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COMMENTARY
Foodborne outbreaks caused by *Cyclospora*: the message is more important than the messenger

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Whenever we eat, we may be consuming ingredients sourced from anywhere in the world. Globalization of our food supply has occurred over the past few decades in response to changing consumer tastes, limited growing seasons in temperate climates, increased costs of food production in developed countries, and decreased costs of shipping food items and ingredients over very long distances across international borders [1–3]. Even the growing popularity of local farmers' markets and the promotion of community-based food movements will not diminish the importance of global food sourcing in the near future. Rather, global climate change and associated weather patterns, such as the prolonged droughts being experienced across major fresh produce growing regions of California and other regions of the world, will increase the need to source these items from foreign markets [4]. Ensuring the safety of foods in a global marketplace requires harmonized food regulations, a high degree of coordination between national food safety authorities, and increased vigilance on the part of food companies that produce, ship and use the imported foods [5, 6].

Effective food safety systems must be able to do the following:

- characterize a food item or process,
- identify hazards associated with that food or process,
- identify points at which the hazards may contaminate the food item, enter the process or can be controlled,
- monitor control points,
- initiate corrective action when the process is out of control.

For an individual food item or process, these are the functions that define a hazard analysis and critical control points (HACCP) system [7, 8]. At the level of a national food system, several of these critical functions are embodied in public health surveillance of foodborne disease. Public health surveillance is a prerequisite for effective food control. It is critical to identify new food safety hazards and provide feedback on the effectiveness of our food control systems.

An outbreak signals that a process is out of control. The speed with which the outbreak can be recognized and investigated may determine the effectiveness of corrective actions to limit its size and scope, particularly if the contaminated food item or ingredient is perishable and moves through the food system quickly. In every instance, the occurrence of an outbreak should result in a determination of why the outbreak occurred and the steps necessary to prevent future outbreaks [9].

Cyclospora cayetanensis is a parasite that has emerged as an important foodborne pathogen during the past 20 years [10]. It causes prolonged and recurrent, watery diarrhoea in patients who are not properly diagnosed and treated. It is not routinely diagnosed because the clinical symptoms are not specific and laboratory confirmation most often requires a special request to clinical laboratories for additional testing [11].

Cyclospora was first recognized as a cause of diarrhoea in travellers returning from underdeveloped,

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tropical countries. During the mid-1990s a series of seasonal outbreaks of cyclosporiasis was linked to raspberries that had been imported from Guatemala [12]. After 2 years of recurrent outbreaks from this source, the FDA banned their import into the United States, and the outbreaks stopped. Canada continued to allow their importation and experienced a third year of outbreaks. Although those outbreak investigations were not able to identify specific sources of contamination, a seasonal import ban imposed on all of Guatemala's raspberry producers effectively prevented additional outbreaks [13].

Since the emergence of these imported foodborne outbreaks, a wide variety of imported fresh produce items have been associated with outbreaks of cyclosporiasis, but the basic epidemiology of infection is unchanged [14]. In the United States, *Cyclospora* is associated with foreign travel and consumption of fresh produce items imported from countries where it is endemic. There is no recognized endemic transmission of *Cyclospora* in the United States. Furthermore, *Cyclospora* is a parasite that only reproduces within a host, and cysts shed in stool require a period of maturation in the environment before they become infective [15]. Thus, infected food handlers cannot contaminate food products at the point of service. The implications of this are that for any foodborne outbreak, the most likely vehicle is an imported fresh food item.

Having a clear hypothesis to test in an outbreak investigation should facilitate the timely collection of exposure histories from cases and the rapid tracing of suspect food items [16]. However, as demonstrated by the two papers published by Buss and colleagues in *Epidemiology and Infection* and a third published earlier by Abanyie and colleagues, the process of coordinating outbreak investigations across states may be difficult, and tracing the source of food items through international food distribution networks even more so [17–19]. The question that faces public health and food regulatory officials is, 'Why is this so hard, and why can't we do anything to improve it?'

During the summer of 2013, 631 cases of cyclosporiasis were reported from 25 states [17]. This represented a marked increase in the number and geographical distribution of cases from that reported in previous years. Relatively few cases had a history of foreign travel. The initial investigation of a large group of cases in the states of Iowa (140 cases) and Nebraska (87 cases) identified that a high proportion of these (71%) had eaten at multiple outlets of one of two restaurant chains that were owned by a common parent company and that shared common produce distributors [18]. One month after the first cases were identified, and 2 weeks after CDC and FDA began coordinating a multi-state outbreak investigation, a salad mix served at these restaurants was identified as the vehicle and the source was traced to a producer in Mexico. It took almost another 3 months to identify cilantro/coriander from Puebla, Mexico as the source for a larger group of cases in Texas (270 cases) [17]. Over the course of several more months, Buss and colleagues successfully linked traceback information from Iowa and Nebraska to identify the Mexican fields of origin for romaine lettuce that was incorporated into the implicated salad mix. They traced the distribution of this romaine lettuce forward to account for cases across 11 central and eastern US states [18, 19]. The results of these investigations clearly distinguished two separate but concurrent outbreaks of cyclosporiasis associated with different growing regions in Mexico. The results also clearly demonstrated that by the time the sources were identified, the outbreaks were long over.

Because *Cyclospora* emerges as an epidemic foodborne pathogen out of defined endemic regions, there is a potential for seasonally recurring outbreaks from the same source. Guatemalan raspberries produced outbreaks over three consecutive spring seasons, until import bans forced most of their raspberry producers out of the industry [13]. We have now seen cilantro from Puebla, Mexico identified as the source for *Cyclospora* each year since 2013 and the FDA has taken action to stop its importation to the United States [20].

What lessons can we learn from these experiences? First, in a possible ranking of foodborne pathogens, *Cyclospora* would not stand out as one of the most important in terms of pathogenicity, severity or burden of illness. Although it can cause prolonged and recurrent diarrhoea, it is not generally life threatening. It can also be treated with antibiotics [10]. However, because it is not endemic to the United States, every foodborne outbreak represents a likely importation of contaminated fresh produce [15]. This is unique among foodborne pathogens under surveillance in the United States. Thus, while foodborne disease surveillance in the United States is a public health function under the jurisdiction of state and local agencies, every outbreak of cyclosporiasis implies the need for a rapid and comprehensive federal regulatory response [21]. The FDA has regulatory authority to trace foods across state lines and international borders. With *Cyclospora*, those tracebacks need to be integrated into the earliest investigation of cases, however small the cluster.

Second, with each outbreak investigated, a watch list of suspected products or ingredients should be generated that can be rapidly assessed during the next investigation of that pathogen. This should increase the efficiency of exposure assessments to speed the conduct of tracebacks and identification of contaminated sources. Plans for these investigations need to be established before the next anticipated outbreak, so that responses can be initiated at the earliest signal. Surveillance, exposure assessment, and food traceback activities need to be much more effectively coordinated between state, local and federal public health and food regulatory officials [21]. The key to *Cyclospora* is for the next outbreaks to be anticipated. If our foodborne disease surveillance system is functioning, each response should be more efficient, and the investigations more effective. Ultimately, recurrent sources should be identified and the risks abated. Ideally, control measures can be put in place that will also benefit the population in the endemic production area.

Third, to make this occur, the investigation of clusters of *Cyclospora* cases needs to be established as a priority for local, state, and federal public health and food regulatory agencies. If local agencies lack the resources to rapidly investigate individual cases and case clusters, they should turn to state and federal partners to do so with speed. Potential sources for all clusters should be immediately traced to identify common distribution pathways that may point to contaminated sources.

Fourth, the lack of available molecular subtyping schemes for *Cyclospora* has been identified as a limitation in determining which cases and clusters may be related. However, as demonstrated by Buss and colleagues [18, 19], good exposure assessment and traceback can link cases by exposure pathway. There should be no barrier to assessing these exposure pathways as they emerge from the investigation. The source for the large grouping of cases linked to chain restaurants in Iowa and Nebraska was traced quickly because of the common menus across restaurants, the limited distribution network supplying the restaurants, and the resources of the restaurant company to assist the investigation. The more diffuse distribution of cilantro to many independent establishments across Texas was more difficult to trace. However, only a small number of clusters were used to try to trace the source. It will be interesting to determine if more aggressive efforts to trace products from a larger number of small case clusters will produce more certain results and more quickly.

The importance of improving outbreak responses goes beyond *Cyclospora*. As culture-independent diagnostic tests become more widely used, we may be confronted with increasing clusters of *Salmonella* and STEC infections that cannot be subtyped because isolates are not available to public health laboratories. Linking these cases by exposure pathways may be critical to identify outbreak sources. Conversely, as whole genome sequencing becomes more widespread, there may be environmental reservoirs for *Salmonella* strains identified that represent hypotheses that need to be evaluated in any cluster investigation [22]. Improving our response to *Cyclospora* outbreaks will better prepare our public health surveillance systems to respond to these other emerging challenges.

While a federal response to foodborne outbreaks caused by *Cyclospora* is needed to assemble and trace rapidly the international movements of suspected foods, it should also be noted that it was the determined efforts of epidemiologists at one state health department that brought much of the picture of this outbreak into focus. As we build public health systems to monitor and respond to problems, we should not forget that it is the motivation and leadership of individuals in those systems that may be critical to achieving the desired outcomes [5]. We acutely need such inspired leaders across global public health systems.

DECLARATION OF INTEREST

None.

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