The Control, Dynamics and Evolution of Emergent and Re-emergent Diseases in the Context of Sustainability

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The complex dynamics of emergent and re-emergent diseases within landscapes living under the tinkering effects of evolution, adaptive human behaviors, and public health policies that include treatment, vaccination or both, are used to highlight, the dynamics of antibiotic resistance including the challenges that emerge in the context of sustainability. On March 11, 2013, the British Chief Medical Officer Dame Sally Davies noted that "the problem of microbes becoming increasingly resistant to the most powerful drugs should be ranked alongside terrorism and climate change on the list of critical risks to the nation … Yet while antibiotic use is rising – not least in agriculture for farmed animals and fish – resistance is steadily growing and the 'pipeline is drying up' of new drugs which can replace those becoming useless. [In fact] No new classes of antibiotics have been developed since 1987, and none are in the pipeline[1]". Professor Nigel Brown, president of the Society for General Microbiology remarks that immediate action by scientists is required if we are going to identify and mass produce new antibiotics; the kind of effort needed to tackle the problem of antimicrobial resistance and its transmission, particularly in the context of nosocomial (hospital) infections. (Ibid.)

Mathematicians use contagion or epidemiological models to study the evolution, dynamics and control of diseases, including nosocomial or hospital infections; that is, the infections most often responsible for the transmission of resistant pathogens in hospitals. The most celebrated epidemic model is due to a medical doctor W.O. Kermack and a statistician A. G. McKendrick[2]. Both researchers modeled disease dynamics under the assumption that transmission depends on the intensity of hosts' interactions (handshakes, kisses, and more) and the frequency of encounters between susceptible and infected individuals.

In 1994, Michael Gladwell, a journalist writing for the New Yorker magazine, re-discovered a plausible explanation for the growth or decay of a different kind of disease, the `disease' responsible for epidemics of crime in the City. He observed that the side of the tipping point that a system was `on' determined whether or not crime was a problem. Hence, the direction of the crossing could mean the difference between "night and day" when it came down to criminal activity.[3] Gladwell saw crime as a contagion process, recognized the existence of a threshold, and understood and appreciated the significance of crossing such a threshold. The insights that he gained from understanding models of contagion led him to the writing of several books.

Kermack and MacKendrick were aware of the ideas popularized by Gladwell. In fact, both had gone further by establishing mathematical results for infectious diseases in 1927. Contagion/contact models are now routinely used in the study of population-level questions in

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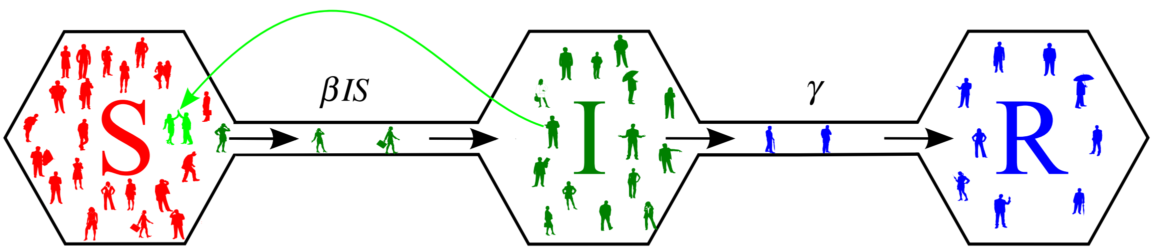
[1] The Independent, Tuesday 12 March 2013
[2] Kermack, W.O. and McKendrick, A.G. (1927), A contribution to the mathematical theory of epidemics, Proc. Royal Soc. London, 115:700-721
[3] Gladwell, M. (2000), The tipping point. Little Brown.

evolutionary biology or public health. The direct use the Kermack-McKendrick 1927 model or its modifications, in the study of the dynamics of antibiotic resistance at the population level, is therefore natural. The simplicity of the Kermack-McKendrick Susceptible-Infected-Recovered or SIR model has increased its popularity. In the transfer diagram below, a population has been divided in three categories: susceptible or S, infected or I (assumed infectious) and recovered or R (assumed immune); there are no births or deaths. That is, we have selected a specific (short) temporal scale to study the dynamics of contagion under this model. It is assumed that all individuals are identical and that the population is large so that the use of differential equations is acceptable. It is further assumed that deaths from the disease under consideration are negligible and that there are no births. Hence, the population is constant and therefore it can (and has been) be normalized to one. It is assumed that infections arise from the interactions between susceptible and infective individuals (modeled via the mass action law) and that recovered individuals cannot get this disease again.



Several things can be deduced from this model (nonlinear system of three differential equations): first that for an outbreak to occur an infectious individual must be introduced (within a purely susceptible population); that over his/her infectious period $1/\gamma$, individuals that recover gain permanent immunity (moving to R); that the success rate is actually β and when it is applied over the window of opportunity $1/\gamma$ it gives the *basic reproduction ratio* or *number*, that is $Ro = \beta/\gamma$. An outbreak is possible if $Ro > 1$ and the disease eventually collapses if $Ro<1$; the assumption of 100% susceptibility.

The issues of the persistence, evolution and the expansion of resistance to antimicrobials are of great importance particularly because the number of drugs is limited and not new ones have been created for nearly three decades. In other words, the predictions made by the British Chief Medical Officer Dame Sally Davies as well as those made a year earlier by the Director General of the World Health Organization, Dr. Margaret Chan are totally consistent. Specifically, we note that head of the WHO while addressing a meeting of infectious disease experts in Copenhagen, noted that we are facing a global crisis in antibiotics, the result of "rapidly evolving resistance among microbes responsible for common infections that threaten to turn them into untreatable diseases … every antibiotic ever developed was at risk of becoming useless. `A post-antibiotic era means, in effect, an end to modern medicine as we know it. Things as common as strep throat or a child's scratched knee could once again kill … 'Antimicrobial resistance is on the rise in Europe, and elsewhere in the world. We are losing our first-line antimicrobials.[4]'"

Computational, Mathematical and Theoretical Biologists, Epidemiologists and Immunologist are trying to find ways of slowing down the evolution of resistance. The goal is to maintain a sustainable pool of antimicrobials available for treating infections and the most effective way of

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[4] The Independent, Friday 16 March 2012

doing this is by slowing down the evolution of resistance. A variety of articles have appeared evaluating the relative efficacy of treatment protocols including the random distribution of antibiotics or drug cycling. The results as it is often the case, depend on the objectives, which may include the reduction of resistance to a single class of drugs or the reduction of multi-drug resistance.

For further reading:

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