CARBON DIOXIDE INTOXICATION: THE CLINICAL SYNDROME, ITS ETIOLOGY AND MANAGEMENT WITH PARTICULAR REFERENCE TO THE USE OF MECHANICAL RESPIRATORS*

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INTRODUCTION

Carbon dioxide intoxication is now recognized as a syndrome that can occur in persons with disorders which greatly reduce alveolar ventilation (3, 7, 13, 14, 33, 37, 42, 61, 63, 70, 79). The symptoms and clinical findings in this condition vary in character and severity and may simulate other disease entities. With moderate acidosis and hypercapnia, the patient may have no complaints, or the only symptoms noted may be weakness, lassitude, irritability, mild confusion, or headache. More severe respiratory acidosis can cause carbon dioxide narcosis with coma, respiratory depression and circulatory failure. Frequently, severe or prolonged narcosis results in the death of the patient.

Retention of carbon dioxide is most commonly observed in individuals with chronic lung disease which results in impaired ventilation, particularly obstructive emphysema and pulmonary fibrosis. On this background carbon dioxide intoxication can develop when ventilation becomes mechanically more difficult; e.g., with a respiratory infection (67, 70, 77). It may also accompany congestive heart failure in patients with cor pulmonale (28, 29). Alveolar ventilation may be impaired when the respiratory center is depressed, particularly by drugs (80). It is now well recognized that carbon dioxide narcosis can be precipitated by the administration of high concentrations of oxygen by mask, nasal catheter or tent to the patient with reduced alveolar ventilation (3, 14, 20, 33, 42, 71, 79).

Hypercapnia is normally a stimulus for hyperventilation. When the ventilatory effort is not easily successful in lowering alveolar carbon dioxide, chronic elevation of blood carbon dioxide occurs and the respiratory center loses its normal responsiveness to hypercapnia. Alveolar hypoventilation necessarily causes hypoxia as well as hypercapnia when the patient is breathing ambient air. As alveolar ventilation progressively decreases, more and more drive is provided through the peripheral chemoreceptors which respond primarily to alterations in arterial oxygen tension. Breathing higher concentrations of oxygen will correct the anoxia, but will also reduce the stimulus to breathe and the retention of carbon dioxide may progress to narcotic levels.

Patients with actual or impending carbon dioxide intoxication and anoxia present a clinical problem in recognition and management. During the past five years, twenty-five examples of carbon dioxide intoxication or narcosis have

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been observed by the authors. The first three cases associated with oxygen therapy have been previously described (33). It is the purpose of this report to present our experience with the clinical features, the etiological factors and the management of this syndrome. The therapeutic measures and the rationale for their use are reviewed with particular emphasis on the aid to ventilation provided by mechanical respirators.

MATERIAL AND METHODS

Twenty-five patients with carbon dioxide intoxication were observed from June 1950 to July 1955. Most of the patients had chronic pulmonary disease (Table 1). Fifteen patients had obstructive emphysema associated with chronic bronchitis. Eight of this group had a prominent history of asthma. Studies of ventilatory function and intrapulmonary gas mixing were done in many of these patients by methods described elsewhere (6) and the clinical impression of emphysema and alveolar hypoventilation confirmed. One patient had asthma without evidence of obstructive emphysema. Three had tuberculosis, either active or inactive, and two had carcinoma of the lung. One had marked kyphoscoliosis with a chest deformity which preceded the development of chronic pulmonary disease. Three patients (cases 10, 20, 23) did not have clinical or autopsy evidence of chronic pulmonary disease which could have been responsible for impaired alveolar ventilation. One had heart failure; another, a cerebral vascular accident; and the third, a staphylococcus pneumonia and pyopneumothorax. Table 1 summarizes the primary pulmonary diseases, the apparent precipitating factors of carbon dioxide intoxication, initial blood gas studies and important individual clinical features.

Arterial blood oxygen saturation, pH and carbon dioxide tension were determined in order to establish the diagnosis and to follow the patient's course. Arterial blood samples were obtained from the brachial, femoral or radial artery through an indwelling Cournand needle. The blood was taken into syringes wet with heparin and stored in ice water for analyses within two to four hours. For pH determinations, sodium fluoride was added as a preservative. Arterial blood oxygen content and percent saturation were determined by a photometric method (30). The pH of whole blood was measured with a Cambridge Model R pH meter equipped with an enclosed glass electrode. Measurements made at room temperature were corrected to 37° C. by Rosenthal's factor (55). The carbon dioxide content of whole blood was determined by the method of Van Slyke and Neill (45), and the plasma carbon dioxide content was calculated from this value, the pH and the hemoglobin by the line chart of Van Slyke and Sendroy (74). From the pH and carbon dioxide content of arterial plasma at 37° C., the carbon dioxide tension of arterial blood was calculated by the Henderson-Hasselbalch equation. Previous studies have demonstrated that this indirect method gives reliable values for the carbon dioxide tension over the wide range of pH values found in these patients (31, 32).

The arterial blood pCO_2 reached extremely elevated levels on occasions when the patient was breathing high concentrations of oxygen. The arterial blood

pCO_2 value obtained in some instances would have been impossible with room air. To review the relative gas pressure relationships in the alveolus of a patient on room air at sea level, the following data are presented. If, for simplicity, the R.Q. is taken to be 1.00, then

760 mm. Hg = atmospheric pressure
−47 mm. Hg = water vapor pressure

713 mm. Hg
−563 mm. Hg = nitrogen tension

150 mm. Hg = oxygen tension + carbon dioxide tension

In this example, as the pCO_2 rises, the pO_2 falls and it would be impossible for the pCO_2 to exceed 150 mm. Hg. Moreover, as this value was approached, the patient would become intolerably anoxic. On higher concentrations of oxygen, however, the arterial blood pCO_2 may exceed 150 mm. Hg as in case 14, without compromising the oxygen supply.

CLINICAL FEATURES OF CARBON DIOXIDE INTOXICATION

Nervous System

The primary symptoms and findings of carbon dioxide intoxication are those of a neurological disorder. However, they may vary in both character and severity, depending in part upon the degree of hypercapnia. Many individuals with obstructive emphysema and an elevated arterial blood pCO_2 appear to have no symptoms referable to hypercapnia (1, 76). Some patients have complaints such as headaches, somnolence, and mental confusion which may be related to carbon dioxide retention. As carbon dioxide intoxication progresses, the patient develops weakness, lassitude, irritability, more marked mental confusion, and drowsiness. The next stage is carbon dioxide narcosis with varying states of unconsciousness, depressed respiration, hyporeflexia, flaccid paralysis, tremors, occasional convulsions, and death. The following case reports are examples of the neurological features of this syndrome.

Case 1

C.H. was a 53-year old man, admitted to the hospital in 1950 with a 12-year history of repeated respiratory infections, during which he had had cough productive of mucopurulent sputum, wheezing and exertional dyspnea. Gradually he developed symptoms of congestive heart failure with orthopnea, ankle edema and ascites. On admission, he was cyanotic and had a large heart with a diastolic gallop, coarse and fine moist rales in the chest, ascites and massive pitting leg edema. By laboratory study he had polycythemia, right axis deviation on electrocardiogram, and the arterial blood gas values shown in Table 1. With digitoxin, diuretics, bronchodilator drugs, dietary salt restriction and low-flow nasal oxygen, the patient improved.

Comment: In spite of an arterial pCO_2 of 81 mm. Hg, this patient had no symptoms which were clearly referable to the hypercapnia. Many patients have chronic respiratory failure with arterial blood pCO_2 of 70 to 80 mm. Hg without symptoms (1). This type of patient, however, may be a candidate for carbon dioxide narcosis if ventilation is impaired enough by heart failure, respiratory infection or the use of oxygen.

TABLE I

Summary chart of patients with carbon dioxide intoxication

Name	Age	Date	Diagnosis	Probable Precipitating Factor	Oxygen % Sat.	pH	pCO_2 mm. Hg	Prominent Neurological Findings	Results
(1) C.H.	53	6-1-50	Obstructive emphysema; cor pulmonale; congestive heart failure	Congestive heart failure	64	7.29	81	Rational; intermittent depression	Recovered
(2) A.M.	25	7-10-50	Asthma; obstructive emphysema	Bronchitis and bronchopneumonia	55	7.10	134	Comatose; shallow respirations; elevated cerebrospinal fluid pressure	Died
(3) J.B.	31	5-27-50	Tuberculosis; thoracoplasty, old	Oxygen therapy in part	85*	7.16	129	Conscious, but lapsed into coma easily	Died
(4) M.M.	23	8-17-50	Asthma; early pregnancy	Status asthmaticus	97*	7.21	—	Comatose; shallow breathing; convulsions; absent deep tendon reflexes	Died
(5) W.D.	64	2-1-51 5-15-51	Asthma; obstructive emphysema Hypertensive cardiovascular lesion	Status asthmaticus Oxygen therapy	95*	7.15	139	Comatose; convulsions; pupils pin-point and react sluggishly; absent deep tendon reflexes	Recovered; died 3rd admission
(6) J.A.	35	4-21-51	Asthma; obstructive emphysema; cor pulmonale; congestive heart failure	Acute bronchitis	87*	7.29	94	Semistuporous; generalized twitching; elevated cerebrospinal fluid pressure	Recovered
(7) J.T.	57	5-12-51	Chronic bronchitis; obstructive emphysema	Drugs (bromides)	92*	7.16	115	Semicomatose; unequal pupils, unequal deep tendon reflexes; papilledema; elevated cerebrospinal fluid pressure	Recovered
(8) G.B.	46	11-16-51	Collapsed lung; obstructive emphysema	Postoperative	99*	6.97	169	Comatose; pupils varied, dilated and pin-point; generalized twitching	Recovered
(9) J.S.	41	6-21-52	Asthma; obstructive emphysema; heart failure	Congestive heart failure	68	7.32	76	Drowsy; shallow depressed respiration	Recovered
(10) W.G.	55	7-16-52	Hypertensive cardiovascular disease; heart failure; obesity	Large pleural effusion	62	7.22	78	Intermittent coma	Died
(11) L.W.	23	10-28-52	Tuberculosis; pneumonectomy	Postoperative	—	6.83	121	Comatose	Died
(12) R.J.	60	11-13-52	Obstructive emphysema; pulmonary fibrosis; chronic bronchitis; cor pulmonale; heart failure	Congestive heart failure	88*	7.17	96	Comatose; unequal pupils; hemiparesis; elevated cerebrospinal fluid pressure	Died
(13) E.H.	66	11-18-52	Carcinoma of lung; asthma; obstructive emphysema	Postoperative	99*	7.12	101	Comatose	Recovered
(14) W.M.	73	10-1-53	Emphysema; pulmonary fibrosis; cor pulmonale	Congestive heart failure	92*	6.84	228	Comatose; depressed respiration	Died
(15) E.E.	56	10-2-53	Asthma; emphysema; chronic bronchitis	Status asthmaticus and acute bronchitis	89*	6.92	194	Comatose; unequal pupils; flaccid paralysis; hypoactive deep tendon reflexes	Recovered
(16) A.D.	65	10-2-53	Asthma; chronic bronchitis; obstructive emphysema	Drugs (sedatives)	99*	7.18	106	Comatose	Recovered
(17) C.D.	33	10-15-53	Kyphoscoliosis; pulmonary fibrosis; heart failure	—	91*	7.07	99	Comatose	Died

(18) M.P.	40	7-21-54	Asthma; obstructive emphysema	Acute bronchitis; status asthmaticus	77	7.19	80	Semicomatose; very irritable; shallow respiration	Recovered
(19) W.P.	74	8-14-54	Asthma; chronic bronchitis; obstructive emphysema	—	—	6.98	168	Comatose; small sluggishly reacting pupils; flaccid paralysis; elevated cerebrospinal fluid pressure	Recovered
(20) R.T.	58	9-15-54	Hypertensive cardiovascular disease; cerebral hemorrhage; no significant lung disease	Intracranial vascular accident	69	6.98	149	Comatose	Died
(21) J.M.	65	10-14-54	Asthma; chronic bronchitis; obstructive emphysema; heart failure	—	79	7.22	78	Semistuporous; later coma	Died
(22) A.H.	61	10-20-54	Carcinoma of lung	Pneumonectomy	74	7.16	97	Comatose	Recovered
(23) M.R.	47	1-7-55	Cushing's syndrome	Staphylococcus pneumonia and pyopneumothorax	79	7.14	151	Comatose	Died
(24) K.S.	67	3-29-55	Obstructive emphysema; obesity	—	77	7.09	138	Comatose; depressed respiration	Died
(25) D.T.	56	6-11-55	Inactive tuberculosis; thoracoplasty; cor pulmonale; heart failure	Congestive heart failure	55	7.20	114	Comatose; generalized twitching	Recovered

* On oxygen at time or recently.

Case 5

W.D. was a 63-year old man, first seen in the hospital in 1950 with a 45-year history of seasonal asthma. His admission was prompted by the onset of confusion associated with a prolonged attack of asthma. On admission he was disoriented and, although no localizing neurological findings were noted, it was the impression of the staff that he had had a cerebral vascular accident. The patient responded well to bronchodilator drugs and expectorants and was discharged from the hospital mentally clear.

The patient was readmitted to the hospital in January 1951, again disoriented and in status asthmaticus. Four days later without having shown improvement he became lethargic and then comatose. Respirations were shallow. The pupils were pin point and reacted only sluggishly to light. At that time he was areflexic and unresponsive to painful stimuli. On several occasions he had a generalized convulsion. Arterial blood gas studies done at that time are recorded in Table 2. The patient ultimately recovered and returned home.

He returned to the hospital in May 1951 in mild status asthmaticus and three days after admission he became confused and drowsy. At that time a moderate elevation in arterial blood pCO_2 was noted (Table 2). Nasal oxygen was started and, because of his cyanosis, it was continued, along with the use of bronchodilator drugs and antibiotics. The following day the patient was comatose and did not respond to painful stimuli. The breathing was rapid and shallow. Perspiration was profuse. The corneal and deep tendon reflexes were absent. There were alternate periods of flaccid immobility and frequent twitching movements of the extremities. He had several generalized convulsions. The patient died on the fifth hospital day.

Comment: This case illustrates some important motor and reflex changes which can occur in carbon dioxide narcosis. Recurrent episodes of carbon dioxide narcosis as exemplified by this man have been observed in other patients in this series.

Case 15

E.E. was a 56-year old woman with a 30-year history of asthma associated primarily with respiratory infections. She was admitted to the hospital in September 1953 after six weeks of almost continuous asthma which had not responded to the usual measures. During the first six days after admission, she became more lethargic and finally lapsed into coma. At that time she had shallow depressed respirations and was perspiring profusely. She did not

TABLE 2

Arterial blood gas studies on patients with carbon dioxide narcosis associated with asthma and pulmonary emphysema

Patient	Date	Comment	Arterial Oxygen % Saturation	Arterial pH	Arterial pCO_2 mm. Hg
W.D. (Case 5)					
Adm. 2	1–31–51	Coma; nasal oxygen	95.2	7.15	139.5
	2–5–51	Recovered; air	89.8	7.49	51.8
Adm. 3	5–15–51	Confused; air	75.7	7.34	69.5
	5–16–51	Comatose; nasal oxygen	91.9	7.10	115.0
	5–17–51	Near death; air	78.0	7.01	152.6
E.E. (Case 15)	10–1–53	Oriented but lethargic; air	—	7.31	74.1
	10–2–53	Comatose; nasal oxygen	89.2	6.92	194.0
	10–5–53	Alert; air	96.1	7.48	47.4
J.T. (Case 7)	5–12–51	Comatose; nasal oxygen	91.9	7.16	115.0
	5–16–51	Improved; nasal oxygen	98.9	7.26	86.5
	5–17–51	Improved; air	86.3	7.35	61.6

respond to painful stimuli. The eyes were deviated to the left. The corneal reflexes were absent. The pupils varied between marked constriction and dilatation, but they did not respond to light. There was a flaccid paralysis and the deep tendon reflexes were absent. The arterial blood gas studies obtained on this patient at various stages of carbon dioxide intoxication are shown in Table 2.

Comment: This patient demonstrated neurological findings commonly associated with carbon dioxide narcosis.

Case 7

J.T., a 57-year old man, was admitted to the hospital in May 1951 in a semicomatose state. He had had asthma and recurrent pulmonary infections for many years. Two weeks before admission he began to act queerly, dragged his left foot and had a staggering gait. Four days before admission he became unresponsive. On physical examination he had unequal pupils, dilated retinal veins and blurred disc margins. There was a right-sided facial weakness and unequal deep tendon reflexes in the lower extremities. Lumbar puncture revealed a spinal fluid pressure of 200 mm. of water, but was otherwise not remarkable. The arterial blood gas studies done on this man are reported in Table 2. This patient also had an elevated blood bromide level. Within 24 hours following measures to improve ventilation the neurological abnormalities had disappeared.

Comment: The rapid disappearance of the neurological symptoms and findings suggests that they were related at least in part to the patient's high arterial blood pCO_2.

Discussion

The outstanding neurological findings and symptoms of each patient are summarized in Table 1. The primary neurological changes in these patients were manifested in the mental state, the motor system and the reflexes.

Carbon dioxide produces unconsciousness and depresses the respirations when administered to normal subjects in high concentrations (41). The narcotic effect of this gas has been known for many years (72). It has had trial as an anesthetic, but was found to produce convulsions in one patient in a small series (75). In lesser concentrations carbon dioxide may produce a variety of mental manifestations including depression, marked irritability, anxiety, somnolence, confusion, and delirium (9, 41). These changes in mental state observed in normal individuals breathing increased concentrations of carbon dioxide resembles the alterations observed in the patients with hypercapnia and respiratory acidosis.

The motor phenomena observed in carbon dioxide intoxication are variable, but the occurrence of some type of muscular movement intermittently during narcosis is quite common (19, 35, 41). This may consist of fine tremor of the facial muscles or intermittent jerking of the fingers and arms (41, 79). Gross clonic movements of the limbs may occur (16, 41, 75) as exemplified by two patients in this series (cases 4 and 5) who had several generalized convulsions. Many of the patients with deep coma have a generalized flaccid immobility which is maintained or intermittent. In cases 15 and 19 this was a particularly prominent finding. In one patient with concurrent bromide intoxication (case 7), there was weakness limited to a portion of the body. Carbon dioxide, in sufficiently large amounts, depresses cortical activity and antagonizes cortical stimulation (46).

A number of different reflex changes were noted in this group of patients. The

pupils were usually constricted with deep coma and did not react, or responded only sluggishly, to light. In some patients the pupils varied between marked constriction and full dilatation. With severe narcosis, loss of the corneal reflex was noted. Many of the narcotized patients had decreased or absent deep tendon reflexes. This has been noted by others (79). The presence of a Babinski reflex has been reported (41) and one patient in this study demonstrated a transient Babinski.

It is now generally believed that carbon dioxide intoxication causes an increase in spinal fluid pressure through its cerebral vasodilator effect (44, 50, 56, 78). The increase in cerebrospinal fluid pressure which occurs with increased arterial blood pCO_2 is probably responsible for the papilledema which may occur in this condition (16, 66, 79). In the group of patients observed by the authors, the cerebrospinal fluid pressure was elevated in those instances in which lumbar punctures were done. In many patients the retinal vessels were reported to be engorged and very dark, and in at least one patient papilledema was observed. It should be noted that many of these patients were hypoxic which was probably more important than hypercapnia in engorging the retinal vessels (64). Administration of oxygen to some patients did not visibly affect the retinal vessels, but in others the vessels decreased in size when oxygen was given.

Relationship Between Arterial Blood pH, pCO_2 and Mental State

The relationship between arterial blood pH, pCO_2 and mental state is summarized in figure 1. There are 35 observations on the 25 patients as they progressed into various stages of carbon dioxide narcosis. In our experience the arterial blood pCO_2 has been as high as 127 mm. Hg and the pH as low as 7.16 in a patient who was still conscious and responsive. As noted in figure 1, the groups of data for rational conscious patients and confused drowsy patients overlap. Westlake, Kaye and Simpson have noted similar overlap in arterial blood pCO_2 and pH values in the two groups of patients (79). In general, if the arterial blood pCO_2 is below 90 mm. Hg and the pH above 7.25, the patient will have no change in mental state or only minimal symptoms of drowsiness and intermittent confusion. Other authors have reported that mental clarity is usually observed wih the pCO_2 below 80 mm. Hg and the pH above 7.20 (79).

The comatose state was observed in patients with arterial blood pCO_2 and pH values ranging from 91 to 228 mm. Hg and 7.25 to 6.86 respectively. In every instance when the arterial blood pCO_2 was above 130 mm. Hg and the pH was below 7.14, a semicomatose or comatose state was present. Previous studies report coma in patients and normal subjects when the pCO_2 was above 100 mm. Hg and the pH below 7.10 (41, 79). As noted in figure 1, when the pCO_2 ranged between 90 and 130 mm. Hg and the pH between 7.25 and 7.14, patients varied from the conscious state to deep coma. This variable level for susceptibility to carbon dioxide has also been previously reported (1, 79). Usually the progression of carbon dioxide narcosis is associated with increase in pCO_2 and decrease in pH. In some patients, however, the mental state ranged between consciousness and semicoma without significant alteration in pH or pCO_2 (e.g., case 25).

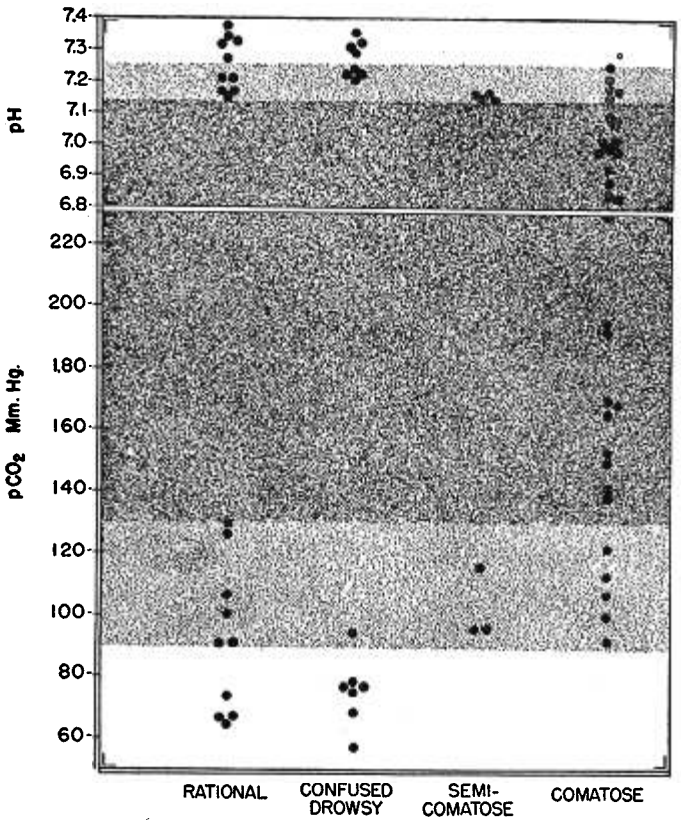

FIG. 1. Relationship of state of consciousness to arterial blood pH and pCO_2 in patients with carbon dioxide retention.

During the recovery from prolonged carbon dioxide narcosis, coma may persist after the carbon dioxide tension has been lowered to levels not ordinarily associated with alterations of consciousness. This tendency is illustrated in figure 2. No patient who was comatose was observed with an initial arterial blood pCO_2 below 90 mm. Hg, but as shown in figure 2, there were two cases in which coma persisted despite reduction of the pCO_2 below 90 mm. Hg by appropriate therapy. The arterial blood pCO_2 and pH were rapidly reversed in these patients. One patient, for example, remained comatose in spite of a change in pCO_2 from 168 to 67 mm. Hg and in pH from 6.98 to 7.27. The mechanism for maintaining coma in spite of the return toward normal arterial blood gas values is not clear. The lag in regaining consciousness occurs in patients who have had prolonged narcosis, but is not usually seen when coma has lasted for less than an hour. This probably represents evidence that alterations have occurred in the brain during the periods of prolonged acidosis and hypercapnia which require time to repair.

The manner in which the retention of carbon dioxide alters the mental state is

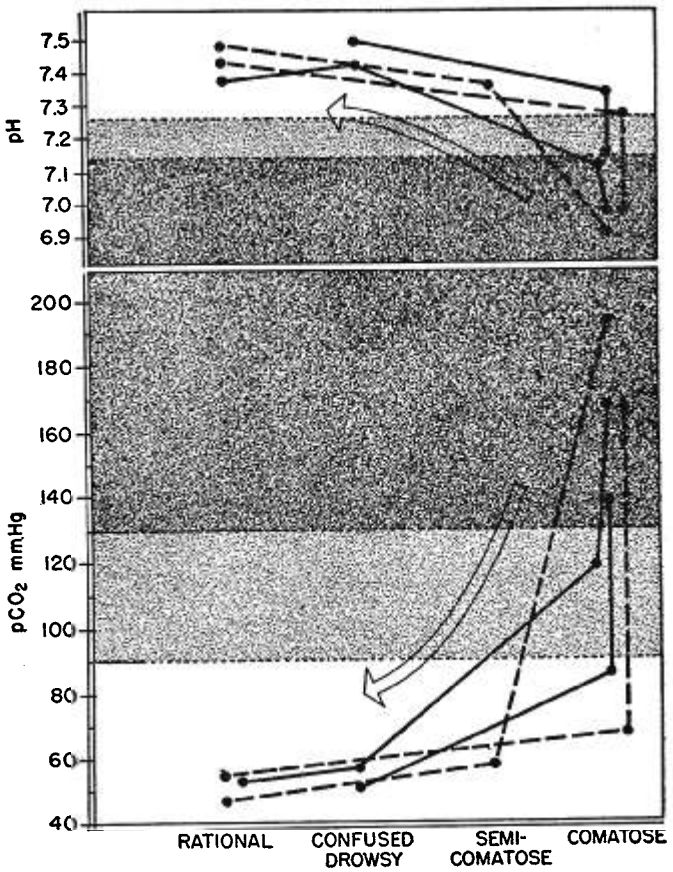

FIG. 2. Relationship of state of consciousness to arterial blood pH and pCO_2 during correction of hypercapnia. Each set of connected points represents one patient.

not known. The relative importance of blood pH and pCO_2 in causing the mental changes is likewise unsettled.

Circulatory System

The circulatory changes most commonly observed in these patients are a warm flushed skin, tachycardia and alterations in the blood pressure. The occurrence of severe, persistent hypotension has not been emphasized in the literature. However, in our experience, severe hypotension is frequently associated with carbon dioxide narcosis, and it may present a major problem in management. This is illustrated by the following case reports.

Case 14

W.M., a 74-year old man, was admitted to the hospital in September 1953. He had a 10-year history of severe respiratory distress related to chronic bronchitis and obstructive emphysema. More recently there had been symptoms of heart failure. The patient was moderately dyspneic and cyanotic. The blood pressure was 140/70; the chest was emphysematous;

and there was pitting edema of the lower extremities. On the sixth hospital day, the respirations became shallower and slower and the patient lapsed into coma. He had been given nasal oxygen and sedatives before this episode. Eight to ten hours later the blood pressure was 90/50 and norepinephrine in intravenous infusion was begun. Four to eight mgm. of norepinephrine were required every twelve hours to maintain a systolic blood pressure of 100 mm. Hg. Despite the continued use of norepinephrine, the blood pressure ultimately became unobtainable and at this time the blood pCO_2 was 228 mm. Hg and the pH was 6.84. The patient died shortly afterward.

Comment: With marked acidosis and hypercapnia, there was circulatory shock which was difficult to treat. Recognition and diagnosis of carbon dioxide narcosis were too late to permit institution of measures to correct hypercapnia.

Case 12

R.J., a male aged 60, was admitted to the hospital with acute respiratory distress in November 1952. He had a 22-year history of recurrent respiratory infections, wheezing, dyspnea, and a productive cough. Six months before admission, he developed ankle edema and marked exertional dyspnea, and appropriate therapy to correct his heart failure was begun. On admission to the hospital the patient was cyanotic and dyspneic; the blood pressure was 140/80; the retinal vessels were dilated; the chest was emphysematous, with many wheezes; a bigeminal pulse was noted; the liver was enlarged; and there was marked ascites and ankle edema.

During the first five days of hospitalization the patient improved, but then was unexpectedly found cyanotic and unresponsive with shallow rapid breathing. Nasal oxygen was started and, within one-half hour, the patient had recovered. Three days later after showing moderate improvement, he was found to be intermittently confused and unresponsive. At that time the blood pressure was 82/50 and norepinephrine in intravenous infusion was begun. A total of 18 mgm. of norepinephrine was required over a 24-hour period to return the blood pressure to normal levels. From that time until his death five days later, the patient required 16 to 24 mgm. of norepinephrine per 24 hours in intravenous fiuids to maintain a systolic pressure of approximately 100 mm. Hg. The arterial blood gas values for this patient were in the range shown in Table 1. At autopsy the patient had marked obstructive pulmonary emphysema, chronic bronchitis, right ventricular enlargement, generalized arteriosclerosis, and infarction of the left frontoparietal lobe of the brain.

Comment: This patient, like many in the study, developed marked intractable shock. At autopsy, in addition to pulmonary disease, the patient had evidence of degenerative vascular disease with cerebral infarction. Although this may have contributed to his altered mental state, it is unlikely that this solely caused his acute prolonged shock.

Case 4

M.M. was a 23-year old woman admitted to the hospital in August 1950 because of a three-day attack of asthma which was difficult to control. The patient had had asthma for two years, beginning with her first pregnancy. The asthma had been easily controlled until the present attack was precipitated, interestingly, by the knowledge that she was again pregnant. The respirations were rapid and labored. The blood pressure was 105/65 and the heart rate was rapid. There was minimal cyanosis of the nailbeds. The chest did not appear emphysematous, but expiratory wheezes were heard over the entire chest.

In the hospital the patient showed little improvement with therapy and on the day of death became markedly cyanotic and comatose. During this period she had several generalized convulsions. Eight hours before death, the blood pressure was 80/40 and, in spite of 500 cc. of whole blood and 4½ mgm. of epinephrine given over an eight-hour period, the blood pressure could not be raised. During the last two hours before death, the systolic blood pressure was in the vicinity of 50 mm. Hg. At autopsy there was marked bronchial and bronchiolar obstruction with mucus and only moderate pulmonary emphysema.

Comment: Circulatory failure was apparently the immediate cause of death in this case of carbon dioxide narcosis. The patient also had generalized convulsions associated with carbon dioxide narcosis.

Discussion

In general, breathing high concentrations of carbon dioxide increases the blood pressure, and voluntary hyperventilation lowers the blood pressure. These effects are believed to be the combined result of changes in carbon dioxide operating both directly on the vessels and by way of the vasomotor center. With hypocapnia there is a predominant vasodepressor effect with a resultant fall in the blood pressure (10). The inhalation of low concentrations of carbon dioxide (7 to 12%) has a powerful stimulant effect on the medullary vasomotor center, as well as the sudomotor and respiratory centers (25, 60). This results in a tachycardia, peripheral vasoconstriction, moderate increase in blood pressure, and sweating. In experimental animals more severe acidosis has been found to produce a large increase in cardiac output, but peripheral vascular resistance is disproportionately decreased and the blood pressure is unaltered or falls to low levels (36). The peripheral vasodilatation and increased blood flow are believed to be the direct effect of acidosis on the peripheral vessels (18). These general cardiovascular effects of increased concentrations of carbon dioxide in experimental animals resemble the picture which develops in patients with carbon dioxide narcosis. These individuals have warm extremities, a bounding rapid pulse which later becomes weak, and slight elevation in blood pressure which may in some cases be followed by hypotension or even severe shock.

ETIOLOGICAL FACTORS IN CARBON DIOXIDE INTOXICATION

Most of the patients in this series had chronic pulmonary disease, primarily obstructive pulmonary emphysema, chronic bronchitis and pulmonary fibrosis, which resulted in impaired ventilation. On this background acute alveolar ventilatory insufficiency was usually precipitated by one or more of the following basic mechanisms: 1) mechanical impairment of ventilation resulting from lung and bronchial infections, status asthmaticus, lung collapse, or chest surgery; 2) hypoventilation associated with congestive heart failure; 3) depression of the respiratory center as by drugs; and 4) elimination of hypoxia as a stimulus to breathing by inhalation of high concentrations of oxygen. Occasionally hypercapneic patients lapsed into coma without any apparent change in ventilation or in the arterial blood pH and pCO_2. Three patients did not have evidence of chronic pulmonary disease and demonstrate that the syndrome of carbon dioxide narcosis can occur whenever alveolar ventilation is sufficiently embarrassed. The following case reports are examples of the various etiological factors which may precipitate this syndrome.

Case 2

A.M., a 25-year old woman, was admitted to the hospital in August 1950 for the sixth time because of a three to four day bout of asthma. The patient had had asthma for 22 years, associated with season change and frequent respiratory infections. On admission the tempera-

TABLE 3

Arterial blood gas studies on a patient with carbon dioxide narcosis precipitated by pulmonary infection

Patient	Date	Comment	Arterial Oxygen % Saturation	Arterial pH	Arterial pCO_2 mm. Hg
A.M. (Case 2)	7-10-50	Comatose; 50% helium and 50 % oxygen	98.9	7.02	129
	(5 hours later)	Comatose; after sodium lactate infusion; nasal oxygen	94.6	7.04	155
		Comatose; air for 10 minutes	55.6	7.10	134

ture was 37.5, and pulse and respiratory rates were rapid. The patient was very apprehensive, had labored breathing, and a cough productive of mucopurulent sputum. The chest was emphysematous, and musical and crepitant rales were heard over both lung fields. A chest roentgenogram showed a diffuse infiltrate in the right upper lung field. Therapy included ACTH, penicillin, nasal oxygen, sedation, bronchoscopy, and the use of bronchodilator drugs. In spite of these measures, the patient became comatose on the third hospital day and died. The arterial blood gas determinations obtained on the first hospital day are shown in Table 3. An attempt was made to correct the patient's acidosis with an infusion of sodium lactate, but no improvement was noted. At autopsy there was severe obstructive pulmonary emphysema, marked tracheobronchitis, and bronchopneumonia of the right middle and lower lobes. *Comment:* This patient had developed obstructive emphysema in the course of a long asthmatic history. With this background, severe ventilatory insufficiency was precipitated by an acute bout of respiratory infection and asthma. In all probability sedation and nasal oxygen, which were indicated for other aspects of her illness, contributed to depression of ventilation. The unsuccessful use of sodium lactate in carbon dioxide narcosis has also been reported by others (79).

Case 11

L.W., a 23-year old woman, was admitted to the hospital in October 1952 for a left pneumonectomy. She had been known to have tuberculosis for three years. Antimicrobial therapy had consisted of para-aminosalicylic acid and streptomycin and the patient had done well. Following pneumonectomy, she remained comatose and an arterial blood sample was obtained which showed marked acidosis and hypercapnia (Table 1). Bronchoscopy with suctioning was performed and intravenous ACTH was started, but the patient died five hours postoperatively. Autopsy showed partial obstruction of the tracheobronchial tree with mucus. *Comment:* A number of factors associated with this patient's operation may have contributed to the accumulation of narcotic levels of carbon dioxide. These include the removal of a lung, depression of respiration and cough with anesthesia, increased secretions in the tracheobronchial tree with impaired drainage, and depression of cough and ventilation due to immobilization of the chest. Such factors are always significant after pneumonectomy, but prolonged hypercapnia of this degree is unusual.

Case 16

A.D., a 66-year old woman, was admitted to the hospital in April 1953. She had had asthma for about 10 years. During her hospital stay, following oversedation, the patient developed shallow respirations, and became cyanotic and comatose. She recovered and did well for a time, but was again admitted in October 1953 because of acute asthma and a respiratory

infection. Ten days after admission while showing marked improvement, she over-sedated herself with whiskey and chloral hydrate, and shortly thereafter became cyanotic and unresponsive. The degree of acidosis and hypercapnia is shown in Table 1. Following therapeutic measures to be discussed later, she recovered. The patient was again admitted in April 1954, because of increased severity of exertional dyspnea and orthopnea. These symptoms were associated with a recent respiratory infection and moderate congestive heart failure. On this occasion, carbon dioxide intoxication did not occur.

Comment: In this patient the respiratory infection and congestive heart failure probably contributed to the tendency to retain carbon dioxide. The episodes of coma, however, were directly related to the use of sedatives in relatively large amounts.

Case 8

G.B. was a 46-year old man, admitted to the hospital in November 1951 with a six-month history of marked exertional dyspnea related to obstructive emphysema. Two months before admission he was found to have a partial pneumothorax which did not re-expand and this prompted the patient's admission for thoracotomy and decortication of the lung. Following operation, the patient began to recover and then unexpectedly, 24 hours after surgery, was found comatose. As indicated in Table 4, he was severely hypercapneic. Nasal oxygen which had been used in a routine fashion was stopped and this measure resulted in the marked fall in arterial blood pCO_2 shown in Table 4.

Comment: This patient had chronic pulmonary disease but even with a pneumothorax managed to prevent marked hypercapnia. Because of the surgery and the patient's moderate hypoxia, nasal oxygen was given as routine postoperative care. In this patient, as demonstrated by the effect of its withdrawal, nasal oxygen depressed the ventilatory drive and caused marked retention of carbon dioxide.

Case 3

J.B. was a 31-year old man who had had tuberculosis for 11 years before his hospital admission in 1950. Following a left thoracoplasty in 1948, the patient had marked dyspnea.

TABLE 4

Alterations in arterial blood pH and pCO_2 in patients with chronic anoxia associated with breathing high concentrations of oxygen

Patient	Date	Comment	Arterial Oxygen % Saturation	Arterial pH	Arterial pCO_2 mm. Hg
G.B. (Case 8)	11–12–51	Preoperatively; air	81.5	7.33	65
	11–16–51	Postoperative; comatose; nasal oxygen	98.8	6.97	169
	11–16–51	Comatose; on air several minutes after oxygen stopped	89.3	7.11	119
	11–17–51	Slightly confused; air	91.3	7.42	57.4
J.B. (Case 3)	4–22–50	Rational; air 10 minutes	67.2	7.30	81
		Rational; mask oxygen, 2½ minutes	98.1	7.24	97
		Rational; mask oxygen, 6 minutes	99.3	7.19	113
		Rational; mask oxygen, 12 minutes	100.0	7.17	124
C.H. (Case 1)	6–1–50	Rational; air	64.4	7.29	81
		Rational; nasal oxygen	100.0	7.24	87

In 1949, one year before his death, he had settled into a bed and chair existence with oxygen for self-administration. He gradually became weaker and more lethargic. In April 1950, observations were made of the effect of breathing increased concentrations of oxygen on the arterial blood pH and pCO_2 (Table 4). Within 12 minutes after beginning nasal oxygen at a flow rate of 5 to 7 L/min., the patient's arterial pCO_2 had increased from 81 mm. Hg to 124 mm. Hg and the pH had changed from 7.30 to 7.17, without any obvious change in the mental state. The effect of hypoxia as a respiratory stimulus was demonstrated in the reverse direction when, during his hospital stay, the patient was found unconscious and breathing at the rate of six per minute. When the nasal oxygen was stopped, the patient became cyanotic, began breathing more rapidly and deeply, and regained consciousness.

Comment: This is an example of the kind of patient who shows marked increase in arterial pCO_2 and decrease in arterial pH when the hypoxic ventilatory stimulus is removed by correcting the hypoxia. It is of interest and a fairly frequent observation in these patients that acute brief episodes of acidosis and hypercapnia precipitated by oxygen breathing are often not associated with mental changes. On the other hand, prolonged use of oxygen gradually causes confusion and coma. Simple removal of the oxygen may then correct the altered mental state.

Case 1

The history of pulmonary disease in patient C.H. has been more fully described in the section on neurological features of carbon dioxide narcosis. The patient had symptoms and findings of marked obstructive pulmonary emphysema, heart failure, and polycythemia. Breathing high concentrations of oxygen did not markedly affect this patient's arterial blood pH or pCO_2 as shown in Table 4. Although his arterial oxygen saturation changed from 64 to 100%, his arterial blood pCO_2 went only from 81 to 87 mm. Hg.

Comment: Not all patients with hypoxia and the tendency to retain carbon dioxide develop immediate symptoms when hypercapnia is induced by oxygen, as shown by case 3. Moreover, as shown by case 1, not all patients with hypoxia and hypercapnia develop a significant further increase in arterial blood pCO_2 when hypoxia is corrected by oxygen.

Case 25

D.T., a 56-year old woman, was admitted to the hospital in June 1955. She was found to have pulmonary tuberculosis in 1928 and was treated with bed rest for the next five years. In 1938 a thoracoplasty was done with resection of seven ribs. Following this she did well, maintained a negative sputum and returned to normal activity. Eight to 12 months before admission, the patient developed exertional dyspnea, then orthopnea and ankle edema, associated with cyanosis. At first, she responded well to digitalis, dietary salt restriction and diamox, but three weeks before admission, there was a return of dyspnea and ankle edema and a productive cough. The patient appeared chronically ill and cyanotic. There was an old right thoracoplasty and there were moist rales at both bases. Only minimal ankle edema was noted at the time of admission. Cor pulmonale and heart failure were thought to be the primary factors accounting for the patient's illness. The effect of breathing high concentrations of oxygen on her acidosis and hypercapnia are shown in Table 5. With a 20 mm. Hg change in arterial carbon dioxide tension, the patient had no apparent mental change. Later in the hospital stay, while she was still rational and oriented, the arterial blood pCO_2 was found to be 106 mm. Hg. One week later with little change in her blood gas values, the patient became comatose. With appropriate therapy she recovered and was discharged from the hospital and followed in the outpatient clinic. Several months later, after relaxing her cardiac regimen, she again developed peripheral edema, cyanosis, and hypercapnia. Successful treatment of congestive failure was once more accompanied by a dramatic improvement in pulmonary function.

Comment: This patient's chronic pulmonary disease was initiated by tuberculosis. She was symptom-free until heart failure resulted from cor pulmonale. It was believed that the symptoms of respiratory failure were precipitated by the presence of congestive failure. This case

TABLE 5

Example of a patient who developed coma without marked change in degree of acidemia or hypercapnia

Patient	Date	Comment	Arterial Oxygen % Saturation	Arterial pH	Arterial pCO_2 mm. Hg
D.T. (Case 25)	6–18–55	Rational; air	55.5	7.27	78.2
		Rational; mask oxygen	100.0	7.17	99.6
	6–21–55	Rational; air	63.6	7.21	105.8
	6–29–55	Comatose; nasal oxygen	99.0	7.28	112.7

illustrates the development of coma with little change in pCO_2 during the course of chronic hypercapnia.

Case 20

R.T., a 58-year old man, was asymptomatic until five to six hours before admission when he suddenly became comatose. He had known hypertension for one year. On admission, September 1954, his blood pressure was 280/140. He was unresponsive, and his respirations were depressed. There was a flaccid paralysis and absent superficial and deep reflexes. Lumbar puncture confirmed the clinical impression that the patient had had an intracranial hemorrhage. An arterial blood sample revealed that marked acidosis and hypercapnia accompanied the depressed respiration (Table 1). At autopsy a massive hemorrhage was found in the region of the pons and the right cerebrum. There was no evidence of lung disease.

Comment: In this particular patient, the acidosis and hypercapnia which were present were of secondary importance. The example does illustrate, however, that narcotic levels of carbon dioxide can be present in patients with conditions which cause alveolar hypoventilation without chronic lung disease. In similar situations, where recovery might otherwise occur, it is possible that persistence of carbon dioxide narcosis could cause death or confuse the clinical management if it remained undiscovered.

Case 23

A patient with Cushing's disease, M.R., was admitted to the hospital for the third time in January 1955. Following completion of bilateral adrenalectomy, she developed staphylococcus pneumonia and a pyopneumothorax. With this complication, she became cyanotic and had marked dyspnea. She gradually became comatose and arterial blood gas analysis showed marked acidosis and hypercapnia (Table 6).

Comment: This case demonstrates that acidosis and hypercapnia may be associated with an infectious process which interferes with adequate ventilation even without a background of chronic pulmonary disease.

TABLE 6

Arterial blood gas values obtained on a patient with staphylococcus pneumonia

Patient	Date	Comment	Arterial Oxygen % Saturation	Arterial pH	Arterial pCO_2 mm. Hg
M.R. (Case 23)	12–30–54	Oriented; air	—	7.36	64.4
	1–7–55	Comatose; nasal oxygen	78.6	7.14	151.0
	1–12–55	Comatose; nasal oxygen	70.0	7.18	143.0

Discussion

Mechanical impairment of alveolar ventilation

Impaired alveolar ventilation is the fundamental cause of respiratory acidosis. This usually occurs in patients with diffuse or generalized pulmonary disease. Mechanical interference with alveolar ventilation primarily involves obstruction of the airways, although changes in the lungs or the chest cage may also impair the ventilatory effort. Restrictive factors such as chest cage deformities, kyphoscoliosis, restrictive pachypleuritis and stiffened lungs do not in themselves usually limit ventilation enough to cause carbon dioxide narcosis, but they may be very important in association with the obstructive factor in producing this syndrome (63). Restrictive chest disorders may also play a significant role in the development of carbon dioxide narcosis by leading in the course of time to obstructive disorders such as chronic bronchitis.

Patients with obstructive emphysema have chronic obstruction of the airway due at least in part to loss of elastic support for the bronchial tree (12, 17). This factor, which is a slow progressive process, in itself does not precipitate acute respiratory insufficiency with acidosis. As shown in Table 1, carbon dioxide intoxication usually occurs after additional embarrassment to alveolar ventilation such as infection, status asthmaticus or chest surgery.

Infection in the lungs or the tracheobronchial tree is a frequent precipitating factor of carbon dioxide narcosis. It is often difficult to find a single agent responsible for the retention of carbon dioxide and the marked anoxia, but in at least four of the patients infection was believed to be the major factor. The association of respiratory infections with this syndrome has been pointed out by others (63, 67, 70). The frequency with which acute respiratory infection, particularly acute bronchitis even without chronic lung disease, is associated with a decrease in arterial oxygen saturation and an increase in carbon dioxide tension has been stressed by Westlake (77). Infection contributes to the bronchial obstruction by increasing the bronchial secretions and by producing edema and engorgement of the bronchial mucosa. The involvement of the lung parenchyma may also interfere with alveolar ventilation by reducing lung compliance or inducing splinting of the chest (39). Parenchymatous infection will interfere with alveolar gas exchange, although this will apply to carbon dioxide excretion much less than to oxygen absorption.

Status asthmaticus or prolonged episodes of asthma are frequently associated with respiratory infections. In many patients with carbon dioxide intoxication, infection and asthma are both implicated in the impairment of alveolar ventilation. This was the situation in at least four patients in his series. Asthma alone, however, may be responsible for carbon dioxide narcosis. Case 4 (Table 1) had had little asthma except at the time of pregnancy and, with the knowledge that she was pregnant, a severe episode of asthma began which was fatal. During an asthmatic attack, obstruction to the airway is increased because of the excessive amounts of thick tenacious mucus, mucosal edema, and bronchospasm.

Surgery and anesthesia may be the factors which embarrass alveolar ventilation. Four patients in the group had had chest surgery and postoperatively had carbon dioxide narcosis. The anesthetist and the surgeon have both been aware of the problem of anoxia and carbon dioxide retention during anesthesia and thoracic surgery (4, 5, 69). The fact that chest surgery postoperatively may be complicated by carbon dioxide narcosis has received little emphasis in the medical literature. Case 8 is an example of this complication. The combination of surgery and anesthesia interferes with ventilation in several ways. Anesthesia increases the bronchial secretions, depresses the ventilatory drive and cough reflex, and predisposes to pulmonary infection. The surgery may remove large portions of the effectively ventilated lung and decrease the motion of the chest. In addition, thoracic surgery necessarily limits postoperative mobility of the chest.

Congestive heart failure

Cor pulmonale and heart failure are circulatory complications of chronic pulmonary disease. Frequently the syndrome of carbon dioxide intoxication is associated with these circulatory complications (79). Cournand and co-workers have stressed the frequent occurrence of heart failure in chronic pulmonary disease and have elucidated the mechanisms by which pulmonary insufficiency may lead to an increased circulatory load and failure of the right ventricle (26, 28, 29). They relate the circulatory changes in pulmonary emphysema to restriction of the pulmonary capillary bed and to anoxia. Both factors contribute to pulmonary hypertension. Chronic anoxia also produces increased cardiac output, polycythemia and hypervolemia, which further contribute to pulmonary hypertension. With the combination of these factors, right heart failure results. Because of the circulatory load which may be imposed by pulmonary insufficiency, right heart failure often follows acute impairment of pulmonary function in these patients. In this way, heart failure may be precipitated by an episode of pulmonary infection.

In addition, we have been impressed by the impairment of pulmonary function which may follow heart failure in these patients. Several patients with cor pulmonale were observed to develop congestive heart failure with relaxation of their cardiac regimen, particularly with reference to sodium restriction. Case 25 demonstrated this on two occasions. In some of these cases, heart failure appeared to precipitate acute pulmonary insufficiency with cyanosis and hypercapnia. The mechanism by which this occurs is not clear. Congestive heart failure is known to decrease pulmonary compliance and this change in the physical properties of the lungs must contribute to impairment of pulmonary function (8, 48). Heart failure in chronic lung disease can apparently cause enough further depression of pulmonary function to account for the development of carbon dioxide narcosis.

Drug depression

Depression of respiration by drugs has been observed as a factor responsible for development of carbon dioxide narcosis in patients with chronic pulmonary

disease. This occurred on two occasions in case 16. Barbiturates and morphine in particular depress the minute volume and the effective alveolar ventilation (73, 80), and morphine in addition depresses the cough reflex.

Oxygen therapy

Oxygen therapy in patients with chronic pulmonary disease and anoxia has been recognized for a long time as a factor leading occasionally to changes in the mental state of some patients (2, 51). Many reports now confirm that this effect of oxygen therapy is due to the retention of carbon dioxide (3, 14, 20, 33, 42, 71, 79, 80). Case reports 3 and 8 demonstrate the marked, rapid elevation in pCO_2 and decrease in pH which can occur when a chronically anoxic patient breathes oxygen. Oxygen therapy was in use when carbon dioxide narcosis developed in most of the patients in this series. However, many patients with chronic anoxia and moderate hypercapnia do not develop carbon dioxide narcosis or even a significant increase in arterial blood pCO_2 when oxygen is administered. Case 1 illustrates this statement. Other reports also indicate that only a small portion of patients with chronic hypoxia develop carbon dioxide retention when oxygen therapy is used (44, 79).

In patients with chronic alveolar hypoventilation and carbon dioxide retention, the respiratory response to carbon dioxide is diminished (22, 27, 47, 58, 71). As indicated earlier these patients are necessarily hypoxic when breathing room air. Hypoxia may be considerably more severe than could be anticipated from the degree of carbon dioxide retention. This is because pulmonary disease which causes hypoventilation often causes changes in diffusing capacity for oxygen and inequalities in pulmonary ventilation-perfusion ratio which affect oxygen absorption more adversely than the excretion of carbon dioxide (23, 52–54). The arterial hypoxia which exists in these patients, acting through the peripheral chemoreceptors, often contributes an important share of the ventilatory stimulus. In this situation when the anoxia is corrected by breathing high concentrations of oxygen, the ventilatory drive may be so reduced that severe carbon dioxide retention develops. The depressant effect of oxygen may be apparent even when the arterial oxygen saturation does not exceed normal values (Table 4, cases 8 and 3). On the other hand, many of these patients show no immediate change in ventilation when oxygen is administered. Under these circumstances ventilation is evidently being driven by stimuli other than hypoxia. However, when such patients are left unattended on oxygen therapy, their ventilatory drive may unexpectedly fail and carbon dioxide retention will then develop.

Other factors

Increased susceptibility to a given level of acidosis and hypercapnia apparently accounted for the episode of carbon dioxide narcosis in some of the patients in this series. Hypercapneic patients occasionally progress from a responsive state into coma with little change in blood pCO_2 or pH, as illustrated by cases 3 and 25. The explanation of this apparent increase in susceptibility to the toxic effects of carbon dioxide and acidosis is not clear, but it may be related to the duration of respiratory acidosis.

Lastly, any illness which impairs alveolar ventilation may lead to carbon dioxide narcosis. If hypoventilation is severe enough to require oxygen therapy, carbon dioxide retention may become significant. Cases 20 and 23 are examples of the fact that carbon dioxide narcosis may be superimposed on another illness without the presence of chronic pulmonary disease. Neuromuscular disease, particularly poliomyelitis, can cause hypercapnia (11, 33). Similarly, oversedation and anesthesia may lead to hypercapnia (5, 80). Carbon dioxide narcosis may also complicate the course of patients whose respirations are depressed because of cerebrovascular accidents or head trauma.

DIAGNOSIS

A change in the mental state of a patient with impairment of alveolar ventilation should lead to a suspicion of the diagnosis of carbon dioxide intoxication. Awareness of the kinds of patients and the etiological factors which result in carbon dioxide narcosis may allow the syndrome to be avoided.

Diagnosis ultimately is made by analysis of an arterial blood sample for carbon dioxide tension and pH. "Arterialized" venous blood obtained from an extremity flushed by heat can be used if arterial blood cannot be obtained. Routine additional laboratory data which may suggest carbon dioxide retention are an acid urine and an elevated carbon dioxide content or combining power. If the blood pH and pCO_2 cannot be measured, these two factors in combination in a patient with lung disease or depressed respiration and cyanosis on room air would certainly be clinical evidence in favor of the syndrome. It must be kept in mind that an elevated serum bicarbonate, an acid urine, and disturbances of consciousness may also be seen in patients with severe hypokalemic alkalosis.

THERAPY

The importance of preventing the development of carbon dioxide narcosis in patients with chronic lung disease has been stressed recently (13, 79). Severe asthma, respiratory infections, heart failure, surgery, oversedation and high concentrations of oxygen are recognizable factors which may precipitate severe carbon dioxide retention. Prevention of this condition, therefore, may be possible by correction of these etiological factors. Bronchodilator drugs, expectorants, steroid therapy, and bronchoscopic drainage are used to decrease airway obstruction. Antibiotics are necessary when infection is present in the respiratory system. The correction of heart failure with digitalis, salt restriction, and diuretics may be an important preventive measure in patients with chronic lung disease and heart failure. Careful use of sedatives and high concentrations of oxygen and particular caution during anesthesia and surgery may also be very important in preventing the development of carbon dioxide narcosis. Unfortunately these measures are not always successful or the patient is seen by the physician after carbon dioxide retention has become severe.

All of the patients in this study had carbon dioxide intoxication with mental changes ranging from intermittent depression to deep coma. Twenty-three of the group were comatose on one or more occasions. Seven of the 13 patients observed from 1950 to 1953 died in coma. In general, therapy in these 13 patients

consisted of the use of bronchodilator drugs, bronchoscopic drainage, expectorants, antibiotics and nasal oxygen. Steroid therapy was used in a few cases. When congestive failure was an apparent feature of the clinical picture, salt restriction, digitalis and diuretics were used. These therapeutic measures which were aimed at correcting the causes for carbon dioxide narcosis were not successful in preventing the death of seven of the patients.

Since 1953, 12 patients with carbon dioxide narcosis have been observed and more intensively treated. Six of this group died in spite of therapy, but two apparently died of associated illnesses even though the hypercapnia was corrected. More intensive use was made of bronchodilator drugs, steroid therapy, bronchoscopic drainage, antibiotics and anticongestive regimens. These measures, however, operate by correcting the acute process which precipitated the carbon dioxide narcosis. Unfortunately the comatose patient with respiratory depression and shock may die before they have time to be effective. For this reason mechanical respirators were used on the last 12 patients to provide adequate alveolar ventilation and correct the severe hypercapnia. It is believed that the mechanical aids to breathing were life-saving in some of the cases of carbon dioxide narcosis by allowing the time necessary for the specific measures to correct the factors which originally initiated the severe carbon dioxide retention.

Based on the experience gained in managing the patients in this study the following program is suggested for the emergency treatment of patients with frank carbon dioxide narcosis. The patient should be bronchoscoped in order to remove excessive mucus and gross obstructing plugs from the airway with suction. At that time isuprel should be instilled into the airway under direct vision. Following bronchoscopy, the trachea is intubated to allow suctioning of the tracheobronchial tree and to maintain a patent upper airway so that a mechanical respirator can be used. Automatic respirators, either a Drinker-type tank respirator or an intermittent positive-negative pressure type resuscitator (32, 49, 59, 65), have been used by the authors to maintain adequate ventilation of the lungs. An increased concentration of oxygen is usually needed to correct the associated anoxia. Intravenous steroid therapy is also instituted. Twenty to 40 units of ACTH in intravenous infusion were used in general in the patients in this report, but we have recently given hydrocortisone, 100 mgm. infused over three to four hours. If hypotension is present, infusion of noradrenaline should be given to maintain the systolic blood pressure at adequate levels. If there is evidence of heart failure, digitalization is begun. Antibiotics are routinely started at this time because infection is so commonly present. With the emergency measures, the severe hypercapnia and its effects may be controlled, allowing sufficient time for steroids, antibiotics and anticongestive therapy to correct the acute factors which precipitated the carbon dioxide narcosis. The following case reports demonstrate various features of the therapeutic program.

Case 15

The description of the clinical history and findings has already been presented. The patient, E.E., was found comatose during her hospital stay in October 1953 and the initial blood gas values shown in Table 7 made it evident that she had carbon dioxide narcosis.

TABLE 7

Examples of the use of a Drinker respirator in conjunction with other medical therapy to correct carbon dioxide narcosis

Patient	Date	Comment	Arterial Oxygen % Saturation	Arterial pH	Arterial pCO_2 mm. Hg
E.E. (Case 15)	10–2–53	Comatose; placed in Drinker respirator; nasal oxygen	89.2	6.92	194.0
	10–3–53	Semicomatose; 24 hours of therapy; nasal oxygen	97.6	7.37	58.5
	10–5–53	Alert; air	96.1	7.48	47.4
	10–10–53	Alert; air	94.2	7.44	44.9
A.H. (Case 22)	10–18–54	4th postoperative day; drowsy; air	74.1	7.38	67.4
	10–20–54	Comatose; nasal oxygen	—	7.16	96.7
	10–21–54	Comatose; 24 hours in Drinker respirator with tracheotomy and ACTH infusion	94.5	7.30	77.5
	10–25–54	Rational; air	87.8	7.41	61.5

She had been on isuprel nebulization, aminophylline retention enemas, and intramuscular epinephrine during the period before coma developed. The patient was bronchoscoped, with clearing of the airway by suction and the instillation of isuprel. She was placed in a Drinker respirator. Intravenous ACTH was given. During the next 24 hours there was correction of the acidosis, hypercapnia and anoxia (Table 7), with a slower clearing of coma over the following two to three days. She later had two more episodes of coma treated elsewhere in a similar fashion with recovery, but ultimately she died in another hospital in a fourth episode of carbon dioxide narcosis when a mechanical respirator was not used.

Comment: The recovery of this woman was probably the result of many factors. The use of a mechanical respirator was believed to be life-saving because her condition had steadily deteriorated as a result of the severe carbon dioxide narcosis. In spite of the rapid return of her arterial blood pCO_2 and pH to near normal levels, the patient remained semicomatose for a period of time as described earlier. The persistence of coma allowed continued use of the respirator to maintain ventilation until other therapy such as ACTH had time to correct the factors which initiated the acute episode of narcosis. With recovery from hypercapnia and acidosis, the patient actually had an increase in arterial pH to 7.48. A similar change has been noted in other patients (case 19, Table 9) with recovery from hypercapnia.

Patients with low arterial blood pH and high arterial blood pCO_2 may show an alkalosis when recovering from carbon dioxide narcosis. They then have a metabolic alkalosis and a slightly elevated arterial pCO_2. In part, this may represent the effect of ACTH or cortisone. More likely, however, is the probability that the metabolic alkalosis represents the delay in excretion of base by the kidney after correction of the respiratory acidosis.

Case 22

A.H., a 61-year old man, had exertional dyspnea for one year before admission. Two months before admission he noted morning cough and blood-flecked sputum. The diagnosis of bronchogenic carcinoma was established and a left pneumonectomy was done. Four days after operation the patient became weaker and more dyspneic. Arterial blood studies showed hypercapnia (Table 7). Intravenous ACTH was started and, because of cyanosis, nasal oxy-

gen was given at low flow rates. Two days later, he was comatose with shallow slow respirations. A tracheotomy was done and a Drinker respirator was used. The patient, though weak and comatose, resisted the respirator to the extent that no reduction in arterial pCO_2 was obtained. Demerol was given to eliminate the patient's resistance and allow the respirator to take over ventilation entirely. As indicated in Table 7, this brought about a definite rapid improvement in blood gas values. Antibiotics which were in use were continued and hydrocortisone was administered by intravenous infusion. Within a few days the patient had become conscious and rational, although he still had moderate hypoxia and hypercapnia.

Comment: This example demonstrates the occurrence of carbon dioxide narcosis in the postoperative patient. The usefulness of a mechanical respirator when the respiratory effort has become ineffective is illustrated. In this instance, the patient attempted to resist the respirator, but the use of demerol permitted the respirator to provide adequate ventilation, correcting the hypercapnia and acidosis.

Case 18

A.M., a 40-year old housewife, was admitted to the hospital for evaluation of seasonal asthma which had been present for 27 years. While in the hospital she had more severe asthma in spite of conventional therapy, including bronchodilator drugs, expectorants, and sedation. Six days after admission she became semi-stuporous. The initial blood gas studies and subsequent course are shown in Table 8. Intravenous ACTH and the use of the Bennett intermittent positive pressure valve with tank oxygen were added to the therapy. Although the Seeler positive-negative resuscitator proved somewhat more effective in lowering the arterial pCO_2, the Bennett valve was used because the patient, in her semi-stuporous state, tolerated this type of mechanical respirator better.

Comment: This case demonstrates that oxygen, when needed by the hypoxic, hypercapneic individual, can be administered without the accumulation of significant additional carbon dioxide if effective alveolar ventilation is maintained with the aid of intermittent positive pressure breathing. The semi-stuporous patient, as shown, may tolerate a non-automatic respirator better than an automatic type because he is able to determine the respiratory pattern more completely.

Case 19

W.P., a 74-year old man, had a ten-year history of recurrent respiratory infections and progressive exertional dyspnea. The clinical impression of obstructive emphysema had been confirmed by pulmonary function studies three years before admission. The patient, however, had been active and continued to work as an engineer until two weeks before admission when the gradual onset of weakness and lethargy forced him to seek medical aid. The morning of

TABLE 8

Illustration of the use of an intermittent positive pressure breathing valve (Bennett)

Patient	Date	Comment	Arterial Oxygen % Saturation	Arterial pH	Arterial pCO_2 mm. Hg
M.P. (Case 18)	7-21-54	Semistuporous; air	77.2	7.19	79.8
		Semistuporous; nasal oxygen	94.2	7.15	95.5
		Semistuporous; Bennett valve 5 min. oxygen	98.6	7.23	75.5
		Semistuporous; Seeler valve 5 min. oxygen	99.2	7.29	62.4
	7-24-54	Alert; air	95.3	7.47	41.2

admission, he became rapidly confused and then comatose. On admission he was cyanotic; respirations were shallow and slow; the pupils were small and fixed to light; and there was a generalized flaccid weakness with hyporeflexia. The cerebrospinal fluid pressure was 300 mm. H_2O. It was the impression of the staff that the patient had had a cerebrovascular accident, but the possibility of carbon dioxide narcosis was considered. The arterial blood pH was found to be 6.98 and therapy for carbon dioxide narcosis was begun. Antibiotics and intravenous ACTH were given. An endotracheal tube was inserted and the Seeler resuscitator was used. The marked improvement in ventilation corrected the acidosis and hypercapnia as shown in Table 9. Within 12 hours the patient responded to questions, and within 24 hours was alert and oriented.

Comment: This case demonstrates the rapid and marked lowering in arterial blood pCO_2 which can be effected by a mechanical respirator in a patient with marked obstructive emphysema.

Case 20

R.T. was admitted to the hospital comatose and proved to have an intracranial hemorrhage and respiratory acidosis. Although he was not expected to live, the automatic resuscitator was used and the results in Table 9 illustrate its effectiveness in increasing alveolar ventilation and lowering the arterial blood pCO_2.

Comment: Although this patient could not be saved by correcting the marked carbon dioxide retention, he does illustrate that carbon dioxide intoxication can occur incidental to any illness depressing respirations. Even though the primary illness may be reversible, the patient may die of carbon dioxide intoxication unless the situation is recognized and narcotic levels of carbon dioxide prevented. The mechanical respirator can do this effectively as demonstrated in the example.

Case 25

The clinical history of patient D.T. has already been given in a previous section. She was believed to have cor pulmonale as a result of extensive inactive tuberculosis and a thoraco-

TABLE 9

Illustrations of the use of an automatic resuscitator (Seeler)

Patient	Date	Comment	Arterial Oxygen % Saturation	Arterial pH	Arterial pCO_2 mm. Hg
W.P. (Case 19)	8-14-54	Comatose; nasal oxygen	—	6.98	168.0
		Comatose; Seeler valve 15 min. oxygen	—	7.27	79.5
		Comatose; air 8 min.	—	7.07	117.0
		Comatose; Seeler valve 20 min. tank air	—	7.30	61.5
	8-15-54	Alert; low flow nasal oxygen	—	7.43	54.1
R.T. (Case 20)	9-15-54	Comatose; air 10 min.	68.8	6.98	149.0
		Comatose; Seeler valve oxygen	100.0	7.17	85.0
		Comatose; air 6 min.	49.4	7.00	140.5
		Comatose; Seeler valve oxygen	100.0	7.05	111.3
	9-15-54	Comatose; Seeler valve 6 hours	99.3	7.34	50.4
	9-16-54	Comatose; Seeler valve continuously	100.0	7.33	53.0

plasty. The primary clinical problem was one of managing marked hypoxia and heart failure. As shown in Table 11, at the time of admission to the hospital she had hypercapnia and showed an increase in arterial blood pCO_2 when breathing high concentrations of oxygen. Intravenous catheterization of the pulmonary artery revealed a pulmonary hypertension of 80/30 mm. Hg and an elevated cardiac output with an index of 4.1 L/min. The patient did not show immediate improvement on dietary salt restriction, diamox, digitalization, and phlebotomy. It was believed that anoxia was an important factor in her illness and nasal oxygen was given at a low flow rate of one L/min. with the intention of increasing the flow gradually. Because respiratory infection or reactivation of the tuberculosis was suspected, the patient received penicillin, streptomycin and isoniozid. No improvement was noted and, by the tenth hospital day, she was comatose. Examination at that time revealed generalized twitchings, constricted unreactive pupils, and occasional periods of flaccid immobility with hypoactive reflexes. The respirations were shallow and depressed. An endotracheal tube was put in place and the patient was resuscitated with the Seeler respirator using tank oxygen. She was maintained by this respirator for the next 24 hours with normal oxygen saturation without further increase in the hypercapnia. The next day a tracheotomy was done and the patient was placed in a Drinker respirator. The tracheotomy permitted frequent suctioning of the airway. Oxygen was administered through the tracheotomy tube. The patient's temperature rose to 40° and 41°C. and she was continued on isoniozid and streptomycin as well as penicillin. Steroid therapy had also been instituted while congestive heart failure was intensively treated. The respirator was used to maintain the patient's respirations and, with moderate diuresis, she eventually lost 22 pounds of weight. Twelve days later the patient was alert. As shown in Table 10, she maintained a near normal oxygen saturation without

TABLE 10

Use of Drinker respirator and correction of heart failure in treatment of carbon dioxide narcosis

Patient	Date	Comment	Arterial Oxygen % Saturation	Arterial pH	Arterial pCO_2 mm. Hg
D.T. (Case 25)					
Adm. 1	6-18-55	Alert; air	55.5	7.27	78.2
		Alert; mask oxygen	99.6	7.17	99.7
	6-21-55	Rational; air	63.6	7.21	105.8
	6-25-55	Rational but lethargic; air	54.5	7.20	114.0
	6-29-55	Comatose; Seeler valve; oxygen	99.1	7.28	112.7
	7-1-55	Comatose; in Drinker respirator; oxygen	99.0	7.26	—
	7-5-55	Unresponsive; out of respirator; nasal oxygen	99.3	7.28	109.0
	7-12-55	Alert; out of respirator 15 min.; air	87.3	7.54	57.0
		Alert; in respirator 15 min.; oxygen	97.5	7.52	61.0
	7-20-55	Alert; air breathing through tracheotomy	88.0	7.51	49.0
		Alert; air breathing through mouth	90.0	7.47	51.0
Adm. 2	11-30-55	Lethargic; room air	61.4	7.28	74.8
		Lethargic; mask oxygen	96.5	7.19	99.0
	12-7-55	Rational; room air	77.4	7.21	82.2

severe hypercapnia while on room air. Twenty days later the patient had near normal arterial blood gas values. She not only recovered from the coma and remained rational and oriented but demonstrated a marked improvement in lung function. She was discharged markedly improved after 9 weeks in the hospital. Therapy to be followed at home included digitalis, dietary salt restriction, diamox as a diuretic, occasional mercurial diuretics, and isuprel by nebulization.

In November 1955 she was re-admitted because of return of her cyanosis and respiratory distress, ascites and 2+ pitting edema. The anticongestive regimen had not been closely followed in the period before admission and digitalis therapy had been stopped by the patient. The results of blood gas studies are shown in Table 10. Therapy for heart failure was again intensively pursued. In addition, the patient was kept in the seated position and given dexedrine to combat drowsiness. Oxygen was given by nasal catheter and positive pressure breathing was intermittently used. Antibiotic therapy was also instituted. On the fifth hospital day the patient began to have a marked diuresis and ultimately lost 15 pounds of weight. Arterial blood gas studies on the seventh hospital day are shown in Table 10. The patient was discharged 13 days after admission markedly improved.

Comment: This patient illustrates a number of important factors in the management of carbon dioxide narcosis. The case is unusual in the prolonged period required for recovery from carbon dioxide narcosis on the first admission. It demonstrates, however, that the arterial oxygen saturation can be maintained by a mechanical respirator without increasing the hypercapnia. It is important to note that the patient's pulmonary function improved enough after correction of heart failure to maintain an arterial oxygen saturation of 90%. Recognition of the relationship of heart failure to pulmonary insufficiency on the second admission enabled institution of intensive anticongestive therapy with rapid improvement of both conditions. Moreover, the use of a mechanical respirator was avoided at that time.

Discussion

The therapy of carbon dioxide narcosis requires the intensive and energetic use of drugs and mechanical measures in an effort to improve alveolar ventilation. For purposes of discussion, the various measures will be considered individually, but it should be remembered that a combination of these measures is necessary in a given patient.

Oxygen

All of the patients in this study and all patients with inadequate alveolar ventilation present the problem of managing hypoxia, either in association with acidosis and hypercapnia or with the anticipation that the syndrome will develop as the hypoxia is corrected. With marked hypoxia, however, oxygen therapy is essential and it should not be withheld because of the fear of developing carbon dioxide narcosis. Anoxia is probably an important factor in precipitating congestive heart failure in patients with cor pulmonale. Correction of anoxia may help prevent pulmonary edema (24), further increase in the pulmonary arterial pressure (43), and an increased cardiac output (29). Anoxia may also result in permanent central nervous system damage and neurological sequelae (15).

Two methods are suggested for administering oxygen to the hypoxic patient in order to avoid the development of carbon dioxide narcosis. Barach has demonstrated that these patients tolerate gradual increases in oxygen concentration, and in the course of several days high concentrations of oxygen can be

given without the development of carbon dioxide narcosis (3). A common procedure is to begin with nasal oxygen at flow rates of about one L/min. Another method for oxygen therapy is to allow the patient to be out of the oxygen tent for 20 minutes in every hour (21). This results in some cyclic variation in the oxygenation and in ventilatory effort. This method has the advantage of automatically insuring close and repeated observation of the patient's condition by ward personnel. Both methods have been useful in some patients but not always successful (case 25). The use of intermittent positive pressure breathing will allow administration of 100%oxygen without increasing the acidosis and hypercapnia. With frank carbon dioxide narcosis, oxygen can be administered while an automatic respirator is being used to correct hypercapnia.

Maintenance of clear airway

Bronchodilator drugs such as isuprel 1:200 by nebulization, intravenous or rectal aminophyllin, intramuscular epinephrine, and antihistamines had been used in the patients in this series. In our experience they were of little value during the period of deep coma. The various drugs are certainly useful and important in the management of less severe cases of carbon dioxide intoxication (13). Isuprel or other bronchodilator drugs were administered as a spray with the intermittent positive pressure device or were placed deep in the airway during bronchoscopy. Similarly, detergents were nebulized into the airway in some patients.

The maintenance of a clear airway, however, is essential for the correction of narcotic levels of carbon dioxide. Three methods were found most useful in the patients vigorously treated in this series. These were bronchoscopy, use of an endotracheal tube, and tracheotomy. Bronchoscopy with suctioning of the airway and installation of bronchodilator drugs under direct vision is frequently extremely important in removing airway obstruction. Occasionally these patients have gross mucus plugs in large bronchi which can be detected and removed during bronchoscopy. For this reason an initial bronchoscopy is a useful procedure. Thereafter, intermittent tracheal suction can often be accomplished in a semicomatose or comatose patient by skillful manipulation of a soft rubber catheter passed through the nose.

The insertion of an endotracheal tube, which may be left in place for periods up to 24 hours, will maintain a patent upper airway, allow suctioning of the tracheobronchial tree, and decrease the dead space. In case 19 it was used effectively with a mechanical respirator, had the advantage of being easily put in place, and within 18 hours was removed without residual damage to the trachea. After 24 hours, however, endotracheal intubation should be discontinued, because of the danger of tracheal ulceration, and a tracheotomy performed if the carbon dioxide narcosis has not been corrected.

Tracheotomy allows better suctioning of the airway and a greater decrease in the dead space than the endotracheal tube. However, it should not be performed without careful consideration. In our opinion the endotracheal tube should be tried first because a tracheotomy has certain disadvantages which are

not easily reversible. It leaves a disagreeable wound, the healing of which may prolong recovery. Although it is well suited to the use of a Drinker respirator, it cannot transmit the high pressures which are required when a positive pressure resuscitator must be used to obtain adequate alveolar ventilation. A tracheotomy also interferes with effective coughing in the convalescent period. Despite these disadvantages it is highly advantageous in cases where a respirator must be used for prolonged periods. A tracheotomy in combination with the Drinker respirator was effective in cases 22 and 25. Theoretically, a tracheotomy would have its greatest usefulness in a patient with marked restriction of chest and lungs, such as case 17 with severe kyphoscoliosis. In this situation ventilation is restricted and maximum decrease in the dead space would be the factor most important in increasing alveolar ventilation.

Antibiotic therapy

Adequate use of antibiotics was an essential feature of the therapy to correct carbon dioxide narcosis. The relationship of infection to impairment of alveolar ventilation and the importance of treating infection of the tracheobronchial tree and lungs have been emphasized (67, 70, 77). In contrast to the use of a tracheotomy and respirator, which are intended to correct the carbon dioxide narcosis without correcting its cause, antibiotic therapy is intended to remove a primary factor in precipitating the retention of carbon dioxide in some patients. Successful antibiotic therapy will reduce bronchial obstruction by decreasing the inflammatory swelling of the bronchial mucosa and the intraluminal exudate. Clearing of pneumonitis will increase the pulmonary aerating surface and will aid over-all ventilation by increasing pulmonary compliance (39). A variety of agents were given including penicillin, gantrisin®, tetracycline, chlortetracycline, oxytetracycline, streptomycin, and erythromycin.

Steroid therapy

ACTH and cortisone have been shown to be effective in the management of acute attacks of asthma and status asthmaticus, and in controlling attacks of asthma in patients who do not respond to bronchodilator drugs, expectorants, antihistamines and sedation (38, 62). They have also been tried by other workers in the therapy of carbon dioxide narcosis (13, 61). ACTH, cortisone or intravenous hydrocortisone were used in most of the patients in this series. In some of the patients early in this series, steroids were started when the patient was terminal and no beneficial effect could have been expected.

The presence of congestive heart failure, or the possibility that it may develop, does not contraindicate the employment of steroid therapy provided dietary salt restriction is adequate. If tuberculosis is suspected or if the diagnosis has been established, antituberculous therapy can be given along with steroid therapy.

The exact mechanism by which ACTH, cortisone or hydrocortisone are effective in the comatose patient with carbon dioxide retention is not known. They probably decrease the inflammatory and allergic process in the bronchial mucosa and reduce bronchial secretion, mucosal edema and bronchospasm.

Treatment of heart failure

Case 25 provides a good example of the effect of heart failure on pulmonary function. The striking feature in this case was the reversibility of the long-standing anoxia and hypercapnia which the patient demonstrated on admission to the hospital. The change was believed to be the result of correcting the heart failure. Cournand and associates have stressed the effectiveness of anticongestive therapy, particularly digitalis compounds, in certain patients with cor pulmonale and heart failure (26, 28, 29).

Dietary salt restriction, particularly with steroid therapy, was important and in several patients a diet containing approximately 150 mgm. of sodium was used during severe failure. Various types of digitalis preparations have been tried and have been effective in right-sided heart failure with cor pulmonale (26). Diamox is particularly effective as a diuretic in heart failure associated with cor pulmonale and a high plasma bicarbonate (57). Venesection may be helpful in decreasing the blood volume and blood viscosity. Lastly, but most important, relief of the marked anoxia is a part of the therapy of heart failure due to cor pulmonale. Maintaining the patient in a chair rather than a bed has been useful in the treatment of congestive failure in some of our cases of cor pulmonale. Treatment for heart failure should be diligently continued though the immediate response is disappointing, because such patients often respond very slowly to therapy.

Mechanical respirators

Recent papers on carbon dioxide narcosis mention that the employment of mechanical respirators is theoretically helpful, but practically difficult to manage (13, 79). In our experience the mechanical respirator has been most helpful in treating the patient with carbon dioxide narcosis. Some type of respirator was used on the last 12 patients reported in this series. In several patients a respirator was not successful in preventing the patient's death. Three types of respirators were used: 1) an intermittent positive pressure breathing valve (Bennett); 2) the Drinker tank respirator; and 3) a positive-negative automatic resuscitator (Seeler).

The Bennett respirator was used on two patients in this series. This respirator allowed the semicomatose patient to control the pattern and rate of breathing. The effectiveness of intermittent positive pressure breathing in improving intrapulmonary gas mixing and faulty distribution of air has been demonstrated (68). Case 18 is an example which confirms the experience of others (68). The intermittent positive pressure breathing valve is most useful in patients with carbon dioxide intoxication who are semi-stuporous and resist an automatic respirator. The patient's breathing cycles the respirator and it simply increases the tidal volume. In patients with frank narcosis, the automatic respirators are more effective in relieving hypercapnia than is intermittent positive pressure breathing.

Four patients were placed in a tank respirator. A tracheotomy was done in addition in three of those cases. Several reports have related good results with

this kind of management of patients with carbon dioxide narcosis (7, 34, 37). Other authors state that the use of respirators has been unsuccessful (13, 61, 79). Three of the four patients with deep carbon dioxide narcosis recovered with a gradual fall in the arterial blood pCO_2 and rise in the pH while maintained in a tank respirator and on tracheal or nasal oxygen. One patient (case 22), although comatose and with depressed respirations, attempted to resist mechanical breathing. Demerol was given to depress the patient's ineffective respiratory effort. The respirator then was effective in lowering the arterial blood pCO_2. The authors have seen in consultation one additional case in which the combination of morphine and a Drinker respirator was successfully used under similar circumstances. The success of respirator therapy in most cases of carbon dioxide narcosis is dependent upon the fact that depression of the central nervous system far outlasts relief of hypercapnia in most of these patients (e.g., case 15). Consequently, use of the respirator can be continued without resistance from the patient until adjuvant therapy has had time to begin correcting the factors which precipitated narcosis.

The Seeler positive-negative automatic resuscitator (32, 49, 59) was used on five patients. Its effectiveness in increasing the alveolar ventilation and correcting the acidosis and hypercapnia was shown by cases 18, 19, and 20 (Tables 8 and 9). This type of respirator allowed free access to the patient for nursing care and diagnostic and therapeutic procedures. It was automatic and allowed changes in flow rate, in positive pressure on inspiration, and in negative pressure on expiration, to meet the needs of the patient. In patients with a high respiratory resistance, the use of negative pressure is relatively ineffective. The Seeler resuscitator has a considerable advantage, however, in allowing control of the rate at which gas is delivered to the patient's lung. With this adjustment it is possible to obtain a much slower flow rate than is delivered by the intermittent positive pressure devices now on the market. Delivery at a slow flow rate permits more even gas distribution throughout the lung of a patient with high respiratory resistance than is the case when the gas is delivered rapidly (40). In addition, when airway resistance is high, a greater tidal volume will be achieved for a given cycling pressure when gas is delivered slowly than when it is delivered rapidly (32). On the other hand, the maximum flow rate which the Seeler resuscitator can provide is not great enough to permit its comfortable use in many patients who are conscious.

The patient with carbon dioxide narcosis, who is comatose with shallow breathing, presents the problem of preventing death until the basic process initiating the narcosis can be corrected. The use of respirators and the various procedures to clear the airways are designed to relieve the carbon dioxide intoxication until antibiotic therapy, steroid therapy, or anticongestive measures can be effective in correcting the precipitating factor. The patient, therefore, presents a problem both in acute life-saving management and in long term corrective and preventive management.

SUMMARY

It is now recognized that carbon dioxide intoxication can occur in persons with disorders that greatly reduce alveolar ventilation. The symptoms and findings in this condition may vary in character and severity, but severe respiratory acidosis can result in coma, respiratory depression, circulatory failure and death. The clinical syndrome of carbon dioxide intoxication, as reviewed in 25 patients, is primarily a neurological and circulatory disorder.

Headache, somnolence, intermittent mental confusion, weakness, lassitude and irritability may be the only manifestations of carbon dioxide intoxication. With more severe carbon dioxide narcosis, as exemplified by most of the patients in this report, varying degrees of unconsciousness are present. Respiratory depression, hyporeflexia, flaccid immobility, pupillary changes, tremors, and convulsion frequently accompany the semicomatose and comatose states. In general, no significant abnormalities in mental state were noted if the arterial blood pCO_2 was less than 90 mm. Hg and the pH was above 7.25. On the other hand, a semicomatose or comatose state was always observed if the arterial blood pCO_2 was above 130 mm. Hg and the pH was below 7.14. During recovery from prolonged carbon dioxide narcosis, coma persisted even after the carbon dioxide tension in the arterial blood had been lowered to levels not ordinarily associated with alterations of consciousness.

Circulatory changes observed with carbon dioxide intoxication are a warm flushed skin, sweating, tachycardia and alterations in blood pressure. In our experience, severe hypotension was frequently associated with carbon dioxide narcosis.

In this study, carbon dioxide intoxication was usually observed in patients with chronic lung disease. Marked impairment of alveolar ventilation was usually precipitated by one of the following more acute processes: 1) mechanical impairment of ventilation with pulmonary or bronchial infection, asthma, lung collapse or chest surgery; 2) hypoventilation associated with heart failure; 3) depression of respiration with drugs; and 4) elimination of hypoxia as a stimulus to breathing by the use of high concentrations of oxygen. In addition, increased susceptibility to a given level of hypercapnia and acidosis apparently accounted for some episodes of carbon dioxide narcosis. Examples of this syndrome have also been noted in patients without chronic lung disease, but with illnesses which embarrassed alveolar ventilation.

Although ideally carbon dioxide intoxication should be prevented, attempts to do this are not always successful, or the patient is seen after carbon dioxide narcosis is severe. Twenty-three of the 25 patients composing this study were comatose on one or more occasions. Therapy in the first 13 patients seen consisted of bronchodilator drugs, bronchoscopic drainage, expectorants, antibiotics and nasal oxygen. Steroids and therapy for heart failure were used in several of those patients. In the last 12 patients more intensive use was made of these measures, which operate primarily by correcting the acute process which precipitated the carbon dioxide narcosis. Unfortunately the comatose patient with respira-

tory depression and shock may die before they can be effective. It has been demonstrated in this group of patients that mechanical respirators can effectively lower the arterial blood carbon dioxide tension. It is believed that the mechanical aids to breathing were life-saving by allowing time for the specific measures to correct the factors which precipitated the severe carbon dioxide retention.

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