

Advances in Studies of Aging and Health 4  
Series Editors: Danan Gu · Qiushi Feng

Giacinto Libertini · Graziamaria Corbi ·  
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Nicola Ferrara

# The Essential Revolution of Evolutionary Medicine

Interpreting Diseases and Population  
Aging

 Springer

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of Evolutionary Medicine

# **Advances in Studies of Aging and Health**

Volume 4

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*To Stanley Boyd Eaton, Marjorie Shostak,  
and Melvin Joel Konner for their vital  
contribution to the birth of Evolutionary  
Medicine*

# Foreword

The renowned geneticist Theodosius Dobzhansky published in 1973 an essay titled “Nothing in Biology makes sense except in the light of Evolution,” pointing to the central position of the Theory of Evolution in understanding Life on our planet. Although this statement has been largely cited and accepted by biologists, it is somehow surprising how the Darwin’s Theory of Evolution is struggling to make its way in many fields of Biology, including Medicine. The Evolutionary Medicine, the topic of this book, is a relatively new discipline, despite Evolutionary Biology is a well-established science since the re-discover of Mendel’s inheritance laws in year 1900 and the formalization of what is called “The modern synthesis” in the early twentieth century.

There are many reasons why the Theory of Evolution is hard to accept, but the main issue is that it proposes that the living beings are basically self-building systems, by a process of billions of attempts and errors, often selected by the environment, a process that ended up in the exploding biodiversity we know today. The process is so deeply affected by chance that there is no reason to think that the entire Evolution on Earth will follow the same pathway if we hypothetically go back in time and start again the history of our planet.

The concept of self-building systems is the trickiest one to accept, as it threatens one of the most intuitive approaches we have when interpreting the world around us. We are a species evolved to build tools, from pebbles to spacecrafts, and our brain is very keen in interpreting what it observes as machines built by a constructor for a given function. Life is not like that. Life is unnecessarily complicated, far from being perfect, as it proceeds by attempts and errors, so what is present today is not the best possible achievement, but a compromise of history, success, failures, and good luck. Understanding life and evolution is accepting that living beings are not machines, at least are not perfect machines built by a skilled constructor. This is like accepting that “a tornado sweeping through a junkyard might assemble a Boeing 747 from the materials therein.” This argument, first presented against evolution (The junkyard tornado, also known as Hoyle’s fallacy), surprisingly tells a true story, besides that the “tornados” lasted for billion years, so a single unlikely event (the assembly of the Boeing) becomes possible over countless attempts. I used to

say to my students: to win a lottery is very unlikely event, but if you buy billions of tickets you win for sure sooner or later. Hard to imagine such big numbers, another “bug” of our brain. Accepting the Theory of Evolution as our way to interpret life, including ourselves, may be somehow disturbing, as it is counterintuitive. I think the struggle that this Theory had to be accepted since its proposal resides in this “unpleasant” feeling it produces. Some react by rejecting it (as is the case for some ultraconservative religious groups), others resolve the issue by avoiding applying the ideas and approaches of Evolutionary Biology in their day-by-day scientific activity. I really think this is what happened in Medicine. Besides countless examples, the COVID Pandemic has once more pointed out that an evolutionary approach to diseases is the best way to reduce their effects in our species. We can use evolutionary approaches to study the origin of COVID, its capacity to spread, the chances of arising new variants, etc., just to name some. For this reason, this book has an important role, and it is absolutely timely, and the Authors have accepted a very important endeavor, which I hope will contribute to a change of paradigm in modern Medicine.

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# Introduction

## Evolutionism as a Revolution in Biology

When Darwin's idea of evolution by natural selection, the subsequent related advances and studies in depth, and the birth of genetics enriched previous biological knowledge, this was not just an addition.

Biology was completely changed by the ideas of evolutionism. For example, in previous times, among the various species one simply saw the affinities or even identities of characteristics and classified the species on the basis of these affinities. With the evolutionism, it became clear that the affinities traced back to a common origin, that is, that there were common ancestors both between similar species and between species that were very different from each other. Furthermore, the affinities were not limited to external aspects but extended to countless previously unknown biochemical characteristics and to every other feature of the living world. More and more, the morphological, physiological, behavioral characteristics, and every other aspect of the species revealed themselves as the fruit of the inheritance of the ancestors and the action of natural selection. Biology became more and more imbued with the ideas of evolutionism so much so that today it is unthinkable to imagine any study of living beings that does not take into account the concepts of evolutionism.

In short, the knowledge of evolutionism has not simply been an enrichment of biology but a profound revolution from the roots of the biological world that in various ways concerns every branch of knowledge and research in that field.

While biology has been completely revolutionized by Darwin's ideas and the subsequent multiple and profound developments, medicine, which is a particular branch of biology with applicative purposes, appears to be only partially and superficially touched by evolutionism. If you tell a doctor today that evolutionism is essential for medical studies and for all that follows as a practical application, he will surely consider this statement as erroneous or at least completely exaggerated.

He will tell you that certainly in some particular cases knowledge of evolutionism is useful, but that in much of medicine such knowledge is entirely secondary or irrelevant. For example, he may tell you that various types of genetically based

anemia are the consequence of genetic adaptations to get at least a partial resistance to malaria. He may also tell you that certain types of malformation (for example those resulting from defective development of the branchial arches) or certain anatomical characteristics (for example the anatomical conformation of the retina) are the consequence of the phylogenetic history of our species. But beyond these particular cases, in general what theoretical and practical importance could the study and application of evolutionary concepts have for medicine?

Yet, as we will see, the importance of evolutionism is not limited to a few particular phenomena of limited importance but affects the very roots of medicine.

It is worth pointing out that medicine was born long before evolutionism and that the objective of this discipline is mainly the practical treatment of suffering and not the mere theoretical knowledge of diseases.

The pre-Darwinian historical origin of medicine is immediately revealed by examining how diseases are classified. In fact, the various official classifications that have followed one another over the years and that are codified worldwide divide diseases on the basis of organs and physiological systems that are affected and on some criteria of opportunity and affinity but without there being a scientific criterion that justifies this subdivision. This is similar to what was the rule for the classification of species in the pre-Darwinian era when empirical and practical criteria allowed the various groups of living species to be distinguished without there being a precise scientific criterion for this subdivision. On the contrary, with evolutionism, species are divided according to their phylogenetic origin and this objective criterion is the rule universally followed to classify species.

Furthermore, in the study of diseases, modern medicine neglects or underestimates the importance of considering the primary origin of a disease in the context of evolution. This has important consequences for both the understanding and prevention of a disease.

Let's look at the case of a very common disease, or rather syndrome, namely essential arterial hypertension, or hypertension for brevity.

The description found on Wikipedia (consulted on 20/10/2024) is:

Essential hypertension (also called primary hypertension, or idiopathic hypertension) is a form of hypertension without an identifiable physiologic cause. It is the most common type affecting 85% of those with high blood pressure. The remaining 15% is accounted for by various causes of secondary hypertension. Essential hypertension tends to be familial and is likely to be the consequence of an interaction between environmental and genetic factors. Hypertension can increase the risk of cerebral, cardiac, and renal events.

The information provided by Wikipedia has no recognized scientific value but is continuously subject to corrections by anyone who is an expert in a subject, and therefore the aforementioned description represents quite faithfully the interpretation of hypertension according to current medicine. However, according to the criteria of evolutionary medicine, this description is seriously deficient with regard to the origin of the disease and misleading for the general interpretation of this syndrome. The questions that evolutionary medicine poses for this disease, and for many others, are the following:

1. If it is true that natural selection favors individuals best suited to survive, how is it possible that it does not seem to be able to defend us from hypertension, a disease so frequent and with fearful consequences?
2. What is the incidence of this disorder in populations that live in conditions similar to those to which our species is adapted?
3. If in such living conditions hypertension is very rare or of irrelevant frequency, why is this not at the center of attention, thus attributing the origin of the disease to altered living conditions and not to different heterogeneous factors?
4. Why is medical attention focused on the treatment of the syndrome and not on the variations in modern lifestyle compared to ancestral conditions, variations that are the likely primary cause of the syndrome and that can be corrected with appropriate measures?

Indeed, for the second question, the answer has been known for at least 30 years and is clear and unequivocal.

As widely documented, in modern populations, systolic and diastolic blood pressure increase with the passage of time (Whelton et al., 1994). On the contrary, as also widely documented (Poulter & Sever 1994), in various isolated populations that follow lifestyles closer to the ancestral ones (e.g., !Kung of Botswana and ten other populations reported in the review), there is no increase in blood pressure in relation to age. Furthermore, the same study (Poulter & Sever, 1994) reports the increase in blood pressure in the transition from primitive living conditions to those of a modern urban condition.

As for the other three questions, they are ignored by modern medicine, or appear not to be considered worthy of attention, or in any case do not determine changes in current practice.

As can be seen from this single example, the attention of modern medicine, following a logic preceding the revolution of evolutionism, seeks the causes of a disease without considering the mechanisms of evolution that instead offer an immediate explanation of the primary origin of the disease.

## **The False Triumph of Modern Medicine**

The results achieved by modern medicine are extraordinary and would once have been inconceivable. Today we have exceptional diagnostic techniques that can investigate any biochemical, morphological, and genetic alteration. Diagnostic imaging techniques allow us to see inside any part of the human body without damaging it in any way. Surgical techniques are increasingly advanced and interventions that were once impossible or devastating are performed even with simple small cuts through which surgical probes are introduced and act with the help of robotic means. We have powerful drugs that can cure even very serious diseases. A detailed list of the conquests of medicine would be very long and astonishing. In short, we can define modern medicine as an enormous triumph of modern science and technology.

Cases that are not yet well treated or solved by modern medicine by virtue of further medical advances in the not too distant future will be adequately addressed.

However, this triumphal and enthusiastic description of modern medicine neglects and underestimates what epidemiological data coldly tell us.

As medicine became more and more effective and capable of previously impossible feats, the incidence of many diseases increased enormously and many previously undescribed diseases appeared and spread. The list of such diseases is considerable. Diseases such as diabetes, hypertension, cardiovascular diseases, allergic diseases, autoimmune diseases, neoplasms, refractive defects, hearing problems, psychiatric diseases, hemorrhoids, sacrococcygeal fistulas, constipation, caries, malocclusion (misaligned teeth), alveolar pyorrhea, which were or are rare or never described for people who lived or are living in primitive conditions have become common and with increasing frequency.

These diseases practically did not exist or do not exist in societies that lived or live in conditions closer to the ancestral ones to which our species is adapted. Today it is statistically normal to suffer from one or more of these diseases. Modern medicine fights these diseases with a success that varies depending on the type of disease and individual cases. If we limit ourselves to considering the improvements obtained by modern medicine in individual cases, the aforementioned triumphal evaluation of the results achieved appears justified. But if we also evaluate the epidemiological data on the number of sick people, even considering the people who have recovered and those with the disease partially controlled or in a quiescent phase, we obtain completely discouraging results. It is like a war in which we boast of countless battles won while in reality the front continues to retreat.

Sometimes this harsh reality is masked or diminished by the realistic prospect of further medical advances and even the development of highly personalized treatments or treatments for specific diseases. For example: (1) the identification of precise individual genetic alterations that can be counteracted by individual genetic treatments; and (2) the development of increasingly specific monoclonal antibodies for particular autoimmune diseases and types of cancer.

These developments are generally very or extremely expensive for each treatment of a single case and are not feasible in non-rich countries or even for individuals who are not covered by sufficient insurance policies.

Furthermore, these treatments are a kind of fog that hides the main problem: why are cases and types of disease increasing despite the ever-increasing effectiveness of medical treatments?

From these considerations arises the need for a different approach that preliminarily provides an answer to these questions.

## **Evolutionary Medicine as Rational Solution for the Problems of Current Medicine**

Evolutionary medicine is a possible rational solution to the failure of current medicine.

The main purpose of this book is to show that evolutionary medicine is not simply an interesting curiosity of only theoretical value but a practical way to overcome the tragic limits of current medicine.

With the simple consideration of evolutionary mechanisms, it is possible to analyze and define the primary cause of the various types of disease, which should be classified precisely according to the type of primary cause.

From the knowledge of the primary causes it is possible to devise a strategy to combat these causes and consequently to prevent many types of disease. This strategy, if managed effectively, reduces the number of new cases of disease and the number of cases of sick people to be treated.

It is good to say that not all types of disease are preventable and that even for preventable diseases a part is caused by genetic alterations that are much less preventable.

The key element is the portion of cases that are preventable with appropriate preventive measures.

The most evident type of cases among the preventable ones are those caused by alterations in lifestyle. A well-known case in current medicine is that of diseases caused by the habit of smoking cigarettes. In smoke there are a myriad of substances for which the body is not adapted and which are therefore harmful. The diseases caused by smoking (chronic bronchitis, emphysema, cardiovascular diseases, cancers of the lung and other organs, etc.) are easily preventable by avoiding cigarette smoking.

In modern medicine, this important prescription arises from the empirical observation of the countless cases of diseases related to the habit of smoking and therefore the prescription to avoid smoking arises from empirical data. For evolutionary medicine, the habit of smoking is not something to which we are evolutionarily adapted. Consequently, *a priori*, it is to be considered—until proven otherwise—something potentially harmful to be avoided. Then, in the comparison between modern populations and others that live in conditions closer to those to which we are adapted, the empirical observation of an increase in various pathologies and the association between the incidence of these pathologies and the habit of smoking indicates that the potential harm of smoking is real harm. Consequently, to combat a series of diseases related to smoking, the priority action is to inform as much as possible about the dangers related to the habit of smoking and to discourage this habit. As a secondary remedy, and as a partial remedy to a lack of primary prevention, it is necessary to proceed with secondary prevention measures and with the appropriate treatment when a disease caused by smoking occurs.

This example can be extended to other types of diseases that are spreading because: (1) the primary cause of a disease is not known or highlighted; (2) primary

prevention measures are not applied, that is, actions on the primary cause of a disease are not taken into account; and (3) attention and efforts are concentrated on the treatment of cases of disease, each of which generally indicates the absence or failure of actions for the primary prevention of the disease.

These simple synthetic considerations indicate that evolutionary medicine is not limited to a simple enrichment of current medical knowledge, but implies a radical rethinking, or rather a profound revolution, of the logic according to which medicine operates.

## Structure of This Book

Let us now see how the exposition of evolutionary medicine is organized in this book.

In Chap. 1, there is the definition of evolutionary medicine and the discussion of the fundamental concepts of evolutionary medicine. Then, there is the comparison between the current classification of diseases and similar conditions (a classification empirical and of historical origin but not based on an objective scientific criterion), and a suggested classification of such conditions based on the objective criterion of their primary causes. The chapter concludes with a brief history of the origins and development of evolutionary medicine.

Chapter 2 discusses the subject of diseases caused by alterations of the genotype, the frequency to be expected for a single disease of this type, and the large overall frequency to be expected for this category of diseases as a whole.

In Chap. 3, there is the first part of the fundamental category of diseases that originate from alterations of our ecological niche. Given that the term holobiont indicates an organism plus the multitude of other living species that live within or on the same, the chapter, which does not include the alterations of the holobiont discussed later, exposes this type of disease with its various subcategories. This category of diseases includes pathologies of great frequency and economic and social impact, all dependent on alterations of the ancestral lifestyle or the environment to which we are adapted. These diseases are largely preventable with the appropriate corrections or at least compensations of the aforementioned alterations.

In Chap. 4, there is the second part of the category of diseases that originate from alterations of our ecological niche, that is, those that originate from alterations of our holobiont. Here too we have a vast category of diseases of great frequency and economic and social impact due to alterations of the ancestral lifestyle or of the environment to which we are adapted, which have consequences on our holobiont and therefore on our health. These diseases are also largely preventable with the appropriate corrections or at least compensations of the alterations mentioned above.

Chapter 5 debates diseases resulting from relationships with other species, such as infections. Diseases resulting from conditions beyond the scope of our adaptations are also discussed.

Chapter 6 addresses physiological phenomena that can cause suffering that are not diseases but adaptations to specific conditions. It is discussed whether and to what extent these phenomena should be counteracted, without causing harm in an attempt to “cure” phenomena that are not pathological.

Chapter 7 introduces the concept of phenoptosis, which includes aging and its complex manifestations, and then expounds some phenoptotic phenomena other than aging.

Chapter 8 discusses aging as a phenoptotic phenomenon. In this regard, the “why” of aging is debated, that is, the mechanisms of natural selection that under certain conditions favor aging. Furthermore, it is explained the unsustainability of the ancient interpretation of aging as an exclusively harmful phenomenon not sufficiently counteracted by natural selection. The “how” of aging is then debated, that is, the specific mechanism of aging at the cellular level and consequently at the level of tissues and organs and of the entire organism. Finally, the relationship between aging and its progressive age-related manifestations and the frequent lack of distinction between physiological aging and the acceleration of aging caused by alterations in lifestyle are discussed. This important topic has been discussed in more detail in the previous book in this series (Libertini et al., 2021), while a substantially complete but more synthetic exposition is reported here.

Chapter 9 presents a varied set of topics that are also the subject of particular studies in terms of evolutionary medicine, including: (a) anatomical constraints and curiosities determined by our phylogenetic history; (b) physiological characteristics that become problems, even very serious ones, in a modified ecological niche; (c) diseases or disorders resulting from conflicting demands of our evolution; (d) enzymatic deficiencies that are not defects but merely the result of our previous evolutionary history; and (e) problems related to the period of birth and the first months of life and caused by altered living conditions.

Chapter 10 addresses the crucial issue of how evolutionary medicine can be implemented in practical reality, not as an addition of knowledge to current medicine, but as a radical transformation of it. In fact, today's medicine is largely oriented toward the treatment of diseases and not on prevention and it is unlikely that a doctor can privilege prevention and avoid treating patients. Treatment and prevention must walk on two parallel tracks in which mechanisms and responsibilities are distinct. The common fundamental principle is that treatment is always due when there is a need, that is, when someone suffers, but that too often the treatment of a disease represents the failure of its prevention.

## References

Libertini, G., Corbi, G., Conti, V., Shubernetskaya, O., & Ferrara, N. (2021). *Evolutionary gerontology and geriatrics. Why and how we age*. Springer.

- Poulter, N. R., & Sever, P. S. (1994). Populations with low blood pressure and the impact of rural-urban migration. In Swales, J. D. (ed.) *Textbook of hypertension*. Blackwell Scientific Publications
- Whelton, P. K., Jiang He, & Klag, M. J. (1994). Blood pressure in western countries. In Swales, J. D. (ed.) *Textbook of hypertension*. Blackwell Scientific Publications



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