

Post-operative aspergillosis

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ABSTRACT

While invasive aspergillosis occurs typically in severely immunocompromised patients, cases of surgical site infection have been reported in immunocompetent individuals. The Medline, LILACS and EMBASE databases were searched for descriptions of cases of post-operative aspergillosis, and references from relevant articles and conference abstracts were reviewed. More than 500 cases of post-operative aspergillosis were found. Cardiac surgery ($n = 188$), ophthalmological surgery ($n > 90$) and dental surgery ($n > 100$) were associated with the majority of cases. Other cases involved wound infections ($n = 22$), bronchial infections ($n = 30$), mediastinitis ($n = 11$), pleural aspergillosis ($n = 1$), infections following orthopaedic surgery ($n = 42$), vascular prosthetic surgery ($n = 22$), breast surgery ($n = 5$), abdominal surgery ($n = 10$) and neurosurgery ($n = 25$). In most patients, the source was presumed to be airborne infection during the surgical procedure. Prevention of these infections requires special care of the ventilation system in the operating room. Successful treatment requires rapid diagnosis, surgical debridement and antifungal therapy, often with voriconazole. In order to improve the outcome, better diagnostic methods are needed, particularly for cases of endocarditis and aortitis.

Keywords *Aspergillus*, neurosurgical infection, nosocomial infection, post-operative infection, review, surgical site infection

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INTRODUCTION

Fungi belonging to the genus *Aspergillus* are ubiquitous and occur in soil, water and decaying vegetation [1,2]. Like other filamentous fungi, *Aspergillus* is acquired primarily from an inanimate reservoir, usually by the inhalation of small airborne spores [3]. While nosocomial aspergillosis typically affects immunocompromised patients [4], post-operative aspergillosis occurs mainly in immunocompetent patients, including some patients who received corticosteroids temporarily. This review is based on a search of the world literature to identify cases of post-operative aspergillosis occurring after surgical procedures that were not secondary to disseminated infection or previous known colonisation by *Aspergillus* spp.

PATIENTS AND METHODS

Search strategy

The Medline, LILACS and EMBASE databases were searched and references from relevant articles were reviewed. Search terms were 'aspergillus', 'surgery', 'surgical site infections', 'cardiovascular surgical procedures', 'endocarditis', 'aortitis', 'mediastinitis', 'breast', 'laparotomy', 'arthroplasty', 'orthopaedic procedures', 'neurosurgery', 'transplantation', 'ophthalmologic surgical procedures', 'osteomyelitis', 'prosthesis', 'treatment' and 'prevention'. Conference abstracts were reviewed using the *Aspergillus* web-site (<http://www.aspergillus.man.ac.uk>). Apart from papers published in Japanese, Russian, Czech or Polish, no language restrictions were applied. Non-surgical cases of primary cutaneous aspergillosis and infections associated with intravascular devices were not considered for this review.

Definitions

Only cases of proven or probable infection were reviewed, which required that all cases included were laboratory-confirmed by culture and/or histology and/or microscopy. These criteria were based on standard definitions for invasive fungal infections in immunocompromised patients for clinical research [5]. As the incubation period of aspergillosis is not well-established, this review was not limited by the CDC definitions of surgical site infection (i.e., infections occurring within 30 days of a surgical procedure if no implant is left in

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place, or within 1 year if an implant is present) [6]. Wound aspergillosis was defined as infections involving only the skin or subcutaneous tissue of the incision. Infections that involved both superficial and deep incision sites were classified as deep surgical site infections, according to the site affected. For classification as a wound infection, in addition to a positive culture of *Aspergillus* spp. taken directly from the wound, the wound itself had to be non-healing following treatment with standard antibiotics, with other pathogens absent or minimally present.

LITERATURE REVIEW

From the initial search, *c.* 450 papers were excluded for several reasons, including cases of aspergillosis unrelated to surgery and disseminated

infections from pulmonary or other sources. Other review articles with no new contributions were also excluded. More than 500 patients with post-operative aspergillosis were included in this review, including cases following heart surgery (188), neurosurgery (25), dental surgery (>100), ophthalmological surgery (>90), orthopaedic surgery (42), vascular prosthetic surgery (22), abdominal surgery (10) and breast surgery (5). Reports of wound infections (22), bronchial infections (30), mediastinitis (11) and pleural aspergillosis (1) were also included. Some cases were reported more than once, *i.e.*, [10] and [11]; [16] and [129]. Table 1 summarises the key aspects of

Table 1. Summary of main clinical presentations, treatment and prophylaxis of cases of post-operative aspergillosis

	Comments
Clinical presentation	
Endocarditis/aortitis (<i>n</i> = 174)	Marked male predominance (<i>c.</i> 70%) Absence of immunosuppression for almost all patients Aortic valve mostly involved (60.5%) Median time from surgery to diagnosis = 2.7 months <i>Aspergillus fumigatus</i> : aetiology in only 58.7% of cases Low ante-mortem diagnosis (43.5%), usually following surgical intervention Blood cultures rarely positive (6.4%) Propensity for late embolisation Mortality >80% despite intervention (overall mortality 92.7%)
Neurosurgery infections (<i>n</i> = 25)	Frequently associated with the use of steroids (52.0%) All proven cases caused by <i>A. fumigatus</i> Median time from surgery to diagnosis = 3 months Higher ante-mortem diagnosis rate (68.0%) than for endocarditis Mortality much lower than observed for immunocompromised patients with aspergillosis disseminated to the central nervous system
Dental surgery infections (<i>n</i> > 100)	Many cases of sinus aspergillosis associated with endodontic treatment Obturing pastes within the maxillary antrum probably a risk-factor
Wound infections (<i>n</i> = 22)	Most patients immunosuppressed Median time from surgery to diagnosis = 17 days <i>A. flavus</i> accounts for 41.2% of cases confirmed by culture Risk of dissemination
Ophthalmological surgery infections (<i>n</i> > 90)	Usually presents as keratitis Diagnosis requires sampling at the site of infection
Vascular prosthesis infections (<i>n</i> = 22)	Almost all patients are male and immunocompetent Median time from surgery to diagnosis = 8 months Clinical picture indistinguishable from <i>Staphylococcus epidermidis</i> infections Usually occurs close to suture lines of previous aortotomy High incidence of embolisation to vertebral disks
Other cases (<i>n</i> = 113)	Frequent association with prosthesis insertion
Treatment	The optimal treatment has not been specifically studied Survival seemingly dependent on excision of the infected tissue; in cases involving a prosthesis, the new prosthesis should be placed in a non-infected field Concomitant use of a systemic antifungal agent is also crucial. Although there are no data favouring any one antifungal drug, the response rates to voriconazole in immunocompromised patients were superior to those in response to amphotericin B. Caspofungin and other echinocandins may also be useful. Longer-term oral extension with itraconazole or voriconazole is appropriate for some patients The optimal duration of therapy is unknown and is likely to differ between patients, but once as much infected tissue as possible has been removed and any immunocompromising factors, such as corticosteroid therapy, are minimised, treatment for 3 months beyond the last evidence of active disease may be appropriate
Prevention	Requires special care with the ventilation system in the operating theatre Proper disinfection and storage of surgical materials

post-operative aspergillosis following different surgical procedures.

The first case reported in the literature

In 1933, a female aged 14 years underwent surgery for an abdominal tumour [7]. After 16 days, the dressing was removed and an ulcer was observed. There were no systemic manifestations of the infection, but *Aspergillus niger* grew in the surgical dressings, which were covered with a 'dark powder'. It was speculated that contamination may have occurred in the operating room, and the authors commented on two previous similar cases of wound aspergillosis in the same medical centre, each exhibiting similar pustulation confined to the area of the gauze dressing, and with rapid healing after local treatment with iodine and alcohol.

Endocarditis, aortitis and other presentations of aspergillosis following cardiac surgery

Table S1 (see Supplementary material) summarises some clinical details for 124 patients with *Aspergillus* endocarditis or aortitis following heart surgery [4,8–91]. The median age of these patients was 43.5 (range 0.8–71) years. Most of the surgical procedures involved the aortic (60.5%) or mitral (30.6%) valve, and no particular prosthesis was associated with the infection. Male patients predominated (69.9%), which may be related to the higher prevalence of coronary and aortic valve surgery in males than in females. The incubation period was variable, with a mean time from surgery to the diagnosis (often following autopsy) of 2.7 (range <1 to >12) months. Two cases [43,88] had possible incubation periods of several years; silent *Aspergillus* fungaemia with late endocarditis is possible in such cases, although there is no direct evidence for such a diagnosis. Forty additional cases were cited in other studies, but without detailed information [92–111], and at least ten additional cases were reported in languages other than English [112–120].

Notably, almost none of the patients were immunosuppressed, and there was no evidence of bronchopulmonary aspergillosis. The post-operative course of these patients was usually consistent with culture-negative endocarditis. Unusual presentations of aspergillosis following heart surgery included osteochondritis and/or

osteomyelitis after sternotomy [78,121–125], and saphenous vein thrombosis [126] or rupture [127] after coronary by-pass surgery.

Aspergillus fumigatus was the aetiological agent in only 58.7% of cases confirmed by culture. Other important species were *Aspergillus terreus* (12.5%), which is resistant to amphotericin B, *A. niger* (11.2%) and *Aspergillus flavus* (11.2%). Most reports associated the infection with contaminated grafts, contaminated sutures or intra-operative dispersion of spores. The prevention of such infections will be considered below.

The difficulty in establishing the diagnosis of *Aspergillus* endocarditis is well-known, since the fungus is isolated infrequently from blood cultures. Only eight cases of post-operative aspergillosis associated with a positive blood culture (6.4% of cases) were found in the literature [11,12,14,36,38,46,61,87]. Pre-autopsy diagnosis was made in only 43.5% of cases. In the vast majority of cases, surgical intervention was crucial in obtaining a definitive diagnosis, often following examination of either the valve (23.4%) or emboli to large peripheral arteries (16.9%). Unfortunately, some surgical specimens were not sent for culture. The diagnosis of *Aspergillus* aortitis is also made more difficult because of the localisation of the infection and the absence of endocarditis vegetation; this condition is therefore often undetected by both trans-thoracic and trans-oesophageal echocardiography. Computed tomography scan, magnetic resonance imaging and angiography might be more helpful for the diagnosis of such cases.

The overall mortality rate was 92.7%. In addition, 83.0% of patients who had an ante-mortem diagnosis died, and a high mortality rate (80.9%) existed even among patients treated with a surgical intervention in the affected valve. This might be related to a delayed diagnosis, which gives the fungus the opportunity to establish large vegetations, to cause extensive local necrosis, and eventually to embolise to large arteries. Many of the patients who underwent valve replacement died during surgery or a few days later. These results indicate an unequivocal need for better diagnostic methods for this condition. At the present time, the role of antibody tests and molecular tests of blood samples has not been properly investigated. In one report, a false-negative galactomannan result occurred for a

patient with non-surgical *Aspergillus* endocarditis, despite a positive blood culture for *A. fumigatus* [128].

Wound infections

For patients with post-operative wound infection caused by *Aspergillus* spp., the interval between surgery and infection is measured in days, rather than the months required for endocarditis (Table S2, see Supplementary material) [5,87,129–143]. In addition, many patients with wound aspergillosis were immunosuppressed, with half of the cases occurring in solid-organ transplant recipients. As this condition can progress to profound or disseminated infection, all patients need to be treated aggressively with combined medical and surgical therapy. *A. flavus* is a particularly important species in wound aspergillosis, accounting for 41.2% of cases confirmed by culture.

Chronic lung disease was the only independent risk-factor for *A. fumigatus* sternal wound infection after open-heart surgery in a case-control study [144]. *A. fumigatus* was grown simultaneously from the bronchial washings of one patient, suggesting that colonised patients may be at increased risk for these infections. In another study, a cluster of four cases of surgical and burn wound aspergillosis was associated with the outside packages of dressing supplies, which had become contaminated during hospital construction work [145]. This resulted in patients with large exposed vulnerable surface areas being inoculated directly with *Aspergillus* spores. When outbreaks of cutaneous aspergillosis occur, wound dressing and tape should be cultured [146,147]. Cases of *A. flavus* sternal wound infection coinciding with hospital renovation activities have also been reported [148].

Neurosurgery

Involvement of the central nervous system in aspergillosis may occur via haematogenous dissemination (usually from the lungs), or by direct extension from nasal or paranasal foci [149]. Table S3 (see Supplementary material) summarises the published literature concerning aspergillosis following neurosurgical procedures [150–168]. In contrast to *Aspergillus* endocarditis, male patients were not over-represented in neurosurgical infections (44.0%). Previous treatment with cortico-

steroids was mentioned in 52.0% of the reports, including patients receiving regimens of pulse therapy, high-dose regimens for periods of weeks to months, and even physiological steroid replacement therapy. The median time from surgery to diagnosis was 3 (range <1 to >12) months. All proven cases were caused by *A. fumigatus*. As shown in Table S3, different presentations of the infection can occur, including meningitis, central nervous system abscesses, mycotic aneurysms and cerebral infarction. Many cases were associated with *Aspergillus* contamination from paranasal sinuses, particularly following trans-sphenoidal surgery.

An ante-mortem diagnosis was performed in 68% of cases, which was a proportion considerably higher than that for cases of *Aspergillus* endocarditis. Most of these cases were diagnosed after abscess drainage (36%), and 20% of patients had a cerebrospinal fluid culture positive for *Aspergillus*. In some cases, a culture positive for *Aspergillus* was considered to be contamination, which was associated with delayed treatment, sometimes with a fatal outcome. All patients who survived received combined aggressive clinical and surgical therapy. The overall mortality rate was 68.0%, which is surprisingly low in comparison with mortality rates of >90% for immunosuppressed patients with disseminated aspergillosis involving the central nervous system. This may reflect an earlier diagnosis, facilitated by imaging techniques, in association with aggressive neurosurgical intervention. Furthermore, dexamethasone therapy could be withdrawn for many of these patients, unlike the situation for patients with more permanent immunosuppression.

Dental surgery

A number of studies have reported a connection between endodontic treatment and non-invasive sinus aspergillosis, mainly in the presence of obturating pastes within the maxillary antrum [169–183]. Experiments with fungal cultures have revealed accelerated growth of *Aspergillus* spp. in the presence of zinc oxide in the culture medium [182]. With respect to treatment, it is necessary to remove surgically the fungal masses in the sinuses, and especially all zinc-containing radiopaque material, and to ensure establishment of adequate sinus drainage and aeration [178,181].

Systemic antifungal agents are generally not recommended to complement the surgical procedure unless there are signs of local invasion [181].

Ophthalmological surgery

Ocular aspergillosis usually presents as keratitis, and rarely as endophthalmitis [92,184–187]. Post-operative infections have been described following penetrating keratoplasty [188–190], radial keratotomy [191–194], excimer laser photorefractive keratectomy [195], laser-assisted in-situ keratomileusis [196–199], pterygium excision [200,201], hydroxyapatite orbital implant surgery [202], cataract surgery [179,184,203–212], scleral buckling procedures [213,214], sutureless surgery [215,216] and trabeculectomy [204,217]. Sampling at the site of infection provides the best chance for obtaining a positive culture [196,218–220]. While some cases of *Aspergillus* endophthalmitis and keratitis have been associated with hospital construction [209,221], others have been linked to contaminated irrigating fluids used during surgery [208]. Many cases of *Aspergillus* keratitis and scleritis following non-surgical corneal trauma have also been reported [209,222–248], frequently in farmers. The efficacy of the antifungal therapy depends to a great extent on the ability of the compound used to penetrate the eye [219,249].

Orthopaedic surgery

A male aged 64 years underwent hip replacement surgery and was admitted after a 9-year interval because of progressive hip pain [250]. *A. niger* grew from aspirated hip fluid, and the patient was treated with amphotericin B and prosthesis replacement. Two cases of aspergillosis following laminectomy were also reported in the same publication. In another report, *A. fumigatus* spondylodiskitis occurred 2.5 months after lumbar disk surgery, and the patient was treated with itraconazole in combination with surgical debridement [251]. Other cases following lumbar surgery have also been reported [252–254].

In a prospective study of 658 consecutive total hip arthroplasty procedures in which cultures were taken at surgery, *Aspergillus* was recovered in 4.1% of cases, and *Aspergillus* was also cultivated from the air in the operating theatre [255]. In another report, a male aged 22 years developed *Aspergillus* osteomyelitis after a closed fracture of

the femur and subsequent surgery [256]. Another male, aged 16 years, developed infection with *A. flavus* following surgery for a fracture of the femur. The infection was associated with pressure and necrosis caused by casts [257]. The first case of aspergillosis complicating total knee arthroplasty was described in a male aged 80 years who was receiving chronic corticosteroid therapy [258]. This patient presented with a popliteal cyst 27 months after surgery, and was cured with a 12-week course of amphotericin B in combination with surgical debridement and prosthesis removal. Other similar cases have been described in the literature [259,260].

Bronchopulmonary surgery

Bronchial stump aspergillosis, i.e., *Aspergillus* infection of bronchial granulation tissue surrounding endobronchial sutures after pulmonary resection, is a rare clinical presentation of *Aspergillus* infection [261–267]. This condition is more common when silk thread is used as the suture material rather than stainless steel [268,269], and should be considered in the differential diagnosis of haemoptysis, coughing and dyspnoea occurring up to several years after lung surgery, although asymptomatic presentation is also possible [262–264,269]. *Aspergillus* suture granuloma may simulate recurrent neoplastic disease in patients undergoing resection for pulmonary cancer [270]. Although no comparative studies exist, removal of the silk suture is probably the key therapeutic intervention for this condition.

An association between the presence of saprophytic fungi in the bronchial anastomosis and the occurrence of serious airway complications following lung transplantation has been proposed [271]. The ischaemic and necrotic airway debris at the bronchial anastomosis provides a fertile environment for *Aspergillus* proliferation. Several reports have also described an increased risk of complications as a consequence of post-transplantation saprophytic *Aspergillus* disease [272–275]. The source of these infections has not been well-studied, but may be related to either colonisation of the diseased or transplanted lungs, or to direct perioperative acquisition.

Pleural aspergillosis has been reported as an iatrogenic complication of lung adenocarcinoma resection [276]. A 14-day course of intravenous caspofungin failed to sterilise the cavity, and

the patient was treated with a combination of intra-pleural and systemic amphotericin B lipid complex.

Infection of vascular prosthesis

Glotzbach [277] seems to have been the first to describe *Aspergillus* infection of a vascular prosthesis in 1982, and this was followed by the report of an immunocompetent patient, aged 73 years, with aortic pseudoaneurysm and contiguous vertebral osteomyelitis, who was treated with graft resection and amphotericin B [278]; as in the previous case [277], this patient presented with back pain *c.* 2 years after surgery. In a study of 14 cases of fungal graft infections [279], only four were caused by *Aspergillus* spp.

Aspergillus graft infections usually occur on the suture line of a previous aortotomy [280]. Definitive diagnostic procedures for these patients generally involve culture of the excised aortic graft or the peripheral embolus, and biopsy of the contiguously affected vertebral disk space [277,281–284]. As with endocarditis, almost all cases have involved immunocompetent males [277,278,281–290]. The median time from the placement of the graft to diagnosis is 8 months, which is a longer period than that for *Candida* graft infections (usually <6 weeks) [279]. Fever is absent in about one-half of the cases. One report associated in-situ replacements or treatment without excision of the infected graft with recurrence and death in all cases, whereas all patients who underwent an extra-anatomical by-pass through a clean field survived [279]. No difference seems to exist between the clinical presentations of fungal and bacterial vascular prosthesis infections, particularly when *Staphylococcus epidermidis* is involved [291].

Abdominal surgery

Multiple abdominal visceral infection by *A. fumigatus* occurred in a female aged 37 years after laparostomy for Crohn's disease [292]. The patient was treated successfully with a 4-week course of amphotericin B. Sampling of air from the patient's environment yielded one isolate of *A. fumigatus* that matched the patient's isolates, suggesting that this patient acquired the infection from air in the intensive care unit. Peritoneal aspergillosis has also been reported following laparotomy in non-trans-

plant patients [4,293,294], and *Aspergillus* cholangitis complicating portoenterostomy for a biliary atresia has also been reported [295]. A case of *A. flavus* renal pelvis infection, following a pyelolithotomy, has been described, with *Aspergillus* around the suture material [296]. Post-operative cases of wound infection [87,138,139,141–143,297], peritonitis [297,298] and renal allograft infection [299] have also been described following solid-organ transplantation. Although not always apparent, it is possible that some of these patients had occult foci from which the *Aspergillus* may have disseminated [299–325].

Mediastinitis

Aspergillus mediastinitis in surgical patients has been described in association with deep sternal wound infection [4,123,125,326], heart transplantation [326–329], aortitis [4,46] and patch infection after repaired tetralogy of Fallot [113]. Two immunocompetent patients were also affected during an outbreak of aspergillosis related to a contaminated air-handling system [4]. The importance of considering aspergillosis in the differential diagnosis of slowly progressive, but destructive, wound infections and culture-negative mediastinitis after cardiac surgery has been emphasised.

Breast surgery

Fungal infections of the soft tissue have been reported in association with prosthetic breast implants [330–333]. A healthy female, aged 39 years, with bilateral inflatable silicone breast implants was colonised by *A. niger* as a possible consequence of massive contamination during surgery [331]. *A. flavus* was also cultured from a saline-filled implant removed from a healthy young patient who developed unilateral breast inflammation 4 years after surgery [332]. It has been shown that fungi can grow and reproduce in a saline-only environment, and that their survival periods differ among species [334–336]. Colonisation of a tissue expander by *A. niger*, resulting in mechanical obstruction of the device, has also been described [337].

Linking the infection with the operating theatre

Many studies have associated the occurrence of post-operative aspergillosis with the dissemin-

ation of *Aspergillus* spores in the operating theatre. In one investigation, pigeon excreta and moss in the immediate vicinity of the ventilator intake port were found to harbour large numbers of *Aspergillus* spores [14]. Similarly, *Aspergillus* was isolated from all areas of the theatre suite in another study [38], except in a room fitted with laminar airflow. Air-conditioner cooling coils and pigeon droppings on the ledges outside the suite were found to harbour large numbers of *Aspergillus* spores.

Environmental studies conducted during an outbreak of *A. flavus* sternal infection [123] revealed massive fungal contamination in some areas of the surgical ward [338]. When isolates from patients and from the environment were typed, the same genotype was detected, implicating a single clonal source for the environmental contamination and intra-operative acquisition of *A. flavus*. Diaz-Guerra *et al.* [339] reported the simultaneous isolation of an *A. flavus* isolate from the aortic prosthesis of a heart surgery patient and two isolates from a dual-reservoir cooler-heater used in the operating theatre where this patient received surgery. Genetic typing of these isolates by random amplified polymorphic DNA analysis revealed identical genotypes, indicating the nosocomial origin of the strain. Similar results were reported in another investigation [51], and during an epidemiological investigation of cases of *Aspergillus* aortitis following cardiac surgery [46], high concentrations of *A. fumigatus* were found in the ventilation system and on the floor of the surgical suite.

Prevention

Most modern operating theatres have conventional ventilation and filters that remove airborne particles $\geq 5 \mu\text{m}$ [340]. However, these filters are not sufficient to remove *Aspergillus* spores (2.5–3.0 μm in size). Laminar airflow systems and HEPA filtration will remove airborne particles $\geq 0.3 \mu\text{m}$ with 99.97% efficiency. These systems are generally used in orthopaedic and other implant surgery [341], as well as in protective environments for high-risk patients [342–347]. Theoretically, these systems are more effective in preventing post-operative aspergillosis, but data demonstrating a survival benefit for patients are lacking [348,349]. Furthermore, these systems are limited by the expense of construction and maintenance, and by a lack

of consensus concerning the level of airborne conidia at which the risk can be numerically defined for aspergillosis [340].

Since outbreaks of post-operative aspergillosis have occurred occasionally in units with HEPA filters [78], periodic maintenance of ventilation systems seems to be warranted [38,346,350]. Some of these incidents were caused by contamination of insulation in variable airflow volume units that had deteriorated after becoming wet. As fungi can inhabit water distribution systems and may cause nosocomial infection, tap water should not be used on surgical wounds. However, larger controlled studies are needed to determine the role of water in the transmission of aspergillosis [2,3]. The patients may also be their own source of infection in some circumstances [159], as has been demonstrated for staphylococcal infections. Prevention of post-operative aspergillosis requires proper disinfection techniques, as well as appropriate storage of surgical materials. A single proven post-operative case of aspergillosis should be sufficient to initiate epidemiological investigations.

CONCLUSIONS

Post-operative aspergillosis seems to be an underappreciated problem, particularly when compared with other extra-pulmonary manifestations of invasive aspergillosis. Mortality is high for non-cutaneous infections. Several organs and surgical procedures may be involved, depending on the surgery performed. These infections are usually indolent, in some cases occurring several months after surgery. In most patients, the source of the spores seems to have originated from the air during surgery, but contamination from paranasal sinuses, bronchopulmonary lesions, haematogenous dissemination and contaminated grafts is also possible. In order to improve the outcome, better diagnostic methods are needed. Infected patients should receive aggressive combined medical and surgical therapy. Prevention of these infections should include special care of the ventilation system in the operating theatre and adequate sterilisation techniques.

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SUPPLEMENTARY MATERIAL

The following supplementary material is available for this article online at <http://www.blackwell-synergy.com>:

Table S1. Case reports of post-operative endocarditis/aortitis caused by *Aspergillus* spp.

Table S2. Case reports of wound infections with *Aspergillus* spp. following surgical procedures.

Table S3. Case reports of central nervous system infections with *Aspergillus* spp. following neurosurgical procedures.

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