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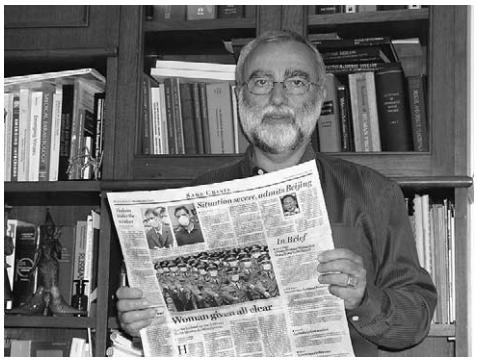
Editorial

SARS: at least and at last, are we learning from the worst?



Diseases are truly emerging, mainly due to the appearance of a pathogen new to Science and, when a disease extends its deadly shrine across new territories or naive populations. However, the concept of "emergence" gradually appears in the collective consciousness, mostly compelled by a never-ending chain of new diseases to confront.

Last March, a disease was discovered. Fitting perfectly with what we consider to be a typical emerging disease: the severe acute respiratory syndrome (SARS) was indeed identified as new when a chain of transmission of severe and unusual cases of pneumonia was observed. Several public hospital staffs in Hong Kong, Singapore and Vietnam were infected and, within 2 weeks, a trans-continental related cases of infection was observed from Hong Kong to Toronto, Canada. In a few days, from the hospital-based first chain of transmission, an index case was identified, as a medical doctor who flew from Shanghai to Hong Kong via Hanoi and, transmitted the disease during his stay at the hotel in Hong Kong, to a Singaporean, a Canadian family and an American businessman, who became the index case of Hanoi nosocomial outbreak. An Italian physician, who unfortunately died form SARS infection, made early epidemiological observations in Hanoi leading to a rapid understanding of the transmission phenomenon.

Meanwhile, the World Health Organization (WHO) started in February investigating on the potential re-emergence of the deadly avian influenza A H5N1virus in Hong Kong, from a traveler from the Fujian province. Also this contextual occurrence coincidental to the turmoil of a World severely shacked by the imminence of a war, probably prompted WHO, to address in less than 2 weeks after the SARS discovery, a Global Alert for the rising epidemic. In addition, because of the unknown etiology of the infection and the involvement of a commercial air traffic as a main factor of it spread, WHO activated the Global Outbreak Alert and Response Network, addressed a Travel Advisory for the SARS and, asked for a collaborative research laboratory network on SARS.

After a month, the Guangdong province of southern continental China was identified as a potential epicenter of the disease where it started in mid-February or a few months before. By the end of March, more than 15 countries around the World reported a thousand of suspected or probable cases of SARS with a case fatality rate not greater than 4%. Under WHO guidance, a group of a dozen of laboratory was gathered to work in synergy in order to identify, isolate, and characterize the etiological agent of SARS and also, to develop specific and sensitive diagnostic tools.

At the beginning of the crisis, it took less than 2 weeks to a team of scientists from Hong Kong University, to isolate and identify by electron microscopy, a Paramyxovirus from a patient lung tissue. The etiological hypothesis, at that time, favored a *Metapneumovirus* sp., a new virus genus identified in Europe a couple of years ago.

Five days later another virus was isolated from a SARS patient and genetically characterized, and, on account of the power of molecular virology, a team in Germany identified a new Coronavirus. Also other scientific teams from Hong Kong, Canada and USA detected the Coronavirus RNA by using RT-PCR. In a few days, researchers from the University of California, San Francisco, using microarray technology, made available a blue print of the all new Coronavirus genome, paving the way for accurate research on specific diagnostic tools, vaccine and, therapeutics.

It is noteworthy to note that, a few weeks before the Coronavirus identification, the avian influenza H5N1 was also identified and genetically characterized by the rapid move of researcher from Hong Kong. They sequenced and characterized in a week 6 of the major internal genes and, in less than 2 weeks, the total sequence was available in order to identify if the deadly avian influenza virus has undergone genetic change since the dramatic 1997 outbreak.

Although, the newly identify Coronavirus seems to have played a major role in the severity of numerous cases of SARS, a *Chlamydia pneumoniae* was also isolated and suspected to be the causative agent of severe pneumonia

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in China in January and overlapping the early phase of the Guangdong province epidemic. The epidemic was thought to probably have started in late October 2002, and to have reached a peak at the beginning of the year when the SARS activity came to public attention and concern. By that time, as early as mid-February, Chinese scientists from Beijing suspected a viral etiology of the Guangdong rising atypical pneumonia epidemic. Two months after, the clinical causality of a hitherto Coronavirus was strongly favored by a Dutch team using an animal model which developed after infection, a pathology mimicking SARS pneumopathia. Nevertheless, after 3 weeks of an intense investigation on the virus etiology, the bacterial hypothesis re-emerged and a *Chlamydia* sp. was again isolated, along with the hitherto Coronavirus, and was also visualized by electron micrograph of seven fatal cases of SARS.

To date,[1] 26 countries have been affected by the importation of SARS patients by commercial airplanes and, in seven instances, an active inter-human chain of transmission was experienced. Also 372 patients have died, with a total of 5 665 cases reported worldwide.

Fifteen years after the concept of emerging diseases has been developed, will we now learn on how to control and prevent such dramatic events? Emerging diseases are, by essence, sudden, devastating, challenging to the health system and, testing the preparedness of health system. Risk factors need to be identified and controlled. Also the increasing population density and, contacts between "culture and nature" are considered the means of intense germ exchanges between human population and other living species of any kind. Such encounters could take place in a close peridomestic disturbed communities as well as in the most remote ecological niche yet accessible by humans. As it occurred centuries ago, for the ancient plagues, the spread of a virus, from an endemic to another non-endemic area, mostly occurs with population migrations. Today, the fast movement of the "migrant air travelers" with a constant increase of travel frequency, and a variety of destinations, has been clearly identified as a main factor of geographical and trans-continental disease diffusion and, pathogen emergence in naïve populations.

Virus ancestors, surely, bacteria and parasite also, preexisted before human beings and will likely survive. We can expect new plagues and germs, emerging in a virgin population or, extending their domain from animal to human, from a tropical to a temperate environment. In regard to "epidemic" and "virus", the collective awareness recall its old fears and ghosts and invite media and public opinion to put more pressure on politics and health responsibles. In a moment of population at war, the world alert increases the feeling of insecurity and forces the actors of health control and prevention to use their skill hastily and share their findings to the best of their abilities.

On the brink of any emerging infectious disease, with reference to the medical and scientific point, which might diverge sometime from public health officers, first the germ needs to be identified in order to provide basic information, which will serve for early control and strategies proceeding by analogy of a previously method developed for known related germs and diseases. This initial attempt to control the disease at the clinical and epidemiological level will give more insight to the nature of the disease and lead to more accurate control and prevention actions with the only objectives to treat patients and limit the spread of the epidemic. These essential steps will only arise with a laboratory network setup at the local, national and international level, and will provide tools to measure and extensively control the threat.

To efficiently address the challenge of the emergence of new diseases, three major components clearly appear crucial for an early detection and control of a new or re-emerging disease: (1) a global laboratory network for the identification of the germ and the development of diagnostic tools, (2) specific skills on clinical epidemiology to raise clinical awareness and response and, (3) a global epidemiological response. The later has been thoroughly developed with the WHO Global Outbreak Alert and Response Network. However, other tasks are poorly advanced.

As mentioned by an European Union Health officer in the early development of SARS epidemic, it is obvious that regional centers of investigation, like an European Center for Disease Control proposed years ago are required.[2] Such centers will provide expertise for an early detection and characterization of pathogen developing skills and global strategies for the control of emerging infectious diseases. According to this concept, at the end of April, the Association of South East Asian Nations (ASEAN) conveyed regional politics and health officer to a SARS summit in Bangkok. Prime ministers of several Asian countries agreed on the principle of developing in the near future an "ASEAN Communicable Diseases Control Center".[3] The establishment of a global laboratory network is imperatively needed and has to include such centers in order to develop permanent observatories focusing on rare or underestimated health related events.[4]

Inadequacies of our global system for tracking events leading to an unexpected germ emergence need to be corrected. In any corner of the World, should be established centers harboring skills and technologies dedicated to detect the emergence of a disease or a new pathogen threatening the global population.[5] Also prospective studies based on the specialization of the risk will be directed to prevent

[1] Thursday, 1 May 2003.

[2] Tibayrenc, M., 1997. European centers for disease control. Nature 389 (2 October), 433.

[3] ASEAN SARS Meeting, Bangkok, 29 April 2003.

[4] Tibayrenc, M., 2001. A European center to respond to threats of bioterrorism and major epidemics. Bull. WHO 79, 1094.

[5] Gonzalez, J.P., 1997. Arbovirus and related viruses as emerging pathogens in Southeast Asia. In: Saluzzo, J.F., Dodet, B. (Eds.), Factors of Emergence of Arbovirus Diseases, vol. 117, Elsevier, Paris, p. 127.

regional or global extension of any pathogen. Communication systems will seal a global network involving expert laboratories, adequate epidemiological skills, university-based expertise for training, altogether the goal will be achieved and, fears subsiding. To quote Louis Pasteur the “patrimoine de l’Humanité” lies in a global quest for pathogens and universally shared research, which must be funded by international sources.

Parasites preceded humanity and, it is not to speculate, that they will survive to any other future. As medical researchers, it is our duty to predict their malignancy and prevent germ nature of subducting human culture.

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