5. A 40-year-old fisherman from the United States gulf coast presents with a complaint of left lower extremity swelling, pain, and "blue" rash. He notes that he was punctured in the right forearm by a fishing hook used in his daily work several days prior to the left leg pain. His past medical history is notable for acute myelogenous leukemia managed with successful bone marrow transplantation 18 months ago. He does not consume alcohol and has no history of liver disease. He received a tetanus booster 3 years ago. The physical examination reveals a blood pressure of 96/60 mm Hg, pulse 120/min, respiratory rate 18/min, and temperature of 37.8ºC. He has a puncture wound on the right forearm with a clear center with a pustule and dark periphery. His left leg is notable for a bluish rash with associated areas of hemorrhage and a central bullous lesion (see Figure 5A). The WBC count is 1400/mm^3 (1.4 x 10^9/L) with a prominence of neutrophils, hemoglobin 10.4 g/dL (104 g/L), and platelet count 18,000 mm^3 (18 x 10^9/L).

The patient is admitted to the ICU, where he becomes progressively more unstable and requires intubation, fluid resuscitation, and increasing vasopressor use. Films of the left lower extremity do not reveal any gas within the tissues. Your surgical consultants are recommending surgical debridement of the leg. The patient is started on vancomycin and levofloxacin. Despite this antibiotic regimen, the patient continues to deteriorate. Within several hours of admission, the laboratory results are complete and note that multiple blood cultures all have positive results. A Gram stain of the buffy coat smear is shown in Figure 5B. What is the most appropriate additional therapy in this patient while awaiting final identification of the organism?

A. Doxycycline and ceftazidime.
B. Drotrecogin alfa.
C. Hyperbaric oxygen.
D. Tetanus immune globulin and tetanus toxoid.
E. Clindamycin.

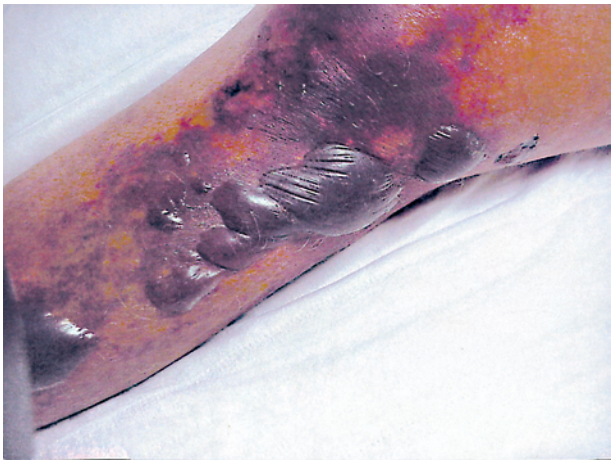

Figure 5A

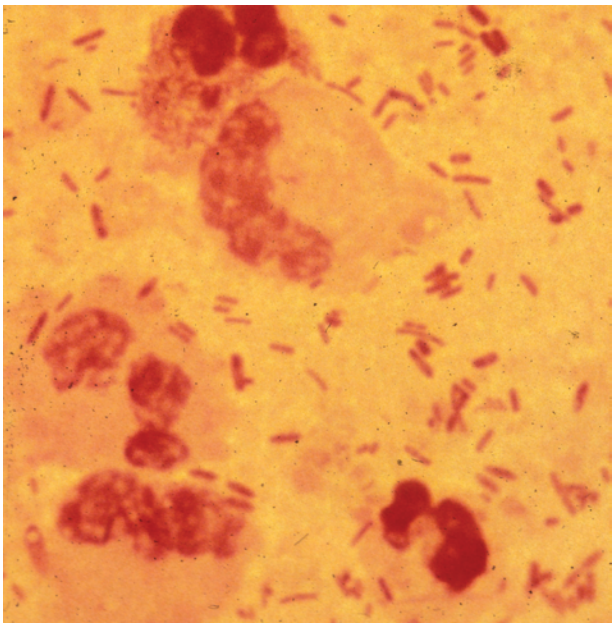

Figure 5B

5. A. Doxycycline and ceftazidime.

The patient's demographic parameters and clinical presentation are classic for sepsis due to *Vibrio vulnificus*. Figure 5A (see item text) shows the skin lesion, which is often found with *V vulnificus,* consisting of a bluish rash with associated areas of hemorrhage and a central bullous lesion. Figure 5B (see item text) shows Gram-negative bacteria, in the buffy coat smear, consistent with *V vulnificus*. The treatment of choice is doxycycline or a combination of doxycycline and ceftazidime (choice A). *V vulnificus* is sensitive to multiple antibiotics. However, *in vitro* studies indicate that tetracycline compounds are very effective. Some authors recommend the addition of ceftazidime. The degree of thrombocytopenia present in this patient is a contraindication to the use of drotrecogin alfa (choice B). Hyperbaric oxygen (choice C) is not indicated in this setting. As the patient is up-to-date in his tetanus immunization, tetanus immune globulin and tetanus toxoid (choice D) are not required at this time. The other antibiotic choice, clindamycin (choice E), is not an agent of choice for *V vulnificus*.

Primary septicemia due to *V vulnificus*, a halophilic Gram-negative bacterium (see Figure 5B), is a leading cause of seafood-related fatalities in the United States. Most cases in the United States occur in states bordering the Gulf of Mexico or states importing oysters from the gulf. Frequently, patients report a recent history of raw oyster consumption and pre-existing chronic liver disease. Chronic liver disease is reported in up to 80% of patients. However, additional risk factors include malignancy, lymphoma, leukemia, immunocompromised states (as in this patient with a bone marrow transplantation), corticosteroid use, diabetes, hemochromatosis, acquired immunodeficiency syndrome, and achlorhydria.

V vulnificus exists as a free-living bacterium in warm, marine environments during the spring and summer months. Filter-feeding shellfish, including oysters, concentrate the organism. Infection occurs through ingestion of contaminated food or through skin contact with contaminated water. Our patient likely acquired his infection through a contaminated fishing hook or exposure to contaminated water at the puncture site from the fishing hook. Two distinct patterns of infection occur. Septicemia may occur with or without a focus of infection and has an associated mortality of up to 53%. Wound infections also occur from pre-existing or newly acquired wound exposure to seawater containing the bacteria.

Onset of symptoms in patients suffering sepsis is abrupt with fever, chills, and shock. Striking skin lesions are an early sign of septicemia and may be seen in 65% of patients. Metastatic skin lesions are usually on the lower limbs. The most characteristic skin lesions, as in this patient, include erythema of the skin and subcutaneous tissues, followed by rapid evolution to indurated plaques. The plaques may be bluish purple and develop vesiculations or bullae. Gangrene of the limb may develop. The organism may be isolated and cultured from blood or cutaneous lesions. Debridement of nonviable and necrotic tissue is central to successful care of these patients.

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23. A 45-year-old man who underwent an allogeneic bone marrow transplant procedure 2 weeks ago for non-Hodgkin's lymphoma is transferred to the ICU for the rapid onset of shortness of breath and requires intubation for hypoxemic respiratory failure. His initial posttransplant course was uncomplicated. His CBC count from the day prior to transfer showed a leukocyte count of 1,900/mm^3 (1.9 x 10^9/L) with 82% segmented neutrophils, 9% monocytes, and 9% lymphocytes, hemoglobin 8.5 g/dL (85 g/L), hematocrit 28% (0.28), and platelets 70,000/mm^3 (70 x 10^9/L). Weights have been stable. No hemoptysis has been reported.

On physical examination, he is intubated and mechanically ventilated. On an FIO_2 of 0.65, his arterial blood gas measurements are PO_2 65 mm Hg, PCO_2 38 mm Hg, and pH 7.37. His temperature is 38.9°C, blood pressure 100/70 mm Hg, pulse 100/min, and respiratory rate is via the ventilator at 15 breaths/minute. His HEENT examination is remarkable for oral mucositis, lung examination reveals diffuse crackles, cardiovascular examination is without murmurs, abdominal examination is benign, and extremities are without rashes, edema, cyanosis, or clubbing. His laboratory tests reveal a leukocyte count of 2,200/mm^3 (2.2 x 10^9/L) with 83% neutrophils, 8% monocytes, and 9% lymphocytes. His hemoglobin is 6 g/dL (60 g/L), hematocrit 22% (0.22), and platelet count 65,000/mm^3 (65 x 10^9/L). Electrolytes and liver function studies are within normal limits. Cultures to date are negative. His immunosuppression regimen includes cyclosporine, prednisone, and azathioprine. His chest radiograph is shown in Figure 23A. The patient undergoes bronchoscopy with bronchoalveolar lavage (BAL). The BAL cytology is shown in Figure 23B. Microbiology studies are pending. The most likely diagnosis in this patient is:

A. Cardiogenic pulmonary edema.
B. Diffuse alveolar hemorrhage.
C. Acute graft-vs-host disease.
D. Idiopathic pneumonia syndrome.
E. Bronchiolitis obliterans.

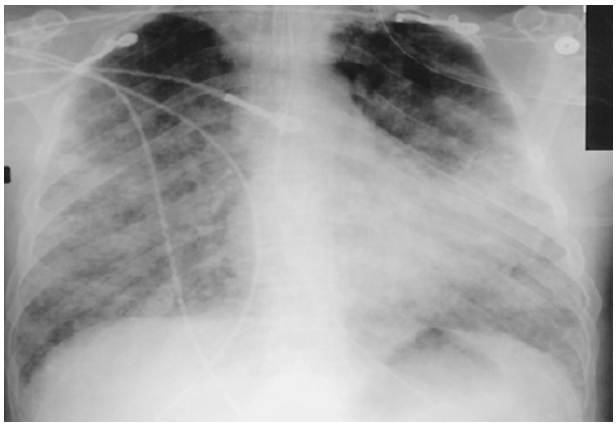

Figure 23A

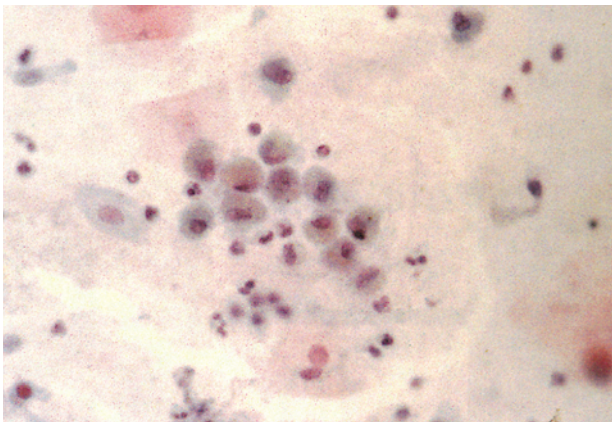

Figure 23B
Papanicolaou stain, original x100

23. B. Diffuse alveolar hemorrhage.

This patient has developed diffuse alveolar hemorrhage (DAH) at the typical time period of 7 to 40 days (mean 12 to 14 days) following bone marrow transplantation (BMT). In general, patients undergoing allogeneic BMT have a greater incidence of pulmonary complications than do the autologous BMT patients. DAH, however, has an equal incidence or is perhaps more frequent in the autologous BMT group. The usual clinical presentation of DAH is the rapid onset of shortness of breath, hypoxemia, diffuse alveolar infiltrates as shown in Figure 23A (see item text), and a decrease in the hematocrit. In addition, there may be hemoptysis, although this is not required for the diagnosis. Risk factors for DAH include age >40 years, fever, total body irradiation as part of the induction regimen, the presence of mucositis, BMT performed for solid tumors, renal insufficiency, and infection, and is usually temporally related to engraftment as in this case. Interestingly, thrombocytopenia is not clearly a risk factor for DAH. DAH can be diagnosed in the appropriate clinical setting by the presence of bloody return on serial bronchoalveolar lavage and the presence of hemosiderin-laden macrophages on cytologic examination (see Figure 23B in the item text). Treatment includes corticosteroids with some reports of success. Mortality from DAH can be as high as 50 to 80%.

Pulmonary edema also commonly develops in the posttransplant period, usually in the first few weeks following transplantation. BMT patients often receive multiple transfusions, antibiotics, and sometimes total parenteral nutrition, all of which can contribute to the development of pulmonary edema. This diagnosis can be made in the appropriate clinical setting with the monitoring of weights and fluid intake and output as well as the presence of edema. The idiopathic pneumonia syndrome is a diagnosis of exclusion made in the 1 to 2 month period following transplantation. This entity occurs more frequently in allogeneic recipients and presents with pneumonic signs and symptoms, gas exchange abnormalities, and radiographic infiltrates, and requires the exclusion of infectious etiologies. There is characteristic pathology including interstitial infiltrates without a clear organism identified. Acute graft-vs-host disease primarily affects the liver, colon, and skin and rarely involves the lung; this is in contrast to chronic graft-vs-host disease, which develops more than 100 days following transplantation and is manifested by bronchiolitis obliterans with a clear or hyperinflated chest radiograph.

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