Tracking Microbes: Defining The Horizon For Molecular Surveillance Of Foodborne Disease

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Foodborne illness sickens an estimated 48 million Americans each year. Yet, many of those sickened never seek medical attention, and very few cases – just the tip of the iceberg – get reported to the public health system. Identifying foodborne illness cases allows public health officials to detect outbreaks, pinpoint contaminated food, and get it off the market to limit the number of people sickened. In addition, the ongoing monitoring of foodborne illnesses by federal, state, local, territorial and tribal governments is the primary tool used to identify outbreaks of foodborne illness and otherwise unrecognized problems with food production and distribution. Investments in foodborne disease surveillance over the past 15 years transformed public health and improved our ability to detect foodborne illness.

Recent advances in science and technology once again hold new promise for revolutionizing foodborne illness surveillance. The use of faster diagnostic tests, using fewer resources, providing rapid “yes-or-no” results, and enabling doctors to treat patients more quickly and accurately, is increasing. However, these new tests do not involve growing the organism that is causing the illness (“culture”) and do not result in a pure sample of the bacteria (“isolate”). They are, in fact, culture-independent and therefore, do not generate the type of information our current surveillance system often relies on to detect many outbreaks of foodborne diseases.

Without new investments to modernize our surveillance infrastructure, these culture-independent diagnostic tests, or CIDTs, could pose a significant threat to the detection of foodborne diseases and, consequently, to public health.

For years, culturing stool samples from patients in clinical laboratories has been the accepted best practice for detecting foodborne pathogens. Much of what we know about foodborne illness has come from the study of patients whose diagnoses have been confirmed using these cultures. While reliable and accurate, this method is time and resource intensive. CIDTs, on the other hand, offer a faster and potentially cheaper alternative that should result in more cases of foodborne illness being diagnosed. Unfortunately, they lack information on serotype, subtype, molecular and antimicrobial susceptibility that is used by our current foodborne disease surveillance system, making it more difficult to identify outbreaks, evaluate trends, and facilitate regulatory oversight of food safety.

A critical piece of our current foodborne illness surveillance system – culture based testing – is in jeopardy. Long-term, we need to develop a new system for tracking microbes that takes advantage of modern molecular methods and is compatible with clinical diagnostics (e.g., is culture-independent), while at the same time utilizing the volumes of information collected through 16 years of PulseNet.

Short-term, the ability to culture foodborne pathogens needs to be maintained and isolates need to be preserved. Simultaneously enhancing other aspects of surveillance, such as improving our ability to identify how people contract foodborne illness (also known as exposure assessment), could offset some of the negative effects of CIDTs by improving our ability to identify potential exposures and link cases at a state and local level.

FINDINGS

(1) Widespread CIDT use may make detecting and investigating outbreaks more difficult.

(2) Changing diagnostic practices could hinder the ability of public health officials to track trends in incidence of foodborne illness and to monitor antibiotic resistance over time.

(3) CIDTs could make the regulatory oversight of food safety more difficult.

(4) With investments in technology and surveillance infrastructure, CIDTs offer an opportunity to increase the detection of foodborne illness in the long run.

(5) Policy makers must develop short- and long-term strategies to prevent disruption to our foodborne illness surveillance network during the transition to CIDTs.

RECOMMENDATIONS

A sudden shift to CIDTs without an appropriate public health response could have a cascading effect with significant consequences that take our surveillance system back decades. At the same time, CIDTs offer a new opportunity to revolutionize food safety surveillance – if the transition is managed properly. There are some immediate needs that, if addressed, could provide a significant first step forward in preserving, and ultimately enhancing, our food safety surveillance system. Specifically, the government should:

(1) Provide resources to public health laboratories to isolate pathogens from patient specimens.

(2) Expand state and local capacity for foodborne illness response.

(3) Invest in infrastructure and research to modernize our foodborne illness surveillance system.
DIAGNOSING FOODBORNE ILLNESSES AND CIDTs

Most of what we know about foodborne illness comes from the study of patients with diagnoses confirmed using culture. Clinically, most foodborne illnesses have similar symptoms (diarrhea, abdominal cramps, nausea, vomiting) and are indistinguishable from each other. To correctly diagnose and treat patients with foodborne disease, clinicians must rely on microbiological testing, which involves collecting a patient’s stool sample and sending it to a clinical laboratory. Depending on the pathogen, state reporting rules typically dictate that public health officials be notified of culture-confirmed cases of particular infections and that the isolates from those patients be submitted to public health laboratories for further analysis.† These state rules form the basis of our current foodborne illness surveillance system.

From a public health perspective, this method is accurate and reliable and provides the isolates needed to identify specific bacterial strains. The isolates, in turn, are used to link illnesses and identify outbreaks. However, from a clinical perspective, where the focus is on treatment of individual patients, this method has drawbacks: it takes time, typically one to two days; and it can be labor-intensive. The method for growing out pathogens is specific to the strain, so one must know what to look for before sending the sample to the lab. Furthermore, certain pathogens, such as norovirus, cannot be grown using culture. This is a problem for the clinicians who are trying to quickly diagnose and treat their patients, for the clinical laboratories that are trying to reduce costs, and for the public health agencies charged with quickly identifying clusters of illness.

Rapid tests for foodborne pathogens have existed for almost 20 years, but until recently, their use has been limited. Newer culture-independent diagnostic tests (CIDTs) potentially offer many advantages for both patients and clinicians. CIDTs are faster, easier to use, and eventually may be cheaper than culture-based tests. Newer tests may also provide information about pathogens that are currently hard to detect or track, such as norovirus. Patient management will improve as physicians more quickly diagnose and more accurately treat their patients. CIDTs also offer potential advantages for public health – if steps are taken to address their short comings. As more foodborne illnesses are diagnosed and reported to public health officials, more outbreaks will be detected* and the time needed to detect them will decrease. A recent study of the timeliness of foodborne illness surveillance found that outbreak recognition was delayed one to three weeks when investigations relied on follow-up of laboratory-confirmed cases or detection of clusters of illness. Time is critical during outbreak investigations - the longer the delay, the less likely the food source will be found and the more people who will be sickened. Thus, quicker diagnosis and the expected increase in numbers of illnesses and outbreaks would, in turn, improve our estimates of the impact of foodborne diseases as well as our ability to attribute illnesses to their food sources, monitor trends, and evaluate food safety efforts.

Case Study: Shiga Toxin-producing E. coli

In 1995, FDA approved the first CIDT for Shiga toxin-producing E. coli (STEC). This test does not differentiate between O157 and non-O157 strains of STEC, so their use was initially limited. However, awareness of the clinical importance of non-O157 STECs has increased in recent years and so has the use of CIDT Shiga-toxin tests. A survey of clinical laboratories serving the Foodborne Diseases Active Surveillance Network (FoodNet) sites found that the percentage of clinical laboratories using CIDTs for Shiga toxin increased from 6 percent in 2003 to 11 percent in 2007. A survey in Washington State found an eight-fold increase in the laboratories using these tests (from 4 percent in 2005 to 33 percent in 2010). A 2010 CDC survey showed that use is continuing to increase. In 2009, anticipating the potential impact on surveillance, CDC issued formal STEC testing recommendations for clinical laboratories, stating that 1) all stool specimens should simultaneously be tested using the Shiga toxin test and a culture-based test and 2) positive specimens for Shiga toxin should be forwarded to the appropriate public health laboratories.


† Not all states mandate that isolates be submitted to public health laboratories.

* The majority of foodborne illness outbreaks are detected through consumer complaint systems, which will not be directly affected by CIDT use. While pathogen-specific surveillance only detects a small fraction of outbreaks, it does enable us to detect large, widely distributed outbreaks and focuses efforts on pathogens of significant public health concern.
Unfortunately, CIDTs cannot yet provide both the rapid results that the clinical community desires and the detailed results that the public health system needs to identify outbreaks and evaluate trends. CIDTs may produce a large number of false positives – a problem for both patients and public health. A patient wrongly diagnosed with an enteric illness may be unnecessarily treated and/or excluded from work, childcare or school. As a result, public health officials may use their limited resources investigating cases that are not true illnesses. Thus, the use of CIDTs for foodborne pathogens has been limited – but that is changing.

With FDA’s recent approval of new CIDTs for foodborne pathogens, CIDT use will likely increase. A CIDT can now detect Salmonella without first isolating it in pure culture. CIDT testing will save time, allowing for earlier diagnosis and intervention, but will not differentiate between the more than 2500 serotypes of Salmonella. Without such differentiation, it is difficult to both identify and link cases and to compare historical and outbreak strains. Of even greater public health concern are the newly introduced tests that can detect multiple bacterial, viral and parasitic enteric pathogens in a fraction of the time needed for traditional culture-based tests. These tests have advantages – the expected organism does not need to be known in advance and multiple organisms can be detected – but, again, they lack the ability to differentiate between various strains of the pathogen (Table 1).

**TABLE 1: CIDT ADVANTAGES AND DISADVANTAGES**

<table>
<thead>
<tr>
<th>CLINICAL</th>
<th>DISADVANTAGES</th>
</tr>
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<tbody>
<tr>
<td>• Faster diagnosis</td>
<td>• Potential false-positives leading to unnecessary treatment</td>
</tr>
<tr>
<td>• Detection of wider range of pathogens</td>
<td>• Loss of antimicrobial sensitivity testing</td>
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<tr>
<td>• Better sensitivity for some pathogens</td>
<td></td>
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<tr>
<td>• Easier specimen collection (potentially)</td>
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<td>• Lower cost (potentially)</td>
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<tr>
<th>PUBLIC HEALTH</th>
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<tr>
<td>• Rapid detection of cases</td>
<td>• Potential false-positives leading to wasted resources on unnecessary follow-up</td>
</tr>
<tr>
<td>• Increased testing leading to increased identification of cases (potentially)</td>
<td>• Incorrect/unstable estimates of number of illnesses</td>
</tr>
<tr>
<td>• Surveillance possible for a wider range of pathogens</td>
<td>• Disruption of trend monitoring</td>
</tr>
<tr>
<td>• Better sensitivity for some pathogens</td>
<td>• Investigation of pseudo-outbreaks</td>
</tr>
<tr>
<td></td>
<td>• Decreased ability to detect outbreaks or monitor trends in subtypes, such as Salmonella Enteritidis</td>
</tr>
<tr>
<td></td>
<td>• Loss of ability to monitor antimicrobial sensitivity or virulence trends</td>
</tr>
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<td></td>
<td>• Increased costs for public health surveillance</td>
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**PulseNet and the Investigation of Pathogens**

Early on, surveillance systems primarily detected outbreaks associated with events that sickened large groups of people at one setting – such as, the church-supper outbreaks. Since most outbreaks are detected and investigated by state and local public health agencies, widely distributed outbreaks – such as national outbreaks – were difficult to detect. However, as technology became more sophisticated, our surveillance systems were able to link cases from across the country and detect these larger outbreaks.

Created in the 1990s, PulseNet – an electronic database of molecular data (known as DNA fingerprints) collected and analyzed using standardized methods – provided public health professionals with the tool to link cases of foodborne illness from across the country and to monitor trends. Over 60,000 “fingerprints” from patients, food, and the environment are uploaded annually by public health laboratories into the PulseNet database. Since 2006, PulseNet has been used to link 15 foods, not previously connected to illnesses or outbreaks. In addition, CDC detects about 70 percent of multistate outbreaks through PulseNet. This ability to constantly identify and investigate clusters of disease significantly benefits both public health and the food industry by providing clues for preventing future failures in the food safety system.

How does PulseNet work?

Source (Figure): Centers for Disease Control and Prevention (CDC), “Pulsed-field gel electrophoresis process.”


<table>
<thead>
<tr>
<th>Sample Collection</th>
<th>When someone becomes sick and seeks medical help, a clinical specimen - usually a stool sample - is collected and sent to a laboratory.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Culture</td>
<td>Living cells are grown (or cultured) using special pathogen-specific enrichments that promote growth. This process usually takes 24-72 hours.</td>
</tr>
<tr>
<td>Isolate Bacteria</td>
<td>If the pathogen grows, the particular species or strain is separated (or isolated) from all other bacteria.</td>
</tr>
<tr>
<td>Notify Public Health</td>
<td>Depending on state laws, public health officials as well as CDC, are notified of positive test results. Often the clinical laboratory is asked to send the isolate to a public health laboratory for DNA fingerprinting.</td>
</tr>
<tr>
<td>Molecular Characterization</td>
<td>The isolates are used to identify the distinct variation of bacteria (known as serotype) as well as the bacteria's ability to cause disease and be treated with antibiotics. DNA fingerprints are also found at this time.</td>
</tr>
<tr>
<td>Submit to PulseNet</td>
<td>DNA fingerprints are submitted to CDC and entered into PulseNet. Regulatory agencies also collect DNA fingerprints from animal, food, and environmental sources for uploading into PulseNet.</td>
</tr>
<tr>
<td>Outbreak Detection</td>
<td>Specialized software is used to compare patterns, identify disease clusters, and link cases from across the country. The emergence of a new pattern or a larger than expected number of matches might suggest a potential outbreak.</td>
</tr>
<tr>
<td>Outbreak Investigation</td>
<td>If an outbreak is suspected, local, state, or CDC epidemiologists are notified, and an investigation may be launched. Identifying the specific food that caused the outbreak and tracing it to its source can take weeks or months.</td>
</tr>
<tr>
<td>Improved Food Safety</td>
<td>Outbreak investigations have led to changes in regulatory oversight/focus and have driven industry-wide changes in food production and processing as well as food safety prevention strategies.</td>
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Without appropriate changes, widespread use of CIDTs could undermine major components of the foodborne illness surveillance system. The focus of healthcare providers is diagnosing and treating their patients. In contrast, the focus of public health is improving population health. Differences in focus result in different priorities for selecting a laboratory method to use. Clinical laboratories typically base decisions about which laboratory methods to use on cost and ease of use—public health impact is usually not emphasized. Public health, on the other hand, needs laboratory methods that distinguish among strains of the same species of a microorganism in order to identify clusters of disease, monitor trends, and initiate other activities to protect the population. Since CIDTs do not provide such differentiation, their use could impact our ability to detect and investigate outbreaks, track trends in illnesses, monitor antibiotic resistance, and take needed regulatory actions.

Widespread CIDT use may make detecting and investigating outbreaks more difficult. Without isolates and the DNA fingerprints they provide being uploaded into PulseNet, major outbreaks might go unnoticed, and many more people will be sickened. For example, PulseNet has identified multiple U.S. *E. coli* outbreaks associated with sprouts over the past 10 years, which has resulted in industry-driven production changes and the development of regulatory guidance. These outbreaks are now generally detected when they are small. In contrast, Germany has had only one reported outbreak—the 2011 *E. coli* O104:H4 outbreak that caused more than 4,000 illnesses and 50 deaths. There are several reasons why Germany was unable to detect this outbreak until it was large, but widespread use of CIDTs certainly played a role (see Case Study: German Outbreak). Widespread implementation of CIDTs in the United States could have similar tragic results.

Changing diagnostic practices could hinder the ability of public health officials to track trends in incidence of foodborne illness and monitor antibiotic resistance over time. For example, not unexpectedly, the increased use of Shiga toxin tests led to an increase in the number of reported non-O157 STEC cases. Since these tests do not differentiate between non-O157 and O157 strains, it is possible that a substantial proportion of STECs identified only by Shiga toxin testing could actually be O157 STEC. Recent declines in reported incidence of O157 might reflect a change in diagnostic practices, rather than a true decrease in incidence.

**Case Study: The German *E. coli* O104:H4 Outbreak**

In May and July 2011, Germany experienced the largest outbreak ever reported of hemolytic uremic syndrome (HUS), a serious and potentially life-threatening disease, and bloody diarrhea related to Shiga toxin-producing *Escherichia coli* (STEC). More than 3,000 STEC cases and 845 HUS cases were reported to the Robert Koch Institute (RKI), Germany’s national agency for infectious disease epidemiology. Epidemiological studies pointed to sprouts as the source of the pathogen: specifically, a single lot of imported fenugreek seeds used to grow sprouts. Molecular analyses of bacterial isolates from raw sprouts obtained from the household of an outbreak patient eventually confirmed this source. This outbreak demonstrates two important implications for the future of outbreak investigations if isolates are no longer obtained and stored.

First, the German outbreak highlights the role of public health surveillance in the detection of outbreaks and the importance of using molecular methods to track disease in a timely manner. Since 2001, Germany has used an electronic reporting system to collect standardized data about HUS and enterohemorrhagic *E. coli* (EHEC) cases. In their system, physicians report suspected HUS cases to public health officials, while laboratories are responsible for reporting EHEC cases. The reporting process can take weeks. Time delays in reporting EHEC cases make outbreak detection difficult. Consequently, outbreaks can go unnoticed until there are several cases of severe disease. The 2011 sprout outbreak was only detected after a cluster of HUS cases in one area of Germany was reported. Routine detection and investigation of less severe cases of disease (e.g., non-HUS cases) could have led to earlier detection of the outbreak earlier and prevented many illnesses and deaths.

Second, this outbreak demonstrates the critical role that isolates play in identifying the source of the outbreak and characterizing the responsible strain. Genomic sequencing of isolates identified several unusual aspects of the outbreak strain early in the investigation—information that helped rule out potential vehicles and zero in on the source. In some ways, the *E. coli* outbreak strain was typical of an enteroaggregative *E. coli* (EAEC), which causes persistent diarrhea but does not cause severe diseases like HUS. However, genomic analyses were also able to determine that the outbreak strain had acquired antibiotic resistance to all penicillins, cephalosporins and co-trimoxazole as well as the gene for the toxin that can cause HUS. Prior to this outbreak, Shiga toxin had rarely been reported among EAEC strains. In the preceding decade, only seven sporadic illnesses from infections with *E. coli* O104:H4 strains that produce Shiga toxin had been reported worldwide. Further, only one of the 588 EHEC strains stored in the German isolate collection belonged to serotype O104:H4. The sequencing information and the German isolate collection provided important guidance about the virulence profile of the outbreak strain. This, in turn, helped public health officials differentiate outbreak cases from other cases and identify the source of the outbreak.
Widespread use of CIDTs would also make it difficult to monitor trends in disease, such as antibiotic resistance, and link animal reservoirs to human disease, even though this type of information is necessary to support policy changes. For example, PulseNet’s sister system, the National Antimicrobial Resistance Monitoring System (NARMS) – which utilizes culture to monitor antibiotic resistance of foodborne pathogens in humans, animals and food – has seen increased trends in antibiotic-resistant Campylobacter in recent years, resulting in a ban of the use of fluoroquinolones in poultry production in the United States in 2005. CIDTs will not necessarily provide such information.

CIDTs will make the regulatory oversight of food safety more difficult. Regulatory agencies rely on microbiological testing to detect pathogens in foods, investigate outbreaks, and take action. These agencies and companies can be reluctant to take regulatory action without epidemiologic and molecular evidence linking contaminated food with a specific human illness. CIDTs do not provide the molecular information needed to link contaminated food with human illness and, consequently, may lead to more outbreaks. Furthermore, regulatory agencies, such as FDA, use human isolates obtained through culture to develop and validate methods for testing for pathogens in food.

**Case Study: Campylobacter**

CIDTs that can detect antigens for Campylobacter directly from stool were approved in the 1990s. However, a 1999 CDC survey found only one of 388 clinical laboratories used this type of CIDT as the sole diagnostic test. More recently, a survey of clinical laboratories in the FoodNet sites found the percentage of labs using antigen testing, a type of CIDT, for Campylobacter had increased from 2 percent in 2009 to 7 percent in 2010. A 2009 survey of clinical laboratories in Pennsylvania found that 16.8 percent were exclusively using antigen assays to detect Campylobacter. Since Campylobacter is not routinely reported in most jurisdictions unless an outbreak is suspected – and outbreaks are rare – the impact of these tests on the surveillance system has been manageable. However a 2011 CDC study - that evaluated the performance of these tests - concluded that stool antigen assay tests should not be used as the sole diagnostic tests for Campylobacter.


**DISCUSSION AND ANALYSIS**

A critical piece of our current foodborne illness surveillance system – culture based testing – is in jeopardy. The clinical laboratories – that culture the organisms needed for the DNA fingerprinting done by public health laboratories – will likely be switching to CIDT and phasing out culture-based testing. Public health laboratories do not have the resources to take over the tasks of acquiring samples, culturing specimens, and obtaining isolates. As a result, the microbial DNA fingerprints will not be uploaded to PulseNet in a timely manner, if they are uploaded at all. Without isolates, or an isolate library such as PulseNet, it will be difficult to link cases and detect outbreaks.

**Long-term solution: Modernize foodborne illness surveillance**

The current foodborne disease surveillance system has significantly benefited public health, but it needs to evolve. The establishment of PulseNet gave us the ability to quickly cluster groups of similar or likely related isolates, thereby making it easier to identify dispersed outbreaks. However, recent advances in technology – CIDTs and next generation characterization methods – make PulseNet seem antiquated and threaten its long-term viability. In order to protect the gains that have already been made, the entire system needs to be modernized.

To protect public health, a foodborne illness surveillance system must be able to detect cases of illness and aggregate them in some meaningful way to detect important trends, such as clusters of disease that may indicate a growing outbreak. Laboratory methods greatly enhance this process by grouping together cases most likely to share a common exposure, such as a contaminated food. Specifically, they enable the system to detect pathogens; determine if a particular pathogen has been seen before; if it is part of an outbreak; if it matches environmental, animal or food isolates; and, if so, what is the level of relatedness. Performance matters: too many false positives or false negatives undermine the system's effectiveness and efficiency. Standardization and consistency matter: stable surveillance methodology is needed to track trends. The system must have the infrastructure and tools necessary for storing, managing, sharing, and analyzing the volumes of molecular data generated. The system needs to provide the level of evidence required by regulatory and public health agencies to initiate action. Finally, the experiences of the past twenty years have taught us much about microorganisms and their evolution, so any new system must be somewhat compatible with existing systems like PulseNet – and must be able to adapt to evolving technology.
Modernizing our foodborne disease surveillance system will require significant investments in strategic planning, research and infrastructure. Efforts to shift the paradigm – such as the 100K Foodborne Pathogen Genome Project† and the Global Microbial Identifier Network‡ – are already underway, but they focus mainly on next generation methods for tracking microorganisms. Many believe that genomic approaches, like whole genome sequencing that use DNA information to map the genetic fingerprint of microorganisms, are the future. They can be used to identify pathogens in raw ingredients, finished products, environmental samples, and fecal samples. They can also characterize microorganisms by strain, source, relatedness to other outbreak strains, and even antibiotic resistance. These genomic approaches require isolates – which may disappear with widespread use of CIDTs – and therefore might not be the only solution for outbreak detection.

Other molecular methods, such as pathogen-specific targeted amplification and sequencing or metagenomics, also have the potential for recovering genetic material directly from samples without culture. In theory, it would be possible to sequence pathogens directly out of a stool sample and even potentially identify clues about potential food sources. While a recent study demonstrated the potential of using culture-independent sequence-based metagenomics to identify and characterize an outbreak strain directly from clinical samples without culture, the authors concluded that the technology was not yet ready for prospective use in a clinical setting. Both genomics and metagenomic approaches require a comprehensive database of pathogen DNA for comparisons. Yet, such a reference database does not currently exist for foodborne pathogens.

Next generation technologies offer many opportunities, but they are not yet ready for widespread implementation. Even if they were, widespread use of CIDTs could negatively impact the ability to detect and track pathogens as this requires a reference database of genetic information obtained from isolates. Until the science develops more fully, intermediate steps can be taken: continue building a reference genomic database; develop culture-independent characterization methods, and explore sentinel surveillance systems that actively seek to culture and isolate pathogens. More immediately, however, solutions that maintain the current capacity to detect, investigate and track foodborne disease are needed.

Short-term: Preserve Isolates and Enhance Surveillance

Maintaining current capacity to detect and investigate large, widespread outbreaks needs to be a priority as we transition to a new paradigm. Requiring clinical laboratories to culture all CIDT positive specimens, increasing state capacity for culturing, and improving exposure assessments to enhance surveillance are steps that could address the immediate threat posed by CIDTs - and may also improve the system in the long run. Each approach has advantages and disadvantages, but due to cost and practicality, none are potential long-term solutions by themselves.

1. Require culture of all CIDT-positive specimens in the clinical laboratory.

One option for maintaining the culture-based system in the near term is to require clinical laboratories to culture all CIDT-positive specimens and continue to forward isolates to public health laboratories. Unfortunately, clinical laboratories have no incentive to use culture methods and forward the resulting isolates. In theory, public health agencies could consider reimbursing clinical laboratories for culture, but doing that would require substantial new funding.

2. Transfer clinical specimens to public health laboratories for culture identification and isolation.

A second approach for maintaining culture capacity would be to transfer clinical specimens (i.e. stool samples) from the clinical laboratories to public health laboratories for culture identification and isolation. Legally, many states have reportable disease laws related to foodborne illness and require the submission of isolates to public health agencies.* Modifying state reporting laws to require submission of specimens, rather than isolates, to public health laboratories is one potential approach. However, changing so many state and local laws and regulations would require significant resources and be time-consuming. Another challenge is that saving samples and sending them to public health laboratories would interrupt workflow in the clinical laboratory and require the development of a new system for saving, tracking, and storing clinical specimens. Smaller clinical laboratories might be able to handle the additional workload, but high-volume laboratories

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* The 100K Genome Project, a collaboration of the FDA, the University of California-Davis and Agilent Technologies, is working to sequence the genomes of 100,000 microbial foodborne pathogens and create a publicly available database of those genomic signatures. For more information, visit http://100kgenome.vetmed.ucdavis.edu.

† The Global Microbial Identifier (GMI) is an informal taskforce of about 140 scientists from 39 countries working to facilitate the sharing and analysis of genomic data from microorganisms. For more information, visit www.g-m-i.org.
would likely have a harder time. Assuming that these hurdles could be overcome, this approach still faces funding challenges. To take responsibility for culture, public health laboratories would need to increase both their workforce and their budgets for specimen transportation and supplies. As discussed below, many public health laboratories barely have the capacity to meet current needs, and in this age of austerity, are under increasing pressure to scale back.

3. Improving exposure assessment to enhance surveillance.

One way to offset the loss of culture is to increase the number of cases of foodborne illness reported to public health agencies and get better information about potential exposures of sickened individuals. While PulseNet has greatly improved our ability to detect large, widespread outbreaks, the vast majority of foodborne illnesses are never reported to public health officials and few have an identified source. Each case that goes unreported or has an unidentified source represents a lost opportunity to control a potential outbreak and prevent a future outbreak.

Modernizing existing and/or developing new exposure assessment tools that improve case follow-up and integrate various streams of information would allow us to take advantage of the opportunities from transitioning to CIDTs and next generation characterization methods. As discussed previously, widespread use of CIDTs will likely increase the number of diagnosed cases of foodborne illness. Since CIDTs provide a quicker diagnosis, delays in identifying cases could be shortened. Further, CIDTs will allow public health agencies to detect illnesses involving multiple organisms. Even so, in order to drive improvements in food safety, illnesses need to be linked to a source.

The critical first step in every foodborne illness investigation is to assess the exposures of those sickened (exposure assessment), but this presents significant challenges. Patients frequently assume the last meal they consumed made them sick, but this is rarely the case. More often, it was eaten days before. For example, with *E. coli* O157:H7, the time from infection to onset of symptoms (also known as the incubation period) is typically three to seven days. By the time the patient seeks medical attention and tests positive for a foodborne pathogen, weeks may have passed, making it difficult for patients to recall what they ate. As a result, exposure information is often missing or unreliable. Electronic surveillance and reporting systems; standardized data elements; and novel approaches to collecting information (e.g., Minnesota’s Team Diarrhea and utilization of shopping card data) have all been successful in improving exposure assessment, but they have not been consistently implemented.

The biggest barriers to improving exposure assessment are funding and epidemiologic capacity. Interviewing patients about potential exposures takes time and resources that many state and local agencies do not currently have. In a 2010 survey, states reported several moderate to substantial barriers to improving outbreak detection, including delayed notification of an outbreak, lack of food safety staff, and inadequate epidemiology expertise. Less than a quarter of epidemiologists in state, regional and local health departments are working as foodborne disease epidemiologists. States estimate that an additional 304 full-time-equivalent (FTE) positions are needed to reach full program capacity – and this assumes no increase in the number of reported cases. Further, many states report a lack of core capacity in electronic surveillance and reporting systems. Data needed for outbreak investigations are inconsistently collected across states or only collected by a few states. The lack of workforce capacity and inadequate IT infrastructure affects the quality and quantity of foodborne disease investigations conducted at the state and local levels – often the first responders to foodborne illness. Addressing these critical needs would greatly improve our ability to investigate and limit outbreaks. Ultimately, improving exposure assessment is a smart investment – with or without widespread use of CIDTs. When coupled with DNA “fingerprints,” better exposure data has a multiplicative effect.

**RECOMMENDATIONS**

A sudden shift to CIDTs could have a cascading effect with significant consequences to take our surveillance system back decades – to a time when only outbreaks associated with church suppers, weddings or other well-defined exposures were detected. At the same time, CIDTs offer a new opportunity to revolutionize food safety surveillance – but we need to properly manage the transition. If immediate needs are addressed, we would take a significant first step forward in preserving, and ultimately enhancing, our food safety surveillance system.

* Reporting and specimen submission requirements vary significantly from state to state, and many laws are outdated.
1. Providing resources to public health laboratories to produce isolates and maintain cultures must be a priority, even as the paradigm for tracking foodborne pathogens shifts.

The reality, however, is that culture is an unfunded mandate. Clinical laboratories are moving quickly away from culture and have no incentive to continue to serve in this capacity. Going forward, culture-based testing will be the responsibility of the states and needs to be funded.

2. Expand state and local capacity for foodborne illness response.

One way to offset the loss of culture is to improve foodborne illness response and exposure assessment, particularly at the state and local levels. Unfortunately, there is heterogeneous commitment to funding foodborne illness surveillance among states – most states rely heavily on CDC Epidemiology and Laboratory Capacity (ELC) grants. Increased funding for ELC grants and the development of new exposure assessment tools are smart investments – with or without widespread use of CIDTs.

3. Invest in infrastructure and research.

In the long-term, we need to modernize our foodborne illness surveillance system. While CIDTs and next generation technologies hold great promise, the science is not yet fully developed, and the necessary infrastructure is not yet in place. Research funding and infrastructure investments now would ensure that our foodborne illness surveillance system would work in the future.

CONCLUSION

With an estimated 1 in 6 Americans affected annually at an estimated $78 billion in health-related costs, foodborne illness is a high-probability, high-impact issue. The changing landscape – from the rising use of CIDTs to the increased pressure to get faster results at a lower cost – requires us to invest in an integrated surveillance system that 1) uses molecular methods to link data from humans, animals, food, and the environment, and 2) can adapt to changing technology.

With advances in molecular methods, fundamental changes are needed to modernize PulseNet and its sister systems, like NARMS. If we do not develop and implement enhancements to our current foodborne illness surveillance system, our ability to link illnesses and detect and investigate outbreaks will be adversely affected. By taking action now, we will protect the gains made with PulseNet and take advantage of the opportunities that newer molecular methods offer.

Transitioning to the “next generation” of surveillance will require strategic planning and collaboration across all levels of government and involve stakeholders, including: public health laboratories, clinical laboratories, clinicians, biotechnology and diagnostic manufacturers, and regulatory and public health agencies. Ensuring the viability of the foodborne illness surveillance system will be a major undertaking, but one that is worth the investment.
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ACKNOWLEDGEMENTS

This report was made possible by support from The Pew Charitable Trusts. The findings and conclusions are exclusively the work of the author and do not necessarily reflect the views of Pew. Special thanks to Patricia Buck, Laura Trivers and Kit Whitley for their contributions to this report.