Respiratory Failure in Pulmonary Tuberculosis*

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Of 852 patients admitted to Cook County Hospital with bacteriologically-proved pulmonary tuberculosis, 16 suffered respiratory failure. Of these 16, 5 died and 11 recovered. On follow-up, the survivors demonstrated significant improvement in oxygenation, but continued to show a severe restrictive ventilatory defect. Our patients, unlike those in previous reports, did not show airway obstruction. The principles of management are the same as for other pulmonary patients. Arterial blood gas analyses should be done on patients with advanced tuberculosis so that abnormalities of gas exchange will not be missed.

Pulmonary tuberculosis is not usually associated with respiratory failure. There are reports of respiratory failure in miliary tuberculosis,¹ ² but there is little information on the more common fibrocavitary pulmonary tuberculosis where arterial blood gas levels have been thought to be near normal because of the concomitant impairment of ventilation and perfusion.³ We report 16 sputum-positive patients with pulmonary tuberculosis who were in respiratory failure.

PATIENTS AND METHODS

From July, 1973 to December, 1975, 852 patients with sputum-positive pulmonary tuberculosis were seen at Cook County Hospital. Sixteen were found to have respiratory failure, each of whom had acid-fast bacilli demonstrated in their sputum smear and a subsequent sputum culture positive for Mycobacterium tuberculosis. A diagnosis of respiratory failure was made after the determination of arterial PaO₂ (PaO₂) level of less than 50 mm Hg, with or without elevation of arterial PCO₂ (PaCO₂) on admission. Other medical problems in these patients consisted of alcoholism, mild-to-moderate liver disease, malnutrition, and anemia (Table 1).

Pulmonary function tests included spirometry, lung volumes by helium dilution, single-breath carbon monoxide diffusing capacity (Dco), and arterial blood gas analyses by standard techniques.⁴–⁷

Antituberculosis chemotherapy was administered to all patients on admission. Patients undergoing repeated treatment received two drugs not used in the past. The management of respiratory failure consisted of oxygen therapy in all 16 patients with mechanical ventilation in 10 (Bennett MA-1 respirator in 7 patients and Emerson Postoperative in 3 patients). Oxygen therapy was given by nasal cannula or by mask when patients were not on mechanical ventilation.

RESULTS

Clinical and laboratory characteristics including admission arterial blood gas levels are presented in Table 1. Age and sex distribution of these patients during the same period showed no statistically significant difference.

Eleven of the 16 patients survived their respiratory failure. All patients responded to oxygen therapy, and after a median of 50 days of hospitalization, the average PaO₂ breathing room air was 77 mm Hg, with a range of 65 to 83 mm Hg in the survivors (Fig 1). At the end of a mean of 137 days of follow-up (range 5 to 681 days), the median PaO₂ on room air was 71 mm Hg, compared with 44 mm Hg on admission. The follow-up PaCO₂ ranged from 21 to 53 mm Hg.

Pulmonary function tests were performed in five patients. At the end of a mean of nine months, these five patients demonstrated a severe restrictive ventilatory defect with reduced forced vital capacity (FVC) (mean 40 percent of predicted), total lung capacity (TLC) (mean 53 percent of predicted) and diffusing capacity (Dco) (mean 52 percent of predicted, Table 2). There was little evidence of obstruction in the group over all, with the mean FEV₁/FVC 76 percent; mild obstruction was present in patient 7 (Table 2) with an FEV₁/FVC of 67 percent.

RESPIRATORY FAILURE IN PULMONARY TUBERCULOSIS 805
Table 1—Clinical and Laboratory Data in Patients with Tuberculosis and Acute Respiratory Failure

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>PPD</th>
<th>Treatment status</th>
<th>Extent</th>
<th>Chemotherapy</th>
<th>Admission Blood Gases</th>
<th>Hospital Stay (days)</th>
<th>Associated Problems</th>
</tr>
</thead>
<tbody>
<tr>
<td>1*</td>
<td>50</td>
<td>M</td>
<td>U</td>
<td>I</td>
<td>FA</td>
<td>INH,RIF,EMB</td>
<td>pH 7.50, PaO2 40</td>
<td>2</td>
<td>Alcoholism</td>
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<tr>
<td>2*</td>
<td>28</td>
<td>F</td>
<td>P</td>
<td>R</td>
<td>FA</td>
<td>INH,RIF,EMB,PZA</td>
<td>pH 7.38, PaO2 40</td>
<td>36</td>
<td>Anemia, alcoholism, arrhythmias, azotemia, electrolyte abnormality</td>
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<tr>
<td>3</td>
<td>27</td>
<td>M</td>
<td>N</td>
<td>I</td>
<td>FA</td>
<td>INH,EMB,RIF</td>
<td>pH 7.37, PaO2 46</td>
<td>10</td>
<td>Anemia, liver disease, alcoholism, hemoptysis</td>
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<tr>
<td>4</td>
<td>29</td>
<td>M</td>
<td>P</td>
<td>R</td>
<td>FA</td>
<td>INH,EMB,RIF</td>
<td>pH 7.32, PaO2 45</td>
<td>9</td>
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<tr>
<td>5</td>
<td>55</td>
<td>M</td>
<td>P</td>
<td>R</td>
<td>FA</td>
<td>INH,RIF,VM,PZA</td>
<td>pH 7.51, PaO2 49</td>
<td>20</td>
<td>Anemia, liver disease, alcoholism, arrhythmias</td>
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<tr>
<td>6*</td>
<td>51</td>
<td>M</td>
<td>P</td>
<td>R</td>
<td>FA</td>
<td>INH,RIF,EMB</td>
<td>pH 7.22, PaO2 59</td>
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<td>7</td>
<td>28</td>
<td>F</td>
<td>P</td>
<td>R</td>
<td>FA</td>
<td>INH,EMB,RIF,SM</td>
<td>pH 7.56, PaO2 49</td>
<td>71</td>
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<tr>
<td>8</td>
<td>57</td>
<td>M</td>
<td>P</td>
<td>R</td>
<td>FA</td>
<td>INH,EMB,RIF</td>
<td>pH 7.51, PaO2 49</td>
<td>58</td>
<td>G-I bleeding, anemia, liver disease</td>
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<tr>
<td>9*</td>
<td>49</td>
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<td>P</td>
<td>R</td>
<td>FA</td>
<td>INH,EMB,RIF</td>
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<tr>
<td>10</td>
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<td>M</td>
<td>P</td>
<td>I</td>
<td>FA</td>
<td>INH,EMB,SM</td>
<td>pH 7.52, PaO2 45</td>
<td>86</td>
<td>Paraplegia, liver disease, alcoholism, anemia</td>
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<tr>
<td>11</td>
<td>48</td>
<td>M</td>
<td>N</td>
<td>I</td>
<td>FA</td>
<td>INH,EMB,RIF</td>
<td>pH 7.39, PaO2 45</td>
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<td>N</td>
<td>I</td>
<td>MA</td>
<td>INH,EMB,SM</td>
<td>pH 7.28, PaO2 47</td>
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<td>Anemia, liver disease, alcoholism, anemia</td>
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<tr>
<td>13</td>
<td>57</td>
<td>M</td>
<td>N</td>
<td>I</td>
<td>FA</td>
<td>INH,EMB,SM</td>
<td>pH 7.47, PaO2 47</td>
<td>56</td>
<td>Anemia, liver disease, alcoholism, anemia</td>
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<tr>
<td>14*</td>
<td>52</td>
<td>M</td>
<td>U</td>
<td>R</td>
<td>FA</td>
<td>INH,RIF,EMB</td>
<td>pH 7.25, PaO2 42</td>
<td>2</td>
<td>Anemia, liver disease, alcoholism, anemia</td>
</tr>
<tr>
<td>15</td>
<td>38</td>
<td>M</td>
<td>P</td>
<td>R</td>
<td>FA</td>
<td>INH,RIF,EMB</td>
<td>pH 7.37, PaO2 38</td>
<td>20</td>
<td>Psychosis, anemia, liver disease, alcoholism</td>
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<tr>
<td>16</td>
<td>41</td>
<td>F</td>
<td>P</td>
<td>R</td>
<td>FA</td>
<td>INH,RIF,EMB,SM</td>
<td>pH 7.35, PaO2 38</td>
<td>14</td>
<td>Alcoholism, liver disease, alcoholism, heroin addiction</td>
</tr>
</tbody>
</table>

*Patient expired; PPD = purified protein derivative; P = positive; N = negative; U = unknown; I = initial; R = retreatment; FA = far-advanced; MA = moderately advanced; INH = isoniazid; RIF = rifampin; EMB = ethambutol; PZA = pyrazinamide; VM = viomycin; SM = streptomycin; PaO2 = arterial O2 tension; PaCO2 = arterial CO2 tension; HCO3 = bicarbonate.

SERIAL ARTERIAL PO2 DETERMINATIONS

Figure 1. Serial arterial O2 tension (PaO2) determinations in each of 16 patients. In survivors, the need for assisted ventilation and supplemental oxygen decreased due to progressive improvement in gas exchange.

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**Table 2—Follow-up Pulmonary Function Tests**

<table>
<thead>
<tr>
<th>Months after recovery</th>
<th>Patients</th>
<th>FEV₁/ FVC, %</th>
<th>TLC (range)</th>
<th>Dco (range)</th>
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</thead>
<tbody>
<tr>
<td>2</td>
<td>1 1/2 months</td>
<td>19</td>
<td>87</td>
<td>22</td>
</tr>
<tr>
<td>3</td>
<td>11 months</td>
<td>72</td>
<td>81</td>
<td>68</td>
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<td>9 months</td>
<td>22</td>
<td>74</td>
<td>52</td>
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<td>7</td>
<td>8 months</td>
<td>39</td>
<td>74</td>
<td>48</td>
</tr>
<tr>
<td>12</td>
<td>1 1/2 months</td>
<td>54</td>
<td>76</td>
<td>57</td>
</tr>
<tr>
<td>Mean* (range)</td>
<td>9</td>
<td>40</td>
<td>76</td>
<td>53</td>
</tr>
</tbody>
</table>

FVC = forced vital capacity; FEV₁ = forced expiratory volume in 1 second; TLC = total lung capacity; Dco = single breath CO diffusing capacity. *In calculation of mean values, only 22-month data of patient 7 were used.

**DISCUSSION**

Before the beginning of this decade, when the treatment of pulmonary tuberculosis began to shift from sanitoriums to general hospitals, many problems, including respiratory failure, may have gone unrecognized. Homan et al., in 1975 reported a patient with miliary tuberculosis in acute respiratory failure. She was unsuccessfully treated using an extracorporeal membrane oxygenator, and a diagnosis of miliary tuberculosis was made at autopsy; no antituberculosis chemotherapy was given.

Bromberg and Robin³ have reviewed a number of papers on the pulmonary function abnormalities in pulmonary tuberculosis. There is no information in the literature on the occurrence of respiratory failure in nonmiliary pulmonary tuberculosis. It has been concluded that arterial blood gas values are near normal in patients with pulmonary tuberculosis because of concomitant impairment of ventilation and perfusion and the maintenance of normal ventilation-to-perfusion relationships.³ The concept of normal ventilation-perfusion relationships is based upon several angiographic and histologic studies.³,⁴ which report parallel involvement of lung parenchyma and vasculature in pulmonary tuberculosis. While such a relationship may exist in most patients with pulmonary tuberculosis, those in the present study exhibited severe hypercarbia on admission. Nine of the 16 patients showed improvement in oxygenation and recovered from respiratory failure, even before roentgenographic improvement was noted. Concomitant suppurative pulmonary disease was unlikely, because serial blood and sputum cultures were negative for nontuberculous microorganisms.

Williams et al.,¹⁰ have demonstrated the usefulness of the Dco in assessing the extent of involvement in acute nonmiliary pulmonary tuberculosis.

The Dco correlated better with the extent of pathologic involvement than did either the vital capacity or roentgenographic appearance. In the present study, the initial diffusing capacity studies in three patients showed severe impairment (11 to 30 percent of predicted) (Table 2). In one patient, the Dco was repeated after 12- and 22-month intervals and showed marked improvement.

In 12 of the 16 patients, significant hypercarbia ranging from 45 to 72 mm Hg occurred at some time during the course of their hospitalization. There was improvement in alveolar ventilation, as indicated by decreases in PaCO₂ among the patients who recovered from respiratory failure. In four of the five patients who died, death was due to progressive respiratory failure despite chemotherapy and mechanical ventilation with high inspired oxygen concentrations. None of the associated conditions was thought to account for the respiratory failure.

The lack of airflow obstruction in the surviving 11 patients was a surprise because several studies¹¹,¹² have indicated that it is a common complication of pulmonary tuberculosis. Gaensler and Lindgren¹¹ found airflow obstruction in 61 percent of tuberculous patients referred for respiratory symptoms and in 43 percent of tuberculous patients studied as part of a preoperative assessment. Many patients at the time of discharge from a tuberculosis sanatorium¹² demonstrated airway obstruction. We are unable to explain our findings; to speculate that more complete resolution of pulmonary tuberculosis may have occurred with use of current antituberculosis drugs does not appear to follow, in view of the severe residual restriction in our surviving patients.

The following two patients are presented in detail to demonstrate the pathophysiology of respiratory failure in pulmonary tuberculosis and to document the potential for recovery.

**CASE REPORTS**

**Case 1**

A 50-year-old man was admitted to the hospital with a three-week history of weakness, a cough productive of yellow sputum, chest pain and loss of appetite. He had lost approximately 40 pounds in weight, but denied having had fever, hemoptysis or a history of tuberculosis. The patient had smoked cigarettes and drunk alcohol excessively for many years. Physical examination revealed a malnourished man with a respiratory rate of 28/min, pulse 104/min and blood pressure 110/70 mm Hg. Auscultation of the chest revealed bilateral coarse crepitations, with scattered rhonchi. Examinations of the heart, abdomen and nervous system were unremarkable. Chest roentgenogram demonstrated extensive bilateral infiltrates, with multiple cavities. Arterial blood gas studies on room air at the time of admission to the hospital...

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revealed PaO₂ 40 mm Hg, PaCO₂ 32 mm Hg, pH 7.50 and a HCO₃⁻ of 24.5 mEq/L. Ziehl-Neelsen stain of his sputum showed acid-fast bacilli, and the culture subsequently grew *M tuberculosis*.

The patient was given oxygen therapy by mask and antituberculosis therapy consisted of isoniazid, ethambutol and rifampin. Because of progressive hypoxemia and the development of hypercarbia and respiratory acidosis, PaCO₂ rose to 51 mm Hg and pH decreased to 7.16. Intubation was instituted and the patient was placed on a Bennett MA-1 respirator. He required a high (80 percent) inspiratory O₂ concentration and a positive end-expiratory pressure (PEEP) of 10 cm was added. He died after a hospital stay of only 44 hours.

**Figure 2.** The lungs of patient 1 at autopsy, showing extensive bilateral consolidation with cavitations.

**Figure 3.** Admission chest roentgenogram of case 7 showing extensive bilateral cavitary disease.

At autopsy, gross examination of the lungs revealed extensive bilateral consolidation with cavitations (Fig 2). Microscopic examination demonstrated areas of exudation, infiltration with leukocytes and numerous acid-fast organisms, consistent with a diagnosis of tuberculous pneumonia.

The pathologic findings easily explain the patient's progressive respiratory failure. The marked disruption of pulmonary architecture and tuberculous pneumonia account for the hypoxemia with severe mismatches of ventilation and perfusion. The extensive consolidation and exudation with a resultant decrease in compliance and increase in the work of breathing likely caused alveolar hypoventilation in this emaciated man.

**Case 7**

A 28-year-old woman was admitted to the hospital with a two-year history of fever, cough productive of yellowish sputum, weight loss, anorexia and progressive shortness of breath. She had been found to have pulmonary tuberculosis two years before, but took antituberculosis drugs irregularly. She was febrile (38.3°C [101.0°F]), her pulse rate was 110/min and blood pressure 90/60 mm Hg. Auscultation of her chest revealed bilateral crepitations with decreased breath sounds at the right apex. Chest roentgenogram showed bilateral extensive infiltrates, with cavities (Fig 3). Arterial blood gas studies on room air at admission revealed: PaO₂ 49 mm Hg and PaCO₂ of 28 mm Hg. Sputum smear revealed acid-fast bacilli and subsequent cultures were positive for *M tuberculosis*. The patient was started on oxygen therapy by mask. Antituberculosis drugs consisting of isoniazid, ethambutol, rifampin and streptomycin were started. Results of the cerebrospinal fluid examination were normal. Tuberculin skin test of 5TU showed a reaction of 15 mm. Since the drug sensitivity study later showed that organisms were sensitive to all the drugs in her regimen, streptomycin was discontinued.

Because of further deterioration of blood gases (PaO₂ 40 mm Hg) and increasing respiratory difficulty, intubation was
initiated and she was placed on a Bennett MA-1 respirator. After use of the respirator for 4 days and oxygen therapy for a total of 50 days, she was discharged from the hospital, at which time arterial blood gas analysis on room air showed PaO₂ 62 mm Hg and PaCO₂ 33 mm Hg. Progressive clinical, bacteriologic and roentgenographic improvement followed, and her chest roentgenogram a year later is shown in Figure 4.

Pulmonary function tests were performed at 8, 12 and 22-month intervals. The FEV₁/FVC showed slight deterioration from 74 percent to 67 percent. There was improvement in predicted TLC from 48 percent to 68 percent and Dco from 11 percent to 69 percent. The PaO₂ increased from 62 mm Hg to 80 mm Hg.

REFERENCES
7 Gaensler EA, Wright GW: Evaluation of respiratory impairment. Arch Envr Health 12:146-189, 1966