Evolution and the curriculum

Given the importance of evolution in explaining disease, **Daniel Racey and Stuart West** believe it merits more teaching time

Charles Darwin began his academic career as a medical student. Fortunately, he found his studies at the University of Edinburgh tedious and unpleasant. He dropped out, took another degree, and embarked on the voyage of the *Beagle*. The rest is history.

Since then medical degrees have changed to prevent talented students such as Darwin leaving the profession. Curriculums have been explicitly designed to promote deep understanding of principles rather than rote learning of facts.[2]

This article assumes that evolution through natural selection has been the major mechanism in shaping the biology of humans and pathogens. This is not a controversial view within the scientific community. However, a substantial minority of medical undergraduates find the concept that humans evolved from apes difficult to accept, even though they may have no problem acknowledging the evidence for microevolution (changes below the level of the species). About 10% prefer literal creationist views for human genesis[3] than the theory of natural selection (at the species level).

Hardly any curriculum time

It seems that a profound understanding of human disease requires some understanding of how diseases evolve. However, medical schools give evolution only a cursory amount of time. In the most recent survey only 11% of UK medical schools included evolutionary biology in the core curriculum.[3] Consequently, 89% of UK medical students will probably not be taught evolutionary principles during their degree. Similar figures have been reported in surveys of medical schools in the United States and Australia.[4 5]

Historically, the content of medical curriculums was decided when physiology and biochemistry were in their heyday and evolutionary biology was not fashionable. Recent surveys of medical school deans have reported a lack of teaching time and a lack of faculty expertise as being the main impediments to teaching evolution.[3 4]

Exposure to evolutionary ideas is important for three reasons. Firstly, a diverse array of clinical decisions requires an understanding of evolution (table). Secondly, there exists a common misunderstanding—that traits evolve for the good of the species. It is more appropriate to consider the gene as the fundamental unit of natural selection. This is important because selection acting at the level of the gene may be detrimental to the species or even the individual (box). And thirdly, a knowledge of evolutionary principles leads to insights about the nature of disease.

The third reason is important. Applying evolutionary thought to disease is not self evident but is profoundly illuminating. A concrete example, the evolution of ageing, shows how studying evolution can lead to deeper medical understanding.

Ageing as an example

Why do we age and die? The proximate reason for ageing is a progressive accumulation of molecular damage. Such damage is intrinsically random in nature, but its rate of accumulation is regulated by genetic mechanisms for maintenance and repair. As cell defects accumulate, the body experiences age related frailty.

A thought experiment is helpful. Consider a population of a theoretical species. This species does not age. It can live and reproduce for an infinite amount of time. However, external catastrophes such as lightning strikes and predation will mean that there are relatively more young individuals than old individuals.

This leads to the key evolutionary principle that the strength of natural selection declines with the age at which a gene is expressed. Natural selection cannot act efficiently on genes that are detrimental to elderly individuals. This is because of the high probability that most carriers will die by other causes before the gene's action is experienced.

Suppose a mutation arises that benefits reproduction in young individuals but disadvantages the survival of old individuals. For instance, a mutation might arise that increases testicular cell division to produce more sperm at young ages at the cost of increased testicular cancer late in life. This mutation will be favoured by natural selection and will result in a decline in survival with age. A large body of experimental and comparative evidence in animals indicates that increased fertility at early ages leads to greater ageing. Death is the price we pay for reproducing.

Biologists have recently begun to elucidate the link between the proximal and ultimate

"Nothing in biology makes sense except in the light of evolution"
Theodosius Dobzhansky, 1973[1]

Evolutionary theory has direct clinical relevance to medicine

Evolutionary concept	Change in clinical understanding or intervention
Evolution of pathogen resistance	Targeted multidrug therapies for specific disease, eg, tuberculosis, HIV Reduction in prophylactic antibiotic use
Evolutionary trees of pathogens	Anticipating epidemics through tracking of genetic change in animal borne diseases, eg, bird flu When and how often drug immunity arises
Distribution of inherited disease	Heterozygote resistance to malaria explains prevalence of sickle cell anaemia in different ethnic groups Kinship theory of genomic imprinting explains persistence of genetic diseases, eg, Prader-Willi syndrome
Evolutionary response to immunisation	Diphtheria has evolved attenuated virulence in response to vaccination Transmission blocking malaria vaccinations may increase malaria virulence
Cancer distribution within the body	The model of cancer as a microevolutionary problem within the body explains timescale and spatial distribution of tumorogenesis, eg, colorectal cancer
Rates of evolutionary change—lack of adaptation to modern lifestyle	Fetuses under nutritional stress switch to a metabolic state that protects against starvation. This interacts with modern diets to predispose individuals to diabetes, hypertension, and obesity Human eyes evolved to look into far distance. Close work such as reading leads the eyeball to develop myopia Changes in lifestyle may leave modern populations vulnerable to certain cancers, eg, breast cancer and reduced birth rate in women

Fig 1 Thomas Henry Huxley (1825-95) was called Darwin's bulldog because of his promotion of the theory of natural selection. He was also a thoughtful medical educator, aware of the importance of well designed medical curriculums

causes of ageing. They have discovered that costly processes, such as somatic repair and reproduction, compete for resources. One of the key pathways that controls allocation between repair and reproduction appears to be the insulin-like growth factor 1 (IGF1)-insulin signalling pathway. If times are lean, it is likely that young individuals will die. Animals cease reproduction in response to environmental scarcity. If an animal's diet is reduced, it diverts its resources from reproduction to somatic repair through changes in IGF1-insulin signalling.[6] Reproduction takes resources that would otherwise be allocated to cell repair, thereby causing ageing. This pathway seems to be conserved in many species, from worms to insects to mammals, and explains why dietary restriction leads to longer life in many species. There is some evidence that a very low food intake prolongs lifespan in humans.[6]

What does this tell doctors? Unfortunately, evolutionary theory predicts that ageing is a programmed inevitability. Ageing will occur in all tissues as the result of the actions of many genes. However, there is hope. Experiments in laboratory animals have shown that the rate of ageing can be slowed and the overall control of the many genes responsible for ageing may involve only a few master genes. The IGF1/insulin pathway switches on or off hundreds of different genes involved in somatic repair.

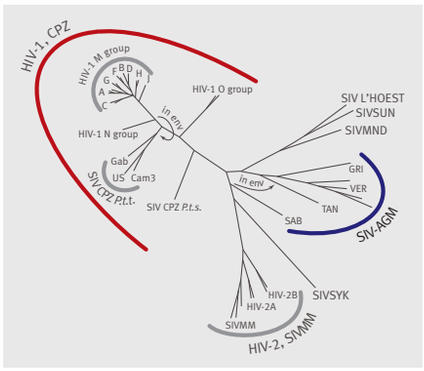

Fig 2 Evolutionary tree of human and simian immunodeficiency viruses, showing how HIV evolved from viruses that affect apes (SIVs)

Conclusion

The discussion of ageing shows how evolutionary biology illuminates a key question in medicine. The prestigious journal *Science* considers the lack of knowledge of evolution among the medical community serious enough to have published a recent editorial entitled "Medicine needs evolution."[7] The authors made a plea to recognise evolution as a basic science for medicine. They recommend that evolution should be incorporated in high school, undergraduate, and graduate courses and that questions about evolution should be included in medical licensing examinations.

The anatomist Thomas Henry Huxley was the key promoter of the theory of natural selection when it was struggling for acceptance. In 1876 he lamented, "The burden we place upon the medical student. . . a system of medical education that is actually calculated to obstruct the acquisition of sound knowledge and to heavily favour the crammer" (fig 1).[3] Medical curriculums have abandoned rote learning to emphasise deep understanding of biological principles. A medical education that neglects evolutionary biology is concerning.[2]

Mothers and fathers: pregnancy and strife

The realisation that the gene is the fundamental unit of selection is a key theoretical advance in evolutionary biology. In most cases, natural selection acts on the gene through its effect on an individual's phenotype. The assumption that natural selection acts at the level of the individual is a good working approximation. However, the selfish gene paradigm is important for doctors to understand because sometimes genes work against an individual's own interests.

An example is natural selection and pregnancy. It is reasonable to assume that the amount a mother invests in a fetus is at the expense of her future reproduction and survival. Fetal genes from a father are under different selection pressures to fetal genes inherited from the mother. If a mother has subsequent offspring with a different father, the genes from a father will not benefit from the later survival and reproduction of the female parent. Evolutionary theory predicts that paternally derived genes will be selected to produce larger placentas that extract more resources from mothers.

Experiments in mice provide support for the theory.[8] A gene called insulin-like growth factor 2 (IGF2) is produced by fetal cells to stimulate fetal growth. Normally only the paternally inherited copy is active. If the father's copy is knocked out experimentally, offspring are born that weigh 40% less. Many genes vary in their expression according to whether they are inherited from a mother or a father. This phenomenon is called imprinting and is the basis for some inherited diseases, such as Prader-Willi syndrome.[8]

Traditionally, medicine has understood the physiology of pregnancy to involve benign hormonal interplay. From an evolutionary perspective, pregnancy is predicted to involve conflict between mother and fetus, driven by paternally derived genes with different evolutionary interests to the mother.

Hormones in pregnancy

Hormonal signalling in pregnancy is almost unique. The mother's hormonal communication systems are under joint control of the mother and the fetus through the fetoplacental unit. The fetoplacental unit secretes several hormones into the mother's body to increase nutrient concentrations in the maternal blood.

Natural selection should favour increased production of hormones by paternally inherited genes to increase fetal nutrition. At the same time it favours maternal genes that conserve resources. About a gram a day of human placental lactogen is secreted into the maternal blood stream but has relatively minor effects.[8] Placental hormones are produced in enormous amounts compared with other hormones, which suggests a conflict between the fetus and the mother about placental development. Paternally derived genes in the fetus may secrete these hormones in an attempt to persuade the mother to act against her best interests.

Current research at Harvard Medical School is exploring whether signalling conflict between mother and fetus can explain pre-eclampsia.[9] In pre-eclampsia, the placenta produces large amounts of the protein Sft1, which circulates systemically. Sft1 causes maternal vasoconstriction, increasing blood supply to the placenta but starving important tissues of blood and leading to kidney and liver failure. Sft1 is raised in women with pre-eclampsia before they become symptomatic and increases as the disease progresses.[8] In addition, pre-eclampsia is associated with twin pregnancies, where there is high fetal demand on nutrients.

Daniel Racey third year medical student, Peninsula Medical School dangling@hotmail.com

Stuart West professor of evolutionary biology, School of Biological Sciences, University of Edinburgh, Edinburgh EH9 3JT

Competing interests: None declared.

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

1 Dobzhansky T. Nothing in biology makes sense except in the light of evolution. *American Biology Teacher* 1973;35:125-9.
2 General Medical Council. *Tomorrow's doctors: recommendations on undergraduate education 2003. London: GMC, 2003*. www.gmc-uk.org/education/undergraduate/tomdoc.pdf
3 Downie JR. Evolution in health and disease: the role of evolutionary biology in the medical curriculum. *Bioscience Education* 2004;4:1-16.
4 Nesse RM, Schiffmann JD. Evolutionary biology and the medical school curriculum. *Bioscience* 2003;53:585-7.
5 Short R. Darwin, have I failed you? *Lancet* 1994;343:528.
6 Partridge L, Gems D. Sex and death: what is the connection? *Cell* 2005;120:461-72.
7 Nesse RM, Stearns SC, Omenn GS. Medicine needs evolution. *Science* 2006;311:1071.
8 Haig D. Genomic imprinting and kinship: how good is the evidence? *Ann Rev Genet* 2004;38:553-85.
9 Yuan HT, Haig D, Karumanchi SA. Angiogenic factors in the pathogenesis of preeclampsia. *Curr Top Dev Biol* 2005;71:297-312.