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CENTER FOR ADVANCING MICROBIAL RISK ASSESSMENT

ADVANCES IN QMRA

INSIDE:

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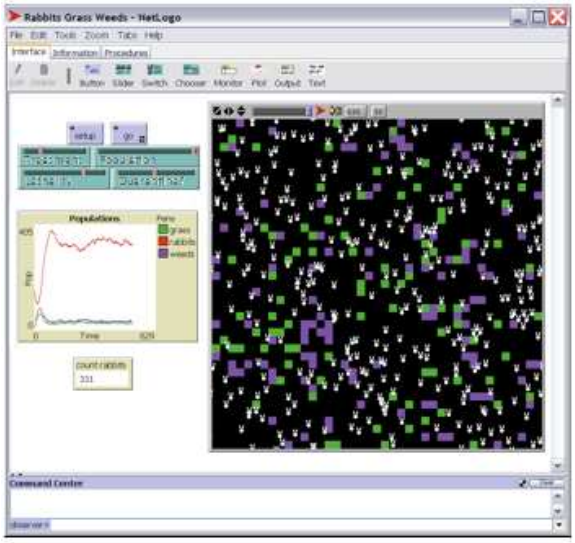
SIMPLE TRANSMISSION MODEL FOR POINT OF USE DEVICE QMRA



Transmission models are an important piece in understanding the dynamics of disease and once developed for specific scenarios can provide a better picture of the risks posed to a population.

Point of use devices are a growing approach for household water treatment (HHWT) and in some cases the sole source of drinking water treatment for communities in developing regions of the world.

Work at MSU has been ongoing, looking at the log reductions of various pathogens from a specific point of use device. This device disinfects water using contact-disinfection with a bromine (Br) chemistry tied to beads and filtration system. Log reductions for specific pathogens of 3 to 6 logs have been found.

To further the understanding of HHWT and the Br disinfection, risks and risk reduction after using the point of use devices for cholera in a small village in a developing region was examined.

The modeling effort was undertaken by Mr. Muhammad Firdaus Hamzah, a visiting undergraduate researcher from Nanyang Technological University (NTU) in Singapore. Firdaus developed a Netlogo model which tracked the movement of a village and their exposure to cholera.

Three main scenarios were examined; where there was no point of use device, ii. all villagers had access to fully operating point of use devices, and iii. where one family unit (5 people) had a faulty device.

Preliminarily we have shown that while person-to-person transmission is relatively low for cholera, there was an effect to the overall risk experienced by the villagers. Although the proper function of the POU device had a greater effect on the risk.

QMRA WORKSHOP SUCCESSFULLY HELD AT INTERNATIONAL WATER ASSOCIATION WORLD WATER CONGRESS, MONTREAL, CANADA

The International Water Association (IWA) World Water Congress is a unique opportunity for delegates from around to world to meet on all topics related to water and water safety. As part of the Congress, Joan Rose (MSU), Charles Haas (Drexel), Gertjan Medema (KWR/TU Delft) and Mark Weir (MSU) presented key aspects of the QMRA framework to the attendees.

The workshop was well attended by delegates with multiple fields of expertise. Topics included, pathogens of interest and their dangers and challenges is control, exposure assessment, and advanced exposure models developed by CAMRA and the dose response assessment and models.

A risk tool from Patrick Gurian's laboratory was highlighted. This comprehensive risk tool developed for biosolids application was of particular interest to the audience, especially since it was based on the Excel platform.

DEVELOPMENT AND APPLICATIONS OF DOSE-RESPONSE TIME MODELING

Contributing Author: Yin Huang, PhD. Michigan State University

A class of time-dose-response models has been previously developed by incorporating time dependencies that model the in vivo bacterial kinetics into the classical dose-response models 1,2. The resulting models demonstrated adequate flexibility in quantifying the time to response caused by disparate pathogens. However, the authors did not provide a direct verification of the biological validity of the models with in vivo pathogen growth. Since the time dependencies are proposed to quantify the time of onset of an effect caused by bacteria proliferation, they should be consistent with the kinetics of in vivo bacterial growth that presumably determine the host response.

The interpretation of the results of host response to inoculation depends on the administered organisms whose germination and growth is believed to be the cause of the response. To study the relationship between the microorganism kinetics and the probability of positive response, it is desirable to compare the proposed time-dependent dose response model with the in vivo bacterial kinetics.

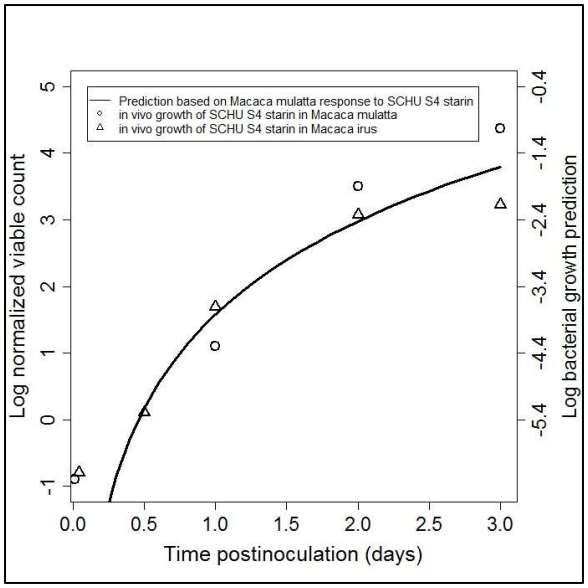


Figure 1. Comparison between the predicted bacterial kinetics and the log normalized viable counts of monkeys exposed to *F. tularensis* SCHU S4 strain.

A recent study3 at Drexel University has shown such verification with data of inhalation tularemia in monkeys. In their study, open literature was searched for survival dose-response data and bacterial viable count data for monkeys infected by F. tularensis via inhalation route. The suggested time-dose-response models were further developed to model quantitatively the hypothetical relationship between the host response and instantaneous microorganism number in vivo. The resulting models were fit to survival dose-response data and the estimates of bacterial dynamics for different aerosol sizes were inferred. The estimates were found consistent with the data of bacterial growth (Figure 1). This preliminary success in developing mechanistic models for tularemia yields information on the mechanism by which the infection develops and potential strategies for controlling it.

To better prepare for public health consequences following an anthrax event, a predictive model associating risks with pathogen doses and time post exposure is desirable. Since an experimental human model does not exist, such a model must be derived from animal studies. For examining the interspecies variation, data of different host species should be analyzed, and resulting models must be verified against human outbreaks. Another study 4 conducted at Drexel University aimed at such validation. They identified eight sets of survival dose-response data of various animals (rhesus monkey, cynomolgus monkey, African green monkey, guinea pig and mouse) exposed inhalationally or intranasally to Bacillus anthracis. Time-dose-response models are examined, expanded and fit to these data. The parameter estimates are generally consistent across species. The low-dose time-to-response distributions estimated by all animal models except African green monkey are clearly aligned with the data from the Sverdlovsk outbreak (Figure 2). This is the first instance that a consistency of time- and dose-dependent host responses to anthrax infection is demonstrated in disparate animals, and the resulting models can be used to predict human response.

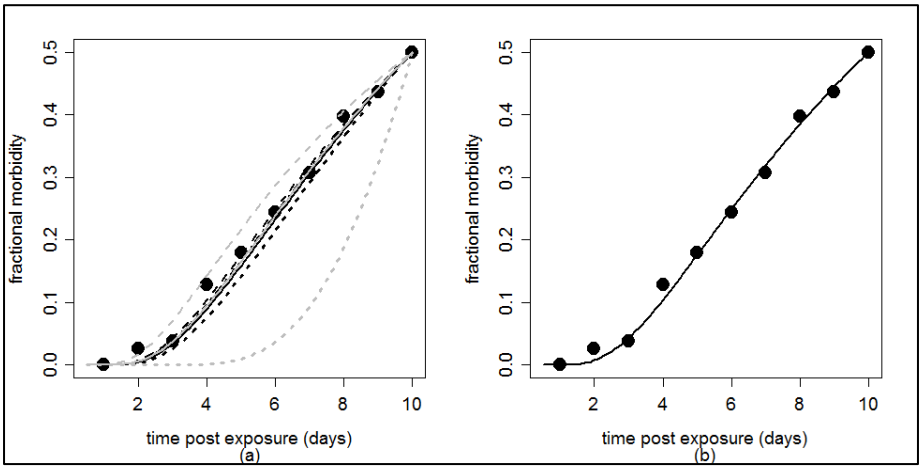


Figure 2. Comparison between the 10-day cumulative incubation distribution (filled circles) of the Sverdlovsk outbreak and the predictions extrapolated solely from the following animal data based on Equation (5.9). (a) black solid curve, rhesus monkey [i]; black dotted curve, rhesus monkey [ii]; black dashed curve, cynomolgus monkey; grey dotted curve, African green monkey; grey dashed curve, guinea pig [i]; grey solid curve, guinea pig [ii]; black dashed-dotted curve, mouse; (b) pooled animal data excluding African green monkey.

References

1. Huang, Y. and Haas, C.N. (2009) "Time-Dose-Response Models for Microbial Risk Assessment," Risk Analysis 29(5): 648-661.

2. Huang, Y., Bartrand, T.A., Haas, C.N. and Weir, M.H. (2009) "Incorporating Time Postinoculation into a Dose-Response Model of Yersinia pestis in Mice," Journal of Applied Microbiology 107(3): 727-735.

3. Huang, Y. and Haas, C.N. "Quantification of the Relationship between Bacterial Knetics and Host Response for Monkeys Exposed to Aerosolized Francisella

ESTABLISHING A WORKABLE SAMPLING STRATEGY: RISK INFORMED ENVIRONMENTAL STANDARDS FOR *BACILLUS ANTHRACIS*

Contributing Author: Tao Hong and Patrick L. Gurian, Drexel University

The 2001 anthrax attacks precipitated an aggressive response in which large numbers of potentially exposed people were treated with prophylactic antibiotics. This also contaminated buildings which then were remediated until no detectable *B. anthracis* spores were present. These actions appear to have been effective in saving lives, but the response was expensive and extremely aggressive, raising the question: how can standards be set that prioritize response actions based on risk?. Therefore an approach to developing environmental standards for *B. anthracis* is needed This work by Tao Hong and Nicholas F. Dudley Ward and Patrick L. Gurian has been accepted for publication in *Risk Analysis* an International Journal.

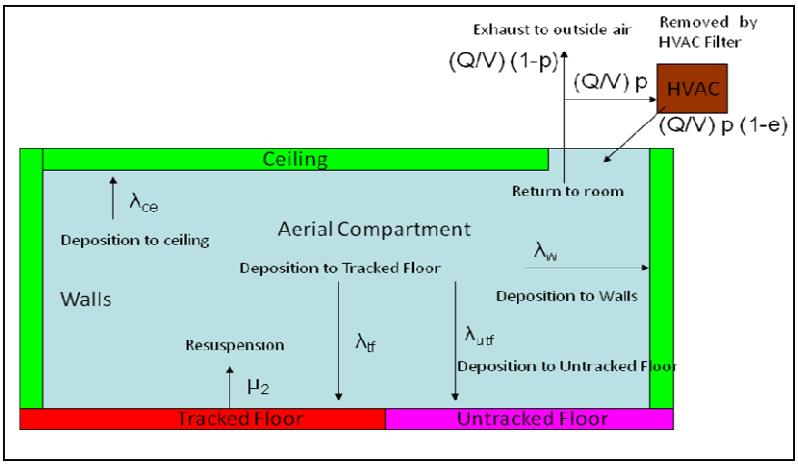


Figure 3. Conceptual diagram of Markov model used for the retrospective and prospective scenarios.

Human health risks from biological agents was associated with aerosol exposures and this environmental fate and transport model was based on a simple office with a heating ventilation and air conditioning (HVAC) system to link environmental concentrations with human health risk. The office was divided into eight internal compartments as shown in Figure 3. The air and tracked floor can exchange spores with each other but the remaining six accumulate spores irreversibly from the air compartment.

Two scenarios were included, retrospective and prospective. In the retrospective scenario all spores were initially present in the air compartment, and surface concentrations at the end of the scenario were linked to risk. In the prospective case all spores were initially present on the tracked floor, and surface concentrations at the start of the scenario were linked to risk (i.e., the initial aerosol release has dissipated).

The relationship between risk of mortality and time for different particle sizes in the retrospective scenario is presented in Figure 4. Risk caused by particles with diameters of 3, 5 and 10μm approached an asymptote after 1.5 hours while it required roughly 4 hours for the risk from 1μm spores to approach its upper bound. If the individual was presented the majority of a working day (8 hours) then risk estimates were not very sensitive to the time of subsequent sample collection, because the most of the risk accrues in less than 8 hours. The accumulated risk over time in the prospective scenario is illustrated in Figure 5.

The surface concentrations corresponding to acceptable risk levels are likely to be very low. For a 10^{-4} retrospective risk from 1 μm particles, the concentration standard for floors would be 3.5 spores/m^2. This raised the question as to whether a negative test result provides sufficient basis for concluding that the risk is below the desired standard. For example, if 11 spores were detected on the floor, then a sampling area of 5.2 m^2 was required for clearance at the 10^{-4} risk level.

The approach presented by Tao et al. served as a beginning for future analysis. They suggested future research should be carried in the following directions: 1) delineating conditions under which this modelling approach is applicable and conditions under which it is not, 2) identifying surfaces in a room which are most reflective of time-integrated human respired air concentrations, 3) quantifying and reducing the degree of variance present within a compartment so that confidence limits can be developed that include these smaller scale variations.

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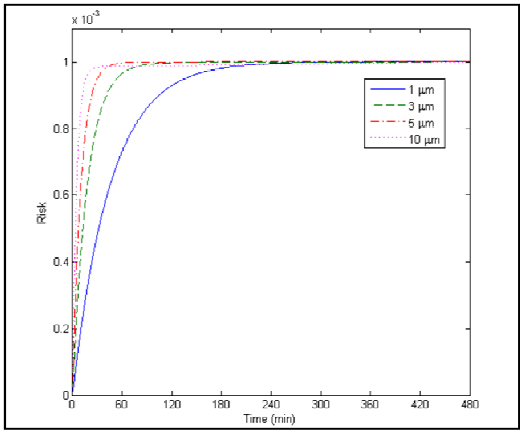

Figure 4. Retrospective risk plots, ultimate risk experienced of 10^{-3}.

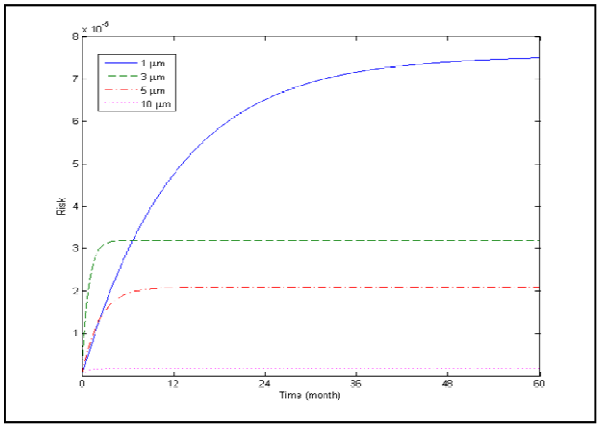

Figure 5. Prospective risk plots, simulated for over 5 years of exposure.

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RISK INFORMED ENGINEERING DESIGN CHANGES FOR RECREATIONAL CENTER TREATMENT SYSTEM.

Contributing Author: Mark H. Weir MSU, and Maria Tereza Pepe-Razzolini, São Paulo University

Recreational outbreaks associated with spray parks are well recognized and in part are problematic because of the engineering designs for reclaiming the water.

CAMRA researcher Mark H. Weir from MSU and visiting researcher Maria Tereza Pepe-Razzolini from the University of São Paulo Brazil developed a QMRA for a design retrofit recommendations for spray park treating *Cryptosporidium*.

This work was based on an actual outbreak of cryptosporidiosis to a population using a recreational spraypark in New York State. An estimation of the dose of oocysts the spray-park users were exposed was developed and Mark and Maria, developed an integrated QMRA to suggest potential design changes to reduce the risk from *Cryptosporidium* exposure to future spraypark users.

Three Markov chain models were developed to understand the effect of the current treatment system as well as the proposed changes to the treatment design. The original treatment system being fairly simplistic is comprised of pipes leading to the treatment system from the spraypad, two holding tanks and a sand filtration system. The original design has a pipe connecting the first tank back with the spraypad which can act as a potential bypass to the treatment system.

The results of the Markov chain models were used to develop distributions of oocysts being delivered to the spraypad from the treatment system. These probability distributions were included in a Monte Calrlo risk model. Those treatment options which allowed the greatest decrease in risk to the population using the spraypad were determined.

The decrease in the risk between the first alternative (removal of bypass) and the second option was not great enough to justify the cost of including the O_3 contactor. Figure 6 shows the last of the design suggestions where an Ozone (O_3) contactor was included in the treatment train (conceptual diagram of the Markov chain model).

Note: This work is in preparation for publication.

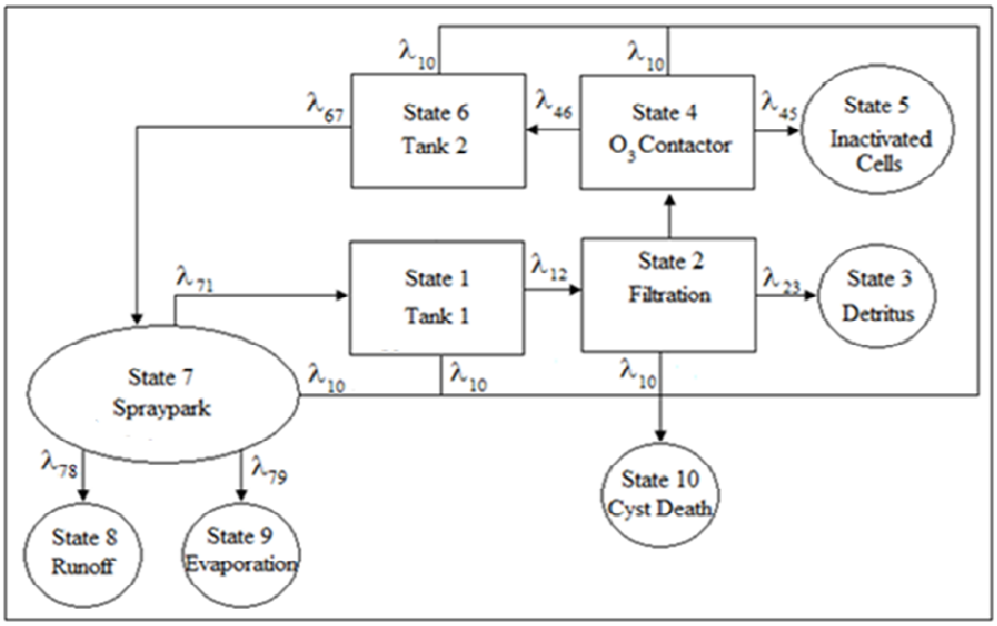

Figure 6. Conceptual diagram of one of the Markov models used for the treatment system..

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