MEETING OF THE STATES PARTIES TO THE CONVENTION ON THE PROHIBITION OF THE DEVELOPMENT, PRODUCTION AND STOCKPILING OF BACTERIOLOGICAL (BIOLOGICAL) AND TOXIN WEAPONS AND ON THEIR DESTRUCTION

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A modelling programme on bio-incidents

Submitted by the United Kingdom

1. The UK has traditionally had strong epidemic and mathematical modelling capabilities, and these are increasingly being applied to enhance response capabilities to future emergency public health situations. Active links have been established between modelling groups in the Department of Health and at HPA Colindale and HPA Porton Down, with groups in other government departments and agencies such as the Ministry of Defence's Defence Science and Technology Laboratory, as well as in university departments in Oxford, Cambridge, Warwick and at Imperial College London. International collaborative efforts are increasingly important, including work related to the Health Security Committee of the EC and the G7 + Mexico Global Health Security Action Group (GHSAG).

The modelling programme at HPA Porton Down

2. HPA Porton Down has a Microbial Risk Assessment Programme based on work over several years, to provide evidence based risk assessment and modelling approaches which can contribute advice to government in the formulation of policy, emergency health planning and disease countermeasures. This programme concentrates on areas of potential public health concern in which HPA Porton Down and collaborating institutes have particular expertise, which include a number of diseases caused by dangerous pathogens in Risk groups 3 and 4 which are not endemic to the UK.

3. The HPA Porton Down programme has a number of key components:

(a) Horizon scanning to "second-guess" the types of event for which modelling applications would be helpful. Events could be natural outbreaks such as pandemic influenza or SARS, or outbreaks deliberately caused by terrorists. Given the potential for spread of infectious diseases into new habitats – as seen in the recent introduction of West Nile virus into the

United States - attention is also being given to future potentials for spread of vector-borne and zoonotic diseases in the UK;

(b) Mathematical modelling tools able to address issues thrown up by horizon scanning;

(c) Underlying data requirements. Geographic Information Systems (GIS) are important because data and the modelling process often rely on specific geographies and spatially referenced data (e.g. human demographic data, population movements, disease vector distributions, and the environmental and ecological factors that determine the distribution of all these). The various data sets currently amount to about 0.6 terabytes;

(d) Dedicated hardware and software to handle, analyse and develop models;

(e) A multidisciplinary team that includes mathematicians, public health microbiologists, epidemiologists and dedicated GIS and IT/database specialists.

4. The overall strategy is to bring together the data and a predictive, adaptable and scalable toolbox of models within an integrated IT/database system, so as to assist in forward planning and for use in real time outbreak/incident management. For forward planning, data that are collected and warehoused regarding past incidents and outbreaks can be fed through into appropriate modelling applications to analyse future "what if" scenarios. In the event of an actual infectious disease emergency, real time data feeds would be rapidly mapped in the GIS and analysed to re-parameterise the models for the particular outbreak in question. These models can then be run in real time to help with outbreak/incident management by making ongoing short/middle term predictions of the likely state of affairs in the upcoming time period, of whether the current interventions are having the required effect in terms of bringing the situation under control, and of the likely time scale for control to be established.

Example of a 'real time' application: the *Legionella* outbreak in Hereford, 2003

5. The health officials investigating an ongoing outbreak of legionellosis in Hereford in 2003 had identified a cooling tower that they felt could have caused the outbreak, consistent with two sets of information: the location of those individuals who did not move out of the area during the outbreak; and the timing and location of the infected individuals from outside Hereford who seemed to have made only one visit to Hereford. HPA Porton Down was asked to help provide confirmatory evidence that the tower could have been responsible for the outbreak.

6. For each person who had developed the disease, the outbreak investigation team had constructed a detailed record of locations visited, with time and date details, during the periods leading up to the onset of their illness. The modellers took this data for each individual and compared it with the emissions that would have been predicted from the tower in the days leading up to the onset of symptoms. Predictions of the likely emissions from the tower for each day of its operation were based on atmospheric dispersion modelling using software called HPAC (Hazard Prediction and Analysis Capability). This required inputs of data on the source characteristics - height and other dimensions of the stack, aerosol flow through the stack, microbial load in aerosol,

survival of pathogen in aerosol - and all relevant meteorological data - such as wind speed, direction, height of boundary layer. The meteorological factors varied considerably both during and between different days. The locations and travel histories of the cases were plotted using GIS, in relation to the predicted plumes of *Legionella* release from the tower for each of the relevant days. By integrating the outputs from the dispersion modelling with the relevant data on the legionellosis cases within the GIS it was possible to demonstrate that the locations and trajectories of the cases were consistent with the postulated exposures from the tower.

7. The analysis was extended to determine whether the timing of the onset of the individual cases was consistent with the timing of the operation of the tower. Luckily, good independent data that could be used to derive an incubation period distribution representative of *Legionella* infection were available from an earlier outbreak in The Netherlands in 1999 following the discrete exposure of individuals at a flower show. Individuals who had visited the show once subsequently developed disease from the single exposure, so providing a clear picture of the individual variation in the length of the incubation period of the disease. In the HPA investigation, an individual-based stochastic model was developed based on the Dutch data. By carrying out Monte Carlo simulations that were fitted to the observed data by maximum likelihood analysis, a predicted Probable Distribution of Exposure times with confidence intervals was derived. (That is, it was "back-calculated" from Observed Distribution of Onset Times). In this way, it was possible to show that the dynamics of the Hereford epidemic were consistent with the predicted operation of (and releases from) the cooling tower, and in particular with the date that the cooling tower was ultimately cleansed, to within 95% confidence limits.

Examples of 'ahead-of-time' applications

8. Three examples are given of how HPA Porton Down is using predictive mathematical models to help in the development of policy and contingency planning ahead of time for potential infectious disease outbreak emergencies in the UK.

(a) An outbreak of smallpox

9. Modelling of a supposed UK smallpox outbreak has been used to investigate the potential impacts of different public health intervention strategies over both time and space – thus allowing comparison of the outcomes of different intervention strategies that are geographically targeted. A typical analysis used administrative districts as the geographic base, and data on the demographics of each 'patch' from the 2001 (population) Census, along with data on the extent to which people move between patches. The model was parameterised based on the published information on past smallpox outbreaks with appropriate adjustments to take account of uncertainties and changes in social structure and demographics. The model can predict the development and transmission of the disease both within and between patches. The model can be run in a stochastic mode – run 1000s of times - with the results being subjected to statistical and sensitivity analysis. It can be used to investigate the potential effect of public health interventions, such as different efficiencies of:

(i) Case finding and isolation;

(ii) Contact tracing, vaccination, monitoring and isolation;

(iii) Vaccination in districts where cases have occurred or may be expected;

(iv) Vaccination on a national scale.

10. The particular problem for smallpox is to optimise for an intervention strategy that minimises the number of cases and deaths from the disease, while at the same time minimising the number of adverse events, including deaths, that would be associated with widespread vaccine use.

(b) An airborne release of anthrax

11. GIS, dispersion modelling (using HPAC) and epidemic modelling have been combined to predict the potential impacts of anthrax aerosol releases on a civilian population in the UK, and the possibilities that may be available for public health interventions. Initial airborne dispersion modelling data for anthrax has been integrated by GIS with representative mapping and demographic layers. This allowed visualisation of the dosage contours for the anthrax exposure of the different parts of the population in relation to a range of useful features, such as the geographic boundaries of health care areas. By taking account of the different population densities in various Census output areas, it is possible to calculate the expected casualty counts and also the relative dosage of anthrax that each exposed individual has received.

12. By applying further bespoke stochastic individual-based models that incorporate appropriate public health responses, including some logistical delays, the anthrax modelling studies have led to a number of conclusions:

(i) With increasing distance from the release site the dosages of anthrax received on the ground get progressively less;

(ii) The probability of infection correspondingly decreases, but the numbers exposed increase as the plume widens;

(iii) As the received dosage decreases, the incubation period of subsequent infections increases considerably, from a time scale measured in hours for the highest dosages to a time scale measured in days and possibly weeks for the lowest dosages;

(iv) People receiving the highest dosages will probably not be identified and treated quickly enough, but these cases will alert the appropriate authorities that there has been a release;

(v) People receiving the lowest dosages, which is the largest proportion of those exposed, could be found and treated with antibiotics.

(c) Future risks from vector-borne diseases in the UK

13. Vector-borne diseases are generally not thought to pose an immediate public health problem in the UK. However, the situation could change with the increasing international movements of people, animals and insects, and increasing trade in exotic items, tourism, etc. These trends could lead to the introduction of new vector-borne zoonotic agents and /or new vectors into the UK.

14. An example of a predictive modelling study being carried out at HPA Porton Down relates to the sheep tick, which can transmit a range of vector-borne diseases, including Congo Crimean Haemorrhagic Fever, Lyme Fever, ehrlichiosis, babesiosis and tick-borne encephalitis.
By undertaking comprehensive ecological and environmental analysis in a sophisticated GIS of the key parameters that impact on tick ecology (such as land cover type, climate, topography, animal host distribution and human demographics), the model can identify potential hot spots for tick distribution and abundance and therefore the potential risk areas for future vector-borne transmission of infection to humans.
