The use of tobacco can be traced back to ancient times. Its popularity grew exponentially during the twentieth century, surging during wartime and with the advent of mass media. The tobacco industry in the United States has been under constant legal pressure during the past 40 years. Despite the well-known and continually increasing morbidity and mortality related to smoking, it continues to be a prominent feature in worldwide culture and health.

Nicotine is a colorless and volatile liquid alkaloid naturally occurring in the leaves and stems of *Nicotiana tabacum* and *Nicotiana rustica*. Nicotine, the primary component of tobacco, is responsible for both tobacco product addiction (with chronic exposure) and the odor associated with tobacco. In addition to cigarettes, nicotine is found in chewing gum, transdermal patches, nasal spray, and sublingual tablets. Following its inhalation and absorption, nicotine and its metabolic products exert diverse physiologic and pharmacologic effects. This article covers the absorption and metabolism of nicotine, nicotine toxicity, pharmacologic effects of nicotine, nicotine-drug interactions, and the use of nicotine for the treatment of disease.

The extensive worldwide disease burden attributable to tobacco smoking is reviewed, with particular attention to the epidemiologic
and clinical aspects, molecular and cellular mechanisms, and pathophysiology of a variety of smoking-related pulmonary diseases, and the epidemiology and clinical presentation of smoking-related atherosclerotic disease as it affects the cardiovascular system cerebral circulation, the aorta, and the peripheral arterial tree.

**Smoking and Systemic Disease**
Antara Mallampalli and Kalpalatha K. Guntupalli

Cigarette smoking is associated with a number of adverse health effects, including well-established links to cardiopulmonary disease and several cancers. Some of the other important systemic diseases associated with smoking are the subjects of this article, such as diabetes mellitus and insulin resistance and thyroid diseases. Also reviewed here is the negative impact of smoking on male and female infertility, on selected dermatologic conditions, and on gastrointestinal diseases including peptic ulcer and inflammatory bowel diseases.

**Cigarette Smoking and Nicotine Dependence**
Susan M. Zbikowski, Gary E. Swan, and Jennifer B. McClure

Tobacco use is the single most preventable cause of death, disability, and disease in the United States and is projected to be the leading cause of death and disability across all developed countries by the year 2020. Understanding nicotine dependence, its causes, consequences, and effective treatments is critical to the nation’s public health agenda. This article presents a brief overview of nicotine dependence with particular emphasis placed on understanding what nicotine dependence is, why it occurs, how it is measured, and how it can be managed through effective treatments.

**Women and Tobacco Dependence**
Virginia Cullen Reichert, Vicki Seltzer, Linda S. Efferen, and Nina Kohn

Millions of American girls and women have been drawn to smoking by an industry that has been clearly and systematically targeting women of all ages and life circumstances. Tobacco marketing strategies skillfully link cigarette use to typical female values. Biologically speaking, women are especially vulnerable to the legion of health problems of tobacco use. Smoking is a critical hazard for women in their reproductive years, particularly when they are pregnant.

**Smoking and Depression**
Khatija N. Paperwalla, Tomer T. Levin, Joseph Weiner, and Stephen M. Saravay

The relationship between smoking and depression is bidirectional. Recent research has focused on nicotine’s neurobiologic impact on
the brain as it relates to depression. Genetic factors are also important and may account for up to 67% of smoking initiation, maintenance, and dependence. Because nicotine withdrawal may mimic and induce depression, appropriate clinical evaluation and treatment are essential to reduce the high morbidity and mortality associated with smoking and depression and maximize smoking cessation rates.

Smoking in Adolescence: What a Clinician Can Do to Help 1495
Suzanne R. Sunday and Patricia Folan

Approximately 4400 adolescents try their first cigarette every day in the United States. Trying a few cigarettes or using tobacco more regularly as an adolescent significantly increases the risk of smoking in adulthood. Adolescents can develop nicotine dependency after smoking relatively few cigarettes. This article points out the prevalence and unique aspects of teenage tobacco use. In addition, current recommendations for treating nicotine dependence in adolescents are reviewed.

Pharmacotherapy of Tobacco Dependence 1517
Arunabh Talwar, Mukesh Jain, and V.K. Vijayan

Smoking cessation activities and support for its implementation should be integrated into the health care system. The outcome of smoking cessation has improved with the availability of proper behavior approaches and medications. Incorporating these guidelines into daily clinical practice ensures that health care providers provide the opportunity for patients to quit smoking. The best hope of improved treatment comes from combining existing and new pharmacotherapies with effective behavioral therapy.

Respiratory Health Consequences of Environmental Tobacco Smoke 1535
Atiya Dhala, Kenneth Pinsker, and David J. Prezant

Over the last several decades there has been a growing interest in examining the health consequences of environmental tobacco smoke (ETS). As a result of a wide body of research, ETS is now considered an unacceptable and entirely preventable public health hazard, and public policy increasingly discourages the presence of tobacco smoke in the public domain. This article provides an overview of the composition of ETS and the major diseases and disorders strongly linked to ETS, emphasizing the effects of ETS on pulmonary function, asthma, and lung cancer.

Promoting Tobacco Cessation and Relapse Prevention 1553
Susan L. Kenford and Michael C. Fiore

Although there is no single cure for tobacco dependence, there are numerous effective treatments for promoting cessation. Using the
chronic disease model of advising and counseling, this article outlines a model for helping patients overcome tobacco dependence. This model consists of the five A's: Ask, Advise, Assess, Assist, and Arrange. Although most of this article focuses on how clinicians who are bound by time constraints can be effective in promoting tobacco cessation, key elements for more intensive interventions are briefly discussed and suggestions for dealing with the less motivated patient are offered.

**Smoking and Sleep Disorders**
Aung Htoo, Arunabh Talwar, Steven H. Feinsilver, and Harly Greenberg

Cigarette smoking is the most important cause of preventable disease, disability, and premature death in the United States. In addition to adverse effects on respiratory, cardiovascular, cerebrovascular, and other systems, accumulating evidence indicates that cigarette smoking may also increase morbidity by adversely affecting sleep. This article focuses on the effects of cigarette smoking, nicotine, and pharmacologic agents used for smoking cessation on neuronal systems regulating sleep and clinically apparent sleep disorders.

**Smokeless Tobacco: An Emerging Addiction**
Jon O. Ebbert, Alan B. Carr, and Lowell C. Dale

Smokeless tobacco (ST) use is an important health issue in the United States, and chronic use leads to significant morbidity. ST users are exposed to levels of nicotine comparable with smokers and experience symptoms of nicotine withdrawal when attempting to stop. Clinical treatment of ST users requires an understanding of the unique characteristics of ST. This article reviews ST products, epidemiology, pharmacology, health risks, and treatment approaches.

**Alternative Therapies for Tobacco Dependence**
Lynn M. Villano and Adrian R. White

This article explores the use of acupuncture and hypnosis to treat tobacco dependence. For both hypnotherapy and acupuncture, the evidence of any effect is anecdotal. There are insufficient rigorous studies that are homogeneous in design or results to allow a reliable conclusion on whether or not these therapies are effective. At best, individual smokers who choose one of these interventions for preference should not be discouraged provided that they are informed about the state of the evidence.

**Office-Based Intervention for Tobacco Dependence**
Susan H. Swartz and J. Taylor Hays

A successful office approach for any behavior change, including for tobacco, makes the intervention part of the everyday work of the
medical practice. This article recommends how to integrate tobacco treatments efficiently into clinical practice. Specific ways to think systematically about smoking cessation and intervene with patients are discussed. Strategies to implement office-based changes to improve tobacco intervention are then presented.

Cigarette Smoking in Interstitial Lung Disease: Concepts for the Internist 1643
Kevin R. Flaherty and Fernando J. Martinez

Cigarette smoking is a common cause of lung disease. It is clearly implicated in the development of chronic obstructive pulmonary disease and lung cancer. Importantly, cigarette smoking has also been implicated in the development of interstitial lung diseases such as respiratory bronchiolitis interstitial lung disease, desquamative interstitial pneumonia, pulmonary Langerhans' cell histiocytosis, and idiopathic pulmonary fibrosis. The exact role of cigarette smoking in the development of interstitial lung diseases is still being defined; the relatively low prevalence of interstitial lung disease makes epidemiologic studies difficult.

Overview of Smoking and All Cancers 1655
Jason S. Levitz, Thomas P. Bradley, and Anne L. Golden

Tobacco consumption has been clearly implicated in the causation of many cancer types, with irrefutable evidence to support the association in multiple organ systems. Tobacco cessation leads to reduced cancer risk and improved survival of those under treatment for their already established cancers. As understanding of the mechanisms by which tobacco products cause cancer increases, clinicians may be able to identify those at highest risk for tobacco-related malignancies and allow for more focused interventions toward risk reduction among current tobacco users. This article reviews the carcinogens present in tobacco products, the mechanisms by which tobacco causes cancer, and the various tumor types causally related to tobacco use.

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