Intravenous feeding in a gastroenterological unit

A prospective study of infective complications

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SUMMARY We have assessed the bacteriological safety of a system of intravenous feeding by culturing catheters on removal, swabs taken from the catheter's skin entry sites, and samples of infusion fluid. Among 38 treatment periods using 51 catheters over 1551 patient days, septicaemia due to Staphylococcus aureus was observed in one treatment period and bacteraemias due to Staphylococcus albus and Diphtheroid species in two others. The Staph. aureus and the diphtheroids probably gained access via the skin entry site along the outside of the catheter. The origin of the Staph. albus was uncertain. Parenteral nutrition over extended periods can be a safe procedure if aseptic precautions are taken. The importance of the catheter's skin entry site as a source of contaminating organisms is emphasised.

Parenteral nutrition is potentially life-saving but we have been very conscious of its bacteriological risks and complications and have attempted to minimise them by refinement of technique. This paper describes the findings of a prospective bacteriological surveillance over the period 1 July 1976 to 31 March 1978, during which a new catheter insertion technique was adopted, nursing protocols for the care of the infusion system were improved, and preparation of infusion fluids was brought under pharmacy control.

Methods

CLINICAL

Our team approach to parenteral nutrition has already been described (Powell-Tuck et al., 1978).

Catheter insertion

This was carried out in a specially cleaned side room observing rigorous aseptic technique. The operator scrubbed and wore hat, mask, sterile gloves, and gown as for any other operation. The patient's anterior chest wall and neck were shaved and prepared with 0·5% chlorhexidine in 70% alcohol, which was allowed to dry before iodophore (povidone-iodine) powder was applied. Catheter insertion used to be by a standard infraclavicular technique, and a Teflon catheter was used.

From January 1977 a skin-tunnelled silicone rubber catheter was used routinely. Such a catheter enters the patient's skin on the anterior chest wall, runs superficially to a point just below the midpoint of the clavicle, and then enters the subclavian vein to end in the superior vena cava. The skin entry site on the anterior chest wall is flat and therefore easy to dress. The technique has been described previously in detail (Powell-Tuck, 1978). After insertion of the catheter, the skin entry site was swabbed again with 0·5% chlorhexidine in 70% alcohol, sealed with a plastic spray (Opsite), dressed with further iodophore powder and covered with a sterile occlusive island dressing (Steripad, Johnson and Johnson Ltd).

Infusion system and fluid preparation

Until June 1977 all infusions were from multiple 500 ml or 1000 ml containers as supplied by the manufacturer. They were infused in pairs at 6- to 8-hourly intervals through a specially designed, single-piece, double-giving set (Travenol Laboratories Ltd). All additives to the containers were made by the pharmacist. From June 1977 a new system was increasingly adopted, which reduced the number of...
bottle changes and therefore the number of manipulations of the infusion system made in the bacteriologically uncontrolled environment of the ward. In this system a single 3-litre Viaflex container (Travenol Laboratories Ltd) was filled by the pharmacist with the patient's principal nutritional requirements for the day. Both additions to the small containers and preparation of the 3-litre containers were done under laminar flow conditions in a room subject to restricted entry, strict daily cleaning schedules, and routine bacteriological monitoring. The pharmacist scrubbed and wore hat, mask, and sterile gloves and gown before following bacteriologically tested procedures for making additions or filling containers. The container was then taken, labelled, to the patient's ward refrigerator where it was kept before use on the same day.

Nursing procedures
All nursing procedures for the care of infusions were written and taught and followed aseptic principles. Ward nurses were under the close supervision of the ward sisters and a nursing sister who specialises in parenteral nutrition.

The giving sets were changed every 24 hours. Before connections or disconnections were made, junctions were sprayed with 0.5% chlorhexidine in 70% alcohol and allowed to dry before manipulations were made. Masks were worn and the nurses handled tubing between chlorhexidine in alcohol-soaked sterile swabs. In six patients the catheter was spigotted and heparinised regularly in between infusions. No other injections were made into the infusion set; no other additives were made to fluid, and no transfusions of blood products were given through the feeding catheter. The skin dressing was changed by the nurses at least weekly or if it became loosened. It was dressed as described under catheter insertion.

Specimen collection
(i) A 10 ml 'midstream' aliquot of the nutrient fluid remaining in the infusion set was obtained daily immediately after the set had been disconnected from the patient. Culture of this specimen aimed principally at monitoring the nursing procedures but also gave information about the pharmaceutical preparation of the fluid.

(ii) The skin tunnels were examined daily for signs of inflammation. Whenever the dressing was changed, the entry site was also inspected for signs of inflammation, and a swab was taken from it before it was recleaned and dressed.

The catheter was left in situ for as long as it was required unless the skin entry site or skin tunnel looked inflamed or a previous pyrexial patient became otherwise inexplicably pyrexial. Blood cultures were obtained if a catheter was removed in these circumstances. In patients apparently pyrexial from causes other than catheter sepsis, regular blood cultures were obtained, and the catheter was removed only if these were positive.

(iii) Attempts were made to culture all catheters routinely after removal. After a swab had been taken, the skin entry site was carefully cleaned with chlorhexidine spirit and allowed to dry before the catheter was withdrawn. At first only the tip was carefully removed with sterile scissors and collected into a sterile container. From August 1977 a small piece of the catheter which had been lying in the skin tunnel (the 'body') was also collected separately.

Bacteriological
Using a standard loop, 0.001 ml of the nutrient fluid samples was inoculated onto blood agar so that colony counts could be made. This detected contamination of greater than 10^2 organisms per ml; 1-3 ml of the fluid was then cultured in both thioglycollate and complete broths1 to detect lower levels of contamination.

Swabs from skin entry sites were cultured on blood agar and MacConkey's medium and Gram stained if purulent.

Catheter tips were initially incubated in thioglycollate broth for up to one week. From August 1977 the semiquantitative method of Maki et al. (1977) was used (modified by the substitution of thioglycollate broth for trypticase soy broth). A 7-cm length of catheter 'tip' or 'body' was rolled backwards and forwards over a blood agar plate four times before being cultured in thioglycollate broth. The blood agar plate was incubated aerobically at 37°C, and colony counts were made of any organisms that grew. This gave a semiquantitative estimate of the number of organisms on the outer surface of the catheter. The thioglycollate broth culture was kept for one week; if any growth occurred it was subcultured and the organisms were identified.

Results
Catheters
The series comprised 34 patients treated over 1551 patient-days and 38 treatment periods using 51 catheters. A treatment period ended when a catheter was removed and there was no intention of continuing the infusion later. In 1976, when Teflon cath-

1Constituents: Bacto casitone (Difco) 10 g, Bacto yeast (Difco) 5 g, K_2HPO_4 3 g, KH_2PO_4 1 g, glucose 5 g, distilled water 1000 ml.
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Table 1 Details of all catheters from which bacteria were grown, including one (4) that was implicated in catheter-related sepsis, although no bacteria were grown

<table>
<thead>
<tr>
<th>No.</th>
<th>Catheter</th>
<th>Organisms grown</th>
<th>Organisms from catheter entry site</th>
<th>Inflammation of entry site or skin tunnel</th>
<th>Patient pyrexial at catheter removal</th>
<th>Clinical correlate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Tip</td>
<td>Staph. albus</td>
<td>—</td>
<td>+</td>
<td>+</td>
<td>Sepsis ?source</td>
</tr>
<tr>
<td>2</td>
<td>Tip</td>
<td>Staph. albus</td>
<td>—</td>
<td>0</td>
<td>0</td>
<td>Catheter-related sepsis — skin infection</td>
</tr>
<tr>
<td>3</td>
<td>Tip</td>
<td>Enterococcus</td>
<td>—</td>
<td>Staph. albus</td>
<td>0</td>
<td>Tunnel infection</td>
</tr>
<tr>
<td>4</td>
<td>Tip</td>
<td>Staph. albus</td>
<td>—</td>
<td>Staph. aureus</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Tip</td>
<td>Staph. albus</td>
<td>—</td>
<td>Staph. aureus</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Tip</td>
<td>Staph. albus</td>
<td>—</td>
<td>Staph. albus</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Tip</td>
<td>Staph. albus</td>
<td>100</td>
<td>Staph. albus</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Tip</td>
<td>Staph. albus</td>
<td>50</td>
<td>Microaerophilic streptococci</td>
<td>0</td>
<td>Touched skin on removal</td>
</tr>
<tr>
<td>9</td>
<td>Body</td>
<td>Staph. albus</td>
<td>50</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Tip</td>
<td>Diphtheroids</td>
<td>200</td>
<td>Microaerophilic streptococci</td>
<td>0</td>
<td>? Catheter-related sepsis</td>
</tr>
<tr>
<td>11</td>
<td>Tip</td>
<td>Proteus sp</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>Skin-tunnel colonisation</td>
</tr>
<tr>
<td>12</td>
<td>Tip</td>
<td>Proteus sp</td>
<td>100</td>
<td>0</td>
<td>0</td>
<td>? Significance</td>
</tr>
<tr>
<td>13</td>
<td>Tip</td>
<td>Staph. albus</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>Tip</td>
<td>Staph. albus</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>Tip</td>
<td>Staph. albus</td>
<td>200</td>
<td>0</td>
<td>0</td>
<td>? Skin-tunnel colonisation</td>
</tr>
<tr>
<td>16</td>
<td>Body</td>
<td>Staph. albus</td>
<td>200</td>
<td>0</td>
<td>0</td>
<td>? Significance</td>
</tr>
</tbody>
</table>

0 No growth. — Not done. + Growth.

eters were predominantly used, mean catheter life was 13 days. After the introduction of the skin-tunnelled silicone rubber catheter, mean catheter life increased to 34 days, and 22 of 27 treatment periods (mean duration 44 days) needed only one catheter. The longest life of a single catheter was 154 days when treatment ended. Of the 51 catheters used, 41 were cultured. In no case was a catheter lost that appeared associated clinically with sepsis.

Table 1 shows bacteriological details of the 14 catheters from which organisms were cultured. It includes also one patient (catheter 4) in whom the culture of the catheter was negative. Staphylococcus aureus was grown from his catheter skin entry site one week before and at the time of an episode of pyrexia, when it was also cultured from the blood. The catheter was removed incorrectly one day after flucloxacillin had been started. He was the only patient in whom a septicemia was clearly related to parenteral nutrition.

A patient (catheter 10) developed a pyrexia which could have been due to acute colitis. Blood cultures were negative but 200 colonies of diphtheroids were isolated from the body and tip of the catheter. The pyrexia resolved when the catheter was removed, but this coincided also with an increase in prednisolone dosage with good clinical effect.

Because of persistent pyrexia, which occurred in a severely malnourished patient (initial weight 51% ideal), four catheters were removed. The first (not shown in Table 1) was sterile. The patient received multiple broad-spectrum antibiotics for pneumonia caused by unknown organisms. The second and the third catheters (Nos 1 and 2 in Table 1) were positive for Staph. albus, as were repeated blood cultures. The fourth catheter (not shown in Table 1) was sterile. The pyrexia subsided after seven weeks. There were growths of Staph. albus from eight fluid samples corresponding to three separate catheters. We think that these catheters were secondarily infected from the blood. Retrograde spread of organisms against the flow of a column of nutrient fluid has been described previously by other authors (Boeckman and Krill, 1970; Freeman et al., 1972; Maki, 1976b).

In two patients, catheters (Nos 6 and 13) were withdrawn because of skin-tunnel inflammation. Both patients remained apyrexial, and therefore there was no evidence of bacteremia in either.

One hundred colonies of Proteus species were grown from the body, and six were grown from the tip of a catheter (No. 11) routinely removed at the end of a single catheter treatment period of 52 days. The patient was apyrexial and neither the
entry site nor the skin tunnel appeared inflamed. A growth of *Staph. albus* was obtained from the body and tip of catheter 15 after routine removal following a single catheter treatment period of 32 days and an excellent clinical result. The patient was apyrexial and the entry site and skin tunnel were not inflamed.

**SKIN SWABS**

A total of 228 swabs from the catheter skin entry sites were examined. Of these, 15 were positive for *Staph. albus* and diphtheroids, six for *Staph. albus* alone, and one for diphtheroids only. None of these was related to either skin-tunnel reddening or positive catheter cultures. The organisms grown from the remaining 12 swabs are shown in Table 2. It can be seen that skin-tunnel inflammation was associated with cultures of *Staph. aureus* (three swabs, catheter 6 in Table 1) and *Pseudomonas* and coliforms (one swab), and *Pseudomonas aeruginosa* (one swab, catheter 13 in Table 1). In one patient, catheter-related septicaemia (catheter 4 in Table 1) seemed to be due to a *Staph. aureus* cultured from two swabs from the skin entry site.

### Table 2  Organisms grown from 228 skin entry-site swabs and their relationship to observed sepsis

<table>
<thead>
<tr>
<th>Organism</th>
<th>No. of positive swabs</th>
<th>Related</th>
<th>Catheter +</th>
<th>Skin-tunnel inflammation</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Staph. aureus</em></td>
<td>6§</td>
<td></td>
<td>1*</td>
<td>1†</td>
</tr>
<tr>
<td><em>Staph. aureus +</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Strep. faecalis</em></td>
<td>1</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><em>Proteus sp</em></td>
<td>1</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>β haemolytic streptocci</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>group G</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><em>Microaerophilic streptocci</em></td>
<td>1</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>1</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>coliform</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><em>Staph. albus and diphtheroids</em></td>
<td>15</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><em>Staph. albus</em></td>
<td>6</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Diphtheroids</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>34</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

*Relate to three separate catheters.
†Relate to three separate catheters.

### DEATHS OCCURRING DURING THE SERIES

Three patients from this series of very ill patients died. Their deaths were not considered to be related to the parenteral nutrition. The first, a man aged 32, died of pneumonia complicating pulmonary fibrosis and systemic sclerosis. The catheter tip was sterile and at necropsy the superior vena cava, where it had been situated, was entirely normal. The second was a woman aged 54, with severe perineal erosion due to Crohn's disease. She had had prolonged treatment with steroids, azathioprine, and antibiotics. At necropsy the cause of death was shown to be disseminated aspergillosis. The catheter tip and body were sterile and necropsy showed no abnormality of the superior vena cava. *Aspergillus* sp had not been isolated from fluid cultures or skin entry sites. The third patient died of the combination of a coronary thrombosis and a subarachnoid haemorrhage.

### Discussion

Parenteral nutrition has become recognised as a cause of both fungal and bacterial septicaemia (Curry and Quie, 1971; Freeman et al., 1972) and stern cautions have rightly been given about this treatment (Duma, 1971). Septicaemia rates associated with parenteral nutrition of around 20-30% are not unusual, and rates as high as 93% have been reported.

Dillon et al. (1973) found 19 of 122 patients undergoing intravenous feeding to have had septicaemia but reminded us that such sepsis does not
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necessarily originate in the intravenous fluids or catheter. Their definition of 'catheter-related sepsis' included patients in whom at least one blood culture was positive, the catheter tip was positive for the same organism within 48 hours, and in whom there was clinical evidence of sepsis with no other site of infection with the same organism. By this definition their incidence was 4.1%.

Another method of assessing sepsis due to parenteral nutrition is routinely to culture all catheters when they are removed. If this approach is adopted, a proportion of catheters will be positive to culture even though they are removed from apyrexial patients with no evidence of catheter site (or skin-tunnel) inflammation. The question then arises whether such organisms are contaminants introduced to the catheter after its removal from the patient or whether they are non-pathogenic commensals of little clinical significance; and if they exist as commensals whether they ever become pathogens. Maki et al. (1977) have demonstrated that septicaemia is associated only with catheters yielding large numbers of colonies of organisms. They had advocated a semiquantitative approach to catheter tip and 'body' culture and suggested 15 colonies as an arbitrary dividing line between those catheter site wounds that are 'infected' and those that are not. Local inflammation was more commonly associated with colony counts of >15 colonies on semiquantitative culture.

Measures taken to prevent sepsis due to parenteral nutrition depend upon a knowledge of how and where organisms can contaminate the infusion system. Much attention has been given to contamination of fluids as supplied by manufacturers after epidemics of septicaemia traced to this source in the USA (Maki et al., 1976) and England (Meers et al., 1973). There is probably little the hospital can do to prevent such episodes. Bottles and containers should be checked for cracks or leaks, and fluids checked for cloudiness. Unfortunately, cloudiness occurs only at very high level contamination and may not be apparent even with levels of 10^6 organisms/ml. The hospital can play a part, however, in tracing such causes of septicaemia by keeping records of batch numbers of fluid infused. Septicaemia due to Klebsiella sp, Pseudomonas sp, Enterobacter cloacae or Erwinia agglomerans occurring in patients receiving intravenous fluids should prompt careful studies of the fluids in stock (Maki, 1976a).

Fortunately, thanks to careful manufacturing techniques, septicaemia due to infected fluid supplies is very unusual. Much more commonly, sepsis arises in the hospital. A full review of the possible causes of this has been made (Maki, 1976b).

The techniques we have adopted have already been described in greater detail elsewhere (Powell-Tuck, 1978; Powell-Tuck et al., 1978). They aim to reduce contamination (i) when additives to a mixture of fluids are made, (ii) during giving set manipulation, (iii) during catheter insertion, and (iv) along the catheter from the skin entry site. This study was designed prospectively to test how bacteriologically safe parenteral nutrition could be rendered by careful aseptic technique and to identify broadly where improvements could be made.

Earlier unpublished studies showed that if a developed pharmaceutical protocol was followed, the viaflex 3-litre containers could be filled under the conditions described without introducing organisms that would grow in nutrient broth. Nevertheless we were aware of the theoretical risk of mixing all the nutrients in one container because mixtures of glucose and amino acids in general support the growth of bacteria better than do individual unmixed solutions (Maki, 1976a). Our studies on the infused fluid samples suggest that this was not a problem in practice. The organisms grown and their numbers do not suggest pharmaceutical contamination and subsequent proliferation of the organisms in the nutrient fluids.

This study emphasises the importance of the catheter's point of entry through the skin as a route of entry for organisms. The one most clear and clinically significant episode of septicaemia (catheter 4, Table 1) arose from this site and, with the exception of one patient in whom endogenous infection of the catheter seems likely (catheters 1 and 2, Table 1), all organisms grown in significant numbers from catheter tips appear to have gained access in this way, as suggested by entry site swab cultures or cultures of the catheter's 'body'. Furthermore, skin-tunnel or entry-site reddening served on two occasions as warnings of impending catheter sepsis and allowed us to remove the catheter before clinical signs of septicaemia occurred. It should have prevented the first case of septicaemia seen (catheter 4, Table 1). It is not clear whether the colonisation of the skin tunnel by apparently non-pathogenic bacteria (catheters 11 and 15, Table 1) is of clinical significance; certainly neither patient exhibited any sign whatever of adverse effect.

From this study we can draw a number of clinical conclusions. Firstly, because so few of the fluid aliquots were positive, we no longer consider daily sampling of infusate to be necessary. The present nursing techniques for changing containers and giving sets, which for simplicity do not include the use of sterile gloves, appear satisfactory. The pharmaceutical techniques seem adequate also, but it must be noted that the nutrient fluid was stored...
before use for only short periods. If longer storage is used, organisms contaminating the fluid have a chance to multiply and produce toxin, and a more sophisticated clean air manufacturing unit may be needed. The potential risks of introducing into nutrient mixtures organisms that subsequently have time to multiply cannot be overemphasised.

The use of microbial filters has not been adopted because it increases the number of manipulations made to the infusion system, and because other studies (Collin et al., 1973; Miller and Grogan, 1975) have not suggested that they reduce the septic caemia rate. Their use could not have improved our sepsis rates because sepsis arose from the skin entry sites and not from the infused fluid. They seem unnecessary if great care is taken in the preparation and infusion of the fluids.

We have learnt that it is a mistake to ignore any degree of skin entry-site or skin-tunnel inflammation. These should be regarded as indications for removal of the catheter.

Because this study draws attention to the skin as a source of infection, we shall continue to obtain and examine routine skin swabs whenever dressings are changed and will further emphasise the importance of cleaning this area at the time of catheter insertion and of redressing the entry site. If organisms other than Staph. albus or diphtheroids are grown, serious consideration will be given to removing the catheter. It seems that if these precautions are added to our present adopted approach, there will be no need for routine catheter changing with its attendant risks and discomfort for the patient. We shall continue routinely to culture the body and tip of all catheters semiquantitatively. Nurses undertaking aseptic procedures are more likely to follow them assiduously if they know that a constant bacteriological interest is being taken in the results of their work.

In summary, we have found, like Ryan et al. (1974), Sanderson and Deitel (1973), and Sanders and Sheldon (1976), that parenteral nutrition can be relatively free of serious bacteriological complications if strict aseptic techniques are employed. We have shown that great attention needs to be paid to preventing organisms from reaching the blood from the skin entry site of the catheter. It appears that a skin-tunnelled catheter has advantages in that organisms are delayed in reaching the patient’s bloodstream and forewarning of their presence is given by visible inflammation.

We thank the nursing staff of St Mark’s Hospital for collecting the specimens; Miss Thalia Nielsen, MSc, SRN, for help in collating the data; the laboratory staff of the Department of Microbiology, St Bartholomew’s Hospital, for taking on the extra workload involved; and the staff of the Cross Infection Reference Laboratory, Colindale, London, for typing the strains of staphylococci.

References


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