

Nosocomial Urinary Tract Infections Caused by Two O-Serotypes of *Providencia stuartii* in One Hospital

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Providencia stuartii nosocomial urinary tract infections occurring in the same hospital over an 18-month period of retrospective study were shown, by serotyping and biotyping, to have been caused by two endemic strains. Two episodes, involving 38 patients in one ward and 11 patients in another, were caused by a mannitol-positive strain of serotype O55. Transmission of the strain through the movements of one patient appeared to have been the basis for the introduction of the agent from one ward to the other. In another episode, involving two patients in a third ward, the infections were caused by a mannitol-negative strain of serotype O49. The study demonstrated the usefulness of serotyping and biotyping in epidemiological studies of infections caused by *P. stuartii*.

The recognition of *Providencia stuartii* as antibiotic-resistant bacteria involved in nosocomial infections has indicated the need for epidemiological studies (1, 2, 4, 9). In the application of the O-typing scheme, it has been noted that endemic strains of different O-serotypes may occur in different hospitals (J. L. Penner, N. A. Hinton, I. B. R. Duncan, and J. N. Hennessey, submitted for publication). This report is concerned with the application of serobiotyping in a retrospective study of urinary tract infections caused by *P. stuartii* in one hospital.

MATERIALS AND METHODS

Bacterial cultures. Isolates identified in the clinical laboratory as *P. stuartii* were submitted for serotyping and biotyping. Included were isolates from urines, environmental samples, and routine specimens.

Serotyping and biotyping. Serotyping was performed with the slide agglutination reaction with O antisera, and each isolate was biotyped according to methods described previously (8).

Antibiotic sensitivity testing. Bacteria were tested for sensitivity to 8- μ g/ml amounts of 12 antibiotics commonly used in the treatment of urinary tract infections, using the multiple inocula-replicating method of Steers et al. (10). Antibiotics were incorporated into disk sensitivity agar (Oxoid). Minimum inhibitory concentration (MIC) values were determined for ampicillin, gentamicin, sulfisoxazole, and cloxacillin. The MIC value was recorded as the minimum concentration of antibiotic that totally inhibited growth.

RESULTS

Outbreak of *P. stuartii* bacteriuria in an 18-bed ward. Episodes of *P. stuartii* hospital-acquired infections were demonstrated previously to be correlated with clusters of isolates of the same O-serotype (Penner et al., submitted). When a group of nine isolates from patients in the same ward in hospital H were all found to be serotype O55 and biochemically different from most other *P. stuartii* in a positive mannitol reaction, an outbreak of cross-infections was indicated. This finding supported the clinical observations of the hospital staff. Subsequent isolates of this species were collected for serobiotyping, and, from the case histories of patients infected with *P. stuartii*, the dates of admission, discharge or death, and the results of urine cultures were recorded to provide data for retrospective studies on the outbreak.

Ward A contained 18 beds and accommodated mostly patients with bladder dysfunction as a result of neurological disease or trauma. The first urine specimen positive for *P. stuartii* was taken as a new case of bacteriuria, and two reinfections that occurred in patients after an apparent cure were considered as new cases in the preparation of the histogram (Fig. 1). On this basis, 40 cases of bacteriuria, involving 38 patients, were diagnosed in an 18-month period. Since all 40 new isolates and five repeat isolates from three patients were mannitol-positive serotype O55, patient-to-patient transmission of

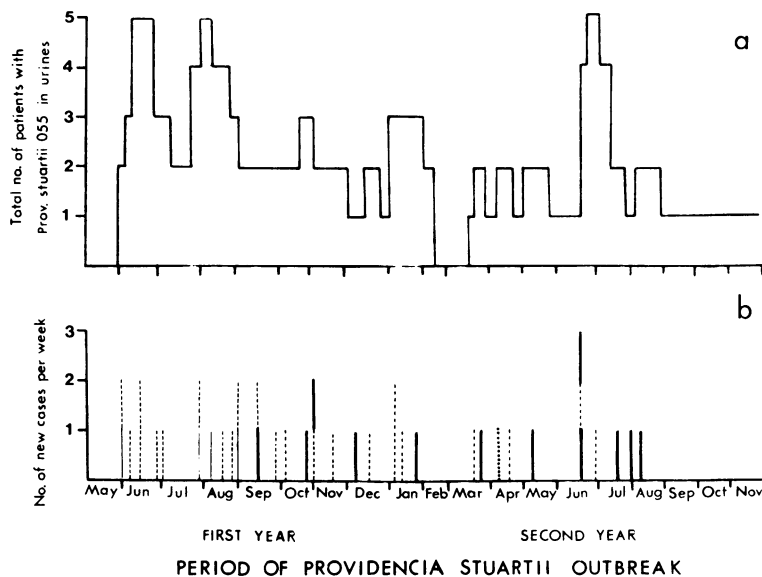


FIG. 1. (a) Total number of patients in ward A with urines positive for *P. stuartii* O55. (b) Number of new cases per week diagnosed on the basis of urines positive for *P. stuartii* O55. Number of isolates per week is indicated by vertical bars. Dashed bars indicate isolates sensitive to 8 μg of gentamicin per ml; dotted bars, thin solid bars, and heavy bars indicate isolates for which the MICs of gentamicin were, respectively, 16, 32, and 64 $\mu\text{g}/\text{ml}$.

an endemic strain appeared to be the most likely cause of the nosocomial bacteriuria.

Some patients had urines positive for the endemic strain for periods as long as 3 months, but others had positive urines for a period of only 1 week. On three separate occasions, five patients simultaneously had urines with this strain (Fig. 1a). During a 3-week period (February and March of the second year) urines of all patients in the ward were negative for *P. stuartii*, and the apparent resolution of the outbreak was attributed to rigorous enforcement of infection control procedures. The use of separate urine measures for each patient was introduced because *P. stuartii* O55 had been isolated from such vessels on this ward. However, the strain re-emerged and, in the course of the next 5 months, 12 more cases were diagnosed. Three months later, in June, an upsurge in new cases coincided with summer vacation changes in staff responsible for the care of these patients. Subsequent revisions in infection control procedures were considered instrumental in lowering again the incidence of new infections. The last patient to acquire the strain did so in the first week in August, and, from then to the end of the study in November, *P. stuartii* O55 was found in this patient's urine. No new infections due to this strain were observed, although the infected patient was in close proximity to other catheterized, infection-susceptible patients.

Examination of case histories showed that antibiotics had been administered at the discretion of the attending physicians for either urinary tract infections or other foci of infections such as wounds to 25 of the 38 patients from whom *P. stuartii* O55 had been isolated. Considerable variation in treatment of patients was noted. One received gentamicin only and seven received gentamicin in combination with ampicillin. Ampicillin, cloxacillin, and sulfisoxazole had been administered alone or in combinations to 17 other patients. Each of the 40 isolates was resistant to ampicillin, cloxacillin, cephalixin, carbenicillin, sulfisoxazole, sulfamethoxazole, tetracycline, chloramphenicol, and nitrofurantoin. Thirty-three isolates were resistant to both nalidixic acid and kanamycin, two antibiotics not used on the ward. Twenty-three were sensitive to gentamicin, and the MICs were determined for the 17 resistant isolates. Four with MICs of 32 $\mu\text{g}/\text{ml}$ were isolated within the first 5 months of the outbreak, but 11 with MICs of 64 $\mu\text{g}/\text{ml}$ occurred thereafter (Fig. 1b). Among the first 20 isolates in chronological sequence, 6 (30%) were resistant, but among the last 20 isolates there were 11 (55%) resistant. The ratio of numbers of resistant to sensitive increased during the course of the outbreak, and the clustering of sensitive isolates near the beginning was in distinct contrast to the clustering of resistant isolates towards the end. In all cases, the

repeat isolates had the same antibiotic susceptibilities as the first. Except for one with an MIC of 16 µg/ml isolated in April, the distribution of isolates was consistent with a pattern of emerging resistance due to a process of preferential selection for resistant forms of an endemic strain.

Interward transmission of *P. stuartii*. No urine specimens from patients in ward B were positive for *P. stuartii* until a specimen from patient R.M. was cultured. Two weeks later, three other patients and, within 1 month, seven more patients had urines positive for *P. stuartii* (Fig. 2). All isolates, like those in ward A, were mannitol positive and serotype O55. Since there was little interward movement of medical staff between ward A, a neurological ward, and ward B, a urological ward, it appeared that transmission of the infectious agent by personnel was unlikely. Records showed that patient R.M. had been temporarily transferred for a 4-day week-end from ward B to A and had been in close

proximity to five patients who, at the time, had urines positive for *P. stuartii* O55. Since a urine sample cultured from patient R.M. the week before the transfer was negative, the positive urine cultures after his return to ward B was most likely due to an infection acquired during his stay in ward A. Hence, the spreading of the strain in ward B could be attributed to case-to-case transmission from patient R.M. as the initial focus, and the interward movement of this patient was considered to be the most highly probable route for the introduction of the infectious strain into the ward.

Second endemic strain of *P. stuartii*. Patient S.S. was first admitted to ward A but after 2 weeks was transferred to ward C. Her urine specimens, regularly cultured, showed no *Providencia*, but after 2 months in ward C debrided tissue from her thigh showed heavy growth of mannitol-negative *P. stuartii* O49, the same strain identified earlier in a contaminated urine-measuring vessel on the same ward. The same serobiotypic was later isolated from urine of the patient in the bed adjacent to patient S.S. and subsequently also from urine of patient S.S. Serobiotyping served to demonstrate the occurrence of a different strain in this ward and showed that the infections were not related to those in ward A, noteworthy because the patient was first located on ward A during the period when patients there were infected with another strain.

DISCUSSION

Urinary tract infections in patients with indwelling catheters have been reported to be the main source of clinical isolates of *Providencia* (3, 6), and, because strains of this group have not been found frequently in urine or feces of patients on first admission to hospital, an exogenous source has been implicated (2). Several reports have noted nosocomial infections caused by *P. stuartii* (5, 7, 11). The epidemiology of these has been investigated with the use of biotypes in combination with antibiograms (5) or with serotypes (11) to define markers in discriminating among infecting strains. The former combination was observed to have limited practicality (5), and our finding of isolates of the O55 strain with different antibiograms supports that observation.

The efficacy of serobiotyping in epidemiological studies was demonstrated by the results in the present study. In the first instance, it was through serobiotyping of nine isolates that specific evidence for the occurrence of cross-infection in a hospital was obtained. Retrospective studies established that, in one ward, 38 patients acquired the organism over an 18-month period.

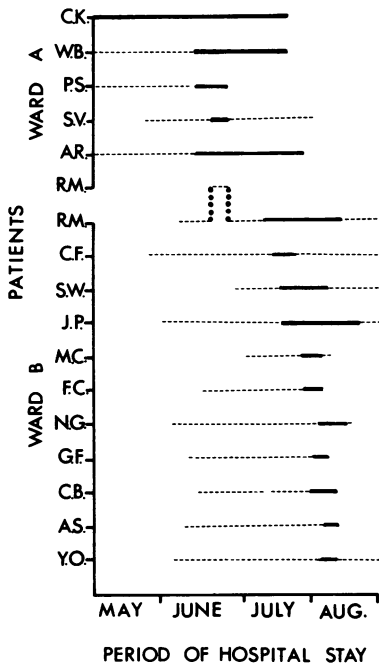


FIG. 2. Interward transmission of *P. stuartii* O-serotype 55. Left end of line corresponds to date of admission to the ward except for four patients already present on the ward before May (C.K., W.B., P.S., and A.R.), and right end corresponds to date of expiration or transfer from the ward except for five patients who remained on the indicated wards at the end of the study (R.M., C.F., S.W., J.P., and Y.O.). Dashed line, Period with urine cultures negative for *P. stuartii*; solid line, period with urine cultures positive for *P. stuartii*; dotted line, interward transfer.

In another ward, serotyping provided results showing that 11 patients were also infected with this strain but that, in a third ward, the infections were caused by another serobiotype. Serobiotyping provided evidence to suggest inter-ward transmission in the case of one ward and, clearly, the absence of such transmission as the cause of infections in the other. Furthermore, serotyping established that infections caused by *P. stuartii* in other areas of the hospital were unrelated to the infections described in three wards, because isolates from the other areas agglutinated in antisera O4, O17, O47, O52, O56, and O63 and not in either O49 or O55.

In considering the different episodes of cross-infection in this study, two features emerged as significant. Once established in the hospital, some strains, at least, have a high potential for spreading among susceptible patients, and rigorous adherence to infection control procedures is necessary to prevent such spread. Epidemiological aspects of nosocomial disease caused by *P. stuartii*, such as the route of introduction into the hospital, the mechanisms of case-to-case transmission, the influence of antibiotics, and the virulence factors of infectious strains, need to be examined, and it is anticipated that O-serotyping will be used in such studies.

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