



CHRISTIAN BRECHOT

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I will focus on how infectious disease fits with the context of global governance. I will make a few general points on this topic, and I have chosen a few examples to illustrate the different contexts for emerging and re-emerging infectious diseases, and then show the changing paradigm of the past 20 years regarding the governance of such challenges.

Firstly, we all know that the 20th century has allowed major breakthroughs in terms of major reductions in mortality from infectious diseases. We also know that this was the century of the discovery of antibiotics, with its major impact, and the breakthrough of the development of vaccines. This led, very inappropriately, around 1967 – and it is always interesting to go back to this – to closing the books on infectious disease and the shift of resources to non-infectious killers.

Then the concept of emerging infections became a reality, and this is related to a major challenge which still remains, animal-transmitted infections, zoonosis. We know that in fact we do have a number of viruses, bacteria, and pathogens all over the world, and the question is not about knowing whether they are new infectious diseases but how they will emerge and re-emerge, and what the prevention and treatment should be.

What are emerging diseases? These are infections transmitted from animals to humans which became epidemics; infections caused by pathogens which mutated and for which there is no immune protection, like some of the influenza-related epidemics which are resistance to anti-infective agents, such as multi-resistant bacteria, which is a major concern; and infections which just spread to new geographic zones.

We know the causes of emergence, but we have not known them for a very long time. These are due to with increasing contact between humans and animals; 75% of emerging infectious diseases are zoonotic. There is also environmental change, growth in population and highly concentrated populations. When you look at the mechanisms for emergence, there is always an animal reservoir, and then an intermediary host where you see the amplification phase of the epidemic, then dissemination to humans, particularly with the much higher number of travellers.

When you want to analyse the factors of emergence, this is really a multidisciplinary and global field, where you have to cope with virological and genetic factors, ecological factors, zootechnical factors such as density of animal breeding, and demographic factors. This is what relates my presentation to the subject of this session, because the Pasteur Institut is a good example. Our research group does not only include scientists working on virology and genetics, but also scientists working in epidemiology and a number of related disciplines.

[Break in audio].

Secondary local outbreaks allow the growth and maturation of epidemics, and then you have the amplification, transmission, and geometric progression of a number of cases. Finally, and it is not always clear why this happens, you have regression. A key point is that during the diffusion phase the virus will adapt to the host, and this is key for transmission; this is the threat for the future. This is what was misleading in the previous conclusion 30 years ago: the key point is not to believe that there are other pathogens, but the capacity through diffusion and amplification to adapt to the human host and to disseminate.

Again, we have very significant numbers of emerging and re-emerging diseases, the latter meaning diseases which were well-known and we thought were gone, but are not, such as tuberculosis or resistance to antibiotics. A more recent example is the infection by *Yersinia pestis*, recorded very recently in Madagascar and also in the US, which is closely related to the level of economic development.

SARS, Severe Acute Respiratory Syndrome, was a breakthrough in the way such crises are handled. SARS, caused by the Coronavirus, has been observed in 8,300 cases in southern China, and about 800 deaths. This is obviously a lot, and too many, but not so many when compared with previous epidemics. However, for a number of reasons, it has



completely overhauled the way we handled this question. It started in Guangzhou Province near Hong Kong, and then a doctor in mainland China went to a hotel in Hong Kong, and this led to complete dissemination all over the world.

What is interesting is that, when you look at the report, the introduction was in November 2002. It only started to be publicised in early 2003. Why is this? Firstly, the advertisements on the Internet were in Chinese, and the global health screening system from Canada which spotted this was only in English. Secondly, China was slow to understand the question, and it only became widely known because an American businessman left from China to Singapore, and the plane had to stop in Hanoi; unfortunately he died from SARS, and this was the moment when it became obvious that there was something going on. Then there were the amplification and the regression phases.

I am very proud, though I was not the president at that time, that the Pasteur Institut was at the forefront of evaluating the first cases in Hanoi. The Institut is a dedicated, multidisciplinary research centre in Paris, and it has an international network with a number of institutes and regional activities throughout the world. This is key to efficient global action, because if you do not have the onsite capacity, if you do not have something linked to the local government, economics and politics, there will be no efficiency in taking on such emerging infectious diseases globally.

The lesson of SARS has been very important. It proves the vulnerability of our societies to new infectious agents, and it led to complete paralysis with major socioeconomic consequences; on the other hand, it has demonstrated our response capabilities, an international network of epidemiological surveillance, new detection tools, and international health regulations. However, we have to be very honest: we have been very lucky, and the reason why the epidemic stopped is that this is an infectious agent which is not easily transmissible and is not infectious after the beginning of the symptoms, which makes a huge difference regarding its diffusion capacity.

I want to show that for other viruses you have different mechanisms. Chikungunya is a virus transmitted by mosquitoes, and this virus has undergone mutations which have allowed it to adjust to a new host, to replicate and to transmit more efficiently. This is another case which presents a new challenge; Filoviruses are very severe and dramatic infections, some of which occur around Central Africa, and are likely to be transmitted by bats, and which include Ebola and Marburg.

Intervention in these countries has led to a misunderstanding by the population as to what has been going on. For example, victims have been buried without ritual ceremonies, and they will become ghosts and haunt the living. This led to an emphasis that you can only be efficient if you have appropriation by the local community of the measures you want to take.

The last part of my presentation concerns the importance of surveillance and alert networks, and I will briefly summarise by saying that a lot of actions have been taken which have reinforced our capacities. I will point to some limitations at the end. I do not want to describe them in detail, but this global network, the Global Outbreak Alert and Response Network, has been a very important step forward to reinforcing global communication about these infectious diseases. You have other warning systems such as the so-called ProMED system, where you have a list of the various events along with reports.

Very importantly, you now have emergency prevention systems for animal-related transmission, for example EMPRES, the emergency prevention system for trans-boundary animal and plant diseases. This is key in the light of the fact that 75% of emerging infectious diseases are zoonotic. Climate change is a key element, along with deforestation. We have a major Pasteur Institute in Guiana, and we are also working on a number of important issues in Asia. This has led to new methodologies for evaluating this risk. You have a multidisciplinary approach where, based on the evolution of climate change, you try to estimate how this might have an influence. You have epidemiological modelling, earth observation, microbiological surveillance, public health computing, etc; this is the way to handle this research.

When you want to tackle these emergent infections, you need to understand what is the reservoir population, what is the target, and this is often very difficult. There are three different tactics. You can target the control, directing your efforts at the target population, with no reference to the reservoir. For example, when you want to vaccinate against yellow fever, may have blocking tactics targeting the control to block transmission between the source and the target



population, such as animal-human transmission, and you can target the reservoir control itself. This is very easy to say and very difficult to achieve.

Looking at the period between 1940 and 2004, you can see the increasing number of factors, and the fact that land use changes, for example, is very important in terms of emergence. This has led to a number of recommendations regarding the prevention measures which would be taken when land use changes. There is the interface between the target population and the reservoir, for example the incredibly large poultry reservoir in China is a key factor in the transmission of avian viruses. The early detection of cases in human by close health monitoring is where you need onsite capacity and diagnostic tools.

Despite this progress, we have not finished with these problems. We had other influenza-related diseases in 2009, and you can see the impact on the population. Finally, there is MERS, Middle East Respiratory Centre Coronavirus, a virus related to SARS but different. It was first reported in Saudi Arabia and is highly pathogenic, fortunately a relative limited dissemination capacity, but causing very significant problems in many countries due to dissemination and travel.

MERS has led to a very significant concern which might be an obstacle to these global actions. The sequence of the virus has been determined by a group in the Netherlands, and this has led to a patent. This patent has led to a block on sample sharing between Saudi Arabia and the other countries. I have shown you some very nice Internet-based programmes which are very efficient, but if you do not get the samples you have nothing, and you do not have the possibility of intervening and making the diagnosis. This is why we need onsite capacity, and this is why we are so active in the Pasteur international network. We will need to address this issue.

Viruses have a great emerging potential, though you also have bacteria, parasites and fungi. What is clear is that you cannot have efficient action on these pathogens if you do not include this in global view which includes deforestation, economics, climate change, global warming and population growth; it is a combination of these which can lead to some concrete actions. International health regulation from the WHO has been a major step forward in combining efforts and integrating the core capacities and global networking activities.

Coming back to SARS, the number of travellers worldwide dropped with concomitant economic loss when the WHO travel recommendations were implemented. I will close with this statement from Charles Nicolle, the founder of Institut Pasteur in Indonesia over a century ago. I like this statement, because it says a lot of things. 'There shall be new disease; that is an inevitable fact. Another fact no less evitable is that we will never be able to detect them from the outset.' Maybe this is not so true now. 'By the time we have some idea of those diseases, they will already be fully formed in their adulthood, so to speak. They will appear like Athena, springing fully-formed from the forehead of Zeus. We must equally resign ourselves to ignorance of the first cases.'

We must understand that we will never have an end of infectious disease. We have a reservoir of disease that is endless. The point is not to dream of suppressing infectious disease; the point is to adjust the follow-up and global governance of this problem.