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A hospital epidemic caused by a gentamicin-resistant *Klebsiella aerogenes*

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SUMMARY

In the 15 months, February 1976 to April 1977, more than 241 patients became colonized with a strain of *Klebsiella aerogenes*, capsular serotype K2, resistant to most antibiotics. Urinary tract infection was the most common clinical manifestation but bacteraemia and, occasionally, infections of other sites were encountered. The main reservoir of the epidemic klebsiella was the gut, urine and skin of colonized patients. Gut carriage among staff was very uncommon. The most susceptible patients were elderly males, with debilitating illnesses and urinary tract abnormalities, especially if they were catheterized or receiving antibiotics. Likely vehicles for spread were the hands of staff, and contaminated bedpans and urinals. Control measures were directed at these factors. At the end of April 1977 no new cases had occurred for 3 months in the ward in which the outbreak began, and which had been the main focus of infection, and only 5 patients in the affected hospitals were known to be colonized by the epidemic klebsiella.

INTRODUCTION

The emergence of klebsiellas, resistant to many antibiotics including gentamicin, and their spread and establishment in urological units have been features of hospital infection in several countries in recent years (Noriega *et al.* 1975; Schaberg, Weinstein & Stamm, 1976; Forbes, Gray, Hurse & Pavillard, 1977; Rennie & Duncan, 1977). We here describe an outbreak in a British hospital group, which began in February 1976 and affected more than 200 patients in the course of the next year. Investigations into the sources of the bacterium and the mode of spread in one heavily infected ward are also reported.

METHODS

Isolation methods

In all patients included in the description of the outbreak, the epidemic klebsiella was isolated from clinical diagnostic specimens by routine laboratory methods. In further investigations, MacConkey's bile salt lactose agar with gentamicin (2 mg/l), and phenol red–lactose broth with gentamicin (2 mg/l) were used; these media were shown to yield, respectively, colony counts of the epidemic

klebsiella equivalent to those on unselective media, and a heavy growth of the epidemic klebsiella from a small inoculum. Swabs were moistened with sterile saline before use and were placed in Stuart's transport medium if any delay in culturing would ensue.

The epidemic klebsiella was recovered from hands, urinals, bedpans and other similar articles by an adaptation of the method of Price (1938). The object being sampled was washed with 90 ml of sterile water to which 10 ml of concentrated phenol red–lactose broth with gentamicin were added subsequently (final concentration of gentamicin 2 mg/l). Volumes ranging from 0·1 to 10 ml were cultured and from the growth obtained the number of colony-forming units (c.f.u.) recovered was estimated (Salzman, Clark & Klemm, 1968).

Characterization of stains isolated

Gram-negative bacteria of suggestive colonial morphology and antibiotic sensitivity were identified to species by the methods of Cowan (1974). Sensitivity to antibiotics was first determined by disk diffusion methods and confirmed by agar dilution.

K. aerogenes isolations were subjected to capsular serotyping by counter-immunoelectrophoresis. The organisms were cultured on Worfel–Ferguson agar for 20 h at 37 °C and the growth was resuspended in distilled water to give a final density of approximately 10^6 c.f.u./ml. Counter-immunoelectrophoresis was carried out in a continuous Veronal buffer system (Coonrod & Rytel, 1973) with Difco antisera (pools and specific). Plates were read after electrophoresis at 2·5 V/cm for 90 min.

Disinfectant tests

Minimum inhibitory concentrations of disinfectants were determined by broth dilution in heart-infusion broth, with an inoculum of approximately 10^5 c.f.u./ml. The activity of disinfectants in conditions simulating use was determined by the methods of Kelsey & Sykes (1969) and of Maurer (1969). 'In-use' tests of disinfectants were performed as described by Maurer (1974).

Ward survey

The patients and staff of the ward chosen for intensive study, and the ward environment, were monitored at weekly intervals for 10 weeks. In addition, the results of the examination of all specimens received from the ward by the laboratory during this period were recorded. Mid-stream or catheter urine specimens, and nasal, perineal and rectal swabs were obtained from all patients. Colonized patients also had hand-washing studies. Staff were examined by hand-washing, and staff faeces were also cultured. The immediate environment of infected patients was intensively investigated, and a large number of environmental sites in the general ward – including sink drains, urinal tanks, ward and kitchen work surfaces, cleaning utensils, baths and showers – were monitored. 'Settle plates' of gentamicin-containing MacConkey agar were exposed in the ward for 6 h periods.

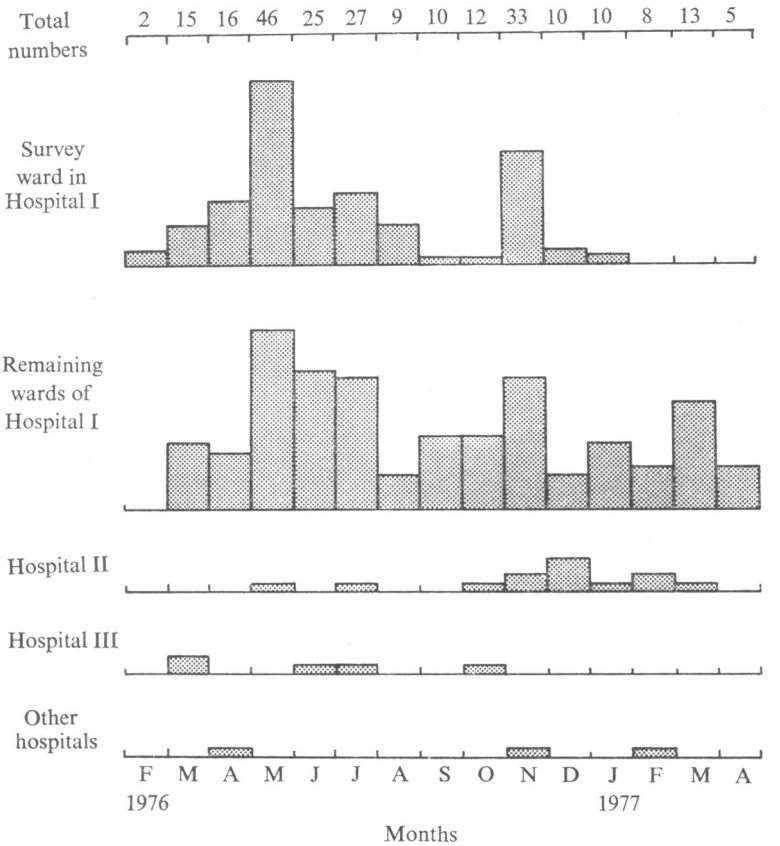

Fig. 1. Incidence of infection by epidemic *Klebsiella aerogenes* (241 patients).

THE EPIDEMIC *KLEBSIELLA* STRAIN

All isolations were of capsular serotype K2. Of the other *K. aerogenes* strains obtained in the hospital during the period of the outbreak which were more sensitive to antibiotics, only one was found to be of serotype K2. Strains isolated were consistently sensitive to cefuroxime, and to amikacin (apart from one resistant to amikacin after treatment of the patient with this antibiotic). All were resistant to ampicillin, carbenicillin, chloramphenicol, gentamicin, streptomycin, sulphonamides and tetracycline, and moderately resistant to tobramycin. Sensitivity to other antibiotics was variable, but treatment with colistin, nalidixic acid and trimethoprim of strains sensitive to these antibiotics resulted in resistant isolations. Although only 33 patients required antibiotic treatment, they presented a considerable therapeutic problem (Speller, Bint & Stephens, 1977).

THE OUTBREAK

The first strains were obtained in February 1976 from urinary infections in two patients, who had undergone prostatectomy, in a general surgical ward of the Bristol Royal Infirmary. The course of the outbreak during the next 15 months is shown in Fig. 1, which represents the 241 patients in whom colonization was

newly detected in specimens received in the laboratory (excluding rectal and skin colonization discovered only in epidemiological surveys). The major focus remained the male surgical wards with urological patients. There was some spread to most other wards in the hospital, including the intensive therapy and the cardiac surgery units. With transfer of urological patients, small outbreaks occurred in several surgical units and a geriatric unit elsewhere in the district. One nurse acquired a urinary tract infection.

Of these 241 patients, 82% were male. More than 85% of the patients had urinary tract colonization; 7% had proved bacteraemia, and the klebsiella infection was known to be the cause of death in 2%. Urinary colonization rapidly reached more than 10^5 colonies/ml; colonization was frequently accompanied by pyuria, but often did not give rise to any symptoms. Bacteraemia was associated with instrumentation, operation, blockage of catheter, etc., and produced a severe clinical illness. Respiratory infection was uncommon, and was of significance only in patients who had had major thoracic or gastro-intestinal surgery.

INVESTIGATION OF MALE UROLOGICAL WARDS

The ward in which the first cases had occurred, and which continued to have many infected patients (see Fig. 1), was an open-plan, 25 bedded, male general surgical ward. About half the patients were under the care of the urology service. This ward was intensively studied for 10 weeks, between November 1976 and February 1977. At the end of this time, when the spread of infection in this ward was better controlled, supplementary observations were made in another similar ward.

Patients

During this ward study 29 patients had urinary tract colonization by the epidemic klebsiella. The other body sites from which the organism was recovered are given in Table 1. Those patients who became colonized were significantly older than the general ward population during the outbreak. In the over-70 age-group, patients infected with the epidemic klebsiella were twice as frequent as expected (χ^2: P less than 0·001). Many factors may account for this. Colonized patients often had debilitating illnesses, such as malignant disease. Urinary colonization was encouraged by urinary tract abnormalities, catheterization and the previous administration of antibiotics, especially broad-spectrum antibiotics such as co-trimoxazole and ampicillin or amoxycillin. Of the 29 patients in the survey who had urinary tract colonization, 21 had indwelling urethral or supra-pubic catheters at the time, and 17 were receiving antibiotics. At the beginning of the outbreak in March 1976 19 of 20 patients, in several wards, were receiving antibiotics when they became infected with the epidemic klebsiella. Neither of these two factors was essential, however, and rapid colonization of the urinary tract could occur in their absence. In the presence of abnormalities urinary colonization sometimes persisted for long periods, and on occasions the urine was the first or the only site of colonization. In other cases gut colonization preceded

Table 1. 29 *patients with urinary colonization: sites yielding epidemic klebsiella*

Urine	29
Rectum/stoma	27
Hands	22
Perineum	20
Nose	14
Sputum	3

Table 2. *Urinary tract infections in survey ward caused by bacteria other than the epidemic klebsiella* (44 *patients*)

Infecting bacteria	Number of cases
Lactose-fermenting coliforms	22
Proteus sp.	7
Pseudomonas aeruginosa	7
Other gram-negative bacilli	3
Streptococcus faecalis	11
Staphylococcus epidermidis	7
Staph. aureus	2

urinary colonization. The prevalence of gut colonization in the ward under survey varied widely, but at times as many as one third of the patients were found to be colonized.

During the course of the investigation urinary tract colonization with other bacteria occurred in 44 patients (Table 2). Ten patients in this group had urinary colonization (more than 10^5 c.f.u./ml) with two or more bacteria. Although many of these infections were present on admission, at least 21 were hospital-acquired. Eight of the patients later acquired urinary colonization with the epidemic klebsiella.

Staff

Routine hand-washing studies failed to reveal the epidemic klebsiella on the hands of staff. It could be recovered, however, if staff hands were sampled immediately after the handling of a patient with heavy colonization of skin sites (not those with rectal, urinary, and perineal colonization only). Faecal carriage by staff was uncommon; only one of 66 staff members sampled yielded small numbers of the epidemic klebsiella. The nurse with the urinary tract infection had heavy faecal carriage.

Environment

The immediate environment of colonized patients was often contaminated (12 of 29 patients) and settle plates placed near their beds frequently yielded a few colonies of the epidemic klebsiella. On the other hand, there was no evidence of persistence in the general ward environment and other settle plates were negative for the epidemic klebsiella. Exceptions were certain sinks and drains which were frequently exposed to infected excreta. Contamination also persisted on a cotton floor-mop.

Bedpans and urinals

The epidemic klebsiella could be recovered in small numbers (less than 10 c.f.u.) from bedpans which had been processed in a Dent and Hellyer washer/disinfector, which was found to be working unsatisfactorily, the maximum temperature reached on a metal or a polypropylene bedpan being 45 °C, rather than the 80 °C (for at least 1 min) which is recommended (Ayliffe, Collins & Deverill, 1974).

Urinals were being decontaminated by rinsing and immersion for at least half an hour in a tank of 1% Clearsol, followed by draining and drying at room temperature. In-use tests of the disinfectant in the tank showed many failures, with the presence of high counts of the epidemic klebsiella and also other gram-negative bacilli, such as proteus and *Pseudomonas aeruginosa*. The worst failures were due to errors in the making up of the disinfectant, with far too low a concentration (less than 0·01%), but in other cases, even when samples of disinfectant taken from the tank passed the in-use test, swabbing of the wall of the tank, when full or after emptying and cleaning, yielded the epidemic klebsiella.

The minimum inhibitory concentration of Clearsol for the epidemic klebsiella was 0·2% and the minimum bactericidal concentration 0·4%. The same results were obtained with clinical strains of *Escherichia coli* and of *K. aerogenes*. which were more sensitive to antibiotics. These gram-negative bacilli all behaved similarly in standard disinfectant tests (see *Methods*) and habituation of the epidemic klebsiella to Clearsol could not be demonstrated in the laboratory.

Other possible sources

The epidemic klebsiella was not isolated from food, medicines, lotions or equipment.

CONTROL MEASURES

Spread of the epidemic klebsiella proved difficult to control at all times. As the investigation proceeded and the major factors involved were determined, it became possible to focus the control measures more accurately.

Surveillance

In the laboratory all isolates from diagnostic specimens, even in scanty growth, with typical colonial appearances, were further investigated. Gentamicin was included as a 'first line' drug for sensitivity testing of all gram-negative bacteria, and in direct sensitivity tests. All patients in the heavily affected male surgical wards had urine specimens examined weekly; and carriage sites of patients in these wards were cultured at intervals. From these data the occurrence of colonization by the epidemic klebsiella throughout the district was charted in the laboratory for daily reference.

Colonized patients

As far as possible, colonized patients were isolated in cubicles, or segregated in one particular area, in the ward in which they had acquired the infection. Transfer

to other wards or hospitals was discouraged, but patients were allowed to go home when fit, even if still carrying the epidemic klebsiella. Colonized patients were supplied with personal bedpans and wash-bowls, and male patients were given disposable urinals. Staff were encouraged to wear disposable gloves when attending these patients, and hand washing afterwards with tablet soap or 'Hibiscrub' chlorhexidine solution was made mandatory.

Staff hygiene

Frequent hand-washing by all staff, after handling patients and before eating, was encouraged. Full and regular screening of all staff faeces was not undertaken, but the two faecal carriers who were detected were not permitted to work on unaffected wards, and were counselled about hygiene.

Catheters

Staff were exhorted to follow scrupulously the procedures already laid down for catheterization and closed catheter drainage (Gillespie, Lennon, Linton & Phippen, 1967). The possibilities of transfer of infection after manipulation of catheters, emptying of urine-collecting bags, etc., were pointed out.

Urinals and bedpan disinfection

It proved impossible in practice to avoid contamination of the disinfectant tanks and an alternative method of cleansing urinals was employed. Urinals were washed in hot water and detergent and dried in air. This method was subsequently shown in the laboratory to leave variable numbers both of the epidemic klebsiella and of other gram-negative bacilli on the urinal. Patients known to be infected were therefore provided with disposable urinals, as described above.

Antibiotic policy

As almost all antibiotics appeared to encourage colonization by the epidemic klebsiella, general restraint in prescribing was advocated. Total prohibition of antibiotic use (Price & Sleigh, 1970) was not thought feasible in the prevailing situation. Spot checks of antibiotic use on severely affected wards were made by microbiology staff.

The few antibiotics to which the epidemic klebsiella was sensitive were reserved for serious clinical situations, for fear of the emergence of resistance if great use were made of these; and so chemotherapy could not be used as a general measure to reduce the reservoir of infection (Schaberg *et al.* 1976).

At the end of April 1977 only 5 patients (distributed among 4 wards) were known to be colonized. No new case had occurred in the past 3 months in the ward in which the major investigation had been carried out, and in which control measures had been most consistently applied.

DISCUSSION

The isolations of *K. aerogenes* obtained from this outbreak were of consistent serotype, but showed slight variation in antibiotic sensitivity and in biochemical reactions, as has been described elsewhere (Eickhoff, 1971). The strain, besides being very resistant to antibiotics, was a successful pathogen for the urinary tract but otherwise only of average virulence. The incidence of proved bacteraemia of 7% is similar to that observed in other such outbreaks (Schaberg *et al.* 1976).

In wards with a high prevalence of infection, patients are undoubtedly the most important reservoir. The bowel has been demonstrated to be a source in other such outbreaks (Selden *et al.* 1971), but the urinary tract may also be significant because of the long persistence of symptomless infection in this site, even months after discharge of the patient from the hospital. Heavy skin carriage is probably secondary to carriage in these sites, but it may lead to contamination of the hands of personnel. In this outbreak staff were not a major reservoir of infection, but it is possible that a few long term faecal carriers were concerned in the transmission of the infection to other wards where sporadic cases occurred. Although the epidemic klebsiella could not be recovered from the hands of staff in routine surveys, indirect evidence suggests that this was an important mode of spread. When a rigid discipline of the wearing of gloves and careful hand-washing in dealings with identified colonized patients was firmly established the incidence of infection declined. Direct transmission of the infection from ambulant heavily colonized patients could not be excluded.

The environment did not appear to provide a long-term reservoir of infection, and, as is usual in hospital infection by gram-negative bacilli, air spread was not significant. Explosive increases in cross infection in the urological wards were closely associated with failures of the urinal tank disinfectant. It is difficult to find an effective method of disinfecting urinals and bedpans which can readily be instituted in older hospital wards. There must be frequent monitoring, to see that the equipment is performing satisfactorily, that the method is being carried out correctly, and that effective disinfection is taking place. Even when disposable equipment is used, with the extensive support services which are necessary, there are still problems (Gibson, 1976).

We have found the control of hospital infection by this resistant klebsiella particularly difficult, as compared with staphylococcal infection (Speller *et al.* 1976). It is clear from our own and others' experience that the appearance of such gram-negative bacilli in a unit must be treated as a serious portent, and immediate stringent measures must be introduced to control the spread of infection. Once a reservoir of bacteria has built up in the hospital population it is extremely difficult to eradicate. In the present outbreak the number of infected patients increased rapidly, and efforts at control were thereafter repeatedly frustrated by the transfer to other wards of patients, whose colonization by the epidemic klebsiella had not been detected, and who initiated further outbreaks. Although at the time of writing only 5 patients in the hospital are known to be colonized, there may be other undetected carriers, and it is still uncertain that this epidemic has been contained.

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