

Medical Ecology

Fernando Dias de Avila-Pires

INTRODUCTION

In 1866, Ernst Haeckel, a German biologist, proposed the name ecology for the study of the relationships between organisms and environment, then known as the balance or the economy of nature (Avila-Pires, 1999b). At that time, Lamarck in France, and Darwin in England, defended distinct mechanisms for biological evolution. Lamarck accepted the inheritance of body parts alterations in response to both external physical environmental factors and internal urges to satisfy new needs and demands. Darwin laid more emphasis on the natural selection of individual variations and, although recognizing the influence of physical factors in evolution, defended the notion that morphological, physiological, and behavioural adaptations gave an organism an edge to survive and to leave viable offspring.

The ensuing arguments concerning the relative importance of the physical environment versus biotic relationships as the main forces acting upon biological evolution resulted in a growing accumulation of ecological lore (Stauffer, 1957).

In 1935, Tansley, an English botanist, defined the ecosystem as the basic unity of the ecological trophic structure of biotic communities. The balance of nature acquired a new meaning, distinct from the simplistic creationist interpretation of Biberg and Linnaeus, in the XVIIIth century, providing the field of ecology with a theoretical model, based on the recycling of nutrients and transfer of energy.

The building of the ecosystem concept had to wait for contributions from chemistry, physics, plant nutrition, photosynthesis, and the elucidation of the processes of synthesis and decay of organic matter. In the XVIIth century, the phenomenon of corruption and the subsequent reorganization of living matter occupied the minds of, and defied explanations from naturalists and philosophers alike (Jacob, 1970; Delaporte, 1979). It had to wait two centuries for the answer.

The German chemists Wöhler and Liebig were responsible for fundamental advances in their own field and for the birth of organic chemistry. Indirectly, they made possible the notion of ecosystem ecology. Wöhler synthesized the first organic compound, urea

(Ramberg, 2000). Liebig elucidated the mechanism of the organic matter synthesis by plants, later detailed by Krebs, and established the foundations of scientific agriculture (Rossiter, 1975). Primary production stands at the first level of an ecosystem, and the organization of mineral radicals and compounds into organic matter is the basic echelon of the trophic chain.

Prominent chemists in the XIXth century defended the theory that putrefaction was a chemical phenomenon. It would be one of their ranks to explain it otherwise, as a biological process. Pasteur began by trying to learn why milk spoil, and what happens during the process of cereals fermentation to make beer, and of grapes, to produce wine. Through a series of famous experiments, Pasteur discovered that yeasts performed the destruction of organic matter, and furthermore that this was a necessary condition for the maintenance of life upon the Earth. In this context he delineated, in 1867, what we nowadays call the biogeochemical cycle:

"It is absolutely necessary that the constituting matter of living beings return, after death, to soil and atmosphere, as mineral or gaseous substances, like water vapour, carbon dioxide, ammonio, nitrogen, elementary traveling principles that atmospheric movements can transport from one pole to another and in which life can sprout the elements of its endless perpetuity. It is mainly through actions of fermentation and slow combustion that the natural law of dissolution and return to the gaseous state of everything that has lived is accomplished. [...] its elementary principles, carbon, hydrogen and oxygen retake the form under which they are ready to reenter a new cycle of life (Pasteur, 1867)."

Contributions from the French physiologist Claude Bernard, lifelong friend of Pasteur, were of fundamental importance for the theory of trophic relations. In 1854, during his second lesson on general physiology at the Faculty of Sciences of Paris, Bernard stated that nutrition is a fundamental property of all living beings, animals and plants; he defined it as a property of living molecules to attract and incorporate other molecules from the environment (Grmek, 1997). Furthermore, we owe him the concepts of the internal and external environments (Avila-Pires, 1978; Grmek, 1967).

Ecology at the level of the community, or synecology, owes much to the concept of plant formation and to phytogeography but it only became a field of its own early in the XXth century, when integrated researches in animal and plant ecology became routine.

MEDICAL ECOLOGY

Although the natural sciences, and particularly botany, were taught at medical schools until the first decades of the XXth century, the reverse did not happen, and the study of diseases fell outside the concerns of early ecologists. The field of medical ecology evolved along two main lines. One, which we must recognize as protoecological, has its roots in the Hippocratic correlation of health and the elements and factors of the physical environment, as he detailed in his famous discourse on airs, waters, and places. Unfounded and spurious beliefs linking meteorological conditions and disease, survives and are still widespread nowadays. The other line derived from modern concepts of general ecology, and arose after the discovery of the vectors of infectious and parasitic diseases (Avila-Pires, 1974; Avila-Pires, 2000).

Parasites are known since early times but many had to wait for the invention of the microscope to be identified, and most were described only after the XVIIIth century, when the field of parasitology was born. (Avila-Pires, 1998). The role of internal parasites was disputed until late in the XIXth century, many authors favouring the idea that they acted as sanitary agents, cleansing the intestines. In the *Origin of Species*, Darwin suggested that parasitic worms, thanks to the facility of contagion, could act as limiting factors of population growth by causing limited epidemics, a notion he maintained in successive editions of the *Origin*.

A long way separated those early conceptions from the advanced views of endogenous ecology of René Dubos (1965), where indigenous microbiota are endemic, and alterations in the internal environment or in the balance of populations is the cause of disease.

Louis Pasteur's contributions to the foundations of scientific medicine opened a new venue for the understanding of the disease's mechanism but delayed the outcome of medical ecology. His demonstration of the theory of infections' specificity and their microbial origins, coupled with the advent of vaccines, led medical doctors and researchers to a hunt for pathogenic agents of diseases and to the simplistic

belief that the threat posed by infections could be eliminated in the near future.

Medicine had been reduced, in the expression of one of its sarcastic critics, to one ill, one pill, one bill. But it gave a mortal blow to the miasmatic theory, and to the climatic determinism, of diseases.

After the Second World War, speed in travel and communications shrank the world and ended the apparent safety afforded by the limited geographical isolation of affluent communities. At the same time, the rapidly accumulating knowledge on infectious diseases and disease transmission began to profit from the advances in ecological thinking, and in the development of ecological methods (Hoogstraal 1956; Carmichael, 1952; Audy, 1958a; Audy, 1958b; Heisch, 1956; Abdusalam 1959), following a pioneer work by Strong (1935). The study and control of diseases could no longer be reduced to the identification of pathogenic organisms in a petri dish, under a microscope.

The ecology of diseases had thus to wait for the realization that there were other important intervening environmental factors in the complex equation of disease causation. Together with the survival of the old notion of the climate determining influence upon health and disease, social and cultural aspects were discounted as important factors of risk.

The circumstance that led to a new way of looking at this issue was the discovery of the part played by vectors in the biological cycles of infectious diseases.

François Delaporte (1986) remarked that the discovery of the role of vectors, at the end of the XIXth century, required, and at the same time imposed, a profound modification in the way we looked at diseases and at disease transmission.

As a young medical doctor working for a British enterprise in China, Patrick Manson was struck by the number of people he saw deformed by elephantiasis (Manson, 1877; Manson, 1878). After a series of incidents in which his very life was threatened, he succeeded in discovering the microfilariae in the blood of infected persons and in dogs. Calculating that an infected dog might harbour up to two million microfilariae in its circulatory system, he realized that before reaching one hundredth of the weight of an adult worm they would weight more than their host. He aptly concluded that the first stage in the natural history of the haematozoan was in the blood, but the nest should be in the animal that fed on that fluid. Following that line of reasoning, Manson tested and proved his hypothesis by examining mosquitoes that fed on one of his patients. The elucidation of the

biological cycle of the filaria worm led him to several important deductions. Manson demonstrated the necessary coincidence of the distribution areas of vectors and of the diseases they transmitted. He went on to explain that the limited geographical distribution of the mosquito vector was the reason why elephantiasis was endemic only in tropical and subtropical climates. He showed a correlation between the presence of microfilariae in peripheral blood vessels and the circadian cycle of activity of vector species, and suggested that the disease could be controlled indirectly through the control of the vector populations.

Veterinarians, used to the practice of collective health assays, had a more epidemiological approach to disease. Theobald Smith, inspired by Laveran's discovery of microorganisms living inside the red corpuscles of the blood of persons suffering from malaria, went on to unravel the complex cycle of the piroplasma, involving ticks as vectors, responsible for the Texas cattle fever in the United States (Smith and Kilborne, 1893). It gave rise to the first campaign in history to eradicate a vector in order to control a disease.

In India, Ronald Ross, an army surgeon and a student of Manson, was engaged in the search for the malarial vector. In 1892, Manson had linked different forms of the parasite to clinical symptoms of the disease, and believed that mosquitoes became infected when feeding on malarial patients. But he also believed that the transmission depended on mosquitoes dying in water and the parasites being released, to infect whoever drank it. Being no taxonomist, Ross was trying to identify the vectors among mosquitoes of the wrong family. Transferred to a malaria-free region, Ross turned to the study of the parasites in birds and eventually demonstrated the real path of transmission, involving culicid mosquitoes. In Italy, the zoologist Grassi worked with the same objective, but following a different line of inquiry. He repeated the method used by Snow for cholera, Simond for plague, and Finlay for yellow fever. Grassi did no preliminary laboratory research, but mapped malarial villages in the Mediterranean region and compared the lists of mosquito species found in each one of them, and those found in malaria-free areas. While Ross demonstrated the role of vectors in the transmission of bird malaria, Grassi concluded, a few months later, that *anopheles maculipenis* was the vector for human beings in Europe (Peller, 1967). But for medical ecologists, the story did not end with the concession of a Nobel Prize to Ross, and with Grassi's discoveries. Many

years later, discrepancies in the distribution of malaria cases in relation to the presence of *anopheles maculipenis* gave rise to a beautiful study that linked taxonomy and ecology and showed that *anopheles maculipenis* was, in reality, a polytypic species (Hackett and Missiroli, 1935; Thorpe, 1940) and not all subspecies were vectors of malaria.

In terms of medical ecology though, the discovery by Adolfo Lutz in 1898 (Lutz, 1903), regarding the association of certain malaria parasites with bromeliad plants in Brazil was more rewarding, as it disclosed a network of relationships involving the biotic and abiotic factors in a complex microecosystem.

Another line of inquiry was inspired by the advances in plant and animal geography. The Swiss Henri C. Lombard (1877-1880) explained in great detail his own ideas about the climatic origin, distribution, and seasonality of diseases. After a discussion on the effects of cold, heat, humidity, drought, air currents, ozone, electricity and magnetism upon the organism, he went on describing the characteristic health conditions of each season. For him, the diseases prevailing in each season in Europe, are those of a corresponding zone of the Earth. Hyperemia and respiratory diseases, common in winter, would be the prevailing ones of the polar regions; parasitic infections, in the tropical belt; anemia in the fall, and plethoria in the spring. Lombard recognized a direct correlation between seasonal diseases and those resulting from geographical circumstances. As Humboldt had stated, altitude corresponds to latitude, as far as the distribution of plants and animals is concerned.

In the XXth century medical ecology became a discipline in its own right.

While epidemiologists searched for the origin and distribution of diseases, and focused on a human population, medical ecology directed its attention to the relationships of biotic and abiotic environmental factors in a pathocenosis. But to succeed, both had to investigate the network involving hosts, vectors, microorganisms, and their ecological relations in all trophic levels. Karl Meyer (1942), one of the pillars of modern medical ecology, describing the ecology of plague, aptly recognized that it is fully realized that the epidemiology of the world rodent disease - the effect of the plague bacillus on the rodent herd - is far more important than the data on human cases.

Of the great epidemic scourges that had a lasting impact upon the humanity, plague is noted for having had a profound influence upon medicine, the arts, religions, and on the weakening of social

and cultural institutions. After the experiments performed in India and published in 1898 by Simond, implicating rats and fleas in the plague transmission, researchers began to look for alternative hosts and reservoirs of *Yersinia pestis*. In April 1911, an international conference was held in Mukden, by invitation of the Chinese government, and the outbreaks of 1910-1911 were scrutinized. One of the participants was R.P. Strong, who, in 1935, was to publish a seminal paper on the ecology of diseases. A Chinese researcher, Wu Lien Teh was in charge of field investigations, and published a number of papers on the role of tarabagans as reservoirs. R. Pollitzer accompanied him and later became one of the pioneers of medical ecology.

In 1925, Charles Elton became interested in the subject and published a paper on the role of plague as a regulating factor of wild mammal populations. He was then interested in the causes of fluctuations of natural populations and in ascertaining the role of climatic cycles and of predation as the main determining factors (Elton, 1924; Elton, 1925).

In 1927, Elton published a text book on general ecology, incorporating his knowledge of disease as an ecological factor.

Russian authors were by then involved in the study of the coincidence of zoonoses and certain aspects of their geographical environment. In 1939, Pavlovsky published his theory stating that the problem of natural natality should be worked out on the basis of zoological, paraistological and ecological studies combined with projects of a microbiologic character and with the participation of epidemiologists.

From 1930 to 1940, a number of projects were engaged in applying ecological research tools to the study and understanding of disease patterns, as for instance, those of Hackett (1937) for malaria in Europe, and Davis (1945) for yellow fever, in Brazil.

After the Second World War, medical ecology grew in status and importance (Dubos and Schaddler, 1964; Dubos, 1965; Dubos, 1968; Sladen and Bang, 1969; Schwabe, 1968; Le Riche and Milner, 1971; Fiennes, 1978; Croll and Cross, 1983).

We owe the modern ecological concept of health as a homeostatic adjustment between an organism and the physical and biotic environment where it normally lives, to J. M. May. In 1958, and again in 1961, he stated that from the ecological point of view, disease is very simply that alteration of living tissues that jeopardizes their survival in their environment.

In the ecological context, infection is the result

of invasion or colonization of a microhabitat in a host organism by symbiotic microorganisms. Veterinarians contributed to endogenous ecology through the investigation of ecological succession and microbial ecosystems in the rumen of ruminants, and studies of the colonization of the human gastrointestinal tract opened a new field of investigation (Sack, 1969).

Infectious diseases, and in special those that involve complicated life cycles with free-living stages and alternation of vertebrate and invertebrate hosts, are of particular interest to ecologists. For them, human and animal patients, as well as infected plants, are ecological indicators. The real focus of interest lies in the unraveling of the relationships of all the elements interlinked in a complex network that results in a disease.

Schistosomiasis provides a good example (Bang, 1969; Dias et al., 1978). For many years it was considered a human infection. The report of introduced monkeys found naturally infected in the Antilles was treated as a freak exception. During the early 1950's, field researchers in Africa and in Brazil published the discovery of wild rodents with the parasites. For the next twenty years, reports of new findings appeared in the medical literature, identifying over one hundred and fifty species of distinct mammalian families and orders as natural hosts. The question of the importance of non-human reservoirs in the maintenance of endemic schistosomiasis, of the possibility of animals spreading the infection to schistosome-free localities, and of their actual contribution to the epidemiology of the disease could not be addressed without a field investigation applying the proper ecological methods. Those methods involved the estimation of the size of several species' wild populations, the study of their natural patterns of behaviour, their territories, movements and home ranges, longevity, food preferences, preferred sites for the deposition of excreta, and responses to human presence and activities. Similar studies had to be made for the intermediate snail hosts. Physical aspects of the environment had to be determined, and the tolerance levels for the larvae, young, and adults of all species concerned had to be established. In water, velocity of flux, pH, temperature showed to be all important ecological factors, as was sunlight. The number of viable eggs of schistosomes excreted by terrestrial hosts that could reach water collections with snail hosts, had to be compared with the contribution from humans to establish their relative importance in the epidemiology of the disease. Long term controlled

experiments had to be made to see if the parasite cycle could be maintained in the absence of human hosts. Complex ecological models have been built to try to estimate risk. They require the evaluation of the chances that eggs of a parasite in the faeces of a land mammal have to eventually reach the water, in condition to infect a snail host, and of all the stages in the life of the parasite to be eventually completed.

ENVIRONMENTAL HEALTH AND SOCIAL RESPONSIBILITY

During the XIXth century a growing concern with the protection of natural habitats led to the establishment of the first national parks in the United States. It represented a new way of looking upon nature, distinct from the logic of the preservation of strategic resources as trees for the building of ships, or game for royal hunts, originated in the Middle Ages. An international movement in response to the warnings of natural scientists, concerned with the threat of extinction of animal and plant species, led to the adoption of laws for the control of hunting, fishing, and the over-exploitation of natural resources around the world and to the creation of the International Union for the Conservation of Nature, later re-named to include Natural Resources. Preservation of habitats evolved into the concept of conservation, or rational use of nature, and recently to that of sustainable development (Avila-Pires et al, 2001). A series of international conferences took place after 1960 (Avila-Pires, 1999a) and thirty years later, in 1992, a summit meeting was held in Rio de Janeiro where the Agenda 21 was drafted and adopted. The inventory of the Earth's biodiversity, an old concern of naturalists and taxonomists became a major preoccupation of governments, thanks to the medical and drug industries.

The modern conception of the biosphere - a name coined in 1875 by Suess, who credited his inspiration to XIXth century's proto-geochemistry of Lamarck - was re-defined by Vladimir Vernadsky (1929), to incorporate the cycles of elements on the Earth's crust. After WW2, the notion of interdependence of living beings and the physical environment gave also rise to the popular movement known as ecologism. Its roots are found in the collective fearsome realization that the Earth was vulnerable and we had the responsibility of leaving a clean environment to our heirs. Atomic bombs, pesticides, pollutants, solid wastes and gaseous emissions could jeopardize the survival of the human race. A popular book by Rachel Carson published in

1962 catapulted medical (or health) ecology from the laboratories to the media. It popularized ecological ideas and originated the concept of environmental health, or health of the environment. Radiations, heavy metals, dumps of radioactive materials, solid waste, polluted water from ponds to oceans, are some of the subjects that became a matter of concern of both scientists and lay people. Theories concerning global warming and climate change became popular subjects in newspaper and magazine articles, news bulletins, conferences, and TV interviews. They are nowadays the subject of complicated international negotiations and the object of agreements, disagreements, and treaties.

A few examples of the growing literature on those subjects are enough to show how important and multivariate they became, and a search at any bibliographic database will disclose dozens, or hundreds of books on each one of them.

A symposium on environmental geochemistry in health and disease took place in 1968 (Cannon and Hopps, 1971). Hinckle and Loring (1979) presented an overview, by several contributors, of the factors in the physical and social components of the residential urban environment that bears upon health, injury and disease. A growing literature on a related topic, development policies on health, was reviewed by Weil et al. (1990). The relationships between health and environment in sustainable development, a concept that arose at the Rio Conference of 1992, was analyzed in a document published by the World Health Organization in 1997. Environmental epidemiology was the subject of a guidebook published by the International Programme on Chemical Safety (1983). A methodology for the preparation of integrated studies on health and environment impact assessment was published by the British Medical Association in 1999. The disputed and complex subject of climate change and human health was covered in a book by McMichael et al. that appeared in 1996. A report by a commission of the World Health Organization encompassed most, if not all, aspects of the problem, in *Our planet, our health* (WHO, 1992).

In spite of the remarkable progress in our understanding of the relationships between human and animal health and our environment, and the generalized concern with the impact of human actions upon the biosphere, a widening gulf separates the approach of scientific medical ecology from an ideal conception of our planet, where nature is seen as perfect, stable, ordained, equilibrated, and healthy. A growing number of ONGs, with support from the

media, spreads such ideal vision of the biosphere, while an increasing number of individuals seek comfort in alternative methods of treatment for real or imaginary health problems. Some of those methods are transplanted from ancient practices, divorced from their cultural settings, and used outside their original contexts. Social relativism and post-modern philosophies have their part of responsibility in this.

The science of ecology, based upon solid scientific foundations has a virtual mirror image which reflects a maze of false beliefs and half-truths interwoven with ideological questions expressed in a politically correct and pseudo-ecologic discourse.

It is a social responsibility of medical ecologists to put this picture right.

KEYWORDS Ecology of Diseases. Environmental Health. Conservation

ABSTRACT The science of ecology, based upon solid scientific foundations has a virtual mirror image which reflects a maze of false beliefs and half-truths interwoven with ideological questions expressed in a politically correct and pseudo-ecologic discourse. It is a social responsibility of medical ecologists to put this picture right.

REFERENCES

- Abdusalam, M.: Significance of ecological studies of wild reservoirs of zoonoses. *Bulletin of the World Health Organization*, **21**: 179-86 (1959).
- Audy, J. R.: The localization of diseases with special reference to the zoonoses. *Royal Society of Tropical Medicine and Hygiene*, **52** (4): 308-338 (1958a).
- Audy, J. R.: Medical ecology in relation to geography. *British Journal of Clinical Practice*, **12**: 2-10 (1958b).
- Avila-Pires, F. D.: Ecology of infectious diseases. *International Journal of Ecology and Environmental Sciences*, **1**: 109-117 (1974).
- Avila-Pires, F. D.: A contribuição de Claude Bernard à ecologia médica. *Revista da Sociedade Brasileira de Medicina Tropical*, **10** (4): 225-230 (1978).
- Avila-Pires, F. D.: Parasites in history. *Revista de Ecologia Latinoamericana*, **5** (1-2): 1-11 (1998).
- Avila-Pires, F. D.: Tropical forest ecosystems. In: B. Nath, L. Hens, P. Compton and D. Devuyt (Eds.): *Environmental Management in Practice*, 3, 151. Routledge, London (1999a).
- Avila-Pires, F. D.: Fundamentos históricos da ecologia. *Holos, Ribeirão Preto*. 278pp (1999b).
- Avila-Pires, F. D.: Princípios de ecologia médica Universidade Federal de Santa Catarina, Florianópolis. 328pp (2000).
- Avila-Pires, F. D., Mior, L., Aguiar, V. P. and Schlemper, S. R.: The concept of sustainable development revisited. *Foundations of Science*, **5**: 261-268 (2001).
- Bang, F. B.: The ecology of schistosomiasis. In: *Biology of Populations*. B. Sladen and F. Bang (Eds.). American Elsevier, New York, p. 380 (1969).
- Biberg, I. J.: Specimen academicum de Oeconomia Naturae, quod praeside Carolo Linnaeo submittit I. J. Biberg d. IV Martii MDCCXLIX. Uppsala. In *L'équilibre de la nature*, C. Limoges. Paris. J. Vrin, Paris p.57 (1749).
- British Medical Association.: *Health and Environmental Impact Assessment*. Earthscan, London. 243pp. (1999).
- Cannon, H. L. and Hopps, H. C.: *Environmental Geochemistry in Health and Disease*. The Geological Society of America, Boulder. 230pp. (1971).
- Carmichael, J.: Animal-man relationship in tropical diseases in Africa. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **46**: 385-94 (1952).
- Carson, R.: *Silent Spring*, Houghton Mifflin, New York. 304pp. (1962).
- Croll, N. A. and Cross, J. H.: *Human Ecology and Infectious Diseases*, Academic Press, New York. 364pp. (1983).
- Darwin, C.: *On the Origin of Species by Means of Natural Selection or the Preservation of Favored Races in the Struggle for Life*. John Murray, London. 513pp. (1859).
- Davis, D. E.: The annual cycle of plants, mosquitoes, birds, and mammals in two Brazilian forests. *Ecological Monographs*, **15** (3): 243-95 (1945).
- Delaporte, F.: *Le second règne de la nature*. Flammarion, Paris. 242pp. (1979).
- Delaporte, F.: *Disease and Civilization* (MIT Press, Cambridge. 250pp. (1986).
- Dias, L. C., Avila-Pires, F. D. and Pinto, A. C.: Parasitological and ecological aspects of schistosomiasis mansoni in the Valley of the Paraíba do Sul river São Paulo State, Brazil. I. Natural infection of small mammals with *Schistosoma mansoni*. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **72** (5): 496-500 (1978).
- Dubos, R.: *Man Adapting*. Yale University Press, N. Haven. 527pp. (1965).
- Dubos, R.: *Man, Medicine and Environment*. Penguin, Harmondsworth. 173pp. (1968).
- Dubos, R. and Schadler, R. W.: The digestive tract as an ecosystem. *American Journal of Medical Science*, **49**: 267-272 (1964).
- Elton, C.: Periodic fluctuations in the numbers of animals: their causes and effects. *British Journal of Experimental Biology*, **2**: 119-163. (1924).
- Elton, C. S.: Plague and the regulation of numbers in wild animals. *Journal of Hygiene*, **24**: 138-163 (1925).
- Elton, C.: *Animal Ecology*. Sidgwick and Jackson, London. 209pp. (1927).
- Fiennes, R.: *Zoonoses and the Origins and Ecology of Human Diseases*. (Academic Press, London.), 196pp. (1978).
- Grmek, M. D.: Evolution des conceptions de Claude Bernard sur le milieu intérieur. In: *Philosophie et méthodologie scientifiques de Claude Bernard*. E. Wolff and C. Fouchet, Masson, Paris. p. 117 (1967).
- Grmek, M. D.: *Le legs de Claude Bernard*. Fayard, Paris. 439pp. (1997).
- Hackett, L. W. and Missiroli, A.: The varieties of *Anopheles maculipennis* and their relation to the distribution of malaria in Europe. *Rivista di Malarologia*, **14**: 45-109 (1935).
- Hackett, L. W.: *Malaria in Europe: An Ecological Study*. Oxford University Press, Oxford. 336pp. (1937).
- Haeckel, E.: *Generelle Morphologie der Organismen: Allgemeine Grundzüge der organischen Formen-Wissenschaft, mechanisch begründet durch die von Charles Darwin reformierte Descendenz-Theorie*. 2 vols. Georg Reimer, Berlin. 684pp. (1866).
- Heisch, R. B.: Zoonoses as a study in ecology. *British Medical Journal*, **2**: 669-673 (1956).
- Hinckle, L. E. and Loring, W.C.: *The Effect of the Man-made Environment on Health and Behaviour*. Castle House,

- Guildford.), 315pp. (1979)
- Hoogstraal, H.: Faunal explorations as a basic approach for studying infections common to man and animals. *East African Medical Journal*, Nov., 1-8 (1956).
- Humboldt, A.: Essai sur la géographie des plantes; accompagné d'un tableau physique des régions équinoxiales. Par Al. de Humboldt et A. Bonpland, rédigé par Al. Humboldt. Levrault, Shoel, Paris. (1805).
- International Programme in Chemical Safety: *Guidelines on Studies in Environmental Epidemiology* World Health Organization, Genève. 351pp. (1983).
- Jacob, F.: La logique du vivant. Galimard, Paris. 328pp. (1970).
- Lamarck, J. B.: Philosophie zoologique ou exposition des considérations relatives à l'histoire naturelle des animaux. Paris (1809).
- Le Riche, W. H. and Milner, J.: *Epidemiology as Medical Ecology*. Churchill Livingstone, Edinburgh. 460pp. (1971).
- Lombard, H. C.: Traité de climatologie médicale. Comprenant la météorologie médicale et l'étude des influences physiologiques, pathologiques, prophylactiques et thérapeutiques du climat sur la santé. 4 vols, 1 atlas, J. B. Baillière, Paris. vol. 1, 552pp.; vol. 2, 694pp.; vol. 3, 771pp.; vol. 4, 687pp. (1877-1880).
- Lutz, A.: Waldmosquitos und Waldmalaria. Centralblatt für Bakteriologie, *Parasitenkunde und Infektionskrankheiten*, 1, 33 (4): 282-292 (1903).
- Manson, P.: Report on Haematozoa. Medical Reports for the half year ended 31st March, 1877, forwarded by the surgeons to the Customs at the Treaty Ports in China. Customs Gazette, pt 6th, 33, Statistical Department of the Inspectorate General of Customs Customs, 12-39 (1877).
- Manson, P.: Further observations on *Filaria Sanguinis Hominis*. Medical Reports for the half-year ended 30th September, 1877. Shanghai Statistical Department of the Inspectorate General, 2, 2, 14, 1-27 (1878).
- May, J. M.: *The Ecology of Human Disease*. MD, N.Y., 327pp. (1958).
- May, J. M.: *Studies in Disease Ecology*. Hafner, N.Y. 613pp. (1961).
- Mayer, K.: The ecology of plague. *Medicine*, 21 (2): 143-174 (1942).
- McMichael, A. J., Haines, A., Sloof, B. and Kovats, S., (Eds.): *Climate Change and Human Health*. World Health Organization, Genève. 297pp. (1996).
- Pasteur, L. Leçons sur le vinaigre du vin, professé à Orléans le 11 novembre 1867. In Étude sur le vinaigre, sa fabrication, ses maladies, moyens de les prévenir; nouvelles observations sur la conservation des vins par la chaleur. Gauthier-Villiers et Victor Masson, Paris 1968. 3, p.78 (1867).
- Pavlovsky, E. N.: *Natural Nidality of Transmissible Diseases in Relation to Landscape. Epidemiology of Zoonanthroponoses* Moscou. 249pp. (1939).
- Peller, S.: *Quantitative Research in Human Biology and Medicine* John Wright, Bristol. 422pp. (1967).
- Ramberg, P. J.: The death of vitalism and the birth of organic chemistry: Wöhler's urea synthesis and the disciplinary identity of organic chemistry. *Ambix*, 47 (3): 170-195 (2000).
- Rossiter, M. W.: *The Emergence of Agricultural Science: Justus Liebig and the Americans, 1840-1880*. Yale University Press, N.Haven. 275pp. (1975).
- Sack, R. B. The ecology of the gastrointestinal tract. In: *Biology of Populations*, B. Sladen and F. Bang, (Eds.). American Elsevier, N.Y. p.35 (1969).
- Schwabe, C. W.: *Medicina veterinaria y salud publica*. Novaro, México, 896pp. (1968).
- Simond, P. L.: La propagation de la peste. *Annales de l'Institut Pasteur*, 12 (10): 625-687 (1898).
- Sladen, B. and Bang, F. (Eds.): *Biology of Populations*. American Elsevier, N.Y. 449pp. (1969).
- Smith, T. and Kilborne, F. L.: Investigations into the nature, causation, and prevention of Texas or Southern cattle fever. *Bulletin of the Bureau of Animal Industry*, 1: 7-301 (1893).
- Stauffer, R. C.: Haeckel, Darwin, and ecology. *Quarterly Review of Biology*, 32 (2): 138-144 (1957).
- Strong, R. P. The importance of ecology in relation to disease. *Science*, 82 (2127): 307-317 (1935).
- Thorpe, W. H. Ecology and the future of systematics. In *The New Systematics*, J. Huxley. (Ed.). Oxford University Press., Oxford. p.341 (1940).
- Vernadsky, V. I.: *La biosphère*. (Félix Alcan), Paris, 267pp. (1929).
- Weil, D. E., Alicbusan, A. P., Wilson, J. E., Reich, M. R. and Bradley, D. J.: *The Impact of Development Policies on Health. A Review of the Literature*. World Health Organization, Geneva, 165pp. (1990).
- World Health Organization: *Health and Environment in Sustainable Development. Five Years after the Earth Summit*. World Health Organization, Geneva, 242pp. (1997).
- World Health Organization. *Our Planet, Our Health. Report of the World Health Organization Commission on Health and Environment*. World Health Organization, Genève, 282pp. (1992).
- Wu, L.T.: A further note on natural and experimental plague in tarbagans. *Journal of Hygiene*, 22; 329-334 (1924).

Author's Address: Fernando Dias de Avila-Pires, Instituto Oswaldo Cruz, Rio de Janeiro, Brasil Rua Bico de Lacre, 79, 88050-150 Florianópolis, SC, BRASIL
E-mail: favila@matrix.com.br