REVISITING DOSE-RESPONSE MODELS OF FOODBORNE PATHOGENS

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Risk assessment of bacterial hazards is an emerging tool for unraveling the factors that contribute to the occurrence of foodborne diseases. It can thus provide useful information for formulating food safety policies. The methodological approach proposed by the Codex Alimentarius Commission includes four very distinct steps: hazard identification, exposure assessment, hazard characterization, and risk characterization.

Hazard characterization, sometimes also called dose-response assessment, is perhaps the least developed component. Although various dose-response functions have been fitted for several foodborne microorganisms, such models are limited in their ability to incorporate differences in strain characteristics of pathogens and in population susceptibility. Moreover, infection rather than disease is in most cases the endpoint. In order to identify opportunities for improvement, the historical origins of hazard characterization of bacterial hazards as well as the current practice are reviewed.

Historical perspective

Covello and Mumper identify a two-fold root of modern risk assessment in probability theory and analytical methods for establishing causal factors of diseases. It is interesting to note that the former still has an important link to medicine. The concept of calculating empirical probabilities was, in fact, introduced by John Gaunt with his "Bills of mortality" published in 1662.

Formal risk assessment was initiated in the United States as early as the 1930s with a focus on noxious agents in industry. Risks posed by ionizing radiation were assessed starting in the 1960s, and carcinogens in food in the 1970s. In the mid-1970s, the Environmental Protection Agency and the Occupational Safety and Health Administration were established, and have become major proponents and users of health risk assessments within the U.S. government.

The body of risk assessment experience in the U.S. was eventually unified in a 1983 document of the National Research Council entitled "Risk Assessment in the Federal Government: Managing the Process", which has become known as "Red Book". Given its genesis, it is not surprising that the focus is on environmental concerns, in particular those posed by carcinogens. A direct inheritance of the industrial setting
and consequent engineering leaning is the tendency to view complex situations as modular, mechanistic systems. Other disciplines, in particular toxicology and epidemiology, are seen more as sources of data than of methods.

The legacy of the Red Book is still apparent in several fields, including food safety. For instance, the four-step approach advocated by the Codex Alimentarius Commission parallels the Red Book paradigm. However, even more than on specific methodological approaches and methods, the most important influence of the Red Book is perhaps in conceptual terms. This might explain why, despite the facts that risk analysis has its ancient roots in medicine and the concept of risk is very much present in medicine (especially in epidemiology), the "biomedical dimension" of current microbial risk assessments is often lacking. This is strikingly evident in hazard characterization.

**Current approach**
While the Codex Alimentarius lays out general guidelines for conducting hazard characterizations, a framework by the International Life Sciences Institute provides more guidance on actual methodological considerations. Three components are described as crucial to hazard characterization: host characterization, evaluation of health effects, and quantification of the dose-response relation. These elements are integrated in a host-pathogen profile, which is the outcome of the process.

With few exceptions (e.g. the risk assessment on *Salmonella enteritidis* in shell eggs and egg products conducted in the USA), hazard characterization is mainly reduced in practice to a dose-response assessment with dose as the major, if not only, factor determining the probability of infection (illness). Other important components comprising host, agent and environment (the epidemiologic triad) factors have not made their way into hazard characterizations to any great extent.

Research has mainly focused on comparing the fitting of statistical models to the results of human feeding trials. In doing that, little attention has been paid to the limitations of the available data. Issues include: use of young, healthy volunteers; repeated dosing of the same subjects (particularly true of Salmonella feeding studies); lack of randomization; fitting of models on few data points; extrapolation beyond the data range.

**Opportunities**
A major involvement of epidemiology in the risk assessment process of bacterial pathogens - be it as source of data, methods, or conceptual approaches - promises ground for advancement. In the specific case of hazard characterization, three major areas of opportunities can be delineated. Firstly, a broader and more critical choice of data should be achieved. Techniques used in meta-analysis potentially offer the opportunity to weight evidence (study quality), to identify homogeneity of findings, and to combine coherently the results. Secondly, the primacy of the biomedical model over the mathematical one has to be reasserted. Methods from epidemiology can be used along those from reliability analysis and statistics to identify model components.
and to organize and integrate them. Thirdly, it must be recognized that the usefulness of risk assessment depends on its ability to represent risk in its multiple dimensions. The use of measures of morbidity as well as of disease burden should be considered at that end.

References
Common Foodborne Pathogens. The U.S. Public Health Service has identified the following microorganisms as being the biggest culprits of foodborne illness, either because of the severity of the sickness or the number of cases of illness they cause. Beware of these pathogens: Fight BAC!®. Campylobacter. Campylobacter is the second most common bacterial cause of diarrhea in the United States. This entailed estimation of dose-response relationship for foodborne pathogens to humans, either by feeding studies or from outbreaks. For certain pathogens, such as Listeria monocytogenes and Escherichia coli O157:H7, there are no feeding studies due to ethical reasons, and the results from outbreaks are normally used to estimate the infectious dose. The focus of this review is to compile dose-response information in volunteers for several foodborne pathogens including Salmonella, Shigella spp., Campylobacter jejuni, Vibrio spp., Escherichia coli, Cryptosporidium parvum and Entamoeba coli. A dose-response model describes the probability of a specified response from exposure to a specified pathogen in a specified population, as a function of the dose. This function is based on empirical data, and will usually be given in the form of a mathematical relationship. The use of mathematical models is needed because: contamination of food and water usually occurs with low numbers or under exceptional circumstances; the occurrence of effects can not usually be measured by observational methods in the dose range needed, and hence models are needed to extrapolate from high doses or frequen This Research Topic titled “Foodborne Pathogens: Hygiene and Safety” focuses on important food safety concerns such as the potential presence of pathogens in food as well as their toxins/metabolites, the resistance to antibiotics or sanitizers and other virulence characteristics. It includes 4 reviews and 44 ori... Foodborne diseases represent one of the most important public health troubles worldwide. The potential of foodborne pathogens to cause illness or even death in consumers highlights the importance of such events and consequent need of their monitoring and prevention. The results showed that the optimal disinfectant dose increased exponentially with the initial bacterial concentration. Infective dose: aka infectious dose; the number of micro-organisms or level of toxin usually required to make you sick. Bacillus cereus. General Characteristics. B. cereus is an aerobic (requires oxygen for growth), spore-forming microorganism. The two basic types of B. cereus illnesses are a diarrheal-type (from consuming microbial cells) and an emetic-type (from consuming the toxin produced by the microorganism). Of reported foodborne illness data, B. cereus is responsible for approximately 2% of the outbreaks, less than 1.0% of the cases, and is usually not fatal. Being a spore-forming m