An Evaluation of the Effectiveness of Different Techniques for Intraoperative Infiltration of Antibiotics Into Alloplastic Implants for Use in Facial Reconstruction

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Background: Reconstruction in the head and neck can be difficult owing to the size of the defect or characteristics of the tissue that needs to be replaced. Facial wounds or reconstruction sites can be subject to contamination, thereby risking infection of any implanted material even under ideal circumstances. Particular areas of concern are sites where minimizing the bacterial contamination prior to placing an implant is difficult (e.g., the oral cavity and internal nose). Reconstruction involves the facial subcutaneous soft tissue and/or bone, and the ideal implant provides support and natural feel, as well as a low risk of infection. The biocompatibility of alloplastic implants depends on the tissue inertness of the implant and the porosity, allowing connective tissue ingrowth, which in turn decreases the susceptibility to infection. Scalafani et al demonstrated that alloplastic implants contaminated prior to fibrovascular ingrowth had a much higher incidence of infection and rejection.

Objective: To examine the effectiveness of several techniques for infiltrating antibiotics into alloplastic implants of different porosity using 2 commonly used alloplastic implants, expanded polytetrafluoroethylene (e-PTFE, or GORE-TEX) and porous high-density polyethylene (Medpor).

Results: Using an in vitro bacterial growth inhibition model, we found that suction infiltration of the implant with antibiotics was the most effective technique, with a statistically significant advantage over other techniques used. The advantages of the suction impregnation were seen to be most effective using alloplasts with a smaller pore size (20-30 µm) (P < .001), but there was a statistically significant difference even with implants with a larger pore size (150-200 µm) (P < .001).

Conclusions: Suction infiltration of antibiotics into porous implants seems to be the most effective method identified using an in vitro testing protocol. Further experiments will be needed to confirm the effectiveness in reducing the perioperative risk of infection in vivo.

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that may have contaminated the implant during reconstruction process. Once bacteria have contaminated a foreign body, then it usually needs to be removed because it cannot be sterilized and will lead to extrusion. To try and prevent infection under these circumstances, surgeons have empirically exposed implants to antibiotics to try and eliminate any bacteria that may have contaminated them during the implantation process. The use of alloplastic material preimplanted with antibiotics is not a new tool and has been described in orthopedic surgery, where the cement can be impregnated with an antibiotic.\textsuperscript{6,8-10} The disadvantage to preimplanted antibiotics is that if the patient has a sensitivity or allergy to them and this fact is overlooked or unsuspected,\textsuperscript{11} difficulties might arise. In addition, it would not be realistic or cost-effective to put a broad spectrum of antibiotics into a variety of alloplastic implants that would be used in different bacterial milieus or in patients who may have an allergy and to keep these stocked for use when urgently needed. A more practical approach would be to place a selected antibiotic into a particular implant when needed. The senior author (M.A.K.) has personally witnessed and used several different techniques in attempting to infiltrate selected antibiotics into porous alloplastic implants during head and neck reconstruction, but we were not able to identify any specific studies performed to determine the most effective methods to accomplish this. Multiple different techniques have been reported to try and infiltrate antibiotics into the implant, including just dipping the implant into the antibiotic, completely immersing the implant in the antibiotic, and, finally, applying negative pressure to create suction and infiltrate the implant with the antibiotic. To our knowledge, there have been no formal studies performed to evaluate these different intraoperative techniques and determine their effectiveness for antibiotic infiltration into alloplastic implants. Our study evaluates several techniques with an in vitro model using bacterial growth inhibition (GI) to determine the optimal technique to infiltrate antibiotics into the GORE-TEX and Medpor alloplasts so that they may function as delayed antibiotic delivery devices, theoretically decreasing the risk of infection in facial reconstruction.

**METHODS**

This protocol did not involve the use of animals or patients and therefore did not require a formal institutional review board protocol. All bacteriologic testing was performed, and materials disposed of, in the microbiology laboratory.

**STANDARDIZATION OF A BACTERIAL COLONY TO BE USED THROUGHOUT THE EXPERIMENT TO DECREASE THE VARIABILITY OF RESULTS OBTAINED**

A culture of non–methicillin-resistant \textit{Staphylococcus aureus} was isolated and purified to be used as the test bacteria for the experiment. The bacteria showed excellent sensitivity to the cefazolin and was then recultured on another chocolate agar plate to ensure the purity of the strain and confirm that the sensitivity to cefazolin was easily reproduced using the standard Kirby-Bauer protocol for disk diffusion testing of antimicrobial sensitivity.\textsuperscript{12} Testing of the alloplasts and controls for the experiment was performed using Mueller-Hinton agar according to a modification of the Kirby-Bauer protocol in using antibiotic-treated alloplasts, as well as control cefazolin antibiotic disks to cause bacterial GI. The concentration of the cefazolin antibiotic used was 1 g in 250 cm\textsuperscript{3} of isotonic sodium chloride solution, which is a common dose given to an adult perioperatively (this concentration was arbitrarily chosen, and a higher concentration could certainly have been used).

**TESTING OF GORE-TEX FOR ANTIBIOTIC INFILTRATION AND DELIVERY IN VITRO USING THE KIRBY-BAUER PROTOCOL ON MUELLER-HINTON AGAR**

Three GORE-TEX blocks, 3 cm \(\times\) 10 cm \(\times\) 7 mm, were obtained from W. L. Gore Associates and under sterile conditions were cut into 1-cm \(\times\) 1-cm \(\times\) 7-mm blocks. These blocks...
were then tested for 1-, 2-, 3-, 4-, 5-, 7-, and 10-minute periods under different experimental test conditions using the cefazolin antibiotic and isotonic sodium chloride solution controls. The specific methods for instilling the antibiotics into the implants included (1) floating the implant on the surface; (2) totally immersing the implant in the antibiotic solution; and (3) suction infiltration of the antibiotic into the implant using a 20-cm³ syringe with 3 seconds of 5-cm negative pressure while tapping the syringe at the same time knocking the bubbles off the implant, followed by relaxation of the pressure for 1 second to allow the antibiotic to infuse into the implant in place of the air. The cycle is then repeated for the prescribed length of time per the protocol. Once this was performed, the GORE-TEX blocks were taken out and dried to remove any excess antibiotic before being placed on the cutting block. Next, 2 mm was shaved off each of the edges, and the resulting rectangular block was placed on its side and 1-mm slices shaved off the ends. Then a 1-mm slice was taken out of the center to test the antibiotic penetration into both the shallow (2-mm) and deeper (5-mm) depths of the GORE-TEX alloplastic block. The edges and center slices were then plated on the Mueller-Hinton agar and tested using the modified Kirby-Bauer protocol for antibiotic GI of the S aureus bacteria. Controls were run using GORE-TEX alone and GORE-TEX that had been suction-infiltrated with isotonic sodium chloride solution for 10 minutes. Three samples were run under each of the antibiotic and control conditions. Photodocumentation of bacterial GI was performed at 48 hours.

**RESULTS**

**GORE-TEX**

The findings for GORE-TEX were as follows:

1. The control test groups of GORE-TEX alone or suction infiltrated with isotonic sodium chloride solution revealed no GI activity against the S aureus bacteria on Mueller-Hinton agar according to the modified Kirby-Bauer protocol used in the experiment.

2. The test groups using suction infiltration to treat the implant showed GI activity against the bacteria even after just 1 minute of suction from the peripheral margin of the implant (Figure 2 and Table 1). Although the activity against the bacteria did not increase proportionally with the length of exposure of the implant to the bacteria, the activity against the bacteria was present throughout all the test groups. Lack of any linear relationship between the exposure time and GI on the agar plates may have been the result of the slight variability in the sample size of the GORE-TEX, which in turn would deliver a variable amount of antibiotic to the agar plate, causing variations in the size of the GI area. Statistical analysis of this data using the analysis of variance (ANOVA) algorithms method revealed a significant main effect (group effect), with P < .001 for single-factor ANOVA with regard to the effect of bacterial GI by the suction-infiltrated implants vs the GORE-TEX or GORE-TEX/isotonic sodium chloride solution controls. Even using a higher α-value and looking at 3 separate test parameters in independent test runs instead of the group effect, the P value was still < .001, which is significant. Only with single-factor ANOVA did time seem to be a factor in the results; with 2-factor ANOVA, time was not a factor.

3. The test groups examining the center of the 1-cm implant for bacterial GI using floating, immersion, and suction infiltration showed delayed bacterial GI activity in the suction infiltration technique only at the 7- and 10-minute points.

4. The floating and immersion technique test groups did not demonstrate any consistent GI activity at any of the experimental time periods from the GORE-TEX peripheral or center test runs.

**MEDPOR**

The findings for Medpor were as follows:

1. The control test groups of Medpor alone or with suction infiltration with isotonic sodium chloride solution revealed no GI activity against the S aureus bacteria plated on Mueller-Hinton agar according to the modified Kirby-Bauer protocol used in the experiment.

2. The test groups using suction infiltration to instill the antibiotic into the implant showed immediate bacterial GI activity even after the first 2-minute period (Table 2). This antibiotic activity continued throughout the remainder of the test periods. These results were
again statistically significant with $P < .001$ for the grouped analysis and $P < .01$ for the individual values. Again, there did not seem to be a directly proportional relationship between the exposure time to the antibi-
otic solution and GI on the agar plates, and time was
not shown to be a significant factor in the statistical
analysis ($P = .001$). However, this will be discussed in
the “Comment” section.

3. Test groups using immersion infiltration to instill
the antibiotic into the implant again showed minimal
variable GI activity that was not consistent throughout
the time periods tested. At no point did all 3 of the Med-
por pieces tested in a particular time run demonstrate
bacterial GI activity.

4. Test groups using suction infiltration and immer-
sion infiltration to instill the antibiotic into the implant
center demonstrated that the suction infiltration test group
showed immediate bacterial GI activity but displayed a
nonlinear relationship with the increasing time of expo-
sure to the amount of GI activity. Minimal variable GI
activity was present in the immersion infiltration group
until the 6-minute interval. Following this, there was con-
sistent GI at the 6- and 8-minute intervals.

5. The final test group evaluated the infiltration of an-
tibiotic into the Medpor while the implant was floating
on the surface of the antibiotic. The test time periods
were again 2, 4, 6, and 8 minutes. The results showed no con-
sistent bacterial GI during any of the time intervals tested.

**COMMENT**

Porous alloplastic implants are commonly used in recon-
struction of head and neck defects and are exposed to risk
of infection at the time of implantation. Strategies commonly used to combat this infectious risk include sterile operative technique and intravenous antibiotics, as well as empirically placing the implants in antibiotic solution. Exposing porous alloplastic implants to antibiotics has been performed using various techniques, including letting the implants float on the surface of an antibiotic solution, totally immersing them in the solution, and using suction infiltration of the solution into the implant, but to our knowledge no formal studies have been conducted to demonstrate the value of any one of these techniques compared with that of the other or compared with a control. In the head and neck, a sterile technique can be especially difficult to achieve because in the nose, mouth, and eye regions it is not easy to create a sterile field in surgery. Hence, the ability to selectively instill appropriate antibiotics into an implant and potentially decrease the infectious risk is an important consideration.

In the experiment described herein, the suction infiltration technique (see Figure 3, which shows the bubbles in a syringe), which shows the air bubbles coming from the implant with negative pressure being applied to be the most effective way to instill the antibiotic into the implants for both alloplasts tested. The results were statistically significant ($P < .001$) with the GORE-TEX alloplast, and the effectiveness may be the result of the smaller pore size, which makes it harder for the antibiotic solution to infiltrate by diffusion action alone. Medpor also demonstrated excellent bacterial GI with suction infiltration compared with the control, even with its larger pore size ($P < .001$). Using suction infiltration, the antibiotic inhibition of bacterial growth was rapid, even as early as 1 (GORE-TEX) and 2 minutes (Medpor) after infiltration, and this did not occur with any consistency in the nonsuction infiltration techniques.

It is also interesting that time did not seem to be a factor in bacterial GI using suction infiltration in our study. This may have been due in part to the minor inaccuracies of cutting the blocks of alloplast, with different amounts of antibiotic being released owing to submillimeter differences in the sizes of the blocks. The implants were cut to their final size by hand with calipers for measurement. This potential variation in size, even though it was a submillimeter difference, could result in a different amount of antibiotics being delivered to the agar plate, and consequently a different zone of bacterial GI. An in vivo or radiolabeled antibiotic study should be considered to determine if there is a time relationship with regard to the effectiveness of suction infiltration of antibiotic solution and decreasing the risk of infection with alloplast implantation.

That implants with a larger pore size will be more easily infiltrated with antibiotic solution, whether using simple immersion infiltration or suction infiltration, would make empirical sense, but this issue was not specifically addressed in our study owing to the limited amount of Medpor blocks that were available. In regard to bacterial GI, only the effectiveness of suction infiltration vs other techniques compared with the control was tested.

In conclusion, although this study determined that alloplastic implants can be used to deliver antibiotics to the implantation site and inhibit bacterial GI compared with a control, and that suction infiltration seems to be the most effective technique to accomplish this, it must be remembered that this is an in vitro study. In vivo studies will be necessary to determine if antibiotic impregnation actually decreases the risk of infection and to evaluate the extent of infiltration that is necessary to actually provide protection against bacterial infection during alloplast implantation (i.e., whether infiltration of the antibiotic all the way to the center of the implant is necessary or whether infiltration to the edges is sufficient to convey protection). In addition, experiments to determine the optimal concentration of the antibiotic being used also need to be considered to optimally decrease the

### Table 2. Medpor Data

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<th>4</th>
<th>6</th>
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<td>0</td>
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</tr>
</tbody>
</table>

**Abbreviations:** Ab, antibiotic; C, control; OGC, overgrown by contaminant; SC, suction center; SE, suction edge; SI, suction infiltration.

*Medpor (porous, high-density polyethylene; Porex Surgical Inc, Newnan, Georgia) data are given as diameter of bacterial growth inhibition, in millimeters.*

![Figure 3. Figure showing bubbles from alloplast in a syringe with negative pressure, indicating air being suctioned out. This allows possible infiltration by antibiotic solution when air bubbles are shaken off and the negative pressure to the alloplast is released. The blue arrow is pointing to bubbles of air coming out of the implant when negative pressure is applied. The air is then replaced by antibiotic suspension using the infiltration technique described in the article.](image-url)
infectious risk and not have any adverse effects on the patient or the implant.

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REFERENCES


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