OPINION ARTICLE

THE TRUE NATURE OF ZOONOSES: THE IDENTITY OF TRANSMISSIBLE DISEASES IN MAN AND IN OTHER VERTEBRATES

Fernando Dias de Avila-Pires1

There appears to me a strong analogy between the same infection or contagion producing the same result, or one closely similar, in two distinct animals, and the testing of two distinct fluids by the same chemical reagent. (Darwin, 1871)

ABSTRACT

This paper argues the nature and identity of diseases as they affect man and other vertebrates, and its importance when selecting animal models for experimental laboratory research (Russell et al., 2017). Here I stress the notion that in the case of the zoonoses, what is transmitted are parasites/microorganisms and not diseases, as the same microorganism may cause distinct clinical symptoms and signs in different hosts.

KEY WORDS: Diseases; zoonoses; animal models; medicine; history.

This article discusses the nature and the assumed identity of diseases that affect man and other vertebrates. In addition to philosophical aspects, this question has a paramount implication when choosing an animal model for the laboratory investigations of human transmissible diseases. My preliminary question is: *Was Darwin right*? Do microorganisms that infect different species of hosts *cause the same disease in all hosts*? What when the signs and symptoms are different in distinct hosts? What is being transmitted?

Disease transmission depends upon the nature of symbiotic relationships among organisms, as parasitism, commensalism, inquilinism, mutualism, and foresia (Dubos, 1965; Whitfield, 1979; Boucher, 1985, Sapp, 1994). Although association is a rule in nature, not an exception, it took a long time in the history of biology before a true understanding of the relationships of animals, plants, and microorganisms, was achieved. We must realize that microbial life became known only after the invention of the microscope in the 17th Century.

Received for publication: 4/8/2017. Accepted: 14/8/2017.

 $^{1.\} Senior\ Researcher, Department\ of\ Tropical\ Medicine,\ Instituto\ Oswaldo\ Cruz,\ FIOCRUZ,\ RJ.\ E-mail:\ favila@matrix.com.br$

For the ecologist, the study of transmissible diseases became a special chapter in the investigation of the relationships between microorganisms and their hosts. In medical terms, the association of an animal with its symbiotic microbiota is an *infection* - the use of *infestation* for helminthes and ectoparasites, is to be forsaken. *Infection*, usually associated with *disease*, has a different meaning in biology (Avila-Pires, 1983). As to the different types of interactions among animals, Darwin dwelt mostly upon the agonistic aspects, as predation and competition leading to natural selection, while cooperation took longer to be investigated (Allee, 1951; Dugatkin, 1997).

The role of microorganisms as the pathogenic agent of transmissible diseases was hardly recognized and understood before the works of Pasteur and Koch, late in the 19th Century. It was only in 1860 that Louis Pasteur began to apply the results of his investigations on fermentation and putrefaction to the study of infectious diseases and to develop the concept of virulence. In spite of the experiments performed by Pasteur, Koch, and those of Claude Bernard upon non-human animals; the notion of the identity of the animal diseases and the diseases of men rested, for most of the 19th Century, upon the philosophical arguments concerning the place of man in the natural world and in the belief in special creation versus organic evolution (Huxley, 1863 and 1867). From then on, modern medical parasitology and microbiology came of age (Kruif, 1926; Cox, 2002).

After Pasteur established the principle of unicausality, meaning that one germ causes a single specific disease, and showed that infectious diseases were caused by biological entities, several authors, among them Friedrich G.J. Henle and Heinrich H. Robert Koch established the criteria for the identification of a specific germ as the causative agent of a particular infectious disease. (King, 1952; Evans, 1976; Carter, 1985; Grimes, 2006; Ulmann, 2007). Although opening a new era for biology and modern medicine, the ideas of Pasteur and Koch were undoubtedly deterministic, and several contemporaneous authors showed cases where the presence of a parasite was not sufficient to provoke a clinical disease, beginning with tuberculosis itself. Different hosts show distinct reactions to an infection, from a clinical disease to asymptomatic tolerance. *Myxoma* virus is a good example: it causes skin tumors in Syvilagus, a deadly one in *Oryctolagus* and no symptoms in human hosts.

The host as a filter

The theory of evolution is based upon the fact that individuals in a population show genetic and resulting phenotypic variations. With the exception of identical twins, no two individuals of the same species are identical. Individual variation is a key to survival of a species when environmental conditions change – the internal environment of the host, in the case of endoparasites. Distinct hosts offer different conditions for the

successful colonization by the same parasite. Those conditions select different lineages (alleles) of parasites of the same species. That is the case of the malaria parasites *Plasmodium simium* and *P. vivax* (Lim, 2005) historically considered to be distinct species, *P. simium* parasitizing non human primates, and *P. vivax*, our own species.

The elusive concepts of Health and Disease

Disease is generally – and loosely – defined as a physiological, genetic, traumatic, psychological, behavioral or mental pathological condition that affects an organism and/or its performance. Clinically verified, objective signs, and individual subjective symptoms are combined to reach a diagnosis.

Illness is a term with special anthropological and sociological connotation. Illness, sickness, impairment, disability, and handicap were aptly discussed by Susser (1990), in the light of a WHO (1980) document, and of Sigerist (1929) and Parsons (1951) theories of disease and social roles. They are not of our concern in this article.

In this paper, we are concerned only with transmissible diseases.

The definition of *health* adopted by WHO (1948) was repeated in the Declaration of Alma-Ata (1978), and paraphrased in Redl & Wattenberg's (1951) definition of psychological adjustment: "...adjustment ...means the 'ability of an individual to live harmoniously with his environment - physical, social, intellectual, and moral..." and describes a condition seldom –if at all – reached by any individual of any species, any time. In daily practice, health is tacitly and loosely defined as the absence of declared disease and the occasional difficulty or impossibility of performing normal physical or social functions.

As I showed elsewhere (Avila-Pires, 1998; 2001 and 2008), pathological lesions are structures that may be identified in fossil plants and animals that lived before the appearance of *Homo sapiens* upon the earth. They may be the result of external causes, as fractures, or of degeneration, or due to an infection. Diseases and the diseased are situated at different levels of complexity: the diseased is an individual affected with a pathological lesion or impairment, while diseases are theoretical constructs or abstractions with different meanings in different epochs and for different contemporaneous societies, cultures and sub-cultures. They are composite categories, constructed from the collected observations of individual cases or episodes. In a text book, the description of the signs and symptoms of a disease usually stress individual variations by stating: *in most cases*, *the virus may cause*, *there could be*, and such qualifying observations. They are as artificial and composite as the schematic drawings of organs and systems in textbooks.

Chagas disease offers a good example. Carlos Chagas described originally a disease he named *parasitic thyroiditis or myxedema*. This construct, based on faulty observations that combined signs and symptoms of distinct pathological conditions evolved in the following years to a recognizable parasitic infection in humans and non-human hosts by a protozoan, *Trypanosoma cruzi*.

Causation and disease: Pasteur's principles and Henle-Koch's postulates. Who gave what to whom?

As a result, distinct parasite variants may cause the same *clinical disease*, meaning conditions presenting the same signs and symptoms, and the same *parasite* may provoke different disease signs and symptoms in the same host species.

This must be the first and foremost consideration when choosing laboratory animals for the investigation of human diseases and for test of new drugs, as many infectious diseases that affect present day humans have disappeared from their original non-human hosts (Russell et al., 2017).

Transmissible diseases in man and in other vertebrates: the zoonoses

In 2015 I discussed the historical origins of the concept of zoonoses, as those diseases that affect men and other vertebrates (Avila-Pires, 2015). This concept has been erroneously credited to Rudolf Virchow, but it was firstly used in the present sense in a book published by Probstmayer (1863).

But we must ask if a disease is the same one in distinct hosts, human and non-human, or even in different individuals, as questioned by Sournia & Ruffié (1984) and Delaporte (1998). Do armadillos as *Dasypus* spp or marsupials as *Didelphis* spp suffer from Chagas disease? Do they present the same signs as humans? Romaña sign, for instance? And what about schistosomiasis, where the parasite infects *Didelphis* but no eggs are eliminated with the stools? *Myxoma* virus causes a deadly disease in rabbits but is harmless in man; several diseases affecting only our species, acquired from other mammals in prehistoric times, lost the ability to infect their original hosts.

As previously implied, the limits of variation in signs and symptoms presented by different individuals are contemplated in the description of each disease catalogued in ICD-10 (International Classification of Diseases). As with the identification of plant and animal species, experts rely on those *diagnostic* characters that allow them to distinguish between closely related or superficially similar kinds, whether species or diseases.

So, what circulates between man and other vertebrates are *parasites*: viruses, fungi, bacteria, protozoans, helminthes – not *diseases*, if we define diseases on the basis of signs and symptoms.

ACKNOWLEDGMENTS

Many thanks to François Delaporte, philosopher, sociologist, historian, and a good friend, for time and again arguing about the reality of diseases. To Adriana, for reading and commenting on the manuscript.

REFERENCES

- Alma-Ata. Declaration of Alma-Ata. International Conference on Primary Health Care, Alma-Ata, USSR, 6-12 September 1978. Available in http://www.who.int/publications/almaata_declaration en.pdf
 Consulted in March 23, 2017.
- 2. Alee WC. Cooperation among animals. Henry Schuman, New York, 1951.
- 3. Avila-Pires F. Princípios de Ecologia Humana. UFRGS/CNPq: Porto Alegre/Brasília, 1983.
- Avila-Pires FD. Medical ecology, holism, and circular reasoning in medicine. *In*: Susanne C, Gallé L. *Ecotechnies and sustainable development*. Officina, Szeged, 1998. p 215-218.
- Avila-Pires FD. On the concept of disease. Revista de Historia & Humanidades Medicas 4: 1-18, 2008.
- Avila-Pires FD. Saúde, doença e teoria de sistemas. Actas 1º Congr Luso-brasil Hist Ciên Técn, Universidade de Évora, 2001. p 606-614.
- Avila-Pires FD. Doenças humanas e doenças de outros animais: origem do conceito de zoonose. Ecologias Humanas 1: 41-48, 2015.
- 8. Boucher D. The biology of mutualism. Croom Helm, London, 1985.
- 9. Carter KC. Koch's postulates in relation to the work of Jacob Henle and Edwin Klebs. *Medical History* 29: 353-374, 1985.
- 10. Cox FEG. History of human parasitology. Clin Microbiol Rev 15: 595-612, 2002.
- 11. Darwin CR. *The descent of man*. John Murray: London. 1871. Available in http://darwin-online.org.uk/content/frameset?pageseq=1&itemID=F937.1&viewtype=text Accessed in May 2, 2017.
- 12. Delaporte F. La nouveauté en pathologie in Vers des nouvelles maladies. Paris, Puf, Paris, 1998. p 9-37.
- 13. Dubos RJ. Man adapting. Yale University Press, New Haven, 1965.
- Dugatkin LA. Cooperation Among Animals: An Evolutionary Perspective. Oxford University Press, Oxford, 1997.
- 15. Evans AS. Causation and disease: the Henle-Koch postulates revisited. *Yale J Biol Med 49*: 175-195, 1976.
- 16. Grimes DJ. Koch's postulates: then and now. Microbe 1: 223-228, 2006.
- 17. Huxley TH. On the zoological relations of Man with the lower animals. *Natural History Review 1*: 67-84, 1867.
- 18. Huxley TH. Evidence as to man's place in nature. Williams and Norgate, London, 1863.
- 19. King LS. Dr. Koch's postulates. J Hist Med Allied Sci 7: 350-361, 1952.
- 20. Kruif P. Microbe hunters. Blue Ribbon Books, New York, 1926.
- 21. Lim CS, Tazi L, Ayala FJ. *Plasmodium vivax*: Recent world expansion and genetic identity to *Plasmodium simium. PNAS 102*: 15523-15528, 2005.
- 22. Parsons T. The social system. The Free Press, Glencoe, 1951.

- 23. Probstmayer W. Etymologisches Wörterbuch der Veterinärmedizin und ihrer ilfswissenschaften. Verlag von Jul, Gubert: München. 1863.
- 24. Redl F, Wattenberg W. *Mental hygiene in teaching*. Hancourt, Brace & World, New York, 1951
- Russell JJ, Theriot JA, Sood P, Marshall WF, Landweber LF, Fritz-Laylin L, Polka JK, Oliferenko S, Gerbich T, Gladfelter A, Umen J, Bezanilla M, Lancaster MA, Shuonan He, Gibson MC, Goldstein B, Tanaka EM, Hu CH, Brunet A. Non-model model organisms. *BMC Biology* 2017: 15:55, 2017.
- Sapp J. Evolution by association: a history of symbiosis. Oxford University Press, Oxford, 1994
- 27. Sigerist H. The special position of the sick. In: Roetner MI, Henry E. Sigerist on the sociology of medicine. MD Publications, New York, 1929. p 9-22.
- 28. Sournia JC, Ruffié J. Les épidémies dans l'histoire de l'homme. Flammarion, Paris, 1984.
- Susser M. Disease, illness, sickness; impairement, disability and handicap. Psych Med 20: 471-473, 1990.
- Ullmann A. Pasteur-Koch: Distinctive ways of thinking about infectious diseases. *Microbe* 2: 383-387, 2007.
- 31. Whitfield PJ. *The biology of parasitism: an introduction to the study of associating organisms*. Edward Arnold. London. 1979.
- 32. WHO. 1948. Preamble to the Constitution of the World Health Organization as adopted by the International Health Conference, New York, 19-22 June, 1946; signed on 22 July 1946 by the representatives of 61 States (Official Records of the World Health Organization. n. 2 p. 100) and entered into force on 7 April 1948. http://www.who.int/governance/eb/who_constitution en.pdf> Accessed in May 2, 2017.
- 33. World Health Organization. *International classification of impairments, disabilities and handicaps*. WHO, Geneva, 1980.