other two (patients 3 and 4) had severe initial insults to the lung and were supported for 45 and 39 days, respectively. Both of these latter two patients were being effectively oxygenated on a concentration of inspired oxygen (FiO₂) of 0.4 or less after ten days, but attempts to discontinue positive end-expiratory pressure (PEEP) resulted in clinical deterioration and recurrent hypoxia. This deterioration was documented by bedside determinations of functional respiratory capacity (FRC) (helium dilution) and static compliance (ambubag and pneumotachograph interfaced to pressure and volume channels of Electronics for Medicine recorder). Only after the addition of prednisone in initial doses of 80 to 100 mg daily did the FRC increase and compliance improve in both of these patients. On six-month follow-up studies, both have residual restrictive lung disease, but neither is now dependent on continuous oxygen.

We believe that early recognition or ARDS, the use of PEEP, careful monitoring of cardiopulmonary function and expectant management of fluids, electrolytes and clotting abnormalities is the most effective way in which to reduce the morbidity and mortality of this severe clinical-pathologic syndrome.

REFERENCES

Functional Effects of Influenza Pneumonia*

Arno F. Fretheimer, M.D.; Stuart M. Brooks, M.D.; Robert G. Loudon, M.B., Ch.B.; Donald B. May, B.S.; and Harold P. Settle, Jr., M.D.

During the months of January and February 1973 an influenza epidemic occurred in Cincinnati, Ohio. Nine patients were admitted to the hospital with the adult respiratory distress syndrome and met the following criteria: (1) the influenza virus A₂, England 42/72 was cultured from sputum and/or at autopsy from the lung; (2) all had an acute febrile respiratory illness; (3) admission chest x-ray films revealed diffuse alveolar infiltrates; and (4) severe hypoxemia was present in all of the patients at the time of admission. The patients ranged in age from 10 to 81 years. All decades from 10 to 80 were represented, and the prevalence of the in-

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INFLUENZAL PNEUMONIA

ADMISSION ARTERIAL BLOOD GASES

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**Figure 1**

Influenza pneumonia was not a matter of extremes of age. There were five females and four males in this series.

All of the patients developed symptoms within the week prior to admission. All complained of difficulty in breathing associated with a usually nonproductive cough. Fever was documented in all at the time of admission to the hospital. Some had chills, myalgia, and pleuritic chest pain.

In our series of patients five had underlying medical conditions: obesity, diabetes, coronary artery disease, prostatic carcinoma and recent renal transplantation.

The chest x-ray films at admission typically showed alveolar infiltrates. White blood cell counts in all of the patients except one were in the range of 5,000 to 15,000 cu mm. The exception occurred in the patient with a white blood cell count of 21,000 cu mm. The differential counts were not helpful.

Admission arterial blood gas levels (see Diagram 1) in all cases revealed severe hypoxemia. Some of the values and all of those above a PaO₂ of 50 were obtained while the patients were receiving oxygen therapy. Three patients had carbon dioxide retention on admission. None of these patients was known or thought to have prior pulmonary disease. Subsequent blood gas levels did not show hypercapnea in any patient. Only the patient with the renal transplant had a significant metabolic problem. Other patients had a mild metabolic acidosis possibly on the basis of hypoxemia and severe muscular exertion secondary to the tremendous work of breathing.

Serum enzyme derangement has been reported in influenzal pneumonia. In all our cases the serum lactic dehydrogenase (LDH) value was elevated, and the serum glutamic oxaloacetic transaminase (SGOT) level was elevated in seven of the nine patients. The severity of enzyme derangements was not a prognostic factor.

Therapy was directed toward adequate oxygenation and supportive measures (Diagram 2). Five patients required assisted ventilation. Four of those required high concentrations of inspired oxygen (FiO₂) to keep the PaO₂ above 60 mm Hg. When excessive FiO₂ was encountered the patient was then placed on continuous positive-pressure ventilation. This technique enabled adequate oxygenation of all patients, keeping the FiO₂ below 50 percent. Using continuous positive-pressure ventilation on four patients, we encountered no adverse effects. Despite the correction of the pulmonary gas exchange, five patients died. The outcome of illness in the patients who died could not have been predicted from the ability to correct the pulmonary gas exchange. At the time the patients died they were all improving as manifested by a continued reduction in FiO₂ necessary for adequate oxygenation, reduction in the need for continuous positive-pressure ventilation, and lower peak pressure for ventilation.

The cause of death in the patient with renal transplantation was determined at autopsy. He had suffered an acute myocardial infarction of the papillary muscles on the left ventricle. The kidney had been totally rejected. The massively obese woman had been successfully treated for her influenzal pneumonia. She required a tracheostomy and continued positive-pressure ventilation for seven days. Her death occurred on the 16th day, 4 days after assisted ventilation had been discontinued. The death was a result of dislodgment of the tracheostomy tube. The third death occurred in an 81-year-old man. He died within 48 hours after hospitalization, secondary to a cardiac arrest. The last two deaths occurred in women ages 45 and 50. Both died within four days of hospitalization. Each required a tracheostomy and continuous positive-pressure ventilation, dying while in this mode of therapy. The pulmonary gas exchange disturbances were corrected despite serial chest x-ray films showing increasing severity of the pulmonary edema pattern. At the time of death arterial PaO₂ was above 60 mm Hg and both had mild hypercapnea. These two patients developed irreversible peripheral vascular collapse.

The autopsy data available for three of the five cases describe the usual pathologic findings in primary viral pneumonia. Grossly, the lungs were edematous with hemorrhagic areas. The microscopic sections were consistent with a hemorrhagic necrotizing pneumonia involving a large proportion of the lungs.

In conclusion, influenzal pneumonia is indeed a severe acute lung injury and, fortunately, strikes only a few persons during an epidemic. The pulmonary gas disturbances were corrected in all our patients, and those who died did so for reasons other than respiratory failure. All ages were represented. The disturbances in enzymes were quite marked in many patients but were not of prognostic value. Positive end expiratory pressure ventilation allowed the use of lower FiO₂ reducing another factor that causes acute lung injury. And finally, predisposing factors were not all that important in determining the existence or outcome of the influenzal pneumonia.