

Septicaemia from prolonged intravenous infusions

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Thong, M. L., and Tay, L. K. (1975). *Archives of Disease in Childhood*, 50, 886. **Septicaemia from prolonged intravenous infusions.** Four cases of septicaemia in children were traced to contaminated intravenous infusions and volume control sets. In each case *Pseudomonas cepacia* was isolated from multiple blood cultures and from intravenous fluid within the volume control set. The first patient died of septicaemia after a long and complicated postoperative period. The other three patients received appropriate antibiotics after removal of the contaminated intravenous sets and they recovered within 2 weeks.

There has been an increasing number of reports in recent years of hospital-acquired infections associated with the use of various types of therapeutic equipment. Some of the important and frequent sources of infection have been ventilatory equipment, indwelling urinary catheters, and indwelling intravenous catheters. This paper reports 4 cases of septicaemia arising from intravenous fluids and volume control sets contaminated by an uncommon organism, *Pseudomonas cepacia*.

Case reports

Case 1. A 2-month-old Chinese boy with imperforate anus, a colostomy, and anoplasty was admitted for reanastomosis of the gut and closure of the colostomy. Postoperatively he was given crystalline penicillin by intravenous infusion and intramuscular streptomycin. On the 12th hospital day he developed a temperature of 39 °C and was thought to have septicaemia. Blood cultures were taken and intravenous cephaloridine was substituted for penicillin and streptomycin. He continued to have a swinging temperature, and on the 25th hospital day he had a laparotomy for intestinal obstruction. Intravenous gentamicin was substituted for cephaloridine. A week later a second laparotomy was required for a subphrenic abscess. Antibiotic treatment was changed to intravenous ampicillin and intramuscular kanamycin. The child remained very ill and finally died on the 44th hospital day.

Three blood cultures taken on the 12th and three on the 43rd hospital day yielded a nonfermenting, Gram-negative bacillus identified finally as *Ps. cepacia*. An intravenous set used for the patient (Fig.) was examined

bacteriologically and the same organism was recovered from the fluid in the calibrated chamber.

Case 2. An 18-month-old Indian boy was admitted with a left chronic subdural empyema. On the 9th hospital day a craniotomy with drainage of abscess was done and intravenous ampicillin was prescribed. The postoperative period was complicated by a swinging temperature, which continued after aspiration of accumulated pus in the subdural space. The subdural fluid grew *Haemophilus influenzae* type b. The antibiotic was changed to intravenous chloramphenicol on the 13th hospital day. Co-trimoxazole was also given from the 20th hospital day.

All of four blood cultures taken between the 14th and 18th hospital days yielded *Ps. cepacia* identical to that in case 1. The intravenous apparatus, removed on the 19th hospital day, was sent for bacteriological examination. The child improved and was well 2 weeks later.

Case 3. A 30-month-old Malay boy was admitted with features suggestive of a partially treated meningitis. He was given crystalline penicillin, chloramphenicol, and sulphadiazine by intravenous infusion. On the 4th hospital day the child developed a temperature of 40 °C associated with rigors. Three blood cultures taken on the 6th to 8th hospital days grew *Ps. cepacia*. The intravenous set was changed and the chloramphenicol and sulphadiazine continued. The child soon became afebrile and was discharged well on the 16th hospital day.

Case 4. A 24-month-old Chinese girl with Hirschsprung's disease was admitted for a rectosigmoidectomy and rectal pullthrough. Postoperatively she was given intravenous penicillin and intramuscular streptomycin. Because of a fear of septicaemia, as seen in the earlier cases, fluid withdrawn aseptically from the intravenous

Received 10 March 1975.

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line below the chamber was cultured 6-hourly from the start of intravenous therapy. The child was quite well until the 5th day of intravenous therapy when she developed a temperature of 39 °C. The intravenous fluid cultures had yielded no growth until the last culture on the 4th day of intravenous therapy, which grew *Ps. cepacia*. Blood cultures taken on the 6th day grew the same organism. The intravenous apparatus was removed and the patient started on intramuscular chloramphenicol. The fever subsided 6 days later and the patient was discharged well.

Bacteriological investigations and results

Blood cultures. The specimens of blood were obtained and processed according to the standard technique in use at the University Hospital. 5–10 ml of peripheral venous blood was drawn aseptically and distributed into a bottle of Liquoid broth (10 ml) and into a bottle of Robertson's cooked meat medium (100 ml). The bottles were incubated at 37 °C and were examined at intervals for up to 2 weeks. Subcultures were made on blood agar plates and appropriate media were used for the biochemical identification of Gram-negative rods as described by Cowan and Steel (1965). Oxoid DST agar plates were also inoculated for antibiotic sensitivity testing with commercial discs.

Intravenous system (Fig.). The intravenous fluid used was 5% dextrose saline. Medications could be added to the fluid inside the calibrated chamber through a cap with an air filter which also served as an air vent. The paediatric measuring units were supplied individually sterilized (Tuta Laboratories, Australia). The intravenous sets used in the 4 cases were examined as soon as they were removed from use. Each entire system was examined for leaks and the fluid used inspected for gross cloudiness. Medication injection caps were inspected for cleanliness and air filters examined for looseness or absence. Samples of fluid were removed aseptically from each cylinder and cultured on blood agar and in nutrient broth. The intravenous fluids in these used cylinders yielded heavy growth of *Ps. cepacia* identical to the isolates from the multiple blood cultures of each case. The air filters in all four cylinders were found to be absent or loose. In addition two unopened, packaged measuring units from the same lot of those currently in use were tested in the same way and were found to be sterile. Volume control sets used for 3 other patients for less than 48 hours were also collected for examination. These patients were not receiving intravenous antibiotics and did not show evidence of septicaemia. Their volume control

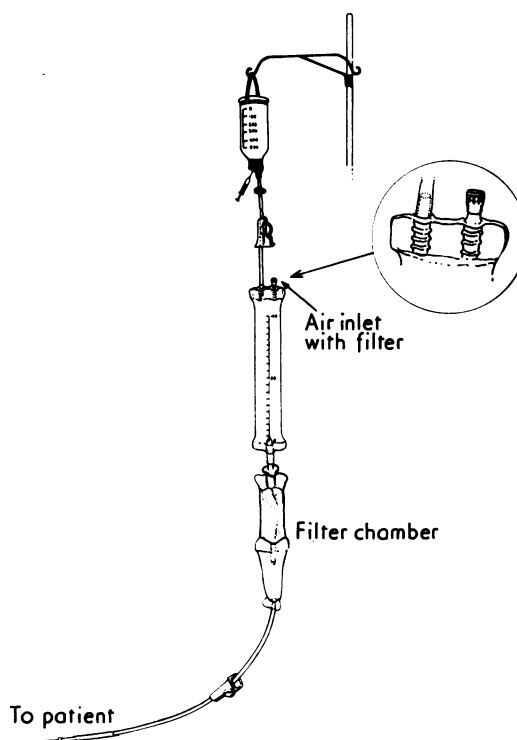


FIG.—Intravenous infusion apparatus as used on all 4 patients.

devices were found to be satisfactory and no organism was isolated from the fluid contained in the cylinders. The bottles of intravenous fluids were all prepared by the pharmacy unit and sterilized by the central supply sterilization unit of the University Hospital. Samples from every batch of intravenous fluids prepared and sterilized have been sent regularly for sterility testing. There has been no record of intrinsic contamination of these bottles.

Organisms. All the organisms isolated from the 4 patients appeared identical in their cultural and biochemical characteristics. They were motile Gram-negative rods, oxidase and catalase positive, and grew well on MacConkey agar. Their colonies measured about 1 mm in diameter after 18 hours at 37 °C. They did not produce haemolysis on human or ox blood agar or form diffusible pigment on nutrient agar. They metabolized glucose oxidatively but did not hydrolyze arginine or oxidize gluconate and could not have been *Ps. aeruginosa*. They also produced acid from 10% lactose agar and reduced nitrate to nitrite. Subcultures of all

isolates were sent to Dr. G. L. Gilardi at the Hospital for Joint Diseases and Medical Centre, New York, who identified them as *Ps. cepacia* (*multivorans*, *kingii*, EO-1). The organisms were thought to be identical because of their unusual antibiotic sensitivity pattern by the disc diffusion method. The strains were sensitive to sulphonamides, co-trimoxazole, and chloramphenicol but resistant to gentamicin, polymixin B, and several other antibiotics. The following MIC determinations ($\mu\text{g/ml}$) by the broth dilution method confirmed this: penicillin >600, ampicillin >200, carbenicillin 100, cephaloridine >200, streptomycin >1200, kanamycin 100, gentamicin 25–50, tetracycline 100, erythromycin 100, rifampicin 100, sulphonamide 50, and chloramphenicol 6.2–12.5. Two of the isolates were examined for growth at room temperature in bottles of 5% dextrose saline. Small inocula of fewer than 10 organisms were used. Viable counts were made by plating serial tenfold dilutions on to nutrient agar in triplicate. The organisms were found to proliferate to a concentration of 6×10^6 organisms/ml within 48 hours and remained viable at about that concentration for at least 2 weeks.

Epidemiological investigations. All pseudomonads isolated from routine clinical specimens by the bacteriology laboratory from September 1971 to January 1973 were examined. It was found that *Ps. cepacia* with the particular antibiotic sensitivity pattern had been isolated from three other sources, all from adult patients nursed in different wards of the University Hospital. These sources were a tracheal secretion, an appendectomy drain swab, and a urine specimen.

Discussion

Usually intravenous infusions and their volume control devices are considered unlikely to be contaminated, since manufacturers adhere to strict sterilization and sterility-testing procedures. However, once they are in use contamination from extrinsic sources is often possible. Duma, Warner, and Dalton (1971) reported 4 cases of septicaemia with contaminated volume control sets in adult patients. They postulated that manipulations of the intravenous apparatus by medical and nursing staff were responsible for the contamination. Contaminating organisms in their cases were coliform bacilli (*Escherichia*, *Klebsiella*, and *Enterobacter*). The patients were receiving antibiotics in their infusions, particularly penicillin, which probably favoured growth of Gram-negative bacilli and

inhibited growth of Gram-positive cocci from the immediate environment.

Investigations in our cases showed that the air vents of the calibrated chambers had not been sealed properly after introduction of medications, particularly antibiotics and mainly penicillin, thus exposing the fluid inside the chambers directly to the ward air. Also the intravenous sets had been used for several days, thus increasing the risk of contamination. In Case 4 the contamination of intravenous fluid was detected only after 4 days of use. Had the entire intravenous system been changed at 24- or even 48-hourly intervals septicaemia might not have occurred in this case. In their review of infection control in intravenous therapy, Maki, Goldmann, and Rhame (1973) stressed the risks and sources of in-use contamination of intravenous fluids. Intravenous systems in use for over 48 hours had five times (15%) the risk of contamination compared with systems used for less than 48 hours (3%). Meyer (1973) showed that *Ps. cepacia* could proliferate in intravenous fluids to reach a concentration of 5×10^5 organisms/ml within 24 hours and 2×10^7 organisms/ml within 72 hours. Our findings are in agreement with this.

Ps. cepacia is generally regarded as a low-grade but potentially dangerous pathogen occasionally causing human infections. Such infections are usually associated with high-inoculum type outbreaks due to contaminated solutions or equipment in hospitals (Ederer and Matsen, 1972). The clinical picture of *Ps. cepacia* septicaemia, as pointed out by Meyer (1973) was different from that of classical Gram-negative septicaemia. *Ps. cepacia* septicaemia was characterized by daily spikes of temperature, anorexia, and a general downhill course until appropriate therapy was started. This organism has a unique drug sensitivity pattern. It is resistant to the aminoglycosides but sensitive to sulphonamides (Gilardi, 1972; Meyer, 1973). Ederer and Matsen (1972) suggested that the drugs of choice for *Ps. cepacia* infections were chloramphenicol and sulphonamides, as most strains were susceptible to these drugs.

In 3 of our cases chloramphenicol and co-trimoxazole were effective after removal of the contaminated apparatus and all 3 cases recovered within 2 weeks. The importance of the organism isolated from blood cultures in Case 1 was not recognized at that time and appropriate antibiotics had not been given. Other pathogenic organisms had been isolated from the patient's surgical wounds and antibiotics prescribed for them. This case illustrates the danger of disregarding unusual organisms as

pathogens, especially when recovered from multiple blood cultures.

The 4 cases occurred between March and June 1972. Since then no other case has been observed in this hospital after it was recommended that entire intravenous systems should be changed at 48-hourly intervals.

We are indebted to Associate Professor K. L. Lam for permission to include the case histories and to Dr. G. L. Gilardi for identifying the organisms.

REFERENCES

Cowan, S. T., and Steel, K. J. (1965). *Manual for the Identification of Medical Bacteria*. Cambridge University Press, London.

Duma, R. J., Warner, J. F., and Dalton, H. P. (1971). Septicemia from intravenous infusions. *New England Journal of Medicine*, **284**, 257.

Ederer, G. M., and Matsen, J. M. (1972). Colonisation and infection with *Pseudomonas cepacia*. *Journal of Infectious Disease*, **125**, 613.

Gilardi, G. L. (1972). Infrequently encountered *Pseudomonas* species causing infections in humans. *Annals of Internal Medicine*, **77**, 211.

Maki, D. G., Goldmann, D. A., and Rhame, F. S. (1973). Infection control in intravenous therapy. *Annals of Internal Medicine*, **79**, 867.

Meyer, G. W. (1973). *Pseudomonas cepacia* septicaemia associated with intravenous therapy. *California Medicine*, **119**, 15.

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