Influenza Pandemic: A Perspective

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Ten years ago, somewhere during January 1999, half of a bucket of transformer mineral oil found its way into the Belgian food chain. A couple of months later, the ingestion of off-odor soft drinks landed a dozen school children in a hospital. Against the background of major police and judicial dysfunction in a highly mediatized pedophile case, both of these incidents triggered the famous "Dioxin and Coca-Cola Crisis" which turned the tiny kingdom of Belgium upside down. There was a nationwide recall of all Coca-Cola products. Worldwide, imports of Belgian meat and dairy products were suspended, with a direct economic cost of 800 million euro. Ministers resigned, careers were broken, the "eternal" Christian-Democratic governemental parties were removed from power—all of this without a single medical casualty.

Thus, we learned that when there is a widespread perception of a major health risk for a community, minor incidents or major non-events can turn into a public health crisis. This is true, especially when there is inadequate information or scientific uncertainty about the causes, nature, or dimensions of (unusual) health hazards against a background of structural problems, unresolved societal tensions, and dysfunctioning or public distrust of state institutions.¹

Therefore, it is not difficult to understand why similar mechanisms and analogous dynamics can turn the threat for an influenza pandemic into a public health crisis—this time, however, on an international scale. In this context, a numbers of issues can be raised with respect to the roles and responsibilities of health professionals and scientists.

Some 3,000 people died at the Trade Towers and the Pentagon following the Al-Quaeda attacks of 11 September, 2001. The same day, and every single day since, somewhere in the world, >16,000 people died—from hunger or malnutrition. Every 24 hours, several thousand people die of malaria, >8,000 of AIDS, and >5,000 of tuberculosis. These are real human beings, dying from well-known, treatable diseases today, not potential victims in hypothetical scenarios. Every year in the developing world, 12.2 million children <5 years of age die, most of them from preventable causes. One billion people live on <\$1/day. In the 44 countries with average per capita income of <\$500/year, the average health expenditure is \$12 per person per year.²⁻⁵

The events of September 11 definitely shaped the international political and ideological landscape, that led to wars in Iraq and Afghanistan. Immediately afterwards, in all of the Western countries, hundreds specimens of dust, sand, sugar, etc. from "suspected" letters were examined in specialized laboratories for anthrax. Ultimately six perons died from anthrax. Although suspicions were raised towards a US defense lab expert, no conclusive evidence was published concerning the source of the anthrax strain used. This was followed by an unresistable bioterrorist hype. All over the world, thousands of papers, courses, guidelines, and exercises emerged concerning CBRN agents and rare diseases. "Dark winter"-type scenarios and risk assessements for so-called low probability events that could have apocalyptic consequences were developed. At huge costs, vaccines for anthrax and smallpox were produced and even tested. Remeniscent of cold-war practices, governments started massively stockpiling drugs and medical and other "crucial" supplies. One cannot stop wondering

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how much of all of these efforts and the money spent then really has been used or still could be useful. By contrast, no facts, no figures, no calculations, nor catastrophic images could motivate the "international community" even to start to respond to the chronically unattended health needs of countries far away or of underpriviliged social groups.^{6,7}

It is unlikely that the potential for an influenza pandemic would have recieved so much attention had the ground not been prepared by the study of potential biological warfare agents. ^{8,9} Out of the shadow of the smallpox-beast came Cinderella in the form of the Influenza virus. And suddenly, there was SARS, the first emerging epidemic of the 21st century. Starting in November 2002 in Guangdong Province, China, a severe acute respiratory syndrome spread rapidly from Eastern Asia around the globe. But, by 05 July 2003, the chain of transmission was broken. Between November 2002 and July 2003, a total 7,768 cases and 727 deaths were reported from 26 countries. ¹⁰

More cynical people would point to the analogy of 19th century bourgeoisie becoming sensitive to sanitary conditions of the working classes, once they realized the importance of a fit working force and of the threat of communicable diseases for their own skin. 11,12 During two decennia, Western establishments failed to acknowledge and contain the AIDS pandemic, under the pretext of individual responsiblity and personal behavior. 13,14 But SARS sounded the alarm and made official experts and agencies aware that, in times of globalization, selective international surveillance and minimal public health services were required in the sake of "national interest". Quite logically, the attention of "Homeland" Security and the like turned toward influenza, pushing WHO officialdom finally into action.¹⁵ Those still reluctant to follow were reminded of the 1918 Spanish Flu that killed more Americans in one year than were killed during the First and Second World Wars, the Korea War, and the Vietnam War combined. 16-18 The death toll of the influenza pandemic of 1918/1919 was in the order of 50 million persons in less than one year. Government and business circles also began calculating the economic costs of influenza, realizing the potential disruption and wider socio-economic implications of a pandemic. The goals as they are bluntly formulated in the National Strategy for Pandemic Influenza announced by President Bush in November 2005, are threefold: (1) stopping or slowing the spread of a pandemic in the United States; (2) limiting its domestic spread; and (3) sustaining infrastructure and mitigating the impact to the economy and functioning of society.¹⁹

Despite the boom in the possibilities of electronic media and information technologies, a number of reasons have made it made more difficult for individual health professionals to be timely and adequately informed with respect to public health problems. First, there has been a decennialong trend of hyper-specialization, growing emphasis on productivity and output, increasing social and professional isolation, lack of clinical supervision and steering mechanisms, and insufficient time and possibilities for exchange, learning, and for cultural or social activities in general. For every person nowadays, there is a continuous bombardment with publicity, messages, news items, and communications in all forms and quality. But, it is an even greater challenge

to keep pace with the rapidly expanding scientific data and professional knowledge, or to develop an adequate search and management strategy for essential and reliable information that is widely dispersed and fragmented. Some help really is needed.

However, when we look at pandemic influenza preparedness, many official websites and planning and guidance documents do no meet the essential standards for peer-reviewed scientific publications. Many do not even include a comprehensive list of citations. Basic asumptions or recommendations are poorly referenced. Uncertainties seem to be banned, scientific controversies are seldom mentioned, and minority points of views and their arguments rarely are described. Innumerable meetings and conferences lack transparancy and accountability concerning the criteria used to invite specific researchers, experts, or keynote speakers—little real scientific exchange or discussion has taken place.

There are many competent, scholarly, and conscientious individuals working for private companies. Many other factors, beside corporate interest, can filter or bias information. But, there must be absolute transparency about financial ties and strict rules concerning possible conflicts of interest, not only for authors, but also for reviewers and editors. ^{20–30}

With the wars on terrorism and in Iraq, credibility of the highest officials and governmental institutions in the USA and the UK suffered major blows, from dys-information on weapons of mass destruction to favors for major business interests like Halliburton. But, many questions and serious concerns can be raised with respect to decision-making for pandemic influenza preparedness. When the US governement allocated lucrative contracts to pharmaceutical companies, former US defense secretary Rumsfeld had major stakes in Gilead Sciences, Inc., which had the original rights on Osseltamivir (Tamiflu®), later sold to drug giant Roche. No doubt many private enterprises try to use every opportunity offered by changing market conditions and swings in public mood, to sell their products and services. Big corporations know the working of state institutions better then anyone else. Powerful lobby work has influenced many budgets and (de)regulations. But mere conspiracy theories do not explain the influenza-boom since 2004.

It is true that each year, influenza-viruses infect roughly one-fifth of the human population, causing significant mortality and morbidity worldwide. 31,32 For Western industrialized countries, Influenza A strains are the main agent causing fatal viral infections. 33,34 Even before the etiological agent became known and understanding of pathogenesis developed, influenza ("La Grippe") could be identified as a separate clinical entity, one of 15 acute respiratory syndromes. 35 Although, following advances in virology and immunology, case definitions became more precise, its seasonal incidence was noted, and several epidemics were recognized. 36

In general, the changing health impact of communicable diseases can be explained by the variable characteristics of three major factors: (1) the infectious agent; (2) the host; and (3) the environment. Remarkably, throughout the 20th century until today, the description of clinical symptoms and signs of uncomplicated influenza, as well as the inefficiency of its symptomatic treatment, have remained essentially the same.^{37–49} However, during epidemics, death rates even

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among healthy young adults can be important. Secondary infection with pathogenic bacteria (as found in post-mortem specimens in 1918) now is thought to be less relevant in the etiology of fatal pneumonia.³⁵ In case of complications and a highly pathogenic strain, symptomatic and supportive treatment has been the major clinical approach. To date, the outcomes of the prophylactic and therapeutic uses of anti-viral drugs have been disappointing.

Therefore, the core strategy for pandemic influenza preparedness in the industrialized world is based on timely and effective immunization of the population-at-risk. But existing technology and production capacity of influenza vaccines fail to guarantee containment, even for the richest nations. Hence, the campaigns for better hygiene and the plans for social distancing have become increasingly important with the hope of reducing transmission of an emerging virus strain or at least slowing down the waves of human infections. ^{32,50} All this compels business continuity planning to be extremely flexible and adaptable to the socioeconomic impact of drastic changes in public health.

Although pandemic influenza preparedness has been improving steadily, many key issues remained unanswered. First and foremost, there are enormous disparities in the strategic arsenal and intervention capacity of developing countries. These countries often house the avian and animal reservoirs with the highest risk for viral antigenic shift and increased infectious and pathogenic potential that may result. As "first line" in the global defence, developing countries are supposed to monitor and try to stop the incipient outbreaks, identify the viral strains involved and—cynically enough—make these factors known to the WHO and private producers of vaccines even though there own population will have no access.⁵¹ For example, the US Navy/Army implemented direct control of at least five key Public Health Surveillance Laboratories and networks in other regions (Peru, Egypt, Kenya, Thailand, Indonesia).⁵²

In official meetings and planning sessions, at some point drastic social measures like closing schools and airports have been mentioned. As was the case in 1918, their theoretical benefits rapidly are undermined by controversy and uncontrollable secondary effects. ⁵³ Despite huge financial investments, many fundamental knowledge gaps remain. These have had a major impact on pandemic risk assessments and practical preventive interventions. For both, a better understanding of the antigenic variability of influenza viruses on the molecular level is crucial. Insight into cellular and humoral immunology and the mechanisms explaining differences in infectiousness and pathogenicity (including for different age groups and chronically ill persons) remains inadequate. ^{54,55}

Finally, as long as transparency and assessments are not improved, much uncertainty will remain concerning the efficacy of vaccines and immunization strategies, and the capacity to deliver them to those in need in time for them to be effective. 56-61 Surprisingly, no comprehensive list has been publicized of the (non)matching results between the chosen strains in annual vaccines and the actually predominant virus responsible for seasonal outbreaks. Although specific vulnerable groups are recommended for priority vaccination, the overwhelming majority of clinical trials have been conduct-

ed on healthy, young military recruits. Follow-up studies on efficacy in cases of repeated annual influenza immunization are equally lacking. Also, one should not forget the health risks involved in influenza vaccinations, as was the case in 1976 in the USA when a mass immunization campaign in the USA was interrupted because of liability for side effects, including some high profile cases of Guillian-Barré syndrome. It remains unclear which of these elements is co-responsible for the fact that—surprisingly, <25% of healthcare workers in Europe are covered by seasonal influenza vaccination. 32

The events following the 2009 H1N1 influenza outbreak cast even more doubt on basic interventional strategies, organisational responsibilities, and critical decision-making processes. Although the strain involved⁶³ results from what could be called an antigenic pseudo-shift, and inter-personal transmission is rapid, the apparent limited virulence makes it difficult to understand why engagements of resources and money are so disproportionate in relation to the actual morbidity and mortality reported. ^{64–67} Some already call it "a pandemic of indecency", because of the relative importance given to H1N1 compared to other global health problems. ⁶⁸

Adequate risk management of the recent H1N1 outbreak has not been helped by current outbreak modelling nor by official communication strategies. Analyzing, not to say predicting, the outbreak dynamics of a genetically unstable and phenotypically changing virus, poorly understood host immunity, diverse populations, and complex environments requires multi-disciplinary and international collaboration. All too often, uncertain parameters have been replaced by simplistic asumptions. Lack of recent or timely data have been jacked-up by a-historic analogies, failing surveillance by wild speculations.⁶⁹ The experience with the avian "cousin" H5NA should have made us more prudent. The WHO projection of 150 million deaths were ventilated, but until today, some 421 human infections were documented and 257 died from highly pathogenic avian influenza. The price has been paid by backyard and subsistance farming—biosafety or zoonotic diseases rarely endanger the practices or profits of agrobusiness.

The 1918 pandemic illustrates that influenza does not spread in a vacuum. The macro-environment of war, censorship, malnutrition, mass transport, and gatherings with inadequate hygiene or social distancing, all played an important role. The World population then was something like two billion, with communication and traveling uncomparable with the modern era of globalization. It is difficult to imagine how little was known about the agent as it only was in 1931 that a swine "filtrable virus" was isolated. Quite rudimentary notions of immunology prevailed. Serological techniques and sequencing were non-existant. Diagnostic chest x-rays, intravenous fluid therapy, and disposables were not available, antibiotics and artificial ventilation⁵⁴ were unknown, as were vaccines and anti-virals. It is not easy to calculate to what extent this would have changed the overall mortality rate of 2% for Americans and Europeans infected in 1918.

Also, at the end of the 20th century, health services and research laboratories were conquered by managerial doctrines, with an evidence base matching that of astrology. Not embarassed by non-existing field experience or scientific illiteracy, managers took over decision-making. Obsessed by

what they called "communication", spokespersons and spin doctors also invaded the field of crises and emergencies. Influenced by the world of publicity and stardom, packaging and image became more important than content and truth. Communication essentially was seduction, often coming very close to manipulation. Commercial ads target hearts and senses, play with emotions and perceptions, but finally, go for your wallet. However, crisis communication is much more complex and long term, involves values of trust and honesty, requires real information, and sometimes, education. Because, as we have learned, major non-events can sometimes turn into public health crises.

So are scientists and health professionals free of blame and shame? Is it enough to do our upmost best in our daily jobs, treating disease, nursing wounds, comforting patients, managing departments, running experiments, and counting the dead? Scientific progress requires transparency and a critical approach. Best practices in health are not served by complacency and peer nepotism. Can we then stay away from the arena of politics and limit ourselves to damage limitation of

decisons made elswhere? Can we continue to try canalize part of the resources spent on inadequate priorities towards more essential objectives?

In our own field, much has to be done. There is a need for health practitioners and clinicians to see their activities in a broader perspective, learn to reflect in terms of communities, and stop ignoring societal problems.⁷¹

But, health practitioners, administrators, and reseracher also should become more active and socially responsible citizens, advocating values, informing the public, contributing to debate, and interfering with the way decisions are taken, budgets are fixed, priorities are set, and investments are made, both locally and internationaly. Reducing the global burden of disease, tackling the unacceptable health disparities, including those within industrialized nations, cannot depend on charity or the foundations of the billionaires of our planet.

If the threat of an influenza pandemic is worth all the efforts already spent on preparedness, then surely, billions more are needed to start dealing with unattended health needs and neglected risk factors elsewhere.

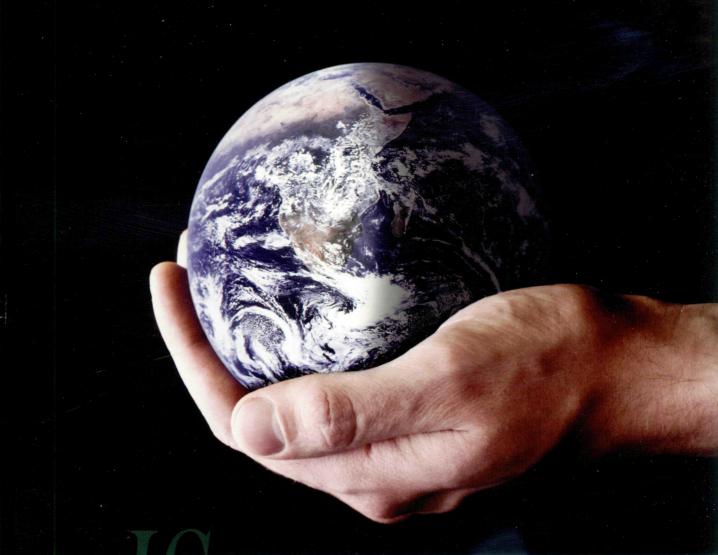
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