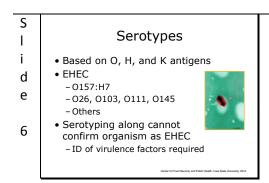
S I d e 1	Enterohemorrhagic Escherichia coli Infections Verocytotoxin producing <i>E. coli</i> (VTEC) Shiga toxin producing <i>E. coli</i> (STEC) <i>E. coli</i> 0157:H7	
S I d e 2	Overview • Organism • History • Epidemiology • Transmission • Disease in Humans • Disease in Animals • Prevention and Control • Actions to Take	<ul> <li>In today's presentation we will cover information regarding <i>Escherichia coli</i> (<i>E. coli</i>) and its epidemiology. We will also talk about the history of the disease, how it is transmitted, species that it affects (including humans), and clinical and necropsy signs observed. Finally, we will address prevention and control measures for <i>E. coli</i>, as well as actions to take if <i>E. coli</i> is suspected.</li> <li>[Photo: Scanning Electron Microscopy (SEM) of <i>Escherichia coli</i> organism. Source: CDC Public Health Image Library]</li> </ul>
S I d e 3	THE ORGANISM	
S I d e 4	<section-header><text><list-item><list-item><list-item><list-item><list-item><list-item><list-item><list-item><list-item><list-item><list-item><list-item><list-item><list-item></list-item></list-item></list-item></list-item></list-item></list-item></list-item></list-item></list-item></list-item></list-item></list-item></list-item></list-item></text></section-header>	<ul> <li><i>Escherichia coli</i> is a Gram negative rod (bacillus) in the family Enterobacteriaceae. Most <i>E. coli</i> are normal commensals found in the intestinal tract. Enterohemorrhagic <i>Escherichia coli</i> (EHEC) is a subset of pathogenic <i>E. coli</i> that can cause diarrhea or hemorrhagic colitis in humans. Hemorrhagic colitis occasionally progresses to hemolytic uremic syndrome (HUS), an important cause of acute renal failure in children and morbidity and mortality in adults. Pathogenic strains of this organism are distinguished from normal flora by their possession of virulence factors such as exotoxins.</li> <li>[Photo: Colorized scanning electron micrograph (SEM) depicting <i>Escherichia coli</i> O157:H7. CDC Public Health Image Library]</li> </ul>

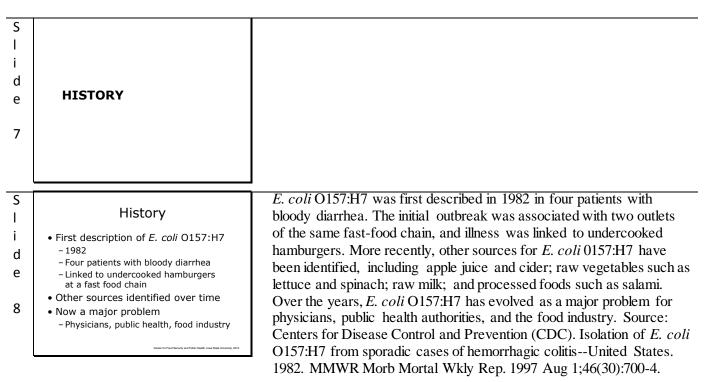
## S I Virulence Factors Verocytotoxigenic *E. coli* (VTEC) Toxins: Vt1, Vt2 Also known as shiga toxin-producing *E. coli* (STEC) EHEC are VTEC that have additional virulence factors Example: genes that produce attaching and effacing lesions in human GI tract

The specific virulence factors can be used, together with the type of disease, to separate *E. coli* into pathotypes. Verocytotoxigenic (or verotoxigenic) *E. coli* (VTEC) produce a toxin that is lethal to cultured African green monkey kidney cells (Vero cells) but not to some other cultured cell types. There are two major families of verocytotoxins, Vt1 and Vt2. A VTEC isolate may produce one or both toxins. Because verocytotoxin is homologous to the shiga toxins of *Shigella dysenteriae*, VTEC are also called shiga toxin-producing *E. coli* (STEC). Enterohemorrhagic *E. coli* are VTEC that possess additional virulence factors. One key characteristic found in EHEC, but not exclusive to these organisms, is the ability to cause attaching and effacing (A/E) lesions on human intestinal epithelium. Some of the genes that are involved in producing A/E lesions can be used, together with the presence of the verocytotoxin, to help identify EHEC.

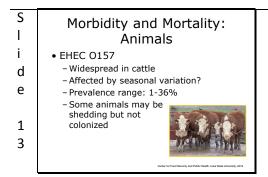


*E. coli* are serotyped based on the O (somatic lipopolysaccharide), H (flagellar) and K (capsular) antigens. Serotypes known to contain EHEC include *E. coli* O157:H7, the non-motile organism *E. coli* O157:H-, and members of other serogroups, particularly O26, O103, O111 and O145 but also O91, O104, O113, O117, O118, O121, O128 and others. Serotyping alone is not enough to identify an organism as an EHEC; virulence factors characteristic of these organisms must also be present. *E. coli* O157:H7 strains are relatively homogeneous, and nearly all of these organisms carry virulence factors associated with hemorrhagic colitis and HUS.

[Photo: Transmission electron micrograph of *E. coli* O157:H7 showing flagella. CDC Public Health Image Library]

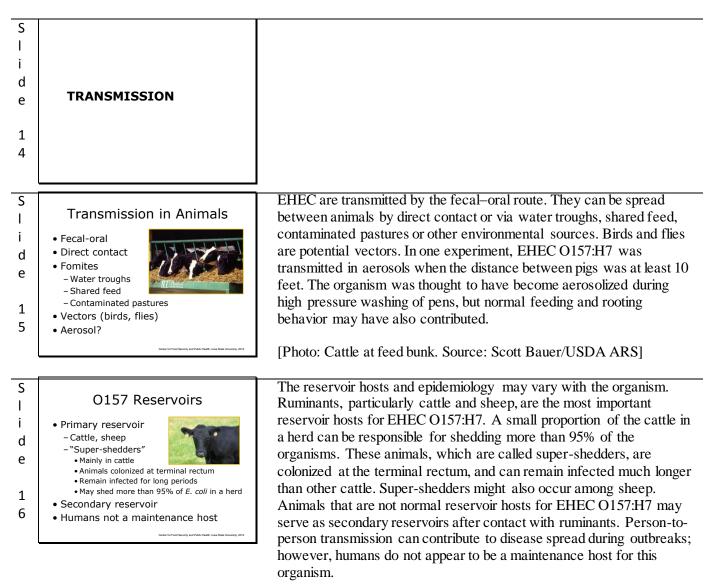


S I d e 9	EPIDEMIOLOGY	
	Center for Food Security and Public Health, leval State University, 2012	
S I d e 1 0	<ul> <li>Geographic Distribution</li> <li>E. coli 0157:H7</li> <li>Found worldwide</li> <li>Exception: Antarctica</li> <li>Other EHEC</li> <li>Wide distribution</li> <li>Prominent serotypes may vary by geographic area</li> </ul>	EHEC O157:H7 infections occur worldwide; infections have been reported on every continent except Antarctica. Other EHEC are probably also widely distributed. The importance of some serotypes may vary with the geographic area.
S I d e 1 1	<ul> <li>Morbidity and Mortality: humans</li> <li>Seasonal variation</li> <li>North America</li> <li>Most infections in summer, autumn</li> <li>Due to seasonal shedding in animals or increase in summer barbecues?</li> <li>Incidence</li> <li>U.S. 1996-2010: 0.9 cases/100,000</li> <li>Mortality</li> <li>HUS: 3-10% (children), 50% (elderly)</li> </ul>	EHEC infections can occur as sporadic cases or in outbreaks. In North America, EHEC O157:H7 infections are most common from summer to autumn. Seasonality might be caused by seasonal shedding patterns in animals, or it could be due to other factors such as eating undercooked meat at summer barbecues. The incidence of EHEC in humans is difficult to determine, because cases of uncomplicated diarrhea may not be tested for these organisms. FoodNet surveillance from 1996 to 2010 showed that O157 infection caused 0.9 illnesses per 100,000; this represents a decrease compared to the period from 1996 to 1998. In clinical cases, the mortality rate varies with the syndrome. Hemorrhagic colitis alone is usually self–limiting, but death is possible. The number of cases that progress to HUS varies with the organism and the outbreak. Approximately 5-10% of patients with hemorrhagic colitis from EHEC O157:H7 usually develop HUS. Complications and fatalities are particularly common among children, the elderly, and those who are immunosuppressed or have debilitating illnesses. HUS is fatal in 3–10% of children and TTP in up to 50% of the elderly.
S I d e 1 2	<section-header><text><figure><footnote><footnote></footnote></footnote></figure></text></section-header>	This image shows the relative rates of laboratory-confirmed infections with <i>Campylobacter</i> , STEC O157, <i>Listeria</i> , <i>Salmonella</i> , and <i>Vibrio</i> , compared with 19961998 rates, by year, according to FoodNet surveillance in the U.S. from 1996-2010. For STEC O157, a 44% decrease was observed. Compared with 2006-2008, the incidence was significantly lower for STEC O157 (29% decrease) in 2010. Source: Centers for Disease Control and Prevention (CDC). Vital signs: incidence and trends of infection with pathogens transmitted commonly through foodfoodborne diseases active surveillance network, 10 U.S. sites, 1996-2010. MMWR Morb Mortal Wkly Rep. 2011 Jun 10;60(22):749-55.



Surveys suggest that EHEC O157:H7 is widespread in cattle herds, but the prevalence in individual animals is low. Some studies have found that this organism is more common in cattle during the summer and early autumn. One study reported that the prevalence was higher when it was cooler, but more bacteria were shed in the summer. Other studies have not found seasonal patterns of shedding. Prevalence rates for EHEC O157:H7 among cattle vary from less than 1% to 36%, depending on the country, type of herd studied and other conditions. Recent studies that use sensitive methods for detection report a higher prevalence than early surveys. However, highly sensitive techniques may also overestimate prevalence, as some animals shedding the organism may not be colonized, but only transiently infected by transmission from super-shedders or the environment.

[Photo: Cattle. Source: USDA ARS]



[Photo: Cow. Source: Larry Rana/USDA]

S I	Transmission in Humans
i d e	<ul> <li>Undercooked or unpasteurized animal products         <ul> <li>Ground beef**</li> <li>Other meats</li> <li>Milk, cheese</li> </ul> </li> </ul>
1 7	<ul> <li>Foods contaminated with feces</li> <li>Fruits</li> <li>Vegetables</li> </ul>

Foodborne outbreaks with EHEC O157:H7 are often caused by eating undercooked or unpasteurized animal products, particularly ground beef but also other meats and sausages, and unpasteurized milk and cheese. Other outbreaks have been linked to alfalfa or radish sprouts, lettuce, spinach and other contaminated vegetables, as well as unpasteurized cider. Irrigation water contaminated with feces is an important source of EHEC O157:H7 on vegetables. This organism can attach to plants, and survives well on the surface of a variety of fruits, vegetables and fresh culinary herbs. Depending on the environmental conditions, small numbers of bacteria left on washed vegetables may multiply significantly over several days. EHEC 0157:H7 can be internalized in the tissues of some plants including lettuce, where it may not be susceptible to washing.

[Photos: (Top) Hamburgers. Source: USDA ARS; (Bottom) Leafy greens. Source: Centers for Disease Control and Prevention]

S I d e 1 8	Foodborne Outbreaks: CDC Investigation Examples • 2012 • Clover sprouts • 2011 • Lettuce, bologna, in-shell hazelnuts • 2010 • Cheese, romaine lettuce, steak • 2009 • Ground beef, cookie dough	Multistate outbreaks of foodborne <i>E. coli</i> are not uncommon; for example, in recent years, the CDC has investigated food products ranging from ground beef to vegetables to prepared foods (e.g., cookie dough).
S I	Transmission in Humans	Some human cases are caused by exposure to contaminated soil or water. EHEC are usually eliminated by municipal water treatment, but
i	Contaminated water	these organisms may occur in private water supplies such as wells.
d	- Private wells - Municipal water treatment	Swimming in contaminated water, especially lakes and streams, has
е	usually eliminates E. coli	been associated with some infections. Soil contamination has caused
	- Swimming (lakes, streams)	outbreaks at campgrounds and other sites, often when the site had been grazed earlier by livestock.
1	Contaminated soil     Campgrounds	grazed carlier by livestock.
9	– Sites grazed by livestock	[Photo: Small lake surrounded by farmland. Source: Neil
	Center for Food Security and Public Health, Iowa Sola University, 2012	Mitchell/geograph.org.uk (Creative Commons) via
		http://commons.wikimedia.org/wiki/File:Small_Lake_surrounded_by_
		farmlandgeograph.org.uk1752021.jpg]
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e	DISEASE IN HUMANS	

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## Disease in Humans

-	
i	Hemorrhagic colitis
d	– Bloody diarrhea
-	<ul> <li>Severe abdominal cramps</li> </ul>
е	-+/- fever, nausea/vomiting
	<ul> <li>Many cases self-limiting</li> </ul>
~	<ul> <li>Resolve in about 1 week</li> </ul>
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## Disease in Humans

i d e	Hemolytic uremic syndrome (HUS)     - Children, elderly, immunocompromised     - Usually develops post-diarrhea     Clinical cianc
2 3	<ul> <li>Clinical signs         <ul> <li>Kidney failure, hemolytic anemia, thrombocytopenia</li> </ul> </li> <li>Thrombotic thrombocytopenic purpura (TTP)</li> </ul>

S I	Diagnosis
i d e	<ul> <li>Culture         <ul> <li>Feces, food, environmental samples</li> <li>Differential and selective media</li> <li>Suspected colonies confirmed with:</li> </ul> </li> </ul>
2 4	<ul> <li>Biochemical tests</li> <li>Immunoassays</li> <li>Phage typing</li> <li>PFGE</li> <li>Serology</li> </ul>

The incubation period for disease caused by EHEC 0157:H7 ranges from one to 16 days. Most infections become apparent after 3-4 days; however, the median incubation period was 8 days in one outbreak at an institution. Person-to-person transmission occurs by the fecal-oral route. Most people shed EHEC O157:H7 for approximately 7 to 9 days; a minority can excrete this organism for 3 weeks or longer after the onset of symptoms. In a few cases, shedding may continue for several months. Young children tend to shed the organism longer than adults. Transmission is particularly common among children still in diapers.

Most symptomatic cases begin with diarrhea. Some cases resolve without treatment in approximately a week; others progress to hemorrhagic colitis within a few days. Hemorrhagic colitis is characterized by diarrhea with profuse, visible blood, accompanied by abdominal tenderness, and in many cases, by severe abdominal cramps. Some patients have a low-grade fever; in others, fever is absent. Nausea and vomiting may be seen, and dehydration is possible. Many cases of hemorrhagic colitis are self-limiting and resolve in approximately a week. Severe colitis may result in intestinal necrosis, perforation or the development of colonic strictures.

Hemolytic uremic syndrome occurs in up to 16% of patients with hemorrhagic colitis. This syndrome is most common in children, the elderly and those who are immunocompromised. It usually develops a week after the diarrhea begins, when the patient is improving. Occasionally, children develop HUS without prodromal diarrhea. HUS is characterized by kidney failure, hemolytic anemia and thrombocytopenia. Extrarenal signs including CNS involvement with lethargy, irritability and seizures are common. In more severe cases, there may be paresis, stroke, cerebral edema or coma. Respiratory complications can include pleural effusion, fluid overload and adult respiratory distress syndrome. The form of HUS usually seen in adults, particularly the elderly, is sometimes called thrombotic thrombocytopenic purpura (TTP). In TTP, there is typically less kidney damage than in children, but neurologic signs including stroke, seizures and CNS deterioration are more common. Death occurs most often in cases with serious extrarenal disease such as severe CNS signs. Approximately 65–85% of children recover from HUS without permanent damage; however, long-term renal complications including hypertension, renal insufficiency and end-stage renal failure also occur.

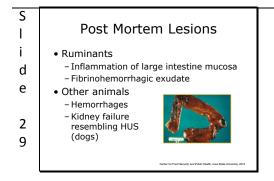
Because humans do not normally carry EHEC, clinical cases can be diagnosed by finding these organisms in fecal samples. Food and environmental samples may also be tested to determine the source of the infection. There is no single technique that can be used to isolate all EHEC serotypes. Selective and differential media have been developed for EHEC O157:H7, including MacConkey agar, hemorrhagic colitis agar, and commercial chromogenic agars. Colonies suspected to be EHEC O157:H7 are confirmed to be E. coli with biochemical tests, and shown to have the O157 somatic antigen and H7 flagellar antigen with immunoassays. A variety of tests

including enzyme-linked immunosorbent assays (ELISAs), agglutination, PCR, immunoblotting or Vero cell assay can be used to detect the verocytotoxin or its genes. Phage typing and pulsed field gel electrophoresis can subtype EHEC O157:H7 for epidemiology; these tests are generally done by reference laboratories. Subtyping is important in finding the source of an outbreak and tracing transmission. Serology is also valuable in humans, particularly later in the course of the disease when EHEC are difficult to find.

[Photo: MacConkey agar culture plate with *Escherichia coli* bacteria. Source: CDC Public Health Image Library]

S I d e 2 5	<ul> <li>Dreatment</li> <li>Mainly supportive</li> <li>Antibiotics</li> <li>Sually avoided</li> <li>Do not reduce symptoms, prevent complications, or reduce shedding</li> <li>Any increase risk of HUS</li> <li>Antimotility drugs</li> <li>Hay increase risk of HUS</li> </ul>	Treatment of hemorrhagic colitis is supportive, and may include fluids and a bland diet. Antibiotics are controversial and are usually avoided: they do not seem to reduce symptoms, prevent complications or decrease shedding, and they may increase the risk of HUS. The use of antimotility (antidiarrheal) agents in hemorrhagic colitis also seems to increase the risk for developing HUS. Patients with complications may require intensive care including dialysis, transfusion and/or platelet infusion. Patients who develop irreversible kidney failure may need a kidney transplant.
S I		
i		
d	DISEASE IN ANIMALS	
e	DISEASE IN ANIMALS	
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S		Ruminants, especially cattle and sheep, are the major reservoirs for
I	Species Affected	EHEC 0157:H7. Bison and deer can be infected. This organism can
i	Ruminants (cattle, sheep)	sometimes be found in other mammals including pigs, rabbits, horses,
d	Pigs     Rabbits	dogs, raccoons and opossums, and in birds including chickens, turkeys, geese, pigeons, gulls, rooks and various other wild birds. In
e	• Horses	some instances, it is not known whether a species normally serves as a
2	• Dogs • Raccoons, opossums	reservoir host or if it is only a temporary carrier. For example, rabbits
2	• Birds	shedding EHEC O157:H7 have caused outbreaks in humans, but most
	Control for Toxad Security and Public Health Linear Solid	infected rabbits have been found near farms with infected cattle. The
ļ		reservoir hosts for non-O157 EHEC are poorly understood.
		[Photo: (Top) Cattle. Source: Alice Welch/USDA; (Bottom) Sheep.
		Source: Danelle Bickett-Weddle/CFSPH]

S	Disease in Animals
I	Disease in Animais
i	• 0157:H7 EHEC
d	- Natural infections • No illness detected
е	- Experimental infections
	<ul> <li>Disease in very young animals</li> </ul>
_	Non-O157 EHEC
2	– Diarrhea, GI signs in young animals
8	<ul> <li>Shedding</li> </ul>
Ũ	<ul> <li>Subclinically infected, young animals</li> </ul>
	Genter for Food Security and Public Health, Iowa State University, 2012



S 	Diagnosis
i	• Culture
d	<ul> <li>Fecal samples, rectoanal swabs</li> <li>Differential and selective media</li> </ul>
е	<ul> <li>Detection of antigens, toxins, genes</li> </ul>
	– Immunological tests – Nucleic-acid based tests
3	<ul> <li>Serology not routinely used</li> </ul>
U	in animals

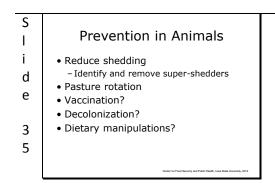
EHEC O157:H7 has not been associated with illness in naturally infected animals. In experimentally infected calves, this serotype does not seem to cause disease in animals older than one week of age. There is one report of bloody or mucoid diarrhea, with some deaths, after experimental infection of neonatal (less than 2-day-old) calves. Another study reported illness in gnotobiotic piglets. Members of some non-O157 EHEC serogroups including O26, O111, O118 and O103 may cause diarrhea and other gastrointestinal signs in young animals. Subclinically infected animals can shed EHEC. Shedding may be transient or intermittent, and animals that have stopped excreting this organism can be recolonized. Calves are more likely to shed EHEC O157:H7 than adult cattle. Experimentally infected pigs could shed this organism for at least 2 months.

EHEC lesions in ruminants are usually characterized by inflammation of the intestinal mucosa, and are generally limited to the large intestine. In some cases, a fibrinohemorrhagic exudate is present. In rabbits experimentally infected with EHEC O153, the cecum and/or proximal colon were edematous and thickened, and the serosal surfaces had petechial or ecchymotic hemorrhages. Pale kidneys were also reported. Dogs infected with EHEC O157:H7 had no significant gross lesions. In dogs inoculated with a non-O157 EHEC strain, the primary cause of death was microvascular thrombosis leading to kidney failure and multiple organ failure. This syndrome resembled HUS. In these dogs, inflammation and edema occurred in the small and large intestines. The kidneys were pale, with a few petechiae on the serosal surface. The liver was enlarged, with inflammation and necrotic lesions. [Photo: Hemorrhagic enteritis in canine small intestine due to E. coli O157:H7. Source: Armed Forces Institute of Pathology/CFSPH]

EHEC can be difficult to identify. They are a minor population in the fecal flora of animals. Carrier animals are usually detected by finding EHEC in fecal samples, which are either freshly voided or taken directly from the animal. Rectoanal swabs may also be used in some cases. Selective and differential media have been developed for EHEC O157:H7, including MacConkey agar, hemorrhagic colitis agar, and commercial chromogenic agars. Selective media and isolation techniques have also been developed for few non-O157 EHEC. Immunological and nucleic acid-based tests that detect O and H antigens, verocytotoxin or various genes associated with EHEC can be used for presumptive diagnosis. These rapid tests can determine whether potential pathogens are present in samples before isolation. They include dipstick and membrane technologies, agglutination tests, microplate assays, colony immunoblotting, PCR, immunofluorescence and ELISAs. Although verocytotoxin production can aid identification, VTEC are common in animals, and these organisms are not necessarily EHEC; additional virulence factors must also be identified. Verocytotoxin-negative derivatives of EHEC can occur. The results from rapid tests are confirmed by isolating the organism. Some kits validated for food and meat samples and kits for human clinical samples may lack sensitivity when testing fecal samples from animals. Although cattle can produce antibodies to O157, serology is not used routinely in animals to diagnose infections with VTEC or EHEC.

S I d e 3 1	PREVENTION AND CONTROL	
S I d e 3 2	Recommended Actions • 0157:H7 nationally notifiable in humans - Contact your physician for guidance • Animal cases may be reportable in some states - State veterinarian http://www.usaha.org/stateanimalhealthofficials. aspx	STEC <i>E. coli</i> infections in humans are nationally notifiable. If you suspect an <i>E. coli</i> infection, contact your physician for additional guidance. Animal cases may be notifiable to in some states. State and/or federal authorities should be consulted for specific guidelines.
S I d e 3 3	<section-header><section-header><section-header><section-header><section-header><section-header><section-header><section-header><section-header><section-header><section-header></section-header></section-header></section-header></section-header></section-header></section-header></section-header></section-header></section-header></section-header></section-header>	Frequent hand washing, especially before eating or preparing food, and good hygiene are important in preventing transmission from animals and their environment. Hand washing facilities should be available in petting zoos and other areas where the public may contact livestock, and eating and drinking should be discouraged at these sites. Thorough hand washing is especially important after changing diapers, after using the toilet, and before eating or preparing food. To protect children and other household members, people who work with animals should keep their work clothing, including shoes, away from the main living areas and launder these items separately. Bed linens, towels and soiled clothing from patients with hemorrhagic colitis should be washed separately, and toilet seats and flush handles should be cleaned appropriately. In some areas, regulations may prohibit infected children from attending daycare or school until they are no longer shedding organisms. Some authors suggest that isolating infected children from their young siblings or other young household members can significantly decrease the risk of secondary spread. [Photo: Hand washing. Source: Centers for Disease Control and Prevention]
S I d e 3 4	<ul> <li>Prevention in Humans</li> <li>Don't cross-contaminate <ul> <li>Wash hands, counters, cutting boards, utensils after contact with raw meat</li> </ul> </li> <li>Thoroughly cook meats <ul> <li>Avoid unpasteurized products</li> </ul> </li> <li>Wash fruits/vegetables before eating</li> <li>Keep livestock away from private water supplies</li> </ul>	To prevent cross-contamination during food preparation, consumers should wash their hands, counters, cutting boards, and utensils thoroughly after they have been in contact with raw meat. Meat should be cooked thoroughly to kill <i>E. coli</i> . Unpasteurized milk or other dairy products and unpasteurized juices should be avoided. Water that may be contaminated should not be used to irrigate vegetable crops, and untreated manure/ effluents should not be used on fruits or vegetables that will be eaten raw. Post-harvest measures include thorough washing of vegetables under running water to reduce bacterial numbers. Vegetables can also be disinfected with a dilute chlorine solution. It is safest to wash vegetables immediately before use; under some environmental conditions, populations of bacteria can build up again after a few days. EHEC carried internally in plant tissues are

difficult to destroy except by irradiation or cooking. Contamination of public water supplies is prevented by standard water treatment procedures. Livestock-should be kept away from private water supplies. Microbiological testing can also be considered. To the extent possible, people should avoid swallowing water when swimming or playing in lakes, ponds and streams.



Prevention of shedding in domesticated animals, particularly ruminants, is expected to decrease the number of human infections. These techniques are still in development. Identifying and targeting super-shedders should be particularly effective. The removal of supershedders from the herd might be helpful. In one study, allowing a pasture to lie fallow for the winter prevented the transmission of EHEC O157:H7 to susceptible animals the following spring. Other proposed interventions include vaccination; the application of disinfectants (e.g., chlorhexidine), various antimicrobial chemicals or bacteriophages to the terminal rectum; and the use of probiotics that would preferentially colonize the gastrointestinal tract. Dietary manipulations have also been proposed. These interventions are still in the research stage.

S I d e 3 6	Additional Resources USDA Food Safety and Inspection Service - http://www.fsis.usda.gov/Factsheets/E_coli/in dex.asp Center for Food Security and Public Health - www.cfsph.iastate.edu CDC <i>E. coli</i> - http://www.cdc.gov/ecoli/	
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S	A alua avula dava avata	Last reviewed: May 2012
5 	Acknowledgments	Last reviewed: May 2012
S   i	Development of this presentation was made possible	Last reviewed: May 2012
S I i d	2	Last reviewed: May 2012
l i	Development of this presentation was made possible through grants provided to the Center for Food Security and Public Health at Iowa	Last reviewed: May 2012
l i d	Development of this presentation was made possible through grants provided to the Center for Food Security and Public Health at Iowa State University, College of Veterinary Medicine from the Centers for Disease Control and Prevention, the U.S. Department of Agriculture, the Iowa Homeland Security and	Last reviewed: May 2012