Minimizing systemic infection during complete parenteral alimentation of small infants

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Nelson, R. (1974). *Archives of Disease in Childhood*, 49, 16. **Minimizing systemic infection during complete parenteral alimentation of small infants.** A regimen of parenteral alimentation for infants was designed to eliminate as many factors responsible for infection as possible.

The most important features of the feeding regimen were as follows. (1) Infants were fed via indwelling silastic catheters inserted into the superior vena cava or the right atrium by a cutdown operation. (2) The parenteral feeding was fat free to simplify the administration system. Y connectors and 2- or 3-way taps were avoided. (3) Extreme care was taken of junctions within the infusion system. Only certain members of the hospital staff were allowed to break such junctions, e.g. during the changing of packs of solution or of the giving sets. These junctions were sprayed with antibacterial aerosols. (4) The hypertonic solutions of nutrients were prepared in plastic packs, which do not require ventilation. The infusion system was therefore not contaminated by the entry of unsterile outside air. (5) The infused solutions were passed through 0.22 μ m millipore filters before entering the patient's blood stream.

There was an infection rate of 9% which was less than the 25 to 45% infection rate previously reported during parenteral feeding through indwelling venous catheters, and is also less than that associated with ventriculoatrial shunts for hydrocephalus. There was no case of systemic candidiasis, which is the most frequent and most serious infection associated with parenteral feeding.

Systemic infection may complicate all forms of parenteral infusions, particularly those using intravenous catheters (Banks *et al.*, 1970). During intravenous alimentation the risk of septicaemia is particularly great (Boeckman and Krill, 1970). If extreme care is not taken, the infection rate during parenteral feeding can become so high that it precludes this form of therapy in all but the most critically ill infant.

A regimen of parenteral feeding has been designed to eliminate as many as possible of the potential avenues of such infection and has been used during the past 10 months to treat 17 infants, all aged less than 12 months. Details of this regimen and the rate of infection experienced are presented.

Parenteral alimentation regimen

The method of parenteral alimentation to be described was used for the prolonged feeding of very small infants. Such patients frequently require feeding through a central venous catheter as available peripheral veins

rapidly become unusable. Because of the known dangers, central venous catheterization should be performed only when other methods of feeding have failed.

A fat-free system was used to simplify administration and to minimize possible infection sites. It is well established that such fat-free parenteral feeding will support optimum growth and development of small infants over several months (Wilmore and Dudrick, 1968).

Preparation of parenteral solutions. Two basic solutions were used. *Solution I* contained over 900 cal/l. as 18% glucose and 3.6% protein hydrolysate. It consisted of a mixture of 200 ml 50% glucose and 500 ml 5% protein hydrolysate/5% dextrose*. *Solution II* contained 660 cal/l. as 12.5% glucose and 4.1% protein hydrolysate. It was a mixture of 100 ml 50% glucose and 500 ml 5% protein hydrolysate/5% dextrose*.

Both solutions were prepared in plastic transfer packs† which do not require ventilation. The essential amino

*Amigen/dextrose solution, Baxter (Travenol Division), Thetford, Norfolk.

†TAI Transfer Packs, Baxter (Fenwal Division).

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acid and ionic content of both solutions are shown in Table I.

After sterilization of all the bottle caps with tincture of iodine, 13 mEq potassium chloride and 5 ml multivitamin infusion (m.v.i.)* were added to each 500 ml bottle 5% protein hydrolysate/5% dextrose.† The required volumes of this and of the 50% glucose solution were then run off into the plastic packs, through the suitably adapted filling tube attached. Each bottle was vented through a 0.22 µm millipore filter. The filling tubes of the packs of solution were finally sealed.

The risk of contamination of the solutions during manufacture is reduced by the use of a laminar air flow hood or similar system. The packs of solution could not be sterilized after manufacture and they were therefore stored until use at 4°C, and not used if over 48 hours old.

TABLE I

Essential amino acid and mineral content of solutions

	Solution I (per l.)	Solution II (per l.)
<i>Amino acids</i>		
Leucine	2.94 g	3.42 g
Valine	2.94 g	3.42 g
Lysine	2.2 g	2.6 g
Isoleucine	1.86 g	2.17 g
Phenylalanine	1.43 g	1.7 g
Threonine	1.36 g	1.6 g
Methionine	930 mg	1.1 g
Histidine	930 mg	1.1 g
Tryptophane	250 mg	290 mg
<i>Minerals</i>		
Sodium	24.0 mEq	28.0 mEq
Potassium	32.0 mEq	37.5 mEq
Calcium	3.5 mEq	4.0 mEq
Magnesium	1.5 mEq	1.7 mEq
Chloride	14.0 mEq	17.0 mEq
Phosphate	21.5 mEq	25.0 mEq

Note: The excess of cations was balanced by anions from the amino acids and stabilizers.

Insertion of the central venous catheters. Silastic catheters, which are probably less likely to perforate the blood vessels than those of more rigid material, were introduced into the right atrium by cutdown operation over an internal jugular vein. The operation was performed under general anaesthesia with strict asepsis in an operating theatre. As has been previously recommended to minimize infection of the blood stream, the venous catheters were tunnelled through the subcutaneous tissues from the vein entry point to a skin exit site 5 cm or more away onto the scalp behind the ear (Harries, 1971; Filler and Eraklis, 1970).

Method of administration of the basic solution. The solution was infused from the plastic pack into the central venous catheter through an administration set, without a connected venting tube.‡ A 0.22 µm

millipore filter was inserted in line immediately proximal to the central venous catheter, to act as a final barrier to particulate matter and micro-organisms before the solution entered the patient's blood stream.

In small infants a constant rate infusion pump is essential to control within narrow limits the volume of fluid administered. Over-transfusion of such hypertonic solutions carries a very great risk from osmotic overload. The pump used must be accurately calibrated to ascertain the relation of the rate of infusion of fluid to the speed of the pump and to the calibre of tubing used in the administration system. Further checks on the volume of fluid being delivered were made by either suspending the packs from a Fenwal infusion scale or by having a Pedatrol* in line in the system. Administration sets with burettes that require venting were not used, as they would have removed the advantage of eliminating contamination of the solutions by unsterile outside air afforded by the plastic packs.

The osmolality of the more concentrated solution I was 1350 to 1400 mOsm/l. Because of the high risk of thrombophlebitis such solutions cannot be infused into peripheral veins. The large blood flow through the superior vena cava allows prolonged infusion via central venous catheters. No case of thrombosis within the superior vena cava or its major tributaries was experienced in the present series of patients. The high glucose concentration accounts for most of the osmolality. 18% glucose solutions contain approximately 1000 mOsm/l. The patient's ability to deal with the osmotic load was monitored by frequent measurements of the blood glucose concentration during treatment.

At the onset of parenteral alimentation, about 150 ml/kg body weight per 24 hours of the less concentrated solution II was transfused at a constant rate. It was usually possible to introduce solution I after 4 to 5 days without producing hyperglycaemia. During the early days of therapy, accurate measurements of fluid intake and output, frequent testing of the urine for sugar, daily serum electrolytes and blood glucose estimations, and twice-daily weighings are required to detect an osmotic overload or diuresis as early as possible. Blood glucose levels should be maintained below 150 mg/100 ml.

At an infusion rate of 150 ml/kg per day, solution I supplied 3.6 mEq/kg per day sodium, 4.3 mEq potassium, 0.23 mEq magnesium, and 1.14 g nitrogen. Solution II supplied 4.2 mEq/kg per day sodium, 5.6 mEq potassium, 0.25 mEq magnesium, and 1.33 g nitrogen.

In addition to the basic solutions I and II, patients also received folic acid 5 mg and vitamin K 1 mg intramuscularly twice weekly; plasma 20 ml/kg body weight intravenously weekly; Imferon 0.5 ml intramuscularly every 2 weeks; and vitamin B₁₂ 100 µg intramuscularly monthly. These injections supplied essential vitamins not contained in the m.v.i., and minerals including trace elements not supplied by the basic solutions (Harries, 1971).

At the end of treatment the intravenous glucose

*S.A.S. Scientific Chemicals Ltd., Liverpool.

†Amigen/dextrose solution.

‡BRIO Administration set, Baxter (Travenol Division).

*Baxter (Travenol Division).

concentration was gradually reduced by infusing 5% dextrose for 12 to 24 hours. Sudden termination of hypertonic glucose administration carries a danger of hypoglycaemia.

Bacteriological studies during parenteral alimentation

Blood cultures. 17 patients aged from 1 day to 12 months were fed intravenously via 21 indwelling central venous catheters. The catheters were maintained *in situ* from 4 to 48 days (Table II) and for an average of 24 days. In Table II the diagnoses and the reasons for parenteral alimentation of each patient are also shown.

At least one 5 ml specimen of blood obtained from each infant through the indwelling catheter was cultured for micro-organisms. 2 ml blood was incubated aerobically at 37 °C in bottles containing 100 ml heart infusion broth with 0.15% glucose and 1 ml added liquid penase (see below for details of this preparation). Subcultures were

made onto blood and chocolate agar after 7 days, or earlier if there was a positive growth. 2 ml blood was incubated anaerobically at 37 °C in 100 ml thioglycollate medium. Aerobic and anaerobic subcultures were made onto blood and chocolate agar after 7 days or when there was a positive growth. 1 ml blood was added to liquid penase medium (0.3% liquid in 0.9% saline with 2% penase (penicillinase)) and a pour plate onto heart infusion agar was incubated at 37 °C. All media were examined daily, and positive growths were sub-cultured.

Blood cultures were obtained at the slightest suspicion of systemic infection. Only two cases had clinical or bacteriological evidence of septicaemia during parenteral feeding, after 25 days and 40 days of such treatment, respectively (Table III). Therefore, cultures of blood obtained from the intravenous catheters showed that only 9% of the catheters became colonized by micro-organisms. In each case the responsible organism was a coagulase negative staphylococcus, and no instance of systemic candidiasis was encountered.

The infected patients were 2 months and 3 months old. They both required complete parenteral feeding for chronic intractable diarrhoea. The infections were successfully eradicated by removal of the catheters and appropriate antibiotic treatment.

Cultures of the packs of solution. Random bacteriological examinations were made on the solutions prepared in the plastic packs. Packs of solutions were cultured after storage at room temperature for up to 6 months. All such cultures were sterile, indicating that the aseptic techniques used in the manufacture of the packs of solution were satisfactory.

TABLE II
Details of total intravenous alimentation

Age	Duration of intravenous catheterization (dy)	Indications for intravenous alimentation
1 dy	(1) 42 (2) 7	Gastroschisis and jejunal perforation; ileal atresia; 2 laparotomies
1 dy	21	Gastroschisis
4 dy	7	Primary repair of oesophageal atresia; prematurity and persistent hypoglycaemia
4 dy	25	Multiple intestinal perforations; intraperitoneal catheter tip after intrauterine transfusion
11 dy	10	Atresia and perforation of the colon; intraperitoneal abscess
2 wk	28	Jejunal atresia; colonic perforation; 3 laparotomies
2 wk	(1) 48 (2) 25	Meconium ileus; recurrent postoperative intestinal obstruction; 3 laparotomies
1 mth	40	Meconium ileus with ileal perforation; postoperative monosaccharide intolerance and intractable diarrhoea
6 wk	13	Gastroenteritis and intractable diarrhoea
6 wk	29	Necrotizing enterocolitis; ileal and colonic perforations
2 mth	(1) 24 (2) 25	Secondary monosaccharide intolerance and intractable diarrhoea
2 mth	15	Intractable diarrhoea
2 mth	24	Intractable diarrhoea
2 mth	36	Hirschsprung's disease of total colon; postoperative diarrhoea and malnutrition
3 mth	(1) 40 (2) 4	Dysmaturity and failure to thrive; Monosaccharide intolerance and intractable diarrhoea
10 mth	15	Coeliac disease; intractable diarrhoea and vomiting
12 mth	26	Immune deficiency; chronic pneumonia; intractable diarrhoea and malnutrition

TABLE III

Results of blood cultures (taken via indwelling catheter)

Patient	Duration of catheter (dy)	No. of cultures	Results of cultures
1	(1) 42	3	Sterile
	(2) 7	1	Sterile
2	21	1	Sterile
3	7	1	Sterile
4	25	2	Sterile
5	10	1	Sterile
6	28	2	Sterile
7	(1) 48	4	Sterile
	(2) 25	2	Sterile
8	40	2	Sterile
9	13	2	Sterile
10	29	3	Sterile
11	(1) 24	2	Sterile
	(2) 25	5	Staph. albus in 2
12	15	3	Sterile
13	24	2	Sterile
14	36	3	Sterile
15	(1) 40	3	Sterile
			Staph. albus in 1
	(2) 4	1	Sterile
16	15	3	Sterile
17	26	9	Sterile

Discussion

Systemic infection is the most frequent serious complication of parenteral alimentation (Moore and Brennan, 1972). Contamination of the infusion system and the patient's blood stream by micro-organisms can occur in several ways.

Local infection at the entry site of the intravenous catheter is a potential precursor to septicaemia. Strict asepsis during the insertion of the catheter is essential and separation of the venous entry site from the skin entry of the catheter probably reduces the risk of septicaemia (Filler and Eraklis, 1970; Harries, 1971). The skin entry site of the catheter was covered with antibacterial and antifungal dressings and these were not changed more than once weekly. Change of dressings have been recommended every 2 to 3 days (Grant, Moir, and Fago, 1969), but Colvin *et al.* (1972) had a low incidence of infection without any change of dressings.

The infused solutions are excellent culture media for micro-organisms (Shadomy and Shadomy, 1972; Brennan *et al.*, 1972) and therefore extreme care was taken to prevent their contamination both during their manufacture in the plastic packs and during the changing of the packs and of the administration sets, which was the responsibility of restricted members of the medical and nursing staff.

The solutions were contained in collapsible plastic packs as they allowed an infusion system which was nonvented and completely closed to the unsterile outside air to be used (Rupp and Forni, 1972).

Packs of solutions were manufactured aseptically as they could not be sterilized afterwards. Contamination during such procedures could not be completely guaranteed, but cultures of packs of solution were all sterile. Packs of solution were stored at 4 °C until given to patients and were not used if over 48 hours old. These precautions were carried out not only to reduce the risk of possible contamination during manufacture but to eliminate possible chemical alterations within the solutions, such as the formation of amino acid—sugar complexes (Coats, 1972).

Junctions within the infusion system, e.g. between the intravenous catheters, the administration sets, and the packs of solution, were potential sites of contamination by micro-organisms. The present regimen of fat-free parenteral feeding reduced such interconnexions to a minimum and eliminated the necessity for complicated systems with Y connectors and 2- or 3-way taps, which significantly increases the danger of infection. Junctions within the present feeding regimen were sprayed with anti-

biotic aerosols containing neomycin, polymyxin, and bacitracin whenever they were changed.

As the solutions infused did not contain fat, it was possible to use a millipore filter to prevent micro-organisms within the solutions from entering the patient's blood stream.

Prophylactic antibiotics cannot be added to the packs of solution because of incompatibility with protein hydrolysates. Their use probably increases the risk of infection by *Candida albicans* (Boeckman and Krill, 1970). As this is the organism most frequently associated with intravenous feeding, their use is probably contraindicated.

Previously reported rates of infection during parenteral feeding through indwelling venous catheters have been between 25 and 45% of those treated (Lloyd-Still, Shwachman, and Filler, 1972). A wide variety of micro-organisms have been cultured from the blood stream during parenteral feeding. *C. albicans* is the most frequent cause of septicaemia (Curry and Quie, 1971), and such systemic candidiasis has carried a 45 to 50% mortality rate (Boeckman and Krill, 1970; Ashcraft and Leape, 1970).

In the present parenteral feeding regimen indwelling central venous catheters were maintained *in situ* for up to 7 weeks and for a mean duration of 24 days. The overall infection rate was 9%, which is lower than previously reported.

It is probably impossible completely to eliminate the problem of infection associated with the prolonged use of central venous catheters. The infection rate associated with ventriculoatrial shunts in hydrocephalus is about 14% (Luthardt, 1970). The infection rate experienced during parenteral feeding was less even though the indwelling catheter was projecting through the skin and was used to infuse fluids capable of supporting the growth of micro-organisms. In the two cases of septicaemia experienced, the causative organism was a coagulase negative staphylococcus, the organism which most frequently colonizes ventriculoatrial shunts.

No case of *C. albicans* septicaemia occurred. It was possible to feed a malnourished infant who had a severe deficiency of both cellular and humoral immunity for 26 days by the parenteral route without developing a systemic infection.

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