

## Triumphs and setbacks in the history of knowledge and in the control of infectious diseases: the pressing need to rethink the future

Infectious diseases have in common a biological agent involved in their occurrence. This agent is commonly, albeit not always, microscopic and includes prions, viruses, fungi, bacteria, parasites, or some arthropods. Tuberculosis was the first disease that was found to be associated with an infectious agent, namely *Mycobacterium tuberculosis*. Its discovery by Robert Koch, in the closing years of the 19th century, revolutionized the knowledge of the time, redefining the causal paradigm of diseases, which altered from miasmas to microbes, and made possible subsequent advances, such as the emergence of immunology and the discovery of antibiotics and vaccines<sup>1</sup>.

In the 1960s, the reduction in the occurrence of infectious diseases that had occurred since the beginning of the 20th century in today's developed countries led many to envisage a world free of them<sup>2</sup> and their replacement by chronic diseases<sup>3</sup>. In poor countries, this would occur when they attained the stage of development of rich countries! From this perspective, the Spanish flu pandemic of 1918-1920, which is estimated to have killed 50 million people, was considered an anomaly in this inexorable trend.

From the 1970s onwards, the emergence or recognition of a series of previously unknown infectious diseases was observed. The most important of these was HIV/AIDS, the respective disease and agent thereof were described in the early 1980s. Thus, emerging infections and diseases returned to haunt the world, even in developed countries<sup>4</sup>. After a series of these events, Covid-19 took the world by storm, which, at the apex of the 21st century, seems to hark back to the time of pestilence and plague.

The erratic path taken by the knowledge of infectious diseases and the inability to predict future events has generated consequences, the effects of which continue to have repercussions in the present and, if not corrected, will multiply in the future. The reaffirmation of the microbial theory stimulated the denial of vigorous ideas in the early years of the 19th century, in Europe, around the social determination of diseases<sup>1</sup>. Under the aegis of microbial theory, sanitarians and hygienists developed and applied prevention and protection models that centered on the idea that microbes are always in readiness to attack and must, therefore, be permanently combated. As a result, human protection focuses on clean and aseptic environments, closing off possible contact routes. This model was also stimulated by the then emerging and profitable cleaning industry, which continues to be applied to the present day<sup>5</sup>.

Since the final decades of the 20th century, new evidence has been emerging that challenges the previous model: (a) non-pathogenic agents circulating in nature, when subjected to anthropogenic pressures, can become pathogenic agents; (b) excessive hygiene and consequent lack of contact with "old friends," can be related to the occurrence of several diseases that are manifested by imbalances in our immune system<sup>6</sup>; (c) skin and mucous membranes are inhabited by a complex microbial flora with important functions in our life and health<sup>7</sup>; (d) in order to flourish fully, this microbiome needs to be embedded in environments with a high degree of biodiversity<sup>8</sup>.

In essence, pathogens are just a tiny part of the complex of microbes that exist in nature; and if, on the one hand, the centuries-old war against them had great successes; on the other hand, it isolated us from the requisite microbial biodiversity. Moreover, predatory human actions on nature trigger the emergence of new pathogens. Therefore, the study of infectious diseases and their agents must be based on a broad framework that understands them in their complex relationships with nature and society and, ultimately, removes them from the exclusive domain of the biomedical and clinical sciences.

Mauricio L. Barreto (<https://orcid.org/0000-0002-0215-4930>)<sup>1</sup>

<sup>1</sup> Centro de Integração de Dados e Conhecimentos para Saúde, Fiocruz. Salvador BA Brasil.

## References

1. Barnes DS. Historical perspectives on the etiology of tuberculosis. *Microbes Infect* 2000; 2(4):431-440.
2. Cockburn A. The evolution and eradication of infectious diseases. Baltimore: Johns Hopkins Press; 1963.
3. Omran AR. The epidemiologic transition. A theory of the epidemiology of population change. *Milbank Mem Fund Q* 1971; 49(4):509-538.
4. Institute of Medicine. *Emerging infections: microbial threats to health in the United States*. Washington: National Academy Press; 1992.
5. Hoy S. *Chasing dirt: the American pursuit of cleanliness*. Oxford: Oxford University Press; 1996.
6. Goerner F, Bourdet-Sicard R, Brandtzaeg P, Gill HS, McQuirk P, van Eden W, Versalovic J, Weinstock JV, Rook GA. Mechanisms of disease: the hygiene hypothesis revisited. *Nat Clin Pract Gastroenterol Hepatol* 2006; 3(5):275-284.
7. Cho I, Blaser MJ. The human microbiome: at the interface of health and disease. *Nat Rev Genet* 2012; 13(4):260-270.
8. von Hertzen L, Beutler B, Bienenstock J, Blaser M, Cani PD, Eriksson J, Färkkilä M, Haahtela T, Hanski I, Jenmalm MC, Kere J, Knip M, Kontula K, Koskenvuo M, Ling C, Mandrup-Poulsen T, von Mutius E, Mäkelä MJ, Paunio T, Pershagen G, Renz H, Rook G, Saarela M, Vaarala O, Veldhoen M, de Vos WM. Helsinki alert of biodiversity and health. *Ann Med* 2015; 47(3):218-225.

