1

AMERICA THE HEALTHFUL: ITS VITAL SIGNS

> Only one in a thousand persons dies a natural death;
> the rest die because of ignorant or aberrant behavior.
> —*Maimonides (1135–1204)*

The best-kept secret of the twentieth century may have been the good health of the public. Even the Russians hadn't gotten onto it. There is no pressing need for this secret to continue into the twenty-first century.

In 1979, Surgeon General Julius Richmond titled his report to President Carter, *Healthy People* [1]. From the first sentence of his report we learn that "the American people have never been healthier." What happened to that tad of good news? Little to nothing. The media deemed it unworthy to pass along. And then, with the new millennium, the Institute of Medicine (IOM), an arm of the National Academy of Sciences, weighed in with its report, *The Future of the Public Health in the 21st Century*, making it satisfyingly clear that the health of the American people at the beginning of the twenty-first century would astonish those living in 1900. "By every measure," it proclaimed, "We are healthier, live longer (as we shall see), and enjoy lives that are less likely to be marked by injuries, ill health or premature death" [2]. If that isn't cause for, and reason aplenty, to shout the good news from our rooftops, what is?

Given the fact that few know this, shouting from rooftops is simply too much to expect. But why the continuing silence by the media? Why haven't our vast communications networks—radio, TV, newspapers, and magazines—

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made much of this uplifting news? Is it that good news doesn't sell? Or is it something else again? Why would anyone want to keep the people ignorant of the sea change that has so affected their lives?

Given the silence of the media, and the public's consequent lack of that knowledge, it is incumbent upon us to provide this remarkable information. And by no means does our good health mean that we don't become ill, or that health has taken a sojourn. Indeed not, but it does mean that by comparison with our parents and grandparents generations, we have made remarkable strides, and that illness and death are no longer constant comparisons.

So, with kudos expressed, we can examine the data for ourselves and see how far we've come. As we journey, we shall ask the pregnant question, which, if any, of our leading causes of death can be ascribed to the food we eat, the water we drink, the air we breathe, and which to our personal behaviors, and which to our inheritance, our genetic constitution.

We begin our trek with a look at the leading causes of death in 2002. Table 1.1 provides a mine of information. At far left, causes of death are ranked from 1 to 12, followed by the total number of deaths for each condition. The fourth column renders the number of deaths per 100,000 populations. By moving the decimal point left, the number of deaths per 10,000, 1000, and 100 can be

TABLE 1.1. Leading Causes of Death, United States, 2002

Rank	Cause	Number	Rate/10^{5a}	Percent of Total (%)
1	Heart disease	696,947	242.0	28.5
2	Cancer	557,271	193.5	22.8
3	Stroke	162,672	56.4	6.6
4	COPB	124,816	43.3	5.1
5	Accidents			
	Motor vehicle	42,281	14.7	1.7
	Other	101,537	35.2	4.1
6	Diabetes	73,249	25.4	3.0
7	Influenza/pneumonia	65,681	22.8	2.7
8	Alzheimer's disease	58,866	20.4	2.4
9	Nephritis/nephrosis, nephrotic syndrome	40,974	14.2	1.6
10	Septicemia	3,865	11.7	1.4
11	Suicide	3,062	10.6	1.2
12	Liver disease	27,257	9.5	1.1
	Total	1,958,478		
	All causes	2,443,387	845.3	100.0

[a] Per 100,000 people.

Note: Total US population on July 1, 2002 was 287,941,220.

Source: National Center for Health Statistics [9].

obtained. The far right column indicates the percent or proportion of deaths contributed by each of the 12. The total of the 12 will yield only 82%. The remaining 18% is contributed by the literally hundred-plus slings and arrows that have found chinks in our armor, our genomes.

From this array it is immediately evident that heart disease lays undisputed claim to the top slot. Since the last edition of *OPH* (this book, *Our Precarious Habitat*), in which heart disease held first place with 323 deaths per 100,000, and was answerable for 37% of all deaths, there has been a gratifying decline of 33%; a triumph of public health. For a longer view, at midtwentieth century, 1950, the death rate was 440.1, a tad less than double our current rate. The numbers do reveal a remarkable achievement, well worth shouting about from rooftops.

Also evident is the fact that once beyond heart disease, the figures in each column of Table 1.1 drop sharply. Quick addition indicates that fully 58% of all deaths are due to heart disease, cancer, and stroke. The top five are responsible for 69% of all deaths. We would be remiss in taking leave of Table 1.1 without noting that the overall death rate stands at less than 1% per year. The rate of 845.3 per 100,000 can be translated as 0.84 per 100 individuals—0.8/100 or 0.8%. The essential takeaway message is that the preponderance of us live full and long lives—well beyond the biblical "fourscore and ten." Most everyone will live to collect their social security benefits for years after retirement. That's part of our current economic problem. When FDR signed the social security legislation into law in 1935, few of us were expected to attain the magic number—65—and collect. Hopefully our length of days will not break the bank. Nevertheless, length of days is the new and assuring message. But there are a clutch of potentially—perhaps more than potentially—deadly myths about heart disease. Heart disease is a man's disease. More men than women die of it. Myths are hard-dying, and this one has had too long a run. For over 20 years more women have died of heart disease than have men. Women put off getting appropriate medical attention, and all too often physicians and hospital personnel have not taken women's heart complaints seriously. Of course, the notion that cancer and AIDS snuff out more lives than does heart disease is laid to rest in Table 1.1, where it is obvious that heart disease is far deadlier than all forms of cancer. As for AIDS, we'll deal with that misperception shortly. We shall also dig deeply into the notion—yes, "notion" is the fit term—that high-dose antioxidant vitamins can protect the heart, is just that: notional. Worse yet, there is highly suggestive evidence that ingesting megadoses of vitamins can blunt the effectiveness of anticholesterol medications.

The myth that your high blood pressure occurs only when you step into the presence of your cardiologist may be the deadliest of all. Too many of us mistakenly believe that our blood pressure is perfectly normal until the white coat appears. True, there is a "white coat" hypertension concern—I know; I'm one of those who manifest that reaction regularly—but too many of us, including physicians, brush it off as nervousness and anxiety. Not a good idea.

Misinformation must not be allowed to make any of us a premature mortality statistic.

Abroad in the land is the extreme misconception that a large number of individuals with coronary heart disease lack any of the major coronary heart disease (CHD) risk factors.

Two recent studies conclude that 80–90% of individuals with CHD have conventional risk factors. Numerous epidemiologic studies have identified cigarette smoking, diabetes, hyperlipidemia, and hypertension as independent risk factors for CHD. Curiously enough, treatment of these risk factors has reduced the risk of a second cardiac event. These four risk factors have been referred to as "conventional risks." However, although well established in the medical literature, it is often stated that more than 50% of those with coronary disease do not exhibit one or more of these conventional risks. Consequently a team of medical researchers from the Cleveland Clinic and the University of North Carolina Medical School set out to determine the prevalence of the four conventional risk factors among patients with CHD, because of the claim that nontraditional and genetic factors play a significant role in the acquisition of heart disease. From their analysis of 122,458 patients enrolled in 14 international randomized clinical trials, they found that at least one of the four risk factors was present in 84.6% of women and 80.6% of men. They concluded that "clinical medicine and public health policies should place significant emphasis on the 4 conventional risk factors and the life-style behaviors causing them to reduce the epidemic of CHD" [3].

Motivated by what they believed to be the same false idea that less than 50% of CHD patients lacked the four conventional risk factors, a team of investigators from Northwestern University School of Medicine, the University of Minnesota School of Public Health, and Boston University School of Medicine set up a study "to determine the frequency of exposure to major CHD risk factors." This team followed 376,915 men and women ages 18–59 for 21–30 years. Among their enrollees, at least one of the four conventional risk factors occurred in 87–100%. Among 40–59-year-olds with a fatal coronary event, exposure to at least one risk factor ranged within 87–94%. For a nonfatal event there was exposure to at least one risk factor in 92% of men and 87% of women. For them, "Antecedent major CHD risk factor exposures were very common among those who developed CHD." They also made the point that, "These results challenge claims that CHD events commonly occur in persons without exposure to at least one major CHD risk factor" [4].

For anyone concerned with prevention of a coronary event, these two statistically powerful studies must be taken seriously, and smoking, high blood pressure, diabetes, and elevated blood lipid levels can no longer be ignored. They can be ignored only at our peril. We will not forget to question, to wonder, whether CHD is an environmental issue or a personal behavioral issue.

Cancer, for which we have an uncommon dread, deserves our scrupulous attention. However, we shall hold it in abeyance until we consider life's less terrifying afflictions.

CHRONIC NONNEOPLASTIC MEDICAL DISORDERS

Cerebrovascular disease (CVD), chronic obstructive pulmonary disease (COPD), diabetes, influenza/pneumonia, Alzheimer's disease, nephritis and nephrosis, septicemia, and liver disease are chronic medical conditions that have emerged as substantial death threats as infectious illness has waned.

Cerebrovascular Disease

Although settled in the number 3 position for generations, cerebrovascular disease (CVD or stroke), with 6.6% of the overall deaths, while not nearly the taker of lives as is heart disease or cancer, is a leading cause of serious, long-term disability. From the numbers we learn that CVD is the cause of one death in every 14, killing 167,661 in the year 2000; 63% of these were women. Stroke deaths afflict Afro-Americans with great force. For every 100,000 men and women the rates are 87 black men, 78 black women; 59 white men, and 58 white women. Current thinking holds this striking racial difference to be a function of genetic inheritance. Why this is so will be revealed by ongoing genetic investigations. As genetic studies indicate that different races are uniquely prone to different diseases, public health policies that recognize this could improve both medical care and the use of prescription drugs that we now know do not provide equal benefit across races [5–7].

Also known is the why of stroke, which occurs as a consequence of oxygen deprivation, when blood flow to the brain is disrupted. This deprivation is the most common cause of disabling neurologic damage and death. Not unlike water through a sediment-clogged pipe, a blood clot or fatty deposition (plaque) (atheroma) can block blood flow anywhere should inflammation narrow blood vessels to the brain. Drugs and hypotension—low blood pressure—can also reduce blood flow.

Chronic Obstructive Pulmonary Disease

Whereas CVD is an obstructive circulatory condition, COPD, chronic obstructive pulmonary disease, the fourth leading cause of death and accounting for the loss of some 125 thousand lives, is the consequence of respiratory obstruction. It is a tenacious blockage of oxygen, often the result of emphysema, chronic bronchitis, and/or asthma.

Our lungs consist of hundreds of millions of tiny airsacs-alveoli—whose walls are astonishingly thin, and necessarily so, permitting the passage of oxygen into and carbon dioxide out of our lungs. The grapelike clusters of alveoli maintain a rigidity that holds the airways open. When the thinner than thinnest tissue-paper thin walls erode, most often the result of cigarette smoke, the alveoli collapse or become hole-ridden, making breathing inordinately

difficult. Death ensues from asphyxiation. In his report on women and smoking, the U.S. Surgeon General [8], states that "mortality rates for COPD have increased among women over the past 20 to 30 years." We are further informed that between 1979 and 1985, the annual age-adjusted rates for COPD among women 55 years and older increased by 73%, from 46.6 per 100,000 to 80.7 per 100,000, and this steep rise continued during 1980–1992. Furthermore, from the CDC's National Vital Statistics Report [9], we learn that for 2002, for all races and all ages, women had a combined COPD death rate of 43.7 per 100,000. This arresting statistic reflects one of the most unfortunate and unnecessary facts of COPD deaths: the increase in smoking by women since World War II. Prevention appears to be entirely in their hands.

Diabetes

In the sixth slot with 3% of total deaths, is diabetes mellitus (literally, "honey sweet" diabetes), a group of diseases in which levels of the sugar glucose, are abnormally high because the pancreas fails to release adequate amounts of insulin, an enzyme that normally metabolizes glucose, maintaining steady levels. Diabetes shows itself in two main forms. Type 1 was until recently called *insulin-dependent diabetes mellitus* (IDDM) or *juvenile-onset diabetes*. Type 1 occurs when the body's immune system destroys pancreatic beta cells, the only cells in the body that make insulin. This form usually occurs in children and young adults; hence juvenile diabetes.

But why does the body harm itself? Why does the immune system destroy beta cells? The essence of the immune system is its ability to distinguish self from nonself. Self is we; our cells, tissues, and organs. Every cell in our tissues contains specific modules that identify it as self. Nonself are foreign objects or conditions that do not belong among us; bacteria, viruses, fungi, and other parasites. Because our bodies provide an ideal environment, with nourishing fluids, parasites are always dying to break in. Our immune system is usually ready and able to detect the presence of foreign substances. Sometimes, not often, the recognition system falters and atttacks tissue carrying the self-marker molecules. When that happens, the body manufactures T cells and antibodies directed against, in this case, the beta cells in the islets of Langerhans that are clustered in the pancreas. With the beta cells destroyed, insulin is not produced, and glucose levels remain uncontrolled. Those T cells ("T" for thymus, the small gland behind the breast bone—the sternum—where these cells are produced) are types of white blood cells—lymphocytes—that normally play a major role in defending the body against foreign invaders.

Type 2 was previously referred to as *non-insulin dependent diabetes mellitus* (NIDD), or adult-onset diabetes. It is type 2 that accounts for the great majority of diabetes cases. Type 2 is associated with older age, obesity, and impaired glucose metabolism. African Americans, Latinos (Hispanics), American Indians, and Pacific Islanders are at unusually high risk [10]. However, the

number of overweight and obese children in the United States has doubled in the past two decades, and 15% of American children are overweight or obese. Type 2 diabetes, which is linked to excess weight, is being found in such high numbers among children that the adult-onset type will need a new designation [11]. We will deal with the obesity problem shortly.

We cannot leave diabetes without considering its future and possible demise. Current immunological research is so vigorous that it is possible to almost see beyond the horizon. In this instance the horizon is T cells, once thought to be of two types, killer T cells that track down virus-infected cells, and helper T cells, which work primarily by secreting lymphokines that accomplish a number of defensive functions. Now, however, a newly found class of T cells, regulatory T cells, are seen as the promise for vanquishing a number of autoimmune diseases including diabetes and multiple sclerosis, diseases in which the body turns on itself. Regulatory T cells are seen as the basis of new therapies, and 5 years on is seen as a reasonable horizon for regulatory T cells to come on line, making diabetes a thing of the past [12]. Hope is on the way.

Influenza/Pneumonia

Influenza/pneumonia, currently in the seventh slot, was the sixth leading cause of death in 1989, which means that life is improving for both the very young and the very old who are at greatest risk for this insidious duo. Influenza and pneumonia are inseparably linked as influenza often leads to pneumonia and death. Influenza is the sixth leading cause of death of infants under one year and the fifth leading cause for those over 65 [13].

Person-to-person spread of the numerous highly contagious and infectious influenza viruses, occurs via inhalation of droplets of saliva expelled when coughing and sneezing. Sneezing is the more troublesome. When someone sneeze, the teeth are clenched, and the intense force of the sneeze squeezes saliva between the teeth, creating a cloud of particles, some of which can hang in the air and drift with the currents—to others nearby, who will breathe them in with their next breath. The risks for complications, hospitalizations, and death increase with such underlying conditions as heart disease, diabetes, stroke, HIV/AIDS, and, of course, pneumonia. Most assuredly the number of influenza deaths will increase along with the number of elderly, unless antiviral medications are discovered and developed. But that is unlikely in the near term, given the complexity of viruses and their adaptive ability. In fact, a new study recently found that influenza vaccination of the elderly may be less effective in preventing death than previously assumed. The possibility is raised that "herd" immunity may be more protective. This would require the vaccination of larger numbers of younger, healthier individuals, children included, the immune herd, to prevent transmission of the viruses to the high-risk elderly [14].

Bacteria, specifically *Streptococcus pneumoniae, Hemophilus influenzae*, and *Klebsiella pneumoniae*, are the microbial villains, among adults, while a

bevy of viruses are children's troublemakers. Here, too, the beasties reach both the upper and lower respiratory tract via inhalation of saliva-bearing organisms sneezed or coughed into the surrounding air. Here again, the elderly and the very young are at increased risk of complications, as are African Americans, Alaska natives, and HIV/AIDS patients. Death occurs in 14–15% of hospitalized patients [13].

Alzheimer's Disease

Alzheimer's disease is a newcomer to the inventory of the leading causes of death. It was not present in 1989, having only recently taken over eighth place, with 59,000 documented deaths, and is currently responsible for over 2% of all deaths. The term "documented" suggests, strongly suggests, that there are many more deaths due to dementia than the numbers indicate [15,16].

Alois Alzheimer, born in Marbreit, Germany, became a medical researcher at Munich Medical School, where he created a new laboratory for brain research. In 1906, he identified an unusual disease of the cerebral cortex that caused memory loss, disorientation, hallucinations, and untimely death. Alzheimer died at the tender age of 51 from complications of pnuemonia and endocarditis [17].

Currently Alzheimer's disease is fairly well understood. It is a disorder that occurs gradually, beginning with mild memory loss, changes in behavior and personality, and a decline in thinking ability. It progresses to loss of speech, and movement, then total incapacitation and eventually death. The brains of Alzheimer's patients have an abundance of plaques and tangles, two abnormal proteins. *Plaques* are sticky forms of β-amyloid; *tangles* are twisted protein fibers called *tau* (τ). Together, these two protein clumps block the transport of electrical messages between neurons that normally allow us to think, talk, remember, and move. Until a medication or procedure is found that can dissolve or prevent the occurrence of these blocking proteins, Alzheimer's can be expected to accumulate victims.

Nephritis and Nephrosis

Nephritis is an inflammation of the kidneys, and *nephrotic syndrome* is a collection of symptoms induced by a number of diseases. Allergies can do it; drugs can do it, and perhaps a dozen ailments, including HIV/AIDS, diabetes, and cancer can cause severe kidney impairment. *Nephrosis* is a severe loss of serum protein that can lead to a number of immunodeficiency disorders and death. Nephritis is usually the consequence of either a streptococcal infection or an adverse immune reaction. Children and adults are equally at risk, and with some 41,000 deaths annually, these kidney miseries have been propelled into the ninth position. However, for infants less than a year, this triad is the seventh destroyer of life [13]. Indeed, they are vulnerable.

Septicemia

Some pathogens can grow and multiply specifically in blood plasma, and their waste products can be toxic and produce septicemia (*septikos*, from the Greek meaning putrefaction, and *haima*, blood). Entry into body cells requires a specialized ability used by various pathogens to produce lytic chemicals capable of dissolving membranes and permitting passage, or via such passive means as entry through breaks in the skin, ulcers, burns, and wounds. They are there waiting an opportunity. By whatever route entrance occurs, toxins shed by the organisms produce a toxic condition, a toxemia, which can be extremely difficult to manage, especially now that many pathogens have evolved resistance to a range of antibiotics.

Sepsis can become risky as a result of surgery and/or the insertion of intravenous catheters, urinary catheters, and drainage tubes. The likelihood of sepsis increases as the time of the indwelling catheters increases. Of course, injecting drug users introduce bacteria directly into their bloodstreams. Also at increased risk are individuals taking anticancer medications, as well as HIV/AIDS patients whose immune systems have been compromised.

Septic shock, in which blood pressure falls to life-threateningly low levels, can be a frightening side effect, occurring most often in newborns, the elderly, and those whose immune systems are in disarray. If infant care is inappropriate, and HIV/AIDS continues unabated as it appears to be doing, septicemia and septic shock will remain integral components of the list.

Liver Disease

Liver disease is in the twelfth position, accounting for some 27,000 annual deaths. Cirrhosis, the primary liver disease, appears to be the end stage of several common causes of liver injury. Cirrhosis (Greek, meaning orange-colored) results in nonfunctioning destroyed liver tissue that can and often does surround areas of viable healthy tissue. Until the cirrhotic condition is well advanced, many people remain a symptomatic, not knowing that they have it. The most common risk factor is alcohol abuse. Among the 45–65-age group cirrhosis is now the sixth leading cause of death [13].

So, here we have gathered the third, fourth, sixth, seventh, eighth, ninth and tenth leading causes of death, which between them account for 24% of what's killing us. Are these environmental?

ACCIDENTS

Although motor vehicle accidents kill over 40,000 men, women, and children every year, and maim hundreds of thousands, this carnage on our highways is considered one of life's less terrifying trials. In fact, it is barely considered.

More to the point, it is accepted as a price to pay for our mobile way of life. Perhaps the numbers that follow will help us see the error of our ways.

Deaths by motor vehicle are synonymous with the advent of the horseless carriage, and have been an integral part of our lives since that crisp September day in 1899 when New York real estate broker H. H. Bliss stepped from a trolley car at 74th Street and Central Park West in New York City and was struck down by an electric horseless carriage [18]. By 1990, 3,000,000 men, women, and children had surrendered their lives to motor vehicles. If this slaughter continues, as it appears to be doing, the fourth million will arrive within 6 years—by 2012. To help comprehend the flaws in our thinking about motor vehicle accidents, we need only revisit Table 1.1. Although this table, which provides substantive information about us as a nation, aggregating all causes of death, is obviously useful, it tends to obscure seminal details. Yes, motor vehicle deaths are the fifth leading cause of death. But the data in Table 1.1 fail to divulge the fact that in 2002, crashes on our highways were the leading cause of death for every age from 3 to 34 [13]. Table 1.2 provides an alternative view of the leading causes of death. By teasing out the top killers by age groups, shock and awe awaits. A new set of risks emerge, which suggest a different approach to prevention. Lest we take some measure of joy that toddlers age 1–3 are not members of this select assembly, I hasten to add that for the 1–3-year-olds, death by motor vehicle is the second leading cause of death. The 35–44-year-olds can take little comfort in the fact that motor vehicle death is the third leading cause of their demise.

Furthermore, motorcycles appear to be the most dangerous type of motor vehicle on the road today. These bikers "were involved in fatal crashes at a rate of 35 per million miles of travel compared with a rate of 1.7 for passenger cars. The peak rate of death among alcohol-impaired cyclists shifted from those 20 to 24, to the 40 to 44 age group" [13]. Stronger law enforcement for this age group would save lives, but any attempt in that direction, will be fought tooth and nail. As for older drivers, Table 1.2 offers yet another surprising and impressive message; those 65 and older do not, repeat, do not appear at any level of leading causes of death by motor vehicle. Now that's a startling and powerful statistic that certainly *does not* accord with conventional wisdom or perception.

The data array in Table 1.2 offers a mother lode of substantive data. We see that for ages 1–34, motor vehicle crashes must or should be their worst nightmare. And as already noted, for those 65 snd older, motor vehicle deaths are not the problem widely thought to be. Continuing to delve into this mine of data, we see that while not on our prime list of the 12 leading causes of death, homicide (e.g., see Table 1.3 for comparisons of firearm homicide rates in three countries) is the second leading cause of death for those aged 16–24, and suicide is the second leading cause of death for the 25–34 age group.

Malignant neoplasms rise to the primary slot for the 35–64 age group, while heart disease deaths takes the top spot for those 65 and older. But who would have believed that homicide is the fourth leading cause of death for toddlers

and youngsters from less than a year old to age 3, along with those those ages 8–15? Suicide emerges as the third leading cause of death for young people ages 8–24. This chart is pregnant with matchless information and worthy of continued mining. For example, the last column on the right discloses the millions of years of life lost by each cause of death, which can be translated as the country's loss of creativity and productivity, losses that cannot be retrieved. In fact, because of the many young lives consumed, motor vehicle traffic crashes rank third in terms of years of life lost—that is, the number of remaining years that someone is expected to live had that person not died—prematurely—behind only cancer and heart disease [19].

Before moving on, it is imperative to note the National Highway Traffic Safety Administration's most recent statistic: 43,443 people killed in roadway *accidents* in 2005. This increase from 2003 and 2004, was attributed to accidents involving motorcycles. In fact, deaths from motorcycles rose by 13% from 2004, and by almost 50% of those who died were not wearing helmets, which are known to reduce the probability of dying in a motorcycle crash by 35–50%. Take note.

It would be remiss not to mention that as national census figures indicate, the 1–34-year-old group comprises some 139 million men, women, and children; not quite 20% of the total population. At 20% they would constitute fully 1 in 5 of all our citizens, representing the heart, the core of young, working America. They are sorely needed. Consequently, for them, prevention would seem a top priority.

Life is not without risks; we know that. But there are risks that need not be taken. In 2002, 18,000 men, women, and children died in crashes involving alcohol [9]. Men, women, and children are included here, rather than people or individuals to make this more personal and perhaps more meaningful. After all, these deaths include parents, relatives, and friends. Nevertheless, those 18,000 deaths do not account for the 500,000 men, women, and children who were injured; many were maimed for life. To edge this a bit more starkly, 18,000 deaths and 500,000 injuries translate into 49 deaths and 1370 injuries each day of the year. Drunk driving deaths have been on the rise since 1999 [20]. Some 25% of the 15–20-year-olds killed on the highways had blood alcohol concentrations (BACs) of 0.08 grams per deciliter (g/dL).

A recent study in the *Journal Psychological Science* informs us that those who drink and drive are at a higher risk of accidents because alcohol distorts depth perception—judging distance from obstacle [21]. It is also troubling that drinking has become more prevalent among teenage girls because of the increased advertisement of alcoholic beverages to teenage groups. Research at Georgetown University revealed a striking increase in such ads in over 100 national magazines. A larger percentage of girls age 12–20 were exposed to alcohol ads than were women ages 21–34. Apparently teenagers are advertisers' primary target [22]. Get 'em young, and you've got them for life.

Again, the numbers continue to tell a grim story. Drivers under 20 were involved in 1.6 million crashes in 2002, with 7772 of them fatal, including 3700

TABLE 1.2. Leading Causes of Death in the United States for 2002 by Age Group[1]

	Cause and Number of Deaths					
RANK	Infants Under 1	Toddlers 1–3	Children 4–7	Young Children 8–15	Youth 16–20	Young Adults 21–24
1	Perinatal period 14,106	Congenital anomalies 474	MV Traffic crashes 495	MV Traffic crashses 1,584	MV Traffic crashes 6,327	MV Traffic crashes 4,446
2	Congenital anomalies 5,623	MV Traffic crashes 410	Malignant neoplasms 449	Malignant neoplasms 842	Homicide 2,422	Homicide 2,650
3	Heart disease 500	Accidental drowning 380	Congenital anomalies 180	Suicide 428	Suicide 1,810	Suicide 2,036
4	Homicide 303	Homicide 366	Accidental drowning 171	Homicide 426	Malignant neoplasms 805	Accidental poisoning 974
5	Septicemia 296	Malignant neoplasms 285	Exposure to smoke/fire 151	Congenital anomalies 345	Accidental poisoning 679	Malignant neoplasm 823
6	Influenza/ Pneumonia 263	Exposure to smoke/fire 163	Homicide 134	Accidental drowning 270	Heart disease 449	Heart disease 518
7	Nephritis/ Nephrosis 173	Heart disease 144	Heart disease 73	Heart disease 258	Accidental drowning 345	Accidental drowning 238
8	MV Traffic crashes 120	Influenza/ Pneumonia 92	Influenza/ Pneumonia 41	Exposure to smoke/fire 170	Congenital anomalies 254	Congenital anomalies 186
9	Stroke 117	MV Nontraffic crashes[4] 69	Septicemia 38	Chronic lower resp. dis. 131	MV Nontraffic crashes[4] 121	Accidental falls 134
10	Malignant neoplasms 74	Septicemia 63	Benign neoplasms 36	MV Nontraffic crashes[4] 115	Acc. dischg. of firearms 113	HIV 130
All[3]	28,034	4,079	2,586	6,760	16,239	15,390

[1] When ranked by specific ages, motor vehicle crashes are the leading causes of death for age 3 through 33.
[2] Number of years calculated based on remaining life expectancy at time of death; percents calculated as a proportion of total years of life lost due to all cause of death.
[3] Not a total of top 10 causes of death.
[4] A Motor Vehicle Nontraffic crash is any vehicle crash that occurs entirely in any place other than a public highway.

Other Adults					
25–34	35–44	45–64	Elderly 65+	All Ages	Years of Life Lost[2]
MV Traffic crashes 6,933	Malignant neoplasms 16,085	Malignant neoplasms 143,028	Heart disease 576,301	Heart disease 696,947	Malignant neoplasms 23% (8,686,782)
Suicide 5,046	Heart disease 13,688	Heart disease 101,804	Malignant neoplasms 391,001	Malignant neoplasms 557,271	Heart disease 22% (8,140,300)
Homicide 4,489	MV Traffic crashes 6,883	Stroke 15,952	Stroke 143,293	Stroke 162,672	MV Traffic crashes 5% (1,766,854)
Malignant neoplasms 3,872	Suicide 6,851	Diabetes 15,518	Chronic lower resp. dis. 108,313	Chronic lower resp. dis. 124,816	Stroke 5% (1,682,465)
Heart disease 3,165	Accidental poisoning 6,007	Chronic lower resp. dis. 14,755	Influenza/ Pneumonia 58,826	Diabetes 73,249	Chronic lower resp. dis. 4% (1,466,004)
Accidental poisoning 3,116	HIV 5,707	Chronic liver disease 13,313	Alzheimer's 25,289	Influenza/ Pneumonia 65,681	Suicide 3% (1,109,748)
HIV 1,839	Homicide 3,239	Suicide 9,926	Diabetes 54,715	Alzheimer's 58,866	Perinatal period 3% (1,099,767)
Diabetes 642	Chronic liver disease 3,154	MV Traffic crashes 9,412	Nephritis/ Nephrosis 34,316	MV Traffic crashes 44,065	Diabetes 3% (1,050,798)
Stroke 567	Stroke 2,425	HIV 5,821	Septicemia 26,670	Nephritis/ Nephrosis 33,865	Homicide 2% (822,762)
Congenital anomalies 475	Diabetes 2,164	Accidental poisoning 5,780	Hypertension renal dis. 17,345	Septicemia 33,865	Accidental poisoning 2% (675,348)
41,355	91,140	425,727	1,811,720	2,443,387	All cause 100% (37,341,511)

Source: National Center for Health Statistics (NCHS), CDC, Mortality Data 2002.

Note: The cause of death classification is based on the National Center for Statistics and Analysis (NCSA) Revised 68 Cause of Death Listing. This listing differs from the one used by the NCHS for its reports on leading causes of death by separating out unintentional injuries into separate causes of death, i.e., motor vehicle traffic crashes, accidental falls, motor vehicle nontraffic crashes, etc. Accordingly, the rank of some causes of death will differ from those reported by the NCHS. This difference will mostly be observed for minor causes of death in smaller age groupings.

TABLE 1.3. Cross-Cultural Differences in Firearm Homicides, 2000

Country	Population (million)	Firearm Homicide	Rate/10^{5a}
United States	275	10,801	39.2
European Union	376	1,260	3.3
Japan	127	22	0.17

[a] Per 100,000 people.

teenagers. Far too many teenagers have neither the skills nor the experience to be permitted full driving privileges. Unfortunately too many parents believe otherwise. And then there is the seatbelt problem, which means the failure to wear them while driving. Highway crashes took the lives of over 19,000 drivers and passengers who failed to wear seatbelts. About a thousand of these were children under 8 who were not buckled up and properly secured in the rear seat of the car [20]. Clearly there is much room for improvement, and much can be readily and easily done to reduce the carnage, but it is difficult to overcome inertia and the tragically mistaken belief that we are all superb drivers. Dispelling that myth could have the salutary affect of relegating the accident death rate to the seventh or eighth position. Would it help to know that the motor vehicle death rates for Mississippi and Massachusetts in 2003 were 31.2 per 100,000 and 8.0 per 100,000, respectively [13]?

The accident equation contains yet another variable: one that cannot be directly attributed to our driving skills, as a third party plays a significant role for which drivers are unprepared. According to the National Safety Council, collisions with animals have risen dramatically from 520,000 animal-related accidents in 2001 to 820,000 accidents in 2002. These collisions resulted in more than 100 deaths and 13,000 injuries [23] as drivers collide with deer bounding across roads, or as we swerve into the path of oncoming vehicles attempting to avoid the creatures. As more of our wilderness gives way to housing developments and animals are forced to seek shelter where they can, their road crossings, day or night, will continue to be a risky business for us both. From the University of North Carolina's Highway Safety Research Center we learn that deer crashes occur most frequently in October, November, and December, and are more likely to occur during 5:00–7:00 A.M. and between 6:00 P.M. and midnight [23].

The National Safety Council maintains that death and injury on our roads and highways is directly related to impulsiveness, alcohol consumption, and poor judgment. It has long been my contention that "accident" is a misnomer for the fateful events that cause the slaughter on our highways. The word should be "purposefuls," as "accident", by definition, means an unforeseen event, or one without an apparent cause. I would imagine that most of us would agree that such a definition fails to adequately describe the crashes, the accidents that permanently removes so many of us prematurely. I'm also com-

fortably certain that many of us could compile lists of good and sufficient risk factors that contribute to untimely motor vehicle deaths.

Unfortunately motor vehicle accidents do not account for all "accidental" deaths and injury. Falls are the greatest single risk; falls from stepladders, and staircases, falls were responsible for 18,044 deaths in 2003. Over 11,000 were in the over 65+ age group [13]. But what actually caused the fall? Was it a toy left on the stairs that a person tripped over; was it a faulty stepladder, or faulty placement of the ladder? Again, "accident" is probably the wrong word. In addition to falls, fires, drownings, poisonings, drugs, knives, and guns drive the nonvehicular deaths to well over 100,000 annually. A chilling statistic. At this point it is worth recalling that although accidents are the fifth leading cause of death nationwide, they are actually the leading cause of death for those ages 1–30—something that Table 1.2 makes abundently clear. Unfortunately, and to their detriment, they are oblivious of this horrific statistic. It would be unimaginable if they were aware; that would suggest total denial. Why hasn't the media made much of this frightful and wasteful cause of death?

SUICIDE

Suicide, the taking of one's own life, while currently the nation's eleventh leading cause of death—with violent death among the 8–24-year-olds, as Table 1.2 informs us—it is the the third leading terminator of life, but slips into second place for the 25–34-year-olds In 2003, 31,484 young lives were snuffed out across the country: 25,203 young men and 6281 young women [13]. Adding these traumatic deaths to the highway deaths, we are looking at some 75,000 deaths annually. Although it is not treated that way, because trauma is not a rubric, a recognized category, trauma is one of the most notorious problems the country must deal with, but doesn't. It is as if it doesn't exist, as it is seen as two separate issues, when it should be seen and dealt with as a single substantive issue. Until it is, expect the numbers to increase. The number of potentially productive years of life lost should give us pause: 1,100,000 years of life lost to suicide. Add another 2 million for motor vehicle deaths. From a purely economic concern, can the country afford the loss of 3 million potentially productive days annually? It's a no-brainer.

According to the American Association of Suicidology (AAS), suicide is, beyond doubt, preventable. Most suicidal individuals, the AAS tells us, want to live but are simply unable to recognize alternatives. Most offer clues, warning signs, but parents, friends, teachers, and physicians fail to read them. With that type of illiteracy, a suicide occurs every 16.7 minutes. Although 31,000 do commit suicide, according to the AAS there are 787,000 attempts: 25 attempts for every death, with an average 3 : 1 female : male ratio for every attempt. I suspect we would agree that this is an intolerable form of illiteracy. But how do we become literate?

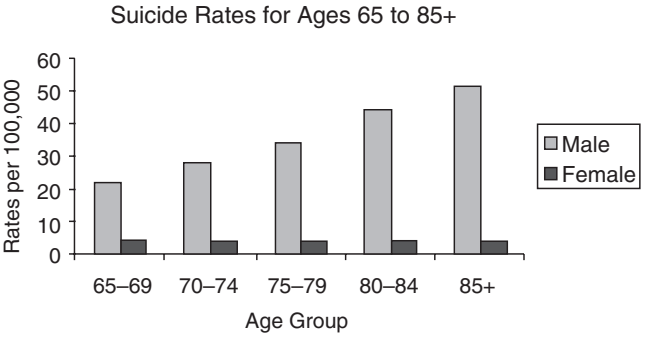

Figure 1.1. Comparison of suicide rates for men and women ages 65–85+. (*Source:* Centers for Disease Control, 2002.)

Surprisingly, winter is not the season of greatest discontent; spring exacts the greatest toll—just the opposite of what I would have imagined. For most of us spring is the season of rebirth and new beginnings, and winter is perceived as cold, damp, and depressing.

At the opposite end of the age spectrum, the elderly, 65 and over, make up 12.4% of the country's total population, yet account for almost 18% of all suicides. According to the AAS, an elderly suicide occurs every 95 minutes. Elderly white men are the highest at-risk group, with some 35 suicides per 100,000. Figure 1.1, shows the rising rates with age and the difference between men and women. Although older adults attempt suicide less often than do others, they have a higher successful completion rate. If all attempts were successful, we would be looking at a 0.75 million suicide deaths a year, which would far exceed the combined death rate due to heart disease and cancer. It boggles the mind. Among the 15–24 age group, which surely must be a terribly fragile age, there is one attempt for every 100–200 attempts. For those over 65, there is one successful suicide for every four attempts. For all age groups, the instruments of most successful attempts are rifles and handguns. Their ready availability speaks for itself. Suffocation and hanging are the second most grizzly choices [24].

The goal of the American Association of Suicidology (AAS) is to understand and prevent suicide. It also serves as a national clearinghouse for information and help, and provides resources and publications on a range of suicide-related topics, including how to read the signs of a potential suicide.

The AAS can be reached at

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Washington, DC 20005
202-237-2283
email: `infor@suicidology.org`
Website: `www.suicidology.org`

If by nature's way, suicide and homicide need not be violent. When "the elders" decided that 70-year-old Socrates was too disturbing an influence on young Athenian boys, he was handed an extract of *Conium maculatum*, spotted hemlock, in wine, of course, with which to dispatch himself to a more propitious environment [25]. Although hemlock's toxic properties were well established by 399 BCE, it was not until modern times that coniine (2-propylpiperidine) was isolated and found to be the active (dispatching) essence [26]. However, I've never been certain whether Socrates' death was a suicide or a homicide. I tend toward homicide, as there is little evidence that at his age he entertained the idea of ending it. *Conium maculatum* is not alone in bringing about the end of days by either suicide or homicide for any number of imbibers.

Recently, another of nature's wonders made headlines. *Cerbera odollam* appears to be a ready-made suicide tree, the cause of widespread death on the Indian subcontinent and environs. The suicide tree is seen as the agent of death for many more than had been imagined. Cerbera, which grows across India and southeast Asia, has a long history of assisted suicide, but the scientists who recently studied the problem indicate that the authorities have failed, and are failing, to determine how often it is used for murder.

Writing in the journal *Ethnopharmacology*, they inform us that cerbera "belongs to the notoriously poisonous Apocynacea family," and they say that the seeds have long been used as an ordeal poison [27]. Ordeal trials were an ancient test used to determine guilt or innocence of sorcery and other crimes. Belief in the infallibility of the poison to make the correct distinction was so strong that innocent people did not hesitate to take a sip.

Cyberin, cerberoside, and odollin, the deadly glycosides, are contained in the kernel. Between 1989 and 1999, 537 deaths were attributed to odollam poisoning. Among those who knowingly took it, 70–75% were women—which continues to speak to their continued oppression. Because of its ready availability, it is the choice poison for both suicides and homicides. For suicide, the kernels are mashed with gur, a form of sweet molasses. For homicide, the kernels are mashed with food containing capsicum-type peppers to mask the bitter glycosides. Death occurs 3–6 hours after ingestion. Although 50 suicides are recorded annually, the actual numbers are unknown, as are the numbers of homicides.

The authors also tell us that "to the best of our knowledge, no plant in the world is responsible for as many suicides as the odollam tree. Mother nature does work in strange ways. The authors further remark that "this study has made it possible to bring to light an extremely toxic plant that is relatively unknown to western physicians, chemists, analysts and even coronors and forensic toxicologists." Yet another caution for our already full agendas.

HIV/AIDS

During the midtwentieth century, the new pathogens human immunodeficincy viruses HIV-1 and HIV-2, which induce AIDS, autoimmune deficincy syn-

drome, crossed over to the human population and was first diagnosed in humans in 1981, in Los Angeles. Although these viruses rapidly adapted themselves to human–human transmission, AIDS has yet to be found in nonhuman primates; nevertheless, HIV-1 appears to have evolved from the simian immunodeficiency virus SIV_{cpz}—specifically the chimpanzee, *Pan troglodytes troglodytes* [28]. Furthermore, over the past quarter-century, it has become clear that human genetic differences determine whether susceptibility or resistance to AIDS will have rapid, intermediate, slow, or no progression from initial virus infection.

Although AIDS neither makes it to the top of the charts nor is among the top 15, and hasn't been in years, AIDS requires examination as it is widely perceived as the top one or two leading causes of death in the United States. The perception arises because of the way the media has dealt with this entirely preventable illness.

For reasons yet to be revealed, AIDS has often been presented to the public by the communications media, in the aggregate, as cumulative numbers. Since its initial detection in 1981, each year's total of new cases and deaths has been added to the previous year's total. Thus, from 1981 to 2004, the total number of deaths stood at 529,000+. When such an overwhelming number is presented on TV and radio, or carried in newspapers and magazines, it must shock readers and listeners. But the fact of aggregation is noted nowhere, and it is assumed that these are current cases and deaths, which most assuredly is shocking. Nevertheless, this is a unique bit of calculus as no other illness is aggregated in this way. All other diseases are presented as annual totals. So, as we see in Table 1.1, heart disease took 697,000 lives in 2002 (the last year for complete numbers). Had heart disease deaths been aggregated for the 22 years 1981–2003, as was done for AIDS, we would be looking at 15–25 million heart disease deaths. Simple arithmetic informs us that over those 22 years, for every AIDS death there was approximately 30 deaths from heart disease.

AIDS receives exuberant media coverage, well out of proportion to its actual numbers. Similar accounting divulges 12–25 million cumulative cancer deaths, which would translate to 24 cancer deaths for every AIDS death. The perception that AIDS is a major killer is a media creation, requiring expeditious revamping.

Be that as it may, AIDS takes its greatest toll of 34–54-year-old African American men and women, with the 25–34-year-olds running a close second. Male–male sexual contact is the primary route of viral transmission for gay men, black or white. Women receive the HIV virus by direct injection of drugs, into their bloodstream, and via sexual encounters with infected men, who all too often do not indicate their HIV positivity. Also, although it is well documented that condoms can be an essential preventive, far too many men eschew them as "a sexual killjoy." In March, 2007, WHO officially recommended circumcision of all men as a way to reduce the worldwide heterosexual spread of the AIDS virus. The intention is to vigorously pursue this means of prevention.

Also well documented and established is the fact that the human immunodeficiency virus (HIV) cannot be picked up by drinking from a water fountain, contact with a toilet seat, or touching an infected person. Neither has saliva been shown to be infectious. HIV can be transmitted by semen and vaginal secretions during intercourse, and is readily transmitted by intravenous injection, by sharing needles used by infected individuals. Accidental needlesticks with a contaminated needle has resulted in infections of health professionals, and infected women can readily transmit the virus to their fetuses during pregnancy.

Early on, as HIV/AIDS spread, scientists discovered that the virus attacks human immune cells. The virus can destroy or disable T cells, which can lay dormant for long periods. As immunity fails, an HIV-infected person becomes prey to life-threatening opportunistic infections and rare cancers. Opportunistic infections, usually bacterial, would be of no consequence to a healthy person, but can be deadly to an individual with a compromised immune system.

HIV tricks the T cell into switching on its copy machine, producing huge numbers of new HIV particles that eventually destroy healthy cells, with the release of vast amounts of virus to continue circulating, infecting, and destroying additional lymphocytes. Over months there is an enormous loss of T lymphocytes (CD4+) cells.

Critical to HIV's lifecycle was protease, a viral enzyme. Researchers expected that by blocking this enzyme virus spread could be prevented. Accordingly, protease inhibitors, saquinivir, ritonavir, indinavir, became available and quickly approved by the Food and Drug Administration (FDA). Unfortunately those protease inhibitors and others that followed did not become the "miracle" cures many had placed their hopes in. HIV produces a variety of versions of itself in a host's cell. Protease inhibitors can kill most, but there are always a resistant few. Not unlike the effect of antibiotics on bacteria, the resistant ones continue the cycle of reproduction, and soon the drug, the inhibitor, is no longer effective. Thus far HIV has eluded all attempts to destroy it [29–31]. So, what remains? Studies have demonstrated that condoms are not a 100% deterrent. It is also evident that safe sexual practices can short-circuit HIV's entrance.

Some 1% of all those infected are "slow progressors," who take years to manifest AIDS. Another 1% are "fast progressors" who develop opportunistic infections in months, when the average time between HIV and AIDS is about 10 years. Should a new and highly drug-resistant viral strain begin to spread via sexual activity, the number of fast progressors could multiply sharply. Consequently, abatement of risky sex is again becoming a priority of public health officials.

At the 2004 International AIDS Conference in Bangkok, Uganda's President Yoweri Musaveni explained that his ABC strategy took Uganda from a 30% infection rate to 6% (A = *a*bstinence—delay having sex if young and unmarried; B = *b*e faithful to your partner—zero grazing; C = use a

*c*ondom properly and consistently if you're going to move around) [32]. But he also noted that condoms have a failure rate, encouraging promiscuity. Conference attendees were turned off by Musaveni's message. Behavior change, self-discipline, and monogamous relationships were not on their agendas.

Although AIDS involves primarily a disruption of the immune system, it can also traumatize the nervous system. While HIV-1 and HIV-2 do not invade nerve cells directly, they do affect their function, causing mental confusion, behavioral changes, migraines, progressive weakness, loss of sensation in arms and legs, and stroke. Additional complications as a consequence of HIV–drug interactions are spinal cord damage, loss of coordination, difficult and painful swallowing, shingles, depression, loss of vision, destruction of brain tissue, and coma. Thus far no single treatment has been able to alter these neurological complications [33].

As of December 2004, an estimated 944,306 individuals had received a diagnosis of AIDS, and of these 529,113 had died: a steep mortality rate of 56% [34]. Furthermore, "since 1994, the annual number of cases among blacks, members of other racial/ethnic minority populations, and those exposed through heterosexual contact has increased" [34], and the number of children reported with AIDS attributed to perinatal HIV transmission peaked at 945 in 1992 and declined 95% to 48 in 2004, primarily because of the identification of HIV-infected pregnant women and the effectiveness of antiretroviral prophylaxis in reducing mother–child transmission of HIV [34].

Of particular importance, 16–22 million people aged 18–64 are tested each year. By 2002, an estimated 38–44% of all US adults had been tested for HIV [34]. Nevertheless, "at the end of 2003, of the approximately 1.0–1.2 million persons estimated to be living with HIV in the United States, an estimated one quarter (250,000–312,000) persons were unable to benefit from clinical care to reduce morbidity and mortality" [34], and "a number of these persons are likely to have transmitted HIV unknowingly." Because treatment has markedly improved survival rates, since the introduction of highly active antiretroviral therapy (HAART), and because progress in motivating earlier diagnosis has been lacking, the National Centers for Disease Control has issued new HIV testing recommendations.

These recommendations, issued in September 2006 for all individuals age 13–64, seek to level the playing field, as previous requirements for written consent and pretest counseling have now been dropped. The federal health officials now see HIV testing as becoming a routine medical/healthcare procedure. HIV testing would be offered by primary care physicians, as well as emergency rooms, substance abuse centers, prisons, and community health centers. Everyone age 13 should be tested at least once, and some sexually active people should be tested annually. According to CDC Director Dr. Julie L. Gerberding, the new recommendations would detect the 250,000 individuals who do not know that they are infected. This would mean saving lives by earlier diagnosis and treatment before the illness advances and becomes more difficult to treat [34]. According to the New York City Health Commisssioner

Dr. Thomas R. Frieden, "The more people who know their status, the fewer infections you're going to get. They're spreading HIV when they wouldn't if they knew" [35].

Which brings us to the future. At the close of the XVI International AIDS Conference (Toronto, Canada, Aug. 13–18, 2006), WHO Acting Director General Anders Nordstrom told the attendees that "This conference has highlighted the importance of an even strongerr focus on women and young people over the world who bear the greatest burden and need particular attention." He concluded by urging the international participants to consider that "we need to invest more in developing new preventive tools, including microbiocides and of course vaccines," but for him, "the most important area to ensure success in achieving universal access, is a skilled and motivated workforce. No improvement in financing or medical products can make a lasting difference to people's lives until the crisis in the health workforce is solved. WHO's "Treat, Train, Retain" plan directly addresses the need for a healthy, skilled, and motivated workforce" [36]. The battle against HIV/AIDS may have begun in earnest—again.

It has become clear that the battle against HIV/AIDS cannot be won by chemical bullets alone, and surely not for years to come. Political correctness has no place in the AIDS equation. Silence is tantamount to death. Ergo, speaking up about this grievous illness that can be readily prevented is long past due. It is time for the country's communications media to take up the issue and challenge of behavior change. If behavior change is the preferred and productive approach for heart disease and cancer, why not HIV/AIDs?

LONGEVITY AND MORTALITY

Life Expectancy

Yet another set of numbers bring a salutary message that can't but elicit delight and satisfaction.

From the National Office of Health Statistics [37], we learn that a person born in 1950 could, on average, be expected to live for 68.2 years. By 1990, life expectancy had climbed to 75.4 years. It is worth recalling that the biblical injunction of "threescore and ten," 70 years, had been attained and passed in 1969. The U.S. Bureau of the Census recently informed us that life expectancy is at an all-time high—77.8 years. Again we want to recall that when FDR signed the Social Security Act of August 14, 1935, few people were expected to make it to 65 when retirement checks would become available. With life expectancy pressing 80, is it any wonder that the country is seeking new ways to ensure that everyone will not only receive their retirement benefits at age 65 but will continue to do so for as long as they live. In 1935, no one would have imagined that most of us would retire in good health and live another 10–30 years. Currently, 12.3% of our population is 65 and older, and that is

TABLE 1.4. Life Expectancy; Gender and Race, United States, 2002

Life expectancy overall	77.3
Female	79.9
Male	74.5
White female	80.3
Black female	75.6
White male	75.1
Black male	68.8

expected to exceed 20% by 2035—when one in every five individuals will be 65 plus. We are indeed experiencing the graying of America. But we are also experiencing great increases in longevity. Between 1950 and 2002, we have gained 9.1 additional years—a stunning 12%. And since 1900, when life expectancy stood at 47 years, the gain has been a bountiful gift of 30+ years—three additional decades! The gains are not universally equal because of gender and racial differences, as we have seen do make a difference, as Table 1.4 shows. Nevertheless, an unprecedented increase in life expectancy has occurred among all segments of our population [13]. However, a note of caution and concern must be injected here. Recently published data indicate that the 77.3 or 78.2 of obesity-related deaths were not the growing problem that they currently are [38]. Obesity deaths, and their prodigious contribution to heart disease, cancer, stroke, and kidney-related deaths has markedly depressed life expectancy. Dr. S. Jay Olshansky, the study's lead author, remarked that the study's projections were "very conservative, and the negative effect is probably greater than we have shown." Obesity shall not go unmentioned. We shall pick it up shortly.

Although we are seeing more gray than ever, the most portentous statistic may just be the proportion of elderly reporting no disabilities. Close to 80% are disability-free, and many are continuing to work—full and part time [39]. Why not? Their experience and judgment serve us well. Cause of elation? You betcha.

Infant Mortality

The National Center for Health Statistics is chock-a-block with good news these days [13]. Having given us upbeat news about longevity and the oldest among us, they come now with lofty data about the youngest. A backward glance at the numbers for 1900 yields the baleful detail that for every 1000 live births, 100 infants died before their first birthday. By 1950, that abysmal statistic had plunged to 28, and the infant mortality rate (IMR) for 2000 was 6.9. What adjective shall we choose to describe this unimaginable reduction? Is "spectacular" overblown?

TABLE 1.5. Infant Mortality Rates per 1000 Live Births, United States, 2002

Race and Gender	Rate
All races, both sexes	6.9
White	5.7
Black	13.5
American Indian	8.3
White female	5.1
Black female	12.1
White male	6.2
Black male	14.8
American Indian male	9.9
American Indian female	6.7

Whenever the subject of the United States IMR is broached, Sweden, Japan, and Norway are trotted out front and center as the class acts of infant survival. True, 6.9 is well above Sweden's 3.0, but 6.9 may be all the more remarkable given the polyglot nature of our country's population. No country in the world has our diversity. Every race, religion, culture, and economic level is represented, and all manner of health/cultural practices arrive with the immigrants. To compare the United States with homogeneous native Swedes or Japanese is to compare apples with onions. Sweden—with a mite over 8 million people, half that of New York State, and 99% white, Lutheran, and highly literate, living in three major population centers, within hailing distance of one another—is both an invidious and ludicrous exercise. Only a glance at Table 1.4 is needed to realize why such comparisons are odious. No other country has our mix of people. These numbers represent a uniquely American experience. No other country, surely neither Japan nor Sweden, has the contrasts evident in Tables 1.4 and 1.5, which must distort the overall IMR. Let us look deeper. Table 1.6 depicts the IMRs for the 10 highest and 10 lowest states. The disparities stand revealed ever more starkly. Clearly, we see a north/south dichotomy. The fact that the District of Columbia, cheek by jowl at the center of political power, has the nation's highest IMR, as well as one of the highest in the Western world, is at once stunning and depressing. Neither Sweden nor Japan has such an enclave. Is it really possible to compare overall rates with such striking national differences? But that is not all. Teasing out additional details provides as with Table 1.7, and yet additional discomfort, as the disparities simply leap off the page. Even among the southern states, the contrasts are awesome. Income levels below the poverty line, high teenage pregnancy rates (accompanied by late or nonexistent prenatal care), and difficult and premature labor with resulting low-weight infants are good and sufficient reasons for the higher rates. Nevertheless, and all the inequalities notwithstanding, and with the stark differences between white and black, we still have

TABLE 1.6. States with the Highest and Lowest Infant Mortallty Rates per 1000 Live Births, 2002

States with the Lowest Rates	
Massachusetts	5.1
Maine	5.3
New Hampshire	5.3
Washington	5.4
Utah	5.4
California	5.5
Oregon	5.5
Minnesota	5.9
Texas	6.0
Iowa	6.2
States with the Highest Rates	
Georgia	8.3
Arkansas	8.4
Tennessee	8.4
North Carolina	9.0
Louisiana	9.1
South Carolina	9.5
Alabama	9.8
Mississippi	10.3
District of Columbia	13.5
Puerto Rico	10.2

TABLE 1.7. IMR's By Gender for Ten Northern and Southern States

State	White	Black
Massachusetts	4.5	9.9
New Jersey	4.9	13.3
Maryland	5.3	13.9
Virginia	5.6	12.5
Wisconsin	5.8	16.7
Iowa	5.8	17.2
Georgia	5.9	13.4
South Carolina	6.3	15.6
Illinois	6.3	17.1
Michigan	6.4	16.4

achieved a single-digit IMR, which must be seen as a triumph of public health. Media take notice.

Furthermore, the precipitous decline from 29.2 in 1950 to the current 6.9 should suggest that "the environment" is not the "ticking bomb" that the spinners have led so many of us to believe it is.

With life expectancy rising to unprecedented levels, and with infant mortality rates falling and substantially decreasing heart disease and cancer rates, is it reasonable to believe that our ambient environment is toxic to children and other growing things? The media have been making much of very little, and not nearly enough of the public's general good health. Why have they not spread the good news of what must be one of the most successful and beneficial accomplishments of the twentieth century—accomplishments that surely blunt the assumption of an environment harmful to our well-being? Overzealous environmentalists have wrought nothing but fear. It's time to repair the damage and realize that we are a healthy people, who will become healthier still as we reduce trauma, and lessen racial and gender disparities. Given the extensive documented data, fear of the environment is unwarranted.

CANCER

It is now altogether fitting and proper that we attend to cancer, which in the hierarchy of mortality is the uncontested occupant of second place. It has been set apart as the very word strikes fear, and for over the past 30 years the so-called war on cancer, initiated by President Richard Nixon, has not been won, and continues unabated. However, new knowledge of the malignant process is beginning to turn the tide of battle. That horizon is coming into view. But let us first consider cancer and its nature.

At the outset, two portentous questions require consideration. Is there a cancer epidemic abroad in the land, as some would have us believe, and, are cancer numbers, cases, and deaths all soaring?

The Chinese scholar who said a good picture is worth 10,000 words, would be pleased with Figures 1.2 and 1.3, which convey literally gobs of information. In seven distinct trendlines, representing major cancer sites, Figure 1.2 conveys the cancer death rates for men over the 72 years 1930–2001. Of the seven major sites, lung cancer makes the most powerful statement. Not only did it rocket upward between 1940 to a peak in 1990, taking many lives with it, but also clearly evident is its decline since 1990. Antismoking campaigns can take well-deserved credit. The stomach cancer trendline tells another wonderful story. If there is a cancer epidemic across the country, stomach cancer surely hasn't contributed, as it has been dropping steadily for 70 years; by 2000 it had the lowest death rates of the seven trendlines. Colorectal cancer, holding steady for 30 years between 1950 and 1980, has also been declining. After a 5-year blip upward, when new screening tests for prostate cancer appeared, it, too, has declined steadily. Hepatic and pancreatic cancers and leukemia have held steady at 5–10 deaths per 100,000 (people) over the past 70 years.

The scenario is much the same for women. From Figure 1.3, we learn that lung cancer is the leading cause of cancer deaths, and still rising. But stomach, uterine, breast, and colorectal cancers have declined sharply, while ovarian and

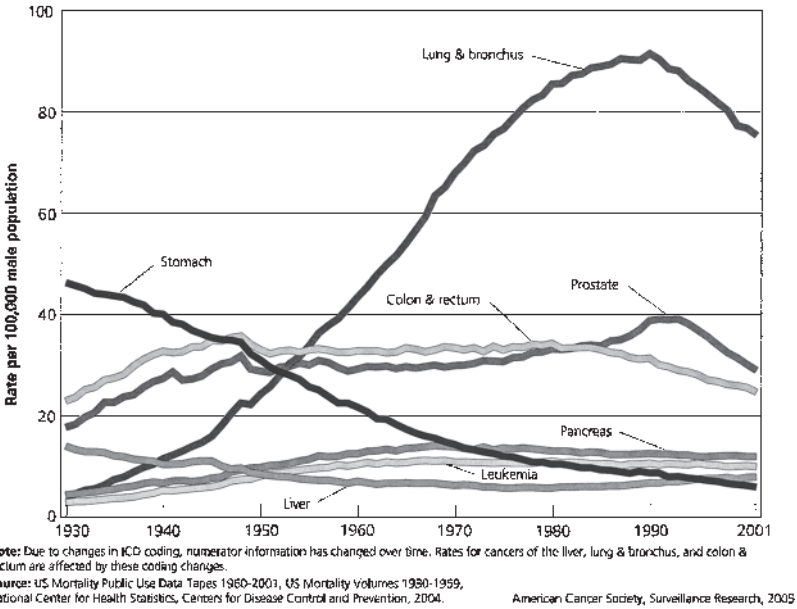


Figure 1.2. Age-adjusted cancer death rates (per 100,000 people, age-adjusted to the 2000 US standard population), males by site, United States, 1930–2001.

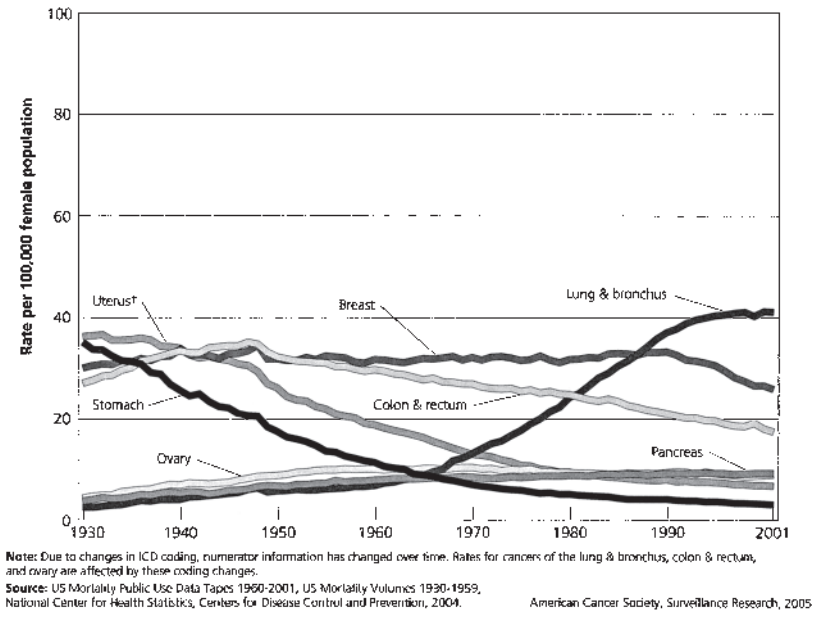


Figure 1.3. Age-adjusted cancer death rates (per 100,000 people, age-adjusted to the 2000 US standard population), females by site, United States, 1930–2001. Uterine cancer death rates are for uterine cervix and uterine corpus combined.

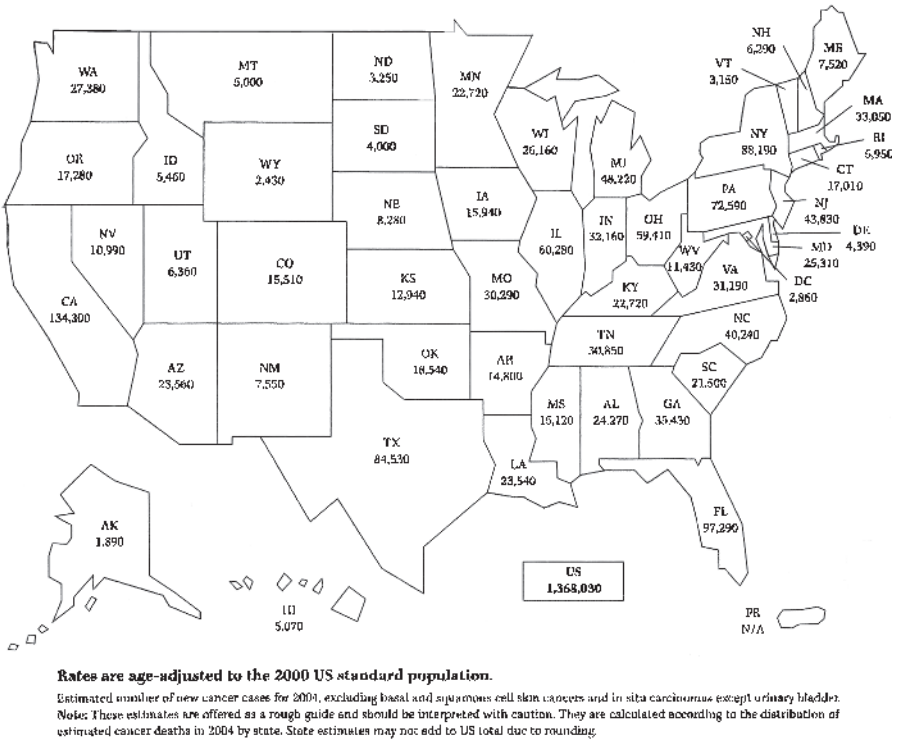
pancreatic cancers have resisted change over 70 years. The answer to the first question seems self-evident. If a cancer epidemic is among us, it is limited to lung cancer in women. We will deal with this shortly. But what is an "epidemic" of any illness or condition? Simply stated, it is a sudden outbreak of an illness above the expected number. Yes, every disease has an expected number of new cases or deaths for each week and month of the year. Should that number be exceeded, it is understood to be of epidemic proportions. Obviously with cancer deaths there have been no sudden increases, and other than lung cancer deaths in women there has been no unusual increase in numbers.

Considering the sweep of time from 1930 to 2001, there appears to be yet another story behind the numbers. Prior to World War II, and well into the 1960s, the United States could be described only as an agriculturally based society. The unprecedented shift to an industrial society, and a giant one at that, was yet to occur. That remarkable shift has occurred over the past 45 years. Yet in these undeniably different environments, most cancer rates have either declined or remained steady. The only soaring cancer rate in sight has been that for lung cancer for both men and women—the result primarily of cigarette smoke.

As for numbers, what we've been experiencing is a statistical artifact—an all-boats-rising phenomenon. Lung cancer is not only the leading cause of cancer deaths; its exceptionally high numbers absolutely skews the rates for all cancer sites combined—an excellent reason for not combining them. This skewing distorts the data and misleads interpretation by falsely implying that cancers of all sites are rising. Can numbers mislead? Indeed, they can. In fact, since 1993, death rates have decreased 1.1% per year—1.5% for men and 0.5% for women—and, perhaps most significantly, from 1950 to 2004, with lung cancer excluded from the total, the combined cancer death rate has dropped by 18%! That's the message the American public should have received, but didn't. That's the message that requires national dissemination—a message that will help dissipate the widespread pall of fear, while bringing a message of hope.

The media totally missed the boat on this. They preferred to trumpet the overall increased rate, rather than explain the distorting effects of lung cancer on the combined rate. Readers, viewers, and listeners are not being served. The media appears to have lost touch with the public. Issues such as this are not of the complexity of the Patriot Act, Social Security reform, or free trade, requiring journalists to have in-depth knowledge of the subject in order to provide the public with comprehensible accounting. By comparison, the facts of life and death, the numbers, are both simple and direct.

Much of the discussion has focused on rates because rates bring unique insights and provide a firm basis for comparing populations, especially populations of diverse sizes. Figure 1.4 shows the estimated number of new cases of cancer for 2004, for each of the 50 states. Glancing east to west, west to east, north to south, or south to north, we see that California with 134,000 new cases is far and away the highest. At the opposite coast is Vermont, with some 3000



Rates are age-adjusted to the 2000 US standard population.

Estimated number of new cancer cases for 2004, excluding basal and squamous cell skin cancers and in situ carcinomas except urinary bladder. Note: These estimates are offered as a rough guide and should be interpreted with caution. They are calculated according to the distribution of estimated cancer deaths in 2004 by state. State estimates may not add to US total due to rounding.

Figure 1.4. Cancer deaths by state. (Figure courtesy of the American Cancer Society.)

cases. Should you be looking for a place to drop anchor, Vermont seems a better bet than California. But is it? Table 1.8 compares five states with the highest number of cancer cases with five of the lowest. But now the populations of all states need to be introduced, and the rates per 1000 population calculated. Without rates per thousand, California appears cancer-prone. But Florida, New York, Pennsylvania, and Illinois (see Fig. 1.4) are not that far behind, and suggest avoidance compared to North Dakota, Idaho, and Montana. By considering their populations, and calculating rates per thousand, a much different picture emerges. California, with 134,000 new cases, is in fact the state with the lowest new-case rate, and Vermont, with 45 times fewer new cases, does in fact have a far higher case rate than does California. So, do you still prefer Vermont to California for setting down roots? California, with the nation's largest population, would be expected to have far more cases of anything simply because of its larger numbers. In order to appropriately compare California with 50 times the population of Vermont, calculating rates per 1000 provides a reasonable basis for comparison and interpretation.

Yet another concern about cancer is its predilection for the elderly. Indeed, as Figure 1.5 so clearly represents, cancer death rates soar with advancing age. Although cancer can occur at any age, it is primarily a disease of the elderly.

TABLE 1.8. Estimated Cancer Incidence, United States, 2004

Five Highest States	
California	134,300
Florida	97,290
New York	88,190
Texas	84,530
Illinois	60,280
Five Lowest States	
Alaska	1,890
Wyoming	2,340
Vermont	3,140
South Dakota	4,000
Delaware	4,390

Source: Cancer Facts and Figures, American Cancer Society, 2004.

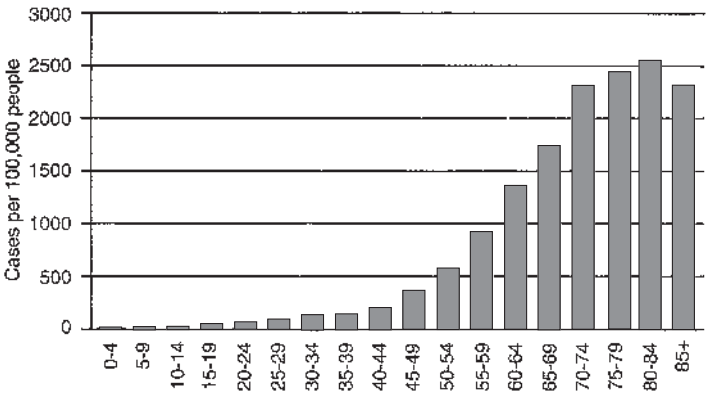


Figure 1.5. Cancer cases by age in the United States. (*Source*: `http://seer.cancer.gov`.)

As indicated in Figure 1.5, the numbers rise after age 40, and began their steep ascent to the 80s, then decline as the number of available folks over 85 disappear, and cancer along with them. One explanation for the fact that cancer occurs more frequently at the older ages may be that for a tumor to develop, cells must accumulate gene alterations, (mutations), which can occur with each cell division and thus accumulate with advancing age. Before raising the question "Why cancer?" a brief discussion of its nature will buttress our perceptions.

Cancer is a group of diseases. More than 100 types are well documented, each with a distinct character and a different trigger. Ergo, lumping them

together gains no understanding, nor does it serve any useful purpose other than gathering numbers. The only commonality among these diseases is that the abnormal cells that they produce have no intention of slowing their runaway division.

Tumors are classified as benign or malignant. Benign tumors are not cancer, and do not spread or metastasize to a new site. They are just lumps. A malignant tumor can and often does enter the bloodstream or lymphatic system to be carried to a site far removed from its original site. Most tumors are named for the organ or cell type in which they began their uncontrolled growth, such as stomach, lung, liver, and breast. Others, such as melanoma, are not as clear. Melanoma is a cancer of melanocytes that produce blue-purple pigments. Melanomas often develop on the skin or in the eyes. Leukemias are cancers of blood cells, and lymphomas are tumors of the lymphatic system.

Around the country, the most common cancers are carcinomas, cancers that develop in the epithelial tissue lining the surfaces of the lung, liver, skin, or breast. Another group of cancers are the sarcomas, which arise in bone, cartilage, fat, connective tissue, and muscle. No tissue or organ has a free pass. Any can become cancerous. And then there is the question "Why?" Why does cancer occur?

We humans have 44 autosomal chromosomes in 22 corresponding pairs. One of each pair is contributed by each parent—which differ in their gene content. In addition to these 22 pairs, normal human cells contain a pair of sex chromosomes. Women carry a pair of X chromosomes, men have an X and a Y, for a total of 23 pairs and 46 chromosomes. A chromosome consists of the body's genetic material, the DNA (deoxyribonucleic acid), along with numbers of other proteins. Within each chromosome, DNA is tightly coiled around these proteins, allowing huge DNA molecules to occupy a tiny space within the cells nucleus. Figure 1.6 shows the tightly coiled DNA strands, which carry the instructions for making proteins. Each chromosome is divided into two segments or "arms"—the short or "p" arm (from the French *petit*, meaning small) and the "q" or long arm. The symbol "q" was chosen simply because it followed "p" in the alphabet and is below the "p" arm The sections are linked at the centromere, the junction where the chromosome attaches during cell division.

Genes are the subunits of DNA. A single chromosome can contain hundreds of protein-encoding genes. Chromosome 16 has 880 genes, including those implicated in breast and prostatic cancers, Crohn's disease, and adult polycystic disease. Chromosome 19, has over 1400 genes, including those that code for cardiovascular disease, insulin-dependent diabetes, and migraines. Cells containing an abnormal number of chromosomes are called *aneuploidic*. It is now evident that cancer cells have either gained or lost entire chromosomes. This loss or gain—this instability, this mutation in chromosome number—can result in cancer. Indeed, the destabilization of a cell's genome is known to initiate cancer. But most cancers are not hereditary, which doesn't end the search for other causes. So, for example, it is also

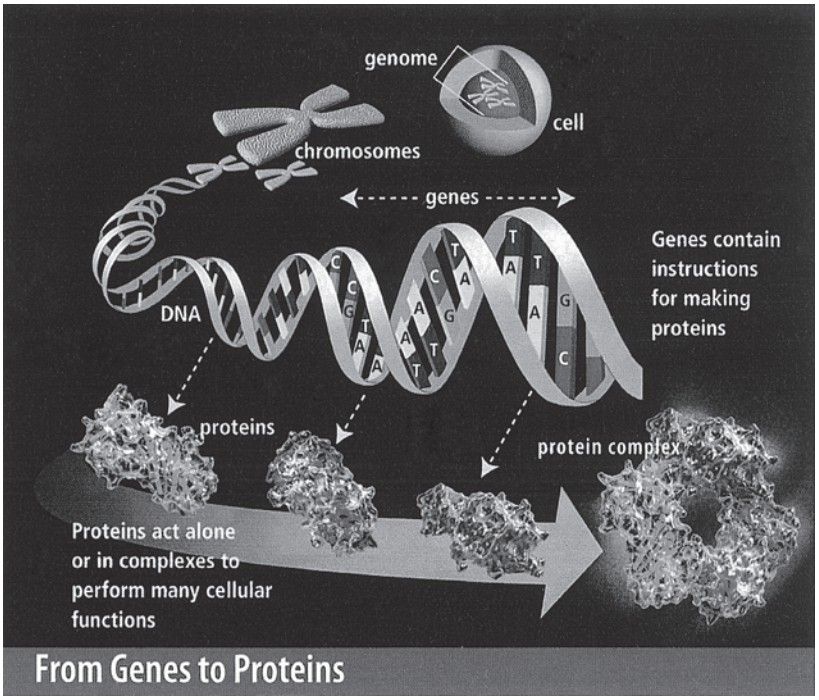


Figure 1.6. The tightly coiled strands of DNA that carry the instructions allowing cells to make proteins are packaged in chromosomal units. (Figure adapted from *Cancer and the Environment*, National Cancer Institute, publication 03-2039.)

known that alterations in oncogenes, can, as shown in Figure 1.7, signal a cell to divide uncontrollably, rather than repair the DNA or eliminate the injured cell.

One of the cell's main defenses against uncontrolled cell growth is the protein p53. Apparently cancer can occur only when the p53 protein, produced by the p53 gene, is damaged. As p53 may be the key that unlocks the riddle of cancer, we shall consider p53.

According to David Lane [40], director of a cancer research group at the University of Dundee, Scotland, and discoverer of p53 in 1979, p53 may just be "The most important molecule in cancer." He believes, as others now do, that faults in this protein or the processes that it oversees may be the cause of all tumors. Lane also gave the chemical its name: "p" for protein and 53 for its molecular weight of 53,000. It is because of p53's presence and vigilance that cancer is so rare [40]. Who would believe that cancer is rare? In his brief and comely book, *One Renegade Cell*, Robert A. Weinberg, director of MIT's Whitehead Institute, asserts that "One fatal malignancy per hundred million billion cell divisions does not seem so bad at all" [41]. He's not saying that anyone's tumor is okay; rather, he's making the momentous point that with

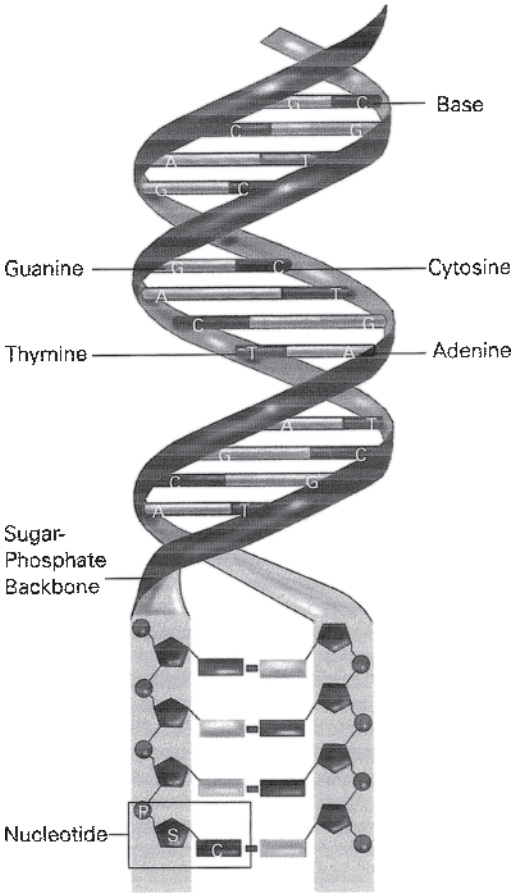


Figure 1.7. DNA—the molecule of life. In double-stranded DNA, the strands are wound about one another in the form of a double helix (spiral) and held together by hydrogen bonds between complementary purine and pyramidine bases. (Figure adapted from *Genetic Basics*, National Cancer Institute, publication 01-662.)

the body's astronomical number of cells (75–100 trillion) and the ongoing addition of new cells as we live and grow, it is simply remarkable how few cancers actually develop. Given the tremendous number of cells available, one can only gasp and wonder at the incredible fact that we do not get cancer soon after we're born. The stark fact is that youngsters with Li-Fraumeni syndrome, a condition caused by inherited mutations, are prone to develop cancer as young as 2 or 3 years. However, this is an extremely rare condition. It is also known that cancer-associated viruses produce proteins that can shut down p53, leaving cells defenseless.

p53 keeps the process of cell division in check by suppressing cancerous growth. p53 was, and still is, a tumor suppressor gene (TSG). When it was

added to cells in culture, those that contained genetic errors made cells cancerous. The normal p53s suppressed cell division. But this protein, which could suppress tumor development, was also the target of cancer-causing viruses and, curiously enough, was found to be mutated in about half of all tumors. It is also odd to find that virologists investigating these unimaginable intracellular events talk of a protein molecule with "godlike properties deciding whether individual cells should live or die." How does this play out? If a cell becomes damaged beyond repair, p53 will force it to self-destruct. Cell suicide or programmed cell death is referred to as *apoptosis* (from the Greek, a "falling off," as leaves from trees) a normal process in which cells perish in a controlled manner. This ability to cause cells to self-destruct is p53's way of protecting us against runaway cell division.

As noted earlier, DNA damage destabilizes genes, promoting mutations. Collections of proteins are constantly traversing genes checking for faulty bases. As shown in Figure 1.6, DNA consists of long, spiral helices—twisted chains—made up of nucleotides. The order of these bases along a strand of DNA is the genome sequence. Each nucleotide contains a single base, one phosphate molecule, and the sugar molecule deoxyribose. The nitrogenous bases in DNA are adenine, thymine, cytosine, and guanine. All instructions in the coded book of life, telling cells what to do, are "written" in an alphabet of just four letters—A, T, C, and G. These bases are strung together in literally billions of ways, which means that billions of coded instructions can be sent to cells. Consider, then, if billions of coded instructions are possible, doesn't this help explain how a single faulty instruction is not only possible but also inevitable? Only a single mutation in the enzyme tyrosinase, an enzyme involved in cat coat color, gives the Siamese cat its dark ears, face, paws, and tail.

So genes do their work by stimulating chemical activity within cells. How? Via proteins, the large complex molecules that require folding into intricate three-dimensional shapes before they can work correctly and provide another possible source of error. (This protein folding ability and requirement will loom large in Chapter 2, during the discussion of several diseases).

These proteins twist and buckle, and only when they settle into their final shape do they become active. Because proteins have many diverse roles, they come in many shapes and sizes. Proteins consist of chains of 20 interlinked amino acids. These chains contain 50–5000 of the 20 amino acids, each with its own amino acid sequence. It is in this sequence that yet additional trouble brews, as an error in just a single amino acid can spell disease. An error, or mutation, can result in an incorrect amino acid at one position in the molecule. So, collections of proteins are searching for faulty bases or breaks in the double helix. If found, they signal p53, which springs into action with an electrifying effect—slamming the brakes on cell division, allowing DNA repair to proceed. As David Lane makes clear, "p53 has earned the title, guardian of the genome." Nevertheless, it can and does malfunction. A variety of triggers can do it. Cigarette smoke and ultraviolet light, among other factors, can damage p53 by

twisting the protein out of shape so that it cannot function correctly. Current research seeks to discover ways of blocking the processes that break down p53, or restoring its shape and thereby its function.

An approach taken by a Chinese biotech company was to use gene therapy—adding back normal p53 via injection of viruses primed to reinsert the healthy gene. When combined with radiotherapy, the gene treatment actually eliminated tumors in a number of patients with head and neck tumors, an authentic and epoch-making achievement. Indeed, the creativity of current research is itself mind-boggling. For example, another route of manipulating faulty p53, should its shape be the problem, like humpty-dumpty, it can be brought back together again [42]. Once p53's power source is revealed, there is every reason to believe that cancer will become little more than a chronic illness. The new approaches, based on intimate knowledge of cell mechanisms, will no longer be a one-size-fits-all, shotgun approach, but more akin to a single bullet fired at a specific cellular element. Consequently, I find it quite reasonable to believe that in the fullness of time, 5–7 years down the road, it will have been worked out, incredible as it sounds.

As if this were not sufficiently exciting, recent research at Baylor College of Medicine, in Houston, by Dr. Lawrence A. Donehower and his team, has taken p53 to new heights [43].

In 2002, the Princes of Serendip passed through Houston. As a consequence of a failed experiment, instead of making a protein that Donehower's group wanted, the mice were making tiny fragments of p53. They noticed, too, that the mice were unusually small and were aging prematurely, getting old before their time. As if that weren't startling enough, these mice appeared to be almost cancer-free—highly unusual for mice. As it turned out, the mouse cells contained an unusually high level of p53, which was vigorously suppressing tumors. Dr. Donehower had some 200 mice that were at once innately protected against cancer, but growing old and decrepit well before their time. A reviewer commenting on the Donehower publication in the journal *Nature* said that the condition of the mice "raise[s] the shocking possibility that aging may be a side effect of the natural safeguards that protect us from cancer" [44]. The possibility was suggested that the Baylor mice with extra p53 may be aging prematurely because too many cells are becoming apoptotic and their tissues cannot function properly. These mice do force the issue as to whether human longevity can be increased? In addition to this issue, there is wonderment as to why we can't maintain p53's cancer-fighting potency and also forestall the aging process. A double whammy if ever there was one. So there appears to be a gene that can limit cancer and accelerate aging. Is aging the price to be paid for a cancer-free life?

Can the next development be the outrageous possibility of manipulating p53 to control both cancer and aging? Are we not living in the best of times? In the most exciting time. We need only live long enough to see this all bear fruit. Just down the road, previously inconceivable cancer therapies are being developed. Truly, the tide is running with us. Stay tuned.

TABLE 1.9. Probability (Chance) of Developing Breast Cancer by Specific Ages among US Women

By Age	1 in
15	763,328
20	76,899
30	2,128
45	101
50	53
60	22
70	13
80	9.1
90	7.8

Source: Ries, L. A. G., Eisner, M. P., Kosary, C. L., eds, *SEER Cancer Statistics Review, 1975–2002,* National Cancer Institute, Bethesda, MD, 2005.

Breast cancer in women (men are not immune) is the most frequently diagnosed nonskin cancer. Some 216,000 new cases were estimated to have occurred in 2004. The risks of being diagnosed with breast cancer increases with age, and the risk increases steadily by decade as shown in Table 1.9. Unfortunately the media also got that one wrong. Recent headlines across the country trumpeted the news: "Cancer now the top killer of Americans" and "Cancer passes heart disease as top killer." The implication is that the war on cancer was lost. What the media so glaringly failed to acknowledge, or failed to understand, was that in their most recent annual report (2005), but whose data were limited to those of 2002, the authors extracted deaths by age, which they had never done before [45]. In doing so, they found that although death rates from all cancer sites combined have been falling steadily since 1993 (by 1.1% per year), the rate of death from heart disease, as shown in Figure 1.8, has been declining since the mid-1970s. Nevertheless, in 1999, for those people under age 85, who constitute 85% of the country's population, cancer deaths surpassed heart disease only because heart disease continued its unflagging descent [45]. As for breast cancer (and here the confusion mounts), another severely abused number is the often cited statistic that over a women's lifetime, the risk (the chance, the odds) of her getting breast cancer, on average, is one in eight, or about 13%. Far too many believe that this number is a woman's current risk. No. The risk involved is in fact a woman's lifetime risk, at age 85, and it works this way. If eight women are followed for their entire lives, one of them, on average, is likely to develop breast cancer. Also recall that with a 1 in 8 chance of developing breast cancer, there remain 7 in 8 chances that it will not occur. Again, as we've seen, cancer is a disease of advancing age, and breast cancer is strongly age-related, as Table 1.7 shows. At age 35, as noted in the table, it is 1 in 99, and at age 45 it is 1 in 101, or a 1% chance of developing breast cancer. Perhaps

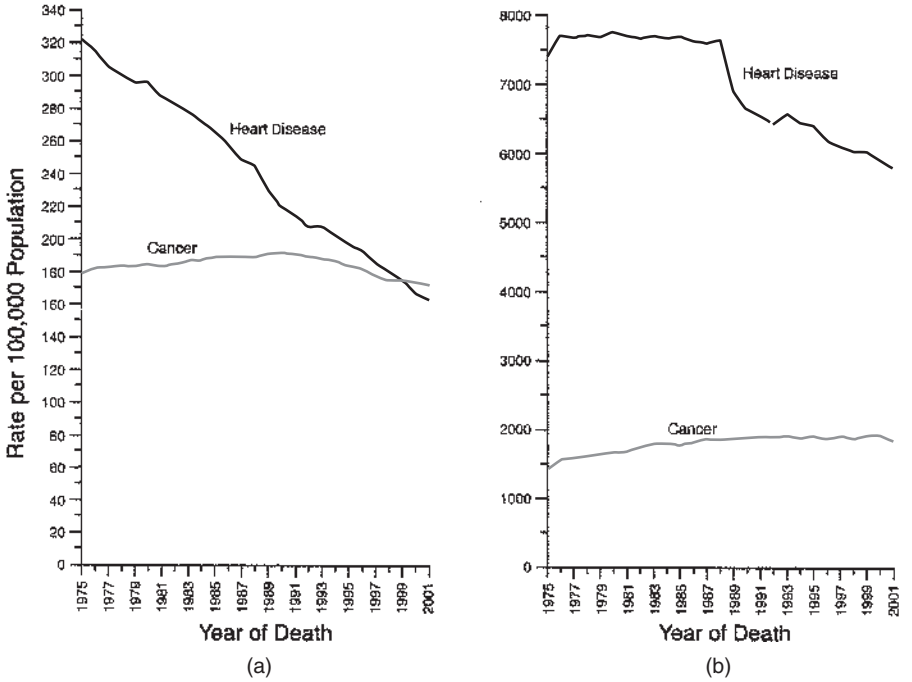


Figure 1.8. Cancer and heart disease death rates (age-adjusted to 2000 US standard population) for individuals younger than (a) and older than (b) age 85. (Figure adapted from American Cancer Society, *CA: A Cancer Journal for Clinicians*.)

more importantly, it is essential to recall that not all women live on to the older ages when breast cancer risk becomes greatest [46].

Much has been made of the fact there are inherited breast cancer susceptibility genes—BRCA1 and BRCA2. But these are responsible for no more than 1 in 10 cases of the disease. Yes, 9 out of 10 cases are not inherited. Of additional importance is yet another number: 0.2% the number of women in the United States whose BRCA genes have mutated. These numbers offer a good deal more than cold comfort.

Furthermore, breast cancer activists have consistently flailed their physical environment as the carcinogenic trigger(s) for breast cancer. One of the most politically active areas has been Long Island, New York, where, as in other areas of the country, breast cancer is commonly reported. In 1993, concerned residents got their Congressional representative to push for legislation requiring epidemiologists to investigate a possible environmental carcinogen/breast cancer link. After a decade of study, the Long Island Breast Cancer Study Project (LIBCSP) began publishing its findings. Among the possible carcinogens under their purview were the polycyclic aromatic hydrocarbons (PAHs). Although the PAHs are potent mammary carcinogens in rodents, their effect on development of human female breast cancer has been equivo-

cal. The LIBCSP wanted to determine whether currently measurable PAH damage to DNA increases breast cancer risk. PAHs are byproducts of the combustion of fossil fuels, cigarette smoke, and grilling of foods and are found in smoked foods. As PAHs can be stored in fatty breast tissue, they were deemed a realistic candidate. The study did not find a relationship between PAH blood levels and exposure to smoked or grilled foods or cigarette smoke, and "no trend in risk was observed" [47]. In addition to PAH, the project studied the relationship between breast cancer and organochlorine pesticide blood levels [48]. Again, no dose–response relationship was uncovered. Nor could they find any support for the hypothesis that organochlorines increase breast cancer risk among the Long Island women.

In another venue, researchers at Maastricht University, in the Netherlands examined the relationship between stressful life events and breast cancer risk [49]. They reported no support for stressful life events and risk of breast cancer.

Although we are most assuredly in an age of breast cancer awareness and breast cancer studies, thus far environmentally related breast cancer carcinogens remain to be discovered. The question at issue is whether heightened awareness and fear are desirable motivators for increasing screening behavior. Clearly the issue is debatable. But overemphasis on breast cancer may well be responsible for inattention to other illnesses. In fact, both heart disease and lung cancer carry greater risks and are greater killers of women than is breast cancer. Shocking though it may be, women worried about breast cancer continue to smoke. According to Dr. Barbara Rimer, Director of the Division of Cancer Control and Population Science at the National Cancer Institute, " We see smokers who are very, very worried about breast cancer, and yet they're continuing to smoke. They have a much better chance of getting and dying of lung cancer than breast cancer, but many women underestimate their chances of getting lung cancer" [50].

Lung cancer is the world's number 1 cancer killer. In the United States, close to 100,000 men and women died of it in 2005. Cigarette smoke is the primary risk. However, another glance at Figures 1.2 and 1.3 shows that men have heeded the antismoking message and their declines in lung cancer deaths are striking whereas women have yet to respond to the messages. Despite the many warnings about the malign affects of smoke, fully 25% continue to do so. Women, especially young women, are the preferred target of cigarette advertisements. And they respond. As many as 20% smoke during their pregnancies. Are they really unaware of the deleterious effects of smoke on the developing fetus? Activists ought to zero in on this curious behavior.

Women and smoking, another cautionary tale that went by the boards, is being given short schrift by the media. However, several of Dr. David Satcher's numbers are devastating. To wit:

- An estimated 27,000+ more women died of lung cancer than breast cancer in 2000.

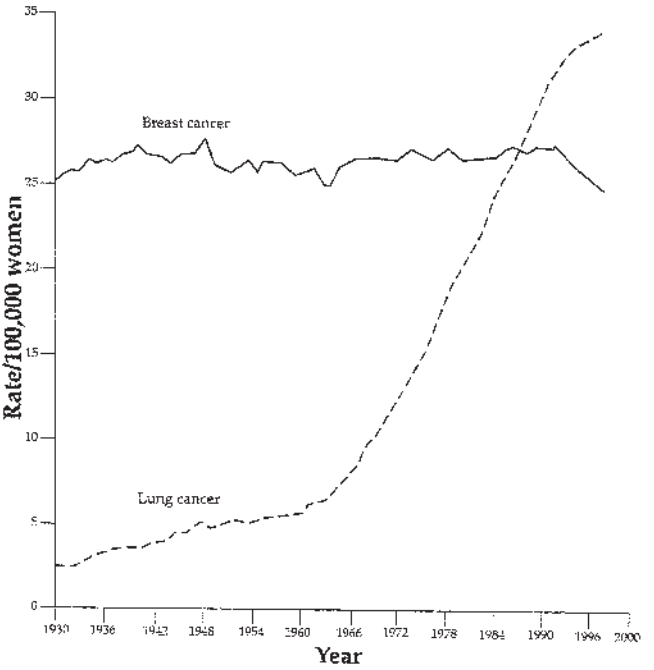


Figure 1.9. Age-adjusted death rates for lung cancer and breast cancer among women, United States, 1930–1997.

- Three million women have died prematurely because of smoking since 1980, and on average, these women died 14 years prematurely.
- For a never-to-be forgotten comparison the US Surgeon General has given us Figure 1.9, for which discussion may even be unnecessary [8].

It has been proposed that there is a higher rate of a specific mutation in the p53 gene in women's lung tumors compared to men. Perhaps. It has also been postulated that women may have a reduced capacity for DNA repair. There is, of course, much yet to be learned. Nevertheless, being female appears to be a factor for extended survival in lung cancer patients. What is not moot is that consequential differences do exist between men and women with lung cancer. Women who have never smoked are more likely to develop lung cancer than are men who have never smoked [51]. The "why" of this and other differences has researchers around the world scurrying for answers. That a number will be found in genes specific to men and in genes specific to women is emerging as a sure bet.

Even though colorectal cancer deaths have been declining over the past 50 years, over 150,000 deaths were expected to occur in 2004. Here again, the primary risk factor is age. Other proposed risks include smoking, alcohol consumption, obesity, and diets high in fat and/or red meats. On the other hand, frequent coffee consumption has been associated with reduced risk of color-

ectal cancer. Bear that word association in mind. We shall consider this possibility in some depth further along, as it can be easily misinterpreted.

Recently, researchers at Harvard University's School of Public Health probed the relationship between coffee, tea, and caffeine consumption and the incidence (new cases) of colorectal cancer [52]. Using data from the well-established Nurses' Health Study and the Health Professionals' follow-up study (physicians), which together provided 2 million person-years of follow-up and 1438 cases of colorectal cancer. They found that "regular consumption of caffeinated coffee or tea or total caffeine intake was not associated with a reduced incidence of colon and rectal tumors." But they did find that decaffeinated coffee did appear to reduce the incidence of these cancers, but also injected the caveat that this association requires confirmation by other studies. It's a start. Advertising by the tea and coffee producers, especially tea (particularly green tea), would have us believe that these are health-promoting beverages. Would that this were true. We shall see.

Cancer Disparities

In 1991, Dr. Samuel Broder, then Director of the National Cancer Institutes, remarked that "Poverty was a carcinogen" [53]. This suggested an interaction between economic and sociocultural factors that could influence human health. It was his contention that poor and medically underserved communities are at higher risk of developing cancer and have less chance of early diagnosis, treatment, and survival. In 2003 the Institute of Medicine (IOM) published a review describing the disparities that can arise from the interplay between economic and sociocultural factors. For the IOM, poverty was the critical factor affecting health and longevity [54].

As we have seen, African Americans have the highest death rate from all cancer sites combined, as well as cancers of the lung, colon, prostate, female breast, and uterine cervix. For all cancer sites combined, male mortality in 1999 was 13% higher in poorer compared to more affluent counties. Similarly, in the poorer counties there was a 22% higher death rate from prostate cancer.

The prevalence of underlying risk factors for some cancers differs among racial and ethnic groups. The higher rates of stomach cancer among Hispanics (Latinos) and Asian Americans reflects in part the higher rates of *Helicobacter pylori* infections in recent immigrants. Similarly, higher rates of liver cancer are found among Hispanics and Asian Americans, who have a higher prevalence of chronic hepatitis infections [55].

Ethnic differences clearly shows itself among eastern European Jewish families who have an almost exclusive susceptibility to Tay–Sachs disease as well as an inordinately high risk of Gaucher's disease, both of which are the product of mutated genes.

The gap we have seen in black life expectancy compared to that of whites is now believed to be due to the higher rates of heart disease, stroke, kidney disease, and hypertension, the consequence of a genetic predisposition to salt

sensitivity—a racial characteristic. Individuals with a higher capacity for salt retention may also retain more water and would tend to be hypertensive (having abnormally high pressure exerted on artery walls), which favors heart disease, stroke, and kidney dysfunction. So, in addition to economic and sociocultural disparities, racial and ethnic differences are at play in cancer and other morbid conditions [5, 6, 56].

How are these disparities to be dealt with? Can they be dealt with? In principle, equal application of existing knowledge about cancer prevention, early detection, and treatment for all segments of the population should substantially reduce these disparities. However, this will require substantial revisions in our healthcare delivery system, which is not known for flexibility. On the other hand, the growing knowledge and acceptance of the idea of racial differences may be a more efficacious stimulus for change, and achieve greater benefits.

OBESITY

"Persons who are naturally fat are apt to die earlier than those who are slender." Hippocrates (circa 460 BCE) was not a man of few words. His many comments have stood the test of time. This quotation is hoary with age, having been written 2500 years ago, and should remind us that fatness is not a new medical concern. What is new is the realization that obesity is a worldwide phenomenon and the consequence of genetic susceptibility, too readily available high-energy foods, and greatly decreased physical activity: a morbid triad [57].

Obesity, unlike AIDS, not only is not on our list of leading causes of death; it is not even in the vicinity of the list. Obesity requires our attention and concern because of its deadly contribution to heart disease, at the top of the charts; to cancer, our second leading cause; to diabetes, the seventh; to hypertension, the fifteenth; to sleep-breathing disorders; and osteoarthritis of large and small joints, and we know, as did Hippocrates, that obesity is inversely related to longevity [57].

Obesity can no longer be regarded as a cosmetic problem, but must be seen as a new pandemic that threatens worldwide well-being. What is obesity? For an answer, dictionaries are to no avail as they speak only of excess weight. Obesity goes beyond excess weight, which raises a second question: How fat is too fat? For Peter Paul Rubens (1577–1640), the great Flemish painter, there was no "too fat." Rubens was the master of rotund femininity. As shown in Figure 1.10, the fatter, the healthier, the more beautiful. But that was then. Today, obesity is our number 1 malnutrition problem, and a major contributor to numerous deaths. It has replaced under nutrition and infectious disease as the most significant contribution to poor health [58].

For adults, *overweight* is defined in terms of body mass index (BMI) and calculated as weight in kilograms [2.2 lb (pounds)], divided by the square of

Figure 1.10. *Bacchus*, by Peter Paul Rubens, 1577–1640.

height in meters, is 25 (55 lb over the ideal weight), and obesity entails a BMI of 30, while extreme obesity is BMI 40 or higher. (To calculate your BMI, multiply your weight in pounds by 700, then divide by your height in inches, and repeat that a second time.) Using these numbers, the prevalence of obesity among adults in the United States is understood to be approximately 30.5% of the total population. For children 2–5 years old, it is approximately 10%, and for those 12–19, it is approximately 22% [59]. Paradoxically, these numbers have markedly increased over the past 30 years, during a time of unimaginable preoccupation with diet(s) and weight control. We Americans spent $46 billion on weight loss products and services in 2004. Unfortunately it is now seen that dieting is either ineffective or counterproductive. Those overweight or obese children must not be given short shrift—not taken lightly. The consequences can be enormous. As noted earlier, type 2 diabetes, closely linked to excess weight, is being diagnosed in such high numbers that it can no longer be referred to as "adult-onset diabetes." But that is not the worst of it. In the recent eye-opening report on obesity, Dr. David Ludwig, Director of the Obesity Program at Children's Hospital, Boston, revealed a threat thus far unmentioned. He warned that the current obesity epidemic has had little public impact, "but when these youngsters start developing heart attacks, stroke, kidney failure, amputations, blindness and ultimately death at younger

and younger ages, that will have a huge effect on life expectancy." This is not something we want to look forward to. Obesity appears to be the result of multiple causes: genetic, environmental, and psychosocial factors acting synergistically with energy intake and expenditure. Obesity is consistently found in single-gene disorders such as Prader–Willi syndrome (PWS), with its upper body obesity (due to uncontrolled appetite), short stature, mental retardation, hypotonia, and hypogonadism. As for an environmental component, "predictions about possible interactions between genes and the environment are difficult because there may be a delay in an individual's exposure to an 'obesogenic' environment, and/or alteration in life style related to living circumstances and uncertainty about the precise timing of the onset of weight gain" [58]. Not so uncertain is the energy intake/expenditure component. Pima Indians of the American Southwest, with a common genetic heritage to Pimas in Mexico, are an average 50 lb or more heavier than those in Mexico. A similar trend is seen with Nigerians living in the United States, who are obese compared to Nigerians in Africa; the former are also twice as likely to exhibit hypertension [58]. Migrants coming into a new culture pick up the habits of the majority culture and soon reflect their medical problems.

As noted earlier, obesity is a significant public health problem given its substantial contribution to morbidity and mortality, but the health risk could be significantly reduced even with modest weight loss. The peptide hormone leptin, which appears to hold the key to weight loss or gain, is produced by adipose tissue, and a decrease in body fat decreases the amount leptin, which triggers food intake; the reverse is also true. More leptin, less food intake. Clearly, leptin and the brain are in this together. When the system works properly, there is maintenance of weight within a narrow range [60]. This raises yet another question. Why are some of us obese and others not? Although not yet fully crystalized, it appears that obese individuals are leptin-resistant. How to modulate this is a high-priority research activity. Furthermore, clarification of the mechanisms and pathways that control food intake and energy homeostasis are of central and crucial importance, and its neurological and hormonal complexity do not suggest a short timeline. However, the enormous cost to human health attributable to obesity is the engine that will drive basic research, leading ultimately to successful medical treatment, and that includes genetic repair, if need be.

THE ENVIRONMENT? WHAT ENVIRONMENT?

We have traveled far and widely, considering and exploring the greatest threats to our well-being. We have seen, too, that we are healthier than ever before. Nevertheless, the threats are there and will remain, but in ever decreasing numbers if we seriously attend to them. To do so, to take appropriate preventive measures, we need to return to the question posed at the outset: Which,

if any, of the adverse conditions that threaten our lives can be attributed to the ambient environment, and what do we mean by "environment"? As we journey into the twenty-first century, is there agreement on the meaning of this word? This is not an idle question, but has profound meaning for our well-being. Consequently it is necessary that it be widely understood.

As has been indicated, the trick of life is to maintain a balance between normal cell division and runaway, uncontrolled growth. For oncogenes to take over, to be turned on, a switch is needed. For the past 30 years, and for far too many people, that switch was the environment.

Misinterpretation and misrepresentation, whether accidental or purposeful, lead directly to misinformation and misunderstanding. This quartet has given "environment" a bad rap, as in "environmental pollution," "tainted environment," "contaminated environment," and "environmental risk." Unrelenting misrepresentation over the past 30 years of "environmental risk factors" has made many of us fear the world. Air, water, food, and soil are seen as polluted and responsible for whatever ails us and as our causes of death.

A 30-year stranglehold on American minds presents some diffiiculties for extirpating this "cancer" on the body politic. But eliminate it we must, if prevention is to work. Misinterpreting what environmental risks are has a long tradition. As far back as 1964, the World Health Organization (WHO) issued its report declaring that the common fatal cancers occur in large part as a result of lifestyle and are preventable. Here are its words [61]:

> The potential scope of cancer prevention is limited by the proportion of human cancers in which extrinsic factors are responsible. These factors include all environmental carcinogens, whether identified or not, as well as modifying factors that favor neoplasia of apparently intrinis origin (e.g., hormonal imbalance, dietary deficiencies, and metabolic defects). The categories of cancer that are influenced by extrinsic factors including many tumors of the skin and mouth, the respiratory, gastro-intestinal, and urinary tracts, hormone-dependent organs (such as the breast, thyroid, and uterus), haematopoietic and lymphopoietic systems, all of which, collectively, account for more than three-quarters of human cancers. It would seem, therefore, that the majority of human cancer is potentially preventable.

From a cursory reading it is evident that the misinterpretation occurred in the United States, where "extrinsic factors" was deleted and "environmental factors" was substituted. And if that wasn't slippage enough, "environmental factors" was translated once again, becoming "man-made [anthropogenic; synthetic] chemicals," which was never WHO's intent. Extrinsic factors are synonymous with lifestyle, our behavior, or what we choose or don't choose to do. Because many people prefer blaming everyone but themselves, it is under-

standable that few complained of the transformation of the English language as it moved from Europe to the United States.

At a conference in Canada in 1969, John Higgenson, founding director of the International Agency for Research on Cancer, a WHO affiliate, stated that 60–90% of all cancers were environmentally induced. That remark was to haunt him and the world for decades. He had no inkling that his use of "the environment" would be so bent out of shape. The floodgates opened wide. Soaring cancer rates could hereafter be attributed to a polluted environment.

In 1979, Higgenson was interviewed by an editor of the journal *Science* to further clarify his 60–90% attribution, and to deal with the seemingly intractable fact that so many Americans "believe that cancer-causing agents lurk in everything we eat, drink, and breathe." That such a perception is wrong is evident from Higgenson's responses. He began by noting, "A lot of confusion has arisen in later days because most people have not gone back to the early literature, but have used the word environment purely to mean chemicals." Further along in the interview, he declared that "Environment thus became identified only with industrial chemicals." Then he said, "There's one other thing I should say that has led to the association of the term environment with chemical carcinogens. The ecological movement, I suspect, found the extreme view convenient because of the fear of cancer. If they could possibly make people believe that pollution was going to result in cancer, this would enable them to facilitate the cleanup of water, of the air, or whatever it was"—a remark not calculated to win friends or attract converts. "I think," he continued, "that many people had a gut feeling that pollution ought to cause cancer. They found it hard to accept that general air pollution, smoking factory chimneys, and the like are not the major causes of cancer" [62]. For all the good it did, that interview might well have never occurred. Dynamic denial, on the hand, and the power of the media to shape opinion prevailed, on the other hand, and this false thesis persists. The media and environmentalists are determined to hold their ill-gotten ground, no matter how wrong the association. But the facts will emerge!

In their now classic publication, "The causes of cancer: Quantitative estimates of avoidable risks of cancer in the U.S. today" [63] ("today" being 1981), Doll and Peto placed numbers and percentages on 12 categories of potential risk factors. Their list, shown in Table 1.10, is worth contemplating.

For Doll and Peto, tobacco and diet were so intimately tied to cancer deaths that their estimates of their importance, their contribution to the disease, ranged from 55% to 100%. The uncertainty factor was apparent, but for them this dynamic duo were cancer risks. At the opposite end of the risk spectrum was pollution, to which they assigned a value of less than 1. Recalling that these estimates were made at the beginning of the 1980s, it is reasonable to ask whether they have withstood the test of time.

A research team of Harvard University's School of Public Health took up the challenge, and in 1996 produced its own estimates (Table 1.11). This list has a familiar look.

TABLE 1.10. Proportions of Cancer Death Attributed to Different Risk Factors, 1981

	Percent of All Cancer Deaths	
	Best Estimate	Range of Acceptable Estimate
Tobacco	30	25–40
Alcohol	3	2–4
Diet	35	10–70
Food additives	<1	<0.5–2
Reproductive and sexual behaviors	7	1–13
Occupation	4	2–8
Pollution	2	<1–5
Medicines and medical products	1	0.5–3
Industrial products	>1	<1–2
Infections	10?	1–?

Source: Ref. 63.

TABLE 1.11. Proportions of Cancer Deaths Attributed to Different Risk Factors, 1996

Cancer Risk Factor	Percent Contribution
Tobacco	30
Diet	30
Hardcore[a]	25
Alcohol	3
Microbial (viral, bacterial)	1–2
Pollution	1–2

[a] "Hardcore" are those cancers that would develop even in a world free of external influences simply because of the production of carcinogens within the body, and the occurrence of unrepaired genetic mistakes.
Source: Ref. 64.

The Harvard list echoes Doll and Peto. Tobacco, diet, infectious agents, and sexual behavior are the primary culprits, while pollution, food additives, and ionizing radiation contribute little if anything to cancer risk or death [64]. Any contribution by the ambient environment must be too small to be measured, and thus is of little or no consequence to our health. They also show that the public has overestimated the risk posed by low levels of radiation, obviously encouraged by the constancy of the media and environmentalist mantra. An objective observer could be forgiven her or his lack of comprehension, wondering out loud how it is possible that misunderstanding of "environment" and its risks has become so entrenched.

Yet another Harvard group, this one from the Department of Medicine, and the School of Public Health, has taken up the cudgel. The researchers intro-

duced their recent study on environmental risk factors and female breast cancer with this caveat [65]:

> It is unfortunate that there is confusion as to what constitutes an environmental exposure. Epidemiologists often label as "environment" any risk factor that is not genetic, including diet, body size, exogenous estrogen use, reproductive factors, and medical treatment. Using this definition, most breast cancer is thought to be due to "environment," as only a small proportion is due to inherited mutations in breast cancer susceptibility genes. The general public, however, often interprets this as evidence that much of breast cancer is due to "environmental" pollution. In this review we restrict the definition of environmental exposures to those which a person experinces passively, due to pollution or other charactreristics of the outside world.

Their study, reported in 1998, concerned the possible risk of breast cancer from exposure to ambient environmental chlorinated hydrocarbons (pesticides), ionizing and electromagnetic radiation, and passive cigarette smoke. And their findings? "Based on current evidence, with the exception of ionizing radiation, no environment exposures can be confidently labeled as a cause of breast cancer." The echoes grow louder. But where are the media? Shouldn't women have gotten this information? Shouldn't everyone know this? This predated the Long Island Breast Cancer Project's reports, which obtained similar results, and has received the same silent treatment.

The leading causes of death have been stable for at least 25 years; heart disease, cancer, and stroke have occupied the top three positions, and suicide, homicide, cirrhosis, diabetes, and accidents switch a position or two every so often. Even Inspector Clouseau would look askance on the ambient environment as the source of these conditions. The assault on the environment, which in fact was an assault on us all, was entirely misplaced and unjustified. Neither evidence nor proof supported such a claim, but there was ever-mounting evidence for the lifestyle and behavior paradigm. What will it take to convince and unshackle the American mind?

If better health for all were in fact the nation's goal, the first priority would be modification of our self-destructive behavior. The environment, as commonly understood, does require vigilance, but for reasons other than human health. We have been flailing at windmills that pose minuscule risk and consume our energy, time, and taxes, whereas the major risks, the real killers, languish for lack of individual and institutional concern and support. If we clasped the lifestyle model to our breasts, our country could follow a path to wholesale reductions in illness and death that no manner of medical intervention could ever hope to match. If we are ready to strike out on the veritable road to personal well-being, it is essential to deal with the enemy within.

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