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From Biosecurity to Emerging Diseases: A Relentlessly Changing Paradigm

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"Diseases are born, live and die" this is the title of one of the most famous works of Charles Nicolle, Nobel Prize of Medicine (1928), illuminating in a few words the general theory of infectious diseases that he developed between 1893 and 1936. In this theory, Nicolle applies the Darwinian principles of evolution for microbiology as follows: "We will never have certainty about how infectious diseases began. When they emerge, we will be unaware of their existence until the day on which the number of reported cases necessitates our knowledge of new evil, even early indications escapes us as we are always looking for infectious diseases as they existed in the past." The concept of "new diseases or better yet, one of "emergence of infectious diseases" dates back to twenty years ago.

The End of an Era, The Beginning of a Concept

The Second World War, WWII, spurred huge technological advances in everything from weapon development to health. The profound leaps in the quality of healthcare throughout the mid-twentieth century bookend the start of the war in 1941. Thus, the output of the war, as often seen in all of them, favored huge technological advances in many areas which obviously affected the weapon development, but also health at large. At the beginning of the World War II in 1941, usual antibiotics included only sulphonamides synthesized eleven years before, and the application of penicillin for bacterial infections was done only after two years after its discovery by Alexander Flemming. In 1944, after the first conclusive trials of penicillin in humans, Pfizer and Merck supplied the troops in the Normandy landings. Among the many fields of research opened by the war efforts, healthcare made tremendous advances including the prevention of wound infections and tuberculosis, the development of the typhus vaccine, the development of surgery and plastic surgery, the treatment of burns, and improvement on existing therapies for combat fatigue and trauma management, etc. Shortly after the war, the Canadian George Klein developed the first model of motorized wheelchair! While for centuries the only effective weapons against epidemics were flying away from the epidemic area and/or having patient strictly, and often brutally isolated, some twenty-five years of the post WWII, a therapeutic armamentarium and efficient control strategies were available capable of pulling of brilliant victories against infectious pathogens. A generation later, it was common to think infectious diseases were relics of a bygone era not to return. Surgeon General William Stewart, a particularly optimistic advocate of this viewpoint, said in December 1967: "the chapter on infectious diseases is closed." On October 26, 1977, the World Health Organization declared a unique victory in the history of mankind's health - the eradication of smallpox. In 1971, Abdel Omran proposed a theory of "epidemiological transition" to explain the eventual paradigm of a society free of pathogens. This theory aligned the health of a society with its age of evolution. Early societies encountered "the age of plagues and famine," with high mortality rates that fluctuated according to infectious epidemics or pandemics. Thanks to the growth of medicine, healthy living, and advanced methods for the control of infectious diseases, later societies at "the age of backing pandemics" saw increased life expectancies. Finally, society would experience the "age of degenerative and chronic diseases" or "societal diseases", along with a decline in mortality and the disappearance of infectious diseases [1]. However, chronic and degenerative diseases will actually grow unevenly in certain populations with often unexpected incidence conversely, even classic infectious diseases appeared to be controlled (immunization campaign, treatments), their prevalence will remain prevalent and eventually decrease unequally in some populations mainly of developed countries. If the theory of epidemiological transition quickly became controversial, particularly in light of immense political and social diversity; it had the advantage of providing a dynamic vision of societies facing their diseases and, prevailing in the discourse on diseases pattern evolution and its dependence on the changing of human and physical environments.

Back to an old values of "déjà vu"

One by one, the great pests were vanquished: the Justinian plague vanished from the Mediterranean Basin after nearly two centuries; John Snow's foundational work in Cholera stemmed the disease's spread by the mid-nineteenth century [2] and finally, leprosy's devastation was halted at the third International Conference on Leprosy organized by Marchoux in Strasbourg in 1923 [3]. By the beginning of the twentieth century, we were convinced that these diseases were behind us and that, with the steady advances of science and technology, we had gained a universal right to health. The WHO expressed this hope in 1991 as "Health for All in 2000"program [4].

At the end of the last millennium, new highly dangerous pathogens emerged. HIV occurs at low levels in the rainforest of the Congo Basin twenty years before the AIDS pandemic is declared on the June 5, 1981; Lassa fever, known since the 1950s, reemerges in Nigeria in 1969; Ebola made a sensational debut in 1976 in Sudan and Zaire (alias Democratic Republic of Congo) with an unusual severe hemorrhagic syndrome and unprecedented mortality; Legionnaires' disease also makes a dramatic appearance in the heart of the New World, in Philadelphia; other viruses appear or reemerge in new locales, such as West Nile or Chikungunya viruses. Finally, as anticipated by Sir Alexander, increasing families of antibiotics give rise to bacterial multidrug resistance beginning in the early 1970s-organisms as common as *Staphylococcus aureus* making lightning – and fast changes to become more resistant. Moreover, if no nosocomial infections have been known for two centuries, antibiotic multi resistant bacteria drove up the severity and incidence of their actual hospital-based emergence.

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From Emerging Diseases to Disease Emergence

Eventually we find ourselves at the end of the century facing both new diseases and unpublished germs. Novelty, suddenness and incomprehensibility are among the recurring characters of this procession of new diseases. In 1992, at the request of the authorities and led by the CDC and NIH, Joshua Lederberg, winner of the 1958 Nobel Prize for Physiology, alongside with Robert Shope and Stanley C. Oaks hosted the first forum on "Emerging Infections: Microbial Threats to Health in the United States" [5]. The concept of Emerging Viral Diseases had been established two years prior, and been brilliantly defended by Morse and Schluederberg [6]. A typology of emergence was born; a specific framework for a new nosology was created to help scientists identify the factors that lead to disease emergence and helping health worker for preparedness. In this new typology of emergence, depending on etiology and risk factors, one distinguished between emerging infectious diseases (EIDs) and chronic and degenerative diseases (CDD). In each of these groups, the nosology is implemented with one hand, the EID using their mode of transmission (direct or indirect) and their origin (zoonotic or expansion) for classification and, on the other hand, the CDD (Cardiovascular Disease, malnutrition, trauma, due to chemical or physical agents, etc.) according to human environments (i.e. societies) and physical environments (i.e. abiotic). Until now, these two groups were not found in a field of common interest, until today international symposium do not mix and continuously speak separately of EID and the rise of CDD which, in specific time and space, would mark an epidemiological transition ultimately depending on the development of societies heavily influenced by globalization but not on the “great cure” form ID, as Omran had previously theorized. With the emergence noumenon, we are still far from a unifying idea of disease emergence, the kind which might enable us develop tools to combat and control ID and build a comprehensive strategy to prevent health risks.

From the concept of emergence a first question arises: where do these diseases- these new germs-come from? Are we witnessing the contents of Pandora's box–that which had hitherto remained hidden from our knowledge? Moreover, a disease emerges only once in space and time eventually followed by reemerging events that has to consider in light of what we know, and not what is there. Therefore the concept of emergence needs to be constantly redefined and re-actualized.

One does not discover the emergence of a disease as Christopher Columbus discovered America by having just the idea, the Columbus egg. Faced with illness, we assemble the pieces of a puzzle comprising a collection of symptoms, patho physiology, etc., in order to finally be able to describe the unique pathological and no sociological framework, which represents the concept of a new disease. Representation is not an element of reality, it is an abstraction allowing a physician to understand the disease and treat their patients efficiently, or an epidemiologist to target their efforts to control and prevent.

Understanding the Emergence, Explaining the Phenomenon

In the transition from nosology to descriptive epidemiology (risk factors, mortality, morbidity), the concept of emerging diseases became more dynamic and the mechanisms of emergence were addressed. The concepts of emergence and reemergence forced the scientific community to understand the need for explanatory research of the described events. For this, a dynamic epidemiology was used to incorporate spatial and temporal analysis of interaction between actors involved in the emergent phenomenon: germs (plasticity, adaptability), hosts (i.e. human and animal, reservoirs and vectors), environmental factors, biotic (e.g.: savanna, equatorial rainforest) and abiotic (e.g. climate, altitude).

The EID inventory shows that more than three quarters of emerging diseases are of zoonotic origin- meaning that that the natural host was an animal- in many cases an arthropod vector or a secondary vertebrate which mediates the transition between the pathogen’s natural host and one which is human. The paradigm is now changed on the dynamic concept of "understanding emergence". With a focus on the environment, territories and germs encountered by hosts and victims, this concept takes into account the spatiotemporal values driving the fundamental of emergence, such as: host factors, germs and parasites biodiversity, hosts and vectors availability. The picture is complex, the emergence is now considered in the context of environmental factors, with a necessary transdisciplinary approach in the service of an explanatory science of emergence. The changed paradigm enables a spatio-temporal approach for the understanding of "disease emergence in a given environment at a given time".

Disease Emergence and Biosecurity

Although Severe Acute Respiratory Syndrome (SARS) was first recognized in 2003 as the first major emergence of the third millennium, it was also the first "expected victim" from a global, rapid and efficient riposte driven by an early comprehensive approach of the first human cases unveiling the transmission mechanism, and the isolation and identification of a previously unknown coronavirus. The WHO played a major role in the coordination of an international response, emphasizing the duty of the mankind to look beyond borders where a pandemic risk is concerned [7].

The paradigm of emergence has become dynamic, beyond an explanatory research on the emergence of pathology, modeling tests are committed to provide otherwise anticipate, prepare for the emergence of novel diseases.

Moreover, on the cusp of the millennium, the events of 9/11 occurred, followed a week later by anthrax attacks. While there is no need to write further these ignominious events, they have changed forever the world’s perception of health risks. Between terrorism and bioterrorism, the international scientific community was tested once again. Those behind the establishment of the concept of emerging diseases were *de novo* engaged. In 2003, under the leadership of Joshua Lederberg, the "Forum of emerging diseases" was changed to the "Forum on Microbial Threats". Along with the wording of the event, the philosophy governing the meeting’s content had changed and the model had been revised. The paradigm had shifted to focus on the “biological risk”-now considered with unity beside different its straightforward origins, including: natural, accidental and voluntary. The framework offered a synthetic approach for understanding "the big picture" of the emergence of diseases and pathogens of all kinds among territories and populations hitherto unscathed.

Emerging diseases have taken 15 years to describe and, 15 more to understand. When the fundamentals and territories of emergence were analyzed, it became clear that by and large we were the agents of our own misfortunes. Humankind was the driver of environmental changes amplified by our constantly growing societies and evolving technologies, agricultural practices and urbanization, as well as other factors. The examples are numerous and emblematic: international trade is associated with the diffusion of mosquitoes and the spread of vector transmitted diseases (e.g. West Nile, Chikungunya); and

likewise, linkages were drawn between agricultural and dissemination of Japanese encephalitis virus; deforestation and Ebola fever; land use and scrub typhus; Dengue fever and urbanization; soil occupancy and Lyme disease, etc.

This paradigmatic shift refocused on biological risk, incorporating the mechanisms of emergence of diseases and targeting the foundations of emergence using upstream determinants of natural, deliberate, or accidental origin. Biosecurity, a set of preventive measures designed to reduce the risk of infection by multiple actions modulated by the foundations of risk (quarantined pests, contain invasive alien species, master living modified organisms, identify pathogen genetic shift, etc.) is in line with the assessment of biological risk. To this end, scientific research became the principal actor in a complex process aimed at understanding and mastering the emergence of pathologies. Fortunately, scientific research-including advances in rapid pathogen detection and the development of tools and strategies to riposte and prevent epidemics-has also progressed dramatically in recent years and -despite the observed life expectancy gap in the 1990s due to the AIDS pandemic-the global life expectancy has continued to grow since the end of WWII [8,9].

Conclusively, following our fatalistic view with respect to new diseases, we experimented with a descriptive approach to the emergence of the disease and finally found an explanatory method of the events that herald disease emergence. That problematic, international riposte against emerging events, must also arise without frontiers, such as diseases today are in line with the population developments, communication becomes also a key factor not only in the control and prevention, but as mean to prepare and convey public message in order to avoid a feeling of fear lived in the time of ignorance behind the past plagues that assaulted frightened people. With new concepts in place to anticipate and predict future emergences: "pathogen discovery" (formerly called in another time "fishing bugs") is now efficiently served by the technology (i.e. high-throughput sequencing, bioinformatics) and the spatial epidemiology using real time satellite imagery to survey landscape changes (climate, urbanization, migration, etc.) associated with the risk of pathogen emergence. The recent history of these needed models to master the concept of emergence shows the dynamic of scientific thinking needed to guide the applied research which best serves health and anticipates pathogenic evil.

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