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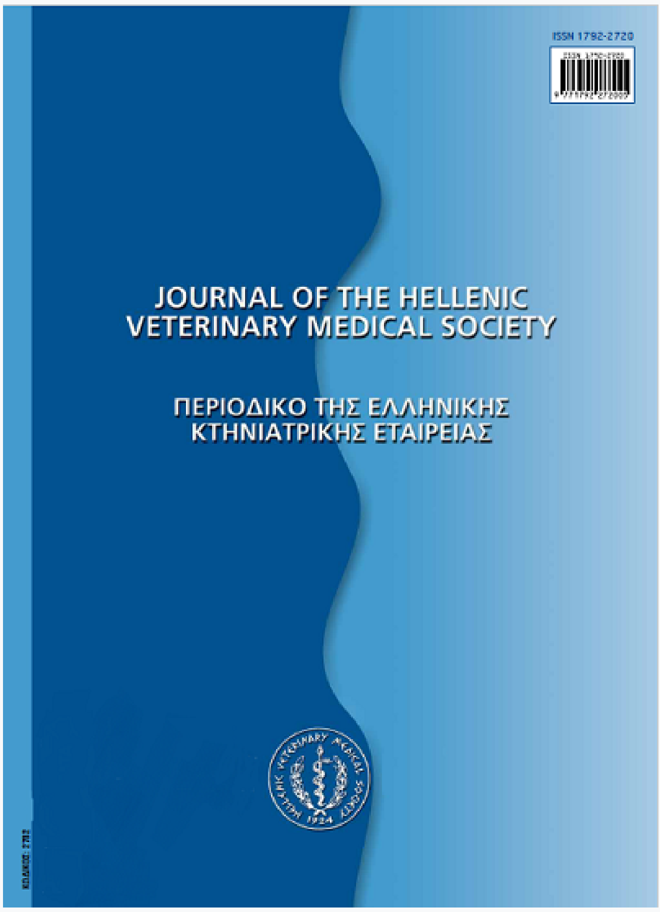

Shiga toxin-producing Escherichia coli (STEC) food-borne outbreaks

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Review article
Ανασκόπηση

Shiga toxin–producing *Escherichia coli* (STEC) food-borne outbreaks

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Τροφιμογενείς επιδημίες από Shiga-τοξινογόνα *Escherichia coli* (Shiga toxin-producing *E. coli*, STEC)

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ABSTRACT. *Escherichia coli (E. coli)* are Gram negative, non-sporulating bacteria, which belong to the normal intestinal flora of humans and animals. Shiga toxin-producing *E. coli* (STEC) are a group of *E. coli* that is defined by the capacity to produce toxins called Shiga toxins (Stx). Following ingestion of STEC, the significant risk of two serious and potentially life-threatening complications of infection, hemorrhagic colitis and hemolytic uremic syndrome (HUS), makes STEC food poisoning a serious public health problem. Besides Stx, human pathogenic STEC harbor additional virulence factors that are important for their pathogenicity. Although human infection may also be acquired by direct transmission from person to person or by direct contact of humans with animal carriers, the majority of STEC infections are food-borne in origin. The gastrointestinal tract of healthy ruminants seems to be the foremost important reservoir for STEC and ingestion of undercooked beef one of the most likely routes of transmission to humans. Other important food sources include faecally contaminated vegetables and drinking water.

The serogroup classification of STEC is based on the somatic (O) and flagellar (H) antigens, and, to date, more than 200 STEC serogroups have been identified. Human STEC infections are, however, associated with a minor subset of O:H serotypes. Of these, the O157:H7 or the O157:H- serogroups (STEC O157) are the ones most frequently reported to be associated with food-borne outbreaks. However other non-O157 STEC serogroups such as *E. coli* O26, O103, O111, O121, O45 and O145 have caused several outbreaks in recent years.

Two outbreaks of gastroenteritis caused by *E. coli* O157:H7 were first reported in the US, following the consumption of undercooked hamburgers, in 1982. Since then several outbreaks were reported worldwide. A major *E. coli* O157:H7 outbreak occurred in Japan and contaminated radish sprouts was identified as the vehicle of infection. More than 6,000 school children were affected, 101 people were hospitalized with HUS and 12 deaths were recorded. The recent outbreak of STEC O104:H4 infection and HUS reported in Germany in the spring of 2011 was one of the largest outbreaks worldwide. As of 27 July, 3126 cases of STEC infections, 773 cases of HUS including 46 deaths linked to the outbreak in Germany and occurring in the European Union (EU) (including Norway). Outside the EU 8 cases of STEC and 5 cases of HUS, including 1 death have been reported in the USA, Canada and Switzerland, all with recent travel history to Germany.

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The present review on major STEC food-borne outbreaks recorded worldwide highlights the need for control measures in order to prevent or at least minimize the occurrence of similar events in the future.

Keywords: *Escherichia coli*, Shiga toxin–producing *Escherichia coli* (STEC), food-borne outbreaks

ΠΕΡΙΛΗΨΗ. Η *Escherichia coli (E. coli)* είναι Gram-αρνητικό μη σπορογόνο βακτήριο που ανήκει στην εντερική χλωρίδα του ανθρώπου και των ζώων. Τα Shiga-τοξινογόνα *E. coli* (Shiga toxin-producing *E. coli*, STEC) αποτελούν μια υποομάδα των *E. coli*, που χαρακτηρίζεται από την ικανότητά τους να παράγουν τοξίνες, που ονομάζονται Shiga τοξίνες (Shiga-toxins, Stx). Οι τροφοδηλητηριάσεις από STEC συνιστούν πολύ σοβαρό πρόβλημα δημόσιας υγείας δεδομένου ότι οι προκαλούμενες λοιμώξεις χαρακτηρίζονται συχνά από σοβαρές και ενίοτε θανατηφόρες επιπλοκές όπως η αιμορραγική κολίτιδα και το αιμολυτικό ουραιμικό σύνδρομο (HUS). Εκτός από τις Stx, τα παθογόνα STEC διαθέτουν επιπρόσθετους παράγοντες παθογένειας που συμβάλλουν σημαντικά στην παθογόνο δράση. Παρότι η μόλυνση του ανθρώπου μπορεί να συμβεί και με άμεση διαπροσωπική επαφή ή μέσω επαφής με ζώα-φορείς του μικροβίου, η πλειοψηφία των περιστατικών είναι τροφιμογενούς αιτιολογίας. Ο εντερικός σωλήνας των θηλαστικών φαίνεται να είναι η σημαντικότερη δεξαμενή των STEC, ενώ η κατανάλωση ανεπαρκώς μαγειρευμένου βόειου κρέατος ένας από τους πλέον συνήθεις τρόπους μετάδοσης του μικροοργανισμού στον άνθρωπο. Νωπά λαχανικά αλλά και νερό που μολύνονται από κόπρανα θηλαστικών μπορούν να αποτελέσουν επίσης πιθανές πηγές μόλυνσης του ανθρώπου.

Η ταξινόμηση των STEC σε οροτυπικές ομάδες (serogroups) βασίζεται στα σωματικά (O) και βλεφαριδικά (H) αντιγόνα και μέχρι σήμερα περισσότερες από 200 οροτυπικές ομάδες έχουν αναγνωριστεί. Ωστόσο, οι λοιμώξεις από STEC φαίνεται να σχετίζονται με ένα περιορισμένο υποσύνολο O:H οροτύπων (serotypes). Από αυτούς οι ορότυποι O157:H7 ή O157:H- (STEC O157) είναι αυτοί που σχετίζονται συχνότερα με την πρόκληση τροφιμογενών επιδημιών. Ωστόσο, και άλλες STEC οροτυπικές ομάδες πέραν της O157, όπως οι E. coli O26, O103, O111, O121, O45 and O145 έχουν προκαλέσει επιδημίες στο πρόσφατο παρελθόν.

Δύο επιδημίες γαστρεντερίτιδας, ύστερα από κατανάλωση ατελώς μαγειρευμένων βόειων μπιφτεκιών μολυσμένων με *E. coli* O157:H7 πρωτοπεριγράφτηκαν στις ΗΠΑ το 1982. Έκτοτε πολλές επιδημίες έχουν περιγραφτεί παγκοσμίως. Μια εκτεταμένη επιδημία από *E. coli* O157:H7 συνέβη στην Ιαπωνία ύστερα από την κατανάλωση μολυσμένων τροφίμων φυτικής προέλευσης (ραπανάκια). Περισσότερα από 6000 παιδιά σχολικής ηλικίας προσβλήθηκαν, 101 άνθρωποι νοσηλεύτηκαν με HUS, ενώ 12 άνθρωποι κατέληξαν. Η πρόσφατη επιδημία από STEC O104:H4 στη Γερμανία την άνοιξη του 2011 ήταν μια από τις μεγαλύτερες σε παγκόσμια κλίμακα. Μέχρι τις 27 Ιουλίου του 2011, 3.126 άνθρωποι νόσησαν, 773 ανέπτυξαν HUS και 46 άτομα απεβίωσαν στην Ευρωπαϊκή Ένωση. Άλλα 8 άτομα νόσησαν σε ΗΠΑ, Καναδά και Ελβετία, από τα οποία 5 ανέπτυξαν HUS και 1 κατέληξε.

Η παρούσα ανασκόπηση που αφορά τις μεγαλύτερες επιδημίες που έχουν προκληθεί παγκοσμίως από STEC υπογραμμίζει την ανάγκη λήψης κατάλληλων μέτρων ελέγχου για την αποφυγή ή τουλάχιστο την ελαχιστοποίηση της επίπτωσης αντίστοιχων κρουσμάτων στο μέλλον.

Λέξεις ευρετηρίασης: *Escherichia coli*, Shiga toxin–producing *Escherichia coli* (STEC), food-borne outbreaks

INTRODUCTION

Shiga toxin–producing *Escherichia coli* (STEC), sometimes referred to as verocytotoxin-producing *E. coli* (VTEC) have emerged as significant etiological agents of food-borne infectious disease in various countries. A total of 3,573 confirmed STEC infections in humans were reported in the European Union in 2009 (EFSA 2011). In the United States it is estimated that STEC O157: H7 causes 63,153 illnesses annually. Non-O157 STEC is responsible for 112,752 illnesses. Foodborne ETEC is responsible for 17,894. Finally diarrheagenic *E. coli* other than STEC and ETEC are responsible for 11,982 illnesses annually (Scallan et al. 2011 a,b)

E. coli is a normal inhabitant of the mammalian intestinal tract (Karmali et al. 2010). Many strains are harmless or even beneficial to the host; however, some strains can be pathogenic to humans and animals since they carry or produce a plethora of virulence factors (EFSA 2011). The mechanisms of pathogenicity include the production of toxins and/or host cell attachment factors, and the invasion of colonic mucosal cells. Usually, a given infection involves more than one virulence factor. Based on virulence properties, mechanisms of pathogenicity, clinical syndromes, and distinct O:H serotypes diarrheagenic *E. coli* isolates are categorized into specific groups (pathotypes). These categories include enteropathogenic *E. coli* (EPEC), enterotoxigenic *E. coli* (ETEC), enteroinvasive *E. coli* (EIEC), diffuse-adhhering *E. coli* (DAEC), enteroaggregative *E. coli* (EAEC or EaggEC) and enterohemorrhagic *E. coli* (EHEC). Verocytotoxin-producing (Verocytotoxigenic) *E. coli* (VTEC) which may be referred to as Shiga toxins (Stx) producing *E. coli* (STEC) especially those causing haemorrhagic illnesses acquired significance for the food industry in the last 30 years (EFSA 2011, Bell and Kyriakidis 2009, Meng et al. 2007, Fratamico and Smith 2006).

STEC classification is based on the somatic (O) and flagellar (H) antigens, and more than 600 STEC serotypes (including 160 O serogroups and 60 H serogroups) have been identified to date. In humans, over 130 STEC serotypes can cause severe inflammation of the large intestine accompanied by haemorrhages of the intestinal mucosa and severe diarrhea (haemorrhagic colitis, HC), or haemolytic uraemic syndrome (HUS), which can lead to renal failure and even death (Thorpe 2004).

The vast majority of STEC reported outbreaks worldwide have been attributed to *E. coli* serogroup O157 and particularly to the *E. coli* O157:H7 serotype. However, other non-O157 *E. coli* serogroups such as *E. coli* O26, O103, O111, O121, O45 and O145 have been implicated in several outbreaks (Karmali 2004). The aim of the present work was to review selected major reported food-borne STEC outbreaks worldwide.

Characteristics of STEC

E. coli is a Gram-negative, facultative anaerobic, non-sporulating, motile bacterium and a member of the Enterobacteriaceae family. Most *E. coli* strains can grow at a temperature range from 10 to 46°C. Although the minimum temperature for growth of *E. coli* O157 in milk has been determined to be 8°C, certain *E. coli* strains can grow in milk at temperatures as low as 6.5 °C (D'Aoust et al. 1988). Optimum growth occurs at a_w 0.995 and the minimum a_w value is 0.950. Salt (NaCl) at 8.5 % inhibits the growth of *E. coli* O157. The optimum pH for growth is 6.0 to 8.0. Reported range for *E. coli* is 4.4 to 9.0 (EFSA 2011, Bell and Kyriakidis 2009, Meng et al. 2007, Fratamico and Smith 2006).

STEC are not heat resistant microorganisms. For *E. coli* O157, a D57°C value of 5 min, and a D63°C value of 0.5 min have been reported in meat. Results reported by D'Aoust et al. (1988) confirm that the high-temperature, short time process (71.7°C, 15 s), which is commonly used to pasteurize milk, is sufficient to kill approximately 1×10^5 *E. coli* O157:H7 ml^{-1}.

Most of STEC strains (including *E. coli* O157:H7) are unusually acid tolerant, being able to withstand exposure to extremely acidic conditions (pH 2.0), particularly when they are previously incubated at acidic pH environments (Brudzinski and Harrison 1998). For example O157:H7 survived for up to 2 months with only two decimal reductions in cell population during fermentation, drying and storage of fermented sausage; for 5-7 weeks in mayonnaise at 5°C and for 10-31 days in apple cider (Fratamico and Smith 2006). The acid resistance of most of STEC strains enables them to survive the acidic milieu of various foods as well as passage through the human stomach. Bacteria that are more resistant to the gastric environment have a greater opportunity to survive and therefore ultimately colonize the intestinal tract and cause illness.

STEC infection

STEC infection is usually acquired by the ingestion of contaminated food or water, by person-to-person transmission or contact with carrier animals (Karmali 2004). The main reservoirs for STEC are cattle and other farm ruminants such as sheep and goats. Wild ruminants, such as deer may also carry the pathogen (Karmali 2010). Foods of animal origin, such as meat (especially ground beef) and unpasteurized milk, are probably the major vehicles of human STEC infection (Karmali 2010). Other types of foods, however, such as unpasteurized fruit juices or raw vegetables contaminated with STEC may also act as vehicles of transmission (EFSA 2011, Karmali et al. 2010). STEC can also be transmitted by direct contact with carrier animals. Person-to person transmission is not uncommon. Waterborne transmission is also becoming increasingly recognized. Outbreaks have been associated with sharing of paddling pools and other communal bathing waters (Coia 1998). Thus, although infection may initially be acquired from a contaminated foodstuff, subsequent outbreak spread can occur by various routes (secondary infections) especially during the late stages of an outbreak.

The infectious dose of *E. coli* O157:H7 is very low, 10 to 100 cells. In one outbreak, the contamination level of *E. coli* O157:H7 in uncooked hamburger meat was found to be less than 700 cells/patty (Griffin 1998). In another outbreak the infectious dose of O157:H7 was found to be less than 50 cells (Tilden et al. 1996), and for the EHEC O111, less than 1 cell/10 g of salami was sufficient to induce HC (Paton et al.

1996). Because the infectious dose is so low, the capacity of *E. coli* strains to survive gastric exposure directly impacts their ability to cause illness.

After ingestion, *E. coli* bacteria rapidly multiply in the large intestine and bind tightly to cells in the intestinal lining. Inflammation caused by the toxins is believed to be the cause of HC, the first manifestation of *E. coli* infection, which is characterized by sudden onset of abdominal pain and severe cramps, followed by diarrhea within 24 hours (Fratamico and Smith 2006). HC typically occurs within 2 to 5 days of ingestion of STEC and is often complicated by potentially fatal systemic sequelae such as neurological damage and HUS, which occur within 2–14 days after the onset of diarrhea (Nishikawa 2011). HUS is defined by the triad of acute renal failure, thrombocytopenia, and microangiopathic hemolytic anemia and occurs in about one-tenth to one-fourth of cases (Karmali 2004). STEC infections that progress to HUS tend to be symptomatic, and there is a bimodal distribution in susceptibility to HUS, with children and the elderly being at highest risk. STEC infections can also result in a variant form of HUS, sometimes referred to as thrombotic thrombocytopenic purpura (TTP). This "diarrhea-associated TTP" is more common in adults, and patients are more often febrile with marked neurological involvement (Paton and Paton 1998). Non renal complications of STEC infections include ischemic colitis with colonic stenosis and, rarely, persistent pancreatitis with diabetes.

By definition, all STEC must produce Stx, but other virulence factors are also involved in pathogenesis and it is the possession of these that seems to determine the virulence of any given serotype. Such well-known factors include the ability to adhere to intestinal cells (*eaeA* gene), and the ability to produce haemolysin (*hlyA* gene) (EFSA 2011, Jaeger and Acheson 2000). The principal virulence factors associated with the severe sequelae of STEC infection are Stx. The Stx family consists of a number of structurally and functionally related protein toxins. The prototype of the family is elaborated by *Shigella dysenteriae* type 1 (Thorpe 2004). Stx are AB5 toxins consisting of an enzymatically active A subunit covalently associated with a pentameric B subunit that mediates binding to host cells. Briefly, Stx act as ribosome-inactivating toxins and inhibit synthesis of critical host proteins needed by the cell to survive and/or properly function (Thorpe 2004). The production of Stx in the gut lumen is strongly associated to HC. A small portion of Stx traverses the epithelium and then translocates to the circulation, where it causes vascular damage in specific target tissues such as the brain and kidneys, resulting in systemic complications (Griffin 1998). Stx are classified into two subgroups, Stx1 and Stx2. A variant of Stx1, named Stx1c, and several variants of Stx2, named Stx2c, Stx2d, Stx2e, and Stx2f, which differ in their biological activities and association with disease, have been reported (Nishikawa 2011, Thorpe 2004).

STEC food-borne outbreaks

Food-borne outbreaks of STEC infection, some involving hundreds of cases, have been documented in various countries and in a variety of settings (Karmali 2010). *E. coli* Serogroup O157 and particularly serotype O157:H7 were identified as the causative agents in most of them. Outbreaks have been caused by both O157 and non-O157 STEC (Tables 1 and 2).

STEC O157 food-borne outbreaks

E. coli O157:H7 was initially recognized as a food-borne pathogen in 1982, during outbreaks that occurred in the US following consumption of undercooked hamburger (Riley et al. 1983). Since then, many additional outbreaks of *E. coli* O157:H7 infections have been linked to the consumption of inadequately cooked hamburger meat. In the US, from 1982 to 2002, 350 outbreaks were reported, 183 (52%) were food-borne and the food vehicle for 41% of these was ground beef (Rangel et al. 2005). A state-wide *E. coli* O157:H7 outbreak in Washington State (US) from December 1992, through February 1993 was associated with the consumption of undercooked hamburger meat at a fast-food chain. In total, 501 cases were reported, including 151 hospitalizations (31%), 45 cases of HUS (9%), and three deaths (Bell et al. 1994). From December 1995 to March 1996, 28 children with HUS in Bavaria, Germany, were identified. This outbreak was caused by *E. coli* O157:H - and the consumption of two types of sausages, including one containing raw beef, was statistically related to illness (Ammon et al. 1999). In France, one outbreak of STEC O157 (69 cases, 17 HUS cases) occurred in 2005, linked to the consumption of contaminated ground beef (King et al. 2009). The same year, in the Netherlands steak

Table 1. Major recorded STEC O157 foodborne outbreaks worldwide.

Year	Country	STEC serogroup /serotype	Implicated food	No of people affected	References
1982-2002	USA	O157:H7	Various (41% ground beef)	183 foodborne outbreaks	Rangel et al. 2005
1992-1993	Washington State, USA	O157:H7	Undercooked hamburger meat	501 cases, 151 hospitalizations 45 HUS cases, 3 deaths	Bell et al. 1994
1995-1996	Bavaria, Germany	O157:H-	Two sausages (including a raw beef-containing sausage)	28 children with HUS	Ammon et al. 1999
1992-2008	England-Wales	STEC O157	Poultry meat (6.8%), bovine and Sheep meat (38.6%), salads, fruit	84 outbreaks; 1,168 cases (286 hospitalizations, 12 deaths)	Gorley et al. 2011
1994	Scotland	STEC O157	Milk	69 cases, 1 death	Upton and Coia, 1994
1995	France	STEC O157	Frozen beef burgers	69 cases, 17 HUS cases	King et al. 2009
1995	Netherlands	STEC O157	Steak tartare (raw beef product)	21 confirmed, 11 probable cases	Doorduyn et al. 2006
1996	Japan	O157:H7	Radish sprouts	> 6,000 (101 HUS cases, 11 deaths)	Michino et al. 1999
1996-2006	France	STEC O157 (66.67%)	Bovine meat, raw milk cheeses	641	Espie et al. 2008
1999	Canada	O157:H7	Sausage	143	McDonald et al. 2004
1999-2008	Scotland	STEC O157	Various types	2,298	Locking et al. 2011
2003	Denmark	O157:H-	Organic cow milk	25	Jensen et al. 2006
2003	Slovakia	STEC O157	Unpasteurised cow milk	9 (3 HUS cases)	Liptakova et al. 2004
2004-2007	New Mexico, USA	STEC O157	No data	4	Lathrop et al. 2009
2005	Holland	STEC O157	Steak tartare (raw bovine meat)	32	Doorduyn et al. 2006
2007	Scotland	STEC O157	Bovine meat	10	McCartney et al. 2010
2007	Iceland	STEC O157	Lettuce	9	Sigmundsdottir et al. 2007
2007	Netherlands	STEC O157	Iceberg lettuce	35	Friesema et al. 2007
2008	Connecticut, USA	STEC O157	Raw milk	14 cases (7 confirmed) (5 hospitalizations, 3 HUS cases)	Guh et al. 2010
2008	USA	STEC O157	Bovine meat	99	Nowicki et al. 2010
2009	Germany	O157:H-	No data	8 (4 HUS cases, 1 death)	Nielsen et al. 2011

tartare (a raw beef product) was revealed as the most likely cause of a STEC O157 outbreak. A total of 21 laboratory-confirmed cases and another 11 probable cases were reported (Doorduyn et al., 2006). In 2007, an outbreak of *E. coli* O157 infection in Scotland, in which 10 people were affected, was linked to cooked meat from a supermarket delicatessen (McCartney et al. 2010). Two multi-state outbreaks of STEC O157 were recorded during 2008 in the US. A total of 99 persons (64 and 35 from the first and the second outbreak, respectively) had confirmed illness after consuming ground beef (Nowicki et al. 2010). In a study of food-borne outbreaks recorded in England and Wales from 1992-2008, 103 STEC outbreaks were reported, 1,168 people affected, with 286 hospitalizations and 12 deaths (Gormley et al. 2011). These outbreaks were associated with consumption of red meats (38.6%), milk and milk products (29.5%), salad, vegetables, fruit (6.8%) and poultry meat (6.8%).

Several outbreaks of STEC infections have been also attributed to the consumption of raw milk and associated dairy products, particularly raw-milk cheeses. Studies show that *E. coli* O157 strains can survive various stages during cheesemaking (Baylis 2009). A milk-borne STEC O157 outbreak (69 cases, 1 death) was recorded in Scotland during 1994 (Upton and Coia 1994). In 2003, an outbreak of STEC O157 infection occurred in Slovakia. Three children suffered from HUS, two children had bloody diarrhoea, and four adults were asymptomatic carriers. Unpasteurised cow's milk was identified as the source of infection (Liptakova et al. 2004). Jensen et al. (2006) described the first outbreak of STEC (*E. coli* O157:H-) with 25 patients in Denmark, after consumption of a particular

Table 2. Major recorded non-O157 STEC food-borne outbreaks worldwide

Year	Country	STEC serogroup /serotype	Implicated food	No of people affected	Reference
1983-2002	USA	non-O157 STEC	Various types	320 (22% O26:H111,16% O111:H8, 12% O103:H2/H11, 8% O121:H19/H7, 7% O45:H2, 5% O145)	Brooks et al. 2005
1986	Japan	O111:H-	No data	23 children affected, 1 HUS cases, 1death	Tanaka et al. 1989
1992	Italy	O111	Unidentified	9 HUS cases; 1 child died	Caprioli et al. 1994
1995	South Australia	O111:H2.	Semi-dry fermented sausage (mettwurst)	21 HUS cases	Paton et al.1996
1996-2006	France	non-O157 STEC (33.33%)	Bovine meat, cheeses made from raw milk	320 (12.3% O26, 2.57% O80, 2.05% O111, 2.05% O55, 13.8% undetermined)	Espie et al. 2008
1999	USA	O111:H8	Lettuce	55 (2 HUS cases)	Brooks et al. 2004
2000	Germany	O26:H11	Bovine meat	11	Werber et al. 2002
2004-2007	New Mexico, USA	non-O157 STEC (64%)	No data	7 (18% O26, 13% O111, 33% O103, O121, O46, O177, O91)	Lathrop et al. 2009
2007	Belgium	O145:H28 O26:H11	Ice cream	12 (5 HUS cases)	Buvens et al. 2011
2008	USA	O158	Raw cow milk	14 (3 HUS cases)	Guh et al. 2010
2011	Germany & other countries	O104:H4	Raw vegetable sprouts	3.134 (778 HUS cases, 47 deaths)	EFSA 2011

kind of organic milk from a small dairy. In 2008, 14 cases (seven confirmed) of STEC infection were identified after consuming raw milk purchased at a retail market and a farm in Connecticut (US). Five patients required hospitalization and three experienced HUS (Guh et al. 2010). In a suspected milk-borne outbreak of *E. coli* 0157:H7-associated illness affecting kindergarten children, the organism was isolated from cattle at a farm where raw milk was served (Borczyk et al. 1987). Other foods that have been incriminated in STEC outbreaks include raw vegetables and salads, and one of the major such outbreaks took place in Japan in 1996. More than 6,000 school children were affected and radish sprouts contaminated with *E. coli* O157:H7 from a single farm were identified as the cause of infection. More than 101 people were hospitalized with HUS and 12 deaths were recorded (Michino et al. 1999). In 2007, a STEC O157 outbreak (33 patients) occurred in the Netherlands. Pre-packaged, shredded iceberg lettuce purchased from several supermarket chains was reported as the possible source (Friesema et al. 2007). Sigmundsdottir et al. (2007) reported that nine domestically acquired cases (seven hospitalizations) of STEC O157 were diagnosed in Iceland. It is interesting that the isolated strain, which was identified as the causative agent, was identical to the strain that caused the outbreak in the Netherlands. Indeed, as verified either by questionnaires or by supermarket purchase records, five cases had consumed lettuce packaged and imported from the Netherlands.

Non-O157 STEC food-borne outbreaks

Non-O157 STEC serotypes are increasingly being recognized as the causative agents in food-borne outbreaks (Table 2). The most striking evidence is the outbreak of STEC O104:H4 infection and HUS reported in Germany in the spring of 2011, which constituted one of the largest outbreaks ever described worldwide. As of 27 July, 3126 cases, including 17 deaths linked to the outbreak in Germany and occurring in the EU (including Norway). In addition, in the EU 773 cases of HUS (including 29 deaths) were linked to the German outbreak. Outside the EU 8 cases of STEC and 5 cases of HUS, including 1 death have been reported in the USA, Canada and Switzerland, all with recent travel history to Germany. The likely source of the outbreak was contaminated raw sprouts from one farm in Germany. An interesting characteristic in this outbreak is that the incriminated *E. coli* strain shows an unusual combination of virulence factors of STEC and EAEC which has been reported sporadically in humans before. Sequence analysis and comparative genomics will be able to show if the German outbreak strain is an EAEC that acquired EHEC virulence determinants or if it is the other way around (EFSA 2011). According to the information reported to the European Center for Disease Prevention and Control (ECDC 2011), there were 10 reported cases of STEC O104 infection in the EU Member States and Norway between 2004 and 2010. Moreover, a case of HUS, which occurred in Italy in 2009 has now been associated with STEC O104, resulting in a total of 11 cases.

Werber et al. (2002) recorded a STEC O26:H11 outbreak (11 cases) in Germany in 2000 and a certain type of beef ("seemerrolle") was revealed as the probable source of infection. In France, in 2005, one outbreak of STEC O26 and O80 involving 16 HUS cases was linked to the consumption of unpasteurized cows' cheese. Also, in France, evidence of STEC involvement in 590 (66%) of 900 HUS cases examined from 1996 to 2006 has been provided; thirty-five (6%) patients had been infected with STEC O26, 15 (2.5%) with O103, 11 (2%) with O145, 4 (0.7%) with O91, 4 (0.7%) with O111, and 4 (0.7%) with O55 (Espie et al. 2008). The most frequent STEC serogroups implicated in STEC food-borne outbreaks and HUS cases in Europe are shown in Table 3 (EFSA 2009).

During 2004-2007, in New Mexico (US) 71 of 111 cases (64%) of sporadic STEC infections were caused by non-O157 STEC with O26 (18%) and O111 (13%) being the most commonly identified serogroups. Serogroups O103, O121, O46, O177 and O91 were responsible for 33% of all STEC infections (Lathrop et al. 2009).

Table 3. The most frequent STEC serogroups implicated in STEC food-borne outbreaks and HUS cases in Europe.

	STEC		HUS	
	No.*	**%**	**No.***	**%**
O157	7,227	66.0	310	68.3
O26	732	6.7	52	11.5
O103	603	5.5	20	4.4
O91	425	3.9	1	0.2
O145	312	2.8	27	6.0
O111	180	1.6	18	4.0
O146	153	1.4	0	0.0
O128	93	0.8	1	0.2
O55	74	0.7	3	0.7
Other	1,199	10.9	22	4.9
Total	**10,998**		**454**	

*(*source: EFSA, 2009)*

According to Brooks et al. (2005) STEC O111 is the second most common bacterial cause of HUS in the US, after STEC O157:H7. It was identified as the etiological agent in three of seven reported outbreaks of non-O157 STEC serotypes. Eleven (52%) of the 21 non-O157 STEC isolates associated with HUS were STEC O111. An outbreak of acute enteritis associated with STEC O111:H- occurred in 1986 in Japan, with 23 children being affected, one developing HUS and dying (Tanaka et al. 1989). In 1992, nine children were hospitalized with HUS and one child died in Italy. The source of the outbreak was not identified, but STEC O111:NM was the most likely cause (Caprioli et al. 1994). In 1995, during an outbreak of HUS (21 children) in South Australia, STEC O111:H2 was identified as the principal cause and a locally produced semidry fermented sausage (mettwurst) as the incriminated vehicle (Paton et al. 1996). In 1999, a STEC O111:H8 outbreak at a youth camp was associated with consumption of lettuce. Fifty-five persons became ill and two women developed HUS (Brooks et al. 2004). In 2007, a mixed-serotype outbreak involving STEC O145:H28 and O26:H11 occurred in Belgium, after consumption of contaminated ice cream. Five girls developed HUS, and seven patients with bloody diarrhea were identified (Buvens et al. 2011). In 2006, a small but severe STEC O103:H25 outbreak, involving 17 persons (10 developing HUS, 1 child died), was reported in Norway, after the consumption of a traditional Norwegian sausage (morrpoelse) made from sheep meat (Schimmer et al. 2008).

This literature review on STEC food-borne outbreaks highlights the need for measures in order to prevent similar events from happening in the future. The main focus in mitigating risks of food contamination and human infection from STEC should be on the prevention of contamination at all production stages reducing the likelihood of STEC to enter the food chain. The application of Good Agricultural Practices, Good Manufacturing Practices, Good Hygiene Practices and of the HACCP system in line with codes available from international organizations is recommended.

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