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COMMENTARY

Investigation of multi-national foodborne outbreaks in Europe: some challenges remain

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In this issue, two reports on foodborne outbreaks caused by the same strain of *Salmonella* serotype Typhimurium DT104 illustrate the value of international collaboration in subtyping and surveillance [1, 2]. This collaboration led to the detection and linkage of two distinct outbreaks caused by the same organism traced to two types of raw beef from the same supplier. Each investigation proceeded independently and used different methods. The Danish investigation [2] relied mainly on the sampling of imported foods, and linkage of those strains with human clinical isolates via multiple laboratory methods, with the limited epidemiological information required to put them together. This worked because most cases were associated with carpaccio consumed at one restaurant, although it did not effectively address the other non-restaurant-associated cases. The Dutch investigation [1] of cases dispersed throughout the country was dependent on a substantial epidemiological effort, and is an excellent example of a multi-jurisdictional case-control study using a novel control selection strategy. In addition to these two recognized outbreaks, the same meats clearly went to other parts of Europe, where they may also have caused illness which was not identified.

These reports also point out some areas for further improvements in the recognition and investigation of multi-national foodborne outbreaks in Europe.

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Recognition of multi-national foodborne outbreaks

There are several ways to discover that an outbreak might be multi-national. During the investigation in one country it might be suspected or even become apparent that the implicated vehicle was distributed to other countries [3]. Routine reporting of outbreaks of particular interest to an established surveillance network (e.g. Enter-net [4]) is one way that other countries may become aware of possible connections. These outbreaks would include those that are large, are caused by an unusual pathogen or pathogen subtype, or that appear to be related to a food in international commerce. Routine examination of the pooled subtype surveillance data in local, national and international databases can also identify hitherto undetected clusters. This happens now in the United States for *Salmonella* serotype data and with PulseNet molecular subtyping data of a number of different foodborne pathogens [5, 6]. Algorithm-based cluster detection is also envisioned for the European Surveillance System (TESSy) at the European Centre for Disease Prevention and Control (ECDC). In this way, a broadly distributed cluster of possibly related cases can be identified, triggering a multi-jurisdictional investigation [7]. Integrated surveillance for foodborne diseases as shown in the Danish example, with comparison of molecular subtypes of isolates from humans, animals and foods can facilitate the detection of an outbreak. These opportunities for unveiling a multi-national outbreak depend largely on the trust among foodborne disease experts in different countries and their willingness to share sensitive information at an early stage, on the timeliness of laboratory subtyping, and on submission of the results to a central national or international database and its analysis there. In the Dutch outbreak the time between peak onset of symptoms and peak in registration in laboratory-based surveillance was 2 weeks. This is quick given the fact that patients had to see a physician after having developed symptoms, and samples for microbiological testing had to be taken, analysed and subtyped, before being reported.

To establish rapidly whether diseases in several countries are caused by the same strain, microbiological methods for molecular typing have to be standardized. This means developing a consensus about the standard method used for each pathogen, the general application of that method in all laboratories in the network as well as agreement about the use of additional methods in particular situations, including phage typing, resistance testing, pulsed-field gel electrophoresis, or sequence-based methods. The capacity to apply these standardized methods in each country enhances the timeliness for exchange of information. Therefore, after having reached a consensus about the 'gold standard' methods, training and quality assurance of laboratories should be an integral part of the standardization process. Under the rubric of 'PulseNet International', molecular subtyping networks are emerging in Europe and around the world all of which use the same methods [8]. This effort also includes the evaluation of new methods, such as the application of multi-locus variable number tandem repeat analysis (MLVA) in the Danish outbreak.

Despite the valuable conclusions that can be drawn from comparisons of molecular typing results both from human and food samples, it should be borne in mind that the exposure of affected persons to the implicated vehicle still needs to be ascertained [9]. Hence the microbiological information has to be combined with the epidemiological investigation.

Response to multi-national foodborne outbreaks

Investigations

In both the Danish and the Dutch outbreaks reported in this issue, investigation by the local and national authorities was sufficient to identify the food vehicles, without pooling epidemiological information across nations. However, in some dispersed outbreaks, it is necessary to combine data across multiple jurisdictions to identify the food vehicle. This can mean that a standard epidemiological approach is needed, requiring substantial coordination. Identifying the lead hypotheses, devising a single questionnaire to gather the critical data from cases and controls, and conducting a rapid statistical analysis can again require active collaboration to gather sufficient information to implicate a specific food.

The main objectives of an investigation are to prevent further cases by an immediate intervention (e.g. by halting distribution of a food or by recalling it from commerce) and by a longer term prevention effort to identify processes or practices that need to be changed to avoid future incidents of contamination [10]. For immediate intervention it is necessary to identify the vehicle of infection, while prevention of future outbreaks requires identification of the source. That means investigating the chain of production sufficiently well to determine how contamination was likely to have occurred.

These outbreaks illustrate why it is essential to tackle the problem at the production and processing plant. Testing a lot of food and destroying the batch that tested positive served as an immediate intervention, but did not prevent the subsequent outbreaks in Denmark and The Netherlands. The key issue here is that whatever the initial control measures that were instituted at the processing facility in the third country were, they were apparently not sufficient, therefore another batch of contaminated meat arrived and caused illness.

In principle, the search for the cause of an outbreak is focused on identifying one food vehicle. These two reports and others [11] are good examples of outbreaks in which different brands or foods can have one single source of contamination.

Communication

During the investigation of foodborne outbreaks, the close collaboration between public health and food safety authorities is pivotal, but achieving this communication is often a challenge even within one country. For multi-national outbreaks this task is even more complex when the contaminated food is traced to a country that may not have recognized any related illnesses and has not previously been involved in the investigation, as was the case in the two outbreaks reported here. Within the United States, such communication occurs rapidly and informally through collegial contacts among neighbouring states, through the electronic networks of

PulseNet and OutbreakNet, through formal liaison arrangements between the CDC, the US Department of Agriculture, and the Food and Drug Administration, through the Epi-X rapid notification system, and through the *Morbidity and Mortality Weekly Report*. In Europe, there are several established means for rapid international exchange of information about foodborne outbreaks. There is the informal exchange of information between public health foodborne disease specialists as established in Enter-net [4], the more formal exchange including the Early Warning and Response System (EWRS) [12], rapid communication of first results in *Eurosurveillance Weekly* [13] and the Rapid Alert System on Food and Feed (RASFF) of the EU Commission [14]. The Danish colleagues used all of these channels to communicate the outbreak, although the actual extent of communication is not explained in detail. It was not made clear whether and how communication was established with the authorities responsible for the production plant and what measures were taken there after the Danish outbreak. It will be crucial to optimize the performance and use of these communication systems as two-way channels in the future.

This pair of reports is a good illustration of why a surveillance network is needed at the European level, why joint investigations are desirable, and why definitive action at the source is imperative for the prevention of future outbreaks. The national authorities remain in charge of establishing the measures to achieve these ends, and of monitoring their effectiveness. Close and timely cooperation between human public health and food safety authorities at the European level, between ECDC and the European Food Safety Authority (EFSA), could enhance such investigations. The added value of a cooperative network would include coordinating multi-national investigations, supporting countries in their investigations upon request, establishing the scientific basis for interventions, providing timely information about events by providing a communication platform and a database with timely reporting and analysis of relevant variables, and developing proposals for a standardized epidemiological approach to investigations.

DECLARATION OF INTEREST

None.

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