pharyngeus muscle. The voluntary relaxation of the upper esophageal sphincter allowed the large coin to pass with minimal resistance.

According to students and tavern owners, the game "Quarters" generally results in substantial consumption of alcohol. As the players become more inebriated, they discriminate less well between liquid and solid as they rapidly drink a glass of beer. Furthermore, alcohol reduces both upper and lower esophageal resting and yield pressures.[8,9] When the patients "chug-a-lugged" their beers, a coin could tumble through a poorly responsive pharynx and through a relaxed upper esophageal sphincter to some portion of the esophagus that was sufficiently extrinsically constricted to stop further progression. Alcohol reduces esophageal peristalsis. In the two patients with esophageal impactions, there was no pathologic lesion found to explain the impactions besides the normal anatomic constrictions and the effect of alcohol.

"Quarters" remains a popular game among college students in the Pacific Northwest. The foreign body ingestions are readily treatable either by time or, if impaction is present, by flexible endoscopy. This report alerts physicians to the game and its consequences.

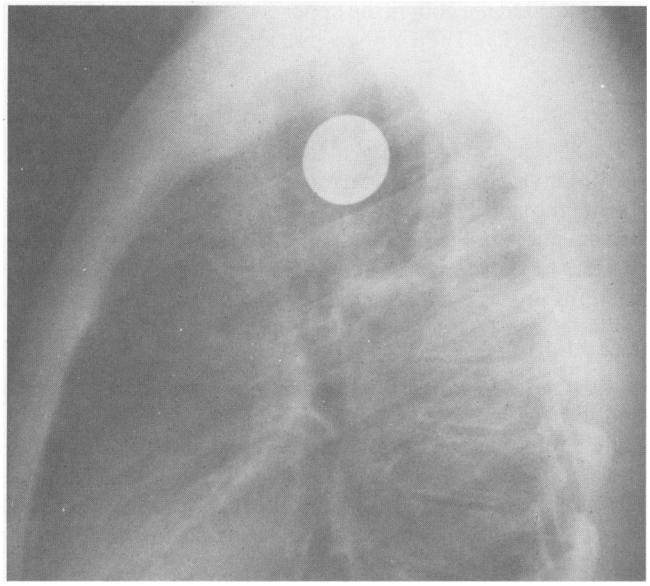

Figure 2.—In patient 2, the ingested 50-cent piece lodged at the thoracic inlet immediately above the aorta.

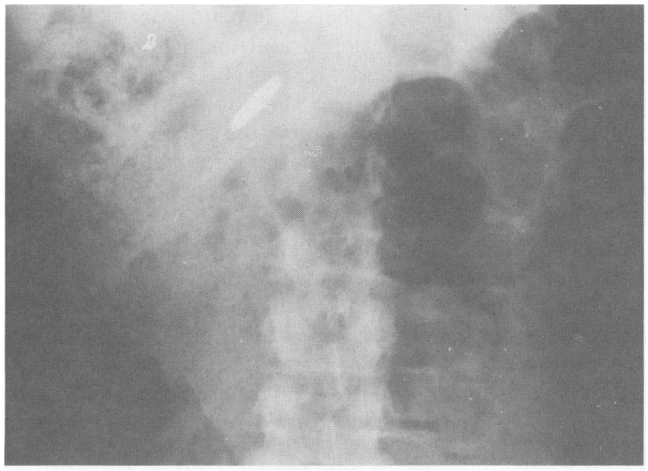

Figure 3.—A radiograph taken of patient 3 shows a quarter located in the duodenal bulb. The patient was asymptomatic and passed the coin without incident.

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Bleomycin-Induced Pulmonary Fibrosis in a Patient With Rheumatoid Arthritis

A Possible Synergistic Effect?

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BLEOMYCIN is the chemotherapeutic agent most frequently associated with pulmonary toxicity.[1-5] Previous or concomitant radiotherapy to the thorax, concomitant chemotherapy, and high inspired oxygen concentrations may enhance the toxicity of bleomycin, producing a toxic reaction at a lower total dose.[6,7] The effect is dose- and age-related,[1] and life-threatening disease is unusual at total doses of less than 150 units.[3]

We report the case of a patient with rheumatoid arthritis and stage IIIB Hodgkin's disease in whom pulmonary fibrosis developed after he received 137 units of bleomycin. This unexpected toxicity at a relatively low cumulative dose raises the possibility that the patient's rheumatoid arthritis may have made him more susceptible to bleomycin-induced pulmonary toxicity.

Report of a Case

The patient, a 51-year-old man, was admitted to Pacific Medical Center (Seattle) in April 1987 because of dyspnea and cough for three months. On examination he was afebrile. There was no finger clubbing or palpable lymphadenopathy. A chest examination revealed bilateral bibasilar crackles. He had characteristic changes of rheumatoid arthritis involving

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his hands, elbows, shoulders, and knees. Symptoms of his rheumatoid arthritis had not recently worsened. Radiographs of the hands showed subchondral erosions with cystic formation.

The patient had been diagnosed as having gout about 15 years previously on the basis of intermittent inflammatory arthritis of the knees and great toes and persistent hyperuricemia. He had been treated with courses of allopurinol and colchicine with reasonable control. In 1978 he presented with symmetric hand and wrist arthritis with morning stiffness and constitutional symptoms. The diagnosis of rheumatoid arthritis was established on the basis of the findings of a physical examination, a rheumatoid factor of 1:160, and hand x-ray films showing erosions, periarticular osteopenia, and soft tissue swelling characteristic of rheumatoid arthritis. He was treated with a gold compound for eight months and had a remission of his joint and constitutional symptoms. A rash developed at a total dose of 945 mg of gold compound, and this therapy was stopped. In March 1985 the patient again had a flare-up of his rheumatoid arthritis and received a second trial of gold therapy, with redevelopment of a rash. From March 1985 his joint symptoms were managed with ibuprofen therapy. There was no clinical evidence of pulmonary toxicity due to gold therapy or to rheumatoid arthritis.

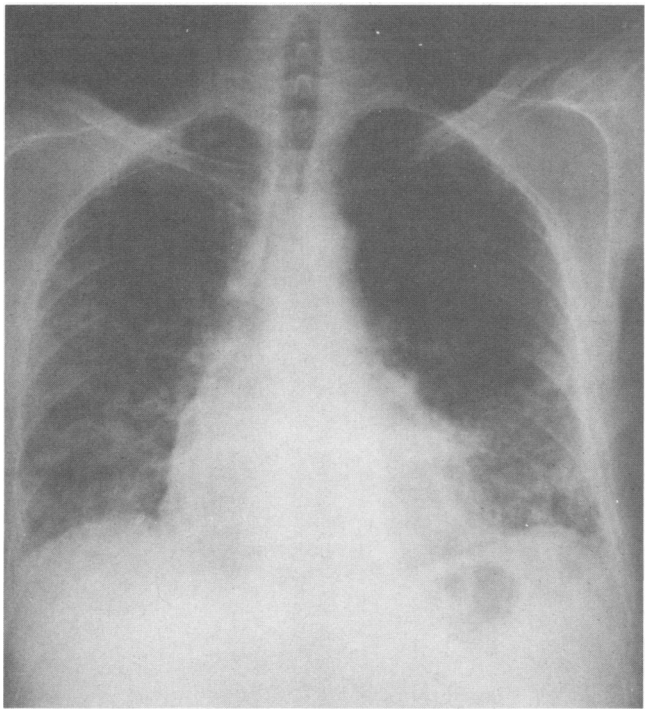

Figure 1.—A chest x-ray film taken immediately before an open-lung biopsy shows diffuse bilateral interstitial changes.

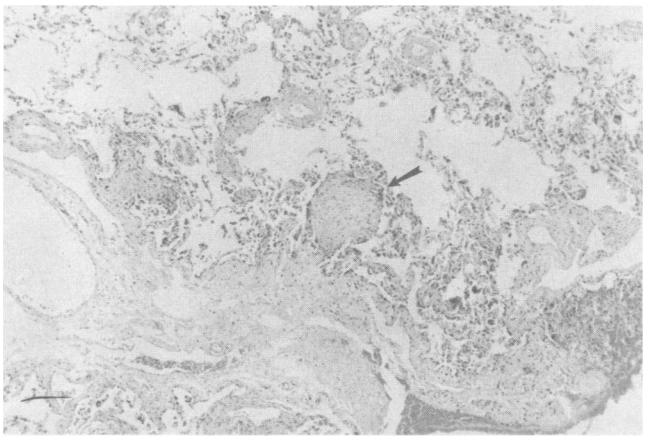

Figure 2.—The biopsy specimen of the left lower lobe of the lung shows areas of active interstitial inflammation **(arrow)** and regions of mature interstitial fibrosis. Little inflammation is present (hematoxylin-eosin, original magnification × 60.5).

The patient was diagnosed with Hodgkin's disease in 1986, nine months before this admission to hospital. He presented with cervical lymphadenopathy and was found to have involvement of the spleen and mediastinal and retroperitoneal nodes. He had been treated with eight courses of mechlorethamine hydrochloride, vincristine sulfate, procarbazine hydrochloride, prednisone, doxorubicin (Adriamycin) hydrochloride, bleomycin sulfate, and vinblastine sulfate (MOPP/ABV). He had received neither supplemental oxygen nor radiation therapy. The cumulative dose of bleomycin was 137 units.

His chest x-ray film (Figure 1) showed decreased lung volumes and abnormal lung parenchyma with diffuse interstitial changes in both lungs for the first time. A radiograph taken immediately before chemotherapy showed a normal lung volume and clear lung fields. Pulmonary function test results indicated progressive deterioration, with a moderate restrictive pattern (total lung capacity 68% of predicted) and a moderate to severe reduction in the diffusing capacity of the lungs for carbon monoxide (42% of predicted). An open-lung biopsy from the left lower lobe was done, and the specimen showed a mixture of acute and chronic changes (Figure 2). There was a background of dense interstitial fibrosis involving pleura and secondary lobular septa. Superimposed on this were nodular areas of active interstitial fibrosis involving alveolar septa, lobular septa, and small confluent areas of lung parenchyma. A few lymphocytes were scattered through the areas of fibrosis, but no eosinophils were seen and neutrophils were rarely seen. There was no evidence of vasculitis or bronchiolitis obliterans. Immunofluorescence studies for immune complexes were not done.

Bleomycin therapy was discontinued from the patient's chemotherapeutic regimen, and a regimen of 60 mg of prednisone daily was begun. The patient continued to deteriorate clinically, however, and two weeks after his open-lung biopsy, he was readmitted to hospital because of progressive dyspnea. There was no evidence of infection, and his chest x-ray film showed no new localized infiltrate. He was afebrile, he had no sputum production, and his blood cultures were negative. He died suddenly within a month of the open-lung biopsy. His death was an acute cardiopulmonary event thought to have been caused by either an arrhythmia or possibly a pulmonary embolus. No autopsy was done.

Discussion

This case shows a recognized complication of bleomycin toxicity at an unexpectedly low dose. We postulate that there may be a synergistic mechanism between rheumatoid arthritis and bleomycin therapy in the pathogenesis of pulmonary fibrosis. Immunologic mechanisms could be responsible for the unusual susceptibility to bleomycin toxicity shown by this patient. Interstitial lung disease has been estimated to occur in 20% to 40% of patients with rheumatoid arthritis. It is often both clinically and radiologically silent. Lung biopsy specimens of patients with rheumatoid arthritis

and interstitial lung disease show immunoglobulin G and complement deposition in pulmonary capillaries.[9] The mechanism is thought to be related to the production of immune complexes, either locally or systemically.

Several mechanisms of bleomycin-related pulmonary injury are suggested. Bleomycin is concentrated preferentially in the lung and is inactivated by a hydrolase enzyme that is relatively deficient in lung tissue. It is unknown whether certain persons are more deficient in this enzyme than others. A second mechanism is that bleomycin may generate reactive oxygen metabolites.[1] Third, there may be a greater influx of polymorphonuclear neutrophils in susceptible persons, thereby causing direct lung injury with their release of oxidants and proteases. Bleomycin has also been shown to affect collagen synthesis inhibitors, resulting in an increase of pulmonary collagen.[1] Finally, it has been noted that bleomycin may stimulate the humoral immune system and that diseases such as rheumatoid arthritis could be exacerbated by an increase in the antibody level. In a rat model of bleomycin-caused lung injury, Struhar and co-workers showed that there was an increase in both the intensity and the distribution of surface antigens of epithelial cells.[8]

There are alternative explanations for the development of pulmonary fibrosis in this patient. He had had exposure to several chemotherapeutic lung toxins in addition to bleomycin. He had recently received procarbazine and vinblastine to treat his Hodgkin's disease.[3] Combination chemotherapeutic regimens are thought to increase the risk of inducing bleomycin pulmonary toxicity.[1] Procarbazine, however, appears to cause a hypersensitivity reaction with eosinophilia,[1] rather than the pattern observed here. Vinblastine used in combination with mitomycin has in rare cases been reported to induce pulmonary fibrosis.[1] In addition, this patient had received gold therapy seven years previously.

In conclusion, a possible mechanism for the apparently increased pulmonary susceptibility to bleomycin toxicity in this patient is complement-mediated immune-complex disease. The simultaneous increase in the surface antigens of the lung epithelial cells induced by bleomycin treatment and a high level of circulating immune complexes—caused by the patient's rheumatoid arthritis—against those antigens may have resulted in severe lung injury. We suggest that patients with rheumatoid arthritis may be more susceptible to bleomycin-induced pulmonary fibrosis by these possible synergistic mechanisms.

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