

they had connected with often followed.”

Despite the usually frantic pace of activity in the NICU, the staff took the flu shot endeavor quite seriously and managed to find the time to talk often with the parents. “We kept track of who was and who was not getting the shots, and we would talk to the ones who had not—to see if they had any questions or concerns that we could address.”

Among the 11 who refused the vaccine, 5 stated that they simply did not believe in immunization, and 2 said they feared that the shots might induce autism. Others cited religious objections or a reluctance to add anything else to

whatever medical care they were already receiving. One cited an allergy to eggs, which is a legitimate concern because the vaccine contains some egg proteins.

Overall, the NYU NICU-based flu shot program was highly successful. Dr. Shah and colleagues hope to do a follow-up to see if the program had any impact on the rate of influenza among the neonates. He cautioned, however, that the sample size may be too small to support any definitive conclusion.

This pilot program did, however, prove that flu shots can be effectively distributed in the NICU setting to parents, who for a variety of reasons, had not previously

gotten immunized. The program created very little additional strain on NICU physicians or nursing staff.

“Administration of the trivalent vaccine is very possible in a busy NICU, and implementation markedly increased compliance with recommendations aimed at protecting high-risk neonates,” Dr. Shah told conference participants. “There will always be a small subset of parents who will refuse, no matter what. But we can get to many parents who are willing to take the shots.” He added that this type of program is highly replicable and could be quickly implemented in any family-centered NICU. ■

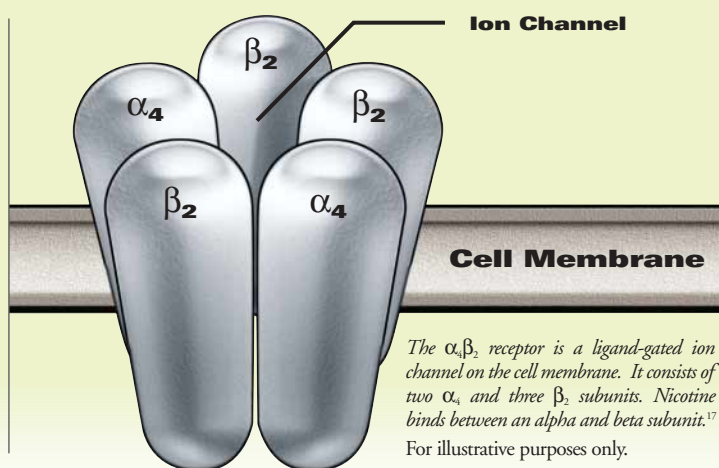
#### 4. An addictive substance causes physical dependence, as evidenced by withdrawal and relapse

The symptoms of nicotine withdrawal have been clearly identified and confirmed. For most smokers, these symptoms include at least one, if not several, of the following: craving, irritability, insomnia, headache, anxiety, depression, and impaired concentration.<sup>11,14</sup> These withdrawal symptoms have been identified as key contributors to relapse, as the smoker often “self-medicates” with nicotine to return to a perceived state of normalcy.<sup>12</sup>

Additionally, chronic stimulation at the receptor site is believed to be responsible for upregulation (an increase) in the number of receptors expressed at the cell surface.<sup>8,10,12</sup> This is likely a result of the brain compensating for the desensitization of existing receptors, as described earlier.

## The $\alpha_4\beta_2$ receptor

Recent evidence suggests that scientists have identified a specific nAChR in the brain that is believed to act as a primary mediator of the addictive properties of nicotine—the  $\alpha_4\beta_2$  receptor.<sup>15-17</sup> The isolation and characterization of this receptor is a significant advancement in the understanding of the neurobiology of smoking addiction.



### Conclusion

Smoking is a chronic, relapsing condition. For most smokers, the compounding effects of behavioral, psychological, and physical triggers make overcoming their addiction extremely difficult. However, given the high morbidity and mortality related to smoking,<sup>3,8</sup> getting smokers to quit is important. Proactive medical intervention for smokers may be beneficial.<sup>1</sup> Recent advancements in the study of nAChRs—specifically the identification and characterization of the  $\alpha_4\beta_2$  receptor—represent a significant advancement in the understanding of the nature of nicotine addiction.

**References:** 1. Fiore MC, Bailey WC, Cohen SJ, et al. *Clinical Practice Guideline: Treating Tobacco Use and Dependence*. Rockville, Md: US Dept of Health and Human Services, Public Health Service; 2000. 2. US Department of Health and Human Services. *The Health Consequences of Smoking: Nicotine Addiction: a Report of the Surgeon General*. Rockville, Md: US Dept of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 1988. Available at: [http://www.cdc.gov/tobacco/sgr/sgr\\_1988/index.htm](http://www.cdc.gov/tobacco/sgr/sgr_1988/index.htm). Accessed October 25, 2005. 3. US Department of Health and Human Services. *Sustaining State Programs for Tobacco Control: Data Highlights 2004*. Atlanta, Ga: US Dept of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2004. Available at: <http://www.cdc.gov/tobacco/datahighlights/>. Accessed October 19, 2005. 4. Foulds J, Burke M, Steinberg M, Williams JM, Ziedonis DM. Advances in pharmacotherapy for tobacco dependence. *Expert Opin Emerg Drugs*. 2004;9:39-53. 5. US Department of Health and Human Services. *Women and Smoking: a Report of the Surgeon General*. Atlanta, Ga: US Dept of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2001. Available at: [http://www.cdc.gov/tobacco/sgr/sgr\\_forwomen/sgr\\_women\\_chapters.htm](http://www.cdc.gov/tobacco/sgr/sgr_forwomen/sgr_women_chapters.htm). Accessed October 26, 2005. 6. Benowitz NL. Nicotine pharmacology and addiction. In: Benowitz NL, ed. *Nicotine Safety and Toxicity*. New York, NY: Oxford University Press; 1998:3-16. 7. Carper K, Machlin SR. Variations in smoking by selected demographic, socioeconomic, insurance, and health characteristics, United States, 2003. October 2005. Available at: <http://www.meps.ahrq.gov/papers/st101/stat101.pdf>. Accessed February 15, 2006. 8. Fagerström K. The epidemiology of smoking: health consequences and benefits of cessation. *Drugs*. 2002;62(suppl 2):1-9. 9. Anthenelli RM. Recent advances in the treatment of tobacco dependence. *Clin Neurosci Res*. 2005;5:175-183. 10. Watkins SS, Koob GF, Markou A. Neural mechanisms underlying nicotine addiction: acute positive reinforcement and withdrawal. *Nicotine Tob Res*. 2000;2:19-37. 11. DiFranza JR, Wellman RJ. A sensitization-homeostasis model of nicotine craving, withdrawal, and tolerance: integrating the clinical and basic science literature. *Nicotine Tob Res*. 2005;7:9-26. 12. Dani JA, De Biasi M. Cellular mechanisms of nicotine addiction. *Pharmacol Biochem Behav*. 2001;70:439-446. 13. Cordero-Erausquin M, Marubio LM, Klink R, Changeux JP. Nicotinic receptor function: new perspectives from knockout mice. *Trends Pharmacol Sci*. 2000;21:211-217. 14. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4th ed. Washington, DC: American Psychiatric Association; 1994. 15. Tapper AR, McKinney SL, Nashmi R, et al. Nicotine activation of  $\alpha_4$  receptors: sufficient for reward, tolerance, and sensitization. *Science*. 2004;306:1029-1032. 16. Picciotto MR, Zoli M, Rimondini R, et al. Acetylcholine receptors containing the  $\beta_2$  subunit are involved in the reinforcing properties of nicotine. *Nature*. 1998;391:173-177. 17. Coe JW, Vetelino MG, Bashore CG, et al. In pursuit of  $\alpha_4\beta_2$  nicotinic receptor partial agonists for smoking cessation: carbon analogs of (-)-cystine. *Bioorg Med Chem Lett*. 2005;15:2974-2979.

# Multidrug Resistance Stalls TB Drop

BY MIRIAM E. TUCKER  
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Tuberculosis cases reached an all-time low in the United States in 2005, but progress toward elimination of the disease has slowed, according to the Centers for Disease Control and Prevention.

Moreover, the number of multidrug-resistant (MDR) TB cases increased 13.3% from 2003 to 2004, marking the largest 1-year increase in such cases since 1993. A greater proportion of foreign-born patients than U.S.-born patients had MDR TB, the CDC said (MMWR 2006;55:305-8).

In 2005, a total of 14,093 TB cases was reported in the United States, representing a decline of 3.8% from 2004 and the lowest recorded rate (4.8 per 100,000 population) since national reporting began in 1953. However, the decline has slowed from an average of 7.1% per year during 1993-2000 to 3.8% per year during 2001-2005.

In 2005, the TB rate in foreign-born persons in the United States was 8.7 times that of U.S.-born persons. Although the total foreign-born population in the United States has increased 61.6% since 1993, the number of TB cases reported in this population hasn't changed substantially, resulting in a 36.0% decline in the TB rate among foreign-born persons. More than half of the 7,656 foreign-born TB patients in 2005 were from Mexico, the Philippines, Vietnam, India, and China, the CDC said.

Race/ethnicity data showed that TB rates in 2005 were increased 19.6 times among Asian Americans, 8.3-fold among blacks, and 7.3 times among Hispanics, compared with whites. But rates declined in almost all racial and ethnic populations from 2003 to 2005, with the most decline among American Indians/Alaska Natives (14.4%) and Asian Americans (14.1%).

The number of MDR TB cases increased from 113 cases in 2003 to 128 in 2004, the most recent year for which complete drug-susceptibility data are available. In 2004, 0.6% of U.S.-born and 1.6% of foreign-born TB patients had MDR TB. Approximately half of the foreign-born patients with MDR TB in 2004 were from Mexico, the Philippines, and Vietnam, the CDC said.

Also reported in the same MMWR issue, the first-ever data from the CDC and the WHO on rates of TB resistant to both first- and second-line antibiotics indicate that “extensively drug-resistant” TB accounted for 2% of all the MDR strains worldwide during the 2000-2004 period (MMWR 2006;55:301-5). ■