



PHILOSOPHY OF MEDICINE

Darwinian medicine – an evolutionary perspective on health and disease

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Evolutionary theory, which gave rise to a new discipline named Darwinian medicine, has had a major impact on modern medical research and practice. This paper focuses on phenomena such as evolved host defences, evolution of virulence, genetic conflicts with other organisms, adaptations to novel environments, and tradeoffs and constraints in biological systems.

Charles Darwin enrolled as a medical student at the University of Edinburgh in 1825.¹ Disturbed by operating theatre scenes, he left medicine and Edinburgh, and in 1827 was studying in Cambridge to become a pastor. Darwin subsequently revolutionised the science of biology with his theory of evolution by natural selection, and deeply influenced biology, many other disciplines, cultural values and society in general.² Medical science, however, has recognised the significance of Darwinian theory only recently. In 1991, the psychiatrist Randolph Nesse and the evolutionary biologist George Williams³ explicated the principles now known as Darwinian, or evolutionary, medicine. Thus, nearly 110 years after his death, Darwin was eponymously re-united with the discipline which he had left as a student before returning to it as a hierophant.

What is Darwinian medicine?

The traditional approach to medicine is to determine the proximate causes for disease, asking questions such as 'what' and 'how'. The Darwinian approach focuses on the ultimate, or evolutionary, reason for the origin of disease, i.e. the 'why'. Biology alone would be useless were it not for the explanatory power of the evolutionary concept that '... nothing in biology makes any sense except in the light of evolution'.⁴ This adaptationist approach can benefit our efforts to combat disease and improve our effectiveness as clinicians, researchers and educators.

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Darwinian medicine comprises five major categories, namely: (i) evolved host defences; (ii) evolution of virulence; (iii) genetic conflicts with other organisms; (iv) adaptation to novel environments; and (v) trade-offs and constraints in biological systems.

Evolved host defences

A principle tenet of evolutionary medicine is to distinguish between clinical signs which are host defences, and those which are pathogen offences, or manifestations of some defect in the host.⁵ Without making this distinction, the clinician may do the patient more harm than good. Host defences are protective mechanisms that have been shaped by natural selection.³ Many host defences, e.g. pain, nausea, vomiting, diarrhoea, fatigue and anxiety, are clearly recognised, and clinicians tussle with the benefits and the costs of intervention medication to combat these. Such interventions, however, while alleviating discomfort associated with the signs and symptoms of disease, may inadvertently suppress the patient's defences, thereby promoting pathogen offences and transmission.

DuPont and Hornick have provided an example of how intervention may block natural defences.⁶ Demonstrating the value of diarrhoea as a host defence, they compared the recovery of patients infected with *Shigella*. Patients not using antidiarrhoeal medication showed reduced recovery time, while those using anti-diarrhoeal medication experienced extended illness, were prone to develop complications, and were more likely to become carriers. Host defences are numerous and include common contraindications for cough suppressants, patients at risk of developing pneumonia shortly after surgery due to subtle defences such as those associated with acute phase response, anxiety,⁷ and the inability to perceive pain.⁸ As a defence mechanism, the acute phase response can manifest behavioural and physiological changes ranging from severe infection to cancer and trauma.⁹ Significant aspects of this response are ensuing fever, loss of appetite, listlessness, increased serum copper concentrations, sequestration of iron and zinc, metabolic alteration, and increased synthesis of C-reactive protein, fibrinogen and ceruloplasmin. From a Darwinian perspective, it is interesting that the acute phase response is initiated by the body's own cytokines (i.e. interleukin 1 and 6; tumour necrosis



factor) and seems to be characteristic of all vertebrates. Even certain invertebrates display a type of 'behavioural fever', indicating that this phenomenon represents a fundamental and well-refined mechanism of defence, as reflected in its long phylogenetic history.¹⁰ While the phylogenetic conservation of this trait, the subcomponents are more difficult to demonstrate as having beneficial value, especially because of their harmful effects, e.g. fever, listlessness and apoptosis.

Evidence in favour of the beneficial effects of these subcomponents has accumulated. A convincing argument for the benefits of fever and the control of infection despite its metabolic costs has been presented,¹¹ and increasing evidence demonstrates the benefit of these subcomponents.¹² Evidence points towards the existence of numerous adaptive host defences. While counter-arguments for intervention suggest that blocking these defences does not result in ill-effects in all cases, a valid explanation for these exceptions is based on the 'smoke detector principle'.³ This may be described as a host defence system modelled by natural selective forces that favour an overly sensitive response, since the cost of numerous 'false alarms/defences' is small compared with no response, which may result in death.

The evolution of virulence

Evolutionary principles have been used to effectively describe and analyse virulence from the pathogen's perspective. Classic arguments held that pathogens evolve towards reduced virulent states as they attempt to balance a need for greater virulence against the avoidance of host death before transmission of pathogenic genes. This concept has been shown to be a simplification and generalisation of what happens in pathogen-host interactions.¹³ The major difficulty with this idea of evolution towards equilibrium is that pathogens acting in a benign fashion are susceptible to 'selfish gene' mutations, which promote faster pathogen replication.¹⁴ Where transmission is rapid, pathogens need have no regard for the host and the level of virulence; but where transmission is slow, they benefit by maintaining the host and increasing the likelihood of transmission.¹³

Diseases that induce actions enhancing transmission tend not to progress towards reduced virulence, and thus behaviours which facilitate the spread of disease can allow greater virulence.¹⁵ Pathogens may even affect the host's behaviour: the fluke *Dicrocoelium dendriticum* affects its intermediate host, the ant, causing it to lock onto the top of grass stems;¹⁵ rats infected with *Toxoplasma* are less fearful of cats, thus aiding transmission;¹⁴ and the *Plasmodium* virus incapacitates its host, thus reducing its ability to fend off attackers. This insight is clinically relevant, as medical practitioners, hospitals and other facilities play a critical role in preventing, or conversely promoting, pathogen transmission. The transmission of

disease has been mathematically modelled, and has shown that vaccines which prevent infection can constrain pathogen prevalence and virulence.¹⁶ However, vaccines that offer only anti-toxin immunity lead predictably to increased disease prevalence and virulence as a by-product of the host being kept alive. This phenomenon in turn leads to propagation of the pathogen, and thus there is no selection against mutant pathogens with increased virulence.

Genetic conflicts with other organisms

The gene is the most basic level where natural selection may take place, although not exclusively so, as selection may occur at the level of the individual, a population, or even of the species. Genetic (or genic) conflicts may arise out of dissimilar survival interests between genes. One can postulate that within the same organism, gene interactions (which may primarily be co-operative) can exhibit a degree of conflict. Genetic conflicts are of particular relevance to infectious diseases, where the complexity of the immune system and its multiple cascading levels of host defences are a direct cause of the race for survival between pathogen and host. It has been argued that the major reason for sexual reproduction is to facilitate rapid genetic change, thus increasing variability and allowing the host to keep a step ahead of pathogens.¹⁷ Even within the individual organism is an evolutionary race for survival between the ever-growing pathogen population and the defences of the individual's lymphocyte population.¹⁸ It has also been argued that the complexity of the female reproductive tract and the vast amount of sperm required for fertilisation indicates a genetic conflict involving passive female choice for high-quality sperm and offspring, and a conflict with male sperm.¹⁹

Adaptation to novel environments

A major area of enquiry in Darwinian medicine stems from the concept that the human body adapted to a Palaeolithic environment and is maladapted to modern lifestyles.²⁰ Popular and scientific authors aplenty have addressed the ills of modern living, such as obesity, lack of exercise, and back pain. The notion of environmental evolutionary adaptation is a reminder of the differences between 'then' and 'now', though it is perhaps too hypothetical, as our hominid ancestors have passed through a gamut of different environments.²¹ While Darwinian enquiry considers past environments, an important concept is that most of today's disease states are the result of novel aspects of our environment to which we have not adapted.²²

A contemporary epidemic accounting for a high proportion of deaths is the triad of hypertension, obesity and atherosclerosis.²³ Compared with Palaeolithic diets, humans now consume much more fat, sugars and salt, but insufficient fibre and phytochemicals.²⁴ This dietary tendency can be regarded as a design defect that goes beyond our metabolism



and arteries to a phylogenetic 'throw-back' as to how our brains perceive and process stimuli from these food sources. Palaeolithic communities had a penchant for sugars and fats, which would have been valuable energy sources when wandering in hostile environments. This proclivity persists, but the availability of these resources has changed dramatically. While hunter-gatherer communities invested substantial time and energy to obtain an occasional taste of salt or sugar, we obtain our 'fix' from supermarkets or home-delivery pizzas. The problem therefore lies not in lack of willpower to stop unhealthy eating but in the very design of the brain which integrates information concerning exercise and diet. Other examples of maladaptation to modern environments include the increasing incidence of breast cancer (most cases shown to be related to genetic abnormalities), drug dependency, and even eating disorders.

Trade-offs and constraints in biological systems

The susceptibility of the human body to disease demonstrates that our designs are sub-optimal and that modifications are possible, although at a cost. A hypothetical increase in the strength of limb bones to prevent fractures may reduce the number of fractures, but at the cost of dexterity and mobility, thus impeding the ability to compete for food and mates. In clinical practice, we are familiar with the consequences of a trade-off between our supposed quadrupedal past and (relatively) recently acquired bipedality. A bipedal gait, while having advantages, has also resulted in uniquely human medical problems such as pressure on the lower spine manifesting as pain, difficulties and complications of childbirth, and a greater tendency to fainting and circulatory problems. The contribution of evolutionary history towards understanding the aetiology of lifestyle diseases may result in yet greater understanding and success in reducing their morbidity and mortality.

Teaching Darwinian medicine

The new discipline of Darwinian medicine has made a significant impression on research in medical and related sciences.³ University courses for science degrees in Darwinian medicine have been introduced, but medical schools are less receptive to the inclusion of evolutionary theory in their curricula.²⁵ In the USA, 48% of deans from 50 medical schools think that the knowledge of evolutionary theory is important for physicians, while 32% stated that their schools teach minimum core subjects on evolutionary biology, and only 8% have staff with PhDs in evolutionary biology.²⁶ Lack of time and qualified staff, which could be circumvented with better organisation and planning,²⁶ were the main impediments to incorporating evolutionary theory into medical curricula.

Including principles of Darwinian medicine in curricula does not necessitate a separate course;²⁷ the subject may be included

in preclinical and clinical years or as a prerequisite to entering medical school.

Practising and teaching science and medicine are strongly influenced by broader social, cultural and political factors. In some countries or sectors of the same society, the teaching of evolution is still taboo. In the USA, the '... education system is experiencing very strong anti-evolutionary feeling coming from certain religious groups'.²⁷ Similarly, in South Africa under National Party rule, evolution was not taught in schools in the second half of the 20th century. Paradoxically, at the same time, major palaeontological and palaeoanthropological discoveries and important theoretical insights were being made in the country.²⁸ Since 1994, however, evolutionism is becoming an integral part of biology curricula in South African schools. But significant academic and non-academic resistance towards Darwinism still persists.²⁸ A challenge for proponents of Darwinian medicine²⁶ is to achieve greater presence in medical curricula – which also might meet considerable resistance and provoke controversy.

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