



SMOKING'S IMMEDIATE EFFECTS ON THE BODY

Many teenagers and adults think that there are no effects of smoking on their bodies until they reach middle age.¹ Smoking-caused lung cancer, other cancers, heart disease, and stroke typically do not occur until years after a person's first cigarette. However, there are many serious harms from smoking that occur much sooner. In fact, smoking has numerous immediate health effects on the brain and on the respiratory, cardiovascular, gastrointestinal, immune and metabolic systems. While these immediate effects do not all produce noticeable symptoms, most begin to damage the body with the first cigarette – sometimes irreversibly – and rapidly produce serious medical conditions and health consequences.

Rapid Addiction from Early Smoking

Many teenagers and younger children inaccurately believe that experimenting with smoking or even casual use will not lead to any serious dependency. In fact, the latest research shows that serious symptoms of addiction – such as having strong urges to smoke, feeling anxious or irritable, or having unsuccessfully tried to not smoke – can appear among youths within weeks or only days after occasional smoking first begins.² The average smoker tries their first cigarette at age 12 and may be a regular smoker by age 14.³ Every day, more 3,500 kids try their first cigarette and about 1,000 other kids under 18 years of age become new regular, daily smokers.⁴ Almost 90 percent of youths that smoke regularly report seriously strong cravings, and more than 70 percent of adolescent smokers have already tried and failed to quit smoking.⁵

Immediate and Rapid Effects on the Brain

Part of the addictive power of nicotine comes from its direct effect on the brain. In addition to the well-understood chemical dependency, cigarette smokers also show evidence of a higher rate of behavioral problems and suffer the following immediate effects:

- **Increases Stress.** Contrary to popular belief, smoking does not relieve stress. Studies have shown that on average, smokers have higher levels of stress than non-smokers.⁶ The feelings of relaxation that smokers experience while they are smoking are actually a return to the normal unstressed state that non-smokers experience all of the time.⁷
- **Alters brain chemistry.** When compared to non-smokers, smokers brain cells- specifically brain cell receptors- have been shown to have fewer dopamine receptors. Brain cell receptors are molecules that sit on the outside of the cell interacting with the molecules that fit into the receptor, much like a lock and key. Receptors (locks) are important because they guard and mediate the functions of the cell. For instance when the right molecule (key) comes along it unlocks the receptor, setting off a chain of events to perform a specific cell function. Specific receptors mediate different cell activities.

Smokers have fewer dopamine receptors, a specific cell receptor found in the brain that is believed to play a role in addiction.⁸ Dopamine is normally released naturally while engaging in certain behaviors like eating, drinking and copulation.⁹ The release of dopamine is believed to give one a sense of reward. One of the leading hypothesis regarding the mechanism of addiction theorizes that nicotine exposure initially increases dopamine transmission, but subsequently decreases dopamine receptor function and number. The initial increase in dopamine activity from nicotine results initially in pleasant feelings for the smoker, but the subsequent decrease in dopamine leaves the smoker craving more cigarettes.¹⁰

New animal studies have shown that brain chemistry and receptors may be altered early in the smoking process.¹¹ Habitual smoking may continue to change brain chemistry, including decreasing dopamine receptors and thus yielding a more intense craving and risk of addiction. These brain chemistry changes may be permanent. In addition, because the role played by receptors in other cognitive functions, such as memory and intelligence, is unknown, how cigarette smoking effects

other brain functions by altering brain chemistry is unknown.¹²

Immediate and Rapid Effects on the Respiratory System

The respiratory system includes the passages from the nose and sinuses down into the smallest airways of the lungs. Because all of these spaces are in direct communication with one another, they can all be affected by tobacco smoke simultaneously.

- **Bronchospasm.** This term refers to “airway irritability” or the abnormal tightening of the airways of the lungs. Bronchospasm makes airways smaller and leads to wheezing similar to that experienced by someone with asthma during an asthma attack.¹³ While smokers may not have asthma, they are susceptible to this type of reaction to tobacco smoke.¹⁴ An asthmatic that starts smoking can severely worsen his/her condition.¹⁵ Bronchospasm makes breathing more difficult, as the body tries to get more air into irritated lungs.
- **Increases phlegm production.** The lungs produce mucus to trap chemical and toxic substances. Small “finger like” hairs, called cilia, coat the lung's airways and move rhythmically to clear this mucus from the lungs. Combined with coughing, this is usually an effective method of clearing the lungs of harmful substances. Tobacco smoke paralyzes these hairs, allowing mucus to collect in the lungs of the smoker.¹⁶ Cigarette smoke also promotes goblet cell growth resulting in an increase in mucus.¹⁷ More mucus is made with each breath of irritating tobacco and the smoker cannot easily clear the increased mucus.
- **Persistent cough.** Coughing is the body's natural response to clear irritants from the lungs. Without the help of cilia (above), a smoker is faced with the difficult task of clearing increased amounts of phlegm with cough alone. A persistent cough, while irritating, is the smoker's only defense against the harmful products of tobacco smoke. A smoker will likely have a persistent, annoying cough from the time they start smoking. A smoker who is not coughing is probably not doing an effective job of clearing his/her lungs of the harmful irritants found in tobacco smoke.¹⁸
- **Decreases physical performance.** When the body is stressed or very active (for example, running, swimming, playing competitive sports), it requires that more oxygen be delivered to active muscles. The combination of bronchospasm and increased phlegm production result in airway obstruction and decreased lung function, leading to poor physical performance. In addition, smoking has been shown to stunt lung development in adolescent girls, limiting adult breathing capacity.¹⁹ Smoking not only limits one's current state of fitness, but can also restricts future physical potential.

Immediate and Rapid Effects on the Cardiovascular System

The cardiovascular system includes the heart and all of the blood vessels that carry blood to and from the organs. Blood vessels include arteries, veins, and capillaries, which are all connected and work in unison with the lungs to deliver oxygen to the brain, heart, and other vital organs.

- **Adverse lipid profile.** Lipids, a form of fat, are a source of energy for the body. Most people use this fat in its good form, called high-density lipoproteins, or HDLs. Some forms of fat, such as low-density lipoproteins (LDLs, triglycerides and cholesterol) can be harmful to the body. These harmful forms have their greatest effects on blood vessels. If produced in excess or accumulated over time, they can stick to blood vessel walls and cause narrowing. Such narrowing can impair blood flow to the heart, brain and other organs, causing them to fail. Most bodies have a balance of good and bad fats. However, that is not the case for smokers. Nicotine increases the amount of bad fats (LDL, triglycerides, cholesterol) circulating in the blood vessels and decreases the amount of good fat (HDL) available.²⁰ These silent effects begin immediately and greatly increase the risk for heart disease and stroke.²¹ In fact, smoking 1-5 cigarettes per day presents a significant risk for a heart attack.²²
- **Atherosclerosis.** Atherosclerosis is a process in which fat and cholesterol form “plaques” and stick to the walls of an artery. These plaques reduce the bloods flow through the artery. While this process starts at a very young age (Some children younger than 1 year of age already show some of the changes that lead to plaque formation.²³), there are several factors that can accelerate atherosclerosis. Nicotine and other toxic substances from tobacco smoke are absorbed through the

lungs into the blood stream and are circulated throughout the body. These substances damage the blood vessel walls, which allow plaques to form at a faster rate than they would in a non-smoker.²⁴ In this way, smoking increases the risk of heart disease by hastening atherosclerosis. In addition, a recent study in Japan showed a measurable decrease in the elasticity of the coronary arteries of non-smokers after just 30 minutes of exposure to second hand smoke.²⁵

- **Thrombosis.** Thrombosis is a process that results in the formation of a clot inside a blood vessel. Normally, clots form inside blood vessels to stop bleeding, when vessels have been injured. However, components of tobacco smoke result in dangerously increased rates of clot formation. Smokers have elevated levels of thrombin, an enzyme that causes the blood to clot, after fasting, as well as a spike immediately after smoking.²⁶ This process may result in blockage of blood vessels, stopping blood flow to vital organs. In addition, thrombosis especially occurs around sites of plaque formation (above). Because of this abnormal tendency to clot, smokers with less severe heart disease, have more heart attacks than nonsmokers.²⁷ In addition, sudden death is four times more likely to occur in young male cigarette smokers than in nonsmokers.²⁸
- **Constricts blood vessels.** It has been shown that smoking, even light smoking, causes the body's blood vessels to constrict (vasoconstriction). Smoking does this by decreasing the nitric oxide (NO₂), which dilates blood vessels, and increasing the endothelin-1 (ET-1), which causes constriction of blood vessels. The net effect is constriction of blood vessels right after smoking and transient reduction in blood supply. Vasoconstriction may have immediate complications for certain persons, particularly individuals whose blood vessels are already narrowed by plaques (atherosclerosis), or partial blood clots, or individuals who are in a hyper-coagulable state (i.e. have sickle cell disease). These individuals will be at increased risk of stroke or heart attack.²⁹
- **Increases heart rate.** Heart rate is a measure of how fast your heart is pumping blood around your body. Young adult smokers have a resting heart rate of two to three beats per minute faster than the resting heart rate of young adult nonsmokers.³⁰ Nicotine consumption increases a resting heart rate, as soon as 30 minutes after puffing; and the higher the nicotine consumption (through deep inhalation or increased number of cigarettes) the higher the heart rate.³¹ Smokers' hearts have to work harder than nonsmokers' hearts. A heart that is working harder is a heart that can tire-out faster and may result in an early heart attack or stroke.
- **Increases blood pressure.** Blood pressure is a measure of tension upon the walls of arteries by blood. It is reported as a fraction, systolic over diastolic pressure. Systolic blood pressure is the highest arterial pressure reached during contraction of the heart. Diastolic blood pressure is the lowest pressure, found during the heart's relaxation phase. Nicotine consumption increases blood pressure.³² Older male smokers have been found to have higher systolic blood pressure than nonsmoking men do.³³ Higher blood pressure requires that the heart pump harder in order to overcome the opposing pressure in the arteries. This increased work, much like that related to increased heart rate, can wear out a heart faster. The higher pressure can also cause organ damage where blood is filtered, such as in the kidneys.³⁴

Immediate and Rapid Effects on the Gastrointestinal System

The gastrointestinal system is responsible for digesting food, absorbing nutrients, and dispensing of waste products. It includes the mouth, esophagus, stomach, small and large intestines, and the anus. These continuous parts are all easily affected by tobacco smoke.

- **Gastroesophageal Reflux Disease.** This disease includes symptoms of heartburn and acid regurgitation from the stomach. Normally the body prevents these occurrences by secreting a base to counteract digestive acids and by keeping the pathway between the esophagus (the tube between the mouth and stomach) and stomach tightly closed; except when the stomach is accepting food from above. The base smokers' bodies secrete is less neutralizing than nonsmokers and thus allows digestive acids a longer period of time to irritate the esophagus.³⁵ Smokers also have an intermittent loosening of the muscle separating the esophagus and stomach, increasing the chance of stomach acid rising up to damage the esophagus.³⁶ These immediate changes in base secretion and esophagus/stomach communication cause painful heartburn and result in an increased risk of long-term inflammation and dysfunction of the esophagus and stomach.³⁷ Smoking also increases reflux of stomach contents into the esophagus and pharynx.³⁸ Occurring regularly over time, this reflux may

cause ulcerations of the lower esophagus, called Barrett's esophagus, to develop.³⁹ Barrett's esophagus may develop into esophageal cancer, which has a poor prognosis in most patients.⁴⁰

- **Peptic Ulcer Disease.** Peptic ulcers are self-digested holes extending into the muscular layers of the esophagus, stomach, and a portion of the small intestine.⁴¹ These ulcers form when excess acid is produced or when the protective inner layer of these structures is injured.⁴² Mucus is produced in the stomach to provide a protective barrier between stomach acid and cells of the stomach. Unlike in the lungs where mucus production is stimulated by cigarette smoke, mucous production in the stomach is inhibited.⁴³ Peptic ulcers usually result from a failure of wound-healing due to outside factors, including tobacco smoke.⁴⁴ Cigarette smoking increases acid exposure of the esophagus and stomach, while limiting neutralizing base production (above).⁴⁵ Smoking also decreases blood flow to the inner layer of the esophagus, stomach and small intestine.⁴⁶ In these ways, cigarette smoking immediately hinders gastrointestinal wound healing, which has been shown to result in peptic ulcer formation, when not treated.⁴⁷ Peptic ulcers are terribly painful and treatment involves the long-term use of medications. Complications of peptic ulcers often require hospitalization and may be fatal secondary to excessive blood loss.
- **Periodontal Diseases.** These occur when groups of bacteria are able to form colonies that cause infections and diseases of the mouth. Smoking quickly changes the blood supply, immune response, and healing mechanisms of the mouth, resulting in the rapid initiation and progression of infections.⁴⁸ In this way, smoking makes the mouth more vulnerable to infections and allows the infections to become more severe. The bacterial plaques of smoking also cause gum inflammation and tooth decay.⁴⁹ In addition, smoking increases tooth and bone loss and hastens deep gum pocket formation.⁵⁰
- **Halitosis.** This is a fancy word for bad breath. Everybody knows that smoking makes individuals and everything around them smell bad. Bad breath, smelly hair and clothes, and yellow teeth are among the most immediate and unattractive effects of smoking.⁵¹

Immediate and Rapid Effects on the Immune System

The immune system is the body's major defense against the outside world. It is a complicated system that involves several different types of cells that attack and destroy foreign substances. It begins in the parts of the body, which are in direct contact with the environment, such as the skin, ears, nose, mouth, stomach, and lungs. When these barriers become compromised, there are serious health consequences. Tobacco smoke weakens the immune system in a number of ways.⁵²

- **Otitis Media.** This is inflammation of the middle ear. The middle ear is the space immediately behind the eardrum. It turns received vibrations into sound. The middle ear is very vulnerable to infection. Children exposed to environmental tobacco smoke (ETS) have more ear infections than those not exposed.⁵³ Tobacco smoke disrupts the normal clearing mechanism of the ear canal, facilitating infectious organism entry into the body. The resulting middle ear infection can be very painful, as pressure and fluid build up in the ear. Continued exposure to tobacco smoke may result in persistent middle ear infections and eventually, hearing loss.⁵⁴
- **Sinusitis.** Sinusitis is sinus inflammation. Sinuses are spaces in the skull that are in direct communication with the nose and mouth. They are important for warming and moisturizing inhaled air. The lining of the sinuses consists of the same finger-like hairs found in the lungs. These hairs clear mucus and foreign substances and are therefore critical in preventing mucus buildup and subsequent infection.⁵⁵ Cigarette smoke slows or stops the movement of these hairs, resulting in inflammation and infection.⁵⁶ Sinusitis can cause headaches, facial pain, tenderness, and swelling. It can also cause fever, cough, runny nose, sore throat, bad breath, and a decreased sense of smell.⁵⁷ Sinusitis is more serious and requires a longer course of medical treatment than the common cold. Long-term smoke exposure can result in more frequent episodes and chronic cases of sinusitis; and the rate of sinusitis among smokers is high.⁵⁸
- **Rhinitis.** This is an inflammation of the inner lining of the nasal passages and results in symptoms of sneezing, congestion, runny nose, and itchy eyes, ears, and nose.⁵⁹ Similar to symptoms of the common cold, rhinitis may begin immediately in the regular smoker. Smoking causes rhinitis by

damaging the same clearing mechanism involved in sinusitis (above).⁶⁰ Rhinitis can cause sleep disturbances, activity limitations, irritability, moodiness, and decreased school performance.⁶¹ Smoking causes immediate and long-lasting rhinitis.

- **Pneumonia.** Pneumonia is an inflammation of the lining of the lungs. This inflammation causes fluid to accumulate deep in the lung, making it an ideal region for bacterial growth. Pneumonia results in a persistent cough and difficulty breathing. A serious case of pneumonia often requires hospitalization. Smoking increases the body's susceptibility to the most common bacterial causes of pneumonia and is therefore a risk factor for pneumonia, regardless of age.⁶² Pneumonia, if left untreated, can lead to pus pocket formation, lung collapse, blood infection, and severe chest pain.⁶³

Immediate and Rapid Effects on the Metabolic System

Your metabolic system includes a complicated group of processes that break down foods and medicines into their components. Proteins, called enzymes, are responsible for this breakdown. The metabolic system involves many organs, especially those of the gastrointestinal tract.

- **Scurvy and Other Micronutrient Disorders.** Micronutrients are dietary components necessary to maintain good health. These include vitamins, minerals, enzymes (above) and other elements that are critical to normal function. They must be consumed and absorbed in sufficient quantities to meet the body's needs. The daily requirement of these micronutrients changes naturally with age and can also be affected by environmental factors, including tobacco smoke.⁶⁴ Smoking interferes with the absorption of a number of micronutrients, especially vitamins C, E, and folic acid that can result in deficiencies of these vitamins.⁶⁵ A deficiency in Vitamin C can lead to scurvy which is a disease characterized by weakness, depression, inflamed gums, poor wound healing, and uncontrolled bleeding.⁶⁶ Vitamin E deficiency may cause blood breakdown, eye disease, and irreversible nerve problems of the hands, feet, and spinal cord.⁶⁷ Folic acid deficiency may result in long-lasting anemia, diarrhea, and tongue swelling.⁶⁸
- **Oxidative Damage.** Oxidants are active particles that are byproducts of normal chemical processes that are constantly underway inside the body. Their formation is called oxidation. These particles are usually found and destroyed by antioxidants, including vitamins A, C, and E. The balance of oxidation and anti-oxidation is critical to health. When oxidation overwhelms anti-oxidation, harmful consequences occur. Oxidants directly damage cells and change genetic material, likely contributing to the development of cancer, heart disease, and cataracts.⁶⁹ Oxidants also speed up blood vessel damage due to atherosclerosis (above) which is a known risk factor for heart disease.⁷⁰ Because smoking increases the number of circulating oxidants, it also increases the *consumption* of existing antioxidants.⁷¹ This increase in antioxidant consumption reduces the levels of antioxidants such as alpha-tocopherol, the active form of vitamin E.⁷² Smoking immediately causes oxidant stress in blood while the antioxidant potential is reduced because of this stress.⁷³ This dangerous imbalance cannot be neutralized and results in immediate cell, gene, and blood vessel damage.⁷⁴ In addition, a National Cancer Institute study found that beta-carotene supplements, which contain precursors of vitamin A, modestly increase the incidence of lung cancer and overall mortality in cigarette smokers.⁷⁵

Immediate and Rapid Effects on Drug Interactions

Drug breakdown, or metabolism, is important to drug effectiveness and safety. Medicines are naturally broken down into their components by enzymes. Factors that effect drug metabolism effect drug function. Factors that speed up drug metabolism decrease drug exposure time and reduce the circulating concentrations of the drug, which compromises the effectiveness of the prescription.⁷⁶ Conversely, factors that slow down drug metabolism increase the circulating time and concentration of the drug, allowing the drug to be present at harmful levels. Tobacco smoke interferes with many medications by both of these mechanisms.⁷⁷ For example, the components of tobacco smoke hasten the breakdown of some blood-thinners, antidepressants, and anti-seizure medications; and tobacco smoke also decreases the effectiveness of certain sedatives, painkillers, heart, ulcer, and asthma medicines.⁷⁸

Especially Vulnerable Populations

- **Asthmatics.** Mainstream or Environmental Tobacco Smoke (ETS) exacerbates asthma symptoms in known asthmatics. In addition, some studies have shown a link between ETS in childhood and a higher prevalence of asthma in adulthood.⁷⁹
- **Infants and Children.** Infants and children exposed to Environmental Tobacco Smoke (ETS) are at increased risk for death and disease. Mothers who smoke during pregnancy are known to have low birth-weight babies. In breastfeeding women who smoke, there is a decrease in maternal milk production and less weight gain in the exposed infant.⁸⁰ In addition, infants whose mothers smoke have an increased risk of Sudden Infant Death syndrome (SIDS), and their overall perinatal mortality rate is 25 to 56 percent higher than those infants of mothers who choose not to smoke.⁸¹ Children exposed to ETS are at increased risk of many infections, most commonly middle ear and respiratory infections, and thus require more doctor visits and hospital stays.
- **Sickle Cell Patients.** Patients with sickle cell anemia who smoke are known to have increased incidence of Acute Chest Syndrome.⁸² Acute Chest syndrome is a condition that presents with severe chest pain, and is a life-threatening emergency.

Conclusion

While some of these effects are wholly or partially reversible upon quitting smoking, research has shown that many are not. Quitting smoking provides enormous health benefits, but some smoking-caused damage simply cannot be reversed.⁸³ Moreover, many of the effects outlined here can cause considerable harm to kids and others soon after they begin smoking and well before they become long-term smokers.

Campaign For Tobacco-Free Kids, September 17, 2009

This report was originally developed by Dr. Jen Doe and Dr. Chris DeSanto from Georgetown Hospital's community pediatrics program while serving as interns at the Campaign for Tobacco-Free Kids, with subsequent work done by Dr. David Granger and Dr. Stacey Cohn during separate internships at the Campaign, and by future doctors Brent Tamamoto and Stacey Smith, while at the Campaign through American Medical Student Association internships.

More information on the health harms of tobacco use is available at
http://www.tobaccofreekids.org/facts_issues/fact_sheets/toll/products/.

¹ American Academy of Pediatrics October 1998 Child Health Month Report: The Risks of Tobacco Use: A Message to Parents and Teens; Milam, JE, "Perceived invulnerability and cigarette smoking among adolescents," *Addictive Behaviors* 25(1):71-80, January-February 2000.

² Russell, MA, "The nicotine addiction trap: A 40 year sentence for four cigarettes," *British Journal of Addiction* 85(2):293-300, February 1990.

³ DiFranza, JR, et al., "Tobacco Acquisition and Cigarette Brand Selection Among Youth," *Tobacco Control* 3:334-38, 1994. Hogan, MJ, "Adolescent Medicine: Diagnosis & Treatment of Teen Drug Use," *The Medical Clinics of North America* 84(4):927-66, July 2000.

⁴ Substance Abuse & Mental Health Services Administration (SAMHSA), HHS, *Results from the 2008 National Survey on Drug Use and Health, NSDUH: Detailed Tables*, <http://www.oas.samhsa.gov/NSDUH/2K8NSDUH/tabs/Sect4peTabs10to11.pdf>.

⁵ DiFranza, JR, et al., "Measuring the loss of autonomy over nicotine use in adolescents: the DANDY (Development & Assessment of Nicotine Dependence in Youths) Study," *Archives of Pediatrics & Adolescent Medicine* 156(4):397-403, April 2002.

⁶ Caumo, W, et al., "Risk factors for preoperative anxiety in adults," *Acta Anaesthesiologica Scandinavica* 45(3):298-307, March 2001.

⁷ Parrott, AC, "Does Cigarette Smoking Cause Stress?," *American Psychologist* 54(10):817-20, October 1999.

⁸ Dagher, A, et al., "Reduced dopamine D1 receptor binding in the ventral striatum of cigarette smokers," *Synapse* 42(1):48-53, October 2001.

⁹ Di Chiara, G, Acquas, E, & Carboni E, « Drug Motivation and abuse: A neurobiological perspective," *Annals of the New York Academy of Sciences* 654:207-219, 1992. Pfaus, JG, et al., "Sexual behavior enhances central dopamine transmission in the male rat," *Brain Research* 430:345-348, 1990.

¹⁰ Gamberino, WC & Gold, MS, "Neurobiology of Tobacco Smoking & Other Addictive Disorders," *The Psychiatric Clinics of North America* 22(2):301-312, June 1999. Shadel, WG, et al., "Current models of nicotine dependence: what is known and what is needed to advance understanding of tobacco etiology among youth," *Drug & Alcohol Dependence* 59(Suppl 1):S9-S21, 2000.

¹¹ Trauth, JA, "An animal model of adolescent nicotine exposure: effects on gene expression and macromolecular constituents in rat brain regions," *Brain Research*, 867(1-2):29-39, June 2000.

¹² Trauth, JA, et al., "Persistent and delayed behavioral changes after nicotine treatment in adolescent rats," *Brain Research* 880(1-2):167-72, October 2000.

¹³ Behrman: *Nelson Textbook of Pediatrics, Sixteenth Edition*, Copyright 2000 W.B. Saunders Company.

- ¹⁴ Behrman: *Nelson Textbook of Pediatrics, Sixteenth Edition*, Copyright 2000 W.B. Saunders Company; Brodish, PH, "The Irreversible Health Effects of Cigarette Smoking," *The American Council on Science & Health*, June 1998.
- ¹⁵ Behrman: *Nelson Textbook of Pediatrics, Sixteenth Edition*, Copyright 2000 W.B. Saunders Company; Brodish, PH, "The Irreversible Health Effects of Cigarette Smoking," *The American Council on Science & Health*, June 1998; Mitchell, B, et al., "Tobacco Use and Cessation: The Adverse Health Effects of Tobacco and Tobacco-Related Products," *Primary Care: Clinics in Office Practice* 26(3):463-98, September 1999; U.S. Department of Health & Human Services (HHS), *Preventing Tobacco Use Among Young People: A Report of the Surgeon General*, 1994.
- ¹⁶ Behrman: *Nelson Textbook of Pediatrics, Sixteenth Edition*, Copyright 2000 W.B. Saunders Company; HHS, *Preventing Tobacco Use Among Young People: A Report of the Surgeon General*, 1994.
- ¹⁷ Takeyama, K, et al, "Activation of epidermal growth factor receptors is responsible for mucin synthesis induced by cigarette smoke," *American Journal of Physiology: Lung Cellular & Molecular Physiology*, 280(1):L165-72, January 2001. Maestrelli, P, et al, "Remodeling in response to infection and injury. Airway inflammation and hypersecretion of mucus in smoking subjects with chronic obstructive pulmonary disease," *American of Respiratory & Critical Care Medicine* 164(10 Pt 2):S76-80, November 15, 2001.
- ¹⁸ Behrman: *Nelson Textbook of Pediatrics, Sixteenth Edition*, Copyright 2000 W.B. Saunders Company; Brodish, PH, "The Irreversible Health Effects of Cigarette Smoking," *The American Council on Science & Health*, June 1998; HHS, *Preventing Tobacco Use Among Young People: A Report of the Surgeon General*, 1994.
- ¹⁹ Behrman: *Nelson Textbook of Pediatrics, Sixteenth Edition*, Copyright 2000 W.B. Saunders Company; Brodish, PH, "The Irreversible Health Effects of Cigarette Smoking," *The American Council on Science & Health*, June 1998; Mitchell, B, et al., "Tobacco Use and Cessation: The Adverse Health Effects of Tobacco and Tobacco-Related Products," *Primary Care: Clinics in Office Practice* 26(3):463-98, September 1999; HHS, *Preventing Tobacco Use Among Young People: A Report of the Surgeon General*, 1994; Gold, DR, "Effects of cigarette smoking on lung function in adolescent boys and girls," *New England Journal of Medicine* 335(13):931-7, September 26, 1996. Louie, D, "The effects of cigarette smoking on cardiopulmonary function and exercise tolerance in teenagers," *Canadian Respiratory : Journal of the Canadian Thoracic Society* 8(4):289-91, July-August 2001.
- ²⁰ Mitchell, B, et al., "Tobacco Use and Cessation: The Adverse Health Effects of Tobacco and Tobacco-Related Products," *Primary Care: Clinics in Office Practice* 26(3):463-98, September 1999.
- ²¹ HHS, *Preventing Tobacco Use Among Young People: A Report of the Surgeon General*, 1994.
- ²² Mitchell, B, et al., "Tobacco Use and Cessation: The Adverse Health Effects of Tobacco and Tobacco-Related Products," *Primary Care: Clinics in Office Practice* 26(3):463-98, September 1999.
- ²³ Cotran, *Robbins Pathologic Basis of Disease, 6th Edition*, 499-503, 1999.
- ²⁴ Mitchell, B, et al., "Tobacco Use and Cessation: The Adverse Health Effects of Tobacco and Tobacco-Related Products," *Primary Care: Clinics in Office Practice* 26(3):463-98, September 1999.
- ²⁵ Otsuka, R, et al., "Acute Effects of Passive Smoking on the Coronary Circulation in Healthy Young Adults," *Journal of the American Medical Association* 286(4):436-41, July 25, 2001.
- ²⁶ Hioki, H, et al, "Acute effects of cigarette smoking on platelet-dependent thrombin generation," *European Heart Journal* 22(1):56-61, January 2001.
- ²⁷ Mitchell, B, et al., "Tobacco Use and Cessation: The Adverse Health Effects of Tobacco and Tobacco-Related Products," *Primary Care: Clinics in Office Practice* 26(3):463-98, September 1999.
- ²⁸ Brodish, PH, "The Irreversible Health Effects of Cigarette Smoking," *The American Council on Science & Health*, June 1998; Mitchell, B, et al., "Tobacco Use and Cessation: The Adverse Health Effects of Tobacco and Tobacco-Related Products," *Primary Care: Clinics in Office Practice* 26(3):463-98, September 1999.
- ²⁹ Barua, RS, et al., "Heavy and light cigarette smokers have similar dysfunction of endothelial vasoregulatory activity: an in vivo and in vitro correlation," *Journal of the American College of Cardiology* 39(11):1758-63, June 5, 2002. Barua, RS, et al., "Heavy and light cigarette smokers have similar dysfunction of endothelial vasoregulatory activity: an in vivo and in vitro correlation," *Journal of the American College of Cardiology* 39(11):1758-63, June 5, 2002. Tsuchiya, M, et al., "Smoking a single cigarette rapidly reduces combined concentrations of nitrate and nitrite and concentrations of antioxidants in plasma," *Circulation* 105(10):1155-7, March 12, 2002. Barua, RS, et al., "Heavy and light cigarette smokers have similar dysfunction of endothelial vasoregulatory activity: an in vivo and in vitro correlation," *Journal of the American College of Cardiology* 39(11):1758-63, June 5, 2002.
- ³⁰ HHS, *Preventing Tobacco Use Among Young People: A Report of the Surgeon General*, 1994.
- ³¹ Rose, JE, et al., "Acute effects of nicotine and mecamylamine on tobacco withdrawal symptoms, cigarette reward and ad lib smoking," *Pharmacology, Biochemistry & Behavior* 68(2):187-97, February 2001. Pickworth, WB, et al., "Sensory and physiologic effects of menthol and non-menthol cigarettes with differing nicotine delivery," *Pharmacology, Biochemistry & Behavior* 71(1-2):55-61, January-February 2002.
- ³² Rose, JE, et al., "Acute effects of nicotine and mecamylamine on tobacco withdrawal symptoms, cigarette reward and ad lib smoking," *Pharmacology, Biochemistry & Behavior* 68(2):187-97, February 2001; Pickworth, WB, et al., "Sensory and physiologic effects of menthol and non-menthol cigarettes with differing nicotine delivery," *Pharmacology, Biochemistry & Behavior* 71(1-2):55-61, January-February 2002.
- ³³ Primates, P, et al., "Association between smoking and blood pressure," *Hypertension* 37:187-193, 2001.
- ³⁴ Righetti, M & Sessa, A, "Cigarette smoking and kidney involvement," *Journal of Nephrology*, 14(1):3-6, January-February 2001.
- ³⁵ Fitzpatrick, TM & Blair, EA, "Smoking and pulmonary and Cardiovascular Disease: Upper Airway Complications of Smoking," *Clinics in Chest Medicine* 21(1):147-157, March 2000; Kadakia, SC, et al., "Original contributions: Effect of Cigarette smoking on Gastroesophageal Reflux Measured by 24 h Ambulatory Esophageal pH Monitoring," *American Journal of Gastroenterology* 90(10):1785-1791, October 1995; Kahrilas, PJ, "Mechanisms of acid reflux associated with cigarette smoking," *Gut* 31(1):4-10, January 1990.
- ³⁶ Brodish, PH, "The Irreversible Health Effects of Cigarette Smoking," *The American Council on Science & Health*, June 1998; Fitzpatrick, TM & Blair, EA, "Smoking and pulmonary and Cardiovascular Disease: Upper Airway Complications of Smoking," *Clinics in Chest Medicine* 21(1):147-157, March 2000; Kadakia, SC, et al., "Original contributions: Effect of Cigarette smoking on Gastroesophageal Reflux Measured by 24 h Ambulatory Esophageal pH Monitoring," *American Journal of Gastroenterology* 90(10):1785-1791, October 1995; Kahrilas, 1990; Wo, JM

- & Waring, JP, "Medical Therapy of Gastroesophageal Reflux and Management of Esophageal Strictures," *Surgical Clinics of North America* 77(5):1041-62, October 1997.
- ³⁷ Fitzpatrick, TM & Blair, EA, "Smoking and pulmonary and Cardiovascular Disease: Upper Airway Complications of Smoking," *Clinics in Chest Medicine* 21(1):147-157, March 2000; Katz, PO, "Gastroesophageal Reflux Disease," *Journal of the American Geriatrics Society* 46(12):1558-65, December 1998.
- ³⁸ Smit, CF, et al., "Effect of cigarette smoking on gastropharyngeal and gastroesophageal reflux" *The Annals of Otolaryngology, Rhinology & Laryngology* 110(2):190-3, February 2001.
- ³⁹ Falk, GW, "Barrett's esophagus," *Gastroenterology* 122(6):1569-91, May 2002.
- ⁴⁰ Swisher, SG, et al., "Gastroesophageal junction adenocarcinoma," *Current Treatment Options in Oncology* 1(5):387-98, December 2000.
- ⁴¹ Goldman, *Cecil Textbook of Medicine, 21st Edition*, 2000.
- ⁴² Coroll, *Primary Care Medicine, 3rd Edition*, 1995.
- ⁴³ Ma, L, et al., "The role of polyamines in gastric mucus synthesis inhibited by cigarette smoke or its extract," *Gut* 47(2):170-7, August 2000.
- ⁴⁴ Mitchell, B, et al., "Tobacco Use and Cessation: The Adverse Health Effects of Tobacco and Tobacco-Related Products," *Primary Care: Clinics in Office Practice* 26(3):463-98, September 1999; Cotran, *Robbins Pathologic Basis of Disease, 6th Edition*, 499-503, 1999; Coroll, *Primary Care Medicine, 3rd Edition*, 1995. Shin, VY, et al., "Cigarette smoke extracts delay wound healing in the stomach: involvement of polyamine synthesis" *Experimental Biology & Medicine (Maywood, NJ)* 227(2):114-24, February 2002.
- ⁴⁵ Fitzpatrick, TM & Blair, EA, "Smoking and pulmonary and Cardiovascular Disease: Upper Airway Complications of Smoking," *Clinics in Chest Medicine* 21(1):147-157, March 2000; Kadakia, SC, et al., "Original contributions: Effect of Cigarette smoking on Gastroesophageal Reflux Measured by 24 h Ambulatory Esophageal pH Monitoring," *American Journal of Gastroenterology* 90(10):1785-1791, October 1995; Kahrilas, 1990.
- ⁴⁶ Sabiston, *Textbook of Surgery, 15th Edition*, 1997.
- ⁴⁷ Mitchell, B, et al., "Tobacco Use and Cessation: The Adverse Health Effects of Tobacco and Tobacco-Related Products," *Primary Care: Clinics in Office Practice* 26(3):463-98, September 1999; Cotran, *Robbins Pathologic Basis of Disease, 6th Edition*, 499-503, 1999; Coroll, *Primary Care Medicine, 3rd Edition*, 1995; Sabiston, 1997.
- ⁴⁸ Palmer, RM, "Potential mechanisms of susceptibility to periodontitis in tobacco smokers," *Journal of Periodontal Research* 34(7):363-9, October 1999; Genco, RJ "Current view of risk factors for periodontal diseases," *Journal of Periodontology* 67(10 suppl):1041-9, October 1996. Obeid, P & Bercy, P, "Effects of smoking on periodontal health: a review" *Advances in Therapy* 17(5):230-7, September-October 2000. Fredriksson, M, Bergstrom, K, & Asman, B, "IL-8 and TNF-alpha from peripheral neutrophils and acute-phase proteins in periodontitis," *Journal of Clinical Periodontology* 29(2):123-8, February 2002.
- ⁴⁹ Fitzpatrick, TM & Blair, EA, "Smoking and pulmonary and Cardiovascular Disease: Upper Airway Complications of Smoking," *Clinics in Chest Medicine* 21(1):147-157, March 2000.
- ⁵⁰ Johnson, GK & Slach, NA, "Impact of tobacco use on periodontal status," *Journal of Dental Education* 65(4):313-21, April 2001.
- ⁵¹ Katz, PO, "Gastroesophageal Reflux Disease," *Journal of the American Geriatrics Society* 46(12):1558-65, December 1998; Belfiglio, G, "Breath Mint'. Two words are the centerpiece of HealthPartners' successful anti-tobacco campaign, the winner of AAHP's Community Leadership Award." *Healthplan* 38(4):46-52, 54, July-August 1997; Lamkin, L & Houston, TP, "Adolescent Medicine: Nicotine Dependency & Adolescents: Preventing & Treating," *Primary Care*, 25(1):123-35, March 1998; U.S. Preventive Services Task Force, *Guidelines from Guide to Clinical Preventive Services, Second Edition*, 1996.
- ⁵² Moszczynski, P, et al., "Immunologic findings in cigarette smokers" *Toxicology Letters* 118(3):121-7, January 3, 2001.
- ⁵³ Fitzpatrick, TM & Blair, EA, "Smoking and pulmonary and Cardiovascular Disease: Upper Airway Complications of Smoking," *Clinics in Chest Medicine* 21(1):147-157, March 2000; DiFranza, JR & Lew, RA, "Morbidity and Mortality in Children Associated with the Use of Tobacco Products by Other People," *Pediatrics* 97(4):560-8, April 1996; Daly, KA, et al., "Knowledge and Attitudes about Otitis Media Risk: Implications for Prevention," *Pediatrics* 100(6):931-6, December 1997; Stenstrom, C, "Otitis-prone Children and Controls: A study of possible predisposing factors. 2. Physical findings, frequency of illness, allergy, daycare, and parental smoking," *Acta Oto-laryngologica* 177(5):696-703, September 1997.
- ⁵⁴ Agius, AM, "Smoking and middle ear ciliary beat frequency in otitis media with effusion," *Acta Oto-laryngologica* 115(1):44-49, January 1995.
- ⁵⁵ Behrman, *Nelson Textbook of Pediatrics, Sixteenth Edition*, 2000.
- ⁵⁶ Behrman, *Nelson Textbook of Pediatrics, Sixteenth Edition*, 2000; Fitzpatrick, TM & Blair, EA, "Smoking and pulmonary and Cardiovascular Disease: Upper Airway Complications of Smoking," *Clinics in Chest Medicine* 21(1):147-157, March 2000; Pedersen, M, "Ciliary activity and pollution," *Lung* 168(supplement):368-76, 1990; Proctor, DF, "Nasal mucus transport and our ambient air," *Laryngoscope* 93:58-62, January 1983.
- ⁵⁷ Behrman, *Nelson Textbook of Pediatrics, Sixteenth Edition*, 2000.
- ⁵⁸ Lieu, JE, Feinstein, AR, "Confirmations and surprises in the association of tobacco use with sinusitis," *Archives of Otolaryngology—Head & Neck Surgery* 126(8):940-6, August 2000.
- ⁵⁹ Lasley, MV & Shapiro, GG, "Pediatric Allergy and Immunology: Rhinitis and Sinusitis in Children," *Immunology & Allergy Clinics of North America* 19(2), May 1999.
- ⁶⁰ Fitzpatrick, TM & Blair, EA, "Smoking and pulmonary and Cardiovascular Disease: Upper Airway Complications of Smoking," *Clinics in Chest Medicine* 21(1):147-157, March 2000.
- ⁶¹ Lasley, MV & Shapiro, GG, "Pediatric Allergy and Immunology: Rhinitis and Sinusitis in Children," *Immunology & Allergy Clinics of North America* 19(2), May 1999.
- ⁶² Coroll, *Primary Care Medicine, 3rd Edition*, 1995; Paul, ME & Shearer, WT, "Pediatric Allergy and Immunology: The Child Who Has Recurrent Infection," *Immunology & Allergy Clinics of North America* 19(2), May 1999.
- ⁶³ Goldman, *Cecil Textbook of Medicine, 21st Edition*, 2000.
- ⁶⁴ Goldman, *Cecil Textbook of Medicine, 21st Edition*, 2000.
- ⁶⁵ Goldman, *Cecil Textbook of Medicine, 21st Edition*, 2000; Munro, LH, "Plasma RRR-alpha-tocopherol concentrations are lower in smokers than in non-smokers after ingestion of a similar oral load of this antioxidant vitamin," *Clinical Science [London]* 92(1):87-93, January 1997.

-
- ⁶⁶ Goldman, *Cecil Textbook of Medicine, 21st Edition*, 2000; Feldman, *Sleisenger & Fordtrans' Gastrointestinal & Liver Disease, Sixth Edition*, 1998.
- ⁶⁷ Goldman, *Cecil Textbook of Medicine, 21st Edition*, 2000; Feldman, *Sleisenger & Fordtrans' Gastrointestinal & Liver Disease, Sixth Edition*, 1998.
- ⁶⁸ Goldman, *Cecil Textbook of Medicine, 21st Edition*, 2000; Feldman, *Sleisenger & Fordtrans' Gastrointestinal & Liver Disease, Sixth Edition*, 1998.
- ⁶⁹ Goldman, *Cecil Textbook of Medicine, 21st Edition*, 2000.
- ⁷⁰ Goldman, *Cecil Textbook of Medicine, 21st Edition*, 2000. Gidding, SS, "Pediatric Cardiology; Preventive Pediatric Cardiology- Tobacco, Cholesterol, Obesity, and Physical Activity," *Pediatric Clinics of North America* 46(2):253-262, April 1999.
- ⁷¹ Goldman, *Cecil Textbook of Medicine, 21st Edition*, 2000.
- ⁷² Traber, MG, et al., "Smoking and Pulmonary and Cardiovascular Disease- Tobacco-Related Diseases: Is there a Role for Antioxidant Micronutrient Supplementation?" *Clinics in Chest Medicine* 21(1):173-87, March 2000. Liu, CS, et al., "Autoantibody against oxidized low-density lipoproteins may be enhanced by cigarette smoking," *Chemico-Biological Interactions* 127(2):125-37, July 3, 2000. Tsuchiya, M, et al., "Smoking a single cigarette rapidly reduces combined concentrations of nitrate and nitrite and concentrations of antioxidants in plasma," *Circulation* 105(10):1155-7, March 12, 2002.
- ⁷³ Durak, I, et al., "Acute effects of smoking cigarettes with different tar content on plasma oxidant/antioxidant status," *Inhalation Toxicology* 12(7):641-7, July 2000.
- ⁷⁴ Goldman *Cecil Textbook of Medicine, 21st Edition*, 2000.
- ⁷⁵ Albanes, D, et al., "Alpha-tocopherol and beta-carotene supplements and lung cancer incidence in the alpha-tocopherol, beta-carotene cancer prevention studye," *Journal of the National Cancer Institute* 88(21):1560-70, November 6, 1996. Albanes, D, "Beta-carotene and lung cancer: a case study," *The American Journal of Clinical Nutrition* 69(6):1345S-1350S, June 1999.
- ⁷⁶ Desai, HD, Seabolt, J, & Jann, MW, "Smoking in patients receiving psychotropic medications," *CNS Drugs* 15(6):469-94, 2001.
- ⁷⁷ Eke, BC, Iscan, M, "Effects of cigarette smoke with different tar contents on hepatic and pulmonary xenobiotic metabolizing enzymes in rats," *Human & Experimental Toxicology* 21(1):17-23, January 2002.
- ⁷⁸ Behrman, *Nelson Textbook of Pediatrics, Sixteenth Edition*, 2000; Goldman, *Cecil Textbook of Medicine, 21st Edition*, 2000.
- ⁷⁹ Larsson, ML, et al., "Environmental Tobacco Smoke Exposure During Childhood is Associated With Increased Prevalence of Asthma in Adults" *Chest* 120(3), September 2001.
- ⁸⁰ Committee on Drugs, 2000-2001, "The transfer of drugs and other chemicals into human milk," *Pediatrics* 108(3):776-789, September 2001.
- ⁸¹ Committee on Artherosclerosis & Hypertension in Children, "Active and Passive Tobacco Exposure: Aserios Pediatric Health Problem," *Circulation* 90(5):2581-2590, November 1994.
- ⁸² Young, RC, et al, "Smoking is a factor in Causing Acute Chest Syndrome in Sickle Cell Anemia," *Journal of the National Medical Association* 84(3):267-271, March 1992.
- ⁸³ Brodish, P, *The Irreversible Health Effects of Cigarette Smoking*, June 1998.