

# CHAPTER 1



## *Introduction*

WE CAN CHOOSE no more appropriate people to introduce *Medical Botany* than Native North Americans (Fig. 1-1). They have long been in harmony and partnership with the elements of our natural world, having used them to survive and to embellish their well-being for centuries. We chose the natives of our continent for still another reason, however: Today we are seeing an important revitalization of interest in situ in their ancient traditions of religion, in their language, and in other aspects of their culture. The young are now aflame with newly developed pride in their heritage, while the elderly are encouraged that after more than a century of indifference to the Native American lifestyle, art, and science, we may be reversing some of the unfortunate attitudes found in the white population, as well as among Native Americans themselves. For all to understand the depth of indigenous use of flora, there now exists the extraordinary catalog *Native American Ethnobotany*, which summarizes this ethnomedical plant wealth in the United States (including Hawaii) and Canada.<sup>1</sup>

For centuries Native Americans and other indigenous peoples worldwide have perpetuated an empirical science of traditional (or folk) medicine.<sup>2</sup> Their traditional healing programs, which may also encompass spiritual and sometimes mythical roles, are often elaborate and lengthy. Apprentices of Navajo healers, for example, learn to use medicinally nearly 200 plants, often applying them for both physical and mental afflictions. In Mexico, the Maya have multifaceted healers. The best known (the h-men) are those who

combine herbal healing with religious aspects; others are midwives, hierbateros (specialists in medicinal plants), and sobadores (giving massages), all using medicinal plants extensively. When conventional (Western, allopathic) health care is available, most Maya prefer treatment by their own healers.<sup>3</sup> Traditional Maori healers of New Zealand have a diagnostic approach similar to that used in conventional medicine, in addition to a spiritual dimension.<sup>4</sup> Knowledge of Samoan herbalists is impressive, with a typical healer able to identify and use medicinally between 100 and 200 species. That know-how involves how to administer the plant, determine dosage, intervene therapeutically during the course of the disease, and advise the patient on dietary taboos.<sup>5</sup> These few examples of traditional medicine in practice can be repeated hundreds of times throughout the world. However, the loss of language and knowledge due to acculturation and plant and habitat destruction is a major concern, particularly among the smaller and more vulnerable tribes near outside influences. However, those traditional systems with long histories of use buffered by having major geographic areas, many users, and trained practitioners are functioning well, as in China and India.

Traditional medicinal techniques in China uniquely involve herbal medicine, acupuncture, and moxa counterirritants. According to legend, Shen Nong, living about 2000 B.C., and considered by many the father of Chinese medicine, was responsible for compiling the first great herbal of 365 drugs and their properties.<sup>6,7</sup> Among the phytomedicinals he is



FIGURE 1-1. Native North Americans: approximate original localities of representative tribes discussed throughout *Medical Botany*.

reputed to have discovered, or used from those known earlier, were ephedra (*Ephedra sinica*), rhubarb (*Rheum*), ginseng (*Panax ginseng*), and cassia bark (*Cinnamomum aromaticum*). In 1083 the *Classified Pharmaceutical Natural History* (*Chêng Lei Pên Tschao*) was published<sup>8</sup> with an excellent likeness of *Ephedra sinica* (ma huang),<sup>9</sup> followed in 1596 by *The Great Pharmacopoeia or The Pandects of Natural History*.<sup>10</sup> The last extraordinary compendium took Li Shih-Chen about 50 years to complete. He included thou-

sands of species from China and abroad, with their uses, pharmacology, and botany. He was not only a consummate physician but a researcher who conducted his own fieldwork in most provinces of China in search and use of medicinal plants. Following the Communist Revolution of 1949, Mao's new directive was to "unite all medical workers, young and old, of traditional and Western schools, and organize a solid united front to strive for the development of people's health work."<sup>6</sup> Today, traditional Chinese medicine

(TCM) is being integrated by varying degrees with conventional medicine, each playing an important role in the Chinese health care system. For instance, in Shenyang (northern China), 80% of Western-trained doctors use TCM to treat patients or they refer patients to TCM specialists.<sup>11</sup>

According to Tang and Leung,<sup>12</sup> the mechanism-centered approach has dominated research and development of TCM in the past 50 years. They state that researchers are preoccupied primarily with the search for molecular, cellular, and pharmacological bases of TCM, with identification of relevant active substances and investigation into the mechanism of individual therapies being uppermost. The question of efficacy has largely been neglected. To many supporters of TCM, the long history of use, tradition, faith, and anecdotal reports are still considered the best evidence for the efficacy of TCM interventions. Tang and Leung's paradigm would represent a middle ground: demonstration of clinical efficacy of material used in TCM in randomized controlled clinical trials as used in conventional medicine, with concomitant toxicity testing in vitro and in vivo and surveillance of harmful effects. If efficacy trials were deemed significant and their potential for use outweighed any toxicity, post-marketing surveillance of long-term, rare adverse events (phase 4 trials) could be studied concurrently with the identification of active substances and the understanding of mechanisms of action. This approach could apply to all herbal traditional medicines being used successfully in systems worldwide.

There has been a recent resurgence in the use of Kampo traditional medicine in Japan, a system long based on introductions of Chinese traditional medicines. Certain Kampo preparations are licensed and approved for health care insurance. In the last decade, these traditional drug sales reached \$56 billion annually.<sup>13</sup>

Not necessarily in harmony, but often in conflict, are the medical practices in the second most populous nation, India, and in much of the Asian subcontinent. Here, ancient practices known as Ayurvedic (Hindu) and Unani (Muslim) medicines do not receive the same treatment in relation to conventional medicine as they do in China. By and large, conventionally trained physicians ignore the practices and teachings of those in traditional medicines, which are neverthe-

less preferred by the population as a whole. On the other hand, Ayurvedic practitioners have been remiss in standardizing their plant drugs so that proper standards in Ayurvedic formulations can be evolved.<sup>14</sup> Moreover, those practicing Ayurveda need to explore new avenues of research and be more open to change and innovation occurring in their culture.<sup>14</sup> Like TCM, Ayurvedic and Unani medicines emphasize body (soma) and psyche as a whole, applying knowledge accumulated over thousands of years of practice. That knowledge concerning drugs and their formulations of plant origin are provided in two recent publications.<sup>14,15</sup>

Although Egyptian medicine dates from at least 3000 B.C., the best known and most important pharmaceutical record is the *Papyrus Ebers* of 1550 B.C., although its content is undoubtedly much older. For example, on discussing the use of *Ricinus* (castor oil), it was said to be "found in old writings," and a hair remedy prescription is said originally to have been prepared for Shesh, the mother of King Teti, who belonged to the VI Dynasty (ca. 2500 B.C.).<sup>16</sup> *Papyrus Ebers* consists, for the greater part, of recipes against various diseases and symptoms, and of those medicines used, an imposing quantity mentioned were taken from plants, animals, and minerals. *Ricinus communis* (castor oil) seeds, Euphorbiaceae, *Citrullus colocynthis* (colocynth, bitter apple), Cucurbitaceae, and *Senna alexandrina* (senna Fabaceae) were used as cathartics, *Punica granatum* (pomegranate) roots (Punicaceae) were taken against intestinal worms, and tannin-containing plants were used as astringents. The best evidence of the quality of ancient Egyptian remedies is that many have survived for millennia—directly to the writings of the great first-century A.D. Greek physician and pharmacologist Dioscorides, and from him to the twenty-first century. Writings of the Greeks, such as Hippocrates (460–377 B.C.) and Galen (A.D. 131–200), are also reminiscent of parts of the *Papyrus Ebers*. "Thus we see that Greek medicine is by no means original, but has taken over very much from Egyptian medicine and can only be looked upon as a further development of the latter. There is, accordingly, every reason to believe that the [Western] science of medicine has its origin in the Nile Valley."<sup>16</sup>

Egyptian–Grecian medicine was kept alive by Avicenna (Ibn Sina), a tenth- to eleventh-century Persian

pharmacist and physician. He wrote in Arabic, his definitive medical work, *Canon Medicinae*, regarded as the final codification of all Egyptian–Grecian–Arabic medicine, accepted as authoritative in the West until the seventeenth century, and still dominant in western Asia.<sup>7</sup>

## PLANTS IN MEDICINE

“Nature has been a source of medicinal agents for thousands of years, and an impressive number of modern drugs have been isolated from natural sources, many based on their use in traditional medicine.”<sup>17</sup> These plant-based traditional medicine systems continue to play an essential role in health care, with about 80% of the world’s inhabitants relying mainly on traditional medicines for their primary health care.<sup>18</sup> Plant products also have an important role in the health care systems of the remaining 20%, who reside in developed countries. About 25% of prescription drugs dispensed from community pharmacies in the United States from 1959 to 1980 contained plant extracts or active principles derived from higher plants. At least 119 chemical substances derived from 90 plant species are important drugs currently in use. Of these 119 drugs, 74% were discovered as a result of research directed at the isolation of active compounds from plants used in traditional medicine.<sup>18</sup> Based on 1991 sales, half of the leading pharmaceuticals were either derived from natural products or contained a pharmacophore that was based on natural products.<sup>19</sup> In 1993, 57% of the top 150 brand-name products prescribed contained at least one major active compound, or were derived or patterned after compounds, reflecting biological diversity.<sup>20</sup>

Many researchers have discussed the importance of medicinal plants as sources of new therapeutic agents,<sup>17,21</sup> and others have effectively focused on the potential of specific chemical classes (e.g., alkaloids)<sup>22</sup> in drug discovery. Recent research continues to validate an ethnobotanically targeted approach to the initial discovery of pharmaceuticals.<sup>23,24</sup> Still others estimate that of about 375 total drugs of pharmaceutical significance in the rain forests of the world, only one-eighth have been discovered. Taken together, they could generate a total value of \$147 billion.<sup>25</sup>

Assessing the worth to humanity of drugs already known and used might be even more relevant. This story begins in 1630, when Peruvian indigenous people (probably Inca or Aguaruna) generously provided Spanish interlopers with their intellectual knowledge of a bark that could treat “intermittent fever” or malaria. Subsequently, *Cinchona* bark has been used since the seventeenth century. In 1820, when Caventou and Pelletier identified its active alkaloid quinine, and later quinidine, along with their analogs, isomers, semisynthetics, and synthetics to treat malaria, heart conditions, and other ailments, sales escalated. World-wide use of these drugs against malaria and arrhythmia generated untold wealth, relieved much suffering, and saved millions of lives. Further, use of the anti-malarial drugs led to the successful habitation of vast areas of tropical to warm temperate regions, making possible new opportunities for progress and riches. Sales of these drugs to the present time amount to an astounding net figure in the tens, if not hundreds, of billions of dollars.

## Medical Ethnobotany

Indigenous peoples use a wide range of plants therapeutically to maintain their health. There is great promise for new drug discoveries based on traditional plant uses.<sup>24,26,27</sup> To be allowed to use this knowledge, researchers must recognize that both intangible resources (knowledge) and tangible resources (genetic material) are being provided. In 1992, the United Nations Convention on Biological Diversity confirmed the rights of source nations over the genetic materials found within their boundaries. That convention also required that local and indigenous knowledge, practices, and innovations be protected and recognized.<sup>28</sup>

Before conducting ethnobotanical research, it is essential to obtain agreements among all parties, addressing prior informed consent, confidentiality, ownership of intellectual property and tangible biological materials, collecting area scope, conservation of medicinal plants and habitats, responsibilities of parties, benefit sharing, compensation due parties at all stages of research, development, and commercialization, and supplier of materials. Appropriate models exist for guidance in developing collaborative agreements, so that the discovery of new natural products

and therapeutics in consort with indigenous and other peoples may proceed.<sup>23,24,27,28,29</sup>

## REVIEW OF CHAPTERS AND PARTS

### Chapter 2: Complementary and Alternative Medicine

About 80% of health care worldwide is delivered by complementary or alternative practices. Although most medicine practiced in the United States is conventional, more than 40% of Americans use some form of complementary and alternative medicine (CAM). In this chapter we describe types of CAM, risk-benefit profiles, interactions, standardization, and regulation of herbal therapies. CAM is here to stay, and conventional medicine and CAM are beginning to work together to provide an integrated health care system to the benefit of all.

### Part I: Injurious Plants

There is no doubt that of all products harmful to people, those of plant origin are important to everyday life, whether one lives in an urban or rural area in a developed country or in a developing nation. Hundreds of plants are known to be injurious if ingested and are capable of causing any number of symptoms, even death (Chapter 3). People in rural settings, of course, are exposed to such organisms every day, but even those in more urban areas must be wary of garden plants introduced from all parts of the world. Houseplants often are poisonous, and children are attracted to the colorful parts of these otherwise harmless organisms in our midst. Few realize, for example, that apple seeds contain cyanide, which may be lethal in large doses; that the alkaloid taxine from the common bedding plant English yew is absorbed rapidly and causes sudden death; that the leaves and twigs of boxwood, so common as a hedging plant, produce another alkaloid, buxine, which contributes to respiratory failure in humans and domestic animals; that children using peashooters made of elderberry stems may be poisoned from exposure to this plant's alkaloids and cyanide; and that the eating of green and

sprouting parts of potatoes may cause poisoning. Similarly, common houseplants such as oleanders, caladiums, and philodendrons must be avoided, for a person ingesting the leaves of oleander, or its sweet nectar, may develop severe vomiting, irregular heartbeat, and respiratory paralysis, followed by death.

Plants have the ability to affect the immune system in ways that are beneficial or deleterious (Chapter 4). *Echinacea* as an immune modifier is the most popular herbal medicine for the treatment of colds and upper respiratory infections. A number of phytochemicals (castanospermine, calanolides, prostratin) are potentially useful in the treatment of human autoimmune deficiency syndrome (AIDS). Cell modifiers of plants that act as mutagens, teratogens, lectins, or mitogens are described. Antimutagenic compounds have important potential roles in cancer chemoprevention.

One out of five, or about 50 million Americans, suffers from an allergic disease (Chapter 5). Two important diseases, hay fever (allergic rhinitis) and asthma, result when atopic (hereditary predisposition to allergy) individuals are sensitized to allergens after repeated exposure. Grasses, trees, weeds, and fungi in our environment produce abundant pollen, spores, and other allergens which lead to allergy that may become severe or life-threatening. A major new source of pollen allergens from *Parthenium hysterophorus* in the southern United States has been shown to cause widespread immediate hypersensitivity. Poison ivy, oak, and sumac exposures lead to contact dermatitis in about 70% of the population, requiring constant vigilance to avoid exposure when outdoors.

### Part II: Remedial Plants

Of the plants found to have remedial properties, none are more welcomed than those that help in the fight against cancer (Chapter 6). How many thousands of lives have been saved or extended by the antineoplastic agents of microorganisms and by the alkaloids vincristine and vinblastine of the Madagascan periwinkle? The dramatic results of using these compounds in combination chemotherapy for treating Hodgkin's disease (80% remission), acute lymphocytic leukemia (99% remission), Wilms' tumor (80% cured), Burkitt's lymphoma (50% cured), and gestational choriocarci-

noma (70% cured) are testimonials to the gigantic strides achieved in using plant products against the most terrifying of all disease complexes. Indeed, the greatest advancement in cancer therapeutics in the last quarter of a century has been the incorporation of compounds and analogs isolated from plants sources and their semisynthetic derivatives.

Almost as valuable to the surgeon as the knife are the curare plants (arrow poisons of South American Indians), which reversibly paralyze skeletal muscles and thus when used as an anesthetic make the surgical process more effective (Chapter 7). Under the skeleton, bone health and injury and degenerative processes are described, the latter including bone fractures, bone repair and regeneration, bone density, slipped disk and lower back pain, dislocated and sore joints, and rheumatism, arthritis, and osteoarthritis. The second part of the functional unit is the muscle, consisting of cardiac, smooth, and skeletal muscles, the latter provided with therapeutics, nutraceuticals, and herbals to facilitate relaxation, pain and swelling, sprain, and muscle mass.

Many plant products affect the peripheral nervous system, and we, like our forefathers, constantly take advantage of developing therapies that either dull or excite the system (Chapter 8). Throughout north temperate America and Eurasia, our ancestors used willows and poplars, which contain an aspirinlike compound, to relieve fever and pain. Eventually, we learned that opium alkaloids also relieve pain, and morphine became the all-important analgesic in conventional medicine.

Our greatest killer is heart disease (Chapter 9), but where would we be if the useful properties of foxglove had not been known empirically in European traditional medicine and then “discovered” by a very astute botanist–physician several centuries ago? The answer is obvious, since 3 million or more Americans daily take compounds from this plant or synthetic compounds modeled on the originals to prolong their lives. Without foxglove, or other plant-producing cardiotonic compounds, congestive heart failure followed by death would occur inevitably for many, but not as quickly for most. High blood pressure was also a quick killer. Before 1950, the inflexible fate of those with this disease was a stroke, heart failure, or kidney failure. With the introduction of *Rauwolfia*, long used in Ayurvedic traditional medicine of India (dating from about

600 B.C.), and the isolation of reserpine, the first hypotensive agent and tranquilizer were born. Eventually, even better compounds were developed to treat both heart disease and hypertension, but without the reserpine model such developments may never have occurred, or at least not as rapidly as they did.

Fundamental to life itself is the ability to metabolize foods into energy (Chapter 10). The selection of appropriate nutrients is essential to a healthy lifestyle. Concerns regarding obesity and diabetes are on the rise, and aspects of these metabolic disorders and the means to control them are discussed. Also discussed are inherent hyperlipidemias and other lipid disorders and the uric acid disease, gout.

The treatment of glaucoma with alkaloids from the calabar bean (*Physostigma*) of Nigeria, or leaves of Brazilian species of *Pilocarpus*, can prevent blindness (Chapter 11). These compounds relieve the pressure within the eye by acting on neural receptor sites in that organ.

The oral cavity is of constant concern (Chapter 12). When oral disease relates to tooth decay and gum disorders, one might well wonder whether preventive dentistry has been adequate, especially when the teeth of the indigenous peoples of western Africa and southern Asia are essentially free of caries. Numerous studies have shown that their cleaning implements—nature’s toothbrush, the chewing stick—contain a number of anticariogenic principles. Fluoride can be found in many of these plants, in addition to anticariogenic beverages such as *Camellia sinensis* teas. Moreover, many plants used to ameliorate gum disease or to treat other oral infections are known to contain styptic tannins, as well as antiinflammatory, antibiotic, and other healing substances. Fundamental to much of this research is the observation that plants favored for these purposes are proving to be the most beneficial. Such studies, which are still evolving, may reveal new substances that could be used by all to promote dental health.

A bewildering array of efficacious plant extracts appears to be available for the alleviation of most symptoms involving the gastrointestinal tract (Chapter 13). Countless plants known to indigenous medicine are used for indigestion and stimulation of digestion, as gastric antacids, antispasmodics, antiemetics and antinausea, purgatives, antidiarrheals, anthelmintics/vermifuges, amebicides, and to treat liver complaints, ileitis and colitis, hemorrhoids, and flatu-

lence. Infectious diarrhea and peptic ulcers are also addressed. In some instances, commercial over-the-counter preparations are available from the same plants that indigenous peoples use.

Discussion of the respiratory tract (Chapter 14) includes treatment with bronchodilators (ephedrine, theophylline), expectorants and mucolytics (bromhexine), antitussives (codeine), bronchitis and asthma treatments, emphysema (theophylline), common cold and flulike treatments (*Echinacea*), adult respiratory distress syndrome (acetylcysteine, rutin), pleurisy, and tuberculosis and related symptoms. Infections of the upper respiratory tract are outlined, with treatments. The chapter concludes with a discussion of tobacco.

Plants have had no greater impact in recent years than in the area of producing the basic steroidal compounds for the efficient development of human sex hormones (Chapter 15). These products are now available cheaply for oral contraception and for treating menopause, improper menstruation, premenstrual tension, and testicular deficiency. Few realize the great contribution made by yams, for example, in stabilizing or decreasing the world population, but perhaps no postwar development has been so relevant in changing the lifestyle of those of reproductive age. Plants are implicated in most folk medicinal aspects of the urogenital system, but none are more extensive than those involved in sexual drive and performance. Perhaps hundreds of aphrodisiac substances are allegedly used by men of certain indigenous populations. Some are available commercially, such as the alkaloid yohimbine, from the bark of the African *Corynanthe*.

The skin is our largest organ (Chapter 16), and a great many herbs have cosmetic uses in perfumes, creams, salves, soaps, oils, and shampoos. Important are plants having properties to stop bleeding, to heal wounds and burns, and as topicals for treating infections, ulcers, eczema, and warts, obtained largely from traditional medicine.

Our defense against specific organisms is extremely relevant to human health, well-being, and often life (Chapter 17). The astonishing developments that have led to novel antiinfective agents, pesticides, antiseptics, and herbicides, often from plant or microbial sources, is testimony to human ingenuity during the twentieth century.

Of all of the panaceas, adaptogens, and tonics (Chapter 18), the "gold standard" is ginseng (*Panax*).

Chemistry, pharmacology, and research involving in vitro, in vivo, and clinical trials are summarized, together with *Eleutherococcus* and other plants. Standardization of ginseng as a dietary supplement and its market are described.

### Section 3: Psychoactive Plants

The central nervous system (CNS) and psychiatry (Chapter 19) involve normal and disturbed function and treatment, describing hypnotics and sedatives, analgesics, migraine, fever, seizure disorders, memory loss and cognitive function (*Ginkgo*), and motion sickness (*Zingiber*). CNS-associated diseases and treatment include hyperactive children; affective disorders, such as bipolar, schizophrenia, depression (*Hypericum*), and anxiety; and dementia, such as Alzheimer's disease (*Ginkgo*), Parkinson's disease, and choreas. The chapter concludes with a discussion of CNS infections.

Stimulants (Chapter 20), such as cocaine, khat, ephedra, amphetamines, and the stimulating beverages (coffee, tea, chocolate), all provide a sense of well-being and exhilaration, of self-confidence, and even power. They also alleviate fatigue and insomnia. In most, increased agitation, apprehension, and anxiety are the inevitable price of overindulgence.

Hallucinogens (Chapter 21) are unique compounds—in nontoxic doses they produce changes in perception, thought, and mood without causing major disturbances in the autonomic nervous system, yet the psychic changes they induce differ completely from ordinary experiences. Described are peyote, nutmeg, sacred mushrooms, snuffs (*Viola*), drinks (ayahuasca), lysergic acid derivatives, iboga, fly agaric, tropane alkaloids, and marijuana.

Depressants (Chapter 22) produce the effects of euphoria and well-being, beginning with sedation and followed by sleep, and ultimately death with high doses. Alcohol, barbiturates, tranquilizers, kava, and the opiates are all drugs of enormous value in medicine, but all are subject to abuse and addiction.

## LITERATURE OF TRADITIONAL AND HERBAL MEDICINE

Many texts and monographs have been studied carefully in selecting the examples of plants useful, harm-

ful, and enjoyable to humans. From these works we have gleaned what our forefathers learned the hard way and passed on to us. They performed experiments over thousands of years by trial and error, and we, with broader insight and scientific expertise, have a much greater opportunity to utilize these data than any who preceded us. Valuable data, however, are not always recorded. It behooves us to study the practices of indigenous populations before they are lost, through either human indifference or our relentless ability to change and destroy the vegetation around us. We hope that this book will stimulate those interested in ethnobotany and human welfare to look closely and seriously at the field data awaiting our scrutiny. We have compiled a list of general and geographically specific herbals, pharmacopeias, materia medicas, and other types of references relative to medical plants and ethnobotany (Appendix B).

#### DANGER OF DRUGS

Plants produce secondary metabolites as defenses against animals, parasites, bacteria, and viruses, and so rely on these chemical and other deterrents for their survival. They do indeed produce them “for their own purposes and not for ours.”<sup>30</sup> Thus, such plant products may be harmful to humans (Chapter 3), so the often repeated adage that “if it’s natural it’s (necessarily) safe” is wrong, sometimes dead wrong if a product is taken in sufficient amounts. Because of their success, many plants have evolved poisonous compounds, and some of these may be the basis of successful pharmaceuticals, herbal preparations, and traditional medicines. Many nontoxic compounds are also found in plants, and they, too, are successful therapeutics alone or in combination with other medicines and the natural components of extracts. Death from plant poisoning is infrequent in general, and rare among medicinal plant users, if doses are not exceeded and the material is labeled correctly.

The risk of side effects from medicinal plants is also low, but if such material is taken together with pharmaceuticals, be aware of potential interactions (Chapter 2). To illustrate, vitamin K (green vegetables such as broccoli) in large amounts can be antagonistic to the effects of anticoagulant therapy, and grape-

fruit juice can lead to the elevation of serum concentrations of medications such as cyclosporine and certain calcium antagonists and coenzyme A reductase inhibitors.<sup>31</sup>

Over 2 billion pharmaceutical drug prescriptions are filled each year in the United States. When taken separately for a specific therapy, they are by and large safe, but when taken together they can be at best risky and at worst deadly. For instance, taking the antihistamine Hismanal (astemizole) for treating allergies, with the topical antifungal Nizoral (ketoconazole) can cause arrhythmia, heart attack, and death. Nizoral inhibits the metabolism of Hismanal, so these drugs should never be prescribed together by a physician or provided to patients by pharmacists. Unfortunately, it does happen.<sup>32</sup> They are contraindicated, as are Rimactane (to treat tuberculosis) and oral contraceptives, since Rimactane diminishes the effect of birth control pills and can render them ineffective; and Vasotec and Dyazide, both used to control hypertension, but when used together may trigger hyperkalemia, which causes dizziness, heart failure, and death. Such medication errors involving drug interactions are an exploding health care problem that sends hundreds of thousands of Americans to the hospital every year.<sup>32</sup>

Pharmaceutical drugs can also be extremely dangerous, even when properly prescribed and administered, as in hospitals. The incidence of adverse drug reactions among hospitalized patients was, in 1994, between the fourth- (after heart disease, cancer, and stroke) and sixth-leading cause of death in the United States: 76,000 to 137,000 patients died, and an additional 2.2 million had serious nonfatal reactions.<sup>33</sup> The numbers shocked even the researchers, who analyzed 39 studies conducted over three decades. Obviously, even in hospitals, powerful pills are given and taken without considering the consequences of patient age, varying physiology, and overall health.

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