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DEVELOPMENT OF A RISK ASSESSMENT MODEL FOR THE EVALUATION OF HACCP-BASED QUALITY ASSURANCE PROGRAMS FOR HUMAN INFECTION FROM *SALMONELLA ENTERITIDIS* : PRELIMINARY ESTIMATES

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Le coût des maladies d'origine alimentaire, aux Etats-Unis, telles que les salmonelloses dont la source est la viande rouge et la volaille a été estimé et varie de 0.3 à 2.6 billions de $. Depuis 1979, les salmonelloses sont classées 4ème dans la liste CDC des maladies. Salmonella enteritidis (S.e) compte parmi les 25 % de salmonelles isolées, une augmentation marquée depuis son taux d'isolation de 5 % en 1976, identifiant S.e comme un agent pathogène en pleine apparition.

Des modèles économiques et d'analyse de risque représentent une approche complète afin d'identifier des stratégies de coût/efficacité pour le contrôle des maladies d'origine alimentaire. Un modèle complet permet l'identification de l'évolution au niveau de la chaîne alimentaire soumise au contrôle des agents pathogènes et évalue simultanément le rapport coût/efficacité de diverses stratégies. Des modèles économiques et d'analyse de risque peuvent fournir aux scientifiques des bases afin de faire évoluer le débat politique autour de la sécurité alimentaire d'une décision (aliment sain ou pas) à une évaluation quantitative du risque. Ce papier décrit le développement d'un modèle d'appréciation du risque.

Les données proviennent de la littérature, des rapports non publiés et de l'opinion des experts. L'estimation de la prévalence montre une distribution trimodale dont la majeure partie est inférieure à 0.008. les résultats temps/température indiquent une bonne adéquation de l'équation de Gompertz avec le modèle de croissance après une phase de latence de 21jours. Les tests du rapport de vraisemblance (Chi 2 = 70.9) pour la différence de virulence entre les souches sont significatifs et basés sur les données d'un essai de nutrition conduit sur l'homme. Les modèles dose/réponse exponentiel, log-normal et logit ont été comparés et l'exponentiel s'est révélé être le plus adéquat. Des efforts complémentaires se feront afin d'affiner les modèles dose-réponse et de croissance (temps-température) en intégrant une analyse de sensibilité et la méthode de simulation de Monté Carlo pour la caractérisation du risque.

INTRODUCTION

Regulatory programs and guidelines for control of foodborne microbial agents have existed for nearly 100 years. However, increased awareness of the scope and magnitude of foodborne disease, as well as the emergence of previously unrecognized human pathogens transmitted via the foodborne route, have prompted regulatory officials to consider new and improved strategies to reduce the health risks associated with pathogenic microorganisms in foods. Implementation of these proposed strategies will involve definitive costs for a finite level of risk reduction.

Quantitative risk assessment (QRA), which is formally defined as the technical assessment of the nature and magnitude of a risk caused by a hazard, provides a framework for the evaluation of health risks from pathogenic microorganisms in food (Jaykus 1996). Integrated risk assessment and economic models represent a comprehensive approach to the identification of cost effective strategies for foodborne disease control. An integrated model allows the identification of stages in the food marketing chain most amenable to pathogen control and simultaneous evaluation of the cost effectiveness of various mitigation strategies. Integrated risk and economic models can provide the scientific basis for shifting the policy (and eventually public) debate in food safety from a "safe or not safe" dichotomy to a quantitative risk-based continuum. Risk and cost based inputs provide sound data for rational decision- making in the face of strident but mutually exclusive demands for both inexpensive and safe food. Risk assessment, management and communication strategies can be utilized in conjunction with HACCP-based approaches to reduce foodborne disease risk and clearly communicate mitigation results to scientists, policy makers and the public.

Foodborne disease from meat and poultry is a major cause of morbidity in the U.S. resulting in estimated annual costs of $7.7 to $8.4 billion (Kvenberg and Archer 1987; Todd 1989). Foodborne illness costs in the U.S. for Salmonellosis from meat and poultry sources have been estimated to range from $0.3 to $2.6 billion. The Centers for Disease Control and Prevention calculates morbidity rates of 6.5 to 33 million cases of foodborne illnesses annually, resulting in 6,000 to 9,000 human deaths (CAST 1994). Since 1979, Salmonellosis has ranked fourth on CDC's list of notifiable diseases. CDC estimates that only 1 in 50 cases of Salmonellosis are reported. Based on notifiable diseases summaries from CDC (1993), the total number of human cases of Salmonellosis in the U.S. is likely to be in the range of 2.5 million per year. Furthermore *Salmonella enteritidis* (S.e.) now accounts for over 25% of the Salmonella isolates, a marked increase from it's 1976 isolation rate of 5%. Recent isolation of phage 4 subtypes in the U.S. clearly which S.e. as an active and emerging pathogen.

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This paper reports the preliminary results of a quantitative microbial risk assessment for the transmission of S.e. in humans due to the consumption of shell eggs. The ultimate goal of this work will be to establish baseline risk levels to be used in conjunction with cost-benefit analysis and other economic approaches for evaluating HACCP-based quality assurance programs. Such programs must be evaluated with respect to their efficiency as market solutions to food safety while identifying optimal control and monitoring strategies to minimize risk to human health.

MATERIALS AND METHODS

The following data and analysis is presented as preliminary results of data acquisition and variable modeling of a quantitative microbial risk assessment for the risk of human Salmonellosis associated with the consumption of raw shell eggs. From an initial quantitative risk assessment (Morales et al., 1995), three variables (prevalence, dose-response, storage conditions) identified as significant for characterizing the probability of illness were chosen for estimation in this study. The following section describes data sources and analyses for each of these variables. All statistical analyses were performed using PCSAS[7].

Prevalence data for S.e. isolation in raw shell eggs was obtained through extensive MEDLINE[7] and AGRICOLA[7] computer data-base searches from 1965-1996. Additional data sources included government and unpublished reports. Prevalence was expressed as the probability of contamination of internal egg contents. Data which included cracked eggs, egg shells and bulk liquid eggs were excluded from the analysis.

Data from human feeding studies as reported by McCullough et al., 1951 and Levine et al., 1973 were utilized for the dose-response modeling. Various combinations of *Salmonella* strains were statistically analyzed for determination of potential to pool data. Three strains (*S. anatum* Strain 1, *S. bareilly*, and *S. newport*) were chosen for pooling based on initial ANOVA statistical results and designated as moderately virulent strains while *S. anatum* Strain 2 and *S. meleagridis* Strain 1 were designated as low virulence strains. Human dose-response data for *Shigella dysenteriae* 1 was used as a proxy for model highly virulent *Salmonella* strains. Dose-response relationships were expressed as the probability of illness at a given dose in log cfu. Dose-response modeling was performed on pooled data using the Beta-Poisson, exponential, log-normal (or probit) and logit models (Proc GENMOD and Proc NLIN SAS[7]).

Growth lags for *Salmonella* in raw shell eggs was modeled using the data of Humphrey and Whitehead, 1993. Data was logarithmically transformed and fitted using the modified Gompertz equation (Skinner et al. 1994).

RESULTS

All prevalence values fell below 1%. Prevalence values were fitted to a truncated log normal distribution for future Monte Carlo simulations (Morales et al. 1996). Initial ANOVA analysis suggested that strain effects were significant and thus a single model based on pooled data from all 9 *Salmonella* strains was not appropriate. However, two different dose-response patterns became apparent from the ANOVA results and it was statistically appropriate to pool certain combinations of strains. These subgroups were designated as moderate and low virulence strains. Since epidemiological evidence indicates the potential for highly virulent strains (Hennessy et al. 1996) and in the absence of human feeding trials representative of high virulence strains, *Shigella dysenteriae* data was used to represent this category. Goodness-of-fit (Pearson P^2) tests favored the exponential model overall. This model had the added advantage of providing the most conservative probability of illness estimates at most doses.

Storage conditions significantly affected yolk membrane breakdown over time (lag phase) and hence growth of S.e. in shell eggs, with prolonged lag phases of up to 21 days under stable storage conditions (Humphrey and Whitehead, 1993). The effect of varying storage conditions on growth of S.e. was simulated using two different lag phase lengths corresponding to stable (21-day lag phase) and temperature-abusive (5-day lag phase) storage conditions. Growth after yolk membrane penetration (post-lag phase) was modeled using the Gompertz equation, again using two different storage temperature profiles (10°C and 20°C) to represent refrigerated and room-temperature storage conditions.

A cumulative frequency distribution for the proportion of eggs consumed at various storage times was developed assuming that 50% of eggs were consumed within 21 days of production, 75% within 29 days, 90% within 35 days and 100% within 44 days.

A first iteration risk characterization for the consumption of raw eggs was done assuming that eggs are held at stable storage conditions of 10°C. A preliminary sensitivity analysis was performed using point estimates for prevalence and virulence, assuming a low, medium and high range for each variable (Table I). The risk estimates presented are for single egg servings, and range from a low of 7.13×10^{-6} to a high of 2.85×10^{-3}. The preliminary risk estimates appear to be more sensitive to prevalence levels than to virulence as represented in this model.

CONCLUSIONS

This preliminary risk characterization has taken 3 major variables into account: prevalence of S.e. in shell eggs, relationship between storage conditions and level of contamination, and the number of organisms consumed and human response defined as the probability of illness. Several conclusions can be drawn at this early stage of analysis. The lag phase takes on particular significance in assessing the growth of S.e. in intact shell eggs, and thus requires special attention when modeling and incorporating this data into a risk assessment. The work is currently being extended to incorporate models of microbial growth with time and temperature abuse during storage into the overall risk model. Preliminary simulations using predictive microbiology indicate that control of storage conditions may significantly impact the levels of S.e. in shell eggs over time. This suggests that such storage control may be an important critical control point in shell egg processing and distribution. These early

findings also suggest that the risk model is particularly sensitive to the prevalence of S.e. contamination in intact shell eggs.

Future endeavors will seek to refine the dose-response and time-temperature growth models incorporating sensitivity analysis and Monte Carlo simulation methods into the risk characterization. By establishing a baseline risk estimate, it will then be possible to incorporate information on various risk mitigation strategies to evaluate them for cost-effective risk management.

Economic analysis and risk assessment are integral to optimal development of food safety and quality assurance programs as they provide information for objective decision making and policy development.

Table I
Sensitivity Analysis – Relationship Between Prevalence of Salmonella Contamination and Dose Response Models, Assuming Stable Storage Conditions.

DOSE-RESPONSE	PREVALENCE		
	Low (0.010%)	Nominal (0.357%)	High (0.983%)
Low Virulence	7.13×10^{-6}	2.55×10^{-4}	7.01×10^{-4}
Mod. Virulence	1.64×10^{-5}	5.86×10^{-4}	1.61×10^{-3}
High Virulence	2.90×10^{-5}	1.03×10^{-3}	2.85×10^{-3}

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