Swine as a Potential Reservoir of Shiga Toxin-Producing *Escherichia coli* O157:H7 in Japan

To the Editor: Shiga toxin-producing *Escherichia coli* (STEC) O157:H7 has become a major meat safety issue worldwide. Cattle, an important reservoir of human infection (1), may not be the only source of this organism (2,3). In a survey of pigs in England (4), non-STEC O157 was isolated from four (0.4%) fecal samples collected (after slaughter) from 1,000 pigs. We found that, although an unlikely source of infection for humans, pigs are a potential reservoir of STEC O157:H7 in Japan.

In 1997, there were 14,400 pig farms and 9,823,000 pigs (average 682 per farm) in Japan. Thirty-five (0.24%) of these farms were randomly selected for study, and rectal swabs were taken from 221 healthy pigs during May and June 1997. The average number of animals examined on each farm was 6.3.

Fecal samples were dipped into test tubes containing Cary-Blair transport medium (Nissui, Japan) and kept refrigerated until processing (usually within 48 hours). Swabs were then incubated overnight at 42°C in 10 ml of mEC broth (Kyokuto, Japan) containing 20 µg/ml of novobiocin (Sigma, USA), after which one loop of the broth was spread onto MacConkey sorbitol agar medium (Difco, USA). After overnight incubation at 37°C, sorbitol-negative colonies from the agar plates were tested by slide agglutination with *E. coli* O157-latex test (Oxoid, UK). Strains that agglutinated were confirmed as *E. coli* by using the API 20E system (BioMerieux, France). Strains confirmed as *E. coli* O157 were subcultured in a motility medium for 3 to 4 days to enhance development of flagella, then they were tested by tube agglutination with *E. coli* H7 antiserum (Denka-seiken, Japan). The swine *E. coli* O157:H7 isolates were examined by polymerase chain reaction for the presence of Shiga-toxin genes *stx1* and *stx2* and to elucidate intimin (*eaeA*) DNA sequences (5), for a plasmid of 92 kb (pO157) by agarose gel electrophoresis (6), and for phage type by the previously described method (7).

Although the numbers sampled were too small to allow comparisons between farms, samples from three (1.4%) apparently healthy pigs (ages: 2, 6, and 9 months) from three farms (8.6%) were positive for STEC O157:H7. The three strains from the pigs were biochemically typical of STEC O157:H7 that did not ferment sorbitol and lacked ß-glucuronidase; agglutinated with *E. coli* O157-latex and with H7 antiserum; possessed *stx1*, *stx2*, and *eaeA* genes; and harbored pO157 plasmid characteristic of STEC O157:H7. The strains belonged to phage type 21, 37, or 43.

The 1.4% carriage rate of STEC O157:H7 in pigs in this investigation is almost the same as that in cattle in Japan (8), which suggests that STEC O157:H7 strains are probably widespread in Japanese pig populations. The STEC O157-positive pigs were each housed in a concrete-floored pen and kept separate from cattle. Whether these pig isolates are the same as cattle or human isolates needs to be clarified; however, they had the same biochemical and genetic markers as STEC O157:H7 isolated from cattle and humans (6,9). The phage type 21 that we found among pig isolates was also observed in bovine and human STEC O157:H7 isolates in Japan (7). These results suggest that common vehicles for dissemination of the organism may exist.

So far, pork has not been identified as a source of human STEC O157:H7 illness in industrialized countries, but our results indicate that eating pork, contact with pigs, and contamination with pig feces should be considered potential sources of this pathogen. This is the first isolation of naturally occurring STEC O157:H7 in pigs in Japan.

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Hospitalizations for Rotavirus Gastroenteritis in Gipuzkoa (Basque Country), Spain

To the Editor: Rotavirus is the main cause of severe acute gastroenteritis among children both in developing and in industrialized countries. The incidence of rotavirus gastroenteritis in northern Europe is similar to or greater than the estimated incidence of the disease in the United States (1-3); however, little is known about the impact of rotavirus infection on health in southern Europe.

We examined the incidence of hospitalization for rotavirus gastroenteritis during 3 years (July 1993-June 1996) in Gipuzkoa (population 400,480, of whom 58,896 are <15 years of age). The presence of rotavirus antigen was prospectively investigated by enzyme immunoanalysis (IDEIA Rotavirus, Dako Diagnostics, UK) in stool samples from all patients <15 years of age in the study area for whom a microbiologic analysis was requested for acute gastroenteritis. Children hospitalized for rotavirus gastroenteritis were sought retrospectively through searching both the computerized records of microbiology laboratory and hospital medical records for the diagnoses 558.9 (other gastroenteritis and presumably noninfectious colitis) and 008.6-009.3 (enteritis due to specific viruses and presumably infectious intestinal disorders) (4). All children in this study lived in the study area, had been hospitalized for gastroenteritis, and had one stool sample positive for rotavirus in the first 5 days of hospitalization without another gastroenteritis agent detected in the stool.

One hundred fifty-two (82 male and 70 female) of 1,004 children <15 years of age with rotavirus gastroenteritititis had been hospitalized for rotavirus infection. No deaths were recorded. Cases usually occurred in epidemic waves, with the highest incidence in January-March. An additional 133 children with rotavirus in stools had been hospitalized but were not included in this study because they had hospital-acquired infections (67 cases), were coinfected by another microorganism (11 cases), came from outside the geographic study area (19 cases), or had a main reason for hospitalization other than gastroenteritis (36 cases). The mean annual incidence of hospitalization was 0.86 per 1,000 children (1 month to 14 years old) and 3.11 per 1,000 children (1 month to 5 years old). The maximum incidence occurred in 6- to 11-month-old children (11.81 per 1,000 children). Children were hospitalized for a mean of 4.8 ± 2.2 days. Rotavirus gastroenteritis was responsible for 152 (2%) of 7,403 pediatric admissions. For the 1- to 35-month age group, community-acquired rotavirus gastroenteritis was responsible for 140 (4.6%) of 3,026 admissions.

Although the incidence is based solely on confirmed cases, the findings closely reflect disease incidence in our region. The National System of Health covers 100% of the reference population, and hospitalization of children in private institutions is rare. Stool cultures were taken for most children for gastroenteritis (94.5%), and the presence of rotavirus was investigated in every case.

The hospitalization rate observed in this study was similar to that reported in other studies from Sweden (2), Denmark (5), and the United States (6) and lower than that found in England and Wales (3). In Spain, reporting of rotavirus infection is not required, is not included in mortality registers, and is not the object of specific vigilance by sentinel surveillance systems. Therefore, information about the incidence and impact of rotavirus infection in Spain is scarce. However, two reports from Spain must be highlighted: one is based on a theoretical prediction using a statistical model (7) and the

other is a small clinical and epidemiologic study of hospitalized children <2 years of age in Santiago de Compostela (8). Data from both studies are consistent with our results. Rotavirus gastroenteritis is a common cause of hospitalization and produces a heavy load on the health-care system in our region. After years of research, vaccines that effectively prevent rotavirus infections in humans have been developed (9,10). These data should be considered in evaluating the potential benefits of introducing rotavirus vaccine in our region and monitoring its effectiveness.

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Israeli Spotted Fever Rickettsia (*Rickettsia conorii* Complex) Associated with Human Disease in Portugal

To the Editor: Mediterranean spotted fever is endemic in Portugal, where it is a reportable disease with approximately 1,000 new cases per year (1). *Rickettsia conorii* has been thought to be the only pathogenic rickettsia of the spotted fever group in Portugal (2), as well as in the Western Mediterranean area. Another rickettsia in this group, the Israeli spotted fever rickettsia, which belongs to the *R. conorii* complex (3-5), was isolated in 1974 from ticks and humans; however, its distribution appeared to be restricted to Israel (6). We report three cases of rickettsiosis in Portugal caused by Israeli spotted fever rickettsia.

Case 1. A 71-year-old woman was hospitalized with a history of fever (39ºC) for 6 days, headache, and icterus. The influenzalike syndrome was treated with an antipyretic. In the next 4 days, the patient had myalgias, malaise, and mental confusion. Ten hours after being transferred to an intensive care unit, she died with septic shock and multiorgan failure, despite intravenous administration of doxycycline and other antibiotics.

Case 2. A 79-year-old woman, who was previously healthy except for high blood pressure, was hospitalized with a 4-day history of gastrointestinal disorders, nausea, and vomiting, which were attributed to food poisoning; high fever (40ºC) developed, and 3 days later a cutaneous rash, which spread to the palms and soles. The diagnosis of Mediterranean spotted fever was made by indirect immunofluorescent assay against *R. conorii* (immunoglobulin [Ig] M 1:40; IgG 1:512). The patient was treated with doxycycline and was discharged from the hospital 20 days after admission.

Case 3. A 65-year-old woman was hospitalized with a 6-day history of fever (39ºC), headache, vomiting, and epigastric pain, which had been treated with penicillin. Rash and

icterus developed, and the patient died of shock and multiorgan failure 9 hours after hospitalization, despite treatment with a mixture of antibiotics, which contained doxycycline.

Rickettsiae of the spotted fever group were isolated by the shell vial technique from the blood of the three patients. Sequences of polymerase chain reaction-amplified fragments of 16SrRNA (1440 bp), citrate synthase (382 bp), and rompA (590 bp) genes of the isolates show 100% similarity with the homologous sequence of Israeli spotted fever rickettsia (4,7,8).

All three patients lived in semirural areas, along the River Tejo (Setubal District). None had left Portugal during the previous year. Although none had a tache noire, contact with ticks cannot be excluded. The absence of tache noire is typical in Israeli spotted fever (6). These findings indicate that the geographic distribution of Israeli spotted fever is wider than had been thought and includes the Iberian Peninsula. Because initial signs and symptoms of the disease are particularly uncharacteristic and appropriate treatment may be delayed, this rickettsia can cause life-threatening disease.

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Avoiding Misdiagnosis of Malaria: A Novel Automated Method Allows Specific Diagnosis, even in the Absence of Clinical Suspicion

To the Editor: We report three cases of malaria to illustrate a novel method that allows diagnosing the disease, even if clinicians do not suspect it or request malaria smears. Lack of clinical suspicion is a well-known factor for malaria misdiagnosis and may be responsible for almost 40% of deaths from *Plasmodium falciparum* infections in industrialized countries (1-3). A recent study from Canada showed that in 59% of cases malaria was initially misdiagnosed, and in 16% three or more physician contacts occurred before malaria smears were ordered (4).

Early diagnosis of malaria relies crucially on clinical suspicion. A clinician suspecting the disease has to explicitly request malaria smears. This problem has not been solved with the advent of several methods alternative to microscopy, including recently introduced rapid dipstick tests (5). Performing any of these tests blindly without a specific request is impractical. On the other hand, routinely performed laboratory tests in the work-up of febrile patients, e.g., automated full blood counts, have so far detected only nonspecific changes, such as anemia or thrombocytopenia, which are associated with many other conditions (6). These changes on their own are therefore not specific enough to trigger malaria smears without an explicit request.

New automated full blood counts-analyzers incorporate flow-cytometric principles. The Cell-Dyn 3500 (Abbott, Santa Clara, CA) uses scattered laser-light of leukocytes at four different angles to generate a white-blood-cell differential (7). Monocytes and neutrophils may

ingest birefringent depolarizing malaria pigment that can be detected by the instrument. The appearance of monocytes (purple dots) above the separation line, in the eosinophil area (green dots), is a highly specific sign of the presence of ingested malaria pigment and consequently malaria.

A study from South Africa investigating 224 directed samples for malaria diagnosis found a sensitivity of 72% and specificity of 96% (8). In Portugal, we observed 45 positives in 120 directed samples. So far, all cases identified by microscopy showed the typical changes in the full-blood-count plots, suggesting a near 100% sensitivity in imported malaria cases. Several thousand full-blood-count plots from patients with a wide range of underlying pathologic features did not show such changes, making them highly specific for malaria diagnosis. However, the changes may persist for some time despite clinical and parasitologic cure, as pigment-containing monocytes may remain in the circulation for 2 to 3 weeks (9). Consequently, the observed changes may not necessarily indicate acute disease but may persist during convalescence.

We report three cases in which clinical suspicion did not lead to the request of a malaria diagnostic test. The final diagnosis of malaria was made only because of the changes observed in the color monitor of the Cell-Dyn 3500. As part of a preliminary investigation of this new method, we reviewed all full-blood-count plots at 24-hour intervals. During a 2-week period, three full-blood-count granularity/lobularity plots compatible with malaria were identified and the full-blood-count results and clinical notes were reviewed. The principal symptoms in the three cases were fever and aches in bones and muscles, case 1; complications of assault, case 2; and feeling generally unwell (from drug abuse), case 3. In all cases, the full-blood-count results were within normal ranges, except for a thrombocyte count of 23,000 in case 2. In cases 1 and 3, the patients were discharged with a clinical diagnosis of flulike syndrome and drug abuse-related problems, respectively, while in case 2, the patient was to be admitted with a diagnosis of assault-related injuries. As attending clinicians had not requested malaria smears, we performed blood films on the recovered specimens that confirmed a diagnosis of malaria. (Case 1: *P. ovale,* 10,000 µl; case 2: *P. falciparum,* 9,000 µl; case 3: *P. falciparum,* 1,500 µl). In case 2, our findings permitted appropriate treatment in the emergency room; in the other two cases, it allowed patients to be contacted at home. All three patients (two male, one female) were of Black African origin but lived in Portugal. They had returned to Portugal after visiting Africa (Angola and Guinea). None of them had taken malaria prophylaxis during their journey.

Anisotropic malaria pigment has been the basis for several microscopy methods for malaria diagnosis (10). However, sensitivities are similar to that of conventional microscopy, and these methods have to be ordered specifically. In contrast, automated full-blood-count is regarded as routine for febrile patients, and the new automated method has the potential to detect additional, unsuspected cases, in which clinical suspicion did not lead to requests for malaria testing. If further studies validate this technique, the instrument could be modified to specifically flag such results, which would alert laboratory staff to perform blood films on these samples, even in the absence of a clinician's request. Finally, if software algorithms are adjusted to enumerate pigment-containing leukocytes, the usefulness of this indicator as a prognostic marker (11) could be further evaluated. The instrument may greatly facilitate quantification of pigment-containing leukocytes, which have been determined by time-honored but cumbersome microscopy.

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The First Reported Case of *Aerococcus* Bacteremia in a Patient with HIV Infection

To the Editor: We report the first case of *Aerococcus viridans* bacteremia in a patient with HIV infection. Two species in the genus *Aerococcus* have been implicated as rare pathogens in humans. *A. urinae* causes urinary tract infections; the other species, *A. viridans*, a gram-positive coccus considered a contaminant in cultures, has been associated with human infections that included bacteremia (1,2), septic arthritis (3), and infectious endocarditis (4,5). Widely distributed in the environment, the organism has been recovered from dust, vegetables, and crustaceans (6) and was isolated from different areas in a hospital (recovery room, intensive care unit, delivery room, treatment room, premature nursery) and from numerous objects (7).

We describe the first case of *A. viridans* bacteremia in a patient with HIV. A 34-year-old man without notable medical history sought medical attention after several weeks of epigastric midabdominal pain associated with a 15-lb weight loss; the pain did not respond to antacid medications. The patient said that he did not have fever, chills, night sweats, or history of transfusions and did not use alcohol, tobacco, or drugs. He had engaged in homosexual activity 2 to 3 years earlier.

Physical examination showed moderate cachexia and low-grade fever (38.8ºC) associated with tachycardia, but the heart and lung examination was otherwise normal. The abdomen was soft, flat, and tender to palpation in the midabdominal epigastric area, without hepatosplenomegaly, guarding, or rebound tenderness. No other abnormalities were identified. The patient was admitted to the hospital, and the initial set of routine blood cultures (Bactec 9240 instrument, Becton Dickinson, Sparks, MD) showed no growth. On hospital day 2, he began to have severe rigors, along with persistent fever. A second set of blood cultures drawn at that time grew paired gram-positive cocci in less than 24 hours. The patient was empirically started on penicillin G, and cefotaxime was added shortly thereafter because of the possibility of intermediately resistant pneumococcus. The rigors responded to antibiotic treatment, and a third set of blood cultures showed no growth. The negative blood cultures before and after appropriate antimicrobial therapy and the short time to detection (which suggests a large initial inoculum) led us to believe that the organism in this case was a true pathogen and not a contaminant.

The patient's work-up included a normal abdominal computer tomography; abdominal ultrasound showed nonobstructing cholelithiasis. Laboratory tests demonstrated anemia of chronic disease diagnosed by a hematocrit of 25% associated with a low reticulocyte production index, high serum ferritin, and an elevated erythrocyte sedimentation rate (91 mm/hr), with polyclonal hypergammaglobulinemia and hypoalbuminemia on serum protein electrophoresis. Stool samples were negative for occult blood, and serologic tests showed no *Helicobacter pylori* antibodies. The patient's total lymphocyte count was 300 cells/µl, HIV serologic testing by enzyme-linked immunosorbent assay and Western blot was positive, and flow cytometry revealed an absolute CD4+ T-lymphocyte count of 19 cells/µl, with an HIV-1 retroviral titer of 280,000 by polymerase chain reaction. Gallium scanning was negative for *Pneumocystis carinii* pneumonia and gastrointestinal lymphoma. A follow-up endoscopy showed esophageal ulcers, with disruption of the mucosal barrier. Blood cultures were negative for cytomegalovirus or mycobacteria, but the aerobic isolate initially reported as paired gram-positive cocci was later identified as *A. viridans*.

The identification of *A. viridans* was made on

the basis of the following characteristics: catalase negativity, α-hemolytic gram-positive cocci forming pairs and tetrads (not chains) in broth culture; growth in the presence of 40% bile and 6.5% NaCl and ability to hydrolyze esculin; pyrrolidony l-aminopeptidase positivity, leucine-aminopeptidase negativity; and production of acid from trehalose, sucrose, maltose, and lactose but not from sorbitol.

Susceptibility testing by the agar dilution method showed that the isolate was susceptible to penicillin-G (MIC = 0.12 µg/ml) and vancomycin (MIC = 0.25 µg/ml). On the basis of this case and previous reports (1,2), we believe that *A. viridans* is a potential pathogen that can cause serious infections in immunocompromised patients. The presumed route of infection in this patient was esophageal ulcers. Clinical microbiologists should pay close attention to α-hemolytic, catalase-negative streptococci recovered from sterile body sites that form tetrads rather than chains on Gram stain.

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Proficiency in Detecting Vancomycin Resistance in Enterococci among Clinical Laboratories in Santiago, Chile

To the Editor: Vancomycin-resistant enterococci (VRE) can be difficult to detect because of limitations in the susceptibility testing methods commonly used in clinical laboratories. Although VRE have not been reported in Chile, clinical isolates have been reported in Argentina (1) and Brazil (2). It is important to detect vancomycin resistance as early as possible, so infection control preventive measures can be instituted when they have their greatest impact. The microbiology laboratory is the first line of defense against VRE, as it plays a critical role in its recognition. In Chile, most laboratories follow the National Committee for Clinical Laboratory Standards recommendations for antimicrobial susceptibility testing and use disk-diffusion methods (3); however, these methods have limitations in detecting low levels of resistance to vancomycin in enterococci.

We evaluated the ability of referral microbiology laboratories in Chile to detect vancomycin resistance in five *Enteroccocus* spp. isolates with different susceptibility patterns for vancomycin, penicillin, and ampicillin. Of six referral laboratories that agreed to participate, four used the disk-diffusion method to evaluate antimicrobial susceptibility. Two used an agar dilution minimum inhibitory concentration (MIC) method, one as the only susceptibility testing method and the other in addition to disk diffusion. The participants correctly evaluated vancomycin susceptibility in 17 (57%) of 30 isolates.

The accuracy of detecting vancomycin resistance varied according to the level of resistance. Isolate 1, which had a high level of resistance (Van A phenotype, MIC 256 µg/ml), was evaluated correctly in 5 (83%) of 6 laboratories. Isolate 2, with a lower level of resistance (Van B, MIC 64 µg/ml), was evaluated correctly in 4 (67%) of 6 laboratories. Isolates 3 and 4, both with intermediate resistance (Van B, MIC 16-32 µg/ml, and Van C, MIC 8 µg/ml, respectively), were evaluated correctly by one laboratory each. Isolate 5 (vancomycin susceptible) was evaluated correctly by all laboratories. Susceptibility to penicillin and ampicillin was correctly identified in 53 (96.4%) of 55 isolates. Although laboratories

correctly identified *E. faecium* and *E. faecalis* to the species level, most (4 of 5) did not correctly identify *E. gallinarum* (three misidentified it as *E. casseliflavus* and one as *E. faecalis*).

The results of this study are consistent with those of previous studies in the United States (4,5), South America (6), Spain (7), and Mexico (8). Although in countries like Chile, disk diffusion is practical and reliable for most susceptibility testing, detecting low-level vancomycin resistance in enterocci is difficult without supplementary testing. In Chile, as in other countries, strategies should be implemented to improve detection of these strains, including improvement of phenotypical and genotypical methods for VRE detection and species identification. Documentation of proficiency in detecting VRE is important for improving laboratory performance, detecting clinical isolates, and accurate and reliable reporting to local, national, and international surveillance systems.

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Food-Related Illness and Death in the United States

To the Editor: Dr. Mead and colleagues should be commended for attempting to estimate the prevalence of foodborne disease in the United States (1). Their study provides more complete estimates than previous studies in terms of the number of foodborne pathogens included; for example, it includes the first realistic estimate of the number of cases of disease due to Norwalk-like caliciviruses. However, the publication of these estimates raises some important issues.

Even though "accurate estimates of disease burden are the foundation of sound public health policy" (2), most of these estimates (in particular, the assumption that unknown agents are transmitted by food in the same proportion as known agents) were derived from assumptions rather than data. Known foodborne agents clearly cannot account for most gastrointestinal illnesses (1). However, illnesses from unknown agents may be as likely to have the transmission characteristics of rotavirus (1% foodborne) or *Cryptosporidium* (10% foodborne) as those of the Norwalk-like viruses (40% foodborne). Furthermore, it was assumed that detecting outbreaks or cases of toxin-mediated illnesses (e.g., due to *Bacillus cereus*, *Staphylococcus aureus*, or *Clostridium perfringens)* follows the model of *Salmonella*. In the authors' entire list of known foodborne agents, data are presented for cases identified both from outbreaks and active surveillance for only three agents: *Salmonella, Shigella*, and *Campylobacter*. *Salmonella* is clearly the most highly characterized, hence the most attractive as a model. However, the ratios of the numbers of cases detected through active surveillance to the numbers of cases detected through outbreaks range from 10 for *Salmonella* to more than 400 for *Campylobacter*. What if the ratios for toxin-mediated illnesses were more

similar to *Campylobacter* than to *Salmonella* ratios? The total estimated cases of these illnesses would increase by a factor of 40. The inadequacy of simply applying a *Salmonella*-based multiplier to the number of cases reported from outbreaks can be demonstrated by applying that multiplier to the total number of cases reported in all foodborne disease outbreaks, typically 15,000 to 20,000 per year (3,4). On the basis of these estimates, the number of foodborne illnesses would range from 5.7 million to 7.6 million, including illnesses caused by unknown agents.

The authors make similar assumptions for hospitalizations and deaths: unknown agents are estimated to account for 81% of hospitalizations and 65% of deaths due to foodborne illnesses. In a retrospective review of death certificate data similar to that used by Mead and colleagues, Perkins et al. projected the number of unexplained deaths possibly due to infectious diseases they expected to find in the Emerging Infections Program sites (5). Prospectively, a much smaller number of unexplained deaths was actually found, because known causes were identified through a detailed review of the death certificates and cases (6). A prospective examination of death certificates for foodborne diseases might also result in a smaller than expected yield.

The need to rely on assumptions to generate estimates highlights the gaps in our understanding of foodborne diseases. A dozen different studies could address these data gaps. However, once the 76 million figure is agreed upon, the perceived need for these studies will decrease.

Finally, if these estimates are accepted as reasonable, do current food safety efforts represent sound public policy? If 82% of foodborne illnesses, 81% of hospitalizations, and 65% of deaths are caused by agents we have not yet identified, where is the commitment of resources needed to identify them? If eradicating *Campylobacter*, *Salmonella, Escherichia coli* O157:H7, and *Listeria* would reduce the number of foodborne illnesses by only 5%, hospitalizations by 10%, and deaths by 25%, why are these agents the primary focus of our national foodborne disease control efforts? Overestimating the occurrence of foodborne diseases caused by unknown agents may lead us to undervalue the public health importance of these and other well-known agents.

Estimating the occurrence of foodborne diseases is daunting. The numerous efforts, including this one by Mead et al., to provide estimates have serious shortcomings. The real challenge is to identify the gaps in our knowledge so that they can be systematically addressed and updated estimates of foodborne illness can be provided to guide prevention efforts and assess the effectiveness of current food safety measures (2).

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Food-Related Illness and Death in the United States–Reply to Dr. Hedberg

To the Editor: Like all scientific undertakings, our estimates require assumptions. Because the actual frequency of foodborne transmission of unknown agents cannot be measured directly, it must be assumed. If unknown agents had transmission characteristics similar to those of rotavirus (1% foodborne transmission) or cryptosporidium (10% foodborne transmission), as Dr. Hedberg suggests, the number of cases of foodborne illness caused by unknown agents would be substantially lower than we estimated. However, unknown agents could just as easily have the transmission characteristics of *Escherichia coli* O157:H7 or *Campylobacter* (80% foodborne transmission), which just 30 years ago

were "unknown agents." For the sake of objectivity, we based our assumption on the aggregate of information for known pathogens rather than on "expert opinion." Interestingly, however, the Council of Science and Technology's "expert opinion" of the percentage of diarrheal illness due to foodborne transmission was 35% (1), nearly identical to the figure we developed.

As noted in our article, pathogen-specific multipliers for underreporting are needed for many diseases. For lack of a better model, we assumed that the underreporting of toxin-mediated diseases follows the model of *Salmonella*. The alternative Dr. Hedberg suggests, *Campylobacter*, is also a nontoxin-mediated bacterial infection like *Salmonella*, but one for which the degree of underreporting is less well documented. Extrapolating from outbreak data to the number of sporadic cases does indeed have limitations, which is the reason we used it for only the few diseases for which other surveillance data were not available.

Regarding deaths attributed to unknown agents, prospective studies may show that some of these deaths are in fact caused by known agents. However, this would not necessarily lessen the overall impact of foodborne illness: it would merely shift the number of deaths from the unknown category to the known category. The possibility that some deaths attributed to unknown agents are in fact caused by *Salmonella* and other known pathogens supports our use of data on known pathogens to estimate the frequency of foodborne transmission for unknown agents.

Improved estimates will require expanded research into the etiologic spectrum of undiagnosed illness. In the meantime, documenting the substantial impact of foodborne illness neither devalues current surveillance and prevention efforts nor undermines future efforts to determine the causes and impact of foodborne diseases. Our estimates help define gaps in existing knowledge and provide a more rational basis for public health policy than reliance on decades-old data.

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Specimen Collection for Electron Microscopy

To the Editor: We read with interest the excellent article "Smallpox: an attack scenario," by Tara O'Toole (1). At a critical point in the scenario, the author states, "The infectious disease specialist takes a swab specimen from the … skin lesions… and requests that it be examined by an experienced technician…. electron microscopy shows an orthopoxvirus consistent with variola." In fact, swab specimens of skin lesions for the detection by electron microscopy of viruses such as pox and herpes viruses are far from ideal; the chances of viral detection would be greatly enhanced if a skin scraping were provided to the electron microscopist.

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