



## **CHAPTER II: DISEASE CHARACTERIZATION AND PATHOGENESIS**

**June 2017**

The majority of foodborne diseases are caused by microbial pathogens such as **viruses**, **bacteria** and **parasites**. Although foodborne diseases are also caused by physical and/or chemical contamination, this chapter will focus primarily on the microbial agents.

Ingested pathogens, transmitted from contaminated foods, enter the body by way of the gastrointestinal (GI) tract. The body has defenses to fight these pathogens, but an overwhelming dose of pathogens or a weakened resistance can lead to illness. Certain populations such as the very young, the elderly, and some immunocompromised persons, are at higher risk for foodborne disease and for serious complications of foodborne disease. The severity of illness may be different among people eating the same contaminated food. The variability in illness severity is due to several factors including: the virulence of the pathogen, the health status of the host, and the concentration of the pathogen. The minimum dose of pathogens necessary to cause illness varies from organism to organism and host to host.

## A. Characteristics of Viruses, Bacteria and Parasites

**1. Viruses:** Viruses are minute organisms, smaller than bacteria and parasites, and are too small to be seen directly with a light microscope. Viruses can only replicate within living cells in the body of the host and cannot multiply in foods. However, some viruses survive in the environment, outside of the host, on objects, food and in contaminated water. Foodborne viruses cause infection and not intoxication.

Viruses that are associated with foodborne diseases are characterized by growth in the intestinal cells and subsequent excretion in the feces or in vomitus. Noroviruses are recognized as the leading cause of viral gastroenteritis and are increasingly being recognized as significant causes of foodborne illness in the U.S.

**2. Bacteria:** Bacteria are single-celled microorganisms which vary in shape and can be as small as 0.2 microns. In contrast to viruses, bacteria can be seen with a conventional microscope. Bacteria multiply by each cell splitting into two identical cells which grow to full size and divide into two again. Unlike viruses or parasites, bacteria ARE able to multiply in, or on, food. Under optimum conditions, large numbers can easily be achieved.

Some pathogenic bacteria, including *Bacillus cereus*, *Clostridium botulinum* and *Clostridium perfringens*, form spores that can survive adverse environmental conditions. Spore-forming pathogens are significant because when the spores occur in foods, they are more difficult to kill.

Pathogenic bacteria can cause foodborne infections OR intoxications. *Salmonella* is the leading documented cause of bacterial foodborne infections in this country. The bacteria that produce foodborne intoxications most often in the U.S. include *Bacillus cereus*, *Clostridium botulinum* and *Staphylococcus aureus*.

**3. Parasites:** Parasites are single or multi-celled organisms where one organism, the parasite, benefits at the expense of a host. Parasites are larger than viruses and bacteria, with dimensions usually greater than 10 microns. With regard to foodborne illness, parasites only cause infection, not intoxication. Similar to viruses, parasites do not multiply in foods, but can survive in the environment and thus be transported through food.

Parasites often go through structural changes during their life cycles. Cysts, eggs, larvae or other life forms can be ingested in food and develop into new parasites in the body. Transmission may also occur through contact with contaminated water, e.g. drinking or recreational. Outbreaks with *Giardia*, *Cryptosporidium* and *Cyclospora* are becoming more common in the U.S. Cases reported with *Trichinella* or *Taenia*, tapeworm, are rare.

## B. Classification of Foodborne Illness

**1. Foodborne Infection:** A foodborne infection is caused by ingestion of food or water contaminated by viruses, bacteria or parasites, and occurs in one of the following two ways:

- a) Viruses, bacteria or parasites in ingested food invade and multiply in the intestinal mucosa and/or other tissues. Examples of these organisms are bacteria such as *Salmonella* spp., *Vibrio parahaemolyticus*, and *Listeria monocytogenes*, parasites such as *Giardia*, *Cyclospora*, and *Cryptosporidium*, and the viruses, hepatitis A and norovirus.
- b) Bacteria in ingested food invade and multiply in the intestinal tract and then release a toxin(s) that damage surrounding tissues or interfere with normal organ or tissue function. This type of infection is sometimes referred to as a **toxin-mediated infection**. Examples of bacteria that cause toxin-mediated infection are Shiga toxin-producing *Escherichia coli* (STEC), *Shigella* spp., *Clostridium perfringens*, and *Clostridium botulinum* in infants. Viruses and parasites are not able to cause a toxin-mediated infection.

Onset of foodborne infections can take varying amounts of time from ingestion of pathogenic organisms to appearance of symptoms in the host. Thus, the incubation period is generally rather long, usually measured in days compared to hours for most foodborne intoxications. Symptoms of infection usually include diarrhea, nausea, vomiting and abdominal cramps. Fever is often associated with infection.

The organisms causing infection often possess colonization or adherence factors, allowing them to attach and to multiply in specific parts of the intestine. These organisms include *Salmonella*, *Shigella*, *Giardia* or *Vibrio*. Other organisms, such as hepatitis A virus and *Salmonella Typhi*, can move beyond the GI tract to infect other body sites such as the liver and blood stream.

Toxins produced by STEC and other toxigenic *E. coli* can adhere to cells in the intestines, kidneys, and central nervous system, prevent protein synthesis and cause cell death. Depending on the site of action, the result can be hemorrhagic colitis, hemolytic uremic syndrome (HUS) or thrombotic thrombocytopenic purpura (TTP).

Figure 2-1: Classification of *Escherichia coli* Associated with Diarrhea

<u>Type of <i>E. coli</i></u>	<u>Epidemiology</u>	<u>Type of Diarrhea</u>
Shiga toxin-producing <i>E. coli</i> (STEC)	Hemorrhagic colitis and hemolytic-uremic syndrome	Bloody or non-bloody in all ages
Enteropathogenic <i>E. coli</i> (EPEC)	Acute and chronic endemic and epidemic diarrhea in infants	Watery
Enterotoxigenic <i>E. coli</i> (ETEC)	Infant diarrhea in resource-limited countries and travelers' diarrhea in all ages	Watery
Enteroinvasive <i>E. coli</i> (EIEC)	Diarrhea with fever in all ages	Bloody or non-bloody, dysentery
Enteraggregative <i>E. coli</i> (EAEC)	Acute and chronic diarrhea in all ages	Watery, occasionally bloody

Source: Adapted from the American Academy of Pediatrics. *Red Book: 2015*. page 343.

Hemolytic Uremic Syndrome (HUS) is a life-threatening illness affecting the kidneys and clotting mechanisms of blood. In North America, it occurs commonly after an *E. coli* O157:H7 infection. It was first described in 1955, but not linked to *E. coli* O157:H7 until 1983. HUS predominantly affects infants and children and is the most common cause of acute renal failure in children. Thrombotic Thrombocytopenic purpura (TTP) is a syndrome similar to HUS, but more often seen in adults. Chronic medical conditions (sequelae) may be associated with infections from foodborne pathogens. The incidence of sequelae is unknown but is believed to be less than 5%.

**2. Foodborne Intoxication:** A foodborne intoxication is caused by ingestion of food already contaminated by a toxin. Sources of toxin are: 1) certain bacteria, 2) poisonous chemicals such as heavy metals, or 3) toxins found naturally or formed in animals, plants or fungi such as certain fish, shellfish and some wild mushrooms. **Viruses and parasites do not cause intoxication.**

Foodborne intoxications most often result from the release of toxins during bacterial growth in the food. The preformed toxin is ingested, thus live bacteria do not need to be consumed to cause illness. Microbial toxins such as botulinum toxin and many of the marine algal toxins are some of the most potent toxins known. Indications that a food contains a preformed toxin, like changes in appearance, odor or taste, are rare.

Illness from an intoxication manifests more rapidly because the body is affected quickly by the toxin or wants to expel it. Time for growth and invasion of the intestinal lining, as in an infection, is not required. The incubation period for intoxications is often measured in minutes or hours. For example, the incubation period for *Staphylococcus aureus* toxin-related illness is one to seven hours, with a mean of 2 to 4 hours. In cases of paralytic shellfish poisoning (PSP), caused by shellfish containing a potent algal toxin, symptoms may be experienced within 15 minutes of ingestion.

The most common or sometimes only symptom of intoxication is vomiting. Other symptoms can range from nausea and diarrhea to interference with sensory and motor functions such as taste, touch and muscle movements. These can include double vision, weakness, respiratory failure, numbness, tingling of the face and disorientation. Fever is rarely present with intoxication. For that reason, the absence of fever is important when trying to determine the cause of illness.

The ability to detect the toxin in food, therefore, is more important than the ability to detect bacterial cells. It is more expensive and technologically difficult to detect toxins than bacteria. Currently, animal bioassays are being replaced by new molecular methods. When testing for toxin in food is unavailable, identification of a large number of bacteria can be circumstantial evidence of toxin presence.

In North America, several kinds of seafood-associated (marine) toxins can cause illness:

- **Paralytic shellfish poisoning (PSP)** is transmitted to humans through mussels, oysters, clams and scallops that have ingested and concentrated toxic marine protozoa. The toxin is found mainly in coastal waters of northwestern and northeastern U.S., southern Chile, Japan and the North Sea and is often associated with a red discoloration of seawater due to algal bloom known as "red tide."
- **Diarrhetic shellfish poisoning** is also caused by ingestion of seafood containing toxic marine protozoa such as certain dinoflagellates which produce okadaic acid and related toxins. Illnesses have occurred in eastern Canada, Japan and Western Europe.
- **Amnesic shellfish poisoning** can result from eating shellfish that are contaminated with algae that produces domoic acid. Cases have occurred in eastern Canada, and northeastern and northwestern U.S.
- **Ciguatera poisoning** is a result of ingestion of ciguatoxin and related toxins, produced in tropical reef fish such as barracuda, snapper, mackerel, grouper and sea bass. Areas of higher risk are the Pacific and northern Caribbean. However, imported fish have occasionally caused outbreaks in the U.S.
- **Scombroid poisoning**, arising from bacterial spoilage of fish and subsequent production of histamine and related compounds, occurs more frequently than other seafood toxin poisonings. Tuna, mackerel, mahi-mahi, bluefish, sardines, and marlin are often implicated. This occurs worldwide with poor conditions of food storage.
- **Neurotoxic poisoning** is caused by another type of dinoflagellate with another toxin that occasionally accumulates in oysters, clams, and mussels from the Gulf of Mexico and the Atlantic coast of the southern states.

**None of these toxins mentioned above are destroyed by cooking.**

## C. Clinical Features of Foodborne Illness

### 1. Transmission of Pathogens

Most foodborne illness occurs through fecal-oral transmission in which a food contaminated with a disease-causing organism is eaten. Since we live in a microbial world there are many opportunities for this to happen in the continuum of food preparation and delivery. Some organisms are naturally found in the soil, can contaminate food and make people ill. Disease-causing organisms can be present in healthy animals raised for

food. These organisms can then be shed in animal feces and be deposited on food items or can infect other animals with which they have contact. Organisms found in the feces of infected animals can also be transferred from the intestines to meat and poultry during slaughter. Some animals harbor these pathogens in areas of their bodies other than their intestinal tract. In addition to being in the intestine, *Campylobacter* has been found in the liver of chickens. We now know that in addition to *Salmonella* being found on the outside of eggs due to fecal contamination, some types of *Salmonella* can silently infect the ovaries of hens which otherwise appear healthy and contaminate the inside of eggs before the shells are formed. In many instances, these animals show no signs of illness. Oysters and other filter feeding shellfish can concentrate organisms such as *Vibrio* and certain foodborne viruses such as norovirus.

A contaminated food item may result in infection if the raw contaminated food is not cooked long enough to kill the pathogen or is consumed raw, such as chicken, eggs or shellfish. Cooking utensils used on a raw contaminated food, then used on another uncooked food, can transfer the pathogen from one food to another, such as preparing raw chicken and using the same knife to prepare a salad. Non-contaminated product may become contaminated when handled by an ill food employee who failed to wash his/her hands after using the bathroom. Any of these routes of contamination may occur in either a home setting or in a commercial operation, such as a restaurant, and may result in one or two cases of illness or a large number of ill individuals.

## 2. Recognizing Foodborne Illness

The site of illness is usually limited to the gastrointestinal tract (GI) but certain pathogens can move beyond the GI tract to infect other areas of the body. The majority of cases can be described as short-term (24 to 48 hours) gastroenteritis of abrupt and sometimes violent onset, with median incubation periods ranging from two to 36 hours. Signs and symptoms of foodborne illness can range from mild gastrointestinal discomfort to severe reactions that can result in death. Although signs and symptoms vary, the most common are vomiting, abdominal cramps and diarrhea. Because many pathogens are excreted in the feces, infected persons not only experience illness themselves, but may be sources of infection to others.

Investigators often face the problem of having to implement control measures before an etiologic agent has been identified. It may be difficult to differentiate between the illnesses and pathogens involved without clinical or lab confirmation. Laboratory analysis is required to make a firm diagnosis, but attention to the onset and presence or absence of some symptoms may indicate the likely cause and permit a more efficient investigation.

Most cases of foodborne disease are single cases, and not associated with a recognized outbreak. Many occur secondary to exposures in the home or at a party, barbecue or picnic, as opposed to restaurant exposure. Single cases are difficult to associate with a particular food or establishment unless there is a distinctive clinical syndrome OR the same agent responsible for the illness is also identified in the food. An example of a distinctive clinical syndrome is fish-borne ciguatera poisoning that produces GI symptoms as well as pronounced and persistent neurosensory symptoms such as a sensation of loose teeth, the inability to identify hot by taste or touch, and numbness and pain in the extremities.

Outbreaks of foodborne disease are usually recognized by the occurrence of illness among people who eat one or more foods in common AND the illness occurs within a short period of time from each other. While laboratory analysis is pending, it is important to focus on the incubation period. The incubation period in relation to the clinical symptoms is useful in determining an etiologic agent.

## 3. High-Risk Populations

Certain populations of people are predisposed to prolonged, more frequent, and often more severe illness. As the population of the U.S. ages, an increasing percentage of the population is becoming more susceptible to



foodborne pathogens. Elderly individuals undergo a decrease in immune function. They are more susceptible to microbial infections and to the complications of diarrheal disease such as dehydration.

Individuals immunocompromised as a result of organ transplants, chemotherapy, or HIV/AIDS are also potentially at higher risk for certain foodborne illnesses. Their immune systems are often weakened from the disease process and/or the side effects of some treatments, reducing their ability to fight off infections and making them susceptible to many foodborne infections such as those caused by *listeria*, *shigella*, *salmonella* and *cryptosporidium*.

Other factors may also increase an individual's risk for foodborne illness. Pregnancy puts a woman and her fetus at risk for infections with *Listeria monocytogenes* or *Toxoplasma gondii*. Each of these organisms may cause abortion, stillbirth or fetal abnormality. According to the CDC, pregnant women are about 20 times more likely than other healthy adults to get listeriosis. Patients with sickle cell disease are at high risk of invasive *Salmonella* infection. Additionally, hospitalized persons are at increased risk for microbial infection. Children, in particular, are at risk of foodborne illness because their immune systems are still developing.

It is especially important for people at higher risk of foodborne illness to not eat unpasteurized milk and milk products, including cheese, butter, yogurt, pudding or ice cream; raw or undercooked eggs in items such as homemade frostings, mayonnaise, sunny-side-up eggs, fresh Caesar salad dressing, Hollandaise sauce, cookie dough and cake batter; raw or undercooked meat, particularly ground beef; unpasteurized juice; raw sprouts; raw nuts; raw shellfish; and honey for children less than a year old. These foods have significant possibilities of being contaminated and are dangerous for those at increased risk of foodborne illness. (1 & 2)

#### 4. Infective or Toxic Dose

The minimum infective or toxic dose of microorganisms needed to cause illness for an individual is difficult to determine because of all the variables described. Not everyone exposed to a contaminated food will become clinically ill. Doses necessary to cause illness can range from one to hundreds to millions of microorganisms.

Predictions have been made to determine the number of pathogens needed to cause illness. These predictions were developed from human feeding studies and are based on probability models, but should be interpreted with caution because of the limitations of sampling and laboratory methodology. The feeding trials are usually done with healthy young men who may report mild or no illness. In an actual outbreak, lower levels of pathogens may cause illness due to the variations of people involved. The food may also have a significant effect on infectivity. Certain foods, such as milk, which is rich in proteins, fats and sugars, may be especially efficient vehicles for transmission of infectious or toxic agents so that they enhance the probability of infection or illness.

Additionally, pathogens that cause illness differ greatly among types, genera, species and strains. Not all microorganisms sharing the same genus and species name (e.g., *Escherichia* is the genus and *coli* is the species) are identical, and they may differ greatly in their infectiousness. In fact, some may not be capable of causing human illness at all, while others are quite hazardous. High-risk individuals may require a much smaller number of pathogens to become ill.

**In summary**, the probability of infection and subsequent illness is a function of:

- the vulnerability of the host (e.g., age and immune response)
- the number of units of the infectious agent ingested (e.g. viral particles, bacterial cells, parasitic cysts); and
- the virulence or pathogenicity of the agent.

## D. The Carrier State

Foodborne disease carriers are individuals who harbor a specific infectious agent but do not exhibit symptoms of illness or disease. Because the agent is excreted in the feces, a carrier is a potential source of infection for others.

**Characteristics of carriers** are listed below:

1. Carriers may be people in the incubation phase (the period before symptoms appear) of an infection. In the period before illness, an infected person may excrete the infectious agent, such as the hepatitis A virus which can be excreted for as long as two weeks before symptoms appear, or norovirus which can be excreted in the few days before illness is noted.
2. Certain individuals who are exposed to a contaminated food, or become infected, never show any signs of illness but as healthy carriers can spread pathogens unknowingly to others. They may show no symptoms, either because they have a subclinical infection, or because they are only mildly infected. This is particularly dangerous in a food-handling setting.
3. Carriers may be people in the convalescent (recovery) stages of an illness. Certain microorganisms can be excreted into feces during the convalescent period, often 24-72 hours after symptoms cease. This is true for noroviruses, *Salmonella* species, and *Shigella* species. A small percentage of patients continue to excrete non-typhoidal *Salmonella* for more than one year.
4. The carrier state can be of short or long duration (temporary or chronic carrier). The carrier state usually ceases spontaneously after several weeks or a few months, but some individuals may become chronic carriers (e.g., for periods exceeding a year, for agents such as *Salmonella* Typhi).

Carrier states are important to remember when investigating and controlling foodborne illness. It is not only individuals with symptoms who are capable of transmission to others, but also those who are in the incubation or convalescent phases of illness and those who are asymptomatic. For example, when determining the close contacts of a hepatitis A case who need prophylactic treatment, it is necessary to identify the onset date of symptoms in the case and identify those individuals who may have had close contact with the case for as long as two weeks prior to that date.

## References:

(1) American Academy of Pediatrics. Appendix VI, Prevention of Infectious Disease from Contaminated Food Products. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report of the Committee on Infectious Diseases*. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015: pages 1004-1007.

(2) <https://www.fda.gov/food/foodborneillnesscontaminants/peopleatrisk//ucm352830.htm>

Website references on food safety from the American Academy of Pediatrics. *Red Book: 2015*:

[www.foodsafety.gov](http://www.foodsafety.gov)

[www.fightbac.org](http://www.fightbac.org)

[www.cdc.gov/food\\_safety](http://www.cdc.gov/food_safety)



For more information on organisms and their unique disease producing factors see:

<https://www.fda.gov/downloads/Food/FoodborneIllnessContaminants/UCM297627.pdf>

Heymann, D., ed. Control of Communicable Diseases Manual, 20th Edition, Washington DC, The American Public Health Association, 2014.