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Editorial: Preventive vaccination

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Microorganisms are believed to exist on the surface of Earth since 3.5-4 billion of years ago. Human knowledge of their existence however, only occurred after the invention of microscopes, in 1670. Since that time, several discoveries contributed to build the *germ theory* that proposed that replicating seeds or germs were responsible for the origin of life, instead of the previous *spontaneous generation theory,* which was prevalent since the Middle age. The conservation of food was a major concern at that time in Europe, where crude winters prevented chase and agriculture activities. Redi, in 1665, studied the development of flies in meets that were exposed to air for drying. Flies were absent however if meets were protected and covered with a tulle, indicating that their development depended on the direct contact and deposit of a larva in the meet. Furthermore, Spallanzani, in 1750, described that boiling prevented the development of microorganisms (animalcules) in infusions, starting, in that way, to derogate the theory of *preformasionism* that defended that organisms develop from miniature versions of themselves and not form replication. Appert, in 1795 observed that long-term conservation of food was possible, in boiled cans that did not contain air. Nevertheless, the final downfall of *preformasionism or spontaneous generation* theories occurred after Pasteur discoveries, which explained that it was the presence of oxygen, and not merely of air, that strongly influenced the growing of microorganisms in broths. Pasteur admired Spallanzani and commissioned a full-length portrait of him, which hung in the dining room of his apartment, at the present Musée Pasteur in Paris.

The knowledge of preservation and control of microorganism growth in food changed the geopolitics and history of humanity. It allowed the owners of this technology, to send armies to conquer territories far away from their own. However, epidemics of pathogenic microorganisms still devastated both, the human populations living in high density and very poor conditions in their countries and the armies far away from home. Mumps, diphtheria and malaria were described by Hypocrites in 400. Pandemics of influenza are known since the XIV century. In the middle age, the disease was named Influenza because it was thought to be related to the influence of planetary conjunctions [1]. Tuberculosis, on the other hand, is supposed to be first acquired in Africa about 5,000 years ago [2]. For many centuries, smallpox devastated humanity [3]. Its origin as a natural disease is lost in prehistory. It is believed to have appeared around10,000 BC, at the time of the first agricultural settlements in northeastern Africa.

Pasteur not only worked on the study of fermentation pathways and the development of sterilization methods for the control of microorganisms but also aimed to prevent the development of diseases in humans by developing vaccines (chicken cholera, rabies) [4]. In 1881, he described the basic paradigm for vaccine development, which included the isolation, inactivation and injection of the causative microorganism. These basic principles have guided vaccine development ever since and during the twentieth century.

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The anti-variola vaccine, on the other hand, started however in 1,100s as variolation, a technique that involved the inoculation of children and adults with dried scab material recovered from smallpox patients. Variations of variolation have been described in Turkey, China, Africa and Europe. Jenner, in 1796, described the use of the heterologous cowpox virus, to obtain, in an eight year´s old child, protection to smallpox. Jenner also succeeded in turning to obligatory worldwide the anti-Variola vaccination. This practice led to the global eradication of the disease in 1966 [4].

Vaccines and antibiotics are therefore, two tools that determined a remarkable revolution of Public Health in XX century. Vaccination is the most effective method of preventing infectious diseases, and widespread immunity due to vaccination is largely responsible for the worldwide eradication of smallpox and the restriction of diseases such as polio, measles, and tetanus from much of the world. The World Health Organization reports licensed vaccines are currently available to prevent, or contribute to the prevention and control of 25 vaccine-preventable infections.

In USA, for instance, where population had access to vaccines and antibiotics, during the first 8 decades of the XX century, the infectious disease mortality rate declined substantially. A total of 797 deaths per 100,000 was recorded in 1900 and only 36 per 100,000 in 1980, consistent with the concept of epidemiological transition from an age of pestilence and famine to an a*ge of degenerative* diseases [5]. Pneumonia, Influenza and Tuberculosis were responsible for the largest number of infectious diseases deaths throughout the century. However, the emergence of AIDS and tuberculosis demonstrated that gain against infectious diseases were not definitive. In high-income countries, 70% of deaths are among people aged 70 years and older. People predominantly die of chronic diseases. Lower respiratory infections remain the only leading infectious cause of death. Only 1% of deaths is among children under 15 years [6].

On the other hand, the global burden of tuberculosis remains enormous in Southeast Asia, Sub-Saharan Africa and Eastern Europe, mainly because of the poor control and high rates of *M. tuberculosis* and HIV co-infection in some African countries. The global case fatality is 23% but exceeded 50% in some African countries with high HIV rates [7]. Every year there are 350–500 million cases of malaria, with 1 million fatalities: Africa accounts for 90 percent of malarial deaths and African children account for over 80 percent of malaria victims worldwide.[8] In low-income countries, nearly 40% of deaths are among children under 15 years and only 20% among people aged 70 years and older. People predominantly die of infectious diseases: lower respiratory infections, HIV/AIDS, diarrheal diseases, malaria and tuberculosis collectively account for almost one third of all deaths in these countries [6].

It has been estimated that vaccination with 7 of the 12 routinely recommended childhood vaccines prevents an estimated 33 000 deaths and 14 million cases of disease in every birth cohort, saves $10 billion in direct costs in each birth cohort, and saves society an additional $33 billion in costs that include disability and lost productivity [9].

While all these evidences strongly stimulated the development of the vaccine industries and of new vaccines, several important problems impeded us from defeating infectious diseases. Among them, we can consider:

Vaccine R&D funded at 10% of which goes to research in therapies [10].

The increased standards of safety regulations applied to vaccines that promoted the evolution from first generation inactivated total germ vaccines to recombinant or synthetic vaccines, which are less immunogenic and demand a more sophisticated industrial technology.

The lack of vaccines based on universal antigens that will exert homologous and heterologous protection and hence, cross-protection to the prevalent variables of all continents.

The lack of vaccines based on conserved antigens that do not show mutagenic variation each new season, and that therefore would not demand annual revaccination.

The increased difficulties in licensing new vaccines. Extensive numbers of Phase II-IIb and Phase III trials are now required before licensing a vaccine. Although these assays disclose very valuable