

## *A Theory of Multimorbidity*

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### **ABSTRACT**

Multimorbidity is the presence of two or more long-term health problems. It often involves the superposition of mental, cardiovascular, diabetes, cancer, and respiratory diseases. It is evident that the accumulation of health problems in a person implies more complexity and difficulties regarding their health care. However, it has not been drawn with sufficient clarity, the path that leads to the accumulation of diseases and if that situation can occasionally be an advantage, rather than a disadvantage, and in what situations It can be intervened to avoid and prevent added risks and more health problems. These multimorbidity paths would be 1. Causality, associations, and links; 2. Coincidences, series, synchronicities; 3. Chance and rearrangement situations; 4. Due to our own interventions to solve other previous problems; 5. The very presence of multimorbidity gives rise to added psychosocial problems; 6. "Two diseases is better than one"; 7. "Multi-problem families"; 8. Co-development; And 9. Rhizome. It is necessary to study the evolutionary perspective and ancestral environments in which humans developed, as well as the paths that lead to the accumulation of diseases and comorbidity and multimorbidity, to see how certain combinations of diseases increase the risk and whether certain diseases could offer protective advantages to the patient. Ockham's maxim must be remembered: It must be looked for simplicity. Perhaps, what we call multimorbidity is not so multiple, and where we believe that 2 or 3 or more diseases are added, we should only see 1 new condition. But, how is it possible to organize almost unlimited data that can be collected from multimorbidity and its accumulation and relationship mechanisms?: finding the system that defines the problem.

**Keywords:** Multimorbidity, Chronic Disease/epidemiology, Comorbidity, Humans, Complexity, Systems Theory.

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### **Introduction**

Multimorbidity is the presence of two or more long-term health problems. It often involves the superposition of mental, cardiovascular, diabetes, cancer, and respiratory diseases. Multimorbidity is now a widespread phenomenon that affects the health of populations around the world, with the greatest burden among people or disadvantaged subpopulations, as it has become a serious public health problem due

to its negative consequences on quality of life, the greater tendency to disability and mortality, polypharmacy and cost of utilization of health services, and that gives rise to a considerable burden of care. Multimorbidity is not simply a problem of chronological aging, nor is it distributed randomly.<sup>1,2</sup>

Currently, one of the main challenges facing the multimorbidity approach is the fact that the current guidelines are not designed to take into account the cumulative impact of treatment recommendations on people with various conditions or to allow the comparison of the relative benefits or risks.<sup>3</sup>

But, not enough attention is paid to the mechanisms of disease production or accumulation and the effects that this accumulation produces on the clinical expression of the diseases. It is evident that the accumulation of health problems in a person implies more complexity and difficulties regarding their health care. This clinical expression of the accumulation of two or more diseases in a person can lead to a clinical aggravation or, conversely, to a survival advantage. However, it has not been drawn with sufficient clarity, the path that leads to the accumulation of diseases and if that situation can occasionally be an advantage, rather than a disadvantage, and in what situations it can be intervened to avoid and prevent added risks and more health problems.

In this scenario, this article aims, based on a selected narrative review and the author's experience, to reflect, synthesize and conceptualize the accumulation and development of health problems in people, and show their possible implications for clinical practice.

## Methods

For the literature review, a pragmatic approach was used that was based on a non-systematic or opportunistic search for information, considering the bibliographic references of selected articles, reviews of

books related to the topic, and searches on the Internet-based on published studies in English and Spanish. The comments in this article should be considered as a personal point of view, based on the author's experience and the review cited above.

## Discussion

It has been observed that most disease pairs occur more frequently than would be expected if the diseases had been independent and that multimorbidity is not limited to specific related or more frequent combinations; about 70% of people with a disease has one or more additional chronic diseases that are not in the top five of the most common diseases; that is, multimorbidity is common in all ages and cannot be captured by some common combinations of diseases.<sup>4</sup>

The accumulation of health problems that leads to multimorbidity is a complex condition and can occur as a result of a genetic predisposition (a natural tendency), environmental or unknown factors. But, a certain history of the pathways of the accumulation of health problems to bequeath multimorbidity can be hypothesized. Multimorbidity paths would be (5-13):

### 1. Causality, Associations and Links

- Through a path of common origin (for example, many digestive diseases and related to the immune system are due to the accumulation of toxins in the intestine), or through a cortico-visceral or psychosomatic route (the origin of many diseases visceral is found in alterations of exteroceptive signaling).
- Through the accumulation of risk factors (for example, cardiovascular,

age, hypertension, obesity, smoking, and sedentary lifestyle, etc.).

- Through genetic bases (the accumulation of genetic and epigenetic alterations). It is a key causal process between the environment and diseases of complex etiology.
- Molecular and biological links (for example, many of the multimorbidities of COPD are related to molecular and biological level, sharing genes, proteins, and biological pathways).
- Biopsychosocial links (pain in all its somatic manifestations and emotional disorders are linked; There are important links that are well established between health and psychosocial conditions, social and material circumstances).

## 2. Coincidences, Series, Synchronicities

The central idea is that coexisting with causality, there is a non-causal non-physical principle of an active nature; It is the simultaneous occurrence of two events that are not causally connected. C. G. Jung and W. Pauli agreed that "there is a principle of non-causal attachment in nature that manifests itself through significant coincidences". That is, there is a close relationship between the internal and external events that we live; It is a type of relationship that cannot be explained by the principle of cause and effect but, nevertheless, makes sense to the observer.

## 3. Chance and Rearrangement Situations

Random fluctuations can occur and their effects can lead to new complexities and sudden reorganizations, such as escapes to a higher-order; internal disturbances of sufficient quantity can lead to higher organizational states. When contradictions, conflicts or multimorbidity, increase in a

patient, there may finally be an "explosion" with a sudden clinical change. For example, a chronic disabling chronic pain clinic of unclear organic origin may improve or disappear when a significant new disease, such as cancer, becomes apparent, and the clinic expressed by the patient will be exclusively referred to the latter problem. Thus, sometimes a "rearrangement" situation may occur when a new situation (or disease) appears. This rearrangement is visible not only in the clinic as physical symptoms that disappear but in changes in experience, thinking, and behavior. An escape is facilitated at a level of greater complexity, of greater awareness of psycho-physical integrality.

## 4. Due to Our Own Interventions to Solve other Previous Problems

For example, pharmacological iatrogenesis with adverse drug reactions and drug-drug-interactions or surgical sequelae; or dependence on the health system with atrophy of the person's own mechanisms to make decisions about their health, etc.

## 5. The very presence of multi-morbidity (presence of multiple biological problems) gives rise to added psychosocial problems

In patients with multimorbidity, there are losses of functional and social roles, they directly influence mood and attract the presence of anxiety and depression (regardless of whether previous psychosocial problems were defined).

## 6. "Two Diseases is Better than One"

On some occasions, suffering from several diseases is an advantage, improving the patient's clinical situation, compared to the situation of presenting those same non-associated diseases. The example of glucose deficiency disease 6-phosphate

dehydrogenase (G-6-PD), caused by a genetic defect, which produces an inappropriate level of an enzyme necessary for the proper functioning of red blood cells can be cited. Under certain physiological conditions of stress, G-6-PD deficiency can cause hemolysis.

In certain areas of Africa, this disease coexists with sickle cell disease. It has been discovered that natives who have sickle cell disease are more resistant to its effects if they concomitantly have a second disease - G-6-PD. In this case, one disease makes them healthier (at least conferring relative resistance against another). Another example, very close to the previous one is sickle cell anemia that confers an advantage to survive against malaria; The hemoglobin gene error was caused by a genetic transformation that took place many thousands of years ago, in people from various parts of Africa, the Mediterranean Basin, the Middle East, and India. At that time a deadly form of malaria was very common, and malaria epidemics caused the death of a large number of people. Studies show that in areas where malaria was a problem, children who inherited a single sickle hemoglobin gene (and, therefore, were carriers of the sickle cell trait), had the advantage to survive, unlike children with normal hemoglobin genes.

On the other hand, sometimes a disease can be an advantage to successfully face adaptive context challenges. Or, there may be a selective advantage for carriers of the disease. Thus, the symptoms of some diseases, at certain times, maybe functionally adequate. And that situation can be view as an adaptation. For example, depression (depressed mood) increases the body's ability to cope with changes in risk situations, where the effort to achieve better results can

probably lead to danger, loss, bodily harm, or lost energy. In such situations, the pessimism and lack of motivation of a depressed mood can be an advantage to inhibit certain actions especially useless or dangerous, or whose results were probably worse.

In addition, depression has a genetic component: parents of people with major depression are 2 or 3 times more likely to have the disease themselves than parents of people without depression. The prevalence of major depression is 16%. The spontaneous mutation rate in humans is 1 per 10,000 to 1 per 1000. Taking conservative values of 1 case of depression greater in 10, and a mutation rate of 1 per 1000, depression is observed with a frequency 100 times greater than mutation rate This indicates that depression must have been a clear advantage for selection in the ancestors of today's human beings, otherwise it should be rare. Of course, not every depression in the modern era is necessarily adaptive. In addition, if some depressions are very disadvantageous in modern conditions, the effect of its negative selection on prevalence will not be apparent for many generations. Thus, depression was an adaptive condition in our ancestors, which was a positive selection. For example, the seasonal depression associated with the climate with few hours of light, could reinforce the reduction of energy consumption, and allow adaptation.

Another example is diabetes, which can be an advantage against the environmental cold. One theory suggests that thousands of years ago, juvenile diabetes could have developed as a way to warm up. The theory states that juvenile diabetes could have developed in ancestral villages that lived in northern

Europe about 12,000 years ago when temperatures dropped 10 degrees on average in just a few decades and a glacial time came almost overnight. Archaeological evidence indicates that countless people died frozen, while others fled south. But some people could have adapted to extreme cold. High blood glucose levels prevent cells and tissues from forming ice crystals. In other words, type 1 diabetes would have prevented these ancestors from freezing to death. At that time, life expectancy was about 25 years. Those with high blood glucose levels did not live long enough to suffer complications. But, despite the extreme cold, they lived long enough to reproduce. Now people live much longer, and therefore the long-term sequels appear.

In fact, many of the metabolic changes observed in type 1 diabetes are also observed in animals that tolerate cold well: the jungle frog, which is found in high latitudes of the Northern Hemisphere, even in the Arctic Circle, is the size of the thumb and as soon as the skin begins to freeze in winter, your liver begins to pour glucose into the blood. This reduces the freezing point of body fluids, similar to a half-melted beverage, and places a protective barrier around the proteins. Finally, the frog makes so much glucose that its tissues are completely protected from the cold though is completely frozen, without heart rate, circulation, breathing or muscle movement. In spring, the frog thaws and returns to normal life; its diabetes is reversible.

The truth is that both humans and other animals exposed to cold tremble to produce heat. But after a while, they generate more heat by burning a special kind of fat: brown

adipose tissue. The ability of this tissue to produce heat depends on whether you have a large amount of glucose; Insulin is not necessary. Therefore, being diabetic would help divert glucose from the blood to the heat-generating path of brown adipose tissue. Thus, mice and rats exposed to cold become insulin resistant.

But there are more examples: a condition that causes harmful levels of iron in the blood, hemochromatosis, protects against bubonic plague. Cystic fibrosis protects against typhoid fever. Tay-Sachs disease may have evolved to fight tuberculosis.

Multiple infections can complicate immunity and treatment, although they can also provide an unexpected benefit for the patient, such as, for example when one organism suppresses the growth of another. Other organisms can act against each other; bacteria, for example, are often quite aggressive around other bacteria to protect their territory, and a coinfection can suppress the growth of an organism.

### **7. "Multi-problem families"**

Many health problems that doctors initially identify as belonging to the individual, actually correspond to the family system. Problems are often shared by more than one individual in the family, and can be seen more appropriately as problems of the family system, and are frequently associated with critical periods of change, transitions, and turning points in families. For example, psychotic episodes are frequently related to the end of adolescence when a person is about to leave the family and start your own home. But, on the other hand, what is called problems, negative emotions, etc., can

potentially be valuable resources and emotions, as they are pointing out undeveloped and repressed elements of potential new abilities.

### **8. Co-development**

There is no individual without context, nor context without individual. One creates the other and vice versa, and they co-evolve. When studying the vital history of the different organisms forces us to study the interaction between the internal and the external. The processes of continuous change during the life of an organism are called "development"; literally unfolding. We have the example of the great climbing plants that grow in the heart of the jungle; It starts being a seed that germinates in the soil. In the first phase of growth, the climbing plant creeps into the ground and grows away from the light, into the darkness of the earth. Later it reaches the base of a tree, and like most plants, ascends the trunk in search of light. During this phase, leaves begin to appear. As it ascends through the tree, the shape of the leaves and the distance between them changes, and the flowers make their appearance. A little higher, the climbing plant is rolled on the branches of the tree, the shape of its leaves changes again and from that moment it hangs from the branches and begins to grow towards the ground. If it runs into a lower branch, an intermediate phase begins again, and when it reaches the ground it resumes its cycle from the beginning. This development is a function of the intensity of the light and the height of the tree.

The information necessary to define an organism is not only contained in its genes, but also in its environment, in the same way the environmental problems of the organism

are a consequence of its genes. For example, penguins, who spend a large part of their lives underwater, have modified their wings to transform them into fins; organisms create their own context, and contexts create their organisms.<sup>14</sup>

### **9. Rhizome**

Multiple morbidities are important. But another related concept must be taken into account: the clinical concept of "rhizome" (15); This is not the presence of two or more diseases, it does not refer to an etiological relationship in the individual, nor to a set of risk factors. This refers to being "among" the problems, in a third dimension: in the complexity of the framework of health-disease phenomena, where each fragment can be read anywhere and related to any other. The doctor should use decentralized knowledge processes, without a single-center, but that is traveling from the node to node. The doctor must be a methodological opportunist in the sense that he is willing to go through several possible ways to achieve his goals in each particular situation.

### **Conclusion**

In summary, it is necessary to study the evolutionary perspective and ancestral environments in which humans developed, as well as the paths that lead to the accumulation of diseases and comorbidity and multimorbidity, to see how certain combinations of diseases increase the risk and whether certain diseases could offer protective advantages to patient. This knowledge can help prevent certain co-or multimorbidities, and to make decisions about the approach to diseases.

Perhaps Ockham's maxim must be remembered, and with respect to the co-presence of several health problems in a person: it should be thought that this interaction can cause modified or new entities that include the previous ones, and thus, it should not be multiplied entities without reason. The evolution in the human being is not a linear process of accumulation or progressive, but a dialectical process in which the crisis of life always imposes a time backwards. Perhaps, what we call multimorbidity is not so multiple, and where we believe that 2 or 3 or more diseases are added, we should only see 1 new condition. We must always go to the simplest hypothesis. Between two explanations, the clearest must be chosen; between two forms, the most elementary; between two expressions, the shortest. It must search the simplicity.

But, how is it possible to organize almost unlimited data that can be collected from multimorbidity and its accumulation and relationship mechanisms? Orientation for this is summed up in finding "the system that defines the problem": the set of problems, both in terms of maintenance (cause) or in its changes (treatment).

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