
CHAPTER 1

Introduction and Overview of Evolutionary Medicine

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INTRODUCTION

In a recent Doonesbury comic strip, Garry Trudeau depicts a 60-ish man who has just been told by his physician that he has tuberculosis. When he asks about his prognosis, the doc says, “Depends—are you a creationist?” The patient answers, “Yes, but what does that have to do with tuberculosis?” Being a good evolutionary medicine proponent, the physician responds, “A creationist would want to be treated with streptomycin, because that worked *before* the tuberculosis strain had evolved. Since you don’t believe in evolution, then streptomycin should work just fine.” “But Doc, aren’t there newer drugs?” “Sure, there are much better ones for the evolved strains of tuberculosis because they have been “intelligently designed.”

Indeed, nothing better illustrates the importance of understanding the role of evolution in medicine than the arms race that infectious agents and drugs have undergone in recent years. During World War II penicillin was found to be extremely effective in reducing the number of deaths from wounds and amputations. In the 1950s, virtually all strains of *Staphylococcus* were vulnerable to streptomycin; today none are. The penicillin used today is no different from that used in World War II, but the strains of bacteria have evolved a resistance to the once-lethal drug. Fortunately, medical and pharmaceutical research has, for the most part, been able to keep up with this arms race by building ever more powerful armaments, but three things stand in the way of continuing success: (1) acceleration of the arms race—because the generation length of bacteria is so short and because they multiply so rapidly they can quickly mutate into an antibiotic-resistant strain; (2) misunderstanding, and even rejection, of the theory of evolution by the vast majority of ordinary citizens in developed countries, where most medical research and health care advances take place; and (3) lack of even a cursory understanding of the scientific basis for human evolution by most of the lay public.

EVOLUTION OF HUMANS

Humans are members of the order of mammals known as Primates, an order that traces its origins to approximately 60 million years ago. Characteristics that define humans as primates include binocular, stereoscopic vision, color vision, a high degree of manual dexterity, which emphasizes opposability by the thumb and first digit, omnivorous dietary adaptations, a tendency to live in complex social groups, and a reliance on learned behaviors rather than simple genetically determined responses for survival. The anatomical characters clearly demonstrate that we are closely related to other primates, and most authorities consider the chimpanzee to be our closest relative, although there are some dissenting opinions that are beyond the scope of this brief introduction.

The taxonomic family and subfamily that include modern humans, Hominidae (family) and Homininae (subfamily), respectively, have been in existence for 5–7 million years, and our genus, *Homo*, for about 2 million years (see Figure 1-1). Members of the genus *Homo* are distinguished in the tribe Hominini (which includes chimpanzees and us) by habitual bipedalism (walking on two legs), large brains relative to body size, and dependency on material culture (tools and technology). Until about 10,000 years ago, humans lived in small, multiaged social groups of about 20–30 individuals, were nomadic, and relied on hunting and gathering of wild foods.

One of the keys to the evolutionary success of humans and many other primate species is behavioral flexibility and the ability to adapt to a wide variety of environments, foods, and lifestyles. As environments changed, people who were able to adjust and continue to reproduce passed those abilities on to their offspring so that today humans continue to live, survive, and reproduce under a variety of conditions, including high altitudes, toxic levels of environmental pollution, dense urban populations, extremes of cold and heat, and diets that differ widely from those of our ancestors. We have survived in an environment that today is radically different from the one our ancestors inhabited only 500 generations ago. The human environment has changed more in the last 10,000 years, or even in the last 200, than in the entire course of human evolutionary history.

Inferences about ancestral diets, lives, and health come from three sources: (1) the living nonhuman primates, especially our closest living relatives the chimpanzees and bonobos; (2) the fossil record of primates and hominins; and (3) the ethnographic studies

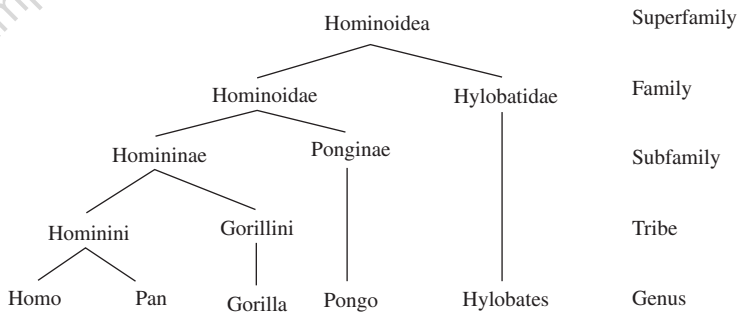


FIGURE 1-1 The hominoid family tree.

of the few remaining populations of hunting and gathering people (e.g., Australian aborigines, Hadza in Tanzania, !Kung of Botswana, Ache of Paraguay, Efé of the Democratic Republic of the Congo, and Agta of the Philippines). Of these three possible sources of data, most of the research discussed in this volume has relied on detailed, ethnographic accounts of the behavior and ecology of living humans. Characteristics reported for contemporary foraging people (hunter-gatherers in the old terminology) include: (1) diets that are composed of from 50 to 80% plant sources; (2) diets that are high in complex carbohydrates and low in saturated fats; (3) high levels of daily activity in search of food, water, and temporary sleeping sites; (4) little to no hypertension and heart disease; (5) near-absence of cancers; and (6) little evidence of psychological and emotional ailments (Eaton, Konner, & Shostak, 1988b). It is tempting to attribute these characteristics to short life expectancies, but more than 8% of the population of most groups studied exceed 60 years of age (Blurton Jones, Hawkes, & O'Connell, 2002). It is true that the exceedingly long lives of many contemporary people is probably of recent origin, but the argument that very few people lived past 50 is unsupported by ethnographic data.

With domestication of plants and animals came numerous changes in human lives, in addition to changes in diet and activity levels. Rather than travel widely foraging for foods, people began to settle in semi-permanent villages where they concentrated their efforts on growing domesticated plants in order to produce sufficient foods to support local families and communities. With increasingly sophisticated agricultural practices came increased population as more people could be supported on the foods grown, fewer died from starvation, and large families became advantageous for working the land. Not only did domestication of plants change the environment, but domestication of animals placed humans in close proximity to a variety of new pathogens, dramatically increasing the risk of infectious disease. It has been estimated that more than 700 microbes known to cause disease in humans were transmitted from animals that we domesticated several thousand years ago (dogs, cats, horses, cattle, goats, sheep, and pigs) (Torrey & Yolken, 2005).¹ In fact, infectious diseases replaced accidents, poisoning, and diseases transmitted by insect bites as the major causes of mortality between the onset of agriculture and industrialization when infectious disease were replaced in developed countries by chronic and noninfectious diseases. These changes in causes of morbidity and mortality have been referred to as “epidemiological transitions,” and there is increasing concern that we are now experiencing a third transition whereby infectious diseases are “re-emerging” (Armelagos, Brown, & Turner, 2005).

EVOLUTION, THEORY, AND BELIEF

One of the major stumbling blocks to the use of evolutionary theory in considering human health is the lack of understanding by many people of what constitutes a theory. For many people, a theory is somehow akin to an opinion, as in “I have a theory about boys” or “a theory about girls.” or “I have a theory about this or that.” In fact, most people do not have real “theories” about much. People have ideas and opinions about how things work, why the weather is what it is, why the opposite sex behaves in the way it does, or why their favorite football team fails to win the big games. These are not theories. A theory is based on repeated observations of a phenomenon that results in an accumulated

wisdom and ability to generalize. There is a theory of gravity. We are comfortable saying that gravity is a theory because we have replicated the crucial experiment millions of times and do so every day—we have seen it work with our very eyes. We are comfortable because there have been no exceptions discovered that contradict this theory. In fact, what we have is a law of physics—a phenomenon that is repeatable with exactly the same results every time.

Unfortunately, when it comes to biological phenomena, there is not the level of certainty, of easy observability, and absolute reproducibility found in physics and chemistry. Because biological systems are always changing, albeit in minute ways, there is not the same certainty of outcome. That lack of complete certainty is what makes many people uncomfortable with theories in biology. Somehow, people have assumed that if a phenomenon is not perfectly and infinitely reproducible that it is not a “real” theory. This is simply not the case. Theories are bodies of knowledge that make predictions about natural phenomena. These predictions are just that—predictions, not fortune telling. The variations we see in the outcome of the evolutionary process are evidence that evolution as a process is a fact. It is a process in which we are immersed just as much as the *Streptococcus* bacteria we discussed earlier. Countless numbers of fossils in museums all over the world, as well as the variation in the roses in a garden, are examples of the process of evolution. Evolution is not a theory, it is a fact.

It is interesting to ask why conversations about evolution in Western cultures often involve whether one “believes in” evolution or not. Quite frankly, the phrase “believe in” is an odd one when discussing a scientific concept, or any scientific process. Can you imagine asking someone if she “believes” in gravity? in the change of seasons? in oceans? in the Krebs cycle? In fact, it is odd to think that anyone need “believe” in evolution at all. Evolution is a body of knowledge that is used to make predictions that are either supported or rejected using the scientific method. But perhaps this ubiquitous tendency to ask “Do you believe in evolution?” provides an important clue as to why evolution in the United States, at least, will always be controversial. Many people view evolution as yet another “belief” system, and one that they perceive as conflicting with religious ways of knowing, just as many people believe that they cannot be both Christian and Jewish (i.e., they cannot believe that Jesus was the Son of God *and* that he was just another man). The idea that a belief system is a dichotomous variable permeates much of Western thought. Either you are for us or you are against us is a common way of thinking. This leads many people to the conclusion that they cannot be both Christian and accept and use evolutionary principles to explain behavior and other natural processes. While it is beyond the scope of this book to offer a full and complete account of the views of those who stand in opposition to the use of evolution as a guiding theory in our everyday lives, it is important to understand that those opposed to using evolution as an explanation have very mixed views on the use of evolution in medicine.

BRIEF HISTORY OF EVOLUTION IN MEDICINE

Evolutionary medicine, as presently constituted with its own name and distinct research area, is a very recent phenomenon. George Williams and Randolph Nesse (Nesse & Williams, 1994b; Williams & Nesse, 1991) are often cited as the first to use explicitly the

term “Darwinian medicine,” which is often used synonymously with “evolutionary medicine” (see Chapters 22 and 23). Although not explicitly referred to as evolutionary medicine, scholars had been “doing” evolutionary medicine for many decades, even if the field did not really achieve professional and public recognition and organization, or its name, until the early 1990s. The publication of the first Williams and Nesse article in the *Quarterly Review of Biology* (Williams & Nesse, 1991) was followed shortly thereafter by a highly publicized American Association for the Advancement of Science (AAAS) symposium in Boston in 1993 entitled “Evolutionary Medicine: Exemplars of An Emerging New Field,” organized by two of the three editors of this volume (McKenna and Smith).

From its beginning, evolutionary medicine received widespread public attention. During the week of the 1993 AAAS symposium in Boston, a number of newspapers, including the *Washington Post*, *Christian Science Monitor*, *Wall Street Journal*, *Los Angeles Times*, *San Francisco Chronicle*, and *Boston Globe*, to name but a few, ran front page stories of the session. AAAS records indicate that almost 500 newspaper and magazine articles were written about the 1993 symposium, exposing about 3.6 million readers worldwide to its content. Many of the authors of the newspaper articles came up with intriguing and thought-provoking titles such as “Evolving Answers” (Anonymous, 1993) in *The Economist*, “Darwin Takes on Mainstream Medicine” (Ezzell, 1993) in the *Journal of NIH Research*, “Diseases That Hark Back to the Stone Age Lifestyle” (Miller, 1993) in the *New Scientist*, “The Flintstone Diagnosis” (Begley, 1993) in *Newsweek*, and “Ancestors May Provide Clinical Answers Say ‘Darwinian’ Medical Evolutionists” (Goldsmith, 1993) in the *Journal of the American Medical Association*. Quite a reception for a symposium proposal that was initially rejected because the first reviewers had no idea what “evolutionary medicine” meant!

It is important to note that that while the “coming-out party” may have been in 1991, and that while Nesse and Williams may have been the first to talk explicitly about Darwinian medicine, the application of evolutionary thinking to medicine has a long and underappreciated history. As Randolph Nesse notes (Chapter 23), Erasmus Darwin (1731–1802) was one of the first physicians to think explicitly about change in nature and how changes observed in nature might be paralleled in humans, writing in his two-volume work, *Zoonomia, or the Laws of Organic Life* (Darwin, 1796). The work is divided into three parts, with Part 2 entitled “A Catalogue of Diseases Distributed into Natural Classes According to Their Proximate Causes, With Their Subsequent Orders, Genera and Species, and With Their Methods of Cure.” So when we refer to Darwinian medicine, we are, in some sense, referring to both Charles Darwin as well as his grandfather.

One of the earliest papers that specifically addressed the place of evolution in medicine was by Dudley J. Morton (1884–1960), an orthopedic surgeon and professor of anatomy at Columbia University. In addition to being a physician, Morton was also a scientist and was interested in the evolution of primate feet. In anthropology, he is best known for his collaboration with Professor W. E. Le Gros Clark in developing ideas about human evolution and locomotion. Morton authored a paper published in *Science* in 1926 (Morton, 1926) entitled “The Relation of Evolution to Medicine.” In this paper he pointed out that science was a direct producer of new and improved methods of curing and preventing human ailments and disease. He observed that medicine was primarily concerned with the recognition and treatment of that which lies beyond the range of

normal human variation. He recognized that understanding what was a true departure from normal, and hence appropriate for clinical intervention, depended directly on knowledge of what constitutes the normal range of human variation and knowledge of what factors maintain normal conditions. He recognized that in order to maintain *normalcy*, medicine had to develop practices that reinforced the natural safeguards the body possessed against forces that would disrupt normalcy. His use of normalcy would likely be problematic today, but the point is clear. In order to understand disease and pathology we have to understand how the body has evolved defenses against possible invasion. He concludes:

... all those to whom we owe our important advances in modern medicine are not only fully assured of the fact of evolution, but, in addition, that they are strongly convinced that the scope and rate of our future advances bear a direct ratio with our better understanding of the biological laws which have guided the course of evolution (Morton, 1926, p. 395).

Interestingly, Morton's call for an understanding of the evolutionary basis for human adaptation against disease went largely unheeded by clinicians. However, some particularly visionary medical schools began to recognize the importance of understanding human evolution, and some were prompted to create departments of physical anthropology. In many cases it was within departments of physical anthropology in medical schools that research into human adaptation and disease, as well as adaptations to environmental extremes, was conducted. In the early twentieth century there was interest among a small group of researchers in the questions of how humans adapted and survived in particular environments. People not only survived, but appeared to thrive at high altitude (above 12,000 feet) and in extremes of hot and cold. In addition, and more important from the perspective of evolutionary medicine, was attention paid to human adaptations and associated diseases. In collaboration with geneticists, physical anthropologists began looking for population differences in particular phenotypic characteristics or physiological processes. By the end of World War II there was an accumulating body of evidence of physiological differences in ability to taste certain substances (e.g., phenylthiocarbamide/phenylthiourea, or PTC), the distribution of color blindness, and population variation in hemoglobin (e.g., sickling in red blood cells).

For biologists interested in human adaptation and disease, the relationship between variation in hemoglobin and malaria was a dream come true. Because of its widespread occurrence and its devastating, lethal effects, malaria was of great concern anywhere female *Anopheles* mosquitoes were found. The relationship between human hosts and the *Plasmodium* parasites provided a natural laboratory for the study of human adaptation to disease. In the early 1950s A. C. Allison published a series of papers that suggested that individuals who were heterozygous for the sickle cell gene possessed a relative immunity to the *Plasmodium falciparum* parasite (Allison, 1953, 1954a, b, c; Allison, Ikin, & Mourant, 1954). Allison also demonstrated that natural selection favored individuals with the sickle cell gene in areas with a high prevalence of malaria.

One of the groundbreaking studies of the complex adaptations of humans to mosquitoes, and in turn malaria, was the work of a physical anthropologist, Frank B. Livingstone. Livingstone published a paper in 1958 in which he summarized what was then known

about the distribution of the sickle cell gene in human populations (Livingstone, 1958) and recognized that the relationship between mosquitoes, malaria, and humans was a complex one. The major vector of malaria in West Africa is *Anopheles gambiae*. This mosquito is drawn to human habitation and resides in the roofs of thatched huts that are ubiquitous in African villages. *A. gambiae* accounts for a majority of the cases of malaria in West Africa and is able to breed in almost any kind of water, except (1) very shaded water, (2) water with a strong current, (3) brackish water, and (4) very alkaline or polluted water.

For Livingstone the key point was the spread of agriculture and the destruction of large areas of natural vegetation and a concomitant rise in the incidence of malaria. With agriculture there were formed large brightly lit pools that were ideal breeding grounds for *A. gambiae*. Human populations increased dramatically in density and provided an almost continuous supply of hosts for the *Plasmodium* parasite. Finally, by destroying the indigenous forest habitat, humans also destroyed many large mammals that traditionally were the hosts for the parasite. So from an evolutionary perspective, Livingstone was able to account for the high frequencies of the sickle cell gene in populations that had not long been exposed to the malarial parasite. The adoption of a particular farming technique brought about environmental changes that had to be considered in understanding the distribution of sickle-cell disease (Livingstone, 1958).

The significance of Livingstone's work is not in its uniqueness, because numerous similar studies would follow, but in his consideration of the complex interaction between a disease vector, the life history of the parasite, and a costly but effective defense against the parasite, all in the context of human populations. It is this kind of research that physical anthropologists interested in evolution and disease had been conducting long before the dawn of Darwinian medicine.

A few studies on evolution and disease were conducted prior to World War II, but after World War II physical anthropologists along with a few other health scientists began studies on the evolution of human disease in earnest. The early 1990s saw a dramatic increase in the number of papers published with an explicit evolutionary orientation applied to pathology and disease (see Figure 1-2).

The topics and subject matter of evolutionary medicine appear to be of interest not only to a small group of academics, but to the public as well. Science writers are attracted to the field and its content because of the potential relevance to immediate human problems. Swine flu, bird flu, West Nile virus, and mad cow disease, as well as other infectious diseases, are expected to appear in future newspaper headlines. These new and potentially deadly infectious diseases and viruses crossing from animal to human, the epidemics of obesity and asthma, the rise in cardiovascular disease, and the rise in breast and colorectal cancer are all topics of considerable popular interest. In addition to this interest in more "popular" diseases, there is also concern about psychiatric disorders such as depression, attention deficit disorder in children, the causes of sudden infant death syndrome (SIDS), and the benefits of breastfeeding. These are all issues that confront people in the industrialized world every day and are the subjects of coverage in the press.

In spite of this interest, evolutionary medicine has made little impact on clinical research and practice in general (see Chapters 22 and 23). As Lewis notes in Chapter 22, most of the "practitioners" of evolutionary medicine are not clinicians or medical researchers but anthropologists, human biologists, and/or psychologists, as are most of

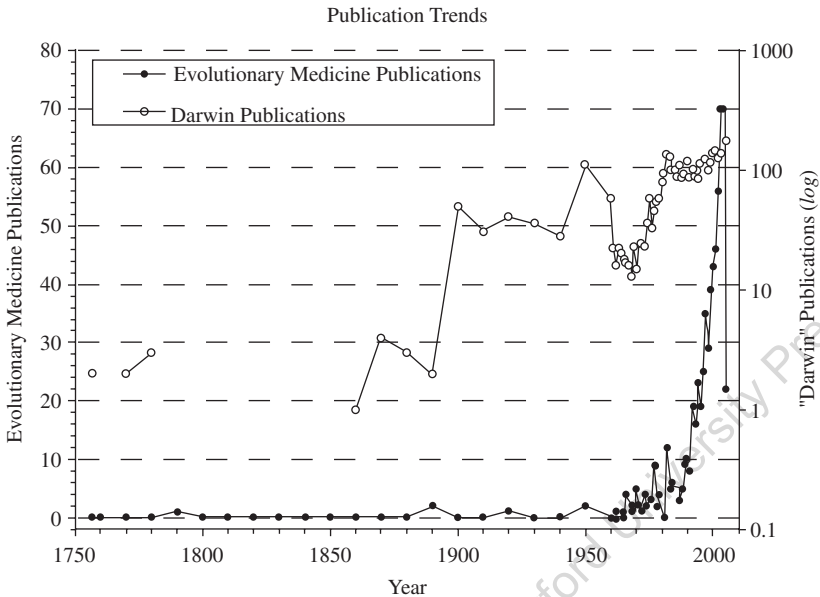


FIGURE 1-2 Publication trends of papers dealing with evolution and medicine. It is easy to see the dramatic increase in published papers in the mid- to late 1990s. Also plotted are the number of papers published over the same period with Darwin or some variant in the title. Data were collected from searches of all major electronic databases (EBSCO, JSTOR, Medline, PubMed, Science Direct, Web of Science). The important point to note is that there was no spike in the Darwin publications at the time when there was a dramatic increase in evolution and medicine papers.

the contributors to this volume. Perhaps the tendency for those not actively involved in clinical medicine and research to write and theorize about evolutionary medicine explains the lack of impact it has had on medicine in general. The lack of widespread, significant impact on the medical profession is understandable (see Chapter 23) for a variety of reasons. Although we have conducted no empirical research to determine the precise reasons for the lack of enthusiasm on the part of clinicians, there are several hypotheses that we might advance. Clinicians have virtually no medical training in evolution. What knowledge they might possess often comes from a few lectures about evolution in their general college biology course. While they might remember something about industrial melanism in the “peppered moth,” if prompted, most simply fail to make the connection when it comes to the indiscriminate prescribing of antibiotics for conditions for which the antibiotics will not be effective. It is much easier, and more profitable, to order a battery of diagnostic tests, regardless of the cost/benefit ratio, than to simply adopt a “watchful waiting” view of treatment. Such watchful waiting is, of course, necessary if we are to let the body’s own elegantly evolved immune system do what it is designed for. And in no small part, we, the consumers, are to blame. We have been seduced into thinking that any pain, itch, slight swelling, or inflammation is something that must be treated, when, in fact, most of these symptoms are simply the responses of our own immune systems.

On the other hand, changes in medical practice and health-related behaviors proceed as much from consumer input as from medical research itself. (Whether this is a particularly good trend or not is not at issue here.) Consumers are more likely to read or hear the work of anthropologists, human biologists and psychologists than they are the work of medical researchers. This is partially because the medical profession has never felt the need or pressure to offer explanations for the layperson. Like any profession, clinical medicine has a language all its own, and rather than trying to make knowledge more accessible, many clinicians have used technical language to obfuscate issues of real concern. On the other hand, nonclinical researchers have always had to justify what they do to a skeptical public and have been pressured into writing to a nonprofessional audience. Medical consumers are more likely to read *Discover* (and watch the Discovery Channel), *National Geographic*, and *Natural History* than they are to read the *New England Journal of Medicine*, the *Lancet*, or *JAMA*. The net result of this bias is that if evolution has a chance of becoming a part of mainstream medicine, it may come from the insistence of consumers, and not the clinicians.

There have been a few areas where evolutionarily based hypotheses about clinical conditions have been sufficiently empirically tested to be recognized by the clinical medicine community. One striking success story is the work on infant sleep and SIDS (see Chapter 12). Evolutionarily based research on infant sleep has been recognized internationally (UNICEF, WHO, American Academy of Pediatrics, Academy of Breastfeeding Medicine, United States Breastfeeding Committee), and researchers have been invited to contribute to policy formulation and general public health recommendations. Those studying SIDS susceptibility in relationship to sleeping arrangements and feeding methods (breast vs. bottle) have participated in the development of large multinational epidemiological studies, and their input has been responsible for important changes in the orientation and emphasis of these surveys. The work of evolutionarily based researchers has not been integrated into mainstream pediatric medicine smoothly or without tensions; nonetheless, the incorporation of an evolutionary perspective into pediatric medicine is ongoing and widespread (Fleming, Blair, & McKenna, 2006).

The other area that has become increasingly important is the coevolution of host and pathogen in the context of infectious disease and antibiotic drugs. Most physicians today realize that the overprescription of antibiotic drugs as well as poor compliance on the part of patients have contributed to the evolution (most would say development) of strains of bacteria that are virtually resistant to all but the most powerful drugs in our pharmaceutical arsenal. Vancomycin has been characterized as the antimicrobial of last resort and, when used in combination with gentamycin and rifampin, was effective against the “superbugs” until recently, when it was displaced by linezolid (Zyvox™) and the carbapenems (β -lactam antibiotics).

FUNDAMENTALS OF EVOLUTIONARY MEDICINE

A number of fundamental concepts from evolutionary theory underlie and are common to work in this field. No matter how divergent the subjects or topics, several common themes consistently emerge. We assume that most readers of this volume have a general understanding of how the evolutionary process works. Nonetheless, throughout the book

authors will introduce or reintroduce basic evolutionary ideas, core concepts, processes, terms, and phrases.

To contextualize a bit, it is important to remember the three basic assumptions of Darwinian evolution. If a trait is to be called Darwinian, it must fulfill these three assumptions. First, for a character or trait to be called Darwinian there must be some phenotypic variation in that character in the population under study. For example, there must be differences in a bacterium's response to a particular antibiotic, some variation in the expression of cardiovascular disease, or the ability of an infant to digest commercial infant formula. Second, some proportion of the phenotypic variation must be the result of an underlying genetic variation. This does not mean that a trait must be under complete genetic control, such as our classic example of the inheritance of a discrete genetic trait like the ability to taste PTC, which is controlled by the presence or absence of a single allele. The ability to taste PTC is a Darwinian trait; it is not the only example. The phenotypic expression of the trait must have some genetic basis, but its phenotypic expression can be profoundly affected by the environment. It turns out that this is very important for the vast majority of human traits that we will consider. For example, individuals may have varying tendencies to express some phenotypic trait, like the ability to digest lactose. In some forms, like kefir or yogurt, lactose may more digestible, but a tall glass of milk is a trigger for extreme gastrointestinal distress for many people (see Chapter 5). Finally, the trait in question must have an effect on fitness—the survival and reproduction of offspring to reproductive maturity. Recall that natural selection operates on individuals who possess traits, behaviors, and characteristics that promote health, survival, and, most importantly, reproductive success over time in a particular environment and gradually eliminates or decreases those traits or characteristics that compromise health or negatively affect reproductive success.

Because health is something that concerns us throughout our entire lives, a number of scholars of evolutionary medicine invoke life history theory as an organizing set of principles to examine how natural selection operates at different stages of the life cycle. Life history theory begins with the premise that there is a finite amount of energy available to an organism for growth, maintenance of life, and reproduction. Allocation of energy to each of these processes represents a series of trade-offs among important aspects of life, such as length of gestation, age at weaning, time spent in growth to adulthood, adult body size, and total life span. Natural selection shapes life history traits, determining which ones will succeed or fail in a given environment. Energy spent in the pursuit of food or mates cannot be used to grow to a larger size, for example. Although some have argued that life history theory may not work in contemporary human populations, it serves as a useful guide for delineating various life cycle phases from the perspective of evolutionary medicine. Thinking in evolutionary terms about life history questions helps us to identify and understand individual decisions about reproduction and patterns of child-care, episodic patterns of growth and development, timing and context for sleep, and susceptibility to certain diseases.

Ultimately, the adaptive value of any particular trait is at least partially determined by the extent to which that trait is congruent, if not complementary, to an overall cluster of functionally related traits—an adaptive suite—of characteristics. Moreover, our evolved physiology ultimately constrains trait variability to a range of “adaptive norms” below or above which life could not be sustained. These limits are the constraints on evolution.

For example, over the course of human evolutionary history there has been increasing pressure for larger and larger brains, but a fundamental constraint or limit on that increase, at least prenatally, is the size of birth canal in an adult female. Although natural selection has “cheated” to an extent, covering the brain in a set of unfused plates, instead of a rigid helmet, allowing humans to be born with brains that are actually too big for the birth canal, there are absolute limits. Our ability to survive at altitude is contingent on the inhalation of oxygen, and for most of us life above 8000 feet is difficult, but there are populations living in the Andes and the Himalayas that survive quite well at that elevation (see Chapter 14). Life, unaided by respiration devices, above 30,000 feet is impossible for humans for any length of time. Populations that have lived at high altitude for generations have adapted to their environment by increases in vital lung capacity, which compensates for the reduced partial pressure of oxygen. These adaptations are true Darwinian traits. Likewise, natural selection ultimately sets limits on our ability to metabolize certain nutrients that are critical for life. Our evolved physiology is designed to accommodate a diet that is drastically different from the typical Western diet. When coupled with a lack of exercise, our chronic consumption of vast quantities of starches (sugars in disguise) and sugars push the capacity of our digestive systems to modulate energy storage with energy consumption leading to a variety of chronic medical conditions (see Chapters 2, 3, 18, and 21).

In a brief overview of Darwinian evolution, it is important to understand *proximate* and *ultimate* causation. This distinction is particularly important for understanding disease. On the one hand we can imagine that the proximate (immediate) cause of a high fever is an infection. In most cases medical practitioners want to treat the proximate cause for the condition, for in doing so they are able to remove unpleasant side effects of the condition. Administration of antiphlogistic (fever-reducing) drugs is a common treatment. However, it has been demonstrated that such treatment rarely reduces the duration or intensity of the infection, although the patient will likely feel better. In fact, an evolutionary perspective suggests that administration of antiphlogistic drugs, except in extreme cases, should be avoided. Humans possess a highly evolved immune system that has many tools to fight off harmful organisms. One of those tools is fever. Fever is a host defense against infection that speeds up certain immunological reactions and reduces the reproduction rate in many pathogens (Kluger, Kozak, Conn, Leon, & Soszynski, 1998). So, in many cases, the treatment of the proximate cause of a condition without an understanding of its ultimate (evolutionary) cause may result in a counterproductive therapy. Certainly this defense (high fever) can exceed an adaptive response (e.g., 105°F in a child), at which point it becomes a defective response that requires intervention. Furthermore, there are some pathogens whose survival and reproduction are enhanced by higher temperatures caused by fever (Ewald, 1994).

Proximate causes denote the more immediate underlying physiological or anatomical factors responsible for a certain expressed behavior or physiological reaction, whereas ultimate causes affect populations and species over much longer spans of time—millions rather than dozens of years. An individual who is gaining excessive weight may ask why, and a polite response might be that the body is absorbing too many calories, which leads to increased fat deposition. A less polite proximate response is: “It’s the food, stupid, you’re eating too much of it and exercising too little!” The overweight person may be counseled to alter the diet while increasing activity levels. From the standpoint of evolutionary

medicine, however, an explanation about the adaptive advantage of being able to store fat during times of excess leading to increased survival and reproductive success in times of scarcity may not be particularly useful or meaningful to a person concerned with looking “fat” or suffering from one of a variety of serious weight-related illnesses like diabetes. In this case, a clinician who focuses on the ultimate or evolutionary explanation (who “practices” evolutionary medicine) will have little or no impact on the patient’s health and well-being when compared to the physician who focuses on and treats the proximate causes.

Another example of a defense against some infectious agents is the withdrawal of iron from the bloodstream (Weinberg, 1978). Many pathogens need iron for their own survival, so if insufficient iron is available, the health of the pathogen is compromised. When a patient presents with classic symptoms of anemia, some clinicians see this defense as a defect and prescribe increased iron intake in the form of pills, diet, or injections. Unfortunately, the administration of exogenous iron produces exactly the opposite effect from that which is desired, and the patient often gets worse. There is some concern that the common practice of encouraging higher iron intake in pregnant women maybe contraindicated in those who are also infected by HIV, in that the iron may worsen the infection (Weinberg, Friis, Boelaert, & Weinberg, 2001).

In sum, we need to keep in mind several important ideas: (1) the three basic assumptions of Darwinian evolution must be met for a trait to evolve; (2) life history theory gives us an important perspective for understanding the adaptive value of traits, with traits being advantageous at one stage of life and deleterious or even lethal at another; and (3) that differences exist between proximate and ultimate causation. With these ideas in mind, we turn to a review of the areas in medicine in which a Darwinian perspective has been applied with some success.

INFECTIOUS DISEASE

The pattern of human variation seen today is due in no small part to infectious agents to which our ancestors were exposed, especially since the origins of sedentary agriculture approximately 10,000 years ago. It is no surprise then that the coevolution of humans and pathogens is the area of evolutionary medicine most accepted by the clinical and medical research communities, but this is also the area in which, for an infected individual, the proximate and ultimate processes may come in conflict. For example, consider that for many years, physicians prescribed antibiotics for common ailments such as colds and ear infections in response to demands from patients who were concerned that their ailments could develop into something more serious. As a result, antibiotic-resistant viruses and bacteria have evolved to the point that some are nearly untreatable with current therapies. Although overuse of antibiotics has a negative impact on individual’s health in that it compromises a person’s ability to respond to other infectious agents, to the person who is ill it seems important to use antibiotics to ward off more serious problems that may develop in the short term.

Immune System

The primary mechanism employed by most vertebrates for responding to invading bacteria, viruses, and helminthes is the immune system. Most significant are immunoglobulins (IgM, IgG, IgA, IgD, and IgE), T-cell receptors, and major histocompatibility complex

(MHC) proteins, also known as the human leukocyte antigen (HLA) complex in humans (Knapp, 2002). Immunoglobins are Y-shaped proteins used by the immune system to identify and neutralize infectious agents like bacteria and viruses. The different types of immunoglobins have evolved to deal with different types of antigens, which are proteins that produce an immune response. IgA is found in areas containing mucus (gastrointestinal tract, respiratory tract, urogenital tract) and prevents colonization of mucosal areas by pathogens. IgD functions mainly as an antigen receptor on B cells. B cells are produced in bone marrow and are referred to as antibody factories. They secrete antibodies that kill microbes, allowing phagocytes (killer cells) to find the microbes more easily. IgE binds to allergens and triggers histamine release from mast cells and also provides protection from helminthes. IgM is expressed on the surface of B cells and is also secreted in a form that has a high affinity for eliminating pathogens in the early stages of B-cell-mediated immunity (before the production of sufficient IgG). T-cell receptors are molecules that are found on the surfaces of T lymphocytes (T cells) and are responsible for recognizing antigens bound to major histocompatibility complex (MHC) molecules. The human leukocyte antigen is the name of a group of genes in the MHC complex region on human chromosome 6 that encodes antigen-presenting protein. The HLA polymorphism is so diverse that it is theoretically possible for every individual to have a unique combination of alleles (Knapp, 2002), enabling our bodies to detect self cells from nonself cells. Infectious diseases are believed to account for the extreme diversity of alleles at this locus, again with the heterozygous form believed to be more resistant. Diseases that may be associated with the HLA polymorphism include leprosy, tuberculosis, malaria, hepatitis B, leishmaniasis, and meningitis (Hill & Motulsky, 1999).

The human genome has evolved a number of defenses against the malaria parasite, such as the sickle cell allele reviewed above. Some scholars have suggested that malaria has been the single biggest killer of humans throughout history, and it has been described as “the strongest known selective pressure in the recent history of the human genome” (Kwiatkowski, 2005, p.171). In addition to sickle cell, malaria appears to be responsible for the distribution of a number of other genetic “disorders” such as glucose 6-phosphate dehydrogenase (G6PD) deficiency, thalassemia, and several hemoglobin variants. All of these alleles cause health problems and even death in some circumstances, but they also confer advantages in the face of chronic malaria infection. Malaria remains high on the list of causes of death throughout the world today, killing as many as 2.7 million people annually (Centers for Disease Control and Prevention, 2004a).

The relationship between infectious disease and genetic polymorphisms has been well known for several decades, but only recently has evolution been integrated into this research. With the addition of evolutionary theory to epidemiology, populations that may be vulnerable to disease outbreaks can be identified and appropriate measures taken. Understanding how genetic resistance to disease has evolved may also lead to discoveries of genotypes that respond differentially to HIV (Samson et al., 1996) or treatments for AIDS, which, in turn, may lead to more effective drugs or vaccines. Furthermore, there is evidence that some polymorphisms that are adaptive in response to infectious diseases may turn out to be maladaptive in certain environments, with certain diets, and with aging, and may lead to greater susceptibility to degenerative or chronic diseases later in life (Hill et al., 1999). Data from the Human Genome Project (HGP) can be used by evolutionary medicine researchers to increase understanding of the origin and distribution of genetic polymorphisms related to infectious and noninfectious diseases.

The role of selection in the development of immune function in the individual throughout the life course is another promising area of research (McDade & Worthman, 1999). Because reproductive rates of most pathogens are so fast and generation lengths so short, long-lived human hosts are at a disadvantage when it comes to the usual work of natural selection on genomes. The response has been that selection has shaped immune systems to develop based on individual experience (e.g., exposure in infancy and early childhood to a variety of pathogens to which immunity develops), “creating a facultative experienced-based system that, on the level of ontogeny, evolves itself” (McDade & Worthman, 1999, p. 715). The lymphatic system develops in response to exposure to varying pathogens, enabling the individual to survive in a specific disease environment. Because of the variation in immune function that results, there is no such thing as a “normal” developmental process, and “culture can interfere in potentially destructive ways when immune defenses are not fully developed” (McDade & Worthman, 1999, p. 715), as with overprotection from pathogen exposure that occurs with using antibacterials in day-to-day activities.

Vaccines and Viruses

As noted previously, in the most developed nations infectious diseases are not a major source of mortality. Improved diet and hygiene (McKeown, 1998), rather than direct medical interventions, have dramatically lowered the life-threatening aspects of infectious disease. Vaccinations, particularly of children, have reduced the incidence of a number of diseases, and smallpox seems to have been completely eliminated as a threat to human health. In fact, diseases that are vulnerable to vaccination are apparently not evolving resistance in the same way as seen with antibiotics (McLean, 1999). This does not mean that viruses cannot evolve such resistance in the future. For example, nucleotide changes in the virus that causes measles have been reported, and there is some evidence that the cessation of vaccination for smallpox may make us vulnerable to related pathogens such as monkeypox, a disease that may have moved into the niche formerly occupied by smallpox (Bangham et al., 1999; McLean, 1999).

Vaccine development is an area that could benefit from an evolutionary approach (Read et al., 1999). The logic of vaccines is to infect a person, typically a child, with a mild strain of the virus, following which immunity typically develops for all strains, including the dangerous ones. This is the procedure used for vaccines for most “childhood” diseases. In areas where vaccines are not available, exposure to mild strains of a virus triggers an immune response that typically works as a good substitute. For example, people who were born before measles vaccines were developed often contracted a mild strain of the virus and became ill, but in the process developed immunity to more virulent strains of the virus. A vaccine designed to kill all strains of a virus may not be the best strategy—better, perhaps, would be the development a vaccine against only the most virulent strains or those likely to evolve virulence, leaving behind mild forms that could “. . . be used like a free live vaccine that will protect those who are not vaccinated and those who develop insufficient immunity to the administered vaccine” (Read et al., 1999, p. 213). In this way, coexistence of humans and relatively mild pathogens may be better, in the long run, than efforts to eradicate all strains, a strategy that could backfire and lead to the most virulent forms “escaping” drug intervention. In fact, there is evidence that

exposure to mild forms of measles, as well as immunization against measles, may provide protection against other pathogens (Aaby, 1995), presumably via stimulation of the immune system. This suggests that total eradication campaigns such as those with smallpox and polio may be ill advised when considered from the standpoint of evolutionary theory because there is always the possibility that defenses against the most hearty (virulent) strains will not be activated by exposure to mild variants, leaving individuals vulnerable to the more virulent strains.

Antibiotic Resistance

When Europeans colonized Africa in the twentieth century, malaria was one of the most dreaded diseases. Quinine, a naturally occurring substance extracted from the bark of the South American cinchona tree, was found to be an effective treatment. Over time drugs used to treat malaria have changed repeatedly as the protozoa have evolved resistance to quinine, chloroquine, primaquine, and mefloquine, among others (Newton & White, 1999). There is some concern that drug development is failing to keep up with pathogen evolution and that preventing exposure to the mosquitoes (or killing them with DDT, as has been recently suggested) may be the best way to curb the spread of this dread disease. And as noted in the Doonesbury comic strip discussed at the beginning of this chapter, tuberculosis is another disease that is evolving drug resistance and that has re-emerged as a feared disease in industrialized nations.

Not only are antibiotics administered to humans of concern, but widespread use of antibiotics in agriculture and animal husbandry (including fish farming) have also contributed to the emergence of drug-resistant strains of pathogens (Bangham et al., 1999). In fact, about half of all antibiotics produced are used in agriculture and animal husbandry (Bangham et al., 1999). Other factors that contribute to the evolution of resistance include failure of patients to follow through on drug regimens. Alexander Fleming, in his Nobel Prize acceptance speech, noted the danger of drug resistance: "It is not difficult to make microbes resistant to penicillin by exposing them to concentrations not sufficient to kill them, and the same thing has occasionally happened in the body. . . . Moral: If you use penicillin, use enough" (Fleming, 1945, p. 11). The failure to kill all the pathogens in the body is usually the result of patients stopping medication when they "feel better." In the case of children, parents often expect that physicians will prescribe antibiotics no matter what the cause of the symptoms may be. Recent studies have shown that doctors prescribe antibiotics about 56% of the time if they perceive that parents expect them and only about 12% if they feel the parents do not expect them (Centers for Disease Control and Prevention, 2003).

A more recent contributor to pathogen resistance is air travel, particularly international travel. A pathogen can leave Bangkok, Thailand, and in no more than a day be in New York City. Such changes in environments open up the possibility of infection to a world of unprepared hosts. Increased urbanization and attendant crowding are also circumstances that enhance transmission, but more recently, crowding seen in refugee camps in the Darfur region of Sudan has produced similar results. Poverty, in general, leads to transmission of pathogens, as well, largely through the lack of public sanitation and clean drinking water. Increased understanding of the evolutionary process will help address some of these factors, but clearly drug resistance is complicated by socio-cultural factors that evolutionary medicine cannot address alone.

Is there a way out of this arms race whereby pathogens develop greater virulence in response to ever more powerful antimicrobials? For a long time, it was assumed that pathogens, most specifically parasites, would evolve toward benign existence rather than increased virulence because their own survival is dependent on the health and survival of the host (Read et al., 1999). This view was based on a false understanding of the evolutionary process and assumed that mutual benefit (and survival) for host and parasite was the “goal.” A more accurate view of host parasite evolution involves analysis of trade-offs for both the host and the parasite. Natural selection will favor organisms that have the greatest reproductive success. Parasites and hosts are designed to maximize their reproductive success, and in doing so one of these competitors will lose.

From the preceding discussion one might conclude that modern medicine is hastening the evolution of pathogens toward increasingly virulent strains. However, there is nothing inherent in the evolutionary process that moves it in one direction or the other, from less to greater lethality, or the reverse. In fact, one of the greatest potentials for thwarting future disease outbreaks is the possibility of reversing the evolutionary process so that pathogens evolve toward less dangerous forms that can coexist with human hosts or forms that may even be beneficial to human hosts (Read et al., 1999). Ewald has referred to this as “domesticating” pathogens (Ewald, 1994). To some extent this has already happened with diphtheria, which has apparently evolved toward less virulence in association with vaccination (Read et al., 1999).

Turning the evolutionary process around may be our best tool for reducing the virulence of pathogens. The problem is that pathogens have a very short generation length and are capable of an extremely rapid evolutionary response to environment change. Where attempts have been made to develop a targeted vaccine, as with HIV, efforts have proved ineffective, and, even worse, by using ineffective vaccines, resistance is enhanced (Ewald, 1999a) and there is no end in sight to this process. Development of a totally successful flu vaccine is also unlikely because vaccines must be developed well in advance of the outbreak based on the best guess of which strains will be most successful in the upcoming flu season. Ewald has proposed that our best hope comes from harnessing evolutionary processes to “mold HIV and other sexually transmitted pathogens into milder forms” (Ewald, 1999a). And who knows what else is lurking out there that may be as devastating as AIDS? Medical interventions that are capable of responding to the processes of disease emergence and evolution are much more likely to be successful in the long run than those that target specific disease variants and their manifestations. But this requires a very sophisticated understanding of the evolutionary process on the part of medical researchers.

Pathogens and Phylogenies

Another important tool from evolutionary biology that has been useful in health-related research is constructing evolutionary relationships (phylogenies) among strains of viruses to assess origins and patterns of distribution. For example, HIV has been traced to multiple central African primate populations, with evidence that it may have entered human populations on more than one occasion. Worldwide geographic maps of the distribution of the various strains of HIV may lead to development of vaccines and treatments that are tailored to specific populations (Holmes, 1999). For example, in some parts of the world injecting drug users tend to be infected with a different strain of HIV than those infected via heterosexual contact (Holmes, 1999). To use the terminology of

evolutionary theory, strains of HIV that are maintained by natural selection show different phylogenies from those maintained by genetic drift (Holmes, 1999). Understanding evolutionary relationships among strains of viruses and among pathogens in general may reveal factors that contribute to their spread and increased virulence (Read et al., 1999) and offer possibilities for control of specific pathogens.

Recent work on unraveling the genomes of humans and chimpanzees has revealed evolutionary relationships and suggested possible reasons for some of the differences in not only development, but also susceptibility to diseases. For example, sialic acid is a sugar molecule on cell surfaces that serves as a binding site for organisms that cause diseases such as cholera, malaria, and some forms of influenza. Interestingly, analysis of the genetics of sialic acid in humans and chimpanzees reveals that they differ by a single oxygen atom (Muchmore, Diaz, & Varki, 1998). The differences in this single gene complex may explain why humans are susceptible to diseases like cholera and malaria, whereas chimpanzees are not, and it may be protective against others of which we are not aware (Varki, 2001). It may also explain why malaria has become such a scourge in the past several thousand years (Martin, Rayner, Gagneux, Barnwell, & Varki, 2005). Because the chimpanzee version of the gene is found in all other mammals studied, it has been suggested that the human version, with its associated disease susceptibilities (or protections), is the derived form. Discovery of this tiny genetic difference may lead to new treatments for infectious diseases to which humans, and not chimpanzees, are susceptible. There are other implications for chronic diseases like cancers and even brain evolution that are beyond the scope of this discussion but are reviewed in Varki (2001). When we say that chimps and humans differ by only a small fraction of their genes or DNA, this does not mean that this seemingly small difference does not have a huge impact on health, just as it apparently does on development.

NUTRITION

That diets of most people in industrialized nations are radically different from the diets of our ancestors is one of the most well-known observations from evolutionary medicine. Human nutritional requirements were shaped by the foods that were consumed during the 5–7 million years of hominin evolution. In the past 10,000 years, many new foods have been introduced into human diets with the domestication of plants and animals. The results of dietary and other behavioral changes brought about by the origin of agriculture have been positive in many ways, but the consequences for human health have not always been so sanguine. Among the reasons for dramatic increases in diseases and disorders such as type 2 diabetes, atherosclerosis, hypertension, some cancers, diverticular diseases, and osteoporosis is the fact that our evolved bodies are “mismatched” with the foods we eat today and the levels of energy expended in our daily lives (Eaton & Konner, 1985b; Eaton, Eaton, III, & Konner, 1999; Eaton, Konner, & Shostak, 1988b; Eaton, Shostak, & Konner, 1988). Chapters 2, 3, and 4 in this volume provide extensive reviews of the hypothesized ancestral diets and the evidence supporting the proposal that many contemporary health problems result from this discordance (but see Strassmann & Dunbar, 1999). In general, the major differences in preagricultural and contemporary diets are seen in percent of calories from fats, protein, and carbohydrates and in intake of sodium, calcium, ascorbic acid (vitamin C), and cholesterol (see Figure 1-3).

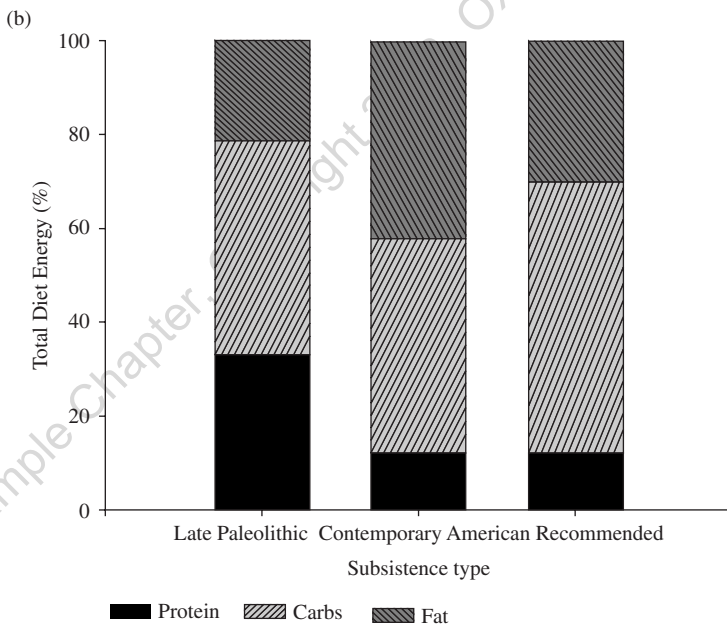
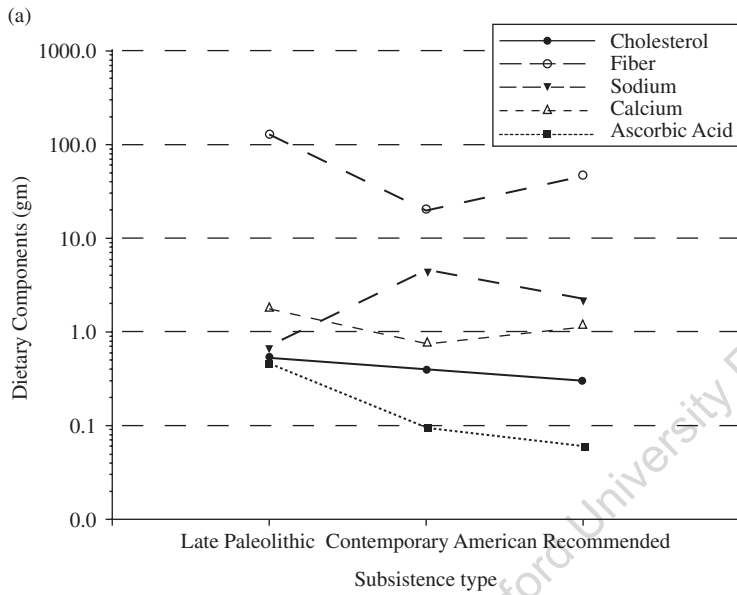


FIGURE 1-3 Late Paleolithic, contemporary American, and recommended dietary composition: a) composition of five components of diet (cholesterol, fiber, sodium, calcium, and ascorbic acid); b) the percent energy intake from protein, carbohydrates, and fats. (From Eaton, Shostak, & Konner, 1988, p. 84.)

Before humans began producing rather than gathering foods, edible components of grasses were consumed rarely and in small quantities; today they comprise more than half of the calories and protein consumed by humans throughout the world (Cordain, 1999). Plants have always made up a substantial part of human diets, but the concentration of food sources in a single family (Gramineae) is relatively recent in human evolutionary history. Furthermore, not only are we consuming considerably more grains than our ancestors, most of the actual cereal-based foods we eat are highly processed and refined so that the more complex carbohydrates of our ancestors' diets have been replaced by highly refined simple sugars. Much of the evidence suggests that the recent changes in food-processing techniques have resulted in declining health for most individuals (see Chapter 2), but if we look at the population level, the production and consumption of cereal grains is the only way to support the world's people. It has been estimated that the number of humans that could be supported on the earth (i.e., the carrying capacity) if they were dependent only on wild resources is approximately 5 million. If this estimate is true we have exceeded the carrying capacity of the earth over three orders of magnitude (1000-fold). It is only through domestication of plants and animals and increased reliance on cereal grains that such population expansion could have occurred.

However, there is a downside to increased grain consumption, especially for populations that have recently begun to depend on wheat as the "staff of life." Diets high in cereal grain lack important vitamins (e.g., vitamins A and C), minerals (e.g., calcium), amino acids (e.g., lysine and methionine), and fatty acids (e.g., linolenic acid) but include antinutrients (e.g., α -amylase and protease inhibitors) that interfere with absorption of other nutrients (Cordain, 1999). Moreover, there is increasing evidence that a number of chronic health problems (e.g., multiple sclerosis, rheumatoid arthritis, celiac disease, and type 1 diabetes) may be due to excessive cereal consumption. In fact, it is possible to map the spread of wheat-based agriculture throughout the world by mapping the prevalence of celiac (gluten intolerance) disease (Simoons, 1981).

Although animal food sources, including insects, have been consumed by humans for thousands of generations, the types of animal products consumed by most people today are much higher in fat than those consumed in the past. The change in the types of animals consumed has important consequences for obesity, heart disease, and cancers. In general the meat of domesticated animals has much higher fat content, than wild animals (see Figure 1-4).

Many of the chapters in this volume reflect the great concern about increasing rates of obesity and type 2 diabetes in many contemporary populations (see Chapters 2, 3, 4, 7, and 8). Because these topics are covered extensively in chapters that follow, they will not be reviewed here. It is absolutely clear, however, that dietary changes are among the best examples of the discordance between ancestral bodies and contemporary lifestyles resulting in a variety of cardiovascular diseases, cancers, and type 2 diabetes.

In summary, the now-familiar refrain that our diets today are different in quality and quantity from those of our ancestors and that the "mismatch" between today's diet and human evolved nutritional needs has negative health consequences has resonated with Western consumers who struggle with weight control, high blood pressure, and diabetes (see Chapter 3). Can "returning to a Paleolithic diet" improve human health? Certainly many contemporary authors of best-selling books on diet and health argue that this is the case, as illustrated by the titles they have chosen: *The Origin Diet: How Eating Like Our*

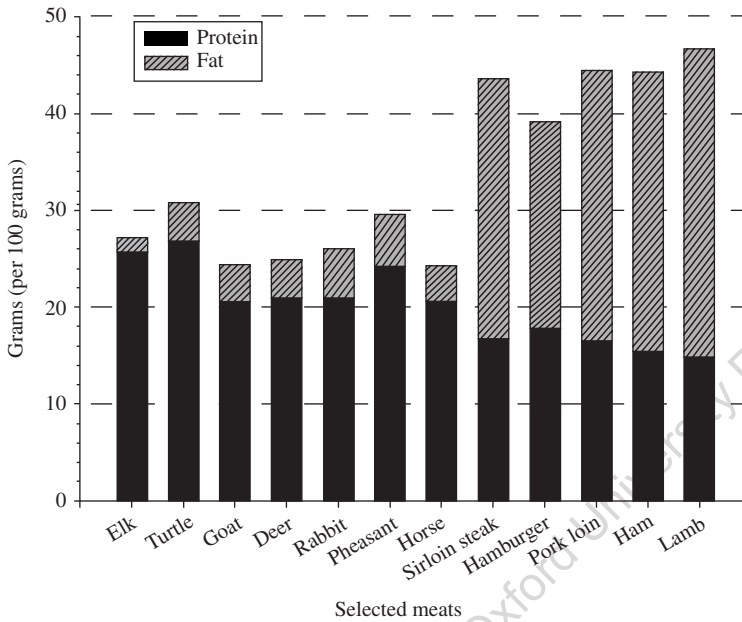


FIGURE 1-4 Fat and protein content of selected wild and domestic meats. (From Eaton, Shostak, & Konner, 1988, p. 108.)

Stone Age Ancestors Will Maximize Your Health (Somer, 2001); *Health Secrets of the Stone Age: What We Can Learn from Deep in Prehistory to Become Leaner, Livelier, and Longer-Lived* (Goscienski, 2005); and *The Paleo Diet: Lose Weight and Get Healthy by Eating the Food You Were Designed to Eat* (Cordain, 2002). However, as noted above, the current world population size is only possible because of the production and consumption of cereal grains. In order for humans to return to Paleolithic food-consumption patterns there would have to be a dramatic reduction in world population, an unlikely scenario, at least voluntarily. Popular authors, like those listed above, argue that by adopting some aspects of ancestral diets (lower fat, more complex carbohydrates, lower sodium, frequent small meals) and lifestyles (more exercise, less alcohol, no smoking, lower stress), we will feel better, live longer, and lose weight. As noted by Turner and her colleagues in Chapter 3, however, many of these popular approaches to incorporating an evolutionary perspective into diet and lifestyle management greatly oversimplify the problem.

HUMAN REPRODUCTIVE HEALTH

Just as contemporary diets are mismatched with evolved nutritional requirements, numerous aspects of contemporary reproductive behavior are mismatched with the reproductive lives of our ancestors, resulting in potential consequences for health, particularly of women. Perhaps the most familiar example is the fewer number of menstrual

cycles experienced by ancestral females when compared to modernday Western females. Given that most of their reproductive years were spent in pregnancy and lactation, it has been estimated that ancestral women had only 100–150 menstrual cycles in their lifetimes (see Figure 1-5). Compare this with the 350–400 cycles experienced by a Western woman using birth control who has two or fewer pregnancies and nurses her infant only a few months, if at all. Women’s reproductive physiology may not be well adapted to the routine monthly fluctuations of ovarian hormones, particularly estrogen and progesterone, that are associated with the typical menstrual cycle. Perhaps Roger Short put it best: “Since natural selection has always operated in the past to maximize reproductive potential, women are physiologically ill-adapted to spend the greater part of their reproductive lives in the non-pregnant state” (Short, 1976, p. 3), i.e., “having an endless succession of menstrual cycles” (Short, 1976, p.21). Perhaps women’s bodies were not “designed” to be exposed to 400 or more monthly surges and falls in estrogen, with the associated effects on cell turnover rates and hormonally sensitive tissue.

It seems likely that these episodic surges have an impact on women’s health. The most probable impact, as proposed by several scholars (Eaton & Eaton, III, 1999; Eaton, Pike, Short, Lee, Trussell, Hatcher, Wood, Worthman, Blurton Jones, Konner, et al., 1994) is on the estrogen-related cancers of the breast, uterus, and ovaries. Although comparative rates are difficult to obtain, the rate of breast cancer for industrialized nations, where birth control is practiced and childbearing is limited and deferred, is considerably higher than for less developed nations and may be as high as 100 times the rate for women who are not using contraception and are spending the bulk of their reproductive lives pregnant or nursing with sufficient frequency to induce lactational amenorrhea (Eaton, S. et al., 1994). For these women, the hormonal milieu to which they are most commonly exposed are high progesterone levels, rather than high estrogen levels. Furthermore, there is evidence that not only do Western women experience more frequent fluctuation in ovarian hormones, but the absolute levels during each cycle are higher in Western women than in women in less industrialized societies (see Chapters 7 and 8).

The mismatch between evolved dietary needs and modern diets seems somewhat easy to resolve, at least in theory, if not in practice. Few would argue that there is a downside

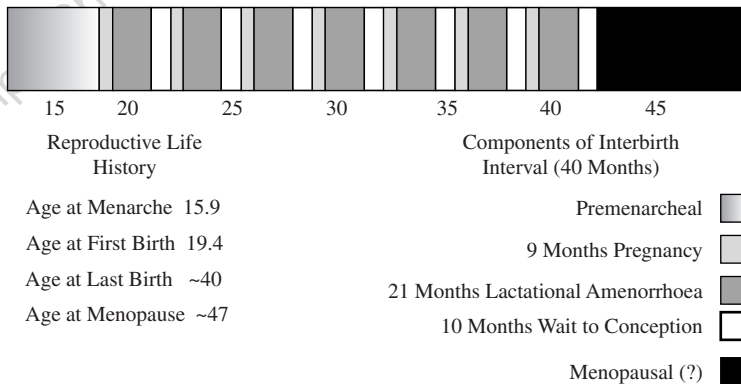


FIGURE 1-5 Hypothetical reproductive history of a female forager. (From Worthman, Smith, & Weil, 1992.)

to reducing fat intake (but see Chapter 4), increasing consumption of complex (rather than simple) carbohydrates, and increasing exercise. Trying to bring women's physiology back in line with ancestral conditions is not as easy to effect, however, because it involves altering reproductive patterns and interfering with hormones. To wit, there are very few popular books written about ways of reducing breast cancer rates by "returning to" reproductive patterns of our ancestors. The point has not been missed by the popular imagination, however, and web sites have sprung up advocating ways of altering menstrual patterns to more closely mimic the hormonal milieu of ancestral women (see Chapter 9). More importantly, pharmaceutical companies have taken note and now are marketing oral contraceptives that not only suppress ovulation, but also suppress menstruation, more closely mimicking the ancestral condition.

Pregnancy

A number of aspects of pregnancy have been subjected to analysis from the perspective of evolutionary medicine, including nausea of pregnancy (commonly called "morning sickness" in the United States), early fetal loss, and eclampsia and preeclampsia. Nausea of pregnancy is an example of a health problem that benefits from questioning whether it is a defense or a defect. Because it can be so debilitating to a woman early in pregnancy, medical approaches in the past sought ways of reducing or eliminating nausea of early pregnancy. A particularly tragic effort to "solve" the problem of morning sickness was the use of thalidomide in the 1950s, resulting in the birth of approximately 12,000 deformed babies and the spontaneous abortion of untold others.

Rather than a problem that has to be fixed, nausea during the first trimester may be a defense, having evolved as a protection against toxins and teratogens that could harm the developing embryo (Profet, 1992). The proximate explanation for nausea and food aversions is likely hormonal (specifically hCG and estradiol, which rise early in pregnancy), but the ultimate explanation may be that women who found potentially harmful food components aversive may have protected their first trimester fetuses from developmental damage, leading to greater reproductive success. Hence, the predisposition toward first trimester nausea could have evolved as a strategy for fetal protection. Certainly there are limits to the adaptive value of nausea and vomiting early in pregnancy. Severe and prolonged nausea results in dehydration and weight loss such that hospitalization is required or death may ensue (Furneaux, Langley-Evans, & Langley-Evans, 2001; Flaxman & Sherman, 2000). This hypothesis, known as the embryo protection hypothesis, has been criticized by some researchers noting that it is based largely on observations of well-nourished women, and that there are potentially severe nutritional consequences among women who were inadequately nourished before pregnancy (Pike, 2000).

It has been estimated that many conceptions are lost before implantation, and 10–20% of those implanted are lost in the first trimester (Haig, 1999). If maximizing reproductive success is how the game of evolution is won, then how can there be benefits to early pregnancy loss? For humans, early pregnancy loss may actually be adaptive under certain circumstances. Quality of offspring overrides quantity because of the huge investment made by women and couples in each pregnancy and the subsequent years of parenting. At the most basic level an evolutionary perspective argues that gestating, giving birth to, nursing, and raising an offspring that is not healthy and capable of reproducing would be

“wasted” energy, energy that could be better allocated to future offspring who are healthier and more likely to reproduce. This is a straightforward resource-allocation problem from the perspective of life history theory. Indeed, most of the pregnancies lost in the first trimester have been found to have chromosomal abnormalities (Haig, 1999; Peacock, 1990). In many cases, however, reproductive failure is seen as pathological by clinicians and preventing it is an overriding goal for physicians, women, and couples, rather than as a solution to an evolutionary mistake. This is a clear example of where medicine and evolution might be at odds (Peacock, 1990). While artificial insemination has solved fertility problems for many couples, it is possible that in some cases this is not a solution that should be attempted.

The fetus is sometimes referred to as a graft, and, just as a skin graft often fails, it should not be surprising that the fetal graft sometimes fails, given that mothers and fetuses share, on average, only about 50% of their genes. From an evolutionary perspective it is useful to consider pregnancy an example of parent–infant conflict in that the interests of the mother do not always coincide with the interests of the fetus (Haig, 1999). Sometimes it may be in the mother’s best interest to abort a pregnancy that interferes with her own health or the health of her current and future offspring, but it is clearly in the interest of the fetus to maintain the pregnancy, no matter how bad the situation is. Consequently, we would predict that fetuses have evolved strategies to minimize pregnancy loss and hence maximize their fitness. Likewise, mothers should have evolved strategies to detect risky fetuses and act accordingly.

Once the pregnancy survives the first trimester, the termination rate declines appreciably (Haig, 1999), but the potential for maternal–fetal conflict continues, especially in competition for nutrients. From a public health perspective one would predict that if the mother experiences severe undernutrition or malnutrition during pregnancy, the uterine environment for the fetus would be compromised and miscarriage would result. Surprisingly, this prediction is not often borne out: women give birth even under severe food restrictions such as occur with famine and war (see Chapters 7, 8, and 18). Some interpret this to mean that the fetus has ways of prolonging the pregnancy, even if there are negative consequences for maternal health. Of course, just because a fetus survives pregnancy and birth does not mean that its health is not compromised by in utero nutritional stress. Such babies are often born small for gestational age (SGA) due to intrauterine growth retardation (IUGR), and there is increasing evidence that nutritional stress in pregnancy has lifelong effects on health (Adair, Kuzawa, & Borja, 2001; Barker, 1995, 1997; Kuzawa, 2005; see also Chapter 18).

Clinical conditions of pregnancy that result from maternal–fetal competition for nutrients include gestational diabetes and eclampsia/preeclampsia. These conditions benefit from consideration from an evolutionary perspective. For both gestational diabetes and eclampsia, changes in maternal physiology designed to increase delivery of oxygen and nutrients to the fetus become so extreme as to become pathological and usually warrant medical treatment. For a woman without diabetes, blood glucose levels rise after a meal and return to normal levels when counteracted by insulin. During late-stage pregnancy, however, both glucose and insulin levels remain elevated for a longer time after a meal to benefit the fetus. This is an example of the fetal interests working against the maternal interests as the fetus works to obtain more and more glucose at the expense of the mother’s health. Elevated glucose levels in mothers can result in hypoglycemia for

mothers, but also result in some compromise in fetal health. Not surprisingly, glucose elevation is also associated with excess nutrient intake in pregnancy and is more common in developed countries. Women who develop gestational diabetes often give birth to large infants who are themselves predisposed to developing diabetes later in life (Power & Tardif, 2005). This suggests that there is likely an optimal level of nutritional intake during pregnancy, and too much or too little food can cause pregnancy complications and lifelong health problems for both mother and infant. Thus, we have an example of stabilizing selection, whereby extremes in food intake result in reduced reproductive success.

A major complication of pregnancy worldwide, found both in developing and developed countries, is preeclampsia and its more severe form, eclampsia. Preeclampsia is associated with hypertension in the mother and is estimated to occur in as many as 10% of births. It is also a common cause of premature birth, because the only “cure” is delivery of the fetus and placenta. If the pregnancy is not interrupted, the mother will experience damage to the kidney, liver, and brain, and if it proceeds to eclampsia, maternal convulsions may result. Furthermore, even though the short-term effects may be improved with delivery, there is evidence that there may be lifelong effects on maternal health (Redman & Sargent, 2005). Unfortunately, there is no animal model for preeclampsia, which has inhibited research on causation and potential interventions. It has been argued that preeclampsia/eclampsia is related to the evolution of increased cranial capacity in *Homo sapiens* and derives from the very deep invasion of the placenta into maternal tissue necessary for adequate oxygen exchange for fetal brain development (Robillard, Chaline, Chaouat, & Hulsey, 2003; Robillard, Dekker, & Hulsey, 1999, 2002; see also Chapter 11).

Preeclampsia is usually restricted to first pregnancies, and ways of reducing the incidence of it have been suggested using evolutionary theory and relating the disorders to other aspects of human reproductive ecology, including the frequency of nonovulatory sexual activity, concealed ovulation, prohibitions of incest, rarity of polyandry, and relatively low fertility rate (see Chapter 11). Although there are other interpretations and recommendations for treatment of preeclampsia (Bdolah et al., 2004; Levine et al., 2006; Signore et al., 2006; Venkatesha et al., 2006), the evolutionary medicine perspective holds promise with its somewhat simple recommendation that pregnancy be delayed until after several months of sexual activity, preventing what is not just a disease of first pregnancy, but a “couple disease” associated with exposure to novel sperm (see Chapter 11). Delaying pregnancy for a few months gives the woman’s immunological system time to adjust to the man’s antigens, decreasing the likelihood that her system will challenge the fetal “allograft” in the early months of pregnancy.

Childbirth

With the origin of bipedalism in our ancestors 5–7 million years ago came alterations in the pattern of childbirth. Birth is not an easy process for most monkeys and the lesser apes, given the close correspondence between the size of the neonatal head and the maternal bony pelvis (see Figure 1-6). Great Apes are the notable exceptions, with humans having a pelvic inlet that is smaller than the head of the neonate.² Bipedalism placed even greater constraints on the birth process through alteration of the dimensions and shape of the pelvic entrance and exit. These anatomical changes can help explain a behavioral

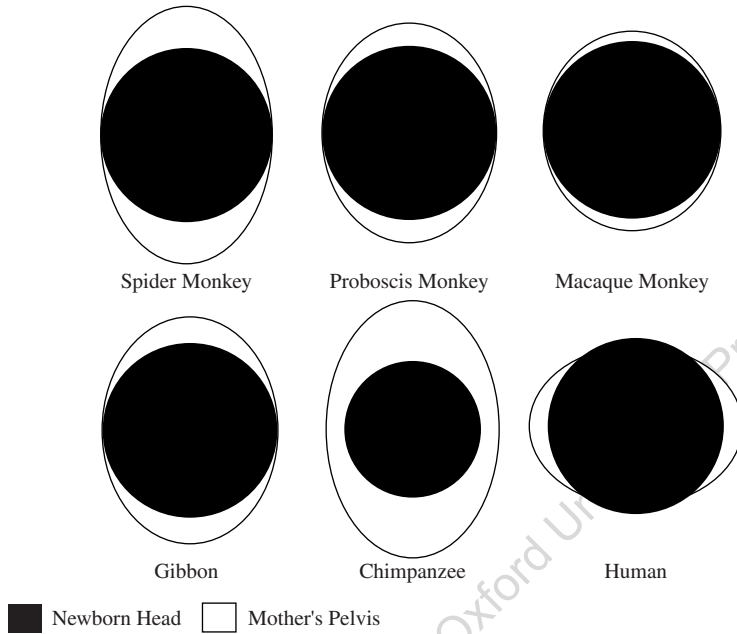


FIGURE 1-6 Representation of the relationship in size between the average diameters of the pelvic inlet of adult females and the average head length and width of newborns of the same species (all diagrams reduced to the same pelvic inlet width). (Adapted from Schultz, 1969, p. 154.)

characteristic of human birth: the tendency for mothers to seek assistance at the time of labor and delivery (Trevathan, 1987, 1999). For most primates and most mammals, birth is a solitary event and parturient females typically seek isolation rather than companionship. For humans, the practice of seeking companionship at birth is found in almost all cultures. While it is possible for women to give birth unattended, Trevathan and Rosenberg have argued that throughout human evolutionary history, those females who sought assistance at birth had more surviving offspring than those who delivered their infants alone (Rosenberg, 1992; Rosenberg & Trevathan, 1996, 2002; Trevathan, 1987, 1999). Even a small difference in mortality and morbidity rates over several hundred generations could account for the near-universal practice of accompanied birth.

Women in the past probably did not seek companionship because of a conscious awareness that assistance would reduce mortality; rather, they likely felt more anxiety and uncertainty about labor and delivery and sought companionship for emotional support (Trevathan, 1999). For thousands of years the emotional needs of women at birth have been met by friends and relatives, most likely women, who possessed no particular skills in midwifery, but who cared about the woman and her newborn and were able, by their mere presence, to reduce emotional stresses that could interfere with labor and delivery. Today, most births in industrialized nations take place in hospitals accompanied by personnel unknown to the laboring woman. In many cases her emotional needs are not

met, resulting in a view that fear and anxiety in labor are “defects” that need to be dealt with medically (with pain-relieving drugs, for example), rather than “defenses” that once motivated women to seek companionship and assistance at delivery, thereby reducing morbidity and mortality.

If efficiency at bipedal walking were the only constraint in the evolution of the human pelvis, it would likely not be the shape we see in modern as well as fossil humans. However, another constraint was imposed on the evolving human pelvis, and that was an upper limit on the size of the neonatal head that could pass through at birth. This put the birth process in direct opposition to selection for increased brain size in human evolution. Apparently the only way for the opposing trends of reducing size of the pelvic opening for bipedal efficiency and increasing size of the brain to continue was for more and more brain development to occur after birth. The result is that human babies today are born with only about 25% of their brain growth completed. This means that a lot of the motor systems necessary for independent function have not yet developed so that the human infant is much more altricial (i.e., less developed) at birth and more dependent on others than are the infants of most monkey and ape species. The other anatomical accommodation for this pressure for larger and larger brains at birth was the lack of fusion of the bony plates that make up the skull. During the birth process the skull can actually be compressed and deformed to allow passage through the birth canal.

Infancy

One of the areas of human biology where evolutionary medicine has made particularly significant impact is human infancy. There are a variety of reasons why this is so, not the least of which is that we were all infants at one time. This is not as silly as it sounds. The ubiquity of childhood is something with which everyone can identify; even if he or she is not a parent, everyone was once an infant.

Given the selective forces that appear to have constrained prenatal processes, including, but not limited to, the biology of birth and fetal sensitivity to the quality of the environments into which it is to be born (see Chapters 2, 8, and 18), the lack of evolutionary constraints on what parents actually do with and for their infants is remarkable. The specific forms of fundamental caregiving activities exhibited today such as feeding, sleeping arrangements, patterns of social affiliation, communication, and parent–infant attachment, appear to vary significantly from the ancestral economic, social, and physical conditions that might have produced them. One would expect, given an evolutionary perspective, that with so much at stake (i.e., the energy and resources invested in mating, conception, gestation and, parturition), natural selection would have designed a “universal” pattern of childcare. Based on cross-cultural ethnographic data, this seems, in fact, not to be the case.

Among the Efé of the Democratic Republic of the Congo, infants are almost continuously attached to mothers and are allowed to nurse frequently, but infants are also passed around to caregivers other than the mother who live in kin-based extended families. Mothers in horticultural groups in East Africa recruit their oldest daughters as babysitters for their infants, while mothers work in the fields. Economically disadvantaged Brazilian mothers provide care for their infants, but seem to withhold the strongest attachment emotions because of the high probability of infant death. Japanese mothers sleep apart

from their husbands with their infants and attempt to minimize the stimulation and excitement of the infants. In traditional Russian families infants are tightly swaddled in blankets, making them easy to handle and restricting their movements. Navajo infants are bound to cradle boards, where they can be easily carried on mother's back (Konner, 1991a).

Human infants are the end product of an evolutionary process that has designed them so that there is the maximum probability that mothers will respond to them. Infants who were slightly less attractive and enticing to mothers would have been ever so slightly less likely to survive. The net result was intense selection for a suite of characteristics that would elicit maximal responsiveness in mothers. While human infants are born to mothers who lack a rigidly programmed set of maternal behaviors, natural selection has favored certain behaviors in infants and certain physiological responses in mothers that increase the likelihood of infants successfully obtaining a meal. The appearance of infants and the concomitant response in mothers makes it likely that infants will be picked up and held. Once that happens, infants have a programmed set of behaviors that guides them towards the nipple. Infant rooting reflex results in the location of the nipple where infants lock on and begin sucking. The ability to suckle and breathe at the same time is particularly advantageous for infants, but is lost in the course of development.³ For mothers, there is certainly a learning component to breastfeeding (Helsing, 1976; Reeve, Gull, Johnson, Hunter, & Streather, 2004). However, once the basics are mastered, maternal physiology takes over. The initial rise in cortisol subsides, and oxytocin levels begin to rise. Maternal blood pressure decreases, and as oxytocin levels continue to rise, mothers experience a kind of calm. Once nursing begins mothers are transformed in ways that will serve the infant's needs and concomitantly increase her fitness. Under past evolutionary conditions maternal physiology takes over and the episodic endocrine and behavioral changes that occur in mothers and their responses to their infants occur with little fanfare.

However, this bond between mother and infant is not immutable. Parents in all cultures are highly susceptible to local cultural assumptions and practices about infant health and well-being. This responsiveness to cultural proscriptions makes sense in so far as the culture is a reliable source of knowledge about infant care. From an evolutionary perspective, such cultural information should have been selected for its reliability and its fidelity. Unfortunately, in modern Western society this is not always the case. Conflicting cultural values come into play in influencing parental decisions to accept or reject popular ideas about childcare, even when these cultural values are not consistent either with parental emotions and/or the ever-changing experientially based caregiving patterns that seem to make their babies happy.

Culture is so powerful that for at least half a century urban Western women were "fooled" by their cultures into thinking that artificial milk and synthetic formulas were either as good as or better than the species-specific milk their own bodies produced. A major epidemiological study of over 8900 infants followed from birth to one year of age, including 1204 infants who died between 28 days and a year from causes other than congenital anomaly and/or tumors, was conducted to determine the effects on the risk of postnatal death of breastfeeding. Overall, researchers concluded that infants who were ever breastfed had 0.79 times risk of the never-breastfed children for dying in the postnatal period. This means that if all infants born in the United States were breastfed after leaving the hospital, approximately 720 postneonatal deaths could be prevented (Chen & Rogan, 2004) For thousands of generations mothers breastfed their infants, and only in

the last century was this tried-and-true childrearing strategy called into question. Not unexpectedly, from an evolutionary perspective, Western mothers have incurred significant costs for following such advice in the form of increased incidence of reproductive cancers (breast, endometrial, or ovarian). Culture has dictated practices that altered human female reproductive physiology in unexpected and even dangerous ways (see Chapter 8).

Breastfeeding is not the only behavior that Western industrialized cultures have attempted to discourage or define as unnecessary. Mothers and infants have slept together for thousands of generations and in much of the world still do so today. Along with the push toward formula feeding in the last century there was pressure for mothers not to sleep with their babies, as well as to distance themselves from their infants at night. Such suggestions are in direct opposition to fundamentally normal and evolutionarily adaptive behaviors and have been based not on empirical scientific studies, but on Western cultural values and ideology. Moreover, the notion that it is important for 2-month-old infants to develop “independence” has become embedded within basic paradigms of pediatric medicine that guide infant care recommendations (McKenna & McDade, 2005). To tell non-Western mothers that infants should be placed alone, in an enclosed pen, in a darkened room, and allowed to cry themselves to sleep would not only be met with astonishment, but would be characterized as child abuse in much of the world.

In addition to solitary sleeping and formula feeding, Westerners fully accepted the advice of Dr. Benjamin M. Spock (1903–1998), who published *The Common Sense Book of Baby and Child Care* (Spock, 1946), a book that by 1998 had sold more than 50 million copies and had been translated into 39 languages. Spock has been considered by many to be overly permissive and indulgent because he advocated that parents be more flexible and affectionate toward their children, but when viewed from an evolutionary perspective he may not seem quite so indulgent. Spock adopted a behaviorist theory of child development that we might call the spoiling theory of development. We should not acquiesce to the every wish of the child lest we spoil the child and produce an adult that is improperly socialized. This idea took hold in Western childrearing practices, particularly around sleep in infancy. Spock advised in the 7th edition of his *Baby and Child Care* book that parents should “. . . put the baby to bed at a reasonable hour, say good night affectionately but firmly, walk out of the room and don’t go back. Most babies have developed this pattern of crying furiously for 20 or 30 minutes the first night, and then they see that nothing happens, they suddenly fall asleep! The second night the crying is apt to last only 10 minutes. The third night there is usually not any at all . . .” (Spock & Parker, 1998, p.210). Interestingly, in the most recent edition (Spock & Needlman, 2004) this idea has been modified and now suggests that infants can sleep in a room by themselves and if they are placed in a crib to sleep it should be done before the infant goes to sleep. While this is certainly a modified version of Spock’s original advice, old ideas die hard. “Steel yourself, go through your bedtime routine, and then after saying goodnight, don’t go back in no matter how much you baby cries. Your baby’s cries may become more and more desperate as time drags on, but if you can bear it, she will eventually wear herself out or give up and fall asleep” (Larson & Osborn, 1997, p. 228–229)

The point here is that an evolutionary perspective on childrearing has influenced pediatricians to rethink some of the advice that had traditionally been given to parents. For example, it is widely accepted that solitary sleeping infants should not be placed on their stomachs for sleeping. Infants who sleep on their stomachs have diminished

nighttime arousal, which promotes artificially prolonged, uninterrupted deep stage sleep among infants. While this may be desirable from a parent's perspective, infants in this sleeping position risk oxygen desaturation, especially when they sleep on soft mattresses, increasing their chances of dying from SIDS (Mosko et al. 1997, 1998). Unfortunately for infant well-being, face-down or prone solitary infant sleep is the most arousal-resistant type of sleep. Under more evolutionarily consistent sleep settings, infants rely on externally based arousals induced by their cosleeping mothers so that their sleep remains more often than not in Stage 1 or 2 (Mosko, Richard, McKenna, Drummond, & Mukai, 1997). In these states, if internal breathing control errors occur, a quick awakening is more likely than if the infant is sleeping solitarily, face-down on its stomach. Frequent waking permits the expulsion of accumulating CO₂, which, while positive in low doses (CO₂ stimulates the breathing reflex), can become fatal if excessive, such as when a baby sleeps face-down into a pillow or soft mattress.

The importance of an evolutionary consideration of patterns of breastfeeding and sleeping has only recently begun to be appreciated. Through the efforts of a number of researchers (Babcock, 1999; Ball, 2002, 2003; Ball, Hooker, & Kelly, 1999; Ball & Panter-Brick, 2001; McKenna, 1986, 2000; McKenna et al., 1993; McKenna & Gartner, 2000; McKenna & Mosko, 2001; see also Chapter 12) public health policy makers are regularly utilizing scientific data on infant sleep patterns in the formation of guidelines. This is clearly an area where the application of an evolutionary perspective has been enormously valuable in dramatically reducing the number of infant deaths due to SIDS.

Childhood

Compared with research in pregnancy and infancy, evolutionary medicine seems to have paid less attention to childhood—the period between weaning and puberty. But there are a number of examples of ways in which childhood health can benefit from evolutionary considerations. The timing of weaning is a topic that evokes discourse that entwines both cultural ideologies and biological processes, and the two may not always be complementary. Among chimpanzees and most human foraging cultures that have been studied, 3–4 years seems to be the typical period of infant breastfeeding, and, perhaps related to that, it is a commonly reported birth interval in great apes and human foraging groups. Some suggest that it is the frequency of nursing bouts by which breastfeeding maintains a 3- to 4-year birth interval. For example, among the !Kung of Botswana and Namibia, mothers were found to nurse their infant more than four times per hour for approximately 2 minutes with a mean interval between bouts of approximately 13 minutes (Konner & Worthman, 1980). This frequent nursing results in elevated levels of 17 β -estradiol and progesterone and is implicated in the inhibition of ovulation. Others argue that the long interbirth intervals are due to maternal nutritional shortages. Age, nutritional status, energy balance, diet, and exercise are all factors that have been associated with variation in ovarian function (Ellison, 1990). But although there is a great deal of debate about what factors are primary in maintaining a 3- to 4-year birth interval, suffice it to say that nursing plays an important role.

Has evolution and natural selection favored a time at which mammals should wean their offspring? It would seem that there should be some optimum time for weaning since there is a point when parents should get on with the business of having additional offspring and existing offspring are sufficiently developed to be able to acquire food on

their own (Trivers, 1972, 1974). Dettwyler (1995) has examined a number of life history variables to determine what she calls the “natural age of weaning” for humans. For example, if you consider that larger animals tend to nurse their infants longer relative to gestation length than smaller animals (e.g., for gorillas and chimpanzees the ratio of nursing to gestation length is 6:1), the expected weaning age for humans is 4.5 years. In another study of growth and development in nonhuman primates, Smith (1991) surveyed 21 species of monkeys and apes and found that weaning occurs at the time of eruption of the first molars, which would be about 6 years in humans (Smith, 1991). In a comparative study of weaning and maternal investment in primates, ungulates, and pinnipeds, when a neonate has grown to four times its birth weight it is weaned. For humans living in a developed country this would mean that a 7.5-lb. infant should be weaned at around 3 years of age (Lee, Majluf, & Gordon, 1991). For those of us in cultures where breastfeeding, if it occurs at all, often lasts less than one year, breastfeeding until age 3–6 years may seem excessive, but for people in parts of the world where access to appropriate and healthful infant foods is limited, nursing for several years (with supplementation from other sources) may mean the difference between a healthy and a sickly child.

Weaning is not the end of parental care, of course. For humans, as well as some other mammals (chimpanzees, bonobos, killer whales, vampire bats, cotton-tops tamarins, lion tamarins, wild dogs) food sharing after weaning is a well-documented behavior (Blurton Jones, 1987; Burrows, Hofer, & East, 1995; de Waal, 1989; de Waal, Luttrell, & Canfield, 1993; Ekman & Rosander, 1992; Feistner & Price, 1990; Hiraiwa-Hasegawa, 1990; Hoelzel, 1991; Hohmann & Fruth, 1993; McGrew & Feistner, 1992; Nishida & Turner, 1996; Price & Feistner, 1993; Silk, 1978; Wilkinson, 1984). However, the food sharing and provisioning that occur in humans is more highly developed and extends for a longer period than in other species that share food (Lancaster & Lancaster, 1983). In the course of human evolution it is possible that provisioning children between weaning and puberty may have doubled or even tripled the number of offspring that survived to adulthood. This long period of extended childcare by older children and adults probably enhanced the time for learning technological and social skills, also contributing to greater survival and reproductive success. Thus, the costs of extensive parental care were outweighed in human evolutionary history by the benefits of greater reproductive success for the recipient offspring.

The major causes of childhood death worldwide are infectious diseases exacerbated by poor nutrition. Pellitier, Frongillo, Schroeder, & Habicht (1995) estimate that about 70% of deaths of children from birth to age 4 years are due to diarrhea, respiratory infections, malaria, and diseases for which immunizations are available, and that as many as 83% of these deaths are indirectly attributable to malnutrition, even in a mild to moderate form. Consider that respiratory infections are a leading cause of death for children, and yet for most of us in developed nations they are merely nuisances. Rarely do we worry that the common cold will kill us or our children. It is notable that the leading causes of deaths of children in developed nations such as the United States and Western Europe are not typically related to malnutrition and include, for children under 5 years of age, accidents followed by preterm births. In the remainder of the world acute respiratory infection followed closely by diarrheal diseases and preterm births were the major sources of mortality (World Health Organization, 2005c) (see Figure 1-7). (Sadly, homicide is ranked fourth on the list of leading causes of death of children under 5 years in the

Unites States.) Furthermore, being born with low birth weight, itself often due to maternal malnutrition, accounts for almost half of the deaths from diarrhea, pneumonia, and malaria (Black, Morris & Bryce, 2003).

Malnutrition affects health and development in a number of ways short of death. As discussed above for intrauterine growth retardation (see also Chapter 18), small adult stature and even compromised brain development are often the outcomes of nutritional deprivation in childhood. It is notable that the first 5 years of life are the period of most rapid brain growth, and most negative effects are irreversible (Bogin, 1998). One of the negative impacts on child health in this early period is competition from other family members, especially younger siblings. An evolutionary perspective suggests that with birth intervals of 4–5 years, as was likely common in the past, nutritional competition among infants was not as big a problem as it is today, where babies may be spaced only a year or two apart. In general, mortality rates for infants and children increase when birth intervals decrease (Panter-Brick, 1998).

Malnutrition and infection are synergistic—one state makes the other worse (Pellitier et al., 1995). As noted above, malnutrition and poor health in utero and in childhood are commonly associated with lower adult stature. There is evidence that overall lowered

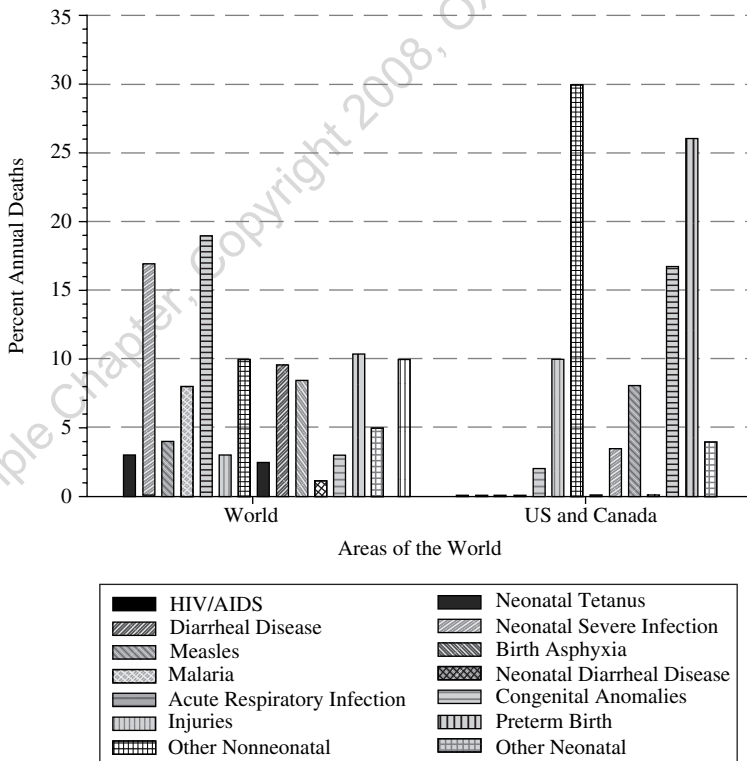


FIGURE 1-7 Mortality data by cause of death for children under 5 years of age including specific sources of mortality for children less than 1 year of age. (From World Health Organization, 2005a.)

immune response may be more directly responsible for slowed growth than nutritional intake itself (Shell-Duncan, 1993). Furthermore, compromised immunocompetence and low food intake also lead to decreased activity levels, themselves linked to chronic diseases throughout the life span.

The effects of psychosocial stress beginning in utero on child health and well-being are explored most directly here in a number of ways and for different purposes by Kuwaza (Chapter 18), Chisholm and Coall (Chapter 6), Núñez de la Mora and Bentley (Chapter 7), and Baker et al. (Chapter 17). Flinn and his colleagues (Chapter 13) studied the stress response in children, by way of measuring levels of salivary cortisol, taking note that cortisol spikes can be correlated with periods of illness. Interestingly (and perhaps predictably, based on the importance of the mother for child health, as discussed above), children who live with their mothers and other close kin have lower cortisol responses to stress than children who live with nonkin or more distant kin, and thus, fewer illness episodes. Even short-term absences of mothers or fathers seemed to have a negative effect on child health among the Caribbean children studied by Flinn.

At one point it was believed that small adult stature under circumstances of low resource availability was adaptive in that small adults would need fewer resources and would fare better under chronically stressful conditions (Seckler, 1982). In fact, a great deal of public policy was based on this “small but healthy” hypothesis, but a broader perspective indicates that small body size also means small organs, less ability to perform work, and lower reproductive success (Martorell, 1989), all of which mean “not healthy” from evolutionary and life span perspectives (especially see Chapters 17 and 18).

Although much of this section has emphasized poor health and causes of child mortality, it is important to note that millions of children survive quite well, even under fairly dire circumstances. In the parts of the world where several million children die every year from diarrhea and respiratory infections, there are also children who had the same levels of infection but did not die—they had social, physical, and behavioral abilities to cope and recover from the illnesses, either on their own or with help from close kin (Panter-Brick, 1998). Imagine two families living in poverty in sub-Saharan Africa in which the toddlers develop severe diarrhea from dirty drinking water—in one family the children die, in the other they live to grow to maturity and have children. In this case, resistance to the effects of diarrhea is a beneficial characteristic, but is it a Darwinian characteristic? Possibly. It is unlikely that there is a diarrhea-resistant gene, but the surviving toddler may have had a slightly stronger immune system, which allowed our survivor to endure severe diarrheal dehydration a bit better. In addition, our survivor’s mother might have been slightly better at getting water or our survivor was a member of a family with a tent with good shade. So what is the point? Our survivor’s slightly better immune system was the critical factor in survival when coupled with a more favorable local environment. So in this case it is natural selection operating on our toddlers, favoring the one that was best able to endure the consequences of drinking polluted water. Diarrhea in this instance is the “agent of natural selection” that selected against the children (and their genes) in one family and favored the children (and their genes) in the other.

There are circumstances under which a mother may consciously or unconsciously neglect her child so that it dies. While maternal neglect, benign or not, seems abhorrent to most Westerners, in fact, there are some situations where it makes perfect sense from

an evolutionary perspective (Hrdy, 1999). For example, when poverty is so grinding that the chances of continued survival are slim (Scheper-Hughes, 1991), it is in the mother's best interest to be indifferent toward the welfare of a child.⁴ This has been seen as evidence against a "maternal instinct" to protect her children at all costs, but an evolutionary perspective suggests that under extreme conditions, it makes sense to "cut your losses" and try again to reproduce later when circumstances for raising a child may be improved. The inclusion of a consideration of future survivorship has implications for public health policy. An emphasis on child immunizations in the context of extreme poverty and malnutrition may be nothing more than prolonging life so that immunized children are able to survive so that they may die later of malnutrition (Dettwyler, 1994). Children who are well nourished and otherwise healthy are usually able to survive bouts of childhood diseases, even without immunization.

Just as there is variation in what is considered optimal and even "normal" infant care (discussed above), there is variation in what is considered "appropriate" child care. For example, in many cultures children begin to contribute economically to the household at very young ages and their contributions are usually very important for family survival. In addition to taking care of younger siblings and relatives, children are recruited to do manual labor in direct support of the household. In many Western nations, however, there are laws against child labor, and the years from infancy to puberty are seen as the time for play and education, not for helping the adults of the family "make a living." In fact, play is seen as critical for normal child development in many cultures, whereas its importance is de-emphasized or ignored in others (Panter-Brick, 1998).

The emphasis on education for children is also highly variable worldwide. One bit of information added by the evolutionary perspective, especially considering evidence from hunter-gatherer populations, is that playing and learning in groups segregated by age is novel in the course of human evolution—most children, until formal schooling changed the rules, spent their childhood in multiaged groups, a setting that is superior for acquiring social skills than age-segregated classrooms (Konner, 1991b). Others have suggested that learning by instruction (as in formal schooling) may not be as effective as learning by observation and doing, the method with the longest association with childhood in our species (Levine, 1998). These are examples of ways in which an evolutionary medicine perspective can help assess intellectual development in children.

There is a relationship between child-rearing practices and infant and child mortality rates (Levine, 1998). Levine argues that generally, and on a universal level, parenting goals can be described in terms of a hierarchy of successive goals to which parents direct their efforts and resources, although the extent of parental resources may prevent parents from achieving any of them. Infant survivorship is the first goal, followed by educating children either formally or informally to become self-sufficient; and, finally, if the first two goals are achieved, parents aim to foster in their children values and ideologies expressed through various societal rituals that affirm their own high status and the validity of the cultural system of which they are a part, therein assuring intergenerational cultural continuities. As regards the process by which the third goal is achieved, for example, only where mortality has been greatly reduced can parents "afford" to spend time and resources on nonutilitarian or non-survival-related activities such as dance, music, theater, and soccer.

Where mortality has been greatly reduced, as in developed nations, environmental causes of developmental disorders are often alleviated, allowing genetic causes to be exposed. This means that genetic contributions are often overestimated and that policies have "...elevated the relative genetic contribution to [child development problems]... and given public salience to genetic problems" (Levine, 1998, p. 125). Thus, in industrialized nations, we have learning disabilities, dyslexia, hyperactivity (attention deficit disorder [ADD] and attention deficit-hyperactivity disorder [ADHD]), and other behavioral problems that would have been unremarkable in the past environments of childhood (Worthman and Kuzara, 2005). For developing nations to take their cue from developed nations in dealing with these genetic diseases of childhood may actually be counterproductive. Resources spent on research into the genetic causes of childhood diseases could be better utilized to raise the standard of living of the poorest of the poor through direct subsidy.

This is not to say that genetic contributions to child development should be ignored. Indeed, there are a number of success stories (Richards, 1998), such as the discovery that a diet low in the amino acid phenylalanine, if implemented early in life, can ward off the dangerous and debilitating disease phenylketonuria (PKU), which causes neurological damage and mental retardation when not treated. Thousands of children have been saved from this disease because of routine genetic testing of newborns that is done in most developed nations, including every state in the United States.

The incidence and prevalence of childhood asthma appear to be increasing in many parts of the world, including industrialized societies such as the United States and the nations of Western Europe, reaching a level that leads some to refer to it as a "world-wide childhood asthma epidemic" (Hurtado, Hurtado, Sapien, & Hill, 1999, p. 104). Unfortunately, most of the treatments that have been developed after years of clinical and pharmacological research are effective only for symptom relief and fail to get at the underlying causes of this potentially debilitating disease. Hurtado and colleagues suggest that an evolutionary perspective may help address the underlying causes of childhood asthma. Given the large number of people in the world with the asthma phenotype, evolutionary theory suggests that the asthma phenotype confers an adaptive advantage now or in the past (i.e., the phenotype and underlying genotype were positively selected over the course of human evolution). In modern environments, the asthma phenotype develops in the context of exposure to indoor allergens (e.g., dust mites, pet dander) and relatively low exposure to endo- and ecto-parasites, especially helminths. Where there is a high prevalence of helminths, there is a low prevalence of asthma, and vice versa (Barnes, Armelagos, & Morreale, 1999). It appears that the immunoglobulin-E (Ig-E) response is triggered by exposure to helminths and exhausts the immune response so that it is relatively unaffected by exposure to allergens like pollen and dust mites. When the helminths are eliminated from the environment, the immune system is free to react, even overreact, to allergens. Thus, what appears to be a defect may be an example of a defense against parasitic infections that were more common in the evolutionary past and likely increased with animal domestication (Barnes, Armelagos, & Morreale, 1999). Now this unbridled IgE response has become a defect in environments that are low in parasites and high in "modern" conveniences like mattresses, rugs, blankets, and insulated homes. Hurtado and colleagues add parental care practices and socioeconomic challenges to the evolutionary perspective on childhood asthma and suggest ways in

which public health measures may be developed to deal with this complex issue (Hurtado et al., 1999).

One characteristic of human reproduction that has changed remarkably is the significant decrease in the age of onset of menarche in recent generations. This decrease in the age at menarche has been referred to as a “secular trend” (see Figure 1-8) and has been recorded in developed nations. The most often cited causes of this secular trend—better nutrition, more protein and calories in infancy, and improvements in health care—are generally assumed to be signs of well-being. It is not clear that lowered age of menarche is actually an improvement in health, since it appears also to be related to mental health problems in adolescence (Kaltiala-Heino, Martunen, Rantanen, & Rimpelä, 2003), increased risk for metabolic syndrome X⁵ (Frontini, Srinivasan, & Berenson, 2003), and increased rates of some reproductive cancers (Eaton et al., 1994).

What does the decreasing age of menarche say about childhood, particularly in girls? Childhood is often defined as that period between weaning and puberty, but given the variation in age of each of these markers, how can it be a defined life cycle phase? Is an 11-year-old girl who has reached menarche no longer a child? And is a 15-year-old who has not yet reached menarche a child, while her peers who have are “adolescents”?

Puberty is fairly well-defined biological event for most mammals and simply refers to the onset of reproductive function. Perhaps unique to humans, the period following puberty is marked by an accelerated rate of skeletal growth that is referred to as the “adolescent growth spurt” (Bogin & Smith, 1996; Krogman, 1972; Tanner, 1962, 1990; Tanner & Taylor, 1965). Human females have a fairly long period of “adolescent sterility”⁶ following menarche when most, if not all, menstrual cycles are nonovulatory. This period

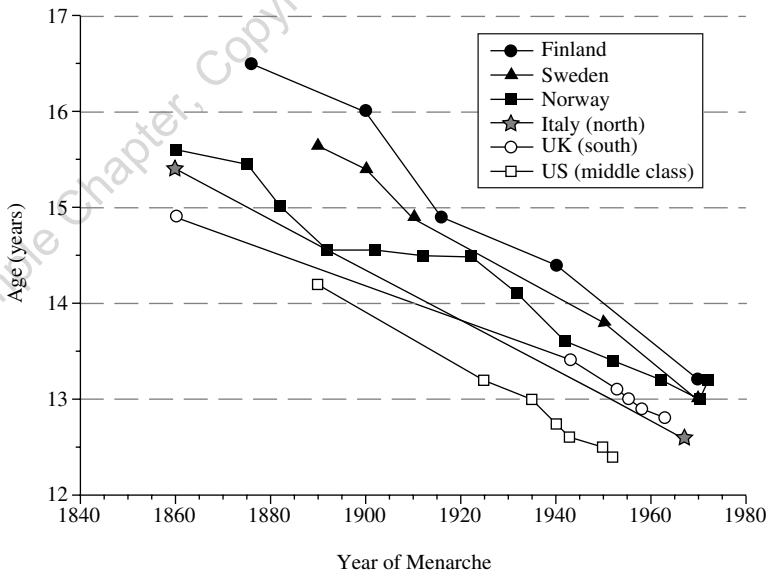


FIGURE 1-8 Secular trends in age at menarche for selected European countries and the United States. (Adapted from Tanner, 1990, p. 160.)

between the appearance of secondary sexual characteristics (enlarged breasts in girls, pubic and axillary hair in both girls and boys) and completion of growth is usually defined as adolescence in humans (Golub, 2000). However, what we are really talking about is puberty, a “universal physiological process” (Worthman, 1998, p. 29), which occurs over time as the body goes through the process of maturing. Adolescence is a cultural construct, and in much the same way as infancy, cultures define the period of adolescence and use it to shape the child into the adult that best fits with the cultural ideal (Worthman, 1998). Thus, adolescence may be seen as a short (or even nonexistent) period or relatively long, depending on how it is defined by a culture. In Western cultures where adolescence may last 10 years (from menarche at age 11 to the age at which alcohol can be legally purchased in the United States and formal education is usually terminated), this long period may be necessary for acquiring the social, intellectual, and technological skills to function as an adult. It should be noted, however, that in some cultures attainment of adult status depends on very specific biological (e.g., birth of the first child) or cultural (e.g., circumcision, marriage) events that may be independent of developmental processes.

Mortality is fairly low during adolescence in most human populations, but this is the time when many emotional (e.g., eating disorders, risk taking behavior) and physical (e.g., obesity, early pregnancy, poor diet) health problems emerge, especially in Western populations (Golub, 2000). It is also a time during which endocrine systems and other physiological processes develop in ways that have a significant effect on later adult health (Worthman, 1999). In fact, just as intrauterine (see Chapter 18) and infant environments have impacts on adult health, so too does the environment of adolescence, with all of these life cycle phases themselves interrelated in their impact on health (Worthman, 1999a, b; see also Chapter 6).

Although we have emphasized the gradual decline in maturation observed in the last century, there is within every population a great range of variation. An important lesson from evolutionary medicine and life history theory is that maturation is sensitive to local environmental situations (including, but not limited to, diet, health care, and parental care practices) and that a textbook-based concept of “normal” adolescence will work only for a small range of the variation observed and primarily what is experienced in the developed world (Worthman, 1999b). As with so many arguments made in this volume, public health measures must look beyond the Western concept of “normal” maturation and “normal” adolescence. Public health policy makers also need to consider the sociopolitical and socioeconomic contexts of developmental problems and intervene at the appropriate level to bring about systemic improvements in health (Chisholm, 1993; see also Chapter 6). “The close associations among resource allocation, pubertal timing, adult competence, and human health make equity in access to resources for child health and development a priority for preventive medicine” (Worthman, 1999, p.154). Improvement in health at all levels requires greater attention to social context than has been given in the past.

CHRONIC DISEASE

Chronic disease is the major source of mortality worldwide, except in sub-Saharan Africa, where infectious disease is the primary cause of death. Worldwide nearly 6 out of

10 deaths (or nearly 35 billion people) are the result of a chronic disease (World Health Organization, 2005c) each year. In the United States it is even worse. Seven of every 10 Americans who die each year, or more than 1.7 million people, will die of a chronic disease (Hoyert, Heron, Murphy, & Kung, 2006) (see Figures 1-9 and 1-10). If there is any area of medicine where an evolutionary perspective might be helpful, it would seem that addressing problems associated with chronic disease should be at the top of the list. It is precisely because humans have developed a robust immunological defense system that works well for short-term problems like infectious disease, but remains highly vulnerable to the slow steady progression of chronic disorders, that an evolutionary perspective might be of help. The prolonged course of illness and disability from chronic diseases like diabetes and arthritis results in extended pain and suffering and decreased quality of life for billions of people worldwide.

There are numerous proximate causes of chronic disease (e.g., obesity, diabetes mellitus, atherosclerosis, hypertension, cancer), but the evolutionary basis for many chronic diseases is poorly understood. The rise of evolutionary medicine has helped place chronic disease in a context where meaningful new therapeutic interventions can be considered. Certainly physicians have been concerned with chronic disease for a long time, but the recommendations for treatment were largely no more than “quick fixes” to the long-term problem. Attention to the evolutionary importance of nutrition and activity as risk factors for chronic disease became apparent in the 1980s, well before the dawn of evolutionary medicine (Eaton & Konner, 1985; Eaton, Konner, & Shostak, 1988a). The general hypothesis that guided this early research was the discordance between the Western diet and the diet of our Paleolithic ancestors (Eaton & Eaton III, 1999b). These differences, not only in diet, but in lifestyle as well, are the underlying cause of many of the chronic diseases that plague modern humans. The research on nutrition and

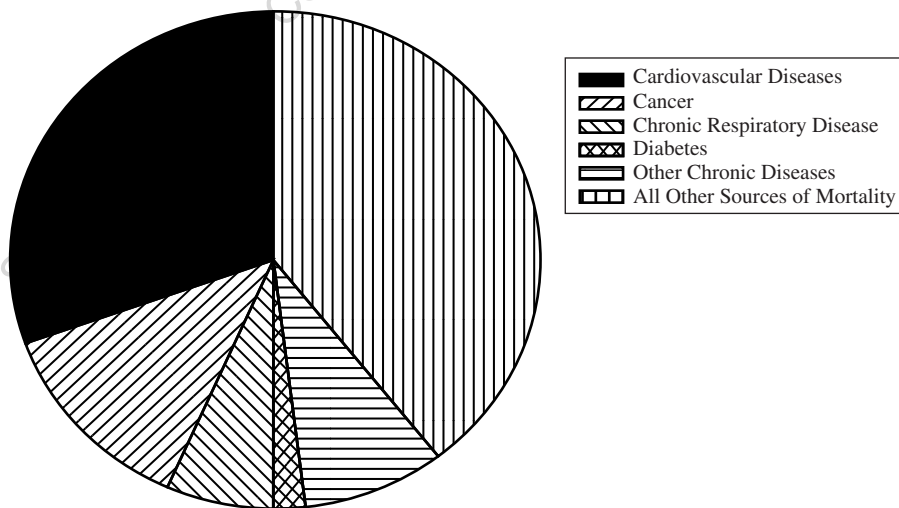


FIGURE 1-9 Causes of mortality worldwide. Data are for 2005. (From World Health Organization, 2005a.)

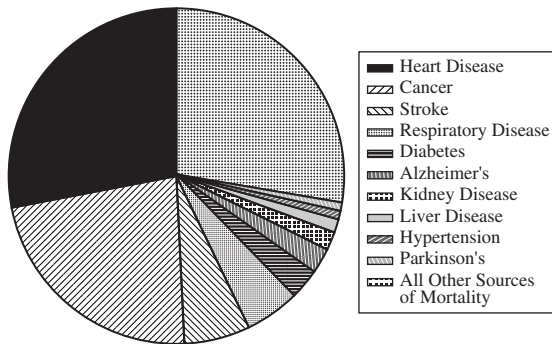


FIGURE 1-10 Causes of mortality in the United States. Data are for 2003. (From Hoyert et al., 2006.)

evolutionary medicine has already been reviewed earlier in this chapter, so here we will confine our discussion to studies of chronic disease.

Exercise

One of the questions that has arisen from the studies of the consequences of modern Western diets and human health concerns the role of exercise in chronic disease. The beneficial effects of exercise on a variety of aspects of health and well-being, not just reduction of chronic disease, have been well documented (Blair, LaMonte, & Nichaman, 2004; NIH Consensus Development Panel on Physical Activity and Cardiovascular Health, 1996; Pate et al., 1995), and considerable effort has been made to make recommended guidelines easily accessible (Centers for Disease Control and Prevention, 2006c). Physical activity recommendations are that adults should: (1) engage in moderate-intensity physical activities (e.g., brisk walking, bicycling, vacuuming, gardening, or anything else that causes small increases in breathing or heart rate) for at least 30 minutes on 5 or more days of the week; or (2) engage in vigorous-intensity physical activity 3 or more days per week for 20 minutes or more per occasion (Centers for Disease Control and Prevention, 2006c). It has been noted, however, that these recommendations may be insufficient to prevent weight gain in some individuals, who will need additional exercise or caloric restriction to minimize the probability of further weight gain (Blair, LaMonte, & Nichaman, 2004).

In spite of the “user friendliness” of these recommendations, Americans are still plagued by a sedentary lifestyle. According to the most recent report from the Centers for Disease Control and Prevention, less than half the adult population surveyed engaged in the recommended level of physical activity, while approximately 35% reported engaging in insufficient levels of physical activity, and 15% of the population reported engaging in less than 10 minutes per week of moderate to vigorous lifestyle activities (Pate et al., 1995). Imagine a Pleistocene ancestor who only engaged in the recommended

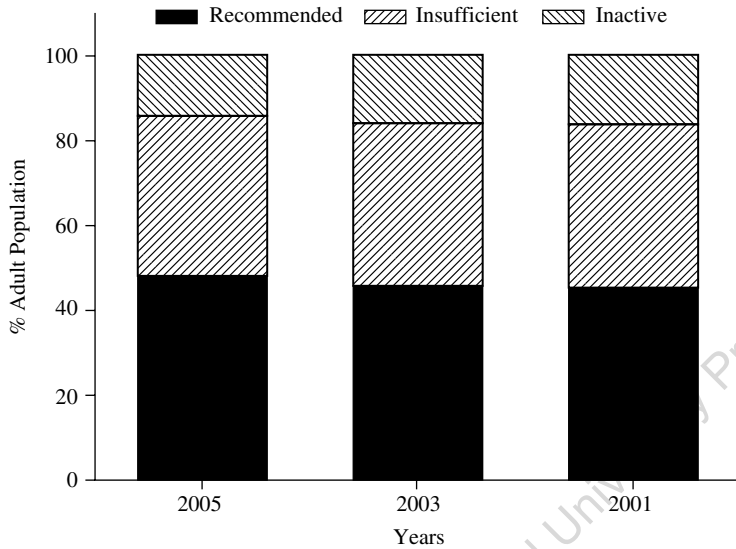


FIGURE 1-11 Prevalence of varying levels of physical activity in adult Americans. Recommended physical activity is defined as moderate-intensity activities in a usual week (i.e., brisk walking, bicycling, vacuuming, gardening, or anything else that causes small increases in breathing or heart rate) for at least 30 minutes per day, or anything else that causes large increases in breathing or heart rate for at least 20 minutes per day, at least 3 days per week. Insufficient physical activity is defined as doing more than 10 minutes total per week of moderate- to vigorous-intensity lifestyle activities (i.e., household, transportation, or leisure-time activity), but less than the recommended level of activity. Inactive is defined as less than 10 minutes total per week of moderate- to vigorous-intensity lifestyle activities (i.e., household, transportation, or leisure-time activity). (From Centers for Disease Control and Prevention, 2006b.)

level of activity. It is not likely that this level of activity would be sufficient to acquire and maintain adequate resources and would enjoy very low reproductive success (see Figure 1-11).

Furthermore, there is considerable evidence that incorporating physical activity into one's life early on is at least one component in lifetime physical fitness. Like their parents, children today are surprisingly sedentary, and in many cases schools are not encouraging physical activity. In a survey of high school students, researchers found that slightly more than half (55.7%) of students were enrolled in a physical education class. Less than one third of those students (28.4%) attended a physical education class daily, and when attending a physical education class, less than 40% (39.2%) were active, that is, exercising or playing sports for more than 20 minutes (Centers for Disease Control and Prevention, 2004b). It is clear from this and numerous other studies that most Americans, young and old, engage in significantly lower levels of physical activity than is recommended—much less than in the recent past, and almost none when compared to our Pleistocene ancestors (Eaton & Eaton, III, 2003).

Our culture has altered not only our dietary patterns, but our activity patterns as well, in ways that are likely to contribute to rise in mortality from chronic disease. While evolutionary medicine has not developed a panacea for this lack of physical activity, it has put the behavior of modern humans living in Western society in context.

Cardiovascular Disease

Diet and exercise are both strongly implicated in the occurrence of cardiovascular disease. Heart disease and stroke are the most common of the cardiovascular diseases and account for about 40% of annual deaths. Almost one fourth of the American population has some form of heart disease. It is important to remember that much of what has been reviewed in the section on nutrition is directly relevant to an evolutionary perspective on cardiovascular disease.

The two major risk factors associated with all cardiovascular diseases are hypertension and serum cholesterol levels. By reducing blood pressure and serum cholesterol Americans could reduce mortality from cardiovascular diseases by 25% and the overall death rate by 13% (Centers for Disease Control and Prevention, 2005a). But what does a view from evolutionary medicine have to see in this case? It should be clear from the preceding discussions that our diet and lifestyle are discordant with our evolved physiology, and this discordance is a major contributing factor to chronic diseases in general, and cardiovascular disease in particular. Evolutionary medicine has been concerned with cardiovascular disease largely from the perspective of prevention and has not focused on the evolutionary adaptations of our cardiovascular systems and how a greater understanding of those adaptations might provide new insights.

Congestive heart disease is one major exception (see Chapter 21). Congestive heart failure (CHF) is often the end stage of cardiac disease. Half the patients who are diagnosed with CHF will die within 5 years, and one in five will die within one year (National Heart Lung and Blood Institute, 1996). CHF is a condition where the heart is unable to pump enough blood to the body's organs. It results from narrowed arteries that supply blood to the heart (coronary artery disease), scar tissue from a past heart attack (myocardial infarction) that interferes with the heart muscle, hypertension, primary diseases of the heart (cardiomyopathy), congenital heart defects, as well as infection of the heart valves or the heart muscle itself (endocarditis or myocarditis). Blood flows out of the heart, but blood returning to the heart backs up, causing accumulation in the tissues. Swelling (edema) in the legs and ankles most often results. Fluid also accumulates in the lungs, and the kidneys are not able to dispose of sodium and water. The sequelae of events associated with CHF is well known to clinicians, but without an understanding of why these events occurred in a particular way. In fact, CHF may not necessarily be a pathological condition and may actually be a defense against blood and fluid loss. That CHF is actually the result of natural selection is considered by Weil (Chapter 21) and is an excellent example of how an evolutionary perspective can change a perceived defect into defense under certain environmental conditions. This new way of conceiving of CHF may lead to new and novel treatments for this major contributor of cardiovascular disease mortality. An understanding of why CHF progresses in a particular way will not quickly offer a magic bullet cure, but by conceiving of diseases from this perspective we can hope to stimulate further research.

Cancer

After cardiovascular disease, cancer is the second leading source of mortality in the United States. Of course, it is impossible to talk about cancer without considering the variety of types of cancers, the array of environmental factors and lifestyle choices, and the genetic factors that affect its prevalence. Epidemiologists generally consider risk factors that are either intrinsic to the individual (age, sex, genetic history) or extrinsic (infections, tobacco use, diet and nutrition, occupational exposure, environmental pollutants). Evolutionary medicine has something to say about both types of cancer risk factor. The intrinsic risk factors are certainly modified by evolution. The risk of most types of cancers increases with age, and certain cancers occur only in one sex due to differences in anatomy. There are some ethnic differences in cancer risk, with genetic inheritance accounting for about 4% of all cancers.

It is clear in Table 1-1 that there are significant differences in the incidence rates of cancers depending on ethnicity. The difficulty, of course, is to tease out the proportion of these differences that are due to genetic factors and/or environmental factors. Given the current state of knowledge, it is unwise to categorically assign certain ethnic groups high-risk status for particular cancers, but the genetic basis for cancers certainly warrants further research (see Chapter 20). There are many factors that contribute to these ethnic differences in cancer incidence, including, but not limited to access to health care, poverty, poor diet, lack of exercise, tobacco use, lifestyle, occupation, as well as some proportion of genetic differences among human populations. Unfortunately, these are questions that have not yet been pursued systematically by many evolutionary medicine researchers. There is some interest among clinicians in the high incidence of hypertension seen in American blacks and the low incidence of certain cancers among Asian and Pacific Islanders, but a discussion of this problem is beyond the scope of this chapter.

We know that inheritance of mutant genes accounts for a proportion of the cancers seen today. Even if there is not a gene for a specific cancer, we know that there is a genetic component. One of the most famous cases is Napoleon Bonaparte. The French have always suspected that the English killed Napoleon by poisoning, but it is much more likely that it was cancer. Napoleon ordered that upon his death an autopsy be performed so that the cause of his death could be immediately confirmed. The determination of the cause of his death was for the benefit of his son, so that he might be able to avoid the disease. The autopsy was conducted by Napoleon's personal physician, Francesco Antommarchi, a Corsican aided by a Scottish army surgeon, Archibald Arnott. Even

TABLE 1-1 Cancer Rates for Men and Women in the United States

Women	Rate^a	Men	Rate
Breast	124.9	Lung	161.2
Lung	38.0	Prostate	86.4
Colorectal	38.3	Colorectal	61.3

^a Rate per 100,000 persons.

Source: Centers for Disease Control and Prevention, 2006a, b.

though several British military surgeons and physicians were in attendance, they were under strict instructions from Napoleon that they were not to touch his body. The autopsy was unequivocal on the cause of death as stomach cancer. In addition, Napoleon's father, his grandfather, one brother, and three sisters died from stomach cancer (Greaves, 2000).

As discussed in the previous section on human reproduction and evolutionary medicine, women's reproductive cancers have benefited from an evolutionary perspective. Breast cancer is a major concern for women all over the world, but much more so for women in the developed world. One of the primary contributors to the high incidence of breast cancer is the pattern of reproduction common in the developed world. Early menarche, delayed first birth, little if any breastfeeding, and reduced number of pregnancies and births have all been identified as key factors in the incidence of reproductive cancers, and in particular breast cancer (Eaton & Eaton, III, 1999a; Eaton et al., 1994).

Cancer is a chronic disease that is not confined to the developed world, but the risk of getting cancer is greater in the developed world, whereas cancers in the developing world are more often fatal. Only 19% of the world population lives in developed countries, but 46% of the new cancer cases occur there. Interestingly, the probability of dying from cancer is not very different in the developed world when compared to the developing world. The types of cancers most frequently presented are different for developed when compared to developing countries (see Table 1-2). This is not surprising when we consider the effects of poverty on lifestyle and the modification of risk factors.

TABLE 1-2 Age-Adjusted Rate for Cancer by Type and Ethnicity, 1999–2002

	Asian and Pacific			
	White	Black	Islanders	Other
All sites combined	471.7	480.6	289.4	1510.2
Brain and nervous system	7.1	3.9	3.5	12.0
Breast, cervical, & uterine	87.9	82.2	53.5	240.3
Colorectal	53.7	59.7	39.0	138.7
Esophagus	4.8	7.1	2.3	9.9
Gallbladder	1.1	1.4	1.5	3.3
Kidney	12.8	13.0	5.3	32.8
Larynx	4.2	6.3	1.4	9.5
Leukemia	12.3	9.3	6.8	39.8
Liver	3.9	6.0	13.3	12.8
Lung	70.2	74.6	37.4	107.3
Skin	17.2	0.9	1.2	104.2
Myeloma	4.9	10.3	3.0	16.7
Non-Hodgkin's lymphoma	19.2	13.3	12.4	57.1
Oral and pharynx	10.2	11.0	7.6	30.8
Ovary	7.7	5.7	5.2	15.3
Pancreas	10.8	14.3	8.1	18.0
Prostate	68.3	97.4	35.4	456.3
Stomach	6.6	12.4	14.1	18.3
Thyroid	7.7	4.6	7.8	22.9
Bladder	22.8	11.2	8.6	60.7

Source: Centers for Disease Control and Prevention, 2006b.

While these data do not directly address the evolutionary question of why there is this geographical dispersion of type of cancers, it is tempting to speculate that as Western culture spreads and many of its features are adopted by people on a worldwide basis, we will continue to see a rise in cancer prevalence due to the modifiable lifestyle risk factors. Of course, the compelling question is what can be done about the spread of Western culture? It is tempting to throw up one's hands and say nothing. We are too far down the road of globalization to halt the exportation of both the positive and the negative aspects of Western culture.

From an evolutionary perspective it is tempting to see cancer as an inevitable consequence of intrinsic evolutionary penalty for two essential characteristics of all living organisms. First, tissue stem cells have the capacity for sustained proliferation and regeneration, as well as a lymphatic system for migration and dispersal. Second, there are mechanisms for shuffling genes and recombination as well as a lack of complete fidelity in DNA copying and repair. While there are multiple physiological systems that have evolved to limit the lifetime risks of these two characteristics, sometimes these protective systems break down. These breakdowns in protection can occur early on in fetal development and give rise to pediatric cancers, but more likely they occur in old age. The average risk of a 25-year-old man dying of cancer by his thirtieth birthday is 50 times less than a man who is 65 reaching his seventieth birthday (Greaves, 2000).

Greaves (2000) has made the observation that for 90% of the cancers, the major risk factors are not our genetic inheritance, but human social engineering, where each of us exercises deliberate and informed choice under normal circumstances. By our own errors we are subjected to repeated and chronic toxic insults that result in proliferative and oxidative stress on tissues, an increased frequency of mutations, and direct damage to DNA. We have taken the basic machinery that is mildly error prone and have significantly ratcheted up the risk for each individual of getting cancer. As we have said so many times before, cancer is another one of those complex chronic diseases that has been present in humans for thousands of generations, but has in recent times markedly increased in prevalence in the population.

While women's cancers have received much attention, men's cancers have not. The leading cause of cancer death among men is lung cancer, followed by prostate cancer (see Table 1-3). Prostate cancer is a common form of cancer and is fast becoming the most commonly diagnosed type of cancer; it will likely soon overtake lung cancer as the leading cause of death in men (Centers for Disease Control and Prevention, 2006d). Current treatments for prostate cancer are crude, feminizing, and not particularly effective. Some 30% of men over 50 have clinically silent prostate cancer, and 50% of men over 80 are affected. So the message is that most men, if they live long enough, will develop prostate cancer, but its potential lethal consequences are preempted by other more acute causes of death.

What are the causes of prostate cancer, and can an evolutionary perspective help us understand this disease? In the United States the primary cause has been thought to be environmental or occupational toxins, but the evidence that has been assembled is very weak. Diet could also play a part, in particular excess caloric intake and reduced energy expenditures, but the mechanisms are unclear at best. Other candidate explanations include high levels of insulin-like growth factor-1 (IGF-1), more cell division, less cell

TABLE 1-3 Cancer Prevalence in Developed and Developing Countries

Developed > Developing	Approximately equal	Developed < Developing
	Lung	
Colorectal		
Breast		
Prostate		
		Stomach
Bladder	non-Hodgkin's lymphoma	
Kidney		
Pancreas		Leukemia
		Liver
	Ovary	
		Oral cavity
		Cervix/Uteri
		Esophagus

Source: Mackay, Jemal, Lee, & Parkin, 2006.

death and hence more cells, more oxidative stress, and greater risk to labile DNA (Greaves, 2000).

A more reasonable explanation first requires an understanding of the physiological function of the prostate, which is to lubricate and facilitate sperm flow and fertilization. The prostate is dependent on a supply of testosterone. Relative to other male mammals, human males have enormous prostates. The only other animals that can claim a comparably sized prostate are dogs (*Canis familiaris*), and they are the only other mammal that experiences an appreciable rate of prostate cancer. The possible function for such large prostates in humans could be related to our mating system. While there are other mildly polygynous mammals today, the degree of polygyny may have been greater in our evolutionary past. Males who were capable of mating often and producing healthy robust sperm could well have had a slight competitive advantage over less well-endowed males. While there is a decrease in testosterone production with age in males, it is nothing like the decline in estrogen production with age in females. Consequently, while the constant bombardment of target-sensitive tissue in males is one factor that allows males to produce viable sperm quite late in life, there is a cost, and that is the likelihood of developing prostate cancer (Greaves, 2000). Again, while this evolutionary explanation does not offer a cure for prostate cancer, it does put this disease in an evolutionary perspective and suggests that it is the outcome of varying selective pressures at different life stages. It is this kind of evolutionary thinking that may produce new and novel treatments for this disease.

While the link between lifestyle and other cancers seems plausible and is based on good scientific evidence, no cancer is more the direct outcome of the discordance between our evolved physiology and our current lifestyle than are lung and throat cancer due to smoking. The relationship between smoking and lung cancer is so well accepted in most developed countries that it does not bear repeating here.

The interesting question is how humans could have begun indulging in a behavior that is so unnatural, initially unpleasant, and clearly learned. The earliest records of smoking are depictions in Mayan art from 2000 years ago. By all accounts Mayans were the originators of the practice, but it became common among many Native American cultures. Tobacco was introduced to England in 1564 by the crew of the *Jesus of Lubeck*, a slave trader captured by Sir John Hawkins (1532–1595). It did not take long for tobacco to make an impact on English society. Inhaled smoke has a long and distinguished history found in many cultures. Perfumed smoke and incense have been used in ceremonies dating back to Greek and Roman times. Pliny recommended that a cure for obstinate coughs was inhaling smoke drawn through a reed (Greaves, 2000).

It did not take long for an elaborate culture to develop around smoking in Europe. While a number of different plants were smoked, one had particular appeal for its powerful narcotic properties. Jean Nicot (1530–1600) was the French ambassador to Lisbon from 1559 to 1561, and upon his return to Paris he brought tobacco plants with him. Tobacco was an instant hit with the affluent and powerful and quickly spread across Europe. The plant is called *Nicotiana tabacum*, and the psychoactive substance nicotine, in his honor (Greaves, 2000). Sailors from European countries succeeded admirably in spreading the use of the tobacco plant around the world. Interestingly, during the Thirty Years War (1618–1648) involving most of the major European continental powers, the Napoleonic Wars (1799–1815), and the Crimean War (1854–1856), smoking was encouraged by commanders, likely because of the narcotic properties of tobacco that blunted fear and hunger. In fact, During World War I tobacco products were included in military rations (Greaves, 2000).

The point of this little historical digression is to demonstrate the power that a narcotic like nicotine has over human behavior. Smoking has worldwide health implications, and the relationship between smoking and lung cancer is widely accepted (Doll & Hill, 1950). In addition to the lungs, smoking increases the risk of cancers in esophagus, larynx, tongue, salivary glands, lips, mouth, pharynx, urinary bladder, kidneys, cervix, breast, pancreas, and colon. In developed countries smoking accounts for approximately 80% of all lung cancers (World Health Organization, 2005a). Tobacco kills more people worldwide than AIDS, legal drugs, illegal drugs, road accidents, homicide, and suicide combined. Today tobacco kills more men in developing countries (1.8 million) than in developed countries (1.6 million), and soon tobacco-related deaths of women in developing countries (0.3 million) will equal the deaths among women in developed countries (0.5 million). Trends in mortality from tobacco show an unabated trend in both the developed and developing world (Mackay & Erikson, 2002) (see Figure 1-12).

So what does this have to do with evolutionary medicine? The reason that smoking is so pervasive and cessation is so difficult is that nicotine is addictive. As one researcher put it, “If it were not for nicotine in tobacco smoke, people would be little more inclined to smoke than they are to blow bubbles” (Jarvis, 2004, p. 279). If a greater understanding of the evolutionary basis for addiction as well as the exact mode of action of psychoactive drugs, including nicotine, were obtained, there would be a significant increase in the likelihood that some effective therapeutic intervention might be discovered. By reducing the number of people addicted to nicotine, a significant savings in lost lives and productivity could be achieved on a worldwide basis.

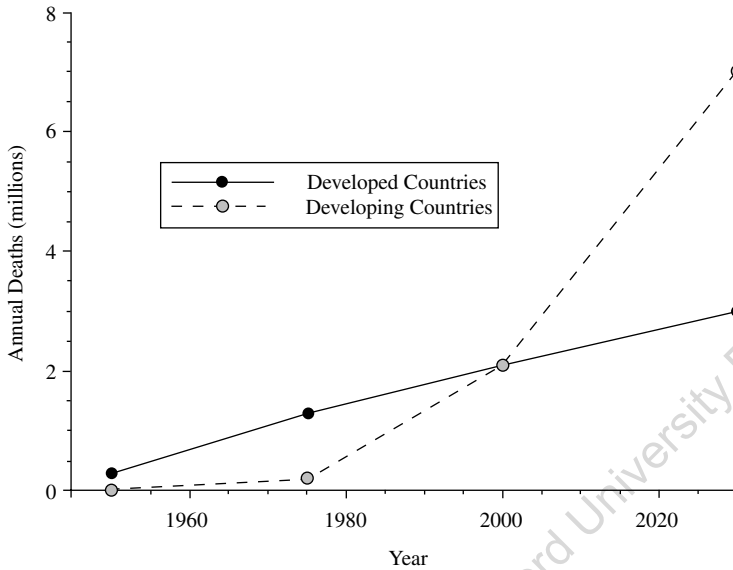


FIGURE 1-12 Annual deaths due to tobacco worldwide from 1950 to 2030 (projected). (From Mackay & Erikson, 2002.)

PSYCHIATRIC DISORDERS

Mental illness is a problem that has been understudied, underdiagnosed, and undertreated on a worldwide basis. It is estimated that 450 million people worldwide are affected by mental, neurological, or behavioral problems at any time. Mental illness is common to all countries, and individuals who suffer from mental illness are subject to social isolation, poor quality of life, and increased mortality. Twenty-five percent of patients visiting a health service worldwide have at least one mental, neurological, or behavioral disorder, but most of these disorders are neither diagnosed nor treated. Mental illness affects and is affected by many chronic diseases such as cancer, cardiovascular disease, diabetes, and HIV/AIDS. Worldwide almost 900,000 people die of suicide every year (World Health Organization, 2005b). Certainly if there is another area where an evolutionary perspective might be helpful, psychiatric disorders is one.

The application of evolutionary theory to psychiatry and the treatment of mental illness has shown great promise and enthusiasm among some clinicians (Nesse, 1984). Mental disorders are different from other kinds of medical problems. While some are caused by primary neural anomalies, many like addiction and mood disorders are often difficult to diagnose and even more difficult to treat. Dysregulated emotions such as anxiety and depression are very common. Mental disorders are widespread, affecting about half of the U.S. population according to some estimates (Nesse, 2006). Additionally confounding the problem is the fact that about 15% of the population accounts for over half of the diagnoses. People who suffer from anxiety are likely to also be depressed, drug users are likely to be depressed or suffer from bipolar disorder, while people suffering

from schizophrenia or obsessive-compulsive disorder or an eating disorder are also likely to suffer from depression or anxiety disorders. Comorbidity is a real problem when dealing with mental illness (Nesse, 2006).

There are at least two broad perspectives on dealing with mental disorders that are common in the psychiatric community. One is the medical model that was a part of the emergence of psychiatry after World War II. The emphasis in the medical model of mental illness is the discovery of a particular neurophysiological basis for a disorder. Along with research into the physiology of mental illness, clinicians became increasingly concerned about accurately defining symptoms of particular conditions and delineating boundaries. While this enterprise increases the precision of discussion of mental disorders among professionals, it also has the added benefit of fitting into the overall diagnostic schema of clinical medicine in general and the rise in importance of insurance companies in orchestrating clinical care. On the other hand, in the 1980s a few psychiatrists began to entertain the possibility that what were considered mental disorders by some could actually be defenses that were shaped and molded by natural selection. Could a mental disorder actually be an individual's way of warding off fitness-reducing events and situations? Alternatively, could some of the mental illnesses actually be the result of selection for other factors that resulted in design compromises? Is it possible that some of the mental illnesses faced by humans today are actually the product of selection for different characteristics that have greater fitness-enhancing properties and these mental illnesses are just the price that we pay for success in other areas?

Possibly because psychiatry found Freudian psychology and Watsonian behaviorism of limited utility in treating a variety of modern psychiatric disorders, clinicians have been willing to accept, at least partially, the tenets of evolutionary theory when applied to treating mental illness. One of the first comprehensive attempts at application of evolutionary theory to mental disorders was a review of how psychotherapy could profit from a greater understanding of the evolution of humans (Glantz, 1987; Glantz & Moehl, 2000; Glantz & Pearce, 1989). One of the areas highlighted in the theories about the evolution of behavior is the importance of reciprocity. Glantz and colleagues recognized that a considerable amount of psychopathology on the individual level had directly to do with emotions and motivations surrounding a lack or a failure of individuals to act in a reciprocal manner. Many people come into therapy without a correct understanding of their emotional rights and duties, their obligations to others, and the obligations of others to them. The whole notion of giving and receiving was shown to be a fundamental aspect of many social relationships that was poorly understood by one or both of the parties.

Why is reciprocity so important in social relations? The answer to that question comes from an understanding of the evolution of social behavior in a more general sense. Briefly, organisms from cockroaches to pine trees to humans are programmed to act in a manner that will maximize their own lifetime reproductive success. In a sense that means that we must act selfishly, and that is the cause for a significant proportion of human interactions. During the course of human evolution, however, there were individuals who would, in addition to acting selfishly, act altruistically to aid a nongenetic relative. Helping kin can actually be seen as selfish behavior because in a sense you are acting to benefit the proportion of your genetic material you and a relative share because of inheritance from a common ancestor. Aiding a potential reproductive competitor is a

big deal, and it is one that has concerned evolutionary theorists since Darwin. The important point here is that it only makes sense to do so if there is some guarantee that your act will be reciprocated. It is easy to imagine the power of cooperative behavior in almost every aspect of life and how individuals who solved this fundamental evolutionary dilemma would enjoy an enormous advantage over those who only acted selfishly. Indeed, humans have evolved elaborate psychological mechanisms to insure that we act reciprocally, and one of the most important is guilt as well as social pressure exerted from peers. In short, an understanding of the evolutionary importance of reciprocity gave psychotherapists new techniques to deal with breakdowns in many human social relationships.

There are three broad categories of mental problems (Nesse, 2006): (1) ones that arise from primary brain abnormalities and have a high heritability (e.g., schizophrenia, autism, obsessive-compulsive disorder, bipolar disorder); (2) ones that arise from emotional and behavioral dysregulation (e.g., depression, anxiety, addiction); and (3) affective states that are aversive or socially unacceptable, but nonetheless may be fitness enhancing.

Mood Disorders

At the top of any list of mood disorders, and by inference emotional disorders, is depression. It is hardly worth citing any prevalence data on depression because it has become so common in the United States. During a 1-year period slightly over 20 million adults or about 9.5% of the population suffer from a depressive illness (National Institute of Mental Health, 2006). While at first blush it might not seem that depression should be anything more than a minor annoyance, the truth is far different. Depression has been linked to a variety of chronic diseases (e.g., cardiovascular disease, cancer, Parkinson's disease, and hormonal disorders), and when accompanied by depression any of these chronic disorders is exacerbated.

Depression is found in both men and women, but has different underlying causes. Women are roughly twice as likely as men to experience depression. While hormonal changes associated with the menstrual cycle (see Chapter 10), pregnancy, childbirth, and menopause are known to effect the incidence of depression in women, there are many aspects of our culture that also seem to be contributing risk factors (work in and out of the home, single parenthood, and caring for aging parents).

For men depression manifests itself differently than in women. Depression is associated with an increased risk of cardiovascular disease in both men and women, but men suffer a higher mortality rate (Ferketich, Schwartzbaum, Frid, & Moeschberger, 2000). Depression in men is often masked by alcohol or drugs or by the socially accepted practice of working excessively long hours. Men are less willing to seek help for depression than are women, and it is more difficult to recognize and diagnose in them. In both sexes, severe depression is marked by disruption of sleep patterns. Depressed patients report under different circumstances both an inability to sleep as well as an inability to stay awake. What constitutes a normal sleep pattern for Westerners would be 8 hours of uninterrupted sleep. Worthman (Chapter 16) alerts to the likelihood that sleep is more complicated than it seems, and ideas of what constitutes normal sleep may be founded on little more than convenience and not on any biological reality.

Given that depression, in its most severe form, can lead to suicide and in less severe manifestations to social isolation and diminished quality of life, how could such a disorder have ever arisen in the population in the first place? Depression is nothing new to the human condition. Hippocrates wrote about melancholia, and from his descriptions it is reasonably certain that he was referring to the condition that we know today as depression. For the Greeks, melancholia was due to the excess accumulation of black bile.⁷ Depression has been recognized in religion (Valley of the Shadow of Death, Psalms 23:4), art (self-portrait of Frida Kahlo), literature (King Lear), and music (American blues), and so has long been a part of the human experience. While clinicians have made attempts to define depression, evolutionary biologist Robert Sapolsky said it best. Depression is a "... genetic/neurochemical disorder requiring a strong environmental trigger whose characteristic manifestation is an inability to appreciate sunsets" (Sapolsky, 1994, p. 197).

An evolutionary perspective on depression asks why such a psychological condition would have arisen when it is associated with so many costs and is so widespread? One possibility is that depression is an adaptive response to defeat and a mediator of social conflict (Price, Sloman, Gardner, Gilbert, & Rohde, 1994; Stevens & Price, 1996). Rather than challenge a competitor to whom you have already lost, it may be that a reduction in activities and a decrease in social interactions is the most adaptive response. Acceptance of defeat has the unanticipated side effect of intensifying social hierarchies and actually promotes an overall reduction in aggressive behavior. Rather than conceive of depression as mental illness, in the evolutionary context it might be viewed as a biopsychosocial adaptation.

Another possibility is that depression signals the loss of resources that are an important part of reproductive success (Nesse, 1991, 2000; Nesse & Williams, 1994a). Depression may be the signal that causes an individual to stop engaging in the behavior that brought about the loss. For example, abandoning a failed relationship certainly results in depression, and there are certainly times that depression may make an individual less likely to abandon an enterprise in which they are heavily invested. Depression and low mood may, however, cause individuals to stop investment in endeavors with a low probability of payoff.

While an evolutionary perspective does not provide a cure for depression or low mood, it does alert us to the range of mood that is part of normal human experience and suggests strategies for elevating mood that are consistent with our overall fitness-maximizing strategies. The question that arises from this view of depression is: Should all depression be treated? As with most such questions, the answer is: It depends. For people who suffer debilitating depression that significantly impairs their health and quality of life, the answer is a resounding yes. However, an evolutionary perspective alerts us to the possibility that depression may serve as an adaptive warning light that signals to us that we should change something that we are doing. For those types of situation and episodic conditions, treatment may not be warranted.

Anxiety is another emotion that is often viewed as a defect. Some people experience excessive anxiety and worry that persists for long periods of time. The anxiety is described as "free floating" and is not triggered by a specific event, unlike phobias, discussed below. People who experience anxiety disorders worry about the everyday aspects of life, many of which are beyond their control. Twitching muscles, dry mouth, clammy hands, sweating, nausea, diarrhea, and frequent urination are typical symptoms. Elevation of

anxiety triggers a cascade of physiological responses in the immune system, as well as in other systems. The activation of the immune system under certain circumstances could have real fitness advantages. Like other systems, our immune system seeks homeostasis. Too much activation leads to autoimmune disorders, and too little results in immune deficiencies. Too much or too little anxiety can be fitness reducing.

“Flight or fight” is the classic response to fear-producing situations and is characterized by sweating, increase in heart rate, increase in respiration rate, increase in blood glucose levels, and the release of epinephrine, as first described scientifically nearly 100 years ago (Cannon, 1914). Of course this response is fitness enhancing in the short run, but we also know that the physiological processes that are incited by the response in long-term health consequences are not positive. On the other hand, too little anxiety does not typically result in a visit to a physician requesting anxiety-inducing drugs, but these individuals can often be found in emergency rooms, standing in a courtroom, or in jail.

Phobic disorders are a classic example of emotions that have been favored by natural selection. Notice that we did not say that the phobic disorders have been favored by natural selection because those responses are extreme manifestations of an adaptive response. In the course of human evolution it is likely that those individuals who were particularly alert or tended to avoid dangerous situations might have enjoyed an evolutionary advantage over those less vigilant or with a slightly blunted sense of danger. While there are certain costs associated with anxiety (e.g., wear and tear on tissues and organs, depletion of hormonal reserves, etc.), there are great advantages to avoiding being eaten. The “smoke detector” principle of the evolution of anxiety suggests that the cost of a few false alarms is significantly less than a positive alarm that goes undetected or ignored (Nesse, 2001; Nesse & Klaas, 1994; Nesse & Williams, 1994a). If these ideas have any merit, that knot in your stomach when entertaining the idea of climbing a tall ladder, or riding the elevator to the top of the Empire State Building, or being slid into a metal cylinder for an MRI exam is the result of natural selection. Carried to an extreme, any of these responses can be debilitating and significantly reduce quality of life, but if experienced acutely under appropriate circumstances, they would be fitness enhancing.⁸ Interestingly, here is another example of discordance between our biology and our culture. If we were really in tune with our environment, we would be inherently afraid of guns, knives, electrical outlets, greasy hamburgers, and cars.

Schizophrenia

Schizophrenia is a mental disorder that has been diagnosed in cultures around the world and has an estimated lifetime prevalence of 0.55% (Goldner et al., 2002) with high variation from country to country. The incidence of schizophrenia of 7.5–16.3 cases per year per 100,000 population gives some idea of the variation. It is characterized by impairment in perception or expression of reality as well as social dysfunction. Patients suffer from delusions, auditory hallucinations, and disorganized thinking. Schizophrenics experience significantly lower fitness (0.7) than nonaffected individuals (Feierman, 1982), and the phenotypic population frequency is difficult to explain exclusively on the basis of mutations.

An evolutionary theory of schizophrenia starts from the perspective that the condition is or was favored by selection and is adaptive. The important point here is that psychiatry

has recognized the genetic component of schizophrenia and is attempting to explain its persistence in modern populations. There have been a number of theories to explain schizophrenia from an evolutionary perspective. Some have suggested that schizophrenia is the outcome of uncontrolled fluctuations of glycemic levels in the brain coupled with insulin resistance (Holden, 1995; Holden & Mooney, 1994). Schizophrenia has also been connected to celiac disease. Individuals affected with celiac disease have an alteration in gut permeability in which the gut may lose its ability to block exogenous psychosis-causing substances, and circulating levels of these substances lead to schizophrenia and other mental conditions (Wei & Hemmings, 2005). Another suggestion relates the disorder to an extreme variation of hemispheric specialization and the evolution of language due to a single mutation located on the homologous regions of the sex chromosomes (Crow, 1995). Another possibility is that schizophrenia is a consequence of intense selective pressures for higher intelligence or verbal abilities in our evolutionary past. In some sense, schizophrenics are the result of intense selection and demonstrate that the costs for such cognitive advances may be individuals with particular mental vulnerabilities (Nesse, 2006). None of these, nor many other hypotheses have been proven, and so we are still left with a disease that is experienced by people living in the developing and developed worlds and results in individuals who are not fully functioning members of society and experience a reduced quality of life.

Addiction

The problem of addiction is a major area of mental health that demands serious attention and can likely be informed by an understanding of evolutionary theory. Approximately 1.2 billion people worldwide are addicted to nicotine, about 70 million are addicted to alcohol, and 5 million inject illicit drugs (World Health Organization, 2001b). If these estimates are even close to reality, that means that about one person out of three is addicted to some type of psychoactive substance. The costs in lives, lost productivity, and quality of life of such a mental illness is difficult to quantify, and attempts to do so produce numbers that are far beyond the abilities of most to comprehend. What can an evolutionary perspective provide?

If we can generate any effective treatment for the abuse of psychoactive substances, it will require an understanding of not only the neurophysiology of addiction and the proximate causal (e.g., environmental, social, familial) circumstances, but also why humans have such a high vulnerability to psychoactive drugs. A search for a particular gene for a susceptibility to drug abuse is a promising area. It is unlikely that a particular gene will be found because drug abuse and dependence are a complex set of genetic disorders that lack a simple pattern of Mendelian inheritance. Much more likely are the discoveries of gene complexes with relatively small effects that play a role in mediating drug–environment interactions.

Psychoactive drug use has a long history in human evolution. Fermented fruits are likely to have played a role in early hominin foraging strategies (Dudley, 2000, 2002, 2004) to the extent that they were a signal for edible resources. The widespread use of psychoactive substances in human evolution has been argued to be a byproduct of selective pressures for increased brain size and cognitive abilities (Smith, 1999). Only in recent times have humans been exposed to sufficient quantities of psychoactive drugs and

in sufficient concentrations that use would be a problem. In the past, consumption of naturally fermenting fruit and the consumption of psychoactive plants was such an infrequent event that it would likely not have been behaviorally disruptive to the individual or to the members of a small close-knit social group. On the other hand, with the improvement in the technology of fermentation and certainly with the advent of distillation, psychoactive substances were available in previously unimaginable volumes and concentrations. Long-term consumption of these drugs is perfectly predictable based on the anatomy of the human brain. These substances are not naturally occurring and consequently represent a novel experience for human brains. They are inherently pathogenic because they bypass the evolved systems of emotional and behavioral control (Nesse & Berridge, 1997). Psychoactive drugs provide the brain with false signals of fitness benefits. The hijacking of normal regulatory processes in the brain can result in continued use of drugs that no longer provide pleasure. Sensory mechanisms that control “liking” and “wanting” may be especially susceptible to drug influence (Lende, 2005; Lende & Smith, 2002). Drugs that block negative emotions may actually be blocking evolved defenses, but under some circumstances this use could actually be fitness enhancing (Nesse & Berridge, 1997).

An evolutionary perspective on substance abuse helps us appreciate how difficult it will be to find effective long-term therapeutic techniques and interventions. As a consequence of our highly evolved big brains and elaborate cognitive abilities, we are also the possessors of neural machinery that is easily derailed by the use of novel psychoactive substances. If nothing else, evolutionary medicine should alert us to any claims of the discovery of a “magic bullet” to cure addiction.

ARE WE LESS HEALTHY THAN OUR ANCESTORS?

Much of the writing on evolutionary medicine, including most of the chapters in this volume, has focused on medical problems or “mismatches,” with the usual claim that our modern lives are incompatible with our evolved bodies. The inference often drawn from this view is that we are not as healthy as our ancestors were. Of course, this is nonsense. If we look only at life expectancy, certainly there has been great improvement in the past century. How about quality of life? Again, 70-year-olds living in nonimpoverished circumstances in the developed world are, for the most part, far healthier than their counterparts in contemporary poor populations or in the past. Most of us who are fortunate to continue active and productive lives into our seventies and eighties marvel at how much healthier we are than our grandparents were. Clearly, by almost any measure, human health has improved. But does this mean that we are healthier?

“Maybe so and then again, maybe not” is probably the most reasonable answer to the question. We certainly live a lot longer than our ancestors, but is that the only measure of health? We certainly hope not. There is no doubt that the technological advances in medicine have contributed enormously to our ability to diagnose and treat disease. Never before in the course of human history have we been able to restore normal functioning to damaged cardiovascular systems, replace failing organs with new ones, treat a variety of

cancers and prolong life, repair limbs lost in battle or in accidents—the list goes on and on. But we can do better. In spite of all of the advances in medicine we have seen since the beginning of the twentieth century, it is striking to note that it took until the last decade of the twentieth century for scientists to recognize the importance of the evolutionary history of the organism they were treating. Even then, an appreciation of the place of evolution in medicine is woefully underappreciated. There are many reasons for this (see Chapters 22 and 23). It is our belief and the belief of the contributors to this volume that only when clinicians and researchers take into account the role of evolution in shaping the organism being treated as well as, in many cases, the organism causing the problem or condition will we achieve something that approaches sustainable health care for all people.

WHAT DOES EVOLUTIONARY MEDICINE HAVE TO OFFER?

Throughout this chapter we have highlighted the contributions that an evolutionary medicine perspective is beginning to make to understanding health and human well-being. Because of its integrative and holistic approach, the field is well suited to drawing together seemingly disparate collections of data and thinking. However, evolutionary medicine has made only a modest impact on clinical medicine. Is changing the way some aspects of clinical medicine are practiced a reasonable or even desirable goal? We think the answer is a qualified yes.

One thing that evolutionary medicine has to offer is the generation of alternative hypotheses for the causation of various conditions. For example, it makes intuitive sense that if a poorly nourished woman receives dietary supplements during pregnancy, her infant's birth weight will increase. An increase in infant birth weight is a desirable outcome because there is a correlation between infant birth weight and reduced mortality. However, supplementation of maternal nutrition to increase birth weight has turned out to be only modestly effective (see Chapter 18). Evolutionarily based research into this seeming paradox suggests that selection has favored buffering mechanisms that enable a woman to respond slowly or not at all to a variety of nutritional changes (both positive and negative) that occur during pregnancy. In other words, the protective/adaptive ability of maternal metabolism to maintain steady supplies of nutrients to the fetus generally works as well whether maternal nutritional intake is increased or decreased. Of course, this does not mean that pregnant women should not be given supplements when necessary, but it does suggest that adaptations that have been successful for generations (i.e., buffering from pregnancy insult due to poor nutrition) may not be very responsive to short-term fixes. Because these nutritional effects are apparently transgenerational, public health measures to improve infant birth weight should likely begin long before pregnancy and should not be judged as success or failure based on data for a single generation. Too often health-related programs are abandoned if positive results are not achieved in a short time. Evolution is typically an extremely slow process. Our expectations of the rapidity of change should be tempered with some knowledge of how evolution works.

SUMMARY

We have attempted to review much of the data concerning evolutionary medicine—in particular material that was unavailable for the precursor to this volume (Trevathan, Smith, and McKenna, 1999). Both in sophistication of theory and in quality of evidence, we feel that the chapters in this volume show a maturation of the field. For the time being evolutionary medicine is likely to remain the province of a relatively small number of specialists working outside of clinical medicine, but we hope that our efforts and others by our colleagues of similar mind will push the awareness and imminent sensibility of an evolutionary approach into larger arenas. To be sure, only time will tell.

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