Aspergillus Infection After Cardiac Surgery

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Aspergillus infections in four patients after cardiac surgery led to intensive search of the hospital environment for fungi and to review of contamination control practice. Aspergillus was grown from pigeon excreta on the outside windowsills and from moss growing on the hospital roof. It was recovered occasionally from the operating room and more often from the postoperative recovery room. Defects in the ventilating system of these areas were identified and corrected in order to reduce air contamination. Patient contamination must be related to the turbulent blood-air interface produced by cardiac suckers during operation, but still the manner of control and even the portal of entry of infection remain obscure and are, therefore, a cause for concern in future operations.

Open heart operations, especially valve replacement, have been vulnerable to complication by endocarditis. Carefully planned antibiotic programs have led to effective control of postoperative bacterial endocarditis, especially that due to staphylococcus, but fungal infections have emerged and become more prominent. The dire consequences of aspergillus endocarditis after open heart surgery have become well known to us.

Report of Cases

Case 1.—A 41-year-old man with mitral stenosis of more than 12 years' duration had excision of the mitral valve on March 8, 1966. A Hufnagel disk prosthesis was used for replacement. Before operation, the patient had been receiving long-term procaine penicillin G prophylaxis. After operation, he was given procaine penicillin G (13 days), streptomycin sulfate (5 days), methicillin sodium (5 days), and then oxacillin sodium for seven days. Postoperative fever lasted five days then subsided. The patient was discharged on April 5, 1966. Two days later, a month after operation, he developed nausea, vomiting, weakness, diaphoresis, and mild fever. These symptoms led to hospitalization on April 14, 1966. Tachycardia, fever (100 F [37.8 C]), and atrial fibrillation were present at that time. Later, petechiae appeared on skin and mucous membranes, and liver and spleen became enlarged and tender. Results of numerous blood cultures were normal. Large doses of antibiotics (procaine penicillin G, streptomycin, methicillin sodium) did not prevent rapid progression of the disease. Severe pulmonary congestion and shock preceded death on April 22, 1966.

At postmortem examination, a large thrombus containing Aspergillus fumigatus occluded the orifice of the prosthetic mitral valve and prevented movement of the disk. The left atrium was filled with recent and old thrombi. Scattered microabscesses were present in the myocardium, lung, liver, and spleen. Aspergillus fungus was identified in the spleen. Death was considered due to aspergillus endocarditis with dissemination (previously reported).

Case 2.—A 36-year-old white man with aortic regurgitation had excision of the aortic valve and replacement with a Starr-Edwards ball-valve prosthesis on Jan 31, 1967. Before operation, he was receiving procaine penicillin G prophylaxis. After operation, he received procaine penicillin G and streptomycin for seven days, methicillin sodium for the first four days, and then oxacillin sodium for three days. Postoperative fever lasted for the first three postoperative days then subsided. The patient was discharged on Feb 27, 1967.

Five weeks later, more than two months after operation, the patient developed weakness, general body pain, and low-grade fever. After hospitalization on April 18, 1967, fever continued and did not respond to large doses of procaine penicillin G and streptomycin. Results of numerous
Fig 1.—Frames of cineangiogram in two phases of heart action show range of abnormal rocking motion of valve. Injection of radio-opaque material shows aorta and mycotic aneurysm near aortic valve (case 2).

Fig 2.—Filamentous septated mycelia of *A fumigatus* on aortic wall close to aortic valve (case 3; Grocotts stain, ×250).

Blood cultures were normal. Cineangiography showed abnormal rocking motion of the prosthetic valve and an aneurysm just above the prosthesis (Fig 1), but the rapidity of progress of symptoms and critical stage of the illness precluded operative treatment. The patient died suddenly on May 5, 1967.

At postmortem examination, the cause of death was endocarditis due to *A fumigatus*. Large, gray-red thrombi covered the prosthetic valve and occluded the lumen. In the region of the right coronary cusp, the ascending aorta was separated from the annulus fibrosis so that prosthetic valve fixation was poor. There was a mycotic aneurysm in this area.

Case 3.—A 43-year-old man with aortic stenosis had excision of the aortic valve and replacement with a Starr-Edwards ball-valve prosthesis on Dec 10, 1968. Antibiotics were not used before operation. After operation, he received procaine penicillin G for 20 days. His temperature after operation ranged from 99 to 102 F (37.2 to 38.9 C) for five days and then fell to normal. On the 25th postoperative day, low fever (99 to 100.5 F [37.2 to 38.5 C], rectal) again developed and continued for three weeks. Poor appetite, night sweats, and weight loss were present during this time. On June 10, growth of *A glaucus* in blood culture was reported, but results of many subsequent blood cultures during this febrile period showed no growth. No antibiotics were given. After June 20, the temperature returned to normal, and the patient's condition progressively improved as all symptoms subsided. He was discharged in July 1969 and has remained well. The final clinical diagnosis was aspergillus bloodstream infection, source unknown. It seems likely that this patient had endocarditis, but this is not certain. His survival is evidence that some patients are able to successfully combat *Aspergillus* infection on their own.

**Diagnosis**

The nature of the infection was difficult to prove before death. Suspicion of fungal heart valve infection was based on symptoms of endocarditis, not responding to antibiotic drugs, with results of blood cultures showing no growth. In only one patient was it possible to grow aspergilli from the blood. Symptoms were late in onset, days after disappearance of the fever that ordinarily follows cardiac operations. The three patients who developed endocarditis had recovered sufficiently to be discharged from the
hospital. Not until one or two months after operation did they return to the hospital with fever, weakness, loss of appetite, weight loss, anemia, and leukocytosis. More specific signs commonly associated with endocarditis, such as petechiae and enlarged liver and spleen, were present in only one patient. There were no major embolic phenomena, though perhaps the seizures in case 3 could have been on an embolic basis.

In the patients who died, the most striking finding was the extensive involvement of the prosthetic valve area with gray red friable thrombi, which filled the lumen of the valve cage and interfered with motion of the ball or disk. The friability of the thrombi, with large fungal vegetations exposed to the flowing blood, easily permitted separation of small emboli, and it was surprising that major emboli did not occur, that microabscesses were not more numerous, and that results of blood cultures were so consistently negative. The final pathological diagnosis was based on characteristic, morphological appearance of the fungus in the tissues (Fig 2).

Source of Infection

As each new infection occurred in the three-year period covered by this report, attention was focused on the operating room, its personnel and equipment, operative techniques, traffic, and ventilation. At first, minor changes in techniques were made, and restrictions on operating room traffic were established. Later, the occurrence of the third infection led to extensive search for fungi in the operating room and postoperative recovery room. Aspergillus was found in an occasional swabbing from room surfaces in both areas and a culture plate exposed to the air in the operating room. These positive cultures were only few in comparison to the many negative swabblings and air samplings by exposed plates made over many days, but still they indicated that occasionally aspergillus were present in the operating room and recovery room and that air contamination was the likely source of infection.

Outside the hospital, aspergillus was identified in two areas in close relation to the operating room. Aspergillus fumigatus was found in the pigeon excreta on the ledges of the windows. In addition, the external roof of the operating room, two stories high and frequently covered...
water, had a luxuriant growth of moss from which *A. fumigatus* was cultured. The window ledges and the roof were close to the intake of the ventilating system of the operating room (Fig 3). Just a few feet separated the potential sources of fungus from the air intake, only a very short distance considering the usual turbulent air currents about the external recesses of the hospital, so the question was whether or not the fungus could pass through the air-conditioning filter system.

The ventilating-cooling system for the operating room had an aerosol filter made of glass microfibers which was considered to have an average dust capture efficiency in the 80% to 85% range, lower than desirable for an operating room but still capable of removing particulate matter over \( \frac{1}{10} \) in diameter. Staphylococci and streptococci, which usually measure between 0.75\( \mu \) and 1.25\( \mu \), would pass through this filter, but the spores (2\( \mu \) to 3\( \mu \)) and the mycelia (4\( \mu \) to 5\( \mu \)) of aspergilli probably would be excluded. In fact, at no time were positive cultures for aspergillus obtained from the ventilating system itself or from large-volume air sampling in the operating room.

The postoperative recovery room had a separate ventilating system. The air intake was on the hospital roof, 12 stories high, and the conduits passed through the hospital structure to the filter system on the second level, close to the recovery room. The aerosol filter was the same type as in the operating room system. The ducts concealed in the ceiling were difficult to clean, and dust removed from the ducts yielded aspergilli in most cultures.

**Portal of Entry**

It seemed most likely that the fungus entered the blood stream during the open heart operation rather than during manipulation of intravascular catheters in the postoperative recovery room. Since the fungus was never found on operating room equipment and since the heart-lung machine parts in contact with the blood were disposable and always sterile on culture after use, we concluded that the susceptibility of cardiac procedures to postoperative fungus infection was related to other features of open heart surgery. The important fact seemed to be that the blood stream and the heart were open to the air during the course of operation, and the possibility of contamination was extraordinarily great. Sucker systems, drawing a mixture of blood and large volumes of air from the heart during valve replacement, created optimum conditions for contaminating the blood with microorganisms.

**Comment**

Faced with four infections from aspergillus, with no effective treatment for the fungal endocarditis, we have sought long for an explanation so that countermeasures could be taken. In considering the problem, it seemed remarkable that other types of fungal infection, such as candida, have not been seen, but perhaps other fungi are not common in the hospital environment. In contrast, aspergillus can be found in many areas in a hospital and also in patients, especially in tracheobronchial secretions. Therefore, perhaps it should not be surprising that even in the operating room an occasional positive culture may be obtained from air sampling. This does not necessarily mean that the ventilating system is at fault because there are other mechanisms of airborne infection, mostly related to contamination from humans. Attention has been directed to the unique way that the human body serves as a source of airborne contamination, with convection currents produced by the heat of the body as the carrier for microorganisms.

The solution to the problem remains obscure because the mechanism of patient contamination has not been certainly established. The operating room proved clean in contrast to the recovery room, but the chances of infection ought to be greater during operation than in the postoperative period, even in a contaminated recovery room. Since we could not prove which area was responsible for infection, our answer was to resort to extraordinary cleaning measures in both areas, including the air ducts. In addition, better filters were placed in the air-conditioning system. Pigeons no longer can roost on the window ledges; the space has been filled with glass blocks. The moss on the hospital roof has been destroyed by chemicals. In application, these changes have gone beyond the ordinary housekeeping techniques and environmental control so long considered adequate in operating and recovery rooms. They were forced upon us by the realization that extraordinary measures were needed to protect the surgical patient suffering from cardiac disease against infection.

George Fazekas, MD, chief, Laboratory Service, gave permission to report the postmortem examinations.

**Nonproprietary and Trade Names of Drug**


**References**


