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Outbreak of Legionnaires' disease in Glasgow Royal Infirmary: microbiological aspects

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SUMMARY

The bacteriological investigation of an outbreak of Legionnaires' disease in Glasgow Royal Infirmary affecting 16 patients is described. Most of the patients had been treated in high-dependency areas on two floors of the hospital supplied by the same two air-conditioned ventilation systems. The source of infection was traced to contamination of a cooling tower from which a plume of spray discharged into the intake vents of the two ventilation systems. Rubber grommets within the cooling tower probably provided a nidus of infection there. The control and management of the outbreak are discussed: a policy of frankness about the course and progress of the investigations was adopted and helped to allay anxiety on the part of both staff and media.

INTRODUCTION

The Royal Infirmary in Glasgow has 918 beds in two main ward blocks. The first and older was opened in 1912, the second, Phase I of a new development, in 1982. In November 1985 15 patients and 1 member of staff in the Phase I block developed Legionnaires' disease. We report here the bacteriological and epidemiological investigations which led to the rapid diagnosis and containment of the oubreak and the problems met by microbiologists in the face of widespread public (and staff) anxiety and media pressure.

MATERIALS AND METHODS

Bacteriological investigations

Patients' specimens were examined in the laboratories in both the Royal Infirmary and Ruchill Hospital. Most of the environmental samples were tested in the Royal Infirmary. The serological identification of isolates from patients and the environment was confirmed at Ruchill Hospital.

Patients

Clinical details have been described by Winter *et al.* (submitted for publication). Briefly, specimens of respiratory secretions were obtained, where possible, by bronchoscopy and lavage and were examined by the direct fluorescent antibody test (DFAT) and by culture on buffered charcoal yeast extract medium (BCYEα) (Edelstein, 1981). A monoclonal antibody specific for *Legionella pneumophila* serogroup 1 and kindly supplied by Inveresk Research International Ltd, Musselburgh, Scotland was used in the DFAT. In two patients, the only respiratory specimens available were samples of sputum. Serum samples were examined by the indirect immunofluorescence test for IgG antibody (IFAT). Specific IgM antibody was not tested. Two laboratories carried out tests in parallel; that in the Royal Infirmary used *L. pneumophila* serogroup 1 (NCTC 11192, Philadelphia 1 strain) suspended in 0·5% (v/v) formol saline. The laboratory at Ruchill Hospital (which provides a diagnostic and reference service for legionella infections) used heat-killed organisms, from an earlier passage of the above strain, suspended in normal yolk sac as described by Wilkinson, Fikes & Cruce (1979). The serological findings reported here were obtained with formalized antigen which gave results that in a comparative study agreed closely with those obtained with heat-killed antigen.

Staff

Members of staff of the Phase I block who had been ill during the relevant period were asked by the Occupational Health Service to give a sample of blood. Later, volunteers who had not been ill were also asked to provide a sample. These blood samples were tested by IFAT.

Environmental sampling

Water samples of approximately 2 l were filtered through nylon membrane filters using a peristaltic pump, pore size 0·2 μm (PALL Ultipore): thereafter the filters were suspended in 50 ml filtrate before shaking and culture. Gravel stones and earth were suspended in 3 l of sterile distilled water (SDW) for 48 h and the supernatant filtered as above. Swabs taken from various appliances and items were shaken in 15 ml SDW per swab and the suspension plated on appropriate media. Grommets and washers were impression-plated before being collected in groups of six and shaken in SDW, which was then plated.

All specimens in SDW or filtrate (with the exception of suspensions of gravel stones or earth) were placed in an orbital shaker for 1 h and then divided into three aliquots. One was cultured without treatment, one was heated at 50 °C for 30 min, and the other treated with hydrochloric acid as described by Bopp *et al.* (1981). A 0·1 ml portion of each aliquot was plated on BCYEα and incubated at 35 °C in a moist chamber for a minimum of 14 days. The BCYEα was supplemented by combinations of various antibiotics.

Plates were examined at 2, 4, 7, 10 and 14 days (and sometimes at 21 days also) and suspicious colonies replated on BCYEα both with and without cysteine and iron. Colonies which grew only on BCYEα with cysteine and iron were confirmed as legionella by DFAT.

Table 1. *Laboratory results on 16 patients with confirmed Legionnaires' disease*

Test	Number positive	Number negative	Number not tested
DFAT	7	3*	6
Culture	7	3*	6
Serology	11	4†	1‡

* One specimen was unsatisfactory

† All four patients were positive by DFAT and/or culture.

‡ One specimen was not tested with formalized antigen but was positive when tested with heat-killed antigen.

Sentinel guinea-pigs in four groups of three were placed in the high-dependency areas of levels 3 and 4. Some were sacrificed at 7 and some at 14 days and examined by culture and serology for evidence of legionella infection.

RESULTS

The outbreak

Legionnaires' disease was diagnosed in seven post-operative patients in the new Phase I ward block of Glasgow Royal Infirmary during the weekend of 2 and 3 November 1985. DFAT was positive on bronchial aspirates from five patients and on sputum in two others. All seven patients had been operated upon in either the Peripheral Vascular or Cardiothoracic Units of the hospital. Laboratory tests confirmed the diagnosis in another four patients during the next 6 days and also in a surgical registrar in the Cardiothoracic Unit who had developed an atypical pneumonia 2 weeks before the outbreak. These 12 patients were recognized early in the outbreak when there was considerable anxiety within the hospital and intense public interest. Some weeks later, four more patients who had been discharged around the time of the outbreak were discovered to have been infected, bringing the total number of cases to 16.

The results of bacteriological tests on the 16 patients are shown in Table 1. The DFAT represented something of a breakthrough in the bacteriology because it confirmed the clinical diagnosis in a matter of hours. *L. pneumophila* was also cultured from patients' specimens within 2–5 days. The organisms were identified by serology and by nutritional requirements. All organisms isolated from patients belonged to *L. pneumophila* serogroup 1. The serogroup 1 strains from patients gave the same reactions with a limited range of monoclonal antibodies and were later confirmed by Dr J. O'H. Tobin as belonging to subgroup Pontiac minor subgroup 1a (Watkins *et al.* 1985).

Legionnaires' disease is usually diagnosed serologically, and 11 of the 16 patients (Table 1) showed either a fourfold rise in titre or stationary high titres of antibody (i.e. 256 or greater). With one exception the fourfold rises in titre were to 64 or greater. Four patients failed to develop significant levels of antibody, one of whom died within 48 h of the onset of illness. Fig. 1 illustrates the results in 10 patients from whom serial samples were available – amongst whom were 3 of the 4 patients mentioned above who did not develop significant antibody titres (nos 1, 9 and 10). It can be seen that a fourth patients (no. 8) showed a rise in titre to only 32.

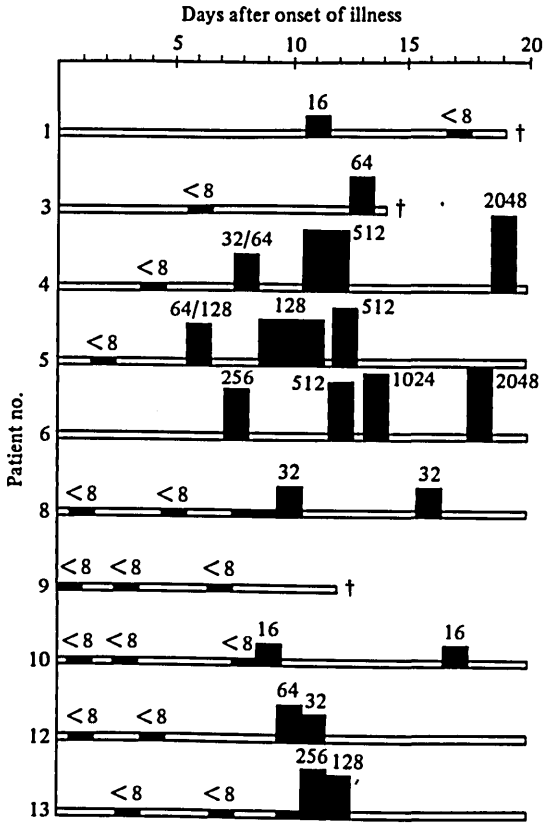

Fig. 1. Antibody titres (by IFAT) in ten patients with Legionnaires' disease from whom serial samples were obtained.

† died.

However, in all 16 patients at least one test (i.e. DFAT, culture or serology) was positive for *L. pneumophila*.

Epidemiology

It was realized at the outset that cases were virtually confined to the two high-dependency areas of the Peripheral Vascular and Cardiothoracic Units. These areas are situated one above the other on levels 3 and 4 respectively and are both ventilated by the same systems, W2 and W5. A diagram of the Phase I block is shown in Fig. 2. The two high-dependency areas are marked 'B'. Tests soon showed that, as in other nosocomial outbreaks, the cooling tower associated with the ventilation systems of the hospital was contaminated with *Legionella* spp. including *L. pneumophila* serogroup 1 (Table 2) and strains identified as Pontiac 1 a.

Cooling tower

The cooling tower which was the source of the outbreak is shown diagrammatically in Fig. 3. Ventilation systems with air conditioning need a source of heating and a source of cooling. Heating is usually provided by steam or hot water. Cooling is provided by a closed chilled-water circulation system in which the water is kept chilled by a refrigerant. During the cooling process heat is removed from the water

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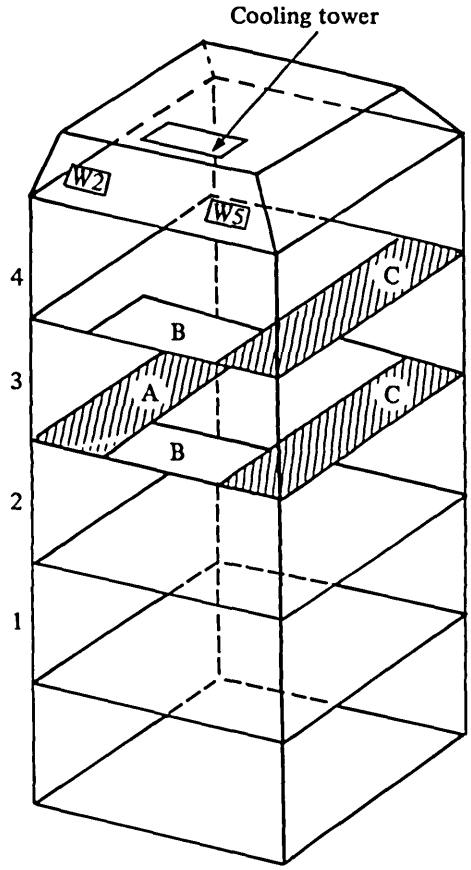

Fig. 2. Three-dimensional diagram of the Phase 1 block of Glasgow Royal Infirmary. On Level 3, Area A is a medical ward, Area C is the Peripheral Vascular ward and Area B is the Peripheral Vascular high-dependency area. On Level 4, Area C is the Cardiothoracic ward and Area B is the Cardiothoracic high-dependency area. W2 and W5 are the ventilation intakes on the roof.

being chilled and transferred to the refrigerant. This heat must be removed – a process that takes place in a condenser, where heat is transferred from the refrigerant to a second circulating water system (the cooling water). Subsequently, the heat transferred to the cooling water is removed in the cooling tower. This water is cooled by a process in which it is sprayed from nozzles over the fill pack (Fig. 3). The fill pack presents a large surface area which is wetted by the water spray. At the same time air is blown upwards by a fan through the fill pack resulting in evaporative cooling. During this process, a cloud or 'plume' of moisture-laden air is discharged into the atmosphere from the top of the cooling tower while the cooled water is pumped from the base of the tower through the circulation system to cool the refrigerant and thence back to the cooling tower. However, water from the cooling tower never comes into direct contact with the air in the ventilation systems.

Table 2. *Environmental samples from the cooling tower from which* Legionella *spp. were isolated*

	L. pneumophila serogroup 1	*Legionella* spp. other than *L. pneumophila*	Legionella not speciated*
Water (various samples)†	+	+	+
Water after cleaning	+	+	−
Water after cleaning and chlorination	+	+	−
Water from cooling tower circulation pump in basement	−	−	+
Sludge from base of tower	−	−	+
Condenser header	+	+	−
Sludge from dead end of header	+	−	−
Spray header pipe	+	−	+
Nozzle swab	−	−	+
Nozzle grommets†	+	+	+
Grommets at base	+	−	+

* All these strains reacted with a monoclonal antibody which recognized *L. pneumophila* and also 'species 1 and 2' (Fallon , 1986).

† Not all samples were positive for all three categories of legionella. +, culture positive; −, culture negative.

Route of contamination

This became apparent when it was realized that the cooling tower was situated on the roof of the Phase I block between the vents of the W2 and W5 ventilation systems (Fig. 2). Smoke bombs set off at the tower showed on two occasions (and depending on the wind direction) smoke drifting into the intake vents of the W2 and W5 systems respectively. The outbreak was therefore concluded to be due to contamination (from the plume of the cooling tower) of air drawn into one or other – or possibly both – of the vents of the W2 and W5 ventilation systems.

Bacteriological investigations

Altogether 529 specimens for culture were taken from numerous sites in the hospital. Among the sites sampled were the air handling and cooling units and the water circulating systems – including stored water, shower fittings and tap washers. Samples were also taken of roof gravel, earth from potted plants and both earth and water from a major road construction site adjacent to the hospital. However, only those from the cooling tower and its water circulating system proved to be positive.

Legionella spp. were isolated from various sites within the cooling tower unit, and these are listed in Table 2. The cooling tower had been well maintained according to the recommendations issued by the Scottish Home and Health Department (1980). Samples examined bacteriologically in June and August 1985, before the outbreak, were negative. Nevertheless, at the time of the outbreak, extensive and heavy contamination was discovered in water, sludge, pipes and rubber grommets. A grommet is illustrated diagrammatically in Fig. 3. Grommets enclose joints in pipes and nozzles and those in the cooling tower remained persistently

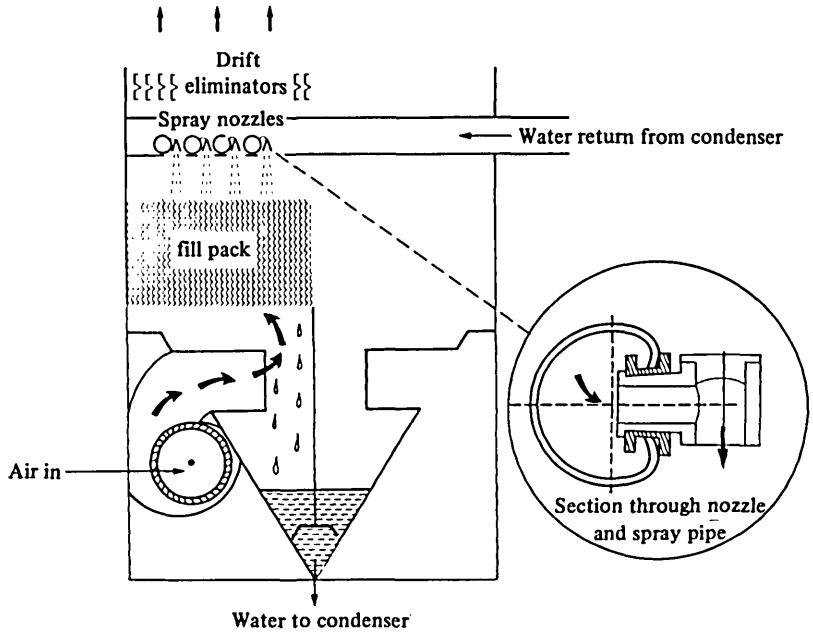

Fig. 3. Cross-section of Glasgow Royal Infirmary cooling tower with (inset) a sectioned drawing of distribution pipe showing nozzle attachment detail. A rubber grommet is shown cross-hatched (▧).

positive over a period of 18 days despite thorough cleaning and repeated chlorination of the system.

The sentinel guinea-pigs placed in the high-dependency areas developed neither disease nor antibodies to *L. pneumophila*.

Seroconversion in staff

Staff in the Phase I block who had reported sick during the time of the outbreak were asked to provide a blood sample. Table 3 shows that seven (7 %) had antibody to *L. pneumophila*. Five members had titres of 64 or higher, but in two the titres were only 32 and 16 respectively. One member who worked as a domestic in the high-dependency area of the Peripheral Vascular Unit had respiratory symptoms suggestive of mild legionellosis: her titre of antibody was 256. The incidence of antibody (1·8 %) in volunteers was lower than that in staff who had been ill. This figure was, in fact, lower than that (2·7 %) found in the general population in this area by the laboratory in Ruchill Hospital using heat-killed antigen (Fallon & Abraham, 1982).

Control of the outbreak

On 3 November, when it was realized that there had beeen nosocomial infection with *L. pneumophila* in Phase 1, the cooling tower was shut down – thereby, although we did not at the time know this, removing the source of the outbreak. Admissions were stopped, with the exception of life-threatening surgical emergencies and the high-dependency areas evacuated, although other patients were kept in until due for discharge. Contamination of the cooling tower was confirmed 4 days after the start of the outbreak. However, other sources of infection (e.g. the

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Table 3. *Incidence of antibody* to* L. pneumophila *in staff working in the Phase I block*

	Number tested	Number seropositive (%)
Staff reporting sick during period of outbreak	98	7(7)
Healthy staff (sampled in 2 months following outbreak)	113	2(1·8)

* Titres of 16 or more were regarded as evidence of seroconversion.

water systems) could not, at that time, be excluded since incubation was continued for up to 3 weeks before cultures were regarded as negative.

The cooling tower was cleaned and repeatedly dosed with sodium hypochlorite to a concentration of free chlorine in the water of 5 parts per million. Table 2 also shows that water from the tower on one occasion (in fact 2 days after the discovery of the outbreak) grew legionella both after cleaning and, surprisingly, also after chlorination. Later, the chlorination was increased to maintain a residual level of 5 parts per million for 1 h after treatment. A particular cause for concern was the grommets in the cooling tower, from which legionella were regularly grown over a period of 18 days after the start of the outbreak and in spite of repeated chlorination. Rubber washers and gaskets have been incriminated as an ecological niche for *L. pneumophila* in plumbing systems (Colbourne *et al.* 1984). As far as we know, the similar danger of rubber grommets in cooling towers has not previously been reported. Because the weather had turned cold, the cooling tower was kept out of commission from the time of the outbreak until the spring of 1986.

Personnel and public relations

During the outbreak, a policy of complete frankness was adopted. Every day a group of microbiologists, administrators, nurses, engineers and the Community Medicine Specialist from the Health Board (TSW) met to discuss developments. A senior registrar in respiratory medicine (JW) was designated in charge of clinical liaison. Regular meetings were held to inform groups of staff and to present as clear a picture as possible of the progress and results of investigations. Similarly, daily bulletins were issued by the Press Officer of the Health Board to the media and, from time to time, press conferences and meetings with trade union officials were held. It was felt by all concerned that this policy was successful, and many members of staff expressed their appreciation of the frankness with which their questions and anxieties were dealt.

DISCUSSION

The outbreak of Legionnaires' disease in Glasgow Royal Infirmary was similar in many ways to other nosocomial outbreaks described previously (McDade *et al.* 1977; Bock *et al.* 1978; Thacker *et al.* 1978; Kirby *et al.* 1980; Dondero *et al.* 1980; Fallon, 1980; Fisher-Hoch *et al.* 1981*a*). As in other outbreaks, the source of

infection was contamination of a cooling tower (Politi *et al.* 1979; Dondero *et al.* 1980; Fisher-Hoch *et al.* 1981*b*). We were fortunate in having the DFAT available as a rapid technique for diagnosis. When applied to well-taken specimens of lavage taken at bronchoscopy, it enabled us to confirm a clinical diagnosis of Legionnaires' disease within hours. Culture of respiratory aspirates and, in two patients, of sputum, gave positive results much earlier than the traditional method of diagnosis by indirect immunofluorescent detection of antibody. Had we relied on the demonstration of antibody alone, the fact that there was an outbreak of Legionnaires' disease in the hospital would not have been known for 7–10 days. Moreover, and in the case of three, and possibly four patients (nos 1, 8, 9 and 10 in Fig. 1), the diagnosis might have been missed altogether.

The source of infection, suspected early in the outbreak from information supplied by the hospital engineers, was confirmed bacteriologically some 4 days later. Bacteriologists were then able to offer informed advice to anxious clinicians and administrators about measures to control the outbreak and the time when Phase I could be reopened to new admissions. Because the cases had virtually been confined to the high-dependency areas and because further contamination of the two ventilation systems was prevented by shutting down the cooling tower, Phase 1 was reopened 10 days after the start of the outbreak. Since numerous cultures were still in progress at that point, there was a calculated risk in this. However, the risk to patient welfare in remaining shut in our view balanced that of infection from an as yet unidentified source. Later on, we learned that rubber grommets within the cooling tower still yielded legionella some days after the hospital had been reopened. Given the repeated chlorination it seems unlikely that the bacteria would have been able to multiply in the cooling tower water. Nevertheless, the grommets clearly represented a continuing nidus of infection from which there might be future contamination of the cooling tower water. Unlike tap washers, there are no official recommendations that grommets in cooling towers and water systems be made from plastic material that does not support the growth of legionella. We think that both Departments of Health (i.e. the D.H.S.S. and the S.H.H.D.) should look into this possibility. Although some of our positive samples grew legionella other than *L. pneumophila* serogroup 1 – the cause of the outbreak – we believe that contamination by any legionella indicates risk in the same way faecal coliforms indicate sewage contamination of drinking water.

A considerably smaller proportion of staff had antibody to *L. pneumophila* than, for example, in the outbreak in Stafford District General Hospital (Report, 1986). Perhaps this indicates that the exposure was limited in time and in the extent of aerial contamination. The patients with Legionnaires' disease were, with two exceptions, post-anaesthetic, which would doubtless enhance their susceptibility to airborne infection. Of the two exceptions, the surgical registrar smoked cigarettes and had been sleeping in a very small room in the Cardiothoracic surgery high-dependency area; he was probably exposed to a heavy airborne dose of organisms. The other exception was a medical patient on steroid therapy.

The outbreak imposed a heavy strain on the bacteriology departments. There was of course a sharp increase in the specimens for examination and senior staff had to attend numerous meetings with administrators, nurses, engineers and clinicians. In addition, bacteriologists were called to address groups, mostly of

nurses and ancillary workers, who were, not surprisingly, worried that they had been exposed to what the media referred to as 'the killer disease'. We felt that our policy of complete frankness was successful and recommend this to other hospitals who may be faced with a similar problem in the future.

Numerous people helped in this investigation, notably the staffs of the hospital administration, engineering and occupational health departments, and the medical laboratory scientific officers of the two bacteriology departments. All worked long hours during the outbreak, and we are grateful to them for their help in preparing this article. Particular thanks are due to Mr D. Campbell and Mr J. Gibson in the Royal Infirmary and Mr W. H. Abraham in Ruchill Hospital for valuable technical assistance.

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