Limitations of Pulsed-Field Gel Electrophoresis for the Routine Surveillance of Campylobacter Infections

To the Editor—Olsen et al. [1] recently provided compelling evidence that an infected food handler was the source of an outbreak of Campylobacter infections at a school luncheon. Their thorough review of events leading to this outbreak and their comparison with the only other reported transmission of Campylobacter species by a food handler reasonably explained both how the outbreak occurred and why such outbreaks are apparently so rare.

The investigation of this outbreak was greatly aided by the use of pulsed-field gel electrophoresis (PFGE) to distinguish outbreak-associated cases from epidemiologically unrelated cases in the community. National standardized methods could allow investigators to link seemingly unrelated outbreaks to a common food source, as has been done with outbreaks of Salmonella and Shigella species and of Escherichia coli O157:H7. However, the usefulness of PFGE for this purpose does not justify the authors’ recommendation that Campylobacter species be added to the national molecular subtyping network, PulseNet.

The usefulness of PulseNet as a national surveillance system to enable rapid detection and investigation of outbreaks is based on the routine submission and subtyping of isolates, with epidemiologic follow-up of cases, as we have demonstrated for both E. coli O157:H7 and Salmonella enterica serotype Typhimurium [2, 3]. Since there are relatively few Campylobacter outbreaks each year, the likelihood of PulseNet being used to identify a common source for these reported outbreaks would be very small. In particular, PulseNet would have contributed nothing to the outbreak investigation reported by Olsen et al. [1].

To be useful in improving surveillance of Campylobacter infections, molecular subtyping would need to be applied to all sporadic isolates, not just to known outbreaks. Because Campylobacter species are the most commonly reported cause of bacterial diarrhea, the additional workload to incorporate Campylobacter species into PulseNet would be large, rather than minimal as suggested by Olsen et al. [1].

In 1994, the Public Health Laboratories of the Minnesota Department of Health began to evaluate the use of PFGE to subtype Campylobacter isolates. Fifteen isolates from 2 unrelated outbreaks that occurred in 1993 were tested initially. The PFGE patterns for these outbreaks were different, and all isolates within each outbreak matched. To determine whether molecular subtyping could enhance outbreak detection for Campylobacter species, all isolates submitted to the Minnesota Department of Health in 1994 were tested by PFGE using Smal and were grouped by exact match for epidemiologic analysis following methods used for both E. coli O157:H7 and Salmonella Typhimurium [2, 3].

Isolates were obtained from 673 (72%) of 941 cases of Campylobacter infections reported among Minnesota residents in 1994. These 673 isolates were grouped into 248 distinct PFGE patterns, 74% of which were represented by only 1 or 2 isolates. Routine epidemiologic methods identified 2 outbreaks and 9 other case clusters involving 4% of all isolates. Use of PFGE revealed 8 more temporal clusters involving 9% of all isolates. Cases that could not be linked with other cases by PFGE pattern, time, and geographic location accounted for 87% of reported isolates. In this instance, use of PFGE increased the identification of clusters that suggested potential outbreaks; however, the large degree of diversity in PFGE patterns among isolates limits the usefulness of PFGE for outbreak detection when resources are scarce.

In a recent survey of retail chicken products in Minnesota, Campylobacter isolates were subtyped by restriction fragment length polymorphism (RFLP) analysis of the flagellin gene amplified by polymerase chain reaction (PCR) [4]. Twelve distinct subtypes were recovered from 13 chicken products positive for Campylobacter species; however, up to 3 subtypes were identified per product. The effect of this Campylobacter strain variability on chicken was demonstrated during the 1998 investigation of a large Campylobacter outbreak that occurred in Minnesota as a result of cross-contamination from raw chicken to chopped lettuce. Of 30 confirmed cases associated with this outbreak that were subtyped by PCR-RFLP, 3 distinct RFLP patterns were detected along with 3 untypeable isolates. This variability on the product limits the potential for molecular subtype-specific surveillance of Campylobacter infections to identify potential common sources among sporadic cases.

PulseNet provides the backbone for a foodborne disease surveillance system that has the potential to improve the sensitivity, specificity, and timeliness of outbreak detection and investigation. However, to reach this potential, all states need to have a system to collect isolates from clinical laboratories, subtype them when they are received, and perform epidemiologic follow-up of individual cases. This type of rapid investigation of E. coli O157:H7 and Salmonella species is not currently conducted in most states. Rather than try to fit pathogens such as Campylobacter into PulseNet, it would be prudent to invest in the public health infrastructure needed to improve PulseNet surveillance for established priorities, such as E. coli O157:H7 and Salmonella Typhimurium.

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To the Editor—Hedberg et al. [1] question the usefulness of adding Campylobacter species to PulseNet, the national molecular subtyping network for foodborne disease surveillance. Their reasoning is that, in order for molecular subtyping to be useful in detecting outbreaks, it must be conducted routinely on all isolates. They present useful data, from the Minnesota Department of Health, suggesting that, despite a large degree of strain diversity, few additional clusters of Campylobacter isolates can be detected by pulsed-field gel electrophoresis (PFGE) and that the added benefit of routine subtyping is minimal when compared with the subtyping of other foodborne pathogens. Thus, routine subtyping of this common cause of diarrheal illness may be neither practical nor cost effective. In contrast, a study conducted in Finland by Hanninen et al. [2] found more strain similarity when routine PFGE was done on Campylobacter isolates; 5 predominant PFGE types represented >40% of the 176 clinical isolates studied [2]. Additional, well-defined studies of sporadic cases will improve our understanding of the usefulness of routine PFGE.

PulseNet, which began in 1996, was designed to have 2 central functions. The first is to use routine subtyping of isolates for the detection of outbreaks that would otherwise be missed. This has proved to be important for outbreaks of Escherichia coli O157: H7, Listeria monocytogenes, and Salmonella enterica serotype Typhimurium. The second purpose is to provide helpful information to epidemiologists during an outbreak investigation [3]. This purpose also has proved to be critically useful in linking individual cases to recognized outbreaks caused by E. coli O157: H7, L. monocytogenes, and a variety of Salmonella serotypes.

We agree with Hedberg et al. [1] that routine subtyping of all Campylobacter isolates may not be feasible or helpful in many state health departments. Instead of proposing the routine use of PFGE and PulseNet for all isolates, we instead suggest that, for Campylobacter species, PFGE and PulseNet should have specific uses in the context of a possible outbreak. Since Campylobacter species are a common cause of diarrheal illness, active case finding during an outbreak will inevitably turn up additional Campylobacter infections that may or may not be related to the outbreak. In this setting, as was the case in an outbreak in Kansas [4], PFGE can be very useful for separating the outbreak-associated cases from the unrelated background cases.

An important feature of the PFGE protocols already used in PulseNet is that they are 1-day, standardized methods that enable a rapid response to the outbreak under investigation and facilitate exchange of data between laboratories. Until now, a wide range of methods have been used for subtyping Campylobacter species by PFGE, making interlaboratory comparisons of PFGE profiles difficult. In addition, the length of time required to perform PFGE (3–5 days) was longer than desired in an outbreak setting. To facilitate outbreak investigations, the Centers for Disease Control and Prevention (CDC) recently developed a rapid (24–30 h) and standardized method for subtyping Campylobacter species [5] that is similar to methods used for other foodborne pathogens in PulseNet. Since outbreaks of campylobacteriosis are relatively rare in the United States, subtyping these additional isolates during investigations should not prove to be too time consuming or cost prohibitive for state public health laboratories. If the standardized protocol had been available for real-time use during the time of the Kansas outbreak, the usefulness of the method would have been even greater.

We currently are in the process of harmonizing our PFGE protocol with that of the European network Campynet (http://www.svs.dk/campynet). Campynet is a network of laboratories with the aim of providing standardized molecular subtyping methods for Campylobacter jejuni and Campylobacter coli. Such standardization of PFGE protocols for Campylobacter species will allow exchange of data at both the national and international levels and will aid in epidemiologic, environmental, veterinary, and medical microbiological studies that are critical for tracing the possible transmission routes of Campylobacter species and for developing effective intervention strategies. PulseNet will continue to evolve as the network expands to include more sites as well as additional pathogens. Over time, the collective experience of state health departments, state public health laboratories, and the CDC will help us define the most appropriate and cost-effective ways in which PFGE subtyping should be used for different foodborne pathogenic bacteria, including Campylobacter species.

References


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