including Medtronic's Endeavor (coated with zotarolimus), Abbott's Xience V (coated with everolimus), and Conor Medsystem's CoStar (coated with paclitaxel); however, given the concerns about late stent thrombosis, the FDA could ask companies for longer-term data before considering newer stents for approval in the United States. How long that term should be is likely to be one more contentious issue at the FDA meeting.

Meanwhile, as clinicians sort through the new information and await the FDA's pronouncements, they are already reducing their use

of the current technology slightly: sales of drug-coated stents have dipped by 5% for Boston Scientific and 6% for Cordis, while sales of bare-metal stents are edging up.

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Don't Eat the Spinach — Controlling Foodborne Infectious Disease

Dennis G. Maki, M.D.

First it was hamburger, then municipal water, apple cider, swimming in the lake, the day-care center, the petting zoo . . . and now, spinach. Is nothing safe?

Between August 19 and September 5, 2006, symptomatic enteritis from Shiga toxin–producing *Escherichia coli* O157:H7 infection was reported in 199 persons in 26 states in association with consumption of fresh spinach or spinach-containing products from commercial brands processed by Natural Selection Foods of San Juan Bautista, California.[1] One hundred two of these persons (51%) had been hospitalized as of October 6, and 31 (16%) had acute renal failure from the hemolytic–uremic syndrome or thrombotic thrombocytopenic purpura, which had developed in 29% of the affected children (<18 years of age), 8% of the affected adults 18 to 59 years of age, and 14% of the af-

fected adults 60 years of age or older. Three persons with confirmed cases had died by mid-October: two elderly adults and
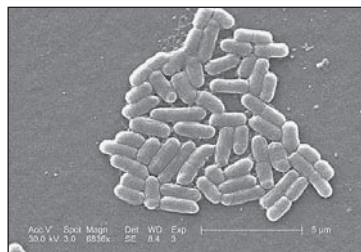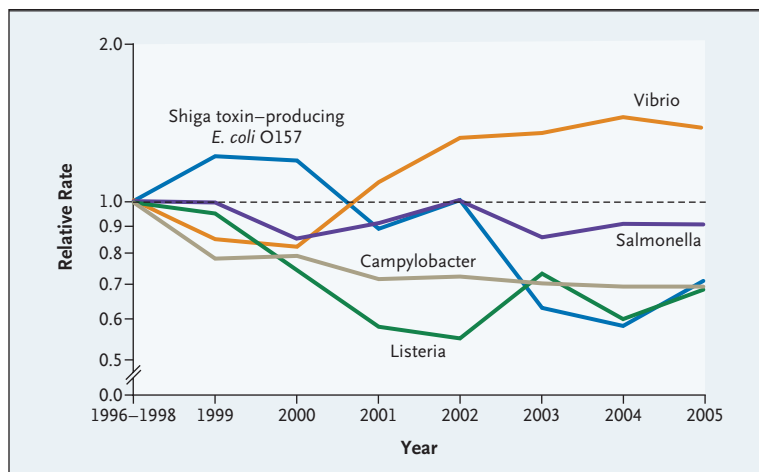

E. coli O157:H7.

a 2-year-old with the hemolytic–uremic syndrome.

E. coli O157:H7 was isolated from 13 opened packages of spinach provided by patients from 10 states; 11 of the packages had lot numbers indicating processing by a single manufacturing facility on the same day. The DNA pattern found in all 13 isolates (by subtyping restriction fragment–length polymorphisms) matches that of the outbreak strain isolated from

numerous patients. The epidemic was quickly controlled by a nationwide ban on the consumption of uncooked spinach, followed by a ban on and recall of all spinach products processed and distributed by Natural Selection Foods. The precise mechanism of contamination remains undetermined, although on October 12, authorities detected the same strain of the bacterium in manure from one of four contiguous cattle ranches that are suspected sources.

This is at least the 26th reported outbreak of *E. coli* O157:H7 infection that has been traced to contaminated leafy green vegetables since 1993, and more than 400 Shiga toxin–producing *E. coli* outbreaks have been reported since enterohemorrhagic *E. coli* O157:H7 was identified as a cause of foodborne disease in 1982.[2] But although this outbreak captured media attention for weeks, it must be put in perspec-

Janice Carr/CDC.

Relative Rates of Laboratory-Diagnosed Foodborne Infection with Vibrio, Salmonella, Campylobacter, Listeria, and Shiga Toxin–Producing *E. coli* O157, as Compared with 1996–1998 Rates.

Data are from FoodNet (the Foodborne Diseases Active Surveillance Network of the CDC, FDA, and USDA).[3]

tive: during each day of the outbreak, there were at least 5 to 10 times as many cases of endemic Shiga toxin–producing *E. coli* infection throughout the country as there were outbreak cases.

Toxigenic and enteroinvasive strains of *E. coli* have long been recognized as the leading cause of foodborne or waterborne traveler's diarrhea, which is typically acquired by Westerners visiting a developing country. Diarrheal illness caused by these strains is rare in North America. So how can more than 110,000 residents of one of the world's wealthiest countries become infected with life-threatening enterohemorrhagic Shiga toxin–producing *E. coli* each year, with as many as 80 dying as a consequence?[2] How do outbreaks continue to occur in a country where food production and distribution are intensively regulated at every level — from farms and ranches to food-processing companies and packing plants to supermarkets and restaurants?

The federal agencies charged with food safety — the Food and Drug Administration (FDA), the U.S. Department of Agriculture (USDA), and the Centers for Disease Control and Prevention (CDC) — have made substantial efforts to improve food safety, particularly in the commercial production and distribution of foods.[3] Moreover, state and regional public health and other agencies have ratcheted up their food-safety activities in recent years. The FoodNet surveillance system of the CDC, FDA, and USDA has been operational in 10 states for a decade, which has allowed for more accurate laboratory-based surveillance of foodborne disease than was possible in the past, and there is evidence that the incidence of foodborne infectious disease in the United States has decreased substantially over the past decade (see graph).[3] Unfortunately, the decline has leveled off since 2000, and achieving substantial further improvements in microbiologic food safety poses formidable challenges, especially if we continue to rely solely on our current strategies.

The complex epidemiology of human infection with *E. coli* O157 and the devastating vasculopathic and prothrombotic disease associated with it (see flowchart) illustrate the complexity of the challenge: of the myriad community-acquired emerging infectious diseases of the past 30 years, few can more justifiably be called a "disease of progress" than enterohemorrhagic infection with Shiga toxin–producing *E. coli*.

Enormous changes in food production during the past half-century underlie the emergence of this unique bacterial enteropathogen as an agent of life-threatening foodborne disease in a developed country. During my childhood in 1950s rural Wisconsin, when I ate a hamburger at home, the ground beef had been produced locally from cuts taken from several sides of beef purchased by the neighborhood grocer from a local farmer, who probably raised no more than 25 pasture-fed cows on a 150-acre farm. If I ate a fast-food hamburger, the ground beef came from a regional packing plant, which processed cattle that had been pasture-raised on a Western ranch of several thousand acres. Today, virtually all beef consumed in North America is produced on a vast industrial scale, starting with a herd of tens of thousands of grain-fed cattle, raised in the final months before slaughter in the constrained environment of a feedlot, with the beef cuts from hundreds of cows to several thousand contributing to a single lot of more than 100,000 pounds of ground beef, shipped to many hundreds of supermarkets in multiple states. Since grain-feeding to enhance meat production — as contrasted with traditional pasturing — promotes enteric colonization by acid-resistant Shiga

| Primary Reservoir of STEC O157:H7 | Colonization of domestic cattle with fecal STEC O157:H7 |
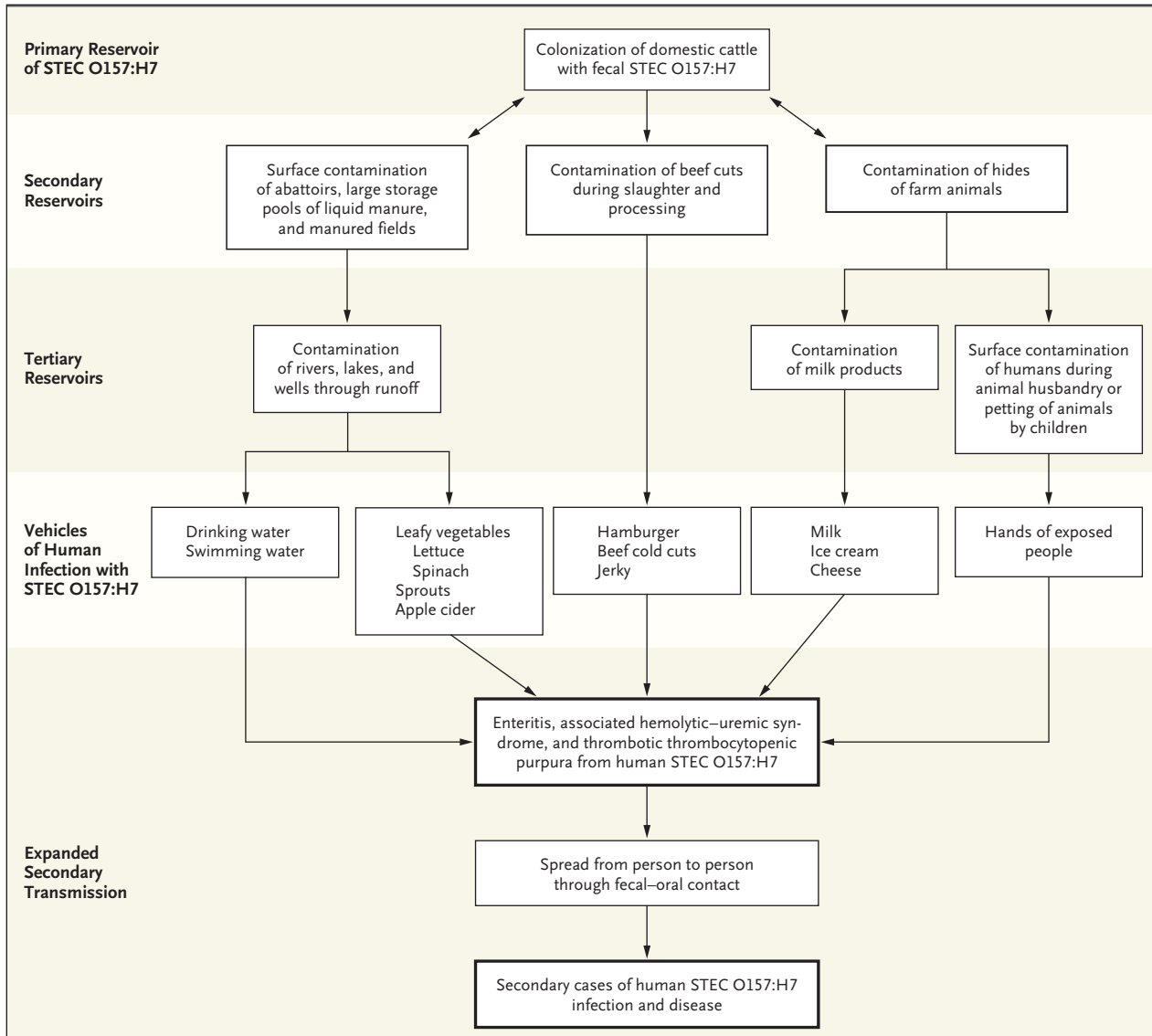
Epidemiology of Shiga Toxin–Producing *E. coli* O157:H7 Infections in North America.

The complex epidemiology of human infection with Shiga toxin–producing *E. coli* (STEC) O157:H7 (and, presumably, non–O157:H7 *E. coli* that produces Shiga toxin), associated with the hemolytic–uremic syndrome and thrombotic thrombocytopenic purpura, underlies the challenge of controlling such infections and other foodborne disease in North America.

toxin–producing *E. coli*,[4] up to 2 to 3% of domestic cattle carry *E. coli* O157 at the time of slaughter, which is nearly universally associated with surface contamination of the carcass. The use of ground beef produced from hundreds or even several thousand animals greatly increases the risk of contamination of the pooled meat product with Shiga toxin–producing *E. coli*.

Moreover, raising thousands of animals with the use of industrial farming techniques generates staggering quantities of manure potentially contaminated with Shiga toxin–producing *E. coli*, far more than any farm can use as fertilizer. Huge lagoons of stored liquid manure are the consequence — as are periodic spills of raw manure into nearby streams. During heavy rains, runoff contami-

nation of fields of commercially raised vegetables and orchards, as well as of rivers, lakes, and wells, results in produce-associated or waterborne outbreaks of *E. coli* infection.

Although most reported infections with Shiga toxin–producing *E. coli* are linked to undercooked ground beef, nearly 25% of outbreaks stem from contamination of commercial produce that is

eaten uncooked — lettuce, spinach, cabbage, sprouts, or tomatoes.[2] Outbreaks have been traced to orchards that market unpasteurized apple cider, made from apples that have dropped from the trees and have become contaminated by *E. coli* O157 from manure used to fertilize the soil. Enteric colonization (and surface contamination) of domestic cattle has resulted in human disease from contaminated milk products and in outbreaks among children visiting petting zoos. Outbreaks at county fairs appear to have been caused by aerosolization of *E. coli* in the animal barns. Finally, since the infective dose of acid-resistant *E. coli* O157 (less than 100 organisms) is much lower than that of most other bacterial enteropathogens, secondary spread through fecal–oral contact further expands the number of Shiga toxin–producing *E. coli* cases in most outbreaks (see flowchart).[2]

Since 2004, there has been a 43% decline in the *E. coli* contamination of ground-beef samples tested by the USDA — a decrease that follows intensified federal regulatory efforts to enhance food-safety systems and microbiologic testing by commercial meat producers.[3] Much less progress has been made in enhancing the safety of commercially produced vegetables. It is hoped that the Lettuce Safety Initiative, which has been expanded to include spinach, will reduce the occurrence of infection related to consumption of lettuce and spinach.

Although the producers and commercial processors of high-risk produce are required to wash products before packaging, washing clearly does not reliably eliminate the risk of contamination. Cooking spinach properly (at 160°F for at least 15 seconds) can eliminate the risk, but undercooking is probably common: the undercooking of foods such as poultry or eggs still causes millions of cases of salmonella and campylobacter infection each year.[3] More than four million tons of lettuce, spinach, and sprouts are consumed in North America every year, and it is unclear how much the risk is reduced by rewashing the produce, even if the consumer bothers to do it. So what is the answer?

As Osterholm and Norgan have proposed,[5] irradiation of high-risk foods after processing could greatly reduce the incidence of all bacterial foodborne disease and save hundreds of lives each year. The efficacy and safety of food irradiation have been established through extensive research, which has demonstrated that irradiation kills or markedly reduces counts of food pathogens without impairing the nutritional value of the food or making it toxic, carcinogenic, or radioactive. Irradiation of food is already approved in the United States for most perishable foods and has been endorsed by the World Health Organization, CDC, FDA, USDA, American Medical Association, and European Commission Scientific Committee on Food. Unfortunately, because of a widespread lack of understanding of the risks and sequelae of foodborne disease and of the effectiveness and safety of irradiation — and because of intense opposition from antinuclear activists and other interest groups — irradiation of food as a public health measure has not yet achieved widespread acceptance.

A number of food products are already commonly irradiated, with no evidence of harmful effects, and for decades, we have sterilized hundreds of millions of implanted medical devices through irradiation each year. The CDC has estimated that irradiation of high-risk foods could prevent up to a million cases of bacterial foodborne disease that result in the hospitalization of more than 50,000 persons and kill many hundreds each year in North America. I believe it is time to overcome our irrational fears and act to ensure the safety of our food.

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