Evolutionary medicine

Update on the relevance to family practice

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ABSTRACT

Objective. *To review the relevance of evolutionary medicine to family practice and family physician training.*

Quality of Evidence. *Articles were located through a MEDLINE search, using the key words* evolution, Darwin, *and* adaptation. *Most references presented level III evidence (expert opinion), while a minority provided level II evidence (epidemiologic studies).*

Main Message. *Evolutionary medicine deals with the interplay of biology and the environment in the understanding of human disease. Yet medical schools have virtually ignored the need for family physicians to have more than a cursory knowledge of this topic. A review of the main trends in this field most relevant to family practice revealed that a basic knowledge of evolutionary medicine might help in explaining the causation of diseases to patients. Evolutionary medicine has also proven key to explaining the reasons for the development of antibiotic resistance and has the potential to explain cancer pathogenesis. As an organizing principle, this field also has potential in the teaching of family medicine.*

Conclusion. *Evolutionary medicine should be studied further and incorporated into medical training and practice. Its practical utility will be proven through the generation of testable hypotheses and their application in relation to disease causation and possible prevention.*

Evolutionary medicine (also called *Darwinian medicine*) refers to the application of the principles of natural selection to the understanding and treatment of disease. The publication of several books on evolutionary medicine aimed at least in part at popular audiences (1-6) has made a basic understanding of this discipline important for family physicians. Physicians, however, are in general poorly prepared to evaluate literature on evolutionary medicine, possibly in part because of a lack of exposure to evolutionary medicine during training. In addition, there is little guidance available to assist family physicians in navigating this literature.

The purpose of this paper is to selectively review the main trends in evolutionary medicine research, emphasizing how these apply to the practice of family medicine. ❑

QUALITY OF EVIDENCE

I searched for relevant articles through MEDLINE, using the key words *evolution, Darwin,* and *adaptation.* Additional articles were found by reviewing the citations of retrieved papers. From these, I selected articles that discussed the clinical relevance of evolutionary medicine or that argued a particular evolutionary explanation for a disease as being necessary for the overall understanding

of that disease. Review papers were excluded unless they offered original arguments for the clinical relevance of evolutionary medicine. The studies I examined logically fell into 3 different categories: articles offering explanations for the existence of specific diseases; articles arguing that evolutionary medicine offers a conceptual framework for medical education; and articles discussing the utility of evolutionary medicine for disease treatment and prevention. For each of these broad categories, I summarized the main arguments relevant to the practice of family medicine. Most papers presented level III evidence (expert opinion). Several papers presented level II evidence (epidemiologic research). ❑

EVOLUTIONARY EXPLANATIONS FOR DISEASES

There are several recurring evolutionary explanations for disease. The 3 most common of these are reviewed here with representative examples. A more complete list of diseases and proposed evolutionary explanations is given in *Table 1*. (7-20)

Table 1. Examples of evolutionary explanations for human disorders

Proposed evolutionary explanation	Disorders
Heterozygote advantage	Sickle cell disease (7) Cystic fibrosis (8) Phenylketonuria (9)
Antagonistic pleiotropy; adaptation to ancestral environment	Hemochromatosis (10,11)
Antagonistic pleiotropy	Gout (12) Atherosclerosis (13) Prostatic hypertrophy (14) Alzheimer disease (15)
Adaptation to ancestral environment	Obesity (16) Type II diabetes (17,18) Essential hypertension (14) Drug abuse (19) Female reproductive cancers (20)

One of the most common evolutionary explanations for disease involves a phenomenon known as *heterozygote advantage*. In diseases caused by heterozygote advantage, certain alleles appear to represent an adaptation in carriers (heterozygotes) but are clearly deleterious in homozygotes. The classic example of this is sickle cell anemia and protection from severe malarial infections. Individuals heterozygous for the HbAS allele (ie, sickle cell trait) demonstrate enhanced phagocytosis of red blood cells infected with the ring form of malaria parasites (particularly *Plasmodium falciparum*). (7) In fact, carriers of the sickle cell trait enjoy a greater than 90% protection against severe malaria. (21) Because infection with *P falciparum* can be fatal, natural selection has favoured maintenance of the HbAS allele in malaria-endemic areas of Africa despite the clear disadvantage to individuals homozygous for HbAS, who contract sickle cell disease. Many other human red blood cell polymorphisms also appear to be adaptations against malarial infection (eg, glucose-6–phosphate dehydrogenase deficiency, pyruvate kinase deficiency, a-thalassemia, hemoglobin C disease, hemoglobin E disease). (22)

Another common evolutionary hypothesis for the origin of human diseases focuses on mismatches between genes and the environment. The basis of this idea is that at some period in the past, human genes adapted to a particular ancestral environment (such as the African savanna). Over time, our physical and cultural environments changed faster than natural selection altered our allele frequencies, resulting in modern-day diseases. Numerous diseases are posited to result from such gene-environment mismatches, including diabetes, cardiovascular disease, and hemochromatosis. For example, the common gene mutation C282Y observed in hemochromatosis might have arisen from an adaptation that occurred when prehistoric humans switched from a Paleolithic hunter-gatherer diet rich in red meat to a Neolithic cereal grain diet relatively low in red meat, resulting in iron deficiency anemia.[10] Because both homozygous and heterozygous carriers of the hemochromatosis C282Y mutation have greater iron stores, this mutation likely provided a fitness advantage in a Neolithic environment, especially to women of childbearing age. The mutation probably only manifested as disease (became disadvantageous) when nutritional intakes improved in recent centuries.

Evolutionary medicine might also have wide-ranging applications in psychiatry. (23,24) For example, it has been postulated that anxiety stems from a mismatch between modern cultural conditions and emotional responses that developed in response to historic (eg, Paleolithic) cultural conditions. This line of reasoning has led to suggestions of preventing the development of anxiety by altering early life experiences in children. (25) However, it must be pointed out that these suggestions remain highly speculative. Among the chief proponents of evolutionary psychiatry is Randolph Nesse. In a 2000 review of evolutionary explanations for depression,

Nesse concluded that in some instances depressive states might be adaptive because they "inhibit dangerous or wasteful actions" in situations that would likely prove futile to the individual. (26)

A third common evolutionary hypothesis for human disease involves a concept known as *antagonistic pleiotropy*. *Pleiotropy* refers to instances where a single gene affects 2 or more traits. *Antagonistic pleiotropy* occurs when one of these traits is advantageous to the organism but the other trait, coded by the same gene, is deleterious. This concept has been central to evolutionary arguments about aging for the last half century. (27) The idea is that alleles that increase reproductive success early in life might also contribute to accelerated aging later in life. Therefore, aging can be considered a trade-off for reproductive success. As natural selection operates through the differential passage of alleles to future generations, it is easy to see how increased reproductive success early in life will be selected, even if it also confers a negative effect (aging) after the reproductive period has passed. ❑

UNIFYING CONCEPT IN FAMILY MEDICINE EDUCATION

Thirty-five years ago, the biologist Theodosius Dobzhansky argued the following:

Seen in the light of evolution, biology is, perhaps, intellectually the most satisfying and inspiring science. Without that light it becomes a pile of sundry facts some of them interesting or curious but making no meaningful picture as a whole. (28)

An analogous argument has been made regarding the study of medicine, with one author writing, "The study of medicine often strikes students as an unsystematic conglomeration of information and skills – relevant to medicine, but gathered from a wide variety of domains without any linking theoretical rational." (29) It has been argued that evolutionary medicine could provide just such a key organizing principle for medical school education. (29-32) This argument also appears to apply to teaching family medicine, where students are presented with a bewildering array of facts and concepts from widely disparate fields.

Despite the fact that proposals for the inclusion of evolutionary medicine in medical school curricula have been made for more than a decade, (29, 31-32) most medical schools have largely or completely ignored this aspect of biologic theory. Nesse and Schiffman conducted a mail survey of all North American medical schools and found that only 48% of responding schools considered evolutionary medicine to be important knowledge for physicians; only 4% had a dedicated course or lecture sequence in evolutionary biology. Among survey respondents, the 2 most important reasons for not teaching evolutionary medicine were that there was not enough curriculum time and that there was a lack of faculty expertise. Concerns about political controversy were cited by 11% of medical schools. (31) While not explicitly addressed in this survey, the risk of misusing evolutionary medicine to naturalize social inequalities could also be raised as a possible concern. A detailed discussion of this is beyond the scope of this review, but interested readers are referred to the recent series of essays by Lewontin and Lewis. (34)

To date, there has been little published experience on the teaching of evolutionary medicine in medical schools. An exception is the Keck School of Medicine at the University of Southern California in Los Angeles, where an evolutionary medicine course was successfully integrated into the curriculum. Students at that school rated the evolutionary medicine course as a highly valuable experience. (33) In an even broader sense, because evolutionary medicine places humanity within the larger ecosystem of the earth and draws attention to the dangers inherent in overpopulation and climate change, its inclusion in family medicine curricula might result in increased awareness of these issues among trainees. To my knowledge, however, there are no published data on the effects of incorporating evolutionary medicine into family medicine training programs. ❑

GENERATING NEW IDEAS FOR TREATMENT AND PREVENTION

One of the most fruitful applications of evolutionary medicine has been in the study of antibiotic resistance and pathogen virulence. (31) It is now clear that bacteria rapidly evolve resistance to antibiotics. (35) Genes that confer antibiotic resistance might arise from new mutations or might be acquired by horizontal gene transfer from other species or strains of bacteria. Once these genes are present in a population of bacteria, exposure to an antibiotic will result in differential survival of individual bacteria possessing the antibiotic-resistance genes. The molecular basis of this evolution has been particularly well studied in *Staphylococcus aureus* (36) and can help to explain the emergence of drug-resistant strains in different parts of the world. Of particular importance are studies of the evolution of pathogen

virulence (37) and the implications of this for emerging epizootic diseases that threaten human populations. The inappropriate use of antibiotics has been implicated as an important factor in the evolution of antibiotic resistance (38-40) ;this is one area where evolutionary medicine has direct relevance to family medicine, as it provides a compelling biological argument for the restrained prescription of antibiotics.

Evolutionary biology has also been influential in the study of oncology, where cancers have been described as "microcosms of evolution." (41) The fundamental idea is that individual cancer cells behave in a fashion analogous to individual organisms and therefore are subject to competition with other cells, from natural selection of cells with survival advantages to predation by the immune system. An understanding of these processes will lead to more effective predictions of the behaviour of tumours as well as potentially more effective treatments. (41) This research has not progressed to the point where it is directly applicable to clinical family practice. A basic familiarity with this topic, however, could prove useful as family physicians play an increasingly important role in community cancer treatment. ❑

CONCLUSION

Although medical schools and physicians have generally been slow to recognize the usefulness of evolutionary medicine, there is increasing public awareness of this area. As the discipline of evolutionary medicine becomes better organized and better integrated into other fields of medicine, its practical utility will be examined in part through the generation of more testable hypotheses, particularly in the areas of disease treatment and prevention. For example, a knowledge of evolutionary medicine could be used to design health promotion programs, especially for diseases that represent adaptations to ancestral environments. (42) It is important that family physicians be aware of this growing field and of its potential applications to the practice of family medicine.

EDITOR'S KEY POINTS

- The purpose of this paper was to selectively review the main trends in evolutionary medicine research.
- The studies fell into 3 different categories: articles offering explanations for the evolutionary existence of specific diseases; articles arguing that evolutionary medicine offers a conceptual framework for medical education; and articles discussing the utility of evolutionary medicine for disease treatment and prevention.
- It is becoming increasingly important that family physicians be aware of this growing field and its potential applications to the practice of family medicine.

Competing interests
None declared

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