ately successful slogan was, “You’ve Come a Long Way Baby.” These data and many more insights can be found in the Speakers Kit of the CHEST Foundation, available from the ACCP.

Once again, the tobacco industry has enlisted the support of Hollywood in portraying cigarette usage as a much-to-be-desired status symbol. Although in 2002 only 19% of Americans of high economic status smoke, 57% of their counterparts in movies puff away.

Our country has changed dramatically in recent decades, but the snake oil pitch of the purveyors of nicotine remains the same. It has been 49 years since I prepared an editorial entitled “Smoke Gets in Your Eyes—and Ears,” and yet a quotation I used then is still fully relevant. I wrote that W. C. Fields was both amused and irritated by the deceptive practices of the tobacco hawkers, as indicated by his biographer, Robert Lewis Taylor:

He often tried to ferret meaning out of sentences like “More doctors smoke Cubebs then formally,” or “Repeated tests have proven that Corn Silks are not responsible for 67% of bad breath originating in the mouth,” or “Your Y zone is safe with Hempies, the middle sized cigarette.” He was ever on the alert for additions of valuable new ingredients such as lataka or chloroform, and he marveled that almost every cigarette was far outselling the competitors. In the wind up he realized that the ultimate end of the fight for mildness was no tobacco at all, and he quit smoking in response to advertising of this sort.

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REFERENCES
2 The management of smoking in the physician’s “workshop”: a report from the ACCP Subcommittee on Smoking in the Physician’s Workshop. Chest 1982; 82:359–361

Pharmacologic Therapy for Nicotine Addiction

Increased mortality among smokers as compared to nonsmokers is well known. A 40-year longitudinal mortality study by Doll et al1 of 34,000 male British physicians from 1951 to 1991, in which smoking status was regularly ascertained, was reported in 1994. The cause of death was determined in > 90% of cases. The absolute all-cause mortality rate in middle-aged patients was twice as high among smokers as compared to nonsmokers, and life expectancy was 8 years shorter among continuing smokers as compared to lifelong nonsmokers. But if a smoker stopped smoking before the age of 35 years, the death rate for the rest of his life was indistinguishable from that of nonsmokers. A similar but progressively lesser effect was noted in successive age groups until groups ≥ 65 years old, for whom smoking cessation no longer caused a measurable effect on continued longevity.

Not only is mortality significantly increased among current smokers but so is morbidity, since diseases that lead to death inevitably cause morbidity along the way, with associated societal cost of care.2–4 Since nicotine addiction is potentially treatable, the more options we have for treatment, the more likely we are to be successful.

The severely addictive nature of nicotine is well known; as a result of its addictive nature, most cigarette smokers fail in attempts to stop smoking. Nicotine replacement therapies, patch, gum, nasal spray, or inhaler, which diminish drug withdrawal symptoms by providing alternate drug delivery, are US Food and Drug Administration (FDA) approved as smoking-cessation aids.5 Of these, various skin-patch nicotine formulations provide sustained blood nicotine levels over the course of 16 to 24 h without surge in blood nicotine levels, and thus their use helps to minimize the systemic symptoms of acute nicotine withdrawal without providing the satisfaction associated with the sudden rise in the blood nicotine level. However, a nicotine inhaler more closely approximates the physiologic effect of inhaled nicotine, while nicotine gum would have a similar effect to that of chewing tobacco. The relative merits of various nicotine-substitution methods in smoking-cessation programs remain to be determined, although the nicotine patch is more effective than nicotine spray in reducing nicotine dependence.6–8

In 1992, Ferry et al9 presented in abstract form the results of a small, double-blind, placebo-controlled study showing the beneficial effect of bupropion on smoking cessation during therapy and 6 months after therapy. The results were comparable to those of nicotine replacement therapy.9 In 1994, a larger study was reported by Ferry and Burchette10 that showed similar results. These studies lead to multiple, larger, placebo-controlled 3-month trials11,12 of the use of sustained-release bupropion for cigarette smoking cessation, and to eventual FDA approval for marketing of the drug as an aid to smoking cessation. The multiple studies show that as compared to placebo, the use of bupropion for
cigarette smoking support results in an approximate doubling of smoking-cessation rate at the end of treatment and at 6 months and 12 months from beginning of treatment. As with other studies, regardless of modality of therapy, by 12 months after beginning treatment (9 months after end of treatment), smoking-cessation rates for both active and placebo study arms fall to approximately 50% of what they were at the end of treatment.6–8,11,12 In follow-up 1 year after therapy, failure rates are not improved by extending bupropion therapy for 1 year beyond the initial 3 months of therapy.12 A trial of 12 weeks of retreatment of 450 smokers who had previously used bupropion in a smoking-cessation attempt resulted in a 6-month smoking-cessation rate of 12% as compared to 2% of those receiving placebo.14 The relative efficacy of bupropion treatment of those in whom nicotine replacement therapy was unsuccessful is unknown.

One year after institution of bupropion or of nicotine therapy in smoking-cessation programs, the success rate is only doubled as compared to placebo, from approximately 10 to 15% to between 20% and 30% regardless of therapy used.5,9,11–13,15,16 Because of the high failure rate of treatment of nicotine addiction, and sometimes intolerance of a given treatment, additional means of treatment are desirable.

The results of a double-blind, placebo-controlled study of the use of the antidepressive drug nortriptyline to aid in the withdrawal from cigarette smoking are described in this issue of CHEST (see page 403). This is the third double-blind, placebo-controlled study of this use of this drug to be reported in a peer-reviewed journal.17,18 The nortriptyline study reported in this issue shows a similar ratio of successful smoking cessation in active treatment arms compared to placebo as those in the two previously reported studies17,18; however, since different ancillary support or nonsupport measures were employed in each study, the percentage of smokers who successfully stopped smoking in treated and control arms of the studies varied between studies, as to be expected. Hughes et al19 compared the results of two previous, double-blind, peer-reviewed nortriptyline studies and one study presented in abstract form to published double-blind bupropion studies and found nortriptyline and bupropion to be equally effective in smoking cessation.

It has been hypothesized that the efficacy of antidepressive drugs in smoking-cessation programs might be a drug-class effect. A number of anxiolytic and antidepressive drugs other than bupropion and nortriptyline have been tested for efficacy in tobacco withdrawal, but despite some studies with large numbers of subjects, no other drugs have been found effective, even though smokers as a group tend to be more depressed than nonsmokers, and depression and anxiety are heightened by nicotine withdrawal.19 At this time, there is no evidence that either bupropion or nortriptyline is effective as a result of antidepressive effects.

It is well known that smokers tend to gain weight on quitting, and weight gain can serve as a motive to start smoking again. Weight gain is less a problem among quitters who take bupropion than those who use nicotine replacement as an aid to quitting, and this has been cited for a possible explanation for the success of bupropion. However, a large multicenter trial of fluoxetine, an antidepressive drug known to cause weight loss, failed to show any benefit in smoking cessation19,20; at the present time, one cannot construct a hypothesis to explain the so-far unique efficacy of bupropion and nortriptyline in smoking cessation. At present, we do not know whether nortriptyline effects smoking-cessation weight gain. Hopefully, future studies of nortriptyline in smoking cessation will monitor body weight.

Bupropion and various nicotine replacement products have FDA approval for use in treatment of nicotine addiction. The monthly cost of bupropion therapy prescribed as Zyban (GlaxoSmithKline; Research Triangle Park, NC) is approximately $120, while the monthly cost of nicotine replacement ranges from approximately $55 for patch formulations to between $160 and $400 dependant on usage of gum, spray, or inhaler formulations. The monthly cost of 75 mg/d nortriptyline is approximately $6. However, since the FDA has not approved nortriptyline use to aid in smoking cessation, prescription for smoking cessation is off label and this will limit its use.

In summary, in three published studies, nortriptyline has been shown to be an attractive and effective low-cost alternative to other more established therapies for treatment of nicotine addiction. Additional studies including head-to-head comparisons of efficacy of nortriptyline relative to nicotine replacement therapy or bupropion therapy will be necessary to determine its ultimate place in treatment of nicotine addiction. As more studies are performed and published, one can hope that eventual FDA approval will be forthcoming for the use of nortriptyline in treatment of nicotine addiction.

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Suffer the Children

Cigarette smoking makes asthma worse. That simple tenet forms one of the most well-known cornerstones of asthma management. Nevertheless, certain studies have suggested that 10 to 30% of adults with asthma continue to smoke cigarettes. They smoke despite intensive efforts at education, smoking cessation therapies, and, most notably, the negative feedback from their own personal experience with acute exacerbations of asthma. Clinical studies have suggested that such patients want to stop cigarette smoking but cannot, perhaps, to a large extent, because of the addictive properties associated with inhaling tobacco smoke.

Worsening of asthma is not limited to active cigarette smoking. Data from adults convincingly show that environmental (involuntary) tobacco smoke inhalation profoundly impacts the management of asthma, causing greater hospitalization rates and worsening of daily asthma symptoms. The impact of environmental tobacco smoke on asthmatic children is not quite as clear as that in adults, possibly because of the complexity of asthma diagnosis and management, especially for younger children. Nevertheless, studies generally show a pattern of more severe respiratory illness in association with childhood environmental tobacco smoke inhalation. Investigators have commonly quantified the extent of environmental tobacco smoke exposure in adults by simply gauging the perceived extent of exposure (questionnaire responses). Estimating smoking exposure in children is more difficult, and many investigators have relied on biochemical markers of tobacco smoke inhalation. One of the most commonly utilized markers is cotinine, a nicotine metabolite that accumulates in the blood and urine following tobacco smoke inhalation.

Mannino and colleagues from the Centers for Disease Control and Prevention have previously utilized blood cotinine and health outcome data from a United States-wide child health survey to provide important insights into the respiratory consequences of involuntary smoke inhalation. These data have shown that, among children within their survey who were aged 4 through 6 years, high blood cotinine concentrations were associated with an increased prevalence of asthma and wheezing. In this issue of CHEST (see page 409), the authors extend these observations with analyses of the subset of children within their survey who already had received a diagnosis of asthma. In the broadest terms, they found that asthma severity generally correlated with blood cotinine concentrations. Worse lung function and more days lost from school occurred for children.