Mathematical Epidemiology with Applications: The Case of Influenza

In a highly interconnected world, epidemic outbreaks become *instant* potential health and/or economic global threats with increasing segments of the population playing active roles on the transmission patterns of infectious diseases like *influenza*. Individual and/or group actions and/or decisions and/or activities can enhance or reduce the effectiveness of intervention/control measures in the Information Era. Travel, social distancing, the availability of medical supplies (antiviral drugs and vaccine) and timely diagnostic tools, and the access to quality medical care are but some of the factors that have been identified as significant during this ongoing influenza pandemic. Varying levels of participation in the implementation of policies aimed at reducing a population's risk of infection are important components not only of disease dynamics but also of their *evolutionary* potential. Hence, the role of changes in the levels of antiviral drug resistance, the impact on transmission patterns, cross-immunity, and the intrinsic ability of diseases like H1N1 that circle the globe to evolve in response to a multitude of *selective pressures* must be studied and assessed. Policy makers have been asked to assess some of these issues during a pandemic that has fortunately not live up to its "expected" potential. Demand for *timely access* for *every* individual to the H1N1 vaccine combined high levels of refusal to get vaccinated, particularly among emergency medical personnel, are but some of the challenges that officials have had to deal with. What can mathematics do to help understand disease dynamics and develop effective control measures? What can mathematics do to help develop resilient approaches for the management of complex adaptive systems of this type? Despite the myriad of complexities associated with disease transmission dynamics, macroscopic epidemic patterns emerge and ways of making use of this knowledge in *real time* can be critically important. In this lecture some of the challenges in the study of the dynamics and evolution of infectious diseases will be addressed. We start with the work of physicians-theoreticians-mathematicians like Bernoulli[1],[2], Ross[3], Kermack and McKendrick[4] who developed key aspects of the mathematical theory of infectious diseases showing that mathematics can be a significant player in epidemiology and public health. A review of some of the mathematical and modeling approaches

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[1] D. Bernoulli, Réflexions sur les avantages de l'inoculation, Mercure de France (1760) 173 (Reprinted in L.P. Bouckaert, B.L. van der Waerden (Eds), Die Werke von Daniel Bernoulli, Bd. 2 Analysis und Wahrscheinlichkeitsrechnung, Birkh€auser, Basel, 1982, p. 268).

[2] Dietz, K and H Heesterbeek, "Daniel Bernoulli's epidemiological model revisited." Mathematical Biosciences 180 (2002) 1–21

[3] Ross, R. "The Prevention of Malaria (2nd edition, with addendum)." John Murray, London 1911.

[4] Kermack, W. O. and A. G. McKendrick (1927), "A contribution to the mathematical theory of epidemics." Proceedings Roy. Soc. London, Ser. A 115:700-721.

common in mathematical epidemiology can be found in the work of Hethcote.[5] This presentation provides an overview of mathematical epidemiology in the context of influenza (including the ongoing pandemic influenza) in order to highlight key questions and approaches and the fundamental role of mathematics in biology.

The presentation will include material from the following co-authored published manuscripts:

1. "Optimal control of influenza pandemics: The role of antiviral treatment and isolation," Journal of Theoretical Biology (in press) (with <u>Lee S.</u> **and G Chowell)**
2. "Pros and cons of estimating the epidemic growth rate of influenza A (H1N1) 2009." Theoretical Biology and Medical Modelling 2010, 7:1 (with Nishiura, H, **G Chowell** and M Safan)
3. "Discrete Epidemic Models," *Journal of Mathematical Biosciences and Engineering*, Volume: 7, Number: 1, January 2010 (with Brauer, F. and <u>Z. Feng</u>).
4. "Transmission potential of the new influenza (H1N1) virus and its age-specificity in Japan." *Eurosurveillance*, Volume 14, Issue 22, pp 1-4, June 4, 2009 (with Nishiura, H, M Safan and **G Chowell**)
5. "Immune Level Structure Model for Influenza Strains," *Journal of Biological Systems*, Volume 17 (4), 713-737, 2009 (with **Nuno, M** and M Martcheva)
6. "Estimation of the Effective Reproductive Number from Disease Outbreak Data," Mathematical Biosciences and Engineering Volume 6, Number 2, April 2009, pp. 261–283 (**Cintron-Arias, A.**, L. M. Bettencourt, A. L. Lloyd and H.T. Banks).
7. "*Mathematical Model of Influenza: The Role of cross-immunity, quarantine and age-structure*" In Mathematical Epidemiology, P. van den Driessche, J Wu and F Brauer, Springer-Verlag (Eds.) 2008 (with **Nuno, M.**, <u>Feng Z.</u> and M. Martcheva)
8. "On the role of cross-immunity, vaccines and 'flu' survival" *Theoretical Population Biology*: 71 20-29 2007 (with **Nuno, M., Chowell, G.** and <u>X Wang</u>).
9. "*The dynamics of two strains of influenza with cross-immunity*," *SIAM J. of Applied Mathematics*, Vol. 65, No. 3, pp. 964–982, 2005 (with **Nuno, M,** <u>Feng, Z.</u> and M. Martcheva)
10. "*Epidemiological Models with Age Structure, Proportionate Mixing, and Cross-Immunity," J. Math. Biology* 27(3): 233-258, 1989 (with Hethcote, H., V. Andreasen, S. A. Levin, S. A. and W-m, Liu)
11. The recent work with <u>Marco Herrera-Valdez</u> and **Maytee Cruz-Aponte** on influenza in Mexico – manuscript—is an important source as well.

Graduate students are in bold and postdocs or former postdocs are underlined.

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[5] H. W. Hethcote, "The Mathematics of Infectious diseases." SIAM Review, Vol. 42 no. 4, pp. 599-653, 2000