INFECTIONS WITH ACHROMOBACTER XYLOSOXIDANS

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SYNOPSIS

Thirty strains of *Achromobacter xylosoxidans* were studied — 24 from clinical specimens and six from fomites. Their biochemical characteristics, antibiotic sensitivity as well as epidemiological data are described. These gram-negative aerobic bacilli were found to be the causal agents of nosocomial infections especially in compromised patients. They were also isolated as contaminants of catheters, surgical drains and incubators. Their resistance to aminoglycoside drugs may have played a significant role in the selection of these organisms as nosocomiants.

INTRODUCTION

Achromobacter xylosoxidans was named and described by Yabuuchi and Ohyama in 1971 after a study of seven strains isolated from purulent ear discharge of patients with chronic otitis media (1). This organism is an aerobic, non-fermentative, gram-negative rod and is not commonly isolated from clinical material. *A. xylosoxidans* can be confused with other non-fermentative gram-negative rods, especially pseudomonas species in clinical specimens, so that its role as a significant pathogen may be underestimated (2). Recently this organisms has been reported to give rise to both community acquired infections (3) as well as nosocomial infections (4, 5).

The purpose of this report is to describe our experience with 30 strains of *A. xylosoxidans* isolated at the University Hospital, Kuala Lumpur between October 1977 and April 1983.

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MATERIALS AND METHODS

Source and Identification of Cultures

Specimens from the hospital were cultured routinely onto blood agar and MacConkey agar plates. Chocolate agar plates were also used for blood cultures, ear swabs and cerebrospinal fluids. Cultures were incubated for one or two days at 37°C. Gram-negative bacilli were subcultured onto MacConkey agar, Kligler's iron agar (Difco) and other media for the determination of additional properties using the methods of Cowan and Steel (6). Strains suggestive of *A. xylosoxidans* were sent for identification and confirmation to the Computer Trials Laboratory, National Collection of Type Cultures, Central Public Health Laboratory, Colindale, London.

Antibiotic Susceptibility Tests

Mueller-Hinton agar (Difco) was used for the plate dilution method to test the antibiotic susceptibilities of the isolates against 20 chemotherapeutic agents. A Denley multipoint inoculator was used to test 25 strains simultaneously. Control organisms used were Oxford *Staphylococcus aureus* NCTC 6571 and *Escherichia coli* NCTC 10418.

Clinical and Epidemiological Observations

Patients' records were reviewed for clinical and epidemiological data. Epidemiologic analysis in all cases included age, sex, site of infection, presence of other pathogens in mixed cultures, time interval between admission and first isolation of the organism, prior antibiotic treatment, presence of underlying diseases and prior surgical procedures and manipulations.

An organism was considered to be hospital acquired if the infection associated with the isolate was not present on admission or the organism was not isolated in previous cultures from the same site. Isolates were classified as "significant" if there was clinical evidence of infection at the time of isolation and the organism was either recovered in pure culture or recovered repeatedly as the predominant organism in mixed cultures.

RESULTS AND COMMENTS

Bacteriology

A. xylosoxidans is a motile gram-negative rod which grows well on both nutrient agar and MacConkey agar. After 24 hours incubation at 36°C the colonies are usually pin-point in appearance. After 48 hours they become 1-2 mm in diameter and are seen to be convex with a smooth, moist surface and an entire margin. Occasionally, the colonies will be so watery that they will run off a plate which is tilted. The organism appears to grow better at room temperature than at 36°C.

Some of the relevant biochemical reactions of the isolates are given in Table 1. All isolates were highly consistent in most of their reactions and compared closely with those of Igra-Siegman *et al* (2) and Holmes *et al* (7). The reactions most useful for identification were: a positive oxidase and catalase reaction, nitrate reduction, an alkaline reaction or no change in Hugh and Leifson's glucose O — F medium, utilisation of citrate and the production of acid from glucose and xylose in ammonium salt sugar medium.

Antibiotic susceptibility

Twenty five strains of *A. xylosoridans* were tested against eleven B-lactam antibiotics, six aminolgycosides, cotrimoxazole, chloramphenicol and colistin. They were found to be fully sensitive to ampicillin, carbenicillin, moxalactam, ticarcillin, piperacillin, azlocillin, cefoperazone and ceftazidime; moderately sensitive to cefotaxime, ceftriaxone and chloramphenicol and mostly resistant to kanamycin, gentamicin, streptomycin, amikacin, tobramycin, netilmicin, colistin and cefuroxime. There appeared to be two sub-populations of *A. xylosoxidans* — one fully sensitive to cotrimoxazole and the other highly resistant. (More comprehensive results of these are being published separately)

TABLE 1
BIOCHEMICAL REACTIONS OF 30 STRAINS OF *A. XYLOSOXIDANS*

Test	Number Positive	Per Cent Positive
Oxidase	30	100
Catalase	30	100
O F Medium		
Alkaline Reaction	14	46.6
No change	16	53.3
Nitrate reduction	30	100
Motility at 37°C	25	83.3
Acid in ammonium salt suger		
Xylose	30	100
Glucose	30	100
Fructose	9	30
Growth at 42°C	18	60

Clinical Data

Some clinical features associated with the recovery of the organism are shown in Table 2. The isolations were mainly from blood cultures, infected wounds and ear discharges.

Six of the strains were recovered together with other organisms. These included *Flavobacterium meningosepticum* (wound swab), B-haemolytic streptococcus (blood culture), Acinetobacter spp. (blood cultures), Proteus spp. (antral wash-out), diphtheroids (ear swab) and Kelbsiella spp. (ear swab).

The ages of the patients ranged from three days to 83 years. Six patients (21%) were less than 12 months old, including two newborn babies. There were twenty males (71%) and eight females (20%) and a predominance of Chinese (61%) over other ethnic groups.

The 28 cases listed in Table 2 can be broadly classified into five groups:-

TABLE 2
CLINICAL DATA OF PATIENTS WITH *A. XYLOSOXIDANS* INFECTIONS

Case No.	Age Sex	Source	Prior antibiotic therapy	No. of days from admission to 1st isolation	Surgery or Instrumentation	Underlying disease
1	7.5 mths. M	Blood culture	+	5	+	Congenital nephrotic syndrome
2	22 yrs. F	Blood culture	+	60	+	Oesophageal stricture, wound infection
3	67 yrs. F	Blood culture	+	8	+	Bleeding gastric ulcer
4	67 yrs. F	Blood culture	+	15	+	Cholangitis, jaundice
5	1.0 mth. M	Blood culture	+	60	+	Multiple congenital abnormalities (died)
6	53 yrs. M	Blood culture	+	45	+	Acute renal failure with urinary tract infection
7	15 days. M	Blood culture	+	17	+	Jaundice, hepatosplenomegaly
8	2 yrs. M	Blood culture	+	4	—	Acute gastroenteritis, shock lung, balanitis
9	83 yrs. F	Blood culture	+	18	+	Carcinoma caecum, diabetes (died)
10	13 yrs. M	Blood culture	+	90	+	Fallot's tetrology (died)
11	4.5 mths. M	Blood culture	+	2	+	VSD, congestive failure, bronchopneumonia
12	23 yrs. M	Wound swab	+	10	+	Nil
13	23 yrs. M	Wound swab	+	3	+	Nil
14	59 yrs. M	Wound swab	+	30	+	Diabetes, gangrene (L) foot
15	30 yrs. M	Wound swab	—	0	—	6% partial thickness burn
16	28 mths. M	Wound swab	+	10	+	Cellulitis
17	43 yrs. F	Ear discharge	—	0	—	Chronic suppurative otitis media

18	41 yrs. M	Ear discharge	+	0	–	Chronic suppurative otitis media
19	22 yrs. F	Ear discharge	+	0	—	Chronic suppurtaive otitis media
20	33 yrs. F	Ear discharge	+	0	+	Chronic suppurative otitis media
21	33 yrs. F	Ear discharge	+	0	—	Chronic suppurative otitis media
22	49 yrs. M	Ear discharge	—	0	—	Chronic suppurative otitis media
23	56 yrs. M	Antral washout	—	0	—	Maxillary sinusitis
24	3.5 mths. M	CSF	+	90	+	secondary hydrocephalus, ventriculitis, jaundice
25	24 yrs. M	Catheter tip	+	18	+	Acute glomerulon-ephritis, peritoneal dialysis, bron-chopneumonia
26	34 yrs. M	Portex drain	+	6	+	Traumatic rupture of spleen
27	3 days. M	Umbilical cath.	+	3	+	Imperforate anus
28	43 yrs. M	Catheter tip	+	24	+	Polycystic kidney, dialysis, hypertension
29		Incubator swab				Routine tests on incubators (prem. babies)
30		Incubator swab				Routine tests on incubators (prem. babies)

1. Septicaemia

There were eleven patients from whom *A. xylosoxidans* was recovered in blood cultures. All the patients had been in hospital for two to 90 days (average 25.9 days) when the infecting organism was isolated. All were on antibiotic therapy and all except one had either surgery or instrumentation or both procedures while in hospital. A variety of underlying disease conditions were associated with these patients all of whom could be considered immunocompromised. There were three deaths due to septicaemia.

2. Infected wounds

Four isolates were recovered from traumatic wounds which were infected following surgical toilet and suturing in the hospital. All four infections apparently subsided with penicillin and streptomycin injections coupled with daily eusol dressings. From one patient with a 6% partial thickness burn on the face the organism was isolated from the burns wound on admission. The patient gave a history of splashing water on his face immediately after the burn had occurred. This water was suspected to be the source of *A. xylosoxidans* contamination. With silver sulphadiazine treatment the burn wound healed without signs of infection.

3. Otitis media and sinusitis

There were six isolates from patients with chronic suppurative otitis media and one from a case of maxillary sinusitis. All seven infections were seen in hospital outpatients. Four had been on antibiotic therapy (ampicillin and chloramphenicol) prior to culture and only one underwent surgery (endaural attico-antrotomy) about one year before the culture specimen was taken.

4. Meningitis

The only strain from the cerebrospinal fluid was isolated from an infant who was diagnosed as a case of Flavobacterium meningitis on the eighth day after birth. He was treated with parenteral and intraventricular rifampicin which failed to control the infection. At three and a half months, he developed secondary hydrocephalus and a ventricular tap yielded *A. xylosoxidans*. He did not respond to empirical treat-

ment with the intraventricular gentamicin and intravenous chloramphenicol. When the laboratory test results were known therapy was changed to intraventricular carbenicillin 60 mg/kg which finally eliminated the infection.

5. Contamination

Four strains were isolated from three catheters and a surgical drain after they had been used on patients. None of the patients showed clinical signs of infection at the time of recovery of the organisms. Two strains were recovered from swabs of premature baby incubators taken during a routine sampling exercise.

DISCUSSION

Although *A. xylosoxidans* was described as a new species in 1971 (1) a search of the literature in English revealed only about a dozen papers on this organism. This may have been partly due to the problematical differentiation of this organism from other non-fermentative, gram-negative bacilli in routine diagnostic laboratories. Many characteristics of *A. xylosoxidans* resemble those of Alcaligenes and Pseudomonas species. However, unlike Alcaligenes, *A. xylosoxidans* produces acid from glucose and xylose in ammonium salt sugar medium and the possession of peritrichous flagellae differentiates it from Pseudomonas (2, 7).

The clinical significance of *A. xylosoxidans* isolates is often difficult to determine. This organism has been described as an opportunistic pathogen causing infection among patients with some breakdown in host defence mechanisms (2). In this series, the majority of strains were isolated from hospitalised patients with severe underlying diseases, who had been subjected to various invasive procedures and given a wide range of chemotherapeutic agents. The pathogenic role of the organism was most apparent for the isolates from CSF and blood but even among the 11 cases of septicaemia, two patients recovered without appropriate antibiotic therapy. Among the five cases of wound infection, none was treated with antimicrobials which showed *in vitro* activity against the infecting strain. The same is true for five of the seven aural and nasal infections. When the organism was isolated in a mixed culture, it was even more difficult to determine to what extent it contributed to the infective process. Raised serum agglutinating antibodies following infection have been reported (10), but unfortunately these antibodies were not sought for in any of our cases.

From the patients who responded favourably to antibiotic therapy carbenicillin, ampicillin and cotrimoxazole appeared to be the most dependable drugs for treatment. On the other hand, prior treatment with these drugs which showed *in vitro* activity against *A. xylosoxidans*, did not prevent infection with this organism.

The source and natural habitat of *A. xylosoxidans* are not known for certain. Shigeta and co-workers (10) isolated four strains from chlorhexidine solution used in the surgical ward. We have found this organism in incubators for premature babies and on catheters and surgical drains used on patients who showed no signs of infection. These fomites could have been contaminated by patients who were carriers or by fluids used for disinfection. Bacterial typing may help to elucidate the epidemiology of nosocomial infections by *A. xylosoxidans*. By the use of the nitrate reduction test, strains can be divided into two biotypes designated groups IIIa and IIIb. Cultures of group IIIa reduce nitrate to nitrite only, whereas strains of group IIIb reduce nitrate to gas (8). Serotyping has also been described by Shigeta *et al* (9) who differentiated 95 strains into seven serogroups by a microtitre agglutination test.

From this study it appears that *A. xylosoxidans* may be a contaminant in the hospital environment but may also cause serious nosocomial infections under certain clinical conditions. Resistance to aminoglycosides like gentamicin and amikacin which are first-line therapy for gram-negative sepsis in many hospitals, may have played a significant role in the colonisation and infection by this organism.

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