1-1-2009

Foodborne or pandemic: An analysis of the transmission of norovirus-associated gastroenteritis and the role of food handlers

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ABSTRACT

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by

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M.S.P.H., Walden University, 2006
M.S., The Ohio State University, Columbus, 1978
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Dissertation Submitted in Partial Fulfillment
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Doctor of Philosophy
Health and Human Services
Epidemiology

Walden University
January 2009

ABSTRACT

This study examined the strength of association between food workers and food to norovirus in comparison to bacteria associated with foodborne-related gastroenteritis by whether norovirus had a direct (physical evidence), indirect (statistical evidence), or suspect (neither of the two) association with food or food handlers. The Centers for Disease Control and Prevention considers norovirus to cause the largest number of foodborne-related gastroenteritis cases in the United States. The association of norovirus with foodborne outbreaks through its information data collection form focuses on the food worker as the typical source. Yet, many outbreaks are not foodborne in nature. The gap in the research is the evidence supporting the theory that norovirus transmission is the same as bacterial transmission. A secondary data anaylsis was conducted on the data from the electronic Foodborne Outbreak Reporting System between 1998 and 2006. An odds ratio analysis showed no similarity between proportion of the implicated and nonimplicated numbers of outbreaks from norovirus and those from *Salmonella*. The odds ratios also showed a stronger similarity between proportions of food handler implicated outbreaks from norovirus than from *Salmonella*. An analysis showed, though, a significant emphasis was not placed on the food handler but on other indirect routes of transmission of norovirus in outbreaks. The analysis also indicated that norovirus transmission was not mainly through food. Norovirus transmission appeared to be through person-to-person rather than food and had more similarities with pandemic influenza than gastroenteritis-associated bacteria. A change in approach to norovirus by local, state, and federal agencies could have social change implications for prevention, surveillance, and public health programs to reduce infection and outbreaks.

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ACKNOWLEDGMENTS

I wish to thank my wife Joyce for her unwavering support of my decision to take on a doctorate and over the years of class work and the time that it took to accomplish writing this dissertation. The understanding and commitment she provided while I spent countless evenings and weekends studying can only come from a family who truly loves you. I thank them sincerely in assisting me in the accomplishment of this personal goal. I could not have done it without them.

I also thank my colleagues, especially Drs. Walter Hill and Uday Dessai at the Microbiology Division, Food Safety and Inspection Service, USDA for their professional advice, encouragement, and overall positive attitudes that helped me reach a goal I have been seeking lo these 30 years. I am fortunate to be able to work with such dedicated professionals and I am proud to call them friends and colleagues.

Lastly, I thank my dissertation committee members, Dr. Talmage Holmes, Dr. Chinaro Kennedy, and Dr. Donald Goodwin, for their dedication and commitment in challenging me, helping me produce this body of work, and their encouragement to complete the degree.

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INTRODUCTION TO THE STUDY

Introduction

Food-handlers not only have to perform quickly in preparing an attractive, acceptable product for consumption, but they must please their clients and managers simultaneously while ensuring their preparation and processing techniques do not introduce foodborne pathogens into the product resulting in illnesses and massive outbreaks. Yet it is on their shoulders that much of the blame for transmitting illness is placed. This may not be appropriate.

Foodborne illness is an ever present and complicated problem. Every year in the United States, foodborne diseases are responsible for 76 million illnesses, 300,000 hospitalizations, 5,000 deaths, and millions of dollars of lost productivity (Mead et al., 1999). The World Health Organization (WHO) estimates suggested that nearly one third of the industrialized countries' populations suffer from a foodborne illness each year (Scott, 2003). Yet, an etiologic agent is identified in less than 10% of these cases (Mead et al.).

Public perception about gastroenteritis typically focuses on the largest outbreaks and food recalls caused by the presence of foodborne bacterial pathogens, typically *E. coli* O157:H7, *Salmonellae*, *Listeria monocytogenes*, and *Campylobacter* species. Because of increased focus on food safety and programs reporting through such programs as the Hazard Analysis and Critical Control Point Program (HACCP) implemented by the National Aeronautics and Space Administration (NASA) and the U. S. Department of

Agriculture's Food Safety and Inspection Service (USDA/FSIS), and supported by the Centers for Disease Control and Prevention (CDC), most bacterial foodborne outbreaks have decreased in the past 5 years (Lynch, Painter, Woodruff, & Braden, 2006). Yet the single leading cause of foodborne illness is viral and under recognized as the largest cause of foodborne illness (Widdowson et al., 2005).

The most commonly attributed source of foodborne viral infection is norovirus. Norovirus, also known as Norwalk, Norwalk-like viruses (NLVs) or small, round structured viruses (SRSVs), cause acute gastroenteritis in humans. An outbreak of explosive gastroenteritis on a single cruise ship five consecutive times was reportedly caused by a parvovirus-like (PVL) agent (also identified as Norwalk agent) affected 521 (64%) cruise ship passengers in 1977 (Gunn et al., 1980). As an emerging infectious disease, it was in 1982 that epidemiologic and clinical criteria were established to identify and characterize norovirus outbreaks (Widdowson, Monroe, & Glass, 2005).

Subsequent to 1982, CDC established criteria for detecting norovirus as a diagnosis in foodborne disease (CDC, 2006). A diagnosis requires one of three conditions: detection of viral RNA in at least two bulk stool or vomitus specimens by real-time or conventional reverse transcriptase-polymerase chain Reaction (RT-PCR), visualization of norovirus by electron microscopy in at least two bulk stool or vomitus specimens, or two or more stool positive by commercial enzyme immunoassay (EIA).

Main sources of all food contamination have been identified as infected animals, fecal material, air, water, and cross-contamination by both equipment (including food contact surfaces) and humans. In a study of 355 cases of norovirus infection that affected

90 patients and 265 health care workers, attack rates were calculated at 5.3% (7 of 133) for patients and 29.9% (29 of 97) for health care workers in the coronary care unit and 16.7% (39 of 233) for patients and 38.0% (76 of 200) for health care workers in the psychiatry units (Johnston et al., 2007). Turcios et al. (2006) in their review of 4,050 outbreaks reported from 1998 to 2000 of AGE estimated an attributable rate of, at a minimum, 28% to norovirus. They noted that the discrepancy of reported rates was due to the laboratory capabilities and test availabilities limitations in those years.

A study of norovirus transmission should consider not only food and food handlers but also other factors such as other modes of transmission and the environment. Kaplan et al., (1982) established the case definition for norovirus associated AGE by stating the disease was characterized by (a) a high attack rate in adults, (b) a high frequency of vomiting, (c) short duration of illness, and (d) absence of identified bacterial pathogens. Data about norovirus induced gastroenteritis from water was last reported to CDC in 2006 (Lianget al., 2006; Dziuban et al., 2006). Drinking water from public water systems is regulated by the U. S. Environmental Protection Agency's (EPA) Safe Drinking Water Act of 1974, which sets standards for microbial contamination under the Total Coliform Rule (TCR), Surface Water Treatment Rule (SWTR), Interim Enhanced SWTR (IESWTR), and the Long Term 1 Enhanced SWTR among others. EPA's role was to protect the public from *Giardia intestinalis, Cryptosporidium* spp., viruses, *Legionella* spp., and other selected pathogens. Between 2003 and 2004 there were only 30 drinking water waterborne disease and outbreak reports by 18 states affecting 2,760 persons and

resulted in four deaths. One of the outbreaks affecting 70 persons was attributed to norovirus.

EPA's reporting of recreational water surveillance reported 207 overall outbreaks between 1991 and 2002 of which only 12 identified norovirus as the etiologic agent affecting 3361 cases (Craun, Craun, Calderon, & Beach, 2006). During 2003-2004, 62 outbreaks resulted in 2,698 ill persons including one death (Dziuban et al., 2006). Of those outbreaks, six were confirmed as viral and five of those were confirmed as norovirus resulting in 300 cases.

Reported cases were those associated with drinking water, contaminated bottled water, ice, beverages made with contaminated water, deficiencies of equipment or devices for which water is used or distributed (Dziuban et al., 2006). No reports involved water used in food preparation even though this is the same potable water supplied to the public.

The epidemiologic evidence for waterborne outbreak classification was based on four classes of evidential quality. The best was adequate epidemiologic data that was provided about exposed and unexposed persons with a relative risk or odds ratio greater than or equal to 2.0 and the water quality data was based on historic or laboratory data (Blackburn et al., 2004). The lowest quality was epidemiologic data provided with limited and water quality data was not provided or inadequate. While these outbreak reports are important, they are too infrequent in surveillance and monitoring to make a substantial analysis of water's contributions to overall outbreaks with norovirus as the etiologic agent. No other databases collected information about water that had traced

such information to outbreaks. A search of other data sources did not yield other information about norovirus.

Environmental transmission of norovirus has rarely been reported in the scientific literature and only as an interesting circumstance. One survey of outbreaks in France between 1999 and 2004 was reported based on genogroup type (Bon et al., 2005). The data found 45 calicivirus outbreaks of which 17 different groups of genotypes were identified. Nursing homes were the location of the most number of norovirus outbreaks (17), schools and holiday camps (9), districts, (7), private homes, (6), hospitals, (4), and hotels (2). The mode of transmission was identified as person-to-person (17), unknown (12), oysters (9), water (5), and food (2). A single genogroup of norovirus, GII, was the most common strain and appeared in nursing homes, hospitals, private homes, and hotels. This same strain was the most predominant in person-to-person, oysters, and food modes. Yet a comprehensive study of the prevalence and persistence in the environment through person-to-person transfer was not possible given the low outbreak numbers and a study in the United States, had not been attempted.

The transmission of norovirus has been stated as person-to-person contact, indirectly through contaminated foods or water, contact with fomites, through infected fecal matter or vomitus and that there are other transmission routes other than foodborne (Kroneman, Verhoef, et al., 2008). There are many published reports of outbreaks based on an ill person's contact or proximity to others who eventually became ill. The difficulty is that infecting a person to follow transmission is no longer acceptable as a research

method and models of transmission risk potential have not been presented to the scientific community for examination.

Data collected about norovirus in the United States are maintained by the CDC's Emerging Infections Program (EIP) in the Foodborne Diseases Active Surveillance Network (FoodNet) electronic Foodborne Outbreak Reporting System (eFORS) database (CDC, 2007). Its focus is foodborne outbreaks and is limited to a minimum amount of information to report as defined by the ingestion of food (see Appendixes A and B).

Limiting CDC's collection of information especially about types of transmission removes important information creating a missing link in the cycle of norovirus spread causing outbreaks. Examination of such facets of transmission would provide a more balanced look at the cycle or cause of transmission (CDC, 2007). Such an ideal situation does not exist for norovirus for practical and cost reasons and this researcher was forced to look at the only available source with all its flaws. Thus, the concentration of the investigation was on the only database about food and food handlers.

General efforts to decrease the number of illnesses were successful for bacterial sources of foodborne gastroenteritis because food handlers, management, and government agencies were aware of potential fatalities and the seriousness of infections. Those efforts included improved sanitation, washing, and maintaining clean facilities and kitchens (Todd, Greig, Bartleson & Michaels, 2007a). These efforts; however, seemed to be ineffective in inactivating the number of Caliciviral associated illnesses (Duizer, Bijkerk, et al., 2004).

The personal hygiene practices of infected food handlers are considered the most important contributor to the spread of foodborne disease (D'Souza, Moe, & Jaykus, 2007). Human contamination of food was presumed to be mitigated by protective barriers such as gloves, aprons, facemasks, and hairnets. Preventive actions focused on hand washing. As food handlers defined their roles as working in wholesale, retail, or home settings, their adherence to the food safety culture was predicated on their social and professional status and outlook.

Food handlers may have been unwitting conveyors of contaminants if professional Sanitation Standards of Operations Practices (SSOPs), common safety tips and personal hygiene efforts, were not effective or properly followed. On-the-job stress from adverse working environments or production schedules could have contributed to the lack of adherence to personal hygiene. Workers, especially in larger establishments, undergo various physical and psychological changes resulting in difficulty adapting to shift work, lack of concentration, and self-perceived constraints (Lac & Chamoux, 2004).

Job-related stress may influence a worker's perception of health and could increase susceptibility to physical and environmental exposures (Chao, Schwartz, Milton, & Burge, 2003). In addition, cleanliness and condition of the kitchen influence the food preparers' persona, projecting attitudes about the environment. All these influences affect how food handlers conduct their business and personal hygiene. Personal behaviors may directly affect food safety and product contamination. Yet, those same factors that contribute to the work or home performance and the contamination of food by viruses have not been critically identified or analyzed.

A survey of food handlers has proven impracticable. The sheer number of potential contributing factors to a person's source of illness, including sick relatives, other foods, water, and environmental conditions is difficult to calculate (Todd et al., 2008a). Isolates from food workers are nearly impossible to obtain and food survey interviews are unreliable and hard to trust (Todd et al., 2008b). Finding the ill food handler may be hard because of low pay, high mobility, fear of officials, and language barriers (Todd, 2008b). Unless viral strains obtained are compared at a genetic level, an ill food handler may not be the actual source and running such analyses is cost prohibitive to most public health programs (Todd, 2008b).

Programs of food safety and hygiene are geared toward food handlers and preparers. Most food outbreaks occurred at restaurants, social gatherings, or in contained environments such as cruise ships. However, there were also many cases of outbreaks documented from water sources and person-to-person contact as seen in hospitals, daycare centers, and schools (Todd, 2007a). In addition, a large proportion of outbreaks were not assigned an etiological cause and plenty of sporadic and isolated incidents were neither reported nor considered outbreaks (Todd, 2007a). Only a single cause was given for illness and outbreaks without consideration of competing pathogens or opportunities for illness to occur (Todd, 2007a).

The only available data file for norovirus is limited and biased towards food and food handlers. A foodborne outbreak is transmitted by a food or from a food handler (Todd, et al., 2007b). A response determining the mode of transmission is only requested in cases of Enterohemorrhagic *E. coli* or *Salmonella* Enteritidis (see Appendix A). No

other options are provided to public health officials in reporting norovirus related illness and so the data will be skewed making objective conclusions difficult (Todd, 2008b).

Statement of the Problem

Because norovirus is the leading cause of viral foodborne outbreaks of gastroenteritis (Widdowson et al., 2005) one could assume that viral foodborne outbreaks follow the same means of dissemination as bacteria. The gap in the research is the evidence demonstrating the assumed transmission routes used as a basis for interventions. Because food handlers are a common element in an outbreak investigation, data collected tend to be biased towards the food handler as a source or contributor (Todd, 2008b).

Almost all foodborne pathogens may be contracted via the oral-fecal transmission route from contaminated feces via the fingers of unsanitary food workers (Jay, Loessner, & Golden, 2005). The data collected and presumed to be norovirus without any confirmed etiology or suspected based on symptoms should be examined more deeply. Having outbreaks occur around food-based events does not mean that food or the handler is always the vehicle enabling transmission (Todd, 2008b). It may not be a given fact that norovirus-like symptoms associated with a food event are really food related or food handler associated. Such a change in assumption could have led to identifying and discovering other pathways of transmission.

The eFORS data contain the only records of norovirus associated illness and outbreaks and while the eFORS data collection form was not designed for answering detailed in depth questions, there is important information that can be derived from an analysis., This study, which must limit itself to the data fields in the forms, questions

what role food or food handlers have in the transmission of norovirus by examining the association between the number of norovirus related and bacterial related foodborne outbreaks and food or food workers. Several specifics from analyses of the eFORS data are needed in order to provide an answer to this question. They are:

1. How is food associated with the direct or indirect transmission of norovirus to acute gastroenteritis outbreaks?
2. Did the evidence implicate food handlers were the direct or indirect source of norovirus outbreaks?
3. Are there other sources identified as the cause of norovirus outbreaks?
4. Considering contributing factors identified for outbreak, how strong is the argument that food or food workers are the major source of transmission of norovirus?

Results should increase understanding about the association between norovirus and food or the food worker. It can also shed light on the appropriateness of the data collection tool. The analysis should provide information to enhance further debate about the status of norovirus as a foodborne pathogen.

Rationale for the Research

The focus of research on foodborne pathogens has been the food itself and its handling by food workers. The use of gloves, facemasks, and cleansing products by food handlers has generally reduced the number of bacterial pathogens from reaching the consumer (Todd, 2007b). Assuming norovirus was solely a foodborne pathogen and sanitation programs worked properly, the number of illnesses due to norovirus should

have been drastically reduced. However, while norovirus is classified as transmitted primarily by oral-fecal routes it is transmitted also by a variety of means including vomitus (D'Souza, Moe, & Jaykus, 2007) and a better understanding of each would explain why intervention in a foodborne route is not producing desired reduced results. Such results could be a result of a general failure of these interventions or other modes of transmission of norovirus not being addressed concurrently. Because acute gastroenteritis as a foodborne disease is presumed to be a result of ingesting food (see Appendix A), it is possible that the emphasis on food handlers will be misplaced. Therefore determining whether the transmission of norovirus is associated with food or food handlers may help develop a better understanding of norovirus and lead to an improved program to prevent the transmission of norovirus and reduce gastroenteritis in the population.

Nature of Study

This study is a secondary data analysis. Typically, all U.S. state or county public health investigations use the electronic Foodborne Outbreak Reporting System (eFORS) to monitor outbreaks and the data are collected by members of CDC's outbreak staff. The data are categorical and odds ratios were calculated estimating the risk when compared to a typical bacterial entropathogen.

The data collected for this study include results of outbreaks as defined by CDC. Each data record is a summary collection of interview results and determinations as to the source and etiologic agent for the outbreak. Within those records, special emphasis is paid to the date, location, type of illness, foods confirmed or suspected, agents of transmission, and demographic information.

Significance of the Research

The importance and significance of this research study is to gain better insight into the classification within eFORS of norovirus as a foodborne pathogen and the contributing factors to norovirus transmission to the population. The gap in the research is the missing evidence that associates norovirus with foodborne outbreaks. It was presumed that any intestinal ailment comes from ingestion of food or water and because norovirus produces acute gastroenteritis, it was presumed that norovirus must be a foodborne pathogen. This study produced information that questions that assumption. This information can be used to design programs to reduce norovirus contamination and spread. As a result, routes of transmission of norovirus can be confirmed and emphasized for designing public health approaches to reducing norovirus associated acute gastroenteritis.

Policy and Social Implications

Norovirus results in low mortality and the level of morbidity is such that required hospitalization is infrequent (Mead et al., 1999). The tendency of health providers and public health officials has been to allow the disease to run its course and to treat the symptoms to alleviate discomfort. Reporting cases of norovirus gastroenteritis is voluntary and not required by state or federal health departments as an ailment and is of interest as a category-B bioterrorism agent and to those who look for trends in foodborne outbreaks.

Use of norovirus as a bioterrorism tool could be used to incapacitate a section of the population or military rendering any response to the attack delayed until a sufficient

portion of those affected could return to their active status (Grabenstein, 2004). This has not only military and public health concerns but can have economic consequences in lost workdays, income, spending, transportation, and function as a society.

The approach of public health officials and hospital administrators in preventing and reducing the incidence of norovirus associated gastroenteritis has been to re-enforce standard personal hygiene and sanitation practices and re-educate those who have the highest risk for transmitting the virus (Martin et al., 2008). This has worked satisfactorily for bacterial foodborne pathogens. Yet, if norovirus- induced gastroenteritis does not have the same transmission traits as other bacterial foodborne cases, then public health programs and policy would need to be addressed. It may be insufficient for current sanitation and personal hygiene techniques and training to be effective in addressing norovirus outbreaks. The emphasis on personal behavior towards sanitation and hygiene could be misdirected and require a change in hygienic programs and behavioral patterns. Social programmatic change would be needed to reduce outbreaks from norovirus as a pandemic pathogen and would require a new approach or shift in research, policy, and administration to contain and control the number of outbreaks similar to other etiologic agents. The potential for positive social change is great if all factors and aspects are investigated. The etiology of norovirus induced gastroenteritis infection, as a potential pandemic virus, would need to be identified and appropriate interventions and counter measures would need to be implemented on the basis of seasonal patterns, genetic evolution, and pandemic spread. Such a conclusion would impact national, state, and local policy; program development, funding, and reporting systems.

Definition of Terms

For the basis of this paper, definitions related to foodborne illness will be expressed in the terms as defined by the surveillance data-collecting group and accepted scientific standards.

Foodborne outbreak or foodborne-disease outbreak: This is defined by CDC (2006) as the, "an incidence in which two or more persons experience a similar illness resulting from the ingestion of a common food" (2nd para.).

Food workers or food handlers: These terms are used interchangeably and are defined as those who serve food to customers in a retail operation or friends or family members in a home setting, and

> Clean and prepare basic food ingredients, such as meats, fish, and vegetables for use in making more complex meals, assemble salads and sandwiches using readily available ingredients, perform simple cooking tasks …, and keep work areas clean. *Dishwashers* clean dishes, glasses, pots, and kitchen accessories by hand or by machine. (U.S. Department of Labor, Bureau of Labor Statistics, 2007, p. 2).

Gastroenteritis: This has been defined as an inflammation of the stomach and small and large intestines. The expression of this ailment is often characterized by vomiting and/or diarrhea (Majowicz et al., 2006). The term has been applied when no etiologic agent was identified.

Norovirus (genus *Norovirus*, family *Caliciviridae*): A group of related, single-stranded RNA, nonenveloped viruses that cause acute gastroenteritis. Originally called the winter vomiting virus, norovirus is also known as Norwalk, Norwalk-like viruses (NLVs), or small round structured viruses (SRSVs) (Reference.MD, 2007).

Norovirus-associated gastroenteritis: The illness caused specifically by Norovirus. Symptoms usually begin 24 to 48 hours after ingestion of the virus, but can appear as early as 12 hours after exposure. The virus can remain in the stool, vomit of infected persons, and shed up to 2 weeks after the illness symptoms have gone (CDC, 2006a).

Acute gastroenteritis (AGE): An infection caused by norovirus that result in typical gastroenteritis. Symptoms include watery diarrhea and vomiting and may include headache, fever, and abdominal cramps (stomach ache). In general, the symptoms begin 1 to 2 days following infection with a virus that causes gastroenteritis and may last for 1 to 10 days, depending on which virus caused the illness. In absence of confirmation of the etiologic agent, this term is applied generically (CDC, 2006b).

Research Delimitations, Limitations, and Assumptions

This study is a secondary data analysis using information from the CDC's Emerging Infections Program (EIP) Enteric Diseases Epidemiology Branch database covering the years 1998 through 2006. The EIP project's purpose is to "better understand the epidemiology of foodborne diseases in the United States" by maintaining active surveillance of foodborne diseases and all related epidemiologic studies (CDC, 2007, p. 1).

Delimitations of the Study

The data are the collection of reports of foodborne outbreaks based on the definition by CDC as two or more cases of a common illness resulting from the ingestion of a common food. Reports submitted are from various locations, times, seasons, or

environmental conditions in the United States over an 8 year period from 1998 through 2006. The data includes information about food and food workers.

Limitations of the Study

The occurrence of norovirus alone is a voluntarily reportable disease agent in the United States that involved in an outbreak. Any data collected has been done by cooperative agreement by those having an interest in its outbreak activity in the CDC and state health departments who then report the results of outbreaks to the CDC. Records held in the EFORS system is limited by the assumption must be made that these reports are truly representative of all norovirus outbreaks.

The scope of this study is limited only to those foodborne outbreaks reported to CDC by all U.S. states and counties. Reports received by CDC follow the pyramid of determining the burden of disease (Griffin, 2008). Of the U.S. population, only a portion is exposed to norovirus, which does not confer lasting immunity to any strain. Of that group, a few contract the disease and only a proportion of those express disease symptoms. The symptoms are severe enough to only a percentage of that group to seek medical care. Doctors take a sample of only a portion of that group. A clinical laboratory is able to isolate and identify the virus from a portion of those samples. A few of those results are reported to local public health officials. Finally, at the top of the pyramid are those few results reported to CDC. Since the eFORS form is a voluntary report of foodborne outbreak information, not all states or counties are obligated to complete and submit the information. Therefore, the data found in the CDC outbreak database may only include the worst of all foodborne outbreaks and not be comprehensive.

Norovirus and acute gastroenteritis (AGE) resulting from an infection is a worldwide phenomenon; the results may not necessarily apply to world conditions or even all of the United States.

As for the data collected, their accuracy could not be verified by this study. The survey instrument reported to CDC through eFORS, was completed after outbreaks occurred and data from interviewees are collected sometimes long after the event. While the form is standard (See Appendix A), the ability of any state or county to do a complete investigation is based on the resources of the public health governmental organization, whether work force or other resources, distance from the outbreak site, or other unidentified cause. In addition, the information collected by different states may not be able to capture the associations because the eFORS survey tool does not allow for an alternative hypothesis. However, this does not mean one cannot exist.

The eFORS form does not provide for sufficient information to determine the food-specific attack rate or attributed risk for a food item. The form allows for indicating a laboratory confirmation of the etiological agent's presence but in absence of such evidence allows for a variety of suspected reasons for implicating a food item making the attribution from a public official's training and experience but unsubstantiated and allowing for bias. In the case of a lack of laboratory tests, the form allows for unconfirmed conclusions about the food handler's contribution to the outbreak and does not consider other sources of contamination from potential environmental factors, such as water or food contact surfaces, or patrons.

The data collected in the eFORS questionnaire was developed and designed by CDC based on the classification of norovirus as a foodborne disease with the conviction that food workers were assumed to be related to the outbreaks. This assumption is based on the premise that standard sanitation and hygiene preventive activities work equally well for both bacterial and viral pathogens and that if food is cooked properly, then any outbreaks must be the result of previous illness and hand washing or personal hygiene failures. The Council of State and Territorial Epidemiologists (CSTE) have challenged this notion by stating there are many enteric disease outbreaks that are due to non-foodborne transmission, specifically mentioning norovirus outbreaks in nursing homes and *Shigella* outbreaks in daycare facilities (CSTE, 2004). Because of the frequency and size of these outbreaks the burden to public health is larger than just from foodborne incidents.

Lastly, the definition of outbreaks limits reportable incidents to two or more cases, which eliminates single incidents and sporadic or unreported household outbreaks from the database.

Assumptions

The number of outbreaks provided in the database is the result of states reporting outbreaks that actually occurred in the United States. Most likely outbreaks are only brought to the attention of public health authorities because they are large, interstate, or restaurant associated or that can cause serious illness, hospitalization, or death (Lynch, Painter, Woodruff, & Braden, 2006). CDC did not include data from five categories of outbreaks:

1. outbreaks that occur on cruise ships,
2. outbreaks in which the food was eaten outside the United States,
3. outbreaks that are traced to water intended for drinking,
4. if the route of transmission from the contaminated food to the infected persons is indirect, and
5. outbreaks that occur as result of direct contact with animals.

Another assumption is that the data provided for this study were edited and validated as correct by CDC, which it does not (Lynch et al., 2006). Additionally, it is possible that state public health officials will not have reported an outbreak of norovirus gastroenteritis because the source was unrelated to food or unidentified. In addition, because norovirus is not a reportable disease, it may not be reported at all adding further bias into the collected reports. The researcher assumed that the reporting agent is an official public health professional and that the department has sufficient resources and work force to do a thorough investigation. Finally, the researcher assumed that the data was collected and recorded accurately and that the conclusions drawn by individual public health officials were correct.

Study Summary

Norovirus outbreaks records are collected within the foodborne outbreak monitoring system. Some researchers and epidemiologists (Cheesbrough, Green, Gallimore, Wright, & Brown, 2000; Isakbaeva et al., 2005) do not agree that norovirus necessarily belongs in such a collection because it presumes that that the outbreak is foodborne related or limited to food related activities. Nevertheless, data about norovirus

outbreaks in such a collection leaves the impression that those outbreaks that have no confirmed etiology allowing norovirus-like symptoms to be classified as foodborne associated (Widdowson et al., 2005).

An analysis of norovirus outbreaks may answer whether a food or food handler association is a justifiable assumption when compared to a bacterial entropathogen. The question then becomes whether or not norovirus data should be included in a foodborne database not currently available from eFORS that would give a more realistic account of norovirus' infectivity and disease burden.

Chapter 2 focuses on the background of norovirus infection and illnesses, the epidemiology of outbreaks, the role of food handlers in such outbreaks, and the reasons for classification of norovirus as a foodborne pathogen. The research design in Chapter 3 focused on examining the data collected from foodborne outbreak reports, data about food handlers, and the means to analyze the data collected. Chapter 4 reported the results and Chapter 5 provided an interpretation of the results and discussed the role of the current transmission model and an alternative model for transmission.

CHAPTER 2:

LITERATURE REVIEW

Introduction

The most commonly identified pathogen-causing foodborne acute gastroenteritis is norovirus. Norovirus, also known as Norwalk, Norwalk-like viruses (NLVs) or small round structured viruses (SRSVs), are a group of related, single-stranded RNA, non-enveloped round viruses that cause significant acute gastroenteritis in humans (CDC, 2006b). The variation in nomenclature reflects the virus' evolving identification. Norovirus causes AGE in numbers far greater than bacterial caused gastroenteritis (Meade et al., 1999). The most recent information estimates 23 million Americans annually become sick from norovirus (Meade, 1999). The next largest groups from a single cause are 2.45 million cases from *Campylobacter* spp. and 1.41 million cases from nontyphoidal *Salmonella.*

Norovirus was described in 1929 but is still considered an emerging infectious disease. Originally called the winter vomiting disease by Zahorsky (Adler & Zickl, 1969), the case definition attributed to norovirus was established in 1982 (Kaplan et al., 1982) and reevaluated in 2006 (Turcios, Widdowson, Silka, Mead, & Glass, 2006). There is a rudimentary but growing knowledge about the virus, its epidemiology, and role in foodborne outbreaks, how it is spread, and how one becomes ill. Information about these viruses been difficult to gather since they do not grow in culture, nor is there an effective animal model for replication (Estes et al., 2000). Since norovirus is considered a

foodborne pathogen, it is important to understand the role of food handlers and their role in transmitting norovirus that may produce outbreaks (Todd, 2008b).

The database mainly utilized was PubMed, a service of the U.S. National Library of Medicine and the National Institutes of Health. The search terms used were Norovirus, Norwalk, Calicivirus, food handler, food worker, and viral transmission. Additional sources were found in scientific peer reviewed journals and discussions with scientific experts on norovirus and infectious diseases.

Norovirus Defined

Norovirus is the prototype strain of genetically and antigenically diverse single stranded 26 to 35-nm nonenveloped RNA viruses. It is a member of the family *Caliciviridae*. Norovirus, first isolated in 1968, was named after the original strain of Norwalk virus that was the source of an outbreak of gastroenteritis in 120 students out of 372 at an elementary school in Norwalk, Ohio (Adler & Zickl, 1969). The attack rate for those who bought lunch in the cafeteria was the same as for those who brought their own lunch. The disease lasted 24 hours and remitted spontaneously (Storr, Rice, Phillips, Price, & Walker-Smith, 1986). Classical confirmation tests showed the virus isolated from rectal swab filtrates induced gastroenteritis in adult volunteers. Typical onset appears to be in spring between March and May (Storr et al.).

Causative Agent – Identification

Norovirus are positive single stranded RNA approximately 7.7 kb in length and constitute their own genus in the *Caliciviridiae* family (Hardy, 2005). The virion is composed of 90 dimers of the major capsid protein VP1 and 1 or 2 copies of the minor

structural protein VP2. This is unique in that only plant viruses contain only a single major capsid protein. Antibody models are currently under development in the form of enzyme-linked immunosorbent assays (ELISAs) and antigen-capture ELISAs (Han, Wang, Smiley, Chang, & Saif, 2005). Some studies have shown replication of the murine norovirus (similar to human norovirus) in cultured macrophages and dendrite cells and molecular cloning with a seroprevalence of 74.1% (Nicollier-Jamot, Pico, Pothier, & Kohli, 2003).

Currently, norovirus contains at least five genogroups, GI, GII, GIII, GIV, and GV, which are divided further into at least 29 genetic clusters. Taxonomic identification is actively occurring and evolving, as the total numbers are not established. Clusters differ by more than 20% amino acid pair-wise distance while genogroups differ by between 44 and 55% pair-wise distance. Most clusters are named after the location in which they were discovered, including Mexico, Toronto, Hawaii, Southampton, Desert Shield, and Norwalk (Koopmanns, van Bonsdorff, Vinje, de Medici, & Monroe, 2002).

The stability of norovirus is difficult to measure since no effective model for replication exists. Other viruses, such as rotavirus, have survived for more than a year at low temperatures in mineral water. Norovirus RNA frozen or found in bottled water has a long survival period (Widdowson et al., 2005; Koopmans & Duizer, 2004).

Infectivity and Clinical Aspects of the Disease

To determine the sole symptoms caused by norovirus, a human trial was conducted consisting of 50 volunteers solicited between 1985 and 1990. The volunteers were orally given norovirus (2 ml of a 1:100 dilution of a stool filtrate) and examined for

health indicators over the following month (Graham et al., 1994). Serum and stool samples were collected. Of the 50 subjects, only 41 became infected, of which 68% were symptomatic and 32% were asymptomatic. Preexisting antibody titers did not confer immunity nor susceptibility to illness. There was a significant correlation between the level of antibody responses with vomiting or vomiting and diarrhea and the magnitude of seroconversion was highest among those who had vomiting. While symptomatic persons who experience vomiting are a significant to epidemiologic studies, reports that one third of those infected are asymptomatic can make investigating the sources and means of transmittal of norovirus difficult unless physical evidence and specimens can be collected.

Norovirus associated gastroenteritis symptoms can last a long period. Symptoms last a median of 5 days with duration of up to 28 days. Viral shedding was observed up to 22 days after the onset of illness, but in only 26% of the cases. Long-term shedding was not associated with increased severity or prolonged duration of clinical symptoms (Goller, Dimitriadis, Tan, Kelly, & Marshall, 2004).

Not all people are susceptible though. While all age groups showed symptoms, from only 78% of patients was the virus able to be detected on the first day of sampling (Rockx et al. 2002).

The youngest afflicted by norovirus were under 5 years of age. Norovirus had the highest proportion of illness in children (aged 0.5 to 17 years) and the elderly (aged above 65 years (Rockx et al., 2002). A total of 13.4% out of 305 stool samples collected from child patients in two major African pediatric hospitals between 1999 and 2001 were

positive for norovirus with mixed viral infections found in 8.9% of the patients (Simpson et al., 2003) while an Australian hospital found norovirus in 30 child patients out of 60 suffering from acute gastroenteritis (Kirkwood & Bishop, 2001).

The most common presentations of illness are nausea, diarrhea accompanied by abdominal cramps, vomiting, and fever, all symptomatic of gastroenteritis (Parashar et al., 2001). Norovirus infections cause an inflammation of the stomach and the small and large intestines. Sudden onset, after an incubation of 24-36 hrs, may be anywhere from 15-75 hrs. Sufferers feel debilitated for 2-3 weeks. Some ill people also complain of headache, fever/chills, and muscle aches. This is rarely a deadly illness and other than drinking liquid to prevent dehydration, no specific treatment is recommended.

Norovirus replication is presumed to occur in the intestine and biopsies have suggested that the virus reproduces within mature enterocytes in the villus tips of the proximal small intestine (Hardy, 1999). Presence of the virus showed broadened and blunted villi and hyperplasia of the crypt cells. Epithelial cell cytoplasm was vacuolized. Large number of polymorphonuclear leukocytes and monocytes were present between the epithelial cells. Enzyme production decreased resulting in transient carbohydrate malabsorption. Further investigation of carbohydrate receptor-binding properties provide a clue into norovirus reproduction by seroconversion from continued passage through pigs (Hutson, Atmar, & Estes, 2004; Cheetham et al., 2006).

The lack of symptoms in some people who have been exposed could be dependent on genetic factors that were common. Risk analysis based on blood type indicates those carrying the O phenotype are more likely to be infected while those who

carry the B phenotype are less likely to become ill (Hutson, Atmar, Graham, & Estes, 2002).

Norovirus is not always the sole virus causing gastroenteritis. Therefore, clinical diagnosis alone is insufficient to point to a cause. In a large cohort of patients in a hospital in England, multiple strains of norovirus, sapovirus, and astrovirus were detected, indicating multiple sources, subclinical infections, and simultaneous infections (Gallimore, Cubitt, Richards, & Gray, 2004).

Diversification of Genetic Strains

The norovirus classification contains five genogroups, which are divided into at least 25 genetic clusters (Lindesmith et al., 2008). Genogroup GII, considered the most common to humans, contains 17 genetic clusters (Monroe, 2001), while Genogroup GI showed up in 25% of all positive gastroenteritis cases (Fankhauser et al., 2002). In Finland, GII always outnumbered GI when the virus was recovered from outbreaks (Maunula & Von Bonsdorff, 2005). Yet, diversification of strains is quite common because of the recombination of nucleic acids that could account for the increasing variety of strains over the past 30 years. Recombinant strains have been noted in Hungary, where 95% of the genogroups determined for 253 cases were GII/Lordsdale strain (Reuter, Vennema, Koopmans, & Szucs, 2005). These strains were subgrouped into 11 genotypes. A new variant, GII.4, was discovered in 2002, and it spread across England, Wales, the Netherlands, Germany, Hungary, and Spain (Lopman, Monroe, et al., 2004). Recombination of genetic material and capsids was found in about 8% of 84 capsid sequences in Germany. Those mixed combinations included GI., GII.1, GII.3,

GII.4, and GII.5 (Rohayem, Munch, & Rethwilm, 2005). Another outbreak of variant type GII.b/Hilversum that began in 2001 was characterized by four different capsid types (Reuter, Vennema, Koopmans, & Szucs, 2006).

New Zealand researchers further characterized 83 samples collected between 1995 and 1999, finding the GII/Lordsdale strain most similar to one isolated. Several other cases showed similarity to the Mexico strain, and in 1996, five other strains of norovirus were detected in New Zealand, including a Desert Storm strain (Greening, Mirams, & Berke, 2001).

In Asia, norovirus strains also maintained genetic diversity. Outbreaks and sporadic cases in Hong Kong between 2001 and 2002 were initially caused by GII (Lau et al., 2004). Subsequently, GII.4 variants C and D became dominant between 2002 and 2004 (Ho, Cheng, Wong, Lau, & Lim, 2006). In the later 6 months, GI and other strains of GII became predominant. A newer GII.4 variant was reported in 2006 (Ho, Cheng, Lau, Wong, & Lim, 2007).

In Japan, capsids of viruses collected between 1997 and 2003 were sequenced and found to be both GI and GII (Seto et al., 2005). In comparison, of the strains isolated from an outbreak from a Japanese restaurant, the GII strains most resembled others found in Mexico (Hirakata, Arisawa, Nishio, & Nakagomi, 2005). As time passed, the diversty in Japan continued. Between 2003 and 2004, outbreaks from five different locations detected subgroups GI.4, GII.2, GII.3, GII.4, and GII.6 (Phan et al., 2006). Variant GII.3 (Arg320 virus cluster) was the most common, consisting of 43.9% of the isolates, followed by GII.4 with 35.1%. In addition, the dominant recombinant strain was GII.3

capsid and GII.12 polymerase. Towards the end of 2005, GII.b within the GII.3 class was being detected in 45.5% of cases (Phan, et al., 2006). In 2006, three genetically distinct norovirus GII.4 subtypes were found in Chiba prefecture, Japan, of that one subtype GII.4f that caused 85% of the outbreaks that year (Okada, Ogawa, Yoshizumi, Kubonoya, & Shinozaki, 2007). Subsequently, the GII.4 variety seen from October 2006 to March 2007 is very similar to the one identified in Europe as GII.4 2006b, which is predominant in Yokohama City, Japan (Kumazaki, Usuku, & Noguchi, 2007).

Diversification of strains is quite common because of the way recombination of nucleic acids occurs, which could account for the increasing variety of strains over the past 30 years. Recombinant strains have been noted in Hungary (Reuter, Vennema, Koopmans, & Szucs, 2005), Australia (Marshall, Dimitriadis, & Wright, 2005), Germany (Rohayem, Munch, & Rethwilm, 2005), England (Green et al., 1994; Lopman, Vennema, et al., 2004), Japan (Seto et al., 2005), Sweden (Thorven et al., 2005), and the United States (Fankhauser, Noel, Monroe, Ando, & Glass, 1998). Examples of dendograms from Ireland and Hungary demonstrate the genographic classification evolution and differences (Figures 1a & 1b).

Seasonal evidence of norovirus activity was determined during a 3-year period in England, between 2003 and 2006. During that time, 2,946 outbreaks occurred, from which 864 strains were obtained (Gallimore, Iturriza-Gomara, Xerry, Adigwe, & Gray, 2007). The researchers investigated three phases of the winter, with September/October as the early period, December/January as the middle period, and March/April as the late period, and looked at only the first 20 outbreaks for each period. A pattern emerged as

each strain appeared or disappeared in the population. In 2003-2004, almost all outbreaks were caused by GII.4 v2. In 2004-5, GI.I4 v3 was far more present and virulent while GII.4 v2 disappeared. In 2005-6, GII.4 v3 continued but diminished greatly, while GII.4 v4 appeared and began to increase. GII.4 v5 rarely was seen and GI.4 v6 was just beginning to be seen towards spring of 2006. No similar seasonal profile has been created for norovirus in the U.S.

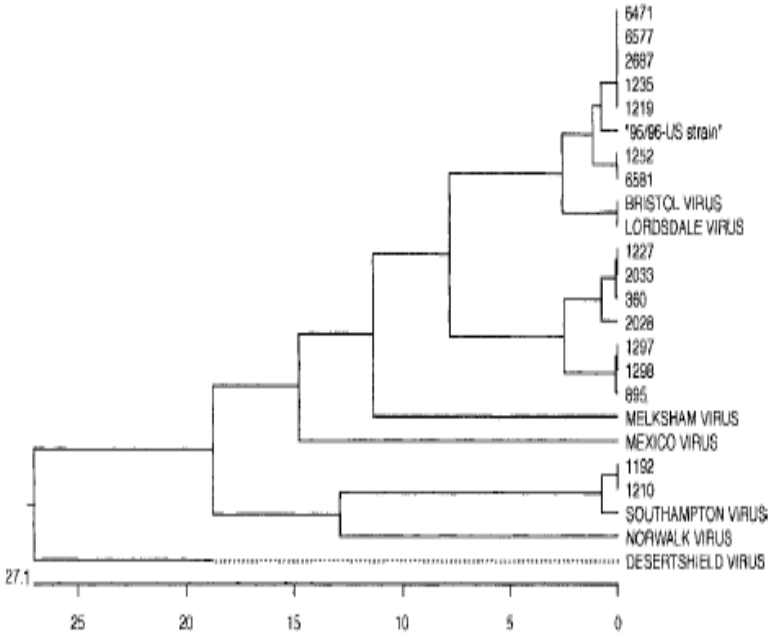

Fig. 2. Phylogenetic alignment of all sequence data obtained from sporadic cases and outbreak specimens in this study. A conserved 72bp fragment between all isolates was aligned. Members of genogroup I viruses (Southampton, Norwalk, and Desert Shield virus) and genogroup II (Bristol, Lordsdale, Melksham, Hawaii, and Mexico virus) obtained from GenBank were included for comparison.

Figure 1a. A dendogram of Norovirus genogroup classification diversity from Ireland. From "Molecular Detection and Sequencing of 'Norwalk-Like Viruses' in Outbreaks and Sporadic Cases of Astroenteritis in Ireland," by B. Foley, J. O'Mahony, C. Hill, & J. G. Morgan, 2001, *Journal of Medical Virology, 65*, p. 390. Copyright 2001 by Name of Copyright Holder. Reprinted with permission.

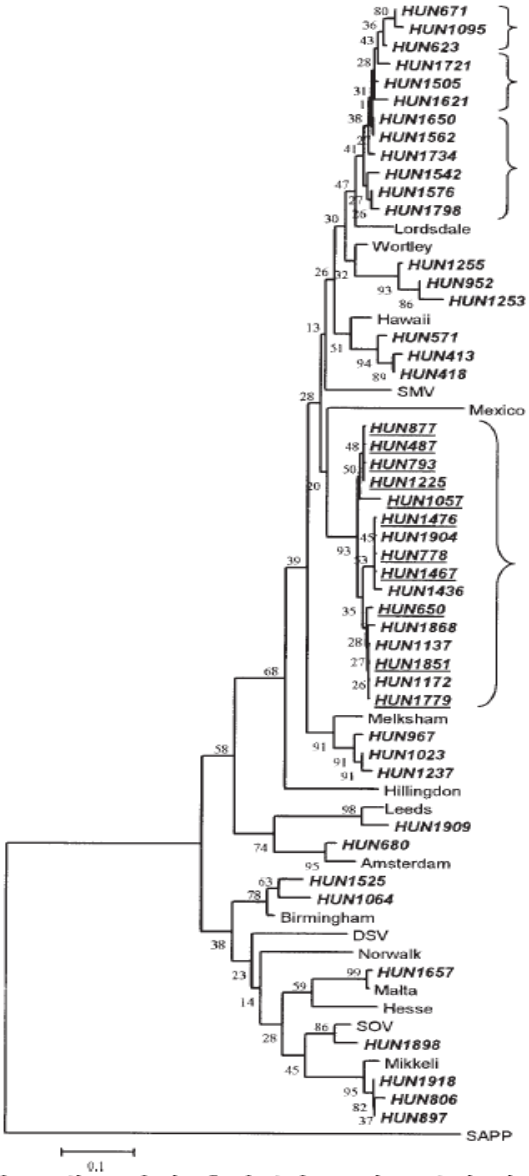

Fig. 3. Phylogenetic analysis of selected norovirus strains in Hungary (bold-italics), including new-variant Lordsdale and recombinant GGIIb/Hilversum polymerase (capsid sequence available: underline) strains observed between 2001 and 2003. The dendrogram was constructed using neighbor-joining clustering method with distance calculation using the Jukes-Cantor correction for evolutionary rate with help of the MEGA version 2.1.

Figure 1b. A dendogram of Norovirus genogroup classification diversity from Hungary. From "Evidence of the etiological predominance of norovirus in gastroenteritis outbreaks--emerging new-variant and recombinant noroviruses in Hungary," by G. Reuter, K. Krisztalovics, H. Vennema, M. Koopmans, & G. Szucs, 2005, *Journal of Medical Virology, 76*(4), p. 603. Copyright 2005 by Name of Copyright Holder. Reprinted with permission.

Norovirus is common as a cause of gastroenteritis for seven main reasons:

1. Low infectious dose.
2. Resistance to most disinfectants.
3. Stable in the environment.
4. Large human reservoir that have prolonged shedding.
5. Immunity is short.
6. Multiple routes of transmission.
7. Strain diversity and genetic plasticity (Estes, Prasad, & Atmar, 2006).

Surveillance of foodborne illness is difficult because many of the same pathogens transmitted through food are also transmitted through water and from person to person obscuring the role of foodborne transmission (Mead et al., 1999). In addition, classification of norovirus as a foodborne pathogen is also difficult because, unlike bacteria, viruses do not replicate in the food; incomplete processing may allow the viruses to reach the consuming public (Hardy, 1999).

Animal Reservoirs

Nonhuman primates may be susceptible to norovirus infections from various genogroups. Oral inoculation on nonhuman primates of several types was observed for symptoms and shedding (Rockx et al., 2005). Marmosets, cotton top tamarins, and cynomolgus macaques showed no clinical symptoms or antibody responses (Rockx et al., 2005). Only rhesus macaques shed the virus and developed specific IgM and IgG antibody responses (Rockx et al., 2005).

A report from Hungary documented young domesticated swine, between 4 days and 2 years of age, that were infected with both enteric sapovirus and norovirus (Reuter, Biro, & Szucs, 2007). The viruses were found in 17 piglets, of which only six had a history of diarrhea. The viruses were confirmed by reverse transcription polymerase chain reaction (RT-PCR) molecular detection and phylogenetic analysis (Reuter, Biro, & Szucs, 2007).

A similar finding in the United States came from 275 fecal samples analyzed from normal adult swine (10-24 weeks of age) on six farms and one slaughterhouse in Ohio, Michigan, and North Carolina. Laboratory analysis of the samples using RT-PCR found six positive DNA sequences for norovirus. One genotype was genetically and antigenically related to human norovirus (Wang et al., 2005).

Swine are not the only major food source animal capable of carrying norovirus. In a study of pigs and cattle, 120 swine fecal samples were taken from 10 Canadian farms over a seven-month period and 179 cattle fecal samples were taken from 45 different dairy farms over a 6 month period (Mattison et al., 2007). In addition, 156 retail meat and poultry samples were collected over the same periods. Of the pigs, 25% had detected norovirus RNA using RT-PCR looking for the GII.4 genetic cluster. In comparison, only 1.6% of the cattle were positive for norovirus RNA. Of the 156 retail samples, only one sample of pork tested positive for the virus. The source of the norovirus in the retail pork sample could not be confirmed (Mattison, 2007). This study suggested that norovirus has the potential to be passed from farm to the consumer's table.

Bovine norovirus was demonstrated in 9.3% of 645 fecal samples in South Korean cows together with a 5.9% mixture of other enteric pathogens, including bovine coronovirus, torovirus, rotavirus, calicivirus, and *E. coli* (Park, Jeong, et al., 2007). Bovine enteric calicivirus produced diarrhea in cows and could be found in two fecal samples from 41 cows of the similar genotypic RNA sequence (Ike, Roth, Bohm, Pfitzner, & Marschang, 2007) while 8.9% of 381 fecal samples were positive for calicivirus (Deng et al., 2003). In England, 11% of 398 bovine fecal samples tested detected norovirus (Milnes, Binns, Oliver, & Bridger, 2007). In the Netherlands, 31.6% of 243 veal calf farms and 4.2% of 312 dairy cattle fecal samples were found positive for norovirus strain that were genetically distinct from human strains of norovirus (van der Poel et al., 2003).

Other mammals are capable of becoming infected with norovirus. Murine norovirus appears to be common in mice, especially those used in many laboratory experiments. Sentinel mice in facilities accounted for three positive norovirus infections. One year later, over 2% of the entire mouse population had antibodies for murine norovirus (Perdue et al., 2007). A study on African lions reported an enteric calicivirus, similar to human norovirus GIV in a lion cub that died in 2006 of severe hemorrhagic enteritis (Martella, Campolo et al., 2007). Given the wide variety of animals, including those kept as pets or used for food, reported with norovirus, it appears that most are capable of harboring and becoming infected with some form of norovirus.

Genetic related animal-human similarity in norovirus found host reactions confirmed by serial passage of the virus through gnotobiotic pigs. In a case control study

in which 65 gnotobiotic piglets that were fed the virus and serially passed were compared to 14-controlled gnotobiotic piglets of similar age, 74% of the infected piglets developed mild diarrhea and 44% shed norovirus while no diarrhea appeared in any of the controls (Cheetham et al., 2006). Histopathological examination of the infected piglets showed mild lesion in one piglet, 59% developed antibodies, and 58% showed duodenal and jejunal enterocytes. Due to the genetic variability of the piglets, a variety of symptoms from diarrhea and shedding to asymptomatic appearance of well-being occurred. It is therefore possible that humans could be the recipients of norovirus from live pigs that have the virus.

Bovine enteric calicivirises morphologically are indistinguishable from human norovirus. Similar genetic varieties of norovirus have been isolated from mice (Widdowson, Monroe, & Glass, 2005), cows in Germany (Deng et al., 2003; Han, Wang, Smiley, Chang, & Saif, 2005) and swine (Wang et al., 2005). Similar genotypes found in both swine and humans posed the question of whether sub-clinically infected adult swine were reservoirs for new human strains or whether recombinants developed. While the potential is considered, antibody- and antigen- capture ELISAs did not show any common antigen relationship with five different genotypes of human norovirus (Han, Wang, Smiley, Chang, & Saif, 2005).

Humans and Host Risk Factors

Foodborne transmission played a significant role in infection. The most likely risk factors involved for gastroenteritis were a household member already infected with gastroenteritis and poor food hygiene (de Wit, Koopmans, & van Duynhoven, 2003).

Noninfectious feline calicivirus, a surrogate for norovirus, was transferred rather easily from contaminated hands to ham, lettuce, and metal disks and, while at lower rates, were then transferred from those products to other hands (Bidawid, Malik, Adegbunrin, Sattar, & Farber, 2004). This similar transference was also seen with Hepatitis A (Mbithi, Springthorpe, Boulet, & Sattar (1992).

Theoretical models have examined the risk of food contamination. The general assumption in these models is that if precautions were taken to avoid the transfer of microorganisms and viruses from raw food to final meal, the probability of foodborne illness was decreased (Todd, 2007a). The probability of ingesting foodborne pathogens was dependent not only on the person preparing the food but on storage of the food, consumption habits of consumers, and the relationship between those preparing and ingesting the food (Christensen et al., 2005). It can have a domino effect; a small number of careless workers about sanitation and hygiene in a food establishment can result in product becoming contaminated and resulting in a high probability of a food preparer receiving contaminated food leading to consumer illness.

The transfer of viral particles to other objects has also been demonstrated. A food handler in England was able to contaminate cold food over 8 days and infect 40 staff members, 70 guests, and 54 others after the illness had apparently ended. He was found to be shedding norovirus up to 48 hours after all symptoms ended (Reid, Caul, White, & Palmer, 1988). In another epidemiologic case, over 275 people were infected over a month's time from food that the chefs prepared. The chefs, while not ill, were all tested for and found to have high levels of antibody titer to the virus taken 12 days after the first

of two outbreaks. One of the chefs was thought to have a long post infection excretion period (Iversen, Gill, Bartlett, Cubitt, & McSwiggan, 1987).

Presymptomatic food handlers are believed to have the same risk as those openly ill for viral spread. A food handler in a hospital was ill the day before reporting to work and contaminated salads served to the patients (Lo et al., 1994). The ill food handler had a child at home who had been sick with gastroenteritis the previous two days. While the food handler showed no symptoms, it was postulated that the virus from the child contaminated the food handler's clothes and hands, resulting in the transmission to the salads in the hospital.

Transmission of norovirus continue to be spread from food or food handlers to others based on their prevalence in the community, the amount of shedding of infectious virus particles from asymptomatic individuals, and the high stability of the virus in the environment (Hutson, Atmar, & Estes, 2004). Contact with an ill person seems to be the most important route of direct community acquired sporadic infection. In Switzerland, a study found 39% of all patients had contact with other ill patients prior to the onset of their symptoms (Fretz, Svoboda, Schorr, Tanner, & Baumgartner, 2005). A substantial portion of the patients contracted the illness from members of their own family. Similarly, the risk of secondary illness was 5.5 times higher in households with sick schoolchildren or adults. The secondary illness rate was related to the age of susceptibility in that preschool illness rates were twice that of adult illness rates. The mode of secondary transmission also favored preschool aged children (Heun, Vogt, Hudson, Parren, & Gary, 1987). A hospital found surface swabs taken were positive for

norovirus from lockers, curtains, commodes, and the immediate surrounding environment to the infected patients (Green et al., 1998). Other risk factors identified included lower socioeconomic status and childcare center attendance (O'Ryan et al., 1998).

Resistance to norovirus has not been reproduced in laboratory experiments and the mechanisms are unclear. Immunity appears to be strain related and lasts only a few months. Patients can become ill again from another variant strain.

Geographical Distribution

Norovirus has been identified worldwide. Norovirus has also been reported in Spain (Sala et al., 2005), Chile (Vidal et al., 2005), Switzerland (Beuret, Baumgartner, & Schluep, 2003), Europe (Kirkwood, 2004), The Netherlands (van Duynhoven et al., 2005), Japan (Inouyeet al., 2000; Kageyama et al., 2004), Hungary (Krisztalovics, Reuter, Szucs, Csohan, & Borocz, 2006), and China (Lau et al., 2004). The majority of norovirus strains that appear in New Zealand are the same ones found around the world (Greening, Mirams, & Berke, 2001).

Diagnostic Methods and Treatment

Most diagnostic tests examine the nucleic acid sequence of the virus by RT-PCR, nucleotide hybridization process, and Enzyme Linked ImmunoSorbent Assays (ELISAs) that used baculovirus-expressed viral antigens (Reuter, Krisztalovics, Vennema, Koopmans, & Szucs, 2005). The predominance of genotype II in patients indicated that this genotype is the most pathogenic. Molecular testing of children in Australia identified 30 norovirus genotype II strains (Kirkwood & Bishop, 2001). Recent studies in Hungary showed variant forms and recently emerged groups of natural recombinant strains with

four capsid types (Reuter, 2005). Using these assays, norovirus was shown to have caused a majority of foodborne gastroenteritis outbreaks in Minnesota and approximately 96% of 90 outbreaks of nonbacterial gastroenteritis reported to the CDC during January 1996-June 1997.

Testing for the virus in patients is a combination of detecting serum antibodies and isolation from stools. The rise in titers is an indication of exposure to norovirus (Black, Greenberg, Kapikian, Brown, & Becker, 1982). The prevalence of antibody to norovirus was approximately 7% in Bangladeshi children less than6 months of age and rose to 80% in children aged 2 to 5.

Typical laboratory isolation and evaluation was from stool samples of infected patients. Laboratory analysis can include immune transmission electron microscopic examination, antigen ELISA, or RT-PCR (Bon et al., 2004; Dimitriadis & Marshall, 2005; Herrmann, Nowak, & Blacklow, 1985; Rabenau et al., 2003). Other studies have shown progress with agarose gel electrophoresis as a viral purification and concentration step (Rosenfield & Jaykus, 1999). Similar concentration steps are taken with immunomagnetic capture RT-PCR in other food outbreaks (Kobayashi, Natori, Takeda, & Sakae, 2004).

The diagnostic gap between identification of agent and illness can be closed if routine sampling is done on all patients, especially children, when presented for diarrhea and gastroenteritis (Simpson, Aliyu, Iturriza-Gomara, Desselberger, & Gray, 2003). Stool samples taken in hospitals and doctors' offices are the easiest way to confirm norovirus (Marshall, Salamone, Yuen, Catton, & Wright, 2001). Stool kits, if employed by sending

them directly to outbreak subjects, could improve the etiology confirmation (Jones, Bulens, et al., 2004). Trial tests found that two-thirds of outbreaks in which kits were employed, an etiologic agent was identified (Jones, 2004). Following illness periods of shedding and excretion in the absence of any clinical symptoms could be determined by nucleic acid amplification and sequencing. Those methods would identify carriers that are reservoirs that could serve to infect others (Marshall, Salamone, et al., 2001).

It is difficult to grow norovirus culturally (Duizer, Schwab, et al., 2004). Extracting viruses from food is more difficult. Food extracts contain a large amount of organic material, making purification difficult. Laboratory methods are taking advantage of RT-PCR amplification to make viral nucleic acid to analyze contaminated hamburger meat by concentrating the filtrated homogenates with some success (Leggitt & Jaykus, 2000). Chemical extract using TRIzol LS Reagent showed promise by extracting detectable norovirus from salami, leftover spareribs, and ham from outbreaks where stool samples were no longer available (Boxman et al., 2007). Using glycine-TRIS (pH 9.5) buffer containing 1% beef extract worked well in isolating norovirus from berries after the extract was treated with pectinase enzyme (Butot, Putallaz, & Sanchez, 2007). Similarly, a technique of removing tissue inhibitors by digestive gland proteases and then treatment by a cell disruptor allowed greater detection of norovirus in oysters (Schultz, Saadbye, Hoorfar, & Norrung, 2007).

Another preventative measure is regulatory sample testing of food products, especially those associated with norovirus. Although expensive and difficult to perform, laboratory methods are taking advantage of RT-PCR to analyze hamburger meat by

concentrating the filtrated homogenates and subjecting the residual to RT-PCR amplification with some success (Leggitt & Jaykus, 2000).

Human Resistance

It has been difficult to understand the mechanism of norovirus replication in humans without some form of cell culture line to develop antibodies or antiviral vaccines. There is no cure for noroviral gastroenteritis (CDC, 2006a). Treatment is to relieve the symptoms and help the body recover (CDC, 2006a). Fluids are useful to prevent dehydration (CDC, 2006a). Antispasmotics, analgesics, and antipyretics are helpful for other symptoms (Wheeler, 2004). Human developed serum antibodies have been seen for quite some time. In a longitudinal study in Bangladesh, seven percent of children younger than 6 months old had antibodies to norovirus. This increased in the population to 80% in children two to five years of age (Black, Greenberg, Kapikian, Brown, & Becker, 1982). Thirty percent of Norwegian military recruits were found to have antibodies to norovirus out of 1,017 tested, with 10.6% testing positive for IgA and 15.4% testing positive for IgM (Myrmel, Rimstad, Estes, Skjerve, & Wasteson, 1996). Over 1,864 blood samples collected in Santiago and Punta Arenas, Chile found sero-prevalence rates of 83% and 67%, respectively (O'Ryan, Vial et al., 1998). The first detection of sero-prevalence in breast milk was reported in Japan from 31 samples. IgG was found in 13% of all samples against norovirus (Makita et al., 2007).

Human histo-blood group antigens (HBGA) have been identified in the past as the receptor sites for viral infection. Such an assumption has been placed on research that showed that type O blood had a far higher risk of infection (OR 11.8, 95% CI 1.3-103)

than type A (OR 0.63, 95% CI 0.14-2.7) or type B (OR 0.027, 95% CI 0.038-1.9). Combinations of blood type genotypes had even less risk (Hutson, Atmar, Graham, & Estes, 2002). Similarly, type A–like HBGA monoclonal antibodies (MAbs) present in oysters, but not type B or H- like HBGA MAbs, were able to bind to human gastrointestinal cells and allowed binding norovirus (Tian, Bates, Jensen, & Mandrell, 2006). Clams and mussels were also found to bind both type A- or type O-like HBGA Mabs with human saliva and could be the means by which bioaccumulation occurs in these bivalves (Tian, Engelbrektson, Jiang, Zhong, & Mandrell, 2007).

A similar process was completed using gnotobiotic pigs for the source of HBGA monoclonal antibodies. Using Type GII4 as the antigen, 18 of 31 piglets showed norovirus infection of the duodenum and jejunal erythrocytes and some cells in the ileum (Cheetham et al., 2006). Additional work revealed that both Type A- and Type H-like HBGA MAbs from gnotobiotic pigs were able to bind in the duodenum and buccal tissues with norovirus GI and GII norovirus but type GII.1 and GII.3 antigens barely bound to the duodenum. These type A- and H-like piglets were more likely to shed virus than other piglets (Cheetham et al., 2007). Immunodeficient mice were found to bind norovirus not only in the duodenum but the liver, lung, peritoneal and pleural cavities (Ward et al., 2006). Another complication for immunocompromised and other patients is that several calicivirus capsids are cross-reactive, suggesting species-specific sites for antibody reactions requiring multiple types of antibodies (Shiota et al., 2007).

HBGAs have been developed for the three main histo-blood groups and eight strain-specific receptor-binding patterns have been described for two major binding sites.

Each of these sites interacted with a carbohydrate side chain of the HBGAs, which can be blocked using human breast milk (Tan & Jiang, 2007). Gut expressed carbohydrates were commonly found to bind norovirus and infection and asymptomatic expression may be related to a person's genetic composition (Hutson, Atar & Estes, 2004). Nonsecretors of viruses and Lewis (FUT3) genotypes had a lower infection rate to type GII than others (Larsson et al., 2006). A homozygous mutation in the human secretor gene (FUT2) for 53 symptomatic and 62 asymptomatic people associated with norovirus outbreaks provided complete resistance for the disease (Thorven et al, 2005).

The development of vaccines to norovirus has been discussed for some time also (Estes et al., 2000). The challenges to vaccine development include: correlation of immune protections that are not completely defined, multiple human forms of the viruses exist, there is limited cross-challenge data concerning other strains of the viruses, the fact that the virus itself had not been cultured and no animal model existed. The development of the vaccine must mimic the protein that makes up the norovirus capsid, which has only 58 kD molecular mass. Resistance to norovirus correlated with the lack of expression of H-type 1 oligosaccharide ligands required for viral binding (Atreya, 2004), but the only measure of actual exposure to norovirus is increased blood titers of serum antibody. Because the viruses recognize human histo-blood group antigens (HBGAs) as receptors, recent research was able to retain the receptor-binding function of the protruding (P) domain of noroviral capsid and form subviral particles in vitro. (Tan, Fang, et al., 2008). Structure reconstruction of the P particle using cryo-EM showed that the P particles were comprised of 12 P dimers that were organized in octahedral symmetry, similar to that in

the norovirus capsid. The P particles are immunogenic and reveal similar antigenic and HBGA-binding profiles with their parental virus-like particle. The P particles are easily produced in *E. coli* and yeast and are stable, which are potentially useful for a broad application including vaccine development against noroviruses. Transgenic plants could provide suitable substitutes in that research has found transgenic potatoes or leaves of Nicotiana benthamiana capable of expressing norovirus capsid protein and showed reduced protection and reduction in intestinal secretion (Tacket, 2005, Santi et al., 2008). Further research must be done to understand the complete cycle of infection, replication, and transmission.

Transmission

The primary transmission mode was considered to be through food. Of the 348 outbreaks of norovirus reported to CDC (January 1996-November 2000) from gastroenteritis, food was implicated in 39%, person to person contact, 12%; water, 3%; and unknown, 18%. Forty-one percent of 295 foodborne outbreaks reported in Minnesota in restaurants during 1981-1998 met the epidemiologic criteria for norovirus gastroenteritis. Norovirus was detected in 70% of 23 foodborne outbreaks investigated during 1996-1998. The risk for food contamination through food handler increased when the food item was consumed without further cooking.

Norovirus has been shown to be transferred via the fingers to water taps, door handles, and telephone receiver surfaces (Barker, Vipond, & Bloomfield, 2004). A contaminated set of fingers could spread norovirus to as many as seven clean surfaces.

Prevention and Control

Improper personal hygiene is considered the third most commonly reported contribution to gastroenteritis (Bean & Griffin, 1990). Clinicians working with potential norovirus infections must be careful not to catch or spread the virus to other patients. Because clinicians and health care workers are exposed to contagious patients, they must minimize actual direct person-to-person contact with contaminated secretions or objects and prevent inhalation of aerosolized secretions through gloves, masks, protective clothing and changing all outer garments prior to attending the next patient (Thornton, Jennings-Conklin, & McCormick, 2004). Patients suspected of norovirus infection or those with undiagnosed acute gastroenteritis were recommended to be placed in contact isolation. All care workers should, as a matter of routine, wash their hands with soapy hot water before and after contact with infected persons and contaminated objects.

Laboratory research into microbiocides is underway as a method to decontaminate the hands of food workers. The evaluation of virucidal activity of microbiocides as decontaminants of medical equipment, contact, and environmental surfaces could prove useful not only in food production facilities but reduce nosocomial infections (Sattar, 2004).

A surveillance system entitled CaliciNet maintains records of all reports of caliciviruses and is operated by CDC with the cooperation of federal, state, local, provincial, and national laboratories that perform routine RT-PCR for norovirus. The network of participants plan on integrating their information into a database called the Infectious Diseases Molecular Epidemiology Database System (IDMEDS), which

contains 2,400 unique sequence entries from multiple pathogens including 575 unique sequences from norovirus GII (Monroe, Ando, & Glass, 2000). The design of IDMEDS is to keep all pathogens independent and provide web interface linking all relational databases of pathogens for sequence, specimen, and epidemiologic information. The advantage of the database system would be to provide users with real-time molecular epidemiology.

Surveillance of activities might help detect outbreaks and ensure proper public health interventions. Screening for GI infection clusters from arrivals to a mass gathering recreational camp included isolating them for 48 hours in discrete facilities that resulted in controlled outbreaks (Coletta et al., 2006). Syndromic surveillance and mass monitoring in New York City for waterborne illness improved detection of substantial city-wide increases in viral illnesses, but not above levels of traditional surveillance (Heffernan et al., 2004). Similar surveillance systems for acute infectious gastroenteritis outbreaks were implemented in North Carolina (Sickbert-Bennett et al., 2005). Other reports indicate syndromic surveillance improves real-time recording and data analysis and can potentially detect high-risk large-scale events (Doroshenko et al., 2005).

Product and process control was essential. Unlike bacterial contamination, viral contamination is not associated with product spoilage or flavor and odor changes (Richards, 2001). The identification of critical control points in a risk hazard analysis once the owners and operators acknowledge that viral contamination is possible and likely to occur is essential to any safe operation. An individualized Hazard Analysis – Critical Control Point (HACCP) program must be developed and implemented for every

establishment that monitors cooking times and temperatures that are set at lethal levels for viruses and maintained, and records of employee illness must be part of the epidemiologic information used to create and validate the HAACP plan.

Food hygiene training is essential to ensuring that food handlers and workers are aware of the risks if they implement appropriate good hygiene practices (Coleman & Roberts, 2005). Adherence to personal plant hygiene, as detailed in sanitation standard operating procedure manuals and the Food and Drug Administration's Food Code, are a reflection of that training and attitudes (Lillquist, McCabe, & Church, 2005). Washing stations and facilities could use foot-operated pedals to avoid hand contact with surfaces recently touched by other workers (Richards, 2001). The behavior of workers in following personal hygiene practices can be influenced by how often stressful situations lead to disregarding required sanitation practices. This working attitude directly affects sanitation implementation and follow-through resulting in whether food products are highly contaminated or not (Marsh, 2005).

Another way to prevent foodborne illness is to inactivate the virus at the food source. Utilization of nonhuman infectious calicivirus has had some success as an indicator organism for norovirus. Heat was useful for inactivation of viruses in shellfish meat at 85-90 ^{o}C for 1 minute (Slomka & Appleton, 1998). UV-B radiation was ineffective at 34 mJ/cm^2, inactivation by 70% ethanol incompletely reduced activity by only 3 D ($\log_{10}$ reduction) after 30 minutes, and sodium hypochlorite solution were effective only over 300 ppm (Duizer, Bijkerk, et al., 2004). Disinfection would be counterproductive if the viruses enter the tissues of fruits and vegetable through cuts and

abrasions in the substrate surface (Richards, 2001). Norovirus was profoundly more resistant to inactivation at low (< 3) and high (> 7) pHs. Reduced temperatures up to 50 ^{o}C at high hydrostatic pressure (200 and 250 Mpa) were effective for inactivation at 4 and 2 minutes, respectively (Chen, Hoover, & Kingsley, 2005).

Disinfectants are difficult to judge when treating contaminated areas. Studies showed that a combination of two-step approach was effective. A combination of detergent-based cleaning followed by a hypochlorite/detergent formulation at 5000 ppm reduced norovirus presence significantly (Barker, Vipond, & Bloomfield, 2004). Other recommended disinfection classes include accelerated hydrogen peroxide, chlorine dioxide and QUAT, hypochlorite, parachormetaxylenol, peroxymonsulfate, or phenol compounds (Wheeler, 2004). Steam cleaning surfaces would raise the surface temperature above viral lethality. Fogging with hypochlorous acid solution, effectively decontaminating large spaces would be good for areas that are difficult to reach or for livestock pens and barns or large areas such as food processing plants (Park, Boston, Kase, Sampson, & Sobsey, 2007).

The most likely concern for hygiene is the place where food is consumed. Adults in private homes need to practice consistent and obvious hygiene and teach these principles to their children based on age, gender, and level of comprehension. This is based on the risk that the hygiene practices of persons preparing the food, consumption patterns of the consumers, and the relationship between people preparing and ingestion of foods are interrelated and contribute to the risk of ingesting a risk meal (Christensen et al., 2005).

Cleaning up after an episode of gastroenteritis is also essential. Vomitus should be cleaned up using protective gloves and a facemask as soon as possible (Wheeler, 2004). Protective clothing would be ideal for this job or clothing that can be washed immediately afterward is a good substitute. All contacted surfaces should be disinfected; bedding, towels, dishes, and washable items need to go through a hot wash cycle. All living quarters and common areas should be cleaned effectively and all waste materials disposed of in contained units such as closed plastic bags. Floors and soiled counter surfaces should receive a 5-10 minute application of disinfectants and allowed to air dry. Especially important are items that are touched by others including television remote controls, keyboards, and other electronic surfaces that might be shared.

Combining temperature and pressure, as used in food processing operations, increased the effective reduction of infection to 4.0 log units when norovirus was exposed to a pressure of 200 Mega Pascal (MPa) pressure at 50^{o}C. The same treatment at 20^{o}C only provided a 0.3 log unit reduction (Chen, Hoover, & Kingsley, 2005).

Knowing the source can contribute to the ability to control and reduce the risk of illnesses. Enteric viruses like norovirus can contaminate food at any time pre- or post-harvest. Produce can be contaminated from improper irrigation and fertilizing, from the field workers or processors, and from water used (Richards, 2001). Interventions such as cooking, irradiation, and improved handling techniques such as robotics could reduce all levels of enteric viruses.

Inactivation

In order to devise inactivation schemes, it was necessary to determine how long norovirus survives in food and on surfaces. Mattison et al. (2007) deposited feline calicivirus on lettuce, strawberries, ham, and stainless steel surfaces for 7 days at room or refrigerated temperatures. It was found that the calicivirus was still detectable on lettuce, ham, and stainless steel until day 7. Ham provided the most protection from inactivation of the virus.

Hospitals, cruise ships, and hotels are not able to sterilize fomites and surfaces the same way as food producers. Use of ozone gas at 25-ppm force sprayed onto surfaces in high humidity was effective to a 3 $\log_{10}$ reduction on plastic, steel and glass surfaces and fabric surfaces such as carpeting, curtains, and cotton materials (Hudson, Sharma, & Petric, 2007). While reduction is effective, it does not eliminate all infectivity. In addition, ozone gas is toxic to the user.

Food systems can use ozone in controlled circumstances, but for large operations it is impractical. Food products are commonly put under high pressure processing for pasteurization and when murine norovirus was exposed to a 5-minute, 400-MPa treatment at 5^{o}C, the infectivity levels were reduced by a level of 4.05 $\log_{10}$ plaque forming units (PFU) (Kingsley, Holliman, Calci, Chen, & Flick, 2007).

Most shellfish prepared within the shell make inactivation difficult. Heat inactivation studies found 30 seconds in a boiling water bath ineffective to inactivate feline calicivirus while different batches of live cockle were reduced to nondetectable levels after 1 to 2 minutes (Slomka & Appleton, 1998). Similar laboratory work found a 3

$\log_{10}$ reduction in activation of feline calicivirus above 56^{o}C, at UV-B radiation, and sodium hyperchlorite >300 ppm, all measured by reverse transcription-PCR (Duizer, Bijkerk, et al., 2004). Seventy percent ethanol was only effective to a 3 $\log_{10}$ reduction after 30 minutes. Exposure to extreme acid (3) or base (>7) demonstrated poor inactivation. Ineffective levels of treatment should be a concern for decontaminating surfaces, fomites, and water.

Chlorine use is commonly applied in cruise ships to inactivate norovirus but the levels of chlorine to be used are in dispute. Using feline calicivirus as a norovirus surrogate, norovirus was found sensitive to free chlorine (10 ug/ml) in a sodium hypochlorite solution but effectiveness was dependent on the volume (Urakami et al., 2007). U.S. regulatory levels for recreational water are 4 ug/ml and the outbreak in Vermont at a swimming pool recorded the chlorine level at 3.5 ug/ml (Podewils et al., 2006). Drinking water is restricted to 1 ug/ml and using a level of free chlorine at 300 ng/ml free chlorine was able to reduce the calicivirus by more than 4.6 $\log_{10}$ after a five minute treatment met the legal requirements, although the virus was still detectable.

Reduction in infectivity

In most cases, improvement in hand hygiene is emphasized as a means of reducing infection. Yet compliance remains difficult to maintain. Overall compliance in hand washing in one hospital in England was less than 50% (Patarakul, Tan-Khum, Kanha, Padungpean, & Jaichaiyapum, 2005). A direct result was high incidences of nosocomial outbreaks at that site. Reasons given by nurses in hospitals included overriding patient need (51.2%), forgetfulness (35.7%), and skin irritation (15.5%).

Hospitals implementing an infection control program, focused education, and frequent performance feedback found a sustained improvement in compliance (Rosenthal, Guzman, Pezzotto, & Crnich, 2003; Rosenthal, Guzman, & Safdar, 2005).

Attempts to identify risks contributing to nosocomial gastroenteritis outbreaks found outbreak rates related to the level of the care unit. The hazard ratio increased when additional beds were added to a unit (HR 1.22 (per 10 additional beds) 95% CI, 1.1-2.6). In addition, the age of the patients was significant with geriatric patients demonstrating the most hazardous (HR 2.6, 95% CI, 1.6-4.3). Overall, general medical care units where patients of all diseases and ailments are housed were high (HR 1.7, 95% CI 1.1-2.6). The length of stay was inversely proportional to outbreak incidence (HR 0.89 per additional week of stay), but those with high throughput increased rates of gastroenteritis (Lopman et al., 2005).

Household transmission from the ill to others was significant. In an outbreak of norovirus gastroenteritis in an elementary school in Vermont in 1984, secondary household transmission from the ill student to others in the house was 5.5 times more likely than it was for well school children. As the number of household members increased, so did the incidence of illness, with pre-school children the most affected (Heun, Vogt, Hudson, Parren, & Gary, 1987). Similar finds were reported crediting contact with a household member with gastroenteritis (population attributable risk fraction [PAR] = 17%), and crediting contact with someone with norovirus gastroenteritis outside the house (PAR=56%) and poor food handling hygiene (PAR=47%) (de Wit, Koopsmans, & van Duynhoven, 2003).

Evidence from a Swiss study held between 2001 and 2003, found no significant associations between consumption of food or bottled mineral water and risk of illness, histo-blood group, household size, or incidence of norovirus gastroenteritis. The authors believed that person-to-person contact was the most important route and contact with ill family members produced a substantial number of mini-outbreaks (Fretz, Svoboda, Schorr, Tanner, & Baumgartner, 2005).

Epidemiology of Norovirus Outbreaks

The numbers of cases of norovirus are probably underestimated because it is a recently discovered agent and methodology was not available to detect it. The number of cases also appears to be increasing. Food handlers were believed to be the source of norovirus infections transmitted through foods. The most common locations for mass gatherings were restaurants and hotels where contamination of food occur and spread among guests.

Foodborne Outbreaks

The virus was first recognized as the cause of an outbreak of gastroenteritis in Norwalk, Ohio in 1968 (Adler & Zickl, 1969). Subsequent outbreaks included one in 1994 on the campus of a Massachusetts university associated with salad consumption affecting 19 students and staff (Kilgore et al., 1996). In another outbreak, a hotel food handler who was shedding viruses after an episode of gastroenteritis infected 40 staff members, 70 residential guests, and 54 persons attending functions in the hotel (Reid, 1988). During this outbreak, staff workers in the kitchen vomited, splattering food preparation surfaces, and stored food with virus particles.

Of the 274 food service-associated outbreaks calculated from all recorded outbreaks between the 1920s and 2006 by the Committee on Control of Foodborne Illnesses of the International Association for Food Protection, 130 of these outbreaks were a result of food contamination by an asymptomatic food worker (Todd, Greig, Bartleson, & Michaels, 2007a). There were an estimated 97 catered, affected events mainly caused by norovirus in 2000. Foods involving the largest numbers of over 1,000 cases were from contaminated frosting and cake and one incident of multiple foods at a single meal.

The number of norovirus cases from the above stated review that required hospitalization of food workers was small, only 113 of 2,740 cases in India (Todd, Greig, Bartleson, & Michaels, 2007b). The largest of these were from salad sandwiches. Of 348 recorded norovirus outbreaks reported to CDC between January 1996 and November 2000, 39% occurred in restaurants, 29% in nursing homes and hospitals, 12% in schools and day care centers, 10% in vacation settings (including cruise ships) and 9% in other settings. Based on these figures, cause of transmission was 57% foodborne, 16% due to person-to-person contact, and 3% waterborne. The remaining cases had no identifiable cause of transmission. An increase in the rate of norovirus outbreaks was also recorded between 1998 (46 outbreaks), 1999 (97), and 2000 (164) (CDC, 2003). Norovirus outbreaks affect almost 50% more people than bacterial-caused gastroenteritis outbreaks (Widdowson, Monroe, & Glass, 2005).

Individual reports gave greater details. In the summer of 1982, 129 of 248 persons interviewed suffered from cases of gastroenteritis in Minnesota (Kuritsky et al., 1984). A

food consumption survey indicated that cake and frosting purchased from a single bakery was the vehicle of transmission. Further investigation found an employee who had a case of vomiting and diarrhea three days prior to the day the cakes were made. It was the employee's custom to reach into the mixing bowl up to his elbows while 76 liters of frosting were being prepared in order to break up clumps of sugar and to scrape the sides. The lack of personal hygiene and fecal contamination was considered the source of the virus. Ultimately, 3,000 cases were associated with this outbreak.

An outbreak of norovirus occurred at a local college campus in Florida in 1980. A survey of 275 cases from students and staff concluded tossed salad served at the cafeteria was the common element in most cases and fecally contaminated lettuce was found (Lieb et al., 1985). The source of the contamination was never identified.

A dinner for 280 persons in a hotel in New York in 1985 resulted in several guests becoming ill with gastroenteritis (Iverson, Gill, Bartlett, Cubitt, & McSwiggan, 1987). A second dinner for 144 persons, one month later, resulted in more persons becoming ill with the same symptoms. Laboratory results isolated norovirus from stool samples. Melon was the suspected vehicle of transmission in the first outbreak and vermicelli in the second outbreak. Serological evidence pointed to one chef who was suspected as a long post-infection excretion period following an episode of gastroenteritis.

Two separate outbreaks in Erie County, New York, were attributed to norovirus. One outbreak affected approximately 350 persons in 13 tour groups that ate at a restaurant over a seven day period in June 1986 (Fleissner, Herrmann, Booth, Blacklow,

& Nowak, 1989). The other outbreak affected 87 persons who attended a catered party in a private home, also in June 1986. Two of the guests, who were relatives of the host, also ate at the same restaurant. The authors could not identify the vehicle of transmission although a food handler at the restaurant who was also a waiter was the first to become ill. This person was singled out as a potential source since he had access to both food and water. On the other hand, contaminated water from a well served in the restaurant could have been cross contaminated with a sewage system. Other public health violations were noted.

An outbreak of gastroenteritis in 1993 was traced to sandwiches eaten at a local sandwich bar (Morgan, Black, Charlett, & John, 1994). Thirty five people were ill from the bar and an investigation showed that the bar owner was ill the day previous to serving food. The owner denied preparing any food and no other food workers were sick.

A single food handler was considered the source of a norovirus gastroenteritis outbreak at a manufacturing company in Ohio in 1997. The worker reported that he had recovered from illness four days prior to the outbreak but was asymptomatic the day the sandwiches were prepared (Parashar et al., 1998). The supplier indicated no other facility who received food had reported any illnesses. Additional investigation found two sisters who worked at the facility were also shedding viruses but did not report ill.

One hundred twenty-five students at a Texas university became ill with gastroenteritis in 1998 and stool samples from nine of 18 students tested positive for norovirus (Daniels et al., 2000). Samples of deli meat was also sampled and found to be positive for norovirus. A food handler who made sandwiches containing the deli meat

reported that her child was ill with diarrhea just prior to the outbreak. Fecal samples from the infant also tested positive for the same strains of norovirus as found in the deli meat and the ill students.

Long distance hikers on the Appalachian Trail became ill with norovirus in spring 1999. Forty-five of 70 hikers became ill after eating at a general store along the trail (Peipins et al., 2002). While norovirus was isolated from stool samples of the hikers, no virus was detected in water samples. Further evidence indicated that some hikers became ill prior to reaching the store so person-to-person contact was most likely the cause. The authors believe poor sanitation, scarce water, and crowding could increase risk of becoming ill.

In Toledo, Ohio, during December 1999, 93 persons reported ill from a banquet made by a local caterer (Kassa, 2001). No primary source of the virus was identified but the author felt that a caterer with a long history of food safety and sanitation violations in the past was more likely to be the cause of foodborne outbreaks than other facilities.

Another common caterer was deigned to be the source of an outbreak of norovirus at a chain of car dealerships nationwide in 2000 (Anderson et al., 2001). Four salads prepared for the 52 nationwide banquets involving 27 states was significantly associated with illness (RR = 3.8, 95% CI 2.5-5.6). A total of 333 persons met the case definitions out of 753 surveyed. Forty-five persons also reported gastroenteritis among family members following the outbreak. Two of 15 food handlers had elevated titers of antibody for norovirus and the authors concluded that one of these two persons had recently been sick even though all workers denied any illness. They suggest that evidence indicates an

ill food handler who had prepared the salads was the source. No virus was detected in any of the salad samples.

A restaurant in Australia that served Mediterranean-style food was considered the source of illness causing three different outbreaks affecting 92 persons (Marshall et al., 2001). Affected food was eaten from a common platter and typically eaten with fingers. Norovirus was found in most of the stool samples taken and it was inferred that the same agent kept re-infecting new cohorts of people. Each outbreak however, was associated with its own strain of norovirus.

A bakery that created seven different types of cakes for 46 different weddings was considered the transmission vehicle for norovirus that directly affected 332 wedding guests and indirectly affected up to 2700 people in 2002. Illness association with the bakery was high (adjusted RR 4.5, $P<0.001$) (Friedman et al., 2005). Two of the bakery workers who directly contributed to making the cakes were ill with gastroenteritis the week prior to the outbreak. The common element was the frosting.

In 2001, an outbreak of norovirus gastroenteritis occurred in Sweden (Le Guyader et al., 2004). An epidemiologic investigation focused on specialty cakes made with frozen raspberries. While multiple strains were found, one strain was predominant. However, investigators did not find that predominant strain in these particular raspberries and hypothesized that another source of norovirus may have been the cause of illness.

A hospital cook was considered the index case of an outbreak of norovirus gastroenteritis that affected 40 hospital workers and relatives in Spain during May 2002. The cook had been ill prior to making sandwiches but decided not to go home. The

cook's husband also became sick the next day. An investigation learned that the cook's son-in-law was ill the day prior to the outbreak. Transmission of the virus was attributed to lapses in personal hygiene (Sala et al., 2005).

In Sweden, again in the summer of 2006, four separate outbreaks of norovirus gastroenteritis affecting 43 people were attributed to raspberries eaten at family gatherings at a school and at a business meeting (Hjertqvist et al., 2006). No attribution to the source of norovirus was provided in the report.

Three norovirus cases and a cluster of community cases occurred in Kent County, Michigan in May of 2005 as a result of sandwiches all prepared by the same restaurant. One food handler reported he was ill the day before with vomiting and diarrhea but returned to work later that day. The worker was exposed to a child relative who had been exposed to norovirus at a day care center. All stool samples from the ill customers and the food worker matched the strain of norovirus identified in the outbreaks (CDC, 2006).

Salad was once again considered the vehicle of transmission in an outbreak in Austria in 2006 (Schmid et al., 2007). An attack rate of 182 persons out of 325 during a four day period was attributed to norovirus. The salad prepared on the third day had the highest adjusted relative risk (RR = 2.82; 95% CI 1.0-7.94). The preparation of the salad was assigned to one employee who later reported she was ill with gastroenteritis that day but continued working for fear of losing her job.

A recent outbreak amongst river rafters down the Colorado River was a result of eating sandwiches prepared by a single food service vendor (Malek et al., 2007). One hundred thirty-seven rafters in 13 of 90 rafting trips became ill with gastroenteritis. A

total of 96% of the rafters ate delicatessen meat that was prepared by one company on contract to the rafting company. All meat was prepared from one processing plant, sliced, vacuum-packed, and frozen up to one month before consumption. A single food handler was determined to be the source when he reported for work and sliced the meat one day after experiencing gastroenteritis. All norovirus strains were found to be identical.

Many other individual reports of foodborne gastroenteritis can be found. Three groups of guests and hotel employees were affected by norovirus gastroenteritis in Virginia (Love, Jiang, Barrett, Fracas, & Kelly, 2002), 220 guests at eight banquets held at a single hotel restaurant became ill from norovirus gastroenteritis (White et al., 1986), as well as diners at a tourist restaurant in Japan (Hirakata, Arisawa, Nishio, & Nakagomi, 2005). Several people became ill for three days with gastroenteritis, following the illness of one woman who vomited in the dining hall but had no symptoms up to that point (Marks et al., 2000). Water supplies were credited with the infection of 448 people at a resort hotel in the Caribbean in 1998 (Brown et al., 2001).

In the United States, between 1991 and 2000, there were over 8,271 foodborne outbreaks (Widdowson, Monroe, & Glass, 2005). Of that number, 1% was norovirus-confirmed from samples collected in 1991. By 2000, the proportion of norovirus-confirmed samples increased to 12%. Minnesota and Ohio reported over 20 outbreaks between 1998 and 2000. Nine states reported between 11 and 20 outbreaks including California, Oregon, Wisconsin, Michigan, Georgia, and Florida. The reason for limitations on making generalizations about the overall number of outbreaks and cases was due to the lack of participation by a number of states.

From 2000 to 2004, there were 270 reported outbreaks of acute gastroenteritis in the U.S. (Blanton et al., 2006). Of the 184 samples collected that tested positive for virus, 79% were norovirus genotype GII strains, and 19% were norovirus genotype GI strains. In the reporting period of October 2005 through December 2006, 1,316 outbreaks of acute gastroenteritis were recorded by 24 states in the U.S. (CDC, 2007b). Of these states, 22 states reported an increase in 2006 in the number of gastroenteritis outbreaks over 2005. A median of 50% of these events occurred in long-term care facilities. Only 26% of the cases were confirmed norovirus. These states without laboratory capability for detecting norovirus had epidemiologic and clinical evidence suggesting norovirus.

Epidemiologic patterns of outbreaks began as early as 1986. Between March 1982 and September 1983, 1360 stool samples were analyzed for norovirus identifying mild diarrhea and vomiting as consistent symptoms (Storr, Rice, Phillips, Price, & Walk-Smith, 1986). In England and Wales between 1992 and 2000, the Public Health Laboratory Service Communicable Disease Surveillance Center found that 79% of 1,877 outbreaks occurred in health care institutions, especially during the winter months. That data suggested a combination of host, virulence, and environmental factors lead to the illnesses (Lopman, Adak, Reacher, & Brown, 2003).

In Europe, norovirus was responsible for 85% of 3,714 cases reported between 1995 and 2000. Food and waterborne outbreaks accounted for 81 of 881 outbreaks (Lopman, Reacher. et al., 2003). The Netherlands found norovirus as the causative agent in 735 (78.1%) of gastroenteritis outbreaks, 54.9% located in residential institutions (Svraka et al., 2007). This incident indicated an increase of three epidemic seasons with

increased infection to GII.4, followed by a period of increased immunity and a decrease in illness numbers (Siebenga, Vennema, Duizer, & Koopmans, 2007). Seventy three outbreaks occurred in Switzerland between 2001 and 2003 and norovirus was identified in 74% of all these cases. Person-to-person contact was credited as 81% of the causes and 13% were related to the food (Fretz, Svoboda, Luthi, Tanner, & Baumgartner, 2005). Hungary had a bad year when 223 norovirus outbreaks in 2006 occurred due to type GII.4 2006b, most of which were credited to drinking water related diseases affecting over 3,000 people (Krisztalovics, Reuter, Szucs, Csohan, & Borocz, 2006). Europe saw an increase in outbreaks in November 2006 due to the same norovirus GII.4 2006b up to 22% of 108 outbreaks (Kroneman et al., 2006).

Between 1994 and 1999, 214 outbreaks in Japan were attributed to norovirus. Over 60% of these were attributed to contaminated food. Raw oysters were the primary source of small outbreaks in school lunches, catered meals, and in banquet halls and hospitals (Inouye et al., 2000). Sixty outbreaks of norovirus gastroenteritis were recorded in Okayama Prefecture, Japan between 1997 and 2004, mainly in the winter months. Transmission routes credited by the authors included shellfish (19%), foods other than shellfish (0%), food handlers (15%), person-to-person contact (24%), and other non-assigned sources (41%) (Hamano, Kuzuya, Fujii, Ogura, & Yamada, 2005).

Based on data from 1996 to 2000, English researchers estimate 61,584 cases of norovirus annually of which only 9,775 victims will see a doctor (Adak, Meakins, Yip, Lopman, & O'Brien, 2005). Australia estimates the number of incidences of gastroenteritis to be 17.2 million cases per year of which 32% are foodborne, meaning 1

in almost every 3 persons has gastroenteritis (Hall et al., 2005). Norovirus accounted for a median of 1.8 million cases and of that, 25% were foodborne. The most common cluster was in the city of Victoria, Melbourne (Hall et al., 2005). The majority of norovirus strains that appear in New Zealand are the same ones found around the world (Greening, Mirams, & Berke, 2001). Seeding effecting can be seen by most countries once the norovirus is introduced through several unrelated outbreaks and secondary infections (Koopmans & Duizer, 2004).

Oysters

Of food types noted, seafood is the most common source of norovirus. Common foods most likely at risk are ready-to-eat products requiring no further heating including salads, peeled fruits, deli sandwiches, finger foods, hors d'oeuvres, dips, and communal foods (Wheeler, 2004). Oysters are considered a special source of foodborne illness that is contaminated with norovirus worldwide. Many introduced to the United States are carried from China (Kingsley, Meade, & Richards, 2002) as seen in a study of imported oysters from 11 countries over a 3 year period in China (Cheng, Wong, Chung, & Lim, 2005) when 53 of 507 samples were positive for norovirus. The relative risk determined of contracting norovirus gastroenteritis was calculated to be 17 (95% CI, 5-51) and 35 (95% CI, 5-243) in two different Australian jurisdictions that experienced 83 cases of illness in the months between November 2003 and January 2004 from a single case of oysters imported from Japan (Webby et al., 2007).

Similarly, oysters imported by the United States from China, originally labeled as cooked but found to be raw, resulted in 5 cases of norovirus gastroenteritis in New York

in 2000 (Kingsley, Meade, & Richards, 2002). As early as 1982, northeastern United States coastal waters were implicated in 103 outbreaks involving 1,017 people from shellfish (clams and oysters) associated gastroenteritis ((Morse et al., 1986). Twenty persons came down with Noroviral gastroenteritis in Florida following the consumption of raw oysters in 1993 (CDC, 1994). Marinating mussels in acidic conditions over a four week period but after simulated commercial sterilization had no effect on detecting norovirus in New Zealand (Hewitt & Greening, 2004). An international outbreak beginning in 2002 was the result of oyster consumption affecting 327 people in Italy and southern France where contamination of the French oyster beds was a result of heavy rainfall allowing the virus to concentrate more viruses in the oysters (Le Guyader et al., 2006). Finally, cooking oysters properly may have the effect of reducing illness however, inadequate monitoring and preparation of oysters served in a Scottish hotel resulted in 15 of 35 guests becoming ill in 1993 (Chalmers & McMillan, 1995).

The similarity of norovirus serotypes from oysters to other species was investigated by sampling oysters from 45 bays along the U.S. coast between summer 2002 and winter 2003. Of the samples, nine were positive for human norovirus GII, seven for porcine norovirus, and two for bovine norovirus. Five of the human samples were similar to cases of diarrhea outbreaks (Constantini, Loisy, Joens, Le Guyader & Saif, 2006). Active surveillance in British Columbia, Canada, identified 26 confirmed and 53 clinical cases from oyster consumption where norovirus GI.2 was present in 50% of the stool specimens and had a direct sequent match between an oyster sample and a human specimen. The purchased oysters came from 18 suppliers and 45 different stores or

merchants. This also demonstrated that the range for finding norovirus in oysters was not a point source but widely distributed and no one harvested area was any more contaminated than any others were (David et al., 2007).

In spite of such evidence, the European Union standards for shellfish (EU Council Directive 91/492/EC) only call for testing for fecal coliforms, *E. coli*, and Salmonellae. Mussels that otherwise meet these standards and deemed safe for consumption have been shown to be contaminated with Hepatitis A virus, enteroviruses and norovirus (Koopmans, von Bonsdorff, Vinje, de Medici, & Monroe, 2002).

The United States northeastern coastal waters were implicated in oyster-associated gastroenteritis (Morse et al., 1986). Outbreaks have been noted following consumption of raw or lightly cooked bivalve shellfish (Hewitt & Greening, 2004), and oysters relocated near sewage contaminated estuaries (Beuret, Baumgartner, & Schluep, 2003; Chen, Hoover, & Kingsley, 2005; CDC, 1995; Ng et al., 2005; Shieh, Baric, Woods, & Calci, 2003), and properly cooked but inadequately monitored oysters (Chalmers & McMillan, 1995).

The origin of the shellfish contamination has been attributed to contaminated water supplies. Bakery plants using drinking water in South Wales and Bristol were the source of outbreaks of 100 cases of illness (Brugha et al., 1999).

Water was identified as the source of the virus in the United States from South Dakota to New Mexico (CDC, 1988). In a Wyoming snowmobile lodge, norovirus was isolated in eight of 13 ill lodgers and was positively associated with the nucleotide sequences of norovirus isolated from the water well (Anderson et al., 2003).

Contaminated drinking water and ice affected 84 of 111 surveyed patrons of a saloon in Wyoming whose odds ratio was 4.5 times were more likely to have been exposed to norovirus than non-ill patients (Parshionikar et al., 2003). No food was found to be involved. In a multiple etiological outbreak in Ohio, of the 1450 ill persons affected, 9 were affected by norovirus (O'Reilly et al., 2007). Sewage contaminated water was considered the likely source.

Several outbreaks were reported in Finland (Horman et al., 2004; Maunula, 2005). An estimated 1,700 to 3,000 residents in a local Finnish town came down with gastro-enteritis in March 1998 and norovirus was isolated from untreated water, treated water and four tap water samples. An insufficient amount of chlorine used to treat water was identified as contributing to the virus' survival (Kukkula, Manunula, Silvennoinen, & von Bonsdorff, 1999). Norovirus was isolated in 22 of 28 stool samples from tourists on an Italian resort. An environmental inspection identified a breakdown in the water system allowing fecal coliforms in tap water. Exposure to norovirus included drinking water, beach showers and drinks with ice (Boccia et al., 2002). Similar reports came from Korea (Kim et al., 2005) and Guatemala (Steinberg et al., 2004). Other water sources for infection included a swimming club (CDC, 2004) and on the Appalachian Trail (Peipins et al., 2002).

Other Outbreaks from Norovirus

Waterborne Sources

The school where Norovirus was first identified in Norwalk, Ohio, in 1968 was the only Ohioan school that had its own well (Adler & Zickl, 1969). Water was suspected

as one vehicle of spread. A second outbreak in Columbus, Ohio, that same year, was in an elementary school that did not serve meals. No vehicle of infection was determined.

To determine a risk assessment of the potential for waterborne norovirus infection, Masago et al., (2006) used the following factors: observed data of norovirus in tap water, distribution of concentration, amount of consumption and dose-response relationship. By using a Monte Carlo analysis, the disease burden and probability of infection were calculated. The estimated mean for norovirus in tap water was 7.0×10^{-4} particles per liter. The probability of infection and the disease burden, when the ID_{50} was 10, the 95^{th} percentile of probability of infection was $10^{-2.1}$ infection/person-year and the disease burden was $10^{-2.1}$ DALY/person-year. The probability of infection and the disease burden, when the ID_{50} was 100, the 95^{th} percentile of probability of infection was $10^{-3.1}$ infection/person-year and the disease burden was $10^{-6.3}$ DALY/person-year. The United States level of acceptable risk was 10^{-4} infection/person-year and the WHO disease burden level of acceptable risk was 10^{-6} DALY/person-year when the ID_{50} was 100.

The difficulty with these estimates is that it is onerous to obtain consistently high-quality quantitative information. In addition, even when levels of infection are high, the disease burden is low because norovirus rarely results in death. No health damage was estimated because most illnesses are quickly resolved without being reported.

Water supplies at a Caribbean resort hotel were credited with the infection of 448 people (Brown et al., 2001). Similarly, 93 guests at a holiday party in Toledo became ill at a catering facility that had been cited several times in the past for food safety and hygiene violations (Kassa, 2001).

In 2004, 53 people developed gastroenteritis after swimming in a Vermont community pool. Fifty-three of 189 of those people had gastroenteritis and five of the 10 stools samples collected were positive for norovirus. An investigation of the operations by the Vermont Department of Health found chlorine failure, poorly trained pool operators, and inadequate maintenance, among other failures. The authors reported that this was a case of norovirus transmittal without the usual vomit or fecal contamination (Podewils et al., 2006; CDC, 2004).

Water samples that were collected and then stored frozen over time before the technology for norovirus detection was developed, were analyzed for norovirus in the Netherlands (Skraber, Italiaander, Lodder, & de Roda Husman, 2005). After sufficient concentration of the effluent, three of four samples were positive for norovirus from RT-PCR analysis. A potential result of insufficient chlorine use was suspected for the presence.

Waterborne disease outbreaks from drinking water dropped slightly in number from 39 in 1999 to 2000 to 36 in 2001-2002 and to 30 in 2003-2004 in the United States (Blackburn et al., 2004); (Liang et al., 2006). The 61 outbreaks between 2001 and 2004 resulted in 3,780 people infected and were linked to 11 deaths. Only 72% were of known etiology. Six outbreaks, or about 10%, affecting 797 people with gastroenteritis were attributed to norovirus. Yet in 2002, noroviruses were the most commonly identified causes (25%) of outbreaks associated with fresh water exposure (CDC, 2004a).

A similar scenario can be seen in recreational water in the United States. Between 2001 and 2004, 127 outbreaks were recorded of that only 60 involved gastroenteritis

(Yoder et al., 2004); (Dziuban et al., 2006). Ten of the outbreaks were attributed to norovirus affecting 446 people with gastroenteritis.

Recreational water and drinking water have been found to be the cause of norovirus gastroenteritis. For example, children playing in an outdoor water fountain became sick in the Netherlands in 2002. Approximately 47% of 191 schoolchildren questioned were ill with diarrhea and vomiting (Hoebe, Vennema, de Roda Husman, & van Duynhoven, 2004). In the Netherlands, norovirus was found in the surface water of rivers that receive treated and untreated water from Belgium, France, and Germany. These rivers feed drinking water for over 30 million people. The concentration of norovirus was detected to be as little as 4 PCR-detectable units (PDU) per liter of river water and as high as 4,900 PDU (in December1998) which is considered high when compared with 896 to 7499 PDU per liter of treated sewage and 5,111 to 850,000 in raw sewage (Lodder & de Roda Husman, 2005). Seven different variants were determined including one that matched those found from fecal samples of patients in the population. The authors state that primary and secondary treatment systems do only a fair job of reducing viral concentration and can overburden the tertiary process.

Water samples taken from the Moselle River in France showed a 38% presence of norovirus and *Enterovirus* species (Skraber, Gassilloud, & Gantzer, 2004). While viral pollution appeared to be the same all year, different viruses exhibited seasonal differences. Seasonally, norovirus GII was common mostly in winter while *Enterovirus* were common in spring and fall. This analysis of water samples during these time periods showed a positive relationship between somatic coliphages and pathogenic viral genome

(Lucena et al., 2006) also suggests that coliphages be added as an indicator tool for pathogens to routine water analysis.

In winter of 2002-2003, norovirus in water was tracked to have high peaks of 1700 PDU per liter in January and October. Without adequate adaptive dynamic filtering, relatively high concentrations could affect the population from drinking water (Westrell et al., 2006).

Norovirus concentrations in sewage were detected as high as 10^5 PDU per liter in raw sewage and 10^3 in treated sewage in the Netherlands (van den Berg, Lodder, van der Poel, Vennema, & de Roda Husman, 2005). Following treatment, 11 different variants of norovirus were detected with up to four variants in a single sewage sample. The most common variant, GGII.b, was also the most predominant cause of human illness in Europe during 2000 and 2001.

Asian countries found similar results. In 2004, 194 students from a total of 516 students were stricken with norovirus gastroenteritis. The students were from two different schools in residence at 2 different hotels about 300 meters apart. Strain identification detected the same genotypes of norovirus in both groups of students, food handlers, and ground water. The authors conclude that the origin of the norovirus was contaminated ground water, which affected the food handlers who in turn infected the students (Kim, Cheong, et al., 2005).

Seasonal presence of norovirus could be seen in sewage, treated sewage, and effluent from a wastewater treatment plant in Japan that was sampled monthly between 2003 and 2004 (Haramoto et al., 2006). Norovirus Genotype GI and GII were seen up to

260 copies/ml and 1900 copies/ml, respectively, mostly in the winter season. Samplings for total coliforms, *E. coli*, and F-specific phages were not correlated to the level or presence of norovirus and the authors do not consider any of these useful indicators of norovirus.

Similarly in Sweden, norovirus was found at an average of $10^{3.29}$ per liter between November and February at the inlet of four wastewater treatment plants (Ottoson et al., 2006). Once treated, norovirus reduction was only 0.9 log. No correlation was found between pathogens and the usual indicator organisms. Another study of water at the inlet to a Swedish wastewater treatment plant found that six of seven samples contained norovirus at an average of $10^{3.28}$ PDU per liter or 1900 MPN per liter with a range of 1200 to 4500 in winter (Ottoson et al.). The mean for the rest of the year was $10^{2.3}$ PDU per liter. Genome variants for norovirus were found all year round. The authors concluded that health significance of these levels was unclear since PCR methods detected most enterovirus particles but not virulence.

Sewage taken from English environmental samples found 1.8 x 106 particle copies per 100 ml and 1.7 x 106 particle copies per liter in effluent (Laverick, Wyn-Jones, & Carter, 2004). Similarly, norovirus particles were found in marine bathing water and recreational river waters.

Of 139 samples of surface water in Finland, norovirus particles accounted for 9.4% of the total enteropathogens and fecal indicators recovered (Horman et al., 2004). Yet the presence of norovirus or other pathogens seemed dependent on the source of contamination and the conditions of discharge into surface water. No clear winter peak in

Finland was seen for norovirus. Test results for coliforms, *E. coli,* and *C. perfringens* saw no correlation with traditional fecal indicators. Similarly, no correlation between norovirus and F-phages was found.

Drinking water in Finland showed another interesting result. Of 16 outbreaks attributed to norovirus, seven were from ground water and 6 were from wells. A total of 28 outbreak samples collected between 1998 and 2003, 18 patient samples, and 10 water samples were found to contain norovirus (Maunula, Miettinen, & von Bonsdorff, 2005). All except one water sample found RNA sequences identical to the patient samples.

Outbreaks in the United States from water sources were seen as early as 1982 when 63% of 25 residents surveyed in a small Georgia town contracted gastroenteritis that were served by a community water system (Goodman, Buehler, Greenberg, McKinley, & Smith, 1982). Those served by wells only showed a 9% gastroenteritis level. In La Crosse, Wisconsin in 2004, viruses including norovirus were found to inhabit municipal drinking water wells as well as Mississippi River water. None of the wells tested (n=4) were positive for typical fecal enterococci contamination, *E. coli* or coliforms.

Water treatment and quality differ around the world but a common issue seems to plague all treatment facilities. Viral particles were found in Columbian water at a level of 7.5% of all samples including two samples of fresh, treated potable water that contained norovirus (Gutierrez, Alvarado, Martinez, & Ajami, 2007). While viral proteins were found but not nucleic acid, it was concluded that complete viruses were in the system at some point at levels higher than the minimum infectious dose. Most likely, the authors

surmised, contaminated feces or infiltration of viruses into the municipal water system are a result of runoff from cattle raising regions where feces are found in the soil. It was also noted that the viral proteins could elicit an antigenic response and that water would play an important role as a vector for viral transmission (Gutierrez et al., 2007).

The quantity and type of viruses in potable water determine the risk of infection. United States monitoring of water for pathogens is minimal at best, limited to coliforms, *Crytosporidium, E. coli* O157:H7, and norovirus and is conducted as passive surveillance (Balbus & Embrey, 2002). Exposure to norovirus in water may confer innate resistance to infection to a portion of the population in the US.

A study in Guatemala found that 56% of 343 subjects in 492 households were responded serologically for norovirus (Crump et al., 2007). Because the level of infant (six to 12 months of age) serological response was determined to be 24%, the authors suggested that environmental transmission may be an important factor in norovirus illness in children aged one to four years.

If water is contaminated with norovirus, the container, if recycled, could contaminate future contents. In a recent study, water samples inoculated with norovirus and other enteric viruses were entered into polyethylene terephthalate (PET) and glass bottles (Butot, Putallaz, Croquet, et al., 2007). Adsorption into the bottle walls was examined after 0, 20, and 62 days with different water brands and deionized water. Adsorption of norovirus increased from 2.5% at day 0 to 75% at 20 days and 91% after 62 days into the PET bottles. In glass, adsorption into the glass ranged from 18% to 73% after 20 days dependent on the type of water. The average glass adsorption rate was 75%

after 62 days. These numbers varied based on storage conditions and autochthonous bacteria present. The findings indicate that loss of detection of the virus may be due to surface adsorption. In addition, if electrostatic repulsive forces between the virus and the PET bottle are changed by cation exchange, hydrogen bonding, van der Waals forces, or hydrophobic interactions, the viruses, once not detectable, could be released and become active.

Monitoring environmental viruses and matching those results to clinical isolates is another way to become aware of potential sources of outbreaks. The clinical data analyzed by (Carducci et al., 2006) indicated a continuous circulation of enteric viruses including norovirus. The same strains of enteric viruses were found in feces and water.

Hospitals and Long-Term Care Facilities

Hospitals are also sources of norovirus contagion not in food but also from transfer through persons, staff, and patients. Surface contamination was credited with the source for norovirus and spread by health care nursing staff in a veteran's hospital (Wu et al., 2005). In an outbreak of 81 patients and 114 staff members of a group of four hospitals, salad was considered the agent of transfer for norovirus (Lo et al., 1994). Significantly, a food handler became ill who also had a child at home who was stricken with gastroenteritis 2 days prior to the outbreak. The authors consider virus transfer possible through clothes and hands of the parent. Another proffered explanation for the food outbreak contamination as a result of fecal contact from the parent who became pre-symptomatic.

A Swiss study found nursing homes and hospitals were responsible for 34% and 25% of norovirus gastroenteritis, respectively (Fretz, Svoboda, Luthi, Tanner, & Baumgartner, 2005). A survey in England and Wales found 97% of all outbreaks occurred in health care institutions, hospitals accounting for 40% and residential care facilities responsible for 39% of all outbreaks (Lopman, Adak, Reacher, & Brown, 2003). In Stockholm, a survey of 4,326 patients and 1,119 staff were exposed on 43 wards that reported 54 outbreaks (Billgren, Christenson, Hedlund, & Vinje, 2002). The index case was deduced to probably be responsible for an outbreak affecting 63 patients and health care workers in a university hospital in Switzerland (Khanna, Goldenberger, Graber, Battegay, & Widmer, 2003) and norovirus was reported as the cause of 54% of all illnesses affecting over 29,000 patients and staff between 1992 and 2000 in hospitals in England and Wales from survey data collected by the Public Health Laboratory Service (Meakins, Adak, Lopman, & O'Brien, 2003).

Additional cases related to hospitals or long term care facilities were noted in Spain (Navarro, Sala, Segura, Arias, Anton, Varela, et al., 2005), half of the 5257 cases reported in England and Wales (Lopman, Reacher, Vipond, Sarangi, & Brown, 2004), Ireland (Foley, O'Mahony, Morgan, Hill, & Morgan, 2000), and pediatric hospitals in London (Gallimore, Cubitt, Richards, & Gray, 2004; Girish, Broor, Dar, & Ghosh, 2002).

Additional cases related to hospitals or long term care facilities due to norovirus were noted in Spain (60 cases during December 2001) (Navarro, Sala, Segura, Arias, Anton, Varela, et al., 2005). Almost half of the 4,378 individuals were hospital patients and 11% were nursing home residents reported in England and Wales, (Lopman,

Reacher, Vipond, Sarangi, & Brown, 2004), 8% of all samples collected from Tralee General Hospital in Ireland over two years were positive for norovirus (Foley, O'Mahony, Morgan, Hill, & Morgan, 2000), pediatric hospitals in London (Gallimore, Cubitt, Richards, & Gray, 2004; Girish, Broor, Dar, & Ghosh, 2002) and six nursing homes in Tel Aviv, Israel affecting 246 residents and 33 staff members (Calderon-Margalit et al., 2005).

A pediatric oncology unit saw 11 patients and two relatives in Germany test positive for norovirus, the symptoms of that were life threatening to three of those patients (Simon et al., 2006). Recently, 20% of hospitalized children (n=318) with acute gastroenteritis in three Rio de Janeiro hospitals were infected with norovirus (Victoria, Carvalho-Costa, Heinemann, Leite, & Miagostovich, 2007). Additionally, six percent (n=237) in Madagascar during 2004-2005 (Papaventsis, 2007), 14.5% of children (n=289) with gastroenteritis in Brazil, (Soares et al., 2007) and 48.4% of children (n=192) in Italy (Colomba et al., 2007).

A total of 77 out of 126 outbreaks in the last six months of 2002 were confirmed norovirus gastroenteritis in Victoria, Australia (Cooper & Blamey, 2005). In one of those cases, 52 patients and 11 staff were affected by a norovirus outbreak in a long term care facility.

One report told of a long-term care facility that had an outbreak of 62% patients and 46% of staff in England (Green et al., 1998). Another survey in England and Wales found 97% of all outbreaks occurred in health care institutions or hospitals accounting for 40% of all outbreaks and residential care facilities responsible for 39% of all outbreaks

(Lopman, Adak, Reacher, & Brown, 2003). In Stockholm, a survey of 4,326 patients and 1,119 staff were exposed on 43 wards that reported 54 outbreaks in 1996 (Billgren, Christenson, Hedlund, & Vinje, 2002).

A farewell party at a nurse's hostel of a civil hospital in Delhi, India, resulted in 130 nurses and staff becoming ill due to norovirus. All infected patients had eaten salad sandwiches but no ingredients were available for testing (Girish, Broor, Dar & Ghosh, 2002).

Because health care workers are more in contact with patients with gastroenteritis and therefore more exposed to the risk of infection, it was recommended that such patients be placed in contact isolation (Thornton, Jennings-Conklin, & McCormick, 2004). Such a recommendation or the closure of medical departments was expanded to all nosocomial outbreaks (Hanson et al., 2007).

Patient isolation may not be enough. Environmental sampling also contamination in a home bedroom and suite facilities in long term care facilities, namely bed wheels, radiator tops, toilets, shower drains, carpet and bed-protective side-covers (Vipond, Barker, & Bloomfield, 2002).

Given the high numbers of norovirus infected patients and rapid spread, it appears that norovirus does not need food to pass from staff and patient to patient and staff.

Person-to-Person Contact

Hospitals are also sources of spread of norovirus by not only the food but from transfer through health care staffs and other patients. As early as 1992, hospital and elderly care facility outbreaks were reported affecting 126 patients and staff in England

(Chadwick & McCann, 1994). Surface contamination was credited with the source for norovirus and spread by health care nursing staff in a veteran's hospital affecting 127 of 246 residents and 84 of 181 staff (Wu et al., 2005).

In a situation where standard precautions were taken with infectious patients, recently another emergency unit was affected by gastroenteritis; over a 51 day period, 45% of the staff became ill from norovirus. Of those affected, 56% were nurses and 58% were SHOs (Vardy, Love, & Dignon, 2007). In this instance, a total of 449.5 working hours were lost. The authors surmised that the infection came from multiple members of the community and was passed among the staff.

Due to extended exposure of health workers to many infected patients, an outbreak in a tertiary care hospital in 2004 resulted in 355 outbreaks of noroviral gastroenteritis that affected 90 patients and 265 health care workers from coronary care and psychiatry units (Johnston et al., 2007). The rates of attack were more than five times that of patients ordinarily in the coronary care unit and almost three times those expected for the psychiatry unit. A patient was probably responsible for an outbreak in a university hospital in Switzerland affecting 63 patients and staff but no evidence was found for a water-borne, food-borne or environment source (Khanna, Goldenberger, Graber, Battegay, & Widmer, 2003). Norovirus was credited with 54% of all illnesses affecting over 29,000 patients and staff in 754 separate outbreaks between 1992 and 2000 in England and Wales (Meakins, Adak, Lopman, & O'Brien, 2003).

The authors of the Norwalk, Ohio, account placed the responsibility for secondary infections in both Norwalk and Columbus on person-to-person spread (Adler & Zickl,

1969). Many of the accounts of norovirus associated gastroenteritis could be attributed to person-to-person contact with food as an intermediary fomite.

Other – Military and Hotels

Another means suspected of transmission of norovirus was by air was seen in an elementary school where 15 children had vomited in 10 classrooms affecting 186 students and five staff members with gastroenteritis (Marks et al., 2003). In another episode, several people became ill three days with gastroenteritis following one woman who had vomited in the dining hall but demonstrated no other contact with the sick patrons (Marks et al., 2000).

Isolated military units have faced norovirus infection. Norovirus was the cause of four large outbreaks on U.S. Navy aircraft carriers between 1992 and 1997 (McCarthy, Estes, & Hyams, 2000). Ninety-nine Army trainees in Texas out of a total of 835 soldiers were infected by norovirus gastroenteritis from carbonated beverage dispensers (Arness et al., 2000; CDC, 1999), contaminated salad resulted in 37 cases among 400 in a British Royal Fleet Auxiliary ship, Argus, in the Northern Arabian Gulf (Gallimore et al., 2005). A total of 159 Israeli soldiers in 1999 suffered a similar fate from norovirus infection (OR = 4.38, 95% CI 1.51-13.35) (Grotto et al., 2004). Various unidentified sources was the only attribution made at a military hospital that affected 30 soldiers in Iraq (Thornton et al., 2005). As many as 2500 soldiers were affected when the virus spread on the spigots of jury rigged faucets (CDC, 2002). Exposure to norovirus by military troops is not uncommon as seen in surveys of Norwegian soldiers who showed 29.5% positive for norovirus total antibodies (Ig) without any associated outbreak.

The most common locations for mass gatherings are restaurants and hotels where contamination of food can occur and spread among guests. A catered affair for car dealership employees was such a site in New York in 2000. Illness was significantly associated with consumption of any of four salads served at the banquet (relative risk = 3.8, 95% confidence interval: 2.5, 5.6) and norovirus was detected by reverse transcription-polymerase chain reaction assay in 32 of 59 stool samples from eight states (Anderson et al., 2001). Other sites included a box lunch affair at a football game affecting 54 persons in Florida (Becker, Moe, Southwick, & MacCormack, 2000), and on a college campuses (Moe, Christmas, Echols, & Miller, 2001). An isolated guest house in Australia was the location of norovirus gastroenteritis affecting 20 people (Oliver et al., 1985). Similarly, a Colorado hotel was the site of norovirus gastroenteritis affecting 69 guests (Dippold, Lee, Selman, Monroe, & Henry, 2003), and a hotel in Virginia had 76 hotel guests and 40 staff become sick from norovirus (Love, Jiang, Barrett, Farkas, & Kelly, 2002). All these places showed that close quarters, just like a hospital or long-term health care facility, are capable of large numbers of cases.

Other locations included three separate house boating trips resulted in an outbreak of norovirus in May, 2004. Twenty of 27 people interviewed (a total of 54 participants on trips) became ill from widespread fomite contamination. While the water supply was clean, norovirus was detected on bathroom surfaces (83%), kitchen surfaces (40%), and doorknobs (100%) on the houseboats (Jones, Kramer, Gaither, & Gerba, 2007).

Uncontrolled natural disasters such as hurricanes can results in outbreaks when the population must be moved and cared for in temporary shelters. Norovirus outbreaks

among evacuees from Hurricane Katrina were reported in Houston, Texas (CDC, 2005) and several gulf coast states (CDC, 2005a). A summary of the cases at the Reliant Park Complex in Houston showed 1173 people treated for gastroenteritis exhibiting vomiting and diarrhea. Of the 78 patients that submitted stool samples 45% were positive for norovirus (Yee et al., 2007).

In all the above situations, close quarters and contacts resulted in quick spread of norovirus regardless of whether food was involved.

Food Workers and Outbreaks

Foods become contaminated by a variety of ways. Contamination of food is most often in contact with unsanitized hands, preparation cutting areas, mixing instruments or equipment or fecally contaminated water. Contact with vomit or vomit contaminated water or working surfaces or aerosols from infected people may contaminate food. Food in contact with environments where infected people were present could become contaminated even if surfaces were not in direct contact with feces or vomit (Koopmans & Duizer, 2004).

The risk of infection has multiple variables. In a cohort community-based prospective study of risk factors for norovirus infection undertaken in the Netherlands in 1999, case patients identified with gastroenteritis were matched by age, degree of urbanization, region, and date of inclusion (de Wit, Koopmans, & van Duynhoven, 2003). Case patients and controls answered questionnaires addressing short term risk factors in a 7 day period before onset of symptoms and submitted stool samples over a three week period. The risk factors focused on food handling and were used as indicators of personal

hygiene. A logistics model was composed by de Wit et al. (2003) based on the weight of each factor to measure food handler hygiene. Population-attributable risk fractions (PAR) were calculated on the basis of multivariate odds ratio. The high PAR calculations demonstrated that viruses were transmitted from person-to-person and could be prevented by intervention of the contact between symptomatic and asymptomatic persons. The risk was greater if a child was in the home and the amount of contact with family (31%), day care center (19%), school (18%), home (10%), or work (22%).

In a review of the literature from 1927 through 2006, the Committee on Control of Foodborne Illnesses of the International Association for Food Protection reviewed 816 reports of outbreaks affecting 80,682 cases where the food worker was found to be the cause or suspected (Greig, Todd, Bartleson, & Michaels, 2007). Norovirus was found to be the top disease producer of 14 main agents. Norovirus was detected or implied in 274 outbreaks and 27,081 cases that stand at approximately one third of all cases involving food workers.

In a study of restaurant-related outbreaks between 2002 and 2003, norovirus was considered the predominant agent of illness. Of all confirmed cases, norovirus accounted for 42% of the outbreaks in 22 restaurants (Hedberg et al., 2006). Most of the cases (65%) were caused by an infected person or a carrier. Researchers at CDC reviewed all foodborne outbreaks recorded from restaurants between 1982 through 1997 found that norovirus accounted for 54% of the cases that had a norovirus-like clinical profile. Of the total of 2,246 cases, 1,549 cases were those whose etiology was unknown (Hedberg, Palazzi-Churas, Radke, Selman, & Tauxe, 2007). Poor hygiene was considered the cause

for norovirus outbreaks and supervision of sanitation policies and monitoring the health of workers was lacking.

The errors or factors identified by health workers investigating scenarios from a norovirus outbreak was caused by a single infected worker who directly infected customers by using bare-handed contact of the food, and by failure to wash hands properly (Todd, Greig, Bartleson, & Michaels, 2007b). The difficulty in investigating these outbreaks were that food workers were no longer available for interview, poor communications due to different languages, failure by the health worker to elicit information, workers giving false information about his/her involvement, or too much time had passed to gain useful information. The culprit in these norovirus cases was or assumed to be a single worker (Todd et al., 2007b).

A survey of food contact with working surfaces in 40 Iowan assisted living facilities found that three quarters of those facility surfaces, work tables, counters, cooking equipment, and cutting boards failed the required sanitation and cleaning requirements. Simple aerobic plates, *E. coli* and *Staphylococcus aureus* were found on each surface. Only two facilities passed for all five surfaces (Sneed, Strohbehn, Gilmore, & Mendonca, 2004). It is believed that if these places could not contain known bacteria, then their chances of controlling norovirus would be the same.

In another study, food consumed outside the home was considered the cause of gastroenteritis. In a random telephone survey of 16,435 U.S. residents, 22% attributed their illnesses to meals eaten away from the home (Green, Selman, Scallan, Jones, & Marcus, 2005). Only 8% of those taken ill specified the restaurant in their reporting of the

illness. Of those reporting gastroenteritis, 54% believed their illness onset was within 5 hours of eating. It is possible that the home environment contributed to the illnesses more than was believed.

Developing a model of risk to foods from hygiene practices found that risk applied to all age groups but critically depended on the hygiene of the food preparer, the consumption patterns of the consumers and the relationship between people preparing food and those ingesting it (Christensen et al, 2005). This implies the likelihood of transfer and illness higher at home situations than in restaurants.

One case described the baker who vomited in 2001 while working in a bakery, cleaned the sink with bleach, and still infected 231 persons after serving a Danish Municipal Health Service luncheon (de Wit et al., 2007). The authors concluded that the baker did not know that the vomit created aerosolized droplets of virus that later contaminated the working counter. In addition, in general, most food handlers are unaware of transmission of viruses and especially norovirus. Later outbreaks in the Netherlands (13 total) and England and Wales (21 total) provided RT-PCR evidence that the same strain was involved making the baker's incident an initiation of a pandemic.

In many countries, street vendors are the source of food for people. In a comparison of 128 street food vendors and 74 food handlers from restaurants, fecal contamination of drinking water, dishwater, and ice cubes were frequent (Vollaard et al., 2004).

While many fault the food as the transmission vehicle, the source in many cases is person first ill, namely, the health worker, customer, patient, or food handler.

Food handler Role

Education and training are the accepted keys to managing safety and preventing foodborne outbreaks from norovirus; but, it is presented from an academic standpoint with some practical training. The academic approach is informative about the pathogens, their spread, harborage sites, and precautions to contaminate the food or contact surfaces (Todd, 2007a). The practical training usually involves methods of proper methods of washing, care of instruments, tools, and equipment (Todd, 2008a). Monte Carlo simulations of risk models showed differences in behavior by age and gender resulting in high risk for young adult males and low risk for those over 60 years old of consuming a risk meal (Christensen et al., 2005). The limitations of this study do not include the probability of not washing hands or applying insufficient cooking, and acknowledge no data exist on the hygiene and consumption of risk products on a detailed level. No current risk models or analyses take into account previous illness history for that institution.

Education cannot make a difference until accurate profiles of food handlers and workers are created for the industrial sector. Food service establishments are typically short-staffed, a reason used by food managers to claim as a barrier to safe food handling (Kendall, Melcher, Pelican, & Paul, 1998). Colorado offered to help managers locate workers in a welfare-to-work program to bolster the workforce while adding training programs, subsidies and tax credits (Hine, Thilmany, Kendall, & Smith, 2003). Yet, managers were reluctant to hire such personnel because persons in the welfare-to-work program would not have the requisite skills to prepare and serve food in a safe and

efficient manner and the employers would need time to adequately train them in sanitation and hygiene practices and behaviors.

Nationally, more than 500,000 food service and drinking establishments employ over 8 million food handlers weekly with a payroll of over $102 billion annually (Census, 2003). Average annual salaries in food preparation are around $11,818, well below the poverty level. Turnover is high and worker stability is unreliable.

For safety sake in a food processing plant, the organizational structure and relationships between management and workers define front line practices and behaviors. In a highly regulated business, such as food production, the plant's food safety culture is affected by management style and communication, responsibility and commitment, risk-taking, job satisfaction, complacency and risk awareness (Harvey et al., 2002). As workers define their roles on the plant floor, their adherence to the food safety culture is predicted by their position in the company. The human element, as expressed in attitude toward work, is a contributing factor to the level of food safety and contamination.

Workers are able to enter and traverse the entire building. These workers may be unwitting carriers of contaminants if SSOPs and personal hygiene requirements are not followed or effective. Meat and poultry plants are highly regulated to prevent food contamination and the working environment and the production schedule can be stressful. Workers, especially those at larger establishments, undergo various physical and psychological changes resulting in difficulties adapting to the shift work, self-perceived constraints and concentration (Lac & Chamoux, 2004). Stress related to job dissatisfaction can influence worker's perceptions of health psychologically and can

increase a worker's susceptibility to physical environmental exposures (Chao, Schwartz, Milton, & Burge, 2003). The cleanliness and condition of the building is influenced by both management and personnel that create a distinctive, unique culture of cleanliness and hygiene. All these influences affect how workers conduct their business and personal hygiene. This then can have a direct effect on product contamination and food safety.

Testing for a correlation between sanitary practices and foodborne illnesses has been conducted in the retail sector but not in production areas. Restaurants that were associated with a food borne illness in Seattle were found to have lower sanitation inspection scores than restaurants with no associated illness (Irwin, Ballard, Grendon, & Kobayashi, 1989; Irwin, Ballard, & Kobayashi, 1989). No statistical difference was found in outcome measures based on frequency of inspection either. When premises were grouped based on the average time between inspections, premises with greater time between inspections scored better compliance measures relative to premises that were inspected more frequently (Newbold, McKeary, Hart, & Hall, 2008). National inspection criteria were questioned after mean inspections scores rose between 1993 and 2000, but no difference was found between scores of restaurants associated with outbreaks (score = 81.2) and those restaurants without association with illness (score = 81.6) (Jones, Pavlin, LaFleur, Ingram, & Schaffner, 2004).

The distribution and demography of food handlers in the United States is not well known. In other countries surveys indicate a wide variety of people in the business. In Thailand, the majority of workers were non-natives or residents (Malays) (98.8%), female (69.5%), married (81.4%), working in food stalls (64.2%), involved in operational

areas (49.3%), and having no license (54.2%) (Zain & Naing, 2002). Their educational levels indicated no education (10.5%), primary school (31.9%), or secondary school (57%). Understandably, because such statistics do not correlate well with United States figures, the influence of differing cultural patterns may affect habits and training abilities of U. S. food handlers.

As a result of little education and poor or ineffective training, food handlers themselves are at risk for transmitting disease. An ill food worker had an onset of *Salmonella* in Australia two days prior to an outbreak that resulted in twenty-eight persons becoming ill with gastrointestinal symptoms (Hundy & Cameron, 2002). In a survey of food handlers in Irbid, Jordan, 48% of non-Jordanian and 12.3% of Jordanian born workers showed enteropathogens in their stools (al-Lahhan, Abu-Saud, & Shehabi, 1990). Such correlations are difficult to match against American food handling and processing but the implication is that the greater the number of non-American workers in the food service industry, the difficulties in language and training may create opportunities for foodborne illness to be transmitted to consumers.

Social Influences

Given the environment of a food preparation establishment, it is not hard to understand the difficulties faced. Job demands and control are very restrictive in a food processing facility. Enforcement of standards and production quotas is driven from not only management but also from state, local, and federal inspectors who demand high adherence to local, state and federal regulations. The work is repetitive, with high demands to fulfill quotas and orders, and almost no decision latitude control. According

to Theorell (2000), job strain is the most relevant outcome to high-demand—low-decision latitudes and most relevant to illness development. Given the overall disparity in income in the United States (Kawachi, 2000), the health and life expectancy of food workers who are near or at the poverty level are probably lower than the average American. Food service industries which are unstable because of irregular contracts, supplies, or work, place food handlers in precarious mental states which can reflect the grieving seen in job loss, unemployment, and future uncertainty (Kasl & Jones, 2000).

Over a long period, this kind of work environment will result in increased sympathoadrenal arousal and decreased stasis (Theorell, 2000). When applied to gastroenteritis, it could translate as an inability to keep normal intestinal flora intact leaving openings for pathogens to exert a change in the immunological balance that results in diarrhea and shedding of pathogens. This could provide a basis for transmission to other persons or foods, which would explain part of the classical fecal-oral route.

Barriers identified by English food handlers were lack of time, lack of staff, and a lack of resources. More than 63% admitted to not carrying out food safety behaviors in spite of receiving food hygiene training. The perception among workers in this study was that the foods they prepared were of relatively low risk for illness while industry identified these food products as high risk (Clayton, Griffith, Price, & Peters, 2002).

Environment

Not only are food handlers and workers subject to difficult social conditions in food production areas, and are also susceptible to chronic and long term diseases (Theorell, 2000). The ease of transmission but unknown mechanism of how norovirus is

transmitted throughout a population must include demographic, occupational, and social epidemiologic studies of food handlers and workers. Workers that do not allow time for recovery from illness, feel pressured to come to work too early, or are asymptomatic pose a great risk for carrying diseases that are considered inconvenient, minor, or nuisances to the work place. Stress from job pressures and demands can undermine health and encourage ill workers to report at work (Theorell). Understanding the factors and influences of the work environment and social context of the employees can lead to better prevention of the disease transmittal through food. The need for more research in this area is critical if the food industry and the government are serious about reducing illness outbreaks.

Syndromic Surveillance

Surveillance of norovirus gastroenteritis is difficult since it is non-fatal and few people go the hospital or for that matter a doctor. In Northern Italy in 2002, norovirus was the cause of 10.4% of gastroenteritis, the second most common agent behind rotavirus (Medici et al., 2006). Most cases occurred in January, September, and November but also were present throughout most of the year. One in six strains of norovirus had already spread through most of the infantile cases before launching into a fully fledged outbreak in Europe. Analyzing by strain, the authors felt that because of sustained incidence of the GII/4 strain, children with sporadic gastroenteritis were probably acting as a reservoir for emerging epidemic Noroviral gastroenteritis.

South India found that both symptomatic and asymptomatic gastroenteritis in children was caused in part by norovirus (15.1%). A community cohort study found

norovirus accounted for 7.6% of the cases. The high prevalence indicates that children routinely circulate the virus and serve as a significant reservoir for infection (Monica et al., 2007).

Using raw sewage as a sample set, a study in Italy found two of 12 samples tested were positive for norovirus and three norovirus GII samples were recovered in sewage plant effluent (Carducci et al., 2006). River water contained norovirus GI and GII in the winter months and seawater contained at least 2 strains of genotype I and II in December. Their findings indicated a scarce reduction of microbial pollution in water treatment waste water that allowed for an increase in river water and a larger increase in seawater. The similarities between strains found in effluent and human cases indicates that gastroenteritis viruses circulate through the populations and that environmental conditions also serve as a resource for norovirus infection.

A recent study in Norway confirmed the emergence of norovirus infection during the winter months as seen in healthcare institutions (Vainio & Myrmel, 2006). They also found that certain strains of norovirus were circulating in the population with some variation appearing in subsequent years.

Tracking norovirus locally can be accomplished only if proper methods are used. In a study from England, clusters of outbreaks were determined to have happened in clusters suggesting local transmission (Lopman et al., 2006). In examining the individuals and pairing them with molecular evidence, it was found that transmission of gastroenteritis was happening between hospital units. They add the caveat that definitions of identity and similarity are still not clear so that some viruses that appear closely related

are in fact not related and that some viruses that appear different from each other are in fact related.

Analysis

Mead et al. (1999) estimated that 66% of all 23,000,000 norovirus cases were foodborne. They also estimate foodborne norovirus-related illness is 40% of the all cases of norovirus illness because other mechanisms of transmission besides food may be in effect.

The problem with relying on domestic technical reports such as the ones detailed here is that there is no national surveillance system in place for acute gastroenteritis or norovirus outbreaks beyond CDC's records of food related outbreaks. Overall transmission estimates are that food is responsible for 39% of outbreaks; person-to-person contact is responsible for 12%, water 3%. Air (aerosolization of vomitus) or environmental (fomites) are not segregated from the foodborne numbers (Parashar et al., 2001). In addition, 46% of all norovirus cases have no known transmission; this skews the data toward foodborne outbreaks reports collected by CDC.

There is no surveillance system for person-to-person transmission, water related, or other methods of transmission. The result is an underestimation of the true number of outbreaks associated with norovirus. Such a reporting system is expected to be in place in 2009; however, results will not be retroactive (CDC, 2007b). The other limitation is that not all states test for norovirus for a variety of reasons including cost so reporting is uneven. In Canada, norovirus infection became a reportable disease in 2006 (Doherty, 2006).

The oral-fecal routes of norovirus spread are well documented through stool samples and assumed to be passed by hands as the classical definition. Oral spread by vomiting has been demonstrated (Marks et al., 2003) but aerosolization is not likely to be considered (Dolin, 2007). Some consider young children a reservoir of norovirus that cycle the virus through the community creating sporadic cases rendering the oral-fecal route theory inaccurate.

Unreported cases are those affecting single individuals or those who decide the symptoms are not worth the cost or time to consult a physician. Symptoms resolve within a few days making a trip to the doctor fruitless. Many people do not consider reporting any disease to a health department. Are these unreported symptomatic cases connected to a larger outbreak, a result of asymptomatic shedding from others, or only a secondary spread? If food was involved, wouldn't more than one person likely be ill and reported if the food was purchased in a store that many people traverse?

Many of the cases provided here demonstrate a clear route of food transmission, especially salads, deli meats, cakes, and raspberries. Some domesticated animals, namely pigs and cows, carry norovirus. Oysters may be the only foodstuffs that can bioaccummulate norovirus.

In many cases mentioned here, the food handler was ill or still shedding viruses. The most common mode of transmission identified in 1998 was consumption of contaminated food from caterers (Fankhauser, Noel, Monroe, Ando, & Glass, 1998). However, re-examining the descriptions of the cases indicates some are a result of secondary infection transfer from ill children.

The asymptomatic person may never have been symptomatic but simply a carrier. A survey of caterers involved in 55 norovirus outbreaks and 35 sporadic cases over a ten year period in Japan found that stool samples from both symptomatic and asymptomatic food handlers were positive for norovirus in 449 of 2376 (19%) persons (Ozawa, Oka, Takeda, & Hansman, 2007). A total of 133 asymptomatic persons were found and tested. That an asymptomatic person's presence may account for person-to-person transfer of the virus without direct contact with food is notable.

Attribution of infection to food is not always a given. The influence of person-to-person transmission has been set at 33 percent among family members and 50 percent among school contacts (Musher & Musher, 2004). Secondary outbreaks indicate person-to-person transmission rather than foodborne transmission. An example of a large foodborne outbreak actually counted patients (20%) that became ill after a university cafeteria was closed (Kilgore et al., 1996). Similarly, secondary cases accounted for 33 percent of all cases in a general outbreak in Sweden (Gotz et al., 2001). In another outbreak, nine of 14 employees in a long term care facility who had gastroenteritis had no direct contact with any of the residents (Gellert et al., 1990).

Commonly norovirus outbreaks occur in nursing homes and hospitals (43%) and restaurants and catered affairs were second most common (26%) (Fankhauser, Noel, Monroe, Ando, & Glass, 1998). Most of these cases were clearly person-to-person transmission and no food transmission was involved.

The waterborne infection cited could have been an isolated incident since no bacteria or virus is evenly distributed throughout an entire system. Person-to-person

contact would also be more likely to affect individuals who determine self treatment to be best and go unreported. Given these possibilities, it is difficult to determine what, if any, is the major transmission route and cause of norovirus gastroenteritis. The assumption that this is a foodborne pathogen and a transmitted a majority of the time by food handlers may fail to take into consideration other potential transmission routes.

Gallimore, Iturriza-Gomara, Xerry, Adigwe, and Gray (2007) considered that the infectiousness of norovirus may provide short-term protective immunity without any lasting ability to protect against other variants. As a major epidemic proceeded with each variant, “herd” immunity was evident. The data they reviewed suggested a new variant every 2.3 years from pools of cocirculating virus variants. The virulence depended on individual susceptibility. They even considered similar changes in influenza A virus to have the same type of evolutionary drift that is replaced every 2-5 years.

Similarly, Anestad, Vanio, and Hungnes (2007) compared the characteristics of norovirus and influenza virus in common. Both viruses are most active in the colder months of the year; both infect a similarly large proportion of the population, both infect epithelial cells, and both show similar symptoms: fever, headache, muscular and abdominal pain, and malaise.

If norovirus has the same pattern of evolutionary drift and spreads by genogroup internationally, it may be similar to pandemic viruses such as influenza virus. In such a case, it is possible that norovirus has been misclassified as a foodborne pathogen.

The analysis was designed to understand whether associations between food, food handlers, and outbreaks existed and the how such associations explained the numbers of

outbreaks seen in scientific reports. The next chapter describes the research methodology and analysis, followed by the results in Chapter 4, and discussion of the analyses in Chapter 5.

CHAPTER 3:

RESEARCH METHODOLOGY AND DESIGN

Introduction

Norovirus in the United States is not a required reportable disease. The CDC does not include information about norovirus in its regular reports. Yet, because of national interest in foodborne outbreaks, the CDC's Emerging Infections Program (EIP) Foodborne Diseases Active Surveillance Network (FoodNet) maintains records of all foodborne outbreaks including norovirus beginning in 1998.

Design

The data used for this study includes all foodborne outbreaks recorded in CDC's eFORS database covering the years 1998 through 2006. The unit of analysis will be the outbreak and not individual persons or clusters of people. All outbreak occurrences are classified into one of three groups:

1. Outbreaks that confirmed norovirus as the source of gastroenteritis.
2. Outbreaks that suspected norovirus as the source of gastroenteritis but could not confirm the source.
3. Outbreaks for which an identified etiological agent that mimics norovirus is credited as the source of gastroenteritis.

The FoodNet project consists of "active surveillance for foodborne diseases and related epidemiologic studies designed to help public health officials better understand the epidemiology of foodborne diseases in the United States" (CDC, 2007, p. 1).

Data Collection

The initial data were collected by local or state officials by a combination of interviews, hospital reports, and laboratory results during an outbreak investigation. All U.S. states or counties that keep statistics will have compiled the data into a summary report for their state or county. None of the reports identify individuals or locations other than the state or counties within the state. Because the submitting officials are state or city Departments of Health personnel, a public health official or an epidemiologist usually completes the form. There is no requirement to be a reporting official as long as the official is willing to be the contact point for feedback or questions.

The county or state will also have completed a separate eFORS form by limited access to a web-based system. The system allows the state to retrieve data but only for that state or county. The data were retrieved from the submittal database by CDC outbreak staff members who then reviewed, cleaned and organized the data into a searchable format. If the reports concerned a multistate outbreak, the submittal by the states or counties will then be compiled by staff at CDC who collapsed the multi-state reports into a single report.

The reporting form used to enter data into eFORS is CDC 52.13, revised November 2004 (see Appendix A), which is broken into six parts. The first part is basic information identifying the number of cases, estimated total ill persons, dates of the cases and exposure, and implicated foods.

Another aspect of the report is the identification of the etiology and whether it was confirmed. Also reported are the contributing factors and whether the food worker

was implicated as the source of the contamination. This last item is stratified into categories of evidence indicating the food worker as the source, including laboratory evidence, epidemiologic evidence, both or prior experience that makes this the likely source.

Part 2 of the report covers the symptoms, signs outcome, incubation period and duration of the illness. The attack rate may be calculated. It also asks for information on location where food was prepared, consumed and whether a trace back was done. The report also requests information if a recall of the food product was done.

Part 3 covers any information if the outbreak involved a school or school-aged children and the food item. Parts four, five and six allows for providing information about ground beef, the mode of transmission for *E. coli* and *Salmonella* Enteritidis, and eggs, respectively.

An analysis of the data described the frequency distribution of outbreaks. Useful information are the counts associated with each etiologic agent, the number of confirmed or suspected etiologic agents, investigation methods, types of foods, and locations of exposure.

Data Description

Walden's Institutional Review Board (IRB) approved the study following CDC's IRB approval (# DREY_06052008) that supplied the information about food handlers, food types, and locations. This researcher applied to CDC's Enteric Diseases Epidemiology Branch officials by email requesting the data collected from the eFORS reports. The data received was in a Microsoft Access file that has been screened by CDC.

Microsoft Access is a relational database management system (RDBMS) which is a database management system (DBMS) that provides the ability to do set-based relational queries, bulk updates, and transfer the data to normalized relational tables that can then be queried and manipulated using Structured Query Language (SQL; Microsoft, 2006). Epi Info, version 3.4.3, was used as the analysis tool. Epi Info is for, "epidemiologists and other public health and medical professionals to rapidly develop a questionnaire or form, customize the data entry process, and enter and analyze data" (CDC, 2007a) providing epidemiologic statistical tables, graphs, and maps (CDC, 2007a). Epi Info is compatible with Microsoft Office Access databases and SQL.

The analysis included the total number of records, number of outbreaks attributed by major etiology, the identified etiology (52.13 field code = SpeciesName, SerotypeName, Confirmed), contamination factor (ContributingFactorCode), the investigation method and the number of types of investigative methods used (investigationmethodname), how the etiology was detected and how often (DetectedInName), location (StateName), where the food was prepared and eaten (WherePreparedName, WhereEatenName), the number of times a food type was implicated (FoodCategoryName), the reason the food was suspected (CookingMethodName), the number of times a food worker was implicated and what basis for that implication (FoodWorkerImlpicatedDescription, ContributingFoodWorker), and other data fields of interest (see Appendixes A and B).

For data analysis purposes, the variables in this study are identified in the Table 1. Because data listed are categorical, analysis calculations only lends itself to odds ratio.

Salmonella will be used as the etiologic agent for comparable purposes because of the high number of reports giving the multivariate analysis study a strong statistical power.

Table 1

Variables used in the study analysis.

Variable name	Dependent/ Independent	Type of data	Potential Confounding factor	eFORS name
Etiology	Dependent	Text: Norovirus, genogroup I		SpeciesName, SerotypeName
Unknown etiology	Independent	0, -1	Yes	Confirmed
Food	Independent	Text: Ground beef, gravy, lettuce	No	EtiologyUndertermined
Unknown Food	Independent	0, -1	No	FoodCategoryName
Etiology Source	Independent	Text: Patient specimen, Food Specimen	Yes	FoodVehicleUndetermined
Food Preparation	Independent	Code: M1 – M15	Yes	DetectedinName
Food Worker	Independent	Text: laboratory and epidemiologic evidence, prior experience makes this the likely source	No	CookingMethodName
Contributing Food Worker	Independent	True, false	Yes	FoodWorkerImplicatedDescription

Contamination Factor	Independent	Code: C1-C15, P1-P12, N/A	Yes	ContributingFoodWorker ContributingFactorCode
table continues				
Unknown Contributing Factor	Independent	0, -1	Yes	
Food Worker Implication	Independent	Code: A, B, C, D, E	Yes	ContributingFactorUnknown
Implication Evidence	Independent	Yes/No	Yes	Supplement file: Question 1 Supplement file: 6A, 6B, 6C, …, 6N

The food variable text name was classified as 1 of 12 categories of food according to the model designed by the Food Safety Research Consortium (Batz et al., 2004).

Missing Data

There is a potential that some data fields were not completed by FoodNet members and those missing data will be included in the data received from CDC. The apparent reasons for the missing data included those lost to follow-up, refused to answer questions or information was not relevant to the investigation. It was possible that physical sampling of food or stools were unable to be done, not collected, analyzed by a laboratory, or that results were inconclusive.

Because of missing data, some analyses may have different population numbers. This researcher will discuss the effect of the missing data later in the analyses.

Descriptive Analysis

Frequency distribution tables will be prepared according to etiology, food, food workers, and all other factors to gain an insight into associations and potential influences.

Table 2

Example of descriptive table of the records for etiological agent in eFORS data.

Etiologic Agent	Number of records	food identified	food undetermined
norovirus			
Sal E			
toxin			
C. perf			
Campy			
E. coli			
S. aureus			
Shigella			
Vibrio			
B. cereus			
Cyclo			
Hep A			
Listeria			
Sal T			
Unknown			
Totals			

Table 3

Example of descriptive table of the records food types in eFORS data.

Food Products	Etiology Identified	Etiology Unidentified
Seafood		
Egg		
Produce		
Beverage		
Dairy		
Breads and Bakery		
Multi-		

ingredient/
other
Game
Beef
Poultry
Pork
Luncheon/
other
meats

Research Questions

Are food handlers more likely to be associated with viral gastroenteritis from norovirus than gastroenteritis from food or other sources? To determine the answer to this question, the following hypotheses were formulated:

Research Question 1: Is food the main transmission agent for norovirus outbreaks? Because eFORS is the only database that contains norovirus information, bias must be considered and is discussed in the Results and Discussion sections. This question that food is the source of the contamination is found in Part 1, Section 8 in eFORS requests information about implicated food where "Foods identified" in the table below are those that have a positive answer of laboratory or statistical evidence (answers 1 or 2). Foods not identified are those that have an undetermined answer or no answer at all).

Ho_1: Food is not directly associated with Norovirus outbreaks.

Ha_1: Food is directly associated with Norovirus outbreaks.

Table 4

Example of 2 x 2 analysis tables for hypothesis 1.

		Etiology	
		Norovirus	*Salmonella*
Foods Identified	Yes		
	No		

		Etiology	
		Norovirus	Other Viral
Foods Identified	Yes		
	No		

An odds ratio (OR) will be calculated from this table to test the association of food identified as the source where outbreaks were attributed to norovirus and to another well established etiologic agent, such as *Salmonella*, and then where the food was not identified.

Reporting differences between *Salmonella* and norovirus complicate the calculation of ORs. Mead et al. (1999) recognized underreporting of *Salmonella* at 38 fold and adjusted the reported figures accordingly. The frequency of *Salmonella* as the suspected etiological agent then confirmed was calculated at 95% and could be used to calculate an adjusted *Salmonella* OR.

Mead et al. (1999) indicated that *Salmonella* reporting was better established and more likely to be done than for norovirus. This means the number for underreporting of norovirus could be many fold higher. Mead et al. then calculated a norovirus reporting rate at 11% of all acute gastroenteritis cases, or 4,180,000 cases. They also calculated a frequency of foodborne transmission at 40% of the total estimated norovirus cases, or

9,200,000 cases. To arrive at an underreporting adjustment figure, the total frequency of norovirus transmission cases divided by the total number of norovirus cases, or 45% could be used to calculate an adjusted norovirus OR.

The adjusted ORs will allow for better comparisons of the pathogen rates by adjusting for the differences in reporting of these two diverse food pathogens. It must be understood though that these adjustments will not account for other factors that cause such a low reporting rate. Such factors would include the method used for testing, capability of the labs, whether the sample was actually analyzed, and other sources not sampled such as food handlers, environmental surfaces, water sources.

Research Question 2: Did the evidence implicate food handlers were the cause of norovirus outbreaks? (This question that food handler is the source of the contamination is found in Part 1, question 11, part 5 where "Food worker implicated" in the table below are those that have a positive answer of laboratory evidence (answers 1 or 3). Food workers not implicated are those that have a "no" answer or no answer at all).

Ho_2: The food handler is not directly associated with Norovirus outbreaks.

Ha_2: The food handler is directly associated with Norovirus outbreaks.

Table 5

Example of 2 x 2 analysis tables for hypothesis 2.

		Etiology	
		Norovirus	*Salmonella*
Food Worker	Yes		
	No		

		Etiology	
		Norovirus	Other Viral
Food Worker	Yes		
	No		

An odds ratio will be calculated from this table to test the association of the food worker identified as the source where outbreaks were attributed to norovirus and to another well established etiologic agent, such as *Salmonella*, and then where the food worker was not identified. Figures will be adjusted based on the above discussion.

Research Question 3: Did the evidence implicate food as an indirect cause of norovirus outbreaks? (Part 1, Section 8 in eFORS requests information about implicated food except that "Foods identified" in the table below are those that have a positive answer of compelling supportive evidence or other indirect evidence (answers 3 or 4). Foods not identified are those that have an "undetermined" answer or no answer at all).

Ho_3: Food is not indirectly associated with Norovirus outbreaks.

Ha_3: Food is indirectly associated with Norovirus outbreaks.

Table 6

Example of 2 x 2 analysis table for hypothesis 3.

		Etiology	
		Norovirus	*Salmonella*
Food Unidentified	Yes		
	No		

		Etiology	
		Norovirus	Other Viral
Food Unidentified	Yes		
	No		

An odds ratio will be calculated from this table to test the association of food identified as the source where outbreaks were attributed to norovirus and to another well established etiologic agent, such as *Salmonella*, and then where the food was not identified. Figures will be adjusted based on the above discussion.

Research Question 4: Did the evidence implicate the food worker as an indirect cause of norovirus outbreaks? (This question is similar to the above in that food handler is the source of the contamination per Part 1, question 11, part 5 except that "Food worker implicated" in the table below are those that have a positive answer of epidemiological evidence only (answers 2). Food workers not implicated are those that have a "no" answer or no answer at all).

Ho_4: The food worker is not indirectly responsible for Norovirus outbreaks.

Ha_4: The food worker is indirectly responsible for Norovirus outbreaks.

Table 7

Example of 2 x 2 analysis table for hypothesis 4.

		Etiology	
		Norovirus	*Salmonella*
Contributing Food Worker	Yes		
	No		

		Etiology	
		Norovirus	Other Viral
Contributing Food Worker	Yes		
	No		

An odds ratio will be calculated from this table to test the association of the food worker identified as the source where outbreaks were attributed to norovirus and to another well established etiologic agent, such as *Salmonella*, and then where the food worker was not identified. Figures were adjusted based on the above discussion.

Research Question 5: Were there other sources identified as the cause of norovirus outbreaks? Part 1, Section 8 in eFORS requests information about implicated food where "Foods identified" in the table below are those that have a positive answer of specific evidence lacking but prior experience makes it a likely source (answer 5) and per Part 1, question 11, part 5 where "Food worker implicated" in the table below are those that have a positive answer of prior experience makes this the likely source (answer 4). Foods not identified and food workers not implicated are those that have an "undetermined or no" answer or no answer at all).

Ho_5: Other causes are not responsible for Norovirus outbreaks.

Ha_5: Other causes are responsible for Norovirus outbreaks.

Table 8

Example of 2 x 2 analysis table for hypothesis 5.

		Etiology	
		Norovirus	*Salmonella*
Other sources	Yes		
	No		

		Etiology	
		Norovirus	Other Viral
Other sources	Yes		
	No		

An odds ratio will be calculated from this table to test the association of sources other than food or food workers where outbreaks were attributed to norovirus and to another well established etiologic agent, such as *Salmonella*, and then where the sources other than food or food workers was not identified. Figures will be adjusted based on the above discussion.

Research Question 6: Considering contributing factors identified for outbreak, how strong is the argument that food workers are the major source of transmission of norovirus?

Ho_6: No association exists between implication of the food workers and the contributing factors.

Ha_6: An association exists between implication of the food workers and the contributing factors.

Table 9

Analysis table for hypothesis 6.

	Implication Justification			
Food-handler Categories	Lab & Epi Evidence	Epi Evidence	Lab Evidence	Likely Source
Outbreak directly associated with food-handler				
Outbreak indirectly associated with food-handler				
Outbreak not associated with food-handler				

Table 10

Contributing Factor variables used to determine food-handler categories.

Food-handler Category	Contributing Factor
Outbreak directly associated with food-handler	Handling by infected person (C12)
	Bare handed contact- food-handler with RTE food (C10)
	Glove handed contact - food-handler with RTE food (C11)
	Toxic substance purposefully added (C2)
	Toxic substance accidental added (C3)
	Excessive addition of ingredient becomes toxic (C4)
Outbreak indirectly associated with food-handler	Inadequate cleaning of utensils/ equipment (C13)
	Cross contamination from raw ingredient of animal origin (C9)
	Storage in contaminated environment (C14)
Outbreak not associated with food-handler	Ingestion contaminated raw ingredient (C7)
	Toxic substance naturally occurring (C1)
	Contaminated raw ingredient (C6)
	Toxic container or pipes (C5)
	Food from polluted source (C8)
	Other source (C15)

Analysis of the variable food handler category as qualified by the implication of evidence will give an idea of the direct, indirect or other association to the outbreak by the contributing factor assigned as listed in Table 9. The contributing factor is the public health official's determination of how those individuals became ill. This analysis would be a chi square analysis. Each category is defined by whether and possibly how the food handler transmitted norovirus to those in the outbreak by the particular contributing factor as listed in Table 10. Only those records that identify one contributing factor will be used since multiple contributing answers can confuse the analysis by adding covariate issues. The outcome would determine how the food handler is viewed by the public health official based on evidence and contributing factors of contamination. It is important to determine how strong the association to the various degrees of implication determined to associate the food handler with the outbreak.

Data Analysis

An odds ratio shows the probability of an occurrence over the probability of a non-occurrence. In this study, the odds ratios to be calculated are the probability of a norovirus foodborne outbreak versus another source of outbreak associated with a food, food worker, or other variable.

There was much information derived from the e FORS data file. The associations of food, food handlers, and the evidence provided an important understanding of how the information was collected and what assumptions were made. The following chapter offers the results and analyses with interpretations discussed in Chapter 5.

CHAPTER 4:

RESULTS

Introduction

Widdowson et al. (2005) reported that norovirus confirmed outbreaks increased from 11 in 1996 to 164 in 2000 from data voluntarily reported by state health departments to CDC for inclusion in the National Foodborne Outbreak Reporting System. Between 1998 and 2000, norovirus confirmed outbreaks accounted for 27% of all reported outbreaks with a determined cause. Mead et al. (1999) estimated that such reports represent approximately 60% of reported illnesses.

Where information provided to the CDC was complete, Widdowson et al. (2005) reported norovirus associated outbreaks were significantly larger than outbreaks of bacterial cause. Of the known bacterial causes, outbreaks are attributed to *Salmonella* (46%), *Clostridium perfringens* (16%), *Staphylococcus aureus* (12%), *Shigella* (11%), *Escherichia coli* (8%), *Bacillus cereus* (3%), and *Campylobacter* (2%). For this study, eFORS data provided from 1998 through 2006 shows a change in that proportion.

Descriptive Analysis

Table 11a shows the results of selected pathogens associated with food resulting in reported foodborne outbreaks. The top six pathogens are norovirus, all *Salmonella* (24.7%), *Clostridium perfringens* (10.6%), *Campylobacter* (6.1%), *Staphylococcus aureus* (4.6%), *Bacillus cereus* (4.1%), and *Escherichia coli* (2.1%). Of the total number of reported outbreaks, 41.7% (5,003) outbreaks had no identified etiology. Slightly more

than half of the etiological agents were confirmed; 4,113 outbreaks had an identified etiologic agent of a total of 6,987 or 58.9%. Tables 11b and 11c describe the breakdown of reported outbreaks from *Salmonella* species and other etiologic agents, respectively.

Table 11a.

Descriptive table of the number and percentage of outbreaks for selected etiological agents in the eFORS database, 1998-2006.

Identified etiologic agent (EA)	Total out-breaks	%	EA confirmed?	Number outbreaks confirmed	% of EA
Norovirus	2,789	23.2%	Yes	1,556	55.8%
			No	1,233	44.2
Other viral	97	0.8	Yes	7	7.7
			No	90	92.3
Hepatitis A	71	0.6	Yes	70	98.6
			No	1	1.4
Total *Salmonella*	1,227	10.2	Yes	1,058	86.2
			No	169	13.8
Other EAs	2,803	23.4	Yes	1,422	50.7
			No	1,381	49.3
Known totals	6,987	58.3	Yes	4,113	58.9
			No	2,874	41.1
Unknown EAs	5,003	41.7			
Total	11,990			6,987	58.3

Table 11b.

Descriptive table of the number and percentage of outbreaks for Salmonella *in the eFORS database, 1998-2006.*

Identified etiologic agent (EA)	Total outbreaks	%	EA confirmed?	Number outbreaks confirmed	% of EA
Salmonella Enteritidis	343	27.9%	Yes	319	93.0%
			No	24	7.0
Salmonella Typhimurium	150	12.2	Yes	143	95.3
			No	7	4.7
S. Heidelberg	96	7.8	Yes	88	91.7
			No	8	8.3
S. Newport	78	6.4	Yes	77	98.7
			No	1	1.3
Groups A, B, C1, C2, D1, E1, and L	51	4.2	Yes	35	68.6
			No	16	31.4
S. Javiana	28	2.3	Yes	26	92.9
			No	2	7.1
S. Montevideo	22	1.8	Yes	21	95.5
			No	1	4.6
S. Thompson	21	1.7	Yes	21	100
			No	0	0
S. Saintpaul	19	1.6	Yes	18	94.7
			No	1	5.3
S. Infantis	17	1.4	Yes	17	100
			No	0	0
S. Oranienburg	14	1.1	Yes	13	92.9
			No	1	7.1
I4,[5],12:i:-	4	0.3	Yes	4	100
			No	0	0
Other *Salmonella*	355	28.9	Yes	258	72.7
			No	96	27.3
Total	1,227	100	Yes	1,058	86.2
			No	169	13.8

Table 11c.

Descriptive table of the records of outbreaks for other etiologic agents in the eFORS database, 1998-2006.

Identified etiologic agent (EA)	Total outbreaks	%	EA confirmed?	Number outbreaks confirmed	% of EA
Toxins	445	3.7%	Yes	360	80.9%
			No	85	19.1
Clostridium perfringens	651	5.4	Yes	218	33.5
			No	433	66.5
Campylobacter spp.	167	1.4	Yes	134	80.2
			No	33	19.8
Escherichia coli	250	2.1	Yes	220	88.0
			No	30	12.0
Staphylococcus aureus	503	4.2	Yes	158	31.4
			No	345	68.6
Shigella spp.	120	1.0	Yes	105	87.5
			No	15	12.5
Vibrio spp.	92	0.8	Yes	50	54.4
			No	42	45.7
Bacillus cereus	458	3.8	Yes	66	14.4
			No	392	85.6
Cyclospora	21	0.2	Yes	19	90.5
			No	2	9.5
Listeria spp.	20	0.2	Yes	18	90.0
			No	2	10.0
Other Bacterial	76	0.6	Yes	74	97.4
			No	2	2.6
Total	2,803	23.4	Yes	1,422	50.7
			No	1,381	49.3

Norovirus appears to be the most common of the foodborne pathogens. From Table 11a, an outbreak where norovirus was implicated occurred 2.27 times more often

than *Salmonella*, 4.28 more often than *C. perfringens*, 5.37 more often than *S. aureus*, 6.09 more often than *B. cereus*, and 11.16 more often than *E. coli*. Yet the number of outbreaks confirmed place doubt in the strength of these numbers. Norovirus was confirmed in 55.8% of the outbreaks. The rest were presumed norovirus based on epidemiologic evidence not provided (Williams, 2008).

Only a proportion of the top bacterial agents were tested, and the evidence of confirmed positives was varied. For *Salmonella*, 86.2% and for *E. coli*, 88.0% of tested outbreaks respectively were confirmed. These two pathogens are common in products under inspection by the U.S. Department of Agriculture; therefore, aggressive testing and recall programs were likely to confirm a high number of cases and outbreaks. The other three pathogens are not tested as often and the confirmation rate is much lower; *C. perfringens*, 33.5%, *S. aureus*, 31.4% and *B. cereus,* 14.4%.

A determination of whether the food was identified was part of the data collected in eFORS. The number of times foods were determined were 6,876 out of 7,480 times, or 91.9%.

Most of the determined foods were identified, (80.3%). Of the outbreaks with an identified etiologic pathogen, the food product was identified in 5,935 outbreaks (79.3%) (Table 12a). Only 25 outbreaks (0.3%) from an identified food had no known etiological source. In some outbreaks, the number of identified foods outnumbered the number of determined foods, most likely due to multiple foods associated with the outbreak.

Table 12a.

Descriptive table of the number and percentage of food determined outbreaks for selected etiological agents in the eFORS database, 1998-2006.

Identified etiologic agent (EA)	Total out-breaks	%	Was food determined?	Number outbreaks w/ determined foods	% of EA
Norovirus	2,789	23.3%	Yes	2,400	86.1%
			No	389	13.9
Other viral	97	0.8	Yes	95	97.9
			No	2	2.1
Hepatitis A	71	0.6	Yes	68	95.8
			No	3	4.2
Total *Salmonella*	1,227	10.2	Yes	1,141	93.0
			No	86	7.0
Other EAs	2,803	23.4	Yes	2,718	97.0
			No	85	3.0
Known totals	6,987	58.3	Yes	6,422	91.9
			No	565	8.1
Unknown EAs	5,003	41.7			
Total	11,990			6,987	

Tables 12b and 12c describe the breakdown of foods determined outbreaks from *Salmonella* species and other etiologic agents, respectively.

Table 12b.

Descriptive table of the number and percentage of food determined outbreaks for Salmonella *in the eFORS database, 1998-2006.*

Identified etiologic agent (EA)	Total out-breaks	%	Was food deter-mined?	Number outbreaks w/ determined foods	% of EA
Salmonella Enteritidis	343	27.9%	Yes	316	92.1%
			No	27	7.9
Salmonella Typhimurium	150	12.2	Yes	133	88.7
			No	17	12.3
Other *Salmonella* spp.	734	59.8	Yes	692	94.3
			No	42	5.7
Total *Salmonella*	1,227	10.2	Yes	1,141	93.0
			No	86	7.0

Table 12c.

Descriptive table of the number and percentage of food determined outbreaks for other etiologic agents in the eFORS database, 1998-2006.

Identified etiologic agent (EA)	Total out-breaks	%	Was food determined?	Number outbreaks w/ determined foods	% of EA
Toxins	445	3.7%	Yes	445	100%
			No	0	0.0
Clostridium perfringens	651	5.4	Yes	640	98.3
			No	11	1.7
Campylobacter spp.	167	1.4	Yes	150	89.8
			No	17	10.2
Escherichia coli	250	2.1	Yes	233	93.2
			No	17	6.8
Staphylococcus aureus	503	4.2	Yes	498	99.0
			No	5	1.0
Shigella spp.	120	1.0	Yes	115	95.8
			No	5	4.2
Vibrio spp.	92	0.8	Yes	85	92.4
			No	7	7.6
Bacillus cereus	458	3.8	Yes	451	98.5
			No	7	1.5
Cyclospora	21	0.2	Yes	17	80.9
			No	4	19.1
Listeria spp.	20	0.2	Yes	18	90.0
			No	2	10.0
Other Bacterial	76	0.6	Yes	66	86.8
			No	10	13.2
Total	2,803	23.4	Yes	2,718	97.0
			No	85	3.0

The 12 groups of the Food Safety Research Consortium (FSRC) (Batz et al., 2004) categorized food types. These 12 groups include seafood, eggs, produce, beverages, dairy products, breads and bakery items, multi-ingredient or other combination products, game meat, beef, poultry, pork, and luncheon/ other combination ready to eat meat products. Tables 13 shows a summary of the known versus unknown etiologic agents and Table 14 show the summary breakdown of foods by known etiologic agents.

Table 13.

Summary of indicated Food Safety Research Consortium (FSRC) food types by etiologic agents in the eFORS database, 1998-2006.

FSRC Indicated Food types	Number Associated w/ Known Etiologic Agents	%	Number Associated w/ Unknown Etiologic Agents	%	Totals	%
Seafood	766	5.9%	312	2.4%	1,078	8.2%
Egg	96	0.7	27	0.2	123	0.9
Produce	1,293	9.9	481	3.7	1,774	13.6
Beverage	148	1.1	51	0.4	199	1.5
Dairy	198	1.5	94	0.7	292	2.2
Breads and Bakery	349	2.7	131	1.0	480	3.7
Multi-ingredient/ other	1,447	11.1	1,056	8.1	2,503	19.1
Game	11	0.1	0	0.0	11	0.1
Beef	371	2.8	212	1.6	583	4.5
Poultry	530	4.1	424	3.2	954	7.3
Pork	222	1.7	94	0.7	316	2.4
Luncheon/ other meats	111	0.9	55	0.4	166	1.3
Known Food Type Total	5,542	42.4	2,937	22.5	8,479	64.8
Unknown Food Type	2,539	19.4	2,066	15.8	4,605	35.2
Totals	8,081	61.8	5,003	38.2	13,084	100

Notes. Seafood included catfish, clams, crab, fish, lobster, mussels, octopus, oyster, salmon, scallops, seafood, shrimp, squid/calamari, sushi, tuna, and whale. Produce included alfalfa sprouts, asparagus, avocado, banana, herbs, broccoli, beets, beans, blueberries, celery, cantaloupe, cabbage, carrots, coleslaw, chutney, corn, cucumber, fruit, guacamole, gelatin, grape, lemon, lettuce, lime, melon, mushrooms, nuts, oil, eggplant, onions, parsley, pear, peas, pickles, peppers, pineapple, popcorn, potato, relish, rice, salad greens, salsa, spinach, squash, strawberries, tomato, vegetables, and watermelon. Beverages included

alcohol, cider, beverage, coffee, ice, juice, infant formula, lemonade, orange juice, punch, soda, tea, and water. Dairy included milk, cheese, ice cream, and butter.

Breads and Bakery included cake, bread, noodles, nachos, pancake, doughnut, macaroni, spaghetti, pasta, cookies, crackers, chips, cream puffs, and desserts. Multi-ingredient foods included buffet, burrito, candy, cerviche, cheeseburger, dips, dressings, sauces, dumpling, ethnic combinations, jello, lasagna, Mexican dishes, multiple, oriental dishes, other, pico de gallo, pizza, pudding, combination salads, sandwiches, soup, stew, taco, and tartar sauce. Game included alligator, rabbit, venison, guinea pig, and bear. Poultry included chicken, turkey, duck, and quail. Luncheon/other meats included deli, liver, lamb, meat, BBQ, hot dogs, and sausage.

The most common foods associated with reported outbreaks with a known etiologic agent were multi-ingredient, produce, and seafood, these representing 19.1%, 13.6% and 8.2% respectively (Table 13). Poultry and beef were also highly associated with outbreaks, 7.3%, and 4.5% respectively.

The association of food with an etiologic agent was more than half the total number of outbreaks. Known etiologic agents represented 61.8% of the total number of outbreaks. Yet 3.7% and 8.1% of the total produce and multi-ingredient categories of food types did not identify an etiologic agent, respectively.

Widdowson et al. (2005) found that norovirus was associated most often with salads, sandwiches and produce, that represented 56% of the norovirus outbreaks in which a food item was identified. In this study, norovirus was most associated with multiingredients products (which included salads and sandwiches) and produce (Table 14a). These two groups represent 64.8% of the norovirus outbreaks in which a food item

was identified. Records identified for sandwiches and salads are 61.1% of multi-ingredients products. In comparison to Widdowson et al.'s findings, this study found that for those three categories 51.2% of the norovirus outbreaks a food item was identified.

The category multi-ingredients of all the identified food types which contained combinations of produce, meat, seafood, breads, and the other food categories, was significant ($p<0.05$) for most of the pathogens (Tables 14a,b,c,d). Produce alone was significant for norovirus ($p<0.10$) (Table 14a), *Shigella* ($p<0.05$) (Table 14d), *B. cereus* ($p<0.05$) (Table 14d), Hepatitis A ($p<0.05$) (Table 14d), and other viral ($p<0.05$) (Table 14a). The number of outbreaks of known etiologies but not known food type when added into the total of identified food types was significant ($p<0.05$) in almost all cases.

Norovirus was implicated with food 7.7 times the number of outbreaks it was not implicated (Table 14). Yet, half the times norovirus was implicated there was no reason listed.

Table 14a.

Descriptive summary of indicated FSRC food types for selected etiologic agents in the eFORS database, 1998-2006.

FSRC food type	Norovirus	% of EA	Other viral	% of EA	Hepatitis A	% of EA	Total *Salmonella*	% of EA	Total other EAs	% of EA	Total	% of kft[a]
Seafood	93	5.2%	5	9.3%	6	15.8%	44	4.5%	618	23.0%	766	13.8%
Egg	7	0.4	0	0.0	0	0.0	86	8.9	3	0.1	96	1.7
Produce	534[b]	29.8	17[c]	31.5	19	50.0	177	18.2	546	20.3	1,293	23.3
Beverage	108	6.0	6	11.1	3	7.9	13	1.3	18	0.7	148	2.6
Dairy	66	3.7	1	1.9	1	2.6	47	4.8	83	3.1	198	3.6
Breads and Bakery	156	8.7	8	14.8	0	0.0	91	9.4	94	3.5	349	6.3
Multi-ingred-ient/other	628[c]	35.0	13	24.1	8	21.01	230	23.7	568	21.1	1,447	26.1
Game	2	0.1	0	0.0	0	0.0	0	0.0	9	0.3	11	0.2
Beef	68	3.8	1	1.9	0	0.0	48	4.9	254	9.5	371	6.7
Poultry	86	4.8	1	1.9	0	0.0	163	16.8	280	10.4	530	9.6
Pork	35	2.00	0	0.0	0	0.0	50	5.2	137	5.1	222	4.0
Luncheon/ other meats	9	0.5	2	3.7	1	2.6	22	2.3	67	2.5	101	1.8
		% for EA		% for EA		% for EA		% for EA		% for EA		% for kft
Known Food Type Total	1,792	55.5	54	49.1	38	50.7	971	69.5	2,687	82.2	5,542	68.6
Unknown FT	1,438[c]	44.5	56[c]	50.9	37	49.3	426	30.5	582	17.8	2,539	31.4
		% total		% total		% total		% total		% total		% total
Totals	3,230	40.0	110	1.4	75	0.9	1,397	17.3	3,269	40.5	8,081	100

Notes. [a]Kft= known food type; [b]p<0.10; [c]p<0.05.

Table 14b.

Descriptive summary of indicated FSRC food types for Salmonella *in the eFORS database, 1998-2006.*

FSRC food type (FT)	*Salmonella* Enteritidis	% of EA	*Salmonella* Typhimurium	% of EA	Other *Salmonella* spp.	% of EA	Total	% of known food type
Seafood	23	5.6%	5	3.1%	16	2.0%	44	3.2%
Egg	60	14.6	2	1.2	24	2.9	86	6.2
Produce	37	9.0	11	6.7	129	15.7	177	12.7
Beverage	2	0.5	2	1.2	9	1.1	13	0.9
Dairy	18	4.4	14	8.5	15	1.8	47	3.4
Breads and Bakery	32	0.4	7	7.8	52	4.3	91	6.3
Multi-ingredient/ other	71[a]	0.9	16	0.2	143[a]	1.8	230	2.9
Game	0	0.0	0	0.0	0	0.0	0	0.0
Beef	10	2.4	6	3.7	32	3.9	48	3.4
Poultry	28	6.8	22[a]	13.4	113	13.8	163	11.7
Pork	7	1.7	9	5.5	34	4.1	50	3.6
Luncheon/ other meats	4	1.0	4	2.4	14	1.7	22	1.6
		% for EA		% for EA		% for EA		% of known food type
Known FT Total	292	71.1	98	59.8	581	70.7	971	69.5
Unknown FT	119[a]	29.0	66[a]	40.2	241[a]	29.3	426	30.5
		% of total		% of total		% of total		% of total
Totals	411	29.4	164	11.7	822	58.8	1,397	100

Notes. [a] $p<0.05$.

Table 14c.

Descriptive summary of indicated FSRC food types for select etiologic agents in the eFORS database, 1998-2006.

FSRC food type (FT)	*C. perfringens*	% of EA	*Campy.* spp.	% of EA	*Escherichia coli*	% of EA	Toxins	% of EA	Other EAs	% of EA	Totals	% of kft[a]
Seafood	26	3.3%	5	2.6%	3	1.1%	422[b]	96.4%	162	10.4%	618	18.9%
Egg	1	0.1	0	0.0	0	0.0	0	0.0	2	0.1	3	0.1
Produce	140	17.5	23	12.1	64[b]	22.9	8	1.8	311	19.9	546	16.7
Beverage	4	0.5	1	0.5	4	1.4	0	0.0	9	0.6	18	0.6
Dairy	3	0.4	46	24.2	12	4.3	1	0.2	22	1.4	83	2.5
Breads and Bakery	20	2.5	3	1.6	12	4.3	6	1.4	58	3.7	58	2.9
Multi-ingredient/ other	206[b]	25.7	21	11.1	17	6.1	0	0.0	318	20.4	568	17.4
Game	0	0.0	0	0.0	1	0.4	0	0.0	8	0.5	9	0.3
Beef	106	13.2	5	2.6	69[b]	24.6	1	0.2	74	4.7	254	7.8
Poultry	109	13.6	27[b]	14.2	2	0.7	0	0.0	141	9.0	280	8.6
Pork	41	5.1	3	1.6	3	1.1	0	0.0	90	5.8	137	4.2
Luncheon/ other meats	21	2.6	6	3.2	5	1.8	0	0.0	45	2.9	67	2.1
		% for EA		% for EA		% for EA		% for EA		% for EA		% for kft
Known FT Total	677	84.5	140	73.7	192	68.6	438	100	1,240	79.5	2,687	82.2
Unknown FT	124[b]	15.5	50[b]	26.3	88[b]	31.4	0	0.0	321	20.6	582	17.8
		% of total		% of total		% of total		% of total		% of total		% of total
Totals	801	24.5	190	5.8	280	8.6	438	13.4	1,560	47.7	3,269	100

Notes: [a]=kft= known food type; [b]$p<0.05$.

Note.

Other pathogens include *Staphylococcus aureus*, *Shigella* spp., *Bacillus cereus, Vibrio* spp., Cyclospora, *Brucella spp., Calicivirus sapovirus, Cryptosporidium parvun, Enterobacter cloacae, Giardia lamblia, Streptococcus* Group A, *Trichinella spiralis, Yersinia enterocolitica,* and "other bacterial

Table 14d.

Descriptive summary of indicated FSRC food types for select other etiologic agents in the eFORS database, 1998-2006.

FSRC food type (FT)	*B. cereus*	% of EA	*Shigella* spp.	% of EA	Hepatitis A	% of EA
Seafood	15	3.7%	6	7.0%	6	15.8%
Egg	0	0.0	0	0.0	0	0.0
Produce	160[b]	39.0	36[b]	41.9	19[b]	50.0
Beverage	2	0.5	3	3.5	3	7.9
Dairy	4	1.0	1	1.2	1	2.6
Breads and Bakery	19	4.6	5	5.8	0	0.0
Multi-ingredient/ other	107	26.1	20	23.3	8	21.1
Game	0	0.0	0	0.0	0	0.0
Beef	27	6.6	5	5.8	0	0.0
Poultry	62	15.1	6	7.0	0	0.0
Pork	6	1.5	1	1.2	0	0.0
Luncheon/ other meats	8	2.0	3	3.5	1	2.6
		% for EA		% for EA		% for EA
Known FT Total	410	76.1	86	61.0	38	50.7
Unknown FT	129[b]	23.9	55	39.0	37[b]	49.3
		% of total[c]		% of total[c]		% of total[c]
Totals	539	16.5	141	4.3	75	2.3

Notes: [a]=kft= known food type; [b]$p<0.05$; c from Table 14c.

The same could be said for *Salmonella* (13.0 times) and most of the other bacterial pathogens. Epidemiologic and statistical evidence was reason for implication for norovirus, *Salmonella, C. perfringens, Campylobacter* spp., *S. aureus*, and *B. cereus* (Table 15). Laboratory evidence was only as important as compelling evidence for *Salmonella, C. perfringens, S. aureus,* and *B. cereus* (Table 15). No data were collected in eFORS in association with foods for other viruses or Hepatitis A.

Widdowson et al. (2005) found that 48% of norovirus outbreaks implicated a food handler but only 20% of outbreaks that involved a bacterial pathogen. In this study, norovirus was found associated with a food handler in only 28.2% of the outbreaks (Table 16). The records for the top five bacterial pathogens totaled 3,089 outbreaks, of that 228 implicated a food worker, representing 7.4%.

The records of outbreaks listed in Table 16 indicated far less certainty of the actual agents causing the outbreaks. Of those positive results, associating a food worker with norovirus, only 274 (34.8%) was associated with laboratory confirmation. The other 65.2% were based on epidemiologic evidence or prior experience of the evaluating health official. For association of a food worker with a bacterial outbreak, the top five pathogens found 154 (67.5%) outbreaks associated with laboratory evidence.

Table 15a.

Summary description of implicated food with each etiologic agent in the eFORS database, 1998-2006.

	Food Implicated	
Etiologic Agent (EA)	Yes	No
Norovirus	3,038	393
Total *Salmonella*	1,420	82
Total	4,458	475
% of Total	90.4	9.6

Table 15b.

Summary description of positively implicated food with each etiologic agent in the eFORS database, 1998-2006.

	How Implicated					
Etiologic Agent (EA)	Epi Evidence	Lab Evi-dence	Compel-ling Support	Other Data	Prior Exper-ience	None listed
	Direct Evidence		Indirect Evidence		Suspect or no Evidence	
Norovirus	911	22	439	2	101	1,563
Total *Salmonella*	336	141	292	28	63	560
Total	1,925	561	1,410	54	405	3,256
% of Total	43.18	12.58	31.63	1.21	9.08	73.04

Table 16a.

Summary description of implicated food worker with etiologic agents in the eFORS database, 1998-2006.

Etiologic Agent (EA)	Food handlers Implicated	
	Yes	No
Norovirus	787	2,002
Total *Salmonella*	127	1,100
Other viral	14	83
Total N/S*	914	3,102
Total N/OV	801	2,085

Notes. * N/S = Norovirus plus Salmonella; N/OV norovirus plus Other Viral

Table 16b.

Summary description of positively implicated food worker with etiologic agents in the eFORS database, 1998-2006.

Etiologic Agent (EA)	How Implicated			
	Lab & Epi evidence	Lab only	Epi only	Prior Experience
	Direct evidence		Indirect Evidence	Suspect Evidence
Norovirus	228	46	346	167
Total *Salmonella*	75	32	12	8
Other viral	1	1	7	5
Total N/S*	303	78	358	175
Total N/OV	229	47	353	172

Notes. * N/S = Norovirus plus Salmonella; N/OV norovirus plus Other Viral

Norovirus was isolated from food only 19 times out of 1,965 outbreaks (Table 17). A majority of the isolates came from patient specimens (84.7%). Norovirus isolated from the food worker represent 14.3% of the outbreaks. However, the collected evidence does not indicate whether the same noroviral strain was isolated from the food handler and the food or patient.

Table 17.

Summary description of the number of outbreaks attributed to a source of evidence for implicating food workers with etiologic agents in the eFORS database, 1998-2006.

	Location of Etiologic Agent Isolation				
Etiologic Agent	Patient Specimens	Food Specimen	Environmental Specimen	Food Worker Specimen	Totals
Norovirus	1,664	19	2	280	1,965
%	84.7%	0.1	0.0	14.3	100
Other viral	12	0	0	2	14
%	85.7	0.0	0.0	14.3	100
Total *Salmonella*	1,101	170	37	170	1,478
%	74.5	11.5	2.5	11.5	100
Other EAs	992	565	31	108	1,696
%	58.5	33.3	1.8	6.4	100
Totals	3,769	754	70	560	5,153
%	73.1	14.6	1.4	10.9	100

Bacterial pathogens show a different picture than that of norovirus. The top five bacterial pathogens were isolated from food only 570 times out of 2,503 or 22.8% (Table 18). A majority of the outbreak-associated isolates came from patient specimens (66.4%). Bacteria isolated from

food workers only 8.6% of the outbreaks. Here also, the collected evidence does not indicate whether the same bacterial strains were isolated from the food handler and the food or patient.

The contributing factors that define direct association of outbreaks with food handlers showed a major preference for handling by infected individuals, especially for norovirus, and bare handling by those same persons (Table 18). Contamination or transmission of etiologic agents when the food handlers were gloved was believed less responsible for outbreaks. Intentional or accidental toxic substance added (C2 or C3 respectively) or excessive addition of contaminated ingredients becoming toxic (C4) received no responses.

Contamination of fomites, equipment surfaces, and unclean utensils was the attributed preference for indirect noroviral transmittal. Raw products of animal origin were not considered a primary concern that is reflected in the results of the food attribution (Table 13). For indirect *Salmonella* transmittal though, attribution to both raw ingredients of animal origin and contamination of fomites, equipment surfaces, and unclean utensils was paramount. When there was no association to food handlers, contamination of raw ingredients and the ingestion of these products were identified as the cause of illness.

Table 18.

Summary of number of outbreaks by contributing factors for transmittal of norovirus, Salmonella *and other viral etiologies with food handlers in the eFORS database, 1998-2006.*

Food handler Category	Contributing Factor	Noro-virus	%	*Salmon-ella*	%	Other viruses	%
Outbreak directly associated with food handler	Handling by infected person (C12)	772	46.3%	117	11.3 %	42	36.8%
	Bare handed contact- food handler with RTE food (C10)	437	26.2	114	11.1	23	20.2
	Glove handed contact - food handler with RTE food (C11)	126	7.6	26	2.5	5	4.4
Outbreak indirectly associated with food handler	Inadequate cleaning of utensils/ equipment (C13)	106	6.4	168	16.3	8	7.0
	Cross contamination from raw ingredient of animal origin (C9)	22	1.3	179	17.3	5	4.4
	Storage in contaminated environment (C14)	16	1.0	40	3.9	0	0.0
Outbreak not associated with food handler	Ingestion contaminated raw ingredient (C7)	45	2.7	95	9.2	9	7.9
	Toxic substance naturally occurring (C1)	0	0.0	2	0.2	0	0.0
	Contaminated raw ingredient (C6)	45	2.7	226	21.9	8	7.0
	Toxic container or pipes (C5) (%)	1	0.1	4	0.4	1	0.9
	Food from polluted source (C8)	13	0.8	6	0.6	1	0.9
	Other source (C15)	83	5.0	55	5.3	12	10.5

Seasonal patterns for norovirus and other foodborne pathogens do not show similarity. In order to show monthly patterns from differing etiologic agents on the same scale, a basis of standard had to be devised. Using the percent change from the annual average required calculating the mean number of outbreaks due to specific etiologic agents listed in Table 11 and then the percent difference of those actual outbreaks per month from annual mean. The results are presented in Figures 2, 3a, and 3b.

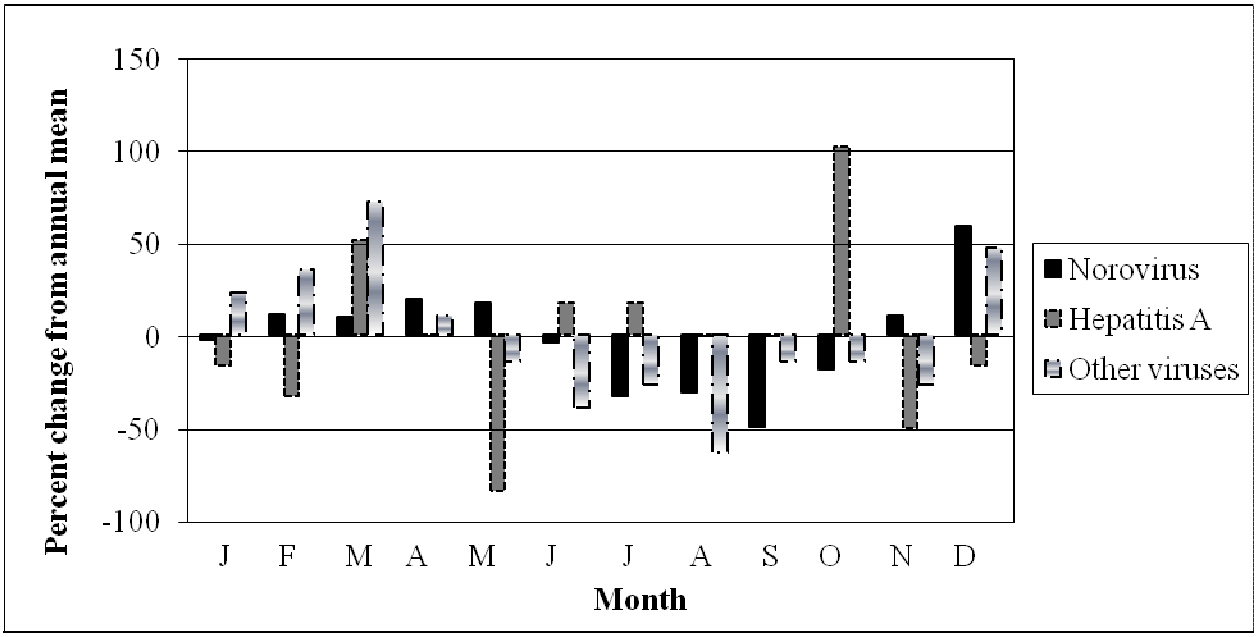

Figure 2. Comparison of monthly outbreak patterns between norovirus with other viruses from the eFORS database, 1998-2006.

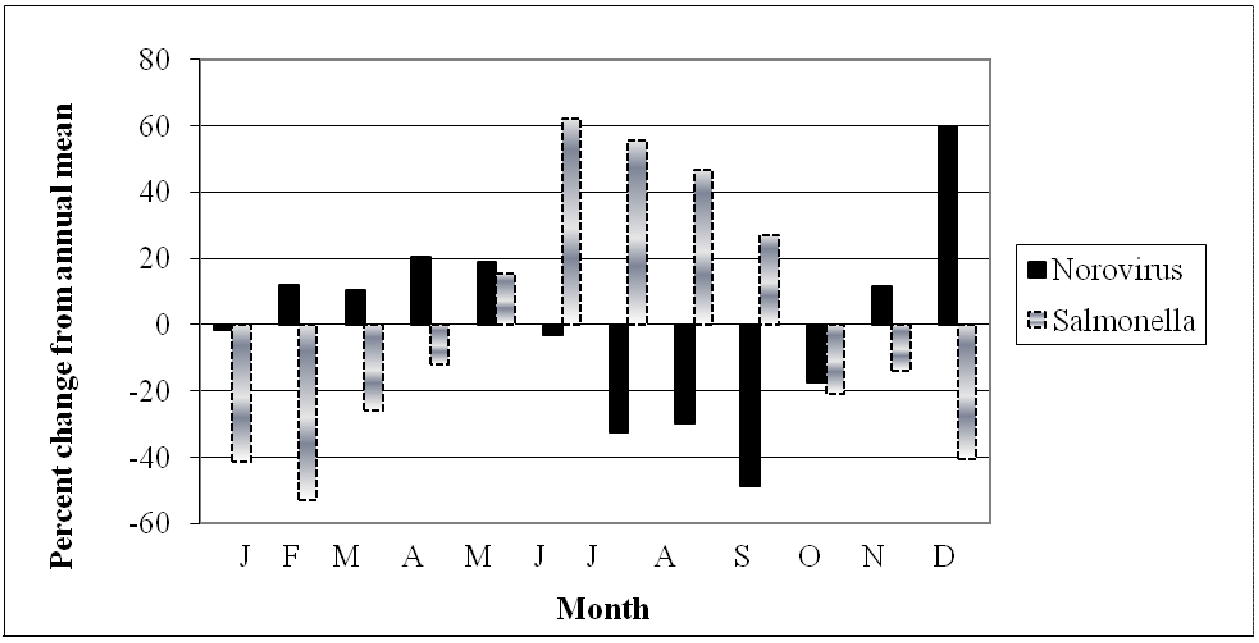

Figure 3a. Comparison of monthly outbreak patterns between norovirus and *Salmonella* from the eFORS database, 1998-2006.

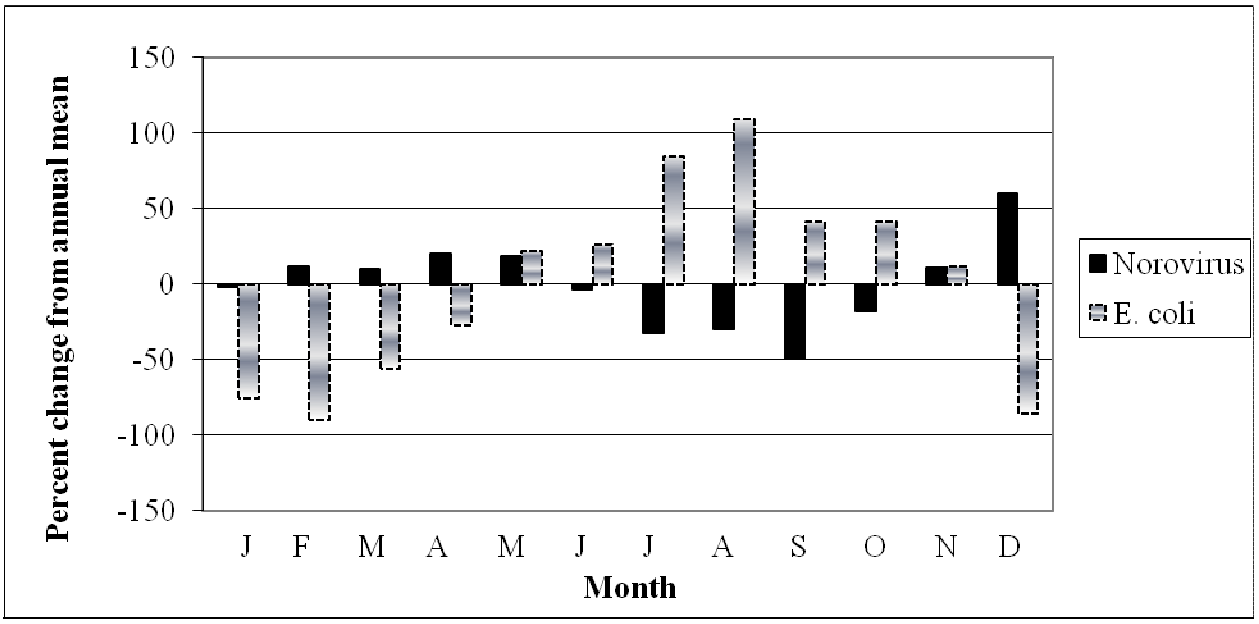

Figure 3b. Comparison of monthly outbreak patterns between norovirus with *E. coli* from the eFORS database, 1998-2006.

In Figure 2, 3a, and 3b, the results showed norovirus up to 25 percent higher from its annual average in the cold months of January through May which then decreased in the hot months (September, $p<0.10$) until November and December ($p<0.05$). In Figure 2, the other viral etiologic agents did not exhibit a consistent pattern indicating that a seasonal variation trend could not be derived from this data. In Figures 3a and 3b, both *Salmonella* and *E. coli* that are a high proportion of all outbreaks, gave the opposite pattern from norovirus; the percent bacteria outbreaks were low in cold months while high in the warm summer months. Other etiologic agents showed a flat pattern with little deviation indicating no seasonal effects.

Research Questions

The number of outbreaks for each etiologic agent varied greatly and the associations had to place on an equal basis for comparison purposes. Before examining the individual research questions that break the data into evidential subgroups, it was necessary to determine whether food overall was associated with norovirus outbreaks by reviewing the number of norovirus-associated outbreaks that had positive and negative indicated food responses were in the same proportion as those of the most common foodborne pathogen *Salmonella* with food (Table 15a). *Salmonella* was used as the standard for food associated outbreaks given its known history and source of contamination or cross contamination emanating from the food source. From the results below, there appeared to be no similarity between proportion of the number of food implicated outbreaks from norovirus and those from *Salmonella*. The overall relationship showed norovirus had an odds ratio of 0.45 (95% CL 0.3490- 0.5710) with *Salmonella* when compared to the total percentage of food identified outbreaks and was significant (Table 19).

Table 19.

Comparison of the proportion of outbreaks associated with food for norovirus and Salmonella *to their total number of outbreaks*.

	Etiologic Agent		
Food Associated	Norovirus	*Salmonella*	total
Yes	3,038	1,420	4,458
Row %	68.1	31.9	100.0
Col %	88.5	94.5	90.4
No	393	82	475
Row %	82.7	17.3	100.0
Col %	11.5	5.5	9.6
TOTAL	3,431	1,502	4,933
Row %	69.6	30.4	100.0
Col %	100.0	100.0	100.0

Notes. p=0.00, $\chi^2 = 43.1466$.

Research Question 1. Foods positively and directly associated with outbreaks were those that were based on laboratory and epidemiologic evidence (Table 15b). As a portion of the overall positively associated number of outbreaks to food, those norovirus outbreaks directly associated (66.2%) when compared to outbreaks directly associated food with *Salmonella* (33.8%) had a ratio of 1.96 and an odds ratio of 0.87 (95% CL 0.7660- 1.0023) with *Salmonella* when compared to their total proportion of food implicated outbreaks (Table 20). In this case, it appeared that the proportion of outbreaks directly associated with foods caused by norovirus were significantly different from those associated with food caused by *Salmonella*. Because no other virus results were found, no viral comparison analyses were done.

Table 20.

Comparison of the proportion of outbreaks directly associated with food for norovirus and Salmonella *to their total number of outbreaks*.

	Etiologic Agent		
Food Associated	Norovirus	*Salmonella*	total
Yes	933	477	1,410
Row %	66.2	33.8	100.0
Col %	30.7	33.6	31.6
No	2,105	943	3,048
Row %	69.1	30.9	100.0
Col %	69.3	66.4	68.4
TOTAL	3,038	1,420	4,458
Row %	68.1	31.9	100.0
Col %	100.0	100.0	100.0

Notes. p=0.05, $\chi^2 = 3.7131$.

The next major question was whether food handlers overall were associated with norovirus outbreaks in comparison to *Salmonella*. To determine this, it was necessary to see whether the number of norovirus-associated outbreaks that had positive and negative indicated food handler responses were in the same proportion as those of *Salmonella* with food handlers. There was a significant association between norovirus and *Salmonella* with food handlers. The overall relationship showed norovirus had an odds ratio of 3.40 (95% CL 2.7839 - 4.1643) when compared to the proportion of food handler identified *Salmonella* outbreaks (Table 21a).

Table 21a.

Comparison of the proportion of outbreaks associated with food handlers for norovirus and Salmonella *to their total number of outbreaks*.

	Etiologic Agent		
Food Handler Associated	Norovirus	*Salmonella*	Total
Yes	787	127	914
Row %	86.1	13.9	100.0
Col %	28.2	10.4	22.8
No	2,002	1,100	3,102
Row %	64.5	35.5	100.0
Col %	71.8	89.6	77.2
TOTAL	2,789	1,227	4,016
Row %	69.4	30.6	100.0
Col %	100.0	100.0	100.0

Notes. p=0.00; $\chi^2 = 154.7494$.

It was also important to determine whether food handlers overall with norovirus outbreaks were similar in comparison to other viruses detected. The overall proportion showed norovirus had an odds ratio of 2.33 (95% CL 1.3150 – 4.1304) when compared to food handler identified other viral outbreaks and was considered significant (Table 21b).

Table 21b.

Comparison of the proportion of outbreaks associated with food handlers for norovirus and other viruses to their total number of outbreaks.

	Etiologic Agent		
Food handler Associated	Norovirus	Other Viral	Total
Yes	787	14	801
Row %	98.3	1.7	100.0
Col %	28.2	14.4	27.8
No	2,002	83	2,085
Row %	96.0	4.0	100.0
Col %	71.8	85.6	72.2
TOTAL	2,789	97	2,886
Row %	96.6	3.4	100.0
Col %	100.0	100.0	100.0

Notes. p=0.00; χ^2 = 8.8837.

Research Question 2.

Food handlers directly associated with outbreaks were those that were based on laboratory and epidemiologic evidence. Food handler associated norovirus outbreaks (71.9%) when compared to food handler associated *Salmonella* outbreaks (28.1%) had a ratio of 2.56. When compared to the proportion of food handler identified outbreaks norovirus had an odds ratio of 0.10 (95% CL 0.0606- 0.1645) with *Salmonella* (Table 22a). In this case, food handlers in outbreaks caused by norovirus were significantly different from *Salmonella*. Norovirus (99.3%) was not significantly different from outbreaks from other viruses (0.07%) with food handlers with a high ratio of 1418.57 and an odds ratio of 3.20 (95% CL 0.7121 - 14.4220) with other viral agents when compared to their proportion of outbreaks (Table 22b).

Table 22a.

Comparison of the proportion of outbreaks directly associated with food handlers for norovirus and Salmonella *to their total number of outbreaks*.

	Etiologic Agent		
Food Worker Associated	Norovirus	*Salmonella*	Total
Yes	274	107	381
Row %	71.9	28.1	100.0
Col %	34.8	84.3	41.7
No	513	20	533
Row %	96.2	3.8	100.0
Col %	65.2	15.7	58.3
TOTAL	787	127	914
Row %	86.1	13.9	100.0
Col %	100.0	100.0	100.0

Notes. p=0.00; $\chi^2 = 109.9418$.

Table 22b.

Comparison of the proportion of outbreaks directly associated with food handlers for norovirus and other viruses to their total number of outbreaks.

	Etiologic Agent		
Food Worker Associated	Norovirus	Other Viral	Total
Yes	274	2	276
Row %	99.3	0.7	100.0
Col %	34.8	14.3	34.5
No	513	12	525
Row %	97.7	2.3	100.0
Col %	65.2	85.7	65.5
TOTAL	787	14	801
Row %	98.3	1.7	100.0
Col %	100.0	100.0	100.0

Notes. p=0.11; $\chi^2 = 2.5671$.

Research Question 3.

Foods indirectly associated with outbreaks were those that were based on statistical or epidemiologic evidence but no laboratory results. Food associated indirectly with norovirus outbreaks (9.9%) when compared to food indirectly associated *Salmonella* outbreaks (22.6%) had a ratio of 0.44. When compared to the proportion of outbreaks, norovirus had an odds ratio of 0.58 (95% CL 0.4973 – 0.6852) with *Salmonella* (Table 23). In this case, foods in outbreaks caused by norovirus were significantly different from the association with outbreaks caused by *Salmonella*.

Table 23.

Comparison of the proportion of outbreaks indirectly associated with food for norovirus and Salmonella to their total number of outbreaks.

	Etiologic Agent		
Food Associated	Norovirus	*Salmonella*	Total
Yes	441	320	761
Row %	58.0	42.0	100.0
Col %	14.5	22.5	17.1
No	2,597	1,100	3,697
Row %	70.2	29.8	100.0
Col %	85.5	77.5	82.9
TOTAL	3,038	1,420	4,458
Row %	68.1	31.9	100.0
Col %	100.0	100.0	100.0

Notes. p= 0.00; $\chi^2 = 43.9573$.

Research Question 4.

Food handlers indirectly associated with outbreaks were those that were based on laboratory and epidemiologic evidence. Food handler associated norovirus outbreaks (59.0%) when compared to the proportion of similar *Salmonella* outbreaks (41.0%), had a ratio of 1.44. When compared to their total number of outbreaks norovirus had a significant odds ratio of 7.52 (95% CL 4.0812 – 13.8522) with *Salmonella* (Table 24a).

Food handlers indirectly associated norovirus outbreaks (97.9%) when compared to similar outbreaks from other viral agents (2.1%), had a ratio of 46.6 but an insignificant odds ratio of 0.78 (95% CL 0.2726– 2.2580) with viral agents when compared to the proportion of outbreaks (Table 24b). Norovirus was not significantly different from other viruses to outbreaks with an indirect association by food handlers.

Table 24a.

Comparison of the proportion of outbreaks indirectly associated with food workers for norovirus and Salmonella *to their total number of outbreaks*.

	Etiologic Agent		
Food Worker Associated	Norovirus	*Salmonella*	Total
Yes	346	12	358
Row %	96.6	3.4	100.0
Col %	44.0	9.4	39.2
No	441	115	556
Row %	79.3	20.7	100.0
Col %	56.0	90.6	60.8
TOTAL	787	127	914
Row %	86.1	13.9	100.0
Col %	100.0	100.0	100.0

Notes. p= 0.00; $\chi^2 = 54.6761$.

Table 24b.

Comparison of the proportion of outbreaks indirectly associated with food workers for norovirus and Salmonella *to their total number of outbreaks.*

	Etiologic Agent		
Food Worker Associated	Norovirus	Other Viral	Total
Yes	346	7	353
Row %	98.0	2.0	100.0
Col %	44.0	50.0	44.1
No	441	7	448
Row %	98.4	1.6	100.0
Col %	56.0	50.0	55.9
TOTAL	787	14	801
Row %	98.3	1.7	100.0
Col %	100.0	100.0	100.0

Notes. p= 0.65; $\chi^2 = 0.2033$.

Research Question 5. Other suspected but not validated evidence associated with outbreaks was those based on presumptive evidence but neither laboratory or epidemiologic evidence. These types of norovirus outbreaks (74.4%) when compared to similar *Salmonella* outbreaks (25.6%), had a ratio of 2.9 and a significant odds ratio 1.30 (95% CL 1.1564 - 1.4701) with *Salmonella* when compared to their proportion of outbreaks (Table 24).

Table 25.
Comparison of the proportion of outbreaks suspected associated with food and food workers for norovirus and Salmonella *to their total number of outbreaks*.

	Etiologic Agent		
Other Association	Norovirus	*Salmonella*	Total
Yes	1,831	631	2,462
Row %	74.4	25.6	100.0
Col %	47.9	41.3	46.0
No	1,994	896	2,890
Row %	69.0	31.0	100.0
Col %	52.1	58.7	54.0
TOTAL	3,825	1,527	5,352
Row %	71.5	28.5	100.0
Col %	100.0	100.0	100.0

Notes. p= 0.00; $\chi^2 = 18.8282$.

Research Question 6: The overall association of contributing factors was very strong with the source of evidence for the determination of the cause of the norovirus (Table 26). In this case, food workers who were determined by the epidemiologist or health official to be the only the direct source of the outbreak were based on laboratory and epidemiologic evidence was significant. Epidemiologic evidence and the perceived likelihood of the source by the health official were also strongly associated with food worker contributing factors. However, laboratory identification was not sufficient to be directly associated to the outbreak. The comparison of classification of indirect association with a food handler to suspect association was not significant. The comparison of laboratory evidence alone or suspected link with indirect or no association to the food worker was significant respectively. These additional analyses indicate that health officials consider food workers the major source of food contamination leading to outbreaks where the source of the outbreak was identified.

Table 26.

Comparison of outbreak association of food workers with contributing factors to norovirus outbreaks.

	Implication Justification					
Outbreak Association	Lab & Epi Evidence	Lab Evidence	Epi Evidence	Likely Source	Totals	p Values
Outbreak directly associated with food handler	476 27.9%	91 5.3	570 33.4	246 14.4	1,383 81.0	0.03
Outbreak indirectly associated with food handler	66 3.9%	28 1.6	52 3.1	39 2.3	185 10.9	0.71
Outbreak suspected associated with food handler	44 2.6%	23 1.3	34 2	38 2.2	139 8.1	0.45
Totals	586 34.4%	142 8.32	656 38.5	323 18.9	1,707 100	

Notes: Likelihood Ratio $p < 0.01$; $\chi^2 = 45.340$.

Yet the additional evidence compiled does not provide strong supporting documentation. Of those etiologic agents identified, 2,874 out of 6,987 outbreaks (41.1%) were not confirmed (table 11a). In addition, only 58.9% of all outbreaks were identified which leaves 34.3% of all outbreaks confirmed. Of the identified etiologic agents, 15.4% came from food (table 17). The majority, 73.1%, came from patient specimens but not necessarily associated with the food or with the food worker. In fact, 10.9% were isolated from food workers but do not necessarily confirm that the pathogen isolated was related to the patient or the food. The information is not apparent in the eFORS records.

For norovirus, the evidence is even more precarious. Norovirus was credited as the cause of most outbreaks. Only those norovirus associated outbreaks, 1,233 out of 2,789 outbreaks

(44.2%) were not confirmed (table 11a). For those norovirus outbreaks that were confirmed (55.8%), norovirus outbreaks were identified were confirmed in 13.0% of all outbreaks. Of the identified norovirus sources, barely 19 outbreaks (0.10%) were associated with food (table 17). The majority, 1,664, came from patient specimens (84.7%) but not necessarily associated with the food or with the food worker. In fact, 14.3% were isolated from food workers but do not necessarily confirm that the pathogen isolated was related to the patient or the food.

The analysis was difficult to understand given the assumptions. It appeared that interpretations could give differing conclusions. Chapter 5 discusses these results against other researcher's understandings and analyses.

CHAPTER 5:

DISCUSSION

Introduction

Widdowson et al. (2005) reported that norovirus confirmed outbreaks increased from 11 in 1996 to 164 in 2000 from data in the National Foodborne Outbreak Reporting System. Between 1998 and 2000, norovirus confirmed outbreaks accounted for 27% of all reported outbreaks with a determined cause. Mead et al. (1999) estimated that such reports represent approximately 60% of reported illnesses.

Where information provided to the CDC was complete, Widdowson et al. (2005) reported foodborne associated outbreaks from norovirus were significantly larger than outbreaks of bacterial cause. Of the known foodborne bacterial causes, outbreaks attributed to *Salmonella* (46%), *Clostridium perfringens* (16%), *Staphylococcus aureus* (12%), *Shigella* (11%), *Escherichia coli* (8%), *Bacillus cereus* (3%), and *Campylobacter* (2%) constituted the largest numbers. Comparisons of the various etiologic agents were not made and difficult to put into context because of varying reporting requirements. Unless there is an unusual situation or a unique set of circumstances, food attribution to an etiologic agent was made based on an assumption mainly through associated evidence.

Because of long proven methodologies in the isolation and identification of bacteria and genetic serology determination, outbreaks from bacterial pathogens were always considered easier to detect. Recent advances in isolation of norovirus from foods or patients for controlled experiments meant that determinations of norovirus attribution to food could be made (Estes et al., 2000). Whether the same criteria for attribution of food and food workers to norovirus

outbreaks when compared to those of bacterial etiology can be made must be examined in light of the results of this study.

Descriptive Analysis

The data reported in eFORS showed that the number of norovirus outbreaks accounts for 39.9% of all outbreaks attributed to identified etiologic agents and 23.26% of all outbreaks that include those of unknown etiologic agents. The general information for each etiologic agent was generally similar, yet fewer outbreaks attributed to norovirus were confirmed (55.8%) than those attributed to bacteria (60.9%). When it comes to food association, norovirus has a very high determination rate (99.9%) while those bacterial etiologic agents had a slightly smaller determination rate relative to food (95.8%).

Etiologic agents were identified in 61.8% of the outbreaks and most often with multi-ingredient foods, produce, and seafood. Norovirus were most identified with multiingredient foods and produce but not seafood even though the literature pointed to oysters quite often. Bacterial etiologic agents were most associated with multi-ingredient foods. This suggested products that required assembly or handling by food workers. Such a conclusion, though, can be questioned because the number of outbreaks with no etiologic association was 31.4%.

Another assumption that can be questioned is that norovirus was associated with food handlers. Of the number of norovirus outbreaks, only in 28.2% were food handlers implicated. In addition, of that number, direct laboratory evidence (with and without epidemiologic evidence) was seen in only 34.8% of those outbreaks. Food workers were presumed to be associated with norovirus with no further evidence in 21.2% of the outbreaks.

These results compared norovirus to the typical bacterial etiologic agent, *Salmonella*, a well-known intestinal pathogen that was associated with animals, in 11.6% of the outbreaks. Moreover, of that number, direct laboratory evidence (with and without epidemiologic evidence) was seen in 84.3% of the outbreaks. Food workers were presumed to be associated with *Salmonella* with no further evidence in only 6.3% of those outbreaks.

Norovirus was isolated from patients associated with the outbreaks in 84.7% of the times. While this is strong epidemiologic evidence, it was still only indirect support. Norovirus identified in food workers occurred 14.3% of the times. Moreover, norovirus was found in food only 0.1% of the outbreaks.

Salmonella was isolated mostly from patients associated with the outbreaks in 74.5% of the times. *Salmonella* was more often identified in food workers (11.5%) than in foods (2.5%).

The contributing factors assigned to contamination of foods by food workers for each etiologic agent also provided different implications. Foods were considered directly contaminated with norovirus (80.2%) mainly by infected food workers. Foods were contaminated with *Salmonella,* on the other hand, mostly by indirect means (37.5%) by cross-contamination from raw ingredients or dirty utensils, or from contaminated raw ingredients (37.6%).

Hypotheses

There appeared to be a conflict of the results from the different research questions. Of the two research questions dealing with direct or indirect association of food with norovirus, it was found that food associated norovirus outbreaks had more suspect association than any other association when compared with *Salmonella.* This strongly suggests that no true relationship

between norovirus and food exists. Of the two research questions dealing with association of food handlers with norovirus, it was found that foods could not be related directly or indirectly with norovirus outbreaks when compared with *Salmonella.* This also shows that food handlers were more likely to have a suspect association with norovirus than with *Salmonella.*

When looking at the contributing factors identified for food workers associated with outbreaks the argument that food workers are the major source of transmission of norovirus found no real association between the implication of the food workers and the contributing factors.

Table 27.

Strength of association of norovirus with food, food workers, or other viruses results of comparative analyses.

Factor	Overall		Direct association		Indirect association		Suspect association	
	OR	p Value	OR	p Value	OR	p Value	OR	p Value
Food	0.45	0.00	0.87	0.05	0.58	0.00	1.30	0.00
Food Workers	3.40	0.00	0.10	0.00	7.52	0.00		
Viruses	2.33	0.00	3.20	0.11	0.78	0.65		
Contributing Factors				0.00		0.91		0.02

The results of this study showed conflicting conclusions from the eFORS data tool collected by CDC. Evidence to associate norovirus with food was weak (OR = 0.45) when

compared to the known foodborne pathogen *Salmonella* (Table 27). There was an association of norovirus with outbreaks from other viruses ($p = 0.00$) but not significantly different when examined for direct or indirect contributions ($p = 0.11$ and $p = 0.65$, respectively). On the other hand, there was a significantly strong association of norovirus to food handlers when compared with *Salmonella* with indirect evidence ($p = 0.00$). Yet, when health officials were asked about the contributing factors that food handlers made to the outbreaks, the overall implication was that both food handlers and food were directly associated ($p = 0.00$). What can be concluded from this study is that outbreaks from norovirus are not like any outbreak from a bacterial pathogen. It is possible that the tool used to collect data about outbreaks from bacterial pathogens is not appropriate for outbreaks from norovirus. The reason for that would be that norovirus is not truly a foodborne pathogen.

Recent literature suggested that the association of norovirus with food is tenuous at best. Several outbreaks at food establishments suggest another mechanism of transmission (CDC, 2007c). An outbreak of norovirus in Michigan was observed following a meal that involved 364 restaurant patrons (CDC, 2007c). The index case, a line cook that prepared antipasti platters, pizza, and salads and who had vomited at his frontline station, became ill from a sibling that had vomited at home (CDC, 2007c). The editors noted that the spread of norovirus is from airborne droplets, food, water environment, environmental surfaces and fomites but in this case, foodborne transmission only “may have” contributed to the outbreak (CDC, 2007c).

In another outbreak case, 27 students and 2 staff members at a school were ill from norovirus (CDC, 2008a). No food was involved since students brought prepared lunches and pre-packaged snacks served in the classrooms and foodborne transmission was ruled out.

Environmental sampling found norovirus on a computer mouse and keyboard in the first grade classroom.

Transmission of genotype GII.4 seems more related to a high concentration of people who have high levels of virus loads in excreta or with a high incidence of vomiting (Kroneman, Harris, et al., 2008). The authors' trend analyses found norovirus spread through person-to-person outbreaks (88%), food (10%), and water (2%). Of all the outbreaks studied in Europe, 72% occurred in a health care setting, 36% in residential institutions, and 35% in hospitals. In Canada, 73.1% in long term care facilities, 10.3% in acute care hospitals, 12.8% in restaurants or social events, and 2.6% in childcare centers, and 1.3% in schools (Lee, Preiksaitis, Chui, Chui, & Pang, 2008). In Japan, 322 outbreaks were considered spread person-to-person involving no less than 10 persons and no incidents of foodborne association (Sakon et al., 2007).

If the number of outbreaks that had an undetermined relation to food actually had no relationship to food and were eliminated from the foodborne pool of outbreaks, then this would reduce the number of outbreaks in food settings to 8.1%. Such a number agrees with the results from Kroneman, Harris, et al., (2008) and Lee et al. (2008) A conclusion reached during cruise ship epidemiologic investigations of outbreaks determined failure to determine a point source of infection strongly signified a non-foodborne mode of transmission (Chimonas et al., 2008).

CDC does not include cruise ship information in its data collection but lessons learned from such outbreaks provide some interesting characteristics to the spread of norovirus associated gastrointestinal illness. A survey of ship passengers found odds ratios of 3.3 of having an ill cabin mate, an ill social contact of 2.1-5.0 and exposure to another person's vomitus or diarrhea of 8.4 (Neri, Cramer, Vaughn, Vinje, & Mainzer, 2008). With a contained population,

the risk for exposure grew with increasing number of passengers and days at sea. Because passengers do not understand the disease well, risk factors for contracting the disease, its mechanism of spread, and procedures to prevent propagation also increase. Cruise ships with inadequate vessel sanitation were also more susceptible to an outbreak and personal behavior and hygiene habits only increased the potential. The most common location that has a contaminated environment was found to be the private cabin and 95% of all vomiting episodes occurred there (Chimonas et al., 2008). Thus, sharing the cabin increased the potential of becoming ill and untrained staff that had to clean up the cabin put themselves at risk and increased potential for spreading the virus.

Person-to-person transmission of norovirus required a higher prevalence of the virus in the population to reconcile the high number of outbreaks not found attributed to food. Norovirus could be found in places where illness or outbreaks were not detected. In a non-outbreak related food catering facility, 159 employees were sampled for norovirus presence (Okabayashi et al., 2008). A total of 20 samples (12.6%) were positive for norovirus genotype GII. Yet all of these employees were asymptomatic.

During the peak outbreak season in Japan, Okabayashi et al. (2008) found that the same asymptomatic staff maintained an 11.9% level of norovirus infection. They concluded that the population normally carried norovirus regardless of the occurrence of norovirus outbreaks and those asymptomatic carriers excreted the virus in similar levels to that of symptomatic carriers. While different individuals were susceptible to different strains at different frequencies due to innate and acquired immunities, the authors concluded that various genotypes of norovirus circulated freely in otherwise healthy individuals.

A similar conclusion was proposed by Ozawa, Oka, Takeda, and Hansman (2007). They found norovirus in 19% of 2,376 samples from both asymptomatic and symptomatic employees of different food catering services and believed that asymptomatic infections are wide-spread in the food catering industry. Their reasoning was that prolonged norovirus shedding made the likelihood of transmission definite but food involvement an uncertainty.

It is also possible that the infectious rate was underestimated. Using a norovirus genome as a measure of infection, Teunis et al. (2008) found the level of dose-dependent probability of becoming ill ranged from 0.1 (10^3 norovirus genomes) to 0.7 (10^8 norovirus genomes), a rate higher than reported for other viruses. Infectivity, though, for different strains of a single pathogen was not always correlated to genetic relatedness and each strain could have its own level.

It is also possible that having the norovirus without symptoms does not mean that the strain present is always the infectious one. In the same above non-outbreak related food catering facility, 20 different strains were found in a phylogenic analysis of the 159 employees and 13 were the genotype GII. One employee was infected with 2 different GII strains (Okabayashi et al., 2008). It is therefore hard to place association of norovirus transmission solely on food handlers in cases of food-associated outbreaks.

The etiologic role of norovirus is similar in range to that of *Salmonella* (Tseng, Leon, MacCormack, Maillard, & Moe, 2007). Norovirus had higher numbers of outbreaks and cases reflecting a large number of secondary transmissions. No doubt food handlers get sick and transmit the disease. Nevertheless, norovirus is extremely widespread and causes asymptomatic infections as well. Thus, when people gather in one location, anyone could be the source. When

looking at food establishments, the customers or patrons could just as well be ill and infect otherwise healthy food handlers who then become ill and continue to spread the virus. This also suggests that infection of the supposed index case in the facility may have occurred days before the spread of the virus.

Norovirus Transmission Model

The model of oral-fecal transmission of norovirus cannot explain the volume of infected people and number of outbreaks. If the person-to-person transmission route is included in a model for norovirus, then people were also contacted with contaminated directly or indirectly with saliva, vomit or aerosol (Conly & Johnston, 2003). This means that norovirus remained in the stomach, esophagus, or mouth and the level of infectivity was dependent on the amount of ingested infectious viral particles (Teunis et al., 2008). Because people breathe through their mouth as well as through their nasal passages, ejection of viral particles via traditional respiratory routes would be understandable.

A better model for person-to-person transmission of norovirus could be a viral model. The same characteristics of norovirus mentioned earlier (p. 94) are shared with other viruses (Estes, Prasad, & Atmar, 2006).

Such a model would include influenza virus. Comparison of norovirus and influenza found that both viruses maintained their activity during the colder months of the year (Figure 4), outbreaks involved a substantial percent of the population, both targeted the epithelial cells; norovirus attacked the gastrointestinal tract while influenza attacked the respiratory tract; and both viruses involved combinations of malaise, fever, and muscular and abdominal pain (Anestad, Vainio, & Hungnes, 2007).

If indeed norovirus was spread as an aerosol and in the colder months, infectivity could be explained by a similar transmission of influenza. Results of recent studies found that transmission efficiency is dependent on relative humidity (Lowen, Mubareka, Stell & Palese, 2007). The authors found the lower the relative humidity (35% or 20%), the greater the transmission efficiency. In addition, transmission efficiency was found to be inversely correlated with temperature; the best transmission of influenza was found at 5^{o} C and not 23^{o} C ($p<0.05$).

A comparison of the monthly pattern of the number of cases from each norovirus outbreak to those monthly percent numbers of cases of influenza as collected by CDC (2008) showed a new association (Figure 4). Like influenza, norovirus is a winter month pathogen in the U.S. They both show decreases from the average in the summer months. Norovirus was typically a winter disease as originally described by Adler and Zickl (1969), but show little similarity to Hepatitis A or other viruses (Figure 2). Bacteria caused outbreaks in spring, summer, or fall or showed no discriminating trend (Figures 3a, 3b).

In addition, viral stability was found greatest at the lowest relative humidity. Lowen et al., (2007) suggested that evaporation of water from exhaled bioaerosols (including regular breathing) occurred rapidly at low humidity forming droplet nuclei that remained in the air for extended periods of time. At high humidity, the droplet would take on water and descend to the

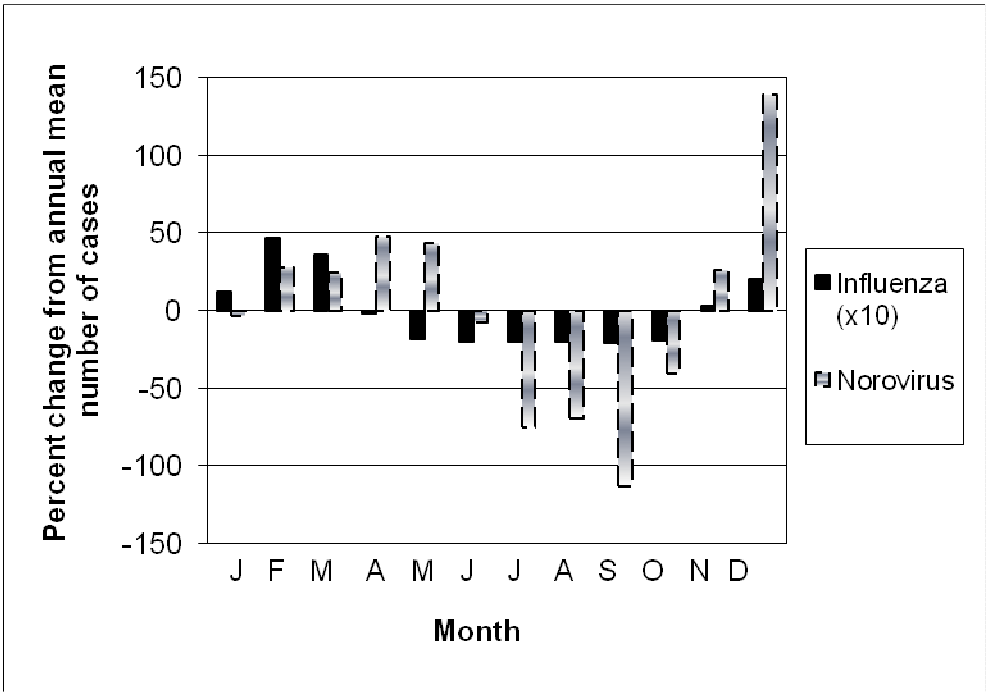

Figure 4. Comparison of percent changes from annual number of cases of norovirus and of influenza by month.

ground or environmental surfaces out of the air. Thus, breathing cold air cleared mucocilliary and amplified the shedding of viruses through the nasal passages. For a gastrointestinal infection, breathing through the mouth, passing gas orally, or vomiting would have had the same effect.

As with influenza, norovirus underwent genetic drift resulting in the increase number of genotypes and changes in levels of infectivity (Lopman, Zombon & Brown, 2008). The accumulation of mutations in the viral particle that are exposed at the outer surface appeared to be from a selective process through step-wise evolution providing for survival in new strains. As the surface-exposed carbohydrate ligand binding ability in the norovirus capsid was targeted by the body's immune system, mutation changes evolved through antigenic drift pressured by

human herd immunity (Lindesmith et al., 2008). The progression of new strains and seasonal peaks of norovirus outbreaks in Europe and the world suggested changes in virulence and behavior of the virus (Kroneman, Harris, et al., 2008). Immune driven changes in the capsid allowed the virus to escape population immunity, which is what happened for influenza viruses.

The differences between influenza and norovirus are important also. Influenza subtypes generally replaced existing types that then become extinct. Norovirus genotypes remained in the population and continued to circulate in low levels. Yet they underwent a genetic drift resulting in a new variety every three years (Lopman, Zombon, & Brown, 2008). The first norovirus genotype GII.4 variant appeared in 1995/6 with high numbers of outbreaks and continued to circulate the world with progressively lowered numbers of outbreaks even when the newest outbreak variant appeared in 2002/3. At spring time and the end of the cold season, population immunity was highest and selective pressure allowed a new pandemic strain to evolve at this time.

Changes Needed and Recommendations

Norovirus is not considered high priority in Europe. Thirteen countries participate in the Foodborne Viruses in Europe (FBVE) network database but France, Denmark and Sweden only report suspected foodborne outbreaks and Italy and Spain do not have a national norovirus surveillance system (Kroneman, Verhoff, et al., 2008). Such a lack of standardization in surveillance systems makes direct analyses of data difficult (Kroneman, 2008). There is also little standardization in case definitions, inclusion criteria, periods covered, methods used for testing, and age groups when reports are filed.

In the United States, reporting is voluntary and inconsistent. During the study period, North Carolina health officials reported only two non-bacterial gastroenteritis outbreaks that did not involve foodborne transmission (Tseng, Leon, MacCormack, Maillard, & Moe, 2007). Only 10 out of 100 counties reported non-bacterial gastroenteritis and 2 counties reported half of the 16 outbreaks.

Recognition of norovirus outbreaks continues to plague medical workers, especially in combination with other diseases. An outbreak of *Clostridium difficile* was hampered by a norovirus outbreak (Bignardi, Staples, & Majmudar (2007). *C. difficile* is usually present in hospitalized elderly patients and norovirus exacerbated the episodes of diarrhea resulting in an increased number of samples and tests. Enzyme-Immunoassay for *C. difficile* was only 87.4% accurate resulting in many false positives. Isolation of patients and containment of the diseases were impeded since those with norovirus and those with *C. difficile* infections or both could not be distinguished.

Containment and control of norovirus also appeared difficult. Continued efforts to educate food workers have not yielded the expected decrease in norovirus outbreaks. Attempts in animal models were only successful in eradicating norovirus through depopulation and disinfection prior to repopulation even though mice were individually caged in ventilated sterile microisolation with hardwood bedding and fed autoclaved pelleted rodent diets (Kastenmayer, Perdue, & Elkins, 2008).

Seafood that was believed to have norovirus also contained other viruses. Japanese clams were found to contain multiple enteric viruses (Hansman et al., 2008). Among those viruses tested were norovirus, Aichivirus, rotavirus, Adenovirus, hepatitis A, and astrovirus. Out of 57

clam packages, 61% had 1 virus, 9% had 2 viruses, 28% had 3 viruses, and 9% had four. Norovirus was found in 54% of the clams.

Taking norovirus seriously will require the tools to understand norovirus. Research needs identified include development of simple, rapid diagnostic assays, determination of the length of norovirus infections, determination of the characteristics of norovirus asymptomatic carriers, whether zoonotic norovirus transfer to humans happens, and effective means of norovirus infection. Potential new hygiene practices may also be needed (Estes, Prasad, & Atmar, 2006).

Programmatic changes are needed on national and international levels. Gauging the true number of norovirus outbreaks and transmission will require mandatory reporting from all states in the United States and countries to their respective surveillance systems. Norovirus surveillance will need a different system and a measuring and reporting tool that reduces the focus on food workers and food transmission to open other venues of transmission possibilities. National databases and reporting systems will need to be established that track and report norovirus outbreaks in a similar manner that influenza is monitored. Population trends and geographical spread should be analyzed through reporting and analysis. Finally other avenues of treatment and prevention of outbreaks, such as vaccination for seasonal norovirus (Tan & Jiang, 2008), could be explored. Without a change in emphasis on the importance of norovirus infection and outbreak, norovirus will continue to spread and evolve and infect millions of people each year.

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APPENDIX A: ELECTRONIC FOODBORNE OUTBREAK REPORTING SYSTEM (EFORS), CDC FORM 52.13, REVISED NOVEMBER, 2004

Form approved OMB No. 0920-0004

Electronic Foodborne Outbreak Reporting System

Investigation of a Foodborne Outbreak

This form is used to report foodborne disease outbreak investigations to CDC. It is also used to report *Salmonella* Enteritidis and *E. coli* O157:H7 outbreak investigations involving any mode of transmission. A foodborne outbreak is defined as the occurrence of two or more cases of a similar illness resulting from the ingestion of a common food in the United States. This form has 6 parts. Part 1 asks for the minimum or basic information needed and must be completed for the investigation to be counted in the CDC annual summary. Part 2 asks for additional information for any foodborne outbreak, while Parts 3 – 6 ask for information concerning specific vehicles or etiologies. Please complete as much of all parts as possible.

CDC Use Only
___-_____

State Use Only
_____

Part 1: Basic Information

1. Report Type

A.
□ Please check if this a final report

B.
□ Please check if data does not support a FOODBORNE outbreak

2. Number of Cases

Lab-confirmed cases_____(A)
Including _____ secondary cases

Probable cases_____(B)
Including _____ secondary cases

Estimated total ill_____
(If greater than sum A + B)

3. Dates
Please enter as many dates as possible

Date first case became ill __ __/__ __/__ __ __ __
Month Day Year

Date last case became ill __ __/__ __/__ __ __ __
Month Day Year

Date first known exposure __ __/__ __/__ __ __ __
Month Day Year

Date last known exposure __ __/__ __/__ __ __ __
Month Day Year

4. Location of Exposure

Reporting state _____

If multiple states involved:
□ Exposure occurred in multiple states
□ Exposure occurred in single state, but cases resided in multiple states
Other states: _____
_____
_____

Reporting county_____

If multiple counties involved:
□ Exposure occurred in multiple counties
□ Exposure occurred in one county, but cases resided in multiple counties
Other counties: _____
_____
_____

5. Approximate Percentage of Cases in Each Age Group

<1 year ____% 20-49 yrs ____%
1-4 yrs ____% ≥50 yrs ____%
5-19 yrs ____% Unknown ____%

6. Sex
(Estimated percent of the total cases)

Male_____%

Female_____%

7. Investigation Methods (Check all that apply)
□ Interviews of only cases
□ Food preparation review
□ Investigation at factory or production plant
□ Investigation at original source (farm, marine estuary, etc.)
□ Food product traceback
□ Environment / food sample cultures
□ Case-control study
□ Cohort study

8. Implicated Food(s): (Please provide known information)

Name of Food	Main Ingredient(s)	Contaminated Ingredient(s)	Reason(s) Suspected (See codes just below)	Method of Preparation (See attached codes)
e.g., Lasagna	e.g., Pasta, sauce, eggs, beef	e.g., Eggs	e.g., 4	e.g., M1
1)				
2)				
3)				

□ Food vehicle undetermined

Reason Suspected (List above all that apply)
1 - Statistical evidence from epidemiological investigation
2 - Laboratory evidence (e.g., identification of agent in food)
3 - Compelling supportive information
4 - Other data (e.g., same phage type found on farm that supplied eggs)
5 - Specific evidence lacking but prior experience makes it likely source

CDC 52.13 revised November, 2004

Public reporting burden of this collection of information is estimated to average 20 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. An agency may not conduct or sponsor, and a person is not required to respond to a collection of information unless it displays a currently valid OMB control number. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to CDC/ATSDR Reports Clearance Officer; 1600 Clifton Road NE, MS D-74, Atlanta, Georgia 30333; ATTN: PRA (0920-0004).

9. Etiology: (Name the bacteria, virus, parasite, or toxin. If available, include the serotype and other characteristics such as phage type, virulence factors, and metabolic profile. Confirmation criteria available at http://www.cdc.gov/foodborneoutbreaks/guide_fd.htm or MMWR2000/Vol. 49/SS-1/App. B)

Etiology		Serotype	Other Characteristics (e.g., phage type)	Detected In (See codes just below)
1)	□ Confirmed			
2)	□ Confirmed			
3)	□ Confirmed			

□ Etiology undetermined

Detected In (List above all that apply)

1 - Patient Specimen(s) 3 -Environment specimen(s)

2 - Food Specimen(s) 4 - Food Worker specimen(s)

10. Isolate Subtype

State Lab ID	PFGE (PulseNet designation)	PFGE (PulseNet designation)	
1)			
2)			
3)			

11. Contributing Factors (Check all that apply. See attached codes and explanations)

□ **Contributing factors unknown**

Contamination Factor

□C1 □C2 □C3 □C4 □C5 □C6 □C7 □C8 □C9 □C10 □C11 □C12 □C13 □C14 □C15 (*describe in Comments)* □ N/A

Proliferation/Amplification Factor (bacterial outbreaks only)

□P1 □P2 □P3 □P4 □P5 □P6 □P7 □P8 □P9 □P10 □P11 □P12 (*describe in Comments)* □ N/A

Survival Factor (microbial outbreaks only)

□S1 □S2 □S3 □S4 □S5 (*describe in Comments)* □N/A

□ **Was food-worker implicated as the source of contamination?** □ Yes □ No

If yes, please check **only one** of following

□ laboratory *and* epidemiologic evidence

□ epidemiologic evidence (w/o lab confirmation)

□ lab evidence (w/o epidemiologic evidence)

□ prior experience makes this the likely source (*please explain in Comments*)

Part 2: Additional Information

12. Symptoms, Signs and Outcomes

Feature	Cases with outcome/ feature	Total cases for whom you have information available
Healthcare provider visit		
Hospitalization		
Death		
Vomiting		
Diarrhea		
Bloody stools		
Fever		
Abdominal cramps		
HUS or TTP		
Asymptomatic		
*		
*		
*		

13. Incubation Period
(Circle appropriate units)

Shortest_____(Hours, Days)
Longest_____(Hours, Days)
Median _____(Hours, Days)
□ Unknown

14. Duration of Illness
(Among those who recovered)
(Circle appropriate units)

Shortest_____(Hours, Days)
Longest_____(Hours, Days)
Median _____(Hours, Days)
□ Unknown

*** Use the following terms, if appropriate, to describe other common characteristics of cases**

Anaphylaxis	Headache	Tachycardia
Arthralgia	Hypotension	Temperature reversal
Bradycardia	Itching	Thrombocytopenia
Bullous skin lesions	Jaundice	Urticaria
Coma	Lethargy	Wheezing
Cough	Myalgia	
Descending paralysis	Paresthesia	
Diplopia	Septicemia	
Flushing	Sore throat	

15. If Cohort Investigation Conducted:

Attack rate* = _____ / _____ x 100 = _____%
(Exposed and ill / Total number exposed for whom you have illness information)

* The attack rate is applied to persons in a cohort who were exposed to the implicated vehicle. The numerator is the number of persons who were exposed and became ill; the denominator is the total number of persons exposed to the implicated vehicle. If the vehicle is unknown, then the attack rate should not be calculated.

16. Location Where Food Was Prepared
(Check all that apply)

□Restaurant or deli
□ Day care center
□ School
□ Office setting
□ Workplace cafeteria
□ Banquet Facility
□ Picnic
□ Caterer
□ Grocery Store
□ Nursing home
□ Prison, jail
□ Private home
□ Workplace, not cafeteria
□ Wedding reception
□ Church, temple, etc
□ Camp
□ Contaminated food imported into U.S.
□ Hospital
□ Fair, festival, other temporary/ mobile services
□ Commercial product, served without further preparation
□ Unknown or undetermined
□ Other (Describe) _____

17. Location of Exposure or Where Food Was Eaten
(Check all that apply)

□ Restaurant or deli
□ Day care center
□ School
□ Office Setting
□ Workplace cafeteria
□ Banquet Facility
□ Picnic
□ Grocery Store
□ Nursing Home
□ Prison, jail
□ Private home
□ Workplace, not cafeteria
□ Wedding Reception
□ Church, temple, etc.
□ Camp
□ Hospital
□ Fair, festival, temporary/ mobile service
□ Unknown or undetermined
□ Other (Describe) _____

18. Trace back:
□ Please check if trace back conducted

Source to which trace back led:

Source (e.g., Chicken farm, Tomato processing plant)	Location of Source State	Country	Comments

19. Recall

□ Please check if any food product recalled

Recall Comments

_____
_____
_____
_____
_____

20. Available Reports (Please attach)

□ Unpublished agency report

□ Epi-Aid report

□ Publication (please reference if not attached)

_____
_____

21. Agency reporting this outbreak

_____

Contact person:

Name _____
Title _____
Phone _____
Fax _____
E-mail _____

22. Remarks

Briefly describe important aspects of the outbreak not covered above (e.g., restaurant closure, immunoglobin administration, economic impact, etc)

_____
_____
_____
_____
_____

Part 3: School Questions

1. Did the outbreak involve a single or multiple schools?

□ Single

□ Multiple (*If yes*, number of schools____)

2. School characteristics (for all involved students in all involved schools)

a. Total approximate enrollment

_____ (number of students)

□ Unknown or Undetermined

b. Grade level(s) (Please check all grades affected)

□ Preschool

□ Grade School (grades K-12)

Please check all grades affected: □K □1st □2nd □3rd □4th □5th □6th □7th □8th □9th □10th □11th □12th

□ College/University/Technical School

□ Unknown or Undetermined

c. Primary funding of involved school(s)

□ Public □ Private □ Unknown or Undetermined

3. Describe the preparation of the implicated item:

□ Heat and serve (item mostly prepared or cooked off-site, reheated on-site)

□ Served a-la-carte

□ Serve only (preheated or served cold)

□ Cooked on site using primary ingredients

□ Provided by a food service management company

□ Provided by a fast food vendor

□ Provided by a pre-plate company

□ Part of a club/ fundraising event

□ Made in the classroom

□ Brought by a student/teacher/parent

□ Other _____

□ Unknown or Undetermined

4. How many times has the state, county or local health department inspected this school cafeteria or kitchen in the 12 months before the outbreak?*

□ Once

□ Twice

□ More than two times

□ Not inspected

□ Unknown or Undetermined

5. Does the school have a HACCP plan in place for the school feeding program?*

□ Yes

□ No

□ Unknown or Undetermined

*If there are multiple schools involved, please answer according to the most affected school

6. Was implicated food item provided to the school through the National School Lunch/Breakfast Program?

- □ Yes
- □ No
- □ Unknown or Undetermined

***If Yes,* Was the implicated food item donated/purchased by :**

- □ USDA through the Commodity Distribution Program
- □ Purchased commercially by the state/school authority
- □ Other_____
- □ Unknown or Undetermined

Part 4: Ground Beef

1. What percentage of ill persons (for whom information is available) ate ground beef raw or undercooked? _____%

2. Was ground beef case ready? (Ground beef that comes from a manufacturer packaged for sale and not altered or repackaged by the retailer)

- □ Yes
- □ No
- □ Unknown or Undetermined

3. Was the beef ground or reground by the retailer?

- □ Yes
- □ No
- □ Unknown or Undetermined

If yes, was anything added to the beef during grinding (e.g., shop trim or any product to alter the fat content)_____

Part 5: Mode of Transmission

(Enterohemorrhagic *E. coli* or *Salmonella* Enteritidis only)

1. Mode of Transmission (for greater than 50% of cases)

Select one:

- □ Food
- □ Person to person
- □ Swimming or recreational water
- □ Drinking water
- □ Contact with animals or their environment
- □ Unknown or Undetermined

Part 6: Additional Egg Questions

1. Were Eggs: (Check all that apply)

- □ in-shell, un-pasteurized?
- □ in-shell, pasteurized?
- □ liquid or dry egg product?
- □ stored with inadequate refrigeration during or after sale?
- □ consumed raw?
- □ consumed undercooked?
- □ pooled?

2. If eggs traced back to farm, was *Salmonella* Enteritidis found on the farm?

- □ Yes
- □ No
- □ Unknown or Undetermined

Comment:_____

Contamination Factors:[1]

C1 - Toxic substance part of tissue (e.g., ciguatera)
C2 - Poisonous substance intentionally added (e.g., cyanide or phenolphthalein added to cause illness)
C3 - Poisonous or physical substance accidentally/incidentally added (e.g., sanitizer or cleaning compound)
C4 - Addition of excessive quantities of ingredients that are toxic under these situations (e.g., niacin poisoning in bread)
C5 - Toxic container or pipelines (e.g., galvanized containers with acid food, copper pipe with carbonated beverages)
C6 - Raw product/ingredient contaminated by pathogens from animal or environment (e.g., *Salmonella* Enteriditis in egg, Norwalk in shellfish, *E. coli* in sprouts)
C7 - Ingestion of contaminated raw products (e.g., raw shellfish, produce, eggs)
C8 - Obtaining foods from polluted sources (e.g., shellfish)
C9 - Cross-contamination from raw ingredient of animal origin (e.g., raw poultry on the cutting board)
C10 - Bare-handed contact by handler/worker/preparer (e.g., with ready-to-eat food)
C11 - Glove-handed contact by handler/worker/preparer (e.g., with ready-to-eat food)
C12 - Handling by an infected person or carrier of pathogen (e.g., *Staphylococcus*, *Salmonella*, Norwalk agent)
C13 - Inadequate cleaning of processing/preparation equipment/utensils B leads to contamination of vehicle (e.g., cutting boards)
C14 - Storage in contaminated environment B leads to contamination of vehicle (e.g., store room, refrigerator)
C15 - Other source of contamination (*please describe in Comments*)

Proliferation/Amplification Factors:[1]

P1 - Allowing foods to remain at room or warm outdoor temperature for several hours (e.g., during preparation or holding for service)
P2 - Slow cooling (e.g., deep containers or large roasts)
P3 - Inadequate cold-holding temperatures (e.g., refrigerator inadequate/not working, iced holding inadequate)
P4 - Preparing foods a half day or more before serving (e.g., banquet preparation a day in advance)
P5 - Prolonged cold storage for several weeks (e.g., permits slow growth of psychrophilic pathogens)
P6 - Insufficient time and/or temperature during hot holding (e.g., malfunctioning equipment, too large a mass of food)
P7 - Insufficient acidification (e.g., home canned foods)
P8 - Insufficiently low water activity (e.g., smoked/salted fish)
P9 - Inadequate thawing of frozen products (e.g., room thawing)
P10 - Anaerobic packaging/Modified atmosphere (e.g., vacuum packed fish, salad in gas flushed bag)
P11 - Inadequate fermentation (e.g., processed meat, cheese)
P12 - Other situations that promote or allow microbial growth or toxic production (*please describe in Comments*)

Survival Factors:[1]

S1 - Insufficient time and/or temperature during initial cooking/heat processing (e.g., roasted meats/poultry, canned foods, pasteurization)
S2 - Insufficient time and/or temperature during reheating (e.g., sauces, roasts)
S3 - Inadequate acidification (e.g., mayonnaise, tomatoes canned)
S4 - Insufficient thawing, followed by insufficient cooking (e.g., frozen turkey)
S5 - Other process failures that permit the agent to survive (*please describe in Comments*)

Method of Preparation:[2]

M1 - Foods eaten raw or lightly cooked (e.g., hard shell clams, sunny side up eggs)
M2 - Solid masses of potentially hazardous foods (e.g., casseroles, lasagna, stuffing)
M3 - Multiple foods (e.g., smorgasbord, buffet)
M4 - Cook/serve foods (e.g., steak, fish fillet)
M5 - Natural toxicant (e.g., poisonous mushrooms, paralytic shellfish poisoning)
M6 - Roasted meat/poultry (e.g., roast beef, roast turkey)
M7 - Salads prepared with one or more cooked ingredients (e.g., macaroni, potato, tuna)
M8 - Liquid or semi-solid mixtures of potentially hazardous foods (e.g., gravy, chili, sauce)
M9 - Chemical contamination (e.g., heavy metal, pesticide)
M10 - Baked goods (e.g., pies, éclairs)
M11 - Commercially processed foods (e.g., canned fruits and vegetables, ice cream)
M12 - Sandwiches (e.g., hot dog, hamburger, Monte Cristo)
M13 - Beverages (e.g., carbonated and non-carbonated, milk)
M14 - Salads with raw ingredients (e.g., green salad, fruit salad)
M15 - Other, does not fit into above categories *(please describe in Comments)*
M16 - Unknown, vehicle was not identified

[1] Frank L. Bryan, John J. Guzewich, and Ewen C. D. Todd. Surveillance of Foodborne Disease III. Summary and Presentation of Data on Vehicles and Contributory Factors; Their Value and Limitations. Journal of Food Protection, 60; 6:701-714, 1997.

[2] Weingold, S. E., Guzewich JJ, and Fudala JK. Use of foodborne disease data for HACCP risk assessment. Journal of Food Protection, 57; 9:820-830, 1994.

APPENDIX B: RETRIEVABLE DATA FROM EFORS RECORDS

Form Name	Data Field Name	Comments
ContributingFactor	EFORSCDCID	
	ContributingFactorCode	
County	EFORSCDCID	
	CountyID	
	CountyName	
	Reporting	
EFORSMain	EFORSCDCID	
	MultiStateResidence	
	MultiStateExposure	
	MultiCountyExposure	
	MultiCountyResidence	
	FirstIll	
	LabCasesPrimary	
	EstimatedTotal	
	AgeUnder1	
	Age1to4	
	Age5to19	
	Age20to49	
	AgeGreater50	
	AgeUnknown	
	SexMale	
	SexFemale	
	FoodWorkerImplicatedDescription	
	ContributingFoodWorker	
.	RecalledFood	
	TracebackConducted	
	EtiologyUndetermined	
	FoodVehicleUndetermined	0:False and -1:True
	ContributingFactorUnknown	
Etiology	EFORSCDCID	
	SpeciesName	
	SerotypeName	
	GenusName	
	Confirmed	0:False and -1:True
	OtherCharacteristics	
EtiologyIsolated	EtiologyID	
	DetectedInName	
GeneralMethodOfPrep	MethodOfPrepID	

	CookingMethodName
GroundBeef	EFORSCDCID GroundBeefConsumed CaseReady GroundBeefReground GroundBeefRegroundComment
ImplicatedFood	EFORSCDCID ImplicatedFoodID FoodCategoryName
Ingredient	IngredientID ContaminatedIngredient
InvestigationMethod	EFORSCDCID InvestigationMethodName
IsolateSubtype	EFORSCDCID StateLabId PFGEType1 PFGEType2
School	SchoolID EFORSCDCID MultipleSchools NumberOfMultipleSchools TotalEnrollment UnknownEnrollmentNumber SchoolFundingName StateInspectedName HACCP NationalSchoolsProgram FoodItemDonatedByName DonatedByOther
SchoolGradeLevel	SchoolID GradeLevelname
SchoolPreparation	SchoolID SchoolFoodPreparationName
State	EFORSCDCID StateName Reporting

WhereFoodEaten	EFORSCDCID	
	WhereEatenName	
WhereFoodPrepared	EFORSCDCID	
	WherePreparedName	
Ingredient	IngredientID	
	ImplicatedFoodID	
	IngredientName	
	ContaminatedIngredient	0:False and -1:True
ReasonSuspected	ReasonSuspectedID	
	ImplicatedFoodID	
	ReasonSuspectedName	

APPENDIX C: REPRODUCTION PERMISSIONS

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A13_Book_Title: J. Medical Virology
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A17_Journal_Year: 2005
A18_Journal_Volume: 76
A19_Journal_Issue_Number: 4
A20_Copy_Pages: Figure 3, page 603
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A23_Your_Title: Foodborne or Pandemic: An Analysis of the Transmission
A24_Publication_Date: 2009
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A41_Ebook_Reader_Type:
A26_If_WWW_URL:
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A45_WWW_Users:
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A48_Intranet_Users:
A34_If_Intranet_Material_Posted_From:
A35_If_Intranet_Material_Posted_To:
A50_If_Software_Print_Type:
A60_If_Other_Type:
A37_Comments_For_Request: □Evidence of the etiological predominance of norovirus in gastroenteritis outbreaks--emerging new-variant and recombinant noroviruses in Hungary,□ by G. Reuter, K. Krisztalovics, , H. Vennema, M.. Koopmans, & G. Szucs, 2005, Journal of Medical Virology, 76(4), p. 603.

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A17_Journal_Year: 2001
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A20_Copy_Pages: Figure 2, page 390
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A24_Publication_Date: 2009
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A26_If_WWW_URL:
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A28_If_WWW_Password_Access:
A45_WWW_Users:
A29_If_WWW_Material_Posted_From:
A30_If_WWW_Material_Posted_To:
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A34_If_Intranet_Material_Posted_From:
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APPENDIX D: EFORS DATA REQUEST APPROVAL

Enteric Diseases Epidemiology Branch
Centers for Disease Control and Prevention
1600 Clifton Rd NE MS A-38,Atlanta,GA30333
Phone: (404) 639-2206 Fax: (404) 639-2205

eFORS Data Request Application

PART I: Individual/Organization Requesting Use of CDC Foodborne Outbreak Reporting System (eFORS) Data

General Information:

Applicant Name: Mark (Moshe) Dreyfuss Position/Title: PhD Candidate

Organization Name: Walden University

Work Address: 901 D St., SW Work Address 2: Aerospace Center, Suite 309

City: Washington State: DC Zip Code: 20024

Phone: 202-690-6379 Fax: 202-690-6364 E-mail address: moshe.dreyfuss@fsis.usda.gov

Type of Organization:

University/college/teaching institution

Provide more information for '***Type of Organizaiton***' if asked to specify

I am currently working at USDA/ FSIS in Washington DC please provide a copy of applications to Kristin Holt

PART II: Intended Use of Data and Project Activities

Intended Data Use:

Research

If '*Other*' ***Intended Data Use***, please specify

If requesting state data, provide state health department contact:

Name: Phone:

Email:

Short Title: An Analysis of the Transmission of Norovirus-Associated Gastroenteritis and the Role of Food Handlers

Brief description of project: This study will examine the strength of association between food, food workers and other potential sources with the spread of norovirus. Odds ratios will be calculated using those categorical outbreak records that report norovirus as the etiologic agent and compared to other bacterial etiologic agents. Data needed within 2 weeks of application submission.

Brief description of subject areas that you plan to investigate (e.g. health outcome, quality, cost, utilization, access, markets, etc.)

Pathogen transmission and contamination routes in the spread of norovirus and worker sanitation effectuveness.

Brief description of potential uses of the final products that you may create using the data (e.g., reports, papers, analyses for public domain and or internal use, etc.) utilization, access, markets, etc.)

For use in my dissertation and potential scientific peer reviewed publications

CDC Data Request Application

PART III: Data Request Specifications

Definition of Data Request
(Please define data request using specific definitions):

Field	data
Dates (Question 3) all records	months, years
Etiology (Question 9)	Species Name
	Serotype Name
	Genus Name
	Other Characteristics
	Detected in
	Confirmed
	Etiology Undetermined

How Data Should Be Provided:

☐ Postal mail (physical disk) ☒ Electronic mail (compressed file) Other _____

Format Data Should Be Provided:

☒ Access database (.mdb) ☐ Extensible Markup Language (.xml) Other _____

Part IV: Data Handling and Security Plan

Please answer the following data handling and security questions:

1. Who has access to the data? — Besides myself, only my Committee Chair, Dr. Talmage Holmes

2. How are you going to limit access to the data? — The data file will be kept on an encripted, security password access only computer. Backup copies will be kept on thumb drives in locked secure area.

3. How are you going to physically protect the data? What are your physical controls (e.g., diskettes locked in filing cabinet, computer located in room only)? — Computers are in locked offices in a guarded building. Any copies of the data will be kept on a thumb drive that will be locked in my desk drawers in my office

4. At the end of the project, how are you going to return or destroy the data? — The data will be destroyed

CDC Outbreak Surveillance Unit Staff Use Only

Request ID: DREY_06052008 Date received: 2008-06-05

Date reviewed by Privacy Board: 2008-09-16 Privacy Board Action: Approved ☒ Data Use Agreement received:

Completed by: _____ Approval and Date: 9/16/08

Date completed: _____ Time spent (hours): _____ Date released: _____

Request folder name: DREY_06052008(ED)_norovirus foodworker and contributing factors

Filename: _____

File format of data released: Access, Email

Reset Form

CURRICULUM VITAE

MARK S. DREYFUSS

mjdreyfuss@verizon.net

EDUCATION

Doctor in Public Health (Epidemiology), January, 2009
Walden University, Minneapolis, MN

Master of Science in Public Health, March, 2007
Walden University, Minneapolis, MN

Master of Science, Food Microbiology, 1978
The Ohio State University, Columbus, Ohio

Bachelor of Science, Microbiology, 1973
The Ohio State University, Columbus, Ohio

PROFESSIONAL EXPERIENCE

Branch Chief, Supervisory Microbiologist, 10/2003 to present
United States Department of Agriculture, Food Safety & Inspection Service (FSIS), Office of Public Health Science (OPHS), Microbiology Division, Microbiological Issues Branch, Washington, D.C. 20024

Food Technologist, 02/2000 to 10/2003
United States Department of Agriculture, Food Safety & Inspection Service, OPPDE & OPAEO, Meat and Poultry Advisory Committee Staff, Washington, D.C. 20250

Food Technologist, 7/1/96 to 02/2000
United States Department of Agriculture, Food Safety & Inspection Service, OPPDE, LCRD, Label Review Branch, Washington, D.C. 20250

Microbiologist, 4/8/91 to 6/30/96
United States Department of Agriculture, Food Safety & Inspection Service
Microbiology Division, Immunology Branch, Beltsville, MD 20705

MASTER'S RESEARCH

The effects of microwave radiation on *E. coli, S. aureus, S. enteritidis,* and *B. cereus*. The Ohio State University, 1978.

SCIENTIFIC PUBLICATIONS

Dreyfuss, M. S., Ransom, G. M., Russell, M. D., Barlow, K. E., Pritchard, K. M., Eblen, D. R., Nadon, C. A., Saini, P. K., Antoine, N. D. O., Rose, B. E., & Zirnstein, G. W. (2007). Pathogen Control in Meat and Poultry Production: Implementing the USDA Food Safety and Inspection Service's Hazard Analysis and Critical Control Point System. In S. Simjee, (Ed.), *Foodborne diseases*, (Chapter 15). Totowa, N. J., Humana Press.

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characterization of tissue distribution and metabolism of ^{14}C-Aflatoxin B_1 in chickens. *Applied Microbiology, 28,* 1027-1029.