PAPER

Significant Reduction in Incidence of Wound Contamination by Skin Flora Through Use of Microbial Sealant

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Hypothesis: Application of skin sealant prior to incision reduces microbial contamination of the wound.

Design: Prospective, randomized, multicenter clinical trial.

Setting: Six teaching hospitals.

Patients: A total of 177 adult patients undergoing elective open inguinal hernia repair were randomized to either standard skin preparation with 10% povidone-iodine or skin preparation followed by cyanoacrylate-based liquid microbial sealant.

Interventions: Wound contamination was assessed during surgery by microbial sampling inside the wound at initiation of skin incision and prior to skin closure.

Main Outcome Measures: The primary outcome measures were the safety and effectiveness of cyanoacrylate-based microbial sealant to reduce bacterial contamination during surgery. The secondary outcome measure was reduction of postoperative surgical site infections using microbial sealant.

Results: Demographics were similar. Patients treated with sealant were more likely to have no bacterial cells found in the wound than control participants (47% vs 31%; $P=.04$). Three patients developed surgical site infections; all were in the control group ($P=.25$). Independent factors that reduced wound contamination were use of microbial sealant (odds ratio, 0.45; confidence interval, 0.23-0.88; $P=.02$) and perioperative antibiotics (odds ratio, 0.24; confidence interval, 0.10-0.58; $P=.001$).

Conclusion: Cyanoacrylate-based microbial sealant may be an important tool to reduce wound contamination and potentially prevent surgical site infections.

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SURGICAL SITE INFECTIONS (SSIs) associated with an incision account for 25% to 38% of nosocomial infections in surgical patients.[1,2] It is estimated that 2% to 5% of all patients who undergo surgery will develop an SSI.[2] These infections are associated with added morbidity, including prolonged hospitalization by approximately 2 weeks, 5 times the risk of readmission, an increase in average health care costs of up to $26 000 per patient, and twice the risk of death.[2-4]

Microbial contamination of the surgical site is a likely precursor of SSI. This is of particular concern for clean wounds where contamination must have originated outside the wound. It is estimated that 1% to 5% of clean surgical procedures performed will result in an SSI.[5] Exogenous sources of contamination include surgical personnel, breaks in sterile technique, the operating room environment, and materials carried into the operating room. A significant alternative source of pathogens is the patient's own skin flora, mucous membranes, and hollow viscera.[6]

In an effort to reduce SSIs, many preventive measures have been proposed, as outlined by the Centers for Disease Control and Prevention and the Medicare Quality Improvement Community's Surgical Care Improvement Project.[3] These include patient and skin preparation, surgical team hand/forearm antisepsis, antimicrobial prophylaxis within 1 hour of incision, restriction of operating room traffic, hair clipping in the operating room, patient core body temperature control, asepsis, meticulous surgical technique, and postoperative incision care. A variety of skin preparation products may be used, including iodophors, alcohol-containing products, and chlorhexidine gluconate. In

Table 1. Inclusion and Exclusion Criteria for Enrollment

Inclusion Criteria	Exclusion Criteria
Scheduled for open, class 1 clean inguinal hernia repair.	Known sensitivity to cyanoacrylate, formaldehyde, or acetone products or iodine or iodine-containing products.
Aged 18 y or older.	Surgical procedures involving mucous membranes or eyes.
Able to complete mean (SD) 30 (5) d follow-up.	Laparoscopic surgical procedures.
Able and willing to provide informed consent.	Evidence of coexistent infection at a remote body site.
	Skin rashes or exfoliative condition on the day of surgery.
	History of keloid formation.
	Currently receiving high-dose steroid treatment.
	Currently receiving immunosuppressive therapy.
	Chemotherapy treatment within 30 d of current surgery.
	Diagnosis of diabetes with $HbA_{1c} > 7.0\%$ obtained within 90 d.
	Use of oral, IV, or topical (in expected area of incision) antibiotics within 10 days prior to the day of surgery.
	Pregnant or nursing.
	Participation in any other study of an investigational drug or device within 2 wk prior to the current surgical procedure.

Abbreviations: HbA_{1c}, hemoglobin A_{1c}; IV, intravenous.

addition, an antiseptic-impregnated adhesive drape may be applied to the operative field (though this has been shown to have no effect on SSI, and in some cases may increase SSI).[7] Despite these perioperative tactics, bacteria continue to survive at the skin level and migrate to contaminate the wound, leading to SSI.[8]

A microbial skin sealant (IntéguSEAL; Kimberly-Clark Healthcare, Roswell, Georgia), has been developed that uses cyanoacrylate technology to seal endogenous skin flora, thus reducing wound contamination. Liquid ethylcyanoacrylate has been determined safe for human use by the National Toxicology Program and the United Kingdom Health and Safety Executive.[9] It is a film-forming liquid that is intended for use following typical perioperative skin preparation, such as iodophors, alcohol-containing products, and chlorhexidine gluconate, and is applied prior to surgical incision. The microbial sealant bonds to the skin with the intent of isolating and immobilizing any surviving resident skin flora, including those remaining in the hair follicles.

The purpose of the sealant is to reduce the risk of surgical wound contamination by skin flora during an operation. This clinical trial was designed to compare the safety and effectiveness of microbial sealant in reducing the incidence of surgical incision bacterial contamination relative to surgical skin preparation alone. The primary outcome measure was to compare the proportion of patients in the 2 study groups who remain without bacterial contamination during surgery. The secondary outcome measures were to quantify the prevalence of antibiotic-resistant *Staphylococcus aureus* (eg, methicillin-resistant *S aureus* [MRSA]) in the wound during surgery, characterize any differences in postoperative SSI, and determine potential factors in developing SSI. The safety outcome was the monitoring of adverse events during the study, giving particular attention to differences in wound healing.

METHODS

PATIENT RANDOMIZATION

This prospective randomized multicenter clinical trial was initiated at 6 high-volume academic institutions in the United States after appropriate institutional review board approval. All patients underwent an open inguinal hernia repair. Inclusion and exclusion criteria for screening are listed in **Table 1**. Patients were randomized using a 1:1 allocation to receive either a standard surgical skin preparation (10% povidone-iodine; control group) or standard skin preparation followed by application of IntéguSEAL (microbial sealant group). The sealant was applied as a single coat to the operative field prior to draping after the povidone-iodine had dried. The sealant was then allowed to dry completely prior to draping. To standardize and ensure correct and safe application of the microbial sealant, all principal investigators were given hands-on instruction regarding use of the applicator prior to enrollment of subjects. Surgeons were allowed to perform the open inguinal hernia repair based on their personal preference with respect to hair clipping, perioperative antibiotics, surgical technique, and use of mesh.

Each investigational site was supplied with sealed envelopes. The randomization schedule was blocked within the investigational center to provide assurance that approximately equal numbers of patients will be randomized to each study group at each center. For randomization development, SAS version 9.1 was used. Owing to the nature of the various skin preparation treatments, it was not possible to mask the surgeon from knowledge of the assigned study group. However, the microbiological evaluation was performed by an independent microbiological core laboratory that had no knowledge of the randomized study group.

MICROBIAL WOUND SAMPLING METHOD

All patients underwent intraoperative microbial wound sampling at 2 stages during the inguinal hernia operation: (1) immediately following the skin incision, prior to the opening of the external oblique muscle and (2) prior to the conclusion of the surgery, immediately after the external oblique muscle was sutured. The sampling method, as previously described by Tammelin et al,[10] was standardized for all the centers using precut sterile 1×4-cm nylon filters. At each sampling point, using separate sterile forceps provided with each filter, 1 filter was placed on each of 2 insides of the incision and allowed to incubate for 30 seconds. Each filter was then transferred to a blood agar plate for culture for a total of 4 samples per patient. In addition, 1 filter per patient per stage served as a control and was transferred directly from the sterile packaging to the agar plate. The microbial wound samples were received and processed at the core laboratory within 24 hours of surgery for both qualitative and quantitative counts of gram-positive bacteria. Patients were considered to have a positive primary outcome if no bacteria were cultured from either stage of the wound sampling, ie, 0 colony forming units (CFUs).

DATA COLLECTION

At the preoperative visit, demographic information and medical histories were obtained from each patient. Select surgical

characteristics were recorded while in the operating room, including incision length, procedure time, antibiotic use, use of mesh, and wound closure methods. Patients were followed up at 2 and 4 weeks postoperatively to assess the incisions for signs of infection such as pain, swelling, erythema, drainage, warmth, and dehiscence. Information on adverse events was collected throughout the study for up to 30 days, and the principal investigator determined their relationship to the investigational device. Deviations from the study protocol and subject withdrawals were also recorded. A patient was considered lost to follow-up following 4 unsuccessful attempts to contact them.

SAMPLE SIZE CALCULATION

Owing to the paucity of wound contamination data available for the unique microbial wound sampling technique used in this trial, a sample size calculation could not be completed prior to enrollment. A porcine study provided preliminary evidence as to how much contamination might be present in human surgical incisions. In this study (data at Kimberly-Clark Health Care), a significantly lower number of bacteria were recovered from incisions where microbial sealant was used (mean, 1.3 CFUs) as compared with the control group (mean, 6.3 CFUs; $P < .002$). Therefore, a sequential design was used to test the data for significance during an interim analysis and to use this interim analysis as an opportunity to power the rest of the study. Based on the animal data, it was assumed that 50% of the control patients had sterile wounds, defined as 0 CFUs. The microbial sealant group was assumed to have 73% of the patients free of wound contamination, a conservative estimate given the findings of the animal study. To have 90% power to detect a difference between 50% and 73% at an experiment-wide, 2-tailed error rate of 5%, a minimum of 103 patients are required per group. The interim analysis was planned to occur when a minimum of 52 patients had been enrolled in each arm of the study (n=104). The O'Brien-Fleming spending function was used to determine the following boundaries: (1) At the interim analysis, the trial will stop if the *P* value in either direction is less than .003. (2) At the final analysis, the *P* value must be less than .047 to claim superiority.

The interim analysis showed that 80% of wounds were sterile immediately following surgical incision, with a 10% observed difference in the incidence of wound contamination between the 2 study groups. This provided a sample size of 742 patients required to detect a 10% difference with 80% power. Enrollment continued after interim analysis until September 2006, when regulatory approval was granted by the Food and Drug Administration for this class II investigational device, based on a parallel path. That is to say, animal data using similar methodology was included to obtain regulatory approval of this investigational device.

STATISTICAL ANALYSIS

For all statistical analyses, SAS version 9.1 (SAS Inc, Cary, North Carolina) was used. A 2-tailed significance level of .05 was used for all comparisons to assess significance. The χ^2 test was used to compare all categorical variables, and the 2-sample *t* test was used for all continuous variables. Multivariate logistic regression was used in the final analysis to determine the odds ratio of all potential factors for wound contamination. For the interim data analysis, the O'Brien-Fleming statistical boundary was used.[11]

RESULTS

From July 2005 to September 2006, 177 patients underwent elective open inguinal hernia repair and were enrolled in the study. Of these, 166 (94%) were evaluable for effectiveness of the sealant and 148 (84%) completed their test of cure after 30 days (**Figure 1**). Patients were equally distributed between the microbial sealant and control groups within each study center.

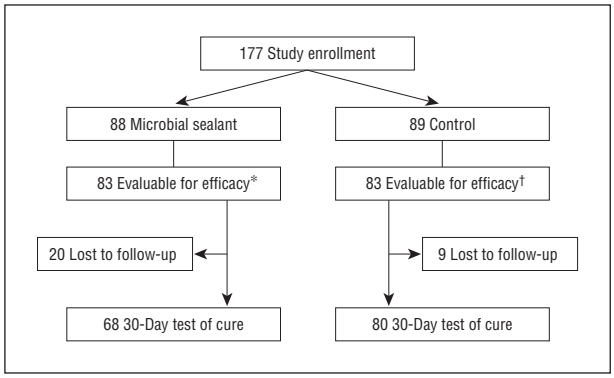

Figure 1. Flow chart of enrollment characteristics. * Indicates 4 protocol deviations, 1 incomplete sampling; †, 5 protocol deviations, 1 incomplete sampling.

Table 2. Patient Demographics and Preoperative Characteristics

Baseline Characteristics	No. (%) Microbial Sealant Group (n=88)	No. (%) Control Group (n=89)	*P* Value
Mean (SD) age, y	52.7 (15.9)	54.1 (14.9)	.55
Male	84 (95.5)	86 (96.6)	.72
Hispanic or Latino	21 (23.9)	22 (24.7)	.89
Race			.43
White, including Hispanic or Latino	66 (75.0)	75 (84.3)	
African, African American	14 (15.9)	10 (11.2)	
Asian or Pacific Islander	5 (5.7)	1 (1.1)	
Other	3 (3.4)	3 (3.4)	
Tobacco use	28 (31.8)	34 (38.2)	.37
Obesity[a]	27 (30.7)	18 (20.2)	.11
Diabetes mellitus	2 (2.3)	4 (4.5)	.68

[a] Defined as body mass index (calculated as weight in kilograms divided by height in meters squared) of 30 kg/m^2 or greater.

Patient demographics and preoperative characteristics are presented in **Table 2**. There were no statistically significant differences between the 2 study group population demographics. The majority of the patients were men (96%), with an average age of 53 years (range, 21-86 years). Six patients (3.4%) had a history of diabetes mellitus, 35% were tobacco users, and 25% were obese, with a body mass index (calculated as weight in kilograms divided by height in meters squared) of 30 kg/m^2 or greater. Only 7 patients had comorbid clinical characteristics that have been reported to be associated with wound complications, such as hyperhidrosis, eczema, psoriasis, or an autoimmune disease. One patient had a history of a previous SSI.

Perioperative care was similar in both study groups (**Table 3**). One patient in the microbial sealant group had missing data. A preoperative antiseptic shower was performed by 47 of 176 (27%) patients. All but 3 patients underwent hair removal. Of those, more than half

Table 3. Preoperative and Operative Characteristics of Patients

Characteristics	No. (%) Microbial Sealant	No. (%) Control	*P* Value
Preoperative	(n=87)[a]	(n=89)	
Antibiotic shower	23 (26.4)	24 (27.0)	.94
Hair removal	84 (96.5)	89 (100)	.12
Clipping[b]	45/80 (56.3)	47/83 (56.6)	
Shaving[b]	35/80 (43.8)	36/83 (43.4)	
Prophylactic antibiotics	61 (70.1)	70 (78.7)	.19
Operative	(n=88)	(n=89)	
Mesh implanted	71 (81.6)[a]	72 (80.9)	.90
Mean (SD) length of incision, cm	7.1 (2.0)	7.1 (2.5)	.99
Mean (SD) duration of surgery, min	73.7 (28.4)	75.6 (31.5)	.66
Skin closure using sutures	87 (98.9)	88 (98.9)	>.99
Wound covered with a dressing	77 (87.5)	80 (89.9)	.62

[a] One patient's data missing.
[b] Data shown for evaluable patients only (n=166).

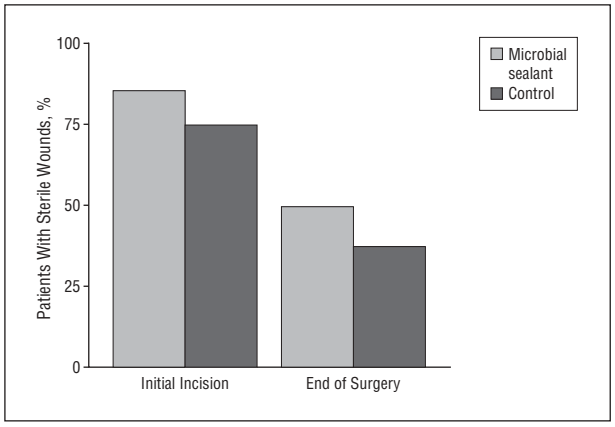

Figure 2. Proportion of patients with sterile wound as a function of time ($P > .05$). Sterility is defined as 0 colony forming units found in a microbial sample of wound both immediately after incision and prior to skin closure.

were done with hair clippers. Prophylactic antibiotics were administered to 131 of 176 (74%) patients. Some surgeons did not routinely administer prophylactic antibiotics for hernia repair surgery. Data regarding the type of antibiotic and the timing of antibiotic administration were not recorded.

There were no statistically significant differences in operative characteristics between the 2 study groups (Table 3). Most patients had mesh implanted during their hernia repair (143 of 176; 81%). All operations used a standard inguinal incision averaging 7.1 cm and were performed in an average of 75 minutes (range, 25-195).

Application of the investigational device was assessed by the surgeons and deemed to be without difficulty. For 4 patients, the surgeons reported some difficulty incising through the clear film, with no difficulties reported with suturing of wounds. One surgeon reported visible flaking of the film during the procedure.

Most patients did not maintain a sterile wound during surgery (101 of 166; 61%). The bacterial contamination in the wounds ranged from 0 to more than 200 CFUs. The median bacterial count was similar between the microbial sealant and control groups (1 CFU vs 2 CFUs, respectively); they also had similar bacterial counts in the 75th percentile (10 CFUs vs 11 CFUs). Patients' wounds that were microbially sealed were more likely to remain sterile throughout the study than those of the control group (39 of 83 vs 26 of 83; $P = .04$). At the initial skin incision, wounds were more likely to be sterile in the microbial sealant group (71 of 83 vs 62 of 83; $P = .08$) (**Figure 2**). With time, the wound bacterial contamination rate increased in both study groups; however, wounds pretreated with microbial sealant were more likely to remain sterile (41 of 83 vs 31 of 83; $P = .11$).

Bacterial contamination by gram-positive organisms was found in 44 of 83 (53%) patients pretreated with microbial sealant and 57 of 83 (68.7%) patients in the control group. The microbial sealant group was most commonly contaminated by gram-positive organisms, of which 43 (97.7%) had gram-positive cocci and 43 (97.7%) had coagulase-negative *S aureus*. In the control group, 56 of 57 (98.2%) had gram-positive cultures, of which 55 (98.2%) had gram-positive cocci and 55 (98.2%) had coagulase-negative *S aureus*. Methicillin-resistant *S aureus* was not identified in any of the cultures.

Of the 166 evaluable patients, 124 (75%) received prophylactic antibiotics. Some centers did not routinely use prophylactic antibiotics for elective inguinal hernia repairs, based on surgeon preference. Of those who received prophylactic antibiotics, 67 patients (54%) had bacterial contamination of their wound. Patients pretreated with microbial sealant in the presence of antibiotic prophylaxis were significantly less likely to have bacterial wound contamination (44% vs 63%; $P = .03$). Hair removal was performed prior to surgery in 163 of 166 (98%) of all evaluable patients. Hair clippers were used for 92 patients (56%), and 60 patients (65%) had bacterial contamination of their wound. Patients pretreated with microbial sealant following clipping were significantly less likely than control participants to have bacterial contamination (53% vs 77%; $P = .02$).

To help differentiate the independent contribution of factors such as prophylactic antibiotics or hair clipping from the bacterial wound contamination rate, multivariate logistic regression analysis was performed. Potential factors that affect SSI rates were included in this analysis, ie, study group, use of prophylactic antibiotics, hair clipping, surgical duration, and length of incision. Hair clipping, length of incision, and surgical duration were not found to have an independent effect on bacterial contamination of the wound (**Table 4**). However, use of prophylactic antibiotics (odds ratio, 0.24; $P = .001$) and pretreatment of the wound with microbial sealant (odds ratio, 0.447; $P = .02$) were both shown to be independent factors that protected against bacterial wound contamination.

ADVERSE EVENTS

Sixty-one percent of the evaluable patients (101 of 166) had wounds with bacterial contamination; however, this did not necessarily translate into an SSI, a secondary out-

Table 4. Independent Factors That Affect Incidence of Bacterial Wound Contamination During Hernia Surgery

Parameters	OR (95% CI)	*P* Value
Microbial sealant[a]	0.447 (0.228-0.875)	.02
Prophylactic antibiotics[a]	0.239 (0.099-0.576)	.001
Hair removal using clippers	1.694 (0.859-3.338)	.13
Length of incision	0.976 (0.646-1.473)	.91
Surgical duration	0.991 (0.979-1.004)	.17

Abbreviations: CI, confidence interval; OR, odds ratio.
[a] Use of prophylactic antibiotics and pretreatment with microbial sealant were found to be statistically significant at independently reducing bacterial wound contamination.

Table 5. Serious Adverse Events by Treatment Group

	No.	
Adverse Event	Microbial Sealant	Control
Admission for SSI due to MRSA	0	1
Groin hematoma	0	1
Chest pain	0	1
Dyspnea	0	1
Scrotal edema	0	1
Knee pain	0	1

Abbreviations: MRSA, methicillin-resistant *Staphylococcus aureus*; SSI, surgical site infection.

come measure for this trial. Only 3 patients developed SSIs; all were in the control group, with all cultures positive for *S aureus*. One of these patients had a deep infection with MRSA and was admitted to the hospital for wound debridement, mesh removal, and intravenous antibiotics. All other serious adverse events also occurred in the control group and resolved at the final follow-up (**Table 5**). Nonserious adverse events are listed in **Table 6**. One patient in the microbial sealant group had skin irritation.

COMMENT

The primary outcome measure of this trial was to determine the effect of InteguSEAL microbial sealant on wound contamination during elective open inguinal hernia repair. Patients who were treated with microbial sealant prior to skin incision had a lower rate of wound contamination immediately after incision; this trend lasted the duration of the surgery. Pretreatment of the incision area with microbial sealant after standard skin preparation was shown to be superior to standard skin preparation alone in preventing wound contamination. Patients in the microbial sealant group were 50% more likely to have sterile wounds than the control group. The effect of microbial sealant on maintaining a sterile wound was even more pronounced when combined with the positive effects of prophylactic antibiotic use and hair clipping on wound contamination. Also, use of microbial sealant was shown to be an independent factor in protecting against wound contamination during surgery. The only other independent protective factor against wound contamination was shown to be use of prophylactic antibiotics.

Table 6. Nonserious Adverse Events by Treatment Group

	No.	
Adverse Event	Microbial Sealant	Control
Scrotal edema, hematoma	3	2
SSIs	0	2
Wound dehiscence	1	0
Incisional pain, swelling	1	1
Skin irritation[a]	1	0
Constipation	0	1
Incisional bleeding	1	0
Urinary frequency	0	1
Numbness in groin	1	0
Sinusitis	0	1
Transsection of spermatic cord	1	0
Urinary retention	1	1
Headache, dizziness	0	1
Epigastric hernia drainage	1	0
Decreased limb sensation	0	1
Spinal headache	1	0

Abbreviation: SSIs, surgical site infections.
[a] Possibly attributable to investigational device; no further treatment needed.

The secondary outcomes of this trial were to assess SSI and the prevalence of MRSA in this population. No MRSA was cultured from the microbial sampling of the wounds. Only 3 patients (1.7%) developed an SSI, with 84% available for follow-up, which is similar to findings reported by specialized hernia surgery clinics.[12] One of the SSIs was due to MRSA, though MRSA was not cultured intraoperatively. All infections were in the control group; however, owing to the low overall incidence, superiority of microbial sealant in preventing SSI cannot be established.

The microbial sealant was deemed safe, as no serious adverse events were reported; 1 patient developed skin irritation that resolved on its own. Surgeons reported no difficulty in applying the microbial sealant; there were 4 reports of difficulty incising through the clear film and 1 episode of visible flaking of the film during surgery.

This is the largest prospective randomized controlled trial using a wound sampling outcome measure. This showed that clean class I wounds will be contaminated with gram-positive organisms up to 60% of the time and that contamination increases as a function of surgical time. The question that remains is whether wound contamination correlates with SSI. Although numerous publications have presented the incidence of surgical site infections and have provided very specific incidence rates depending on factors such as surgery class, patient risk factors, and surgery duration, very little has been published documenting the frequency and/or bacterial counts of surgical wound contamination.[1] Those publications that do exist vary greatly in time, sampling methods, surgical procedures, and most notably, results. Dewan et al[13] reported 18.4% of clean or clean-contaminated surgical procedures exhibiting wound contamination using bacterial culture swabs. Garibaldi et al[5] reported 4% to 15% of clean elective surgical procedures exhibiting more than 50 CFUs using 5-μ Millipore filter pads (Millipore, Billerica, Massachusetts), depending on the skin preparation method used. Whyte et al[14] reported approximately half of 188 patients undergoing cholecys-

tectomies exhibiting wound contamination using 4- × 7.5-cm viscose-polyester-polyamide pads. For cardiac surgery, 100% of patients were found to be contaminated, using 2- × 7-cm viscose-polyester-polyamide pads for microbial sampling.[10]

In this study, though wound contamination rates increased with time, few SSIs developed. Also, there was no correlation between the extent of wound contamination, such as the number of CFUs, and developing an SSI. The median wound contamination in this study was low, at only 1.5 CFUs. Given the low bacterial load within the wound, no correlation between wound contamination and SSI can be made. Though all SSIs occurred in the control group, the low incidence of SSI overall precludes statistical analysis. Perhaps a larger study or one using this microbial sampling method in clean-contaminated wounds may be able to answer the question, "How much wound contamination is clinically significant?"

Another limitation of this study is the lack of standardization of perioperative factors that may influence wound contamination rates, such as appropriate antibiotic selection, prophylactic antibiotic timing, hair clipping, normothermia, euglycemia, and oxygenation. Though most surgeons are aware of the importance of reducing the incidence of perioperative wound contamination, the recent introduction of the Surgical Care Improvement Project guidelines has encouraged, provided incentives for, and provided an infrastructure for national data collection to meet these quality improvement activities.[15] These guidelines have been shown to significantly reduce SSI; however, until now, there has been no data to suggest that intraoperative wound contamination is also affected by these measures. This study has shown that use of prophylactic antibiotics, not hair clipping, surgical duration, or wound length, can significantly reduce wound contamination and lead to a sterile wound throughout surgery. It is possible that a larger sample size would yield different results.

With the growing interest in improving surgical outcomes, surgeons are encouraged to take precautions at multiple levels to reduce SSI.[3,15] Strict adherence to Surgical Care Improvement Project guidelines has been shown to statistically reduce, but not completely prevent, SSIs. The addition of cyanoacrylate-based microbial sealant may be useful as an adjunct to reduce the incidence of wound contamination in all operative fields, even clean ones, and possibly further reduce SSIs.

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Role of the Sponsor: Funding was limited to provision of IntegUSEAL applicator, standardized microbial sampling supplies, and facility reimbursement of study-related costs, such as data collection and patient reimbursement for travel expenses at test-of-cure visit.
Previous Presentation: This paper was presented at the Pacific Coast Surgical Association annual meeting; February 18, 2008; San Diego, California. The discussions that follow this article are based on the originally submitted manuscript and not the revised manuscript.
Additional Information: This clinical study has been classified as a nonsignificant risk study in accordance with 21 Code of Federal Regulations 812.3 by the Food and Drug Administration and was managed in accordance and in full compliance with recognized Good Clinical Practices, 21 Code of Federal Regulations 50 Protection of Human Subjects, and 21 Code of Federal Regulations 56 institutional review boards. Based on this classification, the trial was not enrolled in clinicaltrials.gov. In September 2006, the Food and Drug Administration granted regulatory approval for this product as a class II medical device. The clinical trial was discontinued at that time.

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DISCUSSION

Jonathan R. Hiatt, MD, Los Angeles, California: This contribution comes to us from a group of investigators with a record of many substantial contributions to the study of surgical infectious diseases. In an effort to decrease wound contamination from resident skin flora, Dr Towfigh and colleagues performed a prospective, randomized trial of InteguSEAL, a cyanoacrolate-based liquid microbial sealant in adult patients undergoing elective inguinal hernia repair in 6 academic centers. The sealant is intended to trap bacteria and in this way hinder their migration from skin to wound. Baseline characteristics of 88 study patients who received the sealant and 89 control patients were similar, as were nonstandardized perioperative variables including hair removal, antibiotic prophylaxis, operative duration, length of incision, and use of mesh. The primary reported outcome measure was the presence or absence of organisms in the surgical wound at the beginning and end of the operative procedure. The sealant was somewhat protective in that wounds of study patients were significantly more likely to remain sterile during the procedure. Independent factors affecting wound contamination were microbial sealant and prophylactic antibiotics. Although SSIs with *S aureus* occurred in 3 control patients only, the difference in SSI incidence was not significant. There were no important adverse events related to the sealant device.

A unique observation of the study is that fewer than half of the wounds were sterile at the end of the 75-minute operations, and the usual contaminating organisms, as expected, were gram positive. The degree of contamination was small, and it was not possible to show that this contamination produced clinical infection, but the observation does add to our knowledge about potential epidemiology of SSI.

I have several questions for the authors. First, I note that the InteguSEAL device is available, it has a Web site, and you have to allow 2 minutes for it to dry. Do you recommend that it be used? If so, what are the specific indications? Next, how should we use your observation about wound contamination in clean elective surgery? Is this an avenue for further research, and how might practice be changed? Finally, it was interesting to note that there was considerable variation in academic practices regarding antibiotic showers, shaving, and antibiotic prophylaxis in elective herniorrhaphy. What are the best practices?

Dr Wilson: When should the cyanoacrylate be used, and what are the indications? In the 40 operations that I performed for the study, I found 2 advantages. First is that the skin sealant provides a better physical barrier between the skin and the operative field than standard plastic drapes which lift up at the edges as the operation proceeds. Also, in some areas, such as skin folds in the neck or the groin and the extremities where adhesion of drapes is difficult, it's much easier to apply the skin sealant and have it secure for the duration of the procedure.

The second indication is that the liquid cyanoacrylate adhesive may be a consideration in prosthetic implant surgery where the number of bacteria essential to cause an infection is much lower. In fact, I think Dr Towfigh has opened up a question that deserves further study, specifically in quantization of the number of bacteria necessary to result in infection in certain at-risk procedures.

Dr Hiatt's next question was how should we use this observation? The practical use to me is that the lowest bacterial contamination rate was found in the group that had both perioperative antibiotics plus the skin sealant.

Regarding further research, first of all there has been, since we composed this paper, a publication from the Medical University of Berlin showing a decrease by half, 3.8% to 1.7%, in wound infections after cardiovascular surgery using the cyanoacrylate sealant. What I would like to see would be a large prospective, randomized trial in North America, and I would recommend orthopedic implant surgery.

I feel it a little presumptuous to dictate best practices, Dr Hiatt, but nevertheless I will have a go. I think good practice would be antiseptic showers at home before operation, hair clipping the morning of surgery, and skin prep with either an idophor or chlorhexidine gluconate. Finally, I am convinced more than ever that the routine use of preoperative antibiotics is helpful in preventing wound infections.

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