Fifteen Years' Experience with Carbon Dioxide in the Management of Cough

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Cough is one of the most frequent symptoms for the treatment of which the patient seeks medical attention. The management of a symptom apparently as simple as this is, however, fraught with a number of obstacles. First, often times it is difficult to estimate the usefulness of cough. Secondly, in many instances the potential dangers of certain types of cough are not appreciated and, therefore are left out of consideration. Thirdly, the immediate and incentive causes of cough may not be as obvious as one would be inclined to think at first glance. And finally, a combination of various not readily recognized conditions obviates a priori a stereotyped control of this symptom.

No wonder that the justifiable lament of teachers of medicine, that the management of cough has been more of an art than a science, is being repeated and perpetuated by others. It seems to me that acquiescence is not likely to bring about constructive advances in this field. On the contrary, it seems only as a stamp of approval for using traditional methods of treatment which may not be as competent as they ought to be. It is certain, however, that if the fundamental aspects of this problem are clarified, a great deal can be gained concerning the efficient treatment of cough.

Although cough can be produced voluntarily, it is, in its spontaneous form, a reflex function of the body. Its purpose is the removal of accumulated mucus, inflammatory exudates, products of circulatory stagnation, extravasated blood, or foreign bodies from the respiratory tract and to rid the body from irritation of

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any sort which originates in the air passages. Its most frequent sources are diseases of the lung, the throat and the heart. For the intelligent and efficient treatment of cough it is mandatory to search for its cause and institute appropriate measures accordingly. The multiplicity of lesions which may elicit cough should be recognized. Pathological changes in any part of the respiratory system, whether of infectious, allergic, neoplastic or other etiology, may provoke cough.

The act of coughing consists of three phases, namely the inspiratory, compressive and expulsive. During the first phase an increased amount of air is inspired. At the end of this phase the glottis is closed. During the second phase a forced expiration takes place while the glottis remains closed. In consequence of this forced expiratory effort the chest becomes smaller and the air inhaled during the inspiratory phase is compressed. The consequent pressure of the air contained in the lungs below the closed glottis reaches very high levels. According to Coryllos, it may stand as high as from 80 to 100 mm. of mercury above the normal atmospheric pressure. Other studies revealed as high rise in the intrapulmonary pressure as 160 mm. of mercury. This is equivalent to an increase of about 3 lbs. per square inch above atmospheric pressure. One can readily visualize what a tremendous expulsive force is represented by this high pressure of the air compressed in the lung at the moment the glottis is opened. This initiates the third phase of coughing. The previously compressed air rushes out of the tracheobronchial tubes. Rohrer studied the velocity of air during cough in human beings and found that it varied from \( \frac{1}{2} \) to \( 2\frac{1}{2} \) meters per second in the respiratory bronchioles and from 50 to 120 meters (150-360 feet) per second at the glottis.

According to the concept of Jackson and Jackson, based on their extensive bronchoscopic investigations, the mechanism of cough which results in expectoration consists of two factors: 1, the blast of air ("bechic blast") which is followed by the forcible expulsion of secretions from the larger bronchial tubes; and 2, the tussive squeeze which is a compression of the lung during the expiratory phase of cough. The expiratory contraction of the lung forces the mucopurulent inflammatory products from the alveoli and bronchioles upward into the larger bronchi. Their clear analogy relative to this item is really worth quoting: "For the purpose of illustration, a lobe of a lung may be likened to a sponge partially filled with water. When the sponge is squeezed, the water is forced out."

It is reasonable to assume that these forces of coughing are capable of evacuating inflammatory products or foreign bodies from the respiratory tract. In case of an inflammatory disease
of the lung, such as bronchitis, pneumonia, etc., one would expect a successful drainage under the effect of cough. If this is actually accomplished by coughing, one considers the cough as useful, adequate or beneficial. There is a number of instances, however, when cough is not productive of any sputum or when the amount of sputum expectorated is much less than the coughing effort should have produced. This type of cough is customarily designated as unproductive or useless. Useless or inadequate cough may be brought about by the following circumstances: 1. The source of irritation which initiates the cough reflex is outside of the lung, as for instance in diseases of the paranasal sinuses, an elongated uvula, pressure on the trachea or bronchi by mediastinal inflammation, tumors or dilated blood vessels. 2. Non-inflammatory lesions of the bronchial tubes, such as benign or malignant tumors, may cause persistent, annoying cough without expectoration. 3. During the course of a great many inflammatory involvements of the bronchi or the lung parenchyma there is a phase when the formation of exudate is practically nil, nevertheless the congested state of the involved structures leads to strenuous but useless cough. One of the best examples of this is the first stage of an acute bronchitis with a so-called "dry" cough. 4. A frequent source of inadequate cough is any disease of the lung in which the mucoid or mucopurulent products of inflammation are so tenacious, sticky and adherent to the walls of the respiratory passages that even intense, exhaustive coughing is unable to remove them. The prototype of inadequate cough of this type is that seen in the paroxysmal stage of whooping cough. 5. Accumulation of too much transudation in the alveoli in heart failure may elicit coughing which is insufficient for the cleansing of the lung. 6. There are cases where a retention of pulmonary exudates is taking place because their removal is blocked by pathological structural changes such as the formation of bronchial strictures. Such condition often causes strenuous but ineffective coughing. 7. Atelectasis may be the source of useless cough for the reason that when the lung becomes airless distal to inflamed areas, there is no chance for the inspired air to get behind the inflammatory products which accumulate in the corresponding bronchial tubes and, therefore, it cannot be compressed and act as the normal expulsive force of coughing. 8. Useless cough is common in pulmonary emphysema. It is the result of: a, weakening and destruction of the elastic structures of the lung; b, change in the intrapleural subatmospheric (negative) pressure so that it is near atmospheric (neutral) pressure, and c, the abnormally low (inspiratory) position of the diaphragm. In consequence of these three pathological alterations, the normal phases of coughing cannot be carried through and
cough becomes inefficient, though it is persistent and troublesome. 9. Protracted, unproductive cough may result from fatigue and exhaustion of the expiratory muscles. It is brought about by conditions where there is only slight inflammatory exudation in the lungs but the pathological changes are conducive to coughing. Such is the case in certain types of long-standing tuberculosis, and pulmonary fibrosis.

It is important to realize that oftentimes cough as a reflex mechanism is working with a high degree of failure which may be well designated as tussic insufficiency. Cough of this type is unquestionably a liability rather than an asset. Assuming that there is inflammatory exudation in the lungs, its removal either by resorption or by expectoration is essential for the restoration of the normal anatomical and functional status of this organ. In the presence of tussic insufficiency, an accumulation and retention of mucus and purulent exudate takes place. The stagnation of inflammatory products in the bronchi is dangerous: 1, because it may cause complete bronchial obstruction and a consequent atelectasis in the corresponding distal segment of the lung, and 2, the pathogenic microorganisms which are prevalent in the retained mucopus are likely to lead to pathological changes in the surrounding bronchial walls and thus cause the development of bronchiectasis. When massive atelectasis of one lobe or multiple patchy (lobular) atelectasis develops, not only useful respiratory surface area of the lung is lost but also the atelectatic areas must be looked upon as sites of lesser resistance which favor the development of new foci of infection. New areas of disease, of course, are followed by additional production of inflammatory exudate and consequently, by increased cough. A similar vicious circle is bound to result when the bronchial wall is involved by microorganisms in the stagnating mucopus. The force of the compressed air in the lung at the beginning of the expulsive phase of cough exerts a certain degree of pressure upon the bronchial walls weakened and damaged by a severe or chronic inflammation and thus dilates and deforms them. This chain of events is an important etiological item in the pathogenesis of bronchiectasis. The additional increase in cough associated with bronchiectasis thus becomes a serious problem.

Tussic insufficiency may entail other difficulties. Droplets of purulent, thin exudate may be sprayed from one segment of the lung to another or from one lung to the opposite side. When partial bronchial obstruction is present, it may cause a rebound of droplets of infected material and cause their settling in the deeper parts of the lung. In either instance a spread of the disease, which is the original source of the cough, may ensue. It has been recog-
nized for sometime that long-continued cough is liable to produce emphysema. This concept is clearly formulated by Christie.\footnote{4} He stated that in chronic bronchitis and in any other pulmonary lesion in which the patient coughs scores of times a day the excessive stress and strain, repeated over many years, causes a destruction of the elasticity of the lung tissue. When pulmonary elasticity is lost, the lung will lack its normal capacity to recoil during expiration. Consequently, the traction or suction effect of the intrapleural subatmospheric (negative) pressure maintains the lung in its inspiratory position. This is a plausible explanation of the typical emphysematous or so-called "barrel-chest". In addition to this, the negative intrapleural pressure dilates the individual alveoli by its pulling effect and thus contributes to the degeneration and rupture of interalveolar septa and to the formation of superficial emphysematous bullae. The greater the dilatation of the lung the closer the intrapleural subatmospheric pressure will approach the atmospheric level. This, in turn, implies a deficient function of the lung the consequences of which are the persistence and incompetency of coughing in emphysema. It can be seen from this sequence of events that protracted, useless cough is a self-defeating act.

*Tussic insufficiency* associated with severe coughing interferes with the rest of the patient and with the rest of the lungs. It is a matter of common knowledge that pulmonary rest and relaxation are the cardinal prerequisites of the treatment of tuberculosis. For this reason the harmful effect of inadequate cough in this disease requires no further elucidation. Also, it is known that protracted, hard cough in pulmonary tuberculosis may accelerate the development of specific laryngitis. Pulmonary hemorrhage may be initiated by excessive, strenuous cough. Other possible disagreeable sequelae of severe coughing include spontaneous pneumothorax, vomiting, loss of appetite, exhaustion, headache, insomnia, rise in temperature, marked dyspnea, cyanosis, thoracic pain, fracture of ribs, mediastinal emphysema, subcutaneous emphysema, subconjunctival hemorrhage, urinary incontinence, and, indirectly, myocardial failure.

Reviewing these data and considering the high frequency with which useless and inadequate cough (tussic insufficiency) is encountered in everyday medical practice it is obvious that our efforts must be focused upon the best possible way of its treatment. With this purpose in mind, it is reasonable to say that the efficient management of cough consists of measures which are capable of removing the maximum amount of sputum with the least frequent and most effortless cough.

Reference has been made previously to the muddled state of
affairs which prevails in the treatment of this condition. But how could it be otherwise if the commentary of Clark made only a few years ago is true? He said that unfortunately the pharmacology of cough has scarcely advanced at all in the last half century. Consequently, shot-gun therapy is still popular in this field, and cough mixtures tend to be very complex and completely irrational. Apropos of this, I believe I am not mistaken in stating that such circumstances may explain in a large measure the success of some widely-advertised and euphemistically named pharmaceutical preparations the presumably effective constituents of which are far below the therapeutically useful level.

The correction of this confused situation is attainable only through a more thorough familiarization of ourselves with pertinent physiological facts.

1. The cough center is located in the medulla close to the sensory vagus center and the vomiting center. It is subject to peripheral and central stimuli. It is depressed by alkaloids of opium, alcoholic intoxication and full general anesthesia. With reference to the suppression of cough by some of the opiates, it is well to remember that alleviation of cough in this fashion must not be interpreted as a cure of the underlying disease. Such easy success does not relieve the physician of the obligation of establishing a correct diagnosis.

2. Cough is provoked by the stimulation of the sensory nerve endings of the vagus and glossopharyngeus.

3. The secretory function of the glands of the bronchial mucosa is increased by stimulation of these vagal nerve endings.

4. There is a rich supply of smooth muscles in the wall of the bronchioles. They are arranged in a circular or net-like fashion. It may not be amiss to mention that about one-half of the weight of the lung tissue is made up by these muscles. They have an important role in the normal functioning of the bronchial tubes. Experimental observations revealed that there are a rhythmic systole and diastole of these structures. Spasm of the bronchial muscles is a characteristic feature of bronchial asthma. It occurs also as a result of irritation from other causes, such as the inhalation of irritant gases, fumes, and foreign bodies. Bronchial spasm can easily cause complete occlusion of the smaller branches of the respiratory tract and thereby lead to dyspnea, anoxemia, atelectasis and increased cough.

5. It has been demonstrated with the aid of bronchocinematography that the bronchi and bronchioles have a peristaltic motion directed from the smaller structures toward the larger ones. It is maintained by the smooth muscles, and is independent from the respiratory movement of the lung. The function of this peristaltic
motion is—in analogy to that of the intestinal tract—the evacuation of the bronchial contents. The normal secretion of the mucosal glands as well as inflammatory products or minute dust particles are propelled and expelled by bronchial peristalsis. Drugs of the parasympatheticomimetic group, which cause bronchospasm, also decrease or abolish bronchial peristalsis and thus deprive the lung of one of its natural protective mechanisms. The inhalation of a suitable mixture of carbon dioxide and oxygen is followed by increased peristalsis of the bronchi and the bronchioles. The increased peristalsis is attributable to carbon dioxide.

6. Another factor which is instrumental in the elimination of mucus and foreign particles from the bronchial tract is the function of the cilia. Under normal circumstances ciliary motion is active in the larger as well as in the smaller bronchi. The terminal bronchioles are not provided with cilia. The motion of the cilia is synchronized so that it is capable of driving inert material from the deeper segments of the lung toward the larynx. When a pathological process destroys the sensory nerve endings of the vagus, a cessation of the ciliary function takes place. Also, in areas where the structures of the bronchial wall are lost due to disease, the ciliary action is absent. Such is the case in bronchiectasis. The observations of Negus on the nasal mucosa revealed that the topical application of mildly alkaline solutions of magnesium (pH 8 - 8.5) stimulates ciliary motion. On the other hand, acids paralyze it. In view of this, one could conjecture that some of the benefits derived from the administration of alkaline salts in cough may be due to their effect upon the cilia.

7. Gordonoff considers the kinetic force of the respiratory air a contributory factor in removing secretions and products of inflammatory exudation from the alveoli to the smaller bronchi. Partial bronchial obstruction or spasm of the smooth muscles, which is particularly effective in the terminal bronchioles interferes with or eliminates this force entirely from the corresponding area of the lung.

8. Also there exists a force of the secreted bronchial mucus which maintains a slow but continuous motion toward the tracheal bifurcation. Diseases or drugs which exert an unfavorable influence upon the consistency or the amount of bronchial secretions are likely to upset this process. Such may be the case when prescribing morphine as a cough sedative, for it is known that morphine suppresses normal bronchial secretion.

9. A great many experimental and clinical studies concerning the efficacy of various expectorants are open to criticism because their conclusions were based on measuring the amount of bronchial secretions expectorated or otherwise collected. The weakness of
these data lies in the fact that the resorption of some of the bronchial secretion by the bronchial mucosa itself was left out of consideration. Unquestionably, under favorable circumstances a portion of the bronchial secretions is resorbed by the mucosa. Gordonoff pointed out that the scanty, thick secretions of the alveoli are made resorbable either by a process of digestion in the alveoli themselves or by a dilution and liquefaction through the admixture of secretions of the glands of the bronchial mucosa.

10. In addition to the capacity of the bronchial mucosa to resorb exudates and minute foreign particles, a similar process is being carried out in the alveoli. No doubt these two pathways of elimination are of tremendous importance in ridding a diseased segment of the lung of increased and pathological elements. The resorptive capacity of the lung tissue can be effectively increased by certain medicinal measures.

11. The role played by the respiratory motion of the lung in the removal of inflammatory products from the bronchi is not sufficiently appreciated. Under normal circumstances the inspiratory expansion of the chest wall is associated with an increase in the negativity of the intrapleural negative pressure. This, in turn, causes a stretching and dilatation of the bronchial tubes. These rhythmically repeated motions tend to remove the bronchial contents mechanically. Liquid material is thus readily propelled and tenacious, adherent mucopus is separated from the bronchial wall and expelled. This expulsive force is greatly reduced or entirely missing in superficial respiration because the stretching and dilatation of the bronchi are absent. Patients who are debilitated, those under the effect of general anesthesia following major surgery, and some in whom the respiratory center is depressed by narcotics, particularly morphine, may show evidence of insufficient respiratory excursions of the chest. Henderson emphasized the significance of anoxemia in this respect, stating that oxygen deficiency, if at all intense, acts as a sort of whip, which excites respiration to activity and even to excessive activity, but injures at the same time and is liable to be followed by a subsequent period of depressed breathing. The dangers inherent in the retention of inflammatory exudates in the lung (possible atelectasis, bronchopneumonia, bronchiectasis, dyspnea, increased cough) call for immediate measures which are capable of restoring the normal self-cleansing function of the lung. The sovereign remedy of such condition is the inhalation of a mixture of carbon dioxide and oxygen. Its effectiveness is attributable partly to the fact that carbon dioxide is a powerful respiratory stimulant and induces increased inspiratory movements of the thorax which, in turn, cause a stretching and dilatation of the bronchial tubes.
12. It is of more than academic interest to remember that the presence of inflammatory products in the smaller bronchi does not, as a rule, elicit cough irritation, or when it does so, the consequent cough is feeble and inadequate. The fluoroscopic studies of Reinberg\(^9\) revealed that secretions in the peripheral bronchial tree produced no cough in bronchi of the fifth, fourth and third order. Brown and Archibald\(^10\) recorded their observations while operating under local anesthesia upon a patient with a long-standing pulmonary abscess, in the base of which there opened a number of bronchi and bronchioles. They found that cough was readily initiated when a probe was inserted into one of the larger bronchi, while a similar procedure was without effect in the case of bronchioles. Also Jackson\(^3\) observed during bronchoscopic examinations that the finer subdivisions of the tracheo-bronchial tree and the alveoli showed decidedly less cough production from instrumental contact than the larger bronchi. When a pathological process is localized predominantly to the bronchioles, as is the case in acute bronchiolitis, the accumulation of secretions may lead to considerable respiratory distress, anoxemia and cyanosis. In the absence or insufficiency of cough in these cases, therapeutic intervention is imperative for draining the small bronchi and bronchioles and for the relief of the patients' distress. The method applied must not increase the accumulation of exudate. The administration of a mixture of carbon dioxide and oxygen is the measure of choice.

I have been administering carbon dioxide as an expectorant since 1930. Its administration is a simple and safe procedure which does not interfere with the comfort of the patient. In my experience it proved to be a most efficient expectorant. The benefits derived from its use are noticeable subjectively and objectively: (a) spells of strenuous, exhausting coughing are prevented and thereby rest is secured for the patients and particularly for the lungs; (b) an unproductive cough is transformed into a useful one; (c) directly after inhalation the amount of expectorated sputum is increased and its character changes from a heavy, thick and tenacious type into a thinner, serous and more watery kind; (d) the use of expectorant drugs and narcotics can be reduced.

In addition to its previously mentioned pharmacological actions, carbon dioxide is a good expectorant: 1, because it stimulates the myo-elastic structures of the lung and causes a forceful peristaltic movement of the bronchi; and 2, because it liquefies mucopurulent inflammatory exudates that stagnate in the bronchial tract.

Miescher\(^11\) in 1885 called attention to the importance carbon dioxide plays in respiration and formulated the aphorism: "Over
the oxygen supply of the body carbon dioxide spreads its protecting wings." This was followed in 1905 by the experimental work of Haldane and Priestley\textsuperscript{12} who actually demonstrated that the carbon dioxide of the blood normally controls respiration. They observed that an increase of the carbon dioxide in the pulmonary alveoli was consistently accompanied by an increase of the respiration. As low as a 1 per cent increase was sufficient to stimulate the respiratory center and to cause deeper breathing. Hill and Flack\textsuperscript{13} reported that the inhalation of increasing concentrations of carbon dioxide caused a proportional stimulation of the respiratory center until 10 per cent was reached; higher concentrations led to a progressive depression of respiration. Brown\textsuperscript{14} found that the maximum stimulation of pulmonary ventilation was reached at 10.4 per cent carbon dioxide. The greatest protagonist of the clinical application of carbon dioxide was Henderson,\textsuperscript{6} who with Haggard and other associates made numerous contributions to the medical literature on the practical value of this method of treatment. They used it for controlling the paroxysmal stage of whooping cough, for the prevention and treatment of postoperative massive atelectasis and pneumonia and for the management of a number of other conditions in which the respiratory center is depressed.

Short inhalations of 5 to 10 per cent carbon dioxide with ample oxygen induce no ill effects. The most conspicuous manifestation of their influence is an increase in the respiratory minute volume. In a self-experiment with 10 per cent carbon dioxide and 90 per cent oxygen, taking 6 liters per minute through a well-fitting face mask my respiratory rate rose from 14 per minute before the inhalation to 19 at the end of a fifteen minute observation period. Henderson,\textsuperscript{6} using 5 per cent carbon dioxide, found that the volume of breathing increased more than threefold. Also, marked augmentation in the respiratory minute volume was recorded by Heller and his associates,\textsuperscript{15} Barcroft and Margaria,\textsuperscript{16} Hitzenberger\textsuperscript{17} and Grueneberg and Viethen.\textsuperscript{18} The effect usually becomes noticeable during the first minute of inhalation. Brief interruptions render the respiratory center more sensitive. Carbon dioxide causes one to breathe not only more times per minute but also with fuller lungs. It quickens the rate both of the air inhaled and of the air exhaled. There are considerable variations in the same person on different days. Some persons show only slight increase in minute volume to 5 per cent, even to 7 per cent carbon dioxide. Hartl\textsuperscript{19} found that oxygen intake is increased at the beginning of the inhalations, it may remain the same or may decrease during the treatment. Saklad\textsuperscript{20} observed that when normal oxygenation was accomplished in anoxemic patients, the respiratory rate di-
minished. The experimental studies of Prinzmetal\textsuperscript{21} revealed that the increased respiratory motions of the chest during carbon dioxide inhalations are associated with a greater negativity of the intrapleural pressure on inspiration and a reduced negativity on expiration; both these changes contribute effectively to a competent diastole and systole of the lung. Henderson\textsuperscript{8} postulated an increase in the tonus of the respiratory muscles of the chest, particularly the diaphragm, and of the myoelastic structures of the lung during carbon dioxide inhalations. The latter assumption was proved to be correct by the clinical observations of Brunn and Brill.\textsuperscript{22} They studied the effect of carbon dioxide during bronchoscopy and noted that it induced violent movements of the bronchial tree and alterations in the shape of its branches: consequently bronchial secretions spilled from minor into major bronchi.

The inhalation of 1 to 8 per cent carbon dioxide improves the functional capacity and the ventricular output of the heart;\textsuperscript{17} also it increases both the systolic and the diastolic blood pressure\textsuperscript{23} and is followed by an increase in the pulse rate and in the pulse pressure, particularly after the concentration of carbon dioxide has reached 3 per cent.\textsuperscript{24} Tomaszewski and his co-workers\textsuperscript{25} administered 8 per cent carbon dioxide to healthy persons, and they found, besides the respiratory changes, a slight increase in the metabolism and an initial quickening and then slowing of the pulse. No increase in the metabolic rate was noted by other investigators. Fuchs\textsuperscript{26} observed that a slight increase in the blood carbon dioxide accelerated clotting, while too much carbon dioxide in the plasma caused prolonged coagulation. Tannenberg\textsuperscript{27} considered this accelerated clotting an indirect transient effect of carbon dioxide on the peripheral and central nervous system that leads to an enlarged production of epinephrine.

I have made observations on 40 patients concerning the respiratory pattern during carbon dioxide inhalation. All of them were given inhalations as a therapeutic measure for the treatment of otherwise uncontrollable cough and dyspnea. The patient was seated on a chair, and the technic and purpose of the procedure was explained to remove fear or apprehension. After the determination of the respiratory rate and pulse rate in this position, from two to five counts were taken during a ten to fifteen minute period of inhalation of the gas mixture. Ten of the 40 patients took the treatment with the aid of a face mask, by the closed method; the others inhaled the gas through a glass tube. In the latter cases the patient was instructed to hold the end of the glass tube in his mouth, to inhale the gas coming from the tank and to exhale through the nose. Although the admixture of air with and dilution
of the inhaled gas was unavoidable, judging from the therapeutic response this method of administration proved to be satisfactory. Altogether 275 observations were analyzed: 17 treatments by the closed method and 258 treatments by the open method (through a glass tube).

By the closed method the amount of gas delivered to the patient varied from 4 to 6 liters per minute. The anticipated response to such high concentrations of carbon dioxide was an increase in the respiratory rate. Still, we found this in 3 instances only. The respiratory rate remained unchanged in 3 and decreased in 9 observations. This is at variance with findings in normal persons and can be explained (1) by the reinflation of previously atelectatic areas of the lung with a consequent immediate relief from dyspnea and (2) by the increase in the amplitude rather than in the rate of respiration. In 2 instances the rate dropped in four minutes from 26 to 14 and from 24 to 10, respectively. In 2 patients an initial decrease in the rate was followed by a moderate increase toward the end of the treatment.

With the open method the pattern of respiratory response was similar to that found with the closed method.

Of the 258 observations with the open method, 4 liters of the gas mixture per minute were given in 8 instances, 4.5 in 9; 5 in 181; 5.5 in 3; 6 in 9; 6.5 in 9 and 7 in 39.

At the end of the inhalations the number of respirations was increased in 89 instances. The increase varied from less than 10 per cent to 60 per cent of the initial rate; the great majority showed a rise less than 30 per cent. In 93 instances the number of respirations was decreased; the reduction varied from less than 10 per cent to 42.6 per cent; it was less than 20 per cent in 79 instances.

The initial respiratory rate varied between 16 and 40; the great majority were between 20 and 29. There was a group of observations in which during the inhalation of carbon dioxide the respiratory rate first decreased and then increased; in another group an opposite response was recorded. In cases in which the rate at the end of the observation period was the same as the original rate, there was an intermediate decrease in 27, or 35.5 per cent, and an intermediate rise in 15, or 19.7 per cent. In the group with a final reduction in the respiratory rate an intermediate increase was noted in 31, or 33.3 per cent. In cases in which the final respiratory rate was elevated, an intermediate decrease was seen in 6, or 6.7 per cent. The intermediate increase varied from less than 10 per cent to 60 per cent of the initial rate, the great majority showing a rise between 10 and 29 per cent. The intermediate decrease varied from less than 10 per cent to 42.6 per cent of the
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initial rate, the great majority falling between 6 and 19 per cent.

It is interesting to note that the final respiratory rate was the same as the initial rate in 76 instances, or 29.5 per cent, and it was less than the initial rate in 93, or 36 per cent. Altogether, the final rate remained unchanged or was reduced in 169 instances, or 65.5 per cent, as against 89 instances, or 34.5 per cent, in which the respiratory rate was increased at the end of the inhalation of the gas mixture.

The apparatus used in my work consists of a tank, containing a mixture of 10 per cent carbon dioxide and 90 per cent oxygen or of 5 per cent carbon dioxide and 95 per cent oxygen, mounted on a small platform on casters that makes it possible to give the inhalations to a number of bed patients. Originally, I used an ordinary mask used for general anesthesia; more recently the B.L.B. mask has been found preferable. An oxymeter regulates the flow of gas per minute. The inhaler is connected to the tank by a rubber tubing. A rubber bag which serves as a small reservoir is attached to the inhaler. In some patients it may be expedient to give the inhalations through a glass tube instead of a mask: either because they may be reluctant to accept the mask, or the respiratory stimulation is too strong from the inhalation of 10 per cent carbon dioxide. It is fully realized that when the inhalations are administered through a glass tube held in the patient's mouth, the admixture of air and dilution of carbon dioxide take place; but the results by this so-called open method are quite satisfactory. The open method is recommended for patients who are markedly debilitated or who show some of the possible side-effects when the closed method is used. All patients taking 5 per cent carbon dioxide and 95 per cent oxygen use the closed method (B.L.B. mask).

It is a good policy to explain to the patient briefly the mode of action of the gas inhaled, and the expected changes in respiration, and the probable subjective symptoms. After proper instructions, inhalations through a glass tube can be administered without constant supervision; however, it is the responsibility of the nurse to regulate the flow of the gas, and time of the treatment. As a rule, the meter is set to 4 to 5 liters per minute for closed inhalations and to 5 to 7 liters per minute for the open method. The length of each treatment varies from 5 to 15 minutes; and the inhalations are administered once, twice, or three times a day. It is necessary to observe the patient closely during the first treatment. His respiratory response and subjective reactions determine the conduct of further treatments. They are conscious of breathing deeper and subsequent to the treatment they describe their experience in such terms as "the chest feels clear and cool"
and “the chest feels so much lighter”. If it is noted that the respirations become too strenuous, the inhalations should be given with brief (1 minute) interruptions. In rare instances, when the closed method is used, it may be necessary to reduce the flow to less than 4 liters per minute. Most patients appear quite comfortable, as if in euphoria. The latter can be explained: (1) by the presence of 90 per cent oxygen in the gas mixture that is bound to counteract anoxemia; (2) by loosening up mucopurulent bronchial plugs and obstructive sticky, tenacious inflammatory exudate: the access of air is secured to underinflated regions of the lung; (3) by increased inspiratory expansion of the chest wall and by increased descent of the diaphragm atelectatic areas are stretched out and become aerated. In some of my patients I noted some transient minor side-effects of carbon dioxide inhalations, such as hot sensations, palpitation, weakness, frontal headache, and slight dizziness. None of these symptoms interfered with the treatment when proper adjustments were made in the method of administration. In the beginning, the treatments are given daily; subsequently, the frequency of inhalations can be reduced, depending upon the relief obtained. Some patients are obliged to take them daily for an extended period of time, while in others the interval between inhalations can be increased to a week. Carbon dioxide is an effective therapeutic agent, and in its use utmost individualization is required.

The prompt relief obtainable by this treatment is best expressed in the comments of patients: “the cough is not so dry, it is loose,” “the cough does not jar me any more,” “the cough is less, and not tight as before,” “I do not have to exert myself when coughing,” “I have no more dry spells of coughing,” etc.

I have noted that following inhalations the amount of expectorated sputum is greater than before treatment, and also that adequate evacuation of the bronchi insures for the patient comparatively long periods of rest free of the annoying cough. Incidental by-effects of the satisfactory pulmonary drainage by carbon dioxide are: relief from dyspnea, undisturbed sleep during night, and improvement in the general subjective feeling. Often patients remarked how a feeling of pressure and heaviness was relieved by the treatment, that following inhalations their chest felt freer “like a loose sponge,” and how much easier they were able to move about. Also I have noted the disappearance of chest noises and pharyngeal cough irritation.

When satisfactory evacuation of the bronchi has been accomplished, the amount of sputum becomes gradually less, unless further mucopurulent accumulation takes place during the interval
between treatments. It can be seen, therefore, that the frequency of inhalations and gas flow per minute have to be individualized and adapted to the changing requirements of the patient. I have found that the inhalation of carbon dioxide not only alleviates distressing cough but also enables one to reduce the consumption of narcotics and expectorant drugs.

The recent painstaking investigations of Basch, Holinger and Poncher\textsuperscript{28} concerning the effectiveness of carbon dioxide and of the commonly used expectorants confirm our own clinical findings. They studied the influence of ammonium chloride, potassium iodide, fluid extract of senega, fluid extract of ipecac, and emetine hydrochloride, and compared it with the effect of carbon dioxide. They found that carbon dioxide acts as a real expectorant by diluting the sputum—that is, by lowering its viscosity and reducing its solid contents. They state that in comparing the physical and chemical properties of the sputum after the use of carbon dioxide inhalations with the same properties after the administration of drugs one at once realizes the greater liquefaction of the sputum caused by carbon dioxide: “since in this treatment there is no interference with the chemical properties of the sputum through the secretion of the administered drugs into it, the dried residue, the amount of ash and the total nitrogen content are regularly markedly lowered.”

Striking results were observed by Allison\textsuperscript{29} following the inhalation of carbon dioxide and oxygen in the treatment of acute bronchitis of infants and children. Satisfactory symptomatic relief was seen in bronchial asthma by Tiefensee,\textsuperscript{30} Hurst\textsuperscript{31} and Campbell and Poulton.\textsuperscript{32} Gratifying symptomatic improvement was recorded in bronchopneumonia and in pneumonia in children by Gruenberg and Viethen,\textsuperscript{18} and by Allison.\textsuperscript{29} This procedure can be used with safety in bronchopulmonary infection of any etiology, including tuberculosis.

As to the selection of cases for this treatment, it is indicated whenever there is an accumulation and retention of inflammatory exudate in the bronchial tract and its evacuation—in spite of strenuous cough—is inadequate.

There are patients who should not be given this treatment: (1) patients with recent pulmonary hemorrhage; (2) those with marked emphysema; (3) when widespread pulmonary fibrosis is present without atelectasis, bronchiectasis or mucopurulent retention in the air-passages; (4) cases of acute plastic pleurisy and pleurisy with effusion; (5) hypertensive patients; and (6) when the cause of cough is outside of the lungs.
CONCLUSIONS

1. The rational management of cough depends upon its nature, origin, and upon the associated clinical findings.

2. Cough which originates from the lung may function with a high degree of failure (tussic insufficiency).

3. Ineffective cough harbors a number of potential dangers and, therefore, it should be corrected.

4. Suppression of the cough by depressing the cough reflex by narcotics, though easy to do, does not necessarily mean adequate treatment. As a matter of fact, there are a great many instances when the administration of narcotics may do more harm than good.

5. Unproductive cough may coexist with an accumulation of inflammatory exudate in the lower air passages.

6. No patient should be permitted to become exhausted under the strain of incessant coughing or to drown in his own accumulated pulmonary secretions.

7. Whenever considerable inflammatory exudate is present in the bronchopulmonary tract, relief from cough is best brought about by the adequate evacuation of these structures.

8. Drugs prescribed for the cleansing of the bronchi and alveoli should be selected according to the individual requirements of the case.

9. Expectoration is not the only means for the elimination of inflammatory exudates from the lung. Large amounts of the exudate are resorbed from the respiratory tract under favorable circumstances.

10. Clinical observation of others as well as my own experience have convinced me that carbon dioxide is a most efficient expectorant. It is superior to medicinal doses of potassium iodide, senega, ipecac and emetine hydrochloride. It is much better than steam inhalation. It aids the cleansing of the lungs both by facilitated expectoration and by pulmonary resorption.

11. When it is used as an expectorant, one can administer a mixture of 5 per cent carbon dioxide and 95 per cent oxygen, or 10 per cent carbon dioxide and 90 per cent oxygen. The strength of the gas mixture and the timing of its inhalation should be adjusted to the individual patient.

12. It is of advantage to combine carbon dioxide inhalation with steam inhalation.

13. Postural drainage may be instituted after the inhalation of carbon dioxide for the rapid evacuation of the respiratory tract.

14. Carbon dioxide by inhalation is given only as a symptomatic measure and it must not exclude specific drugs or accepted methods of treatment.
CONCLUSIONES

1. El tratamiento racional de la tos depende de su naturaleza, origen y hallazgos clínicos concomitantes.

2. La tos que se origina en el pulmón puede fracasar en su función (insuficiencia de la tos).

3. La tos ineficaz fomenta un cierto número de peligros potenciales y, por lo tanto, debe ser corregida.

4. La supresión de la tos mediante la depresión del reflejo de la tos por narcóticos, aunque fácil de lograr, no es necesariamente un tratamiento adecuado. En realidad, hay muchas ocasiones en las que la administración de narcóticos puede causar más mal que bien.

5. La tos improductiva puede coexistir con una acumulación de exudado inflamatorio en las vías respiratorias inferiores.

6. No se debe permitir que ningún enfermo se agote debido al esfuerzo excesivo de una tos incesante o que se ahogue en la acumulación de sus propias secreciones pulmonares.

7. Cuando quiera que exista una cantidad considerable de exudado inflamatorio en las vías broncopulmonares, la mejor manera de aliviar la tos es mediante la evacuación adecuada de ese material.

8. Las drogas que se receten para limpiar los bronquios y los alvéolos deben ser escogidas de acuerdo con los requisitos individuales del caso.

9. La expectoración no es el único medio de eliminar los exudados inflamatorios del pulmón. Cuando las circunstancias son favorables se reabsorben grandes cantidades del exudado en las vías respiratorias.

10. La observación clínica de otros, así como mi propia experiencia, me han convencido de que el anhídrido carbónico es un expectorante de lo más eficaz. Es superior a dosis medicinales de yoduro de potasio, sénega, ipecacuana e hidrocloruro de emetina. Es mucho mejor que la inhalación de vapor, y ayuda a limpiar los pulmones, tanto porque facilita la expectoración como por la reabsorción pulmonar.

11. Cuando se usa como expectorante, se puede administrar una mezcla de 5 por ciento de anhídrido carbónico y 95 por ciento de oxígeno, o 10 por ciento de anhídrido carbónico y 90 por ciento de oxígeno. La concentración del gas en la mezcla y la regulación del tiempo de inhalación deben ser adaptados a cada paciente.

12. Es ventajoso combinar la inhalación del anhídrido carbónico con inhalación de vapor.

13. Puede instituirse el drenaje de postura después de la inhala-
ción del anhidrido carbónico para facilitar la evacuación rápida de las vías respiratorias.
14. Se emplea la inhalación del anhidrido carbónico solamente como medida sintomática y no a exclusión de drogas específicas o de tratamientos aceptados.

REFERENCES
14 Brown, A. L.: "Bronchoscopic Observations on Postoperative Atelec-
				


