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Invasive nosocomial pulmonary aspergillosis: risk factors and hospital building works

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SUMMARY

A retrospective epidemiological study of 22 observations of invasive pulmonary aspergillosis, of which 18 were fatal, occurring over a period of 30 months, implicated certain building sites within the hospital. The building works were responsible for the diffusion into the atmosphere of fungal spores from normally closed reservoirs, notably false ceilings, fibrous thermal and/or acoustic insulation materials and roller-blind casings. The results of our study permit us to suggest that protective measures should be set up or that immunodepressed patients are evacuated when such works are to be carried out in an in-patient establishment.

INTRODUCTION

Modern chemotherapy has considerably improved the prognosis of patients with some potentially fatal diseases. Unfortunately, the immunodepression caused by such treatment favours opportunist infections which are sometimes fatal; 30% of such infections are mycoses (Leclerc *et al.* 1982). In more than 90% of cases, the etiological agent is a *Candida* or *Aspergillus* (Leclerc *et al.* 1982), the latter being found seven times more frequently than *Candida* in leukaemic patients.

Invasive nosocomial pulmonary aspergillosis (INPA), generally due to *Aspergillus fumigatus*, is often fatal. The spores penetrate via the pulmonary tract (Prytowski *et al.* 1976; Krick & Remington, 1976) from different reservoirs amongst which ventilation and air-conditioning systems seem to play an important role (Krick & Remington, 1976; Sayer, Shean & Ghosseliri, 1969; Burton *et al.* 1972; Mahoney *et al.* 1979). However, this means of entry is not the only one, and more rarely contaminations can arise from the digestive tract, the skin and the nasopharynx (Prytowski *et al.* 1976; Krik & Remington, 1976).

Following 22 cases of INPA, of which 18 were fatal, in the haematology department in Lyon amongst leukaemic patients in medullary aplasia, we looked for possible spore reservoirs. The absence of an air-conditioning system led us to focus our attention on demolition work being undertaken in the hospital over this period. This study was guided in particular by our knowledge of the work

Table 1. *Patients covered by the study*

Number order	Sex	Age	Haematological diagnosis	INPA diagnostic method			Date of diagnosis	Outcome of INPA
				Sputum	BAL	Histology		
1	F	32	ALL	+	0	+	Aug. 1982	Fatal
2	F	27	AML	0	+	+	Nov. 1981	Fatal
3	M	49	AML	−	0	+	Nov. 1981	Fatal
4	F	32	AML	0	0	+	Nov. 1981	Fatal
5	F	35	SP	0	+	+	Jan. 1982	Fatal
6	M	16	AML	0	+	+	Feb. 1982	Fatal
7	M	45	AML	+	+	0	Mar. 1982	Favourable
8	F	55	CLL	0	0	+	Mar. 1982	Fatal
9	M	67	AML	−	−	+	Apr. 1982	Fatal
10	M	58	AML	0	+	+	Apr. 1982	Fatal
11	M	39	CML	+	−	+	May 1982	Fatal
12	M	71	AML	0	+	0	May 1982	Fatal
13	F	40	AML	0	+	0	June 1982	Favourable
14	F	21	AML	0	+	0	June 1982	Fatal
15	M	17	ALL	+	+	0	Aug. 1982	Favourable
16	F	52	AML	0	+	+	Nov. 1982	Fatal
17	M	19	AML	0	+	+	Feb. 1983	Fatal
18	M	45	AML	0	+	0	Feb. 1983	Favourable
19	M	31	Myeloma	0	+	0	Feb. 1983	Fatal
20	F	51	AML	0	+	0	Apr. 1983	Fatal
21	F	58	AML	0	+	0	Aug. 1983	Fatal
22	F	39	Nodular lymphoma	0	+	0	Aug. 1983	Fatal

bal, Broncho-alveolar lavage; ALL, acute lymphoblastic leukaemia; AML, acute myeloblastic leukaemia; CLL, chronic lymphoid leukaemia; CML, chronic myeloid leukaemia; SP, paramyelosis secondary to an anaplastic carcinoma of the breast; 0, examination not performed.

performed by Aisner *et al.* (1976) and Arnow *et al.* (1978), who had indicated the role played by certain construction materials as a reservoir of *Aspergillus* spores.

METHODS AND RESULTS

The observations

Between 1 July 1981 and 31 December 1983, 22 cases of INPA were observed in the haematology department of the Edouard Herriot Hospital, Lyon, France. Table 1 shows that there was no predominance according to sex, and the age distribution was comparable (median age of women 39 years, of men 45 years). Fifteen patients suffering from acute myeloblastic leukaemia formed the largest group of INPA subjects.

The association of other organisms with *Aspergillus* was important; *Candida albicans* occupied first place, followed by *Staphylococcus epidermidis*. This was not surprising, as all these patients, under antimitotic chemotherapy, were in medullary aplasia with a leukocyte count of less than $0{\cdot}5 \times 10^9/l$.

The outcome was fatal in 18 of the 22 cases. In half of these death occurred in less than 3 weeks. We saw a clinical picture of progressive respiratory insufficiency, with invasion of the entire pulmonary parenchyma visible on successive radiographs. Three of the four patients who survived had another associated

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Table 2. *Diagnosis of pulmonary aspergillosis in 22 patients*

In 18 cases: isolations of *A. fumigatus* during the patient's life
- 16 times in BAL
  - 4 had favourable evolution
  - 6 were confirmed by pathology
  - 6 died without necropsy
- Twice in sputum – 2 confirmed by pathology alone

In 4 cases: post-mortem diagnosis alone (septate hyphae in lungs)

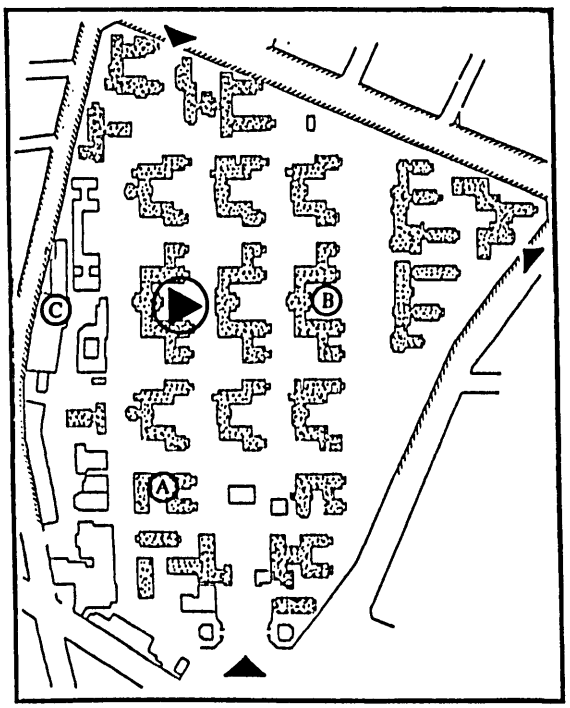

Fig. 1. Hospital plan. □, Technical, administrative and general services: ⊠, in-patients' units.

infection: staphylococcal septicaemia, legionellosis and candidosis. Antimycotic treatment always employed venous amphotericin B (cases 2, 4, 5, 7, 10, 11, 12, 13 and 14), associated with either 5-fluorocytosine (cases 6, 15, 21 and 22) or ketoconazole (cases 9, 16, 18, 19 and 20).

A diagnosis of pulmonary aspergillosis was based on positive broncho-alveolar lavage or sputum culture (Sabouraud's medium) for *A. fumigatus* (18/18), and/or presence of septate hyphae at necropsy performed within 24 h after death (12/18) (Table 2). In 12 out of 22 cases, therefore, diagnosis of pulmonary aspergillosis was based on, or confirmed by pathology, whilst in 10 out of 22 cases broncho-alveolar lavage alone was positive.

The buildings

The hospital (see Fig. 1) is built on a pavilion or block principle. The buildings where works were being carried out and which were considered in our study were

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Table 3. *Wilcoxon table summarizing the number of months during which 0, 1, 2 or 3 new INPA cases were seen, according to the presence or absence of building works in the hospital*

Frequency of new cases	0	1	2	3	Month	Total
With works	7	3	4	1	16	17
Without works	10	3	1	0	14	5
Total	17	6	5	2	30	22

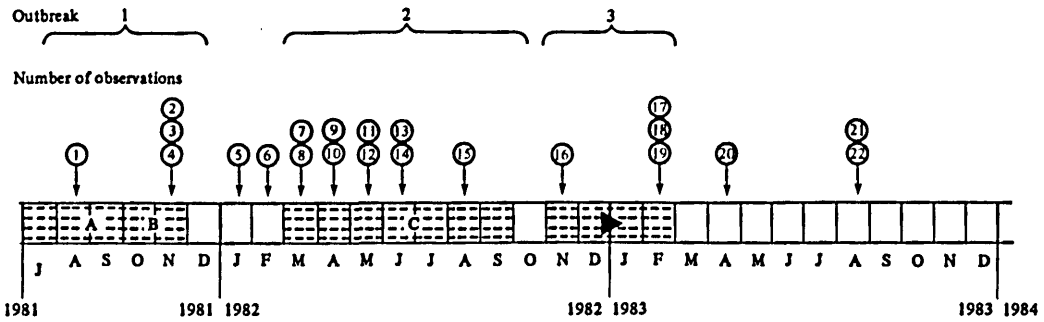

Fig. 2. Chronological order of the appearance of 22 cases of INPA covered by the investigation according to the presence of building works in the hospital. (Hatched zones correspond to periods with works. The blocks concerned are shown in the corresponding hatched zone by their identification symbol as shown in Fig. 1.)

two in-patient blocks, labelled A and B, the heating plant C, and the haematology block itself, indicated on the plan by an arrow.

The clinical haematology department treats adults and consists of a standard in-patient unit and a semi-controlled unit, access to which requires a certain number of precautions (sterile gown, mask, cap, hands washed in antiseptic soap), which is reserved for patients in medullary aplasia.

This department has no air-conditioning, either centralized or individual. Ventilation is natural, via the doors and windows.

Epidemiological investigation

Our retrospective epidemiological investigation covered 30 months (July 1981 to December 1983) during which period 22 cases of INPA were seen. Diagnostic methods for INPA, its treatment and the chemotherapeutic procedures employed did not change significantly over this period. Further, the number of patients in medullary aplasia was more or less constant.

Study of the building works programme within the hospital during these 30 months led us to identify three periods during which work was carried out on the demolition of ducts and false ceilings, the removal of fibrous thermal insulating materials (glass fibre) and work on roller-blind casings, all of which may have freed spores into the atmosphere.

1st period. July–November 1981 (5 months): demolition of ducts and false ceilings during the complete renovation of Block A and one department in Block B. Both blocks are situated 120–150 m from the haematology block.

2nd period. March 1982 to September 1982 (7 months): renovation of the

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heating plant C, situated 60 m from the haematology block, including the removal of large quantities of insulating material.

3rd period. November 1982 to January 1983 (3 months): renovation work in the haematology block itself, with demolition of false ceilings and renovation of roller blinds.

The total of 15 months of work yielded 17 new cases of INPA (average: 1·13 cases per month), whilst the four periods without works covered 14 months and only 5 new cases of INPA were seen (average: 0·35 cases per month). Using the Wilcoxon test, this differs significantly ($P = 0{\cdot}048$) (Table 3). The chronology of new cases and their monthly number with reference to the works programme is shown schematically in Fig. 2.

The works considered were, by their nature, those likely to have freed fungal spores into the atmosphere. Other works undertaken have not been considered as they consisted of simple upgrading without demolition works.

Air sampling was performed in the haematology department in June and September 1982 (Piens *et al.* 1983), then in November 1982 and in February 1983 (unpublished results). There were no significant differences in the number of *A. fumigatus* spores in the air. No air sampling was performed outside the hospital buildings.

DISCUSSION

Similar observations have been made in other hospitals, particularly in the United States, establishing a direct link between cases of INPA seen in patients in medullary aplasia and building or road construction works in and around the hospital, responsible for freeing dusts and fungal spores into the atmosphere (Arnow *et al.* 1978; Sarubbi *et al.* 1982; Lentino *et al.* 1982; Streifel *et al.* 1983).

In another hospital, the ventilation ducts and insulation materials in the false ceilings were responsible for the increase of aspergillosis, as these materials represented an excellent support for the development of *A. niger* (Aisner *et al.* 1976).

The prevention of these particularly dangerous infectious complications – the mortality of these types of aspergillosis reaches more than 80% – requires, when demolition works are to be undertaken nearby, either the hospitalization of subjects in medullary aplasia in isolated rooms with filtered and sterile ventilation systems (Rose, 1972), or the transfer of these patients to another hospital if such facilities are not available. Further, it should be possible to verify and clean air-conditioning systems without the risk of pollution and release of fungal spores.

The chemoprophylaxis of pulmonary aspergillosis is difficult, and trials of ketoconazole disappointing (Tricot *et al.* 1987).

In conclusion, the dangers of demolition and repair work which releases dust loaded with fungal spores into the atmosphere should be recognized. Patients in medullary aplasia are particularly at risk from this danger. Invasive pulmonary aspergillosis is the main manifestation.

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