 100 times greater) than the general population. To ensure adequate protection of this group will require a better understanding of the occurrence of the agents in drinking water and food and the effectiveness of current technology for their control.

Infections in the immunocompromised host constitute a relatively new and severe problem magnified by the current AIDS epidemic and by the escalation in organ

and tissue transplantations. Enteric pathogens are among the many agents that take advantage of the impaired or destroyed immune system to establish persistent and generalized infections in the immunocompromised host. Such infections are difficult to treat, tend to be long term, add to the burden of the debilitation in the patient, and can result in a significant higher mortality (as great as 50% of those clinically ill) than immunocompetent persons. These sensitive populations may need special protection from water and foodborne microorganisms.

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