Risk assessment and food-borne micro-organisms: the difficulties of biological diversity

D.T. Bernard and V.N. Scott*

Quantitative risk assessment to estimate the probability of adverse health consequences from microbial pathogens in foods has developed from techniques used to assess the risk associated with chemicals. The procedure is complicated by numerous variabilities and uncertainties. While many of the microbial hazards have been identified, dose-response data are limited and variable. Little information is available to characterize the potential for exposure. The accuracy of dose-response models used to calculate the probability of infection is highly dependent on the assumptions used. The risk assessment is complicated by the fact that microbial populations are not static in foods. Mathematical models can generate numerical estimates of risk which are used in risk management. An acceptable level of risk should be based on what is technically feasible and economically achievable.

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INTRODUCTION

Risk assessment is the estimation of severity and the likelihood of harm resulting from exposure to a hazard. Whether we are considering public health risk posed by chemicals or micro-organisms in food, the purpose of the risk assessment and the basic steps involved in conducting the assessment will be the same. The purpose is to derive a mathematical statement, based on the probability of certain events, of the chance of adverse health consequences from exposure to an agent capable of causing harm. The risk assessment process involves four steps (NRC, 1983).

1. Hazard identification: the qualitative indication that a substance may cause adverse health effects.

2. Hazard characterization (dose-response assessment): the qualitative and quantitative evaluation of the nature of the adverse health effects; the relationship between the magnitude of the exposure and the probability of occurrence of adverse health effects.

3. Exposure characterization: the qualitative and quantitative evaluation of the degree of exposure likely to occur.

4. Risk characterization: integration of the above steps into an estimation of the adverse effects likely to occur in a population, to be used in decision-making (risk management).

While the basic steps are the same, applying quantitative risk assessment techniques to estimate the probability of adverse health consequences from microbial pathogens in foods has proven even more difficult than for chemicals. Because recent efforts to produce quantitative risk estimates for microbial food-borne disease began with the techniques used for estimation of risk associated with chemicals, we shall briefly review this area.

RISK ASSESSMENT FOR CHEMICALS

In the past, tolerances have been set for foods based on the assumption that there is a threshold dose below which there are no adverse effects. Using a variety of toxicological studies in animals, a no observable effect level (NOEL) is determined and a safety factor is applied to establish an acceptable daily intake (ADI) for the chemical.

There are a number of difficulties with this approach. Toxicological tests generally involve testing animals with relatively high doses of the chemical. In vivo toxicity has a wide range of effects (variability), and the determination of toxicological end-points is a matter of scientific judgement. Interspecies extrapolation is the source of much uncertainty in defining risk. Extrapolation from high doses to low doses introduces additional uncertainties. The normal safety factors of 10–100 are arbitrary numbers and may be increased by considerations such as incomplete data, teratogenic effects, age-related effects etc. The number may also be adjusted if toxicity and dose-response effects in humans are known.

Reliable information on dietary intake of chemical hazards is necessary to assess the health implications of dietary exposure. Accurate data on the actual level of the chemical in foods may not be available. Furthermore, accurate consumption data are difficult to obtain. The assumptions that are used may be very biased for certain segments of the population. Thus, while the ADI or safety factor approach contains many of the elements of a formal risk assessment, it does not represent a quantitative measure of risk.

An alternative approach is the use of quantitative risk assessment (QRA), which provides a statistical estimate of the probability of an event taking place based on exposure and dose-response models. This has been used for risk assessment of carcinogens, and is based on the principle that cancer induction is dose dependent, with no threshold. Mathematical models are used to extrapolate observed data derived from high dose levels to the expected response at low dose levels. Mechanistic multi-stage models are most commonly used. Such models help to standardize approaches, define data needs, and allow the quantitation of risk and uncertainty. However, such models may oversimplify biological mechanisms and imply scientific precision that is not justified.

RISK ASSESSMENT FOR MICROBIAL HAZARDS

QRA applied to microbial hazards is a relatively new approach and has only been applied to drinking water (Regli et al., 1991; Rose and Gerba, 1991: Rose et al., 1991) and most recently to viruses in shellfish (Rose and Sobsey, 1993). Other approaches proposed for conducting a risk assessment for food-borne pathogens include probabilistic scenario analysis, fault tree analysis. However, any method used to assess risk of hazards from food-borne microorganisms will be complicated by factors resulting from methods used to grow, process, store and prepare food for consumption.

Hazard identification

A large number of food-borne microbial hazards have been identified. An excellent summary of these can be found in the CAST report 'Foodborne pathogens: risks and consequences' (CAST, 1994). The biological agents of concern include pathogenic strains of bacteria, viruses, fungi, helminths, protozoa, algae and the toxic products these may produce. Those agents known to cause food-borne disease have been identified by using epidemiologic and other data to link the organism and its source to illness. As only a limited number of outbreaks are adequately investigated for cause, it is likely that agents of disease have yet to be identified.

Another limiting factor in hazard identification is that epidemiological data are expensive to obtain and are typically only available from developed countries which have a health care and surveillance system adequate to produce such data. Thus hazards identified and foods implicated will depend on the food production system and dietary customs of those localities. Such data may be entirely inadequate for accurately identifying hazardous organisms, foods or practices in developing countries.

Dose-response assessment

As with chemical risk assessment, the purpose of this step is to provide an estimate of the quantity of the agent (pathogen) necessary to cause disease in various populations. For many food-borne pathogens, dose-response data are limited or non-existent. Information on which to base dose-response estimates is difficult to obtain and may also be inaccurate for a variety of reasons. For example, dose-response can be highly variable. A food-borne disease organism rarely affects all those ingesting a contaminated food. Thus, the minimum dose to cause illness is difficult to determine. The variables involved include the virulence of the organism, the susceptibility of the host, and the number of micro-organisms that survive the digestive process and other host defences. Foods, drugs and disease states may alter host defence mechanisms such as gastric acidity, indigenous intestinal bacterial flora and the immune system. All of these factors may contribute to the observation that certain populations (elderly, infants, persons with cancer or AIDS etc.) are more susceptible to food-borne pathogens.

Risk assessments for micro-organisms have primarily relied on dose-response data generated from human feeding studies, which have generally been done using healthy male volunteers. Such data may underestimate the risk to certain segments of the population. Since human feeding studies are now considered unaccept-
able, studies to generate dose-response curves where such data are lacking are not possible.

Another means of obtaining dose-response data is from outbreaks. Data from both outbreaks and feeding studies show that the doses required to cause illness differ greatly among types, genera, species and strains of infective micro-organisms (CAST, 1994). Dose-response data currently in the literature may reflect asymptomatic infection (colonization) rather than actual illness.

In addition, estimates of the number of micro-organisms responsible for an outbreak are sometimes inaccurate because the laboratory determination of numbers of organisms in implicated food (the dose) may not reflect the numbers actually consumed as a result of increase or decrease of numbers of micro-organisms between the time of the outbreak and the time of the analysis. Without accurate dose-response data we must extrapolate data from related pathogens, extrapolate dose-response from food-borne disease outbreak data, or use probability functions to simulate hypothetical dose-response curves (or a combination of these methods).

Exposure characterization

Determining the probability of contact with or consumption of a pathogen and the quantity consumed is another area of uncertainty when dealing with micro-organisms. When addressing exposure to many chemicals, certain assumptions can be made regarding use rates and persistence in foods. Micro-organisms, however, occur in foods through various routes which typically relate to the ecological niche of the organism and/or to the production, processing and storage practices used. Thus our current knowledge of where exposures may originate has been developed through studies of foods involved in various outbreaks, analysis of foods for specific pathogens, and ecological studies conducted to determine where specific organisms occur in nature. This leads to the obvious statement that for those recently determined pathogenic organisms, little information is available to characterize the potential for exposure.

The second element to exposure characterization is the concentration (quantity) of the organism in a food. When dealing with chemicals or a toxin, this element is simplified, as concentrations rarely change without some physical change to the food. However, with bacterial pathogens, populations are in a dynamic state. Thus, exposure estimates must be based on predictions which account for potential for bacterial growth and death.

Another factor to be considered in exposure characterization is that micro-organisms are seldom homogeneously distributed in foods. Thus analysing foods for a pathogen to estimate potential exposure will never yield results which are absolute. Numerous studies have focused on the prevalence of pathogens in specific foods. In conducting these studies, samples have frequently been taken at point of sale. While these data may be useful in the risk assessment procedure, storage and preparation steps may increase or decrease the level of pathogens in the foods eaten. Since sampling does not occur at the point of consumption, there will be inherent errors in exposure estimates.

Risk characterization

Dose-response models can be used to define the risk of infection (Haas, 1983). The log-normal model assumes a threshold effect, or that there is a minimum infective dose required to initiate infection. The single-hit exponential model assumes that a single organ ism can cause adverse effects in at least a portion of the population. This model can be revised to take into account assumptions that there is variation in the virulence of individual pathogens or in the sensitivity of the individual hosts or both (β-distributed infectivity probability or β-Poisson model). Haas (1983) applied the three models to data sets on dose-response for viral, protozoan and bacterial pathogens. Of the nine data sets, the beta distribution model fitted seven, the log-normal model fitted five and the single-hit exponential model fitted three. Based on these results, Haas concluded that it is impossible to rule out the hypothesis that one ingested organism can cause infection in at least a portion of the exposed population.

Rose et al. (1991), Regli et al. (1991), and Rose and Gerba (1991) also applied the single-hit exponential and the β-Poisson models to water-borne pathogens. The models were used to calculate the probability of infection from a single organism, the dose for a particular level of infection, daily risk etc.

As with any model, how well these models reflect reality will depend on the assumptions used, the accuracy of the model for characterizing the independent variables, and the data used to develop the dose-response curves and exposure. Many assumptions are made in applying the models. For example, a random Poisson distribution of the micro-organism has generally been assumed. This may accurately characterize the distribution of micro-organisms in water, but is unlikely to be true for foods. In many cases it is assumed that the population is equally susceptible. The β-Poisson model generalizes the host-micro-organism interaction using a β probability distribution to account for heterogeneity of either the infectivity of the micro-organism or the sensitivity of the host or both. Each of the models uses parameters characterized by dose-response curves. As noted above, this is an area where accuracy of available data is questionable.

Monte Carlo simulation can be used for probabilistic modelling when such uncertainties exist. In Monte Carlo simulation, a model is run repeatedly using different values for each of the uncertain input parameters each time. The values of each of the uncertain input parameters are generated based on the probability distribution for the parameter. With all the uncer-
Factors complicating risk assessment for food-borne pathogens

As noted above, there are many factors which complicate the assessment of risk presented by food-borne pathogens. The most significant of these is that, with the exception of shelf stable products, microbial populations are not static in foods. Factors which influence levels of micro-organisms in foods as consumed include the following:

- physical treatments such as hot holding or freezing may kill a portion of the microbial population;
- refrigeration will allow slow growth of some microorganisms, including a few pathogens;
- holding of many foods at temperatures within the range of 5–60°C will allow microbial growth;
- under certain conditions, spoilage organisms may compete with pathogens, reducing their growth and the likelihood of infection; and
- thorough cooking of foods before consumption will kill vegetative cells of pathogenic organisms, thus virtually eliminating the threat of certain types of infection.

Another factor to be considered is the effect of the food itself as a modulator of virulence of a particular pathogenic organism. A graphic example of this effect is the recent occurrence of a widespread outbreak of salmonellosis from ice cream in the USA. It has been reported that the contamination level of Salmonella in the ice cream which caused the outbreak was extremely low but the attack rate was high. This supports a theory postulated earlier that high fat or highly buffered foods provide a certain degree of protection to the micro-organisms which permits them to survive exposure to acidic conditions in the stomach. Similar outbreaks which support this hypothesis have occurred from low levels of Salmonella in chocolate candies.

Because of the above documented difficulties, the art of risk analysis as applied to food-borne micro-organisms has not advanced to the point where it is greatly useful in establishing food safety practices or policies. Therefore both industry and government bodies continue to rely on the judgement of experts who must have a knowledge of the intrinsic properties of foods and the potential for contamination and abuse to provide a qualitative estimate of hazards of public health significance associated with a food or processing operation. This can often times result in very conservative positions when establishing policy.

ACCEPTABLE RISK

Mathematical models can generate a numerical estimate of risk which may be used in decision-making by comparison with socially and politically accepted risk levels. The US Environmental Protection Agency (US EPA) judges pesticides against the negligible risk standard of less than $1 \times 10^{-6}$ additional cases of cancer over a 70 year lifetime. Standards for carcinogens in drinking water supplies are based on a minimal target of protection of between $10^{-4}$ and $10^{-6}$ incremental lifetime risk using a conservative model unlikely to have underestimated risk. US EPA has also promulgated drinking water standards with an acceptable risk level of one infection/10,000/year for infectious agents (Giardia lamblia), which translates to a lifetime risk of $<10^{-2}$ to $10^{-3}$ infections per year (Regli et al., 1991).

Different risk criteria may be appropriate depending on the severity of the disease caused by a particular agent and the potential sequelae. For example, the acceptable risk criterion for E. coli O157:H7 should be more stringent than that for Staphylococcus aureus. It is fair to say, however, that it is much less controversial to consider acceptable levels of risk for conditions which may arise from chronic exposure to chemicals than for acute and sometimes life threatening illnesses which may arise from exposure to pathogenic micro-organisms. In addition, we must consider how we would apply an acceptable level of risk. Should this be based on lifetime exposure as with chemical hazards, on probability of being made ill from eating a single serving, or on probability of being made ill from a food in any one year? For example, Griffin and Tauxe (1991) estimate that in the USA as many as 15,500 cases of illness from E. coli O157:H7 occur each year from eating hamburgers. If these were true and estimates are correct that 28,000,000 hamburgers are consumed each year, the likelihood of becoming ill from eating a single hamburger is about 5.5 in 10,000,000. If, as the beef industry estimates, each person eats the equivalent of about 100 hamburgers each year, the annual risk would be considerably higher. If we were to apply an estimate of the risk based on a lifetime of consumption at a steady rate, the risk would obviously increase proportionately.

While this exercise is very cursory and does not take into account the many factors which will mediate the actual risk (such as proper cooking), consideration of an acceptable level of risk is essential. Since we currently cannot preclude all pathogens from our food supply and the continuation of commerce in foods dictates that reasonable policies for microbial contaminants be established, these policies must be based on acceptable levels of risk. The acceptable safety level or risk level should be based on what is technically feasible and economically achievable with current technologies. As Hathaway (1993) noted, food will always present some minimal level of risk. It is the task of industry to maintain the level of risk at the minimum which is technologically feasible. It should be the role of official bodies to use risk analysis to determine achievable risk levels for food-borne pathogens and to base food safety policies on defensible and practical application of these analyses.
REFERENCES


