sonnel necessary for successful management during acute exacerbations. In our experience the role of the patient becomes critical during the interval periods. His education and understanding of the management program are crucial. His ability to increase or decrease the amount of time devoted to aerosol administration, postural drainage, and maintenance of good bronchial hygiene will be deciding factors in the success of therapy. He should be encouraged to seek immediate physician consultation when there is significant change in symptoms so that adjustment of the treatment regimen or addition of the appropriate antibiotic may avert more serious decompensation.

Additional Measures

Needless to say, smoking should be avoided by all persons who have impairment of bronchial clearance mechanisms as found in bronchiectasis. Irritant dusts and fumes which produce increased symptoms are best avoided. Situations likely to produce dehydration with resultant increase in viscosity of pulmonary secretions may induce an episode of decompensation. Influenza immunization should be recommended on a yearly basis. Avoidance of large crowds in closed areas during periods of high incidence of respiratory infections in the community is advisable. Gamma globulin administration, although popular in the past, probably gives little help, because only traces of the major fraction associated with pulmonary defense (IgA) appear in usual preparations of gamma globulin.

SURGERY

Prior to the availability of present methods for medical management, surgery played a large role in treatment of many patients with bronchiectasis. Currently, most situations are effectively handled by medical methods alone if they are sufficiently intensive and appropriate. On rare occasions one does encounter the patient with relatively localized disease in one lobe or segment of lung whose condition cannot be controlled with a good medical program. In such situations surgery may be indicated. At times serious hemoptysis, usually resulting from aneurysmal vessel deformity in a bronchiectatic cavity, may present a surgical indication.

PREVENTION

Most bronchiectasis in today's clinical experience results from necrotizing lung infections which destroy the integrity of the bronchial wall. Prompt recognition and aggressive treatment of serious lung infections are important for prevention. Recognition of obstructing bronchial lesions such as bronchial plugs warrant prompt attention and removal. A primary dictum of the pulmonary physician has been complete x-ray and clinical resolution of all pneumonic processes. Unless there is adequate explanation for delay in the clinical course of the disease or other explanation for residual findings following pneumonia, diagnostic studies such as bronchoscopy and bronchography are indicated. Foreign bodies, obstructing lymph nodes, or tumor may be the underlying cause. Suspicion of foreign body should always remain paramount in children when recurrent pulmonary infections are encountered. Bronchiectatic changes will result in segments of lung in which mechanical blockage of bronchi is left uncorrected.

CHRONIC BRONCHITIS

method of
W. K. C. MORGAN, M.D.
Morgantown, West Virginia

DEFINITION

Because of the confusion in terms and language that had been prevalent for many years, several years ago The Medical Research Council of Great Britain devised a definition for chronic bronchitis, that is, the presence of cough and sputum for at least 3 months in the year for 2 successive years. Before a diagnosis of chronic bronchitis can be made, not only must the above criteria be met, but it is also necessary to exclude other causes of a productive cough such as bronchiectasis and tuberculosis. While this definition has done much to standardize terms and had been widely accepted, it has several drawbacks. First, many subjects with early chronic bronchitis have cough and sputum for less than the required 3 months each year and thereby fail to fulfill the criteria. Others, especially women, are reluctant to admit to cough and sputum and tend to dismiss their symptoms as a smoker's cough. Second, chronic bronchitis is a clinical diagnosis which is difficult to confirm pathologically in life. Nevertheless, mucous gland hypertrophy and goblet cell hyperplasia may be demonstrated in the larger airways in resected lungs or at autopsy.

While chronic bronchitis in the absence of emphysema can cause shortness of breath and an increase in airway resistance, the disease commonly occurs in association with emphysema. When the two conditions are present in the same patient, either or both may be responsible for dyspnea. If emphysema were the predominate cause of the airway obstruction and if the patient were to give up smoking so that his

chronic bronchitis would clear up completely, shortness of breath would persist largely unchanged. On the other hand, should dyspnea largely be related to chronic bronchitis, cessation of smoking would have a much greater effect on the symptoms.

GENERAL MEASURES

By far the commonest cause of chronic bronchitis is cigarette smoking and it is exceptional to find a patient with this condition who is a nonsmoker. Thus, cessation of smoking is of paramount importance in the treatment of chronic bronchitis. When the bronchitic subject stops smoking, sputum production decreases and may cease altogether within 1 to 2 months. Similarly, but over a longer period (6 months to 2 years), the abnormal histologic features regress and the bronchi become normal or nearly so.

Other agents that have been incriminated to a limited extent in the production of bronchitis include certain dusts, particularly silica and coal. It is felt by some authorities that prolonged exposure to either coal dust or silica produces a form of industrial bronchitis. Although this may well be true, the symptoms and effects are usually negligible unless the man is also a cigarette smoker. It must be conceded, however, that the subject with established chronic bronchitis would be well advised to avoid working in a dusty environment. Severe episodes of air pollution also aggravate chronic bronchitis and, indeed, in subjects with severe disease may induce respiratory failure. Such pollution should be avoided, and if possible the subject should live in a rural rather than an industrial area.

Many chronic bronchitics are obese and those who are will profit by weight reduction. They should also be encouraged to indulge in some form of regular exercise. Needless to say, they must exercise within their physical capacity, but regular mild to moderate exercise increases the efficiency of the muscles and improves exercise tolerance.

SPECIFIC MEASURES

Liquefaction and Removal of Secretions

Unlike the sputum found in the asthmatic subject, that of the chronic bronchitic is usually fairly liquid and can be expectorated with ease unless the patient is grossly short of breath and debilitated. Despite this, expectorants are still commonly administered to patients with chronic bronchitis. and to make matters worse, few of the commonly used expectorants have any therapeutic effect whatsoever. This is especially true of two of the most popular ones, saturated solution of potassium iodide and glyceryl guaiacolate. Although potassium iodide rapidly finds its way into the bronchial secretions, there is no evidence that it in any way aids expectoration. The use of steam mists is more efficacious and far cheaper. An excessively dry atmosphere, such as is produced by forced air central heating, may lead to inspissation of secretions in the chronic bronchitic. This can usually be avoided by installing a humidifier.

The use of mucolytics is currently popular but none of them seems significantly more effective than heated saline solution, and all are associated with undesirable side effects. N-acetylcysteine is currently popular but often induces bronchospasm. Tyloxapol, sodium bicarbonate, and glycerin (Alevaire) sometimes produces a chemical pneumonia and should be avoided. When acetylcysteine is given by nebulization, the dose is 1 ml. of a 20 per cent solution, but either epinephrine (2 mg.) or isoproterenol (0.25 ml. of 1:200 solution) should be added to prevent bronchoconstriction.

Bronchodilators

Chronic bronchitis is usually associated with irreversible obstructive airway disease. In a few instances, up to 10 to 15 per cent improvement in the usual ventilatory tests may occur following the administration of bronchodilators. More commonly, the improvement is around 5 to 10 per cent. When a good response to bronchodilators is obtained, i.e., over 25 per cent, the diagnosis of chronic bronchitis is probably in error, and the patient is usually found to have an atypical form of intrinsic asthma. Despite the generally poor spirometric response, bronchodilators often provide appreciable relief for the chronic bronchitic subject and can be administered by a variety of routes.

Oral Agents

SYMPATHOMIMETIC DRUGS. Ephedrine is still the most effective oral bronchodilator. One 15-mg. tablet three times a day often produces substantial relief. It tends to keep patients awake and may also produce nervousness, palpitations, and difficulty with micturition. To combat these side effects, it is often combined with a small dose of phenobarbital (15 mg.).

THEOPHYLLINE GROUP. Most of these drugs produce gastric irritation before they have an appreciable bronchodilator effect. An exception is oxtriphylline (Choledyl) which is sometimes helpful. It is best given as one 200-mg. tablet three or four times a day.

STEROIDS. Although there is little doubt that

many subjects with irreversible obstructive airway disease feel better while receiving steroids, evidence that these drugs significantly reduce airway obstruction in chronic bronchitis is lacking, and indeed most well-controlled studies have shown that steroids are ineffectual. That they have a euphoric effect cannot be denied; however, when a marked improvement in ventilatory capacity occurs following the administration of steroids in a patient who is presumed to have chronic bronchitis, it is likely that he has either atypical asthma or that asthma and chronic bronchitis coexist. The dangers of steroids are several, and if given for long periods in conjunction with broad-spectrum antibiotics they may predispose the patient to lethal gram-negative bacterial and fungal infections.

Nebulized Agents. The most effective drug for nebulization currently available in the United States is isoproterenol. A hand nebulizer is very effective and a dose of 0.5 ml. of 1:200 isoproterenol is usually sufficient. Pocket pressurized inhalers are also available. These contain either isoproterenol (Medihaler-Iso, Mistometer) or epinephrine (Medihaler-Epi). The pocket inhalers are fairly effective and convenient and a graduated dose of the drug is given with one "squirt." However, they can easily be used too frequently, and there is some evidence to suggest that cardiac arrhythmias and even death may result from overuse.

Intermittent Positive Pressure Breathing (IPPB)

The use of some form of portable IPPB machine daily or twice daily is currently popular and it cannot be denied that many patients feel that IPPB helps them. The basis for this faith can be traced to two sources: first, the power of autosuggestion (a complicated box with a plethora of levers and knobs is always impressive), and second, the fact that most portable IPPB machines are excellent nebulizers and generate a mist that is fine enough to reach the smaller air passages. The latter attribute is helpful to those subjects who are so short of breath that they cannot squeeze their hand nebulizer bulb for any length of time. Several relatively cheap pumps are available on the market for around $30 to $50, and these can be adapted to become effective nebulizers.

Treatment of Infection

The sputum of the usual subject with chronic bronchitis contains numerous organisms, ranging from *Neisseria catarrhalis* to *Escherichia coli, Actinomyces israeli,* and *Klebsiella pneumoniae.* The presence of organisms does not mean that they are acting as pathogens, and indeed many of them originate in the upper passages. During acute exacerbations of chronic bronchitis, i.e., when the sputum changes from mucoid to purulent, two organisms, *D. pneumoniae* and *H. influenzae,* are isolated with increased frequency and monotonous regularity, provided that the right culture media are used. Effective chemotherapy will eliminate or reduce the number of these organisms present in the sputum and in addition will restore its original mucoid character. On the other hand, continuous antibiotic therapy in subjects with chronic obstructive airway disease does not lessen the number of acute exacerbations, although it shortens their duration. This is taken as evidence that most acute exacerbations are a consequence of acute viral infections. As the viral infection subsides, secondary bacterial infection of the bronchi occurs. The commonly used broad-spectrum antibiotics have an effect only on the latter and can do nothing to prevent the antecedent viral infection. Thus there is a good reason to give polyvalent influenza vaccine to every chronic bronchitic each fall, bearing in mind that the majority of acute exacerbations are a consequence of viruses other than that of influenza. During an Asian influenza (A_2 virus) epidemic, a prophylactic course of amantadine hydrochloride is worth trying. This drug is given in a single dose of two 100 mg. tablets a day. It is usual to continue administering the drug for 10 to 30 days during an epidemic; however, duration of prophylaxis should depend on household and other direct contacts plus the prevalence of the disease in the general population. If necessary the drug can be continued for up to 90 days. Amantadine should not be given to patients with central nervous system disease or epilepsy. It is not an effective prophylactic in any except A_2 influenza infections, and should not be used to treat the acute illness.

In regard to the secondary bacterial infection that occurs with the acute exacerbations of chronic bronchitis, the best management remains debatable. There are those who recommend giving antibiotics continuously throughout the winter months. The opposing and, in my opinion, more logical approach, is to start antibiotics as soon as a viral infection occurs. Those who favor the first approach, and this includes The American Thoracic Society's Committee on Therapy, point out that a course of antibiotics given only when an exacerbation occurs is often not very effective. In my opinion, this is related to the tardiness of many patients in starting antibiotic therapy. It cannot be impressed on the patient too often that success depends on instituting antibiotic therapy at the very first symptom. The use of long-term broad-spectrum antibiotics is associated with several side

effects, in particular, the colonization of the respiratory tract with gram-negative resistant organisms such as Pseudomonas, *E. coli,* and Proteus. Rarely, it induces a superinfection with resistant staphylococci. Diarrhea and gastrointestinal candidiasis are common. Finally, the cost of continuous antibiotic therapy is much greater. If use of a continuous regimen is elected, tetracycline, in a dose of 250 mg., four times a day, is preferred.

The following regimens are recommended for short-term treatment of acute exacerbations:

1. The combination of penicillin and streptomycin is the preferred treatment when the patient is in the hospital. The recommended dose is 3 mega-units of benzyl penicillin plus 0.5 gram of streptomycin every 12 hours. Both should be given intramuscularly; because penicillin is painful, 0.5 ml. of 0.5 per cent procaine should be given first, and then the penicillin should be given through the same needle. Seldom is it necessary to give systemic antibiotics for more than 4 to 5 days, after which time an oral preparation will suffice. In seriously ill patients with respiratory failure and cor pulmonale, the above regimen should be first choice.

2. Tetracycline is also fairly effective when given in a dose of 750 mg. orally every 6 hours. The commonest cause of failure of this antibiotic is an inadequate dose, namely, 1.0 to 1.5 grams per day.

3. Ampicillin is also effective but again should be given in a dose of 0.75 to 1.00 gram every 6 hours. Regimens of about 1.0 to 1.5 grams per day are often unsatisfactory and do not eliminate *H. influenzae* from the sputum. This antibiotic has the disadvantage that it is more expensive than both tetracycline or the combination of penicillin and streptomycin.

Cephaloridine and gentamicin should be used only when there is definite evidence of parenchymal involvement of the lung with sensitive organisms. The finding of Pseudomonas or Klebsiella in the sputum in the absence of clinical and radiographic evidence of pneumonia is not an indication for these antibiotics.

RESPIRATORY FAILURE

The long-standing chronic bronchitic with obstructive airway disease is prone to develop respiratory and right-sided heart failure. Cor pulmonale is usually precipitated either by an acute exacerbation of bronchitis or by overt pneumonia. The subject is usually hypoxic and hypercapnic and retains salt and fluid. If arterial Po_2 is below 55 mm. of mercury, he will benefit from oxygen, since a Po_2 below this level causes reflex pulmonary vasoconstriction. Oxygen is best administered slowly and in low concentrations. After the patient is first placed on oxygen, his general condition should be observed closely and arterial blood gases should be monitored. Convenient ways of administering oxygen are either by nasal prongs at a flow rate of 2 liters per minute or with a 24 per cent Ventimask.* If under these circumstances the arterial Po_2 rises to above 50 mm. of mercury and the patient does not become comatose or undergo secondary hypoventilation, all is well. If he does, then it is likely that some form of assisted ventilation is necessary. If the arterial Po_2 remains below 44 mm. of mercury with the above measures, the flow rate can be increased to 3 or 4 liters per minute or a 28 or 35 per cent Ventimask can be used. Again a careful watch for secondary hypoventilation and respiratory depression must be kept.

Any coincident infection should be treated as described above without waiting for cultures. Digitalis is often prescribed but its effect in cor pulmonale secondary to chronic bronchitis is seldom worthwhile. Moreover, subjects with respiratory failure are notoriously susceptible to hypokalemia and refractory digitalis intoxication. Rapid intravenous digitalization is never required in a chronic bronchitic in the absence of an arrhythmia. Diuresis is helpful and in this connection mercurials or thiazides are preferred. Furosemide often precipitates metabolic alkalosis.

If the hematocrit is above 55 per cent, the patient may benefit from a 500-ml. venesection. For subjects in whom arterial Po_2 is below 50 mm. of mercury, whose exercise tolerance is limited, who are polycythemic, and who have no appreciable carbon dioxide retention, continuous oxygen therapy is sometimes helpful. Oxygen can be given at home through nasal prongs and often increases exercise tolerance and lessens the need for repeat venesections.

In conclusion, it must be emphasized that none of the routine and recommended therapeutic measures used in the treatment of chronic bronchitis, namely, bronchodilators, long-term antibiotics, and IPPB, has been shown to do anything to prolong life. In this regard, the one measure of definite benefit is the cessation of smoking. However, symptomatic treatment is well worthwhile for the relief that it affords.

* Bethlehem Corporation, Bethlehem, Pennsylvania.