Eur J Vasc Endovasc Surg **26**, 550–557 (2003)
doi: 10.1016/S1078-5884(03)00344-7, available online at http://www.sciencedirect.com on SCIENCE DIRECT®

Rifampin and Triclosan but not Silver is Effective in Preventing Bacterial Infection of Vascular Dacron Graft Material

T. Hernández-Richter,[1*] H. M. Schardey,[1] F. Wittmann,[1] S. Mayr,[1] M. Schmitt-Sody,[1] S. Blasenbreu,[2] M. M. Heiss,[1] C. Gabka[1] and M. K. Angele[1*]

[1]*Chirurgische Klinik und Poliklinik and* [2]*Institut für Pathologie, Klinikum Großhadern, Ludwig Maximilians-University, Munich, Germany*

Objectives. *To evaluate the efficacy of silver- or Triclosan-coated prosthetic material compared to Rifampin bonded Dacron concerning their resistance to infection following subcutaneous implantation and contamination with* Staphylococcus aureus.
Design. *Animal experimental study in mice.*
Material and methods. *Thirty-six C3H/HcN mice (Charles River Lab., Sulzfeld, Germany) with a weight between 24 and 27 g were randomised into six groups counting six animals each. Group I: control, gel-sealed dacron graft, group II: gel-sealed dacron graft and local contamination, group III: Intergard®-Silver-prosthesis and contamination, group IV: silver/gel-sealed dacron prosthesis (test graft) and contamination, group V: Rifampin-bonded gel-sealed graft and contamination, group VI: Triclosan/collagen-coated dacron graft and contamination. Dacron graft material 0.8 × 1 cm was subcutaneously implanted in mice. Local contamination with* 2×10^7*/0.2 ml* S. aureus *ATCC 25923 was carried out in groups II to VI. On day 14 the animals were killed and the grafts were explanted. The microscopic, histologic and microbiological evaluation of the graft material and the perigraft tissue was performed.*
Results. *In control group I no case of infection was detected. In group II, 6 of 6 animals showed infection. In group III (Intergard®-Silver) and group IV (silver/gel-test graft) were 6 of 6, in group V (Rifampin) only 1 of 6 grafts and in group VI (Triclosan) 4 of 6 grafts were infected. The difference between the low rate of infection in group V (Rifampin) in comparison to the completely infected groups III and IV (Silver) as well as the control group II was significant. Treatment of grafts with Triclosan could prevent infection only in 1/3 of the cases in group IV.*
Conclusion. *Silver coating failed to prevent graft infection material. A potential antimicrobial property was evident for Triclosan whereas Rifampin-bonded grafts exhibit a significantly reduced infection rate. Thus, silver-coated vascular grafts cannot ensure protection from vascular graft infection.*

Key Words: Vascular graft infection; Silver coating; Rifampin; Triclosan; Standardised infection model.

Introduction

The reported incidence of vascular graft infection is between 0.5 and 5%.[1–4] The mortality in the presence of vascular graft infections varies between 25 and 75%,[5,6] and the rate of limb loss in infrainguinal vascular bypass infection may reach 79%.[7,8] Following the manifestation of a vascular graft infection the gold standard in the treatment is the explantation of the infected graft, extensive excision of perigraft tissue followed by the reconstruction with an extraanatomic bypass. In 1990 the reconstruction with in situ graft replacement using antimicrobially protected grafts was introduced. Recently, autologous and homologous graft reconstructions have been performed with promising results. Although homologous and autologous reconstructions lead to good outcome, there availability is limited. In particular cases the use of Dacron material cannot be avoided.

In surgical meetings successful case reports of Dacron vascular grafts coated with the novel agent Triclosan have been propagated for in situ reconstruction in vascular graft infections.[9] Similarly, in a pig vascular graft infection model positive effects of Triclosan on the infection rate have been shown.[10] Presently, silver coated grafts are utilized for in situ reconstruction in case of vascular graft infection,

*Corresponding authors. Priv. Doz. Dr med. Th. Hernandez-Richter, Dr Martin K. Angele, Department of Surgery, Klinikum Grosshadern, Ludwig-Maximilians University, Marchioninistr. 15, Munich 81377, Germany.

1078–5884/03/050550 + 08 $35.00/0

despite the fact that there are no in vivo examinations available proving the efficacy.

The aim of our study, therefore, was to test the antimicrobial properties of dacron grafts treated with silver-or Triclosan and compare those results with the previously established Rifampin bounded prosthetic material. To address this issue a standardised well characterised experimental mouse model was used in which infected graft material treated with various agents was implanted.

Material and Methods

Thirty-six male C3H/HcN mice (Charles River Lab., Sulzfeld, Germany), 6–7 weeks old with a weight between 24 and 27 g were used in the trial. (The C3H/HeN mice were used in this study since they have a balanced Th1–Th2 immune response and are therefore similar to the immune system in humans.) All animal care complied with the principals of Laboratory Animal Care and the Guide for the Care and Use of Laboratory Animals (Tierschutzgenehmigung und Versuchsgenehmigung, Government Oberbayern/Germany).

Graft material. Commercially available standard grafts (Silver Intergard® Intervascular, La Ciotat, France and Uni-Graft® DV, B. Braun Melsungen AG, Melsungen, Germany) as well as a not commercially available silver/gelatine-coated dacron graft were used in the study. All grafts had a diameter of 8 mm. They were cut to a size of 0.8 × 1 cm. The graft material in the groups I, II, III, IV and V were autoclaved and graft material in group VI underwent gamma-radiation. All operations were done under sterile conditions. The grafts were implanted into a subcutaneous pouch. Contamination was not carried out in all groups. The groups undergoing contamination received 0.2 ml 2×10^7 *S. aureus* ATCC 25923 (Max von Pettenkofer-Institut für Hygiene und Medizinische Mikrobiologie, München, Großhadern, Germany) directly onto the graft at the end of the procedure prior to closing the skin. This dosage was used since it caused reproducibly infection of the prosthetic material.[10] There were six animals in each group.

Group I. Control group, gelatine-sealed dacron graft (Uni-Graft®DV); no contamination.

Group II. Control group gelatine-sealed dacron graft (Uni-Graft®DV), local contamination with *S. aureus* (1×10^7).

Group III. Silver/collagen coated dacron graft (Intergard®), local contamination with *S. aureus* (1×10^7).

Group IV. Silver/gelatine-sealed dacron graft not commercially available, local contamination with *S. aureus* (1×10^7).

Group V. Rifampin-impregnated gelatine-sealed dacron graft (Uni-Graft®DV), local contamination with *S. aureus* (1×10^7). The graft material was in analogy to the clinical procedure bathed in a concentration of 60 mg/ml Rifampin (Rifa® parenteral 600 mg, Grünenthal GmbH, Stolberg, Germany) for 15 min at 37 °C.

Group VI. Triclosan/collagen-coated dacron graft (Intergard® Intervascular), local contamination with *S. aureus* (1×10^7). Triclosan (Irgasan®) was bonded directly to the polyester of the graft by means of van der Waal'sche forces as has been reported.[11]

Surgical technique

All mice were anaesthetised with Isofluran (Forene®) employing the Isofluran Vaporiser 19,3 (Dräger AG, Lübeck) in combination with a oxygen laughing gas mixture. The animals were fixed on their back, the abdominal wall was shaved and disinfected with an alcohol 75%. Under sterile conditions the abdominal midline incision was carried out followed by the preparation of a subcutaneous pouch to the left. The 0.8 × 1 cm graft was implanted into this pouch. In groups II–VI local contamination of the graft with *S. aureus* was then carried out. The incision was closed with subcutaneous and skin sutures (Ethicon, Ethibond® 5/0) followed by a spray dressing.

Postoperative course

The animals and the wounds were checked daily for progress in healing and signs of wound infection. Six animals were kept as a group in Macrolon® Nr.2 cages and received a standard diet as well as water ad libitum. During the entire study the animals were kept at the Institute of Surgical Research (LMU Munich) under veterinary supervision.

Euthanasia and sampling

On postoperative day 14 animals were euthanised with an isofluran overdose. This observation has been chosen based on previous studies examining antimicrobial properties of vascular graft material.[12] The explantation of the grafts as well as the perigraft tissue was carried out under sterile conditions; the samples were transferred to sterile vessels and examined.

Microbiological examination

Swabs, grafts and perigraft tissue were examined. The material was stored under sterile conditions. In positive samples the microorganisms were identified with standard techniques used in clinical practice in the Institute of Microbiology of the Ludwig-Maximilians-University, Klinikum Großhadern. In order to improve the yield of the samples the graft tissue and perigraft tissue was trypsinised. One hundred microlitre of the bacterial suspension was applied to blood agar. In positive cultures the microorganisms were identified. If Staphylococci were found a combined latex hemagglutinine test for the proof of clamping factor and protein A as well as other specific antigens of *S. aureus* (Slidex Staph-Kit, Fa. Bio Mérieux) allowed the differentiation between *S. aureus* and coagulase-negative staphylococci. In the case of uncertain reactions further diagnostics were performed using biochemical identification with a commercial identification system (API ID32 Staph, Fa. Bio Mérieux). The degree of bacterial contamination of the perigraft tissue was semiquantitatively assessed two double-blinded researchers and described as low '+', moderate '++' and high '+++'.

Histopathological examination

Material from the graft and perigraft tissue underwent histopathological examination and semiquantitative evaluation concerning the degree of inflammation. A grading from 1 to 3 was carried out: low '1', moderate '2' and high '3'.

Statistics

The aim of the evaluation was to identify infection. It was defined via the criteria 'microbiological contamination' and/or 'histopathological signs'. We are dealing with a dichotome question. The probability of error was calculated with the Fisher's exact test (probability of error $\leq 5\%$).

Results

Group I (control), n6

In all six animals there was no histological sign of infection. In one animal there was erosion of the skin with a migration of the graft material through the incision. Here 10^3 *S. epidermidis* were found.

Group I showed 0 from six infections (see Table 1).

Group II (control, contamination), n6

Five out of six animals showed severe signs of infection on histologic and microbiologic examination. In all five cases *S. aureus* was recovered at numbers of 10^3–10^5. Infection with formation of a fistula led to the loss of the graft material in the sixth animal on postoperative day 7. Thus, further evaluation was not possible. Nonetheless, macroscopically there were clear signs of infection.

Group II was evaluated to have 6 out of 6 infections (see Table 2).

Group III (Intergard®-Silver, contamination) n6

In group III extensive infection was found in all animals. Macroscopically, histologically and microbiologically all grafts were found to be infected. In all animals the inoculated *S. aureus* was recovered in at numbers of 10^4–10^5. One graft sample could for technical reason not be evaluated. The degree of inflammation of the graft material was severe (4×2, 1×3).

In group III 6 out of 6 infections were found (see Table 3).

Group IV (silver test graft, contamination), n6

Extensive infection was present in all cases. The inoculated *S. aureus* was recovered from all grafts. Histologically all grafts were considered to be infected yet infection was not as extensive when compared to the Intergard®-Silver graft. The degree of inflammation of the graft material was low (4×1, 1×2).

In group IV there were 6 out of 6 infections (see Table 4).

Group V (Rifampin, contamination), n6

In group V there was infection only in one animal. 10^5 *S. aureus* was recovered from the graft.

Group V was evaluated to have 1 out of 6 infections (see Table 5).

Group VI (Triclosan, contamination), n6

In group VI there were four cases of infection on histological and microbiological evaluation. One perigraft tissue sample could for technical reasons not be evaluated. The degree of inflammation of the graft material was low (3×1, 3×2).

Table 1. Group I (control), microbiological and histological results: silver-free gelatine-coated dacron graft (Uni-Graft®DV).

Animal no.	Microbiological evaluation		Histolog. Evaluation		
	Graft	Perigraft tissue	Graft	Macroscop.	Comment
1	–	–	1	–	
2	–	–	1	–	
3	–	–	1	–	
4	–	–	1	–	
5	–	–	1	–	
6	10^3 *S. epidermis*	–	1	–	Erosion
Infections	0/6				

–: No infection; 1, 2 and 3: Degree of inflammation after histological evaluation (semiquantitative: 1: low, 2: middle, 3: high).

In group VI there were 4 out of 6 infections (see Table 6). Data is summarised in Table 7.

Discussion

Several studies compare the efficiency of various substances bounded to dacron graft material in preventing graft infection.[11,13–15] The aim of our study was to compare the recently introduced agents with well investigated substance Rifampin in an experimental subcutaneous infection model.

In this regard, the formally tuberculostatic drug Rifampin has been shown to be an effective antimicrobial agent against typical bacteria responsible for vascular graft infections in vitro.[15,16] Due to its very poor water solubility high concentrations of the substance can be reached in the vicinity of the graft over a long period of time.[17,18] Previously, Rifampin was tested with commercially available gelatine-coated dacron grafts demonstrating an adequate affinity between gel-sealed dacron grafts and Rifampin.[15,16,19–21] Those properties of Rifampin appear to be responsible for the positive results of this agent in preventing graft infection in vivo in clinical and experimental studies.[22–26] Conversely, Koshiko et al.[27] points out that Rifampin failed to demonstrate effective antimicrobial effects against certain *S. aureus* strains, i.e. MRSA. This has to be taken into account when interpreting studies using Rifampin as an antimicrobial agent. In our study, we focussed on *S. aureus* (ATCC 25923), a common bacteria involved in graft infections. Our results demonstrate an effective bacterial killing in Rifampin coated vascular graft material. It should be noted that two prospective clinical trials improved local wound healing, however, failed to significantly decrease the local rate of graft infections.[25,28]

Therefore, additional agents have to be tested in experimental studies. In 1996 Manouguian[9] for the first time reported the use of an antimicrobial substance Triclosan binding directly via van der Waal'sche forces to polyester graft material.[11] In this manuscript, the authors only reported the successful clinical use of this Triclosan-coated vascular graft. In a pig animal experimental model our group[10] could demonstrate the efficacy of such Triclosan-coated vascular grafts following femoral vessel replacement. Following local contamination all grafts of the unprotected control group were infected (8 of 8) while none of the Triclosan/collagen-coated dacron grafts developed infection (0 of 7). In vitro it could be shown that Triclosan stays on the graft for more than 4 weeks.[11] In the present infection model with implantation of

Table 2. Group II, microbiological und histological results: silver-free gelatine-coated dacron graft (Uni-Graft®DV) and local contamination with 0.2 ml 2 × 10^7 *Staphylococcus aureus* ATCC 29213.

Animal no.	Microbiological evaluation		Histolog. Evaluation		
	Graft	Perigraft tissue	Graft	Macroscop.	Comment
1	>1000 *S. aureus*	+++	3	+	
2	>1000 *S. aureus*	+++	3	+	
3	/	/	/	+	Graft lost via fistula
4	10^4 *S. aureus*	++	2	+	
5	10^5 *S. aureus*	++	2	+	
6	10^5 *S. aureus*	++	2	+	
Infections	6/6				

+: Macroscopical sign of infection; +, ++ and +++: Positive contamination after microbiological examination of the perigraft tissue(semiquantitative). 1, 2 and 3: Degree of inflammation after histological evaluation (semiquantitative: 1: low, 2: middle, 3: high).

Table 3. Group III, microbiological and histological results: Silver Intergard® graft and local contamination with 0.2 ml 2×10^7 *Staphylococcus aureus* ATCC 29213.

Animal no.	Microbiological evaluation		Histolog. Evaluation		
	Graft	Perigraft tissue	Graft	Macroscop.	Comment
1	10^4 *S. aureus*	++	2	+	Erosion
2	10^5 *S. aureus*	+++	2	+	Erosion
3	10^4–10^5 *S. aureus*	++	3	+	Abscess
4	10^4 *S. aureus*	++	2	+	Abscess
5	10^5 *S. aureus*	++	2	+	abscess
6	10^5 *S. aureus*	++	–	+	
Infections	6/6				

–: No infection; +: Macroscopical sign of infection; +, ++ and +++: Positive contamination after microbiological examination of the perigraft tissue (semiquantitative); 1, 2 and 3: Degree of inflammation after histological evaluation (semiquantitative: 1:low, 2: middle, 3: high).

alloplastic graft material subcutaneously in mice Triclosan also decreased the infection rate. This therapeutic effect, however, was not significant. In contrast, previously our group demonstrate efficacy of Triclosan in preventing graft infection in an arterial interposition model.[10] Thus, decreasing the bacterial load in the present study might better demonstrate the antimicrobial potential of Triclosan also in the subcutaneous area. It should be pointed out, that our model clearly discriminates between Rifampin coated and non-treated prosthetic material. Rifampin-bonded gel-sealed vascular graft almost completely prevented infection of graft material.

In addition, the hemodynamic effect in the pig model in contrast to the subcutaneous model might contribute to the observed difference. This notion remains to be determined.

At the end of the 1980s silver-coated graft material was examined. Silver is a broad-spectrum bacteriostatic agent. Silver binds to the microbial DNA and prevents bacterial replication.[29–31] Medical instruments such as central venous lines, urinary catheters, peritoneal catheters, vascular grafts, cardiac valves, suture material and bone implants have been coated with silver. Already at the end of the 1980s examination of PTFE grafts and silver derivatives was carried out. Coating PTFE grafts with silver derivatives was carried out in order to bind antibiotics. The bonded antibiotics were liberated in two phases. Half of the substance was given off immediately and in the second phase the remaining substance was slowly given off over a longer period to the surrounding tissue.[32] Shah et al.[33] carried out their trials in dogs. Following the challenge with *S. aureus* and *E. coli* after the implantation of a PTFE graft treated with Norfloxacin (control) and silver-norfloxacin (AGNF) they found no infection in seven animals (0 of 7) in compared to 6 of 7 infected grafts in the control group. Kinney et al.[34] also reported after using PTFE grafts with and without silver coating about positive effects of silver in combination with ciprofloxacin bonded to vascular grafts. In an in vivo trial in dogs he only found a moderate reduction of the rate of vascular grafts infection following the challenge with *S. aureus* and *E. coli*.

Benvenisty[35] as well could demonstrate an effect of silver-coated vascular grafts in an animal model in the dog. However, he could only detect a reduction in the

Table 4. Group IV, microbiological and histological results: Not commercially available silver/gelatine-coated dacron graft and contamination with 0.2 ml 2×10^7 *Staphylococcus aureus* ATCC 29213.

Animal no.	Microbiological evaluation		Histolog. Evaluation		
	Graft	Perigraft tissue	Graft	Macroscop.	Comment
1	10^3 *S. aureus*	++	2	+	Abscess
2	10^3 *S. aureus*	–	1	+	
3	10^3 *S. aureus*	–	1	+	
4	10^3 *S. aureus*	++	1	+	
5	10^3 *S. aureus*	++	1	+	
6	10^3 *S. aureus*	–	1	+	Abscess
Infections	6/6				

–: No infection; +: Macroscopical sign of infection; +, ++ and +++: Positive contamination after microbiological examination of the perigraft tissue (semiquantitative); 1, 2 and 3: Degree of inflammation after histological evaluation (semiquantitative: 1:low, 2: middle, 3: high).

Table 5. Group V, microbiological and histological results: gel-sealed dacron graft (Uni-Graft®DV) with Rifampin-impregnation and contamination with 0.2 ml 2 × 10^7 *Staphylococcus aureus* ATCC 29213.

Animal no.	Microbiological evaluation		Histolog. Evaluation		
	Graft	Perigraft tissue	Graft	Macroscop.	Comment
1	–	–	1	–	
2	–	–	1	–	
3	–	–	1–2	–	
4	–	–	0–1	–	
5	10^5 *S. aureus*	+	2	+	
6	–	–	1–2	–	
Infections	1/6				

–: No infection; +: Macroscopical sign of infection; +, ++ and +++: Positive contamination after microbiological examination of the perigraft tissue (semiquantitative); 1, 2 and 3: Degree of inflammation after histological evaluation (semiquantitative: 1:low, 2: middle, 3: high).

concentration of the inoculated *S. aureus* on grafts at the end of the trial. Based on those results recent studies have been initiated determining the effect of silver in protecting graft material infections. Only for silver coating of cardiac valve material and intravenous lines protective effects have been reported. In this respect, Illingworth[29] could show a clear reduction in the number of infections following subdermal implantation of silver-coated polyester cardiac valves in a pig infection model. Collin[36] found a significant reduction of bacterial contamination of central venous lines. Only two of 98 silver-coated central venous catheters showed signs of infection in comparison to 25 out of 139 infected not silver-protected ones.

Although no standardised data exists concerning the antimicrobial properties of silver coated vascular graft material, a commercially available silver coated dacron graft for the treatment of graft infection is used clinically. In the present paper a direct comparison of the silver-coated Intergard®-Silver vascular graft as well as the not commercially available silver-protected vascular graft with antimicrobially impregnated gel-sealed dacron grafts (Rifampin) has been carried out. In contrast to Rifampin, silver coated to vascular graft material had no effect on the infection rate in the present study. Support for these findings comes from studies of Goëau-Brissonnière et al.,[37] who demonstrated no effect of silver in preventing graft infection in a dog infection model. In contrast, Rifampin completely prevented graft infection in the experiments of Goëau-Brissonnière et al.[37]

In summary, the present studies compared the antimicrobial properties of two new prophylactic agents with the established Rifampin in a subcutaneous infection model. The results indicate that silver coating of prosthetic material failed to prevent graft infection. In contrast, Triclosan coating decreased the infection rate of prosthetic material. This effect, however, was not significant. Those findings together with our previous positive results in an arterial reposition pig model suggest that Triclosan exhibits an antimicrobial potential. Rifampin, however, showed the best antimicrobial property. Therefore, silver coated vascular material should not be recommended in case of vascular graft infection.

Table 6. Group VI, microbiological and histological results: Triclosan (10 g/l)/collagen-coated dacron graft and contamination with 0.2 ml 2 × 10^7 *Staphylococcus aureus* ATCC 29213.

Animal no.	Microbiological evaluation		Histolog. Evaluation		
	Graft	Perigraft tissue	Graft	Macroscop.	Comment
1	10^5 *S. aureus*	++	2–3	+	Arrosion
2	10^3 *S. aureus*	++	2–3	+	
3	10^3 *S. aureus*	–	1–2	+	
4	10^5 *S. aureus*	++	2	+	Abscess
5	–	–	1–2	+	
6	–	–	0–1	+	
Infections	4/6				

–: No infection; +: Macroscopical sign of infection; +, ++ and +++: Positive contamination after microbiological examination of the perigraft tissue (semiquantitative); 1, 2 and 3: Degree of inflammation after histological evaluation (semiquantitative: 1:low, 2: middle, 3: high).

Table 7. Infection rate of dacron graft material coated with Silver, Rifampin and Triclosan.

Detected infection	Microbiological evaluation		Histological evaluation	Macroscopic evaluation	Graft infection (summary)	*P* value vs. group II
Group	Graft material	Perigraft tissue	Graft material	Graft material		
I	0/6	0/6	0/6	0/6	0/6	$p < 0.05$
II	5/5	5/5	5/5	6/6	6/6	
III	6/6	3/6	5/5	6/6	6/6	$p > 0.05$
IV	6/6	6/6	6/6	6/6	6/6	$p > 0.05$
V	1/6	1/6	1/6	1/6	1/6	$p < 0.05$
VI	4/6	3/5	4/6	4/6	4/6	$p > 0.05$

Detection of graft or perigraft infection using microbiological, histological, or macroscopic procedures. Six animals per group were incorporated. Group I: control; Group II: control contamination; Group III: Intergard-Silver contamination; Group IV: Silver test graft contamination; Group V: Rifampin contamination; Group VI: Triclosan contamination. Data presented: detected infection/total number, Fisher's exact test, $p < 0.05$.

References

1 Goldstone J, Moore WS. Infection in vascular prosthesis. Clinical manifestations and surgical management. *Am J Surg* 1974; **128**: 225.

2 Kaiser AB, Clayson KR, Mulherin JL, Roach AC, Allen TR, Edwards WH, Dale EA. Antibiotic prophylaxis in vascular surgery. *Ann Surg* 1978; **188**: 283.

3 Spartera C, Morettini G, Bafile G, Di Cesare E, Alage G, Ventura M. Diagnostic imaging techniques and vascular graft infections. *Eur J Vasc Endovasc Surg* 1997; **14**(Suppl. A): 24–26.

4 Szilagi ED, Smith RF, Elliot JB, Vrandecec MP. Infection in arterial reconstruction with synthetic grafts. *Ann Surg* 1972; **176**: 321.

5 Calligaro KD, Veith FJ. Diagnosis and management of infected prosthetic aortic grafts. Clinical review. *Surgery* 1991; **110**: 805–813.

6 Yeager RA, Porter JM. Prosthetic and arterial infections. *Ann Vasc Surg* 1992; **6**: 485–491.

7 Cherry KJ, Roland CF, Pairolero PC, Hallett JW, Meland NB, Naessens JM, Gloviczki P, Bower TC. Infected femorodistal bypass: is graft removal mandatory? *J Vasc Surg* 1992; **15**: 295–303.

8 Kikta MJ, Goodson LJ, Bishara RA, Meyer JP, Schuler JJ, Flanigan DP. Mortality and limbloss with infected infrainguinal bypass grafts. *J Vasc Surg* 1987; **5**: 566–571.

9 Manouguian S. Unsere klinische Erfahrung mit der neuen antimikrobiell beschichteten Inter-Gard-IGK/AM-Gefäßprothese bei der chirurgischen Behandlung des tiefen Wundinfektes mit Beteiligung des Kunststoff-Bypasses: Bericht über zwei Fälle. *Zentralbl Chir* 1996; **121**: 768–772.

10 Hernández-Richter T, Schardey HM, Löhlein F, Redondo-Müller M, Hammer C, Schildberg FW. The prevention and treatment of vascular graft infection with a Triclosan (Irgasan)-bonded dacron graft: an experimental study in the pig. *Eur J Vasc Endovasc Surg* 2000; **20**: 413–418.

11 Hernández-Richter T, Schardey HM, Löhlein F, Fleischer CT, Walli AK, Boos KS, Schildberg FW. Binding kinetics of Triclosan (Irgasan) to alloplastic vascular grafts: an in vitro study. *Ann Surg* 2000; **14**: 370–375.

12 Lehnhardt FJ, Torsello G, Claeys LGY, Pfeiffer M, Wachol-Drewek Z, Grundmann RT, Sandmann W. Systemic and local antibiotic prophylaxis in the prevention of prosthetic vascular graft infection: an experimental study. *Eur J Vasc Endovasc Surg* 2002; **23**: 127–133.

13 Goldmann DA, Hopkins CC, Karchmer AW, Abel RM, McEnany MT, Akins C, Buckley MJ, Moellering Jr. RC. Cephalotin prophylaxis in cardiac valve surgery. *J Thorac Cardiovasc Surg* 1977; **73**: 470–479.

14 Maki DG, Bohn M, Stolz SM, Kroncke GM, Acher CW, Myerowitz PD. Comparative study of Cefazolin, Cefamandole and Vancomycin for surgical prophylaxis in cardiac and vascular operations. *J Thorac Cardiovasc Surg* 1992; **104**: 1423–1424.

15 Chervu A, Moore WS, Chvapil M, Hendersson T. Efficacy and duration of antistaphylococcal activity comparing three antibiotics bonded to dacron vascular grafts with a collagen release system. *J Vasc Surg* 1991; **13**: 897–901.

16 Greco RS, Harvey RA. The role of antibiotic bonding in the prevention of vascular prosthetic infections. *Ann Surg* 1982; **195**: 168–171.

17 Freyrie A, Curti T, Rodio M, Masetti L, Bignozzi L, Sanguinetti V, Joeschler M, D'addato M. Interaction between vascular prosthesis and Rifampicin in the prevention of the graft infection. An experimental study. *Int Angiol* 1992; **11**: 213–216.

18 Malassiney P, Goiëau-Brissonnière O, Coggia M, Pechère JC. Rifampicin loading of vascular grafts. *J Antimicrob Chemother* 1996; **37**: 1121–1129.

19 Greco RS. Utilising vascular prosthesis for drug delivery. *Eur J Vasc Surg* 1991; **5**: 753–757.

20 Harvey RA, Greco RS. The noncovalent bonding of antibiotic to a PTFE graft. *Ann Surg* 1981; **194**: 642–647.

21 Moore WS, Chvapil M, Seiffert G, Keown K. Developement of an infection-resistant vascular prosthesis. *Arch Surg* 1981; **116**: 1403–1407.
22 Goëau-Brissonnière OA, Mercier F, Nikolas MH, Bachourt F, Coggia M, Lebrault C, Pechère JC. Treatment of vascular graft infections by in situ replacement with a rifampin-bonded gelatin-sealed dacron graft. *J Vasc Surg* 1994; **19**: 739–741.
23 Chervu A, Moore WS, Gelabert HA, Colburn MD, Chvapil M. Prevention of graft infection by use of prostheses bonded with a rifampin-collagen release system. *J Vasc Surg* 1991; **14**: 521–524.
24 Lachapelle K, Graham AM, Symes JF. Antibacterial activity, antibiotical retension and infection resistance of a rifampin-impregnated gelatin-sealed dacron graft. *J Vasc Surg* 1994; **19**: 675–682.
25 D'Addato M, Curti T, Freyrie A. The rifampicin-bonded gelseal graft. *Eur J Vasc Endovasc Surg* 1997; **14**: 15–17.
26 Sardelic F, Ao PY, Taylor DA, Fletcher JP. Prophylaxis against *Staphylococcus epidermidis* vascular graft infection with Rifampicin-soaked, gelatin-sealed dacron. *Cardiovasc Surg* 1996; **4**: 389–392.
27 Koshiko S, Sasajima T, Muraki S, Azuma N, Yamazaki K, Chiba K, Tachibana M, Inaba M. Limitations in the use of Rifampicin-gelatine grafts against virulent organisms. *J Vasc Surg* 2002; **35**(4): 779–785.
28 D'Addato M, Curti T, Freyrie A, Abus GB, Bertini D, Biasi GM. Prevention of early graft infection with Rifampicin-bonded gelseal graft: a multicenter experimental study. *Cardiovasc Surg* 1994; **2**: 254–258.
29 Illingworth B, Tweden K, Schroeder R, Cameron JD. In vivo efficacy of silver coated (Silzone) infection-resistant polyester fabric against a biofilm producing bacteria, *Staphylococcus epidermidis*. *J Heart Valve Dis* 1998; **7**: 524–530.
30 Petering HG. Pharmacology and toxicology of heavy metals: Silver. *Pharmacol Ther* 1976; **1**: 127–130.
31 Rabih O, Darouichi E. Anti-ineffective efficacy of silver coated medical prosthesis. *Clin Infect Dis* 1999; **29**: 1371–1377.
32 Schröder A, Goëau-Brissonnière O, Koskas F, Nevelsteen A. *Infektionsprophylaxe mit Rifampicin verbundener Gelatine-imprägnierter Dakron(-Prothesen-Vorläufige Ergebnisse der Europäischen Studie*. Symposium 30 Jahre Gefäßchirurgie im Krankenhaus Friedrichshain-Berlin, 1–2 September; 1995.
33 Shah PM, Modak S, Fox CL, Babu SC, Sampath L, Clauss RH, Stahl WM. PTFE graft treated with silver norfloxacin (AgNF): drug retention and resistance to bacterial challenge. *J Surg Res* 1987; **42**: 298–302.
34 Kinney EV, Bandyk DF, Seabrook GA, Kelly HM, Towne JB. Antibiotic-bonded PTFE vascular grafts: the effect of silver antibiotic on bioactivity following implantation. *J Surg Res* 1991; **50**: 430–435.
35 Benvenisty AI, Tannenbaum G, Ahlborn TN, Fox CL, Modak S, Sampath L, Reemtsma K, Nowygrod R. Control of prosthetic bacterial infection: Evaluation of an easily incorporated, tightly bound silver antibiotic PTFE graft. *J Surg Res* 1988; **44**: 1–7.
36 Collin GR. Decreasing catheter colonization through the use of an antiseptic-impregnated catheter. *Chest* 1999; **115**: 1632–1640.
37 Goëau-Brissonnière OA, Fabre D, Leflon-Guibout V, Di Centa I, Nicolas-Chanoine MH, Coggia M. Comparison of the resistance to infection of rifampin-bonded gelatin-sealed and silver/collagen-coated polyester protheses. *J Vasc Surg* 2002; **35**: 1260–1263.