Cigarette smoking makes asthma worse. That simple tenet forms one of the most well-known cornerstones of asthma management. Nevertheless, certain studies2,3 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 studies1-5 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. Data1 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, studies6 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.7

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.8 These data have shown that, among children within their survey who were aged 4 through 6 years, high blood cotinine concentrations were associated with more severe respiratory illness in association with asthma diagnosis and management, especially for younger children. 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
with the highest blood cotinine concentrations. These findings are consistent with the implications of the data from other pediatric clinical studies.

Two especially interesting features of the latest analyses by Mannino et al raise questions about the pathophysiologic correlates of smoking behavior. The first is that weighted analyses showed that a greater proportion of asthmatic children aged 4 though 6 years had higher blood cotinine concentrations than older children. The authors do not hypothesize as to the basis for this finding, but other studies of household smoke exposure suggest that younger children may experience greater exposure because they are inherently more home-bound than older children. In essence, younger children may be “trapped” within the smoking environment, while the more mobile older children manage to lessen their environmental smoke exposure.6,9 The second interesting observation is that children with the highest blood cotinine concentrations were less likely to have been hospitalized for asthma within the past year. In addition to potential misreporting, the authors hypothesize that this finding may be related to the alteration of home smoking policies in response to asthma hospitalization, which is an attractive hypothesis given the short half-life of cotinine within the blood and some evidence that parents modify their smoking behavior in response to their children’s asthma exacerbations.4 Conceivably, a child’s life-threatening asthma exacerbation might prompt the parents to eliminate cigarette smoke from the home and car.

In addition to facilitating epidemiologic studies, information on blood or urine cotinine levels might be a very effective tool in parental smoking cessation techniques, the concentrations providing tangible evidence to parents of cigarette smoke inhalation by their children. Two recently published clinical studies have examined the impact of this technique in counseling the parents of asthmatic children. Both studies suggested that this information is not as useful as one might anticipate. One of these studies9 compared “usual care” smoking cessation techniques to counseling techniques that included provision of the results of their children’s urine cotinine concentrations. After 6 months, the proportion of homes in which smoking was banned was not remarkably different between the two groups; smoking was banned in 42% of homes in the usual care group and in 50% of homes in the cotinine group. The second study11 also showed no statistically significant difference in banning cigarette smoke from the home. However, this second study showed that active counseling (with feedback on urine cotinine concentrations) lowered the risk for acute asthma exacerbations requiring medical attention. These results underscore the need for additional studies of the components and methods involved in smoking cessation counseling for parents who smoke, especially those with asthmatic children.

Mannino and colleagues provide a snapshot of the consequences of exposing asthmatic children to tobacco smoke. Because of the inherent methodological features of their data, the snapshot is not completely focused as many patients had to be eliminated from the analyses because of missing data points, and very extensive subsetting was performed. Nevertheless, the photograph is clear enough to remind us of one of the common observations from studies of addictive behavior: addicted parents may harm not only themselves but also their children.2 Notably, in a recently published study13 of children seen in a Cincinnati emergency department because of asthma exacerbations, 41% of the parents identified themselves as cigarette smokers. The data of Mannino et al, combined with those from other reports, provide evidence of the harm associated with involuntary smoke inhalation among children, especially children with asthma. These observations support the contention that the addictive properties of cigarette smoking may be profound. Indeed, recovery from tobacco addiction is notoriously difficult, even for highly motivated smokers.14 Because the consequences of parental smoking impact not only the smoker but the smoker’s children, it behooves us all to work diligently with parents who smoke to lower or eliminate tobacco smoke from their homes and cars.

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REFERENCES
Magnesium Treatment for Asthma

Where Do We Stand?

My name is John Doe, and I have asthma. I am concerned about my health, and I’m not sure whether I should take the steroids and other chemicals my physician has ordered me to. A friend suggested I should take magnesium. What shall I do? Well, I’m up-to-date and concerned, hence I consult the World Wide Web. I search for “asthma and magnesium,” and find . . . > 26,600 Web page matches! When looking for “corticosteroids and asthma,” or even for, eg, “anticholinergics and asthma,” I “only” find 17,400, and “only” 2,370 Web sites relate to anticholinergics and asthma. When browsing through the 26,600 pages, the evidence in favor of magnesium seems overwhelming. My friend was right: I should take magnesium!

You are a pulmonologist, and confronted with a concerned and allegedly well-informed John Doe, proudly facing you with > 25 kg of printouts. What do you say? Well, here’s “magnesium and asthma in a nutshell”!

Magnesium is primarily (99%) an intracellular cation. In contrast to calcium, the maintenance of magnesium homeostasis is highly dependent on dietary intake, and there is no known regulatory system that functions to mobilize magnesium from bone or elsewhere to maintain circulating extracellular levels. Magnesium is involved in maintaining the ionic cellular balance, eg, by its role in the function of the cell membrane sodium-potassium adenosine triphosphatase pump. Magnesium is an obligate ion essential for the activation of > 300 enzymes, for virtually all hormonal reactions occurring in the body, and for the activity of adenylate cyclase. Finally, magnesium also acts as a calcium channel blocker. Magnesium thus undoubtedly is a major player in many cellular and hormonal functions. And severe magnesium deficiency is dangerous: in critically ill patients, for instance, hypomagnesemia occurs in up to 65% of patients, and is associated with increased mortality rates. Severe magnesium deficiency can lead, among other things, to a variety of dysrhythmias, seizures, muscle weakness, and mental status changes, various endocrine dysfunctions, but also to bronchospasm and respiratory failure. Magnesium replacement hence undoubtedly is useful in these critically ill patients. But is it useful for John Doe’s asthma? To answer this question, it may be useful to apply Koch’s postulates: (1) Is magnesium a bronchodilator? (2) Is asthma characterized by/associated with magnesium deficiency states? (3) Is magnesium therapy useful in treating asthma?

1. Magnesium has been shown to cause bronchial smooth-muscle relaxation in vitro,7 probably by its action as a “physiologic calcium antagonist,”8 or by its action on adenylyl cyclase activation.9 Magnesium has been shown to cause bronchodilation in vivo in children as well as in adults. Yes, magnesium is a bronchodilator.

2. The question of whether asthma is characterized by/associated with magnesium deficiency is less clear, and much more difficult to answer because of the difficulties in measurement and interpretation of intracellular vs extracellular (protein-bound, chelated, and ionized) forms.11 Although magnesium levels have been shown to appear similar in asthmatics as compared to those in control subjects,14 other data suggest that low magnesium intake (which is a major determinant in magnesium homeostasis) may be involved in the etiology of asthma and chronic obstructive airway disease. Britton et al., for instance, have shown in a random adult population sample study that a 100 mg/d higher magnesium intake was independently associated with a 27.7 mL (95% confidence interval, 11.9 to 43.5 mL) higher FEV1, and a reduction in the relative odds of bronchial hyperreactivity by a ratio of 0.82 (confidence interval, 0.72 to 0.93). Furthermore, β2-receptor agonist use can increase renal magnesium losses and thus lead to magnesium deficiency. Nevertheless, it remains unclear from the available data