

BACTERIA FROM INTRAVENOUS FLUIDS

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Summary Eighty strains of bacteria associated with two outbreaks of infection from contaminated intravenous fluids were identified. Most were common soil or water organisms, chiefly enterobacteria, pseudomonads, and coryneforms.

Introduction

AN outbreak of bacteraemia in the U.S.A. due to infected intravenous fluid has been described in which there were 150 cases and 9 deaths.¹ *Enterobacter cloacae* and strains of the *Erwinia* group were incriminated. The report suggested that the fluids might have become infected from the outer surfaces of the synthetic cap-liners during manipulation of the cap. Phillips et al.² described an outbreak in a hospital in which 40 patients were infected and 8 had bacteraemia. These patients were probably infected during the administration of intravenous fluids. One death was attributed to the infecting organism, *Pseudomonas thomasi*. The intravenous fluids were infected by non-sterile water used for cooling the bottles in the hospital pharmacy.

We describe the identification of eighty strains of bacteria (duplicate cultures are not taken into account) isolated from patients with bacteraemia associated with intravenous fluids, from the fluids themselves, or from the equipment in factories of the two firms concerned (firms A and B).

Methods

Many of the strains were identified on their test results by a computer identification program based on the probability of those test results being given by strains of various species or groups.³ Strains of *Klebsiella oxytoca* are included under *K. aerogenes*, from which *K. oxytoca* differs only in the production of indole and late liquefaction of gelatin; intermediate strains, however, may be found.

Results

Firm A

This firm was implicated during the Plymouth out-

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1. McBride, W. G. *Med. J. Aust.* 1972, i, 492.
2. Rachelefsky, G. S., Flynt, J. W., Jr., Ebbin, A. J., Wilson, M. G. *Lancet*, 1972, i, 838.
3. Banister, P., Dafoe, C., Smith, E. S. O., Miller, J. *ibid.* p. 838.
4. Crombie, D. L., Pinsent, R. J. F. H., Fleming, D. *Br. med. J.* 1972, i, 745.
5. Kuenssberg, E. V., Knox, J. D. E. *ibid.* 1972, ii, 292.
6. Klemetti, A., Saxén, L., Health Services Research of the National Board of Health in Finland 1970, 9, 1.
7. Saxén, L., Klemetti, A., Härö, A. S. Unpublished.
8. King, C. T. G. *Science*, 1963, 141, 353.
9. King, C. T. G., Weaver, S. A., Narrod, S. A. *J. Pharmac. exp. Ther.* 1965, 147, 380.
10. McBride, W. *Aust. N.Z. J. Obstet. Gynaec.* 1969, 9, 103.
11. Yerushalmy, J., Milkovich, L. *Am. J. Obstet. Gynec.* 1965, 93, 553.
12. Sadusk, J. F., Palmisano, P. A. *J. Am. med. Ass.* 1965, 194, 987.

break in March, 1972, in which 5 deaths followed the intravenous administration of fluids infected when the sterilisation process in the factory failed.^{4,5} Twenty-two strains from sources connected with firm A were received from three laboratories and investigated in our laboratory (table 1). Two strains came from patients and eight strains came from a batch of 5% dextrose solution in water from Plymouth, a further eleven strains came from the same batch of dextrose saline solution isolated in other laboratories, and one strain came from the factory of firm A.

TABLE I—22 STRAINS ASSOCIATED WITH ONE BATCH OF 5% DEXTROSE IN WATER OF FIRM A

Source	No. of strains	Taxon
Human urine*	1	<i>K. aerogenes</i>
Human lung*	1	<i>K. aerogenes</i>
5% dextrose	2	<i>K. aerogenes</i> †
	2	<i>Enterobacter cloacae</i>
	3	<i>Erwinia herbicola</i>
	3	<i>Enterobacteriaceae</i> (unspeciated)‡
	4	<i>Ps. thomasi</i>
	5	Coryneform organisms (unspeciated)‡
Washtank stopper at firm A	1	<i>Enterobacter cloacae</i>

* Separate patients.
† Strains of this taxon were isolated from a bottle possibly implicated with isolation of a similar strain from a patient with bacteraemia.
‡ Did not conform to the characteristics of commonly described species.

TABLE II—58 STRAINS ASSOCIATED WITH 11 BATCHES OF INTRAVENOUS FLUIDS OF FIRM B

Source	No. of strains	Taxon
Blood-culture	2	<i>K. aerogenes</i>
	1	<i>Citrobacter</i> sp.*
	3	<i>Enterobacteriaceae</i> (unspeciated)†
	1	Non-fermentative gram-negative organism (unclassified)
Intravenous-infusion apparatus (4)	1	<i>K. aerogenes</i>
	3	<i>Enterobacteriaceae</i> (unspeciated)†
5% dextrose in water	7	<i>K. aerogenes</i> ‡
	1	<i>Klebsiella</i> sp.
	1	<i>Enterobacter cloacae</i>
	1	<i>Erwinia herbicola</i>
	2	<i>Citrobacter koseri</i>
	7	<i>Enterobacteriaceae</i> (unspeciated)†
4.3% dextrose in 0.18% saline solution	3	<i>K. aerogenes</i>
	1	<i>Enterobacter cloacae</i>
	1	<i>C. koseri</i>
	3	<i>Pseudomonas</i> spp.
	1	Coryneform organisms (unspeciated)‡
Normal saline	1	<i>K. aerogenes</i>
	1	<i>C. freundii</i>
Intravenous fluid (unspecified)	1	<i>Citrobacter</i> sp.*
	1	<i>Acinetobacter lwoffii</i>
Cooling-water at factory	4	<i>K. aerogenes</i>
	1	<i>Enterobacter cloacae</i>
	3	<i>Escherichia coli</i>
	4	<i>Pseudomonas</i> spp.
	1	<i>A. anitratus</i>
	1	<i>Streptococcus salivarius</i>
	1	<i>Streptococcus</i> sp.

* Did not conform to *C. freundii* or *C. koseri*.
† Did not conform to the characteristics of commonly described species.
‡ Strains of this taxon were isolated from a bottle directly implicated with isolation of a similar strain from a patient.

Firm B

Between March and October, 1972, after the Plymouth outbreak, 12 laboratories sent fifty-eight strains associated with infected intravenous fluids from 11 batches produced by firm B for identification (table II). Seven of these strains were from patients, four were from intravenous apparatus, thirty-two from infected fluids, and fifteen from cooling water at the factory. This cooling water appeared to be the source of infection of the bottles. In seven instances, additives (e.g., heparin or oxytocin) had been added to the intravenous fluids.

Discussion

The overall distribution of the strains among the taxa is given in table III. Most of these organisms might be expected to be commonly found in water and the environment. The presence of *Escherichia coli* and *Streptococcus salivarius* in the cooling water associated with firm B suggests possible human contamination of that water.

The survival of viable organisms derived from plants (i.e., from the maize from which the dextrose is produced) is most improbable. The production of dextrose involves an initial liquefaction step in which the maize starch is heated under pressure at a temperature of 135°C for seven minutes at a pH of 1.5. This should effectively destroy any original contaminants. However, although the dextrose is manufactured to *British Pharmacopœia* standards and is handled under modern hygienic, but not aseptic, conditions, it is not sold as a sterile product nor is it packed as such.⁶

TABLE III—DISTRIBUTION AMONG TAXA OF 80 STRAINS FROM VARIOUS SOURCES

Organisms	No. of strains from			Total
	Infected patients	Intravenous fluids and apparatus	Factory environment	
<i>Gram-negative organisms:</i>				
<i>K. aerogenes</i>	4	14	4	22
<i>Klebsiella</i> sp.	1	..	1
<i>Enterobacter cloacæ</i>	4	2	6
<i>Erwinia herbicola</i>	4	..	4
<i>C. koseri</i>	3	..	3
<i>C. freundii</i>	1	..	1
<i>Citrobacter</i> spp.	1	1	..	2
<i>Escherichia coli</i>	3	3
<i>Enterobacteriaceæ</i> (unspciated)*	3	13	..	16
<i>Pseudomonadaceæ:</i>				
<i>Ps. thomasi</i>	4	..	4
<i>Pseudomonas</i> spp.	3	4	7
<i>Miscellaneous:</i>				
<i>A. antratus</i>	1	1
<i>A. lwoffii</i>	1	..	1
Non-fermentative (unclassified)	1	1
<i>Gram-positive organisms:</i>				
<i>Str. salivarius</i>	1	1
<i>Streptococcus</i> sp.	1	1
Coryneform organisms (unspciated)*	6	..	6

* Did not conform to the characteristics of the commonly described species.

Despite the wide range of organisms in the intravenous fluids, *K. aerogenes* was predominantly isolated from the patients, whereas strains of *Enterobacter cloacæ* or *Erwinia* were absent from the patients examined. Both *E. cloacæ* and *Erwinia herbicola* are potentially pathogenic, and were implicated in the outbreak in the U.S.A.¹ Perhaps *K. aerogenes* more readily multiplies in the patient, although the other organisms present in the intravenous fluid, whether alive or dead, contribute to the bacteræmic shock and reaction to foreign protein. Additionally, since many of the bottles examined were samples taken from the batches and only a few were directly associated with a patient, the range of organisms isolated from all the bottles might be expected to be wider than from the smaller sample directly associated with patients, unless each bottle contained all the kinds of organisms. This would seem unlikely, and did not appear to be the case.

It is also possible for a patient with bacteræmia to infect a bottle by backflow, especially when the bottle is disconnected. This happened with a strain of *K. aerogenes* isolated from a patient and an associated bottle of dextrose saline.⁷ This case has not been included in the present series.

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REFERENCES

1. Special supplement to Center for Disease Control Morbidity and Mortality Weekly Report, U.S. Department of Health, Education and Welfare, 1971, 20, no. 9.
2. Phillips, I., Eykyn, S., Laker, M. *Lancet*, 1972, i, 1258.
3. Lapage, S. P., Bascomb, S., Willcox, W. R., Curtis, M. A. in *Automation, Mechanization and Data Handling in Microbiology* (edited by A. Baillie and R. J. Gilbert); p. 1. London, 1970.
4. Report of the Committee appointed to inquire into the circumstances, including the production, which led to the use of contaminated infusion fluids in the Devonport Section of Plymouth General Hospital. Cmnd. 5035. H.M. Stationery Office, 1972.
5. *Lancet*, 1972, i, 645.
6. Barber, G. A. Personal communication.
7. Heggie, J. F. Personal communication.

DIMINISHED GROWTH OF PSEUDOMONAS ÆRUGINOSA IN UNVENTED BLOOD-CULTURE BOTTLES

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Summary Strains of eight common pathogenic bacterial species were examined for their growth in commercially prepared, vacuum-exhausted bottles of medium used for the cultivation of aerobic and facultative organisms. When various bacterial inocula were mixed with fresh human blood and injected into culture bottles, most bacteria grew luxuriantly and equally whether the vacuum was preserved or broken by the introduction of air. All three strains of *Pseudomonas æruginosa* which were studied failed to produce visible growth in vacuo but grew rapidly in vented bottles. Quantitative studies indicated that pseudomonas multiplied in vacuo but never to an extent at which the growth was macro-