EDITORIAL

THE ORIGIN OF DISEASES: MUSINGS ON ECOLOGY AND THE EVOLUTION OF MEDICAL IDEAS

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The truth is rarely pure and never simple.
—Oscar Wilde, *The Importance of Being Earnest*, 1895

How extremely stupid not to have thought of that.
—T.H. Huxley's reaction to the reading of Charles Darwin's *The Origin of Species*

THE ORIGIN OF SPECIES: MUSINGS ON TRANSMUTATION OF IDEAS
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Sailing in the equatorial oceanic islands of the Galapagos, retracing Darwin's journey and observing the same phenomena he witnessed 170 years earlier, I was stimulated to consider the unique parallels between pre- and post-Darwinian biology and current trends in medical science and systems biology. I began to consider the confluence of events that led to such a radical change in our view of the world, and how that may help us recognize that we stand on the brink of a similar change in biologic theory as it applies to health and disease.

How did Darwin come to understand the nature of things, the nature of nature? How did an idea arise that was completely different than the collective wisdom of scientists, theologians, and philosophers of his time? How did an idea emerge that contradicted the belief that all animals and living things were the result of spontaneous creation manifested in one instant through the intelligent design of a benevolent god? Darwin said, "Science consists in grouping facts so that general laws or conclusions may be drawn from them."[1]

And how could the observation of exactly the same facts in natural science lead to entirely different conclusions about the nature of reality? It took nearly 20 years from the time 22-year-old Darwin graduated from the seminary at Cambridge University and set out on his 5-year voyage on the *HMS Beagle* as an amateur naturalist until he fully formulated his theory on the origin of species by means of natural selection. He quietly and carefully assembled the observations of his journey. In his mind, Darwin incubated his observations and musings—the fossil records of extinct species, the unique populations of species on the Galapagos Islands, the collective observations and musings of other naturalists and geologic and political observers and thinkers. After he returned from his journey, this coalesced into a novel, radical, and contrary notion of the world.

His perspective on nature did not arise in a vacuum. The ideas of natural selection and the transmutation of species emerged from a few key parallel shifts in understanding the world. First and perhaps most important was the work of Sir Charles Lyell, the 19th-century British geologist who questioned the notion that fossil records were the result of "successive creations" brought about through floods, volcanoes, and earthquakes.[2] Based on his research, he suggested that the geological time not be considered in a few thousand years of biblical time but measured in millions of years. The intellectual tide shifted quickly in the 19th century, exploding the conventional view of a short geological time span. The view that all species of animals arose in an instant from the spontaneous creation of God and that all species appeared in their current form on earth—the belief in the "fixity of species"—was open to question.

Darwin brought the newly published first volume of Charles Lyell's *Principles of Geology* with him on the *HMS Beagle*. It was through the lens of an expanded geological time span that Darwin made his observations of the fossil record and geology of South America and its flora and fauna.

Against this backdrop, Darwin questioned his beliefs learned in the cultural cauldron of early 19th-century England and reinforced during his studies for the clergy. He noticed what otherwise may have been insignificant phenomena that began the crack in the established orthodoxy. Since no animals could be observed to have changed even from the time of the ancient hieroglyphs of the pharaohs, then it must be that the doctrines of spontaneous creation and the fixity of species are true. They matched observed phenomena.

Any extraneous data or contradictory observations are ignored, not seen or witnessed, because our capacity for truly unique observations is inhibited by our beliefs about the nature of things. Theologians encouraged the study of nature, and many clergy were naturalists, as was Darwin. They studied nature as a way to illustrate God's wondrous creation—not to discover new laws or principles. In much the same way, modern medical science has worked to discover subtleties within the existing structure and orthodoxy without questioning the very principles on which it was founded.

When Darwin observed certain facts that contradicted the notion that each species was created individually, he noted them even though at the time they remained only a series of questions, clues, and juxtapositions that did not fit with the existing paradigm. Why, he wondered, did each extinct fossil species show such a close structural relation to living animals? Why did the finches and the giant tortoises in the Galapagos Islands show significant variations from island to island so that the local inhabitants could tell from which island a tortoise had come?

However, the laws of natural selection and the mutability of species, the concepts of evolution and ecology, did not first occur to Darwin on his 5-year voyage on the *HMS Beagle*. It was only after he arrived home and collected and reviewed his observations and let them stir and be stimulated by other thinkers and teachers that he awakened to a new set of natural laws. His observations were illuminated in the context of new geologic theories of Lyell and the economic theories of populations put forth by J.R. Malthus, published in his *An Essay on the Principle of Populations in 1798*. Darwin was deeply influenced by this theory of human populations, which he applied to the rest of the biological world. Malthus asserted that population growth will always tend to outrun food supply unless it is checked by war, famine, disease, or voluntary restraint.[3] How did this theory of populations apply to the natural populations observed by Darwin?

It was not until 20 years after his return from the *Beagle* that Darwin published *The Origin of the Species by Means of Natural Selection* and only under duress because of the parallel discoveries in the field by a young biologist, Alfred Russell Wallace. Darwin's hope was to publish it after his own death because he understood the revolutionary and social impact of the laws of nature he observed. The difficulties and challenges to the prevailing notions of the creation of species—and hence the world itself—were disturbing to a cautious and thoughtful Darwin.

The patterns and relationships he observed between geologic succession, the behavior of whole populations throughout history, and his own young and unblemished observations on his voyage around the world, and particularly the Galapagos—where slight but distinct variations were found among species of animals living in close geologic proximity but separated by different environments—led him to inescapable conclusions despite his beliefs. When observations and facts contradict beliefs and theories, the role of the scientist is to ask why.

Arriving on the Galapagos Islands 170 years after Darwin, not much has changed, except, perhaps, for the decline in the giant Galapagos tortoise population that occurred with the slaughter of 200,000 of these ancient creatures by whalers in the mid-19th century.

By day we explore the perimeter of newly formed volcanic islands, where dense populations of a variety of ancient creatures make their equatorial homes. The Galapagos sea lions descended from canine-like creatures, retaining small external ears, a tail, finger-and-paw-like flippers with vestigial claws placed at their knuckles, which help them scratch away sand fleas like a dog. The Galapagos are the only home of the marine iguana, a large prehistoric creature with serrated teeth that are used to loosen seaweed from the rocks and flattened tails that are adapted to swimming in the sea. Their land cousins, the giant foraging lizards of the Galapagos, adapted to the land and have round tails and are lighter in color. The black marine iguanas lie on the black volcanic lava rocks to warm themselves after their cold ocean-feeding expeditions.

By night we sail on the *Mary Anne*, a 207-foot sailing ship crisscrossing the upwelling fertile equatorial sea from island to island, each distinct in its geography, flora, fauna, and natural history. These undisturbed oceanic islands are close in proximity but separated by insurmountable barriers of sea. On Isabella, the largest of the islands, there are multiple different micro-ecosystems separated by volcanic cauldrons and barren, rough, and scorching lava rock. This caused the parallel development of slight variations among similar species of animals that could not cross the alien lava landscapes, providing clues for Darwin as he mused on the origin and the purpose of his observations.

How was it that the carapace (the enormous exoskeleton shells) of the giant tortoise is different from island to island or even within an island like Isabella, which is separated by insurmountable geological, rather than oceanic, barriers. Why did some have enormous domes by which the tortoise is protected and can grow to an enormous size—reaching 200 to 500 lbs over 200 years—while others, such as the saddleback giant tortoises, had carapaces with wide openings in the front that provided little protection from predators, which were nonexistent in Galapagos, but allowed them to stretch their necks high to reach vegetation that was unique to their islands. These discrepancies and peculiar variations stimulated Darwin to challenge the belief in spontaneous creation and the fixity of species.

THE ORIGIN OF DISEASES: EVOLUTION AND ECOLOGY IN MEDICINE

The climate of 21st-century medical science parallels early pre-Darwinian 19th-century notions of natural history and the origin of species. Current notions on the origins of disease support the theory that disease arises "spontaneously" and is "fixed." We have carefully observed pathology and named and categorized diseases much like the natural historians of yore catalogued, named, and classified species according to Linnaean principles. It is a useful phenomenological classification of disease, but without connection to meaning and purpose in the development of illness. It provides little insight into the functional relationships and patterns and basic laws of nature that inform, shape, and determine the evolution and ecology of disease.

Disease entities are not fixed like species but are mutable and variable, changing in relation to environmental, genetic, and lifestyle influences. Illness is an attempt by the body to adapt to a harsh environment as it struggles to survive. A toxic food landscape, unremitting psychological stressors, and poisons in our water, air, and food force our biology to adapt through the development of disease.

Diseases do not arise spontaneously in a vacuum, as sudden acts of God, as species were once believed to arise, or as a manifestation of evil humors or spirits—although some may be "cursed" by certain genetic polymorphisms or born into social and political environments that foster illness. The study of the "natural history" of disease, just like the study of the natural history of "species," stops short of wisdom. It provides knowledge but stops short of clear understanding. This is the fundamental limitation of medical thought today. In his book on the relationships, patterns, and systems that underlie and unite biological, physical, chemical, social, and political laws, E.O. Wilson, Pellegrino Research Professor in Entomology for the Department of Organismic and Evolutionary Biology at Harvard University and a fellow of the Committee for Skeptical Inquiry, proposes the need for a new theoretical framework for inquiry into phenomena predicated on systems theory.

> *Reductionism is the primary and essential activity of science. Also crucial are synthesis and integration, tempered by philosophical reflection on significance and value. . . . To make any progress [researchers] must meditate on the hidden design and forces of the networks of causation.*[4]

Now, there is a new era of thought, scientific discovery, and social and political realities that reflects a new set of unifying principles that guides us directly into the "hidden design and networks of causation." This is our greatest opportunity in medicine. Our greatest risk lies in ignoring new observations in science and systems biology that shake the root of our current thinking and practice.

CLIMATE CHANGE: CONSILIENCE AND CONCINNITY

> ***Consilience**: the linking together of principles from different disciplines especially when forming a comprehensive theory.*[5]
> ***Concinnity**: harmony or elegance of design especially of literary style in adaptation of parts to a whole or to each other.*[6]

The ideas that shaped a worldview for centuries fell away in the light of new observations by Darwin that was bright enough to reframe our assumptions about the laws of nature. How do current parallel developments in science require us to reframe our notions of biology and disease, to consider new laws of nature? What lessons can be learned from the circumstances that led to the Darwinian shift in biological theory from "spontaneous creation" and "the fixity of species" that happened nearly 2 centuries ago? How do new observations and discoveries in medicine and systems biology require us to question the current paradigm of disease origination?

The principles of natural selection, evolution, ecology, and systems theory are natural laws that apply directly to understanding of health, disease, and illness. We can no longer ignore facts and discoveries that call on us to prioritize the need to understand the relationship of the parts of human biology, rather than simply dissecting and naming the individual parts. A plant, a fungus, an insect, or an animal in the forest is meaningful only in the context of how it forms a larger ecological whole. Health and disease are no different.

Improved understanding of molecular mechanisms, pathologic changes, and genetic polymorphisms, improvements in laboratory analysis; and increasing refinements in imaging technology allow us to have a finer appreciation of the phenomena of disease but rarely provide insight into disturbances at the root of the disharmonious relationship of the parts of our biology. They help us to better frame disease as a fixed entity or external phenomenon. But they do not allow the scientist or clinician to see the harmonious relationship of the parts of our biological systems, nor that, in truth, the parts are relevant only as they enhance our understanding of the whole.

The patterns, connections, networks, and systems of our biology are the critical aspects that demand further inquiry and investigation. Reductionism has reached its limit in medicine. Understanding the parts is only relevant as it illuminates the overall ecology of the organism. Diseases themselves and diagnosis as we know it will become increasingly irrelevant as the principles of concinnity and consilience, of ecology, evolution, and the synthesis of knowledge replace reductionistic "dissection science" and become wisdom.

The kin of ecology is a notion that may inform our new understanding of the biological laws of nature. This is the notion of concinnity. In our current discourse on disease and illness, we would do well to embrace the view that the internal harmony (or disturbance in that harmony) and relationship of the parts to the whole is more relevant in the inquiry of health and disease than further dissection of the parts themselves. This perspective of the intimate relationship of an organism to its environment, influenced by the natural laws of ecology and evolution, can transform the science and practice of medicine.

We can improve medical practice according to the old principles of diseases as fixed entities, perhaps reduce medical errors and improve adherence to current practice guidelines, and optimize treatments within our current framework through the use of information technology. But what if we are improving a flawed system? What if the fundamental foundations and assumptions that guide us in diagnosing and treating disease do not reflect current laws of biology grounded in systems theory, the scientific playground of concinnity and consilience.

E.O. Wilson challenges us to deliberately and seriously take up the act of synthesis. This is the potential of medicine today. Chronic illness and suffering will not be diminished until we reframe our inquiry, release old reductionistic classification models of disease, and understand the critical urgency of creating a medical and healthcare system based on the true origins of disease.

. . . . *In the twenty-first century, the world will not be run by those possessing mere information alone. Thanks to science and technology, access to factual knowledge of all kinds is rising exponentially while dropping in unit cost. It is destined to become global and democratic. Soon it will be available everywhere on television and computer screens. What then? The answer is clear: synthesis. We are drowning in information, while starving for wisdom. The world henceforth will be run by synthesizers, people able to put together the right information at the right time, think critically about it, and make important choices wisely.*[4]

NEW HORIZONS: NAVIGATIONAL LENSES BASED ON SYNTHESIS AND INTEGRATION

A few explorers of 21st-century biological landscapes are reframing the discourse on the origins of disease. One of these, Sidney MacDonald Baker, MD, is a thinker of Darwinian intellect who, after cataloguing observations of a lifetime of medical practice, has offered a new model for understanding how genetics and environment intersect to give rise to the physiology of disease expression. In his ongoing "Lenses" series in *Integrative Medicine: A Clinician's Journal*, he has suggested that rather than classifying disease according to the International Classification of Disease (ICD) based on medical specialties that forms the basis of medical practice, reimbursement, and treatment, we look through another set of lenses when observing the phenomena of ill health.[7] The naming of the disease must become, he suggests, subservient to the understanding of the functional processes of the body.

These lenses, or systems of the body, are a more robust and clarifying perspective for understanding disease. Dr Baker describes 8 lenses through which to view the biology of health and disease: energy, synthesis, detoxification, messaging, membrane function, perception, memory, and timing. Though quite different from our current classification of disease, they may, in fact, be a closer approximation of the ecology of illness.

The creation of energy through the transformation of food and oxygen in the mitochondria into ATP is the foundation of life. Anything that interferes with that process impedes health. Synthesis, the creation of new molecules for metabolism, tissue growth, and repair, must function optimally for health. The processing and excretion of waste or detoxification is another essential system of biology. Proper communication and our messaging systems at all levels—at a molecular level, from cell to cell, and within an organism and in its response to a changing environment—are necessary for health. The body is made up of miles of membranes, from the gastrointestinal barrier to the alveolar membrane to the blood brain barrier, through which molecules transmit messages and information from the internal and external environments. Damaged membranes impair normal physiologic responses. Perception is the process of taking in the world on a macroscopic and microscopic level and encompasses the function of our nervous and immune systems. Disturbances in perception of the immune system, for example, lead to allergy, autoimmunity, infection, or malignancy. Memory is the way in which we recognize things, and it is located within our immune and central nervous systems. Central nervous system and immune system pathologies are a functional unity through their activities of perception and memory. And lastly, timing in biologic systems and rhythmic functioning is critical for health.

Changing our set of lenses is no easy task for those of us who were trained in the "spontaneous creation" and the "fixity of diseases." However, the evolution of science and the ecological imperatives of human biology demand it of the scientist and clinician setting out on a voyage to discover the origins of disease.

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