Molecular, epidemiological, and clinical complexities of predicting patterns of infectious diseases

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The prediction of the future meets an essential need of humanity but it is not possible for the human epidemics. This need results in rites and "sciences" such as haruspices (Etruscan reading the future in entrails of animals) and augurs (Romans reading the flight of birds). They are as old as the human history makes it possible to know. The scientific knowledge in astronomy gives the impression to be able to predict the events of the future thanks to observation of the events of the past. Thus astrology was initially developed by the astronomers such as Ptolemy, who, by their capability to predict the moon's eclipses and the planets movements, were considered like magicians. This vision of the world still remains very vivid since XXV centuries and it is easy to see the echo of it, in all the countries of the world where astrology remains extraordinary prevalent.

Concerning the epidemics, the temptation to predict the future is also important, even more so as politicians are accused of incompetence when an unexpected outbreak appears. This is linked with the reluctance to accept stochastic events. This brought about the development of mathematical models of epidemiology, of which none have been proven to be efficient, but that influenced the human society in a considerable way through the media. Among the examples for which we are involved are mad cow disease (which was predicted to cause hundreds of thousands of deaths), the prediction on evolution of the epidemic of AIDS (that was contradicted by a rapid decline in Africa in the middle of the 90th), the avian influenza (which predicted that the virus was going to be transformed into an agent of inter-human disease), the dramatic decline of Malaria in Africa (that was unpredicted), and, finally, the recent episode on the swine flu.

This episode of A-H1N1 "swine flu" pandemics highlighted the scope of our ignorance by associating elements which had never been seen in the pandemic or seasonal flu (Nougairede et al., 2010).

1. The disease stopped, in Europe and the USA, with the arrival of the cold, which was unique. This is in contrast with the name Influenza that comes from the Italian name "Influenza di fredo" meaning under the influence of cold.
2. The disease diffusion seems to have an alternation with that caused by rhinoviruses, which had never been described (Raoult, 2011).
3. A large part of mortality is not related to the virus itself but on secondary infection (*Pneumococci*, *Staphylococci*, *Haemophilus*), therefore, the prescription of antibiotics is probably changing the fatality rate, as anti-pneumococcus vaccines may do.
4. Paradoxically, in 2010, there was (in spite of all the predictive models), less cases of influenza during the year in temperate countries than in any previous year studied, since the disease has been observed (Jhung et al., 2011). Not only A-H1N1 did not circulate, or very little, but the virus Influenza B did not circulate either, nor the seasonal virus A-H3N2. These events could be explained by an interference between viruses; one can create a new model including this, except that, in the current year, in 2010–2011, flu reappeared in the standard seasonal course in Europe and three viruses circulate together; Influenza virus B, A-H3N2, and A-H1N1 (Cornaglia and Raoult, 2010). This is illustrating our large gap of knowledge of influenza virus transmission.
5. Finally, flu is more common in the inter-tropical region (and specifically in Africa and Asia) in the hot, rainy, summer season and is not linked to cold at all.

A-H1N1 epidemics show that we are completely unable to predict the form of the epidemics of the future, because of our lack of current knowledge, including on seasonality! In contrast, the first great "influenza pandemic" of the century resulted in a dramatic reduction in the number of cases of influenzas during the winter of 2010, which defies all the models. The main lesson is that we need to reduce our dramatic gap of knowledge, starting by careful observation and analysis of cases. Indeed, it is much more valuable to carefully observe the development of a new outbreak and modify accordingly the strategy to fight its extension. The future of the epidemics remains unpredictable because of multiple interference between micro-organisms, of which is still largely unknown to us. This is associated with a deep ignorance of our microbiome. It is critical to study the microbiome and the virome of patients to evaluate their relative composition compared to controls. Therefore, creation of sites that are able to detect, study, and follow outbreaks of the future will be more successful than modeling the future outbreaks based on conditions of the past, that do not exist anymore.

Finally, the permanent social evolution of human beings generates behavioral changes in a permanent way. Indeed, the behavior of the human society, in the medium term, is impossible to predict, in particular, this is explained by the "red queen" theory where each actor, victim of one parasite, is selected and/or generates strategies to avoid this parasitism. In this mind, any previous outbreak modifies the society response to the next one. Finally, the failure of modeling of the epidemics is as obvious as predictions of the future in the field of demographic, or, economic (evidenced by the unpredicted crisis in 2009), or any human activities and it is rather reassuring. In contrast, the recurrence of these never confirmed predictions, in the best journals disguised in Science with the use of mathematic formula, is worrying and may reflect more the anxiety of the future of the editors than true science. It may represent "pseudo-sciences" as astrology, numerology, and other "magic sciences."

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