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Reduction of healthcare-associated infections in a long-term care brain injury ward by replacing regular linens with biocidal copper oxide impregnated linens

A. Lazary [a,*], I. Weinberg [a], J.-J. Vatine [b,c], A. Jefidoff [a], R. Bardenstein [d], G. Borkow [e], N. Ohana [a]

[a] Brain Injury Division, Reuth Medical Center, 2 Ha'Hayil blvd, Tel Aviv 61092, Israel
[b] Outpatient and Research Division, Reuth Medical Center, Tel Aviv, Israel
[c] Department of Rehabilitation Medicine, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel
[d] Microbiology Laboratory, Kaplan Medical Center, Rehovot, Israel
[e] Cupron Scientific, Herzliya, Israel

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SUMMARY

Background: Contaminated textiles in hospitals contribute to endogenous, indirect-contact, and aerosol transmission of nosocomial related pathogens. Copper oxide impregnated linens have wide-spectrum antimicrobial, antifungal, and antiviral properties. Our aim was to determine if replacing non-biocidal linens with biocidal copper oxide impregnated linens would reduce the rates of healthcare-associated infections (HAI) in a long-term care ward.
Methods: We compared the rates of HAI in two analogous patient cohorts in a head injury care ward over two 6-month parallel periods before (period A) and after (period B) replacing all the regular non-biocidal linens and personnel uniforms with copper oxide impregnated biocidal products.
Results: During period B, in comparison to period A, there was a 24% reduction in the HAI per 1000 hospitalization-days ($p < 0.05$), a 47% reduction in the number of fever days (>38.5 °C) per 1000 hospitalization-days ($p < 0.01$), and a 32.8% reduction in total number of days of antibiotic administration per 1000 hospitalization-days ($p < 0.0001$). Accordingly there was saving of approximately 27% in costs of antibiotics, HAI-related treatments, X-rays, disposables, labor, and laundry, expenses during period B.
Conclusions: The use of biocidal copper oxide impregnated textiles in a long-term care ward may significantly reduce HAI, fever, antibiotic consumption, and related treatment costs.

1. Introduction

Copper has been used as a biocide for centuries.[1] The fungicidal, antibacterial, and antiviral properties of copper have been demonstrated in many controlled laboratory studies and are very well documented.[2,3] Copper exerts its toxicity to microorganisms through several parallel non-specific mechanisms, which include damage to the microorganisms' envelope and intracellular proteins and nucleic acids.[3] Many bacteria and fungi have different mechanisms to deal with excess copper.[2] However, above a certain threshold and time of exposure, they cannot deal with the copper overload and die. In contrast to the highly antibiotic-resistant microbes that have evolved over less than 50 years, microorganisms tolerant to copper are extremely rare even though copper has been a part of the earth for millions of years. This can be explained by the multisite and non-specific kill mechanisms of copper.[2] Significantly, copper also displays potent biocidal activity against antibiotic-resistant bacteria and antiviral-resistant viruses.[3–5]

Copper and copper-based compounds are used routinely in several health-related areas. These include the control of Legionella[6] in hospital water distribution systems, reduction of caries in dentistry,[7] reduction of food-borne diseases,[8] and the

* Corresponding author. Tel.: +972 547791928.
E-mail address: lazary@reuth.org.il (A. Lazary).

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prevention of conception.[9] Copper intrauterine devices are widely used by millions of women, are approved by the regulatory agencies, and have been applied for several decades.[9] It has recently been demonstrated in hospitals, clinics, and care homes for the elderly, that substituting the existing hard surfaces with copper-based surfaces reduces the bioburden and the transmission of nosocomial pathogens.[10,11] The US Environmental Protection Agency (EPA) approved the registration of copper alloys and polymeric surfaces containing copper oxide particles as materials with antimicrobial properties that can kill >99.9% of Gram-negative and Gram-positive bacteria within 2 h of exposure, making copper the only metal that can be used in hospitals to reduce the bioburden and for which public health claims can be made.

In the last few years, a durable platform technology has been developed that permanently embeds copper oxide particles into polymeric materials.[4] The introduction of copper oxide particles into polymeric materials endows them with potent broad-spectrum antimicrobial[4,5,12] and anti-mite properties,[4,13] and in some applications has a direct effect on physiological processes, such as enhanced wound healing.[14] Since copper oxide is a non-soluble form of copper, the copper oxide particles do not wash out during laundry and the textile products remain active for the life of the products.[4,12]

Consumer products impregnated with copper oxide particles, such as pillowcases, sheets, and diapers, are extremely safe and do not cause any skin irritation or sensitization, or any adverse reactions, both to intact and breached skin.[15] This has been demonstrated (1) in animal studies;[4,12,16,17] (2) in several double-blind clinical trials;[18–20] (3) with patients who slept on sheets containing copper oxide for a total of 300 nights;[12] and (4) in adult patients using diapers containing copper oxide for a period of 6 months, without even one adverse reaction.[21]

The innovative potential use of this technology in health-related applications include making hospital soft surfaces, like sheets, patient robes, patient pajamas, nurse clothing, and diapers, from copper oxide impregnated biocidal textiles.[4,12,16,22] It was hypothesized that the use of copper oxide containing textiles, especially sheets, pillowcases, robes, and pajamas that are in close contact with the patients, may significantly reduce the bioburden in the products themselves and in the surrounding environment and consequently reduce the risk of HAI.[22] In order to test this hypothesis we examined if the HAI rates in a long-term care ward could be reduced when all the textile products used in the ward were replaced with biocidal copper oxide containing textiles (Figure 1).

2. Materials and methods

The study was conducted in the Head Injury Ward, following approval by the hospital institutional review board. Since all

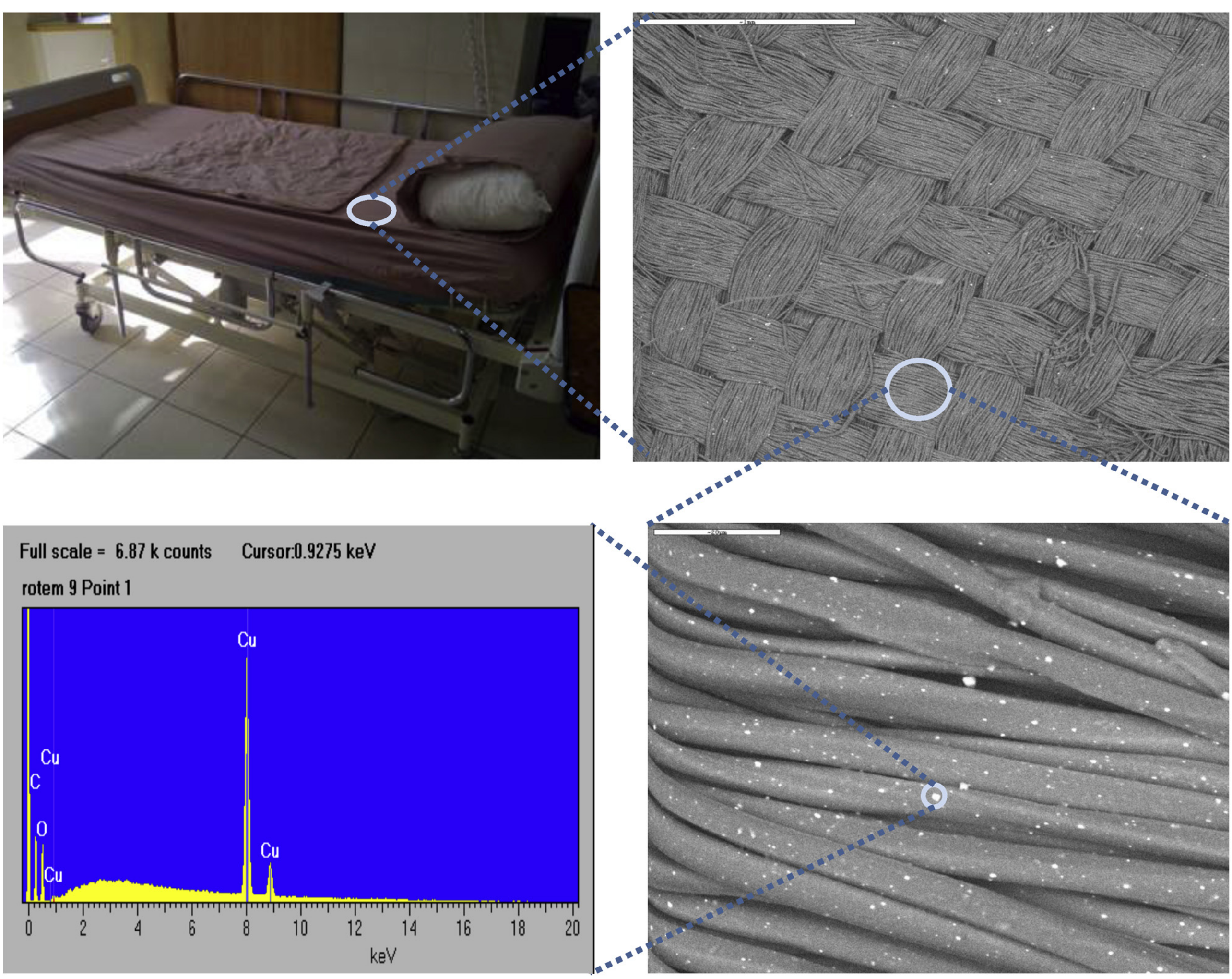

Figure 1. Two scanning electronic microscope images (taken with a Jeol JMS 840 scanning electron microscope) of a representative pillowcase are shown. The white dots are the copper oxide particles embedded in the polyester fibers. The chart is an X-ray photoelectron spectra analysis (done with a Shimadzu XRD 6000, TN-5500 X-ray analysis system) of the encircled white dot, showing a peak at 8 KeV corresponding to copper.

Table 1
Surveillance definitions of HAI used in the study

Type of infection	Criteria
A. Upper respiratory	1. Pharyngitis (at least two criteria outlined below)
	a. Runny nose or sneezing
	b. Stuffy nose (i.e., congestion)
	c. Sore throat or hoarseness or difficulty in swallowing
	d. Dry cough
	e. Swollen or tender neck glands (cervical lymphadenopathy)
	2. Influenza-like illness (both criteria a and b were present)
	a. Fever
	b. At least three of the following influenza-like illness sub-criteria
	• Chills
	• New headache or eye pain
	• Myalgias or body aches
	• Malaise or loss of appetite
	• Sore throat
	• New or increased dry cough
B. Lower respiratory	1. Pneumonia (all three criteria were present)
	a. Positive chest radiograph demonstrating pneumonia or presence of a new infiltrate
	b. At least one of the following respiratory sub-criteria was present
	• New or increased cough
	• New or increased sputum production
	• O_2 saturation $<94\%$ on room air or a reduction in O_2 saturation of $>3\%$ from baseline
	• New or changed lung examination abnormalities
	• Pleuric chest pain
	• Respiratory rate of ≥ 25 breaths/min
	c. At least one of the following sub-criteria was present
	• Fever (single oral/axillary/rectal temperature $>38.5\,^{\circ}C$)
	• Leukocytosis ($>14\times10^9$ leukocytes/l or $>6\%$ bands or $\geq 1.5\times10^9$ bands/l)
	• Acute change in mental status from baseline
	• Acute functional decline
	2. Bronchitis or tracheobronchitis (all three criteria were present)
	a. Chest radiograph not performed or negative results for pneumonia or new infiltrate
	b. At least two of the respiratory sub-criteria listed in section Bb above
	c. At least one of the sub-criteria listed in section Bc above
C. Urinary tract	1. No indwelling catheter (both criteria 1 and 2 were present)
	a. At least one of the following signs or symptom sub-criteria
	• Acute dysuria or acute pain, swelling, or tenderness of testes, epididymitis, or prostate
	• Fever or leukocytosis and at least one of the following
	– Acute costovertebral angle pain or tenderness
	– Suprapubic pain
	– Gross hematuria
	– New or marked increase in incontinence
	– New or marked increase in urgency
	– New or marked increase in frequency
	• In the absence of fever or leukocytosis, then two or more of the following sub-criteria
	– Suprapubic pain
	– Gross hematuria
	– New or marked increase in incontinence
	– New or marked increase in urgency
	– New or marked increase in frequency
	b. One of the following microbiological sub-criteria
	• At least 10^5 CFU/ml of no more than two species of microorganisms in a voided urine sample
	• At least 10^2 CFU/ml of any number of organisms in a specimen collected by in-and-out catheter
	2. With indwelling catheter (both criteria 1 and 2 were present)
	a. At least one of the following signs or symptom sub-criteria
	• Fever, rigors, or new-onset hypotension, with no alternate site of infection
	• Acute change in mental status, with no diagnosis and leukocytosis
	• New onset suprapubic pain or costovertebral angle pain or tenderness
	• Purulent discharge from around the catheter or acute pain, swelling or tenderness of testes, epididymitis, or prostate
	b. Urinary catheter specimen culture with at least 10^5 CFU/ml of any microorganism
D. Skin	At least 1 of the following criteria were found
	a. Pus at a wound or skin site
	b. New or increasing presence of at least four of the following sub-criteria
	• Heat at the affected site
	• Redness at the affected site
	• Swelling at the affected site
	• Tenderness or pain at the affected site
	• Serous drainage at the affected site
	• One of the sub-criteria
	– Fever
	– Leukocytosis
E. Eye	At least one of the following
	a. Pus appearing from one or both eyes, for at least 24 h
	b. New or increased conjunctival erythema, with or without itching
	c. New or increased conjunctival pain for at least 24 h

Table 1 (*Continued*)

Type of infection	Criteria
F. Mouth	Both criteria were present a. Presence of raised white patches on inflamed mucosa or plaques on oral mucosa b. Diagnosis by a medical or dental provider
G. GI	At least two of the following criteria were present a. Diarrhea; ≥2 liquid or watery stools above the normal for the patient within a 24-h period b. Vomiting; ≥2 episodes in a 24-h period c. A stool specimen testing positive for a pathogen
H. Blood	Both criteria were present a. Recognized pathogen isolated from blood culture and pathogen was not related to infection at another site (contamination) b. Clinical sepsis with one of the following clinical signs: • Fever (>38.5 °C) • Chills • Hypotension (systolic pressure ≤90 mmHg) • Oliguria (<20 cm^3/h)
I. Other infections	Osteomyelitis, otitis, orchitis

HAI, healthcare-associated infection; GI, gastrointestinal.

patients included in the study were in a low conscious state and not legally eligible, their custodians signed an informed consent form. The Head Injury Ward is a 35-bed ward in which long-term care patients with severe head injuries are hospitalized. All the patients are confined to bed and wheel chair. They are totally dependent on medical personnel for everyday needs and activities. The most common medical complication that afflicts these patients is infection, which is also the main cause of death.[23–25] Patients are usually hospitalized for a period of a few months to several years. During both study periods, >90% of the patients were immunized against seasonal influenza.

The data were gathered during two 6-month parallel periods: period A, December 2010 to June 2011, and period B, December 2011 to June 2012. Data collected were: patient ID, age, and sex; date of admission to the ward; date of discharge from the ward; main diagnosis and medical background; mobility (yes, no, or confined to bed); tracheostomy (yes or no); urinary catheter (yes or no); feeding tube (yes or no); sores (admitted to the ward with sores, yes or no); drug treatments; antibiotic treatments (types, period of treatment, and times of treatments); steroid treatments (yes or no); inhalations (yes or no); fever (times of fever >38.5 °C); and infection (date of infection, type, and duration). An infection event and the type of infection was determined according to the criteria defined by Embry and Chinnes[26] and in accordance with the revised McGeer criteria for defining an infection event of a patient hospitalized in a long-term care facility.[27] These criteria are detailed in Table 1.

During period A, the regular non-biocidal hospital linens were used in the ward. During period B, all bed sheets, pillowcases, patient shirts, patient pants, patient gowns, towels, underpads, and personnel robes used in the ward were replaced with copper oxide impregnated products. The textile products were distinguished from the regular hospital products by having a different color. They were used exactly as any of the regular hospital products are used. The used products were laundered in the same laundry, where all hospital linens are laundered, using the exact laundry conditions as those used with the regular hospital products. The routine infection control measures, such as standard precautions, isolation of patients infected with antibiotic-resistant bacteria (MDR, multidrug-resistant), and hand hygiene were the same during period A and period B. The standard precautions to prevent cross-contamination were monitored in both studied periods in the same strict and rigorous manner and by the same infection control nurse. No other environmental or treatment modality changes occurred in the ward during the two periods, other than the use of the biocidal textiles. No changes were made or instituted in the ward during the intermediary period (July–November 2011). The hospital staff who actually took care of the patients (i.e., the ward doctors, nurses, and nurse aides) in the ward itself were not involved directly in the trial. The only change that they saw in the ward was the color of the linens. The ward staff were not aware of the parameters monitored and studied. All the data gathered for the study were collected from the patients' medical files, from the pharmacy reports, and from the laboratory reports, without the knowledge or involvement of the ward medical staff.

2.1. Microbiology testing

Forty regular bed sheets and 40 copper oxide impregnated bed sheets were swabbed between 6 to 7 h after being used by patients in a regular ward and in the Brain Injury Ward, respectively, as described previously.[28] An area of 10 cm^2 of each sheet was swabbed in the area that was in contact with the patient's back. The presence of microorganisms, their titers, and characterization were then determined by regular standard microbiology assays.

2.2. Statistical analyses

The statistical analyses were performed by MediStat Ltd, a company that specializes in biostatistical analyses (http://www.medistat.co.il/). The differences between the two populations studied in terms of patient medical characteristics, treatments, and nosocomial infections, were compared. The Chi-square test was applied to test the statistical significance of the differences in frequencies of categorical variables between periods. Weighted Chi-square tests were applied to test the statistical significance of the differences in sum of variables between periods. The two-samples *t*-test was applied to test the statistical significance of the differences in means of continuous variables between periods. The Mann–Whitney rank sum test was used to test the difference between the bacterial loads in the regular and copper oxide impregnated sheets after use. The effect of possible cofounders was analyzed by conducting multivariate analysis of covariance (ANCOVA). All tests applied were two-tailed, and a *p*-value of 0.05 or less was considered statistically significant. The data were analyzed using SAS version 9.1 (SAS Institute, Cary, NC, USA).

3. Results

The patient groups hospitalized during the two periods compared had similar characteristics and underwent similar treatments not related to HAI (Tables 2 and 3). In contrast, as can be seen in Table 4, there was a 24% reduction in HAI events that occurred in period B as compared to period A ($p = 0.046$). Of note was the significant decrease in the number of days the patients had fever (47%; $p = 0.0085$). It should be pointed out that each time a

Table 2
Patient characteristics

Variable	Period A	Period B
Number of patients	57	51
Total hospitalization days	4337	3940
Mean age, years	57 ± 19	49.7 ± 22
Age range, years	18–90	19–83
Female/male ratio	1:2	1:2.6

Table 3
Clinical characteristics of the study populations (%)

Variable	Period A	Period B	*p*-Value
Mobile patients	10.2	13.8	0.797
Patients with tracheostomy	61.0	63.8	0.538
Patients with urinary catheter	31.3	22.2	0.449
Patients with feeding tube	72.5	69.4	0.694
Patient with pressure sores[a]	25.9	16.7	0.298
Patients receiving steroids	30.4	19.4	0.245
Patients receiving inhalations	49.1	41.7	0.482

[a] The patients were admitted to the ward with pre-existing sores. No sores developed in the ward during the study period.

Table 5
HAI distribution

Infection	Period A		Period B		% Decrease	*p*-Value
	Number[a]	%	Number[a]	%		
GI	13	92.86	1	7.14	92.3	0.0013
Eyes	20	68.97	9	31.03	55	0.0411
Respiratory, upper	18	40.91	26	59.09	-	0.2278
Respiratory, lower	23	57.50	17	42.50	-	0.3428
Urinary	9	64.29	5	35.71	-	0.2850
Skin	27	56.25	21	43.75	-	0.3865
Blood	2	100.00	0	0	-	-
Mouth	3	100.00	0	0	-	-
Other infections	3	50.00	3	50.00	-	1.0000

HAI, healthcare-associated infection.
[a] Number of events.

patient had fever, the patient received antipyretic treatment, and in 98.5% of the cases the fever did not persist more than 1 day. In accordance, there was a 23% reduction in the number of events in which patients received antibiotics during period B as compared to period A ($p = 0.052$). Moreover, the total days of antibiotic administration during period B was 32.8% lower than in period A ($p < 0.0001$). The influence of potential confounders, such as patient age, gender, mobility, presence of sores, steroid administration, tracheostomy, urinary catheter, and inhalation treatments, on the differences found in fever days, use of antibiotics, and rates of HAI, was negated by conducting ANCOVA analyses. The HAI distribution is detailed in Table 5. Statistically significant reductions in gastrointestinal (GI) and eye infection events ($p = 0.0013$ and $p = 0.0411$, respectively) occurred in period B as compared to period A. No blood or mouth infections were recorded during period B. No statistical differences were noted in the other HAI events.

Significantly lower loads of Gram-positive and Gram-negative bacteria were found in the copper oxide containing sheets than in regular sheets after 6–7 h of patient use (reductions of approximately 50% and 46%, respectively; Figure 2). The Gram-positive bacteria found were Bacillus and *Staphylococcus epidermis*. The Gram-negative bacteria found were *Acinetobacter baumannii*, *Enterobacter cloacae*, *Escherichia coli* (only on one regular sheet), *Klebsiella pneumoniae*, and *Pseudomonas stutzeri*. *Candida albicans* was found on one regular sheet.

4. Discussion

It was hypothesized that the use of biocidal textiles instead of ordinary textiles may significantly reduce nosocomial infections in hospital wards.[22] This was based on the following: microbial shedding from the living body occurs all the time.[29] When a bacterium is shed into a textile fabric between the patient and the bed, either the pajamas or directly onto the sheet, the moisture and temperature in the textile microenvironment promotes its proliferation. Bed-making releases large quantities of microorganisms into the atmosphere, contaminating the immediate and distant surroundings.[30,31] For example, methicillin-resistant *Staphylococcus aureus* (MRSA) was detected following bed-making on the bed sheets, over-bed tables, and the patients' clothing.[32] Similar results were reported following undressing and redressing of patients.[33] These studies strongly support the notion that disturbance of textiles in clinical settings may contribute to the dispersal of pathogens into the air, which then settle down and contaminate the immediate and non-immediate environment. Healthcare workers can then transport these pathogens to patients by the contact route.[34]

In addition to being a source of aerosol transmission of microorganisms, contaminated textiles can also directly contaminate the hospital personnel. Forty-two percent of personnel who had no direct contact with patients, but who had touched different surfaces including bed linens, contaminated their gloves with MRSA.[35] The transmission of *Streptococcus pyogenes* occurred via contact with the contaminated surface of a vinyl sheet that covered the bed on which the patients were treated.[36] Similarly, bedding was a significant risk factor related to a nosocomial outbreak of Norwalk gastroenteritis.[37] Also staff clothing, such as uniforms, has been found to be highly contaminated with, for example, high levels of MRSA.[38] Hospital staff, even when using protective equipment such as gloves, can become contaminated themselves by touching the contaminated textiles and then transfer the microorganisms to other patients directly or indirectly by contaminating other surfaces, such as door knobs.[35]

While the notion that contaminated textiles in hospitals can be an important source of microbes contributing to endogenous, indirect-contact, and aerosol transmission of nosocomial related pathogens is gaining recognition,[22] the demonstration that the use of biocidal textiles in a clinical environment can be an important simple measure to fight HAI had not been done, until this study.

Table 4
HAI-related events[a]

Variable	Period A		Period B		% Decrease	*p*-Value
	Number[b]	%	Number[b]	%		
HAI	27.4	56.85	20.8	43.15	24	0.046
Fever days	13.4	65.36	7.1	34.63	47	0.0085
Number of times antibiotics given	21.44	56.51	16.5	43.49	23	0.052
Total days of antibiotics	382.7	59.82	257.1	40.18	32.8	<0.0001

HAI, healthcare-associated infection.
[a] Data normalized per 1000 hospitalization days.
[b] Number of events.

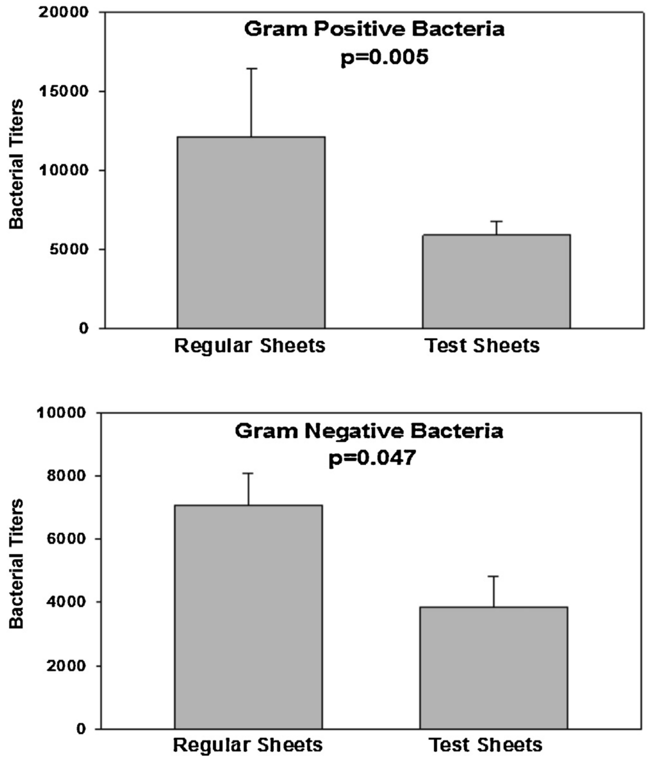

Figure 2. Bacterial loads found on the regular and copper oxide impregnated sheets. Forty regular bed sheets and 40 copper oxide impregnated bed sheets were swabbed immediately after being used by patients for 6–7 h. The swabs were taken from the area that was in contact with the patient's upper back.

We chose to perform the study in a chronic care head injury ward, as most of the patients hospitalized in this ward are very fragile and susceptible to infection. Unfortunately the rate of HAI in these patients is very high and is actually the most common medical complication that afflicts them.[23–25] We assumed that with a cohort of patients suffering from a high rate of infections, it would be appropriate to demonstrate the beneficial effect of using biocidal textiles in reducing HAI in a relatively short period of time, and that results may be more significant.

Indeed, this study indicates that the HAI rates in a long-term care ward could be reduced simply by replacing the textile products used in the ward with biocidal copper oxide containing textiles. As expected, in the copper oxide impregnated fabrics there were significantly lower loads of pathogenic bacteria such as *A. baumannii* and *K. pneumoniae*. A clear indication that there was a reduction in infections when the copper oxide biocidal textiles were used was the significant reduction in the number of events in which patients had a fever $>38.5\ ^{\circ}C$. Such a fever can be a clinical indication of an infection, sometime being the only clinical sign. There was a reduction of approximately 50% in the number of high fever measurements recorded in the ward during period B as compared to the corresponding period A. There was also a clear reduction in the total HAI rates during period B, which resulted mainly from the significant reduction in GI infections and conjunctiva-associated eye infections. The reduction in GI infections can be explained by the reduction in antibiotics given to the patients. It is well known that the use of antibiotics can induce diarrhea and reactivate *Clostridium difficile* in silent carriers. Conjunctiva-associated eye infections may be associated with airborne bacteria released during bed-making,[32,33] since many of the brain injury patients lie down with their eyes open. Thus the reduction in airborne bacteria that results from the use of biocidal linens reduces the risk of contracting an eye infection.

It should be noted that in order to eliminate seasonal variations between the examined periods, the two periods compared were similar, i.e. period A was from December 2010 to June 2011, and period B was from December 2011 to June 2012. There were no statistical differences in the rates of HAI that are often associated with insertion or manipulation of selective biomedical devices, such as urinary catheters, central lines, and respiratory equipment, between the two periods. This can be explained by the fact that most of these infections are caused by the handling of the inhalation tubes by staff and due to constant contamination of the inhalation tubes by the patient's oral secretions, which do not come into contact with the biocidal linens, and thus are not affected by them, and apparently are less related to airborne bacteria. The population studied is not ventilated, thus there is no ventilator-associated pneumonia. The patients with indwelling urinary catheters were identical in the two studied populations. There were no central lines in those patients.

This study demonstrated that the use of copper oxide containing linens reduced HAI in a long-term care ward. There is no reason to believe that reducing the bioburden in a regular ward by using biocidal linens would not affect the HAI rates. The use of biocidal textiles should be a complementary approach to fight nosocomial infections in all medical institutions, as well as care homes for the elderly, where the risks of acquiring an infection are high. Importantly, the biocidal efficacy of the copper oxide has been demonstrated not to be affected even after 100 commercial laundry cycles and years of use.[12,20]

Obviously longer trials, including trials comparing HAI during consecutive 12-month periods rather than parallel 6-month ones, or trials in which two similar wards are supplied with either the copper oxide impregnated linens or non-treated matched linens, without the personnel knowing what the meaning of the colors are, would be better experimental designs and should be used in future studies.

The use of copper oxide containing linens also results in significant cost savings. As calculated by the hospital, there was a dramatic reduction in the costs in treating patients during period B as compared to the parallel period A. The reduction was in the costs of antibiotics, HAI-related treatments, X-rays, disposables, labor, laundry, etc., which averaged a saving of approximately 27% (data not shown). It should be pointed out that in this long-term care ward, patients are hospitalized for many months to years, so if they have an HAI it does not usually result in a prolonged hospitalization as is the case in non-chronic care wards. Most cases of HAI result in prolonged hospitalization and an associated significant increase in the costs, both to the hospital and to the insurance companies. These costs were not taken into consideration in the current study.

The results of this study clearly demonstrate that the use of copper oxide impregnated linens in a long-term care ward reduce HAI and antibiotic and other infection-related treatments, and can be an important addition to the arsenal of measures taken in hospitals to reduce an important source of nosocomial pathogens and the risk of HAI. Due to the good results obtained in reducing infections, the hospital where this study was carried out is in the process of replacing the linens and staff protective clothing throughout the hospital.

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Conflict of interest: Dr Borkow is the Chief Medical Scientist of Cupron Inc. Cupron Inc. is the company that developed the technology of incorporating copper oxide particles into textiles. All other authors have no conflicts of interest.

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