The complications of intravenous cannulae incorporating a valved injection side port

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SUMMARY

In a series of 519 intravenous cannulae with valved injection side-ports the incidence of cannula-related local inflammation was 25·2 % and bacteraemia 0·2 %. Severe local inflammation was associated with a longer mean duration of cannulation, 59·4 *v.* 81·4 h ($P = <0·05$). There was no significant association between the presence of local inflammation and microbial colonization of either the intravascular segment of the cannula, the adjacent skin, or the side-port. The data suggest that colonization of the cannulae was usually secondary to prior skin colonization. Side-port colonization did not predispose to cannula colonization. Organisms colonizing the side-port were biologically different and were possibly derived from the skin of medical attendants. In the final 157 patients, randomized to receive either isopropyl alcohol or 0·5 % chlorhexidine in 70 % spirit skin preparation, there was no difference in the incidence of either local inflammation or microbial colonization.

INTRODUCTION

Over five million plastic intravascular cannulae are used each year in Britain. An increasing proportion of these cannulae incorporate a valved side-port which affords intermittent intravenous access for bolus injections. This design feature has been criticized as it also offers micro-organisms a potential portal of entry to the circulation (Oberhammer, 1980; Peters, Fisher & Mehtar, 1979, 1980, 1981 *a*; Peters, Mehtar & Fisher, 1980; Peters *et al.* 1981 *b*), although evidence linking this with an increased incidence of local or systemic sepsis is lacking (Macfarlane *et al.* 1980, 1981; Cowan, 1982).

In January 1980 a series of studies was initiated to determine the incidence of both local inflammation and microbial colonization associated with the use of such intravenous cannulae. Observations were made regarding the relationship between these complications and methods aimed at their control. The results of the first two studies on 362 cannulae have been published (Macfarlane *et al.* 1980, 1981) and are now included with a further study of 157 patients in this report.

MATERIALS AND METHODS

The Venflon (British Viggo, Swindon) cannula was used exclusively. The cannulae were inserted by junior medical staff into consecutive patients on the coronary care unit and two adjoining medical wards in the first two studies and in the coronary care unit alone in the third study. Skin preparation prior to insertion was performed with a 70 % isopropyl alcohol swab (Mediswab) in the first study involving 102 cannulae. In the second study involving 260 cannulae, 0·5 % chlorhexidine gluconate in 70 % spirit (Dispray No. 3 Stuart Pharmaceuticals) was used. In the final study 157 cannulae were randomized to receive either one or other of these preparations. In all cases the agent was allowed to dry prior to cannula insertion. The cannula was secured with Micropore tape. In the second study a group of 89 cannulae had their insertion sites covered with a sterile dressing which was changed daily, at which time 42 of them were sprayed with povidone-iodine. Drugs administered via the cannula were recorded.

Cannulae were removed when clinically indicated. At the time of removal the insertion site was inspected for the presence of redness and swelling, scored in centimetres measuring the diameter of the area involved, while phlebitis was also sought and scored in centimetres of affected vein. Tenderness was assessed on a 0 to + + + + analogue scale. Definite local inflammation was judged to be present if at least two of the above criteria were present at a score exceeding one centimetre or a single +. Severe local inflammation was present if more than five centimetres of phlebitis was also present.

Immediately prior to removal a saline moistened swab was rubbed over the skin immediately adjacent to the cannula insertion site. A further moistened swab was then vigorously rotated in the side-port (except in the first study). The insertion site was then sprayed with 0·5 % chlorhexidine gluconate in 70 % spirit and allowed to dry. The cannula was then removed and the intravenous segment cut off with a sterile blade into a sterile plastic universal container. The swabs were kept in Stuart's transport medium and the cannula segments at 4 °C until cultured. Within 24 h of removal the swabs were inoculated on agar and the cannulae rolled over a plate to give a semi-quantitative assessment of colonization (Maki, Weise & Sarafin, 1977). The cultures were made on 5 % horse blood agar incubated at 37 °C for at least 48 h in air. A positive cannula roll culture was defined as > 15 colonies growth and a positive swab as > 5 morphologically similar colonies in the first sweep. The tip was finally cultured in nutrient broth (this step was omitted in the second study). A blood culture was taken routinely at the time of removal in the first study, but only if clinically indicated in the other studies. All isolates were identified and saved. In all cases in which there were two or more isolates of the same species from the different sites on the same cannula these were further defined by phage-typing, biotyping and antibiogram.

RESULTS

There was one case of cannula-related bacteraemia in this sample of 519 cannulae, an incidence of 0·2 %. This was due to *Staphylococcus aureus*, and resulted in fatal endocarditis.

Table 1. *Relationship between inflammation at the cannula insertion site, duration of cannulation and site of positive culture*

Inflammation	Number of cannulae (number with side-port culture)	Duration (h) (mean ± s.D.)	Sites with positive culture (%)		
			Skin	Cannula	Side-port
None	388 (321)	59·4±38·2*	41 (11)†	19 (5)	15 (5)
Definite	93 (70)	64·7±44·8	12 (13)	3 (3)	2 (3)
Severe	38 (26)	81·4±69·1*	9 (24)†	4 (11)	2 (8)
Total	519 (417)		62	26	19

* Significant difference at $P = < 0.05$, Student's t test.
† $P > 0.05$ by chi-squared test.

Table 2. *Correlations between cannula tip cultures, skin cultures and side-port cultures for 519 cannulae*

Study number	Number of cannulae	Cannula roll	Site of colonization	
			Skin	Side-port
1	1	*S. aureus**	*S. aureus**	Not tested
	7	*S. epidermidis**	*S. epidermidis**	Not tested
	5	*S. epidermidis*†	*S. epidermidis*†	Not tested
	2	*S. epidermidis*	No growth	Not tested
	16	No growth	*S. epidermidis*	Not tested
	1	No growth	*Candida albicans*	Not tested
2+3	4	*S. epidermidis**	*S. epidermidis**	No growth
	1	*S. epidermidis**	*S. epidermidis**	*S. epidermidis*‡
	2	*S. epidermidis*‡	*S. epidermidis**	*S. epidermidis**
	4	*S. epidermidis*	No growth	No growth
	21	No growth	*S. epidermidis*	No growth
	3	No growth	*P. aeruginosa**	*P. aeruginosa**
	1	No growth	*Klebsiella* sp.†	*Klebsiella* sp.†
	12	No growth	No growth	*S. epidermidis*
Total		26	62	19

* Same ⎱ By phage-typing, biotyping and antibiogram.
‡ Different ⎰
† Non-typable.

The association of local inflammation with culture results and duration of cannulation is shown in Table 1. Overall, 25·2 % of cannulae were associated with local inflammation and in 7·3 % this was severe. There was a trend towards a longer mean duration of cannulation in the local inflammation group but this was only significant for the severe group ($P < 0.05$). The majority (78 %) of the cannulae with local inflammation were culture negative. There was a tendency for positive cultures of skin and cannula to be associated with the presence of severe local inflammation but not lesser degrees of inflammation. This trend however scarcely reached a modest degree of significance ($0.1 > P > 0.05$ by chi-squared test) in the case of skin cultures alone.

The relationship between positive side-port, cannula and skin culture was examined (Table 2 and Fig. 1). There was no common isolate in the three cases
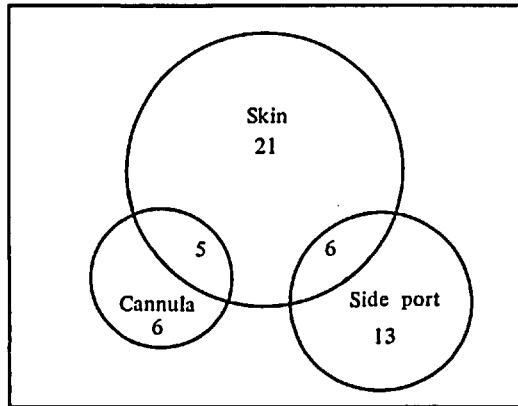
Fig. 1. Venn diagram showing relationship between positive skin, cannula and side-port cultures in 417 cannulas (studies 2 and 3).

Table 3. *Influence of skin preparation on the incidence of local inflammation and skin culture positivity*

	Skin preparation	Number of cannulae	Local inflammation		Positive skin culture	Duration (h) (mean ± s.d.)
			Definite	Severe		
All cannulae	Mediswab	182	32*	20†	41‡	66·2 ± 50·1
	Dispray	337	61*	18†	21‡	59·5 ± 43·8
Randomized	Mediswab	80	9*	8*	8*	50·1 ± 28·3
cannulae	Dispray	77	14*	6*	4*	46·5 ± 25·9

* No significant difference
† Significant difference $P < 0.05$ ⎫
‡ Significant difference $P < 0.001$ ⎭ chi-squared test.

Mediswab; 70 % isopropyl alcohol-soaked swab pre-packed in single sachets. Dispray (no. 3); 0·5 % chlorhexidine in 70 % spirit as an aerosol.

in which both side-port and tip cultures were positive. Skin culture and cannula cultures were found to be of identical phage type, biotype and antibiogram in 13 cases and dissimilar in two. A further seven pairs were not phage-typable. On six occasions similar organisms were grown from both skin and side-port and dissimilar organisms once. Although these associations were highly significant ($P < 0.001$), the positive predictive value of skin culture for either cannula or port culture was only 21 % and 19 % respectively. In 21 instances skin cultures alone were positive (a further 17 in the first study were possibly so, but port cultures were omitted). Likewise 12 port cultures were similarly positive in isolation, while only six cannulae produced lone positive cultures.

The influence of different skin preparation is recorded in Table 3. Taking the whole population there is a significant reduction in the incidence of both severe inflammation and the presence of a positive skin culture in the chlorhexidine-in-spirit group. However, when the randomized groups are considered, although there is still a trend towards a lower incidence of both local inflammation and the

presence of a positive skin culture with chlorhexidine in spirit, it is no longer significant. The randomized groups were well matched for duration of cannulation and drug administration including antibiotics.

The drugs most frequently administered via the cannulae side-ports were diamorphine and prochlorperazine, reflecting the large proportion of patients on the coronary care unit included in these studies. These drugs had no influence on the incidence or severity of local inflammation or on culture results. Antimicrobial drugs exhibiting activity against most strains of *Staphylococcus epidermidis* were administered in 66 cases. Although the incidence of local inflammation was not significantly different in these cases, only two had positive skin cultures, and none produced positive cannula or side-port cultures. Overall 164 (32 %) of the cannulae were not used for drug administration although all cannulae were flushed 4–6 hourly with 0·9 % saline to maintain patency. These cannulae as a group had a reduced incidence of phlebitis, but when stratified for the influence of duration of cannulation this reduction was no longer significant.

Neither the position of the cannulae, skin shaving prior to insertion, nor the application of a sterile dressing had any influence on the incidence of local inflammation or culture results. In none of the 42 cannulae which received a daily povidone–iodine spray was culture of the skin, side-port or cannula positive. Eight of these cannulae were associated with local inflammation and in three this was severe. None of these results was statistically significant by Fisher's exact test.

DISCUSSION

The reported incidence of septicaemia related to the use of plastic peripheral venous cannulae varies between 0 and 3·4 % (Banks *et al.* 1970) while the incidence of local inflammation varies from 9 to 56 % (Smith, Selick & Edelist, 1973; Collin *et al.* 1975). The reasons for this wide variation include differences in the populations and type of cannulae studied, as well as differences in definition of significant local inflammation.

In this study there was only one case of septicaemia in 519 Venflon cannulae with incorporated side-ports. The incidence of local inflammation was 25·2 %, which compares favourably with the incidence observed in several studies using a number of cannula types (Dinley, 1976; Maki & Band, 1981). But the incidence of local inflammation is significantly greater ($P < 0.025$) than the 18·8 % incidence reported in a sample of 468 Teflon cannulae without side-ports (Tully *et al.* 1981). However, these authors employed a more restrictive definition of local inflammation, and their protocol ensured that no cannula remained *in situ* for more than 72 h. Since both these features will tend to reduce the incidence of local inflammation it seems inappropriate to regard this small difference in incidence as established. Furthermore, Noble *et al.* (1980) observed in a sample of 203 Venflon cannulae an incidence of 19·7 %, which is not significantly different from Tully's series.

Local inflammation is believed to be primarily due to the administration of irritant drugs, microparticulate matter introduced via the cannula or irritation related to the cannula material itself. The role of infection, although clearly important in suppurative thrombophlebitis, is less certain in milder degrees of phlebitis. Maki estimates that 20 % of local inflammation is due to infection

although the possibility that an initial 'chemical' phlebitis becomes secondarily infected is hard to exclude (Maki, 1980).

Our studies reveal a weak association between a positive skin culture and evidence of local inflammation but fail to confirm Maki's finding of a strong association with a semi-quantitative roll tip culture growing >15 colonies. The reasons for this may lie in differences in the populations and type of cannulae studied. Another possibility is that our use of chlorhexidine in spirit as opposed to alcohol alone prior to cannula removal caused small quantities of antiseptic to be transferred, giving 'false' negative cannula cultures, although care to allow time for evaporation to dryness was generally observed.

In none of the 19 positive side-port cultures could the same isolate be grown from the tip, although six had skin cultures growing the same isolate. This complete lack of common isolates between side-port and cannula roll culture is surprising in such a large series. It suggests that if microbes are injected down the cannula lumen they rarely subsequently colonize it *in vivo*, although this has been demonstrated *in vitro* (Locci, Peters & Pulverer, 1981). Intraluminal colonization can be missed on roll cultures (Grabe & Jakobson, 1983; Zinganell, Bohme & Schmitt, 1983). It should however be detected on broth culture, but again this was not demonstrated in association with a positive side-port culture in the last 157 cases, the only study in which both broth and side-port cultures were done. While these data indicate that the side-port is an infrequent source of cannula-related infection, the possibility remains that transient undetected side-port colonization may be the cause of some of the positive tip cultures which lack similar skin isolates.

The data suggest that skin colonization is usually the prime event which subsequently leads to cannula colonization, provided the cannula is *in situ* long enough. This presumably occurs by migration along the intracutaneous tract. An alternative explanation is that a small inoculum from the skin is introduced on insertion of the cannula, which then leads to colonization. This seems unlikely; in 20 cannulae *in situ* for less than 2 h no growth was found (Macfarlane *et al.* 1981), although clearly a much larger series would be required to rule this out.

The main source of potential organisms colonizing the port is the skin of patients or hospital staff. Almost one-third of the port isolates were found in conjunction with an identical skin isolate, suggesting that the patient's skin was the source of infection. However, half of these were a cluster of three cases of colonization with an identical strain of *Pseudomonas aeruginosa*, strongly suggesting cross-infection, most probably on the hands of the attending staff. Therefore in 16 out of 19 side-port isolates the data suggest that the source of infection was extrinsic rather than from the patients' own skin.

The conflicting data on the influence of skin preparation may be due to an increasing degree of awareness and greater care being taken by medical staff over the course of the first two studies favourably biasing the second study in which chlorhexidine was used exclusively. The final randomized study suggested that chlorhexidine reduced skin colonization, but that it had no influence on local inflammation. Similarly, in patients receiving anti-staphylococcal antibiotics, although a reduction in skin colonization was noted it had no impact on local inflammation, possibly in this case because of a local irritant effect of the antibiotic.

Although this study suggests that povidone–iodine spray may reduce the incidence of microbial colonization, the number of cannulae so treated was too small to be significant and previous studies have revealed no benefit (Noble *et al.* 1980).

In conclusion our data show that the Venflon cannula is associated with a rate of bacteraemia, local infection and local inflammation which is similar to that found in cannulae not incorporating a valved side-port, although a formal comparative trial has not been carried out. The data also suggest that the pathogenesis of cannula-related local inflammation is multifactorial, with local infection only accounting for about 20% of cases. However, when local infection does occur it is usually secondary to prior skin colonization, there being no evidence to implicate side-port colonization as a precursor.

In the randomized trial comparing 0·5% chlorhexidine in 70% spirit with isopropyl alcohol skin preparation, no statistically significant difference could be detected in the incidence of either local inflammation or positive skin cultures, although the overall trend suggested that alcoholic chlorhexidine was superior.

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