Journal of Food Protection, Vol. 59, No. 1, Pages 102–107

Hazard Analysis: The Link between Epidemiology and Microbiology

FRANK L. BRYAN*

Food Safety Consultation and Training, Lithonia, Georgia 30058 USA

(MS# 95-126: Received 2 June 1995/Accepted 7 September 1995)

ABSTRACT

Epidemiologic inquiry, collation of data and statistical calculations are useful in identifying the place foods were mishandled or mistreated and the probable vehicle of foodborne disease. Biases during collection of information and classification of cases and control can lead to false conclusions. Laboratory analyses can confirm the etiologic agent and vehicle if an appropriate sample is collected, and sometimes trace the source of the etiologic agent. Laboratory analyses may give negative or misleading results depending on the samples collected and the quantity of samples collected. Hazard analyses are necessary to determine the mode of contamination, the means by which the pathogen survived processing, and the conditions that allowed the pathogenic bacteria to increase to populations or elaborate toxins sufficient to cause the illness. Hazard analysis is the link between epidemiology and microbiology that identifies events that contributed to the causation of outbreaks and, hence, provides information upon which to initiate control actions and to base preventive measures.

Key words: Hazard analysis/HACCP, foodborne disease, epidemiology

The major components of a complete investigation of foodborne disease outbreaks are (i) epidemiologic inquiry, collation of collected data, and their interpretation; (ii) sampling and laboratory analysis of foods under suspicion of being vehicles; and (iii) hazard analysis to detect operations by which the food under suspicion became contaminated and the etiologic agent survived and increased to populations or concentrations capable of causing illness. The primary attributes and limitations of each of the components of the investigation process are reviewed.

EPIDEMIOLOGIC INQUIRY

Epidemiological case-control comparisons are commonly used in investigations of outbreaks of foodborne diseases. Foodborne history attack rates provides data on which to form an hypothesis about food vehicles responsible for the disease under investigation and to give an indication of the likelihood that the ingested food was indeed the vehicle.

Epidemiologists commonly use computers to collate data and to form and test hypotheses by calculating rates and probability. These are important aids to an investigation, but they do not give the final answer as to the circumstances that caused the outbreak and that must be controlled to prevent subsequent occurrences of a similar kind.

Looking only at numbers or rates of diseased versus healthy persons, however, can be misleading. Certain biases or errors can occur during collection of data *(1, 33, 36, 43, 47)*. These include chance, selection, information, and confounding. The observed associations may result from sampling variability and hence be caused by chance.

Bias, for example, can result from procedures used to select subjects. Some ill persons never come to the attention of investigators because they do not report their illness, do not seek medical treatment, or have mild illnesses that are ignored because of the case definition set by investigators. This can lead to an underestimate of the total population affected and perhaps a distortion of the proportions at risk. Nonparticipation by potential controls also results in selection bias. Hence, some persons classified as cases may not be cases and those classified as controls may indeed have the disease; hence, misclassification of some persons in both groups or either group can result. These result in a mistaken estimate of an exposure's effect on the risk of disease.

Information obtained during retrospective questioning is imprecise and can be a major source of bias. Interviewers can cause bias by the way they word questions or record what they hear. Recall bias is always a possibility where information about past experiences are sought. When persons know or suspect that a particular vehicle is under suspicion, they may erroneously recall eating it or eating larger portions of it than they actually did. Informational biases also result in a mistaken estimate of an exposure's effect on the risk of disease.

A third factor which is the true risk factor but not necessarily identified can distort or confound the estimate of the true association between an exposure and disease. Mixing of various effects can distort interpretation in either direction and perhaps in the direction opposite to the effect. Furthermore, true association may be indirect rather than

* Author for correspondence. Tel: 770-760-1569.

direct. Such biases, however, do not invalidate a study, but an investigator should be aware of them and try to prevent or control them if possible, or at least to estimate the direction of the biases so as to avoid overinterpreting the data. The most common way to improve precision of a study is to increase the sample size, which is often impossible in outbreak investigations.

Food history attack rate tables are useful in forming an hypotheses as to the responsible vehicle. Such a table is essentially a rate difference comparison between persons who ate foods under investigation and those who did not eat the foods. The disease rate for the control group is subtracted from the disease rate for the affected population to give the rate difference. To provide accurate conclusions, the collected data must be accurate and unbiased, which assumes well-designed questionnaires, good interview technique, and likely vehicles not communicated by the media or interviewer.

Epidemiologic studies focus on analysis of the relationship between groups of persons with a specific disease and otherwise comparable persons who are free of the disease. If significant, the odds of having the disease are significantly higher in an affected population than in the unaffected population being compared, and, hence, there is an association between exposure and disease. Where it can be assumed that the cases under study are representative of the diseased population and that controls represent the nondiseased population, an odds ratio can be calculated. In case-control studies, however, an investigator usually interviews a far greater proportion of all diseased persons than nondiseased persons *(51)*. This leads to bias.

Probability that chance influenced such an association can also be calculated. This provides some degree of confidence (or lack of it) but not proof of association. Such calculations only give the probability that chance alone produced a difference at least as big as that observed between the compared groups. A small probability value indicates that it is unlikely that chance or random error is the explanation for the findings. Proof of causation, however, must come from field and/or laboratory investigations that identify the causative agent and its source, the mode of contamination, survival of the agent of processes or treatments that the foods underwent, and whether the agent increased by either accumulation or multiplication.

LABORATORY TESTING OF SAMPLES

Laboratory detection of the same strain of pathogen in clinical specimens and the epidemiologically implicated food proves causation. The detection of the same strain from a food worker or raw food can prove the source. Detection of large numbers of pathogens from a food eaten at a suspect meal or by several ill persons can strengthen an hypothesis as to the vehicle.

A positive result of an appropriate analytical test can prove that an epidemiologically implicated food is the responsible vehicle. On the other hand, a positive finding in a food without epidemiologic association does not prove that the food was the vehicle. Isolation of an etiologic agent of foodborne illness from a food may indicate contamination in too small quantities to cause illness at the time of eating or contamination or growth in leftovers after eating. Of crucial importance: a negative result does not exonerate a food. It merely indicates that the etiological agent was not isolated from the sample collected. There are many reasons for this; some follow.

(i) The implicated food was no longer available and a subsequently processed or prepared batch was sampled which was not contaminated or not contaminated to the same extent. (ii) Not all units of the batch of food were contaminated, and a uncontaminated unit was collected as a sample. (iii) The batch of food was not uniformly contaminated, and a sample from an uncontaminated region was collected. (iv) Not all units or portions of food were exposed to the same time and temperature conditions during cooking, and portions receiving the greatest exposures were sampled. (v) The sample size was too small to detect the presence of low populations of a contaminant. (vi) Contaminants were located only on the surface of the food, and the geometric center was sampled; (vii) or contaminants multiplied in the geometric center of the food to an extent sufficient to develop an infectious dose, but only the frame or upper portion was sampled. (viii) Competitive microorganisms outgrew the etiological agent between the time that portions were eaten and the time that the sample was collected, and populations of the responsible agent diminished during this interval. (ix) The food was tested for indicator organisms rather than for pathogens or toxins or for microorganisms other than the etiological agent. (x) Heating, freezing, drying, or other processing diminished, injured, or inactivated the pathogen. (xi) The test method was inferior because of media used, incubation temperature, duration of incubation, or other laboratory procedures; and/or perhaps other factors. Furthermore, food laboratories may be either unavailable in a region or limited in the scope of analyses that can be performed.

Assuming homogenous distribution of a contaminant in a batch of food to be sampled, the number of samples collected dictate the probability of identifying defective lots *(38)*. Often during outbreak investigations, only one sample of a suspect food is collected and tested. Yet, if as many as three samples of the suspect food are collected and a pathogen is not isolated, the interpretation with 95% confidence would be that the lot sampled is less than 75% contaminated. Hence, it could be 50% or 30% or 10% (or any number less than 75%) contaminated without detection when maintaining that level of confidence. Correspondingly, 30 samples would give this level of confidence that the lot under investigation is less than 10% contaminated. Approximately 300 samples (a quantity beyond practicality) would have to be collected to have this level of confidence that the lot is less than 1% contaminated; but, yet, any fraction of 1% (e.g., 0.5% or 0.33%) could be contaminated without detection. If contamination is nonhomogenous, the possible contamination levels increase significantly and the confidence level decreases from the previously stated values. Hence, a negative result provides a low and sometimes a very low level of confidence that the food is not contami-

nated and/or is not the vehicle when small numbers of samples are collected. The laws of mathematics set these limits, and an investigator must increase the number of samples to improve the chances of detection and to provide greater confidence of the result.

Samples of foods at various stages of processing, preparation, and storage can provide confirmation of hazards, but not confirmation of the absence of hazards when results are negative. This sort of data is of limited value, however, without accompanying information of time and temperature exposures on which to interpret findings and judge risks.

HAZARD ANALYSES, AN IMPORTANT PART OF OUTBREAK INVESTIGATIONS

With these limitations of both epidemiological and laboratory studies, what can be done to improve foodborne disease investigations? The answer is hazard analyses to detect actual or likely sources and modes of contamination, whether processes inactivated the etiologic agent or whether holding and storage allowed multiplication *(6, 7, 10)*. Hazard analyses can identify actual or potential sources and modes of contamination by foodborne pathogens, processes that allow survival of pathogens, and situations that promote growth of pathogenic bacteria and molds. Thus, they can often identify events that contributed to the illness despite incomplete epidemiological data or lack of laboratory confirmation.

During such hazard analyses, each step of an operation is watched for modes of contamination, time and temperature and/or concentration and time exposures are measured and interpreted in relation to anticipated inactivation of microorganisms or toxins of concern, and time and temperature exposures, pH, water activity, and perhaps redox potential are measured and interpreted in relation to anticipated multiplication of bacteria or molds of concern. When close observations and in-process measurements are being made, some workers modify their behavior or the process to some extent, but this is limited to the extent of their knowledge of hazards and control measures and the capability of the equipment being used. Hence, interpretation of observations and measurements must be tempered with an understanding that operations may have been different at the time that the implicated foods were processed or prepared than at the time of the investigation. This can be done by bracketing or extending graphed data with low and high ranges, and curves can be cut or extended to illustrate anticipated modifications. With the aid of laboratory testing (having the same limitations as described above) proof of some or all of these events as well as indications of contamination, survival, and growth may be obtained when sampling is done following specific operations rather than sampling end products.

Ordinary inspections using typical food-protection check sheets are of little or no value in making hazard analyses, and such an approach may even be distractive and consume time that otherwise could be spent more productively. Many items on typical inspection forms relate to concerns about sanitation and aesthetics or equipment or facility construction and not factors that are likely to contribute to the causation of foodborne illnesses.

Data generated during past epidemiological investigations can be useful in directing attention toward hazards and risks. Of particular importance are the factors that contribute to foodborne diseases *(2, 4, 28, 45, 50, 52)*. Commonly identified contributory factors are (i) allowing cooked foods to remain at room temperature for several hours, (ii) improper cooling (e.g., storing foods in large containers), (iii) preparing foods several hours in advance of serving, (iv) handling cooked foods with bare hands, (v) insufficient cooking or heat processing, (vi) holding foods at warm (but not hot) temperatures for a few hours, (vii) cross-contamination of cooked foods from raw food, (viii) improperly cleaning utensils and equipment, (ix) obtaining contaminated raw foods, and (x) eating raw (contaminated) foods of animal origin. The operations listed indicate hazards and their relative frequencies provide guidance to estimating risks. When these factors occur in proper sequence, risks of occurrence of foodborne disease outbreaks are great. Certain foods (e.g., turkey, chicken, ham, beef, and rice) are frequently identified as vehicles during epidemiological investigations *(3)*. This sort of data provides further information about risks. In developing countries, where foods are often mishandled and improperly held, the risk of acquiring foodborne diseases from them and the occurrences of these contributory factors ought to be far greater than in developed countries.

Research on the ecology of foodborne pathogens (including studies related to their ability to grow under various conditions and to survive when exposed to various sublethal effects) and studies of the prevalence of pathogens in various foods, food-source animals, and the environment provide additional information on which to anticipate hazards and risks.

It is well known, without repeated hazard analyses, that raw foods of animal origin are frequently contaminated with foodborne pathogens *(11, 29, 34, 37, 44)*. Additionally, any one or a combination of the following operations contribute to high populations of microorganisms on or in raw foods: poor hygienic practices on farms and during harvesting, washing or freshening produce with polluted waters, insanitary practices during processing and preparation, and long durations of storage at temperatures that are conducive to microbial growth.

Hazard analyses in developing countries, with few exceptions, revealed that foods are often thoroughly cooked *(19–22, 24–27)*. Hence, vegetative forms of pathogenic bacteria ought to have been killed at least on surfaces if not in the interior during cooking. This, however, may not always be the case. Salmonellosis and enterohemorrhagic *Escherichia coli* enteritis, for example, have resulted from insufficient heat processing or cooking of poultry, eggs, and hamburgers in many nations *(32, 35, 46, 48)*. Outbreaks of hepatitis A have followed insufficient steaming of clams *(39)*. Bacterial spores would survive and germinate later as temperatures become conducive for bacterial growth. For example, *khoa*-based confectionery was subsequently cooked

to temperatures that would be lethal to staphylococci, did not inactivate preformed enterotoxins *(49)*.

The major hazards for cooked foods, however, commence after cooking. There are at least six: (i) handling cooked foods with bare hands; (ii) preparing raw foods on cutting boards, on tables, and/or with utensils that were either not cleaned or improperly cleaned and then used for cooked foods; this is conducive to cross-contamination; (iii) holding foods at warm room or outdoor ambient temperatures for several hours; (iv) holding foods at warm (bacterial-incubating) temperatures for a few hours or longer; (v) insufficient time and temperature exposures during reheating, if indeed the foods were reheated, and (vi) improper (slow) cooling. All of these situations have led to either contamination, survival, and/or growth of foodborne pathogens. Examples from personal observations of situation that could have contributed to foodborne illness and that were detected during hazard analyses are briefly described:

1. Bare hands. The potential for staphylococci to reach cooked potatoes during peeling, cutting, shaping, and garnishing was observed at street vending operations *(24)*. These bacteria (to up to 10^5/g of potato) and enterotoxins were recovered after the contaminated foods were held on display for several hours. Large numbers (usually $>10^5$/g of food) of coliform bacteria and aerobic mesophilic colonies (10^6 to 10^9/g of the food) were isolated from the potatoes and other foods after handling and holding for several hours. Despite cooking to high temperatures, staphylococci and coliforms were often found in high numbers in confectionery products *(49)*. Considerable handling of the cooked confectioneries with bare hands was observed.

2. Cross-contamination. Salmonellae were isolated from raw chickens and wooden (often heavily soiled) cutting boards used for both raw and cooked chickens by street vendors *(27)*. The potential for cross-contamination from the cutting boards, knives, and hands was obvious as operations were watched. Hands after handling raw meat were wiped on cleaning cloths which afterwards were used for wiping surfaces that contacted foods not subsequently cooked. The potential for cross-contamination intensified when the damp cloths remained for several hours on tables or shelves.

3. Holding at ambient temperatures. In Chinese-style restaurants, cooked rice is sometimes held at room temperature for several hours and sometimes overnight *(8)*. If the water activity is sufficiently high, *Bacillus cereus* cells which survive cooking can increase to large populations. Japanese box lunches *(bento)* were held at ambient temperature for several hours and the foods within were at bacterial-incubating temperatures for most of this duration *(12)*. Deep-oil-fried foods (e.g., fish, chicken, or yuca) prepared in the early morning and held until sold or, if not, kept overnight had large ($>10^5$/g of food) aerobic colony populations *(19)*. In confectionery manufacturing plants, bacterial multiplication occurred in the warm environment of the place of manufacture and could continue in products having high water activity during transport and while at retail outlets *(49)*. Foods had lower mesophilic aerobic populations and prevalence of contamination with *Bacillus cereus* when held at temperatures above 54.4°C than those kept at ambient temperature long enough for the product temperatures to fall to between 25 and 35°C. An inverse correlation was seen between temperature at the time of sampling that indicated the duration of holding and aerobic mesophilic populations *(30, 31)*. Populations up to 10^5/g of food *B. cereus* were isolated from the cooked foods after a 6-h or longer holding period *(24, 26, 27)*. Furthermore, the situation described in example 1 showed growth of coliforms and staphylococci and production of enterotoxin during holding on vending stands.

4. Holding at warm temperatures. Hot holding can provide situations during which microorganisms can multiply if the temperatures are sufficiently low and the duration of holding long. Such situations have been observed with the holding of cooked roast beef during hazard analyses following outbreaks due to *Clostridium perfringens (13, 16)*. At street vending operations, large populations (10^4 to 10^7/g of food) of *C. perfringens* were isolated from samples of cooked pulses, ground meat dishes, and chick peas collected during display, 8 to 10 h after cooking despite ineffective attempts to hold foods hot *(24, 26, 27)*.

5. Reheating. Reheating often does not provide sufficient time and temperature exposures to kill vegetative forms of foodborne pathogens generated from spores that survived cooking or microbes that contaminated the products after cooking. For example, foods were merely warmed up for a short time in households in developing countries *(10, 20, 22, 40–42)*. Reheating by microwaves gave inconsistent results and would allow survival of some pathogens in some foods *(14)*.

6. Slow cooling. Improper cooling practices can be seen in developed countries as well as in developing countries. Storing foods in large pots and otherwise in large masses in refrigerators is an operation that frequently leads to the causation of foodborne outbreaks. Poor practices have been illustrated and described in a variety of foods, e.g., beans *(8)*, roast beef *(16)*, turkeys *(15, 17)*, barbecued meat *(18)*, gyros *(23)*, and rice *(9)*.

Observed hazards of food preparation practices in homes usually do not differ greatly from those observed in food-service establishments or by street vendors in any of the cultures in which hazard analyses have been done *(5)*. Variation depends on microorganisms that are likely to reach the foods, composition of the food, preparation and holding practices, and understanding of the person who prepares foods about ways to handle them that reduces contamination, kills pathogens, and prevents or slows bacterial growth.

Critical control points must be determined from the hazards observed or measured during hazard analyses. They are usually one or more of the following: (i) source of foods or ingredients, (ii) formulation (in the case of certain acidified, dried, salted, or sugared foods), (iii) cooking, (iv) manipulation of foods after cooking, (v) holding cooked foods, (vi) cooling, (vii) reheating and/or (viii) cleaning utensils and equipment. The first two steps (identification and assessment of hazards and determination of critical control points) of the hazard analysis critical control point (HACCP) system *(10)* are valuable for detecting foodborne disease hazards during outbreak investigations.

If successful, epidemiologic inquiry, collation of data, and calculation of statistics can identify the place foods were probably mishandled or mistreated and the food that was most probably the vehicle. Hazard analyses are necessary to confirm the former and laboratory analyses coupled with hazard analyses are necessary for the latter. Risky food-processing and preparation practices can be identified during hazard analyses despite limitations of epidemiologic and laboratory phases of an investigation. Hence, hazard analysis is the link between epidemiology and microbiology that identifies events that contributed to the causation of outbreaks; and, being such, it provides information upon which to initiate control action and to base preventive measures.

REFERENCES

1. Austin, H., H. A. Hill, W. D. Flanders, and R. S. Greenberg. 1994. Limitations in the application of case-control methodology. Epidemiol. Rev. 16:65–76.
2. Bryan, F. L. 1978. Factors that contribute to outbreaks of foodborne disease. J. Food Prot. 41:816–827.
3. Bryan, F. L. 1988. Risk associated with vehicles of foodborne pathogens and toxins. J. Food Prot. 51:498–508.
4. Bryan, F. L. 1988. Risks associated with practices, procedures and processes that lead to outbreaks of foodborne diseases. J. Food Prot. 51:663–673.
5. Bryan, F. L. 1988. Safety of ethnic foods through the application of the hazard analysis critical control point approach. Dairy Food Sanit. 8:654–660.
6. Bryan, F. L. 1992. Hazard analysis critical control point evaluations. A guide to identifying hazards and assessing risks associated with food preparation and storage. World Health Organization, Geneva.
7. Bryan, F. L., H. W. Anderson, O. D. Cook, J. Guzewich, K. H. Lewis, R. C. Swanson, and E. C. D. Todd. 1987. Procedures to investigate foodborne illness, 4th ed. International Association of Milk, Food, and Environmental Sanitarians, Ames, Iowa.
8. Bryan, F. L., and C. A. Bartleson. 1985. Mexican-style foodservice operations; hazard analyses, critical control points and monitoring. J. Food Prot. 48:509–524.
9. Bryan, F. L., C. A. Bartleson, and N. Christopherson. 1981. Hazard analysis, in reference to *Bacillus cereus,* of boiled and fried rice in Cantonese-style restaurants. J. Food Prot. 44:500–512.
10. Bryan, F. L., C. A. Bartleson, C. O. Cook, P. Fisher, J. Guzewich, B. Humm, R. C. Swanson, and E. C. D. Todd. 1991. Procedures to implement the hazard analysis critical control point (HACCP) system. International Association of Milk, Food and Environmental Sanitarians, Ames, Iowa.
11. Bryan, F. L., and M. P. Doyle. 1995. Health risks and consequences of *Salmonella* and *Campylobacter jejuni* in raw poultry. J. Food Prot. 58:326–344.
12. Bryan, F. L., Fukunaga, I., Tsutsumi, S., Miyashiro, L., Kagawa, D., Sakai, B., Matsuura, H., and Oramura, M. 1991. Hazard analysis of Japanese boxed lunches (*bento*). J. Environ. Health 54:29–32.
13. Bryan, F. L., and E. G. Kilpatrick. 1971. *Clostridium perfringens* related to roast beef cooking, storage, and contamination in a fast food service restaurant. Am. J. Public Health 61:1869–1885.
14. Bryan, F. L., and J. B. Lyon. 1984. Critical control points of hospital foodservice operations. J. Food Prot. 47:950–963.
15. Bryan, F. L., and T. W. McKinley. 1974. Prevention of foodborne illness by time-temperature control of thawing, cooking, chilling, and reheating turkeys in school lunch kitchen. J. Milk Food Technol. 37:420–429.
16. Bryan, F. L., and T. W. McKinley. 1979. Hazard analysis and control of roast beef preparation in foodservice establishments. J. Food Prot. 42:4–18.
17. Bryan, F. L., T. W. McKinley, and B. Mixson. 1971. Use of time-temperature evaluations in detecting the responsible vehicle and contributing factors of foodborne disease outbreaks. J Milk Food Technol. 34:576–582.
18. Bryan, F. L., K. McNaught, and K. Blehm. 1980. Time-temperature survey at a restaurant that specializes in barbecued food. J. Food Prot. 43:595–600.
19. Bryan, F. L., S. Michanie, P. Alvarez, and A. Paniagua. 1988. Critical control points of street-vended foods in the Dominican Republic. J. Food Prot. 51:373–384.
20. Bryan, F. L., S. Michanie, N. Mendoza Fernandez, M. Moscoso Vizcarra, D. Taboada-P., O. Navarro-S., A. Bravo Alonso, and E. Guerra Requejo. 1988. Hazard analyses of foods prepared by migrants living in a new settlement at the outskirts in Lima, Peru. J. Food Prot. 51:314–323.
21. Bryan, F. L., S. Michanie, M. Moscoso Vizcarra, O. Navarro-S., D. Taboada, N. Mendoza Fernandez, E. Guerra Requejo, and B. Perez Munoz. 1988. Hazard analyses of foods prepared by inhabitants near Lake Titicaca in the Peruvian Sierra. J. Food Prot. 51:412–418.
22. Bryan, F. L., B. Phithakpol, W. Varanyanond, C. Wongkhalaung, and P. Auttaviboonkul. 1986. Phase II: Food Handling: Hazard analysis critical control point evaluations of foods prepared in households in a rice-farming village in Thailand. *For* The Food and Agriculture Organization of the United Nations, Rome.
23. Bryan, F. L., S. R. Standley, and C. Henderson. 1980. Time-temperature conditions of *gyros.* J. Food Prot. 43:346–353.
24. Bryan, F. L., P. Teufel, S. Roohi, F. Qadar, S. Riaz, and Z. Malik. 1992. Hazards and critical control points of street-vended *chat,* a regionally-popular food in Pakistan. J. Food Prot. 55:708–713.
25. Bryan, F. L., P. Teufel, S. Roohi, F. Qadar, S. Riaz, and Z. Malik. 1992. Hazards and critical control points of foods preparation and storage in homes in a village and a town in Pakistan. J. Food Prot. 55:714–721.
26. Bryan, F. L., P. Teufel, S. Riaz, S. Roohi, F. Qadar, and Z. Malik. 1992. Hazards and critical control points of vending operations at a railway station and a bus station in Pakistan. J. Food Prot. 55:534–541.
27. Bryan, F. L., P. Teufel, S. Riaz, S. Roohi, F. Qadar, and Z. Malik. 1992. Hazards and critical control points of street-vending operations in a mountain resort town in Pakistan. J. Food Prot. 55:701–707.
28. Davey, G. R. 1985. Food poisoning in New South Wales: 1977–1984. Food Technol. Aust. 37:453–456.
29. Doyle, M. P. 1989. Foodborne bacterial pathogens. Marcel Dekker, New York.
30. El-Sherbeeny, M. R., M. F. Saddik, H. E.-S. Aly, and F. L. Bryan. 1985. Microbiological profile and storage temperatures of Egyptian rice dishes. J. Food Prot. 48:39–43.
31. El-Sherbeeny, M. R., M. F. Saddik, and F. L. Bryan. 1985. Microbiological profiles of foods sold by street vendors in Egypt. Int. J. Food Microbiol. 2:355–364.
32. Griffin, P. M., and R. V. Tauxe. 1991. The epidemiology of infections caused by *Escherichia coli* 0157:H7, enterohemorrhagic *E. coli,* and the associated hemolytic uremic syndrome. Epidemiol. Rev. 13:60–98.
33. Hill, A. B. 1965. The environment and disease: association of causation? Proc. Royal Soc. Med. 58:295–300.
34. Hui, Y. H., J. R. Gorham, K. D. Murrel, and D. O. Cliver (ed.). 1994. Foodborne disease handbook, vol. 1. Diseases caused by bacteria. Marcel Dekker, New York.
35. Humphrey, T. J., M. Greenwood, R. J. Gilbert, B. Rowe, and P. A. Chapman. 1989. The survival of salmonellas in shell eggs cooked under simulated domestic conditions. Epidemiol. Infect. 103:35–45.
36. Ibrahim, M. A., and W. O. Spitzer. 1979. The case-control study: the problem and the prospect. J. Chron. Dis. 32:139–144.
37. International Commission on Microbiological Specifications for Food. 1980. Microbial ecology of foods, vol. 2. Food commodities. Academic Press, New York.
38. International Commission on Microbiological Specifications for Food. 1986. Microorganisms in foods 2. Sampling for microbiological analysis: principles and specific applications, 2nd ed. University of Toronto Press, Toronto.
39. Koff, R. S., and H. S. Sear. 1967. Internal temperature of steamed clams. N. Engl. J. Med. 276:737–739.
40. Michanie, S., F. L. Bryan, P. Alvarez, and A. Barros Olivo. 1987. Critical control points for foods prepared in households in which babies had salmonellosis. Int. J. Food Microbiol. 5:337–354.
41. Michanie, S., F. L. Bryan, P. Alvarez, A. Barros Olivo, and A. Paniagua. 1988. Critical control points for foods prepared in households whose members had either alleged typhoid fever or diarrhea. Int. J. Food Microbiol. 7:123–134.

42. Michanie, S., F. L. Bryan, N. Mendoza Fernandez, M. Moscoso Vizcarra, D. Taboada-P., O. Navarro-S., A. Bravo Alonso, and L. Santillan-M. 1988. Hazard analyses of foods prepared by inhabitants along the Amazon River. J. Food Prot. 51:293–302.
43. Murphy, P. A. 1990. Avoiding bias: systematic and random error, p. 75–82. *In* G. F. Craun (ed.), Methods for investigation and prevention of waterborne disease outbreaks, EPA/600/1-90/005a. U.S. Environmental Protection Agency, Washington, D.C.
44. Riemann, H., and F. L. Bryan (ed.). 1979. Foodborne infections and intoxications, 2nd ed. Academic Press, New York.
45. Roberts, D. 1982. Factors contributing to outbreaks of food poisoning in England and Wales 1970–1979. J. Hyg. 89:491–498.
46. Rodrigue, D. C., R. V. Tauxe, R. V., and B. Rowe. 1990. International increase in *Salmonella enteritidis:* a new pandemic? Epidemiol. Infect. 105:21–27.
47. Sackett, D. L. 1979. Bias in analytic research. J. Chron. Dis. 32:51–63.
48. St. Louis, M. E., D. L. Morse, M. E. Potter, T. N. DeMelfi, J. J. Guzewich, R. V. Tauxe, P. A. Blake, and the *Salmonella enteritidis* Working Group. 1988. The emergence of grade A eggs as a major source of *Salmonella enteritidis* infections. New implications for the control of salmonellosis. JAMA 259:2103–2107.
49. Teufel, P., F. L. Bryan, F. Qadar, S. Riaz, S. Roohi, and Z. Malik. 1992. Risks of salmonellosis and staphylococcal food poisoning from Pakistani milk-based confectioneries products in Pakistan. J. Food Prot. 55:588–594.
50. Todd, E. C. D. 1983. Factors that contribute to foodborne disease in Canada, 1973–1977. J. Food Prot. 46:737–747.
51. Traven, N. D. 1990. Data analysis: estimating risks, p. 65–74. *In* G. F. Craun (ed.), Methods for investigation and prevention of waterborne disease outbreaks, EPA/600/1-90/005a. U.S. Environmental Protection Agency, Washington, D.C.
52. Weingold, S. E., J. J. Guzewich, and J. K. Kudala. 1994. Use of foodborne disease data for HACCP risk assessment. J. Food Prot. 57:820–830.