Chapter 27
Darwin, Evolution, and Medicine: Historical and Contemporary Perspectives

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Abstract Monographs commemorating the work of Charles Darwin (1809–1882) typically cover a wide range of topics on which the theory of evolution has thrown some light. The influence of evolutionary thought on medicine was, until recently, often left in the dark, however. Yet evolutionary biology has crossed path with medicine more than once during the last 150 years, and the changing nature of these interactions has only begun to be examined historically and philosophically. Since more than 20 years, researchers are increasingly addressing the nature and causes of health and disease from an evolutionary standpoint. In this chapter after surveying the reception of Darwin's work by medical doctors and the relation between evolutionary thinking and eugenics, I argue that distinguishing 'evolutionary' from 'Darwinian' medicine will help us assess the variety of roles that evolutionary explanations can play in a number of medical contexts. Because the boundaries of 'evolutionary' and 'Darwinian' medicine overlap to some extent, they are best described as distinct 'research traditions' rather than as competing paradigms. But while evolutionary medicine does not stand out as a new scientific field of its own, Darwinian medicine is united by a number of distinctive theoretical and methodological claims. For example, evolutionary medicine and Darwinian medicine can be distinguished with respect to the styles of evolutionary explanations they employ. While the former primarily involves 'forward looking' explanations, the latter depends mostly on 'backward looking' explanations. A forward looking explanation tries to predict the effects of ongoing evolutionary processes on human health and disease in contemporary environments (e.g., hospitals). In contrast, a backward looking explanation typically applies evolutionary principles from the vantage point of humans' distant biological past (i.e. the Pleistocene) in order to assess present states

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of health and disease. Both approaches, however, are ultimately concerned with the prevention and control of human diseases. In conclusion, I raise some concerns about the claim that 'nothing in medicine makes sense except in the light of evolution'.

1 Introduction

Centenary commemorations provide long-awaited opportunities to explore the influence of scientific ideas and methods developed previously, but also allow deconstructing myths and revisiting historical claims or omissions. Monographs commemorating the work of Charles Darwin (1809–1882) typically cover a wide range of topics on which the theory of evolution has thrown some useful light. The influence of evolutionary thought on medicine and the health sciences, however, was until recently a rather neglected topic. The essays collected in *Darwinism and Modern Science* (1909) published on the occasion of Darwin's hundredth birthday and the fiftieth anniversary of *On the Origin of Species* (1859), for instance, explored how the theory of evolution impacted on the natural and social sciences, including philosophy and history, but did not consider health or disease. At least one physician addressed the question directly this year, though. In his Bradshaw lecture on "Darwinism and Medicine", J.A. Lindsay considered the "significance of Darwin's great discovery for medical thought and practice" (1909, 1325). Musing on the significance of pathologies, he concluded that disease "becomes something more than a disagreeable and embarrassing fact when we realize how closely it is related to evolutionary processes". Disease, he continues, "even takes its place – a temporary place we may hope – in the eternal order" (1909, 1331). *Evolution in the Light of Modern Knowledge* (1925), published a few years later, contained no contribution on medicine and evolution either. F. W. Andrewes, a professor of pathology in London, spotted this neglect in his paper "Disease in the light of evolution" and hoped, doing so, "to supply the missing chapter" (1926, 1075). The second large-scale commemoration of Darwin's work marked the centenary of the publication of *On the Origin of Species* in 1959 and appeared to have had equally little to say about the relations between evolutionary biology and medicine at the time.[1] The rise and fall of eugenics during the twentieth century played a critical part in this apparent lack of interest (Méthot 2014).

Yet evolutionary biology has crossed path with medicine more than once since the publication of *Origins of Species* in 1859 although the changing nature of these interactions, and that of their current relation, has only begun to be addressed

[1] In her essay, Betty Smocovitis relates the organization of the 1959 centenary in the United States by the Darwin Centennial Committee. To the exception of Ilza Veith who was from the department of medicine and was interested in the history of medicine, the other committee members were from the departments of zoology, geography, and paleontology. Veith's own contribution to the centenary, however, was not on medicine but on "Creation and Evolution in the Far East" (Smocovitis 1999, 318).

historically and philosophically.[2] In 2009, the questions as to how do Darwin's theories relate to medicine historically, and what the relations between the medical sciences and evolutionary biology are today, gained momentum. Those questions were at the forefront of numerous workshops held worldwide in addition to being the focus of publications in medical, science, or education journals.[3] While the progressive growth of mechanistic explanations of disease can be regarded as 'one of the most salient features of the development of medicine over the past three centuries' (Tracy 1992, p. 53; Campaner 2011), we are witnessing rapid developments in evolutionary explanations of disease (Williams and Nesse 1991; Nesse and Williams 1996; Stearns 1999; Trevathan et al. 2008; Stearns and Koella 2008; Gluckman et al. 2009; Perlman 2013). Since more than 20 years, in fact, the nature and causes of health and disease are increasingly being addressed in the light of evolution, a progression indicating a change in both the public and scientific perception of the role of evolutionary biology in medicine as well as the emergence of 'evolutionary medicine as a concept' (Alcock 2012). At a more general level, the steady progression of papers on evolutionary medicine topics signposts a recent convergence between evolutionary and functional biology, or between "why" and "how" questions, as seen in fields such as evolutionary developmental biology and experimental evolution (Morange 2010).

Reflecting this attempt at bridging the gap between evolutionary theory and medicine, two new scientific journals were recently launched: *The Journal of Evolutionary Medicine* (2012), edited by Paul Ewald, and *Evolution, Medicine, and Public Health* (2013), edited by Stephen Stearns. This current interest is also illustrated by the organization of a number of international conferences that aim to assess the medical consequences of the evolutionary past of human beings and to negotiate a space for the teaching of evolution in medical schools (see Nesse et al. 2010). While the introduction of evolutionary courses in the medical curriculum is yet to be achieved, it is noteworthy that university programs dedicated to questions of health and disease from an evolutionary point of view are growing in several distinguished institution (e.g. The Centre for Human Evolution, Adaptation, and Disease at the University of Auckland, the Centre for Evolutionary Medicine at the University of Zurich, and the Center for Evolutionary Medicine at Arizona State University). Despite closer interactions, the application of evolutionary biology to medicine remains controversial (Cournoyea 2013; Valles 2011; Méthot 2009).

[2] See, for example, Buklijas and Gluckman (2013), Cournoyea (2013), Alcock (2012), Ruse (2012), Valles (2011), Antolin (2011), Zampieri (2009a), Bynum (1983, 2002). Needless to say, a complete survey of the complex and changing relations between medicine and evolutionary biology is far beyond the scope of this paper.

[3] See the contributions in the special issue in *The Lancet*, December 2008. See also the more recent special issue "In the Light of Evolution: Interdisciplinary Challenges in Food, Health, and the Environment" in *Evolutionary Applications* 2011 4(2) and the one on "Evolution and Medicine" in *Evolution: Education and Outreach* 2011 4(4).

Sometimes these evolutionary perspectives go under the heading of 'Darwinian medicine', but occasionally, the term 'evolutionary medicine' is used instead. This is done on the grounds that the term Darwinian medicine narrows the concept of evolution to the processes of natural selection and adaptation while evolutionary medicine is more general and acknowledges other important aspects of the theory of evolution such as symbiosis, the role of epigenetic processes, and so on (Swynghedauw 2004; Lewis 2008). However, the nomenclature is not firmly established, and often, the expressions are used interchangeably (Zampieri 2009a, p. 347). As one of my goals for this article, I defend a methodological distinction between two evolutionary approaches that I have sketched elsewhere (Méthot 2009). I argue that the terms Darwinian medicine and evolutionary medicine are useful for expressing the contrast between the two orientations. I follow Stephen Lewis (2008) in drawing this distinction, but in contrast with Lewis, what I propose is informed by David Buller's distinction between Evolutionary Psychology as specific to the work of John Tooby and Leda Cosmides and evolutionary psychology broadly construed (Buller 2007, p. 256). Buller's distinction is important because it permits the distinctiveness of the former to be characterized and contrasted with other kinds of biological explanations of human behaviour, which involve evolutionary biology, such as evolutionary anthropology or human behavioural ecology. Similarly, I want to argue that distinguishing evolutionary from Darwinian medicine will help us assess the variety of roles that evolutionary explanations can play in a number of medical contexts. Because the boundaries of evolutionary and Darwinian medicine overlap to some extent, however, they are best described as distinct 'research traditions' rather than as competing paradigms.[4] Terminology aside, the distinction is not intended to promote a normative division of labor among practitioners but rather to draw attention to the different methodological principles and underlying assumptions that guide research in these areas, in addition to some possible historical connections with older research traditions.

First, I provide an overview of the historical reception of Darwin's theory by medical doctors in order to contextualize the recent development of Darwinian and evolutionary medicine. Then, I survey the relation between evolutionary thought and eugenics. Coming up to more contemporary works, I draw a contrast between evolutionary and Darwinian medicine before giving a more fine-grained critical description of the field of Darwinian medicine. Then, I show that evolutionary and Darwinian medicine can be distinguished with respect to the styles of evolutionary explanations they employ. Whereas the former primarily involves 'forward looking' explanations, the latter depends mostly on 'backward looking' explanations. A forward looking explanation tries to predict the effects of ongoing evolutionary processes on human health and disease in contemporary environments (e.g., hospitals). In contrast, a backward looking explanation typically applies evolutionary

[4] I follow Downes S (2008) "Evolutionary psychology", in *Stanford Encyclopedia of Philosophy*. Recently, Nesse suggested that "in order to provide a designation as general and inclusive as possible" he prefers to call the field neither Darwinian medicine nor evolutionary medicine but "evolution and medicine" (2007, p. 419).

principles from the vantage point of the evolutionary past of humans (here, the Pleistocene epoch) in order to assess present states of health and disease among populations. The contrast between these two explanatory styles can also be captured by the distinction between a theoretically and a practically oriented approach; whereas evolutionary medicine seeks to devise practical solutions to medical problems based on specific applications of evolutionary biology's toolbox, Darwinian medicine, in contrast, stresses the need to compare past and present populations from an evolutionary point of view in order to gain insights into why we in the present get sick. Both approaches, however, are ultimately concerned with the prevention and control of human diseases. To illustrate how forward looking explanations can work I develop the example of the evolution of antibiotic resistance.

2 Charles Darwin and Medicine

Despite not being a doctor himself Charles Darwin (1809–1882) had "medicine in his blood", so historian of medicine William Bynum said ((Bynum 1983), p. 43). Sickened by the sight of blood in the surgical amphitheater in Edinburgh, the young Charles dropped out of his medical curriculum after 2 years (1825–1827) and went on studying theology and natural history in Cambridge. Darwin's time in Edinburgh's stimulating intellectual environment, however, prepared him for a career in science and arguably set the groundwork for his evolutionary vision of life, which would begin to grow while on the *H.M.S Beagle* and developed fully afterwards (Sloan 1985; Bowler 1990). Despite giving up on medicine, Darwin remained for most of his life in close contact with medical doctors, including his own father and grandfather, the colourful Erasmus Darwin, an early proponent of the doctrine of transformism. In Zoonomia, Erasmus Darwin endeavoured to "reduce the facts belonging to animal life into classes, orders, genera, and species; and, by comparing them with each other, to unravel the theory of disease" (1794, vii). Charles Darwin's grandfather's book, also, addressed the problem of hereditary diseases through cases such as gout, consumption, insanity, and epilepsy.[5] Charles would later discuss several of these examples in his book on *Variations in Plants and Animals under Domestication* (1868). As to his father, Darwin recognized and praised his power of observation and diagnostic but did not show clear interest in medical practice as such (Bynum 1983). During most of his career, Charles Darwin's friends and scientific interlocutors included many prominent doctors like Henry Holland, John Scott Burdon-Sanderson, W. B. Carpenter, Lawson Tait, William Roberts, and James Paget (Towers 1968),

[5] In *Zoonomia* (1794), the elder Darwin argued that there is a need in the medical profession for "a theory founded upon nature, that should bind together the scattered facts of medical knowledge and converge into one point of view the laws of organic life" (cited in. Wilson P.K. (2007) "Erasmus Darwin and the 'noble' disease (gout): Conceptualizing heredity and disease in Enlightenment England". In: Mueller-Wille and Rheinberger (eds.) *Heredity Produced: At the Crossroads of Biology, Politics, and Culture, 1500–1870*, MIT Press, pp. 133–153, p. 134.

many of whom corresponded with Darwin. Tait, for instance, was a "disciple" of Darwin and sent him more than 30 letters, along with copies of his work on ovarian cancer in which the latter apparently took great interest. In a letter of 1875, Tait remarked: "the more I think over some of the problems of pathology the more I lean towards the view that their solution will be aided by regarding them from a Darwinian point of view".[6] Darwin's own experience with chronic, but intermittent, illness resulted in his frequently undergoing various medical treatments and suggests another point of contact between medicine and the father of evolutionary theory.[7]

Yet Darwin's remarks on the medical sciences remain overall scarce. In *Descent of Man* (1871) and particularly in *Variations of Plants and Animals Under Domestication* (1868), he made a number of observations on hereditary diseases, citing several authorities on the subject. Appalled by the transmission of "evil qualities" (i.e. diseases) from one generation to the next, he sought comfort in the thought that "good health, vigor, and longevity are equally inherited" (1868, p. 11). In *Descent of Man*, Darwin used communicability of diseases between apes and humans as evidence for their similarity of descent. Overall, medical conceptions of health and disease did not seem to have entered Darwin's work in a significant way, though he followed the development of the medical sciences closely. Toward the end of his life, for example, he was pleased to bear witness to the coming into being of the germ theory of disease, as developed by Pasteur, Koch, and Lister. In a letter to botanist and bacteriologist Ferdinand Cohn in 1877, Darwin wrote:

> I remember saying to myself, between twenty and thirty years ago, that if ever the origin of any infectious disease could be proved, it would be the greatest triumph to science; and now I rejoice to have seen the triumph. (quoted in (Bynum 1983), p. 52)

Whilst the rapid development of the medical sciences during the nineteenth century had relatively little impact on Darwin's own scientific work, the converse is probably not true – indeed quite to the contrary. Even in France, where the introduction of Darwinian thinking was slowed down compared to other countries (Conry 1974), and where physicians tended to see no "raison d'être" for Darwinism in medicine (Bouchut 1873, p. 422), the germ theory of disease developed by Pasteur was rapidly connected to evolutionary dynamics of adaptation and species transformation, for instance by anthropologist Arthur Bordier (1888). It is however the Russian immunologist Ely Metchnikoff who introduced Darwinian thinking and the concept of natural selection inside the walls of the Pasteur Institute in the last decade of the nineteenth century (Moulin 1991). In England, as the London physician K.W. Millican indicated in his monograph on *The Evolution of Morbid Germs*, "the general application of the great doctrine of evolution to disease appears to have been more or less distinctly 'in the air' for some considerable time" (1883, 44).

As Bynum rightly noted (Bynum 1983, p. 46), medical practitioners rapidly turned to Darwin's evolutionary theory (1859) and to his work on heredity (1868) to

[6] Cited in Shepherd (1982). For other examples, see Bynum (2002, 60–62).

[7] The nature and cause(s) of Darwin's illness have been the focus of much speculation and are still debated nowadays. It might have been lactose intolerance. For a recent view see Hayman (2009).

understand both the "diseases of evolution" (i.e. hereditary diseases) and "the evolution of diseases" (i.e. infectious diseases). Drawing on the *Origin of Species* epidemiologists and public health officers relied, on the one hand, on the concepts of natural selection and adaptation to explain the remarkable changes in virulence seen during epidemics in terms of ongoing evolution between hosts and microorganisms (or lack thereof).[8] Evolutionary theory also helped understand how saprophytic microorganisms could transform into parasites by reverting to original type, which in turn explained the changes in local and global manifestation of epidemic patterns (Bynum 2002). Finally, evolutionary thinking provided early bacteriologists a way to reconcile the observable and sometimes puzzling variation in infectious diseases with the claim that diseases have a specific cause (e.g. a bacterium). In the late nineteenth century, the coming into being of virulent germs and disease specificity were recast in the light of evolutionary thinking.

On the other hand, physicians and surgeons who studied the transmission patterns of specific pathologies from one generation to the next, and how these traits sometimes disappear, revert, and suddenly reappear in a discontinuous but heritable fashion in offspring, emphasized yet another aspect of Darwin's work, namely his theory of heredity, or pangenesis.[9] According to the "provisory" hypothesis of pangenesis proposed by Darwin, "the whole organization, in the sense of every separate atom or unit, reproduces itself" (1868, p. 359). In *Variations*, Darwin postulated that "gemmules" – particles of inheritance emitted by bodily cells – move freely in the body, accumulate and hybridize in the gametes, retaining and transmitting some characters acquired from the environment. Building on the breeders' knowledge of inheritance and on Prosper Lucas's (1805–1885) *Traité philosophique et physiologique de l'hérédité naturelle* (1847), Darwin's *Variation of Plants and Animals under Domestication* (1868) supported the view that inheritance can be adaptive as well as maladaptive, as hereditary diseases indicate. This is but one aspect of the "dark side" of evolution that remains an underappreciated aspect of Darwin's work even today (Müller-Wille 2009). In addition, old medical concepts of constitution, predisposition to disease, and diathesis were, at the time, reinterpreted from an evolutionary point of view (Zampieri 2009a). Diseases of evolution also included "disease of modern life" which would later be called "diseases of civilization".[10] On the whole, unraveling the historical trajectory of diseases through Darwinian concepts provided a new understanding of a number of pathologies, social or otherwise, in the late nineteenth century.

One should be careful not to draw the line between the "evolution of diseases" and the "diseases of evolution" too sharply – indeed, germ theorists also believed that some pathogenic germs can undergo "reversion" and "atavism". Moreover, Darwin's theory of heredity was first used to explain changes in infectious diseases. Such was the case of James Ross', *The Graft Theory of Disease, being an Application of Mr Darwin's Hypothesis of Pangenesis to the Explanation of the Phenomena of*

[8] For instance, see Aitken (1885–1886), Millican (1883), Thorne (1882), Airy (1878).

[9] See Paget (1883), Hutchinson (1884), Haycraft (1894).

[10] See Richardson (1889).

the Zymotic Disease (1872).[11] However, late nineteenth and early twentieth century medical scientists appear to have applied Darwin's theories to medicine alongside two broad lines of thinking. Interestingly, one can trace continuities between these two ways of understanding the role of evolution in medicine and today's Darwinian and evolutionary medicine: the former inquiring into the origins and nature of humans' adaptations (and maladaptation) and their hereditary transmission, and the latter focusing on the factors influencing the evolution and transmission of infectious diseases. Like their analogues in the late nineteenth century, these new evolutionary trends to disease and health sometimes overlap while they also bear the marks of older research traditions from which they derive. Before turning to these more recent projects I examine the historical relations between evolutionary thought and eugenics.

2.1 Darwinism and Eugenics

The period spanning 1880–1940 – recently labeled the era of "medical Darwinism" – saw the publication of a large number of medical articles, books, reviews, and letters on "Darwin", "Darwinism" or "evolution" in leading journals such as the *British Medical Journal* and the *Journal of American Medical Association* (Zampieri 2009a, b). This flow of publications, however, radically came to a halt in the aftermath of the Second World War, save for a noticeable peak in the mid-1950s on the occasion of the centenary of the publication of *On the Origin of Species*. It will have escaped no one that eugenics – the idea of artificially selecting for (or against) specific (presumably) heritable traits among human populations – was a major force in shaping the relations between the medical sciences and evolutionary biology from the publication of Darwin's *Origin* until the mid-1940s and beyond.[12] The idea of an organized selective mating process emerged, and gained wide acceptance, within the particular context of Victorian society (though Britain never proclaimed eugenics laws) in which scientists, lay persons, and politicians of all allegiances expressed concerns about the forces of degeneration they perceived to act on the mental, the physical, and indeed the moral, abilities of individuals. To be sure, a large fraction of the population in Britain but also outside of it regarded rather anxiously the long-term impact of medicine on the preservation of the "less-fit" (e.g. the so-called "feebleminded"), as much as they feared its larger effects on the economy, politics, and society.

The idea of eugenics is an old one but it gained a new meaning and applicability following Darwin's works on evolution and heredity as it became entangled with a popular understanding of evolution as the process of the "survival of the fittest", an

[11] Until the end of the nineteenth century, the now common distinction between hereditary and infectious cause of disease was not obvious to most scientists. Even so, several forms of cancer have infectious origins.

[12] On the history of eugenics see Paul (2009), Kevles (1985), Harwood (1989).

expression coined by Herbert Spencer. The then-perceived consequences for society of tampering with the law of natural selection weeding out ill-adapted or diseased individuals, and permitting them instead to live and to reproduce, were regularly addressed from a societal and medical point of view. In a polemical essay titled "On the Failure of Natural Selection in the Case of Man", William R. Greg addressed the possibility that natural selection does not operate in human societies and warn about possible degradation of health following medical progress: "medical science is mitigating suffering, and achieving some success in its warfare against disease; but at the same time it enables the diseased to live" (1868, p. 362). One year later, the Birmingham surgeon Lawson Tait (1845–1899) asked whether "the law of natural selection by survival of the fittest failed in the case of man". Tait, a pioneer of ovarian surgery, painstakingly sought to support Darwin's theories through his own medical work (Shepherd 1982). In his 1869 essay, however, Tait was primarily concerned with the apparent tension that "medical science enables the diseased to live, those whom it saves from dying prematurely it preserves to propagate dismal and imperfect lives" (Tait 1869). Darwin was not estranged to these discussions although he did not himself encourage the practice of eugenics. In *The Descent of Man* (1871), he expressed similar concerns as those voiced by Tait and Greg about the effects of a prolonged relaxation of natural selection – partly made possible thanks to medical advances (e.g. small-pox vaccination) – for the march of societies toward progress (1871, p. 168) but held moderate views.[13] However, and in contrast, Darwin noted that the sympathy instincts that lead us to give protection to the "imbecile, the maimed, and the sick" are themselves the product of evolution by natural selection, and suppressing those instincts would be impossible "without deterioration in the noblest part of our nature" (1871, p. 168–9).

In 1869, Francis Galton (1822–1911), Charles Darwin's cousin, who coined the word "eugenics" in 1883, published *The Hereditary Genius*, an influential book in which he inquired into whether human intellectual abilities were heritable. Separating the realms of nature and culture, this treatise stressed, against Darwin, the "unity of type" over individual variations. Faithful to his eugenics utopia, Galton saw the use of artificial selection as the easiest and quickest way to achieve what natural selection would eventually realize (Gayon, forthcoming). Reacting to the apparent failure of the positive effect of natural selection in the case of human societies and proposing a "hard" conception of hereditary phenomena, Galton proposed to artificially impose constraints on human reproductions. The eugenics ideology he promoted throughout his life became a political project at the turn of the twentieth century, with disastrous consequences culminating during World War II.

Some medical men held less dramatic views on the relations between evolution, heredity, and the medical sciences. In his Bradshaw Lecture on "Darwinism and

[13] In particular, here is Darwin's response to Greg's pamphlet: "Natural selection follows from the struggle for existence; and this from a rapid rate of increase. It is impossible not to regret bitterly, but whether wisely is another question, the rate at which man tends to increase; for this leads in barbarous tribes to infanticide and many other evils, and in civilised nations to abject poverty, celibacy, and to the late marriages of the prudent" (1871, p. 142).

Medicine" delivered at the Royal College of Physicians in 1909, J.A. Lindsay raised doubts regarding the ability of doctors to control births and maintain "the purity of the race". Amidst subtle ethical overtones he warned, however, that "the possibility of reversion and degeneration will always have to be reckoned with" (1909, p. 1331). Others also tried to show how medicine could contribute to the study of evolutionary processes (Adami 1918; Nash 1915).

In 1912, the biometrician and then-director of the Francis Galton Eugenics Laboratory in London, Karl Pearson (1857–1936), gave a Cavendish lecture at the West London Medico-Chirurgical Society titled "Darwinism, Medical Progress, and Eugenics" (Pearson 1912). In his address, Pearson argued that evolutionary theory as formulated by Darwin and medical progress are radically "opposed forces", and that the tension between them could indeed only be resolved through the implementation of strict eugenics policies of birth control (1912, p. 27). With the rediscovery of Mendel's laws of inheritance circa 1900, and the beginning of genetics, Pearson's project of birth control became to a large extent a social and political reality for countless individuals.[14] In effect, in the early to mid-twentieth century positive and negative forms of eugenics practices (e.g. sterilization laws) blossomed in several North American and European countries, including the United States, Canada, Sweden, and Denmark (Kevles 1985). When the association of Nazi crimes during the Second World War with a number of eugenics movements was brought to light, the application of Darwinian concepts to "medical" questions became for a time morally untenable, at least publically. Possibly, *this* is one of the main cause of the discernible "oblivion" of evolutionary approaches to medicine in the second half of the twentieth century (see Zampieri 2009b, p. 24).

As it became clear throughout the 1940s and 1950s that most individuals harbor pathological variation at the genetic level, to various degrees, medical genetics somehow eased concerned about racial degeneration (Gayon 2004). But even so, eugenicist concerns with degeneration, though publically dismissed, did not disappear once and for all after the war and the revelation of the concentration camps and the recognition of biological variation; such concerns, furthermore, continued to be promulgated and defended by prominent medical scientists and geneticists until the 1960s in the United States, Britain, and Germany, but also elsewhere, and afterwards (Paul 1984). For instance, the Australian immunologist and Nobel Prize Winner Frank Macfarlane Burnet (1899–1985) held eugenicist opinions, not too dissimilar from those of Pearson and others before him. During a symposium on *The Impact of Civilization of Man* held in Canberra (Australia) in 1968, and as the chairman of the meeting, Burnet argued that given the social patterns in today's society there was no hope of avoiding "genetic deterioration", and consequently scientists would fail their responsibilities if "opportunities for rational birth control are not made equally effective through all classes of all human communities" (1970, p. xvi–xix).

[14] Pearson, however, was opposed to Mendelian genetics. On the debate between biometricians and Mendelians see Olby (1988).

Forty years on, while new work in genetics and genomics is giving rise to further medical applications such as pre-natal testing, genetic screening for various hereditary diseases, and so on, attempts are frequently made to separate the ‘new genetics’ from the ‘old eugenics’ (Hansen et al. 2008). Yet while the new genetics is often branded as being individually empowering, medically predictive, voluntary, protective of individual rights, and based on accurate science, it is not always possible to demarcate it sharply from old eugenics (Ekberg 2007). In the light of the complex and problematic history of medical progress and evolutionary thinking during the twentieth century, it hardly comes as a surprise that one of the constant challenges faced by any kind of evolutionary approach to health and disease nowadays is to safely distance itself from this eugenic past. Randolph Nesse and George Williams were fully aware of the potential misreading of their project when they labeled it “Darwinian medicine” (Williams and Nesse 1991). As they wrote, one of the main obstacles for physicians to embrace an evolutionary perspective is that “of course, whenever evolution and medicine are mentioned together, the specter of eugenics arises” (Nesse and Williams 1998, p. 92). In subsequent sections I will try to depict how the relations between evolutionary biology and medicine were remade once again from the early 1990s onwards and how we can detect historical and conceptual continuities between some of these new research projects and the way in which medical doctors read Darwin’s work in the late nineteenth century, outside a eugenicist framework.

3 Two Research Traditions

3.1 Evolutionary Medicine

Evolutionary medicine focuses on the large and increasing number of illnesses that evolutionary biology’s conceptual and methodological resources can shed some light on. Typical examples include the evolution of infectious diseases, antibiotic resistance, the evolution of virulence, etc. In that sense, evolutionary medicine has a long tradition that predates the birth of Darwinian medicine by many decades. Indeed, although Charles Darwin himself said little about medicine per se, evolution-oriented accounts of infectious diseases were progressively advanced by medical doctors and epidemiologists a few decades after the publication of *On the Origin of Species*, as discussed above (Bynum 1983). On this view, germs that cause disease result from long evolutionary processes through which they have progressively acquired (or lost) their pathogenic power. Similarly, *in vivo* laboratory experiments provided evidence that some changes induced in microorganisms were heritable. In this sense, Louis Pasteur’s laboratory experiments on variable virulence in bacterial strains for instance could also be regarded as an early example of evolutionary medicine, where evolutionary thinking provided new ways of intervening on disease, for instance, by controlling the level of virulence in the production of standardized vaccines (Mendelsohn 2002). Attempts to understand the origin, evolution and decline of infectious diseases from various viewpoints such as bacteriology and ecology underline another point of contact between evolution and medicine from the late nineteenth century up to the present day (see Anderson 2004; Méthot 2012).

As I see it, evolutionary medicine today does not stand out (yet) as a new scientific field of its own. To put it differently, my claim is that evolutionary medicine is not a theoretically unified scientific domain but, rather, a collection of different research agendas. Scientists doing evolutionary medicine draw on different fields such as population genetics, microbiology, bacterial genetics, ecology, immunology, and, of course, evolutionary biology to understand and regulate medical problems. Accordingly, today's evolutionary ecologists and epidemiologists interested in the dynamics and ecology of infectious diseases, emergent diseases (e.g., HIV-AIDS, H1-N1 flu, Ebola virus, etc.), and host-pathogen coevolution are engaged in evolutionary medicine, sometimes without knowing it. It would be a mistake to think that evolutionary medicine has a strong internal cohesion in terms of epistemology and methodology. Applying Buller's description of evolutionary psychology, evolutionary medicine is not a synthesis but, rather, 'a loose confederation of research programs that differ significantly in theoretical and methodological claims' (Buller 2007, p. 255).

What is central, though, is that in this broader sense, evolutionary theory is employed to provide an additional axis of research to medical researchers, health care practitioners, clinicians, policy makers, etc. What unites evolutionary medicine is mainly the attempt to articulate questions about health and disease with concepts and methods drawn from evolutionary biology in order to devise practical solutions to pressing medical problems. Evolutionary biology provides medicine with an additional level of explanation for disease that can lead to new technological applications, not a theoretical worldview as to why we get sick. In applying evolutionary principles in contemporary environments, for example, in hospital wards, intensive care units, and so on, evolutionary medicine often seeks to address 'real time' evolutionary issues of medical significance such as the prediction and control of the evolution of infectious diseases or the evolution of resistant bacterial strains. In that sense, evolutionary medicine is characterized by what I call a 'forward looking' mode of evolutionary explanation.

3.2 Darwinian Medicine

Within evolutionary medicine, there is a more unified tradition of evolutionary studies of medicine called 'Darwinian medicine'. This tradition began with the work of psychiatrist Randolph Nesse and evolutionary biologist George C. Williams in the early 1990s. It is now pursued by Stephen C. Stearns, Stanley. B. Eaton and others. Although this tradition is more recent, it also has historical roots and predecessors in the late nineteenth century and early twentieth century biological and medical sciences. Indeed, Darwinian medicine, at least as initially conceived, is in many ways analogous to the study of diseases of evolution in the late nineteenth century. Today, practitioners use the neo-Darwinian theory to understand the genealogical patterns of disease transmission; to determine why individuals are, or become, maladjusted to their environment; and to provide an evolutionary explanation of disease susceptibility framed in terms of our evolutionary past. Understanding patterns of disease in the light of the evolutionary trajectory of humankind stands out as a distinctive feature of Darwinian medicine and reflects its historical origin as one of the late nineteenth century answers to Darwin's work.

Whereas the "forerunners" of Darwinian medicine during the second half of the twentieth century were largely unsuccessful in promoting evolution-based medicine among larger audiences, Nesse and Williams's *Evolution and Healing: The New Science of Darwinian Medicine* (Nesse and Williams 1996) rapidly gained worldwide recognition. Nesse and Williams' approach to disease benefited from several recent developments in medical genetics and medical anthropology. Given that their work drew on the work of Harvard evolutionary biologist Edward O. Wilson, who attempted to apply evolutionary principles to human behaviour, it is unsurprising that questions about human evolution, behaviour, and psychology were often intertwined in Darwinian medicine.

Darwinian medicine is generally in favour of the following theoretical and methodological claims that can be summarized as follow:

1. Adaptationism (methodological) is a good heuristic principle in medicine and natural selection is the paramount evolutionary force (empirical);
2. Functional and evolutionary explanations must be systematically articulated in order to understand vulnerability to disease;
3. Evolution provides medicine with an organizing theoretical framework, and the potential domain for the application of evolutionary principles is unbounded;
4. Evolutionary principles are applied from the vantage point of the Pleistocene epoch (backward looking explanations);
5. Humans are generally maladapted to the modern environment (the mismatch hypothesis).

In what follows, I will consider the first three claims one-by-one and then the fourth and fifth claims jointly.

3.2.1 The Adaptationist Program of Darwinian Medicine

Following the paleontologist Stephen J. Gould and the population geneticist Richard C. Lewontin (Gould and Lewontin 1979), Williams and Nesse have described Darwinian medicine as being an 'adaptationist programme' (Williams and Nesse 1991, p. 3). Darwinian medicine's adaptationism is methodological and empirical. A methodological adaptationist assumes that 'looking first for adaptation is a useful research strategy' (Forber 2009, p. 156). In other words, it is 'a suggestion about how… best to organize investigation' (Godfrey-Smith 2001, p. 338). Williams and Nesse seem to satisfy the condition for being methodologically adaptationist by making the following recommendation: 'When confronted with a biological phenomenon, try to envisage it as an aspect of an adaptation' (Williams and Nesse

1991, p. 3). Applying this research strategy to medicine, they argue that 'the adaptationist program predicts otherwise unsuspected adaptive processes' to be medically significant (Williams and Nesse 1991, p. 3; Nesse and Williams 1996, p. 21). Williams and Nesse are also committed to what Peter Godfrey-Smith called empirical adaptationism, namely the claim that natural selection is the most important force driving the evolution of populations over time. This empirical claim about the biological world is expounded in a panselectionnist variety by Williams and Nesse and is found in most of the works they inspired (Valles 2011).[15]

Taken together, methodological and empirical adaptationism lead to the reconsideration of the nature of a number of pathological reactions. One of Darwinian medicine's central claims is that 'many manifestations of illness are not defects in the body's mechanisms, but sophisticated adaptations' (Nesse 1999a, p. 353). This adaptationist stance is intended to provide a new way of looking at symptoms of bodily disease (e.g., pain, fever, iron deficiency, etc.) or mental disorder (e.g., panic attack, depression, etc.). Instead of thinking about these conditions in terms of symptoms of a disease, adherents of an adaptationist perspective stress their selective advantage (Nesse 1999b). All this suggests a practical role for adaptationist thinking in clinical medicine (Nesse and Williams 1996, p. 245–48). In effect, Williams and Nesse have argued that 'clinical practice will also benefit from an evolutionary perspective' in the sense that evolutionary theory has 'immediate practical utility when considering what to do about a low iron level in a person with a chronic infection, whether to suppress cough in a person with pneumonia, or when to adopt new technology' (Williams and Nesse 1991, p. 17). For Williams and Nesse, 'the adaptationist' doctor is thus better equipped to understand why diseases occur (ibid.).

Treatment of disease, however, is unlikely to rest on evolutionary considerations alone (Gammelgaard 2000), as Darwinian medicine's advocates themselves now recognize (Nesse and Stearns 2008). Relying on a panselectionist view can even make evolutionary hypotheses appear stronger than they really are, which can in turn lead to unwanted clinical consequences (see Valles 2011). For instance, deciding whether or not to block fever will depend on a constellation of factors which are only very loosely related to the fact that fever is an evolved mechanism. In cancer, fever is commonly associated with a high mortality rate (Dalal and Zhukovsky 2006). In choosing to suppress fever, the nature of the disease and the patient's sex and age – in addition to his general state of health and other conditions – are arguably of greater relevance than evolutionary knowledge. Although the benefits of applying adaptationist thinking to clinical medicine will require some more empirical work, Williams and Nesse rightly point out that it can lead physicians to better 'appreciate compromises that are responsible for much disease' (Williams and Nesse 1991, p. 17). Overall, Darwinian medicine rarely offers practical guidelines; its aim is to guide research instead (Nesse and Stearns 2008, p. 31).

[15] Williams and Nesse do not seem committed to a form of explanatory adaptationism, namely the idea that organismal design is the most important problem to solve in biology.

3.2.2 Functional and Evolutionary Explanations of Disease Vulnerability

The goal of Darwinian medicine is to gain a better understanding of why members of our species get sick and to do so from an evolutionary standpoint (Nesse and Williams 1996). In other words, Nesse and Williams wonder why the body is not better designed; why has natural selection left us vulnerable to disease? Even if natural selection is seen as the primary cause of organismic design, it cannot optimize the body, and so inevitably there are inbuilt faults that leave it imperfect and prone to diseases. Using Ernst Mayr's terminology (Mayr 1961), they argue that functional (or proximate) biology does not suffice to explain disease, and so they urge that 'each disease needs a proximate explanation of why some people get it and others don't, as well as an evolutionary explanation of why members of the species are vulnerable to it' (Nesse and Williams 1998, p. 93). The case of sickle-cell anemia is one of the clearest examples that bridge the gap between evolutionary and functional (or proximate) explanatory schemes. This emphasis on disease vulnerability is one of the most salient aspects of this research tradition. The idea is that 'natural selection shapes structures and functions that, being imperfect, are vulnerable to disease' (Zampieri 2009a, p. 348). So although natural selection may be the paramount evolutionary force, it does not lead necessarily to optimality in terms of functioning of the body.[16]

Nesse and Stearns have distinguished six main reasons for disease vulnerability (Nesse and Stearns 2008), each one couched in terms of what natural selection can and cannot achieve. First and foremost, natural selection cannot (1) overcome the mismatch between genes inherited from the Pleistocene and modern environments because the response to selection is too slow. The speed at which selection operates also explains why (2) pathogens continually find ways to circumvent our evolved defences. A number of (3) structural constraints and (4) historical trade-offs limit what natural selection can do to decrease disease vulnerability. Finally, the authors argue that natural selection (5) maximizes fitness, not health, and (6) that a number of defences like pain and fever 'are useful despite causing suffering and complications' (Nesse and Stearns 2008, p. 38). In brief, disease is not something that can be completely avoided and pathological situations are sometimes the inevitable downside of evolutionary adaptations.[17]

The emphasis on the principle of natural selection to explain disease (vulnerability) is perhaps overstated, however. Clearly, in most cases, natural selection will not be

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[16] Here is an example of trade-offs between different demands: "No trait is perfect. Every trait could be better, but making it better would make something else worse. Our vision could be as acute as that of an eagle, but the price would be a decreased capacity to detect color, depth, and movement in a wide field of vision. If the bones in our wrists were thicker they would not break so readily, but we would not be able to rotate our wrists in the wonderful motion that makes throwing efficient. It the stomach made less acid we would be less prone to ulcers, but more prone to GI infections. Every trait requires analysis of the trade-offs that limit its perfection" (Stearns, Nesse, and Haigs (2008), p. 11).

[17] For a discussion of how to test and apply evolutionary hypotheses in medicine and in biology see Nesse (2011).

the (relevant) causal factor that doctors will pick to explain the occurrence of pathologies among individual patients (but perhaps so at the population level). Physicians will be more likely to investigate proximate rather than ultimate cause to account for why a patient has got a disease in a given context, because they can act more efficiently on the former than on the latter. Pain and suffering are primarily the result of proximate mechanisms that have gone wrong and need to be corrected by physicians. To put it differently, because medicine is an *interventionist* discipline it often does not require looking into deep evolutionary history to diagnose and treat disease and to relieve pain (Gammelgaard 2000). For example, knowing that the function of the appendix for our ancestors was to digest cellulose-based food is not of immediate help to understand why it becomes inflamed now and how to treat it, though it contributes to the general explanation of appendicitis. Arguably, when physicians ask "why questions" they are generally not concerned with evolutionary explanations but with proximate mechanisms of disease. Counterfactually, though, a charitable interpretation of Darwinian medicine could grant that had the evolution of our species (including our commensal microbes) been different, we may have been less prone to some diseases but perhaps also would have been much more susceptible to others. In that sense, evolutionary biology does account, if only on very general grounds, for why members of our species are vulnerable to disease.

3.2.3 Applying Evolutionary Principles in Medicine: An Unbounded Perspective

Another noticeable aspect of Darwinian medicine is that from its perspective, evolutionary biology is relevant virtually to every medically related discipline. In effect, for Nesse and Williams, 'there is no branch of medicine that cannot benefit substantially from an evolutionary approach in its research and, sometimes, its current clinical practice' (Nesse and Williams 1997, p. 664). In particular, 'evolution provides an otherwise missing paradigm for understanding why our bodies are vulnerable to disease' (Nesse and Stearns 2008, p. 31), in addition to a 'natural framework' that 'can link diverse aspects of medicine' (Williams and Nesse 1991, p. 18). Paraphrasing population geneticist Theodosius Dobzhansky (1973), Nesse and Williams have claimed that 'nothing in medicine makes sense except in the light of evolution' (Nesse and Williams 1996, p. 249). I will return to this formulation in the conclusion. The book edited by Trevathan et al. (Trevathan et al. 2008) exemplifies the scope of Darwinian medicine's research tradition. Indeed, the introductory chapter announces that an evolutionary perspective is crucial to understanding a number of issues in medicine, such as infectious diseases (including, in this regard, vaccines, viruses, antibiotic resistance, and host-pathogen coevolution), psychological disorders (including depression, anxiety, and mood disorders), nutrition (diets), reproduction (including pregnancy, childbirth, infancy, and childhood), chronic diseases (including cardiovascular diseases), etc. In other words, evolutionary principles are used to investigate whether various biological, behavioural, sexual, and psychological aspects of human life are normal or pathological. From a

Darwinian medicine perspective, there are no limits on the extent to which evolutionary explanations can be employed in medicine.

However, it is sometimes unclear in what sense evolutionary principles are explanatory and/or useful. In his *Evolution in Health and Disease*, Stearns asserts that 'Human sexual behaviour, reproduction, and the assurance of parenthood are affected by evolutionary forces, often with consequences for the welfare of sons versus daughters. Some of the reasons for the neglect and abuse of children are evolutionary' (Stearns 1999, p. 6). No one would deny that the abuse of children is a very important and preoccupying social problem with potentially profound consequences for those children's behaviours and psychologies. But it is not clear that child abuse is a medical problem in the same sense that heart disease is. In fact, Stearn's example illustrates that in Darwinian medicine, social, familial, and psychological problems are insufficiently distinguished from genuinely medical ones. Moreover, it illustrates how the methodology of Darwinian medicine is related to that of Evolutionary Psychology. As rightly observed by Cournoyea (2013), Darwinian medicine often fails to distinguish between macro- and micro-domain and, as a result, considers that positive results in one automatically support the other. That is, although antibiotic resistance offers a clear example of how evolutionary dynamics affect human health, this does not provide evidence for Stearn's case of child abuse as having an evolutionary origin. Failure to make this distinction in the literature has resulted in overstating the applicability of evolutionary explanations to disease of civilization (macro domain) based on the more detailed understanding of micro-evolutionary processes. Cournoyea' distinction reinforces the existence of distinct research traditions in what is broadly called "evolutionary medicine".

3.2.4 The Mismatch Hypothesis and Backward Looking Explanations

Unsurprisingly, for Darwinian medicine's theoreticians, the way in which human beings have evolved is of central concern. This facet is reflected in their support of the mismatch hypothesis.[18] It is significant that some have argued that the most 'crucial argument' in Darwinian medicine is that there is a 'mismatch' between our genes, inherited from the Pleistocene era, and 'present environmental conditions' (Swynghedauw 2004, p. 134) that causes a number of diseases (Eaton et al. 2002; Nesse 2001, p. 45). Categories of mismatch range from nutrition, to physiological

[18] It should be noted that Gluckman et al. (2009) are using a different concept of 'mismatch' that brings in epigenetic and other developmental processes. In effect, the term 'mismatch' has changed its meaning in Gluckman et al's work. In classic Darwinian medicine, there is a mismatch between the modern environment and the ancient 'environment of evolutionary adaptedness'. While to some extent this sense persists in Gluckman's explanation, the mismatch that figures in the actual mechanism is a mismatch produced in a single generation by a mechanism of phenotypic plasticity. Whereas Gluckman's concept of mismatch concerns individuals who can be mismatched to their environment to various extents, Nesse's concept bears on *Homo sapiens*. It is the latter concept that is being discussed in this section.

and to reproductive behaviour (Trevathan et al. 2008). In their first coauthored paper, Williams and Nesse (1991) made a distinction between the environment of evolutionary adaptedness (EEA) (see Bowlby (1969), usually thought of as corresponding to the Pleistocene epoch (1.8 million to 10,000 years ago), to which humans are allegedly 'optimally' adapted, and the modern environment, which is 'abnormal', even 'unnatural', and plagued with the 'diseases of civilization', such as diabetes, obesity, cancer, drug addiction, and so on (Williams and Nesse 1991).

The historian of medicine Charles E. Rosenberg once remarked that Darwinian explanations of pathologies in the late nineteenth century conceptualized disease from the perspective of 'humankind's distant biological past' and attempted to derive 'normative lessons about disease prevention and pathogenesis' based on 'speculative models of prehistoric biological and social development' (Rosenberg 1998, p. 338). These remarks can be applied to Darwinian medicine as well. In effect, very much in the manner of Evolutionary Psychologists, Darwinian medicine's theoreticians argue that humans are generally 'maladapted' to modern environments and are, in contrast, well adapted to life in Pleistocene-like environments. Indeed, for Williams and Nesse, 'human biology is designed for Stone Age conditions' (Williams and Nesse 1991, p. 1). Both Darwinian medicine's theoreticians and Evolutionary Psychologists appeal to the EEA concept to contrast variations in health and disease between past and present societies. For example, they argue that 'the current epidemics of arteriosclerosis, stroke, hypertension, diabetes, obesity, alcoholism, drug addiction and eating disorders result from the mismatch between our bodies and the environment in which we live now' (Nesse 2001, p. 45). On this view, the time lag between the evolutionary past of human beings and modern society significantly shapes current states of health and disease among human populations. The argument usually given is that human biology was 'optimally' designed by natural selection to meet a number of challenges under environmental conditions that no longer exist. At a more fundamental level, however, this view also seems to suggest that what is "normal" and what is "pathological" ought to be delineated in the light of this distant and somewhat hypothetical biological past. In other words, it is as if the idea of the normal was shaped during the geological era known as the Pleistocene, so that any deviation from this prior evolutionary state (e.g. following environmental changes) ultimately results in disease, pathology, or abnormality. This is at odd with the emphasis Darwin's theory of natural selection places on the claim that biological forms are not fixed but are fluid and changing, that organisms create new norms of life by adapting to different environments, and that the concept of normal only makes sense when organisms and environment are considered together, and not separately (Canguilhem [1966] 1991).

The mismatch hypothesis is not merely a theoretical concept; it significantly affects how health is understood, how it should be measured, and how such studies should be conducted. Firstly, for Darwinian medicine, the Pleistocene is the gold standard—the environment relative to which health and disease states are to be evaluated. In other words, the Pleistocene epoch operates as a benchmark in understanding common diseases in modern societies. As some have argued, 'the most rewarding research [for understanding health differences] involves contrasts between present and previous humans' (Eaton et al. 2002, p. 115). This is typical of backward looking explanations in the sense that evolutionary principles are applied from the vantage point of the Pleistocene epoch. Secondly, because the paleontological and anthropological records of preagricultural societies are incomplete, contemporary hunter-gatherer populations are used as proxies for understanding the human evolutionary past. 'When looking for risk factors for common disease', Nesse and Stearns contend, 'the first question is whether the condition is equally common in hunter-gatherer populations' (Nesse and Stearns 2008, p. 39). Again, Eaton et al. (Eaton et al. 2002, p. 113) have argued that 'in order to provide an evolutionary foundation for preventive recommendations [in medicine], the most pressing research need is to identify, contact, interview and examine remaining hunter-gatherers and other traditional people throughout the world'.

Although Williams and Nesse do not 'advocate a return to any earlier way of life' (Williams and Nesse 1991, p. 14), it is clear that the proponents of Darwinian medicine account for health and disease variations on the basis of whether individuals comply with regimens, life styles, etc. that prevailed in the social environments of the Stone Age. Cancer research specialist Mel Greaves, for instance, stresses that 'the mismatch that increases the risk of breast (and ovarian) cancer falls on women in modern or affluent societies who do not conform to hunter-gatherer lifestyles with respect to reproductive patterns, including breast-feeding' (Greaves 2008, p. 283). This view, thus, has normative implications regarding what is normal and abnormal beheviour in terms of health, and suggests that a number of diseases result from changes in social and physical environmental conditions broadly construed.

One of the challenges this backward looking style of explanation faces is to give empirical content to the EEA concept on which the mismatch argument rests. There are, however, a number of well-known worries associated with the EEA concept. Firstly, it 'discards human evolution' before and after somewhat arbitrary cutoff points (Strassmann and Dunbar 1999, p. 101), even though human evolution almost certainly began long before and continued on after the Pleistocene era (Downes 2010). From an evolutionary point of view, other transitions, such as to agricultural modes of life, probably played a more crucial role in shaping human health and disease (Strassmann and Dunbar 1999). Interestingly, the evolution of adult tolerance for lactose and resistance to malaria (the latter among heterozygous individuals) are linked to the spread of agriculture and evolved after the end of the EEA, that is, during the last 10,000 years [ibid.]. More importantly, the Pleistocene argument provides a generally inadequate picture of what it means to say that organisms are 'adapted' to their environment. In effect, to say that a trait is 'adapted' to a particular environment 'is simply shorthand to say that the trait was selected over alternative traits in that environment' (Buller 2005), p. 435; emphasis in original]. Thus, saying that the EEA is the normal and natural environment of the human species by no means entails that the phenotypes and genotypes of *Homo sapiens* were 'designed' for or 'optimally' adjusted to their Stone Age surroundings. All it means is that some variants of particular traits scored higher in terms of fitness than others did in that particular environment. But just as some traits that evolved during the Pleistocene era are now maladaptive, others may be even better adapted today, as amply demonstrated by the reproductive success of the human species.

Finally, to suggest that hunter-gatherer populations were 'optimally' adapted to their environment gives the incorrect impression that the Stone Age was a sort of golden age. Anthropologists sometimes (unintentionally) reinforce this perception. For instance, Kiple writes that 'early humans were blessed with nutritional plenty and a life relatively untroubled by disease' and that 'hunter-gatherers were relatively disease-free' (Kiple 2006, pp. 11–24). While Darwinian medicine's advocates do not hesitate to describe the EEA in empirical terms, they acknowledge at the same time that they 'rarely have enough information about past environments and past lifestyles to make a strong assertion about the environment of evolutionary adaptedness'. Yet, they maintain that 'such hypotheses are interesting and worth further exploration' (Stearns and Ebert 2001, p. 427). In light of the conceptual and empirical problems raised by the concept of the EEA one has to be careful in deriving medical recommendations such as 'Stone Age diets', etc., on the basis of the mismatch hypothesis alone (Eaton et al. 2002). However, the main point of the mismatch hypothesis is that bodies are more vulnerable to disease when they exist in environments that differ from those in which they evolved, a point that remains valid despite the series of problems that face the mismatch concept.

4 A Forward Looking View: Predicting Evolution?

We have seen that a backward mode of disease explanation is a central and somewhat problematic aspect of Darwinian medicine. But whether humans have evolved their physiological features during a particular era is largely irrelevant for a physician in his day-to-day practice. Proximate medicine, so to speak, is usually sufficient for treating disease. Yet, it may be that to successfully treat and/or prevent disease, health professionals will sometimes need to understand ongoing evolutionary processes. In this section, I introduce another way of thinking about the role of evolution in medicine by drawing on the notion Paul Griffiths called a 'forward looking' explanation. This approach is underpinned by the idea that what matters for the promotion of health and reduction of disease is not only that (micro) organisms are 'things that have evolved' – the evolutionary history of which we should reconstruct – but also that they are 'things that are evolving' (Griffiths 2009, p. 14). Unsurprisingly, forward looking explanations are mostly used in the context of the interactions of humans and microorganisms (viruses, bacteria, and so on) that can potentially induce health problems. By focusing on the different and much smaller reproductive timescale of these entities we can see evolution at work.

Consider the recent studies on antibiotic resistance and one of its consequences, the spread of nosocomial (i.e., hospital-acquired) diseases. Because the generation time is much shorter for bacteria than for humans, pathogens eventually find ways to circumvent our immunological defences. The evolutionary aspect of antibiotic resistance in bacteria has long been recognized by microbiologists (Davies and Davies 2010) and remains one of the best examples of evolution in 'real time'. However, the selection of resistance genes in bacterial populations continues to be largely under-appreciated by physicians, as a recent study demonstrates (Antonovics et al. 2007). While antibiotic resistance largely remains unacknowledged as a formal 'clinical problem', it nonetheless has begun to be recognized as a 'long-term evolutionary issue', notably in intensive care units where it is most problematic (van Saene et al. 2005, p. 597).

Resistance to drugs means that the efficacy of antibiotic treatments against bacterial infections is decreasing and new treatments have to be developed in order to fight the continually emerging resistant strains that make common diseases more difficult and expensive to treat (Kollef 2006). In effect, from the 1960s until today, bacteria have been developing multiple resistances to a large number of antibiotic classes, including macrolides, methicillin, vancomycyn, and more recently, linezolid (Genereux and Bergstrom 2005). The evolution of drug resistance has many causes, but three main mechanisms are responsible for the augmentation of resistance: (1) the occurrence of mutations on single nucleotides; (2) homologous (or intraspecies) recombination; and (3) heterologous (or interspecies) recombination (Bergstrom and Feldgarden 2008). At the population level, conditions conducive to the development of resistance include the utilization of broad-spectrum antibiotics (i.e., targeting both gram-positive and gram-negative bacteria), the over-the-counter availability of antibiotics (in many developing countries), unnecessary prescriptions (e.g., for upper-respiratory infections that are often of viral origin), and large-scale agricultural use (Cohen 2000). The massive use of antibiotics in hospitals, however, is now widely acknowledged as one of the main factors in the evolution of resistance (Goossens et al. 2005). Indeed, the hospital environment creates a formidable selective pressure, which favours the survival and the reproduction of the most resistant bacteria and thereby diminishes the efficacy of the available treatments. For example, the widespread use of b-lactam antibiotics in clinical contexts has prompted the evolution of resistant strains. The response to this selective pressure has been the evolution of b-lactamase enzymes (encoded by the TEM-1 gene) capable of degrading a large number of b-lactam antibiotics and rendering them inactive (Barlow and Hall 2002a).

One of the most direct consequences of this massive use of antibiotics, and consequently the evolution of resistance, is the increasing number of nosocomial diseases (e.g., blood infections, urinary and respiratory tract infections), which pose a threat to patients, especially in intensive-care units (ICU) where they are immunocompromised and acutely ill (Bergstrom et al. 2004). As many as 90,000 patients may die of nosocomial infections each year in the US alone (Bergstrom and Feldgarden 2008, p. 125).[19] Indeed, the presence of resistant bacterial strains

[19] There are a number of difficulties concerning how to measure the ways in which nosocomial diseases affect mortality, morbidity, and costs that I shall put to one side; see Marshall and Marshall (2005).

that are well adapted to the hospital environment (e.g., methicillin-resistant Staphylococcus aureus) stimulates the multiplication of this particular type of infection. But frequently, nosocomial infections result from commensal bacterial flora that become ‘pathogenic when they multiply in normally sterile sites such as the lower respiratory tract or the blood’ (Lipstich et al. 2000, p. 1938). Hand washing, isolation, and the use of narrow-spectrum antibiotics are among the earliest measures tailored to prevent the spread of infections in hospitals. Recently, more sophisticated methods aimed at counteracting bacterial resistance, based on evolutionary theory and natural selection, have been developed. These include in vitro, or ‘directed evolution’, models (Barlow and Hall 2002a) and ‘cycling’ and ‘mixing’ antibiotics (Kollef 2006). Whereas the former draw extensively on genetic tools and molecular biology, the latter appeal largely to ecological theory to predict the evolution of resistance. This illustrates the heterogeneity of methodologies and approaches in evolutionary medicine. I outline each of them in turn.

4.1 In Vitro Evolution: Predicting Resistance

In vitro evolution is about engineering resistant genes in order to ‘predict’ antibiotic resistance. This technique was precisely developed ‘for the specific purpose of predicting how resistance genes will evolve in nature’ (Barlow and Hall 2002b, p. 1237). TEM-1 resistant genes, in particular, have been extensively studied because they confer resistance to b-lactam antibiotics such as penicillin, which are widely used in the clinic to treat a large number of infections because of their nontoxicity. In vitro evolution consists in evolving a gene (e.g., TEM-1) in a host (usually E. coli) by inducing a number of mutations through a mutagenesis technique. Plasmids are used to express the genes of interest, which are then classified into ‘libraries’ where they are subjected to a number of different antibiotics to see whether resistance mutations will be selected. The in vitro evolution method is based on the assumption that evolution in the lab and evolution in nature are analogous processes. This assumption rests on some evidence provided by Barlow and Hall (2002a; b). Their basic idea was to see whether in vitro evolution would recover the same mutations as those that occurred in nature. In the case of b-lactams, phylogenetic methods had demonstrated that nine amino acid mutations arose multiple times in response to a set of antibiotics known as extended spectrum cephalosporins (Barlow and Hall 2002a, p. 829).

In their experiment, Barlow and Hall recovered seven of the nine mutations that occurred in nature. This is consistent with other work on protein evolution, which has shown that mutational pathways are evolutionarily constrained (Weinrich et al. 2006). Barlow and Hall concluded that their work provides evidence to support the view that in vitro evolution mimics in vivo evolution and that this result allows them to ‘begin making predictions about the evolution of antibiotic resistance’ (Barlow and Hall 2002a, p. 830).

4.2 *Cycling and Mixing Antibiotics: Achieving Heterogeneity in Hospital Wards*

During the last two decades, a number of physicians and health care practitioners have investigated the effects of applying different antibiotics in rotation in order to limit the spread of resistant alleles, an approach that is grounded in evolutionary thinking. The underlying assumption of this method is that varying antibiotics over a determinate period of time 'can minimize the emergence of resistance because selection pressure for bacteria to develop resistance to a specific antibiotic would be reduced as organisms become exposed to continually varying antimicrobials' (Niederman 1997). Cycling is thus one method of achieving heterogeneity in a given environment. The use of specific antibiotics for a given period of time and then withdrawing and reintroducing them at a later stage prevents bacteria from becoming adapted to their environment. Although some studies have reported significant reductions in resistance (see Kollef (2006) for references), this approach is not without limitations. Clinical microbiologists have pointed out that antibiotic cycling raises a number of methodological issues related to the mechanisms of antibiotic resistance, the dynamics of a particular ICU (e.g., transmission between patients and between patients and medical staff), the composition of the antibiotics, etc., that need to be carefully considered if antibiotic cycling is to be effective (van Saene et al. 2005). This is consistent with recent mathematical modelling suggesting that due to the ecological dynamics of the hospital setting, antibiotic resistance is unlikely to decrease with cycling (Bergstrom et al. 2004). In effect, while standardizing antibiotic administration over a period of time increases 'long term' heterogeneity in the hospital, it does not increase 'local' heterogeneity at the patient level (Bergstrom and Feldgarden 2008, p. 135). These ecological models suggest, however, that 'mixing' antibiotics (rather than cycling) holds promise. 'Mixing' roughly amounts to administering 'all or most available antimicrobial classes' (Kollef 2006, p. 85) to different patients in order to create a more heterogeneous environment to which bacteria cannot adapt as easily (Bergstrom and Feldgarden 2008, p. 135). In other words, mixing imposes different selective pressures (at the 'local' level) on bacterial strains as compared to cycling.

The example of antibiotic resistance shows how evolutionary biology can help us gain a better understanding of a complex medical problem – drug resistance – which is influenced by 'ongoing' evolutionary processes. It provides a basis on which to examine proposed alternatives and to devise future solutions.[20] Moreover, antibiotic resistance explains better why in some cases medicine can hardly do without 'forward looking' evolutionary explanations; even a 'medical creationist' cannot avoid the consequences of natural selection on resistant strains of bacteria that are continually evolving.

[20] See for instance Martinez et al. (2007).

5 Discussion and Conclusion

Following an analysis of the dual reception of Charles Darwin's work by medical doctors during the late nineteenth century (i.e. diseases of evolution and evolution of diseases), this chapter sketched how eugenics concerns have shaped the complex, and often disturbing, relations between medicine and evolutionary biology up to the postwar period, and examinined how medical advances came to be progressively seen as acting against the Darwinian law of natural selection by allowing "unfit" individuals to live longer and to reproduce. The sole alternative to degeneration found by Francis Galton, Karl Pearson and others to counter the artificial relaxation of natural selection was the promotion of severely constraining measures of birth control and selective breeding. This project, politically levered, translated into a harsh social reality in the first half of the twentieth century. While Darwin was not himself a eugenicist thinker, no more than many of his contemporaries at least, his scientific work, and particularly his idea of a constant, gradual improvement of organisms by natural selection in the "struggle for life", provided sufficient room to allow for various and sometimes incompatible social and political interpretations of his theory to be promoted at once. Following the 40-year long eclipse of Darwinism in medicine after the Second World War, medical doctors have recently witnessed the flourishing of new evolutionary approaches to health and disease, outside a eugenicist context.

In the second part of this chapter I have shown that Darwinian medicine and evolutionary medicine are distinct research traditions that emerged from two distinct ways of applying Darwin's theories to medicine, and I have explored several points of contrast between them. First, Darwinian medicine generally applies evolutionary principles from the vantage point of the Pleistocene epoch, while evolutionary medicine studies 'real time' evolution occurring in contemporary environments such as hospital wards or laboratory settings. Second, whereas Darwinian medicine systematically articulates evolutionary and proximate causes to explain why humans are vulnerable to disease and extends those principles to (social) issues such as child abuse, evolutionary medicine uses the theory of evolution by natural selection to target specific medical problems. Third, evolutionary biology provides a general paradigm to make sense of disease for Darwinian medicine's theoreticians, whilst from an evolutionary medicine perspective, it offers an additional axis of research. Fourth, whereas Darwinian medicine relies extensively on backward looking explanations, evolutionary medicine depends mostly on forward looking explanations. Importantly, in evolutionary medicine, health and disease are not assessed on the basis of a comparison between different lifestyles or different environments, where one is considered 'natural' and 'normal' and the other aberrant. Fifth, there is a sense in which Darwinian medicine is committed to a particular vision of *Homo sapiens*. This vision shapes the way in which questions about health and disease are investigated and articulated within an evolutionary framework. For example, Darwinian medicine considers humans to be generally maladapted to modern environments but optimally adapted to live in Pleistocene-like environments. Evolutionary medicine, in contrast, is agnostic as to whether humans are maladapted to modern environments. In fact, as pointed out before, just as some traits that evolved during the Pleistocene era are now maladaptive, others may be even better adapted today. Finally, Darwinian medicine is a field of research unified by a set of methodological and epistemological commitments whereas evolutionary medicine is a collection of diverse research programs working with heterogeneous models.

In spite of these differences, there is overlap between the two research traditions in terms of the problems they wish to solve or investigate and in terms of individual collaborations, as reflected in recent publications (see Nesse et al. 2010). For instance, antibiotic resistance is recognized by Darwinian medicine as a relevant problem to be tackled from an evolutionary point of view (Nesse 2007). Also, researchers engaged in evolutionary medicine may need to use a form of the backward looking mode of explanation (e.g., to construct microbial phylogenies), although such a style of explanation does not rest on a comparison between past and present human populations. Darwinian medicine and evolutionary medicine are best seen as different research traditions situated on a historical continuum, and that both are attempting to shed light on medical issues by drawing on different aspects of Darwinian evolutionary theory. Again, this claim is not intended to create divisions among practitioners but rather to highlight the fact that there are several ways in which the relations between evolutionary biology and medicine can be envisaged.

To finish, let me turn to an aphorism that is often used rhetorically (Nesse and Williams 1996), p. 259; (Gluckman et al. 2009, p. 257) but that, unfortunately, distorts the role of evolutionary biology in medicine. Does nothing in medicine make sense outside the light of evolution? One could imagine that Nesse, Williams, and others were simply making a play on Dobzhansky's words. However, the way they characterize the relationship between evolutionary biology, biological sciences, and medicine reveals the basic role they think evolutionary biology has to perform in medicine. In effect, they assume that 'evolutionary biology is, of course, the scientific foundation for all biology, and biology is the foundation for all medicine' (Nesse and Williams 1998, p. 86).[21] Things may not be so straightforward, however. For instance, although biology and medicine have become increasingly intertwined, medicine continues to be largely an art focused on the individual while evolution looks primarily at the fate of populations. Interestingly, the population approach needed to understand the evolution of resistance illustrates the tension between the individual and population levels because what is good for a patient (i.e., receiving antibiotic treatment) does not line up with what is good for the population (i.e., increase in overall resistance). The ethical and methodological challenge is thus to strike a balance between providing appropriate treatment and 'avoiding the unnecessary administration of antibiotics' (Kollef 2006, p. 82)

[21] Revisiting Dobzhansky's quotation Nesse recently emphasized that it is inadequate in relation to biology itself, and is even less appropriate to medicine, precisely because "medicine is not a science, it is a profession" (2007, p. 417).

that increases resistance. Solving this problem would have obvious consequences for medicine and for public health measures more generally. In fact, applying evolutionary concepts and methods to public health might be even more useful than to clinical medicine, because practitioners think precisely in terms of interacting populations, and their evolution.

Finally, what does making sense of something mean? In his article, Dobzhansky (1973) primarily intended to contrast two types of explanations for the diversity of life on earth, namely, the Darwinian theory of evolution with the theories of 'special creation' (Griffiths 2009). He argued that only when looking at the diversity of life from the lens of evolutionary biology can one make sense of the patterns seen in biogeography and comparative anatomy. There is little doubt that evolution can throw some light in various ways on medicine and maybe also on disease patterns. But to say that 'nothing in medicine makes sense except in the light of evolution' makes little sense and perhaps no sense at all if we consider medicine to be primarily a practical discipline, that is, 'an art at the crossroad of many sciences' (Canguilhem [1966] 1991, p. 35). At any rate, functional (or proximate) medicine without evolution remains incomplete in the sense that it leaves unanswered many questions about disease but not in the sense that no aspect of disease can be understood without invoking evolution (Wouters 2005).

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Pierre-Olivier Méthot Discipline: History and philosophy of the life sciences

Research interests: My research focuses on historical and philosophical issues in biology and medicine in the nineteenth, twentieth, and twenty-first centuries. I am particularly interested in the epistemological and historical relations between evolutionary thinking and medicine, the conceptual foundations of bacteriology and immunology, the development of styles of reasoning as well as current modelling practices of host-parasite interactions and in the development of integrated approaches in the history and philosophy of science, especially historical epistemology. Other research interests include the ethics of dual-use technologies in the life sciences.