HEALTH PROMOTION AND DISEASE PREVENTION

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Learning Objectives

1. Discuss the implications of the human genome project and the advent of pharmacogenomics for disease prevention and health promotion initiatives for substance abuse prevention.
2. Outline the Food and Drug Administration's (FDA) five-part strategic action plan, Protect and Advance America's Health.
3. Determine when pharmacotherapies are indicated for disease treatment and/or disease prevention and when they are not indicated because of excessive risk or contraindications.
4. Counsel an alcoholic pregnant woman in her first trimester about the risks to her unborn fetus of continued alcohol consumption.
5. Analyze the design, efficacy, and cost of model substance abuse prevention programs.
6. Recommend drug therapy regimens for disease prevention or health promotion when appropriate.
7. Describe the clinical pharmacist's role in disease state management programs for disease prevention and health promotion.

Introduction

Health promotion is the process of enabling people to increase control of and improve health, and disease prevention is the therapeutic or educational intervention provided by the medical community based on evidence-based medicine and public policy. Health promotion requires action by many individuals and groups not usually identified with the care of the sick or prevention of disease. With health promotion initiatives, patients are empowered to take actions that improve their quality of life. Health advocates regard health promotion as a step toward autonomous decision-making for people who benefit from such measures as fluorinated drinking water, dietary additives (e.g., folic acid supplementation in grains and vitamin D in milk), mass testing and vaccination programs (e.g., tuberculin and rubella), and many others. Although these interventions seem beneficent in nature, controversies arise frequently, especially when people are not given a choice, and when public policy enforced by government weigh benefits and risks for an entire population based on data derived from epidemiological studies. Epidemiological data are subject to bias and limited by confounders; thus, sometimes associations are observed and not confirmed by subsequent prospective experimental studies (e.g., hormone replacement therapy results from the Women's Health Initiative vs. the Nurses Health Study).

Healthy People 2010 is a comprehensive, nationwide health promotion and disease prevention agenda that is designed to guide efforts to improve the health of all people in the United States during the first decade of the 21st century. Its purpose is to promote health and prevent illness, disability, and premature death, and is a continuation of the Healthy People 2000 agenda of similar scope and purpose. Using the public health philosophical doctrine, the health of the individual is closely linked to the health of the community and, hence, the health of the nation. The Healthy People 2010 document provides general goals for 10 leading health indicators (e.g., tobacco use, substance abuse, overweight and obesity, responsible sexual behavior, access to health care, and immunizations). The document is further subdivided into 28 focus areas with quantifiable goals whenever possible.

Two comprehensive review articles recently reviewed the pharmacist's role in helping the nation achieve the

Babb VJ, Babb J. Pharmacist involvement in Healthy People 2010. J Am Pharm Assoc (Wash) 2003;43:56–60.

Abbreviations in this Chapter

FAS	Fetal alcohol syndrome
FDA	Food and Drug Administration

Healthy People 2010 goals. Some interventions outlined in the first article included the conduct of screening programs and provision of specialized services that focus on hypertension, diabetes, asthma, patient education, smoking cessation, or general drug management. Collaborative practice agreements between pharmacists, physicians, and other health care professionals are emphasized. Because the community pharmacist is the most accessible health care provider, pharmacists have a unique opportunity to motivate patients toward achieving these goals, and pharmacy as a profession has been pursuing provider status through collaborative practice agreements for many years, subject to individual state laws and regulations that govern the scope of pharmacists' practice. In addition, because of the emphasis on self-care and the availability of medical information on the Internet, patients are becoming more informed about available drug therapies; however, they often do not understand the information they find. Thus, the role of the pharmacist in verifying the validity and applicability of medical information on the Internet becomes paramount.

An American College of Clinical Pharmacy white paper described the challenges and opportunities for pharmacists with Healthy People 2010 initiatives, and divided the focus areas into four categories: category 1 included areas where the pharmacist's role is well established; category 2 included areas where pharmacists are active but have yet to establish a leadership role; category 3 included areas where pharmacists primarily have a supportive role but have yet to achieve a leadership role because of barriers that include inadequate training and insufficient manpower; and category 4 included areas where little or no role exists for pharmacy in these areas. This chapter examines examples of public health programs targeted toward the most imminent, modifiable threats to the public health. Some initiatives also are emphasized; this chapter focuses on risks to public health that clinical pharmacists have yet to embrace as disease prevention initiatives and those that have new evidence to support potential pharmacotherapeutic interventions, the majority of which are characterized by the American College of Clinical Pharmacy as category 3 focus areas. This chapter helps readers increase awareness and delineate the pharmacist's role in disease prevention and health promotion initiatives, and perhaps encourage pharmacists to capitalize on their unique position as a community health resource in ways not previously pursued.

Pharmacists could contribute substantially more to substance abuse prevention, especially substance abuse during pregnancy which represents preventable, modifiable risk factors for neonatal morbidity and mortality. Neonatal mortality continues to rise in the United States despite the relative wealth of the nation. Pharmacists also can contribute to tobacco use cessation initiatives because tobacco use has been identified as the No. 1 preventable cause of morbidity and mortality in this country. In addition, obesity is occurring in epidemic proportions, according to the Centers for Disease Control and Prevention, and pharmacists are in a unique position to impact this disease state.

Another important role of the clinical pharmacist is to provide accurate drug information, which is especially important in an age where the 10-second sound bite on the evening news leaves patients frightened and confused. Hormone therapy is a subject that has been in both the medical and lay press and has resulted in confusion over the role of such therapy. In the past, hormone supplementation was embraced as a major disease prevention and health promotion initiative. With new research forcing reevaluation of the role of hormone therapy, pharmacists must remain abreast of new developments to guide their recommendations. Pharmacists need to provide accurate information to patients to assist them in making personal choices about whether to take hormones. This chapter also includes a brief introduction to the emerging science of pharmacogenomics with particular focus on its implications for future disease prevention and health promotion initiatives.

Government Initiatives in Public Health

The impetus for public health research and interventions is based on epidemiological studies that document increasing trends of certain diseases and/or modifiable risk factors for diseases in various genders, subgroups, or ethnic groups. Cultural and/or genomic links to various disease states have been identified. Based on these national trends, the United States government has created federally funded programs to try to decrease modifiable risk factors in certain patient populations. Clinical pharmacists have an important role in many of these programs as discussed in the following section.

Developing Disease Prevention Programs

Community health disease prevention and health promotion programs cannot be successful unless health care practitioners have a thorough understanding of the dynamics of the targeted community. Planning a health promotion and disease prevention program is a systematic process. One philosophical dogma is that communities can develop the capacity to deal with their own problems. Another is that people want to change and have the ability to do so. Thus, the community members must be involved

Calis KA, Hutchinson LC, Elliot ME, et al. Healthy People 2010: challenges, opportunities, and a call to action for America's pharmacists. Pharmacotherapy 2004;24:1241–94.

in the planning and developing processes for lasting changes to occur.

The first step in creating a disease prevention and health promotion program is assessing the needs of the target population by gathering data. Then, the data are analyzed and prioritized based on needs that were identified. Next, the needs are validated, and goals and objectives are chosen to measure progress with the initiatives. Once these are drafted, the intervention is implemented. Then the actual outcomes are compared with the expected outcomes, and adjustments are made as necessary to obtain the best possible results.

The Centers for Disease Control and Prevention uses a methodology referred to as scenario planning to anticipate possible future public health problems to address chronic disease prevention and control programs. Scenario planning is a method that is used to anticipate possible alternative futures. It allows planners to anticipate problems and to consider their potential alternative consequences. Using an example from public health, an unhealthy diet and physical inactivity are considered to be key risk factors for cardiovascular disease. Scenarios are presented to allow public health professionals to evaluate the following three consequences: interventions to promote a healthful diet plus an active lifestyle, interventions that promote a healthful diet without interventions to promote an active lifestyle, and interventions to promote an active lifestyle without interventions to promote a healthy diet. This methodology allows the Centers for Disease Control and Prevention to allocate human and monetary resources for disease prevention and health promotion initiatives that are discussed further in the next section.

Centers for Disease Control and Prevention Initiatives

The Centers for Disease Control and Prevention has embraced numerous health promotional initiatives that include adopting healthy behaviors, such as eating nutritionally sound foods, being physically active, and avoiding tobacco use, to protect and control the devastating effects of chronic disease. Some of these programs include the National Multicultural Campaign Promoting Healthy Lifestyles Among Tweens program, the Racial and Ethnic Approaches to Community Health 2010 program, and the Excellence in Curriculum Integration through Teaching Epidemiology programs. In the National Multicultural Campaign Promoting Healthy Lifestyles Among Tweens campaign, Congress directed the Centers for Disease Control and Prevention to create a healthy movement campaign for youths. The program is a planned, 5-year, national, multicultural campaign to promote physical activities among tweens (9–13-year-olds) and the people who influence them. National Multicultural Campaign Promoting Healthy Lifestyles Among Tweens materials available from the Centers for Disease Control and Prevention include interactive computer activities, stickers, posters, and temporary tattoos given as rewards to participating youths.

Table 1-1. REACH 2010 Disease State Targets

Target Disease
Breast and cervical cancer
Cardiovascular diseases
Child and adult immunizations
Diabetes
Elder care
HIV/AIDS
Infant mortality

AIDS = acquired immune deficiency syndrome; HIV = human immunodeficiency virus.

Excellence in Curriculum Integration through Teaching Epidemiology is a collection of teaching materials developed by the Centers for Disease Control and Prevention to introduce students to public health and epidemiology. This program is targeted toward high school students, but could be used for exceptional elementary school students as well. Students will learn about the scientific method of inquiry, basic biostatistics, and outbreak investigation. Excellence in Curriculum Integration through Teaching Epidemiology adapts readily to team-teaching across a variety of subjects, including mathematics, social studies, history, and physical education.

Racial and Ethnic Approaches to Community Health 2010 is a federal initiative to eliminate racial and ethnic disparities in conjunction with the Healthy People 2010 initiatives. Funding was awarded to community coalitions in 18 states to help address racial and ethnic disparities in the United States. Some of these disease state targets are listed in Table 1-1.

The Department of Health and Human Services has selected six focus areas in which racial and ethnic minorities experience disparities in health access and outcomes: 1) infant mortality, 2) cancer screening and management, 3) cardiovascular disease, 4) diabetes, 5) human immunodeficiency virus infection and acquired immune deficiency syndrome, and 6) immunizations. These disease states or conditions have been chosen in consultation with experts in the field of public health because they affect multiple racial and ethnic minorities. Thus, programs have been developed during the past 4 years to target these disease prevention and health promotion initiatives.

The term “health disparities” refers to a difference in incidence, prevalence, mortality, and burden of diseases and other health conditions that exist among specific populations of the United States. According to the National Institutes of Health, the ethnic groups that need to be targeted with these programs include African Americans, Pacific Islanders, Hispanics/Latinos, Native Americans, and Native Alaskans. The National Institutes of Health has awarded grants to three biomedical research institutions to establish Comprehensive Centers on Health Disparities. The goal is to encourage innovative and effective research strategies that ultimately will reduce the burden of diseases that disproportionately affects minority populations. The development of sustainable, effective, and culturally appropriate prevention and intervention strategies targeted

Centers for Disease Control and Prevention. National Center for Chronic Disease Prevention and Health Promotion. Goals for 2010. February 19, 2004. Available at *http://www.cdc.gov/reach2010/goals.htm*. Accessed November 20, 2004.

toward minority populations continue to be a priority for these government-funded initiatives.

A glaring health disparity is evident when examining the rate of occurrence of birth defects in different groups. Birth defects continue to occur with more frequency among minority and less affluent populations. The cause of this higher frequency is multifactorial, and may be because of limited health care access, inadequate nutrition, occupational exposures, pollution, substance use/abuse, or any combination thereof. To further understand the causative factors, with the hope of designing future community health models, the March of Dimes awards several grants for research into the prevention of birth defects. These grants encourage proposals for behavioral research to identify and prevent cognitive and behavioral risk factors that affect outcomes of pregnancy, the perinatal period, and subsequent child development. For example, pharmacogenomics research is being conducted to determine the possible genetic links to the triggering of premature birth, because babies born at 32 weeks or earlier are 40 times more likely to develop cerebral palsy. Even moderately prolonging gestation can have a tremendous effect on disease prevention. Clinical pharmacists often are involved in pharmacogenomics research, especially as it relates to drug metabolism. However, current disease prevention and health promotion initiatives in this area have been minimal and should be a more pronounced focus for research initiatives in the future.

One observational study was conducted to determine if pharmacy interventions to increase periconceptional folic acid supplementation was associated with increased multivitamin use in a sample of women during childbearing years. The effectiveness of two interventions was evaluated: a pharmacy mailing vials containing 100 folate-containing multivitamins and an educational intervention delivered by primary care providers. A total of 3438 women were interviewed after the interventions. A small, significant increase in the percentage of women using multivitamins was found in the group that received information and prenatal vitamins at the beginning of the intervention period ($p=0.006$), but this increase was not sustained after the interventions ended. No other significant changes were observed, and this increase in multivitamin use pales in comparison to other, larger scale governmental initiatives, such as folic acid supplementation in flour and grains. But it shows that pharmacists can have an impact on vitamin use, and results of this study could provide ideas for future programs. Furthermore, it demonstrates the need for continued educational initiatives provided by pharmacists if benefits of initial teachings are to be sustained.

Food and Drug Administration Initiatives and Regulations

The Food and Drug Administration (FDA) has drafted a strategic action plan, Protect and Advance America's Health that encompasses five broad priority goals to address new challenges that face the agency. The first goal is to embrace efficient, scientific-based risk management. This goal requires that the most current biomedical, statistical, managerial, and economic science be used. The second goal is to enhance postmarket monitoring, communication, and regulatory activities to improve patient and consumer safety. Some specific objectives to accomplish this goal include partnering with other government agencies and health care providers and embracing technologies such as bar coding. The third goal is to better inform consumers so that the choices they make on a daily basis will improve their own health and welfare. The fourth goal is to protect the nation from terrorism and its many forms, including protecting the nation's food supply, and to speed the availability of new counter measures against national threats in the form of biological or chemical warfare. The fifth goal is to promote a strong FDA that can protect and advance America's health through the employment of outside experts and collaborators, and to improve employee retention within the FDA.

One strong FDA initiative that is beginning to bear fruit is to improve the regulation of dietary supplements. For example, ephedra is an alkaloid that has been found in many dietary supplements promoted for weight loss. Evidence suggests that ephedra is not effective for long-term weight loss, yet it increases the risk for cardiovascular events and other adverse health outcomes. Its active ingredient, ephedrine, can be chemically modified to methamphetamine in clandestine laboratories. The FDA deemed ephedra-containing nutritional supplements misbranded and adulterated based on several observational studies that documented an increased risk of ischemic stroke and other adverse cardiovascular outcomes in patients who used ephedra for weight loss. Patients with preexisting cardiovascular disease who used ephedra for weight loss were associated with increased cardiovascular risk. The FDA banned the sale of ephedra because it was deemed to pose an unreasonable risk to public health.

Another FDA initiative involves a Nonprescription Drug Task Force that is charged with evaluating the safe and effective use of nonprescription drugs. One recent investigation that this committee has undertaken is to determine the risk of misuse of ipecac syrup as a nonprescription drug, and its marginal therapeutic role for managing poisonings. Many health care practitioners have expressed their desire to have ipecac syrup restricted to prescription drug status to increase monitoring and decrease availability to the untrained user. Several large scale pharmacoepidemiological studies demonstrated that ipecac syrup is used rarely in the community for therapeutic purposes. When community and hospital pharmacists are consulted in cases of drug overdose, most pharmacists defer to the poison control center for treatment recommendations. For acute poisonings, the poison control center refers most patients and their families to the emergency department. Ipecac syrup is rarely the treatment of choice for acute overdoses because of its slow onset of action, variable duration of action, and lack of efficacy for removing many offending drugs. The use of ipecac syrup complicates poison management because it cannot be used concomitantly with activated charcoal or gastric lavage. Thus, the availability of ipecac syrup as a nonprescription drug does not decrease the number of emergency department visits, but often complicates emergency department visits.

Also problematic is the abuse of ipecac syrup by patients with eating disorders. Although not as frequently abused as prescription-controlled drugs, abuse of ipecac syrup may predispose patients to dehydration and associated electrolyte abnormalities. Thus, benefits of nonprescription availability may not outweigh the risks of inappropriate use. The FDA is still accepting comments about this issue and has yet to make a final decision.

To improve the safe and effective use of nonprescription drugs, the FDA has ordered manufacturers to improve product labels. The goal is to improve the way consumers use nonprescription medicines, a need made clear after a survey revealed that most patients do not read or understand nonprescription drug labels. It is hoped the new labels will prove to be easier for laypersons to read and understand.

The FDA has long been concerned about the casual way in which Americans use nonprescription pain relievers and the risks that such use may pose. In January 2004, the FDA launched a national education campaign to provide advice on the safe use of over-the-counter pain relief products. The nationwide campaign focuses on the over-the-counter pain and fever reducers that contain acetaminophen and nonsteroidal anti-inflammatory drugs, including products containing aspirin, ibuprofen, naproxen sodium, and ketoprofen.

Because acetaminophen is found in more than 600 over-the-counter and prescription products, such as pain relievers, cough suppressants, and drugs that treat colds, patients could ingest more of this ingredient than is safe. To minimize the risks of an accidental overdose, consumers are encouraged to avoid taking multiple drugs that contain the same active ingredient at the same time. The risk for acetaminophen liver damage may be increased in consumers who drink three or more alcoholic beverages per day, and the FDA embarked on an educational campaign to raise awareness of the dangers of these familiar drugs.

Nonsteroidal anti-inflammatory drugs can cause gastrointestinal bleeding with an increased risk in patients who are older than 60 years of age, those taking prescription drugs with anticoagulant properties or corticosteroids, or those with a history of gastrointestinal bleeding. Nonsteroidal anti-inflammatory drugs also may increase the risk of renal diseases in consumers with preexisting kidney disease or those taking diuretics.

The FDA's consumer educational initiative includes: 1) an over-the-counter pain reliever brochure to be distributed in pharmacies and by health care providers; 2) a "matte release" newspaper article to be distributed to 10,000 community papers across the country; 3) a reprint of "Use Caution With Pain Relievers", an FDA Consumer magazine article that will be distributed at national health care conferences and available for reprinting in health-related publications; and 4) two print public service advertisements that will be sent to about 100 major magazines. The campaign provides advice on how to avoid inadvertently taking more than the recommended doses of over-the-counter pain relieves, and outlines underlying health conditions that increase risk. Pharmacists are in a key position to distribute some of these materials and to be available to provide advice and counsel those who may have concerns.

Several FDA initiatives are continuing and have already been described in the American College of Clinical Pharmacy white paper on Healthy People 2010. Readers are referred to the white paper for a comprehensive review of the Healthy People 2010 objectives because they have important ramifications for public health.

Pharmacogenomics and Disease Prevention

Pharmacogenomics (which is the focus of an entire chapter in this book) focuses on the genetic variations affecting drug response. The challenge of the field is to understand which genetic variants are biologically relevant, to understand how the combined interaction of genetic variants contributes to disease, and to determine how to achieve optimal drug therapy selection based on pharmacogenomics findings. This area of research has the potential to impact disease prevention and health promotion initiatives substantially in both therapeutic and ethical realms. Understanding 1) why certain patients abuse drugs and others do not and 2) why certain babies are born with major malformations and others are not despite their seemingly similar modifiable risk factors are just two examples of pharmacogenomics research that may affect disease prevention. Both legal and ethical dilemmas arise when scientific knowledge progresses faster than public policy, because acquiring knowledge without means for action does not necessarily improve patient care. For example, in California, comprehensive newborn screening is mandated. However, a recent case describes how ineffective public policy can undermine the effectiveness of such programs. A baby underwent state-mandated newborn screening and was found to have abnormally low levels of thyroxine and thyrotropin, findings consistent with the presence of congenital hypothyroidism. The physician was not notified of these results because the state had chosen not to divulge the actual values and instead had opted to report as abnormal only these results in which thyroxine levels were low and thyrotropin levels were high. As a result, the diagnosis of congenital hypothyroidism and subsequent treatment were seriously delayed, resulting in permanent harm. When the child's family sued the state, the California Supreme Court ruled that the state program could not be held liable, in part to avoid diverting funds that would have been used for other state purposes. By contrast, if a private diagnostic laboratory had given the same report, especially without providing the actual results that would have enabled the newborn's physician to make an independent assessment, the laboratory almost certainly would have been held responsible. In this example, the fault was not with the screening program, but with its implementation. This begs the question as to whether the public health is actually

Clayton EW. Ethical, legal, and social implications of genomic medicine. N Engl J Med 2003;349:562–9.

improved by mere knowledge, for it is public policy decisions that permit actions that improve public health.

Tobacco Use

Tobacco, a substance sold legally in the United States, is a well-known carcinogen when smoked or chewed, and it has adverse effects on the fetus when used during pregnancy. Tobacco use, particularly cigarette smoking, is the leading preventable cause of death in the United States and is responsible for about 440,000 deaths each year. One of the national health objectives for 2010 is to reduce the prevalence of cigarette smoking among adults to less than 12%. During 2001, the median adult current smoking prevalence was 23.4% (range: 13.3–30.9%) for the United States and Washington, D.C., and 12.5% (range: 9.8–31.4%) for Guam, Puerto Rico, and the Virgin Islands. During 1996–2001, the prevalence of current smoking was relatively stable in 41 states and Washington, D.C., and the proportion of current smokers who were "some day" smokers (i.e., smoked cigarettes occasionally, but not every day) increased significantly in 31 of those states and Washington, D.C. Because the only safe alternative to smoking is cessation, interventions should target all smokers to help them quit smoking completely.

In women who use tobacco products during pregnancy, higher nicotine concentrations are found in the fetus/neonate than the mother. Nicotine use is associated with increased maternal and fetal heart rate, preterm birth, decreased birth weight, and an increased risk of abortion and stillbirth.

A prospective, observational study was conduced in 24 pregnant women. Maternal heart rate, blood pressure, fetal heart rate, and fetal aortic and umbilical vein blood flow increased after nicotine exposure. Pulsatility indices of the fetal aortic and umbilical artery blood velocity waveforms decreased with increasing maternal nicotine levels. These results suggest that maternal nicotine intake is associated with changes in fetal blood flow that may contribute to decreased fetal birth weight. Despite these known risks, women continue to smoke during pregnancy. Is it because they are unaware of the health risks to themselves and their fetuses, or is it because of nicotine dependence and addiction, and can public policy address these issues? Current research seeks to understand the process and mechanism of nicotine dependence.

Much research in smoking cessation is targeted toward adolescents because this age typically is when tobacco use begins. A recent report from the continuing McGill University Study on the natural history of nicotine dependence found an association between nicotine dependence symptoms and increased smoking in adolescents. This result challenges previous dogma that nicotine dependence occurs only after long-term, heavy smoking. In the McGill study, 17% of adolescents, 19% of weekly smokers, and 66% of daily smokers who had smoked during the previous 3 months were tobacco-dependent.

The link between pharmacogenomics and tobacco dependence was evaluated prospectively in adolescents. A protective association between the tyrosine hydroxylase gene and tobacco smoking in adolescents was found. Adolescents positive for the K4 allele of the tyrosine hydroxylase gene were less likely to smoke tobacco as adolescents. Further study may elucidate the means to identify interventions that target high-risk populations, as well as the possibility to learn from low-risk populations.

Pharmacist-managed smoking cessation programs have been described in great detail in the pharmacy literature. These interventions are perhaps even more important in pregnant patients, because maternal smoking increases the risk of spontaneous abortion, low birth weight, premature delivery, sudden infant death syndrome, and learning and behavioral problems in offspring. In addition, prospective data from the National Collaborative Perinatal Project found that children of mothers who smoked more than a pack of cigarettes during pregnancy were at an increased risk of developing nicotine dependence. Furthermore, children of two smoking parents are associated with higher nicotine dependence scores.

A multimodal approach to smoking cessation in pregnant women was more effective than counseling alone when smoking cessation rates were measured at 37 weeks' gestation. This multimodal approach involved initial individual smoking cessation counseling supplemented by an invitation to join a smoking cessation program with nicotine replacement therapy as a voluntary option. All pregnant women involved in the study received standard smoking cessation counseling. Despite evidence for effectiveness of smoking cessation programs, a recent survey of 354 programs reported that less than 50% provided training on smoking cessation/reduction methods, and 28% said that smoking cessation counseling had a high priority in comparison to other objectives. Thus, public policy must put greater emphasis and encouragement on evidence-based interventions.

Primary Prevention of Chronic Disease

For the past 12 years, the prevalence of patients with one or more major risk factors for heart disease and stroke has increased. As a result, the national burden of heart disease and stroke may increase substantially during the next 10

Andres RL, Day MC. Perinatal complications associated with maternal tobacco use. Semin Neonatol 2000;5:231–41.

O'Loughlin J, DiFranza J, Tyndale RF, et al. Nicotine-dependence symptoms are associated with smoking frequency in adolescents. Am J Prev Med 2003;25:219–25.

Olsson C, Anney R, Forrest S, et al. Association between dependent smoking and a polymorphism in the tyrosine hydroxylase gene in a prospective population-based study of adolescent health. Behav Genet 2004;34:85–91.

Klerman LV, Spivey C. Smoking-related activities in prenatal care programs. Am J Prev Med 2003;25:129–35.

years. Nationally sponsored prevention programs to increase awareness of and reduce high blood pressure, high blood cholesterol, smoking, diabetes, and obesity are more important now than ever and should remain a public health priority. See the Annotated Bibliography for information regarding the latest clinical practice guidelines for preventing these chronic diseases. The Prevention of Cardiovascular Disease chapter in the Cardiology book of PSAP-V discusses the role of the pharmacist in disease prevention and health promotion, highlighting pharmacotherapy as appropriate. This chapter focuses on obesity because obesity is of epidemic proportions in the United States and continues to rise, and it affects the development of cardiovascular disease as well as the development of many other chronic diseases.

Obesity

During the past 30 years, the prevalence of obesity in the United States has increased from 14.5% to 30.9%. If current trends continue, obesity will surpass tobacco smoking as the No. 1 preventable cause of death in the United States. During the past 30 years, mean carbohydrate intake per person increased and total dietary fat consumption decreased, which is consistent with the current recommendations of the United States Dietary Guidelines. Because of this increasing obesity prevalence, an expert advisory committee appointed by the United States Department of Health and Human Services and the United States Department of Agriculture is conducting a review of the dietary guidelines for Americans that is expected to be published in 2005. In the meantime, the United States Preventive Services Task Force recommends that clinicians screen all patients for obesity and offer intensive counseling and behavioral interventions at each appointment or interview. Body mass index between 25 kg/m^2 and 29 kg/m^2 is considered overweight and a body mass index greater than 30 kg/m^2 is defined as obesity; obesity is further divided into three classes to assess severity and treatment strategies. Evidence-based medicine confirms that decreasing weight, even modestly, is beneficial; a 3–5 kg weight loss can improve glucose metabolism, have a beneficial effect on lipid levels, and decrease blood pressure in obese patients if maintained for more than 1 year.

The five As, (assess, advise, agree, assist, and arrange) are used as a framework for behavioral counseling for obesity. These same interventional strategies are used in smoking cessation counseling, and are discussed in great detail in the public health literature. Incorporating non-nutritive sweeteners is one intervention that is used by many Americans to decrease daily caloric consumption. These sweeteners are contained in several consumer products from soft drinks to diet aids. The American Dietetic Association has addressed public health concerns about non-nutritive sweeteners. Dietary quality suffers when sweetener intake is more than 25% of the total nutrition consumed, according to the Institutes of Medicine's suggested maximal intake level. Yet, in the United States, one in four children surpasses this level. Polyols (sugar alcohols) add sweetness with reduced energy and functional properties to foods/beverages and promote dental health. Five non-nutritive sweeteners have FDA-approved labeling (acesulfame-K, aspartame, neotame, saccharin, and sucralose) at estimated intakes below the acceptable daily intake (level that a person can safely consume everyday during a lifetime without risk). Although evidence does not support an association between elevated intake of nutritive sweeteners and increased obesity risk, or non-nutritive sweetener consumption and behavioral disorders, the American Dietetic Association recommends that consumers enjoy both nutritive and non-nutritive sweeteners as part of their healthful dietary program.

Sometimes, for several reasons, behavioral modification, education, and non-nutritive sweetener supplementation is not enough to promote weight loss in specific patients. In these obese patients, pharmacotherapy along with behavioral and lifestyle interventions is necessary to promote weight loss. Surgical therapy also may be used when the benefits outweigh risks. Medicare is evaluating stomach bypass surgery for coverage because this modality has proven to be more effective for long-term weight loss than other therapeutic modalities, although many questions still remain.

Pharmacotherapy for Obesity

Preventing and treating obesity can decrease obesity-related sequelae. Of the drug therapies used in this setting—metformin, acarbose, orlistat, sibutramine, diethylpropion, phentermine, and others—orlistat and sibutramine are the only drugs with FDA-approved indications for long-term use. These drug therapies promote modest weight loss when combined with lifestyle and behavioral interventions. Drug therapy must be continued to maintain weight loss and weight loss typically peaks after 6 months. For these reasons, many insurance companies do not cover the costs of drug therapies for obesity treatment. Public policy must address the ethics of denying obesity treatment, knowing that obesity is one of the most prevalent causes of preventable death in the United States. More insurance companies, including Medicaid, cover drug therapy for erectile dysfunction than drug therapies for obesity treatment.

Drug therapy for obesity is contraindicated during pregnancy for several reasons, including the lack of safety data for mother and fetus. Table 1-2 shows the patient types in whom pharmacotherapy is indicated. Orlistat is a nonsystemic inhibitor of gastrointestinal lipases that are necessary for dietary fat breakdown. This inhibition prevents absorption of dietary fats from the intestines. At 18 months follow-up, 33% of patients randomized to orlistat lost more than 10% of their baseline body weight versus 25% of patients randomized to placebo. Successful

Centers for Disease Control and Prevention. Trends in intake of energy and macronutrients—United States, 1971–2000. MMWR Morb Mortal Wkly Rep 2004;53:80–2.

Whitlock EP, Orleans T, Pender N, Allan J. Evaluating primary care behavioral interventions: an evidence-based approach. Am J Prev Med 2002;22:267–84. Also available at *http://www.ahrq.gov/clinic/3rduspstf/behavior/behsum1.htm*. Accessed November 20, 2004.

Table 1-2. Indications for Pharmacotherapy for Obesity

Indication[a]
1. Patients at risk for disease from their level of obesity
2. Patients committed to losing weight
3. Patients who understand the risks for long-term therapy
4. Patients who understand the success rates
5. Patients with BMI greater than 30
6. Patients with BMI greater than 27[b]
7. Women with a waist circumference greater than 35 inches[b]
8. Men with a waist circumference greater than 40 inches[b]
9. Patients with no contraindications to the drugs

[a]Patients need to have indications 1–4, plus at least one of 6–9.
[b]With two or more associated comorbidities.
BMI = body mass index.

treatment with orlistat results in improvements in cardiovascular risk factors that include obesity, lipid profile, blood pressure, waist circumference, and fasting insulin and glucose levels. More patients with impaired glucose tolerance who are treated with orlistat have normal glucose tolerance after 2 years compared with a matched placebo group. Half as many patients progressed to a diabetic state.

Diets high in fat (greater than 30% of total caloric intake) can increase the adverse effects associated with orlistat that include fecal urgency, incontinence, oily spotting, and flatulence. These adverse effects may become less frequent or diminish in patients who consume a high-fiber diet. Psyllium 3 times/day with orlistat and taken with meals may decrease gastrointestinal symptoms. Orlistat decreases absorption of fat-soluble vitamins, particularly vitamin E and vitamin D, especially in obese adolescents treated for 3–6 months. Orlistat also decreases vitamin K absorption from the intestines and, thus, attenuates warfarin efficacy in anticoagulated patients; increased monitoring and dose adjustments may be necessary to prevent bleeding complications. The pharmacist is invaluable in counseling patients about methods to decrease the severity of these common adverse effects.

Sibutramine is a nonamphetamine appetite suppressant that also has slight antidepressant properties. Its pharmacological action involves the blocking of neuronal uptake of norepinephrine, serotonin, and (weakly) dopamine. Its approved indications include weight loss in adolescents and patients 16 years of age and older; it also is effective for patients with hypertension and diabetes who have additional risk factors for cardiovascular disease. Sibutramine is well tolerated, but it can cause increased blood pressure, heart rate, and palpitations in some patients. Thus, cardiovascular risks must be considered, and adverse effects must be monitored along with weight loss progress. Drug therapy should be discontinued if ineffective or adverse effects are intolerable. A recent randomized, prospective, clinical trial demonstrated that low-dose metoprolol improved compliance rates and decreased the cardiovascular adverse effects without adverse metabolic sequelae combined with sibutramine therapy in patients who may otherwise discontinue treatment.

Metformin commonly is prescribed for women with insulin resistance that manifests as type 2 diabetes, prediabetes, or polycystic ovary syndrome. Polycystic ovary syndrome is a common cause of infertility and recurrent pregnancy loss. It also is associated with central adiposity and increased cardiovascular risk that commonly is referred to as metabolic syndrome. Metformin has an array of complex actions yet to be fully elucidated. Hypoglycemia is rare and modest weight loss is promoted. Although metformin is not effective enough as a sole treatment for obesity, it is useful as an adjunct for insulin-resistant obese patients to prevent the development of diabetes. Women have been able to take metformin throughout pregnancy without adverse consequences to the mother or the baby. See the Annotated Bibliography for clinical practice guidelines endorsed by the American Heart Association; National Heart, Lung, and Blood Institute; and the American Diabetes Association for managing metabolic syndrome.

Patients often ask the community pharmacist about the efficacy of various nonprescription drugs and nutritional supplements. The majority of these products do not have evidence to support long-term safety or efficacy. This is the perfect opportunity for clinical pharmacists to advise patients that nonprescription drugs and nutritional supplements are of limited value for weight loss, and to emphasize effective lifestyle modifications for weight loss that include a calorie-restricted, well-balanced diet, and the benefits of increased physical activity in the form of aerobic, anaerobic, and weight bearing exercise 3–5 times/week.

Surgical Treatments of Obesity

Gastric bypass, vertical banded gastroplasty, and adjustable gastric banding can result in substantial weight loss (28–40 kg). This effective intervention is reserved for patients with class 3 obesity or those with class 2 obesity and one other obesity-related illness. Some patients (about 25%) will require subsequent operations. Vitamin supplementation is necessary. Some authors suggest an oral multivitamin, whereas others suggest intramuscular B_{12}, folate, vitamins A and D, and others.

The long-term sequelae of these procedures remain unknown, and short-term severe complications are rare (0.5–1.5% mortality). To identify the factors that increase mortality after either open or laparoscopic Roux-en-Y gastric bypass, a retrospective analysis was conducted in the bariatric outcomes database at a university teaching hospital (n=2000). A multivariate logistic regression analysis was used to identify factors related to perioperative mortality. Factors examined included age, gender, body mass index, preoperative weight, hypertension, diabetes mellitus, sleep apnea, obesity hypoventilation syndrome, venous stasis ulcers, intestinal leak, small bowel obstruction, and pulmonary embolus. Results indicated that independent risk factors associated with perioperative death included leak, pulmonary embolus, preoperative weight, and hypertension. Thus, surgery should not be reserved as a desperate last measure for weight loss when the benefits of long-term weight loss are weighed with the risks of surgery.

Fernandez AZ Jr, Demaria EJ, Tichansky DS, et al. Multivariate analysis of risk factors for death following gastric bypass for treatment of morbid obesity. Ann Surg 2004;239:698–702.

Differences in absorption of drug therapies in patients after gastric bypass remain unknown. Clinical pharmacists should help gastric bypass patients choose appropriate multivitamin supplements, as well as counsel patients on the importance of long-term adherence to vitamin supplementation. Gastric bypass patients consume low-calorie diets that do not provide sufficient vitamins and minerals per American Dietary Association recommendations for preventive health. Also, the surgical procedure bypasses part of the small intestine, which decreases nutrient absorption from food and the bioavailability of drugs taken orally. In general, drugs with a narrow therapeutic window taken orally require more frequent monitoring and dose adjustments after gastric bypass procedures, but little information has been published to assess the clinical significance of altered drug and nutrient absorption. In the future, as bariatric surgery (obesity management) becomes more prevalent, clinical pharmacists should publish case reports and observational, cohort studies that assess the clinical significance of altered nutrient and drug therapy absorption, especially in patients who receive drugs with a narrow therapeutic window.

Hormone Therapy

The FDA has launched a collaborative campaign to inform women that hormone therapy is no longer appropriate for primary or secondary prevention of cardiovascular disease, according to the Women's Health Initiative, the Heart and Estrogen/Progestin Replacement Study, and Heart and Estrogen/Progestin Replacement Study 2. Proven benefits of hormone therapy include reduction of hot flashes, vaginal dryness, and bone loss. These benefits must be weighed against the confirmed increased risk of stroke, heart disease, and breast cancer.

In January 2003, based on the findings of the Women's Health Initiative, the FDA advised women and health care professionals that menopausal hormone therapy—estrogen and estrogen with progestin—is associated with an increased risk of heart disease, heart attacks, strokes, and breast cancer. The warning emphasized that these products are not labeled or intended for heart disease prevention. The FDA also has modified the approved indications of these menopausal hormone therapies to clarify that these drugs should be used only when the benefits clearly outweigh risks.

With a clearer picture of who should and who should not take hormones, the next challenge is in communicating the importance of weighing benefits and risks for potential users. In the spring of 2003, Congress directed the FDA to develop and execute an informational campaign targeting women through partnerships with organizations nationwide. Working in collaboration with the National Institutes of Health and other Department of Health and Human Services agencies, the FDA has developed science-based informational materials on its latest guidance on menopausal hormone therapies (estrogens and estrogens with progestins), and is working closely with women's health organizations, community-based organizations, and other experts to get this information out to women and health care providers. The main tools of the campaign are fact sheets about menopause and hormone therapy and a purse guide that provides questions for discussion with a health professional.

Future research may focus on understanding the distribution and regulation of estrogen receptors in vascular tissue; genomic interactions of estrogens and progestins; and the interaction between inflammatory cytokines, coagulation proteins, platelets, and the endothelium. Genetic variations of estradiol metabolism have been described as significant contributors to disease susceptibility that include recurrent pregnancy loss (typically at least three or more), preeclampsia, endometriosis, breast cancer, and hormone therapy-related complications including thrombosis. The research should result in an increased ability to target hormone therapy to those best suited for intervention.

Clinical pharmacists have the necessary skills to evaluate critically the medical literature, and to interpret the data appropriately for patients, health care providers, and the press as appropriate. Clinical pharmacists work in collaboration with physicians and other health care practitioners to evaluate the appropriateness of hormone therapy for patients, together weighing benefits and risks in each individual case. The risks of osteoporosis, thromboembolism, and breast cancer for one symptomatic perimenopausal patient may be totally different from another. Clinical pharmacists explain benefits and risks of hormone therapy during counseling sessions and provide recommendations or prescriptions for hormone therapy, depending on the pharmacists' scope of practice.

Preterm Labor

Preterm birth occurs in about 11.5% of all live births, resulting in 500,000 premature infants per year. Despite improvements in medical care, the preterm birth rate increased by 10% in the United States during the past 10 years. This rate is highest for African-American women, followed by Native Americans, Hispanics, Caucasians, and Asians. Premature births result in significant neonatal morbidity and mortality; surviving neonates often must endure long-term neurological manifestations. With substantial economic consequences resulting in a cost of $12 billion (United States dollars) per year, research is continuing to seek solutions to this significant source of morbidity and mortality.

Premature labor is defined as regular uterine contractions that occur before 37 weeks of gestation and are associated with cervical changes. One cause of premature labor is postulated to be an imbalance between estrogen and progesterone because both hormones in combination are thought to prevent uterine contractions. Trauma and inflammation of the cervix both have been associated with preterm labor. Although the causes of premature labor remain poorly understood and currently are being researched, risk factors, diagnosis, treatment, and consequences of premature labor for both mother and neonate have been identified.

Modifiable risk factors in the mother include family stress, domestic abuse, tobacco use, sexually transmitted diseases, illicit substance abuse, inadequate nutrition, low preconception body mass index, and slow prenatal weight gain. Patients with these characteristics should be referred to the appropriate support services for follow-up strategies to prevent preterm birth, even though few prevention methods have been proved. There is conflicting evidence whether treating bacterial or viral infections prevents premature labor, but prophylactic antibiotics in patients with intact membranes are not recommended outside of clinical trials. Despite vast medical advances in neonatal care, the fetus cannot survive outside the uterus before 22 weeks' gestation. Therefore, supportive measures for the mother are used, and tocolysis rarely is initiated at this stage. Educational initiatives geared toward women at high risk for preterm labor can make a difference. A recent landmark clinical trial demonstrated that preventing the start of preterm labor with hydroxyprogesterone caproate in certain patients can be more effective than trying to stop preterm labor with tocolytic therapy once it begins. It is ironic that at the time of this writing, hydroxyprogesterone caproate is not available commercially from a manufacturer; thus, pharmacists compound hydroxyprogesterone caproate as a sterile, pyrogen-free injectable solution for intramuscular injection. Pharmacists teach patients how to administer the intramuscular injections; how to dispose of needles; and counsel patients about the benefits and risks of therapy, including the importance of drug therapy adherence to obtain optimal outcomes.

Hydroxyprogesterone Caproate

A recent randomized, double-blind, placebo-controlled trial evaluated the efficacy of 17-α-hydroxyprogesterone caproate for preventing preterm labor in high-risk women. Women were enrolled if they had a documented history of spontaneous preterm delivery. The drug (17-α-hydroxyprogesterone caproate) or placebo was administered weekly after randomization, starting at 15–20 weeks' gestation. Results indicate that intramuscular administration of 17-α-hydroxyprogesterone caproate at 250 mg/week in high-risk women resulted in an 18.6% absolute risk reduction in preterm delivery before 37 weeks' gestation ($p<0.05$). For every five patients treated with 17-α-hydroxyprogesterone caproate, one preterm birth before 37 weeks' gestation is prevented. Similarly, for every 10 patients treated, one preterm birth before 35 weeks' gestation is prevented, and 12 high-risk patients were treated to prevent one preterm birth before 32 weeks' gestation is prevented. Additional beneficial results were observed in infants born to women who received 17-α-hydroxyprogesterone caproate, including decreased occurrence of enterocolitis, intraventricular hemorrhage, and need for supplemental oxygen. As previously discussed, 17-α-hydroxyprogesterone caproate is not available commercially, necessitating pharmaceutical compounding in hospitals and special compounding pharmacies.

Candidates for hydroxyprogesterone caproate therapy must have a history of preterm birth, be free of fetal anomalies per ultrasound diagnosis, and must be between 15 and 20 weeks' gestation. Patients with a history of hypertension or a seizure disorder are not candidates. Intramuscular injections are given weekly until 36 weeks' gestation or delivery. If an injection is missed or forgotten, it should be administered as soon as remembered and the schedule readjusted to be weekly thereafter. In this study, injections were administered by the nurse and directly observed; patients can be taught to administer their own injections. Patients should be followed up in clinic and monitored as a high-risk pregnancy.

Tocolytic Therapy

Although halting uterine contractions in preterm labor is not a labeled indication, nifedipine is used to do just that. This treatment is preferred to the once popular β-sympathomimetic drugs because it is associated with fewer maternal adverse effects. Compared to both magnesium sulfate and β-sympathomimetic drugs, nifedipine also has been associated with better neonatal outcomes and is discontinued less often because of adverse effects. Fewer neonates are transferred to neonatal intensive care units when nifedipine tocolysis is used versus β-sympathomimetic drugs. In the studies analyzed, nifedipine doses ranged from 30 mg/day to 160 mg/day.

Clinical pharmacists in hospitals should encourage the use of nifedipine tocolysis as opposed to β-sympathomimetic drugs or magnesium. Institutionally approved standard order forms and clinical pathways endorsed by the medical staff help to improve prescribing patterns. The combination of education, policy changes, and clinical interventions provided by clinical pharmacists are more effective than education alone.

Recurrent Pregnancy Loss

Polycystic ovary syndrome is the most common form of infertility and is responsible for both poor conception rates and pregnancy loss. First trimester spontaneous abortions can occur as frequently as 50% in patients with this syndrome. The mechanism involves both insulin resistance and an increase in endothelin-1, a marker of vasculopathy. Although the specific mechanism of action remains unknown, both retrospective and prospective, observational studies have shown that metformin administration throughout pregnancy is associated with a decrease in spontaneous abortions and without known adverse fetal sequelae in patients with polycystic ovary syndrome. Metformin during pregnancy also has been associated with a decreased rate of gestational diabetes in these women. Children of mothers who received metformin throughout pregnancy have been followed up to 6 months without signs of motor and social developmental sequelae.

In addition to polycystic ovary syndrome, antiphospholipid syndrome is another frequent cause of

King JF, Flenady VJ, Papatsonis DN, Dekker GA, Carbonne B. Calcium channel blockers for inhibiting preterm labour. Cochrane Database Syst Rev 2003;(1):CD002255.

recurrent pregnancy loss. Antiphospholipid syndrome is a condition characterized by a hypercoagulable state secondary to autoantibodies that bind to anionic phospholipid-protein complexes. The diagnosis of antiphospholipid syndrome is based on finding of "moderate to high" anticardiolipin antibody titers and/or a positive lupus anticoagulant test with a syndrome of episodes of thrombosis in arteries or veins, pregnancy loss, and/or thrombocytopenia. In patients with systemic lupus erythematosus, the prevalence of anticardiolipin antibodies ranges from 12% to 30% and 15% to 34% for lupus anticoagulant. Patients with recurrent thromboses require lifelong anticoagulation; patients with recurrent spontaneous abortions require anticoagulation with heparin or low-molecular-weight heparin and aspirin throughout most of gestation. Once diagnosed and adequately treated, women given low-molecular-weight heparin and aspirin had a higher rate of live births than those treated with intravenous immunoglobulin alone, aspirin alone, or placebo.

Low-molecular-weight heparin typically is the anticoagulant of choice for pregnant patients with antiphospholipid syndrome. A prospective, clinical trial evaluated the efficacy of enoxaparin for preventing spontaneous abortions in patients with a history of recurrent spontaneous abortions. Twenty-six of the 37 pregnancies (70%) in treated patients resulted in live births, compared with 21 of 48 (44%) in untreated patients ($p<0.02$; odds ratio = 3.03; 95% confidence interval = 1.12–8.36). The beneficial effect was seen mainly in women with no previous live births ($p<0.008$; odds ratio = 9.75; 95% confidence interval = 1.59–52.48). For pregnant patients with thrombophilic defects, recurrent miscarriages during and after the second trimester, preeclampsia, or intrauterine growth restriction, 40 mg once daily of subcutaneous enoxaparin or heparin is recommended. For pregnant patients, those with antiphospholipid syndrome and those with a history of long-term anticoagulation therapy, 1 mg/kg subcutaneous enoxaparin 2 times/day or subcutaneous heparin is recommended. Patients are taught to administer the subcutaneous injections of 17-α-hydroxyprogesterone caproate in the thigh at alternating sites.

Another risk factor for recurrent pregnancy loss is hyperhomocysteinemia. A meta-analysis of case control studies found an association between recurrent pregnancy loss and hyperhomocysteinemia. Hyperhomocysteinemia may be related to a hereditary defect within the methionine-homocysteine pathway. It also may be acquired as a result of a deficit of vitamin B_{12} and vitamin B_9. Elevated homocysteine levels greater than 18 micromol/L are considered a risk factor for recurrent pregnancy losses. Supplementation with 400 mcg/day folic acid 4 weeks before conception and for the first 12 weeks of gestation decreases homocysteine levels and the onset of spontaneous/recurrent miscarriage.

To ensure adequate folic acid consumption in women of childbearing years, especially because more than 50% of pregnancies are not planned, grains in the United States, as well as several other countries, are now fortified with folic acid. After this folic acid addition in 1998, a 54% reduction in open neural tube defects was observed. Women in intermediate- to high-risk categories for neural tube defects (previous pregnancy affected by neural tube defect, family history, insulin-dependent diabetes, and epilepsy treatment with valproic acid or carbamazepine) should be advised that high-dose folic acid (4–5 mg/day) supplementation is recommended.

Community pharmacists who dispense insulin or antiepileptic drugs to women of childbearing years should counsel them about the elevated folic acid requirements to prevent neural tube defects. Also, pharmacists working in collaboration with physicians and other health care practitioners in primary care settings should educate all women of childbearing years about the importance of folic acid supplementation, regardless of whether the patients are planning to conceive in the near future. Colorful signs should be posted in waiting areas in community pharmacies and clinics reminding women and practitioners about folic acid supplementation.

Preventing Drug-induced Birth Defects

About 150,000 babies are born each year with birth defects. The parents of one out of every 28 newborns are confronted with the news that their baby has a birth defect. The causes of about 60–70% of birth defects currently are unknown; hence, prevention efforts are difficult if not impossible. Drugs and environmental chemicals account for an estimated 2–3% of all birth defects. Pharmacists can emphasize the importance of a woman's prepregnancy visits to her health care provider. A prepregnancy visit is especially crucial for women with medical problems, such as diabetes, high blood pressure, and epilepsy or any other condition for which drugs are required. This visit would be a good time to ensure that all vaccines are up to date.

All women who could become pregnant should take a daily multivitamin containing 400 mcg of the B vitamin, folic acid. A woman who is pregnant or planning pregnancy should avoid alcohol, smoking, and drugs of abuse because these can cause birth defects and other pregnancy complications. Pharmacists who maintain good patient profiles are in a position to monitor the drugs a woman may be taking and to suggest she should check with her health care provider about continuing the therapy.

There are more than 4 million chemical mixtures (e.g., drugs, cleansers, and pest control agents) in homes and businesses in this country, with little information on the effects of most of them during pregnancy. Certain drugs and

Carp H, Dolitzky M, Inbal AJ. Thromboprophylaxis improves the live birth rate in women with consecutive recurrent miscarriages and hereditary thrombophilia. J Thromb Haemost 2003;1:433–8.

Brouwer IA, van Dusseldorp M, Thomas CM, et al. Low-dose folic acid supplementation decreases plasma homocysteine concentrations: a randomized trial. Am J Clin Nutr 1999;69:99–104.

chemicals are known to increase the risk of birth defects, and pharmacists should be aware of these. Efforts can be undertaken to prevent drug-induced birth defects.

Phenytoin is one drug with known adverse effects on the fetus. Fetal abnormalities associated with its use during pregnancy include facial dysmorphism, epicanthal folds, hypertelorism, broad flat bridge of the nose, upturned tip of the nose, and prominent lips. This syndrome, collectively referred to as the fetal hydantoin syndrome, occurs in 11–17% of exposed pregnancies. Other anticonvulsant drugs have been implicated. A recent retrospective, case-control study (n=128,049) did not detect a difference in major malformation incidence among newborns exposed to various anticonvulsant drugs (e.g., phenytoin, carbamazepine, or phenobarbital), but the total incidence of growth retardation, midface hypoplasia, and hypoplasia of the fingers was greater in those exposed to anticonvulsant therapy than those not exposed to anticonvulsant drugs in mothers with no seizure history. Developmental delays also have been observed more often in children exposed to monotherapy and polytherapy with anticonvulsant drugs in utero than nonexposed children.

Pregnancy and Live Vaccines

Rubella, also known as German measles, was associated with major fetal abnormalities in the early 1940s. A survey determined that offspring of all mothers infected with rubella before week 7 of pregnancy were abnormal; 80% of those infected between weeks 7 and 12; 65% between weeks 13 and 16; and 4% at week 17 or greater. Heart, eye, and central nervous system defects were all associated with exposures during weeks 3–12 and deafness between weeks 3 and 16. Isolation of the measles virus, development of the vaccine, and mass vaccination has virtually eradicated congenital rubella syndrome. The Centers for Disease Control and Prevention recommends that vaccines should not be administered to women who are pregnant or might become pregnant within 4 weeks after vaccination because of the risk for fetal vaccinia.

Isotretinoin

A well-known teratogen, isotretinoin, is a retinoid that is a synthetic analogue of vitamin A. Retinoic acid embryopathy is characterized by malformations of the fetal cranium and face, heart, thymus, and central nervous system. Microtia and anotia with atresia or stenosis of the external auditory canal are the most commonly observed fetal anomaly. Because all retinoic acid derivatives are teratogenic in both humans and animals, isotretinoin has been contraindicated in pregnancy after it was first brought to market in the early 1980s. Yet, accidental exposures have occurred, and the incidence of observed malformations is between 20% and 80%. By 1999, 2.5 of 1000 women of reproductive age had been exposed to isotretinoin. Thus, public policy changes were needed to protect the public.

The program designed to protect the public from isotretinoin's known teratogenicity is called the System to Manage Accutane-Related Teratogenicity. Isotretinoin is contraindicated in women during childbearing years, except for patients with all of these characteristics: 1) not pregnant, 2) uses two forms of contraception if fertile, and 3) is compliant with the contraceptive methods chosen. To prescribe isotretinoin, the prescriber must obtain a supply of yellow self-adhesive isotretinoin qualification stickers. To obtain these stickers, prescribers must agree to educate patients about the risks of isotretinoin use; they must discuss the need for two forms of contraception while patients are taking isotretinoin and for 1 month after drug therapy discontinuation. The prescriber obtains the first pregnancy test when the decision is made to pursue qualification of the patient for isotretinoin therapy. The second pregnancy test (a confirmation test) is conducted during the first 5 days of the menstrual period immediately preceding the beginning of isotretinoin therapy. For patients with amenorrhea, the second test should be done at least 11 days after the last act of unprotected sexual intercourse.

Each month of therapy, the patient must have a negative result from a urine or serum pregnancy test. A pregnancy test must be repeated every month for therapy continuation. Patients must receive written warnings about the rates of possible contraception failure (included in patient education kits). The patient must sign an informed consent form and an informational sheet that describes the isotretinoin survey and information for participation. The prescriber may then prescribe isotretinoin and place a yellow isotretinoin qualification sticker on the prescription. This sticker signifies that the patient has had two negative urine or serum pregnancy tests with a sensitivity of at least 25 mIU/ml before receiving the initial prescription.

Despite all the precautions taken to prevent isotretinoin-induced malformations, there are still birth defects caused by prenatal exposure to this drug. With the growing problem from underground sources (e.g., rogue Web sites), women may obtain drugs illegally and unwittingly harm their babies by ingesting this drug. The manufacturer of isotretinoin created an internal watch group that discovered 108 Internet sites in the United States and abroad that illegally offer its acne drug, isotretinoin, for sale. A bottle of 60 capsules of isotretinoin 20 mg could be purchased for the price of $123.20 from a Web site traced to the South Pacific Island nation of Vanuatu. Pharmacists should be on the lookout for patients showing an interest in obtaining isotretinoin in this manner and cautioned strenuously against pursuing this source of supply.

Thalidomide

Thalidomide is a drug initially marketed in Germany starting in the 1950s as a nonprescription sedative, antinausea, and antiemesis drug. It was available in several other countries including Great Britain, Sweden, Belgium, and Canada. Thalidomide has caused more than 6000 major fetal malformations, not including the abortions or fetal deaths attributable to the drug. A highly specific syndrome, known as phocomelia, results in the reduction of upper limbs, and sometimes results in digits emerging from the shoulder. Other skeletal and nonskeletal malformations also occur. The mechanism is still poorly understood today

Holmes LB, Harvey EA, Coull BA, et al. The teratogenicity of anticonvulsant drugs. N Engl J Med 2001;344:1132–8.

because the teratogenesis witnessed in humans is not easily reproduced in animals.

Thalidomide was reintroduced into the market for treating erythema nodosum leprosum, prompting the development of a safeguard program called System for Thalidomide Education and Prescribing Safety. However, the majority of thalidomide use today is off label for its immunomodulatory and anti-inflammatory properties. It has demonstrated benefits in a variety of diseases, including aphthous and genital ulcers, cancer cachexia, human immunodeficiency virus infection, tuberculosis, and chronic graft versus host disease. Thalidomide also is being studied in clinical trials for treatment of renal cell carcinoma, and liver and thyroid cancers.

Much like the System to Manage Accutane-Related Teratogenicity program, the System for Thalidomide Education and Prescribing Safety program was designed to protect patients from the teratogenic effects of thalidomide. With this program, only prescribers and pharmacists registered with the program are allowed to prescribe and dispense thalidomide. Pregnancy must be avoided by using two reliable forms of contraception simultaneously or by continuous abstinence from heterosexual sexual contact. A pregnancy test must be conducted within 24 hours before beginning thalidomide therapy. The prescriber must not issue a prescription for thalidomide for a woman of childbearing potential until a written report of a negative pregnancy test has been obtained. Because thalidomide is present in the semen of patients receiving the drug, men taking thalidomide must use a latex condom during any sexual contact with women of childbearing potential, even after vasectomy. Pregnancy tests should occur every 4 weeks thereafter. If menstrual cycles are irregular, the pregnancy testing should occur every 2 weeks. Pregnancy testing and counseling should be performed if a patient misses her period or if there is any abnormality in menstrual bleeding. If pregnancy occurs during thalidomide treatment, thalidomide must be discontinued immediately. All inadvertent exposures should be reported to the Celgene pregnancy registry program. Patients must receive both oral and written warnings before thalidomide is dispensed. Thus, the role of the pharmacist is to ensure that the patient complies with all requirements for thalidomide treatment, and that the patient has been counseled on all of the benefits and risks associated with it. Patients must be counseled on the safe maintenance of their supply of thalidomide to prevent family members or others from illegally obtaining this drug without knowledge of the potential sequelae.

Fetal Alcohol Syndrome

Ethanol is one of the most prevalent human teratogens with a myriad of fetal adverse effects collectively referred to as the fetal alcohol syndrome (FAS) and characterized by growth retardation, central nervous system damage, and facial dysmorphology. Cognitive delays and motor deficits also are attributed to this syndrome. Short palpebral fissure is observed in the neonate, along with midfacial hypoplasia, long flat filtrum, and a long convex upper lip with a thin vermilion border. See Table 1-3.

Problems caused by FAS often lead to difficulties in school and problems socializing. Fetal alcohol syndrome is a permanent, lifelong condition that affects every aspect of a child's life and the lives of the child's family. However, FAS is completely preventable, provided the woman does not drink alcohol while she is pregnant.

Table 1-3. Characteristics of Children with Fetal Alcohol Syndrome

Characteristic
Small for gestational age or small in stature in relation to peers
Facial abnormalities such as small eye openings
Poor coordination
Hyperactive behavior
Learning disabilities
Developmental disabilities (e.g., speech and language delays)
Mental retardation or low IQ
Problems with daily living
Poor reasoning and judgment skills
Sleep and sucking disturbances in infancy

IQ = intelligence quotient.

In 1981, public health concern about drinking during pregnancy was first voiced by the Office of the Surgeon General in the form of a public health advisory. Women who were pregnant or planning a pregnancy were warned to abstain from alcohol use because of the potential risks to the fetus. The United States Department of Health and Human Services issued additional advisories in 1990, 1995, and 2000. Despite the clear links between the consumption of alcohol during pregnancy and adverse outcomes, pregnant women continue to consume alcohol. Although the overall rate of alcohol use (at least one drink) among pregnant women has declined after 1995, frequent (seven or more drinks per week) and binge (five or more drinks on any one occasion) drinking continues to occur. One in 30 women who know they are pregnant reports "risk drinking" (seven or more drinks per week or five or more drinks on any one occasion). One in seven women of childbearing age (18–44 years of age) who report not being pregnant engages in "risk drinking."

During 1999, about 500,000 pregnant women reported having one or more drinks during the preceding month, and an estimated 130,000 pregnant women per year in the United States consume alcohol at levels shown to increase the risk of having a baby with FAS or other prenatal alcohol-related conditions.

As previously discussed, FAS and other prenatal alcohol-related conditions are completely preventable by ensuring that a woman does not drink alcohol while she is pregnant or when she could become pregnant. If a woman is drinking during pregnancy, benefits from stopping can still occur. The sooner a woman stops drinking, the better it will be for both her baby and her.

How to Counsel Pregnant Alcoholic Women

About 20–25% of women drink some alcohol during pregnancy, even though no universally safe level of alcohol consumption has been identified. About 50% of pregnant women spontaneously reduce or discontinue alcohol consumption while pregnant. By implication, this means that the other 50% continue to drink, some maintaining drinking behaviors consistent with alcoholism. Counseling such patients would be similar to counseling the

nonpregnant patient, but women may not know the seriousness of the risk at which they are placing their babies. The pharmacist should explore the knowledge and attitudes of the patient, which may help tailor an individualized treatment approach likely to be effective. Pharmacists should teach patients that there is no safe level of alcohol intake and that cumulative exposure of the baby to alcohol increases risk. At the same time, women should be advised that it is never too late to quit drinking.

Patients with a strong physical addiction to alcohol should be referred to a practitioner with skills and experience in dealing with alcohol withdrawal and detoxification. Specialized programs for dealing with alcoholic expectant mothers are available at select places in the country. Traditional after care programs, such as Alcoholics Anonymous, or similar programs would be necessary. Regular contact with the patient should be maintained to monitor for relapse and to institute a sobriety plan for the duration of the pregnancy and beyond.

Clinical pharmacists in hospital settings provide recommendations for treating acute alcohol withdrawal during pregnancy. Benzodiazepines typically are not prescribed during pregnancy, but are the class of drugs usually prescribed for acute alcohol withdrawal in nonpregnant patients. Barbiturates, such as phenobarbital and secobarbital, are more likely options for acute alcohol withdrawal during pregnancy. A new drug therapy to help maintain abstinence from alcohol after detoxification is acamprosate. There are no data to support the safety or efficacy of acamprosate in pregnant women. Thus, psychosocial therapeutic modalities should be used to maintain abstinence from alcohol for the pregnancy duration. Clinical pharmacists can educate patients and other health care practitioners about acamprosate use postpartum. Clinical pharmacists can alleviate fears by explaining that acamprosate does not affect the mesolimbic dopaminergic pathways and, thus, is not associated with a known abuse potential. The recommended dosage of acamprosate is 666 mg orally 3 times/day.

Targeted Media Campaigns to Reduce FAS

The media can be powerful tools to create awareness, change attitudes, and motivate individuals and communities to engage in healthy behaviors. Campaigns can be targeted to specific audiences, taking into account the specific attributes and requirements of particular groups. The targeted media campaign can be used to enhance current prevention efforts related to FAS and other prenatal alcohol-related effects.

One example of a targeted media campaign is a program aimed at African-American women, 18–35 years of age, at risk for pregnancy. The primary purpose of the campaign is to increase knowledge and change attitudes about alcohol use during pregnancy. The campaign was designed to deliver four core messages: 1) drinking alcohol during pregnancy harms unborn babies; 2) pregnant women should abstain from alcohol; 3) sexually active women should not drink if they could be pregnant; and 4) women at risk for an alcohol-exposed pregnancy should see a physician.

Another media campaign is taking place at the University of Iowa where reduction of prenatal alcohol use in rural areas is targeted at women enrolled in the Women, Infants, and Children program. Through formative research, project staff is producing commercial-quality materials (a broad-based 30-second television commercial for dissemination on three channels; an 8-minute video for localized distribution in Women, Infants, and Children clinics; and a printed pamphlet for distribution in Women, Infants, and Children clinics) to increase awareness about the dangers of alcohol use during pregnancy. Women, Infants, and Children clinics in rural Iowa will be paired and randomly assigned to usual care or awareness intervention groups.

A project based at the University of Texas at San Antonio is exploring characteristics regarding alcohol use and pregnancy, and plans to demonstrate the effectiveness of a social action approach to prevent alcohol-exposed pregnancies among Latinos in San Antonio. The project will investigate the values, attitudes, and behaviors of Latinos regarding motherhood and pregnancy, patterns of alcohol use and familial patterns, sexual activity, and knowledge of FAS. The study will pilot-test a social action intervention model that aims to alter normative drinking behavior and/or sexual behavior.

Health professionals, including pharmacists, have a responsibility to their patients and to society to effectively counsel pregnant women and those at risk for becoming pregnant of the dangers of prenatal alcohol use. Prevention of FAS and other alcohol-related birth defects requires the active involvement of all health professionals with whom the patient may come into contact. Yet, in one recent survey, only 1% of obstetric physicians reported asking about alcohol use at every prenatal visit and 70% reported time limitations as a barrier to assessment.

Many health professionals receive little or no training on substance abuse issues and when they do, the message often is not clear. Despite public health recommendations that pregnant women abstain from drinking during pregnancy, a recent review of 81 obstetrical textbooks found that only 17% consistently recommended that pregnant women should not consume alcohol. Although there was a slight upward trend toward recommendations for abstinence in more recent texts, only 24% of the 29 texts published after 1990 made this recommendation. Fifty-three percent of all texts and 52% of texts published after 1990 contained a sentence condoning drinking at some level. The remaining texts (30%) contained no recommendations. Many texts, even those published recently, have not embraced public health recommendations and, in some instances, contradict them.

For some time now, it has been known that the incidence of alcoholism is affected by genetic factors. A recent study of identical twins demonstrated that not only alcoholism,

Ingersoll K, Floyd L, Sobell M, Velasquez MM; Project CHOICES Intervention Research Group. Reducing the risk of alcohol-exposed pregnancies: a study of a motivational intervention in community settings. Pediatrics 2003;111:1131–5.

Loop KQ, Nettleman MD. Obstetrical textbooks: recommendations about drinking during pregnancy. Am J Prev Med 2002;23:136–8.

but also certain medical complications of alcoholism including alcoholic psychosis and cirrhosis, also are genetically influenced. It is thought that 50% of the overall variance in these traits is because of additive genetic factors. Susceptibility to FAS is not because of a mutation in a single gene, but rather of the action of both genes and environmental risk factors including exposure to alcohol.

Identifying the precise genes that might contribute to the risk of a complex disorder such as FAS is not an easy task. Using the case-control approach, researchers can evaluate the role of a particular candidate gene on a disease phenotype. To study the genes responsible for FAS, two samples would need to be studied: a group of FAS patients and a control group of non-FAS patients. The goal would be to find a sample of individuals whose mothers consumed similarly large amounts of alcohol. Ideally, the two groups would be matched (e.g., ethnically) so that they differ only in the presence or absence of FAS. The allele frequencies at a marker within or near the candidate gene of interest are then compared in the two groups, and evidence of differences in allele frequencies between the two groups typically is interpreted as causal evidence that the candidate gene contributes to disease susceptibility. In the mixed ancestry population of the Western Cape Province in South Africa, this approach has found that the ADH2*2 allele is significantly more common in controls compared to the children with FAS and their mothers. Thus, the ADH2*2 allele is protective against FAS, as is the ADH2*3 allele. The isoenzyme forms containing the β2 and β3 subunits and encoded by the variant ADH2*2 and ADH2*3 alleles metabolize alcohol faster than those encoded by the ADH2*1 allele that encodes for the β1 subunit. In the future, perhaps it will be possible to develop methods to test a patient's genotype, thereby identifying a high-risk population for developing FAS. In this way, specific programs targeting these individuals could be developed.

Preventing Substance Abuse Among Children and Adolescents

Abuse of alcohol, tobacco, and other drugs is considered by some to be the nation's No. 1 health problem. There are more deaths, illnesses, and disabilities from substance abuse than from any other preventable health condition. The economic cost of substance abuse to the United States economy each year is staggering, estimated at more than $414 billion. Reducing the abuse of drugs and other substances would result in enormous cost-savings to the health care system, not to mention the immeasurable benefits to those whose pain and suffering would be prevented.

Considerable research has been conducted to determine how the problem of drug abuse starts and how it progresses. Studies indicate that some children are already abusing drugs by 12 or 13 years of age. Early abused drugs include tobacco, alcohol, inhalants, marijuana, and pharmaceutical drugs. If drug abuse persists into later adolescence, abusers typically become more involved with marijuana and then advance to other illegal drugs, while continuing their abuse of tobacco and alcohol. Studies also have shown that early initiation of drug abuse is associated with greater drug involvement in the long term, whether with the same or different drugs.

Scientists have proposed several hypotheses as to why individuals first become involved with drugs and then escalate to abuse. One explanation is a biological cause, such as having a family history of drug or alcohol abuse, which may genetically predispose a person to drug abuse. Another explanation is that starting to abuse a drug may lead to affiliation with more drug-abusing peers which, in turn, exposes the individual to other drugs. Many other factors may be involved.

Research has shown that the key risk periods for drug abuse occur during major transitions in children's lives. These transitions include significant changes in physical development (e.g., puberty) or social circumstances (e.g., divorce or relocation) when children experience heightened vulnerability for problem behaviors. Children often experience the first big transition when they leave the sanctuary of the family and begin their schooling. New academic and social circumstances accompany the move from elementary school to middle or junior high school. Learning to get along with a broader group of peers and having greater pressure to earn good grades create an environment where children are likely to encounter drug use for the first time.

In high school, there are new social, psychological, and educational challenges. Children are more likely to encounter greater availability of drugs, drug abusers, and social circumstances involving drugs. A particularly risky period occurs in late adolescence when students move away from home for the first time to live without parental supervision, perhaps to attend college or other schooling. Substance abuse, particularly of alcohol, remains a major public health problem for college populations. Life is filled with all types of transitions, but the news is not all bad: research has shown that some new lifestyles, such as marriage and parenthood, serve as protective factors—the new roles become more important than being involved with drugs in some cases.

Pharmacists consider themselves to be knowledgeable about drugs and pride themselves on being able to deliver "antidrug" messages, focusing primarily on information about the drugs themselves. Information refers to facts about drugs and their effects, as well as drug laws and policies. However, drug information alone has not been an effective drug abuse deterrent. Combining information with skills, methods, and services produces more effective results. Table 1-4 describes the type of content included in effective prevention programs. Skills development training is aimed at building and improving behaviors in important areas, such as communication within the family, social and emotional development, academic and social competence in children, and peer resistance strategies in adolescents.

Risk Factors and Protective Factors

Many factors have been discovered that help identify individuals more likely to abuse drugs compared with those

Table 1-4. Content Areas for Effective Drug Abuse Prevention Programs

Program Types	Information	Skills Development	Methods	Services
Community	Drug trends	Social skills	Tolerance policies	Drug-free zones
School	Drug effects	Resistance skills	Norms change	School counseling and assistance
Family	Drug abuse symptoms	Parenting skills	Home drug testing Curfew	Family therapy

less likely to get involved. Factors associated with greater potential for drug abuse are called "risk" factors, and those associated with reduced potential for abuse are considered "protective" factors. It would seem intuitive that if people could work to eliminate or decrease the risk factors or improve the protective factors, then the likelihood of individuals becoming involved in drugs would be diminished. Indeed, research shows this to be the case.

Table 1-5 provides a framework for identifying risk and protective factors in five settings or domains. As the first two examples suggest, some risk and protective factors are mutually exclusive. That is, the presence of one means the absence of the other. For example, in the individual domain, early aggressive behavior is a risk factor that indicates the absence of impulse control, a key protective factor. Helping a young child learn to control impulsive behavior is a focus of some prevention programs. Prevention programs should be aimed at changing the balance between risk and protective factors so that protective factors outnumber the risk factors.

Table 1-5. Risk Factors and Protective Factors for Substance Abuse

Risk Factors	Domains	Protective Factors
Early aggressive behavior	Individual	Impulse control
Lack of parenteral supervision	Family	Parental monitoring
Substance abuse	Peer	Academic competence
Drug availability	School	Antidrug use policies
Poverty	Community	Strong neighborhood attachment

Long-term research studies have led to the development of some guiding principles common to effective prevention programs. These can be used to guide prevention practitioners in setting up programs to decrease drug use among children and adolescents. The earlier an intervention is made to change the risk factors (e.g., aggressive behavior and poor self-control), the greater its effect. Prevention programs should address all forms of drug abuse, alone or in combination, including the underage use of legal drugs (e.g., tobacco or alcohol); the use of illegal drugs (e.g., marijuana or heroin); and the inappropriate use of legally obtained substances (e.g., inhalants, prescription drugs, or nonprescription drugs). Programs also should address the type of drug abuse problem in the local community, target modifiable risk factors, and strengthen protective factors that might be present. To improve program effectiveness, prevention programs should be designed to address risks specific to the population or audience characteristics, such as age, gender, and ethnicity,

Family-based prevention programs should enhance family bonding and relationships and include parenting skills; practice in developing, discussing, and enforcing family policies on substance abuse; and training in drug education and information. Prevention programs can be designed to intervene as early as preschool to address risk factors for drug abuse, such as aggressive behavior, poor social skills, and academic difficulties

Prevention programs for elementary school children should target improving academic and social-emotional learning, such as early aggression, academic failure, and school dropout, to address risk factors for drug abuse. Education should focus on skills, such as self-control, emotional awareness, communication, social problem-solving, and academic support, especially in reading. Programs for middle or junior high and high school students should increase academic and social competence with the following skills: study habits and academic support, communication, peer relationships, self-efficacy and assertiveness, drug resistance skills, reinforcement of antidrug attitudes, and strengthening of personal commitments against drug abuse.

Prevention programs aimed at general populations at key transition points, such as the transition to middle school, can produce beneficial effects even among high-risk families and children. Community prevention programs that combine two or more effective programs, such as family-based and school-based programs, can be more effective than a single program alone. Community prevention programs reaching populations in many settings (e.g., schools, clubs, faith-based organizations, and the media) are most effective when they present consistent, community-wide messages in each setting.

Prevention programs should be long-term with repeated interventions (i.e., booster programs) to reinforce the original prevention goals. Research shows that the benefits from middle school prevention programs diminish without follow-up programs in high school. Teacher training on good classroom management practices, such as rewarding appropriate student behavior, are necessary in effective prevention programs. These techniques help to foster students' positive behavior, achievement, academic motivation, and school bonding. Peer discussion groups and parent role-playing allow for active involvement in learning about drug abuse and reinforcing skills.

Research-based prevention programs can be cost-effective. For example, in a recent study, investigators performed cost-effectiveness and cost-benefit analyses on

Hawkins JD, Catalano RF, Arthur MW. Promoting science-based prevention in communities. Addict Behav 2002;27:951–76.

data from two long-term interventions previously shown to be effective in preventing substance abuse. Both interventions were found to be cost-beneficial by preventing adult cases of alcohol abuse, thereby saving future costs for treatment of alcohol abuse. For each $1 invested in one of these programs, there was a benefit of $9.60 in prevention. For the other program, $5.85 of benefit was derived from each $1 invested. For each family in the first program, there was a benefit of $5,923, and for the second program a benefit of $2,697 per family was observed.

Drug Abuse Resistance Education (DARE) is a long-standing and highly acclaimed drug abuse prevention program that was estimated to reach 26 million school children in the United States in 2004. It is the most widely implemented drug use prevention program in the United States and has considerable community support. According to its organizers, this program, founded in 1983 in Los Angeles, is now being implemented in almost 80% of the nation's school districts and in more than 54 countries around the world. Drug Abuse Resistance Education is a police officer-led series of classroom lessons that teaches children from kindergarten through 12th grade how to resist peer pressure and live productive drug-free and violence-free lives.

Despite the excellent reputation of this program, research has questioned its effectiveness in changing drug abuse behaviors. A recent study was conducted to evaluate the effect of the middle and junior high school Drug Abuse Resistance Education and an enhanced program called Drug Abuse Resistance Education Plus on drug use and violence. The study was a randomized, controlled trial of 24 schools and neighborhoods, primarily in Minneapolis-St. Paul, Minnesota. The research included all 7th-grade students in 24 schools in the academic year 1999–2000. The outcomes measured were self-reported tobacco, alcohol, and marijuana use; multidrug use; violence; and victimization. These outcomes were assessed at the beginning and end of 7th grade and at the end of 8th grade. There were no significant differences between children who attended a Drug Abuse Resistance Education program and children who did not. There were significant differences among boys undergoing the expanded version of the program and those who did not, with positive results for tobacco, alcohol, and multidrug use and victimization. Researchers concluded that Drug Abuse Resistance Education Plus significantly enhanced the effectiveness of the Drug Abuse Resistance Education curriculum among boys and was more effective than the delayed program controls, underscoring the potential for multiyear, multicomponent prevention programs, and demonstrating gender differences in response to intervention programs.

Are there prevention programs that do work? In the Annotated Bibliography is a reference that will direct the interested reader to a Web site discussing such prevention programs.

Treatment of Opiate Dependence with Buprenorphine

Typically, opioid dependency is treated initially with detoxification, usually in an inpatient setting. Some individuals remain drug-free, but a large number of patients require long-term maintenance therapy. Until recently, the cornerstone of opioid-dependency treatment was methadone or levomethadyl acetate. However, federal restrictions limited distribution of these drugs to a small number of "methadone clinics" with limited provision for take-at-home dosing of methadone or levomethadyl because of concern about the diversion of these drugs to illicit use.

In October 2003, the FDA-approved labeling of two new formulations of buprenorphine indicated for treating opiate dependence. The first of these formulations contained only buprenorphine, and is intended for use at the beginning of treatment for opiate abuse. A second product contains both buprenorphine and naloxone, and is the formulation used for maintenance treatment of opiate addiction. Naloxone was added to buprenorphine, so that the formulation cannot be ground up and injected intravenously, lest the naloxone negate the pharmacological actions of buprenorphine. These drugs represent the first therapy available for in-office prescribing for opioid dependence; yet, not every physician is permitted to prescribe these new drugs. To qualify, physicians must be board certified in addiction medicine/psychiatry or have other special credentials, and physicians are required to obtain 8 hours of authorized training before they can prescribe drugs for office-based treatment of opioid dependence. They also must agree to treat no more than 30 opioid-dependent patients at any one time, and they must obtain special Drug Enforcement Administration numbers indicating that they are authorized to prescribe under the provisions of the Drug Addiction Treatment Act of 2000.

In a multicenter, randomized, placebo-controlled trial, 326 people addicted to opiates were assigned to office-based treatment with sublingual tablets consisting of buprenorphine (16 mg) in combination with naloxone (4 mg), buprenorphine alone (16 mg), or placebo given daily for 4 weeks. The primary outcome measures were the percentage of urine samples negative for opiates and the patients' self-reported craving for opiates. Safety data were obtained on 461 people addicted to opiates who participated in the open-label phase of buprenorphine and naloxone (at daily doses of up to 24 mg and 6 mg, respectively) and another 11 people who received this combination only during the trial.

The double-blind trial was terminated early because both buprenorphine and naloxone in combination and buprenorphine alone had greater efficacy than placebo. The proportion of urine samples that were negative for opiates was greater in the combined treatment and buprenorphine groups (17.8% and 20.7%, respectively) than in the placebo group (5.8%; $p<0.001$ for both comparisons with each buprenorphine group); the active

Spoth RL, Guyll M, Day S. Universal family-focused interventions in alcohol-use disorder prevention: cost effectiveness and cost-benefit analyses of two interventions. J Stud Alcohol 2002;63:219–28.

treatment groups also reported fewer opiate cravings ($p<0.001$ for both comparisons with placebo). Rates of adverse events were similar in the active treatment and placebo groups. During the open-label phase, the percentage of urine samples negative for opiates ranged from 35.2% to 67.4%. Results from the open-label follow-up study indicated that the combined treatment was safe and well tolerated. The authors concluded that the combination of buprenorphine and naloxone and buprenorphine alone are safe and reduce the use of and craving for opiates among people addicted to opiates who receive these drugs in an office-based setting.

Physicians will use sublingual buprenorphine alone during induction and will give a small supply of the product directly to the patient (clinical studies used buprenorphine-only tablets for the first 2 days). Community pharmacists typically will see prescriptions for the combination of buprenorphine and naloxone. If patients present prescriptions for either drug from more than one prescriber for the same time period, the pharmacist should assume that diversion or abuse is occurring, refuse to fill the prescriptions, and notify both prescribers. Likewise, prescriptions for the single-entity product should be verified with prescribers, as the combination is preferred for long-term therapy.

Conclusions, Challenges, and More Questions

Pharmacists have an opportunity to provide pharmaceutical care and clinical pharmacy services in conjunction with interdisciplinary teams to optimize drug therapy regimens. They also have the expertise to research the etiology, behaviors, and other potentially modifiable risk factors associated with diseases, especially those that affect public health and that may benefit from existing or future pharmacotherapeutic interventions. Pharmacists teach and promote disease prevention and health promotion to laypersons, patients, pharmacy students, and other health care professionals as opportunities arise. Disease prevention and health promotion are as important, if not more important than the treatment of already existing disease. The examples discussed in this chapter are some of the most imminent risks to public health today. Educational interventions, grants, research, and other initiatives should focus on these disease states to improve public health as a whole, and to empower patients to make a difference for their own health and welfare.

The concept that it is easier to prevent than treat disease is an intuitive one. Yet, the real work begins when modifiable risk factors and pharmacogenomics variables that affect pharmacotherapy decision-making and disease state management are identified. More research is needed to learn what interventions can be made, and how these modifiable risk factors can be decreased.

Annotated Bibliography

1. Department of Health and Human Services, Centers for Disease Control and Prevention. Health Promotion. Available at *http://www.cdc.gov./node.do/id/0900f3ec80059b1a*. Accessed November 20, 2004.

   Adopting healthy behaviors, such as eating nutritious foods, being physically active, and avoiding tobacco, can prevent or control the devastating effects of many diseases. The Centers for Disease Control and Prevention is committed to programs that reduce the health and economic consequences of the leading causes of death and disability and that ensure a long, productive, healthy life for all people. This Web site provides information about health promotion efforts that would be useful to pharmacists who need resources to help start health promotion campaigns. Topics are divided into the following areas: adolescent health, aging and elderly health, bone health, breastfeeding, correctional health, faith-based and community initiatives, global health, health-related quality of life, men's health, minority health, nutrition, oral health, physical activity, pregnancy, reproductive health, school health, tobacco, and women's health. There are many helpful links to other electronic sources of information, such as the link to a subpage called, "preventing chronic disease." This is a useful source of information; however, it does not provide extensive referencing for it content, which is the case with many Web sites.

2. The March of Dimes Birth Defects Foundation. Birth Defects: Strategies for Prevention and Ensuring Quality of Life. Available at *http://www.marchofdimes.com/professionals/*. Accessed November 20, 2004.

   The March of Dimes supports education, research, and public policies that promote the health and welfare of babies. This Web page contains an excellent overview of the problems of birth defects and efforts under way to prevent them. There are sections on the background on birth defects, major legislation aimed at preventing birth defects, and a discussion on federally sponsored birth defects research and services. Although this resource provides an excellent overview of efforts to prevent birth defects, its greatest value is the links to other resources. Special sections focus on drug-induced birth defects (e.g., those caused by isotretinoin and alcohol); an overview of the mechanisms of drug-induced dysmorphosis would be a welcomed addition. There are extensive bibliographies on a variety of patients for a pharmacist who is interested in more detail. There also are continuing education programs that focus on genetics, resources that link to perinatal statistics, and patient education materials.

3. World Health Organization Technical Report Series No. 916. Diet, Nutrition, and the Prevention of Chronic Diseases. Available at *http://www.who.int/hpr/NPH/docs/who_fao_expert_report.pdf*. Accessed November 20, 2004.

   These recommendations, drafted at a joint meeting of the World Health Organization and the Food and Agricultural Organization of the United Nations, are part of the World Health Organization Technical Report Series. This report focuses on modifiable risk factors, interventions to decrease risk, and evidence-based medicine from clinical trials. It follows a template for each disease that consists of the

Boatwright DE. Buprenorphine and addiction: challenges for the pharmacist. J Am Pharm Assoc 2002;42:432–8.

following: background, trends, diet, physical activity, strength of evidence, disease-specific recommendations, and references. Some diseases addressed include obesity, diabetes mellitus, cardiovascular disease, hypertension, stroke, osteoporosis, and cancer. It also addresses genetic susceptibility to chronic disease and gives recommendations for diet, nutrition, and physical activity. The report is 149 pages long and, at times, can be tedious to read. It is well referenced, allowing the interested reader to access primary literature and more detail on a given subject. Particularly useful is the chart at the end of the report that summarizes the strength of evidence for nutritional strategies in preventing obesity, type 2 diabetes, cardiovascular disease, cancer, dental disease, and osteoporosis.

4. United States Department of Health and Human Services, Substance Abuse and Mental Health Services Administration, Center for Substance Abuse Prevention. Bringing Effective Prevention to Every Community. Available at *http://www.mentalhealth.samhsa.gov/cmhs/specialpopulations/*. Accessed November 20, 2004.

   The Substance Abuse and Mental Health Services Administration is the federal agency charged with improving the quality and availability of prevention, treatment, and rehabilitative services to reduce illness, death, disability, and costs to society that result from substance abuse and mental illnesses. A workplace resource center on the Web site provides centralized access to information about drug-free workplaces and related topics. Also included are two Web casts featuring two model drug abuse prevention programs. The Centers for the Application of Prevention Technologies teaches people how to apply skills that have proven effectiveness for substance abuse prevention. This Web site is a comprehensive resource for the pharmacist who may wish to become involved in substance abuse prevention. It provides an evidence-based approach to evaluate what does and what does not work to reduce the burden of substance abuse in our country.

5. Grundy SM, Hansen B, Smith SC Jr, Cleeman JI, Kahn RA; American Heart Association; National Heart, Lung, and Blood Institute; American Diabetes Association. Clinical management of metabolic syndrome: report of the American Heart Association/National Heart, Lung, and Blood Institute/American Diabetes Association conference on scientific issues related to management. Circulation 2004;109:551–6.

   The metabolic syndrome consists of a constellation of factors that raise the risk for cardiovascular disease and type 2 diabetes. The National Cholesterol Education Program's Adult Treatment Panel III report identified metabolic syndrome as a multiplex risk factor deserving of more clinical attention. Subsequently, the National Heart, Lung, and Blood Institute, in collaboration with the American Heart Association, convened a conference to examine scientific issues related to the definition of metabolic syndrome. This paper summarizes a second conference devoted to clinical management of metabolic syndrome, which was sponsored by the American Heart Association in partnership with the National Heart, Lung, and Blood Institute and cosponsored by the American Diabetes Association.

   The second conference considered the following issues: 1) pathogenesis and presentation of metabolic syndrome, 2) management of underlying risk factors, 3) management of metabolic risk factors, and 4) unresolved issues and research challenges.

   The original conference identified six major components of the syndrome: abdominal obesity, atherogenic dyslipidemia, elevated blood pressure, insulin resistance with or without glucose intolerance, a proinflammatory state, and a prothrombotic state. The follow-up conference on management was structured around therapies for these components.

   Because of the increasing frequency of obesity in the United States, metabolic syndrome also has increased. Adult Treatment Panel III introduced metabolic syndrome into its clinical guidelines to achieve cardiovascular disease risk reduction beyond low-density lipoprotein-lowering therapy. All pharmacists, especially those working in primary care clinics and adult internal medicine programs, should find this report useful. The report is quite lengthy, but fortunately there are summaries and overviews that condense the information into a useable format.

6. Kalter H. Teratology in the 20th century: environmental causes of congenital malformations in humans and how they were established. Neurotoxicol Teratol 2003;25:131–282.

   This article is the most comprehensive reference that puts the issue of congential malformations in humans in a clinical perspective. It establishes a common set of definitions and a system of classification of malformations. The author created a historical approach to the study of environmental causes of birth defects. The author is able to maintain a writing style that is captivating. The article begins with a discussion of congenital malformations caused by x-irradiation and rubella. There is a fascinating historical account of a thalidomide episode as it relates to teratogenic effects of drugs. There are sections that discuss the difficulty in studying teratogenic effects of drugs as well as interesting accounts of the purported teratogens: doxylamine-pyridoxine, blighted potatoes, female sex hormones, and diethylstilbestrol.

   There is discussion of environmental hazards, such as iodine deficiency, organic mercury, Agent Orange, and such environmental disasters as the radiation leak at Chernobyl. The style of this article is such that it is difficult to read just a small section. It is clear that the author has conducted years of research to compile this paper. Without question, this is an indispensable reference for anyone interested in the subject of drug-induced birth defects.

7. Griffin KW, Botvin GJ, Nichols TR, et al. Effectiveness of a universal drug abuse prevention approach for youth at high risk for substance use initiation. Prev Med 2003;36:1–7.

   Targeting school aged children for substance abuse prevention continues to be an important disease prevention initiative but has met with mixed success. This study evaluated the effectiveness of a program designed to prevent the use of alcohol, tobacco, and other drugs of abuse in school age children. A strength of this particular study is that instead of targeting all of the students in these middle schools, only the students deemed to be at high risk for developing substance abuse problems received the substance abuse intervention. Twenty-nine innercity middle schools participated in the substance abuse prevention program. General social skills, antidrug norms, and drug refusal skills were taught to students identified as high risk for substance use initiation (n=426). The high-risk students who received the educational interventions reported less tobacco use, less alcohol use, less inhalant use, and less polydrug use at 1 year after education versus high-risk students who did not participate in the program. Whether these differences in substance abuse continue long term remain to be seen.

Although this research looked at programs in innercity middle schools, the paper would be useful for pharmacists working in substance abuse prevention who want to incorporate an evaluation component of the program.

8. Svikis DS, Reid-Quinones K. Screening and prevention of alcohol and drug use disorders in women. Obstet Gynecol Clin North Am 2003;30:447–68.

   Effective drug abuse prevention programs often need to target special populations at risk. For example, many treatments are available for women with substance use disorders. Some of these available treatments include psychosocial interventions, cognitive-behavioral therapy, and 12-step recovery programs. Drug therapies, such as acamprosate, buprenorphine, methadone, and naltrexone, also are available to be used in combination with cognitive interventions. This comprehensive review article describes the clinical trials that have documented the efficacy of pharmacotherapy and cognitive therapy in combination to decrease substance abuse. Although a challenging proposition, physicians and pharmacists can use this review article to identify effective interventions to decrease the onset and recidivism of substance abuse problems with their patients. The article encourages more primary care practitioners to screen for substance abuse, and intervene quickly and efficiently. This paper looks at new strategies to enhance practitioner feelings of self-efficacy about their ability to identify and intervene early in the progression from alcohol use to abuse to dependence.

9. Substance Abuse and Mental Health Services Administration. Model Programs: Effective Substance Abuse and Mental Health Programs for Every Community. Available at *http://modelprograms.samhsa.gov/template.cfm?page=default.* Accessed November 20, 2004.

   This PSAP chapter talked about the elements of an "ideal" or model program for delivering substance abuse prevention messages. Can there possibly be programs that meet or exceed these standards? Indeed, programs have been identified as model programs, described as well-implemented, well-evaluated programs. The Substance Abuse and Mental Health Services Administration of the United States Department of Health and Human Services maintains this Web site identifying such "model programs." To be acknowledged by the Substance Abuse and Mental Health Services Administration as a model program requires review by the National Registry of Effective Programs according to rigorous standards of research. In return for being recognized as model programs, program developers have coordinated and agreed with Substance Abuse and Mental Health Services Administration to provide quality materials, training, and technical assistance for nationwide implementation. This site would be particularly useful for those who wish to begin providing prevention services without having to start from scratch.

SELF-ASSESSMENT QUESTIONS

Questions 1 and 2 pertain to the following case.
One hundred thirty male, Mexican-American alcoholics who met Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, criteria for alcohol dependence were recruited for a study. Two hundred fifty-one Mexican-Americans were in the control group. Peripheral blood samples were collected, and deoxyribonucleic acid was isolated, amplified, and sequenced for genotypic analysis. The table below lists the results of genotypic analysis.

Genotype and allele frequency of dopamine type 2 receptor *Taq*I A, B, and -141C insertion/deletion polymorphisms; serotonin transporter-linked polymorphic region; and gamma aminobutyric acid A receptor β_3 subunit gene in Mexican Americans.

1. Based on the results in the table, which one of the following can be concluded from this study?

A. A positive association was found between alcoholism in Mexican Americans and the serotonin transporter-linked polymorphic region S allele.
B. A positive association was found between alcoholism in Mexican Americans and the dopamine dopamine type 2 receptor *Taq*I A allele.
C. No positive association was found between alcoholism in Mexican Americans and the serotonin transporter-linked polymorphic region S allele.
D. A positive association was found between alcoholism in Mexican Americans and the dopamine type 2 receptor *Taq*I B allele.

2. You are a clinical pharmacist employed by the National Institute on Drug Abuse. Based on this clinical data from the case, which one of the following is the best next step in the interest of public health?

	n	Genotype (%)			Frequency (%)	
*DRD2 Taq*I		*A A1/A1*	*A1/A2*	*A2/A2*	*A1_A2/A2_A2*	*A2*
Nonalcoholic patients	251	81 (32.3)	121 (48.2)	49 (19.5)	170 (67.7)	43.6
Alcoholic patients	130	42 (32.3)	64 (49.2)	24 (18.5)	88 (67.7)	43.1
*DRD2 Taq*I		*B B1/B1*	*B1/B2*	*B2/B2*	*B1_B2/B2_B2*	*B2*
Nonalcoholic patients	251	92 (36.7)	123 (49.0)	36 (14.3)	159 (63.3)	38.8
Alcoholic patients	130	52 (40.0)	57 (43.8)	21 (16.2)	78 (60.0)	38.1
*DRD2 Taq*I -141C *Ins/Del*		*Del/Del*	*Ins/Del*	*Ins/Ins*[a]	*Ins/Del_Ins/Ins*	*Ins*
Nonalcoholic patients	251	7 (2.8)	70 (27.9)	174 (69.3)	244 (97.2)	83.3
Alcoholic patients	130	6 (4.6)	18 (13.9)	106 (81.5)[a]	124 (95.4)	88.5
5-HTTLPR		*L/L*	*L/S*	*S/S*	*L/S_S/S*[b]	S[c]
Nonalcoholic patients	251	63 (25.1)	111 (44.2)	77 (30.7)	188 (74.9)	52.8
Alcoholic patients	130	19 (14.6)	62 (47.7)	49 (37.7)	111 (85.4)[b]	61.5[c]
*GABR*b3		*G1/G1*[a]	*G1*/n*G1*	n*G1*/n*G1*	*G1*/n*G1*_n*G1*/n*G1*	n*G1*
Nonalcoholic patients	251	22 (8.8)	81 (32.2)	148 (59.0)	229 (91.2)	75.1
Alcoholic patients	126a	12 (9.5)	41 (32.6)	73 (57.9)	114 (90.5)	74.2

[a]p=0.007; $\chi^2 = 9.888$.
[b]p=0.018; $\chi^2 = 5.574$, nonalcoholic patients versus alcoholic patients.
[c]p=0.021; $\chi^2 = 5.316$, nonalcoholic patients versus alcoholic patients.
5-HTTLPR = serotonin transporter-linked polymorphic region; DRD = dopamine type 2 receptor; GABRb3 = gamma aminobutyric acid A receptor β_3 subunit gene; Ins/Del = insertion/deletion polymorphisms.

A. Choose goals and objectives for public health initiatives based on these data.
B. Use scenario planning to anticipate future public health issues.
C. Prioritize public health needs to determine prevention programs necessary.
D. Gather and analyze more data before planning public health initiatives.

3. B.J. is a 24-year-old woman who has been a patron of your community pharmacy for several years. Recently, she delivered a healthy baby boy weighing just more than 8 pounds. With all good intentions, B.J.'s mother has taken it on herself to prepare her daughter's house for the new baby. She prepared a checklist of things for her daughter to do. Among these things was the recommendation to purchase a 2-ounce bottle of ipecac syrup from the pharmacy. When B.J. asks for this product, you tell her that ipecac syrup is no longer recommended to be kept in the home. Which one of the following is the best explanation as to why ipecac syrup should not be kept in the home?

A. It has abuse potential similar to benzodiazepines and opiates.
B. Its use does not decrease emergency department visits or improve patient outcome.
C. Cardiac monitoring is necessary because of central nervous system stimulation and arrhythmias.
D. Its rapid action requires monitoring by a health care practitioner in a hospital.

4. The Food and Drug Administration (FDA) recently revised the requirement for labeling of nonprescription drugs. Which one of the following is the best explanation for this revision?

A. Encourage laypersons to use nonprescription drugs more frequently.
B. Research suggests laypersons do not understand nonprescription drug labels.
C. Nonprescription drugs are not safe when used per label instructions.
D. Pharmacists do not understand nonprescription drug labels.

5. In early 2004, the FDA banned the sale of ephedra-containing dietary supplements. The agency deemed that ephedra posed a risk to the public health. Patients taking which one of the following drugs are at an increased risk for the adverse effects attributable to ephedra?

A. Amoxicillin 500 mg 3 times/day for 7 days.
B. Orlistat 120 mg 3 times/day.
C. Fluoxetine 20 mg/day.
D. Carvedilol 25 mg 2 times/day.

6. R.L. is a 47-year-old Hispanic man who is 5'7" and 265 pounds. His current drugs include atorvastatin 10 mg once daily for hyperlipidemia, metformin 1000 mg 2 times/day for type 2 diabetes, metoprolol XL 50 mg once daily for hypertension, and phenytoin 125 mg 3 times/day for epilepsy. His physician recommends that he undergo a gastric bypass procedure because all other modalities for weight loss have failed in R.L., and he is at high risk for cardiovascular comorbidities because of obesity. Which one of the following is the best clinical pharmacy intervention after surgery?

A. Assess liver function tests and R.L.'s complaints of muscle aches.
B. Assess R.L. for hyperglycemia, hypoglycemia, or drug-induced diarrhea.
C. Assess blood pressure, heart rate, and add low-dose aspirin or an angiotensin-converting enzyme inhibitor.
D. Assess phenytoin serum concentrations and R.L.'s seizure history.

7. Which one of the following patients is the best candidate for orlistat drug therapy?

A. Patients with body mass index greater than 40 and renal dysfunction.
B. Patients with polycystic ovary syndrome, recurrent spontaneous abortion history, and insulin resistance.
C. Patients with hyperlipidemia, high-fiber diet, and body mass index greater than 27.
D. Patient with irritable bowel syndrome and an eating disorder.

8. Which one of the following is the best candidate for sibutramine drug therapy?

A. Patient with body mass index greater than 40 and renal dysfunction.
B. Patient with polycystic ovary syndrome, recurrent spontaneous abortion history, and insulin resistance.
C. Patient with uncontrolled hypertension, high-fiber diet, and body mass index greater than 27.
D. Normotensive patient with dysthymia and body mass index greater than 27.

9. You are volunteering at your local community health fair and staffing a booth with a sign that reads, "Ask the Pharmacist." A patient asks if she should continue to take her estrogen and progestin supplement for "her heart". She says her physician told her it will prevent cardiovascular disease. Which one of the following is the best response?

A. Hormone therapy is only marginally effective for primary prevention.
B. Hormone therapy is no longer appropriate for primary prevention.
C. Short-term compared to long-term hormone therapy is associated with more cardiovascular risk.
D. Stop taking hormone therapy immediately because of increased cardiovascular risk.

A randomized, double-blind, placebo-controlled, multicenter study was conducted in 463 women with a history of spontaneous preterm delivery. Women were enrolled between 16 and 20 weeks' gestation, and randomly assigned in a 2:1 ratio to receive weekly injections of 250 mg of 17-α-hydroxyprogesterone caproate or weekly

injections of inert placebo. Injections were continued to week 36 or delivery. The following data were collected:

	Pregnancy-related Complications No. (%)	Progesterone No. (%)	Placebo Relative Risk (95% CI)
Delivery before 37 weeks' gestation	111 (36.3)	84 (54.9)	0.66 (0.54–0.81)
Indicated because of complications	21 (6.9)	15 (9.8)	0.70 (0.37–1.32)

CI = confidence interval.

10. Which one of the following statements is most correct according to recently published data regarding the risk of delivery before 37 weeks' gestation?
    A. Patients in the placebo group had a decreased risk of preterm delivery.
    B. Patients in the hydroxyprogesterone group had a decreased risk of preterm delivery.
    C. Patients in the placebo group had more pregnancy-related complications.
    D. Patients in the hydroxyprogesterone group had more pregnancy-related complications.

11. Dr. Watkins is a general practitioner who works in a remote county in one of the southwestern states. He is treating a patient with premature labor at 29 weeks' gestation. Dr. Watkins asks you, the clinical pharmacist for obstetrics and gynecology, why you have recommended nifedipine monotherapy. Which one of the following is the best response to his question?
    A. Nifedipine is more effective than terbutaline.
    B. Nifedipine is available intravenously and orally.
    C. Combining tocolytic drugs increases the rate of maternal pulmonary edema.
    D. Magnesium sulfate is associated with less maternal and fetal adverse effects.

12. You are a pharmacist volunteering your time in a medical clinic for homeless people. In the waiting room, you overhear two young women arguing about drinking alcohol during pregnancy. One woman contends that it is safe, just as long as you do not drink "excessively." The other woman believes differently. Based on the current scientific evidence, which one of the following statements is most correct regarding alcohol consumption during pregnancy?
    A. No amount of alcohol is safe during pregnancy.
    B. Moderate alcohol during the second trimester is not harmful.
    C. Less than two alcoholic beverages per day is not harmful.
    D. Alcohol consumption has not been definitively associated with fetal anomalies.

13. According to substance abuse specialists, which one of the following statements about fetal alcohol syndrome (FAS) is the most accurate?
    A. Mothers of children with FAS have an increased risk for future children with FAS.
    B. Fetal alcohol syndrome can be diagnosed with amniocentesis and ultrasonography.
    C. Mothers of children with FAS typically are of low socioeconomic status.
    D. Alcohol exposure during the first trimester causes FAS.

Question 14 pertains to the following table, which presents results from an evaluation of a substance abuse prevention program. Substance use was compared at the end of each "wave" of multidisciplinary interventions.

Variable	Wave 2	Wave 3	Wave 4
	Decrease in self-reported substance abuse compared to baseline (percentage)		
Recent Substance Use	6%	10%[b]	16%[c]
Alcohol	15%[b]	15%[a]	23%[c]
Cigarettes	4%	10%[a]	7%
Marijuana	1%	6%	18%[c]

[a]$p<0.05$.
[b]$p<0.01$.
[c]$p<0.001$.

14. Which one of the following statements is the best interpretation of these data?
    A. Alcohol, cigarettes, and marijuana use was decreased at study completion.
    B. Alcohol and marijuana use was decreased at study completion.
    C. Recent substance use and cigarette use decreased throughout the study.
    D. No conclusions can be drawn from these data.

Questions 15–17 pertain to the following case.

A.N. is a healthy 25-year-old who is 4 months pregnant. She is having difficulty quitting smoking but expresses a sincere desire to quit. She comes to see her pharmacist and asks if smoking cessation aids, such as bupropion or nicotine patches, are an option for her.

15. Which one of the following is the best response?
    A. Nicotine replacement therapy has been associated with congenital malformations.
    B. Nicotine replacement is contraindicated in pregnancy.
    C. Nicotine does not cross the placenta to a significant degree.
    D. Nicotine replacement poses similar risks to the fetus as smoking tobacco.

16. A.N.'s doctor is not comfortable prescribing nicotine replacement therapy to help her quit smoking. The physician asks you for an alternative recommendation. Which one of the following is the best response?
    A. Nicotine replacement therapy is contraindicated, so bupropion is her best choice.
    B. Behavioral modification therapy without nicotine patches is her best option.

C. Both behavioral modification and nicotine replacement therapy is her best option.
D. Bupropion is classified as pregnancy category C; therefore, it is not an option for A.N.

17. According to clinical practice guidelines, which one of the following most accurately describes A.N.'s risks of tobacco smoking on the fetus?

A. Smoking increases the risk of spontaneous abortion.
B. Smoking decreases the risk of low birth weight.
C. Smoking increases the risk of major teratogenesis.
D. Smoking is more harmful to the mother than the fetus.

18. A.J. is a 22-year-old Caucasian woman with a past medical history of heroin abuse for 4 years, cocaine abuse for 5 years, and alcohol abuse for 8 years. You are the clinical pharmacist at the emergency department she went to about 24 hours ago with an acute heroin overdose, as evidenced by respiratory depression, pinpoint pupils, ventricular dysrhythmias, and mental status changes leading to unconsciousness. Opiate concentrations consistent with toxicity were confirmed through drug screen. Intravenous naloxone 2 mg was administered every 3 minutes for three doses until A.J. regained consciousness; it was ordered as needed for symptom recurrence. After 24 hours of intravenous fluids and psychosocial support, A.J. was discharged with follow-up by social services. Which one of the following prescriptions is the best discharge drug to prevent opiate abuse?

A. A 30-day supply of acetaminophen-codeine orally 3 times/day.
B. A 30-day supply of extended-release oxycodone 10 mg orally 3 times/day.
C. A 30-day supply of methadone 10 mg/day.
D. A 30-day supply of buprenorphine 8 mg sublingually daily.

19. M.J. is a 32-year-old Caucasian woman in the ambulatory care clinic with a history of nausea and vomiting and general malaise occurring throughout the past 3 weeks. As the clinical pharmacist, you have been asked to do a drug history on M.J. At some point during your discussion, she tells you she thinks she is pregnant. As you talk with her, you notice a strong smell of residual alcohol on her breath, perhaps indicating a heavy night's drinking the evening before. When you inquire about her drinking habits, she tells you that she has a drink only occasionally. Which one of the following is the best thing you can do?

A. Perform a urine test to determine if she has used alcohol in the past 24 hours.
B. Recommend disulfiram or acamprosate for alcohol abstinence.
C. Give her the phone number to the local Alcoholics Anonymous chapter.
D. Explain the dangers of alcohol consumption during pregnancy.

20. A friend of yours works for a local community service agency that is applying for a grant to establish a drug abuse prevention program for children and adolescents. Knowing that you are a pharmacist, your friend asks for your help in completing the grant application. For the application section called "program description", he has proposed that you and he formulate a plan in which the county pharmacy association would develop a speaker's bureau through which pharmacists could go to local elementary schools and middle schools to explain the dangers of drugs. Which one of the following is the best response that you can give your friend?

A. Research what constitutes effective prevention programs and change accordingly.
B. Begin calling all the pharmacists that you know and ask for volunteers who would be willing to do these programs.
C. Advise him to discontinue substance abuse prevention as these programs are futile.
D. Order enough books about the adverse effects of abused drugs so that the pharmacists can present factual information to scare potential substance abusers.