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Mini-Review

# From Patho-puzzle to Epidem-puzzle? New Concepts in Completing Disease Puzzle

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## ABSTRACT

Ecosystems are rife with various kinds of microscopic organisms or microbes. These microorganisms are responsible for a wide range of natural phenomena and functions in the environment and within other organisms. Some microbes, also known as pathogens, cause diseases and could be fatal for the host organisms and the communities. Though the epidemics are primarily initiated by pathogenicity, little is known regarding the process through which pathogens lead to mass infections. This process is similar to a puzzle with a lot of missing pieces between the starting and endpoint. The gaps in this puzzle between pathogenicity and epidemiology need to be identified to make the decision-making process effective. In this study, we propose several new concepts in which the patho-puzzle is the first step of the disease puzzle. Viewing the link between pathogenicity and epidemiology as a puzzle with multiple gaps provides a novel perspective into studying the role of microbes in epidemics.

**Keywords:** Microbes; Pathogens; Epidemiology

## INTRODUCTION

Microorganisms are found all through ecosystems, playing an indispensable role in human health, environment, and the lives of plants and animals. Microbes involve bacteria, fungi, and viruses, as well as archaea and protozoa [1]. The dynamics and function of Microbial Communities (MCs) are not perfectly clear and understandable. Thus, it is not possible to predict and manage MCs behaviors in soils, plants, atmospheres, animals, and humans [2]. Understanding microbial functions and structures, from metagenomics to metaphenomics in community and environment [3], and holobiont and eco-holobiont, can help our ecological understanding of multitrophic interactions and multifunctional roles between microorganisms and their environment and host [4].

## LITERATURE REVIEW

The microbiota (ecological communities of commensal, symbiotic, and pathogenic microorganisms) regulate the pathogenesis, improvement and therapy of diseases ranging from metabolic to neurological disorders and diseases [5]. In the meantime, the pathogens are the most harmful organisms in the world. They evolve quickly and permanently, causing diseases in the plants and animals [6] and threatening the humans' health. The pathogens impose their damages either directly or indirectly using various mechanisms. They have been divided into opportunistic, facultative, and obligate pathogens [7]. The diseases caused by pathogens are enormous threats for the food security and safety, world economy, and biodiversity in the environment [8].

In recent times, the climate changes and globalization have been identified as the agents of dissemination and spreading of infectious diseases. Throughout the years, human actions have endangered and exacerbated these issues [9]. For example, anthropogenic climate changes have been exacerbated by the finding new hosts and new locations [10], and the spreading of vector-borne, water-borne, food-borne, and air-borne pathogens. In addition to contributing in the disruption of normal ecosystem functions, they have increased the antimicrobial resistance of microorganisms and diseases caused by phytopathogens [11], as well as biodiversity changes in belowground and underground in global scale [12]. The pathogenicity of some pathogens are correlated with the climate changes [13], and the temperatures required for growth and virulence, such as *Agrobacterium*, *Pectobacterium atrosepticum*

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(including plant pathogens in elevated temperature) [14], *Vibrio cholerae* (including human pathogen in increased temperature) and *Batrachochytrium dendrobatidis* (including frog pathogen in temperature fluctuations owing to host susceptibility) [15].

Although the plant diseases can have a high economic loss in the world [16], the epidemic modeling of infectious diseases is mostly studied on human populations. Modeling epidemics in plants, humans, and animals involve four sections including focal systems, data revolution, types of modeling approaches, and forecasting and control [17]. Additionally, Geographic Information System (GIS) have been used in epidemiological studies using the disease mapping [18,19]. Likewise, a combination of some approaches such as histological monitoring, macroscopic identifications, microscopic studies such as scanning electron micrographs, and next-generation barcoding of pathobiomes would be utilized in calculation of the pathogen outbreaks [20].

## THE NEW CONCEPTS

As it was already mentioned, diverse scientific approaches could be involved in comprehending the gap between pathogenicity and epidemiology (Table 1).

| New concepts | Recommended definition |
|---|---|
| **Disease-puzzle** | Put all the components together to form a complete picture of the disease. The components of one puzzle include micro-puzzle, patho-puzzle, myco-puzzle, bacto-puzzle, viro-puzzle, nemato-puzzle, vecto-puzzle, parasito-puzzle, epidemo-puzzle and domino-puzzle. |
| **Micro-puzzle** | The comprehensive study of microbe (s) or microbiome and all relevant factors that affect, predict, promote, prevent and analyze them in and on host and environment (all related scientific approaches and technologies on microorganisms or microbiome). |
| **Patho-puzzle** | The comprehensive study of the pathogen (s) or pathobiome or pathosystem, and all relevant factors that affect, predict, promote, prevent and analyze them in and on host and environment (all related scientific approaches and technologies on pathogens or pathobiome or pathosystems). |
| **Myco-puzzle** | The comprehensive study of fungus (fungi) or mycobiome, and all relevant factors that affect, predict, promote, prevent and analyze them in and on host and environment (all related scientific approaches and technologies on fungi or mycobiome). |
| **Bacto-puzzle** | The comprehensive study of bacterium (bacteria) or bacteriome, and all relevant factors that affect, predict, promote, prevent and analyze them in and on host and environment (all related scientific approaches and technologies on bacteria or bacteriome). |
| **Viro-puzzle** | The comprehensive study of virus (es) or viome, and all relevant factors that affect, predict, promote, prevent and analyze them in host and environment (all related scientific approaches and technologies on viruses or virome). |
| **Nemato-puzzle** | The comprehensive study of nematode (s) or nematobiome or its (their) microbiome, and all relevant factors that affect, predict, promote, prevent and analyze them in and on host and environment (all related scientific approaches and technologies on nematodes or nematobiome). |
| **Vecto-puzzle** | The comprehensive study of the vector (s) and its (their) microbiome, and all relevant factors that affect, predict, promote, prevent and analyze them in and on host and environment (all related scientific approaches and technologies on vectors and their microbiome). |
| **Parasito-puzzle** | The comprehensive study of parasite (s) or its (their) microbiome, and all relevant factors that affect, predict, promote, prevent and analyze them in and on host and environment (all related scientific approaches and technologies on microorganisms). |
| **Epidemo-puzzle** | The comprehensive study of the epidemic, and all relevant factors that affect, predict, promote, prevent and analyze it in the host and environment in spatio-temporal conditions (all related scientific approaches and technologies on epidemiology). |
| **Domino-puzzle** | All domino effects must be assessed for the above-considered parts, either together or alone in host and environment (using the required scientific approaches or technologies). |

**Table 1:** Introducing new concepts related to the disease puzzle and all agents playing a role in the infection process. The puzzle has been designed to find and solve the problems related to the diseases. Each concept in the puzzle has a specific definition which involves all of the scientific approaches and technologies that are typically interrelated.

## DISEASE PUZZLE STUDIES

Disease puzzle is defined as application of all scientific approaches and technologies for detection, manipulation, control, and ultimate decision-making related to the disease components from pathogenicity to epidemiology.

In moving from patho-puzzle to epidem-puzzle, we will confront new concepts and several perspectives that reinforce our projects for reaching target points. Patho-puzzle is the first step in identifying pathogenicity and the influencing factors before and after pathogenicity. Biotic and abiotic agents cooperate in all aspects from pathogenicity to epidemiology. There are many questions and gaps in the link between patho-puzzle and epidem-puzzle.

Disease puzzle could indicate various data and information for correct and perfect decision making about the diseases. This puzzle includes controls, forecasting, drug consumptions, pesticide applications, prevention, monitoring, whole genome sequencing, genomic manipulation, pathogenicity modes, pathogenicity conditions, pathogen diverse functions, signaling pathways, co-infections, microbiome, pathobiome, holobiont, eco-holobiont, vectors, reservoirs, weaknesses of the host, spread, transmission, persistence, implications and population dynamics of infectious diseases, type of hosts and pathogens, nutrition, diets, immunities, nerves systems, mathematical models, statistics, bioinformatics, meta-omics, dynamics at the individual level, biology, ecology, evolution, population genetics of infectious agents, microorganisms or pathogens interactions, interaction with the environment, climate change effects, GIS, Remote Sensing (RS), chemical and physical investigations, software for data analysis, etc (Figure 1).

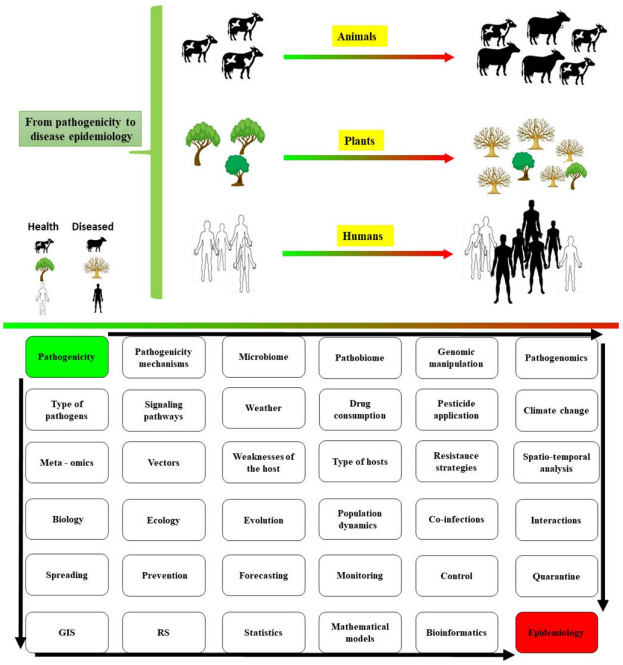


**Figure 1:** The 'Disease puzzle' conceptual framework. We express that biotic and abiotic agents and their bitrophic, tritrophic and multitrophic interactions participate in causing disease in hosts and epidemics in other hosts, other regions, or countries. These scientific approaches are examples in completing puzzle.

## CONCLUSION

As a result, complete information and data from pathogenicity on hosts, the intervening processes, and epidemic conditions on hosts' high populations are the best assets in understanding the disease loop. According to the data and information packages, disease puzzle can provide a perfect schematic picture of the disease cycles in the epidemic, in which manipulating disease components or other related conditions will lead to disruption in the disease loop. Finally, the base of any action about a disease is *disease puzzle* by which a comprehensive database for proper decision making will be provided. Hence, all this information is imperative. However, using them is a big first step. In fact, innovative technologies combined with obtained data can rejuvenate the databases of the disease puzzle.

## FUTURE REQUIREMENTS

Each of the components in the puzzle could be utilized in a particular period of the disease. Furthermore, without considering the intervening gaps between pathogenicity and epidemiology, all elements are essential in various parts of disease interpretation. These various scientific approaches could not have the sufficient information about the diseases by themselves. Thus, a comprehensive database must be made using different pieces of the puzzle for each disease and the obtained data must be updated monthly or annually.

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## AUTHORS' CONTRIBUTIONS

The author contributed to the study conception.

## CONFLICT OF INTEREST

The author declares that, I have no conflict of interest.

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