Hamman-Rich Syndrome
(Diffuse Interstitial Pulmonary Fibrosis)

ROBERT B. WHITE, M.D., F.C.C.P.*
Aurora, Illinois

JOHN T. CRAIGHEAD, LT., MC, USN**
Oakland, California

In 1935, Hamman and Rich1 of Johns Hopkins first described a syndrome which they had observed in three patients, characterized by a gradual onset of cough, dyspnea, and cyanosis; and in whose lungs pathologic studies revealed a diffuse interstitial fibrosis, involving the interalveolar septa in particular. In the discussion they emphasized that the causative factors and associated findings commonly seen in the recognized type of pulmonary fibrosis were not found and, indeed, that this was a new entity of unknown etiology.

Since the appearance of their original paper2-7 and following the appearance of a stimulating editorial in the Journal of the American Medical Association in 1953,8 approximately 46 additional cases have been reported, of whom 20 have not had all the clinical and pathologic manifestations. An additional case is presented here which conforms to the classical description by Hamman and Rich but in which additional findings of an unusual nature were encountered.

A. L. (USNH OP2169): This 42 year old white woman was admitted to the United States Naval Hospital, Oakland, California, on January 15, 1964, with a history of chronic, productive cough, progressive dyspnea, weight loss, recurrent episodes of spontaneous pneumothorax, and increasing cyanosis of 13 months' duration. She stated she had been in robust health until 18 months prior to admission, at which time it became evident to her that while she had been athletic in the past, she was experiencing for the first time increasing exertional dyspnea. A pre-employment x-ray film taken one year prior to admission was reported as showing "fibrosis of the lungs" (Figure 1). For the six months prior to admission she became dyspneic even when crossing the kitchen. She recalled that the cough was insidious in onset and was interpreted as "smoker's cough." During this same period she had frequent colds with slight elevations of temperature. Penicillin, streptomycin, terramycin, and combinations of these were used at various times to control a nonproductive cough. The symptoms, however, were not appreciably altered. Careful questioning concerning the inhalation of dusts, etc. in her occupation, environment, and housework failed to elicit any of the agents commonly responsible for pulmonary fibrosis.

Her past and family history were noncontributory.

A bedridden, thin, cyanotic woman, both acutely and chronically ill, weighing 86 pounds, and standing 62 inches. Temperature and pulse were within the limits of normal; respirations, 22 per minute. Blood pressure was 120/80 millimeters of mercury. A few, scattered, fine, moist rales were heard in the lung bases. The vital capacity was 0.7 liters. There was no evidence of clubbing or skin manifestations. The remainder of the physical examination was within normal limits.

†From the Medical Service, United States Naval Hospital, Oakland, with the approval of the Commanding Officer. The opinions or assertions contained herein are the private ones of the authors and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large.

*436 Gladstone Avenue, Aurora, Illinois (formerly on the staff at the United States Naval Hospital, Oakland).

**Resident in Internal Medicine, United States Naval Hospital, Oakland.
Figure 1: A routine pre-employment roentgenogram taken one year prior to hospitalization showing a diffuse, reticular pattern throughout both lung fields. **Impression:** Chronic interstitial fibrosis.

---

Figure 2: Roentgenogram, taken at the time of admission to the U. S. Naval Hospital, Oakland (one year after Figure 1), reveals left pneumothorax and pleural effusion but little significant change in the degree of interstitial fibrosis.
HAMMAN-RICH SYNDROME

The x-ray films of her chest revealed a diffuse, reticular pattern throughout both lung fields which was interpreted as representing “chronic interstitial fibrosis of unknown etiology.” The admission film showed evidence of pneumothorax and minimal pleural effusion on the left side. Comparison with earlier films showed little change. The heart size and configuration were unchanged and within normal limits (Figure 2) X-ray films of the hands were also normal.

Purified protein-derivative tuberculin skin tests both in the first and second strengths (on three occasions) were negative; coccidioidin and histoplasmin skin tests were also repeatedly negative; sputum smears and culture (10 specimens) for acid-fast bacilli and fungi were negative. One routine bacterial smear was found to contain non-hemolytic staphylococcal organisms on culture; however, repeat cultures were negative for predominant bacteria. Repeat Papanicolaou smears for malignant cells in the sputum were negative. Urinalysis and blood Kahn were negative. The white blood cell count was 8,600 with normal differential; hemoglobin, 12 grams; hematocrit, 42 volumes per cent; red blood cells, 4.1 million. The sedimentation rate ranged between 4 and 32 millimeters per hour during the period of hospitalization. The total protein, and albumin/globulin ratio, the blood CO2, and other electrolytes and two electrocardiograms were within normal limits.

A biopsy of the right paratracheal lymph node was negative. A lung biopsy studied by direct smear and culture for Coccidioides, Histoplasma, tubercle bacillus, fungi, and inclusion bodies was negative.

She remained confined to her bed throughout most of the hospital stay because of marked exertional dyspnea and, in spite of inactivity and bed rest, she experienced four additional episodes of spontaneous pneumothorax. These crises of pulmonary insufficiency necessitated emergency treatment with needle aspiration, oxygen, intercostal tube, and water-seal bottle. On February 10, 1954 left thoracotomy for parietal pleurectomy (to prevent recurrent collapse) was done. At operation a lung biopsy was obtained, and on the basis of the microscopic findings a diagnosis of Hamman-Rich syndrome was established (Figure 3). The postoperative course was not complicated. On February 23, 1954 she was started on cortisone, 100 milligrams four times daily. This dosage schedule was subsequently reduced to 37.5 milligrams per day.

The clinical course was complicated subsequently by spontaneous pneumothorax on the right and this recurred while a catheter was in the chest. On April 21, 1954 right pleurectomy was performed. Again the postoperative course was not complicated; however, two weeks following cessation of cortisone therapy she became morose, aprehensive, and cyanotic despite prolonged use of oxygen by tent. Cortisone in the dosage of 37.5 milligrams per day was again started, the need for oxygen was gradually reduced, and she rapidly improved mentally. By July 10, 1954, however, there was evidence of progressive, generalized, peripheral edema which did not respond to vigorous therapy and she expired in pulmonary insufficiency on July 15, 1954.

Autopsy observations will be limited to the heart and lungs since the remainder of the examination was not unusual. The lungs were cyanotic as was the entire body. Shaggy adhesions were observed between the lungs and chest wall except for a small apical and basal pneumothorax on the right. The lungs were of equal weight, totaling 1200 grams. On cut section they had a honeycombed appearance as the result of the many emphysematous blebs (Figure 4). Blood vessels stood out with a somewhat evertting, erectile appearance in some focal areas. The bronchi and bronchioles when opened contained a small amount of watery, viscous, reddish fluid. The lymph nodes were not unusual. The heart was of normal size, weight and configuration. The right ventricular wall measured 0.3 to 0.4 centimeters in thickness, while the left ventricle averaged 1.0 centimeters. The valves were normal.

Microscopic sections revealed marked distortion of the pulmonary architecture characterized by thickening of the alveolar walls by fibrosis; numerous scattered areas of dense interstitial fibrosis interspersed by areas of emphysema (Figure 5); and hypertrophy of smooth muscle of the bronchi and periarteriolar areas. The thickening of the alveolar walls in some areas was twice normal, whereas in others the walls were so irregularly thickened and nodular that the lumina of many adjacent alveoli were obliterated. The air sacs whose walls were not greatly involved formed blebs. In general the alveolar spaces were empty. An occasional space was filled with an eosinophilic protein material. Red blood cells were rare as were macrophages. Within and surrounding the interstitial fibrotic areas were numerous, round, inflammatory cells, most marked in the perivascular areas. In small focal areas were neutrophilic polymorphonuclear leukocytes.

DISCUSSION

This patient was unusual in that she experienced no less than six episodes of spontaneous pneumothorax during her last nine months of illness. These
Figure 3: Lung biopsy taken at the time of parietal pleurectomy revealing marked hypertrophy of the alveolar walls, capillary proliferation, interstitial fibrous reaction, and moderate round-cell infiltration in the interstitial perivascular areas.—Figure 4: Cross section of the lung showing a honeycombed appearance as the result of numerous emphysematous blebs.
collapses were subsequently shown to be the result of widespread emphysematous bleb formation. Other observers have described blebs associated with the Hamman-Rich syndrome but without pneumothorax.

Because of recurring bilateral pneumothoraces in a patient already dyspneic, a thoracotomy for parietal pleurectomy and incidental lung biopsy were carried out. At a later date this procedure was repeated on the opposite side. The autopsy demonstrated, as did the clinical course, that the pleurectomy was effective in preventing further episodes of pneumothorax. The small collapses which occurred following operation did so only in the areas where the parietal pleura was left.

At the time of operation it was most interesting to see and palpate the inflated and functioning lung. The surface of the lung was diffusely studded with small blebs, giving a cobblestone appearance. This is well illustrated in Peabody’s Case No. 3. The lung was darker than normal, congested, and beefy red. It inflated poorly and deflated slowly. Palpation revealed the increased crepitation of emphysema and the nodular solidity of bronchopneumonia. Bleeding from the biopsy site was no greater than one sees in the normal individual. The parietal pleura was thickened slightly and was hyperemic.

The use of cortisone was obviously a desperate measure which proved futile; and it seems evident that, as in the cases of Keeton et al. and Peabody et al., sudden withdrawal of the drug is an extremely hazardous procedure in any patient who has little pulmonary reserve.

Cor pulmonale, as seen in 50 per cent of the previous reports, did

![FIGURE 5: Autopsy specimen revealing distortion of alveolar architecture by interstitial fibrosis and rupture of alveolar walls resulting in the pattern of emphysema.](http://journal.publications.chestnet.org/pdfaccess.ashx?url=data/journals/chest/21290/)
not appear, and the heart size and ventricular walls were normal. There was no evidence of polycythemia reported in many of the previous cases. Thorough questioning regarding the patient's past history, as well as exhaustive laboratory and clinical study, failed to give evidence of known etiologic agents.

Last, the illness of our patient extended over a period of more than 18 months and therefore could not be classed as an acute or fulminating type of disease. Indeed, it would best be placed in the category described by Callahan et al. as chronic interstitial pulmonary fibrosis.

Acknowledgments: The authors wish to express their appreciation for the encouragement and assistance given by Captain Christopher C. Shaw, MC, USN (then Chief of the Medical Service); Doctor Gerald L. Crenshaw, Consultant in Chest Diseases at the U. S. Naval Hospital, Oakland, who was most helpful in the management of this case; and Lieutenant Commander Leonard J. Kreissl, Jr., MC, USNR, who provided the gross and microscopic diagnoses.

REFERENCES