특별강연 논문 I

An Industry View of the Role of Epidemiology in Public Health Policy

Jenny Scott and Dane Bernard

(National Food Processors Association)

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Jenny Scott and Dane Bernard
Food Safety Programs
National Food Processors Association

The science/art of epidemiology is not always understood and, for this reason, and because of the way it has sometimes been used, it is not always trusted. However, industry does recognize that epidemiology is necessary and can be good.

Epidemiology can identify the foods involved in outbreaks:

- Epidemiology identified unpasteurized juices as the cause of infections with *E. coli* O157:H7 in the fall of 1996.
- It pinpointed hamburgers sold at Jack in the Box as the cause of similar infections in 1992-93.
- It identified ice cream as the source of a multistate *Salmonella* Enteritidis outbreak in 1994.
- Epidemiology has demonstrated that *Campylobacter* is the most frequent bacterial cause of diarrhea in the US.
- Epidemiology identified a specific brand of hot dogs as the source of a wide-spread outbreak of listeriosis in the US in 1998-99.

The laboratory confirmation aspects of epidemiologic studies can help identify the causative agent, such as when *E. coli* O157:H7 was first identified as the agent of illness in 1982 outbreaks involving hamburgers.

Epidemiology can help us identify risk factors:
CDC reports on the sentinel site active surveillance study for diarrheal illnesses indicates that risk factors associated with death from *Salmonella* may include infection with serotype Typhimurium and that persons with underlying illness such as AIDS may be at greater risk for fatal disease. The study also shows that age is a risk factor for infection by several foodborne disease organisms: children between 1 and 10 years old are at greater risk from *E. coli* O157 and from *Shigella*, whereas people over 59 are at greater risk from *Listeria monocytogenes*.

Epidemiology can also identify practices leading to adverse health consequences:
An outbreak in Oregon of illness from *E. coli* O157 from venison jerky led to the recognition that home dehydrators may not provide adequate inactivation of the organism, especially if used at the lower temperature setting. Not pasteurizing apple cider can be risky, as can using un-composted

manure (both things we learned as part of epidemiologic investigations).

Epidemiology can help us identify new sources of foodborne pathogens:

- *Cryptosporidium* and *E. coli* O157 in apple juice
- *E. coli* O157:H7 in fermented sausages
- *E. coli* O157:H7 in venison
- *Yersinia* in chitterlings (pork intestines an ethnic food)

Knowing where organisms come from and practices that are risky can allow us to implement corrective actions and preventive procedures at appropriate points in the food chain.

So, with all these good things epidemiology can do, why does industry have concerns about its use?

For one thing, industry recognizes that good epidemiology is not easy and that a good epidemiologic study may be difficult to find. I'm by no means an expert in epidemiology, but I do know some of the difficulties. For example, there are many epidemiologic study design issues that can impact on the outcome of the study. Many books chronicle the abuse and misuse of the statistics, but it is often the way the data are collected that results in such misinterpretations. Epidemiologic studies are only as good as the data collected.

Study design issues that need to be addressed often involve how and when the food histories were taken. Were the food histories obtained from representative cases? Were they taken in close conjunction time-wise with the outbreak, or were they taken some time later when memories may have dimmed? As we all know, often times foodborne outbreaks can occur days, even weeks, after the consumption of the product. How much do you remember about what you ate 10 days ago? This tends to cloud the accuracy of the food histories. Who was it that gave the history? Was it the patient, or a parent, sibling, or friend of the affected individual? This affects the accuracy of the information. How was the history taken? Was it volunteered or prompted? Were lists of potential foods consumed provided, which may have biased answers? Often times these lists can provide biased results; however, it is also often the only way to get a complete food history, by providing information that may jog the memory. But incompleteness will also leave out sometimes valuable information. Completeness of the epidemiologic study also depends on the willingness of a subject to participate. If information is obtained from only a few of those who became ill because of the unwillingness of others to participate, again the data may be biased.

In the case of a foodborne illness outbreak, the patients or cases are asked about the foods eaten

within a specific time period. This time period is selected based on the normal incubation time of the illness. However, we know that there can be a range of incubation times. So while an epidemiologist may use 48-72 hours for a *Salmonella* outbreak, what happens if this is one of those times when the incubation period was >128 hours, as can occur with a low dose exposure? The source will either be missed or mis-identified.

Let's assume the epidemiologist in on track with the incubation time, and the interviews suggest a likely food vehicle. Just determining that the ill persons all ate a particular food is not enough. It's necessary to have a healthy group that might have had the same exposure for comparison. Ideally the controls and the cases are matched for factors such as sex, age, geographic location, etc. in a case-control study. Note that with multi-jurisdictional outbreaks, case-control studies may be conducted at several locations at once. This requires careful coordination and consistency to avoid errors.

One other issue to address in the epidemiologic study is whether or not the cases belong to the outbreak. Fingerprinting has revolutionized epidemiologic investigations. In the 1996 Odwalla apple juice outbreak 6 cases of illness from *E. coli* O157 were identified by fingerprinting as a smaller outbreak due to apple cider pressed at a church social. In fact, fingerprinting may indicate that there is no outbreak at all.

In Minnesota, fingerprinting of *Salmonella* isolates has indicated lots of mini-outbreaks and sporadic cases in what would on first blush appear to be a potential large outbreak. In June/July of 1994, there were 46 confirmed cases of *E. coli* O157:H7 reported to the New Jersey Department of Health (compared to 5 in 1993). No common source could be identified. Fingerprinting confirmed that among 23 isolates tested, there were 17 different organisms. This "outbreak" was really an artifact of enhanced detection (labs culturing diarrheal specimens for O157 increased from 2 (10%) to 18 (90%) in this period).

And epidemiologists shouldn't forget to consider demographic and cultural factors. Food preparation, handling and storage practices may differ depending on cultural background, and certain ethnic food handling practices may not be readily apparent to those gathering food histories. It is sometimes these practices which may have resulted in the outbreak rather than overt problems with the food product itself.

Statistics are used to evaluate the data obtained from epidemiologic studies. We must remember that when a statistically significant factor is identified at the .05 level, there is a one in 20 chance that the association is just that, chance. In such cases, more information, such as laboratory

confirmation may be warranted.

To illustrate the fact that mistakes sometime happen, a couple of the more well-chronicled goofs in epidemiologic history are listed here. These are documented in the literature.

- One study chronicled the fact that "airport noise kills." This was based on the premise that death rates per capita were higher in the general vicinity of airports than they were in other communities. A reanalysis of information compared with the socioeconomic data of communities which typically surround airports found that, in general, populations in that area were lower income and also engaged in certain higher risk behaviors which resulted in a higher mortality rate, not airport noise.
- A similar study found that, based on heart attack rates in areas like Denver, high altitude protected against heart attacks. Once again, what was really at work here was the lifestyle of those involved rather than a single factor such as high altitudes.

Of course, this never happens in the epidemiology of foodborne disease - or does it?

In the 1970's there was an outbreak of salmonellosis that was statistically associated with ham. *Salmonella* serotype Muenchen was the organism involved, however the outbreak seemed to involve different brands of ham eaten in different places and at different times, which didn't make much sense. On closer investigation, the hypothesis fell apart. An investigator went to the homes of the cases to conduct additional investigations and noticed a strange smell, which he was able to identify. Sure enough, samples of marijuana were positive for *Salmonella* of the same serotype and plasmid type as the patient isolates.

So, while industry is generally supportive of epidemiology because we recognize the good things it can do, we have concerns about accuracy and completeness of information. We also have concerns about how such information will be used.

One example of a use we may not be too fond of is the use of epidemiologic evidence alone to initiate actions against a food without an opportunity for laboratory confirmation when necessary. I emphasize "when necessary."

The Odwalla apple juice outbreak is a good example of an outbreak where the epidemiologic information was well-done and solid, and the actions initiated before laboratory confirmation were indeed appropriate. On the other hand, the release of information by the Houston Department of Health regarding the *Cyclospora* outbreak in 1996 being related to strawberries was certainly premature, damaging, and in all likelihood diluted the effectiveness of subsequent warnings when a

more accurate diagnosis was made. Not only did the premature release of this information cause the California strawberry industry a $20 million loss, by getting it wrong, there may have been more illnesses resulting from restaurants substituting raspberries for strawberries. From a public health viewpoint, it would seem prudent to warn consumers rather than to wait, however, when multiple warnings have to be issued and there is controversy regarding the initial results, it may be best to wait for additional information rather than run the risk of issuing warnings which are false, misleading and dilute the effectiveness of correct information when it is obtained. Even today there are many who associate strawberries with causing illnesses from *Cyclospora*.

The regulatory agencies are well intentioned and take their mandate of protecting the public health seriously. But when one looks at the outcomes of epidemiologic investigations and public warnings in terms of the regulatory agencies, we can see that if there is in fact illness, and action is taken, there certainly is no adverse consequence to the regulatory agency. In fact, that is what should happen. If there is illness caused by a food and no action had been taken by the regulatory agencies, invariably there is criticism of the regulatory agency bad news. An example of this happened in Oregon at Crater Lake in 1977. An outbreak of diarrheal illness occurred at the lodge. The National Park Service and the state called in CDC. Pressure was on to close the park, but data were incomplete, and CDC wanted time to analyze and investigate the situation. 24 hours later, it was determined that the water was contaminated and all agencies agreed to close the park. This was one of CDC's fastest investigations. Yet the 24 hour delay in closing the park became the subject of a Congressional hearing.

If, however, there is in fact no illness caused by a product, and action was taken against that product, once again the regulatory agencies are not likely to be criticized publicly for having taken precautionary action in the public interest. Also, if there is no illness and no action is taken, obviously there isn't any adverse consequence for the regulatory agency either. So, in most situations, except when there is an illness and no action is taken, the regulatory agencies really pay no price for having been incorrect from taking an action.

However, from an industry standpoint, if there is an illness and action is taken, that has a negative impact on the industry, and rightfully so. If there is no action taken by the regulatory agency, the industry still pays a high price for that particular illness, as a product type becomes associated with causing an adverse impact on consumers. If, however, there is no illness from a particular product but epidemiologic evidence indicates there is a problem and regulatory agencies take action against the product which is, in fact, not at fault, industry suffers the negative consequence for no particular reason other than perceived protection of the public health and the agency itself. The only situation in which the industry wins is where the product is not involved in any illness and

the regulatory agencies determine to take no action.

So we can see that there is considerable momentum for agencies to take action rather than to completely study a situation and run the risk of taking action which is too late to prevent or reduce illness. This works against the industry position of wanting to assure that problems are well-documented before action is taken.

In Italy in the 1970's there was an outbreak of cholera associated with oysters. CDC was called in to consult. The Italians decided to use mines to destroy the oyster beds, in spite of CDC's recommendation to wait for more information. The beds were destroyed to the cost of $36 million. Further investigations revealed that the oysters were indeed the source of the cholera, but they were not contaminated in the beds - they were contaminated by a water spray used to clean the oysters after harvest. The agency took some criticism here, but there were much more negative consequences here for the industry than for the agency involved.

So, industry's worry is that regulatory action up to and including the need for a recall will be taken, but in fact no microorganisms are found and the product is, in fact, not a hazard. That is our biggest worry. Looking at the costs of recalls and regulatory actions, obviously there is a cost to the regulatory agencies in terms of manpower and hours spent, but that is in fact what the job entails. For industry , however, we suffer the actual direct cost associated with any recall, but we also have many indirect costs, including future costs done to our brand name and the reputation of our company and its brands, and other factors including the loss of public confidence in the company, loss of profitability, difficulties in obtaining inventory loans, and many other consequences that may not be offset by appropriate insurance.
However, monetary costs are only part of the story -- the effectiveness of the public health message may be even more important. If consumers avoid strawberries because of a public health warning, but not the real culprit, raspberries, the consumer is not well-served. And if the second warning says don't eat raspberries, what kind of confusion does that cause? Of course, some of our regulatory colleagues have told us that if you have ever made a mistake and been called before Congress or a legislature to testify, as was the case with the Crater Lake outbreak, you know there are additional costs to a regulatory agency as well. Recalling the wrong product can also erode consumer confidence in future actions taken by the agency.

Another part of the epidemiologic picture that isn't often explored is that a food may be associated with an illness but it is not the food's fault. It may be faulty practices down the line. Some notable examples may be the identification by USDA of chicken fried steak fingers as being the cause of an outbreak in a school system in Texas several years ago. On further investigation it

turned out that there was no problem with practices in the plant, and if the chicken fingers were indeed the vehicle at all, it was probably due to mishandling or cross contamination after the product left the manufacturer's establishment. However, significant financial damage was done to the establishment as the result of actions taken against this product.

There was also a 1993 outbreak of *E. coli* O157:H7 associated with a mayonnaise-based product in Oregon. Even though the salad dressing involved was formulated from commercial mayonnaise, it is suspected that cross-contamination occurred at the restaurant where ingredients, including mayonnaise, were stored in coolers suspected of having allowed cross-contamination from other products. However, the commercially prepared mayonnaise got most of the publicity and the company producing this product suffered financial consequences because of these reports. Even the American Gastroenterological Association consensus statement on *E. coli* O157:H7 listed mayonnaise as one of the sources of the organism!

And in another incident a botulism outbreak in Georgia was caused by consumption of baked potatoes served with cheese sauce. Commercially canned, aseptically-processed cheese sauce was determined to be the cause. Even though it was well documented by the producer that the product had been commercially sterile when it left the processing facility, reactions to this are still being felt in terms of potential FDA regulations or guidelines regarding labeling of all canned foods "IMPORTANT Must Be Refrigerated After Opening to Maintain Safety." The company producing this cheese sauce was not at fault, since this cheese sauce was re-contaminated by the customer, and was left at room temperature for an extended period of time. Once again, it was the practice used, rather than the product, that should have been the target of subsequent publicity; however, the firm involved once again suffered consequences because of warnings to the public. And now the entire canned food industry may suffer the consequences from this incident.

So, when is there sufficient evidence? What do we recommend on the use of epidemiologic data? Let me emphasize that we do support epidemiologic studies. Epidemiology is a very powerful tool, no doubt about it! However, as with any tool, it must be used carefully and correctly. We encourage remembering Koch's postulates. (Koch isolated the tubercle bacillus from ill patients, he was unable to recover it from patients without the disease, and he inoculated guinea pigs and rabbits with a pure culture and reproduced the disease. In this case we would be looking to demonstrate that ill persons ate a particular food, those not eating the food did not become ill, and the organism could be found in the food.) Not only is it preferable to have linkages based on case control studies, but it is also preferable to close the loop in terms of finding problems through laboratory tests. We recognize that in some situations we cannot isolate the organism from the food (we may not have the techniques, as with *Cyclospora* or foodborne viruses). Again, in all

instances this may not be necessary. A strong statistical association in a well-conducted case control study may be enough. This is especially true when there are serious consequences, such as long-term sequelae or even death.

We recognize that it becomes a judgment call for the public health agency: action in the face of incomplete data becomes a balancing act between the need for action to protect the public health and not causing unnecessary harm to industry. Make sure the response is appropriate for the threat; there must be a balance between rapidity and restraint.

Hindsight is always 20/20. In the Crater Lake outbreak, hindsight may suggest that the agencies should have acted sooner. But the illness was not life-threatening. Hindsight on the *Cyclospora* problem in raspberries says the agencies should have waited. Both these outbreaks point out the problem with the tiered public health structure in the US (local, state, CDC). When several agencies are involved, it can be difficult to establish who's in charge. With widely distributed product, lots of jurisdictions react as if they are dealing with a local problem. Having the bigger picture may be necessary to provide the information needed to appropriately address the situation. In the *Cyclospora* problem, analysis of 55 events in the US and Canada indicated that strawberries were not served at more than 24% of the events. Also, if strawberries were the culprit, the number of cases in the US would have been larger and there would have been cases in the West, not just the mid-West and East.

Thus we have been pleased to nationally recognized foodborne illness epidemiologists espouse the need for a national response team to review and evaluate all information before taking action. As we experience more diffuse outbreaks with low level contamination, we will have to deal with multi-jurisdictional issues, and this type of review will be essential. The *Cyclospora* outbreak involved 20 states, the District of Columbia, and 2 Canadian provinces. The Council of State and Territorial Epidemiologists has proposed an Emergency Consultation structure. A crisis coordination group that would develop standards and criteria for use of epidemiologic data in future situations would go a long way in enhancing the effectiveness of actions based on epidemiologic studies in protecting public health. the necessity of. These types of controls are important in addressing industry's concerns.

Nevertheless, when significant doubts arise, either from the way data are collected or the statistical significance of data, one must make a decision on whether it is appropriate to issue public warnings and take action. We feel that there should be an equal focus on food handling practices rather than investigations that focus solely on the food as potential cause. In conducting epidemiologic studies there must be considerations on the quality and the completeness of data

developed and some common sense factors in addition to the statistical interpretation. Even in cases where a statistical significance is found, even a high statistical significance, if it doesn't make sense some additional investigation may be in order (remember the ham).

And another suggestion, would be that if they're wrong why shouldn't the government help pay for the damages to a company. While I say that tongue in cheek, if that were to happen, I guarantee we would have fewer errors in the future.