WHERE THE HELL DID SHIGA TOXIN E. COLI COME FROM? A LITERATURE REVIEW

In recent months, a surge of papers have appeared in the literature describing findings from the deadly 2011 *E. coli* O104:H4 outbreak in Germany linked to sprouts (8, 11-12, 14, 17-18, 21, 24, 29, 37, 38, 41, 51). The speed at which this information is being published in the literature—much of it free to the public through open access journals—is a testament to the advances in biotechnology available to scientists that study emerging foodborne pathogens. However, despite all the impressive molecular tools the researchers' have at their disposal, the origin of the unusual strain associated with the outbreak in Germany is still unknown. In fact, the origin of *E. coli* O157:H7, a bacterium first described in the 1970s and currently the most well studied shiga toxin-producing *E. coli* (STEC) strain, also (despite conventional wisdom) remains elusive.

PART 1: INTRODUCTION

So, I ask, where the hell did *E. coli* O157 and other STECs come from?

If you read the media stories and foodist blogs, it would seem that this question has been answered with total certainty. The popular belief is that "superbugs" in the food system are the product of industrial agriculture. The dogma is that feedlots (also called concentrated animal feeding operations or CAFOs), grain-feeding, and genetically modified organisms (GMOs) are the root cause of everything wrong in our food system including food safety problems.

For example, Michael Pollen said in a 2010 editorial, "The Food Movement Rising" (35):

"The 1993 deaths of four (sic, three) *children in Washington State who had eaten hamburgers from Jack in the Box were traced to meat contaminated with E. coli O157:H7, a mutant strain of the common intestinal bacteria first identified in feedlot cattle in 1982."*

But, Dr. Thomas Whittam (1954-2008), a pioneer in the study of *E. coli* O157:H7 evolution, said in a 1998 paper published in Emerging Infectious Diseases (52):

"It has been proposed that an increased mutation rate (indicated by the frequency of hypermutable isolates) has facilitated the emergence of Escherichia coli O157:H7. Analysis of the divergence of 12 genes shows no evidence that the pathogen has undergone an unusually high rate of mutation and molecular evolution."

Then in 2011, Dr. Eric Denamur, a French expert in the ecology and evolution of microorganisms, pointed out in Clinical Microbiology and Infection that the shiga toxin-producing *E. coli* German outbreak teaches us a lesson in genome plasticity (14):

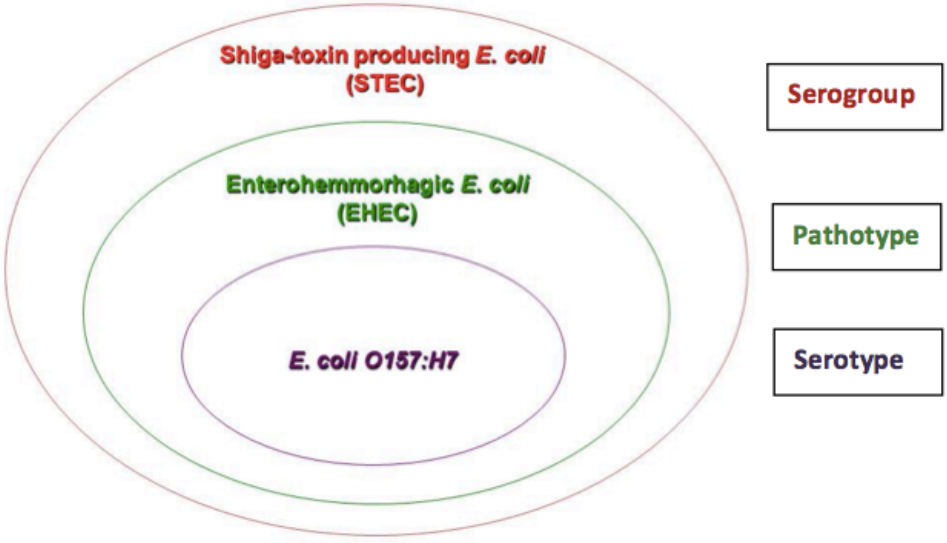
"The main lesson from this outbreak is that we should be aware of the capacity of the E. coli species to produce new combinations of genes, leading to the emergence of highly aggressive strains. Furthermore, antibiotic pressure in human and veterinary medicine should be kept as low as possible, as it will select for such strains once they become resistant."

So, I jumped into the literature to gain a deeper understanding of the question about the origin of *E. coli* O157:H7 and other STECs, especially the role industrial agriculture may or may not have played in their evolution and emergence as human pathogens. What was the ultimate answer to the question of whether STECs are old or new pathogens, and where they arose? I would have loved a clear answer, but only came up with "it depends."

This 3-part series summarizes my findings from the literature review.

Terminology

Escherichia coli was named after its discoverer, Theodor Escherich. The current terminology and nomenclature (naming) of *E. coli* strains can be confusing. There are over 700 *E. coli* "serotypes" described. Most of these *E. coli* strains are harmless inhabitants of the intestinal tract of humans and other warm-blooded animals (15).



An *E. coli* serotype is named based on its numbered "O" (letter capital "O," not zero) and "H" antigen types. *E. coli* O157:H7 is the prototype of a subset of pathogenic strains called enterohemorrhagic *E. coli* (EHEC). EHEC is a "pathotype" associated with human infections that may cause gastrointestinal and hemorrhagic symptoms such as bloody diarrhea and hemolytic uremic syndrome (HUS). *E. coli* O157:H7 and other EHEC pathotypes belong to a broader group of *E. coli* called shiga toxin-producing *E. coli* (STEC) as shown in the figure. Members of the STEC "serogroup" carry shiga toxin genes (*stx1* and/or *stx2*). STEC strains (including *E. coli* O157) are found primarily in healthy animal hosts (e.g., cattle, goats, sheep, pigs, deer, elk). The harmful strains may be transmitted to humans through contaminated food, water, contact with infected animals, or person-to-person transmission via fecal-oral ingestion.

Interestingly, according to recent research in Germany (2), the *E. coli* O104:H4 strain linked to raw sprouts is a combination of two different pathotypes: entero-aggregative *E. coli* (EAEC) and EHEC. A proposed name for the new pathotype is entero-aggregative-hemorrhagic *Escherichia coli* (EAHEC). It is unknown if the natural reservoir of this new EAHEC type is of human or animal origin.

Bacterial Evolution

Understanding the terminology used in describing *E. coli* strain relationships is important in deciphering the research into STEC evolution, including how fast these strains mutate into new variants. Serotyping is based on differences in surface antigens, which are likely encoded by genes that evolve slowly. In contrast, "virulence factors" describe generally a broad group of molecules or proteins that affect the bacteria's ability to cause disease in humans. Shiga toxins and proteins or enzymes that confer antibiotic resistance are examples of virulence factors. Virulence factors are usually encoded by genes in the bacteria's chromosomal DNA, or genes encoded by bacteriophage or plasmid DNA carried inside the bacteria. The ability of some of these virulence factor genes to move rapidly between different populations of *E. coli* may explain short-term changes in the virulence potential of some strains.

In Part 2, the discovery of *E. coli* O157:H7 and evidence of long and short-term evolutionary changes influencing its emergence as a human pathogen will be explored. In Part 3, evidence for and against the importance of agriculture practices (e.g., feedlots, GMOs) in the spread of *E. coli* O157:H7 and other STECs will be reviewed.

PART 2: THE DISCOVERY OF E. COLI O157:H7 AS A CAUSE OF HUMAN DISEASE

The discovery of E. coli O157:H7 as a cause of human disease was a relatively humble, unpublicized event in comparison to the identification of the E. coli O104:H4 strain that exploded in international headlines during the summer of 2011 following an outbreak in Germany**.**

In contrast, the E. coli O157:H7 story emerged quietly in 1975, two years after the Centers for Disease Control and Prevention (CDC) implemented a serotyping service for E. coli isolates. That year, the CDC reference laboratory received a single E. coli strain from a California patient with bloody diarrhea, which typed as "O" antigen 157 and "H" antigen 7 (50). It is worth noting that the E. coli O157 serotype was also described previously in the veterinary literature in the early 1970's, but not linked to human illness (19-20).

The CDC subsequently described four sporadic illnesses caused by E. coli O157:H7, a publication that received little fanfare in a 1982 issue of CDC's Morbidity and Mortality Weekly Report (9). The original write-up was later highlighted in a 1997 MMWR commemoration of the agency's 50th anniversary (10).

Looking back, the earliest recognized outbreak may have occurred in 1980, as described by Steele and colleagues (47). The authors reported an outbreak of hemolytic uremic syndrome

(HUS) in Toronto, Canada associated with ingestion of fresh apple juice. The etiologic agent was not identified during the investigation, but it is likely the illnesses were due to E. coli O157:H7 infections (10). Another early outbreak of HUS probably due to E. coli O157:H7 was reported in Sacramento, California in July and November 1982, but the agent was not isolated from patient specimens (44).

In February and March 1982, the obscure E. coli O157:H7 strain was "re-discovered" during the investigation of two outbreaks of hemorrhagic colitis in Oregon and Michigan, respectively (42). Dr. Lee Riley (pictured above) and colleagues authored the first paper describing an outbreak of hemorrhagic colitis associated with E. coli O157:H7. The outbreaks involved 47 people who became ill from consumption of undercooked hamburgers prepared by Restaurant A (McDonalds) restaurant chains in Oregon and Michigan. E. coli O157:H7 was isolated from patient stool, and the "smoking gun" was found in a raw ground beef hamburger patty from one of the fast-food restaurants implicated during the outbreak investigation (42, 50).

During the same year, Canadian health officials were investigating cases of hemorrhagic colitis and diagnosed E. coli O157:H7 as the cause of another outbreak (22). At this point, it appeared E. coli O157:H7 was a rare emerging foodborne disease in North America.

Throughout the 1980's additional reports of sporadic- and outbreak-associated E. coli O157:H7 were published with a predominance of illnesses among children and the elderly (32, 40, 49). However, the bacterium did not become a "household name" until 1993, when it made national headlines following a highly publicized multistate outbreak due to consumption of undercooked hamburgers served at Jack in the Box fast-food restaurants in the western United States (4). With approximately 700 illnesses and 4 deaths, this outbreak was the impetus for policy changes in the ground beef industry, and pushed health officials in 1995 to add E. coli O157:H7 to the list of nationally reportable diseases the United States. Likewise, Health Canada classified E. coli O157:H7 as a nationally notifiable disease in 1990. E. coli O157:H7 infections from a wide range of food vehicles, as well as person-to-person transmission and direct contact with animals, have been described worldwide since the pathogen's discovery in North America.

Did E. coli O157:H7 Cause Human Illness Before the 1970s-1980s?

An intriguing question is whether E. coli O157:H7 was an unrecognized cause of HUS before its link to outbreaks of hemorrhagic colitis. E. coli O157:H7 is now recognized as the leading cause of HUS in children. Karmali et al (1985) published an early report describing the association between HUS and vero (shiga) toxin-producing E. coli (23). Interestingly, the authors point out that HUS was first described in 1955, which was twenty-years before the identification of E. coli O157:H7 as a human pathogen and pre-dated development of diagnostic assays for the strain. In 1963, the first outbreak of HUS was reported in Wales (28). Notably, the cases were all among children (range 6 weeks to 8 years old), and 7 of 10 patients had gastrointestinal illness with or without bloody diarrhea preceding onset of HUS. The cause of the outbreak was not determined, but the authors speculated that the syndrome was initiated by an exogenous agent. Was the cause E. coli O157:H7?

It is unknown how many early cases of E. coli O157:H7 were missed pre-1970's due to lack of awareness, diagnostic tests, and reporting. Diagnosticians realized early on the need for appropriate laboratory tests to detect E. coli O157:H7, as well as proper specimen collection (10). Even today, diagnosis of E. coli O157:H7 and other shiga toxin-producing E. coli (STEC) strains may be challenging and is dependent on the use of specific protocols for diagnosis in clinical, food, and environmental specimens.

Given what we know today about evolutionary changes and pathogenesis, these early HUS reports may very well have been due to E. coli O157:H7 or another STEC.

Was E. coli O157:H7 Born in a Feedlot in 1982? Not According to the Molecular Clock

The molecular revolution in bacterial genetics began to really take off in the 1990's with technological advances allowing researchers to study the genome sequences of microorganisms and identify genes associated pathogenic strains. The complete genome sequence of E. coli O157:H7 was published in Nature in 2001 (34). The first sequenced strain, EDL933, was isolated from hamburger meat associated with the 1982 McDonald's outbreak (42).

Molecular biologists use the term "molecular clock" to describe the theory that evolutionary changes in bacterial strains can be measured over time by studying mutations in specific DNA sequences or the proteins they encode. The theory assumes that these spontaneous mutations occur at constant rates, which allows calculation of an estimate of how long ago two related organisms diverged from a common ancestor.

The molecular clock theory is still a hypothesis and time estimates vary widely between papers depending on the genes or proteins studied and the methodology. In a 2000 paper from the Whittam Lab, seven housekeeping genes and phylogenetic analysis were used to trace the history of virulence gene acquisition in pathogenic E. coli (39). The authors estimated that E. coli O157:H7 separated from a common E. coli ancestor as long as 4.5 million years ago. However, in a more recent paper, Leopold and co-authors examined E. coli O157:H7 strains from three continents over three decades from humans, cattle, and food (26). They estimated the dominant E. coli O157:H7 cluster evolved on the in last millennium. Similarly, Zhou et al (2010) conducted an analysis of mutation frequency to estimate the divergence of E. coli O157:H7 from E. coli O55:H7, its closest genetic relative (56). These authors estimated the divergence occurred as recently as 400 years ago, or from 14,000 to 70,000 years ago depending on the clock rate used.

"Stepwise" Long-term Evolution of Shiga Toxin-Producing E. coli

Feng and colleagues described a "stepwise" model for sequential evolution of E. coli O157:H7 from an ancestor (16). The model shown in the figure below suggests an explanation for gentotypic and phenotypic differences between strains including changes in acquisition of shiga toxin genes, gain/loss of motility, and the ability to ferment sorbitol. These findings have been exploited in the development of diagnostic assays including protocols that detect E. coli O157 based on a point mutation at +92 in the uidA gene (53-54).

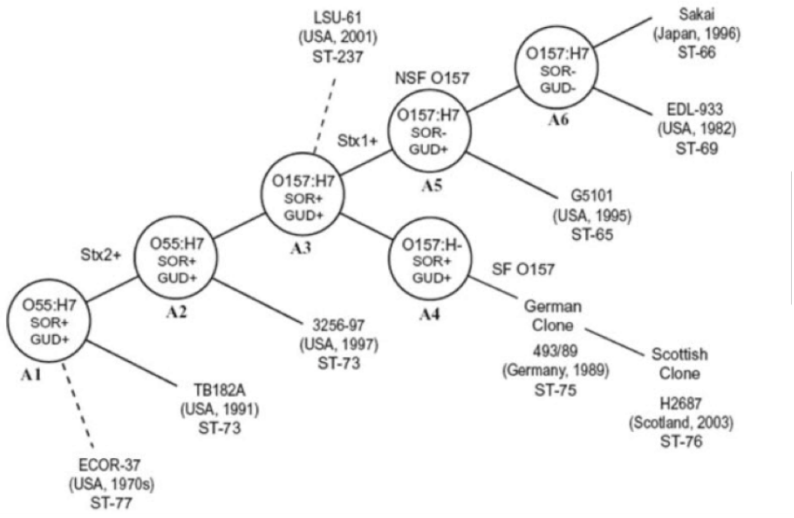


Figure 1. Evolution model for *Escherichia coli* O157:H7. Figure modified and updated from (1) to include the sequence type (ST) data showing subclones within clonal complexes. Some strains, whose position on the model remains to be determined, are shown with dashed lines (16).

The Whittam Lab subsequently published a detailed genetic analysis of E. coli O157:H7 associated with disease outbreaks thereby providing a deeper understanding of the relationship between genetics and pathogenesis (27). They discovered nine distinct clades with Clade 8 containing strains linked to spinach and lettuce outbreaks that caused unusually high rates of hospitalizations and HUS. The 1982 outbreak strain reported by Riley et al (1983) belonged to Clade 3, while the 1993 outbreak strain linked to Jack in the Box hamburgers belonged to clade 2.

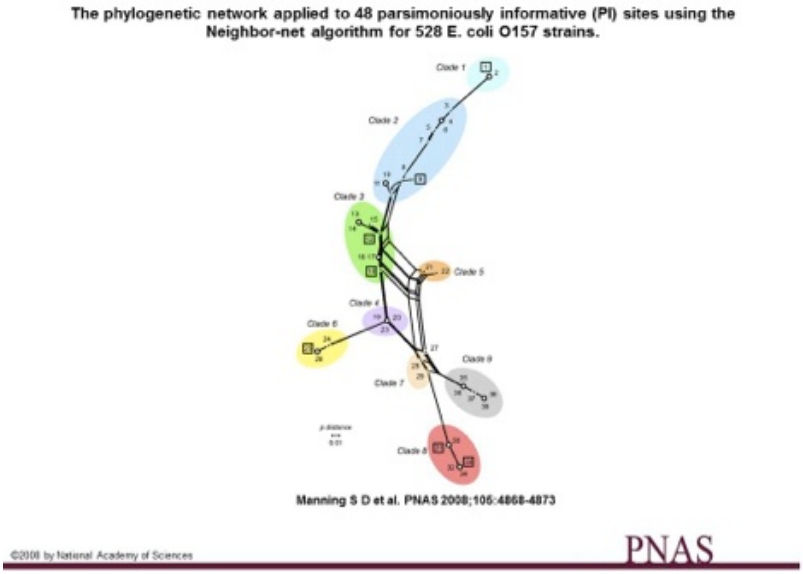


Figure 2. The phylogenetic network applied to 48 parsimoniously informative (PI) sites using the Neighbor-net algorithm for 528 E. coli O157 strains. The colored ellipses mark clades

supported in the minimum evolution phylogeny. The numbers at the nodes denote the SNP genotypes (SGs) 1–39, and the white circle nodes contain two SGs that match at the 48 PI sites. The seven SGs found among multiple continents are marked with squares (27).

The Relentless Short-term Evolution of Pathogenic E. coli

Regardless of whether the E. coli O157:H7 serotype evolved hundreds or millions of years ago, it certainly did not suddenly mutate in a U.S. feedlot 30 years ago then spread worldwide as suggested by Pollan and other foodists. However, their broad statements are supported, in part, by the ability of pathogenic E. coli strains to rapidly gain or lose virulence determinants through genetic mutations and gene transfer (13, 25, 33, 55). These genetic changes can impact the ecology, epidemiology and pathogenesis of E. coli O157:H7 in a relatively short time period. Specifically, mobile genetic elements such as bacteriophages and plasmids play a major role in the genetics of pathogenic E. coli, and can change significantly the virulence of a population of E. coli O157:H7 in as short as a single generation.

Dr. Roy M. Robins-Browne reminds us of this relentless evolution of E. coli in an editorial published in Clinical Infectious Diseases (43):

"...bacterial evolution is an ongoing process that undoubtedly will lead to the emergence of other successful pathogenic clones of E. coli in the future."

Notably, early in the recognition of E. coli O157:H7 as a human pathogen, shiga toxins (also referred to as vero toxins or cytotoxins) were characterized as important virulence factors in the pathogenesis of the syndrome (31). These toxins do not originate from the bacterium, but rather from two lambda-like bacteriophages that infect the E. coli O157:H7 cell then integrate into its chromosome (43). Bacteriophages carry the stx1 and stx2 genes responsible for shiga toxin-related disease. We now understand that these toxins act like the ricin causing damage to the vascular system and potentially leading to HUS. Other accessory virulence determinants include "pathogenicity islands" such as the locus for enterocyte effacement (LEE), which contains genes encoding virulence factors that assist E. coli in host invasion and influence the manifestation of diarrhea and other gastrointestinal signs and symptoms (43).

As shown in the diagram below, the hallmark of a pathogenic strain of E. coli is the presence of these additional mobile elements or gene clusters that convert a harmless, commensal E. coli strain into a potentially dangerous human pathogen (1).

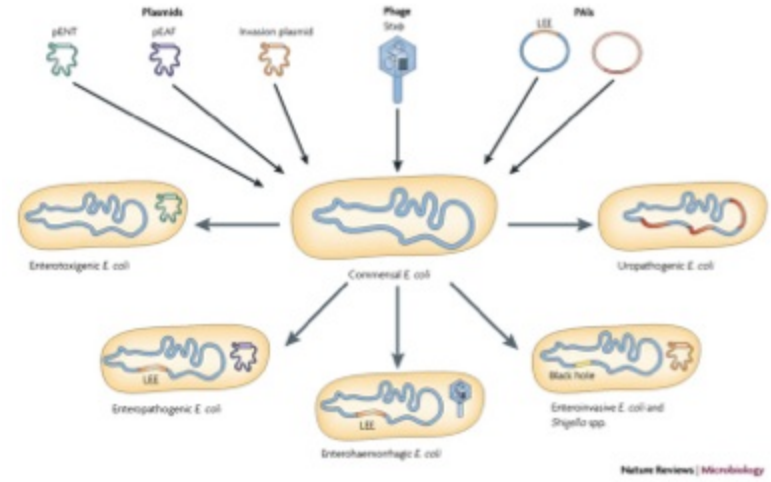


Figure 3. Contribution of horizontal acquisition of mobile genetic elements to the evolution of Escherichia coli pathotypes.The uptake of mobile genetic elements (phages, virulence plasmids and pathogenicity islands), as well as the loss of chromosomal-DNA regions in different E. coli lineages, has enabled the evolution of separate clones, which belong to different E. coli pathotypes and are associated with specific disease symptoms. LEE, locus of enterocyte effacement; PAI, pathogenicity island; pEAF, enteropathogenic E. coli adhesion-factor plasmid; pENT, enterotoxin-encoding plasmids; Stx, Shiga-toxin-encoding bacteriophage (1).

Summary

In summary, an overview of the literature demonstrates the importance of differentiating between a newly recognized pathogen versus a newly evolved organism. The E. coli O157:H7 serotype clearly is not "new," although its remarkable ability to evolve and adapt to different environments, particularly through acquisition and loss of mobile genetic elements, may result in new mechanisms of transmission and strain-dependent variations in pathogenicity.

In Part 3, the role of agriculture, food distribution systems, and human activities in the spread of E. coli O157:H7 will be explored.

Did humans turn an obscure E. coli strain into a dangerous emerging infectious disease?

PART 3: HOW HUMANS COULD HAVE TURNED AN OBSCURE E. COLI STRAIN INTO A DANGEROUS EMERGING INFECTIOUS DISEASE?

The furor of "pink slime" politics and unrelenting reports of foodborne illnesses in 2012 adds new meaning to the conclusion of Part 1 and Part 2, a series started earlier this year. On the surface, one might think E coli evolution is a purely scientific, apolitical topic. Is it? The review ends with a brief exploration of host, environmental, and social factors that may influence selective pressures favoring the evolution and emergence of highly virulent STECs. The findings are put in perspective with regard to making evidence-based policy decisions to prevent foodborne disease from these pathogens.

Under Pressure: Selecting for Virulent E. coli

The theory (promoted by movies like Food, Inc.) of E. coli O157:H7 being "born" on a feedlot just 30 years ago was debunked (see Part 2 of this series). As discussed previously, current estimates of the age of the O157 serotype range from hundreds to many thousands of years. However, the ability for E. coli strains to evolve rapidly through gene acquisition and mobile elements may influence short-term evolutionary events resulting in increased risk of contamination of the food supply and human foodborne disease. Host and environmental factors including medical and agricultural practices can directly and indirectly influence the selective pressure on E. coli O157:H7 to develop and maintain new characteristics including virulence factors such as toxins and antibiotic resistance.

Armstrong et al. (1996) outlined three broad hypotheses that may have led to the emergence and recognition of E. coli O157:H7 in beef products (2). Given new information including recognition of novel vehicles of transmission ranging from fresh produce to cookie dough, a modification of their hypotheses might be:

1) Conditions for the spread of E. coli O157:H7 and other pathogenic STECs from animals to humans have always existed, but these organisms have only recently emerged in animal populations.

2) E. coli O157 and other pathogenic STECs have always been widespread in animal populations, but slaughter and meat processing practices have changed in such a way as to promote contamination of meat with this organism, and allowed dissemination from the farm environment to surrounding fresh produce or other food crops.

3) E. coli O157:H7 and other pathogenic STECs has always been present in the food supply but consumer practices have changed such that contaminated undercooked meat, raw milk, raw produce and other raw foods now lead to human infection.

4) A combination of one or more of the above.

The Price of Fast, Cheap Burgers

Major structural changes in the U.S. agriculture and food processing industries promoting mass production of ground beef occurred concomitantly with the emergence of E. coli O157:H7 as a cause of foodborne illness (2). Coincidence? Not likely.

It is important to consider the dynamics surrounding the first recognized outbreaks in the context of the evolution of this organism. Specifically, what were the potential selective pressures that favored the emergence and persistence of E. coli O157:H7 as an important cause of human foodborne disease?

As described in Part 2 of this series, the first recognized E. coli O157:H7 outbreaks were linked in the early 1980's to undercooked hamburgers served at McDonald's chain restaurants in Oregon and Michigan (42). A decade later, another E. coli O157:H7 outbreak linked to burgers

served at a fast-food restaurant chain (Jack in the Box) shook the beef industry (4). The 1993 Jack in the Box outbreak that sickened nearly 700 and killed 4 people was perhaps the most significant driving factor in public health reform of the meat industry since Upton Sinclair published his book, The Jungle, where he exposed filthy conditions in America's slaughterhouses and corruption in the meatpacking industry in the early 20th century (46). Similarly, the Jack in the Box outbreak exposed for the first time the numerous vulnerabilities in late 20th-century industrial agriculture that contributed to the tragic event in 1993 as expressed eloquently by Benedict in his book, "Poisoned," published in 2011 (5).

Today, a myriad of potential contributing factors related pre- and post-harvest production, transportation, and preparation of ground beef have been recognized. For example, it is well documented that high concentrations of cattle in crowded pens before slaughter increase the opportunity for transmission of STECs between animals and into the environment (2-3). The subsequent sourcing and mixing of cattle from numerous farms and mass production of ground beef products provide many opportunities for cross-contamination. For example, the traceback conducted during the 1993 Jack in the Box outbreak revealed that meat used in the implicated lots of ground beef could have come from 443 individual cattle from six different states and three different countries (2).

It is not difficult to envision retrospectively how changes in industrial agriculture practices combined with faster line speeds in the 1980's could have promoted transfer of E. coli O157 from the hide or gut of beef carcasses to the finished product. Additionally, The public's enthusiasm for fast, cheap food and the restaurant chain industry's desire to meet this demand even at the cost of food safety clearly gave E. coli O157:H7 a new niche and pathway into the human gut.

Small Farms Not Exempt

Ironically, the increased popularity of raw, unprocessed foods perceived as more healthy may also be a factor contributing to increased human exposure to E. coli O157 and other STECs in the 21st Century. Following the Jack in the Box outbreak, and a string of other outbreaks associated with industrial agriculture and fast food, the public became increasingly disillusioned with modern food systems. Fears over antibiotics, chemicals, and genetically engineered food further fueled the emergence of the so-called "foodist" movement. Popular books and movies shunning modern agriculture brought a new hope to the health- and environmentally-conscious population by portraying small-scale, family farms and cows eating a "natural," grain-free diet on pasture as a panacea for the problem with E. coli O157:H7. Although changes in U.S. industrial agricultural obviously played an important role in the pathogen's short-term evolution and emergence as a human disease threat (see above), simple solutions such as "grass only" feeding have not panned out, as illustrated by continued E. coli O157:H7 outbreaks on both small and large farms. For example, the popularity of raw milk and cheeses made from raw milk correlates with an increase in E. coli O157 illnesses from dairy products. Similar to outbreaks linked to industrial foods, children have been the most severely affected by contaminated raw dairy products.

Super Bug or Super Cow

Since the early ground beef-related outbreaks in the 1980's, there have been a number of important new discoveries in the transmission dynamics and ecology of E. coli O157:H7 among cattle. The interplay of animal host-pathogen relationships and the influence of genetics on both is an active area of research. A hot topic in this field of research involves the phenomenon of "supershedders." A supershedder is an animal that excretes a much higher concentration of E. coli O157 and has a higher rate of transmission to other animals (6). Supershedders expel more than 1 million E. coli O157 cells in every gram of feces (a gram is less than the weight of one penny). As a result, the environment where the cattle live can become heavily contaminated. It remains unknown if the driving selective factor in the occurrence of supershedders is the cattle host, the bacterial population, the environment, or a combination of both.

The Accidental Tourist

Humans do not appear to play any significant role in the natural history of E. coli O157:H7 or other STECs. The human gut is likely an "accidental host" of E. coli O157:H7 and has minimal influence on the evolution, ecology or long-term maintenance of this pathogen in nature. If humans are not the natural STEC host, it may explain in part why humans become severely ill, and even die from these infections, while cattle and other animal hosts carry the bacteria in their gut asymptomatically.

One explanation for the difference in pathogenicity involves the presence/absence of host receptors for the shiga toxins (stx1, stx2) produced by bacteriophages carried by STEC strains (36). In short, some research shows that cattle may lack shiga toxin receptors, thus do not succumb to the damaging effects of these toxins. In contrast, humans carry genes that express shiga toxin receptors and thus may suffer severe illness ranging from hemorrhagic colitis to HUS when exposed to these toxins during infection. Additional research is needed to further characterize these host-pathogen interactions and how they relate to clinical disease.

Virulence Factors – E. coli Super Powers or Evolutionary Baggage

If humans are indeed accidental hosts, what, if any, evolutionary benefit exists for E. coli O157 and other STECs (and their bacteriophages) in retaining virulence genes?

An intriguing theory was published by Steinberg and Levin (2007) suggesting that some of the virulence factors of E. coli O157:H7 provide protection against predation by grazing protozoa found in soil, water, and ruminant hosts such as cattle (48). Grazing protozoa are single cell parasites that "feed" on E. coli O157 bacterial populations. The authors hypothesize that the stx-encoding bacteriophage carried by E. coli O157:H7 may help it survive in food vacuoles after being consumed by protozoan parasites.

Another concern in medicine and agriculture that has a direct relationship to selective pressure on bacterial populations is the use/misuse of anitbiotics (14). There is evidence of antibiotic resistance among STEC strains from human and animal sources (30, 45). While antibiotics are generally contraindicated during E. coli O157:H7 infections due to increased risk of the patient developing HUS, antibiotic resistance may complicate therapeutic options in rare situations where treatment with antibiotics is needed.

The Elephant in the Room

It is worth making a final comment on factors that do not influence the evolution or ecology of E. coli O157:H7 and other pathogenic STECs. Despite the hype and sensationalism, there is no evidence or biological plausibility of genetically modified organisms (GMOs) being involved in the ecology or evolution of E. coli O157 or other pathogenic strains of E. coli. The non-pathogenic E. coli strain used in the cloning process to create genes that will be inserted into seeds to confer a specific genetic trait to future generations of plants (7). As such, laboratory E. coli is not present in the seed or the plant at the end of the process, and there is no opportunity for a person or animal that eats a transgenic plant being exposed to an E. coli lab strain.

Conclusions and Recommendations

The reality is that E. coli O157:H7 and other pathogenic STECs are entrenched in our food animal populations, especially ruminants. There is likely no turning the clock back on the evolution of these pathogens, which will continue to stay a step ahead of us through their evolutionary processes. However, there are medical, agricultural, and social practices that may strongly influence the potential for these organisms to cause human foodborne disease. Thus, the hope in combatting these food safety threats lies in embracing scientific advancements that can inform evidence-based policy in best practices throughout the food chain.

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