

tor input into the afferent arc of the reflex. Maguire et al. found that the pupillary light reflex in treated patients became asymmetric, consistent with a marked increase in signal input from the retina of the treated eye. These objective data are very useful in monitoring the outcome of intervention in this group of patients with retinal degenerations and severely limited vision function, in which changes in more standard clinical outcomes (visual acuity and visual fields) are difficult to quantify.

Maguire et al. observed the development of a macular hole in one patient, which they believed was caused by contraction of a preexisting epiretinal membrane after surgery. Alternatively, as the authors note, subretinal injections in atrophic retina may cause complications, and this observation warrants further study. Given the limited central vision in the enrolled patients, the hole was of no clinical significance; however, it would be clinically significant in patients with better baseline retinal function. Both groups of investigators followed patients with optical coherence tomography, which provides some retinal anatomic detail. High-resolution spectral-domain optical coherence tomography provides greater resolution of the retinal-cell layers before and after treatment; this approach should be considered as these studies move forward and in future studies.¹⁰

The preliminary results from these investigations suggest that in the short term, the procedure is safe. Moreover, the data are suggestive of efficacy. Both groups recognize that longer follow-up and additional subjects are necessary to provide satisfying safety data. Certainly, efficacy data will be available only in larger trials. Some of the remaining issues include the reproducibility and persistence of the improved retinal function and whether further retinal degeneration is delayed or averted. In addition, systemic or ocular complications may yet be encountered with the treat-

ment of additional patients, with higher doses of vector, and with longer follow-up. One might also speculate that treatment of younger patients with less advanced retinal degeneration might allow greater improvement of visual function. Finally, larger studies may show advantages of a particular vector preparation, promoter selection, or technique.

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Stranded in the Periphery — The Increasing Marginalization of Smokers

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One of the greatest health advances in the past three decades has been the continuing decline in the prevalence of smoking, which recently hit a modern age-adjusted low of 19% of adults in the United States, down from a high of 57% of men

in 1955 and 34% of women in 1965.¹ Credit for these spectacular decreases has rightly focused on policy interventions such as increases in tobacco taxes, ordinances requiring smoke-free public places, countermarketing, and better ways to

help smokers quit.²⁻⁴ These policy interventions are important tools, but how they have accomplished their results has not been clear. In this issue of the *Journal*, Christakis and Fowler,⁵ whose previous social-network analysis of subjects in the Framingham Heart Study indicated that social contacts may be a more important factor in the development of obesity than genes,⁶ report that family members and friends also exert powerful influences on smoking behavior.

Observing data on more than 12,000 people during a 32-year span, the authors found a major decrease in the prevalence of smoking, mirroring the national decline. For example, in persons between 40 and 50 years of age, the prevalence of smoking decreased from 66% to 22%. It is intriguing that they also documented major shifts in the social positioning of smokers. In 1971, smokers were indistinguishable from nonsmokers in terms of integration in their social networks. But three decades later, reflecting major shifts in societal views of smoking, smokers were at the periphery of social networks and aligned with other smokers. Christakis and Fowler also observed that clusters of smokers tended to quit all at once rather than by gradual attrition.

Smokers were differentially influenced by the smoking behavior of others. Smoking cessation by the spouse decreased a person's probability of smoking by 67%, smoking cessation by a friend decreased the probability by 36%, and smoking cessation by a sibling decreased the probability by 25%. Coworkers were influential only in small firms, where smoking cessation by a colleague yielded a 34% decrease in the chances of smoking. The stronger the friendship and the better educated the friend, the greater the influence on smoking behavior. Social marginalization was more likely to occur among highly educated smokers as compared with less well-educated smokers. The influence of a person's spouse and family remained significant regardless of whether the relative was a heavy or a light smoker, but the influence of friends on smoking cessation was limited to the influence of light smokers only.

As Barabási has noted, the ability to use the data from the Framingham Study to analyze social networks arose through serendipity: the names of close friends of subjects were ascertained at the beginning of the Framingham Study to facilitate the tracking down of subjects, not as an additional explanatory variable.⁷

Is it really so startling that behaviors such as

smoking and eating are influenced by friends and family, or that smoking and smokers have become increasingly marginalized over the past three decades? The answers are both yes and no. The progressive denormalization of tobacco use in most regions of the United States and in parts of Western Europe stands in stark contrast to how smoking was viewed when this particular segment of the Framingham Study began in 1971. In my state, California, there are now local ordinances against smoking at public parks and beaches and in shared housing such as condominiums, and state legislation has been proposed to prohibit smoking in automobiles when children are present. The growing backlash against tobacco use has resulted from an increasing body of evidence that links both active and passive smoking with an expanding host of diseases and a still staggering burden of morbidity and mortality.^{8,9} Just as clever marketing by the tobacco industry led to the normalization of smoking in the first half of the 20th century,¹⁰ the initial findings about tobacco's toll were used by health professionals, social advocates, and government officials to reverse that epidemic.

Can the network phenomena documented by Christakis and Fowler be applied to limit the disease burden of tobacco use further, or are these merely passive indicators of major social trends? It would be easier to answer these questions if we understood better the reasons for the large regional and social disparities in the prevalence of smoking. People in Kentucky, for example, are twice as likely to smoke as those in California. In addition, 25 to 43% of people with a high-school education or less are likely to smoke; they are much more likely to smoke than people with graduate education (7%) or physicians (1%).⁹

Some firms are now refusing to hire smokers. What do these trends portend for the success of smoking-cessation efforts in the future if smokers find themselves in the social periphery, surrounded by fellow smokers? Will that make it harder to quit, because smokers are now occupying a social island wherein smoking is still "normal"? Or are these islands merely the last bastions of smokers, soon to be overtaken by the rising tide of antitobacco sentiment? There are many more tools to help smokers quit now than there were in 1971, when even hospitals permitted smoking and no medicines to help with smoking cessation were approved by the Food and Drug Administration. Today, seven different forms

of medication have been shown to improve the chances of smoking cessation, toll-free telephone quitlines exist in every state (1-800-QUITNOW), and there are more exsmokers than current smokers. However, will marginalized smokers have less access to these tools, and will they be less motivated to use them?

A risk of the marginalization of smoking is that it further isolates the group of people with the highest rates of smoking — persons with mental illness, problems with substance abuse, or both.¹¹ These people are already stigmatized by their underlying psychiatric condition. Adding the further burden of the stigma associated with smoking makes it even harder for them to achieve the wellness that they and their families seek. Somehow we must find a way to integrate the twin goals of reducing smoking and integrating people with mental illness into mainstream society. Perhaps the strategy of “love the smoker, hate the smoke” could help these smokers quit while avoiding further stigmatization.

Despite the tremendous recent progress against tobacco use, it is premature to declare victory. Tobacco remains our nation’s number one health problem. More than 400,000 people die every year from smoking, and 20 times that number of people struggle with severe smoking-related disability. If the United States is to improve its current dismal performance in health status as compared with that of other countries, it must do better in reducing tobacco use.¹² The findings that smokers are increasingly peripheral resonate with how we encounter smokers in the United States today, many of whom we see furtively puffing outside their places of employment. If these findings ap-

ply more broadly — which appears to be likely — a further reduction in the burden of smoking will require focusing on people who are socially marginalized and whose social networks may be limited, and it will require figuring out ways to harness the potent social forces that shape behavior.

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