Bad Bug Book

Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

The *"Bad Bug Book"*

This handbook provides basic facts regarding foodborne pathogenic microorganisms and natural toxins. It brings together in one place information from the Food & Drug Administration, the Centers for Disease Control & Prevention, the USDA Food Safety Inspection Service, and the National Institutes of Health.

Some technical terms have been linked to the National Library of Medicine's Entrez glossary. Recent articles from Morbidity and Mortality Weekly Reports have been added to selected chapters to update the handbook with information on later outbreaks or incidents of foodborne disease. At the end of selected chapters on pathogenic microorganisms, hypertext links are included to relevant Entrez abstracts and GenBank genetic loci. A more complete description of the handbook may be found in the Preface.

PATHOGENIC BACTERIA

- *Salmonella* spp.
- *Clostridium botulinum*
- *Staphylococcus aureus*
- *Campylobacter jejuni*
- *Yersinia enterocolitica* and *Yersinia pseudotuberculosis*
- *Listeria monocytogenes*
- *Vibrio cholerae* O1
- *Vibrio cholerae* non-O1
- *Vibrio parahaemolyticus* and other *vibrios*
- *Vibrio vulnificus*

- *Clostridium perfringens*
- *Bacillus cereus*
- *Aeromonas hydrophila* and other spp.
- *Plesiomonas shigelloides*
- *Shigella* spp.
- Miscellaneous enterics
- *Streptococcus*

ENTEROVIRULENT ESCHERICHIA COLI GROUP (EEC Group)

- *Escherichia coli* - enterotoxigenic (ETEC)
- *Escherichia coli* - enteropathogenic (EPEC)
- *Escherichia coli* O157:H7 enterohemorrhagic (EHEC)
- *Escherichia coli* - enteroinvasive (EIEC)

PARASITIC PROTOZOA and WORMS

- *Giardia lamblia*
- *Entamoeba histolytica*
- *Cryptosporidium parvum*
- *Cyclospora cayetanensis*
- *Anisakis* sp. and related worms
- *Diphyllobothrium* spp.
- *Nanophyetus* spp.
- *Eustrongylides* sp.
- *Acanthamoeba* and other free-living amoebae
- *Ascaris lumbricoides* and *Trichuris trichiura*

VIRUSES

- Hepatitis A virus
- Hepatitis E virus
- Rotavirus
- Norwalk virus group

- Other viral agents

NATURAL TOXINS

- Ciguatera poisoning
- Shellfish toxins (PSP, DSP, NSP, ASP)
- Scombroid poisoning
- Tetrodotoxin (Pufferfish)
- Mushroom toxins
- Aflatoxins
- Pyrrolizidine alkaloids
- Phytohaemagglutinin (Red kidney bean poisoning)
- Grayanotoxin (Honey intoxication)

OTHER PATHOGENIC AGENTS

- Prions

APPENDICES

- Infective dose
- Epidemiology summary table
- Factors affecting microbial growth in foods
- Foodborne Disease Outbreaks, United States 1988-1992
- Additional Foodborne Disease Outbreak Articles and Databases.

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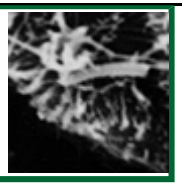


Salmonella spp.

Education | CDC/MMWR | NIH/PubMed

1. Name of the Organism:
Salmonella spp.

Salmonella is a rod-shaped, motile bacterium -- nonmotile exceptions *S. gallinarum* and *S. pullorum*--, nonsporeforming and Gram-negative. There is a widespread occurrence in animals, especially in poultry and swine. Environmental sources of the organism include water, soil, insects, factory surfaces, kitchen surfaces, animal feces, raw meats, raw poultry, and raw seafoods, to name only a few.

2. Nature of Acute Disease:

S. typhi and the paratyphoid bacteria are normally caused septicemic and produce typhoid or typhoid-like fever in humans. Other forms of salmonellosis generally produce milder symptoms.

3. Nature of Disease:

Acute symptoms -- Nausea, vomiting, abdominal cramps, minal diarrhea, fever, and headache. Chronic consequences -- arthritic symptoms may follow 3-4 weeks after onset of acute symptoms.

Onset time -- 6-48 hours.

Infective dose -- As few as 15-20 cells; depends upon age and health of host, and strain differences among the members of the genus.

Duration of symptoms -- Acute symptoms may last for 1 to 2 days or may be prolonged, again depending on host factors, ingested dose, and strain characteristics.

Cause of disease -- Penetration and passage of Salmonella organisms from gut lumen into epithelium of small

intestine where inflammation occurs; there is evidence that an enterotoxin may be produced, perhaps within the enterocyte.

4. Diagnosis of Human Illness: Serological identification of culture isolated from stool.

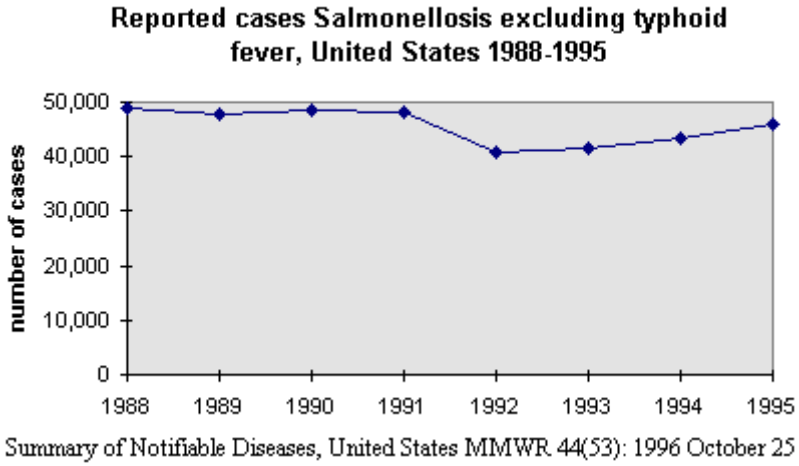
5. Associated Foods: Raw meats, poultry, eggs, milk and dairy products, fish, shrimp, frog legs, yeast, coconut, sauces and salad dressing, cake mixes, cream-filled desserts and toppings, dried gelatin, peanut butter, cocoa, and chocolate.

Various Salmonella species have long been isolated from the outside of egg shells. The present situation with *S. enteritidis* is complicated by the presence of the organism inside the egg, in the yolk. This and other information strongly suggest vertical transmission, i.e., deposition of the organism in the yolk by an infected layer hen prior to shell deposition. Foods other than eggs have also caused outbreaks of *S. enteritidis* disease.

6. Relative Frequency of Disease:

It is estimated that from 2 to 4 million cases of salmonellosis occur in the U.S. annually.

The incidence of salmonellosis appears to be rising both in the U.S. and in other industrialized nations. *S. enteritidis* isolations from humans have shown a dramatic rise in the past decade, particularly in the northeast United States (6-fold or more), and the increase in human infections is spreading south and west, with sporadic outbreaks in other regions.



Reported cases of Salmonellosis in the U.S. excluding typhoid fever for the years 1988 to 1995. The number of cases for each year varies between 40,000 and 50,000. From Summary of Notifiable Diseases, United States MMWR 44(53): 1996 (October 25).

7. Complications: *S. typhi* and *S. paratyphi* A, B, and C produce typhoid and typhoid-like fever in humans. Various organs may be infected, leading to lesions. The fatality rate of typhoid fever is 10% compared to less than 1% for most forms of salmonellosis. *S. dublin* has a 15% mortality rate when septicemic in the elderly, and *S. enteritidis* is demonstrating approximately a 3.6% mortality rate in hospital/nursing home outbreaks, with the elderly being particularly affected.

Salmonella septicemia has been associated with subsequent infection of virtually every organ system.

Postenteritis reactive arthritis and Reiter's syndrome have also been reported to occur generally after 3 weeks. Reactive arthritis may occur with a frequency of about 2% of culture-proven cases. Septic arthritis, subsequent or coincident with septicemia, also occurs and can be difficult to treat.

8. Target Populations: All age groups are susceptible, but symptoms are most severe in the elderly, infants, and the infirm. AIDS patients suffer salmonellosis frequently (estimated 20-fold more than general population) and suffer from recurrent episodes.

9. Foods Analysis:

Methods have been developed for many foods having prior history of Salmonella contamination. Although conventional culture methods require 5 days for presumptive results, several rapid methods are available which require only 2 days.

10. Selected Outbreaks:

In 1985, a salmonellosis outbreak involving 16,000 confirmed cases in 6 states was caused by low fat and whole milk from one Chicago dairy. This was the largest outbreak of foodborne salmonellosis in the U.S. FDA inspectors discovered that the pasteurization equipment had been modified to facilitate the running off of raw milk, resulting in the pasteurized milk being contaminated with raw milk under certain conditions. The dairy has subsequently disconnected the cross-linking line. Persons on antibiotic therapy were more apt to be affected in this outbreak.

In August and September, 1985, *S. enteritidis* was isolated from employees and patrons of three restaurants of a chain in Maryland. The outbreak in one restaurant had at least 71 illnesses resulting in 17 hospitalizations. Scrambled eggs from a breakfast bar were epidemiologically implicated in this outbreak and in possibly one other of the three restaurants. The plasmid profiles of isolates from patients all three restaurants matched.

The Centers for Disease Control (CDC) has recorded more than 120 outbreaks of *S. enteritidis* to date, many occurring in restaurants, and some in nursing homes, hospitals and prisons.

In 1984, 186 cases of salmonellosis (*S. enteritidis*) were reported on 29 flights to the United States on a single international airline. An estimated 2,747 passengers were affected overall. No specific food item was implicated, but food ordered from the first class menu was strongly associated with disease.

S. enteritidis outbreaks continue to occur in the U.S. (Table 1). The CDC estimates that 75% of those outbreaks are associated with the consumption of raw or inadequately cooked Grade A whole shell eggs. The U.S. Department of Agriculture published Regulations on February 16, 1990, in the Federal Register establishing a mandatory testing program for egg-producing breeder flocks and commercial flocks implicated in causing human illnesses. This testing should lead to a reduction in cases of gastroenteritis caused by the consumption of Grade A whole shell eggs.

Salmonellosis associated with a Thanksgiving Dinner in Nevada in 1995 is reported in MMWR 45(46):1996 Nov 22.

MMWR 45(34):1996 Aug 30 reports on several outbreaks of *Salmonella enteritidis* infection associated with

the consumption of raw shell eggs in the United States from 1994 to 1995.

A report of an outbreak of *Salmonella* Serotype Typhimurium infection associated with the consumption of raw ground beef may be found in MMWR 44(49):1995 Dec 15.

MMWR 44(42):1995 Oct 27 reports on an outbreak of Salmonellosis associated with beef jerky in New Mexico in 1995.

The report on the outbreak of Salmonella from commercially prepared ice cream is found in MMWR 43 (40):1994 Oct 14.

An outbreak of *S. enteritidis* in homemade ice cream is reported in this MMWR 43(36):1994 Sep 16.

A series of *S. enteritidis* outbreaks in California are summarized in the following MMWR 42(41):1993 Oct 22.

For information on an outbreak of Salmonella Serotype Tennessee in Powdered Milk Products and Infant Formula -- see this MMWR 42(26):1993 Jul 09.

Summaries of Salmonella outbreaks associated with Grade A eggs are reported in MMWR 37(32):1988 Aug 19 and MMWR 39(50):1990 Dec 21.

For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.

11. Education: The CDC provides an informational brochure on preventing Salmonella enteritidis infection.

Food Safety Facts for Consumers (July 1999)

12. Other Resources: A Loci index for genome *Salmonella enteritidis* is available from GenBank.

CDC/MMWR

The CDC/MMWR link will provide a list of Morbidity and Mortality Weekly Reports at CDC relating to this organism or toxin. The date shown is the date the item was posted on the Web, not the date of the MMWR. The summary statement shown are the initial words

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Clostridium botulinum

Education | CDC/MMWR | NIH/PubMed

1. Name of the organism:
Clostridium botulinum

Clostridium botulinum is an anaerobic, Gram-positive, spore-forming rod that produces a potent neurotoxin. The spores are heat-resistant and can survive in foods that are incorrectly or minimally processed. Seven types (A, B, C, D, E, F and G) of botulism are recognized, based on the antigenic specificity of the toxin produced by each strain. Types A, B, E and F cause human botulism. Types C and D cause most cases of botulism in animals. Animals most commonly affected are wild fowl and poultry, cattle, horses and some species of fish. Although type G has been isolated from soil in Argentina, no outbreaks involving it have been recognized.

Foodborne botulism (as distinct from wound botulism and infant botulism) is a severe type of food poisoning caused by the ingestion of foods containing the potent neurotoxin formed during growth of the organism. The toxin is heat labile and can be destroyed if heated at 80°C for 10 minutes or longer. The incidence of the disease is low, but the disease is of considerable concern because of its high mortality rate if not treated immediately and properly. Most of the 10 to 30 outbreaks that are reported annually in the United States are associated with inadequately processed, home-canned foods, but occasionally commercially produced foods have been involved in outbreaks. Sausages, meat products, canned vegetables and seafood products have been the most frequent vehicles for human botulism.

The organism and its spores are widely distributed in nature. They occur in both cultivated and forest soils, bottom sediments of streams, lakes, and coastal waters, and in the intestinal tracts of fish and mammals, and in the gills and viscera of crabs and other shellfish.

2. Name of the Disease:

Four types of botulism are recognized: foodborne, infant, wound, and a form of botulism whose classification is as yet undetermined. Certain foods have been reported as sources of spores in cases of infant botulism and the undetermined category; wound botulism is not related to foods.

Foodborne botulism is the name of the disease (actually a foodborne intoxication) caused by the consumption of foods containing the neurotoxin produced by *C. botulinum*.

Infant botulism, first recognized in 1976, affects infants under 12 months of age. This type of botulism is caused by the ingestion of *C. botulinum* spores which colonize and produce toxin in the intestinal tract of infants (intestinal toxemia botulism). Of the various potential environmental sources such as soil, cistern water, dust and foods, honey is the one dietary reservoir of *C. botulinum* spores thus far definitively linked to infant botulism by both laboratory and epidemiologic studies. The number of confirmed infant botulism cases has increased significantly as a result of greater awareness by health officials since its recognition in 1976. It is now internationally recognized, with cases being reported in more countries.

Wound botulism is the rarest form of botulism. The illness results when *C. botulinum* by itself or with other microorganisms infects a wound and produces toxins which reach other parts of the body via the blood stream. Foods are not involved in this type of botulism.

Undetermined category of botulism involves adult cases in which a specific food or wound source cannot be identified. It has been suggested that some cases of botulism assigned to this category might result from intestinal colonization in adults, with in vivo production of toxin. Reports in the medical literature suggest the existence of a form of botulism similar to infant botulism, but occurring in adults. In these cases, the patients had surgical alterations of the gastrointestinal tract and/or antibiotic therapy. It is proposed that these procedures may have altered the normal gut flora and allowed *C. botulinum* to colonize the intestinal tract.

3. Nature of the Disease:

Infective dose -- a very small amount (a few nanograms) of toxin can cause illness.

Onset of symptoms in foodborne botulism is usually 18 to 36 hours after ingestion of the food containing the toxin, although cases have varied from 4 hours to 8 days. Early signs of intoxication consist of marked lassitude, weakness and vertigo, usually followed by double vision and progressive difficulty in speaking and swallowing. Difficulty in breathing, weakness of other muscles, abdominal distention, and constipation may also be common symptoms.

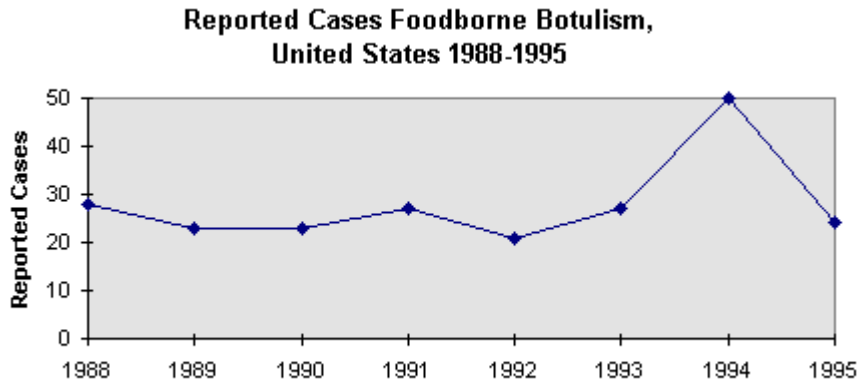
Clinical symptoms of infant botulism consist of constipation that occurs after a period of normal development. This is followed by poor feeding, lethargy, weakness, pooled oral secretions, and wail or altered cry. Loss of head control is striking. Recommended treatment is primarily supportive care. Antimicrobial therapy is not recommended. Infant botulism is diagnosed by demonstrating botulinal toxins and the organism in the infants' stools.

4. Diagnosis of Human Illness: Although botulism can be diagnosed by clinical symptoms alone, differentiation from other diseases may be difficult. The most direct and effective way to confirm the clinical diagnosis of botulism in the laboratory is to demonstrate the presence of toxin in the serum or feces of the patient or in the food which the patient consumed. Currently, the most sensitive and widely used method for detecting toxin is the mouse neutralization test. This test takes 48 hours. Culturing of specimens takes 5-7 days.

5. Associated Foods: The types of foods involved in botulism vary according to food preservation and eating habits in different regions. Any food that is conducive to outgrowth and toxin production, that when processed allows spore survival, and is not subsequently heated before consumption can be associated with botulism. Almost any type of food that is not very acidic (pH above 4.6) can support growth and toxin production by *C. botulinum*. Botulinal toxin has been demonstrated in a considerable variety of foods, such as canned corn, peppers, green beans, soups, beets, asparagus, mushrooms, ripe olives, spinach, tuna fish, chicken and chicken livers and liver pate, and luncheon meats, ham, sausage, stuffed eggplant, lobster, and smoked and salted fish.

6. Frequency:

The incidence of the disease is low, but the mortality rate is high if not treated immediately and properly. There are generally between 10 to 30 outbreaks a year in the United States. Some cases of botulism may go undiagnosed because symptoms are transient or mild, or misdiagnosed as Guillain-Barre syndrome.



Summary of Notifiable Diseases, United States MMWR 44(53): 1996 October 25

7. The Usual Course of Disease and Complications:

Botulinum toxin causes flaccid paralysis by blocking motor nerve terminals at the myoneural junction. The flaccid paralysis progresses symmetrically downward, usually starting with the eyes and face, to the throat, chest and extremities. When the diaphragm and chest muscles become fully involved, respiration is inhibited and death from asphyxia results. Recommended treatment for foodborne botulism includes early administration of botulinal antitoxin (available from CDC) and intensive supportive care (including mechanical breathing assistance).

8. Target Populations:

All people are believed to be susceptible to the foodborne intoxication.

9. Food Analysis:

Since botulism is foodborne and results from ingestion of thet toxin of *C. botulinum*, determination of the source of an outbreak is based on detection and identification of toxin in the food involved. The most widely accepted method is the injection of extracts of the food into passively immunized mice (mouse neutralization test). The test takes 48 hours. This analysis is followed by culturing all suspect food in an enrichment medium for the detection and isolation of the causative organism. This test takes 7 days.

10. Selected Outbreaks:

Two separate outbreaks of botulism have occurred involving commercially canned salmon. Restaurant foods such as sauteed onions, chopped bottled garlic, potato salad made from baked potatoes and baked potatoes themselves have been responsible for a number of outbreaks. Also, smoked fish, both hot and cold-smoke (e.g., Kapchunka) have caused outbreaks of type E botulism.

In October and November, 1987, 8 cases of type E botulism occurred, 2 in New York City and 6 in

Israel. All 8 patients had consumed Kapchunka, an uneviscerated, dry-salted, air-dried, whole whitefish. The product was made in New York City and some of it was transported by individuals to Israel. All 8 patients with botulism developed symptoms within 36 hours of consuming the Kapchunka. One female died, 2 required breathing assistance, 3 were treated therapeutically with antitoxin, and 3 recovered spontaneously. The Kapchunka involved in this outbreak contained high levels of type E botulinal toxin despite salt levels that exceeded those sufficient to inhibit *C. botulinum* type E outgrowth. One possible explanation was that the fish contained low salt levels when air-dried at room temperature, became toxic, and then were re-brined. Regulations were published to prohibit the processing, distribution and sale of Kapchunka and Kapchunka-type products in the United States.

A bottled chopped garlic-in-oil mix was responsible for three cases of botulism in Kingston, N.Y. Two men and a woman were hospitalized with botulism after consuming a chopped garlic-in-oil mix that had been used in a spread for garlic bread. The bottled chopped garlic relied solely on refrigeration to ensure safety and did not contain any additional antibotulinal additives or barriers. The FDA has ordered companies to stop making the product and to withdraw from the market any garlic-in-oil mix which does not include microbial inhibitors or acidifying agents and does not require refrigeration for safety.

Since botulism is a life-threatening disease, FDA always initiates a Class I recall.

January 1992

An incident of foodborne botulism in Oklahoma is reported in MMWR 44(11):1995 Mar 24.

A botulism type B outbreak in Italy associated with eggplant in oil is reported in MMWR 44(2):1995 Jan 20.

The botulism outbreak associated with salted fish mentioned above is reported in greater detail in MMWR 36(49):1987 Dec 18.

For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.

11. Education:

The December 1995 issue of "FDA Consumer" has an article titled Botulism Toxin: a Poison That Can Heal which discusses Botulism toxin with an emphasis on its medical uses.

12. Other Resources: FDA Warns Against Consuming Certain Italian Mascarpone Cream Cheese Because of Potential Serious Botulism Risk (Sept. 9, 1996)

A Loci index for genome *Clostridium botulinum* is available from GenBank.

CDC/MMWR

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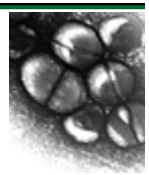

Staphylococcus aureus

CDC/MMWR NIH/PubMed

1. Name of the Organism: ***Staphylococcus aureus***

S. aureus is a spherical bacterium (coccus) which on microscopic examination appears in pairs, short chains, or bunched, grape-like clusters. These organisms are Gram-positive. Some strains are capable of producing a highly heat-stable protein toxin that causes illness in humans.

2. Name of Acute Disease:

Staphylococcal food poisoning (staphyloenterotoxicosis; staphyloenterotoxemia) is the name of the condition caused by the enterotoxins which some strains of *S. aureus* produce.

3. Nature of the Disease:

The onset of symptoms in staphylococcal food poisoning is usually rapid and in many cases acute, depending on individual susceptibility to the toxin, the amount of contaminated food eaten, the amount of toxin in the food ingested, and the general health of the victim. The most common symptoms are nausea, vomiting, retching, abdominal cramping, and prostration. Some individuals may not always demonstrate all the symptoms associated with the illness. In more severe cases, headache, muscle cramping, and transient changes in blood pressure and pulse rate may occur. Recovery generally takes two days, However, it us not unusual for complete recovery to take three days and sometimes longer in severe cases.

Infective dose--a toxin dose of less than 1.0 microgram in contaminated food will produce symptoms of staphylococcal intoxication. This toxin level is reached when *S. aureus* populations exceed 100,000 per gram.

4. Diagnosis of Human Illness:

In the diagnosis of staphylococcal foodborne illness, proper interviews with the victims and gathering and analyzing epidemiologic data are essential. Incriminated foods should be collected and examined for

staphylococci. The presence of relatively large numbers of enterotoxigenic staphylococci is good circumstantial evidence that the food contains toxin. The most conclusive test is the linking of an illness with a specific food or in cases where multiple vehicles exist, the detection of the toxin in the food sample(s). In cases where the food may have been treated to kill the staphylococci, as in pasteurization or heating, direct microscopic observation of the food may be an aid in the diagnosis. A number of serological methods for determining the enterotoxigenicity of *S. aureus* isolated from foods as well as methods for the separation and detection of toxins in foods have been developed and used successfully to aid in the diagnosis of the illness. Phage typing may also be useful when viable staphylococci can be isolated from the incriminated food, from victims, and from suspected carrier such as food handlers.

5. Foods Incriminated: Foods that are frequently incriminated in staphylococcal food poisoning include meat and meat products; poultry and egg products; salads such as egg, tuna, chicken, potato, and macaroni; bakery products such as cream-filled pastries, cream pies, and chocolate eclairs; sandwich fillings; and milk and dairy products. Foods that require considerable handling during preparation and that are kept at slightly elevated temperatures after preparation are frequently involved in staphylococcal food poisoning.

Staphylococci exist in air, dust, sewage, water, milk, and food or on food equipment, environmental surfaces, humans, and animals. Humans and animals are the primary reservoirs. Staphylococci are present in the nasal passages and throats and on the hair and skin of 50 percent or more of healthy individuals. This incidence is even higher for those who associate with or who come in contact with sick individuals and hospital environments. Although food handlers are usually the main source of food contamination in food poisoning outbreaks, equipment and environmental surfaces can also be sources of contamination with *S. aureus*. Human intoxication is caused by ingesting enterotoxins produced in food by some strains of *S. aureus*, usually because the food has not been kept hot enough (60°C, 140°F, or above) or cold enough (7.2°C, 45°F, or below).

6. Frequency of Illness: The true incidence of staphylococcal food poisoning is unknown for a number of reasons, including poor responses from victims during interviews with health officials; misdiagnosis of the illness, which may be symptomatically similar to other types of food poisoning (such as vomiting caused by *Bacillus cereus* toxin); inadequate collection of samples for laboratory analyses; and improper laboratory examination. Of the bacterial pathogens causing foodborne illnesses in the U.S. (127 outbreaks, 7,082 cases recorded in 1983), 14 outbreaks involving 1,257 cases were caused by *S. aureus*. These outbreaks were followed by 11 outbreaks (1,153 cases) in 1984, 14 outbreaks (421 cases) in 1985, 7 outbreaks (250 cases) in 1986 and one reported outbreak (100 cases) in 1987.

7. Complications: Death from staphylococcal food poisoning is very rare, although such cases have occurred among the elderly,

infants, and severely debilitated persons.

8. Target Population: All people are believed to be susceptible to this type of bacterial intoxication; however, intensity of symptoms may vary.

9. Analysis of Foods: For detecting trace amounts of staphylococcal enterotoxin in foods incriminated in food poisoning, the toxin must be separated from food constituents and concentrated before identification by specific precipitation with antiserum (antienterotoxin) as follows. Two principles are used for the purpose: (1) the selective adsorption of the enterotoxin from an extract of the food onto ion exchange resins and (2) the use of physical and chemical procedures for the selective removal of food constituents from the extract, leaving the enterotoxin(s) in solution. The use of these techniques and concentration of the resulting products (as much as possible) has made it possible to detect small amounts of enterotoxin in food.

There are developed rapid methods based on monoclonal antibodies (e.g., ELISA, Reverse Passive Latex Agglutination), which are being evaluated for their efficacy in the detection of enterotoxins in food. These rapid methods can detect approximately 1.0 nanogram of toxin/g of food.

10. Typical Outbreak: 1,364 children became ill out of a total of 5,824 who had eaten lunch served at 16 elementary schools in Texas. The lunches were prepared in a central kitchen and transported to the schools by truck. Epidemiological studies revealed that 95% of the children who became ill had eaten a chicken salad. The afternoon of the day preceding the lunch, frozen chickens were boiled for 3 hours. After cooking, the chickens were deboned, cooled to room temperature with a fan, ground into small pieces, placed into l2-inch-deep aluminum pans and stored overnight in a walk-in refrigerator at 42-45°F.

The following morning, the remaining ingredients of the salad were added and the mixture was blended with an electric mixer. The food was placed in thermal containers and transported to the various schools at 9:30 AM to 10:30 AM, where it was kept at room temperature until served between 11:30 AM and noon. Bacteriological examination of the chicken salad revealed the presence of large numbers of *S. aureus*.

Contamination of the chicken probably occurred when it was deboned. The chicken was not cooled rapidly enough because it was stored in l2-inch-deep layers. Growth of the staphylococcus probably occurred also during the period when the food was kept in the warm classrooms. Prevention of this incident would have entailed screening the individuals who deboned the chicken for carriers of the staphylococcus, more rapid cooling of the chicken, and adequate refrigeration of the salad from the time of preparation to its consumption.

11. Atypical Outbreaks:

In 1989, multiple staphylococcal foodborne diseases were associated with the consumption of canned mushrooms. (CDC Morbidity and Mortality Weekly Report, June 23, 1989, Vol. 38, #24.)

Starkville, Mississippi. On February 13, 22 people became ill with gastroenteritis several hours after eating at a university cafeteria. Symptoms included nausea, vomiting, diarrhea, and abdominal cramps. Nine people were hospitalized. Canned mushrooms served with omelets and hamburgers were associated with illness. No deficiencies in food handling were found. Staphylococcal enterotoxin type A was identified in a sample of implicated mushrooms from the omelet bar and in unopened cans from the same lot.

Queens, New York. On February 28, 48 people became ill a median of 3 hours after eating lunch in a hospital employee cafeteria. One person was hospitalized. Canned mushrooms served at the salad bar were epidemiologically implicated. Two unopened cans of mushrooms from the same lot as the implicated can contained staphylococcal enterotoxin A.

McKeesport, Pennsylvania. On April 17, 12 people became ill with gastroenteritis a median of 2 hours after eating lunch or dinner at a restaurant. Two people were hospitalized. Canned mushrooms, consumed on pizza or with a parmigiana sauce, were associated with illness. No deficiencies were found in food preparation or storage. Staphylococcal enterotoxin was found in samples of remaining mushrooms and in unopened cans from the same lot.

Philipsburg, Pennsylvania. On April 22, 20 people developed illness several hours after eating food from a take-out pizzeria. Four people were hospitalized. Only pizza served with canned mushrooms was associated with illness. Staphylococcal enterotoxin was found in a sample of mushrooms from the pizzeria and in unopened cans with the same lot number.

For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.

12. Other Resources:

A Loci index for genome *Staphylococcus aureus* is available from GenBank.

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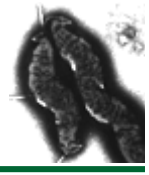
Foodborne Pathogenic Microorganisms and Natural Toxins Handbook



Campylobacter jejuni

Education | CDC/MMWR | NIH/PubMed

1. Name of the Organism: *Campylobacter jejuni* (formerly known as *Campylobacter fetus* subsp. jejuni)

Campylobacter jejuni is a Gram-negative slender, curved, and motile rod. It is a microaerophilic organism, which means it has a requirement for reduced levels of oxygen. It is relatively fragile, and sensitive to environmental stresses (e.g., 21% oxygen, drying, heating, disinfectants, acidic conditions). Because of its microaerophilic characteristics the organism requires 3 to 5% oxygen and 2 to 10% carbon dioxide for optimal growth conditions. This bacterium is now recognized as an important enteric pathogen. Before 1972, when methods were developed for its isolation from feces, it was believed to be primarily an animal pathogen causing abortion and enteritis in sheep and cattle. Surveys have shown that *C. jejuni* is the leading cause of bacterial diarrheal illness in the United States. It causes more disease than *Shigella* spp. and *Salmonella* spp. combined.

Although *C. jejuni* is not carried by healthy individuals in the United States or Europe, it is often isolated from healthy cattle, chickens, birds and even flies. It is sometimes present in non-chlorinated water sources such as streams and ponds.

Because the pathogenic mechanisms of *C. jejuni* are still being studied, it is difficult to differentiate pathogenic from nonpathogenic strains. However, it appears that many of the chicken isolates are pathogens.

2. Name of Disease: Campylobacteriosis is the name of the illness caused by *C. jejuni*. It is also often known as campylobacter enteritis or gastroenteritis.

3. Major Symptoms: *C. jejuni* infection causes diarrhea, which may be watery or sticky and can contain blood (usually occult) and

fecal leukocytes (white cells). Other symptoms often present are fever, abdominal pain, nausea, headache and muscle pain. The illness usually occurs 2-5 days after ingestion of the contaminated food or water. Illness generally lasts 7-10 days, but relapses are not uncommon (about 25% of cases). Most infections are self-limiting and are not treated with antibiotics. However, treatment with erythromycin does reduce the length of time that infected individuals shed the bacteria in their feces.

The infective dose of *C. jejuni* is considered to be small. Human feeding studies suggest that about 400-500 bacteria may cause illness in some individuals, while in others, greater numbers are required. A conducted volunteer human feeding study suggests that host susceptibility also dictates infectious dose to some degree. The pathogenic mechanisms of *C. jejuni* are still not completely understood, but it does produce a heat-labile toxin that may cause diarrhea. *C. jejuni* may also be an invasive organism.

4. Isolation Procedures:

C. jejuni is usually present in high numbers in the diarrheal stools of individuals, but isolation requires special antibiotic-containing media and a special microaerophilic atmosphere (5% oxygen). However, most clinical laboratories are equipped to isolate Campylobacter spp. if requested.

5. Associated Foods:

C. jejuni frequently contaminates raw chicken. Surveys show that 20 to 100% of retail chickens are contaminated. This is not overly surprising since many healthy chickens carry these bacteria in their intestinal tracts. Raw milk is also a source of infections. The bacteria are often carried by healthy cattle and by flies on farms. Non-chlorinated water may also be a source of infections. However, properly cooking chicken, pasteurizing milk, and chlorinating drinking water will kill the bacteria.

6. Frequency of the Disease:

C. jejuni is the leading cause of bacterial diarrhea in the U.S. There are probably numbers of cases in excess of the estimated cases of salmonellosis (2- to 4,000,000/year).

7. Complications:

Complications are relatively rare, but infections have been associated with reactive arthritis, hemolytic uremic syndrome, and following septicemia, infections of nearly any organ. The estimated case/fatality ratio for all *C. jejuni* infections is 0.1, meaning one death per 1,000 cases. Fatalities are rare in healthy individuals and usually occur in cancer patients or in the otherwise debilitated. Only 20 reported cases of septic abortion induced by *C. jejuni* have been recorded in the literature.

Meningitis, recurrent colitis, acute cholecystitis and Guillain-Barre syndrome are very rare complications.

8. Target Populations:

Although anyone can have a *C. jejuni* infection, children under 5 years and young adults (15-29) are more frequently afflicted than other age groups. Reactive arthritis, a rare complication of these infections, is strongly

associated with people who have the human lymphocyte antigen B27 (HLA-B27).

9. Recovery from Foods:

Isolation of *C. jejuni* from food is difficult because the bacteria are usually present in very low numbers (unlike the case of diarrheal stools in which 10/6 bacteria/gram is not unusual). The methods require an enrichment broth containing antibiotics, special antibiotic-containing plates and a microaerophilic atmosphere generally a microaerophilic atmosphere with 5% oxygen and an elevated concentration of carbon dioxide (10%). Isolation can take several days to a week.

10. Selected Outbreaks:

Usually outbreaks are small (less than 50 people), but in Bennington, VT a large outbreak involving about 2,000 people occurred while the town was temporarily using an non-chlorinated water source as a water supply. Several small outbreaks have been reported among children who were taken on a class trip to a dairy and given raw milk to drink. An outbreak was also associated with consumption of raw clams. However, a survey showed that about 50% of infections are associated with either eating inadequately cooked or recontaminated chicken meat or handling chickens. It is the leading bacterial cause of sporadic (non-clustered cases) diarrheal disease in the U.S.

In April, 1986, an elementary school child was cultured for bacterial pathogens (due to bloody diarrhea), and *C. jejuni* was isolated. Food consumption/gastrointestinal illness questionnaires were administered to other students and faculty at the school. In all, 32 of 172 students reported symptoms of diarrhea (100%), cramps (80%), nausea (51%), fever (29%), vomiting (26%), and bloody stools (14%). The food questionnaire clearly implicated milk as the common source, and a dose/response was evident (those drinking more milk were more likely to be ill). Investigation of the dairy supplying the milk showed that they vat pasteurized the milk at 135°F for 25 minutes rather than the required 145°F for 30 minutes. The dairy processed surplus raw milk for the school, and this milk had a high somatic cell count. Cows from the herd supplying the dairy had *C. jejuni* in their feces. This outbreak points out the variation in symptoms which may occur with campylobacteriosis and the absolute need to adhere to pasteurization time/temperature standards.

Although other *Campylobacter* spp. have been implicated in human gastroenteritis (e.g. *C. laridis*, *C. hyointestinalis*), it is believed that 99% of the cases are caused by *C. jejuni*.

Information regarding an outbreak of Campylobacter in New Zealand is found in this MMWR 40(7):1991 Feb 22.

For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.

11. Education: The Food Safety Inspection Service of the U.S. Department of Agriculture has produced a background document on *Campylobacter*.

12. Other Resources: A Loci index for genome *Campylobacter jejuni* is available from GenBank.

CDC/MMWR

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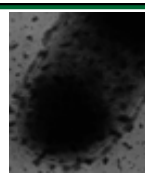

Yersinia enterocolitica

CDC/MMWR NIH/PubMed

1. Name of the Organism: *Yersinia enterocolitica* (and *Yersinia pseudotuberculosis*)

Y. enterocolitica, a small rod-shaped, Gram-negative bacterium, is often isolated from clinical specimens such as wounds, feces, sputum and mesenteric lymph nodes. However, it is not part of the normal human flora. *Y. pseudotuberculosis* has been isolated from the diseased appendix of humans.

Both organisms have often been isolated from such animals as pigs, birds, beavers, cats, and dogs. Only *Y. enterocolitica* has been detected in environmental and food sources, such as ponds, lakes, meats, ice cream, and milk. Most isolates have been found not to be pathogenic.

2. Name of Disease: Yersiniosis

There are 3 pathogenic species in the genus Yersinia, but only *Y. enterocolitica* and *Y. pseudotuberculosis* cause gastroenteritis. To date, no foodborne outbreaks caused by *Y. pseudotuberculosis* have been reported in the United States, but human infections transmitted via contaminated water and foods have been reported in Japan. *Y. pestis*, the causative agent of "the plague," is genetically very similar to *Y. pseudotuberculosis* but infects humans by routes other than food.

3. Nature of Disease: Yersiniosis is frequently characterized by such symptoms as gastroenteritis with diarrhea and/or vomiting; however, fever and abdominal pain are the hallmark symptoms. *Yersinia* infections mimic appendicitis and mesenteric lymphadenitis, but the bacteria may also cause infections of other sites such as wounds, joints and the urinary tract.

4. Infective dose: Unknown.

Illness onset is usually between 24 and 48 hours after ingestion, which (with food or drink as vehicle) is the usual route of infection.

5. Diagnosis of Human Illness: Diagnosis of yersiniosis begins with isolation of the organism from the human host's feces, blood, or vomit, and sometimes at the time of appendectomy. Confirmation occurs with the isolation, as well as biochemical and serological identification, of *Y. enterocolitica* from both the human host and the ingested foodstuff. Diarrhea is reported to occur in about 80% of cases; abdominal pain and fever are the most reliable symptoms.

Because of the difficulties in isolating *yersiniae* from feces, several countries rely on serology. Acute and convalescent patient sera are titered against the suspect serotype of *Yersinia spp*.

Yersiniosis has been misdiagnosed as Crohn's disease (regional enteritis) as well as appendicitis.

6. Associated Foods: Strains of *Y. enterocolitica* can be found in meats (pork, beef, lamb, etc.), oysters, fish, and raw milk. The exact cause of the food contamination is unknown. However, the prevalence of this organism in the soil and water and in animals such as beavers, pigs, and squirrels, offers ample opportunities for it to enter our food supply. Poor sanitation and improper sterilization techniques by food handlers, including improper storage, cannot be overlooked as contributing to contamination.

7. Frequency of the Disease: Yersiniosis does not occur frequently. It is rare unless a breakdown occurs in food processing techniques. CDC estimates that about 17,000 cases occur annually in the USA. Yersiniosis is a far more common disease in Northern Europe, Scandinavia, and Japan.

8. Complications: The major "complication" is the performance of unnecessary appendectomies, since one of the main symptoms of infections is abdominal pain of the lower right quadrant.

Both *Y. enterocolitica* and *Y. pseudotuberculosis* have been associated with reactive arthritis, which may occur even in the absence of obvious symptoms. The frequency of such postenteritis arthritic conditions is about 2-3%.

Another complication is bacteremia (entrance of organisms into the blood stream), in which case the possibility of a disseminating disease may occur. This is rare, however, and fatalities are also extremely rare.

9. Target The most susceptible populations for the main disease and possible complications are the very young, the

Populations: debilitated, the very old and persons undergoing immunosuppressive therapy. Those most susceptible to postenteritis arthritis are individuals with the antigen HLA-B27 (or related antigens such as B7).

10. Food Analysis: The isolation method is relatively easy to perform, but in some instances, cold enrichment may be required. *Y. enterocolitica* can be presumptively identified in 36-48 hours. However, confirmation may take 14-21 days or more. Determination of pathogenicity is more complex. The genes encoding for invasion of mammalian cells are located on the chromosome while a 40-50 MDal plasmid encodes most of the other virulence associated phenotypes. The 40-50 MDal plasmid is present in almost all the pathogenic *Yersinia* species, and the plasmids appear to be homologous.

11. Selected Outbreaks: 1976. A chocolate milk outbreak in Oneida County, N.Y. involving school children (first reported yersiniosis incident in the United States in which a food vehicle was identified). A research laboratory was set up by FDA to investigate and study *Y. enterocolitica* and *Y. pseudotuberculosis* in the human food supply.

Dec. 1981 - Feb. 1982. *Y. enterocolitica* enteritis in King County, Washington caused by ingestion of tofu, a soybean curd. FDA investigators and researchers determined the source of the infection to be an non-chlorinated water supply. Manufacturing was halted until uncontaminated product was produced.

June 11 to July 21, 1982. *Y. enterocolitica* outbreak in Arkansas, Tennessee, and Mississippi associated with the consumption of pasteurized milk. FDA personnel participated in the investigation, and presumptively identified the infection source to be externally contaminated milk containers.

A report of *Yersinia enterocolitica* incidents associated with raw chitterlings may be found in MMWR 39(45):1990 Nov 16

For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.

12. Other Resources: A Loci index for genome *Yersinia enterocolitica* and Loci index for genome *Yersinia pseudotuberculosis* are available from GenBank.

CDC/MMWR

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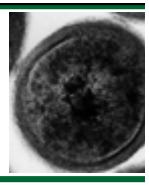

Listeria monocytogenes

Education | CDC/MMWR | NIH/PubMed

1. Name of the Organism: *Listeria monocytogenes*

This is a Gram-positive bacterium, motile by means of flagella. Some studies suggest that 1-10% of humans may be intestinal carriers of *L. monocytogenes*. It has been found in at least 37 mammalian species, both domestic and feral, as well as at least 17 species of birds and possibly some species of fish and shellfish. It can be isolated from soil, silage, and other environmental sources. *L. monocytogenes* is quite hardy and resists the deleterious effects of freezing, drying, and heat remarkably well for a bacterium that does not form spores. Most *L. monocytogenes* are pathogenic to some degree.

2. Name of Acute Disease:

Listeriosis is the name of the general group of disorders caused by *L. monocytogenes*.

3. Nature of Disease:

Listeriosis is clinically defined when the organism is isolated from blood, cerebrospinal fluid, or an otherwise normally sterile site (e.g. placenta, fetus).

The manifestations of listeriosis include septicemia, meningitis (or meningoencephalitis), encephalitis, and intrauterine or cervical infections in pregnant women, which may result in spontaneous abortion (2nd/3rd trimester) or stillbirth. The onset of the aforementioned disorders is usually preceded by influenza-like symptoms including persistent fever. It was reported that gastrointestinal symptoms such as nausea, vomiting, and diarrhea may precede more serious forms of listeriosis or may be the only symptoms expressed. Gastrointestinal symptoms were epidemiologically associated with use of antacids or cimetidine. The onset time to serious forms of listeriosis is unknown but may range from a few days

to three weeks. The onset time to gastrointestinal symptoms is unknown but is probably greater than 12 hours.

The infective dose of *L. monocytogenes* is unknown but is believed to vary with the strain and susceptibility of the victim. From cases contracted through raw or supposedly pasteurized milk, it is safe to assume that in susceptible persons, fewer than 1,000 total organisms may cause disease. *L. monocytogenes* may invade the gastrointestinal epithelium. Once the bacterium enters the host's monocytes, macrophages, or polymorphonuclear leukocytes, it is bloodborne (septicemic) and can grow. Its presence intracellularly in phagocytic cells also permits access to the brain and probably transplacental migration to the fetus in pregnant women. The pathogenesis of *L. monocytogenes* centers on its ability to survive and multiply in phagocytic host cells.

4. Diagnosis of Human Illness: Listeriosis can only be positively diagnosed by culturing the organism from blood, cerebrospinal fluid, or stool (although the latter is difficult and of limited value).

5. Associated Foods: *L. monocytogenes* has been associated with such foods as raw milk, supposedly pasteurized fluid milk, cheeses (particularly soft-ripened varieties), ice cream, raw vegetables, fermented raw-meat sausages, raw and cooked poultry, raw meats (all types), and raw and smoked fish. Its ability to grow at temperatures as low as 3°C permits multiplication in refrigerated foods.

6. Frequency of the Disease: The 1987 incidence data prospectively collected by CDC suggests that there are at least 1600 cases of listeriosis with 415 deaths per year in the U.S. The vast majority of cases are sporadic, making epidemiological links to food very difficult.

7. Complications: Most healthy persons probably show no symptoms. The "complications" are the usual clinical expressions of the disease.

When listeric meningitis occurs, the overall mortality may be as high as 70%; from septicemia 50%, from perinatal/neonatal infections greater than 80%. In infections during pregnancy, the mother usually survives. Successful treatment with parenteral penicillin or ampicillin has been reported. Trimethoprim-sulfamethoxazole has been shown effective in patients allergic to penicillin.

8. Target Populations: The main target populations for listeriosis are:

- pregnant women/fetus - perinatal and neonatal infections;
- persons immunocompromised by corticosteroids, anticancer drugs, graft suppression therapy, AIDS;
- cancer patients - leukemic patients particularly;

- less frequently reported - diabetic, cirrhotic, asthmatic, and ulcerative colitis patients;
- the elderly;
- normal people--some reports suggest that normal, healthy people are at risk, although antacids or cimetidine may predispose. A listerosis outbreak in Switzerland involving cheese suggested that healthy uncompromised individuals could develop the disease, particularly if the foodstuff was heavily contaminated with the organism.

9. Food Analysis:

The methods for analysis of food are complex and time consuming. The present FDA method, revised in September, 1990, requires 24 and 48 hours of enrichment, followed by a variety of other tests. Total time to identification is from 5 to 7 days, but the announcement of specific nonradiolabled DNA probes should soon allow a simpler and faster confirmation of suspect isolates.

Recombinant DNA technology may even permit 2-3 day positive analysis in the future. Currently, FDA is collaborating in adapting its methodology to quantitate very low numbers of the organisms in foods.

10. Selected Outbreaks:

Outbreaks include the California episode in 1985, which was due to Mexican-style cheese and led to numerous stillbirths. As a result of this episode, FDA has been monitoring domestic and imported cheeses and has taken numerous actions to remove these products from the market when *L. monocytogenes* is found.

There have been other clustered cases, such as in Philadelphia, PA, in 1987. Specific food linkages were only made epidemiologically in this cluster.

CDC has established an epidemiological link between consumption of raw hot dogs or undercooked chicken and approximately 20% of the sporadic cases under prospective study.

For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.

11. Education:

The FDA health alert for Hispanic pregnant women concerns the risk of listeriosis from soft cheeses. The CDC provides similar information in Spanish.

The Food Safety and Inspection Service of the U.S. Department of Agriculture has jointly produced with the FDA a background document on *Listeria* and Listeriosis. FSIS also has updated consumer information on Listeria dated February 1999.

The CDC produces an information brochure on preventing Listeriosis.

12. Other Resources: A Loci index for genome *Listeria monocytogenes* is available from GenBank.

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Vibrio cholerae Serogroup O1

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism:
Vibrio cholerae Serogroup O1

This bacterium is responsible for Asiatic or epidemic cholera. No major outbreaks of this disease have occurred in the United States since 1911. However, sporadic cases occurred between 1973 and 1991, suggesting the possible reintroduction of the organism into the U.S. marine and estuarine environment. The cases between 1973 and 1991 were associated with the consumption of raw shellfish or of shellfish either improperly cooked or re-contaminated after proper cooking. Environmental studies have demonstrated that strains of this organism may be found in the temperate estuarine and marine coastal areas surrounding the United States.

In 1991 cholera was reported for the first time in this century in South America, starting in Peru. The outbreaks quickly grew to epidemic proportions and spread to other South American and Central American countries, and into Mexico. 1,099,882 cases and 10,453 deaths were reported in the Western Hemisphere between January 1991 and July 1995.

Although the South American strain of V. cholerae O1 has been isolated from Gulf Coast waters, presumably transmitted by ships off-loading contaminated ballast water, no cases of cholera have been attributed to fish or shellfish harvested from U.S. waters. However, over 100 cases of cholera caused by the South American strain have been reported in the United States. These cases were travelers returning from South America, or were associated with illegally smuggled, temperature-abused crustaceans from South America.

In the Autumn of 1993, a new strain, a non-O1 never before identified, was implicated in outbreaks of cholera in Bangladesh and India. The organism, V. cholerae serogroup O139 (Bengal), causes characteristic severe

cholera symptoms. Previous illness with V. cholerae O1 does not confer immunity and the disease is now endemic. In the U.S., V. cholerae O139 has been implicated in one case, a traveller returning from India. The strain has not been reported in U.S. waters or shellfish.

2. Nature of Acute Disease:

Cholera is the name of the infection caused by *V. cholerae*.

3. Nature of Disease:

CDC Case Definition

What is a "Case Definition"?

Overview of Public Health Surveillance

Symptoms of Asiatic cholera may vary from a mild, watery diarrhea to an acute diarrhea, with characteristic rice water stools. Onset of the illness is generally sudden, with incubation periods varying from 6 hours to 5 days. Abdominal cramps, nausea, vomiting, dehydration, and shock; after severe fluid and electrolyte loss, death may occur. Illness is caused by the ingestion of viable bacteria, which attach to the small intestine and produce cholera toxin. The production of cholera toxin by the attached bacteria results in the watery diarrhea associated with this illness.

Infective dose -- Human volunteer feeding studies utilizing healthy individuals have demonstrated that approximately one million organisms must be ingested to cause illness. Antacid consumption markedly lowers the infective dose.

4. Diagnosis of Human Illness:

Cholera can be confirmed only by the isolation of the causative organism from the diarrheic stools of infected individuals.

5. Associated Foods:

Cholera is generally a disease spread by poor sanitation, resulting in contaminated water supplies. This is clearly the main mechanism for the spread of cholera in poor communities in South America. The excellent sanitation facilities in the U.S. are responsible for the near eradication of epidemic cholera. Sporadic cases occur when shellfish harvested from fecally polluted coastal waters are consumed raw. Cholera may also be transmitted by shellfish harvested from nonpolluted waters since *V. cholerae* O1 is part of the autochthonous microbiota of these waters.

6. Relative Frequency of Disease:

Over 200 proven cases of cholera have been reported in the U.S. since 1973, with 90% occurring within the last 5 years. Most of these cases were detected only after epidemiological investigation. Probably more sporadic cases have occurred, but have gone undiagnosed or unreported.

7. Course of Disease and Complications:

Individuals infected with cholera require rehydration either intravenously or orally with a solution containing sodium chloride, sodium bicarbonate, potassium chloride, and dextrose (glucose). The illness is generally self-limiting. Antibiotics such as tetracycline have been demonstrated to shorten the course of the illness. Death occurs from dehydration and loss of essential electrolytes. Medical treatment to prevent dehydration prevents all complications.

8. Target Populations:

All people are believed to be susceptible to infection, but individuals with damaged or undeveloped immunity, reduced gastric acidity, or malnutrition may suffer more severe forms of the illness.

9. Food Analysis:

V. cholerae serogroup O1 and O139 may be recovered from foods by methods similar to those used for recovering the organism from the feces of infected individuals. Pathogenic and non-pathogenic forms of the organism exist, so all food isolates must be tested for the production of cholera enterotoxin.

10. Selected Outbreaks:

Literature references can be found at the links below.

MMWR 47(19):1998

In April 1997, a *Vibrio cholera* outbreak occurred among 90,000 Rwandan refugees residing in three temporary camps between Kisangani and Ubundu, Democratic Republic of Congo (formerly Zaire).

MMWR 44(20):1995

Since the onset of the *Vibrio cholera* epidemic in Latin America in 1991, most cases of cholera in the United States have occurred among persons traveling to the United States from cholera-affected areas or who have eaten contaminated food brought or imported from these areas. In December 1994, a cluster of cholera cases

occurred among persons in Indiana who had shared a meal of contaminated food brought from El Salvador.

MMWR 44(11):1995	The cholera epidemic caused by Vibrio cholerae O1 that began in January 1991 has continued to spread in Central and South America. In southern Asia, the epidemic caused by the newly recognized strain V. cholerae O139 that began in late 1992 also has continued to spread. This report updates surveillance findings for both epidemics.
MMWR 42(33):1993	Following the epidemic spread of cholera in Peru (1), in April 1991, health officials in neighboring Bolivia established a surveillance system to detect the appearance and monitor the spread of cholera in their country. The first confirmed case in Bolivia was reported on August 26, 1991; by December 31, 1991, a total of 206 cases had been reported, and 21,324 probable and confirmed cases were reported during 1992. This report summarizes cholera surveillance in Cochabamba.
MMWR 42(26):1993	Epidemics of cholera-like illness caused by a previously unrecognized organism occurred recently in southern Asia. This report documents the first case of cholera imported into the United States that was caused by this organism, the newly described toxigenic Vibrio cholerae O139 strain.
MMWR 42(21):1993	During February 7-May 10, 1992, an epidemic of cholera caused by *Vibrio cholerae* O1, serotype *Ogawa*, affected 1044 persons in Western Burundi, a small country in central Africa.
MMWR 42(05):1993	On July 2, 1991, during routine monitoring, the Food and Drug Administration (FDA) isolated toxigenic *Vibrio cholerae* O1, serotype Inaba, biotype El Tor from oysters and intestinal contents of an oyster-eating fish taken from closed oyster beds in Mobile Bay. This isolate was indistinguishable from the Latin American epidemic strain and differed from the strain of *V. cholerae* O1 that is endemic to the Gulf Coast.
MMWR 41(36):1992	Approximately one case of cholera per week is being reported in the United States. Most of these cases have been acquired during international travel and involve persons who return to their homelands to visit family or foreign nationals visiting relatives in the United States. The following report summarizes case reports from four states during 1992.
MMWR 40(49):1991	During August 1991, three cases of cholera in Maryland were associated with the consumption of frozen coconut milk imported from Asia. Following an investigation, the product was recalled, and no other cases have been reported.
MMWR 40(30):1991	Through June 26, 1991, four cases of cholera had been reported in New York and this report described a new

	laboratory procedure used to confirm the vehicle of transmission in this outbreak.
MMWR 40(17):1991	Through April 30, 1991, epidemic cholera has been reported from five countries in South America: Brazil, Chile, Colombia, Ecuador, and Peru. In addition, in the United States a total of 10 confirmed cases of epidemic-associated cholera have been reported in Georgia, New Jersey, and Florida. This report summarizes information regarding the cases reported in New Jersey and Florida.
MMWR 40(15):1991	A case of importation of cholera from Peru to the United States is detailed.
MMWR:40(6):1991 and MMWR 40(13):1991	The cholera outbreak in Peru is reported on and the update of the South American endemic.
MMWR 38(2):1989	On August 17, 1988, a 42-year-old man was treated at an emergency room in Rifle, Colorado. On August 15, he had eaten approximately 12 raw oysters from a new oyster-processing plant in Rifle.The patient had no underlying illness, was not taking medications, and had not traveled outside the region during the month before onset. The oysters had been harvested on August 8, 1988, in a bay off the coast of Louisiana. During a 6-day period, eight other persons shared the oysters purchased by the patient. None became ill.
MMWR 35(38):1986	Four cases of cholera acquired in Louisiana and one case acquired in Florida have been detected since mid-August 1986. All five patients were hospitalized with severe diarrhea and had stool cultures yielding toxigenic *Vibrio cholerae* 01, serotype Inaba.
MMWR 35(44):1986	Since mid-August 1986, a total of 12 cases of cholera have been identified among nine families living in New Orleans and in other towns in six parishes within a 200-mile radius to the south and west of New Orleans. None of the patients had traveled abroad within the past year. All patients recovered following intravenous fluid therapy. Seven patients had stool cultures yielding toxigenic *Vibrio cholerae* O1, biotype El Tor, serotype Inaba. The remaining five patients did not have stool cultures performed but had vibriocidal antibody titers greater than or equal to 1280, suggesting recent infection with *V. cholerae* O1.
Morbidity and Mortality Weekly Reports	**For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.**

11. Education and Background

Literature references can be found at the links below.

Resources:

English Spanish Portuguese	**CDC brochures on the prevention of cholera**.
Cholera Prevention FAQ's	Center for Disease Control and Prevention of Food Illness Fact Sheet
"Produce Handling and Processing Practices" (1997) Emerging Infectious Diseases 3(4).	In the past decade, outbreaks of human illness associated with the consumption of raw vegetables and fruits (or unpasteurized products produced from them) have increased in the United States. Pathogens such as *Listeria monocytogenes*, *Clostridium botulinum*, and *Bacillus cereus* are naturally present in some soil, and their presence on fresh produce is not rare. Salmonella, *Escherichia coli* O157:H7, *Campylobacter jejuni*, *Vibrio cholerae*, parasites, and viruses are more likely to contaminate fresh produce through vehicles such as raw or improperly composted manure, irrigation water containing untreated sewage, or contaminated wash water. Treatment of produce with chlorinated water reduces populations of pathogenic and other microorganisms on fresh produce but cannot eliminate them. Reduction of risk for human illness associated with raw produce can be better achieved through controlling points of potential contamination in the field; during harvesting; during processing or distribution; or in retail markets, food-service facilities, or the home.
Loci index for genome *Vibrio cholerae*	Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.
12. Molecular Structural Data:	None currently available.

CDC/MMWR

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Bad Bug Book

Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Vibrio cholerae Serogroup Non-O1

CDC/MMWR NIH/PubMed Agricola

1. Name of the Organism:
Vibrio cholerae Serogroup Non-Ol

This bacterium infects only humans and other primates. It is related to *V. cholerae* Serogroup O1, the organism that causes Asiatic or epidemic cholera, but causes a disease reported to be less severe than cholera. Both pathogenic and nonpathogenic strains of the organism are normal inhabitants of marine and estuarine environments of the United States. This organism has been referred to as non-cholera vibrio (NCV) and nonagglutinable vibrio (NAG) in the past, although at least 139 "O" serogroups have been identified. (Note: for V. cholerae O139, see Chapter 7).

2. Nature of Acute Disease:

Non-Ol *V. cholerae* gastroenteritis is the name associated with this illness. Although rare, septicemic infections have been reported and deaths have resulted. Some cases are similar to the primary septicemia caused by V. vulnficus.

3. Nature of Disease:

Diarrhea, abdominal cramps, and fever are the predominant symptoms associated with this illness, with vomiting and nausea occurring in approximately 25% of infected individuals. Approximately 25% of infected individuals will have blood and mucus in their stools. Diarrhea may, in some cases, be quite severe, lasting 6-7 days. Diarrhea will usually occur within 48 hours following ingestion of the organism. It is unknown how the organism causes the illness, although an enterotoxin is suspected as well as an invasive mechanism. Disease is

caused when the organism attaches itself to the small intestine of infected individuals and perhaps subsequently invades.

Disease caused by V. cholerae O139 is indistinguishable from cholera caused by V. cholerae O1. See chapter 7.

Infective dose - It is suspected that large numbers (more than one million) of the organism must be ingested to cause illness.

4. Diagnosis of Human Illness:

Diagnosis of a *V. cholerae* non-Ol infection is made by culturing the organism from an individual's diarrheic stool or from the blood of patients with septicemia.

5. Associated Foods:

Shellfish harvested from U.S. coastal waters frequently contain *V. cholerae* serogroup non-Ol. Consumption of raw, improperly cooked or cooked, re-contaminated shellfish may lead to infection.

6. Relative Frequency of Disease:

No major outbreaks of diarrhea have been attributed to this organism. Sporadic cases occur frequently mainly along the coasts of the U.S., and are usually associated with the consumption of raw oysters during the warmer months.

7. Course of Disease and Complications:

Diarrhea resulting from ingestion of the organism usually lasts 7 days and is self-limiting. Antibiotics such as tetracycline shorten the severity and duration of the illness. Septicemia (bacteria gaining entry into the blood stream and multiplying therein) can occur. This complication is associated with individuals with cirrhosis of the liver, or who are immunosuppressed, but this is relatively rare. FDA has warned individuals with liver disease to refrain from consuming raw or improperly cooked shellfish.

8. Target Populations:

All individuals who consume raw shellfish are susceptible to diarrhea caused by this organism. Cirrhotic or

immunosuppressed individuals may develop severe complications such as septicemia.

9. Food Analysis:

Methods used to isolate this organism from foods are similar to those used with diarrheic stools. Because many food isolates are nonpathogenic, pathogenicity of all food isolates must be demonstrated. All virulence mechanisms of this group have not been elucidated; therefore, pathogenicity testing must be performed in suitable animal models.

10. Selected Outbreaks:

Literature references can be found at the links below.

Sporadic cases continue to occur all year, increasing in frequency during the warmer months.

MMWR 44(11):1995

The cholera epidemic caused by *Vibrio cholerae* O1 that began in January 1991 has continued to spread in Central and South America. In southern Asia, the epidemic caused by the newly recognized strain *V. cholerae* O139 that began in late 1992 also has continued to spread. This report updates surveillance findings for both epidemics.

MMWR 42(26):1993

Epidemics of cholera-like illness caused by a previously unrecognized organism occurred recently in southern Asia. This report documents the first case of cholera imported into the United States that was caused by this organism, the newly described toxigenic *Vibrio cholerae* O139 strain.

MMWR 31(39):1982

In September 1981, an isolated case of non-O1 *Vibrio cholerae* gastroenteritis occurred in a Laconia, New Hampshire, resident following consumption of raw clams harvested from New England coastal waters. The patient was a previously healthy 40-year-old woman; her recent travel and personal-contact histories were unremarkable. Within 26 hours after eating the clams, she developed acute abdominal cramps, followed by fever and bloody diarrhea. She was treated symptomatically with rest and oral hydration and recovered without sequelae. Her stool culture grew *V. cholerae* (Smith serotype 361) and no other enteric pathogens.

Morbidity and Mortality Weekly Reports

For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.

11. Education and Background Resources:	*Literature references can be found at the links below.*
Loci index for genome *Vibrio cholerae*	Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.
12. Molecular Structural Data:	None currently available.

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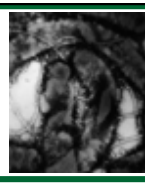

Vibrio parahaemolyticus

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism:
Vibrio parahaemolyticus (and other marine *Vibrio* spp.**)

This bacterium is frequently isolated from the estuarine and marine environment of the United States. Both pathogenic and non-pathogenic forms of the organism can be isolated from marine and estuarine environments and from fish and shellfish dwelling in these environments.

2. Nature of Acute Disease:

V. parahaemolyticus-associated gastroenteritis is the name of the infection caused by this organism.

3. Nature of Disease:

Diarrhea, abdominal cramps, nausea, vomiting, headache, fever, and chills may be associated with infections caused by this organism. The illness is usually mild or moderate, although some cases may require hospitalization. The median duration of the illness is 2.5 days. The incubation period is 4-96 hours after the ingestion of the organism, with a mean of 15 hours. Disease is caused when the organism attaches itself to an individuals' small intestine and excretes an as yet unidentified toxin.

Infective dose -- A total dose of greater than one million organisms may cause disease; this dose may be

	markedly lowered by coincident consumption of antacids (or presumably by food with buffering capability).
4. Diagnosis of Human Illness:	Diagnosis of gastroenteritis caused by this organism is made by culturing the organism from the diarrheic stools of an individual.
5. Associated Foods:	Infections with this organism have been associated with the consumption of raw, improperly cooked, or cooked, recontaminated fish and shellfish. A correlation exists between the probability of infection and warmer months of the year. Improper refrigeration of seafoods contaminated with this organism will allow its proliferation, which increases the possibility of infection.
6. Relative Frequency of Disease:	Major outbreaks have occurred in the U.S. during the warmer months of the year. Sporadic cases occur along all coasts of the U.S.
7. Course of Disease and Complications:	Diarrhea caused by this organism is usually self-limiting, with few cases requiring hospitalization and/or antibiotic treatment.
8. Target Populations:	All individuals who consume raw or improperly cooked fish and shellfish are susceptible to infection by this organism.
9. Food Analysis: FDA's Bacteriological Analytical Manual *Vibro parahaemolyticus*	Methods used to isolate this organism from foods are similar to those used with diarrheic stools. Because many food isolates are nonpathogenic, pathogenicity of all food isolates must be demonstrated. Although the demonstration of the Kanagawa hemolysin was long considered indicative of pathogenicity, this is now uncertain.

10. Selected Outbreaks:

MMWR 48(03):1999

During July-September 1998, an outbreak of *Vibrio parahaemolyticus* infections associated with consumption of oysters and clams harvested from Long Island Sound occurred among residents of Connecticut, New Jersey, and New York. This is the first reported outbreak of *V. parahaemolyticus* linked to consumption of shellfish harvested from New York waters.

MMWR 47(22):1998

During July-August 1997, the largest reported outbreak in North America of culture-confirmed *Vibrio parahaemolyticus* infections occurred. Illness in 209 persons was associated with eating raw oysters harvested from California, Oregon, and Washington in the United States and from British Columbia (BC) in Canada; one person died.

**OTHER MARINE VIBRIOS IMPLICATED IN FOODBORNE DISEASE:

Several other marine vibrios have been implicated in human disease. Some may cause wound or ear infections, and others, gastroenteritis. The amount of evidence for certain of these organisms as being causative of human gastroenteritis is small. Nonetheless, several have been isolated from human feces from diarrhea patients from which no other pathogens could be isolated. Methods for recovery of these organisms from foods are similar to those used for recovery of *V. parahaemolyticus*. The species implicated in human disease include:

Vibrio alginolyticus	*Vibrio furnissii*
Vibrio carchariae	*Vibrio hollisae*
Vibrio cincinnatiensis	*Vibrio metschnikovii*
Vibrio damsela	*Vibrio mimicus*
Vibrio fluvialis	

Morbidity and Mortality Weekly Reports

For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.

11. Education and Background Resources:	*Literature references can be found at the links below.*
Loci index for genome *Vibrio parahaemolyticus*	Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.
US. FDA Risk Assessment for *Vibrio parahaemolyticus*	In response to the 1997 and 1998 outbreaks of *V. parahaemolyticus* infections in the United States, the Food and Drug Administration (FDA) conducted a risk assessment to characterize the public health impact associated with consumption of raw oysters harboring pathogenic *V. parahaemolyticus*. This risk assessment focused specifically on oysters, because this was the food predominantly linked to the outbreaks. The risk assessment structures our knowledge of *V. parahaemolyticus* in a systematic manner, and includes sophisticated, mathematical models developed to estimate exposure to this microorganism and the dose-response relationships between the consumer and *V. parahaemolyticus*.
12. Molecular Structural Data:	None currently available.

CDC/MMWR

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Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Vibrio vulnificus

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism:
Vibrio vulnificus

Vibrio vulnificus, a lactose-fermenting, halophilic, gram-negative, opportunistic pathogen, is found in estuarine environments and associated with various marine species such as plankton, shellfish (oysters, clams, and crabs), and finfish. It is found in all of the coastal waters of the United States. [Cases of illness have also been associated with brackish lakes in New Mexico and Oklahoma.] Environmental factors responsible for controlling members of *V. vulnificus* in seafood and in the environment include temperature, pH, salinity, and increased dissolved organics.

2. Nature of Acute Disease:

This organism causes wound infections, gastroenteritis, or a syndrome known as "primary septicemia."

3. Nature of Disease:

Wound infections result either from contaminating an open wound with sea water harboring the organism, or by lacerating part of the body on coral, fish, etc., followed by contamination with the organism. The ingestion of *V. vulnificus* by healthy individuals can result in gastroenteritis. The "primary septicemia" form of the disease follows consumption of raw seafood containing the organism by individuals with underlying chronic disease, particularly liver disease (see below). In these individuals, the microorganism enters the blood stream, resulting in septic shock, rapidly followed by death in many cases (about 50%). Over 70% of infected individuals have

distinctive bulbous skin lesions.

Infective dose -- The infective dose for gastrointestinal symptoms in healthy individuals is unknown but for predisposed persons, septicemia can presumably occur with doses of less than 100 total organisms.

4. Diagnosis of Human Illness:

The culturing of the organism from wounds, diarrheic stools, or blood is diagnostic of this illness.

5. Associated Foods:

This organism has been isolated from oysters, clams, and crabs. Consumption of these products raw or recontaminated may result in illness.

6. Relative Frequency of Disease:

No major outbreaks of illness have been attributed to this organism. Sporadic cases occur frequently, becoming more prevalent during the warmer months.

In a survey of cases of *V. vulnificus* infections in Florida from 1981 to 1987, Klontz et al. (Annals of Internal Medicine 109:318-23;1988) reported that 38 cases of primary septicemia (ingestion), 17 wound infections, and 7 cases gastroenteritis were associated with the organism. Mortality from infection varied from 55% for primary septicemia cases, to 24% with wound infections, to no deaths associated with gastroenteritis. Raw oyster consumption was a common feature of primary septicemia and gastroenteritis, and liver disease was a feature of primary septicemia.

7. Course of Disease and Complications:

In healthy individuals, gastroenteritis usually occurs within 16 hours of ingesting the organism. Ingestion of the organism by individuals with some type of chronic underlying disease [such as diabetes, cirrhosis, leukemia , lung carcinoma, acquired immune deficiency syndrome (AIDS), AIDS- related complex (ARC), or asthma requiring the use of steroids] may cause the "primary septicemia" form of illness. The mortality rate for individuals with this form of the disease is over 50%.

8. Target Populations:

All individuals who consume foods contaminated with this organism are susceptible to gastroenteritis. Individuals with diabetes, cirrhosis, or leukemia, or those who take immunosuppressive drugs or steroids are particularly susceptible to primary septicemia. These individuals should be strongly advised not to consume raw or inadequately cooked seafood, as should AIDS / ARC patients.

9. Food Analysis:

Methods used to isolate this organism from foods are similar to those used with diarrheic stools. To date, all food isolates of this organism have been pathogenic in animal models.

FDA has a genetic probe for *V. vulnificus*; its target is a cytotoxin gene which appears not to correlate with the organism's virulence.

10. Selected Outbreaks:

Sporadic cases continue to occur all year, increasing in frequency during the warmer months.

MMWR 45(29):1996

Of all foodborne infectious diseases, infection with Vibrio vulnificus is one of the most severe; the case-fatality rate for V. vulnificus septicemia exceeds 50% (1,2). Cases are most commonly reported during warm-weather months (April-November), and often are associated with eating raw oysters. During April 1993-May 1996, a total of 16 cases of V. vulnificus infection were reported in Los Angeles County.

MMWR 42(21):1993

Vibrio vulnificus is a gram-negative bacterium that can cause serious illness and death in persons with preexisting liver disease or compromised immune systems. From 1981 through 1992, 125 persons with V. vulnificus infections, of whom 44 (35%) died, were reported to the Florida Department of Health and Rehabilitative Services (HRS). This report summarizes data on these cases and presents estimates of the at-risk population in Florida.

Morbidity and Mortality Weekly Reports

For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.

11. Education and Background Resources:	*Literature references can be found at the links below.*
Vibrio vulnificus FAQ's from the CDC.	What is *Vibrio vulnificus*? What sort of germ is it? How can an infection be diagnosed? How can the infections be treated?
Loci index for genome Vibrio vulnificus	Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.
If You Eat Raw Oysters, You Need to Know . . .	More information for consumers of raw shellfish is available at this FDA brochure.

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Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Clostridium perfringens

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism: *Clostridium perfringens*

Clostridium perfringens is an anaerobic, Gram-positive, sporeforming rod (anaerobic means unable to grow in the presence of free oxygen). It is widely distributed in the environment and frequently occurs in the intestines of humans and many domestic and feral animals. Spores of the organism persist in soil, sediments, and areas subject to human or animal fecal pollution.

2. Nature of Acute Disease:

Perfringens food poisoning is the term used to describe the common foodborne illness caused by *C. perfringens*. A more serious but rare illness is also caused by ingesting food contaminated with Type C strains. The latter illness is known as enteritis necroticans or pig-bel disease.

3. Nature of Disease:

The common form of perfringens poisoning is characterized by intense abdominal cramps and diarrhea which begin 8-22 hours after consumption of foods containing large numbers of those *C. perfringens* bacteria capable of producing the food poisoning toxin. The illness is usually over within 24 hours but less severe symptoms may persist in some individuals for 1 or 2 weeks. A few deaths have been reported as a result of dehydration and other complications.

Necrotic enteritis (pig-bel) caused by *C. perfringens* is often fatal. This disease also begins as a result of

ingesting large numbers of the causative bacteria in contaminated foods. Deaths from necrotic enteritis (pig-bel syndrome) are caused by infection and necrosis of the intestines and from resulting septicemia. This disease is very rare in the U.S.

Infective dose--The symptoms are caused by ingestion of large numbers (greater than 10 to the 8th) vegetative cells. Toxin production in the digestive tract (or in test tubes) is associated with sporulation. This disease is a food infection; only one episode has ever implied the possibility of intoxication (i.e., disease from preformed toxin).

4. Diagnosis of Human Illness:

Perfringens poisoning is diagnosed by its symptoms and the typical delayed onset of illness. Diagnosis is confirmed by detecting the toxin in the feces of patients. Bacteriological confirmation can also be done by finding exceptionally large numbers of the causative bacteria in implicated foods or in the feces of patients.

5. Associated Foods:

In most instances, the actual cause of poisoning by *C. perfringens* is temperature abuse of prepared foods. Small numbers of the organisms are often present after cooking and multiply to food poisoning levels during cool down and storage of prepared foods. Meats, meat products, and gravy are the foods most frequently implicated.

6. Relative Frequency of Disease:

Perfringens poisoning is one of the most commonly reported foodborne illnesses in the U.S. There were 1,162 cases in 1981, in 28 separate outbreaks. At least 10-20 outbreaks have been reported annually in the U.S. for the past 2 decades. Typically, dozens or even hundreds of person are affected. It is probable that many outbreaks go unreported because the implicated foods or patient feces are not tested routinely for *C. perfringens* or its toxin. CDC estimates that about 10,000 actual cases occur annually in the U.S.

7. Course of Disease and Complications:

The disease generally lasts 24 hours. In the elderly or infirm, symptoms may last 1-2 weeks. Complications and/or death only very rarely occur.

8. Target Populations: Institutional feeding (such as school cafeterias, hospitals, nursing homes, prisons, etc.) where large quantities of food are prepared several hours before serving is the most common circumstance in which perfringens poisoning occurs. The young and elderly are the most frequent victims of perfringens poisoning. Except in the case of pig-bel syndrome, complications are few in persons under 30 years of age. Elderly persons are more likely to experience prolonged or severe symptoms.

9. Food Analysis: Standard bacteriological culturing procedures are used to detect the organism in implicated foods and in feces of patients. Serological assays are used for detecting enterotoxin in the feces of patients and for testing the ability of strains to produce toxin. The procedures take 1-3 days.

10. Selected Outbreaks: *Literature references can be found at the links below.*

MMWR 43(8):1994

Clostridium perfringens is a common infectious cause of outbreaks of foodborne illness in the United States, especially outbreaks in which cooked beef is the implicated source. This report describes two outbreaks of *C. perfringens* gastroenteritis following St. Patrick's Day meals in Ohio and Virginia during 1993.

In November, 1985, a large outbreak of *C. perfringens* gastroenteritis occurred among factory workers in Connecticut. Forty-four percent of the 1,362 employees were affected. Four main-course foods served at an employee banquet were associated with illness, but gravy was implicated by stratified analysis. The gravy had been prepared 12-24 hours before serving, had been improperly cooled, and was reheated shortly before serving. The longer the reheating period, the less likely the gravy was to cause illness.

Since December 1981, FDA has investigated 10 outbreaks in 5 states. In two instances, more than one outbreak occurred in the same feeding facility within a 3-week period. One such outbreak occurred on 19 March 1984, involving 77 prison inmates. Roast beef served as a luncheon meat was implicated as the food vehicle and *C. perfringens* was confirmed as the cause by examining stools of 24 patients. Most of the patients became ill 8-16 hours after the meal. Eight days later, on 27 March 1984, a second outbreak occurred involving many of the same persons. The food vehicle was ham. Inadequate refrigeration and insufficient reheating of the implicated foods caused the outbreaks. Most of the other outbreaks occurred in institutional feeding environments: a hospital, nursing home, labor camp, school cafeteria, and at a fire house luncheon.

Morbidity and Mortality Weekly Reports	**For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.**

11. Education and Background Resources:	*Literature references can be found at the links below.*
Loci index for genome Clostridium perfringens	Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.

12. Molecular Structural Data:	None currently available.

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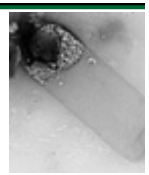

Bacillus cereus and other *Bacillus* spp.

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism:
Bacillus cereus and other *Bacillus* spp.

Bacillus cereus is a Gram-positive, facultatively aerobic sporeformer whose cells are large rods and whose spores do not swell the sporangium. These and other characteristics, including biochemical features, are used to differentiate and confirm the presence *B. cereus*, although these characteristics are shared with *B. cereus* var. mycoides, *B. thuringiensis* and *B. anthracis*. Differentiation of these organisms depends upon determination of motility (most *B. cereus* are motile), presence of toxin crystals (*B. thuringiensis*), hemolytic activity (*B. cereus* and others are beta hemolytic whereas *B. anthracis* is usually nonhemolytic), and rhizoid growth which is characteristic of *B. cereus* var. mycoides.

2. Nature of Acute Disease:

B. cereus food poisoning is the general description, although two recognized types of illness are caused by two distinct metabolites. The diarrheal type of illness is caused by a large molecular weight protein, while the vomiting (emetic) type of illness is believed to be caused by a low molecular weight, heat-stable peptide.

3. Nature of Disease:

The symptoms of *B. cereus* diarrheal type food poisoning mimic those of *Clostridium perfringens* food poisoning. The onset of watery diarrhea, abdominal cramps, and pain occurs 6-15 hours after consumption of contaminated food. Nausea may accompany diarrhea, but vomiting (emesis) rarely occurs. Symptoms persist for 24 hours in most instances.

The emetic type of food poisoning is characterized by nausea and vomiting within 0.5 to 6 h after consumption of contaminated foods. Occasionally, abdominal cramps and/or diarrhea may also occur. Duration of symptoms is generally less than 24 h. The symptoms of this type of food poisoning parallel those caused by *Staphylococcus aureus* foodborne intoxication. Some strains of *B. subtilis* and *B. licheniformis* have been isolated from lamb and chicken incriminated in food poisoning episodes. These organisms demonstrate the production of a highly heat-stable toxin which may be similar to the vomiting type toxin produced by *B. cereus*.

The presence of large numbers of *B. cereus* (greater than 10^6 organisms/g) in a food is indicative of active growth and proliferation of the organism and is consistent with a potential hazard to health.

4. Diagnosis of Human Illness:

Confirmation of *B. cereus* as the etiologic agent in a foodborne outbreak requires either (1) isolation of strains of the same serotype from the suspect food and feces or vomitus of the patient, (2) isolation of large numbers of a *B. cereus* serotype known to cause foodborne illness from the suspect food or from the feces or vomitus of the patient, or (3) isolation of *B. cereus* from suspect foods and determining their enterotoxigenicity by serological (diarrheal toxin) or biological (diarrheal and emetic) tests. The rapid onset time to symptoms in the emetic form of disease, coupled with some food evidence, is often sufficient to diagnose this type of food poisoning.

5. Associated Foods:

A wide variety of foods including meats, milk, vegetables, and fish have been associated with the diarrheal type food poisoning. The vomiting-type outbreaks have generally been associated with rice products; however, other starchy foods such as potato, pasta and cheese products have also been implicated. Food mixtures such as sauces, puddings, soups, casseroles, pastries, and salads have frequently been incriminated in food poisoning outbreaks.

6. Relative Frequency of Disease:

In 1980, 9 outbreaks were reported to the Centers for Disease Control and included such foods as beef, turkey, and Mexican foods. In 1981, 8 outbreaks were reported which primarily involved rice and shellfish. Other outbreaks go unreported or are misdiagnosed because of symptomatic similarities to *Staphylococcus aureus* intoxication (*B. cereus* vomiting-type) or *C. perfringens* food poisoning (B. cereus diarrheal type).

7. Course of Disease and Complications:

Although no specific complications have been associated with the diarrheal and vomiting toxins produced by *B. cereus*, other clinical manifestations of *B. cereus* invasion or contamination have been observed. They include bovine mastitis, severe systemic and pyogenic infections, gangrene, septic meningitis, cellulitis, panophthalmitis, lung abscesses, infant death, and endocarditis.

8. Target Populations:

All people are believed to be susceptible to *B. cereus* food poisoning.

9. Food Analysis:

A variety of methods have been recommended for the recovery, enumeration and confirmation of *B. cereus* in foods. More recently, a serological method has been developed for detecting the putative enterotoxin of *B. cereus* (diarrheal type) isolates from suspect foods. Recent investigations suggest that the vomiting type toxin can be detected by animal models (cats, monkeys) or possibly by cell culture.

10. Selected Outbreaks:

Literature references can be found at the links below.

MMWR 43(10):1994

On July 21, 1993, the Lord Fairfax (Virginia) Health District received reports of acute gastrointestinal illness that occurred among children and staff at two jointly owned child day care centers following a catered lunch. Of the 80 persons, 67 ate the catered lunch. Chicken fried rice prepared at a local restaurant was the only food significantly associated with illness; illness occurred in 14 (29%) of 48 persons who ate chicken fried rice, compared with none of 16 who did not. *Bacillus cereus* was isolated from leftover chicken fried rice and from vomitus from one ill child but not from samples of leftover milk.

MMWR 35(25):1986

On September 22, 1985, the Maine Bureau of Health was notified of a gastrointestinal illness among patrons of a Japanese restaurant. The customers exhibited symptoms of illness while still on the restaurant premises. While the question of the specific vehicle remains incompletely resolved, the clinical and laboratory findings substantially support *Bacillus cereus* as the cause of the outbreak.

Morbidity and Mortality Weekly Reports

For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.

11. Education and Background Resources:	*Literature references can be found at the links below.*
Loci index for genome Bacillus cereus	Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.
"Produce Handling and Processing Practices" (1997) Emerging Infectious Diseases 3(4).	In the past decade, outbreaks of human illness associated with the consumption of raw vegetables and fruits (or unpasteurized products produced from them) have increased in the United States. Pathogens such as *Listeria monocytogenes*, *Clostridium botulinum*, and *Bacillus cereus* are naturally present in some soil, and their presence on fresh produce is not rare. Salmonella, *Escherichia coli* O157:H7, *Campylobacter jejuni*, *Vibrio cholerae*, parasites, and viruses are more likely to contaminate fresh produce through vehicles such as raw or improperly composted manure, irrigation water containing untreated sewage, or contaminated wash water. Treatment of produce with chlorinated water reduces populations of pathogenic and other microorganisms on fresh produce but cannot eliminate them. Reduction of risk for human illness associated with raw produce can be better achieved through controlling points of potential contamination in the field; during harvesting; during processing or distribution; or in retail markets, food-service facilities, or the home.
12. Molecular Structural Data:	None currently available.

CDC/MMWR

The CDC/MMWR link will provide a list of Morbidity and Mortality Weekly Reports at CDC relating to this organism or toxin. The date shown is the date the item was posted on the Web, not the date of the MMWR. The summary statement shown are the initial words of the overall document. The specific article of interest may be just one article or item within the overall report.

NIH/PubMed

The NIH/PubMed button at the top of the page will provide a list of research abstracts contained in the National Library of Medicine's MEDLINE database for this organism or toxin.

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January 1992 with periodic updates

Bad Bug Book

Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Aeromonas hydrophila

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism:
Aeromonas hydrophila, *Aeromonas caviae*, *Aeromonas sobria* & (*Aeromonas veronii*?)

Aeromonas hydrophila is a species of bacterium that is present in all freshwater environments and in brackish water. Some strains of *A. hydrophila* are capable of causing illness in fish and amphibians as well as in humans who may acquire infections through open wounds or by ingestion of a sufficient number of the organisms in food or water.

Not as much is known about the other *Aeromonas* spp., but they too are aquatic microorganisms and have been implicated in human disease.

2. Nature of Acute Disease:

A. hydrophila may cause gastroenteritis in healthy individuals or septicemia in individuals with impaired immune systems or various malignancies.

A. caviae and *A. sobria* also may cause enteritis in anyone or septicemia in immunocompromised persons or those with malignancies.

3. Nature of Disease:

At the present time, there is controversy as to whether *A. hydrophila* is a cause of human gastroenteritis. Although the organism possesses several attributes which could make it pathogenic for humans, volunteer

human feeding studies, even with enormous numbers of cells (i.e. 10^11), have failed to elicit human illness. Its presence in the stools of individuals with diarrhea, in the absence of other known enteric pathogens, suggests that it has some role in disease.

Likewise, *A. caviae* and *A. sobria* are considered by many as "putative pathogens," associated with diarrheal disease, but as of yet they are unproven causative agents.

Two distinct types of gastroenteritis have been associated with *A. hydrophila*: a cholera-like illness with a watery (rice and water) diarrhea and a dysenteric illness characterized by loose stools containing blood and mucus. The infectious dose of this organism is unknown, but SCUBA divers who have ingested small amounts of water have become ill, and *A. hydrophila* has isolated from their stools.

A general infection in which the organisms spread throughout the body has been observed in individuals with underlying illness (septicemia).

4. Diagnosis of Human Illness:

A. hydrophila can be cultured from stools or from blood by plating the organisms on an agar medium containing sheep blood and the antibiotic ampicillin. Ampicillin prevents the growth of most competing microorganisms. The species identification is confirmed by a series of biochemical tests. The ability of the organism to produce the enterotoxins believed to cause the gastrointestinal symptoms can be confirmed by tissue culture assays.

5. Associated Foods:

A. hydrophila has frequently been found in fish and shellfish. It has also been found in market samples of red meats (beef, pork, lamb) and poultry. Since little is known about the virulence mechanisms of *A. hydrophila*, it is presumed that not all strains are pathogenic, given the ubiquity of the organism.

6. Relative Frequency of Disease:

The relative frequency of *A. hydrophila* disease in the U.S. is unknown since efforts to ascertain its true incidence have only recently been attempted. Most cases have been sporadic rather than associated with large outbreaks, but increased reports have been noted from several clinical centers.

7. Course of Disease and Complications:

On rare occasions the dysentery-like syndrome is severe and may last for several weeks.

A. hydrophila may spread throughout the body and cause a general infection in persons with impaired immune systems. Those at risk are individuals suffering from leukemia, carcinoma, and cirrhosis and those treated with immunosuppressive drugs or who are undergoing cancer chemotherapy.

8. Target Populations:

All people are believed to be susceptible to gastroenteritis, although it is most frequently observed in very young children. People with impaired immune systems or underlying malignancy are susceptible to the more severe infections.

9. Food Analysis:

A. hydrophila can be recovered from most foods by direct plating onto a solid medium containing starch as the sole carbohydrate source and ampicillin to retard the growth of most competing microorganisms.

10. Selected Outbreaks:

Literature references can be found at the links below.

Most cases have been sporadic, rather than associated with large outbreaks.

MMWR 39(20):1990

Aeromonas species are associated with gastroenteritis and with wound infections, particularly wounds incurred in outdoor settings. On May 1, 1988, isolates of Aeromonas became reportable in California, the first state to mandate reporting of isolates of and infections with these organisms. From May 1, 1988, through April 30, 1989, clinicians and clinical laboratories in California reported 225 Aeromonas isolates from 219 patients. Cases were reported on Confidential Morbidity Report cards to local health departments, which then conducted case investigations and forwarded their reports to the California Department of Health Services.

Morbidity and Mortality Weekly Reports

For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.

11. Education and Background Resources:	*Literature references can be found at the links below.*
Loci index for genome Aeromonas hydrophila	Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.
12. Molecular Structural Data:	None currently available.

CDC/MMWR

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AGRICOLA

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Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Plesiomonas shigelloides

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism: *Plesiomonas shigelloides*

This is a Gram-negative, rod-shaped bacterium which has been isolated from freshwater, freshwater fish, and shellfish and from many types of animals including cattle, goats, swine, cats, dogs, monkeys, vultures, snakes, and toads.

Most human *P. shigelloides* infections are suspected to be waterborne. The organism may be present in unsanitary water which has been used as drinking water, recreational water, or water used to rinse foods that are consumed without cooking or heating. The ingested *P. shigelloides* organism does not always cause illness in the host animal but may reside temporarily as a transient, noninfectious member of the intestinal flora. It has been isolated from the stools of patients with diarrhea, but is also sometimes isolated from healthy individuals (0.2-3.2% of population).

It cannot yet be considered a definite cause of human disease, although its association with human diarrhea and the virulence factors it demonstrates make it a prime candidate.

2. Nature of Acute Disease:

Gastroenteritis is the disease with which *P. shigelloides* has been implicated.

3. Nature of Disease: *P. shigelloides* gastroenteritis is usually a mild self-limiting disease with fever, chills, abdominal pain, nausea, diarrhea, or vomiting; symptoms may begin 20-24 hours after consumption of contaminated food or water; diarrhea is watery, non-mucoid, and non-bloody; in severe cases, diarrhea may be greenish-yellow, foamy, and blood tinged; duration of illness in healthy people may be 1-7 days.

The infectious dose is presumed to be quite high, at least greater than one million organisms.

4. Diagnosis of Human Illness: The pathogenesis of *P. shigelloides* infection is not known. The organism is suspected of being toxigenic and invasive. Its significance as an enteric (intestinal) pathogen is presumed because of its predominant isolation from stools of patients with diarrhea. It is identified by common bacteriological analysis, serotyping, and antibiotic sensitivity testing.

5. Associated Foods: Most *P. shigelloides* infections occur in the summer months and correlate with environmental contamination of freshwater (rivers, streams, ponds, etc.). The usual route of transmission of the organism in sporadic or epidemic cases is by ingestion of contaminated water or raw shellfish.

6. Relative Frequency of Disease: Most *P. shigelloides* strains associated with human gastrointestinal disease have been from stools of diarrheic patients living in tropical and subtropical areas. Such infections are rarely reported in the U.S. or Europe because of the self-limiting nature of the disease.

7. Course of Disease and Complications: *P. shigelloides* infection may cause diarrhea of 1-2 days duration in healthy adults. However, there may be high fever and chills and protracted dysenteric symptoms in infants and children under 15 years of age. Extra-intestinal complications (septicemia and death) may occur in people who are immunocompromised or seriously ill with cancer, blood disorders, or hepatobiliary disease.

8. Target Populations: All people may be susceptible to infection. Infants, children and chronically ill people are more likely to

experience protracted illness and complications.

9. Food Analysis:

P. shigelloides may be recovered from food and water by methods similar to those used for stool analysis. The keys to recovery in all cases are selective agars which enhance the survival and growth of these bacteria over the growth of the background microflora. Identification following recovery may be completed in 12-24 hours.

10. Selected Outbreaks:

Literature references can be found at the links below.

Gastrointestinal illness in healthy people caused by *P. shigelloides* infection may be so mild that they do not seek medical treatment. Its rate of occurrence in the U.S. is unknown. It may be included in the group of diarrheal diseases "of unknown etiology" which are treated with and respond to broad spectrum antibiotics.

Most cases reported in the United States involve individuals with preexisting health problems such as cancer, sickle cell anemia, immunoincompetence, the aged, and the very young, who develop complications.

MMWR 47(19):1998

On June 24, 1996, the Livingston County (New York) Department of Health (LCDOH) was notified of a cluster of diarrheal illness following a party on June 22, at which approximately 30 persons had become ill. This report summarizes the findings of the investigation, which implicated water contaminated with Plesiomonas shigelloides and Salmonella serotype Hartford as the cause of the outbreak.

MMWR 38(36):1989

In July 1988, a community hospital in southeastern Missouri reported isolating Plesiomonas shigelloides from the stool of a 14-month-old girl with watery diarrhea (no blood or mucus) and fever. Her highest recorded rectal temperature was 102 F (38.9 C). The child was treated with trimethoprim/sulfamethoxazole, and her illness resolved after 5 days.

Morbidity and Mortality Weekly Reports

For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.

11. Education and

Background Resources:	*Literature references can be found at the links below.*
Loci index for genome Plesiomonas shigelloides	Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.
12. Molecular Structural Data:	None currently available.

CDC/MMWR

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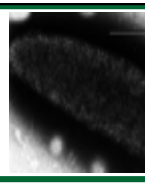


Shigella spp.

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism:
Shigella spp. (*Shigella sonnei*, *S. boydii*, *S. flexneri*, and *S. dysenteriae*)

Shigella are Gram-negative, nonmotile, nonsporeforming rod-shaped bacteria. The illness caused by *Shigella* (shigellosis) accounts for less than 10% of the reported outbreaks of foodborne illness in this country. *Shigella* rarely occurs in animals; principally a disease of humans except other primates such as monkeys and chimpanzees. The organism is frequently found in water polluted with human feces.

2. Nature of Acute Disease:

Shigellosis (bacillary dysentery).

3. Nature of Disease:

CDC Case Definition

What is a "Case Definition"?

Symptoms -- Abdominal pain; cramps; diarrhea; fever; vomiting; blood, pus, or mucus in stools; tenesmus.

Onset time -- 12 to 50 hours.

Infective dose -- As few as 10 cells depending on age and condition of host. The *Shigella spp.* are highly infectious agents that are transmitted by the fecal-oral route.

Overview of Public Health Surveillance

The disease is caused when virulent *Shigella* organisms attach to, and penetrate, epithelial cells of the intestinal mucosa. After invasion, they multiply intracellularly, and spread to contiguous epitheleal cells resulting in tissue destruction. Some strains produce enterotoxin and Shiga toxin (very much like the verotoxin of *E. coli* O157:H7).

4. Diagnosis of Human Illness:

Serological identification of culture isolated from stool.

5. Associated Foods:

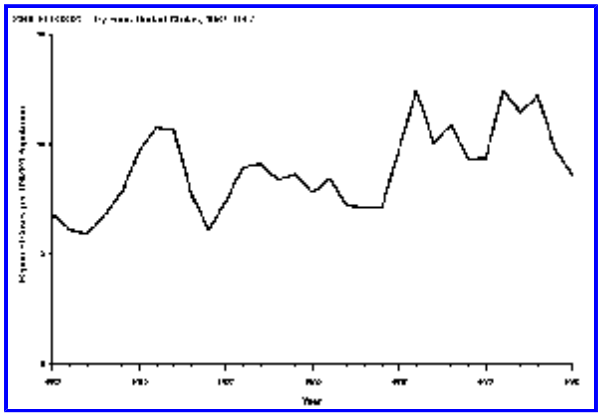
Salads (potato, tuna, shrimp, macaroni, and chicken), raw vegetables, milk and dairy products, and poultry. Contamination of these foods is usually through the fecal-oral route. Fecally contaminated water and unsanitary handling by food handlers are the most common causes of contamination.

6. Relative Frequency of Disease:

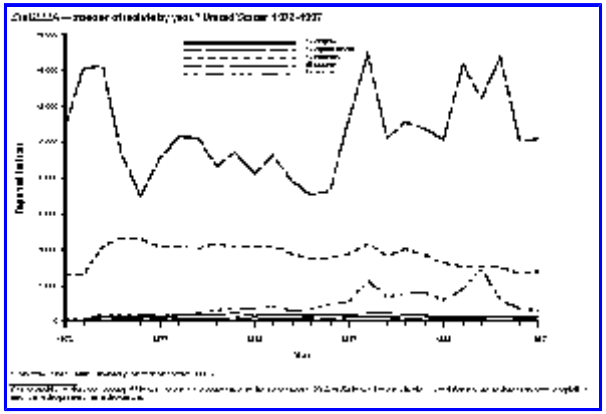
An estimated 300,000 cases of shigellosis occur annually in the U.S. The number attributable to food is unknown, but given the low infectious dose, it is probably substantial.

Reported cases of Shigellosis, United States 1967-1997

Summary of Notifiable Diseases, United States, 1997:MMWR 46(54)



Reported isolates of Shigella, United States 1972-1997



Summary of Notifiable Diseases, United States, 1997:MMWR 46(54)

7. Course of Disease and Complications: Infections are associated with mucosal ulceration, rectal bleeding, drastic dehydration; fatality may be as high as 10-15% with some strains. Reiter's disease, reactive arthritis, and hemolytic uremic syndrome are possible sequelae that have been reported in the aftermath of shigellosis.

8. Target Populations: Infants, the elderly, and the infirm are susceptible to the severest symptoms of disease, but all humans are susceptible to some degree. Shigellosis is a very common malady suffered by individuals with acquired immune deficiency syndrome (AIDS) and AIDS-related complex, as well as non-AIDS homosexual men.

9. Food Analysis: Organisms are difficult to demonstrate in foods because methods are not developed or are insensitive. A genetic probe to the virulence plasmid has been developed by FDA and is currently under field test. However, the isolation procedures are still poor.

10. Selected Outbreaks: *Literature references can be found at the links below.*

MMWR 48(14):1999 — In August 1998, the Minnesota Department of Health reported to CDC two restaurant-associated outbreaks of *Shigella sonnei* infections. Isolates from both outbreaks had two closely related pulsed-field gel electrophoresis (PFGE) patterns that differed only by a single band. Epidemiologic investigations implicated chopped, uncooked, curly parsley as the common vehicle for these outbreaks.

MMWR 45(11):1996 — On August 20, 1995, the District 7 Health Department requested the Idaho Department of Health to assist in investigating reports of diarrheal illness among visitors to a resort in Island Park in eastern Idaho; *Shigella sonnei* had been isolated from stool cultures of some cases. This report summarizes the findings of the investigation, which implicated contaminated drinking water as the cause of the outbreak.

MMWR 43(35):1994 — During August 29-September 1, 1994, an outbreak of gastrointestinal illness occurred on the cruise ship Viking Serenade (Royal Caribbean Cruises, Ltd.) during its roundtrip voyage from San Pedro, California, to Ensenada, Mexico. A total of 37% of passengers and 4% of the crew who completed a survey questionnaire reported having diarrhea or vomiting during the cruise. One death occurred. Investigation of the mode of transmission is under way.

MMWR 41(25):1992 — In January 1991, the Lexington-Fayette County (Kentucky) Health Department (LFCHD) received three reports of *Shigella sonnei* infections from the University of Kentucky microbiology laboratory. The infections occurred in children aged 2-3 years, each of whom attended a different child day care center in Lexington-Fayette County

(population:200,000).

MMWR 40(25):1991

On March 14, 1991, physicians at a hospital in Guatemala City reported to the Institute of Nutrition of Central America and Panama (INCAP) that a 2-year-old boy living in an orphanage in Guatemala City had been hospitalized with dysentery. Another child from the orphanage had recently died from dysentery. During March 18-21, two other young children from the orphanage were diagnosed with *Shigella dysenteriae* type 1. On March 21, health officials in Rabinal, in the department of Baja Verapaz, reported more than 100 cases of dysentery to the Division of Epidemiology and Disease Control of the Ministry of Health (MOH).

MMWR 39(30):1990

From 1986 to 1988*, the reported isolation rate of Shigella in the United States increased from 5.4 to 10.1 isolates per 100,000 persons. In addition to the increase in Shigella isolation rates, many communitywide shigellosis outbreaks that have been difficult to control have been reported. This report describes four community outbreaks of shigellosis during 1986-1989 in which innovative public health control measures were used.

MMWR 37(31):1988

From January 1 to August 1, 1988, 17 cases of diarrheal disease caused by *Shigella dysenteriae* type 1 (*Shiga bacillus*) were reported to CDC. Three cases were reported to CDC during the same period in 1987. Fifteen of the patients with shigellosis had visited Cancun, Mexico, andd two had visited other areas in Mexico in the weeks before or during onset of their illness. The patients had no common exposures in hotels or restaurants. An epidemiologic and laboratory investigation is under way in Mexico.

In 1988, numerous individuals contracted shigellosis from food consumed aboard Northwest Airlines flights; food on these flights had been prepared in one central commisary. No specific food item was implicated, but various sandwiches were suspected.

MMWR 36(38):1987

In early July 1987, an outbreak of multiply resistant *Shigella sonnei* gastroenteritis occurred among persons who attended the annual Rainbow Family gathering in North Carolina. Since that time, four clusters of gastroenteritis due to multiply resistant *S. sonnei* have been reported among persons who had no apparent contact with gathering attendees. Basic hygiene and sanitary precautions remain the cornerstones of control measures for shigellosis outbreaks, including those due to multiply resistant strains. Vigorous emphasis on handwashing with soap after defecation and before eating has been shown to reduce secondary transmission of shigellosis.

MMWR 36(27):1987

CDC has received reports that shigellosis outbreaks have occurred in several states, affecting related religious communities. Dates of onset range from November 1986 through June 1987. The largest outbreak was in New York City, and outbreaks in other states began soon after the Passover holiday in April, when many persons

visited relatives in New York. Epidemiologic data are incomplete, but in some of these outbreaks new cases continue to occur.

MMWR 35(48):1986

Between October 10 and November 6, 1985, 15 children at a day-care center in Diboll, Texas, developed a diarrheal illness. *Shigella sonnei* was isolated from 10 ill children and from two of 19 asymptomatic children who were cultured on November 7. All isolates were colicin type 9, resistant to ampicillin, carbenicillin, streptomycin, cephalothin, and trimethoprim/sulfamethoxazole (TMP/SMX), and sensitive to tetracycline, nalidixic acid, chloramphenicol, and gentamicin. The attack rate was highest among the 12- to 22-month-old group. Family members of this group had the highest secondary attack rate. No cases occurred among the 22 staff members.

In 1985-1986, several outbreaks of shigellosis occurred on college campuses, usually associated with fresh vegetables from the salad bar. Usually an ill food service worker was shown to be the cause.

In 1985, a huge outbreak of foodborne shigellosis occurred in Midland-Odessa, Texas, involving perhaps as many as 5,000 persons. The implicated food was chopped, bagged lettuce, prepared in a central location for a Mexican restaurant chain. FDA research subsequently showed that *S. sonnei*, the isolate from the lettuce, could survive in chopped lettuce under refrigeration, and the lettuce remained fresh and appeared to be quite edible.

MMWR 34(39):1985

In 1984, 12,790 Shigella isolates from humans were reported to CDC. This is a 14.4% decrease from the 14,946 isolates reported in 1983. The number of isolates continues to be less than the 15,334 reported during the peak year, 1978.

MMWR 33(43):1984

In 1983, 14,946 Shigella isolates from humans were reported to CDC. This is a 10.5% increase from the 13,523 isolates reported in 1982. The number of isolates is still less than the 15,334 reported during the peak year, 1978.

MMWR 32(34):1983

In 1982, 13,523 Shigella isolations from humans were reported to CDC. This represents a 9.9% decrease from the 15,006 isolations reported in 1981. The number of isolations has continued to decline from the 15,334 reported during the peak year, 1978.

MMWR 32(19):1983

An outbreak of severe dysentery caused by *Shigella dysenteriae* type 2 recently occurred at the U.S. Naval Hospital, Bethesda, Maryland. Epidemiologic investigation implicated the salad bar in the active-duty staff cafeteria as the source of infection.

MMWR 31(50):1982	In 1981, 15,006 Shigella isolations from humans were reported to CDC. While this represented a 6% increase over the 14,168 isolates reported in 1980, it remained 2% below the 15,334 reported during the peak year, 1978. ****NOTE -** Although all *Shigella* spp. have been implicated in foodborne outbreaks at some time, *S. sonnei* is clearly the leading cause of shigellosis from food. The other species are more closely associated with contaminated water. One in particular, *S. flexneri*, is now thought to be in large part sexually transmitted.
Morbidity and Mortality Weekly Reports	**For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.**

11. Education and Background Resources:	*Literature references can be found at the links below.*
Loci index for genome *Shigella spp.*	Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.
ShigellosisFAQ's from the CDC.	What is Shigellosis? What sort of germ is it? How can an infection be diagnosed? How can the infections be treated?

CDC/MMWR

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Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Miscellaneous enterics

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism:
Miscellaneous enterics, Gram-negative genera including: *Klebsiella, Enterobacter, Proteus, Citrobacter, Aerobacter, Providencia, Serratia*

These rod-shaped enteric (intestinal) bacteria have been suspected of causing acute and chronic gastrointestinal disease. The organisms may be recovered from natural environments such as forests and freshwater as well as from farm produce (vegetables) where they reside as normal microflora. They may be recovered from the stools of healthy individuals with no disease symptoms. The relative proportion of pathogenic to nonpathogenic strains is unknown.

2. Nature of Acute Disease:

Gastroenteritis is name of the disease occasionally and sporadically caused by these genera.

3. Nature of Disease:

Acute gastroenteritis is characterized by two or more of the symptoms of vomiting, nausea, fever, chills, abdominal pain, and watery (dehydrating) diarrhea occurring 12-24 hours after ingestion of contaminated food or water. Chronic diarrheal disease is characterized by dysenteric symptoms: foul-smelling, mucus-containing, diarrheic stool with flatulence and abdominal distention. The chronic disease may continue for months and

require antibiotic treatment.

Infectious dose--unknown. Both the acute and chronic forms of the disease are suspected to result from the elaboration of enterotoxins. These organisms may become transiently virulent by gaining mobilizeable genetic elements from other pathogens. For example, pathogenic *Citrobacter freundii* which elaborated a toxin identical to *E. coli* heat-stable toxin was isolated from the stools of ill children.

4. Diagnosis of Human Illness: Recovery and identification methods for these organisms from food, water or diarrheal specimens are based upon the efficacy of selective media and results of microbiological and biochemical assays. The ability to produce enterotoxin(s) may be determined by cell culture assay and animal bioassays, serological methods, or genetic probes.

5. Associated Foods: These bacteria have been recovered from dairy products, raw shellfish, and fresh raw vegetables. The organisms occur in soils used for crop production and shellfish harvesting waters and, therefore, may pose a health hazard.

6. Relative Frequency of Disease: Acute gastrointestinal illness may occur more frequently in undeveloped areas of the world. The chronic illness is common in malnourished children living in unsanitary conditions in tropical countries.

7. Course of Disease and Complications: Healthy individuals recover quickly and without treatment from the acute form of gastrointestinal disease. Malnourished children (1-4 years) and infants who endure chronic diarrhea soon develop structural and functional abnormalities of their intestinal tracts resulting in loss of ability to absorb nutrients. Death is not uncommon in these children and results indirectly from the chronic toxigenic effects which produce the malabsorption and malnutrition.

8. Target Populations: All people may be susceptible to pathogenic forms of these bacteria. Protracted illness is more commonly experienced by the very young.

9. Food Analysis:

These strains are recovered by standard selective and differential isolation procedures for enteric bacteria. Biochemical and in vitro assays may be used to determine species and pathogenic potential. Not being usually thought of as human pathogens, they may easily be overlooked by the clinical microbiology laboratory.

10. Selected Outbreaks:

Literature references can be found at the links below.

Intestinal infections with these species in the U.S. have usually taken the form of sporadic cases of somewhat doubtful etiology.

MMWR 32(41):1983

Citrobacter freundii was suspected by CDC of causing an outbreak of diarrheal disease in Washington, DC. Imported Camembert cheese was incriminated.

MMWR 33(2):1984

Cases of similar clinical illness have subsequently been identified in four states (Colorado, Georgia, Illinois, and Wisconsin) associated with eating the same brand of semi-soft cheese (either Brie or Camembert). The lots implicated in these states included at least one lot produced approximately 40 days after the cheese that caused the District of Columbia cases.

Morbidity and Mortality Weekly Reports

For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.

11. Education and Background Resources:

Literature references can be found at the links below.

Loci index for genome
Klebsiella spp.
Enterobacter spp.
Proteus spp.
Citrobacter spp.

Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.

Providencia spp.
Serratia spp.

12. Molecular Structural Data: None currently available.

CDC/MMWR

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NIH/PubMed

The NIH/PubMed button at the top of the page will provide a list of research abstracts contained in the National Library of Medicine's MEDLINE database for this organism or toxin.

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Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Streptococcus spp.

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism:
Streptococcus spp.

The genus Streptococcus is comprised of Gram-positive, microaerophilic cocci (round), which are not motile and occur in chains or pairs. The genus is defined by a combination of antigenic, hemolytic, and physiological characteristics into Groups A, B, C, D, F, and G. Groups A and D can be transmitted to humans via food.

Group A: one species with 40 antigenic types (*S. pyogenes*).

Group D: five species (*S. faecalis*, *S. faecium*, *S. durans*, *S. avium*, and *S. bovis*).

2. Nature of Acute Disease:

Group A: Cause septic sore throat and scarlet fever as well as other pyogenic and septicemic infections.

Group D: May produce a clinical syndrome similar to staphylococcal intoxication.

3. Nature of Disease:

Group A: Sore and red throat, pain on swallowing, tonsilitis, high fever, headache, nausea, vomiting, malaise, rhinorrhea; occasionally a rash occurs, onset 1-3 days; the infectious dose is probably quite low (less than 1,000 organisms).

Group D: Diarrhea, abdominal cramps, nausea, vomiting, fever, chills, dizziness in 2-36 hours. Following ingestion of suspect food, the infectious dose is probably high (greater than 107 organisms).

4. Diagnosis of Human Illness:

Group A: Culturing of nasal and throat swabs, pus, sputum, blood, suspect food, environmental samples.

Group D: Culturing of stool samples, blood, and suspect food.

5. Associated Foods:

Group A: Food sources include milk, ice cream, eggs, steamed lobster, ground ham, potato salad, egg salad, custard, rice pudding, and shrimp salad. In almost all cases, the foodstuffs were allowed to stand at room temperature for several hours between preparation and consumption. Entrance into the food is the result of poor hygiene, ill food handlers, or the use of unpasteurized milk.

Group D: Food sources include sausage, evaporated milk, cheese, meat croquettes, meat pie, pudding, raw milk, and pasteurized milk. Entrance into the food chain is due to underprocessing and/or poor and unsanitary food preparation.

6. Relative Frequency of Disease:

Group A infections are low and may occur in any season, whereas Group D infections are variable.

7. Course of Disease and Complications:

Group A: Streptococcal sore throat is very common, especially in children. Usually it is successfully treated with antibiotics. Complications are rare and the fatality rate is low.

Group D: Diarrheal illness is poorly characterized, but is acute and self-limiting.

8. Target Populations:

All individuals are susceptible. No age or race susceptibilities have been found.

9. Food Analysis: Suspect food is examined microbiologically by selective enumeration techniques which can take up to 7 days. Group specificities are determined by Lancefield group-specific antisera.

10. Selected Outbreaks: *Literature references can be found at the links below.*

Group A: Outbreaks of septic sore throat and scarlet fever were numerous before the advent of milk pasteurization. Salad bars have been suggested as possible sources of infection. Most current outbreaks have involved complex foods (i.e., salads) which were infected by a food handler with septic sore throat. One ill food handler may subsequently infect hundreds of individuals.

Group D: Outbreaks are not common and are usually the result of preparing, storing, or handling food in an unsanitary manner.

MMWR 45(30):1996 During December 1995-February 1996, four cases of a bacteremic illness (three accompanied by cellulitis and the fourth with infective endocarditis, meningitis, and probable septic arthritis) were identified among patients at a hospital in Ontario. *Streptococcus iniae*, a fish pathogen not previously reported as a cause of illness in humans (1-3), was isolated from all four patients.

MMWR 35(40):1986 In the period October 17, 1985-January 9, 1986, 44 episodes of pyoderma occurred among 32 workers in an Oregon meat-packing plant. Most of the 44 reports involved impetigo-like lesions on the hand, wrist, and forearm, but six episodes of cellulitis and two of lymphangitis were also reported. The same epidemic strain of Group-A, -B hemolytic Streptococcus (GAS) isolated from skin lesions was also isolated from meat in the plant.

MMWR 33(47):1984 Two large outbreaks of foodborne group A streptococcal pharyngitis have been reported to CDC during 1984. The Puerto Rico Department of Health was notified of the outbreak on August 8. Because of the high attack rate and the clustering of cases, the outbreak was presumed to be foodborne. Another outbreak occurred among participants from seven states at a meeting held at a Kansas City, Missouri, hotel from May 31, to June 1, 1984. Clustering of cases and a high attack rate suggested a foodborne source.

MMWR 32(39):1983 Between July 25 and September 9, 1983, 16 cases of invasive group C streptococcal infection were identified in northern New Mexico. The group C streptococcus was isolated from the blood of 15 patients and the pericardial

	fluid of one patient. The organism isolated from 14 of the patients has been identified as a group C B-hemolytic streptococcus--species *Streptococcus zooepidemicus*; the species of the remaining two isolates have not yet been determined. Initial questionnaires identified eating "queso blanco," a homemade white cheese, as the only risk factor associated with illness.
Morbidity and Mortality Weekly Reports	**For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.**

11. Education and Background Resources:	*Literature references can be found at the links below.*
Loci index for genome Streptococcus	Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.
Streptococcus A FAQ's from the CDC.	What is streptococcus A? What sort of germ is it? How can an infection be diagnosed? How can the infections be treated?

12. Molecular Structural Data:	None currently available.

CDC/MMWR

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Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Enterotoxigenic *Escherichia coli*

CDC/MMWR NIH/PubMed Agricola

1. Name of the Organism: Enterotoxigenic *Escherichia coli* (ETEC)

Currently, there are four recognized classes of enterovirulent *E. coli* (collectively referred to as the EEC group) that cause gastroenteritis in humans. Among these are the enterotoxigenic (ETEC) strains. They comprise a relatively small proportion of the species and have been etiologically associated with diarrheal illness of all age groups from diverse global locations. The organism frequently causes diarrhea in infants in less developed countries and in visitors there from industrialized countries. The etiology of this cholera-like illness has been recognized for about 20 years.

2. Nature of Acute Disease:

Gastroenteritis is the common name of the illness caused by ETEC, although travelers' diarrhea is a frequent sobriquet.

3. Nature of Disease:

The most frequent clinical syndrome of infection includes watery diarrhea, abdominal cramps, low-grade fever, nausea and malaise.

Infective dose--Volunteer feeding studies indicate that a relatively large dose (100 million to 10 billion bacteria) of enterotoxigenic *E. coli* is probably necessary to establish colonization of the small intestine, where these organisms proliferate and produce toxins which induce fluid secretion. With high infective dose, diarrhea can be

induced within 24 hours. Infants may require fewer organisms for infection to be established.

4. Diagnosis of Human Illness: During the acute phase of infection, large numbers of enterotoxigenic cells are excreted in feces. These strains are differentiated from nontoxigenic *E. coli* present in the bowel by a variety of in vitro immunochemical, tissue culture, or gene probe tests designed to detect either the toxins or genes that encode for these toxins. The diagnosis can be completed in about 3 days.

5. Associated Foods: ETEC is not considered a serious foodborne disease hazard in countries having high sanitary standards and practices. Contamination of water with human sewage may lead to contamination of foods. Infected food handlers may also contaminate foods. These organisms are infrequently isolated from dairy products such as semi-soft cheeses.

6. Relative Frequency of Disease: Only four outbreaks in the U.S. have been documented, one resulting from consumption of water contaminated with human sewage, another from consumption of Mexican food prepared by an infected food handler. In two others, one in a hospital cafeteria and one aboard a cruise ship, food was the probable cause. The disease among travelers to foreign countries, however, is common.

7. Course of Disease and Complications: The disease is usually self-limiting. In infants or debilitated elderly persons, appropriate electrolyte replacement therapy may be necessary.

8. Target Populations: Infants and travelers to underdeveloped countries are most at-risk of infection.

9. Food Analysis: With the availability of a gene probe method, foods can be analyzed directly for the presence of enterotoxigenic *E. coli*, and the analysis can be completed in about 3 days. Alternative methods which involve enrichment and

plating of samples for isolation of *E. coli* and their subsequent confirmation as toxigenic strains by conventional toxin assays may take at least 7 days.

10. Selected Outbreaks:

Literature references can be found at the links below.

MMWR 43(5):1994

Outbreaks of ETEC in Rhode Island and New Hampshire are reported.

In the last decade, four major common-source outbreaks of ETEC gastroenteritis occurred in the U.S. In late 1975 one-third of the passengers on two successive cruises of a Miami-based ship experienced diarrheal illness. A CDC investigation found ETEC to be the cause, presumably linked to consumption of crabmeat cocktail. In early 1980, 415 persons eating at a Mexican restaurant experienced diarrhea. The source of the causative organism was an ill food handler. In 1981, 282 of 3,000 personnel at a Texas hospital acquired ETEC gastroenteritis after eating in the hospital cafeteria. No single food was identified by CDC.

Morbidity and Mortality Weekly Reports

For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.

11. Education and Background Resources:

None currently available.

12. Molecular Structural Data:

None currently available.

CDC/MMWR

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Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Enteropathogenic *Escherichia coli*

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism:
Enteropathogenic *Escherichia coli* (EPEC)

Currently, there are four recognized classes of enterovirulent *E. coli* (collectively referred to as the EEC group) that cause gastroenteritis in humans. Among these are the enteropathogenic (EPEC) strains. EPEC are defined as *E. coli* belonging to serogroups epidemiologically implicated as pathogens but whose virulence mechanism is unrelated to the excretion of typical *E. coli* enterotoxins. *E. coli* are Gram-negative, rod-shaped bacteria belonging the family Enterobacteriaceae. Source(s) and prevalence of EPEC are controversial because foodborne outbreaks are sporadic. Humans, bovines, and swine can be infected, and the latter often serve as common experimental animal models. *E. coli* are present in the normal gut flora of these mammals. The proportion of pathogenic to nonpathogenic strains, although the subject of intense research, is unknown.

2. Nature of Acute Disease:

Infantile diarrhea is the name of the disease usually associated with EPEC.

3. Nature of Disease:

EPEC cause either a watery or bloody diarrhea, the former associated with the attachment to, and physical alteration of, the integrity of the intestine. Bloody diarrhea is associated with attachment and an acute tissue-destructive process, perhaps caused by a toxin similar to that of *Shigella dysenteriae*, also called verotoxin. In most of these strains the shiga-like toxin is cell-associated rather than excreted.

Infective dose -- EPEC are highly infectious for infants and the dose is presumably very low. In the few documented cases of adult diseases, the dose is presumably similar to other colonizers (greater than 10^6 total dose).

4. Diagnosis of Human Illness: The distinction of EPEC from other groups of pathogenic *E. coli* isolated from patients' stools involves serological and cell culture assays. Serotyping, although useful, is not strict for EPEC.

5. Associated Foods: Common foods implicated in EPEC outbreaks are raw beef and chicken, although any food exposed to fecal contamination is strongly suspect.

6. Relative Frequency of Disease: Outbreaks of EPEC are sporadic. Incidence varies on a worldwide basis; countries with poor sanitation practices have the most frequent outbreaks.

7. Course of Disease and Complications: Occasionally, diarrhea in infants is prolonged, leading to dehydration, electrolyte imbalance and death (50% mortality rates have been reported in third world countries).

8. Target Populations: EPEC outbreaks most often affect infants, especially those that are bottle fed, suggesting that contaminated water is often used to rehydrate infant formulae in underdeveloped countries.

9. Food Analysis: The isolation and identification of *E. coli* in foods follows standard enrichment and biochemical procedures. Serotyping of isolates to distinguish EPEC is laborious and requires high quality, specific antisera, and technical expertise. The total analysis may require from 7 to 14 days.

10. Selected Outbreaks:	*Literature references can be found at the links below.*
	Sporadic outbreaks of EPEC diarrhea have occurred for half a century in infant nurseries, presumably derived from the hospital environment or contaminated infant formula. Common-source outbreaks of EPEC diarrhea involving healthy young adults were reported in the late 1960s. Presumably a large inoculum was ingested.
Morbidity and Mortality Weekly Reports	**For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.**
11. Education and Background Resources:	None currently available.
12. Molecular Structural Data:	None currently available.

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Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Escherichia coli O157:H7

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism: *Escherichia coli* O157:H7 (enterohemorrhagic *E. coli* or EHEC)

Currently, there are four recognized classes of enterovirulent *E. coli* (collectively referred to as the EEC group) that cause gastroenteritis in humans. Among these is the enterohemorrhagic (EHEC) strain designated *E. coli* O157:H7. *E. coli* is a normal inhabitant of the intestines of all animals, including humans. When aerobic culture methods are used, *E. coli* is the dominant species found in feces. Normally *E. coli* serves a useful function in the body by suppressing the growth of harmful bacterial species and by synthesizing appreciable amounts of vitamins. A minority of *E. coli* strains are capable of causing human illness by several different mechanisms. *E. coli* serotype O157:H7 is a rare variety of *E. coli* that produces large quantities of one or more related, potent toxins that cause severe damage to the lining of the intestine. These toxins [verotoxin (VT), shiga-like toxin] are closely related or identical to the toxin produced by *Shigella dysenteriae*.

2. Nature of Acute Disease:

Hemorrhagic colitis is the name of the acute disease caused by *E. coli* O157:H7.

3. Nature of Disease:

The illness is characterized by severe cramping (abdominal pain) and diarrhea which is initially watery but becomes grossly bloody. Occasionally vomiting occurs. Fever is either low-grade or absent. The illness is usually self-limited and lasts for an average of 8 days. Some individuals exhibit watery diarrhea only.

Infective dose -- Unknown, but from a compilation of outbreak data, including the organism's ability to be passed person-to-person in the day-care setting and nursing homes, the dose may be similar to that of *Shigella* spp. (as few as 10 organisms).

4. Diagnosis of Human Illness:

CDC Case Definition

Hemorrhagic colitis is diagnosed by isolation of *E. coli* of serotype O157:H7 or other verotoxin-producing *E. coli* from diarrheal stools. Alternatively, the stools can be tested directly for the presence of verotoxin. Confirmation can be obtained by isolation of *E. coli* of the same serotype from the incriminated food.

5. Associated Foods:

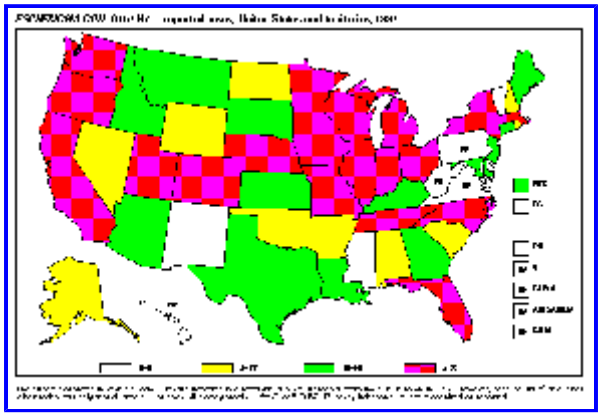
Undercooked or raw hamburger (ground beef) has been implicated in many of the documented outbreaks, however *E. coli* O157:H7 outbreaks have implicated alfalfa sprouts, unpasteurized fruit juices, dry-cured salami, lettuce, game meat, and cheese curds. Raw milk was the vehicle in a school outbreak in Canada.

6. Relative Frequency of Disease:

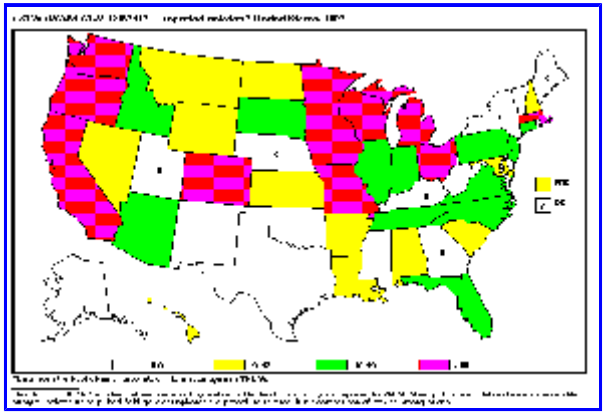
Hemorrhagic colitis infections are not too common, but this is probably not reflective of the true frequency. In the Pacific Northwest, *E. coli* O157:H7 is thought to be second only to Salmonella as a cause of bacterial diarrhea. Because of the unmistakable symptoms of profuse, visible blood in severe cases, those victims probably seek medical attention, but less severe cases are probably more numerous.

Reported cases of Ecoli O157, United States 1997

Summary of Notifiable Diseases, United States, 1997:MMWR 46(54)



Reported isolates of Ecoli O157, United States 1997



Summary of Notifiable Diseases, United States, 1997:MMWR 46(54)

7. Course of Disease and Complications: Some victims, particularly the very young, have developed the hemolytic uremic syndrome (HUS), characterized by renal failure and hemolytic anemia. From 0 to 15% of hemorrhagic colitis victims may develop HUS. The disease can lead to permanent loss of kidney function.

In the elderly, HUS, plus two other symptoms, fever and neurologic symptoms, constitutes thrombotic thrombocytopenic purpura (TTP). This illness can have a mortality rate in the elderly as high as 50%.

8. Target Populations:

All people are believed to be susceptible to hemorrhagic colitis, but young children and the elderly appear to progress to more serious symptoms more frequently.

9. Food Analysis:

FDA's Bacteriological Analytical Manual Escherichia coli

Several microbiological methods can be used to isolate *E. coli* O157:H7 from foods. Unlike typical *E. coli*, isolates of O157:H7 do not ferment sorbitol and are negative with the MUG assay; therefore, these criteria are commonly used for selective isolation. Sorbitol-MacConkey agar has been used extensively to isolate this organism from clinical specimens. Hemorrhagic colitis agar, a selective and differential medium, is used in a direct plating method to isolate O157:H7 from foods. A third procedure uses Sorbitol-MacConkey medium containing potassium tellurite and Cefixime. It includes an enrichment step and is a new method developed as result of the recent foodborne outbreaks. Rapid methods using a variety of technologies, including recombinant DNA methods, are being developed.

10. Selected Outbreaks:

Literature references can be found at the links below.

MMWR 49(40):2000

On June 15, 1998, the Division of Public Health, Wisconsin Department of Health and Family Services, was notified of eight laboratory-confirmed and four suspected Escherichia coli O157:H7 infections among west-central Wisconsin residents who became ill during June 8--12. This report summarizes the outbreak investigation, which implicated fresh (held <60 days) cheese curds from a dairy plant as the source of infection.

MMWR 49(15):2000

In June 1999, the Tarrant County Health Department reported to the Texas Department of Health (TDH) that a group of teenagers attending a cheerleading camp during June 9--11 became ill with nausea, vomiting, severe abdominal cramps, and diarrhea, some of which was bloody. Two teenagers were hospitalized with hemolytic uremic syndrome (HUS), and two others underwent appendectomies. Routine stool cultures from eight ill persons failed to yield a pathogen. Stools subsequently were sent to laboratories at the Texas Department of Health and CDC, where *Escherichia coli* O111:H8 was isolated from two specimens.

MMWR 48(36):1999	On September 3, 1999, the New York State Department of Health (NYSDOH) received reports of at least 10 children hospitalized with bloody diarrhea or Escherichia coli O157:H7 infection in counties near Albany, New York. All of the children had attended the Washington County Fair, which was held August 23-29, 1999; approximately 108,000 persons attended the fair during that week. Subsequently, fair attendees infected with Campylobacter jejuni also were identified. An ongoing investigation includes heightened case-finding efforts, epidemiologic and laboratory studies, and an environmental investigation of the Washington County fairgrounds.
USDA announcement (12 Aug 1997) and follow-up announcement (15 Aug 1997)	These reports announce a recall of Hudson frozen ground beef.
MMWR 46(33):1997	The same recall investigation reported by the CDC.
MMWR 46(32):1997	In June and July 1997, simultaneous outbreaks of Escherichia coli O157:H7 infection in Michigan and Virginia were independently associated with eating alfalfa sprouts grown from the same seed lot. The outbreak strains in Michigan and Virginia were indistinguishable by molecular subtyping methods. This report summarizes the preliminary findings of the outbreak investigations.
MMWR 46(30):1997	As part of its commemoration of CDC's 50th anniversary, MMWR is reprinting selected MMWR articles of historical importance to public health, accompanied by current editorial notes. Reprinted below is a report published November 5, 1982, which was the first in MMWR to describe diarrheal illness attributable to Escherichia coli serotype O157:H7 infections.
Odwalla brand apple juice products	The FDA has issued on 31 October 1996 a press release concerning an outbreak of *E. coli* O157:H7 associated with Odwalla brand apple juice products.
MMWR 46(01):1997 and MMWR 45 (44):1996	In October 1996, unpasteurized apple cider or juice was associated with three outbreaks of gastrointestinal illness. These reports summarizes the clinical and epidemiologic features of the two apple cider-related outbreaks, one infection the Western US and the other in the Northeast.
MMWR 45(21):1996	On July 5, 1995, the Winnebago County Health Department (WCHD) in northern Illinois received a report from the local hospital of five cases of Escherichia coli O157:H7 infection among children who resided in Rockford.

Interviews of the children's parents revealed no common food source; however, on June 24-25, they all had visited an Illinois state park with a lake swimming beach. On July 6, the Illinois Department of Public Health (IDPH) closed the swimming beach because of suspected transmission of infection through lake water. While, the source of the outbreak is thought to be waterborne, the article is linked to this chapter to provide updated reference information on enterohemorrhagic *E. coli*.

MMWR 45(12):1996

On June 26, 1995, the Division of Public Health, Georgia Department of Human Resources (GDPH), was notified of three cases of Escherichia coli O157:H7 infection among residents of a community in north Georgia who had onsets of illness within a 24-hour period . Because of the proximity of this community to the Tennessee border, on June 28 GDPH notified the Tennessee Department of Health (TDH) about these cases. TDH subsequently identified two confirmed cases with onsets of illness during June 23-24. Both of these cases were among persons residing in eastern Tennessee approximately 100 miles from the community in Georgia, and one occurred in an 11-year-old boy who was hospitalized with hemolytic uremic syndrome (HUS). This report summarizes the investigation of this outbreak, which implicated eating hamburgers purchased at a fast-food restaurant chain as the source of infection.

MMWR 44(29):1995

Post diarrheal hemolytic uremic syndrome (HUS) is characterized by microangiopathic hemolytic anemia, renal injury, and thrombocytopenia and is associated with infection with Shiga-like toxin-producing Escherichia coli (SLTEC). From January 4 through February 20, 1995, the South Australian Communicable Disease Control Unit of the Health Commission (SACDCU) received reports of 23 cases of HUS among children aged less than 16 years who resided in South Australia. In comparison, during 1994, a total of three cases of HUS was reported in South Australia (1991 population: 1.4 million).

MMWR 44(27):1995

During February-March, 1994, four persons in Helena, Montana (1995 population: 24,569), developed bloody diarrhea and severe abdominal cramps. Stool cultures for Salmonella, Shigella, Campylobacter, and Escherichia coli O157:H7 were negative; however, sorbitol-negative E. coli colonies were identified in stools from all four patients. Isolates from three patients were identified at CDC as a rare serotype, E. coli O104:H21, that produced Shiga-like toxin II. Although other SLTECs also have been identified in sporadic cases of diarrhea and HUS, the findings in this report document the first reported outbreak of a non-O157 SLTEC in the United States, and the first documentation of illness attributable to Shiga-like toxin-producing E. coli O104:H21. The clinical manifestations of infection in this outbreak were similar to those reported for patients infected with E. coli O157:H7.

MMWR 44(22):1995

In 1993, the Council of State and Territorial Epidemiologists recommended that clinical laboratories begin culturing all bloody stools -- and optimally all diarrheal stools -- for E. coli O157:H7. This report describes the

investigation of a pseudo-outbreak of E. coli O157:H7 infection that occurred in New Jersey during July 1994 after a year-long increase in the number of laboratories culturing all diarrheal specimens for this pathogen.

MMWR 44(22):1995 — On August 8, 1994, the Virginia Department of Health was notified that several campers and counselors at a summer camp had developed bloody diarrhea. The outbreak began during the July 17-30 session at a rural camp where activities included frequent overnight trips at which meals were cooked over a campfire. This report summarizes the findings from the investigation, which confirmed E. coli O157:H7 as the causative agent.

MMWR 44(09):1995 — From November 16 through December 21, 1994, a total of 20 laboratory-confirmed cases of diarrhea caused by Escherichia coli O157:H7 were reported to the Seattle-King County Department of Public Health (SKCDPH). In comparison, three cases were reported during October 1994. Epidemiologic investigation linked E. coli O157:H7 infection with consumption of a commercial dry-cured salami product distributed in several western states. Three additional cases subsequently were identified in northern California.

MMWR 43(12):1994 — Most epidemiologic investigations of illness associated with E. coli O157:H7 infections have been directed at restaurant-associated outbreaks, and the sources of infection for sporadic cases rarely have been identified. In July 1993, three cases of culture-confirmed E. coli O157:H7 infection among persons residing in a small community in California were traced to consumption of hamburger purchased from a local grocery store; E. coli O157:H7 was isolated from that meat. This report summarizes the investigation of these cases by local and state public health officials.

MMWR 43(10):1994 — Reports on laboratory screening for *E. coli* O157 in Connecticut.

MMWR 42(14):1993 — From November 15, 1992, through February 28, 1993, more than 500 laboratory-confirmed infections with E. coli O157:H7 and four associated deaths occurred in four states -- Washington, Idaho, California, and Nevada. This report summarizes the findings from an ongoing investigation (see next paragraph) that identified a multistate outbreak resulting from consumption of hamburgers from one restaurant chain.

MMWR 42(04):1993 — During January 1-29, 1993, 230 persons with culture-confirmed infection with Escherichia coli O157:H7 resulting in bloody diarrhea and, in some cases, hemolytic uremic syndrome (HUS) were reported in the state of Washington. Culture results are pending for 80 others with similar illnesses. Preliminary investigations by public health agencies linked cases to consumption of hamburgers from one fast-food restaurant chain. E. coli O157:H7 has been isolated from epidemiologically implicated lots of ground beef; an interstate recall was initiated by the restaurant on January 18.

MMWR 40(16):1991	In late July and early August 1990, an outbreak of gastroenteritis occurred among persons who had eaten a meal while attending an agricultural threshing show in North Dakota on July 28-29. At least 70 (3.5%) of the more than 2000 attendees were affected. Analysis of food histories obtained from 157 persons implicated a buffet-style dinner on July 28. Although food samples were not available at the time of the investigation, food history analysis indicated that roast beef served at the dinner was the most likely source of infection.
MMWR 35(34):1986	A patient recently died in Seattle with a clinical and pathologic diagnosis of TTP had bloody diarrhea associated with E. coli O157:H7 infection for 1 week before the onset of her other symptoms. This patient's clinical course suggested that E. coli O157:H7 infection may have been related to the development of thrombotic thrombocytopenic purpura (TTP).
MMWR 32(10):1983	In November 1982, 31 (8.8%) of 353 residents at a home for the aged in Ottawa, Ontario, Canada, became ill with gastrointestinal symptoms. Cases occurred over an 18-day period. None of the usual enteric pathogens (Salmonella, Shigella, Campylobacter, Yersinia, or Amoeba) were found in stool specimens obtained from the 31 affected residents. Escherichia coli O157:H7 was isolated from the stools of 17 patients.
MMWR 31(43):1982	Since the beginning of August 1982, stool isolates of Escherichia coli serotype 0157:H7 have been identified at CDC from specimens obtained from four patients in two states. The four patients with sporadic cases in which E. coli was isolated from stools and 24 of the remaining 25 patients with sporadic cases had eaten hamburgers from a variety of sources (including homes and/or local or national-chain restaurants) within the week before they became ill. Additionally, as part of its commemoration of CDC's 50th anniversary, MMWR is reprinting selected MMWR articles of historical importance to public health, accompanied by current editorial notes.
Morbidity and Mortality Weekly Reports	**For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.**

11. Education and Background Resources:	*Literature references can be found at the links below.*
Loci index for genome Escherichia coli O157:H7	Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.

USDA (Aug 11 1998)	USDA Urges Consumers To Use Food Thermometer When Cooking Ground Beef Patties
Preventing *Escherichia coli* O157:H7 infections	A CDC information brochure.
"Produce Handling and Processing Practices" (1997) Emerging Infectious Diseases 3(4).	In the past decade, outbreaks of human illness associated with the consumption of raw vegetables and fruits (or unpasteurized products produced from them) have increased in the United States. Pathogens such as *Listeria monocytogenes*, *Clostridium botulinum*, and *Bacillus cereus* are naturally present in some soil, and their presence on fresh produce is not rare. Salmonella, *Escherichia coli* O157:H7, *Campylobacter jejuni*, *Vibrio cholerae*, parasites, and viruses are more likely to contaminate fresh produce through vehicles such as raw or improperly composted manure, irrigation water containing untreated sewage, or contaminated wash water. Treatment of produce with chlorinated water reduces populations of pathogenic and other microorganisms on fresh produce but cannot eliminate them. Reduction of risk for human illness associated with raw produce can be better achieved through controlling points of potential contamination in the field; during harvesting; during processing or distribution; or in retail markets, food-service facilities, or the home.
CDC *Escherichia coli O157:H7* FAQ'S	Frequently Asked Questions about *Escherichia coli O157:H7*.
Emerging Infectious Diseases (1995)1(2)	A monograph on *E. coli* O157:H7, written Dr. Feng of FDA/CFSAN
USDA's *E. coli* O157:H7 risk assessment	The overall goal of this risk assessment is to assess the likelihood of human morbidity and mortality associated with E. coli O157:H7 in ground beef in the United States. The risk assessment identifies the occurrence and concentration of this pathogen at specific points from farm-to-table and will assist FSIS in reviewing and refining its risk reduction strategy for *E. coli* O157:H7 in groun beef. In addition, the risk assessment will identify future research needs.
12. Molecular Structural Data:	None currently available.

CDC/MMWR

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NIH/PubMed

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Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Enteroinvasive *Escherichia coli*

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism: Enteroinvasive *Escherichia coli* or (EIEC)

Currently, there are four recognized classes of enterovirulent *E. coli* (collectively referred to as the EEC group) that cause gastroenteritis in humans. *E. coli* is part of the normal intestinal flora of humans and other primates. A minority of *E. coli* strains are capable of causing human illness by several different mechanisms. Among these are the enteroinvasive (EIEC) strains. It is unknown what foods may harbor these pathogenic enteroinvasive (EIEC) strains responsible for a form of bacillary dysentery.

2. Nature of Acute Disease:

Enteroinvasive *E. coli* (EIEC) may produce an illness known as bacillary dysentery. The EIEC strains responsible for this syndrome are closely related to *Shigella* spp.

3. Nature of Disease:

Following the ingestion of EIEC, the organisms invade the epithelial cells of the intestine, resulting in a mild form of dysentery, often mistaken for dysentery caused by *Shigella* species. The illness is characterized by the appearance of blood and mucus in the stools of infected individuals.

Infective dose -- The infectious dose of EIEC is thought to be as few as 10 organisms (same as *Shigella*).

4. Diagnosis of Human Illness:

The culturing of the organism from the stools of infected individuals and the demonstration of invasiveness of isolates in tissue culture or in a suitable animal model is necessary to diagnose dysentery caused by this organism.

More recently, genetic probes for the invasiveness genes of both EIEC and *Shigella* spp. have been developed.

5. Associated Foods:

It is currently unknown what foods may harbor EIEC, but any food contaminated with human feces from an ill individual, either directly or via contaminated water, could cause disease in others. Outbreaks have been associated with hamburger meat and unpasteurized milk.

6. Relative Frequency of Disease:

One major foodborne outbreak attributed to enteroinvasive *E. coli* in the U.S. occurred in 1973. It was due to the consumption of imported cheese from France. The disease caused by EIEC is uncommon, but it may be confused with shigellosis and its prevalence may be underestimated.

7. Course of Disease and Complications:

Dysentery caused by EIEC usually occurs within 12 to 72 hours following the ingestion of contaminated food. The illness is characterized by abdominal cramps, diarrhea, vomiting, fever, chills, and a generalized malaise. Dysentery caused by this organism is generally self-limiting with no known complications. A common sequelus associated with infection, especially in pediatric cases, is hemolytic uremic syndrome (HUS).

8. Target Populations:

All people are subject to infection by this organism.

9. Food Analysis:

Foods are examined as are stool cultures. Detection of this organism in foods is extremely difficult because undetectable levels may cause illness. It is estimated that the ingestion of as few as 10 organisms may result in dysentery.

10. Selected Outbreaks:

Literature references can be found at the links below.

Several outbreaks in the U.S. have been attributed to this organism. One outbreak occurred in 1973 and was due to the consumption of imported cheese. More recently, a cruise ship outbreak was attributed to potato salad, and an outbreak occurred in a home for the mentally retarded where subsequent person-to-person transmission occurred.

Morbidity and Mortality Weekly Reports

For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.

11. Education and Background Resources:

None currently available.

12. Molecular Structural Data:

None currently available.

CDC/MMWR

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FDA/Center for Food Safety & Applied Nutrition
Hypertext updated by mow/las/dav/ear June 14, 2006

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Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Giardia lamblia

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism:
Giardia lamblia

Giardia lamblia (intestinalis) is a single celled animal, i.e., a protozoa, that moves with the aid of five flagella. In Europe, it is sometimes referred to as Lamblia intestinalis.

2. Nature of Acute Disease:

Giardiasis is the most frequent cause of non-bacterial diarrhea in North America.

3. Nature of Disease:

CDC Case Definition

What is a "Case Definition"?

Overview of Public Health Surveillance

Organisms that appear identical to those that cause human illness have been isolated from domestic animals (dogs and cats) and wild animals (beavers and bears). A related but morphologically distinct organism infects rodents, although rodents may be infected with human isolates in the laboratory. Human giardiasis may involve diarrhea within 1 week of ingestion of the cyst, which is the environmental survival form and infective stage of the organism.

Normally illness lasts for 1 to 2 weeks, but there are cases of chronic infections lasting months to years. Chronic cases, both those with defined immune deficiencies and those without, are difficult to treat.

The disease mechanism is unknown, with some investigators reporting that the organism produces a toxin while others are unable to confirm its existence. The organism has been demonstrated inside host cells in the duodenum, but most investigators think this is such an infrequent occurrence that it is not responsible for disease symptoms. Mechanical obstruction of the absorptive surface of the intestine has been proposed as a possible pathogenic mechanism, as has a synergistic relationship with some of the intestinal flora.

Giardia can be excysted, cultured and encysted in vitro; new isolates have bacterial, fungal, and viral symbionts. Classically the disease was diagnosed by demonstration of the organism in stained fecal smears.

Several strains of *G. lamblia* have been isolated and described through analysis of their proteins and DNA; type of strain, however, is not consistently associated with disease severity. Different individuals show various degrees of symptoms when infected with the same strain, and the symptoms of an individual may vary during the course of the disease.

Infectious Dose - Ingestion of one or more cysts may cause disease, as contrasted to most bacterial illnesses where hundreds to thousands of organisms must be consumed to produce illness.

4. Diagnosis of Human Illness:

Giardia lamblia is frequently diagnosed by visualizing the organism, either the trophozoite (active reproducing form) or the cyst (the resting stage that is resistant to adverse environmental conditions) in stained preparations or unstained wet mounts with the aid of a microscope. A commercial fluorescent antibody kit is available to stain the organism. Organisms may be concentrated by sedimentation or flotation; however, these procedures reduce the number of recognizable organisms in the sample. An enzyme linked immunosorbant assay (ELISA) that detects excretory secretory products of the organism is also available. So far, the increased sensitivity of indirect serological detection has not been consistently demonstrated.

5. Associated Foods:

Giardiasis is most frequently associated with the consumption of contaminated water. Five outbreaks have been traced to food contamination by infected or infested food handlers, and the possibility of infections from contaminated vegetables that are eaten raw cannot be excluded. Cool moist conditions favor the survival of the organism.

6. Relative Frequency of Disease:

Giardiasis is more prevalent in children than in adults, possibly because many individuals seem to have a lasting immunity after infection. This organism is implicated in 25% of the cases of gastrointestinal disease and may be present asymptomatically. The overall incidence of infection in the United States is estimated at 2% of the population. This disease afflicts many homosexual men, both HIV-positive and HIV-negative individuals. This is presumed to be due to sexual transmission. The disease is also common in child day care centers, especially those in which diapering is done.

7. Course of Disease and Complications:

About 40% of those who are diagnosed with giardiasis demonstrate disaccharide intolerance during detectable infection and up to 6 months after the infection can no longer be detected. Lactose (i.e., milk sugar) intolerance is most frequently observed. Some individuals (less than 4%) remain symptomatic more than 2 weeks; chronic infections lead to a malabsorption syndrome and severe weight loss. Chronic cases of giardiasis in immunodeficient and normal individuals are frequently refractile to drug treatment. Flagyl is normally quite effective in terminating infections. In some immune deficient individuals, giardiasis may contribute to a shortening of the life span.

8. Target Populations:

Giardiasis occurs throughout the population, although the prevalence is higher in children than adults. Chronic symptomatic giardiasis is more common in adults than children.

9. Food Analysis:

Food is analyzed by thorough surface cleaning of the suspected food and sedimentation of the organisms from the cleaning water. Feeding to specific pathogen-free animals has been used to detect the organism in large outbreaks associated with municipal water systems. The precise sensitivity of these methods has not been determined, so that negative results are questionable. Seven days may be required to detect an experimental infection.

10. Selected Outbreaks:

Literature references can be found at the links below.

Major outbreaks are associated with contaminated water systems that do not use sand filtration or have a defect

	in the filtration system.
MMWR 38(23):1989	In April 1988, the Albuquerque Environmental Health Department and the New Mexico Health and Environment Department investigated reports of giardiasis among members of a church youth group in Albuquerque. The first two members to be affected had onset of diarrhea on March 3 and 4, respectively; stool specimens from both were positive for Giardia lamblia cysts. These two persons had only church youth group activities in common.
MMWR 32(50):1983	On August 8, 1983, the Utah Department of Health was notified by the Tooele County Health Department (TCHD) of an outbreak of diarrheal illness in Tooele, Utah, possibly associated with a contaminated public water supply that resulted from flooding during Utah's spring thaw.
Morbidity and Mortality Weekly Reports	**For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.**

11. Education and Background Resources:	*Literature references can be found at the links below.*
Loci index for genome Giardia lamblia	Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.
CDC *Giardiasis* FAQ'S	Frequently Asked Questions about *Giardiasis*.
FSIS Parasites and Foodborne Illness Resource page	*Giardia duodenalis*, cause of giardiasis (GEE-are-DYE-uh-sis), is a one-celled, microscopic parasite that can live in the intestines of animals and people. It is found in every region throughout the world and has become recognized as one of the most common causes of waterborne (and occasionally foodborne) illness.

12. Molecular Structural Data:	None currently available.

13. FDA Regulations or Activity:

Bacteriological Analytical Manual.	Current recovery methods are published in this FDA methodology reference. The FDA continues to actively develop and improve methods of recovering parasitic protozoa and helminth eggs from foods.

CDC/MMWR

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Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Entamoeba histolytica

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism:
Entamoeba histolytica

This is a single celled parasitic animal, i.e., a protozoa, that infects predominantly humans and other primates. Diverse mammals such as dogs and cats can become infected but usually do not shed cysts (the environmental survival form of the organism) with their feces, thus do not contribute significantly to transmission. The active (trophozoite) stage exists only in the host and in fresh feces; cysts survive outside the host in water and soils and on foods, especially under moist conditions on the latter. When swallowed they cause infections by excysting (to the trophozoite stage) in the digestive tract.

2. Nature of Acute Disease:

Amebiasis (or amoebiasis) is the name of the infection caused by *E. histolytica*.

3. Nature of Disease:

CDC Case Definition

What is a "Case Definition"?

Infections that sometimes last for years may be accompanied by 1) no symptoms, 2) vague gastrointestinal distress, 3) dysentery (with blood and mucus). Most infections occur in the digestive tract but other tissues may be invaded. Complications include 4) ulcerative and abscess pain and, rarely, 5) intestinal blockage. Onset time is highly variable. It is theorized that the absence of symptoms or their intensity varies with such factors as 1) strain of amoeba, 2) immune health of the host, and 3) associated bacteria and, perhaps, viruses. The amoeba's enzymes help it to penetrate and digest human tissues; it secretes toxic substances.

Overview of Public Health Surveillance	Infectious Dose--Theoretically, the ingestion of one viable cyst can cause an infection.
4. Diagnosis of Human Illness:	Human cases are diagnosed by finding cysts shed with the stool; various flotation or sedimentation procedures have been developed to recover the cysts from fecal matter; stains (including fluorescent antibody) help to visualize the isolated cysts for microscopic examination. Since cysts are not shed constantly, a minimum of 3 stools should be examined. In heavy infections, the motile form (the trophozoite) can be seen in fresh feces. Serological tests exist for long-term infections. It is important to distinguish the *E. histolytica* cyst from the cysts of nonpathogenic intestinal protozoa by its appearance.
5. Associated Foods:	Amebiasis is transmitted by fecal contamination of drinking water and foods, but also by direct contact with dirty hands or objects as well as by sexual contact.
6. Relative Frequency of Disease:	The infection is "not uncommon" in the tropics and arctics, but also in crowded situations of poor hygiene in temperate-zone urban environments. It is also frequently diagnosed among homosexual men.
7. Course of Disease and Complications:	In the majority of cases, amoebas remain in the gastrointestinal tract of the hosts. Severe ulceration of the gastrointestinal mucosal surfaces occurs in less than 16% of cases. In fewer cases, the parasite invades the soft tissues, most commonly the liver. Only rarely are masses formed (amoebomas) that lead to intestinal obstruction. Fatalities are infrequent.
8. Target Populations:	All people are believed to be susceptible to infection, but individuals with a damaged or undeveloped immunity may suffer more severe forms of the disease. AIDS / ARC patients are very vulnerable.

9. Food Analysis:

E. histolytica cysts may be recovered from contaminated food by methods similar to those used for recovering *Giardia lamblia* cysts from feces. Filtration is probably the most practical method for recovery from drinking water and liquid foods. *E. histolytica* cysts must be distinguished from cysts of other parasitic (but nonpathogenic) protozoa and from cysts of free-living protozoa. Recovery procedures are not very accurate; cysts are easily lost or damaged beyond recognition, which leads to many falsely negative results in recovery tests. (See the FDA Bacteriological Analytical Manual.)

10. Selected Outbreaks:

Literature references can be found at the links below.

The most dramatic incident in the USA was the Chicago World's Fair outbreak in 1933 caused by contaminated drinking water; defective plumbing permitted sewage to contaminate the drinking water. There were 1,000 cases (with 58 deaths). In recent times, food handlers are suspected of causing many scattered infections, but there has been no single large outbreak.

MMWR 34(9):1985

In October 1983, the Los Angeles County (California) Department of Health Services was notified by a local medical laboratory of a large increase in the laboratory's diagnoses of intestinal amebiasis (Entamoeba histolytica infection). Thirty-eight cases were identified from August to October. The laboratory staff estimated that, before August, they had diagnosed approximately one E. histolytica infection per month. A preliminary investigation failed to identify a common source of the infection.

Morbidity and Mortality Weekly Reports

For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.

11. Education and Background Resources:

Literature references can be found at the links below.

Loci index for genome Entamoeba histolytica

Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.

Amebiasis (*Entamoeba*

What is amebiasis? What are the symptoms of amebiasis? How soon after exposure do symptoms appear? How

histolytica) infection FAQ's	can I get it? Who is at risk? What should I do if I think I have it? How is it diagnosed and how is it treated? How can it be prevented during travel in developing countries? Should I be concerned about spreading infection to the rest of my household?
Nonpathogenic Intestinal Amebae Infection FAQ's	Where do these amebae live in the body? How did they get there? How long do these amebae stay in my body? Should I be treated for these amebae?
12. Molecular Structural Data:	None currently available.

CDC/MMWR

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Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Cryptosporidium parvum

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism: *Cryptosporidium parvum*

Cryptosporidium parvum, a single-celled animal, i.e., a protozoa, is an obligate intracellular parasite. It has been given additional species names when isolated from different hosts. It is currently thought that the form infecting humans is the same species that causes disease in young calves. The forms that infect avian hosts and those that infect mice are not thought capable of infecting humans. *Cryptosporidium* sp. infects many herd animals (cows, goats, sheep among domesticated animals, and deer and elk among wild animals). The infective stage of the organism, the oocyst is 3 um in diameter or about half the size of a red blood cell. The sporocysts are resistant to most chemical disinfectants, but are susceptible to drying and the ultraviolet portion of sunlight. Some strains appear to be adapted to certain hosts but cross-strain infectivity occurs and may or may not be associated with illness. The species or strain infecting the respiratory system is not currently distinguished from the form infecting the intestines.

2. Nature of Acute Disease:

Intestinal, tracheal, or pulmonary cryptosporidiosis.

3. Nature of Disease:

Intestinal cryptosporidiosis is characterized by severe watery diarrhea but may, alternatively, be asymptomatic. Pulmonary and tracheal cryptosporidiosis in humans is associated with coughing and frequently a low-grade

CDC Case Definition

What is a "Case Definition"?

Overview of Public Health Surveillance

fever; these symptoms are often accompanied by severe intestinal distress.

Infectious dose--Less than 10 organisms and, presumably, one organism can initiate an infection. The mechanism of disease is not known; however, the intracellular stages of the parasite can cause severe tissue alteration.

4. Diagnosis of Human Illness:

Oocysts are shed in the infected individual's feces. Sugar flotation is used to concentrate the organisms and acid fast staining is used to identify them. A commercial kit is available that uses fluorescent antibody to stain the organisms isolated from feces. Diagnosis has also been made by staining the trophozoites in intestinal and biopsy specimens. Pulmonary and tracheal cryptosporidiosis are diagnosed by biopsy and staining.

5. Associated Foods:

Cryptosporidium sp. could occur, theoretically, on any food touched by a contaminated food handler. Incidence is higher in child day care centers that serve food. Fertilizing salad vegetables with manure is another possible source of human infection. Large outbreaks are associated with contaminated water supplies.

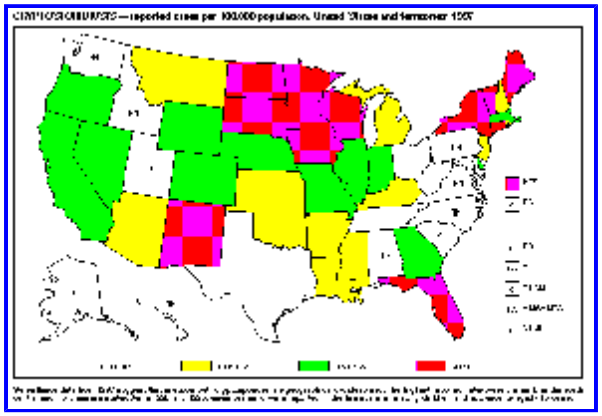
6. Relative Frequency of Disease:

Direct human surveys indicate a prevalence of about 2% of the population in North America. Serological surveys indicate that 80% of the population has had cryptosporidiosis. The extent of illness associated with reactive sera is not known.

Reported cases of Cryptosporidiosis, United States 1997

Summary of Notifiable Diseases, United States,

1997:MMWR 46(54)



7. Course of Disease and Complications: Intestinal cryptosporidiosis is self-limiting in most healthy individuals, with watery diarrhea lasting 2-4 days. In some outbreaks at day care centers, diarrhea has lasted 1 to 4 weeks. To date, there is no known effective drug for the treatment of cryptosporidiosis. Immunodeficient individuals, especially AIDS patients, may have the disease for life, with the severe watery diarrhea contributing to death. Invasion of the pulmonary system may also be fatal.

8. Target Populations: In animals, the young show the most severe symptoms. For the most part, pulmonary infections are confined to those who are immunodeficient. However, an infant with a presumably normal immune system had tracheal cryptosporidiosis (although a concurrent viremia may have accounted for lowered resistance). Child day care centers, with a large susceptible population, frequently report outbreaks.

9. Food Analysis: The 7th edition of FDA's Bacteriological Analytical Manual will contain a method for the examination of vegetables for *Cryptosporidium* sp.

10. Selected Outbreaks:

Literature references can be found at the links below.

MMWR 47(40):1998

This report summarizes the investigation of a large outbreak of cryptosporidiosis associated with exposure to a water sprinkler fountain at the Minnesota Zoo. The initial cases were not diagnosed as cryptosporidiosis by the health-care system despite patients seeking care, underscoring the need for increased awareness of cryptosporidiosis and routine laboratory diagnostic practices among health-care providers.

MMWR 47(27):1998

On December 29, 1997, the Spokane Regional Health District received reports of acute gastroenteritis among members of a group attending a dinner banquet catered by a Spokane restaurant on December 18. The illness was characterized by a prolonged (3-9 days) incubation period and diarrhea, which led public health officials to suspect a parasitic cause of the illness. Eight of 10 stool specimens obtained from ill banquet attendees were positive for Cryptosporidium using both modified acid-fast and auramine-rhodamine staining of concentrated specimens.

MMWR 46(16):1997

To improve disease reporting and identify exposures associated with infection, New York City designated cryptosporidiosis a reportable disease in January 1994, and the New York City Department of Health (NYCDOH) initiated active surveillance in November 1994. Each of the clinical laboratories are routinely contacted (usually monthly) for reports of new cases, and each case is investigated by telephone interview and/or chart review. Of the 289 cases of cryptosporidiosis reported in New York City during 1994, most (72%) occurred among men and among persons aged 20-44 years (63%).

MMWR 46(01):1997

In October 1996, unpasteurized apple cider or juice was associated with *Cryptosporidium parvum* infections in the Northeast. Apple cider is a traditional beverage produced and consumed in the fall. Cider often is manufactured locally at small cider mills where apples are crushed in presses, and the cider frequently is not pasteurized before sale.

MMWR 45(36):1996

On September 29, 1995, the Minnesota Department of Health (MDH) received reports of acute gastroenteritis among an estimated 50 attendees of a social event in Blue Earth County on September 16. This report summarizes the epidemiologic and laboratory investigations of the outbreak, which indicate the probable cause for this foodborne outbreak was *Cryptosporidium parvum*.

MMWR 45(21):1996

On July 27, 1995, the Alachua County Public Health Unit (ACPHU) in central Florida was notified of an outbreak of gastroenteritis among children and counselors at a day camp on the grounds of a public elementary school. This report summarizes the outbreak investigation, which implicated *Cryptosporidium parvum* as the

causative agent and underscores the role of contaminated water as a vehicle for transmission of this organism.

MMWR 43(31):1994	In March and April 1993, an outbreak of cryptosporidiosis in Milwaukee resulted in diarrheal illness in an estimated 403,000 persons. Following that outbreak, testing for Cryptosporidium in persons with diarrhea increased substantially in some areas of Wisconsin; by August 1, 1993, three of six clinical laboratories in Dane County were testing routinely for Cryptosporidium as part of ova and parasite examinations. In late August 1993, the Madison Department of Public Health and the Dane County Public Health Division identified two clusters of persons with laboratory-confirmed Cryptosporidium infection in Dane County (approximately 80 miles west of Milwaukee).
MMWR 43(36):1994	On December 6, 1993, water-treatment plant operators in the District of Columbia (DC) began to have difficulty maintaining optimal filter effectiveness. On December 7, filter performance worsened, and levels of turbidity (i.e., small suspended particles) exceeded those permitted by U.S. Environmental Protection Agency (EPA) standards. On December 8, DC residents were advised to boil water intended for drinking because of high municipal water turbidity that may have included microbial contaminants. Although adequate chlorination of the DC municipal water was maintained throughout the period of increased turbidity, the parasite *Cryptosporidium parvum* is highly resistant to chlorination.
MMWR 39(20):1990	From July 13 through August 14, 1988, 44 persons in five separate swimming groups developed a gastrointestinal illness after using a swimming pool in Los Angeles County. The outbreak began several days after an unintentional human defecation in the pool during the first week of July. When the outbreak was reported to the Los Angeles County Department of Health Services (LACDHS) in early August, LACDHS initiated an epidemiologic investigation.
MMWR 36(33):1987	Between July 1 and October 1, 1986, 78 laboratory-confirmed cases of cryptosporidiosis were reported to the Office of Epidemiology at the New Mexico Health and Environment Department. Because the source of infection in these cases was unclear, investigators conducted a case-control study to establish risk factors for infection.
MMWR 33(42):1984	During 1984, CDC has received several reports of cryptosporidiosis among children attending day-care centers. Seven investigations conducted in five states are summarized.
Morbidity and Mortality Weekly Reports	**For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.**

11. Education and Background Resources:	*Literature references can be found at the links below.*
Loci index for genome Cryptosporidium parvum	Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.
FAQ's	Fact Sheet: Cryptosporidiosis
Control and Prevention	Cryptosporidiosis Control and Prevention
Child Care	The ABCs of Safe and Healthy Child Care: Cryptosporidiosis in the Child Care Setting
Cleaning and Disinfecting	The ABCs of Safe and Healthy Child Care: Cleaning and Disinfection
HIV/AIDS	Cryptosporidiosis: A Guide for Persons with HIV/AIDS
Source of Infection	Cryptosporidiosis: Sources of Infection and Guidelines for Prevention
Emerging Infectious Disease 1(2)1995	Waterborne Cryptosporidiosis Threat Addressed
Emerging Infectious Disease 3(1)1997	Cryptosporidiosis: An Emerging, Highly Infectious Threat
Emerging Infectious Disease 3(4)1997	Genetic Polymorphism Among Cryptosporidium parvum isolates: Evidence of Two Distinct Human Transmission Cycles
FSIS Parasites and Foodborne Illness Resource page	*Cryptosporidium parvum*, cause of the disease cryptosporidiosis (KRIP-toe-spo-RID-e-O-sis), is a one-celled, microscopic parasite, and a significant cause of waterborne illness worldwide. It is found in the intestines of many herd animals including cows, sheep, goats, deer, and elk.

12. Molecular Structural Data:	None currently available.
13. FDA Regulations or Activity:	
Bacteriological Analytical Manual.	Current recovery methods are published in this FDA methodology reference. The FDA continues to actively develop and improve methods of recovering parasitic protozoa and helminth eggs from foods.

CDC/MMWR

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Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Cyclospora cayetanensis

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism:

2. Nature of Acute Disease:

3. Nature of Disease:

CDC Case Definition

What is a "Case Definition"?

Overview of Public Health Surveillance

4. Diagnosis of Human Illness:

5. Associated Foods:

6. Relative Frequency of Disease:

7. Course of Disease and Complications:

8. Target Populations:

9. Food Analysis:

10. Selected Outbreaks: *Literature references can be found at the links below.*

MMWR 47(38):1998 During May-June 1998, the Ontario Ministry of Health and local health departments in Ontario received reports of clusters of cases of cyclosporiasis associated with events held during May. This report describes the preliminary findings of the investigation of a cluster in Toronto, Ontario, and summarizes the findings from investigations of 12 other clusters.

MMWR 46(30):1997	During July 1997, state and local health departments in Virginia, the District of Columbia (DC), and Maryland received reports of clusters of cases of cyclosporiasis associated with events (e.g., luncheons) held in their jurisdictions during June and July. This report describes the preliminary findings of the investigation of a cluster in Virginia and summarizes the findings from ongoing investigations of the other clusters. Fresh basil has been implicated as the probable vehicle of infection.
MMWR 46(23):1997	Since April 1997, CDC has received reports of outbreaks of cyclosporiasis in the United States and Canada (1,2). As of June 11, there have been 21 clusters of cases of cyclosporiasis reported from eight states (California, Florida, Maryland, Nebraska, Nevada, New York, Rhode Island, and Texas) and one province in Canada (Ontario). These clusters were associated with events (e.g., receptions, banquets, or time-place-related exposures {meals in the same restaurant on the same day}) that occurred during March 19-May 25 and comprise approximately 140 laboratory-confirmed and 370 clinically defined cases of cyclosporiasis.
MMWR 46(21):1997	During April and May 1997, CDC received reports of clusters of cases of cyclosporiasis in the United States (1). This report describes the preliminary findings of an investigation of an outbreak in New York and summarizes the findings from on-going investigations in other states.
MMWR 46(20):1997	In April and May 1997, CDC received reports of seven event-associated clusters of cases of cyclosporiasis from five states (California, Florida, Nevada, New York, and Texas). Approximately 80 cases of infection with human-associated Cyclospora, a recently characterized coccidian parasite, have been laboratory-confirmed. State and local health departments, CDC, and the Food and Drug Administration are conducting investigations to identify the vehicles of infection. Both foodborne and waterborne outbreaks of cyclosporiasis have previously been reported in the United States during spring and summer months.
MMWR 46(16):1997	Until 1996, most cases of cyclosporiasis in the United States occurred among international travelers, and information about modes of transmission of C. cayetanensis was limited. Waterborne transmission had been documented, but direct person-to-person transmission was considered unlikely. During the summer of 1995, in response to an outbreak of Cyclospora infection among Florida residents with no history of international travel, the state health department initiated surveillance for the organism.
MMWR 45(28):1996	Since May 1996, CDC has received reports of clusters and sporadic cases of infection with the parasite Cyclospora cayetanensis that occurred in May and June in the United States and Canada. This report describes preliminary findings of an investigation by the New Jersey Department of Health and Senior Services (NJDHSS) and updates the findings of other ongoing investigations.

MMWR 45(25):1996	Cyclospora cayetanensis (previously termed cyanobacterium-like body) is a recently characterized coccidian parasite; the first known cases of infection in humans were diagnosed in 1977. Before 1996, only three outbreaks of Cyclospora infection had been reported in the United States. This report describes the preliminary findings of an ongoing outbreak investigation by the South Carolina Department of Health and Environmental Control (SCDHEC) and summarizes the findings from investigations in other states.
FDA talk paper, 10 June 1997	FDA has released a talk paper on outbreaks of cyclosporiasis and Guatemalan raspberries.
Morbidity and Mortality Weekly Reports	**For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.**

11. Education and Background Resources:	*Literature references can be found at the links below.*
Loci index for genome Cyclospora cayetanensis	Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.
Information for the general public	What is Cyclospora and how is it spread? Who is at risk for infection? What are the symptoms of infection and how soon after infection will symptoms begin? How long will symptoms last? How is it infection diagnosed and treated? How is infection prevented?
Information for health professionals	What is Cyclospora and how is it spread? Who is at risk for infection? What are the symptoms of infection and how soon after infection will symptoms begin? How long will symptoms last? How is it infection diagnosed and treated? How is infection prevented? **Key points for the laboratory diagnosis of Cyclospora.**
The FDA method *Cyclospora cayetanensis* Protocol	Concentration and Preparation of Oocysts from Produce for the Polymerase Chain Reaction (PCR) and Microscopy.
A FDA Laboratory Information Bulletin 4044	"Differentiation of *Cyclospora* sp. and *Eimeria* spp. by Using the Polymerase Chain Reaction Amplification Products and Restriction Fragment Length Polymorphisms."

FSIS Parasites and Foodborne Illness Resource page	*Cyclospora cayetanensis* (SIGH-clo-SPOR-uh KYE-uh-tuh-NEN-sis), cause of cyclosporiasis, is a one-celled, microscopic parasite. Currently little is known about this organism, although cases of cyclosporiasis are being reported from various countries with increasing frequency.
12. Molecular Structural Data:	None currently available.

CDC/MMWR

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Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Anisakis simplex and related worms

CDC/MMWR NIH/PubMed Agricola

1. Name of the Organism:
Anisakis simplex and related worms

Anisakis simplex (herring worm), *Pseudoterranova (Phocanema, Terranova) decipiens* (cod or seal worm), *Contracaecum* spp., and *Hysterothylacium (Thynnascaris)* spp. are anisakid nematodes (roundworms) that have been implicated in human infections caused by the consumption of raw or undercooked seafood. To date, only *A. simplex* and *P. decipiens* are reported from human cases in North America.

2. Nature of Acute Disease:

Anisakiasis is generally used when referring to the acute disease in humans. Some purists utilize generic names (e.g., contracaeciasis) in referring to the disease, but the majority consider that the name derived from the family is specific enough. The range of clinical features is not dependent on species of anisakid parasite in cases reported to date.

3. Nature of Disease:

In North America, anisakiasis is most frequently diagnosed when the affected individual feels a tingling or tickling sensation in the throat and coughs up or manually extracts a nematode. In more severe cases there is acute abdominal pain, much like acute appendicitis accompanied by a nauseous feeling. Symptoms occur from as little as an hour to about 2 weeks after consumption of raw or undercooked seafood. One nematode is the usual number recovered from a patient. With their anterior ends, these larval nematodes from fish or shellfish usually burrow into the wall of the digestive tract to the level of the muscularis mucosae (occasionally they

penetrate the intestinal wall completely and are found in the body cavity). They produce a substance that attracts eosinophils and other host white blood cells to the area. The infiltrating host cells form a granuloma in the tissues surrounding the penetrated worm. In the digestive tract lumen, the worm can detach and reattach to other sites on the wall. Anisakids rarely reach full maturity in humans and usually are eliminated spontaneously from the digestive tract lumen within 3 weeks of infection. Penetrated worms that die in the tissues are eventually removed by the host's phagocytic cells.

4. Diagnosis of Human Illness:

In cases where the patient vomits or coughs up the worm, the disease may be diagnosed by morphological examination of the nematode. (*Ascaris lumbricoides*, the large roundworm of humans, is a terrestrial relative of anisakines and sometimes these larvae also crawl up into the throat and nasal passages.) Other cases may require a fiber optic device that allows the attending physician to examine the inside of the stomach and the first part of the small intestine. These devices are equipped with a mechanical forceps that can be used to remove the worm. Other cases are diagnosed upon finding a granulomatous lesion with a worm on laparotomy. A specific radioallergosorbent test has been developed for anasakiasis, but is not yet commercially marketed.

5. Associated Foods:

Seafoods are the principal sources of human infections with these larval worms. The adults of *A. simplex* are found in the stomachs of whales and dolphins. Fertilized eggs from the female parasite pass out of the host with the host's feces. In seawater, the eggs embryonate, developing into larvae that hatch in sea water. These larvae are infective to copepods (minute crustaceans related to shrimp) and other small invertebrates. The larvae grow in the invertebrate and become infective for the next host, a fish or larger invertebrate host such as a squid. The larvae may penetrate through the digestive tract into the muscle of the second host. Some evidence exists that the nematode larvae move from the viscera to the flesh if the fish hosts are not gutted promptly after catching. The life cycles of all the other anisakid genera implicated in human infections are similar. These parasites are known to occur frequently in the flesh of cod, haddock, fluke, pacific salmon, herring, flounder, and monkfish.

6. Relative Frequency of Disease:

Fewer than 10 cases are diagnosed in the U.S. annually. However, it is suspected that many other cases go undetected. The disease is transmitted by raw, undercooked or insufficiently frozen fish and shellfish, and its incidence is expected to increase with the increasing popularity of sushi and sashimi bars.

7. Course of Disease and Complications:

Severe cases of anisakiasis are extremely painful and require surgical intervention. Physical removal of the nematode(s) from the lesion is the only known method of reducing the pain and eliminating the cause (other than waiting for the worms to die). The symptoms apparently persist after the worm dies since some lesions are found upon surgical removal that contain only nematode remnants. Stenosis (a narrowing and stiffening) of the pyloric sphincter was reported in a case in which exploratory laparotomy had revealed a worm that was not removed.

8. Target Populations:

The target population consists of consumers of raw or underprocessed seafood.

9. Food Analysis:

Candling or examining fish on a light table is used by commercial processors to reduce the number of nematodes in certain white-flesh fish that are known to be infected frequently. This method is not totally effective, nor is it very adequate to remove even the majority of nematodes from fish with pigmented flesh.

10. Selected Outbreaks:

Literature references can be found at the links below.

This disease is known primarily from individual cases. Japan has the greatest number of reported cases because of the large volume of raw fish consumed there.

A recent letter to the editor of the New England Journal of Medicine (319:1128-29, 1988) stated that approximately 50 cases of anisakiasis have been documented in the United States, to date. Three cases in the San Francisco Bay area involved ingestion of sushi or undercooked fish. The letter also points out that anasakiasis is easily misdiagnosed as acute appendicitis, Crohn's disease, gastric ulcer, or gastrointestinal cancer.

Morbidity and Mortality Weekly Reports

For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.

11. Education and Background Resources:	*Literature references can be found at the links below.*
Loci index for genome Anisakis sp.	Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.
12. Molecular Structural Data:	None currently available.
13. FDA Regulations or Activity:	FDA recommends that all fish and shellfish intended for raw (or semiraw such as marinated or partly cooked) consumption be blast frozen to -35°C (-31°F) or below for 15 hours, or be regularly frozen to -20°C (-4°F) or below for 7 days.

CDC/MMWR

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FDA/Center for Food Safety & Applied Nutrition
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Bad Bug Book

Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Diphyllobothrium spp.

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism:
Diphyllobothrium spp.

Diphyllobothrium latum and other members of the genus are broad fish tapeworms reported from humans. They are parasitic flatworms.

2. Nature of Acute Disease:

Diphyllobothriasis is the name of the disease caused by broad fish tapeworm infections.

3. Nature of Disease:

Diphyllobothriasis is characterized by abdominal distention, flatulence, intermittent abdominal cramping, and diarrhea with onset about 10 days after consumption of raw or insufficiently cooked fish. The larva that infects people, a "plerocercoid," is frequently encountered in the viscera of freshwater and marine fishes. *D. latum* is sometimes encountered in the flesh of freshwater fish or fish that are anadromous (migrating from salt water to fresh water for breeding). Bears and humans are the final or definitive hosts for this parasite. *D. latum* is a broad, long tapeworm, often growing to lengths between 1 and 2 meters (3-7 feet) and potentially capable of attaining 10 meters (32 feet); the closely related *D. pacificum* normally matures in seals or other marine mammals and reaches only about half the length of *D. latum*. Treatment consists of administration of the drug, niclosamide, which is available to physicians through the Centers for Disease Control's Parasitic Disease Drug

Service.

4. Diagnosis of Human Illness: The disease is diagnosed by finding operculate eggs (eggs with a lid) in the patient's feces on microscopical examination. These eggs may be concentrated by sedimentation but not by flotation. They are difficult to distinguish from the eggs of *Nanophyetus* spp..

5. Associated Foods: The larvae of these parasites are sometimes found in the flesh of fish.

6. Relative Frequency of Disease: Diphyllobothriasis is rare in the United States, although it was formerly common around the Great Lakes and known as "Jewish or Scandinavian housewife's disease" because the preparers of gefillte fish or fish balls tended to taste these dishes before they were fully cooked. The parasite is now supposedly absent from Great Lakes fish. Recently, cases have been reported from the West Coast.

7. Course of Disease and Complications: In persons that are genetically susceptible, usually persons of Scandinavian heritage, a severe anemia may develop as the result of infection with broad fish tapeworms. The anemia results from the tapeworm's great requirement for and absorption of Vitamin B12.

8. Target Populations: Consumers of raw and underprocessed fish are the target population for diphyllobothriasis.

9. Food Analysis: Foods are not routinely analyzed for larvae of *D. latum*, but microscopic inspection of thin slices of fish, or digestion, can be used to detect this parasite in fish flesh.

10. Selected Outbreaks:	*Literature references can be found at the links below.*
	An outbreak involving four Los Angeles physicians occurred in 1980. These physicians all consumed sushi (a raw fish dish) made of tuna, red snapper, and salmon. Others who did not consume the sushi made with salmon did not contract diphyllobothriasis. At the time of this outbreak there was also a general increase in requests for niclosamide from CDC; interviews of 39 patients indicated that 32 recalled consuming salmon prior to their illness.
Morbidity and Mortality Weekly Reports	**For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.**

11. Education and Background Resources:	*Literature references can be found at the links below.*
FDA recommendations	The FDA is determining whether the freezing recommendations (see chapter 25) for raw or semiraw seafood with anisakid nematodes will also prevent infections with the broad fish tapeworms.
Loci index for genome *Diphyllobothrium spp.*	Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.

12. Molecular Structural Data:	None currently available.

CDC/MMWR

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Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Nanophyetus spp.

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism:
Nanophyetus spp.

Nanophyetus salmincola or *N. schikhobalowi* are the names, respectively, of the North American and Russian troglotrematoid trematodes (or flukes). These are parasitic flatworms.

2. Nature of Acute Disease:

Nanophyetiasis is the name of the human disease caused by these flukes. At least one newspaper referred to the disease as "fish flu." *N. salmincola* is responsible for the transmission of *Neorickettsia helminthoeca*, which causes an illness in dogs that may be serious or even fatal.

3. Nature of Disease:

Knowledge of nanophyetiasis is limited. The first reported cases are characterized by an increase of bowel movements or diarrhea, usually accompanied by increased numbers of circulating eosinophils, abdominal discomfort and nausea. A few patients reported weight loss and fatigue, and some were asymptomatic. The rickettsia, though fatal to 80% of untreated dogs, is not known to infect humans.

4. Diagnosis of Human

Detection of operculate eggs of the characteristic size and shape in the feces is indicative of nanophyetiasis. The

Illness: eggs are difficult to distinguish from those of *Diphyllobothrium latum*.

5. Associated Foods: There have been no reported outbreaks of nanophyetiasis in North America; the only scientific reports are of 20 individual cases referred to in one Oregon clinic. A report in the popular press indicates that the frequency is significantly higher. It is significant that two cases occurred in New Orleans well outside the endemic area. In Russia's endemic area the infection rate is reported to be greater than 90% and the size of the endemic area is growing.

6. Relative Frequency of Disease: Nanophyetiasis is transmitted by the larval stage (metacercaria) of a worm that encysts in the flesh of freshwater fishes. In anadromous fish, the parasite's cysts can survive the period spent at sea. Although the metacercaria encysts in many species of fish, North American cases were all associated with salmonids. Raw, underprocessed, and smoked salmon and steelhead were implicated in the cases to date.

7. Course of Disease and Complications: Mebendazole was ineffective as a treatment; patients kept shedding eggs, and symptoms gradually decreased over 2 months or more. Treatment with two doses of bithionol or three doses of niclosamide resulted in the resolution of symptoms and disappearance of eggs in the feces. These drugs are available in the U.S. from the Centers for Disease Control's Parasitic Drug Service.

8. Target Populations: Consumers of raw or underprocessed freshwater or anadromous fish, especially salmonids.

9. Food Analysis: There are no tested methods for detection of *Nanophyetus* spp. in fishes. Candling with the aid of a dissecting microscope, or pepsin HCl digestion should detect heavily infected fish.

10. Selected *Literature references can be found at the links below.*

Outbreaks:	
	None
Morbidity and Mortality Weekly Reports	**For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.**
11. Education and Background Resources:	*Literature references can be found at the links below.*
Loci index for genome Digenea (Fluke family)	Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.
12. Molecular Structural Data:	None currently available.
13. FDA Regulations or Activity:	FDA has no specific regulation or activity regarding these trematodes. As pathogens, however, they should not be live in fish consumed raw or semiraw.

CDC/MMWR

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Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Eustrongylides sp.

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism: *Eustrongylides* sp.

Larval *Eustrongylides* sp. are large, bright red roundworms (nemotodes), 25-150 mm long, 2 mm in diameter. They occur in freshwater fish, brackish water fish and in marine fish. The larvae normally mature in wading birds such as herons, egrets, and flamingos.

2. Nature of Acute Disease:

If the larvae are consumed in undercooked or raw fish, they can attach to the wall of the digestive tract. In the five cases for which clinical symptoms have been reported, the penetration into the gut wall was accompanied by severe pain. The nematodes can perforate the gut wall and probably other organs. Removal of the nematodes by surgical resection or fiber optic devices with forceps is possible if the nematodes penetrate accessible areas of the gut.

3. Nature of Disease:

One live larva can cause an infection.

4. Diagnosis of Human Illness:

In three of the five reported cases, the worms were diagnosed by surgical resection of the intestine. In one case, there was no clinical data and in one other, the patient was treated medically and recovered in 4 days.

5. Associated Foods: Fish from fresh, brackish or salt water.

6. Relative Frequency of Disease: The disease is extremely rare; there have been only five cases reported in the U.S.

7. Course of Disease and Complications: Septicemia, which is due to the perforated digestive tract.

8. Target Populations: Those consuming whole minnows are at greatest risk. One case was reported from the consumption of sashimi.

9. Food Analysis: These large worms may be seen without magnification in the flesh of fish and are normally very active after death of the fish.

10. Selected Outbreaks: *Literature references can be found at the links below.*

There have been no major outbreaks.

MMWR 31(28):1982 CDC received reports that three fishermen in Baltimore, Maryland, swallowed live minnows and developed severe abdominal pain within 24 hours. Although data are incomplete, infection by larval Eustrongylides spp. is widespread and common in numerous species of freshwater fish. The high rates of infection for minnows (Fundulus spp.) reported here and earlier may indicate a high degree of risk for persons who choose to eat these fish without cooking them first.

Morbidity and Mortality Weekly Reports	**For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.**
11. Education and Background Resources:	*Literature references can be found at the links below.*
Loci index for genome Nematoda (Roundworm family)	Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.
12. Molecular Structural Data:	None currently available.
13. FDA Regulations or Activity:	FDA has no specific regulation or activity regarding these worms; however, as pathogens, no live *Eustrongylides* sp. should be present in fish consumed raw or semiraw.

CDC/MMWR

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Bad Bug Book

Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Acanthamoeba spp., *Naegleria fowleri* and other amobae

CDC/MMWR NIH/PubMed Agricola

1. Name of the Organism: *Acanthamoeba spp.*, *Naegleria fowleri* and other amobae

Members of the two genera named above are the principal examples of protozoa commonly referred to as pathogenic free-living amoebae.

2. Nature of Acute Disease:

Primary amoebic meningoencephalitis (PAM), *Naegleria fowleri* and granulomatious amoebic encephalitis (GAE), acanthamoebic keratitis or acanthamoebic uveitis.

These organisms are ubiquitous in the environment, in soil, water, and air. Infections in humans are rare and are acquired through water entering the nasal passages (usually during swimming) and by inhalation. They are discussed here because the FDA receives inquiries about them.

3. Nature of Disease:

PAM occurs in persons who are generally healthy prior to infection. Central nervous system involvement arises from organisms that penetrate the nasal passages and enter the brain through the cribriform plate. The organisms can multiply in the tissues of the central nervous system and may be isolated from spinal fluid. In untreated

cases death occurs within 1 week of the onset of symptoms. Amphotercin B is effective in the treatment of PAM. At least four patients have recovered when treated with Amphotercin B alone or in combination with micronazole administered both intravenously and intrathecally or intraventrically.

GAE occurs in persons who are immunodeficient in some way; the organisms cause a granulomatous encephalitis that leads to death in several weeks to a year after the appearance of symptoms. The primary infection site is thought to be the lungs, and the organisms in the brain are generally associated with blood vessels, suggesting vascular dissemination. Treatment with sulfamethazine may be effective in controling the amobae.

Prior to 1985 amoebae had been reported isolated from diseased eyes only rarely; cases were associated with trauma to the eye. In 1985-1986, 24 eye cases were reported to CDC and most of these occurred in wearers of contact lenses. It has been demonstrated that many of these infections resulted from the use of home-made saline solutions with the contact lenses. Some of the lenses had been heat treated and others had been chemically disinfected. The failure of the heat treatment was attributed to faulty equipment, since the amoebae are killed by 65°C (149°F) for 30 minutes. The failure of the chemical disinfection resulted from insufficient treatment or rinsing the lenses in contaminated saline after disinfection. The following agents have been used to successfully eliminate the amoebic infection in the eye: ketoconazole , microconazole, and propamidine isothionate; however, penetrating keratoplasty has been necessary to restore useful vision.

4. Diagnosis of Human Illness:

PAM is diagnosed by the presence of amoebae in the spinal fluid. GAE is diagnosed by biopsy of the lesion. Ocular amoebic keratitis may be diagnosed by culturing corneal scrapings on nonnutrient agar overlaid with viable *Escherichia coli*; amoebae from PAM and GAE may be cultured by the same method. Clinical diagnosis by experienced practitioners is based on the characteristic stromal infiltrate.

5. Associated Foods:

Transmission is through water based fluids or the air.

6. Relative Frequency of Disease:

PAM and GAE are rare in occurrence; fewer than 100 cases have been reported in the United States in the 25 years since these diseases were recognized.

7. Course of Disease and Complications: PAM and GAE both lead to death in most cases. Eye infections may lead to blindness.

8. Target Populations: Immunodeficients, especially those infected with HIV, may be at risk for atypical infections. PAM, GAE, and eye infections have occurred in otherwise healthy individuals.

9. Food Analysis: Foods are not analyzed for these amoebae since foods are not implicated in the infection of individuals.

10. Selected Outbreaks: *Literature references can be found at the links below.*

These diseases are known only from isolated cases.

MMWR 35(25):1986

Twenty-four patients with Acanthamoeba keratitis have been reported to CDC from 14 states in the last 9 months. Although onset of illness for some patients dates to as early as 1982, most had onset of illness in 1985 or 1986. In two patients, the infected eye was enucleated; 12 patients underwent corneal transplantation. Twenty (83%) of the patients wore contact lenses. Of these, two wore hard lenses (one hard, the other rigid gas-permeable); four wore extended-wear soft lenses; and 14 wore daily-wear soft lenses. Ten of these 20 patients cleaned their lenses with home-made saline solution prepared by mixing salt tablets with bottled, distilled, nonsterile water; four used commercially available lens-cleaning solutions followed by a tap water rinse; one used commercial bottled saline; and one cleaned lenses with tap water pumped from a private well.

Morbidity and Mortality Weekly Reports

For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.

11. Education and

Background Resources:	*Literature references can be found at the links below.*
Loci index for genome Acanthamoeba	Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.
12. Molecular Structural Data:	None currently available.
13. FDA Regulations or Activity:	Since infection is not known to be by way of the digestive tract, the FDA has no regulations concerning these organisms. Eye infections are indirectly regulated by FDA's Center for Medical Devices and Radiological Health; FDA's Center for Drug Evaluation and Research regulates heat sterilization units and saline solutions for ophthalmological use. FDA has published a paper documenting the presence of amoebae in eye wash stations, and warning about the potential danger of such contamination.

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Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Ascaris lumbricoides and *Trichuris trichiura*

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism:
Ascaris lumbricoides and *Trichuris trichiura*

Humans worldwide are infected with *Ascaris lumbricoides* and *Trichuris trichiura*; the eggs of these roundworms (nematode) are "sticky" and may be carried to the mouth by hands, other body parts, fomites (inanimate objects), or foods.

2. Nature of Acute Disease:

Ascariasis and trichuriasis are the scientific names of these infections. Ascariasis is also known commonly as the "large roundworm" infection and trichuriasis as "whip worm" infection.

3. Nature of Disease:

Infection with one or a few *Ascaris* sp. may be inapparent unless noticed when passed in the feces, or, on occasion, crawling up into the throat and trying to exit through the mouth or nose. Infection with numerous worms may result in a pneumonitis during the migratory phase when larvae that have hatched from the ingested eggs in the lumen of the small intestine penetrate into the tissues and by way of the lymph and blood systems reach the lungs. In the lungs, the larvae break out of the pulmonary capillaries into the air sacs, ascend into the throat and descend to the small intestine again where they grow, becoming as large as 31 X 4 cm. Molting (ecdysis) occurs at various points along this path and, typically for roundworms, the male and female adults in the intestine are 5th-stage nematodes. Vague digestive tract discomfort sometimes accompanies the intestinal

infection, but in small children with more than a few worms there may be intestinal blockage because of the worms' large size. Not all larval or adult worms stay on the path that is optimal for their development; those that wander may locate in diverse sites throughout the body and cause complications. Chemotherapy with anthelmintics is particularly likely to cause the adult worms in the intestinal lumen to wander; a not unusual escape route for them is into the bile duct which they may occlude. The larvae of ascarid species that mature in hosts other than humans may hatch in the human intestine and are especially prone to wander; they may penetrate into tissues and locate in various organ systems of the human body, perhaps eliciting a fever and diverse complications.

Trichuris sp. larvae do not migrate after hatching but molt and mature in the intestine. Adults are not as large as *A. lumbricoides*. Symptoms range from inapparent through vague digestive tract distress to emaciation with dry skin and diarrhea (usually mucoid). Toxic or allergic symptoms may also occur.

4. Diagnosis of Human Illness: Both infections are diagnosed by finding the typical eggs in the patient's feces; on occasion the larval or adult worms are found in the feces or, especially for *Ascaris* sp., in the throat, mouth, or nose.

5. Associated Foods: The eggs of these worms are found in insufficiently treated sewage-fertilizer and in soils where they embryonate (i.e., larvae develop in fertilized eggs). The eggs may contaminate crops grown in soil or fertilized with sewage that has received nonlethal treatment; humans are infected when such produce is consumed raw. Infected foodhandlers may contaminate a wide variety of foods.

6. Relative Frequency of Disease: These infections are cosmopolitan, but ascariasis is more common in North America and trichuriasis in Europe. Relative infection rates on other continents are not available.

7. Course of Disease and Complications: Both infections may self-cure after the larvae have matured into adults or may require anthelmintic treatment. In severe cases, surgical removal may be necessary. Allergic symptoms (especially but not exclusively of the asthmatic sort) are common in long-lasting infections or upon reinfection in ascariasis.

8. Target Populations: Particularly consumers of uncooked vegetables and fruits grown in or near soil fertilized with sewage.

9. Food Analysis: Eggs of *Ascaris* spp. have been detected on fresh vegetables (cabbage) sampled by FDA. Methods for the detection of *Ascaris* spp. and *Trichuris* spp. eggs are detailed in the FDA's Bacteriological Analytical Manual.

10. Selected Outbreaks: *Literature references can be found at the links below.*

Although no major outbreaks have occurred, there are many individual cases. The occurrence of large numbers of eggs in domestic municipal sewage implies that the infection rate, especially with *A. lumbricoides*, is high in the U.S.

Morbidity and Mortality Weekly Reports **For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.**

11. Education and Background Resources: *Literature references can be found at the links below.*

Loci index for genome *Ascaris lumbricoides* *Trichuris trichiura* Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.

12. Molecular Structural Data: None currently available.

13. FDA Regulations or Activity:	Ascarids and trichurids are considered pathogens and foods eaten without further cooking should not be contaminated with viable embryonated eggs of either genus.

CDC/MMWR

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NIH/PubMed

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Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Hepatitis A Virus

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism:
Hepatitis A Virus

Hepatitis A virus (HAV) is classified with the enterovirus group of the Picornaviridae family. HAV has a single molecule of RNA surrounded by a small (27 nm diameter) protein capsid and a buoyant density in CsCl of 1.33 g/ml. Many other picornaviruses cause human disease, including polioviruses, coxsackieviruses, echoviruses, and rhinoviruses (cold viruses).

2. Nature of Acute Disease:

The term hepatitis A (HA) or type A viral hepatitis has replaced all previous designations: infectious hepatitis, epidemic hepatitis, epidemic jaundice, catarrhal jaundice, infectious icterus, Botkins disease, and MS-1 hepatitis.

3. Nature of Disease:

CDC Case Definition

What is a "Case Definition"?

Hepatitis A is usually a mild illness characterized by sudden onset of fever, malaise, nausea, anorexia, and abdominal discomfort, followed in several days by jaundice. The infectious dose is unknown but presumably is 10-100 virus particles.

Overview of Public Health Surveillance

4. Diagnosis of Human Illness:

Hepatitis A is diagnosed by finding IgM-class anti-HAV in serum collected during the acute or early convalescent phase of disease. Commercial kits are available.

5. Associated Foods:

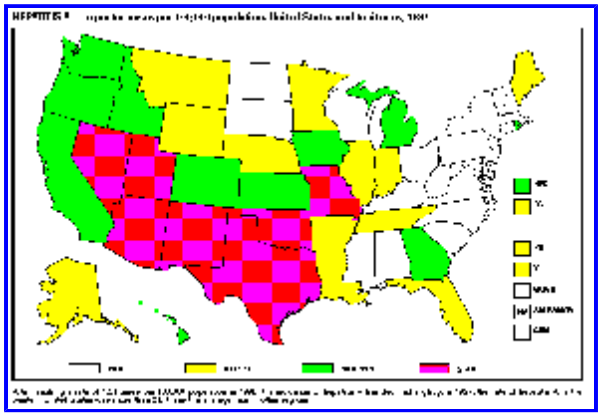
HAV is excreted in feces of infected people and can produce clinical disease when susceptible individuals consume contaminated water or foods. Cold cuts and sandwiches, fruits and fruit juices, milk and milk products, vegetables, salads, shellfish, and iced drinks are commonly implicated in outbreaks. Water, shellfish, and salads are the most frequent sources. Contamination of foods by infected workers in food processing plants and restaurants is common.

6. Relative Frequency of Disease:

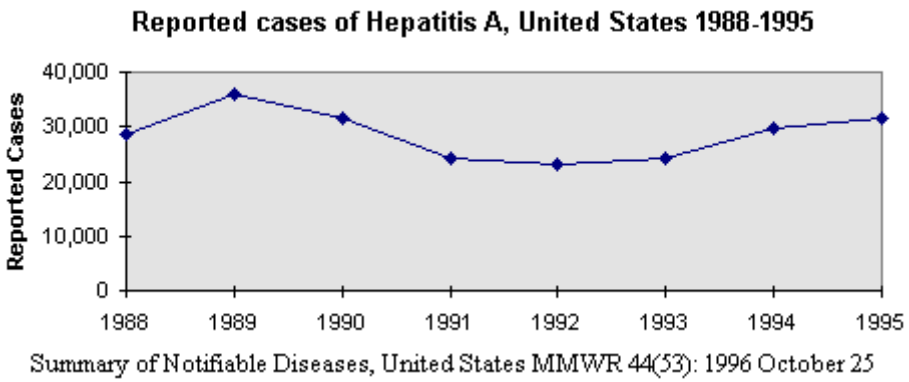
Hepatitis A has a worldwide distribution occurring in both epidemic and sporadic fashions. About 22,700 cases of hepatitis A representing 38% of all hepatitis cases (5-year average from all routes of transmission) are reported annually in the U.S. In 1988 an estimated 7.3% cases were foodborne or waterborne. HAV is primarilly transmitted by person-to-person contact through fecal contamination, but common-source epidemics from contaminated food and water also occur. Poor sanitation and crowding facilitate transmission. Outbreaks of HA are common in institutions, crowded house projects, and prisons and in military forces in adverse situations. In developing countries, the incidence of disease in adults is relatively low because of exposure to the virus in childhood. Most individuals 18 and older demonstrate an immunity that provides lifelong protection against reinfection. In the U.S., the percentage of adults with immunity increases with age (10% for those 18-19 years of age to 65% for those over 50). The increased number of susceptible individuals allows common source epidemics to evolve rapidly.

Reported cases of Hepatitis A, United States
1997

Summary of Notifiable Diseases, United States, 1997:MMWR 46(54)



Summary of Notifiable Diseases, United States, 1996:MMWR 44(53)



7. Course of Disease and Complications:

The incubation period for hepatitis A, which varies from 10 to 50 days (mean 30 days), is dependent upon the number of infectious particles consumed. Infection with very few particles results in longer incubation periods. The period of communicability extends from early in the incubation period to about a week after the development of jaundice. The greatest danger of spreading the disease to others occurs during the middle of the incubation period, well before the first presentation of symptoms. Many infections with HAV do not result in clinical disease, especially in children. When disease does occur, it is usually mild and recovery is complete in 1-2 weeks. Occasionaly, the symptoms are severe and convalescence can take several months. Patients suffer

from feeling chronically tired during convalescence, and their inability to work can cause financial loss. Less than 0.4% of the reported cases in the U.S. are fatal. These rare deaths usually occur in the elderly.

8. Target Populations: All people who ingest the virus and are immunologically unprotected are susceptible to infection. Disease however, is more common in adults than in children.

9. Food Analysis: The virus has not been isolated from any food associated with an outbreak. Because of the long incubation period, the suspected food is often no longer available for analysis. No satisfactory method is presently available for routine analysis of food, but sensitive molecular methods used to detect HAV in water and clinical specimens, should prove useful to detect virus in foods. Among those, the PCR amplification method seems particularly promising.

10. Selected Outbreaks: *Literature references can be found at the links below.*

Hepatitis A is endemic throughout much of the world. Major national epidemics occurred in 1954, 1961 and 1971. Although no major epidemic occurred in the 1980s, the incidence of hepatitis A in the U.S. increased 58% from 1983 to 1989. Foods have been implicated in over 30 outbreaks since 1983. The most recent ones and the suspected contaminated foods include:

- 1987 - Louisville, Kentucky. Suspected source: imported lettuce.
- 1990 - North Georgia. Frozen strawberries. - Montana. Frozen strawberries. - Baltimore. Shellfish.

MMWR 42(27):1993 On November 26, 1990, hepatitis A was diagnosed in an employee of a restaurant in Cass County, Missouri. The employee's duties involved washing pots and pans in the restaurant. From December 7, 1990, through January 9, 1991, hepatitis A was diagnosed in 110 persons, including four waitresses, who had eaten at the restaurant; two persons died as a result of fulminant hepatitis.

MMWR 39(14):1990 From 1983 through 1989, the incidence of hepatitis A in the United States increased 58% (from 9.2 to 14.5

	cases per 100,000 population). Based on analysis of hepatitis A cases reported to CDC's national Viral Hepatitis Surveillance Program in 1988, 7.3% of hepatitis A cases were associated with foodborne or waterborne outbreaks (1). This report summarizes recent foodborne-related outbreaks of hepatitis A in Alaska, Florida, North Carolina, and Washington.
MMWR 32(50):1983	Two unrelated outbreaks of hepatitis A, involving a total of 326 people, occurred in Oklahoma and Texas during September and October 1983. Both were associated with restaurant food. Hepatitis A was defined as: (1) jaundice or (2) serum glutamic oxalacetic transaminase enzyme (SGOT) greater than 100 mIU/ml plus nausea, vomiting, or fever or (3) a positive serum anti-hepatitis A virus (HAV) immunoglobulin (IgM).
MMWR 31(12):1982	An increase in the number of hepatitis cases in Monmouth County, New Jersey, was reported to the New Jersey Department of Health on June 15, 1981. Investigation by state and local area health departments revealed that 56 cases of hepatitis had occurred during the first 3 weeks of June in an area of Monmouth County where the usual average is 3-4 cases/ month. Detailed food histories revealed that, within the appropriate incubation period for hepatitis A, 55 of the 56 patients had eaten at a Mexican style restaurant.
Morbidity and Mortality Weekly Reports	**For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.**

11. Education and Background Resources:	*Literature references can be found at the links below.*
Loci index for genome Hepatitis A	Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.
CDC/Centers for Inectious Diseases Fact File	Important information and statistics about Hepatitis A.

12. Molecular Structural Data:	None currently available.

CDC/MMWR

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Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Hepatitis E Virus

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism:
Hepatitis E Virus

Hepatitis E Virus (HEV) has a particle diameter of 32-34 nm, a buoyant density of 1.29 g/ml in KTar/Gly gradient, and is very labile. Serologically related smaller (27-30 nm) particles are often found in feces of patients with Hepatitis E and are presumed to represent degraded viral particles. HEV has a single-stranded polyadenylated RNA genome of approximately 8 kb. Based on its physicochemical properties it is presumed to be a calici-like virus.

2. Nature of Acute Disease:

The disease caused by HEV is called hepatitis E, or enterically transmitted non-A non-B hepatitis (ET-NANBH). Other names include fecal-oral non-A non-B hepatitis,and A-like non-A non-B hepatitis.

Note: This disease should not be confused with hepatitis C, also called parenterally transmitted non-A non-B hepatitis (PT-NANBH), or B-like non-A non-B hepatitis, which is a common cause of hepatitis in the U.S.

3. Nature of Disease:

CDC Case Definition

Hepatitis caused by HEV is clinically indistinguishable from hepatitis A disease. Symptoms include malaise, anorexia, abdominal pain, arthralgia, and fever. The infective dose is not known.

What is a "Case Definition"?

Overview of Public Health Surveillance

4. Diagnosis of Human Illness: Diagnosis of HEV is based on the epidemiological characteristics of the outbreak and by exclusion of hepatitis A and B viruses by serological tests. Confirmation requires identification of the 27-34 nm virus-like particles by immune electron microscopy in feces of acutely ill patients.

5. Associated Foods: HEV is transmitted by the fecal-oral route. Waterborne and person-to-person spread have been documented. The potential exists for foodborne transmission.

6. Relative Frequency of Disease: Hepatitis E occurs in both epidemic and sporadic-endemic forms, usually associated with contaminated drinking water. Major waterborne epidemics have occurred in Asia and North and East Africa. To date no U.S. outbreaks have been reported.

7. Course of Disease and Complications: The incubation period for hepatitis E varies from 2 to 9 weeks. The disease usually is mild and resolves in 2 weeks, leaving no sequelae. The fatality rate is 0.1-1% except in pregnant women. This group is reported to have a fatality rate approaching 20%.

8. Target Populations: The disease is most often seen in young to middle aged adults (15-40 years old). Pregnant women appear to be exceptionally susceptible to severe disease, and excessive mortality has been reported in this group.

9. Food Analysis: HEV has not been isolated from foods. No method is currently available for routine analysis of foods.

10. Selected Outbreaks: *Literature references can be found at the links below.*

Major waterborne epidemics have occurred in India (1955 and 1975-1976), USSR (1955-1956), Nepal (1973), Burma (1976-1977), Algeria (1980-1981), Ivory Coast (1983-1984), and most recently in Borneo (1987). To date, no outbreak has occurred in the U.S., but imported cases were identified in Los Angeles in 1987. There is no evidence for immunity against this agent in the American population. Thus, unless other factors (such as poor sanitation or prevalence of other enteric pathogens) are important, the potential for spread to the U.S. is great. Good sanitation and personal hygiene are the best preventive measures.

MMWR 36(36):1987 — Two outbreaks of enterically transmitted non-A, non-B (ET-NANB) hepatitis occurred during the late summer and fall of 1986 in rural villages in the State of Morelos, Mexico. This is the first reported instance of epidemic transmission of this disease in the Americas.

MMWR 36(16):1987 — Outbreaks of enterically transmitted non-A, non-B hepatitis occurred in 1985 and 1986 at refugee camps for Ethiopians in Somalia and the Sudan.

Morbidity and Mortality Weekly Reports — **For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.**

11. Education and Background Resources: *Literature references can be found at the links below.*

Loci index for genome Hepatitis E — Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.

12. Molecular None currently available.

Structural Data:

CDC/MMWR

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Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Rotavirus

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism:
Rotavirus

Rotaviruses are classified with the Reoviridae family. They have a genome consisting of 11 double-stranded RNA segments surrounded by a distinctive two-layered protein capsid. Particles are 70 nm in diameter and have a buoyant density of 1.36 g/ml in CsCl. Six serological groups have been identified, three of which (groups A, B, and C) infect humans.

2. Nature of Acute Disease:

Rotaviruses cause acute gastroenteritis. Infantile diarrhea, winter diarrhea, acute nonbacterial infectious gastroenteritis, and acute viral gastroenteritis are names applied to the infection caused by the most common and widespread group A rotavirus.

3. Nature of Disease:

Rotavirus gastroenteritis is a self-limiting, mild to severe disease characterized by vomiting, watery diarrhea, and low-grade fever. The infective dose is presumed to be 10-100 infectious viral particles. Because a person with rotavirus diarrhea often excretes large numbers of virus (108-1010 infectious particles/ml of feces), infection doses can be readily acquired through contaminated hands, objects, or utensils. Asymptomatic rotavirus excretion has been well documented and may play a role in perpetuating endemic disease.

4. Diagnosis of Human Illness:

Specific diagnosis of the disease is made by identification of the virus in the patient's stool. Enzyme immunoassay (EIA) is the test most widely used to screen clinical specimens, and several commercial kits are available for group A rotavirus. Electron microscopy (EM) and polyacrylamide gel electrophoresis (PAGE) are used in some laboratories in addition or as an alternative to EIA. A reverse transcription-polymerase chain reaction (RT-PCR) has been developed to detect and identify all three groups of human rotaviruses.

5. Associated Foods:

Rotaviruses are transmitted by the fecal-oral route. Person-to-person spread through contaminated hands is probably the most important means by which rotaviruses are transmitted in close communities such as pediatric and geriatric wards, day care centers and family homes. Infected food handlers may contaminate foods that require handling and no further cooking, such as salads, fruits, and hors d'oeuvres. Rotaviruses are quite stable in the environment and have been found in estuary samples at levels as high as 1-5 infectious particles/gal. Sanitary measures adequate for bacteria and parasites seem to be ineffective in endemic control of rotavirus, as similar incidence of rotavirus infection is observed in countries with both high and low health standards.

6. Relative Frequency of Disease:

Group A rotavirus is endemic worldwide. It is the leading cause of severe diarrhea among infants and children, and accounts for about half of the cases requiring hospitalization. Over 3 million cases of rotavirus gastroenteritis occur annually in the U.S. In temperate areas, it occurs primarily in the winter, but in the tropics it occurs throughout the year. The number attributable to food contamination is unknown.

Group B rotavirus, also called adult diarrhea rotavirus or ADRV, has caused major epidemics of severe diarrhea affecting thousands of persons of all ages in China.

Group C rotavirus has been associated with rare and sporadic cases of diarrhea in children in many countries. However, the first outbreaks were reported from Japan and England.

7. Course of Disease and Complications:

The incubation period ranges from 1-3 days. Symptoms often start with vomiting followed by 4-8 days of diarrhea. Temporary lactose intolerance may occur. Recovery is usually complete. However, severe diarrhea without fluid and electrolyte replacement may result in severe diarrhea and death. Childhood mortality caused by rotavirus is relatively low in the U.S., with an estimated 100 cases/year, but reaches almost 1 million

cases/year worldwide. Association with other enteric pathogens may play a role in the severity of the disease.

8. Target Populations: Humans of all ages are susceptible to rotavirus infection. Children 6 months to 2 years of age, premature infants, the elderly, and the immunocompromised are particularly prone to more severe symptoms caused by infection with group A rotavirus.

9. Food Analysis: The virus has not been isolated from any food associated with an outbreak, and no satisfactory method is available for routine analysis of food. However, it should be possible to apply procedures that have been used to detect the virus in water and in clinical specimens, such as enzyme immunoassays, gene probing, and PCR amplification to food analysis.

10. Selected Outbreaks: *Literature references can be found at the links below.*

MMWR 48(27):1999

On August 31, 1998, a tetravalent rhesus-based rotavirus vaccine (RotaShield[Registered]*, Wyeth Laboratories, Inc., Marietta, Pennsylvania) (RRV-TV) was licensed in the United States for vaccination of infants. The Advisory Committee on Immunization Practices (ACIP), the American Academy of Pediatrics, and the American Academy of Family Physicians have recommended routine use of RRV-TV for vaccination of healthy infants (1,2). During September 1, 1998-July 7, 1999, 15 cases of intussusception (a bowel obstruction in which one segment of bowel becomes enfolded within another segment) among infants who had received RRV-TV were reported to the Vaccine Adverse Event Reporting System (VAERS).

Outbreaks of group A rotavirus diarrhea are common among hospitalized infants, young children attending day care centers, and elder persons in nursing homes. Among adults, multiple foods served in banquets were implicated in 2 outbreaks. An outbreak due to contaminated municipal water occurred in Colorado, 1981.

Several large outbreaks of group B rotavirus involving millions of persons as a result of sewage contamination of drinking water supplies have occurred in China since 1982. Although to date outbreaks caused by group B rotavirus have been confined to mainland China, seroepidemiological surveys have indicated lack of immunity to this group of virus in the U.S.

The newly recognized group C rotavirus has been implicated in rare and isolated cases of gastroenteritis. However, it was associated with three outbreaks among school children: one in Japan, 1989, and two in England, 1990.

MMWR 47(45):1998	In August 1998, the first live attenuated rotavirus vaccine (Rotashield{registered} {Wyeth Lederle Vaccines and Pediatrics}) was approved for use in infants by the Food and Drug Administration. The Advisory Committee on Immunization Practices has recommended that this vaccine be given as a three-dose schedule to infants aged 2, 4, and 6 months. Since 1991, rotavirus activity in the United States has been prospectively monitored by the National Respiratory and Enteric Virus Surveillance System (NREVSS), a voluntary, laboratory-based system. This report summarizes surveillance data from NREVSS during the 1997-1998 rotavirus season and reviews issues related to rotavirus surveillance that are important for a national rotavirus vaccine program.
MMWR 47(19):1998	On June 24, 1996, the Livingston County (New York) Department of Health (LCDOH) was notified of a cluster of diarrheal illness following a party on June 22, at which approximately 30 persons had become ill. This report summarizes the findings of the investigation, which implicated a deficient water supply system as the cause of an outbreak of diarrheal illness caused by Salmonella serotype Hartford and P. shigelloides. Unfiltered, untreated surface water led to contamination of food during its preparation.
MMWR 40(5)1991	A discussion of rotavirus surveillance in the US.
Morbidity and Mortality Weekly Reports	**For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.**

11. Education and Background Resources:

Literature references can be found at the links below.

"ABC's of Rotavirus Diarrhea in the Child Care Setting"	Rotavirus is one type of virus that causes diarrhea, especially in young children. It is a common cause of infection is a common cause of diarrhea in the child care setting. Rotavirus infection usually occurs during the winter months. Some children have no symptoms of rotavirus infection while others may have severe vomiting , watery diarrhea, and fever. In some instances, there may also be a cough or runny nose.

Viral Gastroenteritis FAQ's	Center for Disease Control and Prevention of Food Illness Fact Sheet
Loci index for genome Rotavirus sp.	Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.
12. Molecular Structural Data:	None currently available.

CDC/MMWR

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Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

The Norwalk virus family

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism:
The Norwalk virus family

Norwalk virus is the prototype of a family of unclassified small round structured viruses (SRSVs) which may be related to the caliciviruses. They contain a positive strand RNA genome of 7.5 kb and a single structural protein of about 60 kDa. The 27-32 nm viral particles have a buoyant density of 1.39-1.40 g/ml in CsCl. The family consists of several serologically distinct groups of viruses that have been named after the places where the outbreaks occurred. In the U.S., the Norwalk and Montgomery County agents are serologically related but distinct from the Hawaii and Snow Mountain agents. The Taunton, Moorcroft, Barnett, and Amulree agents were identified in the U.K., and the Sapporo and Otofuke agents in Japan. Their serological relationships remain to be determined.

2. Nature of Acute Disease:

Common names of the illness caused by the Norwalk and Norwalk-like viruses are viral gastroenteritis, acute nonbacterial gastroenteritis, food poisoning, and food infection.

3. Nature of Disease:

The disease is self-limiting, mild, and characterized by nausea, vomiting, diarrhea, and abdominal pain. Headache and low-grade fever may occur. The infectious dose is unknown but presumed to be low.

4. Diagnosis of Human Illness:

Specific diagnosis of the disease can only be made by a few laboratories possessing reagents from human volunteer studies. Identification of the virus can be made on early stool specimens using immune electron microscopy and various immunoassays. Confirmation often requires demonstration of seroconversion, the presence of specific IgM antibody, or a four-fold rise in antibody titer to Norwalk virus on paired acute-convalescent sera.

5. Associated Foods:

Norwalk gastroenteritis is transmitted by the fecal-oral route via contaminated water and foods. Secondary person-to-person transmission has been documented. Water is the most common source of outbreaks and may include water from municipal supplies, well, recreational lakes, swiming pools, and water stored aboard cruise ships.

Shellfish and salad ingredients are the foods most often implicated in Norwalk outbreaks. Ingestion of raw or insufficiently steamed clams and oysters poses a high risk for infection with Norwalk virus. Foods other than shellfish are contaminated by ill food handlers.

6. Relative Frequency of Disease:

Only the common cold is reported more frequently than viral gastroenteritis as a cause of illness in the U.S. Although viral gastroenteritis is caused by a number of viruses, it is estimated that Norwalk viruses are responsible for about 1/3 of the cases not involving the 6-to-24-month age group. In developing countries the percentage of individuals who have developed immunity is very high at an early age. In the U.S. the percentage increases gradually with age, reaching 50% in the population over 18 years of age. Immunity, however, is not permanent and reinfection can occur.

7. Course of Disease and Complications:

A mild and brief illness usually develops 24-48 h after contaminated food or water is consumed and lasts for 24-60 hours. Severe illness or hospitalization is very rare.

8. Target Populations:

All individuals who ingest the virus and who have not (within 24 months) had an infection with the same or related strain, are susceptible to infection and can develop the symptoms of gastroenteritis. Disease is more

frequent in adults and older children than in the very young.

9. Food Analysis: The virus has been identified in clams and oysters by radioimmunoassay. The genome of Norwalk virus has been cloned and development of gene probes and PCR amplification techniques to detect the virus in clinical specimens and possibly in food are under way.

10. Selected Outbreaks: *Literature references can be found at the links below.*

MMWR 48(11):1999 During August 27-September 1, 1998, 99 (12%) of 835 soldiers in one unit at a U.S. Army training center in El Paso, Texas, were hospitalized for acute gastroenteritis (AGE). Their symptoms included acute onset of vomiting, abdominal pain, diarrhea, and fever. Review of medical center admission records for AGE during the previous year indicated that fewer than five cases occurred each month.

MMWR 44(2):1995 A report on the multistate outbreak of viral gastroenteritis associated with consumption of oysters from Apalachicola Bay, Florida, December 1994-January 1995.

MMWR 43(24):1994 During November 20-30, 1993, four county public health units (CPHUs) of the Florida Department of Health and Rehabilitative Services (HRS) in northwestern Florida conducted preliminary investigations of seven separate outbreaks of foodborne illness following consumption of raw oysters. On December 1, the HRS State Health Office initiated an investigation to characterize the illness, examine risk factors for oyster-associated gastroenteritis, and quantify the dose-response relation. In four specimens, small round-structured viruses were detected by EM; in one specimen, a Norwalk-like genome was confirmed by RT-PCR.

MMWR 42(49):1993 On November 17, 1993, the state health departments of Louisiana, Maryland, and Mississippi notified CDC of several outbreaks of gastroenteritis occurring in their states since November 12. Preliminary epidemiologic investigations identified consumption of oysters as the primary risk factor for illness. On November 16, the Louisiana Department of Health and Hospitals (LDHH) had identified the Grand Pass and Cabbage Reef harvesting areas off the Louisiana coast as the source of oysters associated with outbreaks in Louisiana and Mississippi. Tagged oysters associated with outbreaks in Maryland were traced to the same oyster beds. Small round structured viruses or Norwalk-like viruses were detected by EM and confirmed by RT-PCR in 13 of 26

stool specimens from ill persons in Louisiana, Maryland, Mississippi, and North Carolina.

MMWR 37(5):1988

An outbreak of diarrhea occurred among the 331 participants in an outing held at a South Dakota campground on August 30 and 31, 1986. A biotin-avidin immunoassay performed at CDC yielded a fourfold rise in antibody titer to Norwalk virus in seven of 11 paired human serum specimens. No pathogenic bacterial or parasitic agents were identified from stool samples. Illness was strongly associated with the consumption of water or the reconstituted powdered soft drink made with water.

Snow Mountain virus was implicated in an outbreak in a retirement community in California (1988) which resulted in two deaths. Illness was associated with consumption of shrimp probably contaminated by food handlers.

Preliminary evidence suggests that large outbreaks of gastroenteritis which occurred in Pennsylvania and Delaware in September, 1987, were caused by Norwalk virus. The source of both outbreaks was traced to ice made with water from a contaminated well. In Pennsylvania, the ice was consumed at a football game, and in Delaware, at a cocktail party. Norwalk virus is also suspected to have caused an outbreak aboard a cruise ship in Hawaii in 1990. Fresh fruits were the probable vehicle of contamination.

MMWR 35(23):1986

Three outbreaks of gastroenteritis occurred on two Caribbean cruise ships between April 26, and May 10, 1986. More than 1,200 persons developed gastrointestinal illness; no deaths were reported. At least one of the outbreaks appears to be associated with Norwalk virus. An outbreak of gastroenteritis caused by the Norwalk virus recently occurred in Tate, a rural community in north Georgia. An investigation implicated the community water system as the source of infection---see MMWR 31(30):1982 Aug 06

Foodborne outbreaks of gastroenteritis caused by Norwalk virus are often related to consumption of raw shellfish. Frequent and widespread outbreaks, reaching epidemic proportions, occurred in Australia (1978) and in the state of New York (1982) among consumers of raw clams and oysters. From 1983 to 1987, ten well documented outbreaks caused by Norwalk virus were reported in the U.S., involving a variety of foods: fruits, salads, eggs, clams, and bakery items.

Morbidity and Mortality Weekly Reports

For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.

11. Other Resources:	*Literature references can be found at the links below.*
Viral Gastroenteritis FAQ's	Center for Disease Control and Prevention of Food Illness Fact Sheet
Loci index for genome Norwalk virus	Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.
12. Molecular Structural Data:	None currently available.

CDC/MMWR

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Other Gastroenteritis Viruses

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism:
Other viruses associated with gastroenteritis

Although the rotavirus and the Norwalk family of viruses are the leading causes of viral gastroenteritis, a number of other viruses have been implicated in outbreaks, including astroviruses, caliciviruses, enteric adenoviruses and parvovirus. Astroviruses, caliciviruses, and the Norwalk family of viruses possess well-defined surface structures and are sometimes identified as "small round structured viruses" or SRSVs. Viruses with smooth edge and no discernible surface structure are designated "featureless viruses" or "small round viruses" (SRVs). These agents resemble enterovirus or parvovirus, and may be related to them.

Astroviruses are unclassified viruses which contain a single positive strand of RNA of about 7.5 kb surrounded by a protein capsid of 28-30 nm diameter. A five or six pointed star shape can be observed on the particles under the electron microscope. Mature virions contain two major coat proteins of about 33 kDa each and have a buoyant density in CsCl of 1.38 - 1.40 g/ml. At least five human serotypes have been identified in England. The Marin County agent found in the U.S. is serologically related to astrovirus type 5.

Caliciviruses are classified in the family Caliciviridae. They contain a single strand of RNA surrounded by a protein capsid of 31-40 nm diameter. Mature virions have cup-shaped indentations which give them a 'Star of David' appearance in the electron microscope. The particle contain a single major coat protein of 60 kDa and have a buoyant density in CsCl of 1.36 - 1.39 g/ml. Four serotypes have been identified in England.

Enteric adenoviruses represent serotypes 40 and 41 of the family Adenoviridae. These viruses contain a double-stranded DNA surrounded by a distinctive protein capsid of about 70 nm diameter. Mature virions have a

buoyant density in CsCl of about 1.345 g/ml.

Parvoviruses belong to the family Parvoviridae, the only group of animal viruses to contain linear single-stranded DNA. The DNA genome is surrounded by a protein capsid of about 22 nm diameter. The buoyant density of the particle in CsCl is 1.39-1.42 g/ml. The Ditchling, Wollan, Paramatta, and cockle agents are candidate parvoviruses associated with human gastroenteritis.

2. Nature of Acute Disease: Common names of the illness caused by these viruses are acute nonbacterial infectious gastroenteritis and viral gastroenteritis.

3. Nature of Disease: Viral gastroenteritis is usually a mild illness characterized by nausea, vomiting, diarrhea, malaise, abdominal pain, headache, and fever. The infectious dose is not known but is presumed to be low.

4. Diagnosis of Human Illness: Specific diagnosis of the disease can be made by some laboratories possessing appropriate reagents. Identification of the virus present in early acute stool samples is made by immune electron microscopy and various enzyme immunoassays. Confirmation often requires demonstration of seroconversion to the agent by serological tests on acute and convalescent serum pairs.

5. Associated Foods: Viral gastroenteritis is transmitted by the fecal-oral route via person-to-person contact or ingestion of contaminated foods and water. Ill food handlers may contaminate foods that are not further cooked before consumption. Enteric adenovirus may also be transmitted by the respiratory route. Shellfish have been implicated in illness caused by a parvo-like virus.

6. Relative Frequency of Disease: Astroviruses cause sporadic gastroenteritis in children under 4 years of age and account for about 4% of the cases hospitalized for diarrhea. Most American and British children over 10 years of age have antibodies to the virus.

Caliciviruses infect children between 6 and 24 months of age and account for about 3% of hospital admissions for diarrhea. By 6 years of age, more than 90% of all children have developed immunity to the illness.

The enteric adenovirus causes 5-20% of the gastroenteritis in young children, and is the second most common cause of gastroenteritis in this age group. By 4 years of age, 85% of all children have developed immunity to the disease. Parvo-like viruses have been implicated in a number of shellfish-associated outbreaks, but the frequency of disease is unknown.

7. Course of Disease and Complications:

A mild, self limiting illness usually develops 10 to 70 hours after contaminated food or water is consumed and lasts for 2 to 9 days. The clinical features are milder but otherwise indistinguishable from rotavirus gastroenteritis. Co-infections with other enteric agents may result in more severe illness lasting a longer period of time.

8. Target Populations:

The target populations for astro and caliciviruses are young children and the elderly. Only young children seem to develop illness caused by the enteric adenoviruses. Infection with these viruses is widespread and seems to result in development of immunity. Parvoviruses infect all age groups and probably do not ilicit a permanent immunity.

9. Food Analysis:

Only a parvovirus-like agent (cockle) has been isolated from seafood associated with an outbreak. Although foods are not routinely analyzed for these viruses, it may be possible to apply current immunological procedures to detect viruses in clinical specimens. Gene probes and PCR detection methods are currently being developed.

10. Selected Outbreaks:

Outbreaks of astrovirus and calicivirus occur mainly in child care settings and nursing homes. In the past decade, 7 outbreaks of calicivirus and 4 of astrovirus have been reported from England and Japan. In California, an outbreak caused by an astrovirus, the Marin County agent, occurred among elderly patients in a convalescent hospital. No typical calicivirus has been implicated in outbreaks in the U.S. However, if Norwalk and Norwalk-like viruses prove to be caliciviruses, they would account for most food and waterborne outbreaks of

gastroenteritis in this country.

MMWR 46(47):1997	Viral gastroenteritis outbreaks caused by caliciviruses (i.e., Norwalk-like viruses or small round-structured viruses) have been associated with eating contaminated shellfish, particularly oysters (Crassostrea virginica). This report describes the findings of the investigation of an outbreak of oyster-associated viral gastroenteritis in Louisiana during the 1996-97 winter season and implicates sewage from oyster harvesting vessels as the probable cause of contaminated oysters.
	Outbreaks of adenovirus have been reported in England and Japan, all involving children in hospitals or day care centers.
	The small featureless, parvo-like viruses caused outbreaks of gastroenteritis in primary and secondary schools in England (Ditchling and Wollan) and Australia (Paramatta). The cockle agent caused a large community-wide outbreak in England (1977) associated with consumption of contaminated seafood. Parvo-like viruses were also implicated in several outbreaks which occurred in the States of New York and Louisiana in 1982-1983.
Morbidity and Mortality Weekly Reports	**For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.**

11. Education and Background Resources:	*Literature references can be found at the links below.*
Loci index for genome astrovirus calicivirus enteric adenovirus parvovirus	Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.
Viral Gastroenteritis FAQ's	Center for Disease Control and Prevention of Food Illness Fact Sheet

12. Molecular Structural Data: None currently available.

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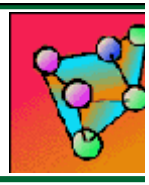

Ciguatera

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism:

Ciguatera

2. Nature of Acute Disease:

Ciguatera Fish Poisoning

Ciguatera is a form of human poisoning caused by the consumption of subtropical and tropical marine finfish which have accumulated naturally occurring toxins through their diet. The toxins are known to originate from several dinoflagellate (algae) species that are common to ciguatera endemic regions in the lower latitudes.

3. Nature of Disease:

Manifestations of ciguatera in humans usually involves a combination of gastrointestinal, neurological, and cardiovascular disorders. Symptoms defined within these general categories vary with the geographic origin of toxic fish.

4. Diagnosis of Human

Clinical testing procedures are not presently available for the diagnosis of ciguatera in humans. Diagnosis is

Illness: based entirely on symptomology and recent dietary history. An enzyme immunoassay (EIA) designed to detect toxic fish in field situations is under evaluation by the Association of Official Analytical Chemists (AOAC) and may provide some measure of protection to the public in the future.

5. Associated Foods: Marine finfish most commonly implicated in ciguatera fish poisoning include the groupers, barracudas, snappers, jacks, mackerel, and triggerfish. Many other species of warm-water fishes harbor ciguatera toxins. The occurrence of toxic fish is sporadic, and not all fish of a given species or from a given locality will be toxic.

6. Relative Frequency of Disease: The relative frequency of ciguatera fish poisoning in the United States is not known. The disease has only recently become known to the general medical community, and there is a concern that incidence is largely under-reported because of the generally non-fatal nature and short duration of the disease.

7. Course of Disease and Complications: Initial signs of poisoning occur within six hours after consumption of toxic fish and include perioral numbness and tingling (paresthesia), which may spread to the extremities, nausea, vomiting, and diarrhea. Neurological signs include intensified paresthesia, arthralgia, myalgia, headache, temperature sensory reversal and acute sensitivity to temperature extremes, vertigo, and muscular weakness to the point of prostration. Cardiovascular signs include arrhythmia, bradycardia or tachycardia, and reduced blood pressure. Ciguatera poisoning is usually self-limiting, and signs of poisoning often subside within several days from onset. However, in severe cases the neurological symptoms are known to persist from weeks to months. In a few isolated cases neurological symptoms have persisted for several years, and in other cases recovered patients have experienced recurrence of neurological symptoms months to years after recovery. Such relapses are most often associated with changes in dietary habits or with consumption of alcohol. There is a low incidence of death resulting from respiratory and cardiovascular failure.

8. Target Populations: All humans are believed to be susceptible to ciguatera toxins. Populations in tropical/subtropical regions are most likely to be affected because of the frequency of exposure to toxic fishes. However, the increasing per capita consumption of fishery products coupled with an increase in interregional transportation of seafood

products has expanded the geographic range of human poisonings.

9. Food Analysis:

The ciguatera toxins can be recovered from toxic fish through tedious extraction and purification procedures. The mouse bioassay is a generally accepted method of establishing toxicity of suspect fish. A much simplified EIA method intended to supplant the mouse bioassay for identifying ciguatera toxins is under evaluation.

10. Selected Outbreaks:

Literature references can be found at the links below.

MMWR 47(33):1998

This report summarizes an investigation of this outbreak by the Texas Department of Health (TDH), which indicated that 17 crew members experienced ciguatera fish poisoning resulting from eating a contaminated barracuda.

MMWR 42(21):1993

Twenty cases of ciguatera fish poisoning from consumption of amberjack were reported to the Florida Department of Health and Rehabilitative Services (HRS) in August and September 1991. This report summarizes the investigation of these cases by the Florida HRS.

MMWR 35(16):1986

On October 29, 1985, the Epidemiology Division, Vermont Department of Health, learned of two persons with symptoms consistent with ciguatera fish poisoning. Both had eaten barracuda at a local restaurant on October 19.

MMWR 31(28):1982

On March 6, 1982, the U.S. Coast Guard in Miami, Florida, received a request for medical assistance from an Italian freighter located in waters off Freeport, Bahamas. Numerous crew members were ill with nausea, vomiting, and muscle weakness and required medical evacuation for hospitalization and treatment. There findings were consistent with ciguatera fish poisoning.

Morbidity and Mortality Weekly Reports

For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.

11. Education and

Literature references can be found at the links below.

Background Resources:

Loci index for genome	Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.

12. Molecular Structural Data:

This structure was created by Fred Fry, Ph.D, CFSAN.

Ciguatoxin

CDC/MMWR

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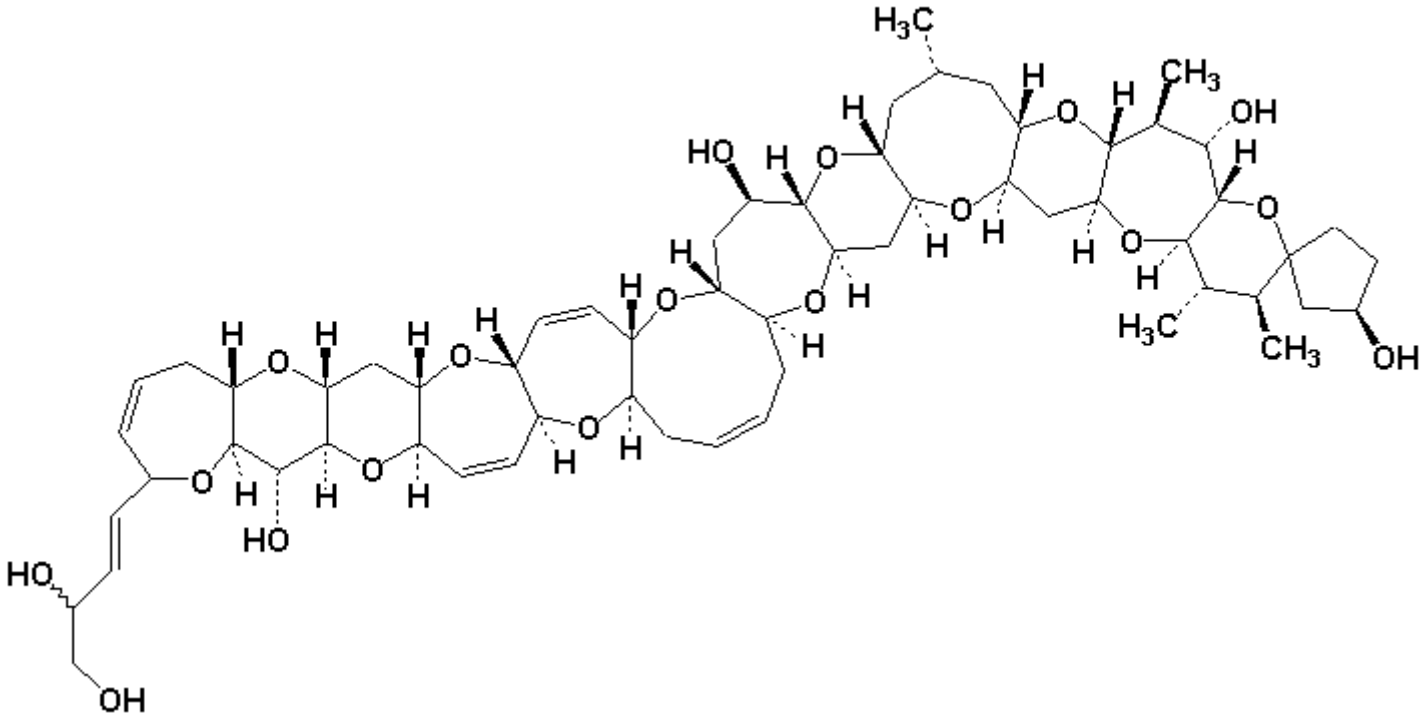
Ciguatera

Ciguatoxin (CTx-1)

Toxin produced by the Dinoflagellate *Gambierdiscus toxicus* and isolated from the flesh and viscera of ciguatoxic fish.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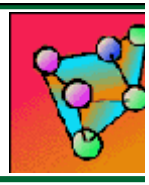

Various Shellfish-Associated Toxins

CDC/MMWR NIH/PubMed

1. Name of the Organism:
Various Shellfish-Associated

Shellfish poisoning is caused by a group of toxins elaborated by planktonic algae (dinoflagellates, in most cases) upon which the shellfish feed. The toxins are accumulated and sometimes metabolized by the shellfish. The 20 toxins responsible for paralytic shellfish poisonings (PSP) are all derivatives of saxitoxin. Diarrheic shellfish poisoning (DSP) is presumably caused by a group of high molecular weight polyethers, including okadaic acid, the dinophysis toxins, the pectenotoxins, and yessotoxin. Neurotoxic shellfish poisoning (NSP) is the result of exposure to a group of polyethers called brevetoxins. Amnesic shellfish poisoning (ASP) is caused by the unusual amino acid, domoic acid, as the contaminant of shellfish.

2. Nature of Acute Disease:

Types of Shellfish Poisoning.

Agricola — Paralytic Shellfish Poisoning (PSP)

Agricola — Diarrheic Shellfish Poisoning (DSP)

Agricola — Neurotoxic Shellfish Poisoning (NSP)

Agricola — Amnesic Shellfish Poisoning (ASP)

3. Nature of Disease: Ingestion of contaminated shellfish results in a wide variety of symptoms, depending upon the toxins(s) present, their concentrations in the shellfish and the amount of contaminated shellfish consumed. In the case of PSP, the effects are predominantly neurological and include tingling, burning, numbness, drowsiness, incoherent speech, and respiratory paralysis. Less well characterized are the symptoms associated with DSP, NSP, and ASP. DSP is primarily observed as a generally mild gastrointestinal disorder, i.e., nausea, vomiting, diarrhea, and abdominal pain accompanied by chills, headache, and fever. Both gastrointestinal and neurological symptoms characterize NSP, including tingling and numbness of lips, tongue, and throat, muscular aches, dizziness, reversal of the sensations of hot and cold, diarrhea, and vomiting. ASP is characterized by gastrointestinal disorders (vomiting, diarrhea, abdominal pain) and neurological problems (confusion, memory loss, disorientation, seizure, coma).

4. Diagnosis of Human Illness: Diagnosis of shellfish poisoning is based entirely on observed symptomatology and recent dietary history.

5. Associated Foods: All shellfish (filter-feeding molluscs) are potentially toxic. However, PSP is generally associated with mussels, clams, cockles, and scallops; NSP with shellfish harvested along the Florida coast and the Gulf of Mexico; DSP with mussels, oysters, and scallops, and ASP with mussels.

6. Relative Frequency of Disease: Good statistical data on the occurrence and severity of shellfish poisoning are largely unavailable, which undoubtedly reflects the inability to measure the true incidence of the disease. Cases are frequently misdiagnosed and, in general, infrequently reported. Of these toxicoses, the most serious from a public health perspective appears to be PSP. The extreme potency of the PSP toxins has, in the past, resulted in an unusually high mortality rate.

7. Course of Disease and Complications: PSP: Symptoms of the disease develop fairly rapidly, within 0.5 to 2 hours after ingestion of the shellfish, depending on the amount of toxin consumed. In severe cases respiratory paralysis is common, and death may

occur if respiratory support is not provided. When such support is applied within 12 hours of exposure, recovery usually is complete, with no lasting side effects. In unusual cases, because of the weak hypotensive action of the toxin, death may occur from cardiovascular collapse despite respiratory support.

NSP: Onset of this disease occurs within a few minutes to a few hours; duration is fairly short, from a few hours to several days. Recovery is complete with few after effects; no fatalities have been reported.

DSP: Onset of the disease, depending on the dose of toxin ingested, may be as little as 30 minutes to 2 to 3 hours, with symptoms of the illness lasting as long as 2 to 3 days. Recovery is complete with no after effects; the disease is generally not life threatening.

ASP: The toxicosis is characterized by the onset of gastrointestinal symptoms within 24 hours; neurological symptoms occur within 48 hours. The toxicosis is particularly serious in elderly patients, and includes symptoms reminiscent of Alzheimer's disease. All fatalities to date have involved elderly patients.

8. Target Populations: All humans are susceptible to shellfish poisoning. Elderly people are apparently predisposed to the severe neurological effects of the ASP toxin. A disproportionate number of PSP cases occur among tourists or others who are not native to the location where the toxic shellfish are harvested. This may be due to disregard for either official quarantines or traditions of safe consumption, both of which tend to protect the local population.

9. Food Analysis: The mouse bioassay has historically been the most universally applied technique for examining shellfish (especially for PSP); other bioassay procedures have been developed but not generally applied. Unfortunately, the dose-survival times for the DSP toxins in the mouse assay fluctuate considerably and fatty acids interfere with the assay, giving false-positive results; consequently, a suckling mouse assay that has been developed and used for control of DSP measures fluid accumulation after injection of the shellfish extract. In recent years considerable effort has been applied to development of chemical assays to replace these bioassays. As a result a good high performance liquid chromatography (HPLC) procedure has been developed to identify individual PSP toxins (detection limit for saxitoxin = 20 fg/100 g of meats; 0.2 ppm), an excellent HPLC procedure (detection limit for okadaic acid = 400 ng/g; 0.4 ppm), a commercially available immunoassay (detection limit for okadaic acid = 1 fg/100 g of meats; 0.01 ppm) for DSP and a totally satisfactory HPLC procedure for ASP (detection limit for domoic acid = 750 ng/g; 0.75 ppm).

10. Selected Outbreaks:

Literature references can be found at the links below.

MMWR 40(10):1991 and Errata Notice MMWR 40(14):1991

Paralytic shellfish poisoning (PSP) is a foodborne illness caused by consumption of shellfish or broth from cooked shellfish that contain either concentrated saxitoxin, an alkaloid neurotoxin, or related compounds. This report summarizes outbreaks of PSP that occurred in Massachusetts and Alaska in June 1990.

PSP is associated with relatively few outbreaks, most likely because of the strong control programs in the United States that prevent human exposure to toxic shellfish. That PSP can be a serious public health problem, however, was demonstrated in Guatemala, where an outbreak of 187 cases with 26 deaths, recorded in 1987, resulted from ingestion of a clam soup. The outbreak led to the establishment of a control program over shellfish harvested in Guatemala.

ASP first came to the attention of public health authorities in 1987 when 156 cases of acute intoxication occurred as a result of ingestion of cultured blue mussels (Mytilus edulis) harvested off Prince Edward Island, in eastern Canada; 22 individuals were hospitalized and three elderly patients eventually died.

The occurrence of DSP in Europe is sporadic, continuous and presumably widespread (anecdotal). DSP poisoning has not been confirmed in U.S. seafood, but the organisms that produce DSP are present in U.S. waters. An outbreak of DSP was recently confirmed in Eastern Canada. Outbreaks of NSP are sporadic and continuous along the Gulf coast of Florida and were recently reported in North Carolina and Texas.

Morbidity and Mortality Weekly Reports

For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.

11. Education and Background Resources:

Literature references can be found at the links below.

Loci index for genome Gonyaulax spp.

Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.

12. Molecular Structural Data: These structures were created by Fred Fry, Ph.D, CFSAN.

Dinophysis Toxin

Brevetoxin

Saxitoxin

Okadaic Acid

Domoic

Yessotoxin

Pectenotoxin

CDC/MMWR

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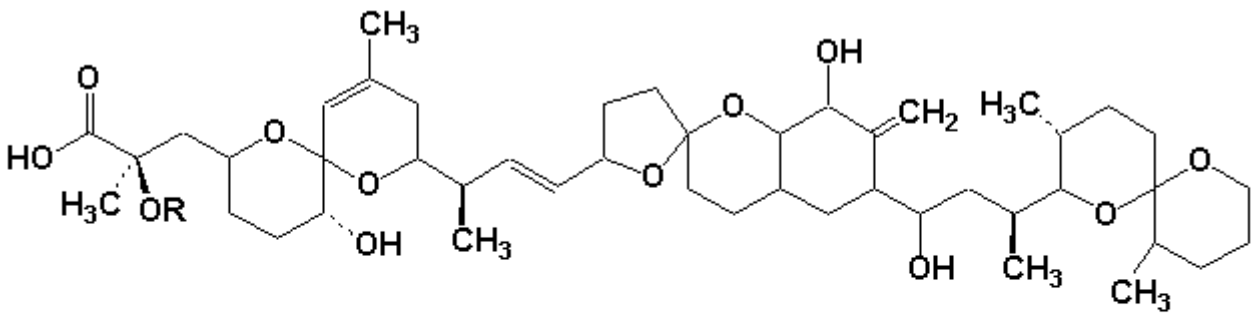
Various Shellfish-Associated Toxins

Dinophysis Toxin

Toxin produced or elaborated by planktonic algae (dinoflagellates, in most cases) upon which the shellfish feed.



DTX	R
DTX1	H
DTX3	Ac

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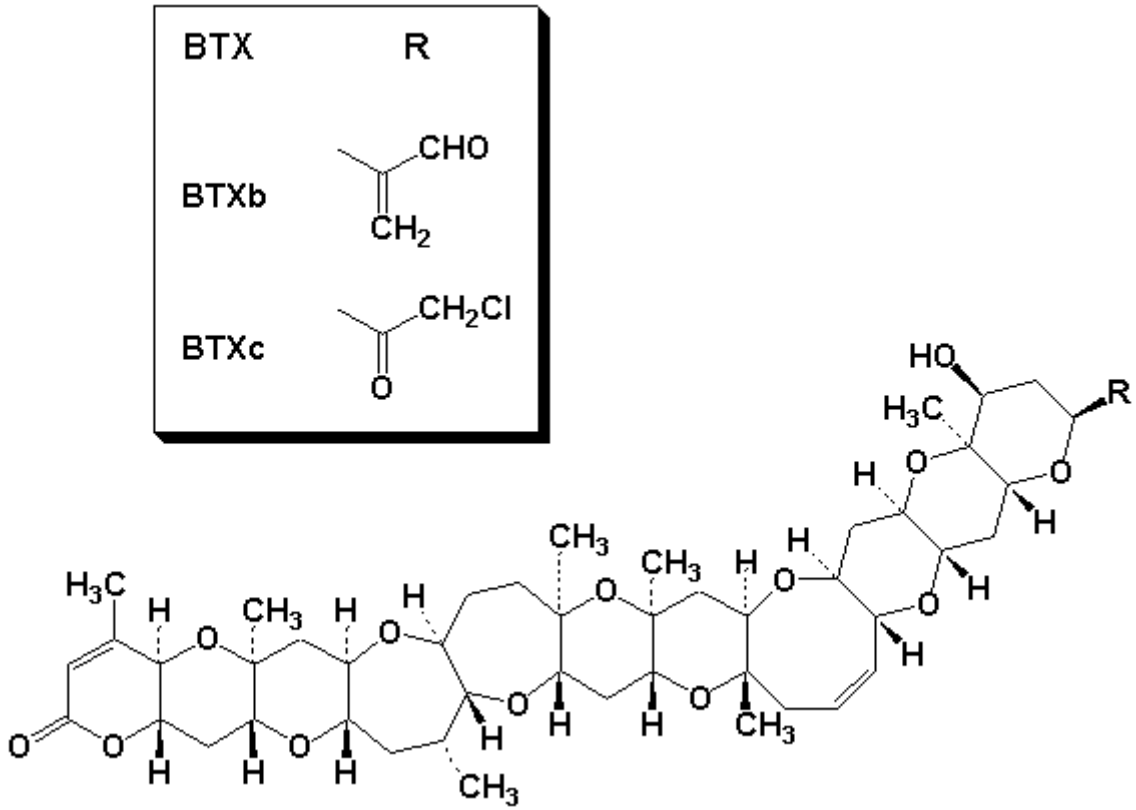
Various Shellfish-Associated Toxins

Brevetoxin

Toxin produced or elaborated by planktonic algae (dinoflagellates, in most cases) upon which the shellfish feed.



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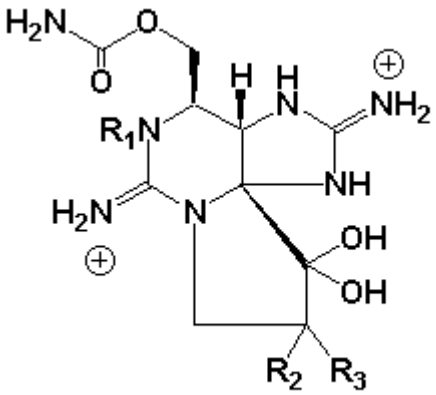
Various Shellfish-Associated Toxins

Saxitoxin

Paralytic shellfish toxin produced or elaborated by planktonic algae (dinoflagellates, in most cases) upon which the shellfish feed.



STX	R_1	R_2	R_3
STX	H	H	H
GTX-II	H	H	OSO_3^-
GTX-III	H	OSO_3^-	H
NeoSTX	OH	H	H
GTX-I	OH	H	OSO_3^-
GTX-IV	OH	OSO_3^-	H

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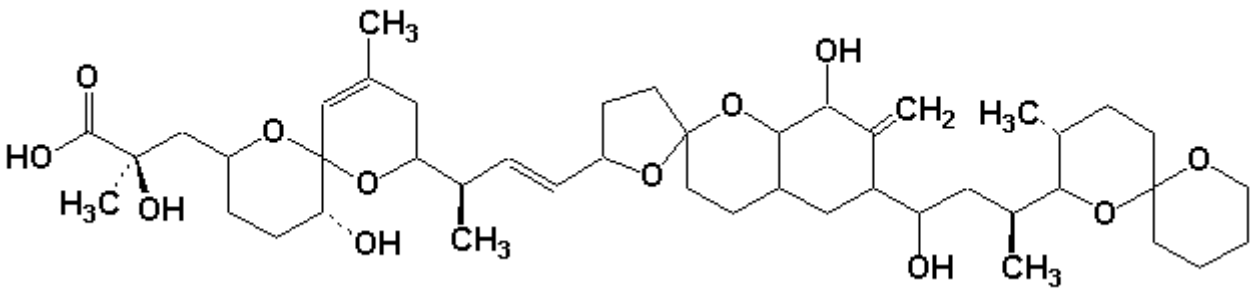
Various Shellfish-Associated Toxins

Okadaic Acid

Toxin produced by planktonic algae (dinoflagellates, in most cases) upon which the shellfish feed.



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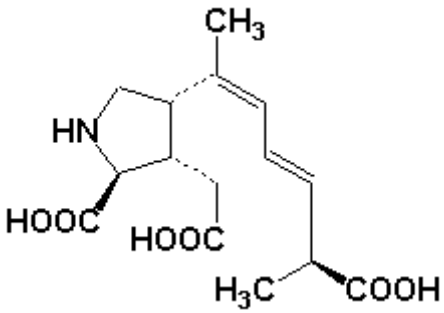
Various Shellfish-Associated Toxins

Domoic Acid

Toxin produced by planktonic algae
(dinoflagellates, in most cases)
upon which the shellfish feed.



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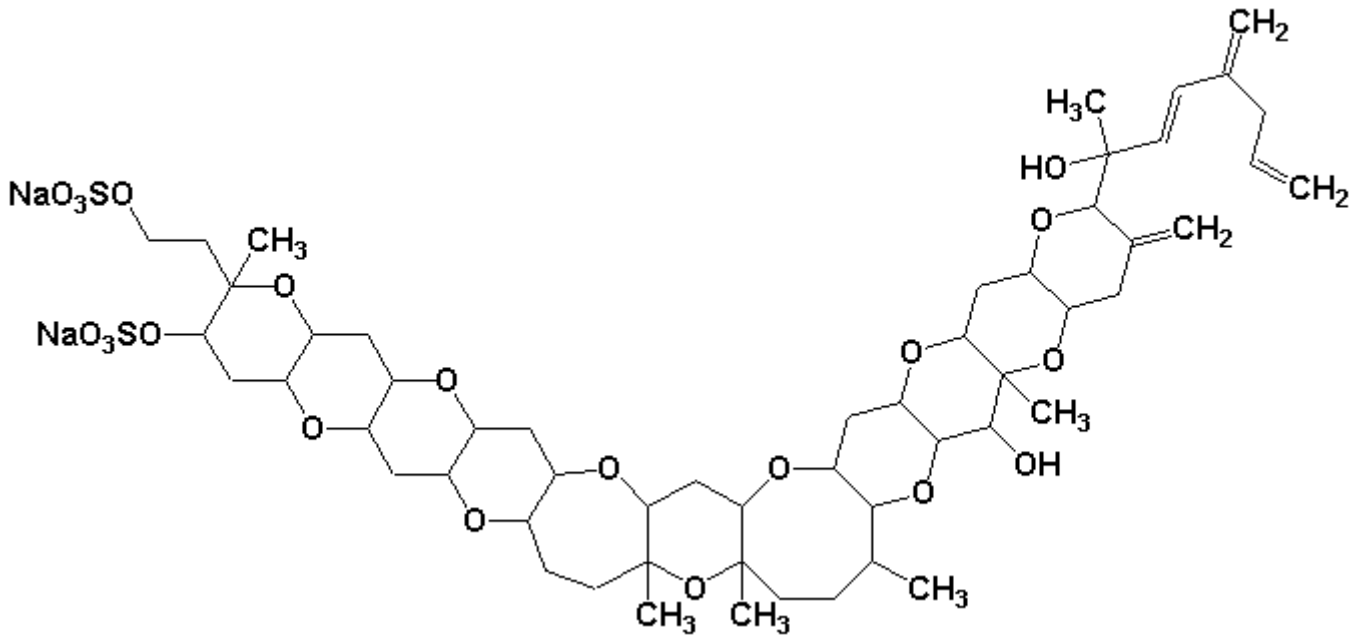
Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Various Shellfish-Associated Toxins

Yessotoxin

Toxin produced by planktonic algae (dinoflagellates, in most cases) upon which the shellfish feed.



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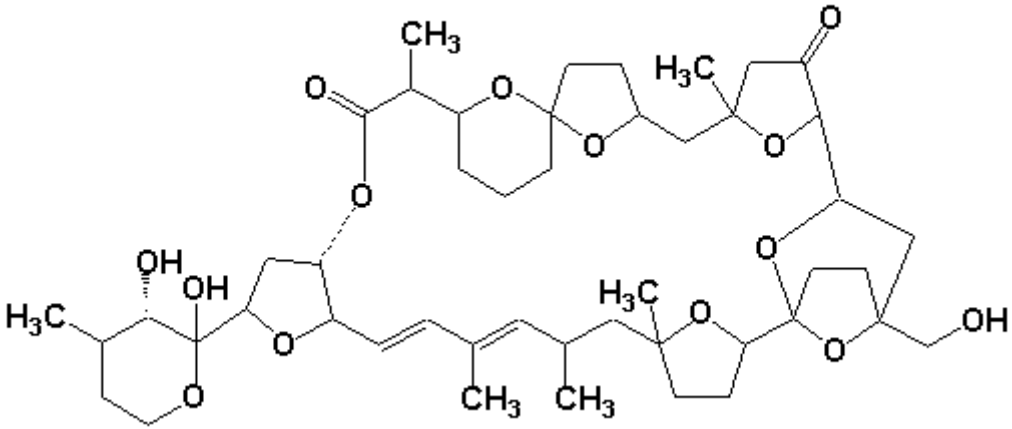
Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Various Shellfish-Associated Toxins

Pectenotoxin

Toxin produced or elaborated by planktonic algae (dinoflagellates, in most cases) upon which the shellfish feed.



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Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Scombrotoxin

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism:

Scombrotoxin

2. Nature of Acute Disease:

Scombroid Poisoning (also called Histamine Poisoning)

Scombroid poisoning is caused by the ingestion of foods that contain high levels of histamine and possibly other vasoactive amines and compounds. Histamine and other amines are formed by the growth of certain bacteria and the subsequent action of their decarboxylase enzymes on histidine and other amino acids in food, either during the production of a product such as Swiss cheese or by spoilage of foods such as fishery products, particularly tuna or mahi mahi. However, any food that contains the appropriate amino acids and is subjected to certain bacterial contamination and growth may lead to scombroid poisoning when ingested.

3. Nature of Disease:

Initial symptoms may include a tingling or burning sensation in the mouth, a rash on the upper body and a drop in blood pressure. Frequently, headaches and itching of the skin are encountered. The symptoms may progress to nausea, vomiting, and diarrhea and may require hospitalization, particularly in the case of elderly or impaired patients.

4. Diagnosis of Human Illness:

Diagnosis of the illness is usually based on the patient's symptoms, time of onset, and the effect of treatment with antihistamine medication. The suspected food must be analyzed within a few hours for elevated levels of histamine to confirm a diagnosis.

5. Associated Foods:

Fishery products that have been implicated in scombroid poisoning include the tunas (e.g., skipjack and yellowfin), mahi mahi, bluefish, sardines, mackerel, amberjack, and abalone. Many other products also have caused the toxic effects. The primary cheese involved in intoxications has been Swiss cheese. The toxin forms in a food when certain bacteria are present and time and temperature permit their growth. Distribution of the toxin within an individual fish fillet or between cans in a case lot can be uneven, with some sections of a product causing illnesses and others not. Neither cooking, canning, or freezing reduces the toxic effect. Common sensory examination by the consumer cannot ensure the absence or presence of the toxin. Chemical testing is the only reliable test for evaluation of a product.

6. Relative Frequency of Disease:

Scombroid poisoning remains one of the most common forms of fish poisoning in the United States. Even so, incidents of poisoning often go unreported because of the lack of required reporting, a lack of information by some medical personnel, and confusion with the symptoms of other illnesses. Difficulties with underreporting are a worldwide problem. In the United States from 1968 to 1980, 103 incidents of intoxication involving 827 people were reported. For the same period in Japan, where the quality of fish is a national priority, 42 incidents involving 4,122 people were recorded. Since 1978, 2 actions by FDA have reduced the frequency of intoxications caused by specific products. A defect action level for histamine in canned tuna resulted in increased industry quality control. Secondly, blocklisting of mahi mahi reduced the level of fish imported to the United States.

7. Course of Disease and Complications:

The onset of intoxication symptoms is rapid, ranging from immediate to 30 minutes. The duration of the illness is usually 3 hours, but may last several days.

8. Target Populations: All humans are susceptible to scombroid poisoning; however, the symptoms can be severe for the elderly and for those taking medications such as isoniazid. Because of the worldwide network for harvesting, processing, and distributing fishery products, the impact of the problem is not limited to specific geographical areas of the United States or consumption pattern. These foods are sold for use in homes, schools, hospitals, and restaurants as fresh, frozen, or processed products.

9. Food Analysis: An official method was developed at FDA to determine histamine, using a simple alcoholic extraction and quantitation by fluorescence spectroscopy. There are other untested procedures in the literature.

10. Selected Outbreaks: *Literature references can be found at the links below.*

MMWR 38(9):1989 — Scombroid fish poisoning is an acute syndrome resulting from consumption of fish containing high levels of histamine. This report summarizes investigations of two outbreaks of scombroid fish poisoning in Illinois and South Carolina in 1988.

MMWR 37(29):1988 — In July 1987, state and local public health officials in New Mexico investigated two cases of scombroid fish poisoning (histamine poisoning) in persons living in Albuquerque. A husband and wife had become ill within 45 minutes after eating dinner. Their symptoms included nausea, vomiting, diarrhea, headache, fever, flushing, and rapid pulse rate. An investigation by the Albuquerque Environmental Health Department found that the couple had shared a meal of grilled mahi mahi, pasta, salad, water, and wine. Their dog had eaten some of the fish and had vomited. Both of the patients had been treated with Benadryl, activated charcoal, and ipecac in a hospital emergency room. Their symptoms resolved within 36 hours of onset of illness.

MMWR 35(16):1986 — Between December 31, 1985, and January 4, 1986, three restaurants in Alabama and Tennessee received complaints of illness from nine customers and one employee who ate Pacific amberjack fish (also called yellowtail or kahala). One restaurant cook, who did not eat the fish, reported a transient red rash on the hands shortly after handling the fish. Ill persons reported no other menu items in common. The fish meals were prepared by grilling or frying. Three people sought medical evaluation. One had diastolic hypotension, and one had bronchospasm. All three were diagnosed as having food or fish allergy and were treated with an antihistamine. The symptoms of scombroid fish poisoning resemble those of a histamine reaction. Scombroid

poisoning is a response to toxic by-products--not an allergic reaction to fish.

Several large outbreaks of scombroid poisoning have been reported. In 1970, some 40 children in a school lunch program became ill from imported canned tuna. In 1973, more than 200 consumers across the United States were affected by domestic canned tuna. In 1979-1980 more than 200 individuals became ill after consuming imported frozen mahi mahi. Symptoms varied with each incident. In the 1973 situation, of the interviewed patients, 86% experienced nausea, 55% diarrhea, 44% headaches and 32% rashes.

Other incidents of intoxication have resulted from the consumption of canned abalone-like products, canned anchovies, and fresh and frozen amberjack, bluefish sole, and scallops. In particular, shipments of unfrozen fish packed in refrigerated containers have posed a significant problem because of inadequate temperature control.

Morbidity and Mortality Weekly Reports

For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.

11. Education and Background Resources:

Literature references can be found at the links below.

Loci index for genome

Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.

12. Molecular Structural Data:

This structure was created by Fred Fry, Ph.D, CFSAN.

Scombroid Toxin

CDC/MMWR

The CDC/MMWR link will provide a list of Morbidity and Mortality Weekly Reports at CDC relating to this organism or toxin. The date shown is the date the item was posted on the Web, not the date of the MMWR. The summary statement shown are the initial words of the overall document. The specific article of interest may be just one article or item within the overall report.

NIH/PubMed

The NIH/PubMed button at the top of the page will provide a list of research abstracts contained in the National Library of Medicine's MEDLINE database for this organism or toxin.

AGRICOLA

The AGRICOLA button will provide a list of research abstracts contained in the National Agricultural Library database for this organism or toxin.

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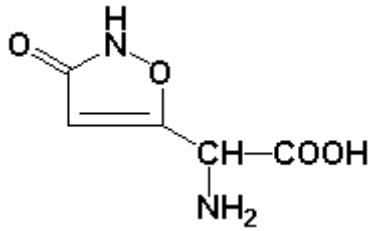
Scombrotoxin

Scombrotoxin

Toxin produced by the growth of certain bacteria and the subsequent action of their decarboxylase enzymes on histidine and other amino acids in food.



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Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Tetrodotoxin

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism: Tetrodotoxin (anhydrotetrodotoxin 4-epitetrodotoxin, tetrodonic acid)

2. Nature of Acute Disease: Pufferfish Poisoning, Tetradon Poisoning, Fugu Poisoning

3. Nature of Disease: Fish poisoning by consumption of members of the order Tetraodontiformes is one of the most violent intoxications from marine species. The gonads, liver, intestines, and skin of pufferfish can contain levels of tetrodotoxin sufficient to produce rapid and violent death. The flesh of many pufferfish may not usually be dangerously toxic. Tetrodotoxin has also been isolated from widely differing animal species, including the California newt, parrotfish, frogs of the genus Atelopus, the blue-ringed octopus, starfish, angelfish, and xanthid crabs. The metabolic source of tetrodotoxin is uncertain. No algal source has been identified, and until recently tetrodotoxin was assumed to be a metabolic product of the host. However, recent reports of the production of tetrodotoxin/anhydrotetrodotoxin by several bacterial species, including strains of the family Vibrionaceae, *Pseudomonas sp*., and Photobacterium phosphoreum, point toward a bacterial origin of this family of toxins. These are relatively common marine bacteria that are often associated with marine animals. If confirmed, these

findings may have some significance in toxicoses that have been more directly related to these bacterial species.

4. Diagnosis of Human Illness:

The diagnosis of pufferfish poisoning is based on the observed symptomology and recent dietary history.

5. Associated Foods:

Poisonings from tetrodotoxin have been almost exclusively associated with the consumption of pufferfish from waters of the Indo-Pacific ocean regions. Several reported cases of poisonings, including fatalities, involved pufferfish from the Atlantic Ocean, Gulf of Mexico, and Gulf of California. There have been no confirmed cases of poisoning from the Atlantic pufferfish, Spheroides maculatus. However, in one study, extracts from fish of this species were highly toxic in mice. The trumpet shell Charonia sauliae has been implicated in food poisonings, and evidence suggests that it contains a tetrodotoxin derivative. There have been several reported poisonings from mislabelled pufferfish and at least one report of a fatal episode when an individual swallowed a California newt.

6. Relative Frequency of Disease:

From 1974 through 1983 there were 646 reported cases of pufferfish poisoning in Japan, with 179 fatalities. Estimates as high as 200 cases per year with mortality approaching 50% have been reported. Only a few cases have been reported in the United States, and outbreaks in countries outside the Indo-Pacific area are rare.

7. Course of Disease and Complications:

The first symptom of intoxication is a slight numbness of the lips and tongue, appearing between 20 minutes to three hours after eating poisonous pufferfish. The next symptom is increasing paraesthesia in the face and extremities, which may be followed by sensations of lightness or floating. Headache, epigastric pain, nausea, diarrhea, and/or vomiting may occur. Occasionally, some reeling or difficulty in walking may occur. The second stage of the intoxication is increasing paralysis. Many victims are unable to move; even sitting may be difficult. There is increasing respiratory distress. Speech is affected, and the victim usually exhibits dyspnea, cyanosis, and hypotension. Paralysis increases and convulsions, mental impairment, and cardiac arrhythmia may occur. The victim, although completely paralyzed, may be conscious and in some cases completely lucid until shortly before death. Death usually occurs within 4 to 6 hours, with a known range of about 20 minutes to 8 hours.

8. Target Populations:

All humans are susceptible to tetrodotoxin poisoning. This toxicosis may be avoided by not consuming pufferfish or other animal species containing tetrodotoxin. Most other animal species known to contain tetrodotoxin are not usually consumed by humans. Poisoning from tetrodotoxin is of major public health concern primarily in Japan, where "fugu" is a traditional delicacy. It is prepared and sold in special restaurants where trained and licensed individuals carefully remove the viscera to reduce the danger of poisoning. Importation of pufferfish into the United States is not generally permitted, although special exceptions may be granted. There is potential for misidentification and/or mislabelling, particularly of prepared, frozen fish products.

9. Food Analysis:

The mouse bioassay developed for paralytic shellfish poisoning (PSP) can be used to monitor tetrodotoxin in pufferfish and is the current method of choice. An HPLC method with post-column reaction with alkali and fluorescence has been developed to determine tetrodotoxin and its associated toxins. The alkali degradation products can be confirmed as their trimethylsilyl derivatives by gas chromatography/mass spectrometry. These chromatographic methods have not yet been validated.

10. Selected Outbreaks:

Literature references can be found at the links below.

MMWR 45(19):1996

On April 29, 1996, three cases of tetrodotoxin poisoning occurred among chefs in California who shared contaminated fugu (puffer fish) brought from Japan by a co-worker as a prepackaged, ready-to-eat product. The quantity eaten by each person was minimal, ranging from approximately 1/4 to 1 1/2 oz. Onset of symptoms began approximately 3-20 minutes after ingestion, and all three persons were transported by ambulance to a local emergency department.

Pufferfish poisoning is a continuing problem in Japan, affecting 30 - 100 persons/year. Most of these poisoning episodes occur from home preparation and consumption and not from commercial sources of the pufferfish. Three deaths were reported in Italy in 1977 following the consumption of frozen pufferfish imported from Taiwan and mislabelled as angler fish.

Morbidity and Mortality Weekly Reports	**For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.**

11. Education and Background Resources:	*Literature references can be found at the links below.*
Loci index for genome Tetraodontidae (Pufferfish family)	Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.

12. Molecular Structural Data:	This structure was created by Fred Fry, Ph.D, CFSAN.
	Tetrodotoxin

CDC/MMWR

The CDC/MMWR link will provide a list of Morbidity and Mortality Weekly Reports at CDC relating to this organism or toxin. The date shown is the date the item was posted on the Web, not the date of the MMWR. The summary statement shown are the initial words of the overall document. The specific article of interest may be just one article or item within the overall report.

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AGRICOLA

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January 1992 with periodic updates

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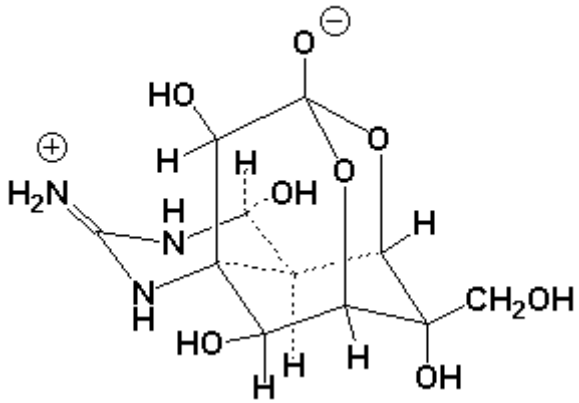
Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Tetrodotoxin

Tetrodotoxin

Toxin produced by members of the order Tetraodontiformes. The metabolic source of tetrodotoxin is uncertain.



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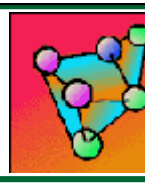

Mushroom toxins

1. Name of the Organism: Amanitin, Gyromitrin, Orellanine, Muscarine, Ibotenic Acid, Muscimol, Psilocybin, Coprine

2. Nature of Acute Disease: Mushroom Poisoning, Toadstool Poisoning

Protoplasmic
Neurotoxins
Gastrointinstinal
Irritants
Disulfiram-like
Miscellaneous

Types of Poisons.

Mushroom poisoning is caused by the consumption of raw or cooked fruiting bodies (mushrooms, toadstools) of a number of species of higher fungi. The term toadstool (from the German Todesstuhl, death's stool) is commonly given to poisonous mushrooms, but for individuals who are not experts in mushroom identification there are generally no easily recognizable differences between poisonous and nonpoisonous species. Old wives' tales notwithstanding, there is no general rule of thumb for distinguishing edible mushrooms and poisonous toadstools. The toxins involved in mushroom poisoning are produced naturally by the fungi themselves, and each individual specimen of a toxic species should be considered equally poisonous. Most mushrooms that

cause human poisoning cannot be made nontoxic by cooking, canning, freezing, or any other means of processing. Thus, the only way to avoid poisoning is to avoid consumption of the toxic species. Poisonings in the United States occur most commonly when hunters of wild mushrooms (especially novices) misidentify and consume a toxic species, when recent immigrants collect and consume a poisonous American species that closely resembles an edible wild mushroom from their native land, or when mushrooms that contain psychoactive compounds are intentionally consumed by persons who desire these effects.

3. Nature of Disease:

Mushroom poisonings are generally acute and are manifested by a variety of symptoms and prognoses, depending on the amount and species consumed. Because the chemistry of many of the mushroom toxins (especially the less deadly ones) is still unknown and positive identification of the mushrooms is often difficult or impossible, mushroom poisonings are generally categorized by their physiological effects. There are four categories of mushroom toxins: protoplasmic poisons (poisons that result in generalized destruction of cells, followed by organ failure); neurotoxins (compounds that cause neurological symptoms such as profuse sweating, coma, convulsions, hallucinations, excitement, depression, spastic colon); gastrointestinal irritants (compounds that produce rapid, transient nausea, vomiting, abdominal cramping, and diarrhea); and disulfiram-like toxins. Mushrooms in this last category are generally nontoxic and produce no symptoms unless alcohol is consumed within 72 hours after eating them, in which case a short-lived acute toxic syndrome is produced.

4. Diagnosis of Human Illness:

A clinical testing procedure is currently available only for the most serious types of mushroom toxins, the amanitins. The commercially available method uses a 3H-radioimmunoassay (RIA) test kit and can detect sub-nanogram levels of toxin in urine and plasma. Unfortunately, it requires a 2-hour incubation period, and this is an excruciating delay in a type of poisoning which the clinician generally does not see until a day or two has passed. A 125I-based kit which overcomes this problem has recently been reported, but has not yet reached the clinic. A sensitive and rapid HPLC technique has been reported in the literature even more recently, but it has not yet seen clinical application. Since most clinical laboratories in this country do not use even the older RIA technique, diagnosis is based entirely on symptomology and recent dietary history. Despite the fact that cases of mushroom poisoning may be broken down into a relatively small number of categories based on symptomatology, positive botanical identification of the mushroom species consumed remains the only means of unequivocally determining the particular type of intoxication involved, and it is still vitally important to obtain such accurate identification as quickly as possible. Cases involving ingestion of more than one toxic species in which one set of symptoms masks or mimics another set are among many reasons for needing this

information. Unfortunately, a number of factors (not discussed here) often make identification of the causative mushroom impossible. In such cases, diagnosis must be based on symptoms alone. In order to rule out other types of food poisoning and to conclude that the mushrooms eaten were the cause of the poisoning, it must be established that everyone who ate the suspect mushrooms became ill and that no one who did not eat the mushrooms became ill. Wild mushrooms eaten raw, cooked, or processed should always be regarded as prime suspects. After ruling out other sources of food poisoning and positively implicating mushrooms as the cause of the illness, diagnosis may proceed in two steps. The first step, outlined in Table 1, provides an early indication of the seriousness of the disease and its prognosis.

As described above, the protoplasmic poisons are the most likely to be fatal or to cause irreversible organ damage. In the case of poisoning by the deadly Amanitas, important laboratory indicators of liver (elevated LDH, SGOT, and bilirubin levels) and kidney (elevated uric acid, creatinine, and BUN levels) damage will be present. Unfortunately, in the absence of dietary history, these signs could be mistaken for symptoms of liver or kidney impairment as the result of other causes (e.g., viral hepatitis). It is important that this distinction be made as quickly as possible, because the delayed onset of symptoms will generally mean that the organ has already been damaged. The importance of rapid diagnosis is obvious: victims who are hospitalized and given aggressive support therapy almost immediately after ingestion have a mortality rate of only 10%, whereas those admitted 60 or more hours after ingestion have a 50-90% mortality rate. Table 2 provides more accurate diagnoses and appropriate therapeutic measures. A recent report indicates that amanitins are observable in urine well before the onset of any symptoms, but that laboratory tests for liver dysfunction do not appear until well after the organ has been damaged.

5. Associated Foods:

Mushroom poisonings are almost always caused by ingestion of wild mushrooms that have been collected by nonspecialists (although specialists have also been poisoned). Most cases occur when toxic species are confused with edible species, and a useful question to ask of the victims or their mushroom-picking benefactors is the identity of the mushroom they thought they were picking. In the absence of a well- preserved specimen, the answer to this question could narrow the possible suspects considerably. Intoxication has also occurred when reliance was placed on some folk method of distinguishing poisonous and safe species. Outbreaks have occurred after ingestion of fresh, raw mushrooms, stir-fried mushrooms, home-canned mushrooms, mushrooms cooked in tomato sauce (which rendered the sauce itself toxic, even when no mushrooms were consumed), and mushrooms that were blanched and frozen at home. Cases of poisoning by home-canned and frozen mushrooms are especially insidious because a single outbreak may easily become a multiple outbreak when the preserved toadstools are carried to another location and consumed at another time.

Specific cases of mistaken mushroom identity appears frequently. The Early False Morel *Gyromitra esculenta* is easily confused with the true Morel *Morchella esculenta*, and poisonings have occurred after consumption of fresh or cooked *Gyromitra*. *Gyromitra* poisonings have also occurred after ingestion of commercially available "morels" contaminated with *G. esculenta*. The commercial sources for these fungi (which have not yet been successfully cultivated on a large scale) are field collection of wild morels by semiprofessionals. Cultivated commercial mushrooms of whatever species are almost never implicated in poisoning outbreaks unless there are associated problems such as improper canning (which lead to bacterial food poisoning). A short list of the mushrooms responsible for serious poisonings and the edible mushrooms with which they are confused is presented in Table 3. Producers of mild gastroenteritis are too numerous to list here, but include members of many of the most abundant genera, including *Agaricus, Boletus, Lactarius, Russula, Tricholoma, Coprinus, Pluteus*, and others. The Inky Cap Mushroom (*Coprinus atrimentarius*) is considered both edible and delicious, and only the unwary who consume alcohol after eating this mushroom need be concerned. Some other members of the genus *Coprinus* (Shaggy Mane, *C. comatus*; Glistening Inky Cap, *C. micaceus*, and others) and some of the larger members of the *Lepiota* family such as the Parasol Mushroom (*Leucocoprinus procera*) do not contain coprine and do not cause this effect. The potentially deadly Sorrel Webcap Mushroom (*Cortinarius orellanus*) is not easily distinguished from nonpoisonous webcaps belonging to the same distinctive genus, and all should be avoided.

Most of the psychotropic mushrooms (*Inocybe* spp., *Conocybe* spp., *Paneolus* spp., *Pluteus* spp.) are in general appearance small, brown, and leathery (the so-called "Little Brown Mushrooms" or LBMs) and relatively unattractive from a culinary standpoint. The Sweat Mushroom (*Clitocybe dealbata*) and the Smoothcap Mushroom (*Psilocybe cubensis*) are small, white, and leathery. These small, unattractive mushrooms are distinctive, fairly unappetizing, and not easily confused with the fleshier fungi normally considered edible. Intoxications associated with them are less likely to be accidental, although both *C. dealbata* and *Paneolus foenisicii* have been found growing in the same fairy ring area as the edible (and choice) Fairy Ring Mushroom (*Marasmius oreades*) and the Honey Mushroom (*Armillariella mellea*), and have been consumed when the picker has not carefully examined every mushroom picked from the ring. Psychotropic mushrooms, which are larger and therefore more easily confused with edible mushrooms, include the Showy Flamecap or Big Laughing Mushroom (*Gymnopilus spectabilis*), which has been mistaken for Chanterelles (*Cantharellus* spp.) and for *Gymnopilus ventricosus* found growing on wood of conifers in western North America. The Fly Agaric (*Amanita muscaria*) and Panthercap (*Amanita pantherina*) mushrooms are large, fleshy, and colorful. Yellowish cap colors on some varieties of the Fly Agaric and the Panthercap are similar to the edible Caesar's Mushroom (*Amanita caesarea*), which is considered a delicacy in Italy. Another edible yellow capped mushroom occasionally confused with yellow *A. muscaria* and *A. pantherina* varieties are the Yellow Blusher (*Amanita flavorubens*). Orange to yellow-orange *A. muscaria* and *A. pantherina* may also be confused with the Blusher

(*Amanita rubescens*) and the Honey Mushroom (*Armillariella mellea*). White to pale forms of *A. muscaria* may be confused with edible field mushrooms (*Agaricus* spp.). Young (button stage) specimens of *A. muscaria* have also been confused with puffballs.

6. Relative Frequency of Disease:

Accurate figures on the relative frequency of mushroom poisonings are difficult to obtain. For the 5-year period between 1976 and 1981, 16 outbreaks involving 44 cases were reported to the Centers for Disease Control in Atlanta (Rattanvilay et al. MMWR 31(21): 287-288, 1982). The number of unreported cases is, of course, unknown. Cases are sporadic and large outbreaks are rare. Poisonings tend to be grouped in the spring and fall when most mushroom species are at the height of their fruiting stage. While the actual incidence appears to be very low, the potential exists for grave problems. Poisonous mushrooms are not limited in distribution as are other poisonous organisms (such as dinoflagellates). Intoxications may occur at any time and place, with dangerous species occurring in habitats ranging from urban lawns to deep woods. As Americans become more adventurous in their mushroom collection and consumption, poisonings are likely to increase.

7. Course of Disease and Complications:

The normal course of the disease varies with the dose and the mushroom species eaten. Each poisonous species contains one or more toxic compounds which are unique to few other species. Therefore, cases of mushroom poisonings generally do not resembles each other unless they are caused by the same or very closely related mushroom species. Almost all mushroom poisonings may be grouped in one of the categories outlined above.

PROTOPLASMIC POISONS

CDC/MMWR

Agricola

Amatoxins:

Several mushroom species, including the Death Cap or Destroying Angel (*Amanita phalloides*, *A. virosa*), the Fool's Mushroom (*A. verna*) and several of their relatives, along with the Autumn Skullcap (*Galerina autumnalis*) and some of its relatives, produce a family of cyclic octapeptides called amanitins. Poisoning by the amanitins is characterized by a long latent period (range 6-48 hours, average 6-15 hours) during which the patient shows no symptoms. Symptoms appear at the end of the latent period in the form of sudden, severe seizures of abdominal pain, persistent vomiting and watery diarrhea, extreme thirst, and lack of urine production. If this early phase is survived, the patient may appear to recover for a short time, but this period will generally be followed by a rapid and severe loss of strength, prostration, and pain-caused restlessness. Death in

50-90% of the cases from progressive and irreversible liver, kidney, cardiac, and skeletal muscle damage may follow within 48 hours (large dose), but the disease more typically lasts 6 to 8 days in adults and 4 to 6 days in children. Two or three days after the onset of the later phase, jaundice, cyanosis, and coldness of the skin occur. Death usually follows a period of coma and occasionally convulsions. If recovery occurs, it generally requires at least a month and is accompanied by enlargement of the liver. Autopsy will usually reveal fatty degeneration and necrosis of the liver and kidney.

Agricola
NIH/PubMed

Hydrazines:

Certain species of False Morel (*Gyromitra esculenta* and *G. gigas*) contain the protoplasmic poison gyromitrin, a volatile hydrazine derivative. Poisoning by this toxin superficially resembles *Amanita* poisoning but is less severe. There is generally a latent period of 6 - 10 hours after ingestion during which no symptoms are evident, followed by sudden onset of abdominal discomfort (a feeling of fullness), severe headache, vomiting, and sometimes diarrhea. The toxin affects primarily the liver, but there are additional disturbances to blood cells and the central nervous system. The mortality rate is relatively low (2-4%). Poisonings with symptoms almost identical to those produced by *Gyromitra* have also been reported after ingestion of the Early False Morel (*Verpa bohemica*). The toxin is presumed to be related to gyromitrin but has not yet been identified.

Agricola
NIH/PubMed

Orellanine:

The final type of protoplasmic poisoning is caused by the Sorrel Webcap mushroom (*Cortinarius orellanus*) and some of its relatives. This mushroom produces orellanine, which causes a type of poisoning characterized by an extremely long asymptomatic latent period of 3 to 14 days. An intense, burning thirst (polydipsia) and excessive urination (polyuria) are the first symptoms. This may be followed by nausea, headache, muscular pains, chills, spasms, and loss of consciousness. In severe cases, severe renal tubular necrosis and kidney failure may result in death (15%) several weeks after the poisoning. Fatty degeneration of the liver and severe inflammatory changes in the intestine accompany the renal damage, and recovery in less severe cases may require several months.

NEUROTOXINS

Poisonings by mushrooms that cause neurological problems may be divided into three groups, based on the type of symptoms produced, and named for the substances responsible for these symptoms.

CDC/MMWR

Muscarine Poisoning:

Agricola

Ingestion of any number of *Inocybe* or *Clitocybe* species (e.g., *Inocybe geophylla*, *Clitocybe dealbata*) results in an illness characterized primarily by profuse sweating. This effect is caused by the presence in these mushrooms of high levels (3- 4%) of muscarine. Muscarine poisoning is characterized by increased salivation, perspiration, and lacrimation within 15 to 30 minutes after ingestion of the mushroom. With large doses, these symptoms may be followed by abdominal pain, severe nausea, diarrhea, blurred vision, and labored breathing. Intoxication generally subsides within 2 hours. Deaths are rare, but may result from cardiac or respiratory failure in severe cases.

CDC/MMWR
NIH/PubMed
Agricola

Ibotenic acid/Muscimol Poisoning:

The Fly Agaric (*Amanita muscaria*) and Panthercap (*Amanita pantherina*) mushrooms both produce ibotenic acid and muscimol. Both substances produce the same effects, but muscimol is approximately 5 times more potent than ibotenic acid. Symptoms of poisoning generally occur within 1 - 2 hours after ingestion of the mushrooms. An initial abdominal discomfort may be present or absent, but the chief symptoms are drowsiness and dizziness (sometimes accompanied by sleep), followed by a period of hyperactivity, excitability, illusions, and delirium. Periods of drowsiness may alternate with periods of excitement, but symptoms generally fade within a few hours. Fatalities rarely occur in adults, but in children, accidental consumption of large quantities of these mushrooms may cause convulsions, coma, and other neurologic problems for up to 12 hours.

CDC/MMWR
NIH/PubMed
Agricola

Psilocybin Poisoning:

A number of mushrooms belonging to the genera *Psilocybe, Panaeolus, Copelandia, Gymnopilus, Conocybe*, and *Pluteus*, when ingested, produce a syndrome similar to alcohol intoxication (sometimes accompanied by hallucinations). Several of these mushrooms (e.g., *Psilocybe cubensis, P. mexicana, Conocybe cyanopus*) are eaten for their psychotropic effects in religious ceremonies of certain native American tribes, a practice which dates to the pre- Columbian era. The toxic effects are caused by psilocin and psilocybin. Onset of symptoms is usually rapid and the effects generally subside within 2 hours. Poisonings by these mushrooms are rarely fatal in adults and may be distinguished from ibotenic acid poisoning by the absence of drowsiness or coma. The most severe cases of psilocybin poisoning occur in small children, where large doses may cause the hallucinations accompanied by fever, convulsions, coma, and death. These mushrooms are generally small, brown, nondescript, and not particularly fleshy; they are seldom mistaken for food fungi by innocent hunters of wild mushrooms. Poisonings caused by intentional ingestion of these mushrooms by people with no legitimate religious justification must be handled with care, since the only cases likely to be seen by the physician are overdoses or intoxications caused by a combination of the mushroom and some added psychotropic substance (such as PCP).

Agricola

GASTROINTESTINAL IRRITANTS

Numerous mushrooms, including the Green Gill (*Chlorophyllum molybdites*), Gray Pinkgill (*Entoloma lividum*), Tigertop (*Tricholoma pardinum*), Jack O'Lantern (*Omphalotus illudens*), Naked Brimcap (*Paxillus involutus*), Sickener (*Russula emetica*), Early False Morel (*Verpa bohemica*), Horse mushroom (*Agaricus arvensis*) and Pepper bolete (*Boletus piperatus*), contain toxins that can cause gastrointestinal distress, including but not limited to nausea, vomiting, diarrhea, and abdominal cramps. In many ways these symptoms are similar to those caused by the deadly protoplasmic poisons. The chief and diagnostic difference is that poisonings caused by these mushrooms have a rapid onset, rather than the delayed onset seen in protoplasmic poisonings. Some mushrooms (including the first five species mentioned above) may cause vomiting and/or diarrhea which lasts for several days. Fatalities caused by these mushrooms are relatively rare and are associated with dehydration and electrolyte imbalances caused by diarrhea and vomiting, especially in debilitated, very young, or very old patients. Replacement of fluids and other appropriate supportive therapy will prevent death in these cases. The chemistry of the toxins responsible for this type of poisoning is virtually unknown, but may be related to the presence in some mushrooms of unusual sugars, amino acids, peptides, resins, and other compounds.

Agricola

NIH/PubMed

DISULFIRAM-LIKE POISONING

The Inky Cap Mushroom (*Coprinus atramentarius*) is most commonly responsible for this poisoning, although a few other species have also been implicated. A complicating factor in this type of intoxication is that this species is generally considered edible (i.e., no illness results when eaten in the absence of alcoholic beverages). The mushroom produces an unusual amino acid, coprine, which is converted to cyclopropanone hydrate in the human body. This compound interferes with the breakdown of alcohol, and consumption of alcoholic beverages within 72 hours after eating it will cause headache, nausea and vomiting, flushing, and cardiovascular disturbances that last for 2 - 3 hours.

Agricola

NIH/PubMed

MISCELLANEOUS POISONINGS

Young fruiting bodies of the sulfur shelf fungus *Laetiporus sulphureus* are considered edible. However, ingestion of this shelf fungus has caused digestive upset and other symptoms in adults and visual hallucinations and ataxia in a child.

8. Target Populations: All humans are susceptible to mushroom toxins. The poisonous species are ubiquitous, and geographical restrictions on types of poisoning that may occur in one location do not exist (except for some of the hallucinogenic LBMs, which occur primarily in the American southwest and southeast). Individual specimens of poisonous mushrooms are also characterized by individual variations in toxin content based on genetics, geographic location, and growing conditions. Intoxications may thus be more or less serious, depending not on the number of mushrooms consumed, but on the dose of toxin delivered. In addition, although most cases of poisoning by higher plants occur in children, toxic mushrooms are consumed most often by adults. Occasional accidental mushroom poisonings of children and pets have been reported, but adults are more likely to actively search for and consume wild mushrooms for culinary purposes. Children are more seriously affected by the normally nonlethal toxins than are adults and are more likely to suffer very serious consequences from ingestion of relatively smaller doses. Adults who consume mushrooms are also more likely to recall what was eaten and when, and are able to describe their symptoms more accurately than are children. Very old, very young, and debilitated persons of both sexes are more likely to become seriously ill from all types of mushroom poisoning, even those types which are generally considered to be mild.

Many idiosyncratic adverse reactions to mushrooms have been reported. Some mushrooms cause certain people to become violently ill, while not affecting others who consumed part of the same mushroom cap. Factors such as age, sex, and general health of the consumer do not seem to be reliable predictors of these reactions, and they have been attributed to allergic or hypersensitivity reactions and to inherited inability of the unfortunate victim to metabolize certain unusual fungal constituents (such as the uncommon sugar, trehalose). These reactions are probably not true poisonings as the general population does not seem to be affected.

9. Food Analysis: The mushroom toxins can with difficulty be recovered from poisonous fungi, cooking water, stomach contents, serum, and urine. Procedures for extraction and quantitation are generally elaborate and time-consuming, and the patient will in most cases have recovered by the time an analysis is made on the basis of toxin chemistry. The exact chemical natures of most of the toxins that produce milder symptoms are unknown. Chromatographic techniques (TLC, GLC, HPLC) exist for the amanitins, orellanine, muscimol/ibotenic acid, psilocybin, muscarine, and the gyromitrins. The amanitins may also be determined by commercially available 3H-RIA kits. The most reliable means of diagnosing a mushroom poisoning remains botanical identification of the fungus that was eaten. An accurate pre-ingestion determination of species will also prevent accidental poisoning in 100% of cases. Accurate post-ingestion analyses for specific toxins when no botanical identification is possible may be essential only in cases of suspected poisoning by the deadly *Amanitas*, since prompt and aggressive therapy (including lavage, activated charcoal, and plasmapheresis) can greatly reduce the mortality rate.

10. Selected Outbreaks:

Literature references can be found at the links below.

Isolated cases of mushroom poisoning have occurred throughout the continental United States.

MMWR 46(22):1997

The popular interest in gathering and eating uncultivated mushrooms has been associated with an increase in incidents of serious mushroom-related poisonings. From December 28, 1996, through January 6, 1997, nine persons in northern California required hospitalization after eating *Amanita phalloides* (i.e., "death cap") mushrooms; two of these persons died. Risks associated with eating these mushrooms result from a potent hepatotoxin. This report describes four cases of *A. phalloides* poisoning in patients admitted to a regional referral hospital in northern California during January 1997 and underscores that wild mushrooms should not be eaten unless identified as nonpoisonous by a mushroom expert.

Another one occurred in Oregon in October,1988, and involved the intoxication of five people who consumed stir-fried *Amanita phalloides*. The poisonings were severe, and at this writing three of the five people had undergone liver transplants for treatment of amanitin-induced liver failure.

Other cases have included the July, 1986, poisoning of a family in Philadelphia, by *Chlorophyllum molybdites*; the September, 1987, intoxication of seven men in Bucks County, PA, by spaghetti sauce which contained Jack O'Lantern mushroom (*Omphalotus illudens*); and of 14 teenage campers in Maryland by the same species (July, 1987). A report of a North Carolina outbreak of poisoning by False Morel (*Gyromitra* spp.) appeared in 1986. A 1985 report details a case of *Chlorophyllum molybdites* which occurred in Arkansas; a fatal poisoning case caused by an amanitin containing *Lepiota* was described in 1986.

MMWR 31(21):1982

In 1981, two Berks County, PA, people were poisoned (one fatally) after ingesting *Amanita phalloides*, while in the same year, seven Laotian refugees living in California were poisoned by Russula spp.

In separate 1981 incidents, several people from New York State were poisoned by *Omphalotus illudens*, *Amanita muscaria*, *Entoloma lividum*, and *Amanita virosa*.

An outbreak of gastroenterititis during a banquet for 482 people in Vancouver, British Columbia, was reported by the Vancouver Health Department in June, 1991. Seventy-seven of the guests reported symptoms consisting of early onset nausea (15-30 min), diarrhea (20 min-13 h), vomiting (20-60 min), cramps and bloated feeling.

Other symptoms included feeling warm, clamminess, numbness of the tongue and extreme thirst along with two cases of hive-like rash with onset of 3-7 days. Bacteriological tests were negative. This intoxication merits special attention because it involved consumption of species normally considered not only edible but choice. The fungi involved were the morels *Morchella esculenta* and *M. elata* (*M. angusticeps*), which were prepared in a marinade and consumed raw. The symptoms were severe but not life threatening. Scattered reports of intoxications by these species and *M. conica* have appeared in anecodotal reports for many years.

Numerous other cases exist; however, the cases that appear in the literature tend to be the serious poisonings such as those causing more severe gastrointestinal symptoms, psychotropic reactions, and severe organ damage (deadly *Amanita*). Mild intoxications are probably grossly underreported, because of the lack of severity of symptoms and the unlikeliness of a hospital admission.

Morbidity and Mortality Weekly Reports

For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.

11. Education and Background Resources:

Literature references can be found at the links below.

Loci index for genomes
| *A. arvensis* | *L. sulphureus* | *V. bohemica* | *G. esculenta* | *I. geophylla* | *C. dealbata* | *A. muscaria* | *A. pantherina* | *Psilocybe spp.* | *C. rickenii* | *P. acuminatus* | *Pluteus spp.* |

C. molybdites | *T. pardinum* | *O. illudens* | *P. involutus* | *A. virosa* | *Cortinarius spp.* | *C. atramentarius* |

Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.

12. Molecular

These structures were created by Fred Fry, Ph.D, CFSAN.

Structural Data:

Amanitin

Orellanine

Muscarine

Ibotenic Acid

Muscimol

Psilocybin

Gyromitrin

Coprine

CDC/MMWR

The CDC/MMWR link will provide a list of Morbidity and Mortality Weekly Reports at CDC relating to this organism or toxin. The date shown is the date the item was posted on the Web, not the date of the MMWR. The summary statement shown are the initial words of the overall document. The specific article of interest may be just one article or item within the overall report.

NIH/PubMed

The NIH/PubMed button at the top of the page will provide a list of research abstracts contained in the National Library of Medicine's MEDLINE database for this organism or toxin.

AGRICOLA

The AGRICOLA button will provide a list of research abstracts contained in the National Agricultural Library database for this organism or toxin.

mow@cfsan.fda.gov
January 1992 with periodic updates

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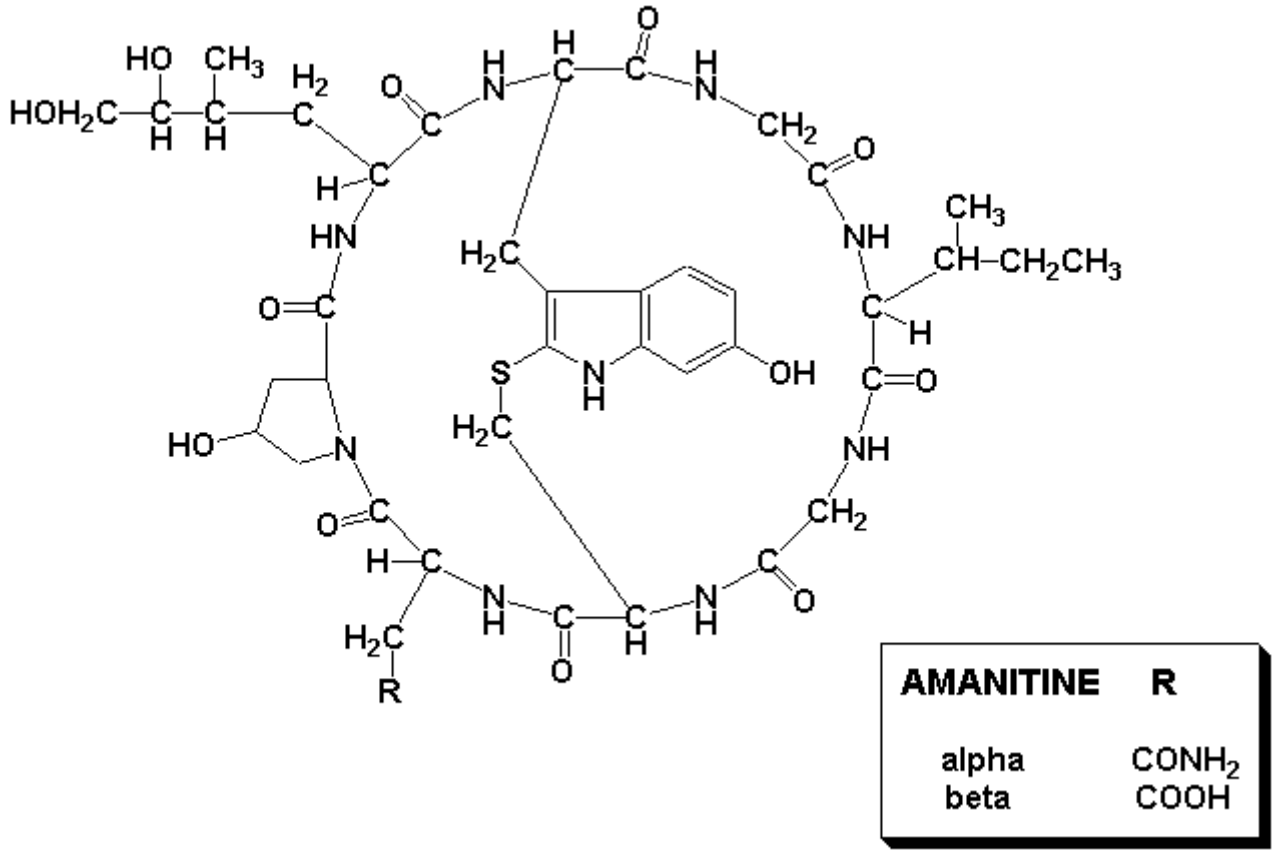
Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Mushroom Toxins

Amatoxin

Toxin produced by several mushroom species, including the Death Cap or Destroying Angel (*Amanita phalloides*, *A. virosa*), the Fool's Mushroom (*A. verna*) and several of their relatives, along with the Autumn Skullcap (*Galerina autumnalis*) and some of its relatives.


AMANITINE R
alpha CONH2
beta COOH

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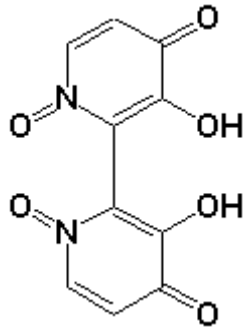
Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Mushroom Toxins

Orellanine

Toxin produced by the Sorrel Webcap mushroom (*Cortinarius orellanus*) and some of its relatives.



FDA/Center for Food Safety & Applied Nutrition
Hypertext updated by mow/las/acr December 9, 2005

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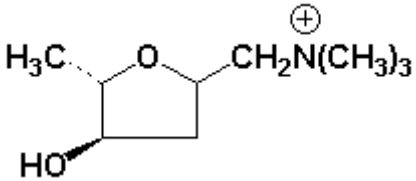
Mushroom Toxins

Muscarine

Toxin produced by any number of Inocybe or Clitocybe species (e.g., *Inocybe geophylla*, *Clitocybe dealbata*).



FDA/Center for Food Safety & Applied Nutrition
Hypertext updated by mow/las/acr December 9, 2005

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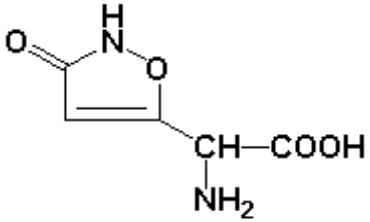
Mushroom Toxins

Ibotenic Acid

Toxin produced by Fly Agaric (*Amanita muscaria*) and Panthercap (*Amanita pantherina*) mushrooms.



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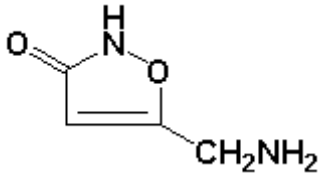
Mushroom Toxins

Muscimol

Toxin produced by Fly Agaric (*Amanita muscaria*) and Panthercap (*Amanita pantherina*) mushrooms.



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Hypertext updated by mow/las/acr December 9, 2005

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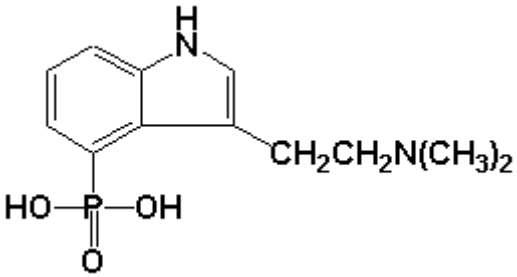
Mushroom Toxins

Psilocybin

Toxin produced by a number of mushrooms belonging to the genera *Psilocybe*, *Panaeolus*, *Copelandia*, *Gymnopilus*, *Conocybe*, and *Pluteus*.



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Hypertext updated by mow/las/acr December 9, 2005

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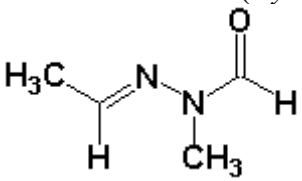
Mushroom Toxins

Gyromitrin

Toxin produced by certain species of False Morel (*Gyromitra esculenta* and *G. gigas*).



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Hypertext updated by mow/las/acr December 9, 2005

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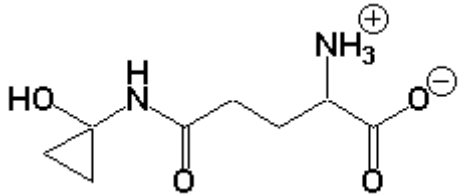
Mushroom Toxins

Coprine

Toxin produced by the Inky Cap Mushroom (*Coprinus atramentarius*).



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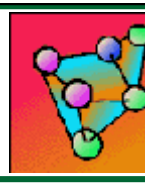

Aflatoxins

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism: Aflatoxins

2. Nature of Acute Disease: Aflatoxicosis

Aflatoxicosis is poisoning that results from ingestion of aflatoxins in contaminated food or feed. The aflatoxins are a group of structurally related toxic compounds produced by certain strains of the fungi *Aspergillus flavus* and *A. parasiticus*. Under favorable conditions of temperature and humidity, these fungi grow on certain foods and feeds, resulting in the production of aflatoxins. The most pronounced contamination has been encountered in tree nuts, peanuts, and other oilseeds, including corn and cottonseed. The major aflatoxins of concern are designated B1, B2, G1, and G2. These toxins are usually found together in various foods and feeds in various proportions; however, aflatoxin B1 is usually predominant and is the most toxic. When a commodity is analyzed by thin-layer chromatography, the aflatoxins separate into the individual components in the order given above; however, the first two fluoresce blue when viewed under ultraviolet light and the second two fluoresce green. Aflatoxin M a major metabolic product of aflatoxin B1 in animals and is usually excreted in the milk and urine of dairy cattle and other mammalian species that have consumed aflatoxin-contaminated food or feed.

3. Nature of Disease:

Aflatoxins produce acute necrosis, cirrhosis, and carcinoma of the liver in a number of animal species; no animal species is resistant to the acute toxic effects of aflatoxins; hence it is logical to assume that humans may be similarly affected. A wide variation in LD50 values has been obtained in animal species tested with single doses of aflatoxins. For most species, the LD50 value ranges from 0.5 to 10 mg/kg body weight. Animal species respond differently in their susceptibility to the chronic and acute toxicity of aflatoxins. The toxicity can be influenced by environmental factors, exposure level, and duration of exposure, age, health, and nutritional status of diet. Aflatoxin B1 is a very potent carcinogen in many species, including nonhuman primates, birds, fish, and rodents. In each species, the liver is the primary target organ of acute injury. Metabolism plays a major role in determining the toxicity of aflatoxin B1; studies show that this aflatoxion requires metabolic activation to exert its carcinogenic effect, and these effects can be modified by induction or inhibition of the mixed function oxidase system.

4. Diagnosis of Human Illness:

Aflatoxicosis in humans has rarely been reported; however, such cases are not always recognized. Aflatoxicosis may be suspected when a disease outbreak exhibits the following characteristics:

- the cause is not readily identifiable
- the condition is not transmissible
- syndromes may be associated with certain batches of food
- treatment with antibiotics or other drugs has little effect
- the outbreak may be seasonal, i.e., weather conditions may affect mold growth.

The adverse effects of aflatoxins in animals (and presumably in humans) have been categorized in two general forms.

A. (Primary) Acute aflatoxicosis is produced when moderate to high levels of aflatoxins are consumed. Specific, acute episodes of disease ensue may include hemorrhage, acute liver damage, edema, alteration in digestion, absorption and/or metabolism of nutrients, and possibly death.

B. (Primary) Chronic aflatoxicosis results from ingestion of low to moderate levels of aflatoxins. The effects are usually subclinical and difficult to recognize. Some of the common symptoms are impaired food conversion and slower rates of growth with or without the production of an overt aflatoxin syndrome.

5. Associated Foods:

In the United States, aflatoxins have been identified in corn and corn products, peanuts and peanut products, cottonseed, milk, and tree nuts such as Brazil nuts, pecans, pistachio nuts, and walnuts. Other grains and nuts are susceptible but less prone to contamination.

6. Relative Frequency of Disease:

The relative frequency of aflatoxicosis in humans in the United States is not known. No outbreaks have been reported in humans. Sporadic cases have been reported in animals.

7. Course of Disease and Complications:

In well-developed countries, aflatoxin contamination rarely occurs in foods at levels that cause acute aflatoxicosis in humans. In view of this, studies on human toxicity from ingestion of aflatoxins have focused on their carcinogenic potential. The relative susceptibility of humans to aflatoxins is not known, even though epidemiological studies in Africa and Southeast Asia, where there is a high incidence of hepatoma, have revealed an association between cancer incidence and the aflatoxin content of the diet. These studies have not proved a cause-effect relationship, but the evidence suggests an association.

One of the most important accounts of aflatoxicosis in humans occurred in more than 150 villages in adjacent districts of two neighboring states in northwest India in the fall of 1974. According to one report of this outbreak, 397 persons were affected and 108 persons died. In this outbreak, contaminated corn was the major dietary constituent, and aflatoxin levels of 0.25 to 15 mg/kg were found. The daily aflatoxin B1 intake was estimated to have been at least 55 ug/kg body weight for an undetermined number of days. The patients experienced high fever, rapid progressive jaundice, edema of the limbs, pain, vomiting, and swollen livers. One investigator reported a peculiar and very notable feature of the outbreak: the appearance of signs of disease in one village population was preceded by a similar disease in domestic dogs, which was usually fatal. Histopathological examination of humans showed extensive bile duct proliferation and periportal fibrosis of the liver together with gastrointestinal hemorrhages. A 10-year follow-up of the Indian outbreak found the survivors fully recovered with no ill effects from the experience.

A second outbreak of aflatoxicosis was reported from Kenya in 1982. There were 20 hospital admissions with a 60% mortality; daily aflatoxin intake was estimated to be at least 38 ug/kg body weight for an undetermined number of days.

In a deliberate suicide attempt, a laboratory worker ingested 12 ug/kg body weight of aflatoxin B1 per day over

a 2-day period and 6 months later, 11 ug/kg body weight per day over a 14-day period. Except for transient rash, nausea and headache, there were no ill effects; hence, these levels may serve as possible no-effect levels for aflatoxin B1 in humans. In a 14-year follow-up, a physical examination and blood chemistry, including tests for liver function, were normal.

8. Target Populations:

Although humans and animals are susceptible to the effects of acute aflatoxicosis, the chances of human exposure to acute levels of aflatoxin is remote in well-developed countries. In undeveloped countries, human susceptibility can vary with age, health, and level and duration of exposure.

9. Food Analysis:

Many chemical procedures have been developed to identify and measure aflatoxins in various commodities. The basic steps include extraction, lipid removal, cleanup, separation and quantification. Depending on the nature of the commodity, methods can sometimes be simplified by omitting unnecessary steps. Chemical methods have been developed for peanuts, corn, cottonseed, various tree nuts, and animal feeds. Chemical methods for aflatoxin in milk and dairy products are far more sensitive than for the above commodities because the aflatoxin M animal metabolite is usually found at much lower levels (ppb and ppt). All collaboratively studied methods for aflatoxin analysis are described in Chapter 26 of the AOAC Official Methods of Analysis.

10. Selected Outbreaks:

Literature references can be found at the links below.

Very little information is available on outbreaks of aflatoxicosis in humans because medical services are less developed in the areas of the world where high levels of contamination of aflatoxins occur in foods, and, therefore, many cases go unnoticed.

Morbidity and Mortality Weekly Reports

For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.

11. Education and

Literature references can be found at the links below.

Background Resources:

Loci index for genome Aspergillus flavus Aspergillus parasiticus	Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.

12. Molecular Structural Data:

These structures were created by Fred Frye of the FDA.

Aflatoxin B_1 and M_1

Aflatoxin G_1

CDC/MMWR

The CDC/MMWR link will provide a list of Morbidity and Mortality Weekly Reports at CDC relating to this organism or toxin. The date shown is the date the item was posted on the Web, not the date of the MMWR. The summary statement shown are the initial words of the overall document. The specific article of interest may be just one article or item within the overall report.

NIH/PubMed

The NIH/PubMed button at the top of the page will provide a list of research abstracts contained in the National Library of Medicine's MEDLINE database for this organism or toxin.

AGRICOLA

The AGRICOLA button will provide a list of research abstracts contained in the National Agricultural Library database for this organism or toxin.

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January 1992 with periodic updates

FDA/Center for Food Safety & Applied Nutrition
Hypertext updated by mow/las/dav/acr/ear June 14, 2006

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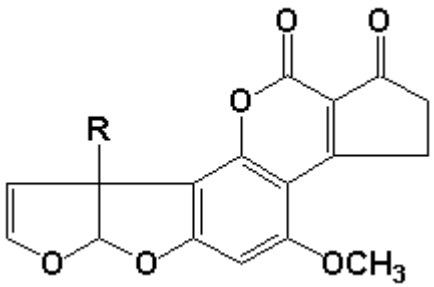
Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Aflatoxins

Aflatoxin B_1 and M_1

Toxin produced by certain strains of the fungi *Aspergillus flavus* and *A. parasiticus*.



AT	R
ATB_1	H
ATM_1	OH

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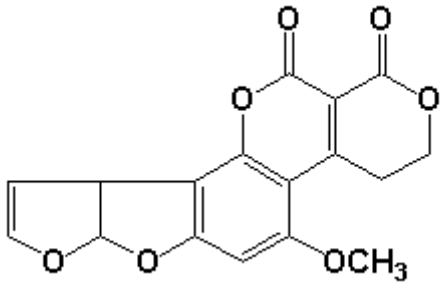
Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Aflatoxins

Aflatoxin G_1

Toxin produced by certain strains of the fungi *Aspergillus flavus* and *A. parasiticus*.



FDA/Center for Food Safety & Applied Nutrition
Hypertext updated by mow/las/acr December 9, 2005

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Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Pyrrolizidine Alkaloids

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism: Pyrrolizidine Alkaloids

2. Nature of Acute Disease: Pyrrolizidine Alkaloids Poisoning

Pyrrolizidine alkaloid intoxication is caused by consumption of plant material containing these alkaloids. The plants may be consumed as food, for medicinal purposes, or as contaminants of other agricultural crops. Cereal crops and forage crops are sometimes contaminated with pyrrolizidine-producing weeds, and the alkaloids find their way into flour and other foods, including milk from cows feeding on these plants. Many plants from the Boraginaceae, Compositae, and Leguminosae families contain well over 100 hepatotoxic pyrrolizidine alkaloids.

3. Nature of Disease: Most cases of pyrrolizidine alkaloid toxicity result in moderate to severe liver damage. Gastrointestinal symptoms are usually the first sign of intoxication, and consist predominantly of abdominal pain with vomiting and the development of ascites. Death may ensue from 2 weeks to more than 2 years after poisoning, but patients may recover almost completely if the alkaloid intake is discontinued and the liver damage has not been

too severe.

4. Diagnosis of Human Illness: Evidence of toxicity may not become apparent until sometime after the alkaloid is ingested. The acute illness has been compared to the Budd-Chiari syndrome (thrombosis of hepatic veins, leading to liver enlargement, portal hypertension, and ascites). Early clinical signs include nausea and acute upper gastric pain, acute abdominal distension with prominent dilated veins on the abdominal wall, fever, and biochemical evidence of liver disfunction. Fever and jaundice may be present. In some cases the lungs are affected; pulmonary edema and pleural effusions have been observed. Lung damage may be prominent and has been fatal. Chronic illness from ingestion of small amounts of the alkaloids over a long period proceeds through fibrosis of the liver to cirrhosis, which is indistinguishable from cirrhosis of other etiology.

5. Associated Foods: The plants most frequently implicated in pyrrolizidine poisoning are members of the Borginaceae, Compositae, and Leguminosae families. Consumption of the alkaloid-containing plants as food, contaminants of food, or as medicinals has occurred.

6. Relative Frequency of Disease: Reports of acute poisoning in the United States among humans are relatively rare. Most result from the use of medicinal preparations as home remedies. However, intoxications of range animals sometimes occur in areas under drought stress, where plants containing alkaloids are common. Milk from dairy animals can become contaminated with the alkaloids, and alkaloids have been found in the honey collected by bees foraging on toxic plants. Mass human poisonings have occurred in other countries when cereal crops used to prepare food were contaminated with seeds containing pyrrolizidine alkaloid.

7. Course of Disease and Complications: No information currently available.

8. Target Populations: All humans are believed to be susceptible to the hepatotoxic pyrrolizidine alkaloids. Home remedies and

consumption of herbal teas in large quantities can be a risk factor and are the most likely causes of alkaloid poisonings in the United States.

9. Food Analysis:

The pyrrolizidine alkaloids can be isolated from the suspect commodity by any of several standard alkaloid extraction procedures. The toxins are identified by thin layer chromatography. The pyrrolizidine ring is first oxidized to a pyrrole followed by spraying with Ehrlich reagent, which gives a characteristic purple spot. Gas-liquid chromatographic and mass spectral methods also are available for identifying the alkaloids.

10. Selected Outbreaks:

There have been relatively few reports of human poisonings in the United States. Worldwide, however, a number of cases have been documented. Most of the intoxications in the USA involved the consumption of herbal preparations either as a tea or as a medicine. The first patient diagnosed in the USA was a female who had used a medicinal tea for 6 months while in Ecuador. She developed typical hepatic veno-occlusive disease, with voluminous ascites, centrilobular congestion of the liver, and increased portal vein pressure. Interestingly, the patient completely recovered within one year after ceasing to consume the tea. Another herbal tea poisoning occurred when Senecio longilobus was mistaken for a harmless plant (called "gordolobo yerba" by Mexican Americans) and used to make herbal cough medicine. Two infants were given this medication for several days. The 2-month-old boy was ill for 2 weeks before being admitted to the hospital and died 6 days later. His condition was first diagnosed as Reye's syndrome, but was changed when jaundice, ascites, and liver necrosis were observed. The second child, a 6-month-old female, had acute hepatocellular disease, ascites, portal hypertension, and a right pleural effusion. The patient improved with treatment; however, after 6 months, a liver biopsy revealed extensive hepatic fibrosis, progressing to cirrhosis over 6 months. Another case of hepatic veno-occlusive disease was described in a 47-year-old nonalcoholic woman who had consumed large quantities of comfrey (Symphytum species) tea and pills for more than one year. Liver damage was still present 20 months after the comfrey consumption ceased.

Morbidity and Mortality Weekly Reports

For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.

11. Education and

Literature references can be found at the links below.

Background Resources:

Loci index for genome Senecio spp.	Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.

12. Molecular Structural Data:

These structures were created by Fred Fry, Ph.D, CFSAN.

Pyrrolizidine Alkaloids of *Symphytum* spp.

Pyrrolizidine Alkaloids of *Senecio longilobus* Benth.

CDC/MMWR

The CDC/MMWR link will provide a list of Morbidity and Mortality Weekly Reports at CDC relating to this organism or toxin. The date shown is the date the item was posted on the Web, not the date of the MMWR. The summary statement shown are the initial words of the overall document. The specific article of interest may be just one article or item within the overall report.

NIH/PubMed

The NIH/PubMed button at the top of the page will provide a list of research abstracts contained in the National Library of Medicine's MEDLINE database for this organism or toxin.

AGRICOLA

The AGRICOLA button will provide a list of research abstracts contained in the National Agricultural Library database for this organism or toxin.

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January 1992 with periodic updates

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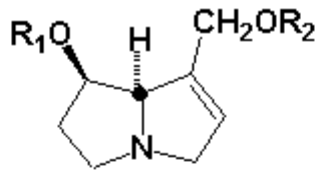
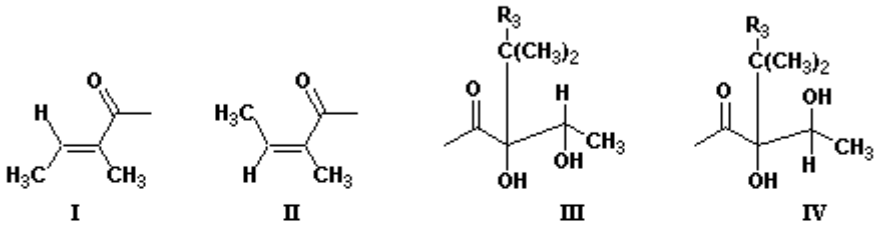
Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Pyrrolizidine Alkaloids

Pyrrolizidine Alkaloids of *Symphytum* spp.

Toxin produced by plants from the Boraginaceae, Compositae, and Leguminosae families.





Name	R_1	R_2	R_3
retronecine	H	H	H
lycopsamine	H	III	H
intermedine	H	IV	H
7-acetyllycopsamine	CH_3CO	III	H
7-acetylintermedine	CH_3CO	IV	H
symphytine	I	III	H
symlandine	II	III	H
echimidine	II	III or IV	OH
uplandicine	CH_3CO	III or IV	OH

FDA/Center for Food Safety & Applied Nutrition
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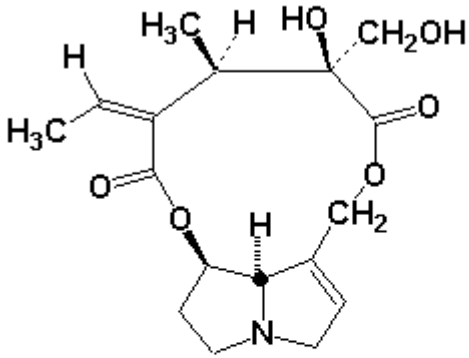
Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Pyrrolizidine Alkaloids

Pyrrolizidine Alkaloids of *Senecio longilobus* Benth.

Toxin produced by plants from the Boraginaceae, Compositae, and Leguminosae families.



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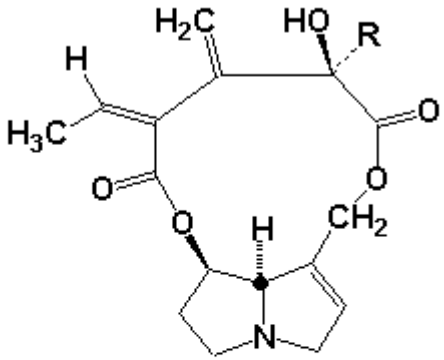

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Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Phytohaemagglutinin

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Organism:
Phytohaemagglutinin (Kidney Bean Lectin)

This compound, a lectin or hemagglutinin, has been used by immunologists for years to trigger DNA synthesis in T lymphocytes, and more recently, to activate latent human immunodeficiency virus type 1 (HIV-1, AIDS virus) from human peripheral lymphocytes. Besides inducing mitosis, lectins are known for their ability to agglutinate many mammalian red blood cell types, alter cell membrane transport systems, alter cell permeability to proteins, and generally interfere with cellular metabolism.

2. Nature of Acute Disease:

Red Kidney Bean (*Phaseolus vulgaris*) Poisoning, Kinkoti Bean Poisoning, and possibly other names.

3. Nature of Disease:

The onset time from consumption of raw or undercooked kidney beans to symptoms varies from between 1 to 3 hours. Onset is usually marked by extreme nausea, followed by vomiting, which may be very severe. Diarrhea develops somewhat later (from one to a few hours), and some persons report abdominal pain. Some persons have been hospitalized, but recovery is usually rapid (3 - 4 h after onset of symptoms) and spontaneous.

4. Diagnosis of Human Illness:

Diagnosis is made on the basis of symptoms, food history, and the exclusion of other rapid onset food poisoning agents (e.g., *Bacillus cereus*, *Staphylococcus aureus*, arsenic, mercury, lead, and cyanide).

5. Associated Foods:

Phytohaemagglutinin, the presumed toxic agent, is found in many species of beans, but it is in highest concentration in red kidney beans (*Phaseolus vulgaris*). The unit of toxin measure is the hemagglutinating unit (hau). Raw kidney beans contain from 20,000 to 70,000 hau, while fully cooked beans contain from 200 to 400 hau. White kidney beans, another variety of *Phaseolus vulgaris*, contain about one-third the amount of toxin as the red variety; broad beans (*Vicia faba*) contain 5 to 10% the amount that red kidney beans contain.

The syndrome is usually caused by the ingestion of raw, soaked kidney beans, either alone or in salads or casseroles. As few as four or five raw beans can trigger symptoms. Several outbreaks have been associated with "slow cookers" or crock pots, or in casseroles which had not reached a high enough internal temperature to destroy the glycoprotein lectin. It has been shown that heating to 80°C may potentiate the toxicity five-fold, so that these beans are more toxic than if eaten raw. In studies of casseroles cooked in slow cookers, internal temperatures often did not exceed 75°C.

6. Relative Frequency of Disease:

This syndrome has occurred in the United Kingdom with some regularity. Seven outbreaks occurred in the U.K. between 1976 and 1979 and were reviewed (Noah et al. 1980. Br. Med. J. 19 July, 236-7). Two more incidents were reported by Public Health Laboratory Services (PHLS), Colindale, U.K. in the summer of 1988. Reports of this syndrome in the United States are anecdotal and have not been formally published.

7. Course of Disease and Complications:

The disease course is rapid. All symptoms usually resolve within several hours of onset. Vomiting is usually described as profuse, and the severity of symptoms is directly related to the dose of toxin (number of raw beans ingested). Hospitalization has occasionally resulted, and intravenous fluids may have to be administered. Although of short duration, the symptoms are extremely debilitating.

8. Target Populations:

All persons, regardless of age or gender, appear to be equally susceptible; the severity is related only to the dose

ingested. In the seven outbreaks mentioned above, the attack rate was 100%.

9. Food Analysis:

The difficulty in food analysis is that this syndrome is not well known in the medical community. Other possible causes must be eliminated, such as *Bacillus cereus*, *staphylococcal* food poisoning, or chemical toxicity. If beans are a component of the suspected meal, analysis is quite simple, and based on hemagglutination of red blood cells (hau).

10. Selected Outbreaks:

Literature references can be found at the links below.

As previously stated, no major outbreaks have occurred in the U.S. Outbreaks in the U.K. are far more common. The syndrome is probably sporadic, affecting small numbers of persons or individuals, and is easily misdiagnosed or never reported due to the short duration of symptoms. Differences in reporting between the U.S. and U.K. may be attributed to greater use of dried kidney beans in the U.K., or better physician awareness. The U.K. has established a reference laboratory for the quantitation of hemagglutinins from suspected foods.

Morbidity and Mortality Weekly Reports

For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.

11. Education and Background Resources:

Literature references can be found at the links below.

Loci index for genome *Phaseolus vulgaris*

Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.

NOTE: The following procedure has been recommended by the PHLS to render kidney, and other, beans safe for consumption:

Soak in water for at least 5 hours.

Pour away the water.
Boil briskly in fresh water, with occasional stirring, for at least 10 minutes.
Undercooked beans may be more toxic than raw beans.

12. Molecular Structural Data:

Data and images are from the C Lectin Database at the French Center for National Scientific Research.

Phytohemagglutinin Structural Information Database

Phytohemagglutinin Image

Chime and Rasmol

You will will need to download these free browser plugins to view the image data.

CDC/MMWR

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AGRICOLA

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January 1992 with periodic updates

Bad Bug Book

Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Grayanotoxin

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Toxin: Grayanotoxin (formerly known as andromedotoxin, acetylandromedol, and rhodotoxin)

2. Nature of Acute Disease: Honey Intoxication

Honey intoxication is caused by the consumption of honey produced from the nectar of rhododendrons. The grayanotoxins cause the intoxication. The specific grayanotoxins vary with the plant species. These compounds are diterpenes, polyhydroxylated cyclic hydrocarbons that do not contain nitrogen. Other names associated with the disease is rhododendron poisoning, mad honey intoxication or grayanotoxin poisoning.

3. Nature of Disease: The intoxication is rarely fatal and generally lasts for no more than 24 hours. Generally the disease induces dizziness, weakness, excessive perspiration, nausea, and vomiting shortly after the toxic honey is ingested. Other symptoms that can occur are low blood pressure or shock, bradyarrhythima (slowness of the heart beat associated with an irregularity in the heart rhythm), sinus bradycardia (a slow sinus rhythm, with a heart rate less than 60), nodal rhythm (pertaining to a node, particularly the atrioventricular node), Wolff-Parkinson-White syndrome (anomalous atrioventricular excitation) and complete atrioventricular block.

4. Diagnosis of Human Illness:

The grayanotoxins bind to sodium channels in cell membranes. The binding unit is the group II receptor site, localized on a region of the sodium channel that is involved in the voltage-dependent activation and inactivation. These compounds prevent inactivation; thus, excitable cells (nerve and muscle) are maintained in a state of depolarization, during which entry of calcium into the cells may be facilitated. This action is similar to that exerted by the alkaloids of veratrum and aconite. All of the observed responses of skeletal and heart muscles, nerves, and the central nervous system are related to the membrane effects.

Because the intoxication is rarely fatal and recovery generally occurs within 24 hours, intervention may not be required. Severe low blood pressure usually responds to the administration of fluids and correction of bradycardia; therapy with vasopressors (agents that stimulate contraction of the muscular tissue of the capillaries and arteries) is only rarely required. Sinus bradycardia and conduction defects usually respond to atropine therapy; however, in at least one instance the use of a temporary pacemaker was required.

5. Associated Foods:

In humans, symptoms of poisoning occur after a dose-dependent latent period of a few minutes to two or more hours and include salivation, vomiting, and both circumoral (around or near the mouth) and extremity paresthesia (abnormal sensations). Pronounced low blood pressure and sinus bradycardia develop. In severe intoxication, loss of coordination and progressive muscular weakness result. Extrasystoles (a premature contraction of the heart that is independent of the normal rhythm and arises in response to an impulse in some part of the heart other than the sinoatrial node; called also premature beat) and ventricular tachycardia (an abnormally rapid ventricular rhythm with aberrant ventricular excitation, usually in excess of 150 per minute) with both atrioventricular and intraventricular conduction disturbances also may occur. Convulsions are reported occasionally.

6. Relative Frequency of Disease:

Grayanotoxin poisoning most commonly results from the ingestion of grayanotoxin-contaminated honey, although it may result from the ingestion of the leaves, flowers, and nectar of rhododendrons. Not all rhododendrons produce grayanotoxins. *Rhododendron ponticum* grows extensively on the mountains of the eastern Black Sea area of Turkey. This species has been associated with honey poisoning since 401 BC. A number of toxin species are native to the United States. Of particular importance are the western azalea (*Rhododendron occidentale*) found from Oregon to southern California, the California rosebay (*Rhododendron*

macrophyllum) found from British Columbia to central California, and *Rhododendron albiflorum* found from British Columbia to Oregon and in Colorado. In the eastern half of the United States grayanotoxin-contaminated honey may be derived from other members of the botanical family Ericaceae, to which rhododendrons belong. Mountain laurel (*Kalmia latifolia*) and sheep laurel (*Kalmia angustifolia*) are probably the most important sources of the toxin.

7. Course of Disease and Complications:

Grayanotoxin poisoning in humans is rare. However, cases of honey intoxication should be anticipated everywhere. Some may be ascribed to a increase consumption of imported honey. Others may result from the ingestion of unprocessed honey with the increased desire of natural foods in the American diet.

8. Target Populations:

All people are believed to be susceptible to honey intoxication. The increased desire of the American public for natural (unprocessed) foods, may result in more cases of grayanotoxin poisoning. Individuals who obtain honey from farmers who may have only a few hives are at increased risk. The pooling of massive quantities of honey during commercial processing generally dilutes any toxic substance.

9. Food Analysis:

The grayanotoxins can be isolated from the suspect commodity by typical extraction procedures for naturally occurring terpenes. The toxins are identified by thin layer chromatography.

10. Selected Outbreaks:

Literature references can be found at the links below.

Several cases of grayanotoxin poisonings in humans have been documented in the 1980s. These reports come from Turkey and Austria. The Austrian case resulted from the consumption of honey that was brought back from a visit to Turkey. From 1984 to 1986, 16 patients were treated for honey intoxication in Turkey. The symptoms started approximately 1 h after 50 g of honey was consumed. In an average of 24 h, all of the patients recovered. The case in Austria resulted in cardiac arrhythmia, which required a temporal pacemaker to prevent further decrease in heart rate. After a few hours, pacemaker simulation was no longer needed. The Austrian case shows that with increased travel throughout the world, the risk of grayanotoxin poisoning is possible outside the

areas of Ericaceae-dominated vegetation, namely, Turkey, Japan, Brazil, United States, Nepal, and British Columbia. In 1983 several British veterinarians reported a incident of grayanotoxin poisoning in goats. One of the four animals died. Post-mortem examination showed grayanotoxin in the rumen contents.

Morbidity and Mortality Weekly Reports	**For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC.**

11. Education and Background Resources:	*Literature references can be found at the links below.*
Loci index for genome Rhododendron spp.	Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.
12. Molecular Structural Data:	This structure was created by Fred Fry, Ph.D, CFSAN.
	Grayanotoxin

CDC/MMWR

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AGRICOLA

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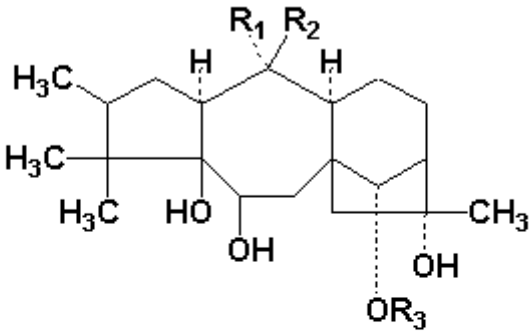
January 2001 with periodic updates

Grayanotoxin

Grayanotoxin (andromedotoxin, acetylandromedol, rhodotoxin)

Toxin produced from the nectar of rhododendrons, occassionally found in honey.



GRAY	R_1	R_2	R_1R_2	R_3
GRAY1	OH	CH_3	-	H
GRAY2	-	-	$=CH_2$	H
GRAY3	OH	CH_3	-	Ac

FDA/Center for Food Safety & Applied Nutrition
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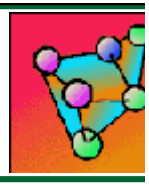
Foodborne Pathogenic Microorganisms and Natural Toxins Handbook



Prions and Transmissible Spongiform Encephalopathies

CDC/MMWR | NIH/PubMed | Agricola

1. Name of the Agent:

The prion. Prions are normal proteins of animal tissues that can misfold and become infectious: they are not cellular organisms or viruses. In their normal noninfectious state, these proteins may be involved in cell-to-cell communication. When these proteins become abnormally shaped i.e., infectious prions, they are thought to come into contact with a normally shaped protein and transform that protein into the abnormally shaped prion. This process causes a geometric increase of abnormally shaped prion proteins until the number of abnormally shaped protein causes overt illness. When consumed by animals, prions are thought to be absorbed into the body during digestion where they begin the process of changing their normal protein counterparts into abnormal proteins; however infectious prions from one species of animal have less of a potential of causing the abnormal shape in the normally shaped prion proteins of another species (the "species barrier"). While the "prion theory" of Transmissible Spongiform Encephalopathies (TSEs) is widely accepted, there are other theories of the cause of these illnesses.

2. Nature of Acute Disease:

Prions are associated with a group of diseases called Transmissible Spongiform Encephalopathies (TSEs). In humans, the illness suspected of being foodborne is variant Creutzfeldt-Jakob disease (vCJD). The human disease vCJD and the cattle disease, bovine spongiform encephalopathy (BSE), also known as "mad cow" disease, appear to be caused by the same agent. Other similar but not identical TSE diseases exist in animals, but there is no known transmission of these TSEs to humans. Included among these is chronic wasting disease (CWD) of deer and elk, and the oldest known of these diseases - scrapie - which occurs in sheep and goats. No

early acute clinical indications for TSEs have been described. After an extended incubation period of years, these diseases result in irreversible neurodegeneration.

3. Nature of Disease: The neurodegenerative phase of vCJD in humans typically involves the formation of "daisy-shaped" areas of damage in the central nervous system. There is also, in common with other TSEs, vacuolization (formation of holes) that gives brain tissue a spongy appearance when examined under a microscope. It is thought that the build-up of the abnormally shaped prion proteins causes the observed neurodegeneration.

4. Diagnosis of Human Illness: The most reliable means for diagnosing any TSE is the microscopic examination of brain tissue - a post-mortem procedure. Preliminary diagnoses of vCJD are based on patient history, clinical symptoms, electroencephalograms, and magnetic resonance imaging of the brain.

5. Associated Foods: The major concern for consumers is the potential contamination of meat products by BSE contaminated tissues or the inclusion of BSE contaminated tissues in foods, including dietary supplements. High risk tissues for BSE contamination include the cattle's skull, brain, trigeminal ganglia (nerves attached to the brain, eyes, tonsils, spinal cord, dorsal root ganglia (nerves attached to the spinal cord), and the distal ileum (part of the small intestine). The direct or indirect intake of high-risk tissues may have been the source of human illnesses in the United Kingdom and elsewhere. Bovine meat (if free of central nervous system tissue) and milk have, to date, shown no infectivity in test animals. Gelatin, derived from the hides and bones of cattle, appears to be very low risk , especially with adequate attention to the quality of source material and effectiveness of gelatin-making process. Based upon many studies, scientists have concluded that forms of CJD other than vCJD do not appear to be associated with the consumption of specific foods.

6. Relative Frequency of Disease: There is one reported human cases of vCJD in the United States in a woman that appears to have aquired the illness from consumption of contaminated food when growing up in the United Kingdom. In the U. K., there have been around 143 human cases of suspected or confirmed vCJD from 1993, when the illness was first recognized, through December 2003. There have been six reported cases of vCJD in France and one in Italy.

Since 1986, more than 180,000 cases of BSE have occurred in the U.K.in cattle, particularly dairy cattle. BSE cases have also been identified in 20 European countries, Japan, Israel, and Canada. The feeding of rendered TSE-infected animal by-products to cattle is believed to have caused the epidemic of BSE. Practices such as this have now been prohibited, resulting in a dramatic decline in the number of cases. There is one reported case of BSE in the U.S. which appears to be the result of importing cattle from Canada that may have been exposed to feed which contained meat and bone meal from rendered cattle.

7. Course of Disease and Complications:

Cases of vCJD usually present with psychiatric problems, such as depression. As the disease progresses, neurologic signs appear -- unpleasant sensations in the limbs and/or face. There are problems with walking and muscle coordination. Sometimes, late in the course of the disease, victims become forgetful and then experience severe problems with processing information and speaking. Patients are hospitalized and are increasingly unable to care for themselves until death occurs.

8. Target Populations:

All cases of vCJD to date have occurred in individuals of a single human genotype that is methionine homozygous at codon 129 of the prion protein. About 40% of the total human population belongs to this methionine-methionine homozygous state. The susceptibility of other genotypes is not yet known.

9. Food Analysis & Reconditioning:

No practical detection methods exist, at present. The abnormally shaped prions are resistant to most heat and chemical treatments, however certain food manufacturing processes (e.g. gelatin production) do result in significant decrease in prion infectivity through exclusion. There are no known means of reconditioning contaminated foods. The key to food protection is obtaining bovine meat and meat byproducts from animals not infected with BSE and protecting against contamination of food with high risk tissues, especially brain and spinal cord tissue.

10. Selected Outbreaks:

Significant numbers of vCJD cases have occurred only in the United Kingdom; isolated cases have been reported in other countries.

11. Education and Background Resources:

Literature references can be found at the links below.

CDC's Emerging Infectious Diseases

Bovine Spongiform Encephalopathy and Variant Creutzfeldt-Jakob Disease: Background, Evolution, and Current Concerns

The epidemic of bovine spongiform encephalopathy in the United Kingdom, that began in 1986 and during its course affected nearly 200,000 cattle, is waning. It leaves in its wake a human outbreak of variant Creutzfeldt-Jakob disease, most probably resulting from the consumption of beef products contaminated by central nervous system tissue. Although averaging only 10-15 cases a year since its first appearance in 1994, the future magnitude and geographic distribution of this illness cannot yet be predicted. The possibility that large numbers of apparently healthy persons might be incubating the disease raises concerns about iatrogenic transmissions through instrumentation (surgery and medical diagnostic procedures) and blood and organ donations. Government agencies in many countries continue to implement new measures to minimize this risk.

APHIS USDA Background document on BSE

BSE has had a substantial impact on the livestock industry in the United Kingdom. The disease also has been confirmed in native-born cattle in Belgium, Denmark, France, Germany, Italy, Ireland, Liechtenstein, Luxembourg, the Netherlands, Northern Ireland, Portugal, Spain, Switzerland, and Canada. The Animal and Plant Health Inspection Service (APHIS) of the U.S. Department of Agriculture (USDA) is enforcing import restrictions and conducting surveillance for BSE to prevent this serious disease from becoming established in the United States. APHIS surveillance detected the single BSE occurance in the U.S.

Centers for Disease Control and Prevention Background document on CJD

Since 1996, evidence has been increasing for a causal relationship between ongoing outbreaks in Europe of a disease in cattle, called bovine spongiform encephalopathy (BSE, or "mad cow disease"), and a disease in humans, called variant Creutzfeldt-Jakob disease (vCJD). Both disorders are inevitably fatal brain diseases with unusually long incubation periods measured in years, and are caused by an unconventional transmissible agent.

Food and Drug Administration

Update on Ruminant Feeding Ban

Rendered feed ingredients contaminated with an infectious agent are believed to have been the source of BSE infection in cattle in the United Kingdom. Some of the feed given to cattle included remnants of the slaughtering process, such as the brain and spinal cord, which harbor the agent that is believed to cause BSE. Although the material is cooked during the rendering process, the BSE agent can survive cooking.

To prevent the establishment and amplification of BSE through feed in the United States, FDA implemented a final rule that, in most cases, prohibits the feeding of mammalian protein to ruminant animals. This rule, Title 21 Part 589.2000 of the *Code of Federal Regulations*, became effective on August 4, 1997.

Food and Drug Administration Q and A's on BSE	• What is BSE? • What causes BSE? • Where is the BSE agent found in infected cattle? • Which countries have reported BSE? • How was BSE spread? • What has the British government done in response to the BSE epidemic? • Does BSE occur in the US?
Loci index for PrP of Homo sapiens	Available from the GenBank Protein database, which contains the protein sequences for many organisms.

12. Molecular Structural Data:

PrP Protein in Humans

PrP Protein in Cattle

CDC/MMWR

The CDC/MMWR link will provide a list of Morbidity and Mortality Weekly Reports at CDC relating to this organism or toxin. The date shown is the date the item was posted on the Web, not the date of the MMWR. The summary statement shown are the initial words of the overall document. The specific article of interest may be just one article or item within the overall report.

NIH/PubMed

The NIH/PubMed button at the top of the page will provide a list of research abstracts contained in the National Library of Medicine's MEDLINE database for this organism or toxin.

AGRICOLA

The AGRICOLA button will provide a list of research abstracts contained in the National Agricultural Library database for this organism or toxin.

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January 2004 with periodic updates

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Foodborne Pathogenic Microorganisms and Natural Toxins Handbook

Infective Dose Information

Most chapters include a statement on infectious dose. These numbers should be viewed with caution for any of the following reasons:

- Often they were extrapolated from epidemiologic investigations.
- They were obtained by human feeding studies on healthy, young adult volunteers.
- They are best estimates based on a limited data base from outbreaks.
- They are worst case estimates.
- Because of the following variables they cannot be directly used to assess risk:

Variables of the Parasite or Microorganism

- Variability of gene expression of multiple pathogenic mechanism(s)
- Potential for damage or stress of the microorganism.
- Interaction of organism with food menstruum and environment
- pH susceptibility of organism
- Immunologic "uniqueness" of the organism
- Interactions with other organisms

Variables of the Host

- Age

- General health
- Pregnancy
- Medications--OTC or prescription
- Metabolic disorders
- Alcoholism, cirrhosis, hemochromatosis
- Malignancy
- Amount of food consumed
- Gastric acidity variation: antacids, natural variation, achlorhydria
- Genetic disturbances
- Nutritional status
- Immune competence
- Surgical history
- Occupation

Because of the complexity of factors involved in making risk decisions, the multidisciplinary Health Hazard Evaluation Board judges each situation on all available facts.

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Onset, Duration, and Symptoms of Foodborne Illness

Approximate onset time to symptoms	Predominant symptoms	Associated organism or toxin
Upper gastrointestinal tract symptoms (nausea, vomiting) occur first or predominate		
Less than 1 h	Nausea, vomiting, unusual taste, burning of mouth.	Metallic salts
1-2 h	Nausea, vomiting, cyanosis, headache, dizziness, dyspnea, trembling, weakness, loss of consciousness.	Nitrites
1-6 h mean 2-4 h	Nausea, vomiting, retching, diarrhea, abdominal pain, prostration.	*Staphylococcus aureus* and its enterotoxins
8-16 h (2-4 h emesis possible)	Vomiting, abdominal cramps, diarrhea, nausea.	*Bacillus cereus*
6-24 h	Nausea, vomiting, diarrhea, thirst, dilation of pupils, collapse, coma.	Amanita species mushrooms
Sore throat and respiratory symptoms occur		

12-72 h	Sore throat, fever, nausea, vomiting, rhinorrhea, sometimes a rash.	*Streptococcus pyogenes*
2-5 days	Inflamed throat and nose, spreading grayish exudate, fever, chills, sore throat, malaise, difficulty in swallowing, edema of cervical lymph node.	*Corynebacterium diphtheriae*
Lower gastrointestinal tract symptoms (abdominal cramps, diarrhea) occur first or predominate		
2-36 h, mean 6-12 h	Abdominal cramps, diarrhea, putrefactive diarrhea associated with *C. perfringens*, sometimes nausea and vomiting.	*Clostridium perfringens, Bacillus cereus, Streptococcus faecalis, S. faecium*
12-74 h, mean 18-36 h	Abdominal cramps, diarrhea, vomiting, fever, chills, malaise, nausea, headache, possible. Sometimes bloody or mucoid diarrhea, cutaneous lesions associated with V. vulnificus. Yersinia enterocolitica mimics flu and acute appendicitis.	*Salmonella* species (including *S. arizonae*), *Shigella*, enteropathogenic *Escherichia coli*, other *Enterobacteriacae*, *Vibrio parahaemolyticus*, *Yersinia enterocolitica*, *Aeromonas hydrophila*, *Plesiomonas shigelloides*, *Campylobacter jejuni*, *Vibrio cholerae* (O1 and non-O1) *V.vulnificus*, *V. fluvialis*
3-5 days	Diarrhea, fever, vomiting abdominal pain, respiratory symptoms.	Enteric viruses
1-6 weeks	Mucoid diarrhea (fatty stools) abdominal pain, weight loss.	*Giardia lamblia*
1 to several weeks	Abdominal pain, diarrhea, constipation, headache, drowsiness, ulcers, variable -- often asymptomatic.	*Entamoeba histolytica*
3-6 months	Nervousness, insomnia, hunger pains, anorexia, weight loss, abdominal pain, sometimes gastroenteritis.	*Taenia saginata, T. solium*

Neurological symptoms (visual disturbances, vertigo, tingling, paralysis) occur		
Less than 1 h	*** SEE GASTROINTESTINAL AND/OR NEUROLOGIC SYMPTOMS (Shellfish Toxins) (this Appendix)	Shellfish toxin
	Gastroenteritis, nervousness, blurred vision, chest pain, cyanosis, twitching, convulsions.	Organic phosphate
	Excessive salivation, perspiration, gastroenteritis, irregular pulse, pupils constricted, asthmatic breathing.	Muscaria-type mushrooms
	Tingling and numbness, dizziness, pallor, gastro-hemmorrhage, and desquamation of skin, fixed eyes, loss of reflexes, twitching, paralysis.	Tetradon (tetrodotoxin) toxins
1-6 h	Tingling and numbness, gastroenteritis, dizziness, dry mouth, muscular aches, dilated pupils, blurred vision, paralysis.	Ciguatera toxin
	Nausea, vomiting, tingling, dizziness, weakness, anorexia, weight loss, confusion.	Chlorinated hydrocarbons
2 h to 6 days, usually 12-36 h	Vertigo, double or blurred vision, loss of reflex to light, difficulty in swallowing. speaking, and breathing, dry mouth, weakness, respiratory paralysis.	*Clostridium botulinum* and its neurotoxins
More than 72 h	Numbness, weakness of legs, spastic paralysis, impairment of vision, blindness, coma.	Organic mercury
	Gastroenteritis, leg pain, ungainly high-stepping gait,	Triorthocresyl phosphate

	foot and wrist drop.	
Allergic symptoms (facial flushing, itching) occur		
Less than 1 h	Headache, dizziness, nausea, vomiting, peppery taste, burning of throat, facial swelling and flushing, stomach pain, itching of skin.	Histamine (scombroid)
	Numbness around mouth, tingling sensation, flushing, dizziness, headache, nausea.	Monosodium glutamate
	Flushing, sensation of warmth, itching, abdominal pain, puffing of face and knees.	Nicotinic acid
Generalized infection symptoms (fever, chills, malaise, prostration, aches, swollen lymph nodes) occur		
4-28 days, mean 9 days	Gastroenteritis, fever, edema about eyes, perspiration, muscular pain, chills, prostration, labored breathing.	*Trichinella spiralis*
7-28 days, mean 14 days	Malaise, headache, fever, cough, nausea, vomiting, constipation, abdominal pain, chills, rose spots, bloody stools.	*Salmonella typhi*
10-13 days	Fever, headache, myalgia, rash.	*Toxoplasma gondii*
10-50 days, mean 25-30 days	Fever, malaise, lassitude, anorexia, nausea, abdominal pain, jaundice.	Etiological agent not yet isolated -- probably viral
Varying periods (depends on specific illness)	Fever, chills, head- or joint ache, prostration, malaise, swollen lymph nodes, and other specific symptoms of disease in question.	*Bacillus anthracis, Brucella melitensis, B. abortus, B. suis, Coxiella burnetii, Francisella tularensis, Listeria monocytogenes, Mycobacterium tuberculosis, Mycobacterium* species, *Pasteurella multocida,*

		Streptobacillus moniliformis, Campylobacter jejuni, Leptospira species.
Gastrointestinal and/or Neurologic Symptoms - (Shellfish Toxins)		
0.5 to 2 h	Tingling, burning, numbness, drowsiness, incoherent speech, respiratory paralysis	Paralytic Shellfish Poisoning (PSP) (saxitoxins)
2-5 min to 3-4 h	Reversal of hot and cold sensation, tingling; numbness of lips, tongue & throat; muscle aches, dizziness, diarrhea, vomiting	Neurotoxic Shellfish Poisoning (NSP) (brevetoxins)
30 min to 2-3 h	Nausea, vomiting, diarrhea, abdominal pain, chills, fever	Diarrheic Shellfish Poisoning (DSP) (dinophysis toxin, okadaic acid, pectenotoxin, yessotoxin)
24 h (gastrointestinal) to 48 h (neurologic)	Vomiting, diarrhea, abdominal pain, confusion, memory loss, disorientation, seizure, coma	Amnesic Shellfish Poisoning (ASP) (domoic acid)

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Factors Affecting the Growth of Microorganisms in Foods

Food is a chemically complex matrix, and predicting whether, or how fast, microorganisms will grow in any given food is difficult. Most foods contain sufficient nutrients to support microbial growth. Several factors encourage, prevent, or limit the growth of microorganisms in foods, the most important are a_w, pH, and temperature.

a_w: (Water Activity or Water Availability). Water molecules are loosely oriented in pure liquid water and can easily rearrange. When other substances (solutes) are added to water, water molecules orient themselves on the surface of the solute and the properties of the solution change dramatically. The microbial cell must compete with solute molecules for free water molecules. Except for *Staphylococcus aureus*, bacteria are rather poor competitors, whereas molds are excellent competitors.

a_w varies very little with temperature over the range of temperatures that support microbial growth. A solution of pure water has an a_w of 1.00. The addition of solute decreases the a_w to less than 1.00.

Water Activity of Various NaCl Solutions

Percent NaCl (w/v)	Molal	Water Activity (a_w)

0.9	0.15	0.995
1.7	0.30	0.99
3.5	0.61	0.98
7.0	1.20	0.96
10.0	1.77	0.94
13.0	2.31	0.92
16.0	2.83	0.90
22.0	3.81	0.86

The a_w of a solution may dramatically affect the ability of heat to kill a bacterium at a given temperature. For example, a population of *Salmonella typhimurium* is reduced tenfold in 0.18 minutes at 60°C if the a_w of the suspending medium is 0.995. If the a_w is lowered to 0.94, 4.3 min are required at 60°C to cause the same tenfold reduction.

An a_w value stated for a bacterium is generally the minimum a_w which supports growth. At the minimum aw, growth is usually minimal, increasing as the a_w increases. At a_w values below the minimum for growth, bacteria do not necessarily die, although some proportion of the population does die. The bacteria may remain dormant, but infectious. Most importantly, a_w is only one factor, and the other factors (e.g., pH, temperature) of the food must be considered. It is the interplay between factors that ultimately determines if a bacterium will grow or not. The a_w of a food may not be a fixed value; it may change over time, or may vary considerably between similar foods from different sources.

pH: (hydrogen ion concentration, relative acidity or alkalinity). The pH range of a microorganism is defined by a minimum value (at the acidic end of the scale) and a maximum value (at the basic end of the scale). There is a pH optimum for each microorganism at which growth is maximal. Moving away from the pH optimum in either direction slows microbial growth.

A range of pH values is presented here, as the pH of foods, even those of a similar type, varies considerably. Shifts in pH of a food with time

may reflect microbial activity, and foods that are poorly buffered (i.e., do not resist changes in pH), such as vegetables, may shift pH values considerably. For meats, the pH of muscle from a rested animal may differ from that of a fatigued animal.

A food may start with a pH which precludes bacterial growth, but as a result of the metabolism of other microbes (yeasts or molds), pH shifts may occur and permit bacterial growth.

Temperature. Temperature values for microbial growth, like pH values, have a minimum and maximum range with an optimum temperature for maximal growth. The rate of growth at extremes of temperature determines the classification of an organism (e.g., psychrotroph, thermotroph). The optimum growth temperature determines its classification as a thermophile, mesophile, or psychrophile.

INTERPLAY OF FACTORS AFFECTING MICROBIAL GROWTH IN FOODS: Although each of the major factors listed above plays an important role, the interplay between the factors ultimately determines whether a microorganism will grow in a given food. Often, the results of such interplay are unpredictable, as poorly understood synergism or antagonism may occur. Advantage is taken of this interplay with regard to preventing the outgrowth of *C. botulinum*. Food with a pH of 5.0 (within the range for *C. botulinum*) and an a_w of 0.935 (above the minimum for *C. botulinum*) may not support the growth of this bacterium. Certain processed cheese spreads take advantage of this fact and are therefore shelf stable at room temperature even though each individual factor would permit the outgrowth of *C. botulinum*.

Therefore, predictions about whether or not a particular microorganism will grow in a food can, in general, only be made through experimentation. Also, many microorganisms do not need to multiply in food to cause disease.

Factors affecting growth of pathogens in foods.

pH values of some foods

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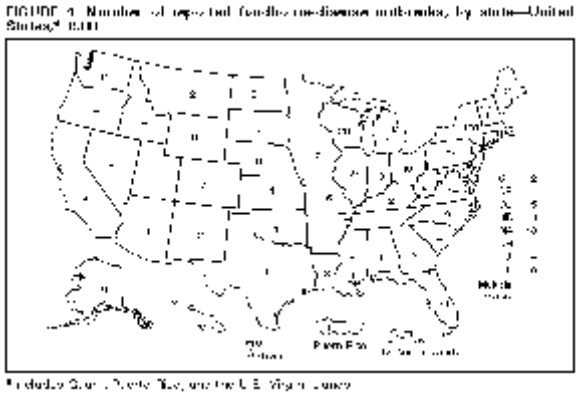
Foodborne Disease Outbreaks in the United States, graphs for 1988-1992

- Click on the links below the image to see a large version of each annual graph.



Outbreaks 1988

Outbreaks 1989

Outbreaks 1990

Outbreaks 1991

Outbreaks 1992

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Foodborne Disease Outbreak Articles and Databases of Interest

"Impact of Changing Consumer Lifestyles on the Emergence and Reemergence of Foodborne Pathogens", Emerging Infectious Diseases 3(4)1997.	Foodborne illness of microbial origin is the most serious food safety problem in the United States. The Centers for Disease Control and Prevention reports that 79% of outbreaks between 1987 and 1992 were bacterial; improper holding temperature and poor personal hygiene of food handlers contributed most to disease incidence. Some microbes have demonstrated resistance to standard methods of preparation and storage of foods. Nonetheless, food safety and public health officials attribute a rise in incidence of foodborne illness to changes in demographics and consumer lifestyles that affect the way food is prepared and stored. Food editors report that fewer than 50% of consumers are concerned about food safety. An American Meat Institute (1996) study details lifestyle changes affecting food behavior, including an increasing number of women in the workforce, limited commitment to food preparation, and a greater number of single heads of households. Consumers appear to be more interested in convenience and saving time than in proper food handling and preparation.
"Quantitative Risk Assessment: An Emerging Tool for Emerging Foodborne Pathogens", Emerging Infectious Diseases 3(4) 1997.	New challenges to the safety of the food supply require new strategies for evaluating and managing food safety risks. Changes in pathogens, food preparation, distribution, and consumption, and population immunity have the potential to adversely affect human health. Risk assessment offers a framework for predicting the impact of changes and trends on the provision of safe food. Risk assessment models facilitate the evaluation of active or passive changes in how foods are produced, processed, distributed, and consumed.

"Outbreak Investigations: A Perspective", Emerging Infectious Diseases 4(1) 1998.	Outbreak investigations, an important and challenging component of epidemiology and public health, can help identify the source of ongoing outbreaks and prevent additional cases. Even when an outbreak is over, a thorough epidemiologic and environmental investigation often can increase our knowledge of a given disease and prevent future outbreaks. Finally, outbreak investigations provide epidemiologic training and foster cooperation between the clinical and public health communities.
National Center for Environmental Health, Diseases Transmitted through the Food Supply	The objective of Environmental Health Services (EHS) is to strengthen the role of state, local, and national environmental public health programs and professionals to better anticipate, identify, and respond to adverse environmental exposures and the consequences of these exposures to human health. Section 103(d) of the Americans with Disabilities Act of 1990, Public Law 101-336, requires Secretary the Department of Health and Human Services to: 1. Review all infectious and communicable diseases which may be transmitted through handling the food supply; 2. Publish a list of infectious and communicable diseases which are transmitted through handling the food supply; 3. Publish the methods by which such diseases are transmitted; 4. Widely disseminate such information regarding the list of diseases and their modes of transmissibility to the general public; 5. Additionally, update the list annually.
Food Safety and Inspection Service Pathogen Reduction/HACCP & HACCP Implementation	FSIS links to federal documents concerning "Hazard Analysis Critical Control Points" implementation.
Food Safety and Inspection Service Active Recall Information Center	This page contains summary data on active recall cases. When a recall is completed, it will be removed from this listing, but will be included in the Recall Case Archive.
Food Safety and	The Office of Public Health and Science (OPHS) provides expert scientific analysis, advice, data, and

Inspection Service Office of Public Health and Science Publications	recommendations on all matters involving public health and science that are of concern to FSIS.
Food Safety and Inspection Service Food Safety Publications	Disaster Assistance, Fact Sheets, Food Safety Features, Food Safety Focus (Background), Seasonal Features (Press Kits) from the Meat and Poultry Hotline, Consumer Information From USDA, some available as one-page reproducibles), Brochures, Graphics, For Children, News Feature Stories and Technical Information From FSIS.

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NCBI/NLM/NIH Entrez Glossary

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acanthamoeba
A genus of free-living soil amoebae that produces no flagellate stage. Its organisms are pathogens for several infections in humans and have been found in the eye, bone, brain, and respiratory tract

acanthamoeba keratitis
Infection of the cornea by an ameboid protozoan which may cause corneal ulceration leading to blindness

acquired immunodeficiency syndrome
An acquired defect of cellular immunity associated with infection by the human immunodeficiency virus (HIV), a CD4-positive T-lymphocyte count under 200 cells/microliter or less than 14% of total lymphocytes, and increased susceptibility to opportunistic infections and malignant neoplasms. Clinical manifestations also include emaciation (wasting) and dementia. These elements reflect criteria for AIDS as defined by the CDC in 1993

adenosine diphosphate glucose
Serves as the glycosyl donor for formation of bacterial glycogen, amylose in green algae, and amylopectin in higher plants

adenoviridae
A family of non-enveloped viruses infecting mammals (MASTADENOVIRUS) and birds (AVIADENOVIRUS). Infections may be asymptomatic or result in a variety of diseases

adenoviridae infections
Virus diseases caused by the ADENOVIRIDAE

aeromonas hydrophila
A species of gram-negative, facultatively anaerobic, rod-shaped bacteria that may be pathogenic for frogs, fish, and mammals, including man. In humans, cellulitis and diarrhea can result from infection with this organism

aflatoxin b1
6aR-cis-2,3,6aalpha,9aalpha-Tetrahydro-4-methoxycyclopenta(c)furo(3',2':4,5)furo(2,3-h)(1)benzopyran-1,11-dione. The compound is a potent hepatotoxic and hepatocarcinogenic mycotoxin produced by the Aspergillus flavus group of fungi. It is also mutagenic, teratogenic, and causes immunosuppression in animals. It is found as a contaminant in peanuts, cottonseed meal, corn, and other grains. The mycotoxin requires epoxidation to aflatoxin B1-2,3-oxide for activation. Microsomal monooxygenases biotransform the toxin to the less toxic metabolites aflatoxin M1 and Q1

aflatoxins
A group of closely related toxic metabolites that are designated mycotoxins. They are produced by Aspergillus flavus and A. parasiticus. Members of the group include AFLATOXIN B1, aflatoxin B2, aflatoxin G1, aflatoxin G2, AFLATOXIN M1, and aflatoxin M2

aids-related complex
A prodromal phase of infection with the human immunodeficiency virus (HIV). Laboratory criteria separating AIDS-related complex (ARC) from AIDS include elevated or hyperactive B-cell humoral immune responses, compared to depressed or normal antibody reactivity in AIDS; follicular or mixed hyperplasia in ARC lymph nodes, leading to lymphocyte degeneration and depletion more typical of AIDS; evolving succession of histopathological lesions such as localization of Kaposi's sarcoma, signaling the transition to the full-blown AIDS

amanitins
A group of very potent toxins from Amanita species which cause lethal liver and kidney damage and inhibit some RNA synthesis

amebiasis
Infection with any of various amebae. It is an asymptomatic carrier state in most individuals, but diseases ranging from chronic, mild diarrhea to fulminant dysentery may occur

amphotericin b
Polyene antifungal antibiotic produced by Streptomyces nodosus obtained from soil of the Orinoco river region of Venezuela

ampicillin

6-((Aminophenylacetyl)amino)-3,3-dimethyl-7-oxo-4-thia-1- azabicyclo(3.2.0)heptane-2-carboxylic acid. Semi-synthetic derivative of penicillin that functions as an orally active broad-spectrum antibiotic

ampicillin resistance
Nonsusceptibility of a microbe to the action of ampicillin, a penicillin derivative that interferes with cell wall synthesis

anaphylatoxins
The family of peptides C3a, C4a, C5a, and C5a des-arginine produced in the serum during complement activation. They produce smooth muscle contraction, mast cell histamine release, affect platelet aggregation, and act as mediators of the local inflammatory process. The order of anaphylatoxin activity from strongest to weakest is C5a, C3a, C4a, and C5a des-arginine. The latter is the so-called "classical" anaphylatoxin but shows no spasmogenic activity though it contains some chemotactic ability

anemia hemolytic
Anemia due to decreased life span of erythrocytes

antacids
Substances that counteract or neutralize acidity. They are used mainly for the treatment of gastrointestinal irritation or ulcers

antinematodal agents
Substances used in the treatment or control of nematode infestations. They are used also in veterinary practice

appendicitis
Acute inflammation of the vermiform appendix

astroviruses
Small (approximately 28nm diameter) circular viruses sometimes showing a star-shaped surface configuration, found in stools of vertebrates with infantile gastroenteritis. The taxonomic status is uncertain though a relationship to Picornaviridae has been suggested

atropine
A toxic alkaloid, originally from Atropa belladonna, but found in other plants, mainly Solanaceae. It is used as an antimuscarinic agent for relaxation of smooth muscle, to increase heart rate, as an anesthetic premedication, as an antispasmotic, in anticholinesterase poisoning, in aspiration pneumonitis, in bronchial disorders, or to dilate the pupil, among other uses

atropine derivatives
Analogs and derivatives of atropine

bacillus anthracis

A species of bacteria that causes ANTHRAX in humans and animals

bacillus subtilis
A species of gram-positive bacteria that is a common soil and water saprophyte

bacillus thuringiensis
A species of gram-positive bacteria which may be pathogenic for certain insects. It is used for the biological control of the Gypsy moth

bacteremia
The presence of viable bacteria circulating in the blood. Fever, chills, tachycardia, and tachypnea are common acute manifestations of bacteremia. The majority of cases are seen in already hospitalized patients, most of whom have underlying diseases or procedures which render their bloodstreams susceptible to invasion

bacterial toxins
Toxic substances formed in or elaborated by bacteria; they are usually proteins with high molecular weight and antigenicity; some are used as antibiotics and some to skin test for the presence of or susceptibility to certain diseases

botulinum toxins
Toxins produced by Clostridium botulinum. There are at least seven different substances, most being proteins. They have neuro-, entero-, and hemotoxic properties, are immunogenic, and include the most potent poisons known. The most commonly used apparently blocks release of acetylcholine at cholinergic synapses

botulism
A disease caused by potent protein neurotoxins produced by CLOSTRIDIUM BOTULINUM. Characteristics include abdominal pain, vomiting, motor disturbances, and visual difficulties. The Centers for Disease Control and Prevention classify botulism into four types: (1) food-borne; (2) infant; (3) wound; and (4) indeterminate

bungarotoxins
Neurotoxic proteins from the venom of the banded or Formosan krait (Bungarus multicinctus, an elapid snake). alpha-Bungarotoxin blocks nicotinic acetylcholine receptors and has been used to isolate and study them; beta- and gamma-bungarotoxins act presynaptically causing acetylcholine release and depletion. Both alpha and beta forms have been characterized, the alpha being similar to the large, long or Type II neurotoxins from other elapid venoms

calicivirus
A genus in the family Caliciviridae containing many species including feline calicivirus (CALICIVIRUS, FELINE), VESICULAR EXANTHEMA OF SWINE VIRUS, and San Miguel sea lion viruses

campylobacter
A genus of bacteria found in the reproductive organs, intestinal tract, and oral cavity of animals and man. Some species are pathogenic

campylobacter coli
A species of gram-negative, rod-shaped bacteria isolated from the intestinal tract of swine, poultry, and man. It may be pathogenic

campylobacter fetus
A species of bacteria present in man and many kinds of animals and birds, often causing infertility and/or abortion

campylobacter infections
Infections with bacteria of the genus CAMPYLOBACTER

campylobacter jejuni
A species of bacteria that resemble small tightly coiled spirals. Its organisms are known to cause abortion in sheep and fever and enteritis in man and may be associated with enteric diseases of calves, lambs, and other animals

cd4-positive t-lymphocytes
A critical subpopulation of regulatory T-lymphocytes involved in the induction of most immunological functions. The HIV virus has selective tropism for the T4 cell which expresses the CD4 phenotypic marker, a receptor for HIV. In fact, the key element in the profound immunosuppression seen in HIV infection is the depletion of this subset of T-lymphocytes, which includes both the helper-inducer (T-LYMPHOCYTES, HELPER-INDUCER) and suppressor-inducer (T-LYMPHOCYTES, SUPPRESSOR-INDUCER) T-cells

cd8-positive t-lymphocytes
A critical subpopulation of regulatory T-lymphocytes involved in MHC Class I-restricted interactions. They are include both cytotoxic T-lymphocytes (T-LYMPHOCYTES, CYTOTOXIC) and suppressor T-lymphocytes (T-LYMPHOCYTES, SUPPRESSOR-EFFECTOR)

chlortetracycline
(4S-(4 alpha,4a alpha,5a alpha,6 beta,12a alpha))-7-Chloro-4-dimethylamino-1,4,4a,5,5a,6,11,12,12a-octahydro-3,6,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenecarboxamide. An antibiotic substance isolated from the substrate of Streptomyces aureofaciens and used as an antibacterial and antiprotozoal agent

cholecystitis
Inflammation of the gallbladder

cholera
An acute diarrheal disease endemic in India and Southeast Asia whose causative agent is VIBRIO CHOLERAE. This condition can

lead to severe dehydration in a matter of hours unless quickly treated

cholera toxin
The exotoxin from Vibrio cholerae. It is a protein that consists of two major components, the heavy (H) or A peptide and the light (L) or B peptide or choleragenoid which binds the whole protein to cell membranes, is nontoxic, but immunogenic. The A fragment causes cholera, probably due to the activation of adenylate cyclase; it consists of two polypeptide fragments

cimetidine
Blocker of histamine H2 receptors that decreases gastric acid secretion and reduces pepsin output. It is used to treat gastrointestinal ulcers

citrobacter freundii
A species of gram-negative, facultatively anaerobic, rod-shaped bacteria found in man and other animals including mammals, birds, reptiles, and amphibians. Its organisms have also been isolated from soil and water as well as from clinical specimens such as urine, throat, sputum, blood, and wound swabs as an opportunistic pathogen

clostridium perfringens
The most common etiologic agent of GAS GANGRENE. It is differentiable into several distinct types based on the distribution of twelve different toxins

colitis ulcerative
Inflammatory disease of unknown cause which involves the mucosa of the colon. Onset may be acute and fulminant, and its course often continues chronically in an intermittent or continuous form. Diarrhea is a common symptom and bleeding an almost constant concomitant symptom

coma
A profound state of unconsciousness. It includes "stupor" from which the patient can be partially roused, as well as complete unconsciousness in which there is no response to sensory stimuli, even at the reflex level

convulsions
Seizures manifested by discontinuous involuntary skeletal muscular contractions, either brief contractions repeated at short intervals or longer ones interrupted by intervals of muscular relaxation

convulsions febrile
Seizures occurring in young children during febrile episodes due to a low convulsive threshold. The convulsions are usually a self-limiting disorder after the age of 5 years

crohn disease
Gastrointestinal disorder characterized by chronic inflammatory infiltrates, fibrosis affecting all layers of the serosa, and development of noncaseating granulomas. The most common site of involvement is the terminal ileum with the colon as the second most common

cryptosporidiosis
Parasitic intestinal infection with severe diarrhea caused by a protozoan, CRYPTOSPORIDIUM. It occurs in both animals and humans

cytotoxins
Substances elaborated by microorganisms, plants or animals that are specifically toxic to individual cells; they may be involved in immunity or may be contained in venoms

dermotoxins
Specific substances elaborated by plants, microorganisms or animals that cause damage to the skin; they may be proteins or other specific factors or substances; constituents of spider, jellyfish or other venoms cause dermonecrosis and certain bacteria synthesize dermolytic agents

diabetes mellitus
A heterogeneous group of disorders that share glucose intolerance in common

dinoflagellida
Protozoans of the class PHYTOMASTIGOPHORA, found mainly in the oceans. They are characterized by the presence of transverse and longitudinal flagella which propel the organisms in a rotating manner through the water

endotoxins
Toxins closely associated with the living cytoplasm or cell wall of certain microorganisms, which do not readily diffuse into the culture medium, but are released upon lysis of the cells

enterobacteriaceae
A family of gram-negative, facultatively anaerobic, rod-shaped bacteria that do not form endospores. Its organisms are distributed worldwide with some being saprophytes and others being plant and animal parasites. Many species are of considerable economic importance due to their pathogenic effects on agriculture and livestock

enterobacteriaceae infections
Infections with bacteria of the family ENTEROBACTERIACEAE

enterotoxins
Substances that are toxic to the intestinal tract causing vomiting, diarrhea, etc.; most common enterotoxins are produced by bacteria

enzyme-linked immunosorbent assay
An immunoassay utilizing an antibody labeled with an enzyme marker such as horseradish peroxidase. While either the enzyme or the antibody is bound to an immunosorbent substrate, they both retain their biologic activity; the change in enzyme activity as a result of the enzyme-antibody-antigen reaction is proportional to the concentration of the antigen and can be measured spectrophotometrically or with the naked eye. Many variations of the method have been developed

eosinophils
Granular leukocytes with a nucleus that usually has two lobes connected by a slender thread of chromatin, and cytoplasm containing coarse, round granules that are uniform in size and stainable by eosin

erabutoxins
Toxins isolated from the venom of Laticauda semifasciata, a sea snake (Hydrophid); immunogenic, basic polypeptides of 62 amino acids, folded by four disulfide bonds, block neuromuscular end-plates irreversibly, thus causing paralysis and severe muscle damage; they are similar to Elapid neurotoxins

erythromycin
Antibiotic substance produced by Streptomyces erythreus found first in a soil sample from the Philippines. Three erythromycins are produced during fermentation - A, B, and C. Erythromycin A is the major component

exotoxins
Toxins produced, especially by bacterial or fungal cells, and released into the culture medium or environment

gastric acid
Hydrochloric acid present in gastric juice

gastric acidity determination
Gastric analysis for determination of free acid or total acid

giardiasis
An infection of the small intestine caused by the flagellated protozoan GIARDIA LAMBLIA. It is spread via contaminated food and water and by direct person-to-person contact

glucose
D-Glucose. A primary source of energy for living organisms. It is naturally occurring and is found in fruits and other parts of plants in its free state. It is used therapeutically in fluid and nutrient replacement

glucose-6-phosphatase

An enzyme that catalyzes the conversion of D-glucose 6-phosphate and water to D-glucose and orthophosphate. EC 3.1.3.9

glucose dehydrogenases
D-Glucose:1-oxidoreductases. Catalyzes the oxidation of D-glucose to D-glucono-gamma-lactone and reduced acceptor. Any acceptor except molecular oxygen is permitted. Includes EC 1.1.1.47; EC 1.1.1.118; EC 1.1.1.119 and EC 1.1.99.10

gram-negative bacteria
Bacteria which lose crystal violet stain but are stained pink when treated by Gram's method

gram-negative bacterial infections
Infections caused by bacteria that show up as pink (negative) when treated by the gram-staining method

gram-positive bacteria
Bacteria which retain the crystal violet stain when treated by Gram's method

gram-positive bacterial infections
Infections caused by bacteria that retain the crystal violet stain (positive) when treated by the gram-staining method

gram-positive cocci
Coccus-shaped bacteria that retain the crystal violet stain when treated by Gram's method

gram-positive endospore-forming bacteria
Bacteria that form endospores and are gram-positive. Representative genera include BACILLUS, CLOSTRIDIUM, MICROMONOSPORA, SACCHAROPOLYSPORA, and STREPTOMYCES

gram-positive rods
A large group of rod-shaped bacteria that retains the crystal violet stain when treated by Gram's method

hemagglutinins
Agents that cause agglutination of red blood cells. They include antibodies, blood group antigens, lectins, autoimmune factors, bacterial, viral, or parasitic blood agglutinins, etc

hemolytic-uremic syndrome
Syndrome of hemolytic anemia, thrombocytopenia, and acute renal failure, with pathological finding of thrombotic microangiopathy in kidney and renal cortical necrosis

hepatitis a

Hepatitis caused by HEPATOVIRUS. It can be transmitted through fecal contamination of food or water

hepatitis a virus
A genus of PICORNAVIRIDAE causing infectious hepatitis naturally in humans and experimentally in other primates. It is transmitted through fecal contamination of food or water

hepatitis antibodies
Immunoglobulins raised by any form of viral hepatitis; some of these antibodies are used to diagnose the specific kind of hepatitis

hepatitis e virus
A positive-stranded RNA virus causing enterically-transmitted non-A, non-B hepatitis (HEPATITIS E). The morphological and physiochemical properties suggest that it is a member of the calicivirus family (CALICIVIRIDAE)

histamine
The procedure of assaying for histamine concentration

hla-b27 antigen
Human histocompatibility (HLA) surface antigen encoded by the B locus on chromosome 6. It is strongly associated with acute anterior uveitis, ankylosing spondylitis, and Reiter's disease

hla-b7 antigen
Human histocompatibility (HLA) surface antigen encoded by the B locus on chromosome 6. There is a weak association between the presence of the HLA-B7 antigen and the diseases of narcolepsy and idiopathic hemochromatosis. HLA-B7 is in linkage disequilibrium with HLA-A3 and HLA-DR2

ibotenic acid
alpha-Amino-3-hydroxy-5-isoxazoleacetic acid. Neurotoxic isoxazole substance found in Amanita muscaria and A. pantherina. It causes motor depression, ataxia, and changes in mood, perceptions and feelings, and is a potent excitatory amino acid agonist

immunocompromised host
A human or animal whose immunologic mechanism is deficient because of an immunodeficiency disorder or other disease or as the result of the administration of immunosuppressive drugs or radiation

ketoconazole
1-Acetyl-4-[4-[(2-(2,4-dichlorophenyl)-2- (1H-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl)methoxy] -phenyl]-cis-piperazine. Broad spectrum antifungal agent used for long periods at high doses, especially in immunosuppressed patients

lectins
Protein or glycoprotein substances, usually of plant origin, that bind to sugar moieties in cell walls or membranes and thereby change the physiology of the membrane to cause agglutination, mitosis, or other biochemical changes in the cell

leukocytes
White blood cells. These include granular leukocytes (BASOPHILS, EOSINOPHILS, and NEUTROPHILS) as well as non-granular leukocytes (LYMPHOCYTES and MONOCYTES)

listeria
A genus of bacteria which may be found in the feces of animals and man, on vegetation, and in silage. Its species are parasitic on cold-blooded and warm-blooded animals, including man

listeria infections
Infections with bacteria of the genus LISTERIA

listeria monocytogenes
A species of gram-positive, rod-shaped bacteria widely distributed in nature. It has been isolated from sewage, soil, silage, and from feces of healthy animals and man. Infection with this bacterium leads to encephalitis, meningitis, endocarditis, and abortion

liver cirrhosis
Liver disease in which the normal microcirculation, the gross vascular anatomy, and the hepatic architecture have been variably destroyed and altered with fibrous septa surrounding regenerated or regenerating parenchymal nodules

marine toxins
Toxic or poisonous substances elaborated by marine flora or fauna. They include also specific, characterized poisons or toxins for which there is no more specific heading, like those from poisonous fishes. Clupeotoxin, pahutoxin, prymnesin, scombrotoxin go here

mebendazole
Methyl-5-benzoyl-2-benzimidazolecarbamate. A nematocide in humans and animals. It acts by interfering with the carbohydrate metabolism and associated energy production of the parasite

monocytes
Large, phagocytic mononuclear leukocytes produced in the vertebrate bone marrow and released into the blood; contain a large, oval or somewhat indented nucleus surrounded by voluminous cytoplasm and numerous organelles

muscarine
2-Methyl-3-hydroxy-5-(aminomethyl)tetrahydrofuran, trimethylammonium salt. A toxic alkaloid found in Amanita muscaria (fly

fungus) and other fungi of the Inocybe species. It is the first parasympathomimetic substance ever studied and causes profound parasympathetic activation that may end in convulsions and death. The specific antidote is atropine

muscimol
5-(Aminomethyl)-3-isoxazolol. Neurotoxic isoxazole isolated from Amanita muscaria and A. phalloides and also obtained by decarboxylation of IBOTENIC ACID. It is a potent agonist at GABA-A receptors and is used mainly as an experimental tool in animal and tissue studies

naegleria fowleri
A species of parasitic protozoa having both an ameboid and flagellate stage in its life cycle. Infection with this pathogen produces primary amebic meningoencephalitis

nematoda
A class of unsegmented helminths with fundamental bilateral symmetry and secondary triradiate symmetry of the oral and esophageal structures. Many species are parasites

ochratoxins
Toxins produced by Aspergillus ochraceus. Occurring widely, ochratoxins have been found as natural contaminants on storage grains, corn, peanuts, cottonseed, and decaying vegetation. They are produced by several other species of Aspergillus as well as by Penicillium viridicatum

oxytetracycline
(4S-(4 alpha,4a alpha,5a alpha,6 beta,12a alpha))-4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,6,10,12,12a-hexahydroxy-6-methyl-1,11-dioxo-2-naphthacenecarboxamide. An antibiotic substance isolated from the actinomycete Streptomyces rimosus and used in a wide variety of clinical conditions

paratyphoid fever
A prolonged febrile illness commonly caused by serotypes of Salmonella paratyphi. It is similar to typhoid fever but less severe

parvoviridae
A family of very small DNA viruses containing a single linear molecule of single-stranded DNA and consisting of three genera: DENSOVIRUS, DEPENDOVIRUS, and PARVOVIRUS. They infect both vertebrates and invertebrates

parvoviridae infections
Virus infections caused by the PARVOVIRIDAE

penicillin v

(2S-(2 alpha,5 alpha,6 beta)-3,3-Dimethyl-7-oxo-6-((phenoxyacetyl)amino)-4-thia-1- azabicyclo(3.2.0)heptane-2-carboxylic acid. A broad-spectrum penicillin antibiotic used orally in the treatment of mild to moderate infections by susceptible gram-positive organisms

peptic ulcer
Ulcer that occurs in those portions of the alimentary tract which come into contact with gastric juice containing pepsin and acid. It occurs when the amount of acid and pepsin is sufficient to overcome the gastric mucosal barrier

peptic ulcer perforation
Penetration of a peptic ulcer through the stomach wall. May be free, i.e., at a point where the stomach wall faces a real or potential space,, or confined, i.e., at a point where the stomach wall is defended by contiguous or adjacent structures, such as the pancreas

phytohemagglutinins
Mucoproteins isolated from the kidney bean (Phaseolus vulgaris); some of them are mitogenic to lymphocytes, others agglutinate all or certain types of erythrocytes or lymphocytes. They are used mainly in the study of immune mechanisms and in cell culture

phytoplankton
Minute plant organisms which live in practically all natural waters

picornaviridae
A family of small RNA viruses comprising some important pathogens of humans and animals. Transmission usually occurs mechanically. There are five genera: APHTHOVIRUS, CARDIOVIRUS, ENTEROVIRUS, HEPATOVIRUS, and RHINOVIRUS

picornaviridae infections
Virus diseases caused by the PICORNAVIRIDAE

plague
An acute infectious disease caused by YERSINIA PESTIS that affects humans, wild rodents, and their ectoparasites. This condition persists due to its firm entrenchment in sylvatic rodent-flea ecosystems throughout the world. Bubonic plague is the most common form

purpura
A group of disorders characterized by purplish or brownish red discoloration, easily visible through the epidermis, caused by hemorrhage into the tissues

purpura thrombocytopenic
Any form of purpura in which the platelet count is decreased. Many forms are thought to be caused by immunological mechanisms

reiter's disease

A triad of nongonococcal urethritis followed by conjunctivitis and arthritis, of unknown etiology

reoviridae
A family of unenveloped RNA viruses with cubic symmetry. The eight genera include ORTHOREOVIRUS, ORBIVIRUS, COLTIVIRUS, ROTAVIRUS, Aquareovirus, Cypovirus, Phytoreovirus, and Fijivirus

reoviridae infections
Infections produced by reoviruses, general or unspecified

reye's syndrome
An acute disease in children characterized by vomiting, hepatic injury with fatty vacuolization, central nervous system damage, and hypoglycemia

salmonella food poisoning
Poisoning caused by ingestion of food harboring species of SALMONELLA. Conditions of raising, shipping, slaughtering, and marketing of domestic animals contribute to the spread of this bacterium in the food supply

sanitation
The development and establishment of environmental conditions favorable to the health of the public

saxitoxin
Poison found in certain edible mollusks at certain times; elaborated by Gonyaulax species (Dinoflagellate protozoans) and consumed by mollusks, fishes, etc. without ill effects; it is neurotoxic and causes respiratory paralysis and other effects in mammals, known as paralytic shellfish poisoning

scarlet fever
Infection with group A streptococci that is characterized by tonsillitis and pharyngitis. An erythematous rash is commonly present

shigella
A genus of gram-negative, facultatively anaerobic, rod-shaped bacteria that ferments sugar without gas production. Its organisms are intestinal pathogens of man and other primates and cause bacillary dysentery (DYSENTERY, BACILLARY)

shigella boydii
One of the SHIGELLA species that produces bacillary dysentery (DYSENTERY, BACILLARY)

shigella dysenteriae
A species of gram-negative, facultatively anaerobic, rod-shaped bacteria that is extremely pathogenic and causes severe dysentery.

Infection with this organism often leads to ulceration of the intestinal epithelium

shigella flexneri
A bacterium which is one of the etiologic agents of bacillary dysentery (DYSENTERY, BACILLARY) and sometimes of infantile gastroenteritis

shigella sonnei
A lactose-fermenting bacterium causing dysentery

sinoatrial node
The small mass of modified cardiac muscle fibers located at the junction of the superior vena cava and right atrium. Contraction impulses probably start in this node, spread over the atrium and are then transmitted by the atrioventricular bundle to the ventricle

sodium channels
Cell membrane glycoproteins selective for sodium ions. Fast sodium current is associated with the action potential in neural membranes

spores
The reproductive elements of lower organisms, such as protozoa, fungi, and cryptogamic plants

staphylococcal food poisoning
Poisoning by staphylococcal toxins present in contaminated food

tetracycline
(4S-(4 alpha,4a alpha,5a alpha,6 beta,12a alpha))-4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,6,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenecarboxamide. An antibiotic originally produced by Streptomyces viridifaciens, but used mostly in synthetic form

tetracyclines
Broad-spectrum natural and semisynthetic antibiotics with a naphthacene structure obtained from various Streptomyces species

tetrodotoxin
Octahydro-12-(hydroxymethyl)-2-imino-5,9:7,10a-dimethano- 10aH-(1,3)dioxocino(6,5-a)pyrimidine-4,7,10,11,12-pentol. An aminoperhydroquinazoline poison found mainly in the liver and ovaries of fishes in the order Tetradontiformes (pufferfish, globefish, toadfish), which are eaten. The toxin causes paresthesia and paralysis through interference with neuromuscular conduction

thrombocytopenia
Decrease in the number of blood platelets

thrombosis
Formation, development, or presence of a thrombus. (Dorland 27th ed

toxins
Specific, characterizable, poisonous chemicals, often proteins, with specific biological properties, including immunogenicity, produced by microbes, higher plants, or animals

trimethoprim-sulfamethoxazole combination
4-Amino-N-(5-methyl-3-isoxazolyl)benzenesulfonamide mixture with 5-((3,4,5-trimethoxyphenyl)methyl)- 2,4-pyrimidinediamine. This drug combination has proved to be an effective therapeutic agent with broad-spectrum antibacterial activity against both gram-positive and gram-negative organisms. It is effective in the treatment of many infections, including Pneumocystis carinii pneumonia in AIDS, but is the drug of choice for urinary infection

typhoid
An acute enteric infection caused by SALMONELLA TYPHI

vibrio cholerae
The etiologic agent of CHOLERA

viremia
The presence of viruses in the blood

zooplankton
Minute free-floating animal organisms which live in practically all natural waters