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Rapid diagnosis of an outbreak of legionnaires' disease at Glasgow Royal Infirmary

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ABSTRACT In the last three months of 1985 there was an outbreak of legionnaires' disease at Glasgow Royal Infirmary affecting 15 patients and one surgeon; five patients died. Legionnaires' disease was first suspected when a second case of severe nosocomial pneumonia occurred in a high dependency unit. The application of the direct fluorescent antibody test to specimens obtained at bronchoscopy was responsible for the rapid diagnosis of legionnaires' disease, which led to the prescription of appropriate antibiotic treatment and the shutting down of the contaminated cooling tower, thereby containing the outbreak. It also led to a search for further cases. It is suggested that these diagnostic techniques should be included in the investigation of affected patients in an outbreak of pneumonia.

Legionnaires' disease is an important cause of outbreaks of nosocomial pneumonia,[1] some outbreaks of which have been associated with a high mortality rate.[2] *Legionella pneumophila* serogroup (SG) 1 is responsible for most cases. Such outbreaks are usually related to contamination of water or cooling towers of ventilation systems by *L pneumophila*; thus it is of great importance to establish whether an outbreak of pneumonia is caused by *L pneumophila*, so that prompt measures can be taken to identify the source, eradicate the organism, and thereby halt the outbreak. Rapid diagnosis led to the early containment of a recent outbreak of legionnaires' disease at Glasgow Royal Infirmary, details of which are given elsewhere.[3]

Methods

Glasgow Royal Infirmary is a teaching hospital with 918 beds. The infirmary has two buildings, one of traditional Victorian design and a new four floor building opened in 1983. Levels 3 and 4 contain respectively the peripheral vascular and cardiothoracic surgical units.

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DIAGNOSIS OF LEGIONNAIRES' DISEASE

Bronchial aspirates and sputum samples were examined by a direct fluorescent antibody test with monoclonal antibody to *L pneumophila* SG1. These samples were also cultured on buffered charcoal yeast extract agar with and without added antibiotics and incubated at 37°C in the presence of 5–10% carbon dioxide. Plates were examined daily for one week. Serum samples were assayed by the indirect fluorescent antibody test.[3] A diagnosis of legionnaires' disease was made if one of the following criteria was met: (1) *L pneumophila* SG1 present in respiratory secretions (culture or direct fluorescent antibody test); (2) a fourfold rise in antibody titre to *L pneumophila* SG1; (3) a convalescent antibody titre to *L pneumophila* SG1 of $\geqslant 256$.

Results

The diagnosis of nosocomial legionnaires' disease was first contemplated on 1 November, when a second case of severe postoperative pneumonia occurred in the high dependency area of the vascular surgery unit. Serum and respiratory tract secretions were obtained from both patients for *Legionella* serological tests and culture respectively. On 2 November three further patients with pneumonia were identified in the same unit and one of the initial patients died. Sputum from

Table 1 *Diagnosis of 16 cases of legionnaires' disease, 1985*

Patient No	Direct fluorescent antibody test for L pneumophila serogroup 1			Culture for L pneumophila serogroup 1		Serum antibody titre to L pneumophila serogroup 1			
						First sample obtained		Earliest sample giving diagnostic	
	Specimen	Date	Result	Result	Days taken for culture	Date	Titre	Date	Titre
1	Tracheal aspirate Bronchial lavage	1 Nov 4 Nov	Negative Negative	Positive Positive	5 4	31 Oct	<16	No diagnostic titre obtained	
2	Sputum Post mortem lung	1 Nov	Positive Positive	Positive Positive	3 5	31 Oct	<16	No diagnostic titre obtained	
3	Sputum	2 Nov	Positive	Positive	5	4 Nov	<16	11 Nov	64
4	Bronchial lavage	2 Nov	Positive	Positive	3	4 Nov	<16	11 Nov	512
5	Bronchial lavage	2 Nov	Positive	Positive	3	4 Nov	<16	8 Nov	128
6	Bronchial lavage	3 Nov	Negative*	Negative*	—	7 Nov	256	7 Nov	256
7	Bronchial lavage Sputum (28/10/85)	3 Nov 4 Nov	Positive NT	Negative Positive	— 2	1 Nov	256†	1 Nov	256†
8	Bronchial lavage	3 Nov	Positive	Negative	—	4 Nov	<16	19 Nov	32
9	Tracheal aspirate	4 Nov	Positive	Negative	—	4 Nov	<16	No diagnostic titre obtained	
10	Bronchial lavage	5 Nov	Negative	Positive	3	5 Nov	<16	No diagnostic titre obtained	
11	—	—	—	—	—	15 Nov	256	15 Nov	256
12	—	—	—	—	—	4 Nov	256	4 Nov	256
13	—	—	—	—	—	4 Nov	<16	12 Nov	256
14	—	—	—	—	—	2 Dec	2048	2 Dec	2048
15	—	—	—	—	—	29 Nov	256	29 Nov	256
16	—	—	—	—	—	4 Nov	<16	13 Nov	64

*Unsatisfactory specimen.
†Result of test with heat killed antigen.[4]
‡indirect fluorescent antibody test with formalin-killed agar grown antigen.
NT—not tested.

patients 2 and 3 (table 1) was thought possibly to be positive for *L pneumophila* on examination by the direct fluorescent antibody test; but in patients 4 and 5, who underwent fibreoptic bronchoscopy, *L pneumophila* SG1 was identified without doubt by the direct fluorescent antibody test in the bronchial lavage samples. This established the existence of an outbreak of legionnaires' disease at the Royal Infirmary and led to action to define and contain the outbreak.

A search of the new building for patients with pneumonia was made and by 4 November a total of seven cases of legionnaires' disease had been diagnosed by the direct fluorescent antibody test from bronchial aspirates (five cases) and sputum (two cases). These patients had all been nursed in the high dependency units on the third and fourth floors of the new building; these areas had been closed on 2 and 3 November respectively and the use of the new building was restricted to emergency admissions only. Over the next four days a further four cases were diagnosed, two by culture and two by serology. In addition, a member of the medical staff who had been resident in one of the high dependency units was shown on serological investigation to have had legionnaires' disease. Some weeks later a diagnosis of legionnaires' disease was made by serology in four patients who had been discharged from the affected areas of the Royal Infirmary; three had had mild respiratory symptoms but one had been symptom free.

The direct fluorescent antibody test confirmed the clinical diagnosis, within a few hours, in seven patients. Cultural confirmation was obtained within two to four days in seven patients. Serological study of blood samples from the first 10 patients at time of diagnosis was, in general, unhelpful; results of microbiological investigations are summarised in table 1.

Details of the individual cases are given in table 2. With the exception of the staff member (case 11) and one medical patient (case 10), all patients had recently undergone major surgery. The four patients who were discovered after discharge from hospital to have been infected are shown in the lower part of the table (cases 13–16).

The antibiotics used in this outbreak and their daily dosages were erythromycin 4 g, ciprofloxacin 800 mg, and rifampicin 1·2 g; patient 2 received only erythro-

Table 2 *Details of 16 patients with legionnaires' disease**

Patient No	Age	Sex	Operation	Outcome
1	71	M	Aorta biprofundoplasty	Died
2	57	M	Patch angioplasty to aortic bifurcation graft	Died
3	63	M	Extension to aortic bifurcation graft	Died
4	59	M	Aortic bifurcation graft	Survived
5	70	F	Aortic bifurcation graft	Survived
6	60	M	Coronary bypass graft	Survived
7	57	M	Coronary bypass graft	Died
8	66	F	Aortic bifurcation graft	Survived
9	67	M	Resection of abdominal aortic aneurysm	Died
10	58	M	None; polyarthritis: having prednisolone 50 mg daily	Survived
11	27	M	None; staff member sleeping in affected area	Survived
12	64	M	Aortic bifurcation graft	Survived
13	65	F	Aortic bifurcation graft	Survived
14	60	F	Mitral valve replacement	Survived
15	59	F	Mitral valve replacement; coronary bypass graft	Survived
16	56	M	Coronary bypass graft	Survived

*Cases 13–16 were diagnosed serologically after discharge.

mycin, patient 10 received erythromycin with ciprofloxacin, and seven patients were treated with a combination of all three drugs. Patients 6, 11, and 12 received a course of erythromycin even though they were already recovering from their pneumonia.

Five patients died. Patient 2 had fulminating disease and died 48 hours after the first clinical suspicion of pneumonia; patients 1 and 7 had required intermittent positive pressure ventilation for six and four days respectively before the diagnosis was made and both had renal failure. Patients 3 and 9 received erythromycin, ciprofloxacin, and rifampicin within 24 hours of becoming dependent on a ventilator; patient 3 died from the adult respiratory distress syndrome rather than from the infection per se, and patient 9 made a good recovery from pneumonia but suffered a fatal pulmonary embolism.

A search of hospital records of patients who had died of pneumonia or respiratory failure of unknown aetiology some weeks before the outbreak, revealed a case in September 1985. This patient developed fever, bilateral pulmonary infiltrates, and respiratory failure after coronary artery surgery; an initial diagnosis of the adult respiratory distress syndrome was made at necropsy. The diagnosis of legionnaires' disease was established late in November by the demonstration of *L. pneumophila* SG1 by direct fluorescent antibody test in postmortem lung tissue. Review of the notes suggest that the infection was acquired in hospital.

Discussion

This was, in many ways, a typical nosocomial outbreak of legionnaires' disease. It affected predominantly surgical patients who after operation had been housed in high dependency areas of the peripheral-vascular and cardiothoracic units. Some cases were recognised only as a result of a deliberate search. Of the 12 patients who developed the disease while in hospital in the Royal Infirmary, all had pneumonia, and four showed the multisystem disease reported by others.[5] Most were men, probably reflecting the preponderance of men admitted to the peripheral vascular and cardiothoracic surgical units. Two patients were immunocompromised; patient 3 had undergone splenectomy in the past and patient 1 was receiving prednisolone for polyarteritis. The remaining patients may have been vulnerable to infection by the respiratory route because they had recently had anaesthetics for major surgery. In addition, all of these patients received prophylactic antistaphylococcal antibiotics at operation and immediately afterwards; possibly such treatment affected the resident bacterial flora and thereby facilitated invasion by *L pneumophila*. Members of staff rarely develop clinical disease in nosocomial outbreaks[1] but here a healthy young surgeon who had slept in a small room in the cardiothoracic high dependency area did become ill. Two of his colleagues who also occupied this room during their nights on duty were unaffected and did not develop antibody to *L pneumophila*.

Although the number of patients was too small to allow statistical analysis, there was a clinical impression that early treatment with erythromycin and ciprofloxacin with or without rifampicin was an effective treatment in this disease. Despite intensive treatment, however, five of the nine patients who were severely ill died.

The most notable feature of this outbreak of legionnaires' disease was the rapidity with which a firm diagnosis was made. As has previously been illustrated in a group of immunocompromised patients, the application of the direct fluorescent antibody test to bronchial lavage specimens obtained at bronchoscopy resulted in a confident diagnosis within a few hours.[6] As a result the contaminated hospital cooling tower was immediately shut down, although microbiological proof of contamination was not obtained until some days later.[3] Legionnaires' disease is most commonly diagnosed by serological techniques, but positive serological results may not be obtained until some weeks after the onset of disease.[7] If we had relied on serological techniques for diagnosis, the outbreak might not have been recognised for some time, and if the number of patients had been small it might have been missed altogether, like the case diagnosed retrospectively on examination of postmortem tissue.

Postoperative respiratory complications, including

pneumonia, are common in patients recovering from major surgery and it is exceedingly difficult, if not impossible, to make a clinical diagnosis of legionnaires' disease. We would suggest that the methods outlined above should be used in the investigation of nosocomial pneumonia so that *Legionella pneumophila*, if it is the cause, can be identified, appropriate antibiotic treatment can be administered, and immediate measures can be taken to identify the source and eradicate the organism.

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