stance was secondary to the damage inflicted on the alveolar-capillary membrane via hypersensitivity of the host to viable and dead tubercle bacilli and tuberculous protein and the subsequent response of the lung to this injury. This syndrome was diagnosed and treated in its early stages, thus avoiding the necessity for mechanical ventilation.

Efficient functioning of the normal lung is dependent upon the integrity of the alveolar-capillary membrane. Impaired function of this vital structure is recognized in the adult respiratory distress syndrome, the pathophysiology being reasonably well described in endotoxin shock, hypovolemic shock, and trauma.

In these investigated syndromes, the etiologic factors causing the adult respiratory distress syndrome are pathologic; they depend upon the occurrence of abnormal factors, such as endotoxin, hypovolemia, the product of traumatized tissues, or the release of platelet factors; however, appropriate pathophysiologic responses may predispose to the occurrence of the adult respiratory distress syndrome. Examples include diffuse viral and bacterial pneumonias and, in the present case, endobronchial spread of tuberculosis. In these conditions the existence of increased permeability of capillaries is due both to damage from the offending agent and also to the physiologic response for the migration of leukocytes and macrophages to the site of the causative organisms.

In the exudative phase of tuberculosis, acute inflammation of the air spaces occurs without necessarily causing permanent injury to the lung. The initial reaction to the tubercle bacillus consists of dilation of capillaries, swelling of endothelial and alveolar lining cells, and an outpouring of protein-rich fluid with polymorphonuclear leukocytes and macrophages into the alveolar spaces. The initial polymorphonuclear reaction is rapidly replaced by large mononuclear cells whose source is uncertain. The duration of this completely reversible phase varies but may last several weeks in the human lung. If untreated, a productive reaction with distortion and destruction of normal pulmonary architecture and formation of caseating granulomas occurs.

With the existence of this increased permeability of the capillaries, any increment in total body water, whether due to increased intake, decreased excretion, or the syndrome of inappropriate secretion of antidiuretic hormone (as in the present case), will result in increasing interstitial and alveolar edema, with a resultant increase in right-to-left shunt and alveolar-arterial oxygen gradient. The syndrome of inappropriate secretion of antidiuretic hormone was documented in this situation by hyponatremia, an augmented urinary excretion of sodium, and an inappropriately high osmolality of the urine without concomitant renal, cardiac, or hepatic disease. The serum level of urea nitrogen was at the lower levels of normal, and no edema was evident. Vorherr et al10 demonstrated an antidiuretic principle in tuberculous pulmonary tissue and concluded that "tuberculous lung tissue may either produce antidiuretic hormone or absorb an inappropriately released hormone from the posterior pituitary." A knowledge of the pathophysiology should emphasize the need for judicious administration of fluids in the prevention of the adult respiratory distress syndrome in patients with pneumonia, and the effectiveness of diuretic therapy when the syndrome occurs. All diseases manifest a spectrum. In the present case the adult respiratory distress syndrome was diagnosed in an early phase and was treated promptly, avoiding the necessity for mechanical ventilation. Tuberculous pneumonia, like any diffuse viral or bacterial pneumonia, can be a cause of the adult respiratory distress syndrome in the appropriate setting.

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REFERENCES

Endocarditis due to Hemophilus aphrophilus

Report of a Case with Possible Transmission from Dog to Man

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A 44-year-old man was treated for bacterial endocarditis due to Hemophilus aphrophilus. The characteristics of the organism are reviewed, along with other cases of

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endocarditis. There is an association of this organism with dogs and a potential for transmission from this source to man.

The organism, *Hemophilus aphrophilus*, has been reported as a rare cause of bacterial endocarditis, affecting normal, as well as damaged, valves. The case reported here is of interest because of the rarity of endocarditis produced by this organism and the difficulty encountered in its routine isolation. In addition, the possible acquisition of this organism from a canine source is described.

**CASE REPORT**

A 44-year-old white man was well until six weeks prior to hospitalization, when he developed fever, chills, and malaise. He was treated with two courses (five days each) of therapy with tetracycline, with subjective improvement each time. Fever returned after the second course of therapy. The patient experienced an episode of hematuria, followed by acute respiratory distress, and was admitted to the hospital on April 13, 1976.

The patient owns a livestock farm and has a dog and two cats. There was no prior history of significant illnesses or cardiac murmurs. The patient had undergone thorough dental work two weeks prior to the onset of his illness.

The findings from physical examination on admission were normal, except for fever. No cardiac murmurs were detected. The following values were determined: hemoglobin level, 11.8 gm/100 ml; hematocrit reading, 35.5 percent; white blood cell count, 11,600/cu mm, with normal differential count; and erythrocyte sedimentation rate, 64 mm/hr. The results of all studies of blood chemistry were normal, except for a serum glutamic-oxaloacetic transaminase level of 70 international units (IU) and an alkaline phosphatase level of 118 IU. Urinalysis revealed a trace of protein and two to five white blood cells and zero to two red blood cells per high-power field. Serologic tests and latex-fixation tests were negative.

X-ray films of the chest, skull, and paranasal sinuses and the results of an upper gastrointestinal series, barium enema, gall bladder series, intravenous pyelogram, and brain scan were normal. The electrocardiogram was normal. Lumbar puncture revealed the following values for the cerebrospinal fluid: protein level, 21 mg/100 ml; glucose level, 78 mg/100 ml; and ten white blood cells per cubic millimeter (nine polymorphonuclear neutrophils and one lymphocyte). Therapy with cephalaxin was begun, and three cultures of blood drawn after the onset of therapy grew tiny gram-negative aerobic bacilli later identified as *H. aphrophilus*. Six more cultures of blood drawn during the next 48 hours were negative.

Subsequent antibiotic therapy included the use of cephalothin, ampicillin, penicillin, clindamycin, chloramphenicol, and isoniazid. The patient developed a maculopapular rash while he was receiving therapy with penicillin, which was then discontinued. He continued febrile, diaphoretic, and anorectic and had recurrent episodes of abdominal pain.

Consultation with a specialist in infectious diseases was obtained on May 6, 1976. Physical examination revealed a depressed obese man in no distress, with the following physical findings: blood pressure 130/70 mm Hg; temperature, 39.5°C (103.1°F); pulse rate, 120 beats per minute; and respiratory rate, 14/min. The head, ears, and nose were normal. A single flame-shaped hemorrhagic lesion with three small central white areas was seen on the right inferior palpebral conjunctiva. The fundi were normal. There was good dentition, without gingival or dental lesions. The chest was clear to percussion and auscultation. There was no cardiomegaly. A grade 3/6 high-pitched apical and left sternal holosystolic murmur was heard for the first time. The abdomen was without organomegaly. There was no clubbing, cyanosis, splinter hemorrhages, or other signs of embolization. Findings from the remainder of the physical examination were normal.

A diagnosis of bacterial endocarditis due to *H. aphrophilus* was made. Cultures were obtained from the mouth of the patient and his dog. *Hemophilus aphrophilus* was grown from the dog's culture, but not from the patient's culture. Because of allergy to penicillin, the patient was treated with cephalothin (2 gm intravenously every four hours). After one week, he continued febrile, and therapy with gentamicin (100 mg intravenously every eight hours), was added. The patient remained febrile and was transferred to the University of Louisville Associated Hospitals on May 20, 1976.

Physical examination showed fever and splenomegaly, with other findings unchanged. The white blood cell count was 6,700/cu mm with 86 neutrophils, two band cells, 22 lymphocytes, five eosinophils, and five monocytes. The hematocrit reading was 22.5 percent. A nitroblue tetrazolium dye test showed 20 percent positive cells (normal, 0 to 12 percent). Latex fixation was positive at a titer of 1:32 and a week later at 1:64. The results of studies of blood chemistry were all normal. The ECG and chest x-ray film were normal. The patient continued febrile during therapy and developed significant eosinophilia. With the assumption that the patient had drug-induced fever, therapy with gentamicin and cefazolin was continued for four weeks, and upon discontinuance of therapy, his fever abated, and he remained afebrile. At discharge from the hospital, the patient was normal, except for mild splenomegaly and a grade 3/6 holosystolic murmur suggesting mitral insufficiency. He remains free of infection at the time of this report.

**DISCUSSION**

In 1940, Khairat isolated *H. aphrophilus* from a patient with endocarditis. This organism has since been implicated in a variety of human infections, the majority being endocarditis or brain abscesses. Endocarditis due to *H. aphrophilus* is rare. Page and King reported 41 cases of infections with *H. aphrophilus*, of which 17 were bacteremias and 24 were localized infections. Fifteen of the patients with bacteremia had endocarditis. Goldsweig et al analyzed 28 cases of endocarditis due to *H. aphrophilus*, including 18 male and 10 female patients. Patients ranged in age from 7 to 82 years, and predisposing factors included dental procedures or chronic infections. Twenty patients had preexisting heart disease. Elster et al reviewed 23 cases of endocarditis due to *H. aphrophilus*; seventeen patients had preexisting heart disease prior to the onset of endocarditis.

Two cases of infection with *H. aphrophilus* have been associated with canine contact, and this organism was isolated from the dog's mouth in both cases. The present patient had a normal heart prior to the onset of endocarditis, and the organism was isolated from his dog's mouth. This is the third reported case of possible
canine transmission of this organism, and the first case of endocarditis associated with such transmission.

Since the first report in 1940, more cases of endocarditis associated with *H. aphrophilus* have been described. The organism is a small, gram-negative nonencapsulated cocccobacillus resembling species of Hemophilus group B1, *Actinobacillus actinomycetemcomitans*, and *Brucella* species.

Kraut et al isolated *H. aphrophilus* from the mouths of normal persons. The mouth and respiratory tract are presumed to be the portals of entry in many cases. In the case presented here, the patient had undergone dental work two weeks prior to his illness, and although the organism was not isolated from his oral cavity, he had already been on therapy when the cultures were obtained.

*Hemophilus aphrophilus* is sensitive to penicillin, streptomycin, gentamicin, kanamycin, ampicillin, chloramphenicol, rifampin, cephalothin, and tetracycline. The organism is resistant to vancomycin, lincomycin, and bacitracin. The clinical manifestations of endocarditis due to *H. aphrophilus* are indistinguishable from those due to *Streptococcus viridans*. Embolization appears to occur more frequently in endocarditis due to *H. aphrophilus*. Hematuria, respiratory distress, pleocytosis, splenomegaly, conjunctival hemorrhage, and repeated episodes of abdominal pain occurred in the patient described herein. These are all suggestive of episodes of embolization. It was once thought that *H. aphrophilus* affected only deformed valves. It is now apparent that it affects normal valves, as in the present case. Bactericidal drugs should be used to treat endocarditis due to *H. aphrophilus*. The use of a single drug vs two drugs in the therapy of this type of endocarditis is still debated. Most authors recommend two drugs for six weeks. Indications for surgical intervention, treatment of embolism, and therapy for congestive cardiac failure are the same as in any other type of endocarditis.

**REFERENCES**