

REVIEW ARTICLE

**EMBEDDING THE CONCEPT OF PATHOCENOSIS INTO A MULTI-DIMENSIONAL HEALTHCARE MODEL FOR A GLOBAL PERSPECTIVE OF THE HEALTH SCENARIO IN THE 21<sup>ST</sup> CENTURY.**

**Sethuraman KR**

*Faculty of Medicine, AIMST University, Malaysia*

**Corresponding Author**

Prof. Sethuraman K. R.

AIMST University, 08100, Malaysia.

Email: [kr.sethuraman@aimst.edu.my](mailto:kr.sethuraman@aimst.edu.my)

**Abstract**

The 21<sup>st</sup> Century physicians need awareness of the complex linkages between human activities and global health risks resulting from pollution, climate change, and disease outbreaks due to emerging and re-emerging infections. Pathocenosis and anthropocenosis conceptualise these complex linkage. A multi-dimensional healthcare model extends the conventional doctor-patient interaction to include the various factors and linkages, which greatly influence the process and the outcome. A qualitative pilot study among medical interns and resident revealed that the model helped them to go beyond the traditional case based approach to view the individual healthcare problems from a global and holistic perspective.

**Keywords:** Pathocenosis, anthropocenosis, global perspective, anthropogenic health crisis

*“We must connect the dots between climate change, water scarcity, energy shortages, global health, food security and women's empowerment. Solutions to one problem must be solutions for all.” – Ban Ki-moon, Secretary-General of the UN (2011)*

## Introduction

This review attempts to highlight why the students of Medicine and other healthcare professions, who will have to face more pandemics and health crises in the 21<sup>st</sup> Century, need to be aware, in a holistic manner, of the complex linkages between human activities and health risks. They need to consider these global issues to the care of an individual patient as well as that of the community at large.

In 1933, Charles Nicolle in 1933 proposed the concept of ‘birth, life and death of infectious diseases’.<sup>[1]</sup> The natural history of an outbreak is a record of sequential biological events from the initial action of the causative factors, the onset and progress of the outbreak to the outcomes, which might be cure, healing, non-healing chronic stage, disability or death.

The evolving COVID-19 pandemic is a remarkable example of the concept put forth by Nicolle. The pandemic has revealed the importance of synergies among global health crisis, socio-political milieu, environmental health, and humanity’s resilience. The hard lessons of this pandemic may lead to a better cooperation and collaboration among the agencies that work on global health issues, such as outbreak preparedness, disaster risk reduction, and the activists working on environmental health, socio-economic determinants of health and health equity. If humanity acts in unison and solidarity, it could lead to proactive actions and promote effective societal resilience on a global scale.

### From Biocenosis to Pathocenosis and Anthropocenosis

Biocenosis, a term used in ecology and biology, which was coined by Karl Möbius in 1877, indicates a community of interacting organisms (*biome*) and their environment (*biotope*) that constitutes an ecological unit. Further, these three words, viz., zoocenosis, phytocenosis, and microbiocenosis, signify "a community of fauna, flora, and microbes, interacting with their

respective milieu to form a natural ecological unit”.<sup>[2]</sup> By extrapolation, “anthropocenosis” signifies a community of human population interacting with its environment in a particular period of time to form an ecological whole. This word is not listed in English language yet, though it has been used in Ukrainian scientific literature in the recent past.<sup>[3]</sup>

Extrapolating the concept of biocenosis to infections and infestations, Mirko Grmek, coined the term ‘pathocenosis’. Pathocenosis signifies all the infections and parasitic diseases in a given population, including its historical, geographic and ecological dimensions during a time period.<sup>[4]</sup>

He proposed that the occurrence of these diseases depended on the following factors:

- (i) Endogenous factors or ‘endopathocenosis’ that signify the internal ecology of the host — inborn genetic & epigenetic factors, and the nurtured life-style, nutrition etc,— and the internal ecology of the cohabiting microbiome, such as virulence, infectivity, vector, route of infection, etc.
- (ii) Ecological factors, such as climate, pollution, flood, drought etc.
- (iii) The prevalence of other co-morbidities in the population.

Even though the concept of pathocenosis could be applied to the communicable and non-communicable diseases, the scanty published literature is restricted to the pathocenosis of infections. (See figure 1)

An adaptation of pathocenosis/anthropocenosis concept to place the “Big-5” non-communicable diseases, i.e. hypertension, diabetes mellitus, cardio vascular diseases, chronic obstructive pulmonary disease and cancer, is shown in figure 2.

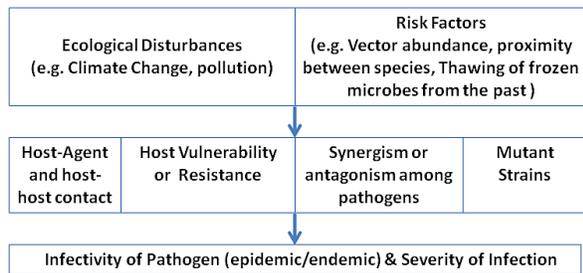


Figure 1. The interplay among ecological factors, risk factors, the host, and the agent determine the infectivity of the pathogen and its severity.

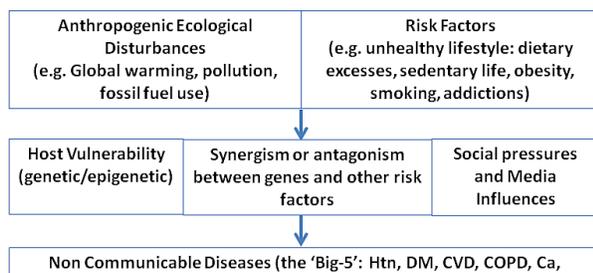


Figure 2. The interplay among ecological, life-style, social and genetic factors that influence the occurrence of non-communicable diseases.

### Some examples of pathocenosis

#### *Herpes Viruses and the Host:*

During childhood, most humans get exposed to various herpes viruses. When the host defences combat the acute infection, these viruses enter in to a dormant phase, known as latency. Latent phase is life-long and this phase is currently considered a parasitic phase, as the individual is at risk for subsequent reactivation and disease. Varicella-Zoster virus is well-documented example, which causes chicken pox during childhood and herpes zoster decades later.

However, herpes virus latency could also be beneficial to the host. Mice infected with murine virus strains, which are similar to the human pathogens Epstein-Barr virus and cytomegalovirus, are subsequently resistant to infection with the bacterial pathogens *Listeria*

*monocytogenes* and *Yersinia pestis*. Latency activates the innate immunity against subsequent infections by these bacteria.

Therefore, latency and persistence of herpes viruses, which we consider as a health hazard is not always so. At times, the latency offers immune benefits in these symbiotic relationships. [5]

#### *Nematodes – Human host Interactions:*

Murray *et al* reported that heavy infestation with *Ascaris lumbricoides*, while causing signs of malnutrition in the host, protected from malaria. [6] After deworming the population, there was an increase in the incidence of malaria in that cohort. [7]

Gut nematode infections regulate the appetite, food intake and body weight of the host and significantly improve of the metabolic syndrome, obesity and type-2 diabetes mellitus. In an adult population in rural Indonesia, gut helminths were negatively associated with body mass index, waist-to-hip ratio, and lipid profile, thereby reducing some of the modifiable coronary risk factors. [8]

Several studies have revealed an inverse association between helminth infections and allergy, auto-immunity, and inflammatory bowel diseases. [9]

#### *Malaria and Red Cell dyscrasias:*

Sickle cell trait, i.e., those who are heterozygous for haemoglobin-S (HbS) are relatively resistant to falciparum malaria infection. This is of survival benefit in areas where malaria had been rampant for centuries, such as Africa. By the process of natural selection, sickle cell trait is now more prevalent among the people of African ancestry. Certain other dyscrasias, viz., HbC, thalassemia, G6PD deficiency, are more prevalent in endemic areas for malaria and presumably provide resistance to malarial disease. Duffy-negative blood group is protective against *vivax* malaria infection; by natural selection,

majority of Africans are Duffy negative. However, while *vivax* malaria is rare in West Africa, this pathocenotic lacuna has been filled by infection by *P. ovale* as it can infect Duffy-negative persons. <sup>[10]</sup>

### **From Pathocenosis to Anthropocenosis (Humans versus Planet)**

Earth System Science, using various has opened our eyes to the disproportionate role of humanity as a driver of change in the eco-system of the planet Earth. ‘Anthropocene’ is a recent concept of a new geological epoch of human actions that determine the massive geological effects on a global scale. These human-induced adverse influences on the biosphere and the climate, such as the loss of biodiversity, the atmospheric pollution, global warming, ozone depletion, and other environmental issues are subsumed within the concept of anthropocene. In addition, other human activities, such as the high and unsustainable consumption of natural resources like the fossil fuel, the growing socio-economic inequalities and unbridled urbanization, are discussed within the same framework. <sup>[11,12]</sup>

Several studies have revealed how enthusiastic human interferences with Nature have had unintended consequences resulting in ‘anthropogenic’ health hazards. Whereas the ecological changes in Nature occur over millennia, giving adequate time span for most species to adapt and survive, anthropogenic (man-made) ecological changes are too rapid for most species, –including human themselves– to adapt. In Ukrainian literature, anthropocenosis refers to the mutual interaction among, i) the human beings, ii) rest of the biosphere and iii) the ecology, and how these interactions are detrimental in ways we cannot anticipate. The following case study is a telling example.

### *HIV/AIDS Pandemic – a case study in Anthropocenosis:*

Jacques Pepin, in his book “The Origins of AIDS” has said that the greatest danger to humankind came from other humans, especially when they mess with nature, without realising the complex and intricate inter-relationship between the mother earth and the biosphere. In this book, he starts with his theories on the origin of HIV in the jungles of Africa nearly 100 years ago and traces its spread to become a pandemic 5 decades later. <sup>[10]</sup> He noted that only chimpanzees in the jungles of Congo harbour the SIV strain that closely resembles HIV-1. Pepin adopts the “cut hunter” theory to explain how the virus made the jump from apes to humans: a hunter, or a butcher, while cutting up an infected chimpanzee, perhaps injured himself and the virus could make the species jump to infect a human. Carrying out genealogical analysis of molecular inheritance, he has proposed around 1921 as the year when the critical incident occurred.

Study of archives revealed to Pepin that enthusiastic health workers had injected thousands of people in remote villages without adequately sterilizing the reusable needles and syringes. While these efforts controlled target diseases, they promoted a rapid and silent spread of HIV to the point that its sexual transmission became a significant risk. Using the documented rates of sero-conversion after needle-stick injuries, he has demonstrated the probability of this occurrence. His argument is corroborated by the documented outbreaks of hepatitis that followed the mass-treatment campaigns. Additionally, if one accepts the concept of pathocenosis, the massive immunization drive against diphtheria, measles, mumps, polio, and smallpox in Africa presumably created a “pathocenotic” window of opportunity for HIV to gain entry in to the humans. <sup>[13]</sup>

As an ancient proverb has said it, at times, “*the road to hell is paved with good intentions*”.

## From Earth System Science to the Healthcare Professions

The medical professionals must realise that the anthropogenic climate crisis is a major health crisis and not merely an ecological threat. <sup>[14,15]</sup>

- Polluted air, in urban areas is a causative factor for seven million deaths per annum.
- The noxious emissions, which result in global warming, also are major factors in deaths from cardiovascular diseases, chronic airways disease and lung cancer.
- Global warming is now causing many more extreme weather events with associated mortality and morbidity.
- Climate change aggravates malnutrition and the spread of infectious diseases.
- Mitigation of the adverse impact on human health from climate change needs a coordinated global effort in reversing the current trend.
- The mortality from dengue has been increasing in Southeast Asia and America.
- Malignant melanoma, due to increased exposure to ultraviolet radiation, has increased in the Western nations.
- The climate change impacts, exposure to various hazards, and population vulnerability point to an increasing level of risk for human health across the globe.

### Teaching Learning of Holistic Approach to Healthcare Incorporating Anthropocenos

We have designed a multidimensional model of health care, which we believe facilitates medical students to adopt a holistic approach to health care in the context of a modern teaching hospital. Since 1991, I have been using this model to discuss the complex inter-relationship among various factors this model and encourage the medical students to cultivate a more inclusive and holistic approach to the cases they examined. <sup>[16,17]</sup>

### The Multi-dimensional JIPMER Model:

To make the starting point easily comprehensible to the medicos, this model has placed the four visible elements of a healthcare consultation at the apex of four pyramids, viz., i) Patient (Pt), ii) Doctor (Dr), iii) Disease and iv) Treatment (Rx) as shown on the diagram. What most healthcare professionals often ignore are the various factors that link these four elements, viz., telecommunication, transport and media. These are placed in the outer ring linking the four pyramids. The inner ring plays the vital roles of regulating and supporting the four elements: regulation by the Governing bodies and support by non-governmental agencies like the WHO. (See figure 3).

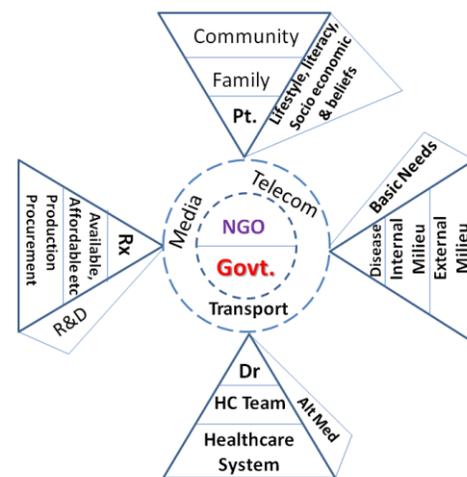


Figure 3. Extrapolation of the traditional healthcare model of Doctor-Patient-Disease-Treatment to a Multi-dimensional model of holistic healthcare.

In the first pyramid, the patient is at the apex with the family in the middle and the community at the bottom. The patient carries with him/her, the knowledge, attitude and practices of the family and the community. He/she also reflects the literacy, social, cultural and economic status of the family and the individual. The hidden parts of the pyramid have to be considered to get a

comprehensive picture of the patient's life world as the patient's expectations and own agenda for seeking healthcare are greatly influenced by these factors.

The disease pyramid has the following components – the illness (what the patient perceives), the disease (what the doctor perceives), the internal environment and causative agent/factor, and finally, the external environment. The internal and external milieus that influence illness/disease constitute this pyramid. The basic needs of a human being viz., food, water, clothes, shelter and energy as well as personal habits, life-style form another face of this. This pyramid and various factors are very important in comprehending how pathocenosis influences healthcare processes. An experienced clinical or a public health educator will be able to narrate several examples of how some of these components, such as high-risk lifestyle (internal factor) or air pollutions (external factor) influence the healthcare decisions and long term outlook for the case under study,

The doctor, the health care team and the system form the third pyramid. To a patient, the individual physician is the most visible part of this pyramid. The doctor is supported by a health care team and the diagnostic facilities. Health care systems at the secondary and tertiary levels are at the bottom of the pyramid. Complementary and Alternative systems of medicine form another face of the pyramid, which the patients often use but kept hidden from the doctor. A medical professional with a holistic outlook would be able to elicit the details of alternate therapies the patient may be taking, which helps avoid interventions contraindicated during such therapies.

The fourth is the treatment pyramid: the visible part is the drug and non-drug therapy advised by the doctor. Availability, accessibility and affordability of these therapies form the mid-portion. Production and procurement at a macro level forms the bottom of this pyramid.

To get the medical students started on using a holistic approach to patients admitted for

treatment, they were told several real-life anecdotes to show them how factors in any of the component of these pyramids or the connecting circles could affect the healthcare process and outcome. We encouraged them to wear a 'holistic hat' and look at the big picture each individual patient, in addition to bookish approach to the diagnosis and management of the case.

#### *Utility of the Model at the bedside – Perceptions of Interns and Residents*

The interns and residents could use the model to elicit case details that are beyond the scope of conventional case history. The following are some interesting examples, all from India, presented by them:<sup>[17]</sup>

1. Malaria in a 19-year-old male:
  - The patient was aware that malaria is caused by mosquito bite but was not aware of its symptoms.
  - Health education posters in his village were about guinea worm infection but not about malaria. (incidentally, the village was known to have guinea worm infection)
  - There was no control procedure against mosquito in his village
  - The community and his family did not use mosquito net or any repellents

The resident's opinion: Community health literacy regarding malaria was poor. Vector control measures were non-existent. Under these circumstances, 'cure' of his malaria became meaningless as he would surely get another attack soon and return to the hospital with recurrence.

2. Typhoid in a 45-year-old housewife that was resistant to most antibiotics:
  - unaware of typhoid or its endemicity at her place of stay
  - lack of simple hygienic measures; uses open air toilet
  - local administration does not provide potable water, community toilets or control houseflies

- when she got fever, she self medicated with one or two few doses powerful antibiotics but stopped as she 'felt better' until these capsules did not work,

The resident's opinion: Typhoid fever would persist in her locality as an endemic with no immediate end in sight. Self-medication of antimicrobials is rampant in the community. There is no antibiotic stewardship even in the teaching hospital. The community faces the hazard of resistant typhoid infections.

3. Miliary tuberculosis in a 23 year old man in a TB – prone family (father and a brother had got treated for 'lung TB')
  - while the family knew about 'lung TB', all were ignorant about other forms of TB
  - failure of primary health care to even suspect TB in this man who presented there with prolonged fever
  - media campaigns on TB do not inform the public about non-pulmonary TB
  - people in his community clear the throat and spit phlegm in public spaces

Intern's opinion: Any persistent symptom in a contact of TB for > 3 weeks could be due to an extra-pulmonary form of the disease. This needs stress in curriculum as well as in public health campaigns. Health literacy in TB is confined to the Lung TB. Civic sense and practice of hygiene in the community are deficient. Public health efforts should effectively address these issues.

4. Deliberate self-harm (para-suicide) using yellow oleander seeds by a 27-year-old man. This was a sequel to family quarrel over some property. He got the idea after watching a few TV serials, where the characters attempt suicide whenever faced with dilemma or inter-personal conflicts.

Resident's opinion: The society perceives deliberate self-harm as a coping mechanism for solving problems and for resolving conflicts in the family. The media (TV and Movies)

propagate these myths repeatedly and persistently. Unless we are either curb these maladaptive coping behaviours, or counter act them by showing several examples of adaptive coping behaviours on the media, the societal practice of resorting to deliberate self-harm will continue.

These examples provide qualitative proof of concept that the medical interns and residents, when provided a framework for a holistic approach to individual patients, are able to think of the big picture and plan possible remedial actions. They could "think globally; act locally."<sup>[18]</sup>

### Conclusion

- The stark reality of the human actions that cause major changes to the life-supporting natural cycles and eco-systems of Earth is very evident and can no longer be '*an elephant in the room*' that no one talks about.
- These global crises will have increasing healthcare, social, economic, political and philosophical implications over the coming decades. It will put the healthcare systems under increasing stress, just as the current Covid-19 pandemic has demonstrated to us all over the globe.
- The healthcare professionals of the future must comprehend the big picture of pathocenosis, and get actively involved in designing and implementing possible solutions to prevent or mitigate the adverse events in their communities.
- The multi-dimensional healthcare model has the potential to link hospital based clinical practice with the big picture of pathocenosis and anthropocenosis.
- "Think globally, Act locally" is a thought to begin our journey along these lines.

## References

1. Nicolle C (1933) Lecons du College de France: Destin des maladies infectieuses, Paris: Felix Alcan (in French) quoted in, Gonzalez JP et al, Pathocenosis: A Holistic Approach to Disease Ecology. *EcoHealth*, 2010 (online). DOI: <https://doi.org/10.1007/s10393-010-0326-x>
2. Biocoenosis, in Wikipedia. URL: <https://en.wikipedia.org/wiki/Biocoenosis> (accessed on 20-10-2020)
3. Lukanova, V. V. (2018). Phenomenon of pandemy from the point of view of system theory: to the formulation of the problem. *Grani*, 2018; 21: 70-76. <https://doi.org/10.15421/171896> (accessed on 20-10-2020)
4. Gonzalez, J. P., Guiserix, M., Sauvage, F., Guitton, J. S., Vidal, P., Bahi-Jaber, N., Louzir, H., & Pontier, D. Pathocenosis: a holistic approach to disease ecology. *EcoHealth*, 2010; 7: 237–241. <https://doi.org/10.1007/s10393-010-0326-x> (accessed on 20-10-2020)
5. Barton, E., White, D., Cathelyn, J. et al. Herpesvirus latency confers symbiotic protection from bacterial infection. *Nature*, 2007; 447:326–329. <https://doi.org/10.1038/nature05762> (accessed on 20-10-2020)
6. Murray MJ, Murray AB, Murray MB, Murray CJ: Parotid enlargement, forehead edema, and suppression of malaria as nutritional consequences of ascariasis. *Am J Clin Nutr* 1977, 30:2117-2121.
7. Murray J, Murray A, Murray M, Murray C: The biological suppression of malaria: an ecological and nutritional interrelationship of a host and two parasites. *Am J Clin Nutr* 1978, 3:1363-1366.
8. Wiria AE, Sartono E, Supali T, Yazdanbakhsh M. Helminth Infections, Type-2 Immune Response, and Metabolic Syndrome. *PLOS Pathogens* (online) 2014; 10(7): e1004140. <https://doi.org/10.1371/journal.ppat.1004140>
9. Shea-Donohue, T et al. Parasites, nutrition, immune responses and biology of metabolic tissues. *Parasite immunology*, 2017; 39,5 (online): 10.1111/pim.12422. doi: <https://doi.org/10.1111/pim.12422> (accessed on 20-10-2020)
10. Human Factors in Malaria. CDC online, 2018. URL: <https://www.cdc.gov/malaria/about/biology/index.html#tabs-1-3> (accessed on 20-10-2020)

11. Lewis, S., Maslin, M. Defining the Anthropocene. *Nature* 2015; 519: 171–180. <https://doi.org/10.1038/nature14258> (accessed on 20-10-2020)
12. Markley, M. Humanities perspectives on the Anthropocene. *Nat. Geosci.* 2020; 13: 394–395. <https://doi.org/10.1038/s41561-020-0588-z> (accessed on 20-10-2020)
13. Jacques Pepin. *The Origins of AIDS*. Cambridge University Press; 2011. (306 pp) ISBN 0521186374, 9780521186377. Available at [https://books.google.com.my/books/about/The\\_Origins\\_of\\_AIDS.html?id=Vh6oMgEACAAJ&redir\\_esc=y](https://books.google.com.my/books/about/The_Origins_of_AIDS.html?id=Vh6oMgEACAAJ&redir_esc=y) (accessed on 21-10-2020)
14. WHO News (online) <https://www.who.int/news-room/photo-story/photo-story-detail/urgent-health-challenges-for-the-next-decade> (accessed on 22-10-2020)
15. Watts N, et al. The 2018 report of the Lancet Countdown on health and climate change. *The Lancet*, 2018; 392:2479-2514. [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(18\)32594-7/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)32594-7/fulltext) (accessed on 22-10-2020)
16. Sethuraman K.R., A holistic perspective in Medicine. In S. Chandrasekar *et al*, *Beyond Rational Therapy* (1991). Pondicherry, EQUIP Society. (pages 81-84)
17. Sethuraman K.R., Multi Dimensional Model of Health care. In *Communication Skills in Clinical Practice – 2<sup>nd</sup> Edition* (2017) Jaypee Brothers, New Delhi. (Pages 212-214)
18. Think globally, act locally. Wikipedia (online) URL: [https://en.wikipedia.org/wiki/Think\\_globally,\\_act\\_locally](https://en.wikipedia.org/wiki/Think_globally,_act_locally) (accessed on 25-10-2020)