AN EXTENSIVE OUTBREAK OF *KLEBSIELLA PNEUMONIAE* BACTEREMIAS FROM IN-USE CONTAMINATION OF I.V. BOTTLES[1]

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A large outbreak of Klebsiella *septicemia at a hospital in Cali, Colombia, was found to be caused by in-use contamination of I.V. fluids. Contamination was largely the result of practices based on the false assumption that in-use I.V. equipment is internally sterile. Potentially, such circumstances are very apt to recur wherever strict aseptic technique is hard to maintain and where economic restraints tend to encourage compromises with the proper practice of I.V. fluid therapy.*

Introduction

Large-scale outbreaks of bacteremias associated with intravenous (I.V.) fluid therapy are known to have resulted from intrinsic contamination of I.V. fluids or bottle caps during the manufacturing process (*1-6*). In-use contamination of I.V.s has frequently been a factor in sporadic cases of bacteremia, but the scale of outbreaks associated with in-use contamination has been small (*7, 8*). Our purpose here is to report on a very large outbreak of bacteremias linked to in-use contamination of I.V. solutions in hospital wards rather than to production-related contamination.

Description of the Outbreak

As seen in Figure 1, the isolation of *Klebsiella* resistant to ampicillin, tetracycline, carbenicillin, chloramphenicol, kanamycin, and gentamicin but susceptible to colistin and cephalosporins began increasing at the University Hospital in Cali, Colombia, in late 1976. We began our investigation at the peak of the epidemic on 9 February 1977. The epidemic occurred among pediatric patients, no parallel rise in resistant *Klebsiella* bacteremias being observed in adult patients.

Figure 2 shows that the epidemic was associated with an increase in pediatric deaths requiring autopsy and with increased isolation of *Klebsiella* from autopsy material. Only a small portion of the fatalities were autopsied, and only one of the autopsied patients had had a blood culture taken while alive. In the case of this patient, both the blood culture and autopsy culture were positive for resistant *Klebsiella*.

Table 1 shows that the recovery of resistant *Klebsiella* in blood cultures was significantly associated with the length of the patients' hospital stay, while recovery of other organisms was not. Table 2 shows a very strong association between *Klebsiella* isolation and administration of I.V. fluids in the same group of patients and cultures. One of the septicemic patients with *Klebsiella* who had not received I.V. fluid was an infant born to a mother with amnionitis.

Since patients who received I.V. fluids

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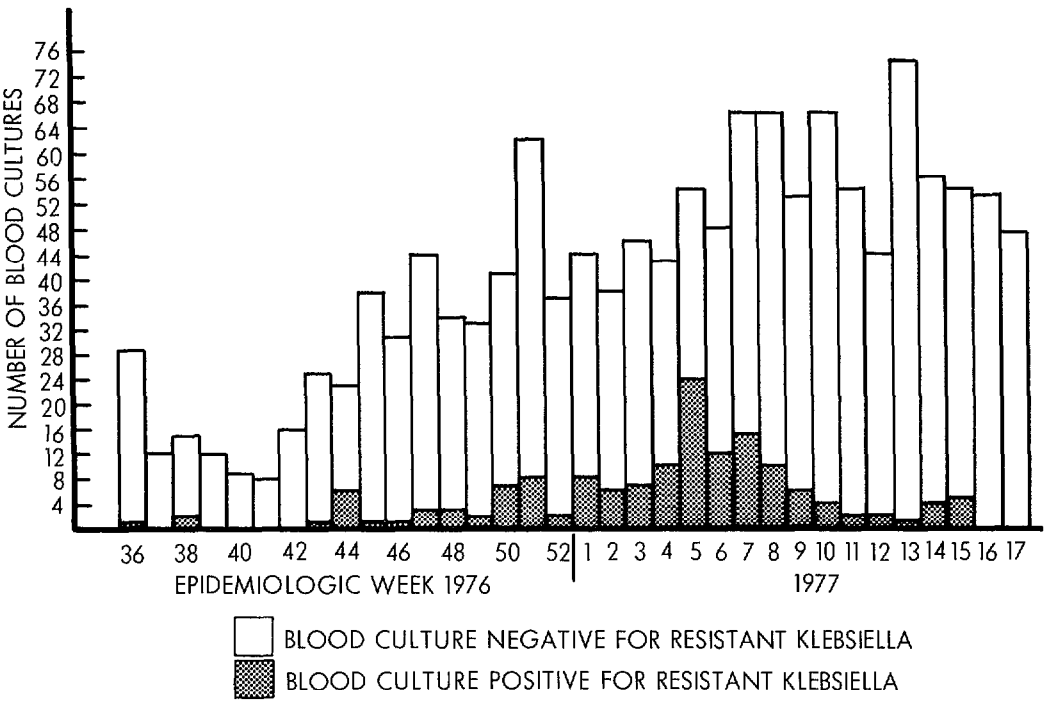
Figure 1. Culture results for blood samples from pediatric patients at the University Hospital in Cali, by epidemiologic week.



were apt to have stayed in the hospital longer than patients who did not, the *Klebsiella* infections could conceivably have been associated with some other hospital-related factor. Therefore, the data were grouped by both length of stay and administration of I. V. fluid. As shown in Table 3, the association between administration of I. V. fluid and isolation of resistant *Klebsiella* remained strong.

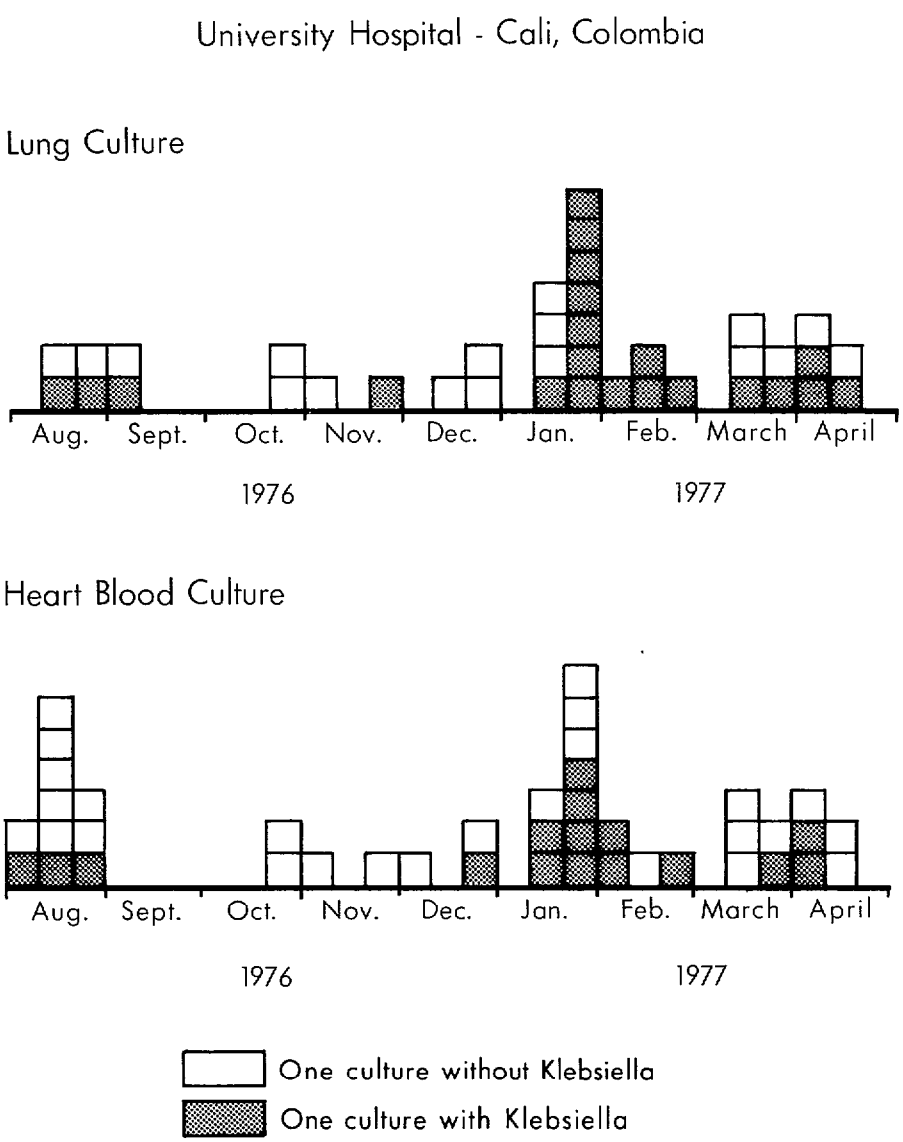
This statistical association between use of I.V.s and *Klebsiella* septicemias was confirmed by finding *Klebsiella* in four bottles of I.V. fluids being administered to newborns. An investigation was undertaken to determine the source of this contamination.

Studies of Intrinsic Contamination

The only I.V. additives that were common to more than 40 per cent of the cases were Na + Cl- and K + Cl-. Eight sealed ampules of each additive were found to be sterile, but contamination was found in opened ampules that had been covered with adhesive tape.

Staphylococcus aureus and *Klebsiella* were found in the I.V. fluids before bottling and sterilization. These organisms most likely came from used bottles returned to the I.V. bottling room for cleaning. After sterilization, however, fluid from 1 bottle out of every lot of 100 prepared was routinely incubated in brain heart infusion broth for 72 hours, and these cultures were always negative throughout the epidemic period. Once the outbreak became evident, the number of bottles cultured was increased; and the fluid from the bottles was also inoculated into chopped meat broth and left for 8 days. All these cultures continued to be negative. From December 1976 to March 1977 cultures were made of fluid from 164 bottles of

Figure 2. Culture results for heart blood and lung samples obtained at autopsy from pediatric patients at the University Hospital in Cali, by thirds of each month.



5 per cent dextrose and 127 bottles of 5 per cent dextrose and normal saline in these media; all were negative.

Experimental contamination of I.V. fluids with *Klebsiella* and subsequent tests run with a range of possible sterilization conditions showed inadequate sterilization to be very unlikely.

When the rubber stoppers from routinely sterilized bottles were cultured separately, no

Table 1. Results of blood cultures from pediatric patients at the University Hospital in Cali, Colombia, in January and February 1977, by days since admission of each patient.

Days since admission	Cultures positive for resistant *Klebsiella*		Cultures negative for resistant *Klebsiella*				Total cultures	
			Positive for other bacteria		Negative			
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Day 1	5	(6.9%)	20	(27.8%)	47	(65.3%)	72	(100%)
Day 2	3	(10.7%)	2	7.1%)	23	(82.2%)	28	(100%)
Days 3-5	14	(42.4%)	4	(12.1%)	15	(45.5%)	33	(100%)
> Day 6	21	(41.2%)	6	(11.8%)	24	(47.0%)	51	(100%)

Table 2. Results of the same blood cultures, grouped according to whether the patient had or had not received I.V. therapy.

Sample source	Cultures positive for resistant *Klebsiella*		Cultures negative for resistant *Klebsiella*				Total cultures	
			Positive for other bacteria		Negative			
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Patients who had not received I.V. therapy	2	(2.7%)	16	(21.6%)	56	(75.7%)	74	(100%)
Patients who had received I.V. therapy	41	(35.7%)	16	(13.9%)	58	(50.4%)	115	(100%)

Table 3. Results of the same blood cultures, grouped by days since admission and by whether the patient had or had not received I.V. therapy (January-February 1977).

Days since admission	Samples from patients who had not received I.V. therapy				Samples from patients who had received I.V. therapy			
	Cultures positive for resistant *Klebsiella*		Cultures negative or only positive for other bacteria		Cultures positive for resistant *Klebsiella*		Cultures negative or only positive for other bacteria	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Day 1	2	(3.6%)	54	(96.4%)	3	(18.8%)	13	(81.2%)
Day 2	0		10	(100%)	3	(16.7%)	15	(83.3%)
> Day 3	0		8	(100%)	35	(46.1%)	44	(53.9%)

Klebsiella were found, but other species of bacteria were isolated on several occasions. Our attention had been drawn to the I.V. bottles' rubber stoppers because a supply problem had forced the use of unlacquered stoppers since December 1976, and bits of rubber could occasionally be seen in the I.V. fluid.

Special attention was also given to scalp-vein needles because these were used almost exclusively by the pediatric service, and hence their contamination might explain

why the outbreak occurred mainly in pediatric wards. However, examination of 16 unopened scalp-vein needles from three lots revealed no contamination.

Studies of Extrinsic Contamination

There was considerable manipulation of I. V. bottles in the pediatric wards—sodium, potassium, or bicarbonate being added to almost every bottle. Also, antibiotics were being given through the I.V. tubing. In most cases no special handwashing procedures were taken before carrying out these procedures, and the procedures were usually performed by the same nurses' aides who changed diapers and dressed wounds.

Some of the most serious errors found in I. V. asepsis were was as follows:

1) mixing the fluids for one patient in a bottle that had already been used for another patient;
2) using the same air-vent needle for several bottles;
3) occasionally using the same I.V. tubing for two patients;
4) using the same needle and syringe to add medication to several bottles;
5) covering opened ampules with adhesive tape for later use and occasionally penetrating this adhesive tape with a needle when using the ampule a second time. One ampule stored this way was found to contain ants.

After taking steps to correct these errors, we began a study of in-use contamination of I.V. fluids and scalp-vein needles. A total of 87 scalp-vein needles (along with samples of the I.V. fluids that they had been administering) were cultured upon being removed from patients. Of these, 23 scalp-vein needles and 20 I.V. fluids were positive for *Klebsiella*. Other bacteria were found in 27 of the scalp-vein needles and 14 of the I.V. fluids.

The role of unlacquered bottle stoppers was also investigated. Lacquered and unlacquered stoppers were first contaminated with the epidemic organisms and then wiped with iodinated alcohol. It was found that unlacquered stoppers (but not lacquered stoppers) treated in this way could cause contamination of I.V. fluids when normal saline was injected.

Studies of the *Klebsiella* Reservoir

Table 4 shows that *Klebsiella* urinary tract infections were associated with exposure to hospital conditions. Therefore, the frequency of *Klebsiella* urinary tract infections over time should indicate whether *Klebsiella* became generally more common in the hospital or whether it merely became more likely that the organism would get into I.V. fluids. No significant change was observed in the frequency of *Klebsiella* urinary tract infections during the period in question, so it can be concluded that the latter explanation applies.

It also appears that *Klebsiella's* establishment of intestinal colony reservoirs in patients was related to patterns of antibiotic use. None of 25 patients in the general pedi-

Table 4. Antibiotic-resistant *Klebsiella* and other bacteria isolated in urine cultures from pediatric and adult inpatients and outpatients at the University Hospital in Cali, Colombia, from May 1976 to February 1977.

	Urine cultures with resistant *Klebsiella*	Urine cultures with other bacteria	% of positive cultures with resistant *Klebsiella*
Pediatric outpatients	3	77	3.8%
Pediatric inpatients	40	148	21.3%
Adult outpatients	12	393	3.0%
Adult inpatients	67	300	18.3%

atric ward harbored the organism in their feces; antibiotics were rarely used in this ward. On the other hand, 6 of 26 children in the infectious disease ward and 6 of 24 subjects in the neonatal intensive care unit were positive for *Klebsiella;* antibiotics were used heavily in these wards.

Even the use of antibiotics to which the organism was sensitive seemed to increase the *Klebsiella* reservoir. Of 5 infants in the neonatal intensive care unit receiving colistin or cephalosporins to which the resistant *Klebsiella* was susceptible, 4 were colonized. But only 1 of the 7 infants not receiving these antibiotics was colonized. This suggests that an intestinal flora not altered by antibiotics might offer resistance to *Klebsiella* colonization, a fact also suggested by the finding that none of the heavily exposed neonatal intensive care unit personnel who were cultured harbored resistant *Klebsiella.*

Discussion

The outbreak of *Klebsiella* pneumonia bacteremias reported here was large and intense.

We rejected intrinsic contamination as the source of the epidemic because the same techniques that showed growth of the epidemic *Klebsiella* in 6 hours during the study of in-use I.V.s showed no growth in 291 cultures of I.V. fluids from unopened bottles during the epidemic period.

Extensive contamination of in-use I.V. fluids and scalp-vein needles was demonstrated. Overall, 20 of 87 in-use I.V. bottles were found to be contaminated with *Klebsiella.* This contamination rate is far above I. V. bottle contamination rates reported in other studies (*9-15*).

Scalp-vein needle contamination was also considerably above contamination rates reported in the literature (*16-18*). It should be noted that the culture methods we used were poorly suited to detecting many organisms found in other studies, but were far better suited to detecting contamination of I.V. fluids than the methods used by other investigators.

Ascending contamination of I.V. bottles from I.V. tubing has been demonstrated (*19*). Nevertheless, our data do not show whether the contamination of I.V. bottle fluids in this outbreak could have arisen from the scalp-vein infection site. Contamination of the fluids during addition of electrolytes and medications seems to have been the most probable source of infection. The extent of I. V. bottle contamination due to contaminated air has been studied (*10,14,15*). It is far too low for that mechanism to be implicated in this outbreak.

The fact that the personnel mixing I.V. medications had frequent contact with patients' fecal material and excretions points to the possibility that their hands were involved in the initial contamination of I.V. fluids. It does not seem possible, however, that hand contamination alone could have achieved the high rates of contaminated fluids we observed. Growth of the organism in the fluids and subsequent bottle-to-bottle transmission must have been involved.

It has been shown that contamination of I. V. fluids with the *Klebsiella* tribe relates to the ability of these bacteria to proliferate in dextrose solutions (*19*). We found that the *Klebsiella* involved in this outbreak grew well in 5 and 10 per cent dextrose solutions to which one-fourth to one-third normal saline and potassium had been added. These are the solutions commonly used in the pediatric wards. The *Klebsiella* did not grow in the 5 per cent dextrose normal saline solution used in the hospital, and only occasional strains grew in plain 5 per cent dextrose solution. This very probably explains why adults were not involved, since the normal saline and plain 5 per cent dextrose solutions were used almost exclusively on adults.

Contamination spread from one bottle to another was probably the most important mechanism acting in this outbreak. A practice of mixing the I.V. fluids and electrolytes to be used during each eight-hour shift in a

bottle that had already been emptied probably created a chain of contamination from one bottle to another. The use of the same air-vent needle or the same I.V. tubing for several bottles would have had the same effect; so would using the same syringe and needle to inject several bottles. This hypothesis is supported by the fact that the wards that had taken the strictest measures to avoid bottle-to-bottle contamination, by insisting on a change of I.V. tubing with each bottle change, were the wards showing the lowest *Klebsiella* isolation rates in our cultural survey of I.V. fluids.

The practices permitting bottle-to-bottle transmission were not new to the hospital, so we must ask what led to the outbreak at the particular time it occurred. To begin with, we investigated the possible role of antibiotics in building up the *Klebsiella* reservoir. The increasing importance of the *Klebsiella* tribe as a cause of hospital infections throughout the world (*20-23*) is probably related to antibiotic use (*24-27*). But even though antibiotic use and abuse probably account for the long-term increase of resistant *Klebsiella* populations, we found no evidence that antibiotics were directly responsible for the outbreak at our hospital. Among other things, it seems unlikely that there was a short-term increase in the *Klebsiella* reservoir among patients because there was no concomitant increase in *Klebsiella* urinary tract infections.

The use of unlacquered bottle stoppers was related over time to the rise in *Klebsiella* bacteremias, but the outbreak was controlled long before lacquered stoppers again became available. Unlacquered stoppers have been shown to create particle and fungal contamination problems in I.V. fluids by providing air pockets that can protect organisms against sterilization procedures. Subsequently, I.V. fluids can be exposed to infection when pieces of the rubber break off (*28*). Nevertheless, in this outbreak we could not demonstrate such an effect. It seems more likely that the bottle stoppers encouraged the spread of fluid contamination by permitting greater adhesion or easier penetration by the *Klebsiella* organisms involved.

Whatever the initiating event, however, failure to consider in-use I.V. bottles, tubing, and air-vent needles as potentially contaminated permitted practices that established a chain of contamination from one bottle to another and that amplified the epidemic.

SUMMARY

The University Hospital in Cali, Colombia, experienced a large-scale outbreak of antibiotic-resistant *Klebsiella* bacteremias in late 1976. The outbreak, apparently limited to pediatric patients, was traced to contaminated intravenous (I.V.) fluids in which the bacteria could multiply.

Further investigation showed that inappropriate handling of I.V. fluids and equipment, rather than faulty production or sterilization procedures, was responsible for the epidemic. The false assumption that in-use I.V. equipment was internally sterile played an important role in creating circumstances that allowed the outbreak to occur. Potentially, there is an excellent opportunity for such circumstances to recur wherever aseptic technique is difficult and where economic restraints encourage compromises with proper I.V. fluid therapy.

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