Evolutionary biology within medicine: a perspective of growing value

Evolutionary biology provides an essential perspective on the determinants of health and disease, believe Peter Gluckman and Carl Bergstrom. It needs to be further integrated into medical research and teaching.

Peter D Gluckman professor¹, Carl T Bergstrom professor² ³

¹Centre for Human Evolution, Adaptation and Disease, and the National Research Centre for Growth and Development, Liggins Institute, The University of Auckland, Private Bag 92019, Auckland 1142, New Zealand; ²Department of Biology, University of Washington, Seattle, Washington, USA; ³Santa Fe Institute, Santa Fe, New Mexico, USA

In the preface to his 1794 treatise *Zoonomia*—perhaps the first book in English to present concepts from which modern evolutionary thought eventually arose—Erasmus Darwin, scientist and grandfather of Charles Darwin, wrote that the purpose of such studies is to elucidate the origins of disease. Yet evolutionary biology has had little explicit role in the training of health professionals¹ and thus in how medicine is practised and research questions are developed.

Over the past decade, however, the explicit application of evolutionary principles has started to appear within a small but increasing number of medical schools, reflecting a growing recognition of the important perspectives offered on the determinants of health and disease both in individuals and across populations.² ³ ⁴ ⁵ The American Association of Medical Colleges has recently recommended establishing evolutionary biology as a required premedical competency and emphasised the value of evolutionary approaches within the medical curriculum itself.¹

Key developments in evolutionary biology and its insights for medicine include the recognition that contemporary evolutionary change is ubiquitous; the accumulation of data on genomic variation within and between human populations; a growing understanding of coevolutionary relationships between host and pathogen; the emergence of major research programmes into symbioses, particularly in relationship to the gastrointestinal microbiome; and an understanding of how evolutionary principles explain the implications of rapidly changing environments for disease susceptibility and human behaviour.⁴ ⁵ A broader understanding of symptoms of illness such as pain and fever can be developed from an evolutionary perspective and this has clinical implications, such as when to use antipyretics.

How should medical schools and programmes for undergraduate, specialist, and continuing medical education training incorporate evolutionary biology into medicine?²

**Major themes in evolutionary medicine**

Evolutionary science addresses medicine in a manner distinct from but complementary to other basic sciences, and provides hypotheses to explain many aspects of human biology and anatomy.

Some of these hypotheses are adaptive explanations that tell us about the functional significance of traits. For example, human infants are the fattest of all mammals at birth and this has implications for the propensity for humans to develop obesity and its complications later in life. This trait probably has its origin in the need to defend the rapidly growing brain against undernutrition that was likely during weaning.⁷ Understanding this could have direct implications for optimal approaches to infant nutrition.

Others are phylogenetic explanations that explain the evolutionary history of traits. Our inability to synthesise vitamin C, for example, has its origin in our frugivore primate ancestry, and is exposed as scurvy only when humans encountered atypical diets such as those on 18th century ship voyages.⁶ Life history perspectives have allowed a better understanding of the significance of the changing age of puberty and provide an explanation of how developmental factors increase the risk of disease later in life. Studies of coevolution are essential to understanding antibiotic resistance and the role of the gut microbiome.

Importantly, evolutionary principles generally provide explanations of the origins of individual variation in vulnerability to disease rather than the cause of disease itself.
Different levels of explanation

The distinction between explanations at the proximate level (pertaining to direct physiological and ontogenetic causes), and explanations at the ultimate level (pertaining to the evolutionary origins, history, and reasons for the persistence of a trait), has useful heuristic value. Proximate explanations lay out the mechanistic chain of disease development and cause along which we hope to intervene; their study and application dominates in medical research, training, and practice. Ultimate explanations, however, interpret how these vulnerabilities came to be in the first place, which has implications for patient and population management. Taken together, proximate and ultimate understandings provide a comprehensive view of a particular clinical state.

Type two diabetes mellitus, for example, can be understood in terms of altered insulin release by the pancreatic beta cell and impaired action via its receptor and signalling cascade (proximate causation); or as a mismatch between evolved biology and the evolutionarily novel nutritional and energetic environments in which most humans now live (ultimate causation).

Both approaches have clear value in explaining the problem to the patient and both lead to potential therapeutic approaches, whether pharmacological or lifestyle based. Proximate explanations are the basis of classifications of disease causation generally used in pathology (neoplastic, inflammatory, immune, and so on). Classifications based on ultimate explanations to explain vulnerability have also been developed. The distinction and synthesis of these two levels of explanation provides an integrative view of human biology and enhances clinical practice. Patients often find the ultimate levels of explanation easy to comprehend and satisfying.

Health, longevity, and fitness

Human evolution is based on selection for maximal reproductive success (which evolutionary biologists term fitness) rather than for health or longevity; this is a fundamental evolutionary principle yet tends to be poorly appreciated within medicine. Survival to reproduction and throughout reproductive life will be the focus of natural selection; survival later in life will be less strongly selected and thus selection may have compromised health in middle and old age. The principle of fitness provides a partial explanation for the emergence of non-communicable diseases in middle age and the failure of natural selection to minimise the risk of such disease.

The concept of trade-offs

Organisms cannot be perfect at everything. Selection typically drives the evolution of a beneficial trait until the marginal benefits of continuing are balanced out by the marginal costs of doing so. So the size of the fetal head is constrained by mechanisms limiting fetal growth to maternal pelvic size, contributing to the challenges of human obstetrics, as distinct from the ease of delivery in other primates. Long human postnatal dependency is thus explained; we are more immature at birth than the other great apes because brain development must be abbreviated in utero for successful delivery.

Life history trade-offs between early investment in reproduction versus later investment in repair and maintenance are at the basis of our understanding of the biology of ageing, and provide explanations for many other aspects of the human condition. For example, individuals living in uncertain circumstances are likely to deploy strategies appropriate for a shorter life span, such as earlier puberty, as evidenced by the younger age at menarche of girls born into disadvantaged environments in the developing world and migrating to the West, and by earlier menarche of girls in Western populations of lower birth weight. There may be broader public health implications for such trade-offs, where investment is made for the present rather than later.

Similar arguments have been applied to explain the relationship between early life exposures and later risks of disease. Low birth weight can be seen as an essential trade-off for immediate survival within a poor intrauterine milieu, but being born small has the consequences of greater postnatal morbidity and mortality. More subtle changes in maternal nutrition that need not affect birth size may induce epigenetic changes in the offspring. Such changes generate a metabolic physiology appropriate for a low quality nutritional environment, but the individual is then placed at greater risk of developing metabolic disease in nutritionally rich environments. This may explain population and individual variations in the sensitivity to obesogenic environments.

Understanding the dynamics of ongoing change

The human organism is a complex multi-species assemblage. Our somatic cells are outnumbered 10 to one by prokaryotic symbionts, commensals, and pathogens present within our body. We have only recently started to understand the significance of this microbial flora. Understanding that host and microbe alike have been shaped by ongoing selection allows us to make sense of how such communities are assembled and regulated by our own physiology and experiences. For example, alterations in gut microbiota are associated with both caesarean section and lack of exposure to breast milk, and both have been implicated in the increased prevalence of allergic disease; these findings have given rise to the growing study of the use of probiotics as components of infant formula.

We are now able to comprehend and model medically relevant contemporary evolutionary changes. Many involve pathogen evolution, either at the scale of an individual host (such as the evolution of the human immunodeficiency virus in response to antiretroviral therapy) or at the population level (such as annual evolution of the influenza virus, and the evolution and spread of antibiotic resistant bacteria). Evolutionary models at the level of a single organism have proved useful in understanding the progression of neoplasia and the development of resistance to chemotherapy.

Impact of recent rapid environmental change

Given the rapid environmental changes resulting from our evolved technological capacity and affecting our nutritional, social, and physical environments, mismatches can occur between our present environmental exposures and those for which our physiology has evolved, as illustrated by the example of metabolic disease.

The place of evolutionary medicine in practice and research

Evolutionary thought will only on occasion directly affect individual therapeutic decisions. Yet it will form a critical part of the worldview for the practice of medicine. Evolutionary reasoning provides a conceptual framework within which to situate the profusion of facts that constitute medicine, and so helps organise knowledge of biological systems. It allows the physician to answer patients’ questions about the origin of
The future of evolutionary medicine

Evolutionary medicine will not—and should not—emerge as a distinct clinical discipline. Rather, evolutionary reasoning is a core competency just as anatomy and communication skills are core competencies for most physicians. Evolutionary reasoning will only rarely lead to different therapeutic choices, as in the case of antibiotic management, although it may lead to new clinical insights. Evolutionary biology provides a worldview for the physician—an integrated view of human biology, and a powerful paradigm for generating a broader research agenda. Evolutionary explanations may offer the patient valuable insights into their condition: “Why is this happening to me? Why is my body letting me down?” Science, through an understanding of our evolutionary history and the evolutionary processes that constructed our physiology, will come closest to answering the question, “What does it mean to be a human organism?”

Acknowledgments: The authors thank Jevin West, Tatjana Buklijas, Alan Beedle, and Felicia Low for their helpful comments and suggestions. PDG is funded by the National Research Centre for Growth and Development. CTB is funded by the National Institute of General Medical Sciences Models of Infectious Disease Agent Study program cooperative agreement 5U01GM07649.

PDG heads the Centre for Human Evolution, Adaptation and Disease, which investigates how ecological and evolutionary-developmental interactions with the environment influence human health and non-communicable disease. He is a co-author of a textbook on evolutionary medicine, and has introduced evolutionary medicine to the medical curriculum at the University of Auckland. CTB is an evolutionary biologist whose mathematical modelling and computer simulation work has contributed to studies of the role of information in social and biological systems. His recent projects have contributed to a number of applied studies in disease evolution, including analysis of antibiotic resistant bacteria in hospital settings and models of the interaction between ecology and evolution in novel emerging pathogens. Both authors contributed to the preparation and review of the article. PDG is guarantor.

Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; and no other relationships or activities that could appear to have influenced the submitted work.

Provenance and peer review: Not commissioned; externally peer reviewed.

1 AAMC-HHMI Scientific Foundation for Future Physicians Committee. Scientific foundations for future physicians. American Association of Medical Colleges and Howard Hughes Medical Institute, 2009.
2 Nesse RM, Williams GC. Why we get sick: the new science of Darwinian medicine. Times Books, 1995.
3 Stearns SC, Koella JC. Evolution in health and disease. Oxford University Press, 2008.
4 Nesse RM, Stearns SC. The great opportunity: evolutionary applications to medicine and public health. Evol App 2008;1:29-48.
5 Gluckman PD, Beedle AS, Hanson MA. Principles of evolutionary medicine. Oxford University Press, 2009.
6 Nesse RM, Bergstrom CT, Ellson PT, Flier JS, Gluckman PD, Govindaraju DR, et al. Evolution in health and medicine: Sackler colloquium: making evolutionary biology a basic science for medicine. Proc Natl Acad Sci USA 2010;107:1800-7.
7 Kuzawa CW, Gluckman PD, Hanson MA. Developmental perspectives on the origin of obesity. In: Funtuzi G, Mazzone T, eds. Adipose tissue and adipokines in health and disease. Humana Press, 2007:207-19.
8 Tinbergen N. On aims and methods of ethology. Z Tierpsychol 1963;20:410-33.
9 Gulickman P, Hanson M, Mismatch: Why our world no longer fits our bodies. Oxford University Press, 2006.
10 Kirkwood TB, Austad SN. Why do we age? Nature 2000;408:223-9.
11 Gulickman PD, Hanson MA. Evolution, development and timing of puberty. Trends Endocrinol Metab 2006;17:7-12.
12 Nettle D. Dying young and living fast: variation in life history across English neighbourhoods. Behav Ecol 2010;21:387-95.
13 Gluckman PD, Hanson MA, Spencer HG, Bateson P. Environmental influences during development and their later consequences for health and disease: implications for the interpretation of empirical studies. Proc Biol Sci 2005;272:671-7.
14 Godfrey KM, Sheppard A, Gluckman PD, Lillycrop KA, Burdge GC, McLean C, et al. Epigenetic gene promoter methylation at birth is associated with child's later adiposity. Diabetes 2011;60:1528-34.
15 Berg RD. The indigenous gastrointestinal microflora. Trends Microbiol 1996;4:430-5.
16 Kaza U, Knight A, Bahna SL. Risk factors for the development of food allergy. Curr Allergy Asthma Rep 2007;7:182-8.
17 Merlo LM, Peppard JP, Reid BJ, Maley CC. Cancer as an evolutionary and ecological process. Nat Rev Cancer 2006;6:924-35.
18 Marks IM, Nesse RM. Fear and fitness: An evolutionary analysis of anxiety disorders. Ethol Sociobiol 1994;15:247-81.
19 Young JH, Chang YP, Kim JD, Chretien JP, Klug RJ, Levine MA, et al. Differential susceptibility to hypertension is due to selection during the out-of-Africa expansion. PLoS Genet 2005;1:e32.
20 Bergstrom CT, Lo M, Lipsitch M. Ecological theory suggests that antimicrobial cycling will not reduce antimicrobial resistance in hospitals. Proc Natl Acad Sci USA 2004;101:13268-90.
21 Gluckman PD, Lew PM, Franks K. Puberty and adolescence: transitions in the life course. Improving the transition: reducing social and psychological morbidity during adolescence. Office of the Prime Minister's Science Advisory Committee, 2011.
22 Lipsitch M, Bergstrom CT, Levin BR. The epidemiology of antibiotic resistance in hospitals: paradoxes and prescriptions. Proc Natl Acad Sci USA 2000;97:1938-43.
23 Bergstrom CT, Feldgarden M. The ecology and evolution of antibiotic-resistant bacteria. In: Stearns SC, Koella JC, eds. Evolution in health and disease. 2nd ed. Oxford University Press, 2008:125-37.
24 Nesse RM. Ten questions for evolutionary studies of disease vulnerability. Evol Appl 2011;4:264-77.

Cite this as: BMJ 2011;343:d7671
© BMJ Publishing Group Ltd 2011
Figure

Scurvy, cephalopelvic disproportion, and antibiotic resistance: evolutionary biology offers invaluable insights

[Image: Robert McGinnis/NGIC/Bridgeman / no credit / Doncaster and Bassetlaw Hospitals (SPA)]