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Infusion Thrombophlebitis: A Prospective Comparison of 645 Vialon® and Teflon® Cannulae in Anaesthetic and Postoperative Use

P. B. GAUKROGER,* J. G. ROBERTS** AND T. A. MANNERS†
Department of Anaesthesia and Intensive Care, Flinders Medical Centre, Adelaide

SUMMARY
A prospective study of the incidence and severity of infusion thrombophlebitis in peripheral intravenous infusions used for anaesthetic and postoperative purposes in 645 patients was conducted over a four-month period. Conditions of insertion were carefully controlled while ward management was according to standard practice. A total of 330 polyurethane Vialon® and 315 FEP-A Teflon® cannulae were used. The results show that the nature of the cannula was the single most important factor in the incidence and severity of infusion thrombophlebitis, Vialon® cannulae being associated with a 46% lower incidence than the Teflon® type. Less important but significant factors included intravenous antibiotics, duration of infusion, cannula tip damage and caesarean section. Factors not associated with infusion thrombophlebitis included potassium therapy, blood transfusion or site of insertion in the upper limb. Heparinisation increased duration of infusion without affecting the incidence of infusion thrombophlebitis.

Key Words: VEINS: damage, thrombophlebitis, anaesthetic drugs; INFUSION: intravenous, antibiotics, IV fluids; CANNULA: peripheral intravenous, material, Teflon®, Vialon®, polyurethane

Intravenous cannulation is the most common invasive procedure performed in acute care hospitals. Over 25% of adult patients in our university teaching hospital receive an intravenous infusion as part of their treatment,[1] and this is almost invariably administered via a cannula placed in a peripheral vein of the upper limb.

The most frequent complication of intravenous therapy is infusion thrombophlebitis. This is characterised by a painful local reaction often with erythema, swelling and palpable thrombosis of the vein. Thrombophlebitis leads to much patient discomfort and necessitates the reinsertion of the cannula into another peripheral vein if intravenous therapy is to continue. The inflammatory reaction is usually sterile. However, patients with catheter-associated phlebitis do have an increased risk of septicaemia.[2] The incidence of septicaemia related to peripheral intravenous cannulae is low, in the order of 1:1000 (J. Turnidge personal communication, 1988). But as infusion thrombophlebitis may take several weeks to resolve and during that period can seriously impair function in the upper limb concerned, any reduction in its incidence would be of great benefit to patients.

Many factors have been implicated in the

*F.F.A.R.A.C.S., Anaesthetic Senior Registrar.
**F.F.A.R.A.C.S., D.Phil., Senior Specialist, Senior Lecturer.
†M.B., B.S., Anaesthetic Registrar.
Address for Reprints: Dr. J. G. Roberts, Department of Anaesthesia and Intensive Care, Flinders Medical Centre, Bedford Park, South Australia 5042.

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genesis of infusion thrombophlebitis. These can be divided into chemical factors such as irritant drugs and fluids, and physical factors such as cannula composition and the site and duration of cannulation.

A review of the literature shows a great difference of opinion between authors in the perceived relative importance of these factors in the aetiology of infusion thrombophlebitis. There have also been further advances in polymer technology which have resulted in cannula materials which on physicochemical grounds should be less thrombogenic than earlier materials. An example is a member of the polyurethane group of compounds (Vialon®) which has shown very favourable in vivo characteristics in animal studies.[3]

We therefore designed an extensive prospective study to re-examine the relative roles of a large number of potential factors including cannula material in the aetiology of infusion thrombophlebitis associated with intravenous infusions used for anaesthetic and postoperative purposes in an Australian teaching hospital.

MATERIALS AND METHODS

Two types of peripheral intravenous cannulae were compared under conditions of normal clinical practice. They were Jelco® brand 1.75" FEP-A Teflon® 18 gauge and 16 gauge (Critikon Inc.) and Insyte® brand 2" polyurethane hybrid co-polymer Vialon® 18 gauge and 16 gauge (Deseret Medical Inc.).

As our anaesthesia staff had become very familiar with the Teflon® type over several years, the newer Vialon® cannulae were made freely available for a familiarisation period of one month before commencement of the study. The study then ran for the subsequent four calendar months.

The entry criteria were that the patient was adult, that a cannula was inserted by anaesthesia medical staff imediately prior to surgery in the operating theatre suite, that it was used for fluid infusion and drug administration during operation and that the infusion was continued beyond the postoperative recovery phase. Institutional Committee on Clinical Investigation approval was given and although individual consent was not required an information sheet was given to all patients.

The anaesthetist in each case nominated the gauge of cannula required (18 gauge or 16 gauge) and was given one or other brand by the anaesthesia nurse in alternating order of patient presentation to that room. The site of cannulation in the upper limb was also chosen by the anaesthetist. Insertion technique was standardised. The skin was prepared with chlorhexidine 0.5% in ethanol 70% and intradermal procaine 1% was used as deemed appropriate. The cannula was inserted percutaneously without prior skin incision. The insertion site was covered with a transparent adhesive dressing (OpSite®, Smith and Nephew) and adhesive tape applied to anchor the tubing of the giving set. Stickers showing a unique identifying number were attached to both the dressing and the giving set.

The cannulae were subsequently managed according to the normal practice of the attending medical and nursing staff. The investigators took no active part in subsequent management. The cannulae were removed by the ward staff on their usual criteria and were retained for subsequent macroscopic and microscopic examination.

The data collected at the time of insertion included patient details, age, sex, time of cannulation, seniority of insertor, use of local anaesthesia, perceived quality of vein, site of insertion, flow through the cannula and ease of insertion through the skin as well as into the vein. The nature of the surgery was noted.

The infusion sites were examined daily by one of the investigators until removal. All drugs and fluids which had passed through the cannulae were recorded. In addition other potentially significant concomitant medication such as anticoagulants were noted. An assessment of the degree of thrombophlebitis was made by recording the presence of pain, redness, swelling, palpable thrombosis or presence of overt infection. Using these findings any thrombophlebitis present was scored each day according to a severity scale modified from that of Dinley (1976)[4] (Table 1). This score had a potential range of zero to 5, where zero represented no evidence of phlebitis and 5 represented obviously infected and extensive phlebitis.

Upon removal, the cannulae were placed by

TABLE 1
Thrombophlebitis grading
(After Dinley 1976[4])

0	No reaction
1	Tender to touch over intravascular portion of cannula
2	Continuous pain ± redness
3	Continuous pain and palpable thrombosis within length of cannula ± swelling
4	Continuous pain and palpable thrombosis beyond cannula ± swelling
5	As for 4 with overt infection

ward nursing staff into a numbered double-wrap soft plastic bag. At this time, nursing staff were asked to record reason for and time of removal. The cannulae were collected daily by the investigators. The retained cannulae were examined for the presence of kinking, and, with the aid of an operating microscope, for evidence of distortion of the tip. The degree of tip distortion was graded according to the scale shown in Table 2. Photomicrographs of typical damage grades are shown in Figure 1.

All the information for each of the cannulae was subsequently entered onto computer coding sheets to facilitate data entry and enable various statistical tests to be applied. This was done with the aid of a Statistical Package for the Social Sciences (SPSS-X) programme running on a Prime 750 mainframe computer (Flinders University Computing Services). Factors influencing the incidence and severity of infusion thombophlebitis were examined by stepwise regression using an entry criterion of $P < 0.05$ and a removal criterion of $P > 0.1$.[5] Statistical comparisons of mean phlebitis scores and other variables between brands of cannula were performed using Student's 't' test for unpaired data and the Wilcoxon Rank-Sum test for ordinal level data. Survival analysis was performed using Cox's proportional hazards model for multivariate analysis and survivals were compared by Cochran-Mantel-Haenzel Chi-Square test.

A mean phlebitis score was calculated for each cannula (Figure 3). This scoring system facilitated comparisons of different groups of potential aetiologic factors. Its was calculated by dividing the sum of the daily thrombophlebitis scores by the duration of

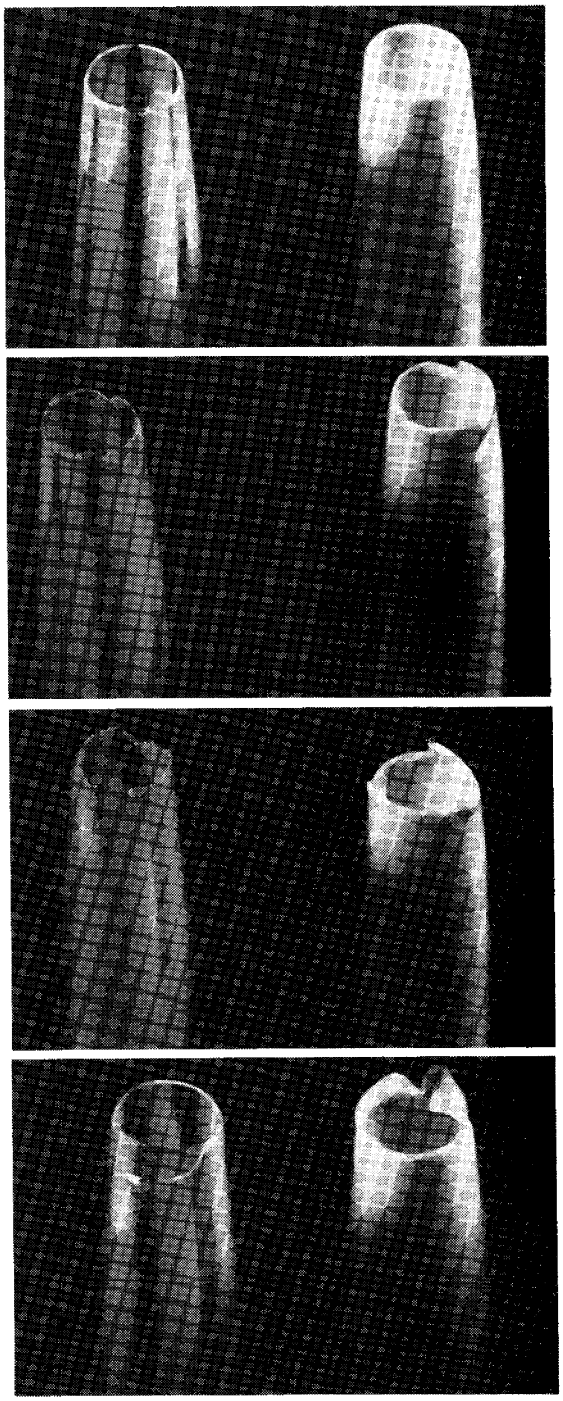

FIGURE 1 a, b, c, d.—Photomicrographs of typical tip damage gradings after rinsing in water. In each panel the Vialon® cannula is shown on the left with the Teflon® type on the right. Damage gradings of zero and one are shown in the top two panels with grades 2 and 3 in the lower two panels.

TABLE 2
Cannula tip damage grading

Damage grade	Appearance of tip	Associated mean phlebitis score
0	No distortion present	1.07
1	Minor deformation of tip	1.25
2	Major distortion, minor cracking	1.41
3	Severe disruption, major cracking, fragmentation	1.58 ($P < 0.05$)

cannulation (in days). This score was very useful for comparative purposes as it took into account the duration of cannulation as well as the degree of thrombophlebitis present.

RESULTS

At the conclusion of the predetermined study period, the performance of 645 cannulae had been assessed. Of these 330 were the Vialon® type (16 gauge n = 138; 18 gauge n = 192) and 315 were the Teflon® type (16 gauge n = 134; 18 gauge n = 181).

The overall thrombophlebitis rate (i.e. infusions with any degree of thrombophlebitis) was 51.9%, and cannulae were in place for a mean of 40.7 hours. The Vialon® cannulae showed a phlebitis rate of 40.9% and the Teflon® cannulae a phlebitis rate of 63.5% ($P < 0.0001$).

Table 3 and Figure 2 describe the thrombophlebitis scores for each day with each type of cannula. With both types there was a progressive increase in the degree of phlebitis with increasing duration of cannulation. Statistically significant differences existed between the Vialon® and Teflon® cannulae for each day of cannulation, with the Vialon® cannulae always being associated with a lower incidence of phlebitis. We observed no case with an infusion thrombophlebitis score of 5 (severe with overt infection). Survival analysis indicated a significantly higher 'survival' (infusion still in progress) for Vialon® cannulae than for the Teflon® type on any day post insertion ($P < 0.001$). Overall, in the infusions studied, the risk for phlebitis of severity greater than one with Vialon® was 54% of the risk with Teflon® cannulae ('prevented fraction' = 46%).

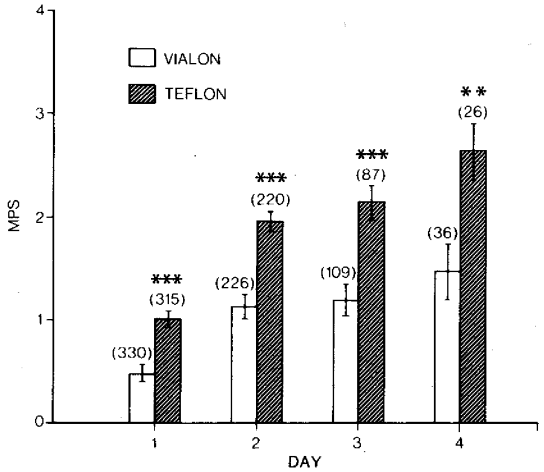

FIGURE 2.—Mean Phlebitis Score (MPS)) by Day. Error bars indicate SEMS. Significance: $^{**}P < 0.01$, $^{***}P < 0.001$.

The mean phlebitis scores were used for evaluation of factors which may have had an effect on thrombophlebitis rate or severity. The mean phlebitis score for all cannulae in the study was 1.15.

The cannula material proved to be the most significant factor affecting infusion thrombophlebitis in all our comparisons. The Vialon® cannulae had an overall mean phlebitis score of 0.81 and the Teflon® cannulae had an overall score of 1.46 ($P < 0.0001$). The difference between materials was more marked with the 16 gauge cannulae than the 18 gauge cannulae, and this may be a reflection of the differing uses to which smaller and larger sizes were put. The 18 gauge cannulae tended to be used for more minor operative procedures. They were less used for the injection of drugs shown to be irritant such as antibiotics, had lower volumes of fluids infused and were more likely to be

TABLE 3
Mean thrombophlebitis scores for each day of cannulation (with standard deviations in brackets)

	Vialon®	Teflon®	% of cannulae Remaining in situ	*P* Value
Day 1	0.48 (1.04) n = 330	1.02 (1.36) n = 315	100%	< 0.0001
Day 2	1.16 (1.43) n = 226	1.95 (1.49) n = 220	69.1%	< 0.0001
Day 3	1.20 (1.48) n = 109	2.15 (1.51) n = 87	30.4%	< 0.0001
Day 4	1.47 (1.63) n = 36	2.65 (1.41) n = 26	9.6%	< 0.003

removed because there was no longer a need for infusion therapy. The duration of cannulation was shorter with 18 gauge cannulae compared to 16 gauge cannulae (35.8 vs 46.6 hours). The 16 gauge cannulae were used for more major procedures, had more irritant drugs and fluids and were less likely to be removed because they were no longer required. The 16 gauge Teflon® cannulae remained in for 40.8 hours while the 16 gauge Vialon® cannulae were in for 50.9 hours.

Cannula tip damage was more common with the Teflon® cannulae (37.3%) than with the Vialon® cannulae (16.6%). This tip damage was significantly associated with higher mean phlebitis scores as indicated in Table 2, where the most severe grade of tip damage had a score of 1.58 ($P < 0.05$).

Kinking was not found in any of the Vialon® cannulae after removal. However, 29.3% of the Teflon® cannulae had visible kinks of the cannula shaft, usually at its junction with the hub.

The only surgical procedure which was found to affect infusion thrombophlebitis rates was caesarean section. Patients undergoing caesarean section (70% under epidural; 30% GA) had scores of 1.77 which has the highest thrombophlebitis score of any operative group in the study. This was despite the fact that infusions in these patients were only maintained for an average of 26 hours and that very few drugs (in particular no antibiotics) passed through these cannulae.

At least one dose of antibiotic was administered via 320 of the cannulae (49.6%). Of these 34.6% were cephalosporins, 11.0% were penicillins and 4.0% were other antibiotics which included gentamicin and metronidazole.

In all, 203 cannulae (31.5%) were used for continued intravenous antibiotic courses. The administration of a course of antibiotics was associated with a higher mean phlebitis score (1.37) than when either only a single dose or no antibiotic at all was given (1.02, $P < 0.002$), a single intraoperative dose of antibiotic not affecting the phlebitis score. Duration of cannulation for cannulae used for antibiotic courses was longer than average (54.0 hours vs 34.2 hours, $P < 0.001$).

We grouped antibiotics into major categories. These were penicillins, cephalosporins, metronidazole and a small group of others. Penicillins and cephalosporins had similar phlebitis scores. Metronidazole however, was associated with a much greater degree of infusion thrombophlebitis and despite the small number in this group (n = 12), this was a highly significant correlation ($P < 0.0001$).

Veins which were judged to be of poor quality at insertion had a significantly increased incidence of phlebitis ($P < 0.05$).

The site of insertion did *not* affect rates of infusion thrombophlebitis as measured by mean phlebitis score. Twenty-five per cent of cannulae were inserted in veins in the back of the hand, 30% were at the wrist and 44% were in the forearm.

Other factors which were examined, but which had no significant effect on mean phlebitis score, were the use of blood transfusions, colloids, potassium supplements, the age or sex of the patient, kinking of the cannulae, thiopentone or opioids.

No change in mean phlebitis score was observed with heparin administration by any route. We examined the use of subcutaneous heparin, single IV bolus, and heparin administered as an infusion for anticoagulation after vascular surgery and found no significant change in phlebitis score in any of the groups when compared with patients not receiving heparin. The heparin infusion group, however, did have longer duration of cannulation (74 hours vs 38.9 hours, $P < 0.0001$) suggesting that these lines may have remained patent for longer.

The effect of size of cannula was not adequately examined in our study because only two sizes (18 gauge and 16 gauge) were used and, as mentioned previously, the 16 gauge cannulae received more fluids and irritant drugs.

Anaesthetic staff had been asked to judge ease of penetration through skin and ease of insertion into the vein, with each cannulation. Ease of penetration through skin was significantly better with the Vialon® cannulae ($P < 0.01$) being judged 'good' in 94.5% of cases versus 88.9% with the Teflon® cannula. Ease of penetration into the vein was equal in the two groups.

Cannulae were removed at the discretion of the ward medical and nursing staff. A total of 405 cannula (62.7%) were removed because they were no longer required (they may have had some degree of infusion thrombophlebitis as well); 207 (32.1%) were removed solely for infusion thrombophlebitis and 30 (4.7%) were removed because they had stopped running adequately. Of the 207 cannulae removed for phlebitis, 89 were Vialon® and 118 were Teflon®. Only three (0.5%) were removed because of the standing order that cannulae be changed at 48 hours.[6]

The seniority of the inserting anaesthetist did not correlate with mean phlebitis score or cannula tip damage: 47.1% were inserted by specialists; 34.6% by registrars and 18.3% by resident medical officers or interns under supervision.

DISCUSSION

The literature contains a multitude of factors said to affect the likelihood of an intravenous infusion vein developing infusion thrombophlebitis.[7] As this condition is a common, painful and troublesome complication of intravenous therapy, we considered it worthwhile to re-examine these factors to see what factors really were important in our own everyday perioperative practice. Clearly, cannulae used in this period are usually used for infusion of a large number of intravenous drugs and fluids and may be considered to be more at risk of inducing infusion thrombophlebitis for this reason. On the other hand a high degree of control over the circumstances and method of insertion was possible in this study. All cannulae were inserted by, or under the direction of, experienced operators in an unhurried manner in well lit and clean surroundings. This control avoided many potential risk factors which may be associated with intravenous lines hastily inserted by unsupervised junior staff or in urgent situations where aseptic and antiseptic precautions so frequently break down.[1]

We found that several factors previously implicated in the pathogenesis of infusion thrombophlebitis were not significant correlates in this series while cannula material had a greater influence that previously reported. That duration of cannulation was clearly associated came as no surprise as it has frequently been observed that the longer a cannula is left in situ, the more likely thrombophlebitis is to develop. Rothman (1986) summarises the position. *'The value of risk is time dependent... During a long period of time risk or cumulative incidence will approach unity no matter what the values of the underlying incidence rates are. This is an epidemiologic manifestation of the aphorism "In the long run, we are all dead"'.* Should all cannulae be removed after a fixed period of time (e.g. 48 hours)? We think not, because many cannulae in the study developed infusion thrombophlebitis after as little as six hours, while others remained free of phlebitis for as long as ten days. It would be more logical for ward staff to be educated to replace cannulae at the first sign of phlebitis. Such education is obviously required as this study shows that our nursing staff pay little heed to the requirements of their nursing procedures manual[6] which, inter alia, requires removal of any peripheral cannula at the first sign of

phlebitis or at least after 48 hours of cannulation.

There was a marked difference between the performance of the two different cannula materials. Vialon® cannulae had much lower rates of thrombophlebitis, longer durations of cannulation, less tip distortion and showed no shaft kinking when examined after removal. Teflon® cannulae were more often removed because of phlebitis than were the Vialon® type (37.5% vs 27.0%, $P < 0.0001$).

Administration of a course of antibiotics caused increased phlebitis rates. This is probably due to the direct irritant effect of the antibiotic on vein endothelium but we also noted that cannulae used for antibiotics remained in situ for ten hours longer than the average cannula in the study. This indicates that these cannula were left in situ because they were still needed for therapeutic purposes even though they exhibited signs of infusion thrombophlebitis. A single dose of antibiotics made no difference to thrombophlebitis rates.

The addition of heparin to the intravenous infusion in a full anticoagulating dose did not affect phlebitis rates as measured by our scoring system. However, the duration of infusion in this group was significantly longer (74.0 hours). This presumably reflects the fact that most of these patients had undergone major vascular surgery and required prolonged intravenous fluid therapy as well as antibiotic cover.

Women undergoing lower segment caesarean section had very high rates of thrombophlebitis despite a short duration of infusion and a general lack of irritant drugs administered. We can only attribute this to patient factors such as the markedly increased likelihood of spontaneous venous thrombosis and phlebitis in term pregnant patients.[9]

We conclude that the Insyte® cannulae (made from Vialon®) were significantly much less likely to develop infusion thrombophlebitis than the Jelco® cannulae (made from FEP-A Teflon®) in the two sizes tested (18 gauge and 16 gauge) and that, in this large prospective series involving 645 intravenous cannulae used in the operative and postoperative period, there were only a few factors which were otherwise found to increase the likelihood of infusion thrombophlebitis. These were the duration of cannulation, cannula tip damage, caesarean section, intravenous antibiotic courses, and poor quality veins as adjudged prior to insertion.

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