What to Expect From Expectorants

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DO MEDICATIONS really help mobilize mucus from the respiratory tract? Are the traditional physicians correct when they try to get the asthmatic child to "vomit" sputum out of the lungs? Do all the numerous cough and cold mixtures have any more effect on expectoration than the glass of water used to wash the medication down? Are inhaled agents superior to those administered by mouth? These are difficult questions to answer, and reliable information is scanty—mainly because of the well-recognized difficulty in quantifying and qualifying a patient's sputum. Nevertheless, many physicians and more patients are convinced that certain favored prescriptions do have a beneficial effect on respiratory secretions.

Traditional and Modern Expectorants

The various American formularies and pharmacopeias are relatively reluctant to praise the traditional expectorants, but an English drug encyclopedia, Martindale's *Extra Pharmacopoeia,* lists a surprisingly large range of such medications that are undoubtedly foisted by British physicians on their phlegmatic patients. The 26th edition of Martindale (1973) lists the following traditional expectorants: cocillana, creosote, eriodictyon, euphorbia, grindelia, guaiacol and guaifenesin and derivatives, glycyrrhiza, primula, senega, squill, terpin hydrate, and various salts including sodium chloride, ammonium bicarbonate, ammonium chloride, and potassium iodide. Most of these agents are still used in proprietary mixtures, in both the United Kingdom and the United States, although most physicians are familiar only with glyceryl guaiacolate (Guaifenesin), terpin hydrate, and potassium iodide.

Few advances have been made in the pharmacologic development of oral expectorants in the United States, whereas in Britain two new drugs have been introduced recently and have won some acclaim: bromhexine hydrochloride (Bisolvon) and carbocisteine (Mucodyne). In the United States, more attention has been directed at inhalational agents such as acetylcysteine (Mucomyst), tyloxapol (present in Alevaire), and sodium ethasulfate (present in Tergemist), as well as various concentrations of sodium chloride and sodium bicarbonate solutions and water itself. In Britain, these aerosol drugs are not popular, and in the United States, the popularity of at least two proprietary inhalational agents has diminished. Traditional aromatic vapors are still used: decongestant vapor ointment (Vick's Vaporub) and many similar agents enjoy public confidence, although they may engender professional disdain. Boyd, who has done extensive investigational work in this area, found that most of the popular over-the-counter agents are relatively ineffective, including a British favorite compound benzoin tincture (Friar's Balsam), although the camphor and cedar leaf oil that are in Vick's Vaporub may be effective.

Actions of Expectorant Drugs

It is particularly interesting to find that a lot of support persists for the use of syrup of ipecac, which has long been used as an expectorant when given in subemetic doses. As Gunn suggested nearly 50 years ago, there is evidence that this drug stimulates vagal afferents in the gastric mucosa, resulting in activation of the vomiting center in the lateral reticular formation of the medulla oblongata. A sufficiently strong stimulus results in a vagal reflex to the stomach, causing vomiting. It may be postulated that a weaker stimulus activates vagal efferents to the bronchial glands, resulting in an augmentation of respiratory tract secretion and an increase in expectoration. The theory that subemetic doses of emetics cause expectoration rather than vomiting is strengthened by the fact that large doses of most expectorants, such as glyceryl guaiacolate, act as emetics. It is perhaps surprising that the evidence suggests that most of the more popular expectorants have to be given in almost nauseating doses to have any effect on expectoration, and that smaller, conventional doses of guaiacolate and terpin hydrate are

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virtually ineffective.

There is some slight redeeming evidence in favor of guaiacolate-type drugs: these agents enter the blood stream from the stomach and are then taken up by the bronchial glands. The expectorant then directly stimulates secretion by the glands, and the drug accompanies the mucus outflow. Thus, these dubious expectorants may have direct and indirect action that allows success even if the dosage is insufficient for the primary vagal indirect mechanism to be activated. Unfortunately, there is no laboratory evidence to suggest that glyceryl guaiacolate, terpin hydrate, and other commercial favorites have any further mucolytic effect on the mucoid secretions in which they find themselves. Oral agents that appear to cause an augmentation of the secretions produced by the respiratory mucosa are often classified as bronchomucotropic agents, and most "expectorants" act in this fashion. Few oral agents seem to directly affect the quality of the mucoid secretions, although it is claimed that the European drugs bromhexine and carboxymethylcysteine do have such an action.

A favorite oral expectorant is saturated solution of potassium iodide (SSKI), 10 to 20 drops (1 to 2 gm), given three or four times a day. Not only is this drug an emetic when given in larger doses (thus qualifying as a vagal bronchomucotropic when given in subemetic dosage), but it has several other important qualities. The drug is absorbed into the blood stream and is selectively and actively removed by various glands, including the salivary, lacrimal, and mucous glands of the nose and tracheobronchial tree. These glands are directly stimulated, and expectoration may be accompanied by lacrimation, rhinorrhea, and salivation (perhaps with salivary gland enlargement in susceptible patients). Furthermore, iodide appears to stimulate natural proteases in the respiratory tract secretions, thereby enhancing the endogenous enzymic breakdown of viscous mucoproteins. Another important advantage of iodide is its ability to stimulate ciliary activity; this property, incidentally, is also shown by aerosolized adrenergic bronchodilators, such as isoproterenol. A further important advantage of SSKI is that it is given in a glass of water, which contributes a major expectorant effect to the therapy (pace, cynics).

Obviously, numerous variables govern a patient's response to expectorant medications. The state of hydration, the pathological condition of the respiratory tract, the presence of various diseases and drugs, and the dose and timing of the medication may all influence the outcome of the therapy. Thus, Boyd found that seasonal factors had a profound effect on the response to various bronchomucotropic drugs: marked augmentation of secretions was induced only in the autumn months of the year in his laboratory, which was situated in Ontario. A further interesting speculation concerns the oral expectorants, which are believed to act mainly through a vagal reflex. Are these agents as effective in patients who have undergone surgical vagotomy? Most of these quandaries concerning the efficacy of expectorant agents await definitive studies, and it is not surprising that many physicians are not, at present, too impressed with the pharmacologic evidence underlying routine expectorant therapy.

Possible Value of Chicken Soup

Various food stuffs have long been credited with beneficial qualities that make them suitable for the treatment of respiratory tract infections, and it is interesting to find that Martindale still includes garlic as an expectorant. One would expect strongly flavored foods and condiments to have a significant effect on the bronchial glands, since many of these agents stimulate secretory activity by the lacrimal, nasal, and salivary glands, and they have a stimulatory effect on the gastric mucosa. Agents such as chiles, horseradish, and pepper often cause sneezing, and may also induce coughing, and ingestion of concentrated solutions of salt or mustard are traditional, time-tested, and well-proved emetics. Furthermore, pimetine, a drug derived from black pepper, has been shown to be a mucolytic.

Thus, there is reason to expect that a spicy diet may activate the "gastric-pulmonary" vagal reflex, thereby augmenting the production and loosening of respiratory tract secretions, with a consequent enhancement of expectoration. It is not unreasonable to suggest that the notoriously bland British diet may contribute to the notoriously high incidence of bronchitis in Britain when compared to countries where the weather, the temperament, and the diet contain more heat. Undoubtedly, the Englishman's bronchial glands are not subjected to the beneficial stimulation that the Mexican or Indian cigarette smoker (who is at similar risk of developing bronchitis) receives in his vagus-activating diet. The irritated lung produces, and retains, very viscous mucus, and probably this would be thinned out if its possessor also enjoyed the benefits of a bronchomucotropic diet. Statistics suggest that the smoking Englishman appears to be at greater risk of sputum retention than his counterparts in those cultures that indulge in highly flavored foods.

Would it be reasonable to expect spices, relishes, and condiments to enter a future edition of Martindale as ideal expectorants for the prophylaxis and treatment of diseases such as bronchitis? Perhaps this is the one disease that could truly benefit from that oft-touted panacea of therapeutics, the overworked nostrum of materia medica—namely, chicken soup. But the full prescription also calls for the addition of plenty of pepper and garlic, and possibly curry powder as well.

Additional Readings

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