

APPENDIX A BENEFITS STUDY SUMMARY

Topical antimicrobial products used to address the risks of infection can be broken into two broad groups: those used in association with invasive procedures, and those used in infection control not associated with invasive procedures (non-invasive).

Benefits from the use of topical antimicrobial products can be split into two classifications:

1. Interruption of infection in invasive situations due to the transfer of resident bacteria into wounds, incisions, injection sites or damaged skin.
2. Interruption of disease transmission in non-invasive situations to others and oneself due to the acquisition of transient bacteria and their transfer to a point of entry into the host, and to oneself due to skin infections from one's own resident skin flora.

A review of the literature demonstrated the varied benefits of use of topical antimicrobial products in both invasive and non-invasive situations.

A. TOPICAL ANTIMICROBIAL PRODUCTS IN INVASIVE PROCEDURES

Interruption of infection in invasive situations due to the transfer of resident bacteria into wounds, incisions, injection sites or damaged skin

The risk of infection associated with breaking the skin barrier during invasive procedures such as surgery, catheterization, and injection is very real. The aim of skin disinfection is the quick removal and killing of as many of the skin flora as possible at the site of a planned invasive procedure in order to prevent their translocation into the underlying tissues by a knife blade or a needle. The organisms that are primarily associated with these types of infections are Gram positive bacteria derived from the patient or from the caregiver.

The examples provided below demonstrate the importance of a topical antimicrobial product in the overall infection control regimen. Many of the studies presented change more than one variable including the topical antimicrobial regimen. However, the use of the topical antimicrobial plays a critical role in infection control.

Clinical Settings

- No endocarditis was contracted during 86 surgeries over a 29-month period using a 3% Hexachlorophene product (Hughes 1966).

This study describes the measures taken to control an abnormal incidence of bacterial endocarditis associated with prosthetic valve replacement. Changes included interrupting the transmission of bacteria to the patient by incorporating a 5 minute soak in 3% hexachlorophene into the pre-operative bathing routine of the patient (3 times daily for 5 days) and requiring the surgical team to scrub for 10 minutes immediately before surgery using a 3% hexachlorophene product. Other changes included prophylactic use of antibiotics by the patient and surgical staff. Following institution of these and other changes, no endocarditis was contracted during 86 surgeries over a 29-month period. This early study, while not conclusive, points to the importance of managing the skin flora of both the patient and the surgical team.

- Decrease in the overall rate of infection for intrathoracic infections following median sternotomy to < 0.5% by use of a 10% povidone-iodine preparation compared to rates of 0.4 - 6% seen elsewhere in the literature (Klovekorn, W.P. *et al.* 1985).

This study used a 10% povidone-iodine preparation pre- intra- and post-operatively for skin and wound disinfection in 7,566 patients undergoing open-heart surgery. One day prior to surgery an alcohol containing disinfectant shaving foam was used followed by bathing with a PVP-I solution for 30 minutes. Then a 10% available iodine PVP-I solution was applied to the surgical site. This results in an immediate reduction in the skin flora of 97%; the following morning the reduction is 75% of baseline. At surgery, a prophylactic antibiotic is administered via *iv*. The skin is washed for 5 minutes with PVP-I scrub, and treated four times with a 10% PVP-I solution. The overall rate of infection for intrathoracic infections following median sternotomy was < 0.5%. This compares favorably with rates of 0.4 - 6% seen elsewhere in the literature. Again, while not conclusive, this study points to the importance of managing the skin flora of the patient.

- Reduced infection rate from 11.3% to 4.0% in 1,017 hysterectomy patients using a povidone-iodine pre-operative regimen (Beaton, undated).

In a study evaluating the decontamination of the vagina prior to hysterectomy, a 7.5% povidone-iodine soak reduced the infection rate from 11.3% to 5.0% in a study of 1,017 patients.

- An infection rate of 0.254% after 393 neurological operations using a 7.5% povidone-iodine formulation for surgical scrubbing and pre-operative preparation (Jackson 1972).

The use of a povidone-iodine formulation for surgical scrubbing and pre-operative preparation was seen to have materially contributed to the extremely low incidence of infections in a military hospital.

- A significant reduction in the incidence of coagulase negative staphylococci related peritonitis was achieved by treating patient skin with a CHG detergent followed by 70% ethanol or the use of povidone-iodine with or without a subsequent alcohol rinse (Gruer *et al.* 1984).

In a 3-month study of 31 continuous ambulatory peritoneal dialysis patients showed a reduction in coagulase negative staphylococci related peritonitis when a regimen including a topical antimicrobial product was conscientiously used for handwashing and site preparation.

- A significant decrease in intra-abdominal sepsis was noted with the use of a Chlorhexidine spray as a pre-operative preparation (Brown *et al.* 1984).

A prospective randomized comparison of infection rates among 737 surgical patients at two hospitals showed no significant difference between a routine using 7.5% PVP-I surgical scrub/aqueous iodine paint and a 0.5% CHG/70% IPA spray as preoperative skin preparations. However, a significantly lower incidence of intra-abdominal sepsis was noted in the group using the CHG spray (0.26%, $p < 0.05$).

- Use of a povidone-iodine surgical scrub in a vascular surgery unit controlled an outbreak of surgical site infections (Grinbaum *et al.* 1995).

Upon comparison of risk factors such as duration of surgery, wound class, use of antibiotics, remote site infection, and hand scrubbing procedure, Grinbaum *et al.* concluded that the only significant factor related to an outbreak of surgical site infections (SSIs) was hand scrubbing. A prospective study was conducted to compare SSI cases that occurred during a period when PVP-I was not provided to surgeons for pre-operative scrubbing to times when PVP-I was used. Scrubbing with bland soap by surgeons in the vascular surgery unit was the only factor that could be linked to the outbreak ($p < 0.00001$). 100% of cases displaying SSIs (9/9) were those where bland soap was used, as opposed to control cases (PVP-I used) where the infection rate was 0% (0/18). Further support of the authors' findings was the fact that no increase of SSIs was detected in other departments where 2% PVP-I in alcohol was used when PVP-I surgical scrub was unavailable. Finally, when PVP-I again became available for presurgery scrubs, the outbreak was controlled.

- Vascular surgery patients who showered with Chlorhexidine prior to surgery had a lower infection rate than those who did not (Denton 1991).

Vascular surgery patients showering with Chlorhexidine three to eight times prior to surgery had a lower infection rate than those who did not (8% vs. 17.5%) even though both groups received the same pre-operative skin preparation immediately prior to surgery.

- No incidences of surgical site infection were found in 150 elective surgeries using a povidone-iodine regimen for surgical scrubbing and pre-operative preparation (Georgiade *et al.* 1990).

In an open study of 150 hospitalized patients undergoing elective surgery, a pre-operative regimen of a 7.5% surgical scrub followed by a 10% povidone-iodine paint was used. No incidences of surgical site infection were found. Of the patients presenting with bacterial colonization prior to surgery, 85% ($p=0.004$) had no detectable levels of bacteria following the procedure.

- A significant decrease in the number of post-operative infections among patients with groin incisions was affected by using repeated shower-baths with 4% CHG prior to standard surgical preparations (Brandberg *et al.* 1981).

With repeated use (3-8 times), the number of infections decreased from 17.5% to 8% in the group using Hibiscrub versus the control group (local washing only).

- A reduction in clean wound infections resulted from use of a pre-operative hexachlorophene shower and from the use of Chlorhexidine skin pre-operative preparations (Cruse and Foord 1973).

A five-year prospective study showed that in addition to education of hospital staff and improved aseptic technique, the pre-operative hexachlorophene showers decreased the rate of clean wound infection from 2.3% (no shower) to 1.3% (Cruse and Foord 1973). In addition, the authors found that PVP-I sponge scrubbing in hospital wards and Chlorhexidine skin prep of operative sites was associated with an infection rate of 1.2%. This was an improvement over the infection rate of the previous four years when green soap and alcohol were used in the pre-operative skin prep regimen (2.0%).

- A lower incidence of post-operative wound infection was found with the use of a 10% povidone-iodine antiseptic solution and a 7.5% povidone-iodine surgical scrub (Connell and Rousselot 1964).

Both skin cultures and biopsies were used to compare 10% PVP-I antiseptic solution and 7.5% PVP-I surgical scrub to 3% hexachlorophene. Bacterial samples were obtained four minutes after scrubbing and 1.5 hours after surgery. Surgical site reductions were 98 and 78% respectively for 10% PVP-I. Three percent hexachlorophene performed comparably, achieving 96 and

68% reductions at each interval. Surgical hand scrub results for each product were again similar (7.5% PVP-I, 98 and 88%; 3% hexachlorophene, 84 and 66%). Although the authors did not note the significance, there was a lower incidence of post-operative wound infection (1%) in the PVP-I group than the hexachlorophene group (6%).

- A significant reduction (85%) in the incidence of early post-operative onset class III or IV capsular contracture among mammoplasty augmentation patients was effected by irrigation with 5% povidone-iodine solution as well as other antibiotic treatments (Burkhardt *et al.* 1986).

In a prospective, random, double-blind and concurrently controlled clinical study of 124 patients having augmentation mammoplasty, the use of a topical antibacterial product in or around inflatable retromammary prosthetic implants reduced the early post-operative onset of class III to IV capsular contracture by sevenfold (85%) and the final incidence by more than 50% ($p < 0.01$).

- A significant reduction in clean non-abdominal surgeries was found when Chlorhexidine was used as a pre-operative preparation and surgical scrub (Berry *et al.* 1982)

In a prospective, randomized study of 866 surgical patients, no statistical difference in the incidence of post-surgical wound infections was shown between patients and surgeons whose skin was disinfected with PVP-I (10% prep, 7.5% surgical scrub) versus those who used CHG (0.5% prep, 4% surgical scrub). However, the wound infection rates were significantly lower among biliary surgical patients and patients undergoing other “clean” non-abdominal surgeries when CHG was used.

- Use of Chlorhexidine preparations resulted in a significantly lower rate of infection in an ICU (Denton 1991).

This study compared 4% CHG with liquid soap followed by an alcohol rinse.

- A significant reduction in surgical wound infections was found with use of 0.23% hexachlorophene in 46% ethanol by surgical teams in 3,480 surgeries over 8 years (Rubio 1987).

The rate of post-operative infections during the study was 0.3%. The authors cited reports that normal nosocomial wound infection rates ranged from 3 to 5%, 30% of which were surgical. Therefore, “normal” surgical wound infection rates would be ~1 to 1.7%, 70 to 82% higher than the infection rate found during the study.

- A significant reduction in surgical wound infection rates was reported with the use of a 0.05% iodine complex soap at a teaching hospital (Onesko and Wienke 1987).

Bland soap was replaced with soap containing 0.05% iodine throughout the hospital. A significant reduction of surgical wound infections was seen in this two-year prospective study.

- Decrease in subclavian catheter related infections of hemodialysis patients with use of a 10% povidone-iodine ointment (Levin *et al.* 1991).

A 10% povidone iodine ointment applied routinely to temporary hemodialysis catheter sites was shown effective in decreasing subclavian catheter related infections vs. a control group ($p < 0.01$).

- A 2% Chlorhexidine skin prep used on catheter insertion sites was associated with significantly fewer catheter-related infections (Maki *et al.* 1991).

In a randomized clinical study, a 2% CHG skin prep (Hibiprep, Stuart, USA) used on catheter insertion sites was associated with significantly fewer catheter related infections than 10% povidone iodine (Betadine, Purdue-Frederick, USA) and 70% isopropyl alcohol. The authors concluded that 2% CHG, used for disinfection prior to catheter insertion and for post-insertion site care, can reduce the incidence of intravascular device related infection.

- A significantly lower number of catheters were colonized when the catheter site was prepared with 0.5% Chlorhexidine gluconate in 70% isopropyl alcohol (Garland *et al.* 1995).

A 12-month study of neonatal intensive care units identified factors related to catheter colonization in infants. Although antibiotic use, gestational age, heavy skin colonization and duration of catheterization were significant factors influencing colonization, the authors demonstrated that a significantly lower number of catheters were colonized when the catheter site was prepared with 0.5% CHG in 70% IPA (4.7%) than when 10% PVP-I was used (9.3%, $p = 0.01$). The number of positive blood cultures was equal in both groups, but a greater number of catheters were identified as being colonized with more than one organism in the group using PVP-I ($p = 0.003$).

- A significant reduction in the rate of ventilator associated pneumonia, bacteremia and vancomycin resistant enterococci was found with the institution of a Chlorhexidine gluconate mouthwash and Triclosan bathing regimen (Beneda and Finney 2000).

A prospective study of MRSA colonized or infected patients compared the effects of CHG mouthwash and Triclosan bathing following antibiotic

treatment on the incidence of nosocomial infections and colonization. Treatment effected a 45% decrease in the incidence of MRSA positive cultures and reduced the use of vancomycin among patients in the study group. The rate of ventilator associated pneumonia, bacteremia and vancomycin resistant enterococci were 0, 0, and 6.9% in the study group. The control group rates for the same parameters were 40, 10 and 20%, respectively.

- A significant reduction in skin bacteria at central venous catheter sites was seen following use of a Chlorhexidine preparation in the care of 113 patients (Tuominen *et al.* 1981)

Patients were randomized to sterile gauze placed over the catheter insertion site, or sterile gauze wetted with 0.05% Chlorhexidine placed over the insertion site. A significantly lower number of skin cultures were positive for bacteria in the Chlorhexidine treated group (17% vs 25% control, $p < 0.05$). Another significant difference was noted when comparing catheters inserted after incision (cutdown). Only 10% of Chlorhexidine treated sites were positive, while 28% of untreated sites yielded bacteria ($p < 0.01$). This was seen by the authors as an indication of a lower rate of infection among treated catheter sites.

- Central venous line related infections, as well as infections at all body sites were reduced through the use of a 60% ethanol hand gel in the Neonatal ICU and Pediatric ICU units of a children's hospital (Gould, 2000).

Comparison of infection rates, maintained for over one quarter, with data from the previous year revealed that the hypoallergenicity and moisturizing properties of the product may have led to increased compliance with handwashing, thus reducing the incidence of nosocomial infections.

- Routine use of a Chlorhexidine surgical hand scrub eradicated an epidemic strain of *S. epidermidis* from a carrier (Boyce *et al.* 1990).

Investigation of post-operative wound infections and endocarditis caused by a single strain of *S. epidermidis*, including examination of surgical equipment, staff and unaffected patients revealed the outbreak was related to the identical strain on one surgeon's hands. The surgeon was prohibited from performing cardiac surgery and required to use a Chlorhexidine surgical scrub routinely. Two weeks later cultures taken immediately after scrubbing and 3-4 hours after gloving failed to grow the epidemic strain and the surgeon was reinstated. No epidemic strain related infections were detected for 24 months after implementation of the infection control measures.

- Methicillin resistant *S. aureus* ventilator associated pneumonias decreased from 92% to 0% over approximately 3 years following introduction of a foamed alcohol hand antiseptic (Brooks *et al.* 1999).

The institution of infection control measures, including the placement of foamed alcohol hand antiseptic in all patient areas and handwashing signs at all sinks, decreased the rate of ventilator associated pneumonia (VAP) from 92% to 0% during a 3 year period at a medical facility. The estimated extra charges of VAP decreased from \$120,764 (October 1995 through September 1996) to \$7,013 (October 1997 through September 1998).

- Ventilator-associated pneumonia was reduced by 76% and catheter-related bloodstream infections were reduced 65% during a 6 month period using an alcohol based antimicrobial hand gel as compared to infection rates measured 18 months previous to the hand sanitizer introduction (Jones and Newman 2000).

A 60% ethanol hand gel was placed in all patient care areas, except surgical scrub areas, in a hospital. All health care workers were educated on the use of the gel as well as when traditional handwashing was necessary. Following institution of routine hand sanitizer use, ventilator associated pneumonia was reduced by 76% and catheter related bloodstream infections were reduced 65% during the 6-month study period as compared to infection rates measured 18 months previous to the hand sanitizer introduction.

- A significant decrease in bacterial colonization rates and Gram negative infection rates was seen with use of a Chlorhexidine preparation (Amarante *et al.* 2000).

The influence of PVP-I and CHG care of central venous catheters (CVC) along with systematic changing of catheters on fungal colonization and infection rates was investigated among 3,124 patients. CHG care and systematic changing of CVCs led to significantly lower fungal colonization and infection rates than unregulated catheter changing (with CHG care). While PVP-I care with systematic CVC changes yielded lower fungal colonization and infection rates than either CHG treated group, it was also related to higher colonization and infection rates for Gram positive and Gram negative colonization and infection rates.

- A sustained decrease in the rate of central venous line infections was attained with institution of new infection control practices including use of topical antimicrobial products (Fauerbach *et al.* 2000).

An increase on central venous line (CVL) related infections at a tertiary transplant center prompted assessment of infection control practices. Education and communication plans as well as using antimicrobial

impregnated CVLs and 0.5% CHG in 70% alcohol for CVL site prep led to a sustained decrease in the rate of CVL associated blood stream infections in 15 of 19 units.

- A povidone-iodine ophthalmic solution applied prior to surgery was shown to prevent an increase in conjunctival bacteria within the first 24 hours and after one week as compared to an antibiotic preparation or no treatment, respectively (Isenberg *et al.* 1985; Isenberg *et al.* 1997; Apt *et al.* 1989).

Isenberg *et al.* (1997) confirmed that one week post-surgery, the eyes treated with 1.25 or 2.5% iodine solution had a lower mean bacterial concentration as compared to untreated eyes. Apt and coworkers (1989) demonstrated that a 5% povidone-iodine solution instilled in the eye immediately before surgery significantly reduced conjunctival flora.

- Significant reductions in skin graft donor body contamination were found with use of a Chlorhexidine gluconate preparation (May *et al.* 1991).

Significant reductions in skin graft donor body contamination were found when a 4% CHG scrub (Hibiclens, Stuart Pharmaceuticals, Division of ICI Americas, Wilmington, DE) was substituted for povidone-iodine preparations (Betadine Surgical Scrub and Betadine Solution, Purdue Frederick Co., Norwalk, CT). The amount of skin from donor cadavers that was negative for bacterial contamination increased from 86.3% to 94.4% in a study of 342 donors from two skin banks.

- Replacing 70% IPA pads with 10% acetone/70% IPA scrub dispensers in blood culture collection kits significantly reduced the number of contaminated blood cultures of 1,546 blood cultures (Schifman and Pindur 1993).

The contamination incidence using conventional blood culture kits was the same as that of the previous year.

- Use of 0.2% benzalkonium chloride in 70% ethanol on caregivers' hands reduced the incidence of *P. cepacia* in arterial blood cultures (Tanaka *et al.* 1988).

The routine method of hand disinfection in an ICU involved immersion of hands in a basin containing 0.02% aqueous Chlorhexidine. Changing this method for dispensers containing 0.2% benzalkonium chloride in 70% ethanol reduced the incidence of *P. cepacia* in arterial blood cultures of suspected septicemia patients. 46% of cultures taken during the four years of aqueous Chlorhexidine use were positive for *P. cepacia*. This rate was reduced to 13% during the year when benzalkonium chloride in ethanol was used.

- Furuhashi and Miyamae (1979) demonstrated that 10^3 to 10^4 colony-forming units of skin bacteria escaped through the pinholes of experimentally punctured gloves during a period of 5 minutes when hands had been scrubbed earlier without a disinfectant. However, when the hands and forearms had been brushed with a disinfectant, bacterial counts were no more than 100, even 3-4 hours after handwashing.

Although evidence that surgical hand disinfection is really necessary is lacking from epidemiological data, it is a logical consequence of the concept of asepsis in surgery. Indirect evidence found that using a 4% CHG scrub (Hibiscrub) or a 10% benzethonium chloride detergent followed by scrubbing with 90% ethanol containing 0.5% of the corresponding active resulted in 99.7% reductions. Bacterial reductions of 99.9% were maintained for up to 3 hours. As skin bacteria are known to cause infections, especially in operations involving prosthetic surgery, it is sensible to prevent them from entering the surgical wound.

- A significant reduction in the number and frequency of total counts and *S. aureus* on patient's skin was effected with a total body wash with 4% CHG (Stuart 1986).

Contact plate sampling showed that total body washing with 4% CHG (Hibiscrub, Stuart Pharmaceuticals) as an adjunct to pre-operative prepping with 4% CHG effected significant decreases in the numbers and frequency of total and *S. aureus* counts on patients' skin overall as well as at the operation site.

- Significant bacterial reductions were seen in surgical patients who used 4% Chlorhexidine gluconate products in post-operative showers (Garibaldi *et al.* 1988; Denton 1991).

A blinded, randomized, prospective study involving 575 surgical patients showed significantly greater bacterial reductions were achieved by using 4% CHG (Hibiclens, Stuart Pharmaceuticals, Wilmington, DE) in post-operative showers than with 7.5% PVP-I (Betadine, Purdue Frederick, Norwalk, CT) or 1-4% TCC bar soap ($p < 0.001$). Two successive showers with 4% CHG effected a 2.44 \log_{10} reduction of bacteria at surgical sites when compared to preshower counts. Although 7.5% PVP-I did not perform as well, causing a 1.62 \log_{10} reduction, it did perform significantly better than TCC (0.87 LR, $p < 0.01$). All three agents maintained reductions below baseline for up to 11 hours. Positive intra-operative cultures, used as an indicator of the possibility of wound infection showed that CHG showering and pre-operative skin preparation again performed significantly better than PVP-I ($p < 0.025$) and TCC ($p < 0.001$). Although the authors found no relation between wound infection rates and antibacterial agent due to the small number of subjects in each group, they noted that the infection rate for patients with positive intra-

operative cultures (6.8%) was almost twice that for patients with negative cultures (3.8%). Another clinical trial with 700 surgical patients reinforced the findings of this study. Using the same methods, the author showed that 4% CHG effected ~2.1 log₁₀ reduction at the surgical site after two showers, while 7.5% PVP-I and 1% TCC bar soap effected ~1.1 and ~0.5 log₁₀ reductions, respectively.

Another study showed that vascular surgery patients showering with Chlorhexidine three to eight times prior to surgery had a lower infection rate than those who did not (8% vs. 17.5%) even though both groups received the same pre-operative skin preparation immediately prior to surgery. A similar controlled study compared infection rates for surgical patients using CHG in pre-operative showers versus those using bland soap. The group using CHG had a significantly lower infection rate (9%) than the control group (12.5%).

- Significant reductions in staphylococci were shown at both subclavian and inguinal sampling sites following two pre-operative showers with 4% Chlorhexidine gluconate (Kaiser *et al.* 1988).

Significant reductions of staphylococci at subclavian (2.07 log₁₀, p<0.05) and inguinal (1.61 log₁₀) sites were effected by two pre-operative showers with 4% CHG (Hibiclens). A prospective, blinded, randomized study of 39 surgical patients also showed that no significant change from baseline counts was achieved by one or two showers with 7.5% PVP-I (Betadine) or by bland soap.

- Two pre-operative showers with 4% CHG produced significantly lower (p<0.05) wound infection rates than showers with bland soap (bar soap) (Hayek *et al.* 1987).

A randomized crossover study monitored 2,015 surgical patients who used 4% CHG, placebo or bar soap. Total wound infection rates were 9% for CHG, 11.7% for placebo and 12.8% for bland soap. The respective rates for wound infections by *S. aureus* were 2.6%, 4.0% and 5.3% and clean wound infections were 3.0%, 4.0% and 6.0%. Although the only significant difference in infection rates was between CHG and bar soap, the authors noted that antibacterial activity by the placebo was detected and the placebo had to be replaced during the study. Therefore, no true placebo was tested.

B. TOPICAL ANTIMICROBIAL PRODUCTS IN NON-INVASIVE PROCEDURES

Interruption of disease transmission in non-invasive situations to others and oneself due to the acquisition of transient bacteria and their transfer to a point of entry into the host, and to oneself due to skin infections from one's own resident skin flora.

Infection can be associated with non-invasive procedures. In non-invasive situations, the aim of skin disinfection and killing or inhibition of the skin flora is: a) to prevent the conveyance of bacteria from one person or fomite to the self or another person; or b) to reduce the resident bacteria and thereby control the risk of pyogenic infection or to decrease the numbers of bacteria associated with diseases such as atopic dermatitis. The organisms that are associated with these types of infections can include Gram positive and Gram negative bacteria.

The examples provided below demonstrate the importance of a topical antimicrobial product in the overall infection control regimen. Many of the studies presented change more than one variable including the topical antimicrobial regimen, however, the use of the topical antimicrobial is seen by the authors to play a critical role in infection control.

Clinical Settings

- Staff handwashing and infant bathing with 3% Hexachlorophene reduced staphylococcal infection among infants in 26 hospitals (Frappier-Davignon *et al.* 1959).

The incidence of staphylococcal infection among infants in 26 hospitals was shown to be related to the handwashing practices of staff and bathing of infants. (Frappier-Davignon *et al.* 1959) While the study showed that the transfer of infants in and out of nurseries had a significant effect on infection rates, handwashing with 3% hexachlorophene or bland soap by staff also reduced infection rates. Bathing infants with hexachlorophene further reduced these infection rates.

- Bathing infants in 3% hexachlorophene significantly reduced the incidence of infection and staphylococcal nasal colonization (Johnson *et al.* 1976).

Staphylococcal colonization and infection rates among infants in a well baby nursery were measured to compare the effects of 3% hexachlorophene, and bland soap bathing of infants. Initially, infants were bathed with 3% hexachlorophene. This practice was alternated for three-month periods with bland soap bathing followed by alcohol cleansing of the umbilical stump. During the final comparative period infants were bathed with bland soap and the umbilical stump was treated with bacitracin. The incidence of infection/nasal colonization was 0.7%/4.4% and ~4%/9.6% during the periods of hexachlorophene use. In contrast, the infection/colonization rates were 9.5%/30.8% and ~10%/16% during the same respective periods of bland soap use.

- Bathing of infants with hexachlorophene eliminated a staphylococcal outbreak in a hospital nursery (Cooper and Gibson 1974).

An outbreak of staphylococcal infection occurred in a nursery where hexachlorophene use was discontinued. Reinstitution of post-partum and weekly bathing of infants eliminated the problem.

- A significant decrease in *S. pyogenes* infections occurred when hexachlorophene was used for infant bathing (Forfar *et al.* 1968).

Two maternity wards were monitored for over 10 years, during which over 29,000 infants were born, to determine the effect of hexachlorophene use. Periods in which hexachlorophene was not used were compared to those in which hexachlorophene was used daily on infants and by nursing staff for handwashing. A significant decrease of *S. pyogenes* infections in infants occurred in the hospital that used hexachlorophene on the infants (from 11.1 to 2.8%). At the same time, an increase in Gram negative bacterial infections was noted. In the second hospital, hexachlorophene was not used for the first eight years, and only used on nurses' hands the last two years. The infection rates did not change significantly for either organism in this hospital. Bacterial sampling of nasal carriers of *S. pyogenes* showed that handwashing with hexachlorophene in both hospitals did not significantly reduce the number of carriers.

- Reduced incidence and severity of staphylococcal infections was associated with use of Chlorhexidine preparations (Murray and Calman 1955).

In a maternity hospital, use of 1% Chlorhexidine diacetate and dihydrochloride decreased the resident and transient flora measured on hands.

- A significant reduction in nosocomial infections was associated with the use of Triclosan-containing foam in an in-patient dialysis unit over a four-month period (Malone and Larson 1996).

A prospective study of the hospital in-patient dialysis unit demonstrated lower infection rates during the four months when staff used the barrier foam (5.3%) than in the six months when no barrier foam was used (13.4%, $p < 0.006$).

- Lack of use of an antimicrobial soap was implicated in the transmission of a staphylococcal bacteremia among bone marrow transplant patients (Klausner *et al.* 1999).

Three fatal cases of *S. maltophilia* bacteremia among bone marrow transplant patients were investigated. Pulsed field gel electrophoresis revealed that all three patients were infected with identical isolates. Further investigation showed that the same health care worker attended to the case-patients. During the outbreak, it was determined that foamed lotion was mistakenly

installed in one of the case patients' room in place of 2% CHG foam soap. Since none of the control patients acquired *S. maltophilia* infections or was treated by the suspected health care worker, the authors reported there was a strong association between the worker and the case isolates. They went on to suggest that the health care worker may have treated one infected patient, used the lotion instead of the antimicrobial soap and then treated the other two patients who subsequently acquired bacteremia.

- Use of an alcohol based hand sanitizer as part of an overall infection control regimen stemmed an outbreak of Vancomycin-resistant *Enterococcus* patients in a liver transplant program (Thompson *et al.* 2000).

An outbreak of VRE among patients in the Mayo Foundation liver transplant program prompted increased infection control measures including patient isolation, increased surface disinfection, staff education, increased surveillance for patient colonization and introduction of an alcohol based hand sanitizer. Enforcement of the infection control measures controlled the outbreak.

- Hand disinfection system using 4% Chlorhexidine gluconate reduced nosocomial infection rates (Doebbeling *et al.* 1992).

This study concluded that a hand disinfection system using 4% Chlorhexidine gluconate (Hibiclens, Stuart Pharmaceuticals, Wilmington, DE) reduced nosocomial infection rates more effectively than one using 60% IPA and nonmedicated soap. Use of these systems was alternated monthly between intensive care units in a hospital for 8 months. Health care personnel were instructed to use the alcohol product routinely and the soap when hands were visibly soiled. Although nosocomial infection rates were reduced in the units using Chlorhexidine compared to alcohol and soap, the authors found there was significantly less compliance with handwashing instructions in the units using alcohol and soap.

- A 50% reduction in nosocomial infections was reported following a six-week use period of a 4% Chlorhexidine formulation in a surgical intensive care unit (Maki and Hecht 1982; Maki 1989).

Following a six-week use period of a 4% Chlorhexidine formulation (Hibiclens, Stuart) in a surgical intensive care unit, a 50% reduction in nosocomial infections was reported as compared to a non-medicated soap ($p > 0.001$). During CHG use period hospital staff were randomly cultured, the authors recovered 3.56 ± 0.09 cfu aerobic skin flora and 0.13 ± 0.78 cfu *S. aureus* compared to 4.22 ± 0.12 cfu and 0.22 ± 0.09 cfu with plain soap.

- Significant reductions in nosocomial infection rates were reported with the use of a 0.05% iodine complex soap at a teaching hospital in a two year

prospective study prompted by an increase of MRSA infections in two units of the hospital (Onesko and Wienke 1987).

Bland soap, commonly used in the intensive care and geriatric units (sites of increased nosocomial infections), was replaced with soap containing 0.05% iodine complex. In addition, all other soaps in the hospital were replaced with the test product. Nosocomial infections were determined according to CDC guidelines and compared between the year before and after use of the iodine soap was instituted. A 21.5% reduction, although not statistically significant, was effected on the overall nosocomial infection rate at the hospital. Significant reductions ($p < 0.005$ to 0.05) were achieved for MRSA, MSSA, *Pseudomonas* spp., *Enterobacter* spp., normal flora related infections and surgical wound infections in the two test units.

- An outbreak of *Acinetobacter anitratus* septicemia in a neonatal ICU was controlled by institution of an infection control regimen including use of an alcohol spray (Sakata *et al.* 1989).

Over a three-year period, 19 of 42 septicemic infants were infected by *A. anitratus*. A new infection control regimen was instituted including: encouraging staff to wash hands before entering the NICU and to disinfect hands before handling infants, isolating colonized infants from non-colonized infants, shortening antibiotic therapy when possible and switching from a 0.02% aqueous Chlorhexidine dip to an ethanol spray. Although the number of *A. anitratus* isolates from environmental surfaces did not change, fingerprint samples revealed that the next nine months, the number of isolates on staff hands was 0. Approximately 9% of cultures from hands yielded *A. anitratus* in the period preceding increased infection control measures. During the same nine months, no septicemia cases occurred, and the number of infants colonized was reduced.

- Use of a 4% Chlorhexidine hand product in conjunction with education and enforcement programs significantly decreased the rate of nosocomial infection in a medical ICU (Conly *et al.* 1989).

The rate of nosocomial infections decreased from 33 to 12% after the first intervention, and fell from 33 to 8.5% following the second intervention ($p = 0.02$).

- Elimination of MRSA from the Intensive Care Nursery and Special Care Unit after introduction of a 1% Triclosan hand wash formulation (Webster *et al.* 1994).

A 7-week trial of a 1% Triclosan hand wash formulation led to a reduction in the number of new MRSA isolates in the Intensive Care Nursery. An extension of the trial to 12 months and the inclusion of the Special Care Unit

of that facility (Royal Women's Hospital in Brisbane Australia) completely eliminated MRSA from the units.

Reduction of new cases of MRSA in a neonatal Intensive Care Nursery after 7 weeks of use of 4% Chlorhexidine gluconate or a 1% Triclosan handwash.

In a 7-week trial, the average number of new cases of MRSA per week was reduced from 3.4 to 0.14 ($p < 0.0001$) in the ward using 1% Triclosan handwash as compared to the ward using 4% Chlorhexidine gluconate.

- A significant reduction in the number of MRSA carriers and infections was observed following a whole-body wash of patients with 1% Triclosan and a decrease the length of use of peri-operative antibiotics (Brady *et al.* 1990).

An increase in the prevalence of MRSA in a cardiothoracic surgical unit prompted a prospective study to determine the carrier status of patients. A whole-body wash of patients with 1% Triclosan (Novaderm R, Novapharm) and the length of peri-operative antibiotic usage were shortened. As a result, during the 18 months following implementation of these practices a significant reduction in the number of MRSA carriers and infections was observed.

- Use of a 2% Triclosan antiseptic liquid exclusively 3 times daily for bathing/showering as well as handwashing eradicated an epidemic MRSA strain from all carriers within an average of 22 days and all carriers remained negative for three months after treatment (Bartzokas *et al.* 1984).

The vascular surgical unit of an 800-bed hospital experienced an outbreak of methicillin resistant *S. aureus* (MRSA) that included 15 patients and 3 staff members as carriers.

- A methicillin-resistant *S. aureus* (MRSA) outbreak in a neonatal nursery was eradicated through the use of a 0.3% Triclosan Healthcare Personnel Antiseptic Handwash for handwashing and bathing (Zafar and Butler 1999).

After eight years of continued use of the product, the Nursery remains MRSA free.

- A significant reduction in bacteremia and MRSA infection rates occurred following institution of an infection control program including use of 7.5% PVP-I in a 332 bed hospital (Tyzack 1985).

Handwashing by all staff and visitors with 7.5% PVP-I (Betadine) was an integral part of an infection control program that eliminated bacteremia in a 332 bed hospital and significantly decreased MRSA infection rates (Tyzack 1985). In addition to handwashing, the hospital retrained staff, created an isolation ward for MRSA cases, gave total body washes with PVP-I to MRSA

patients, treated wounds and pressure sores with PVP-I and administered PVP-I nasal ointment to all intensive care and MRSA patients. During the two year study, total MRSA infections were reduced from 74 in the four months prior to institution of the program to 5 in the last four months of the study. The rate of infections per discharges also significantly changed. In the four months prior to the study the rate was ~8.1%. This was reduced to ~4.6% two years later.

- Reduction of MRSA carriage by 135 patients was seen with the use of Chlorhexidine baths as an adjunct to topical and oral antibiotic therapy (Majury *et al.* 2000).

CHG bathing was used as an adjunct to topical and oral antibiotic therapy in a 21 month study of 135 patients colonized or infected with methicillin resistant *S. aureus* (MRSA). Although the risk of relapse was greater for patients not receiving oral antibiotics, both topical antibiotic used with CHG bathing and topical ointment used with CHG bathing and oral antibiotics were effective at eradicating MRSA. Seventy-three percent of patients were free of MRSA one month after treatment and 48% were free of MRSA at two months.

- A significant reduction of nasal MRSA carriage and colonization rates was seen following use of povidone-iodine cream (Mitsuda *et al.* 1999).

The relationship of MRSA colonization and persistent MRSA carriage by health care workers at a hospital was studied in a 5- year study. In addition, transmission to the families of colonized workers was investigated. MRSA isolates in 65% newborns at the hospital were identical to strains found in two colonized nurses in the unit. Some of the nurses' family members also were persistent or transient carriers with identical MRSA strains (within each family). Following povidone-iodine cream treatment, nasal MRSA was eradicated in the nurses and the MRSA colonization rate, which had been as high as 26% remained below 5% in newborns for over 3 years.

- Use of a Triclosan handwash reduced the rate of MRSA infection in a hospital outbreak (Tuffnell *et al.* 1987).

Prior to and during the outbreak, MRSA patients were isolated in their rooms and treated with mupirocin cream. When the outbreak was detected, an isolation ward was created and patients were bathed with 3% hexachlorophene. Staff in contact with the patients also washed their hands with hexachlorophene. Affected staff were treated in the same manner as affected patients, but not isolated. When the outbreak was not controlled, hexachlorophene was replaced with 2% Triclosan. In the nine months after Triclosan use was begun, eight MRSA infections occurred. Fifty-six MRSA infections occurred in the previous two years when hexachlorophene was used.

- A significant decrease in the number of staff related colonization/infections among patients followed institution of routine use of 4% Chlorhexidine gluconate handwash by hospital staff (Casewell and Phillips 1977).

Serotyping *Klebsiella* spp isolated from patients and staff at an intensive care unit demonstrated the effect of education and routine use of 4% CHG in reducing bacterial colonization and infection. Upon identifying the routes of *Klebsiella* spp transmission, the authors instructed the staff of the ICU on the importance of handwashing and introduced the use of 4% CHG as a routine procedure. A significant decrease ($p < 0.001$) in the number of staff related colonization/infections among the patients occurred following the intervention. During the two years prior to intervention the rate was 22.0 to 22.6%. This rate dropped to 15.5% after the intervention.

- Staff handwashing with 3% hexachlorophene was associated with a lower rate of nosocomial *S. aureus* acquisition in a hospital nursery (Mortimer *et al.* 1962).

Nurses were cohorted with infants in the nursery and instructed to handle an index patient before handling their assigned patients. Nurses in the test group washed their hands for 10 seconds with hexachlorophene between patient contacts. Nurses in the control group did not. *S. aureus* acquisitions, as determined from umbilical and nasal cultures, occurred in ~53% of test group infants and ~92% of control group infants. Infants in the control group acquired the organism more quickly than test infants at an average of 35 hours before acquisition (test group 133 hours). Infants in the main nursery acquired the organism from control group nurses at a higher rate (~17%) than from test group nurses (2.3%). A subsequent trial to determine the effect of airborne bacteria on carrier rates showed that handwashing was the only significant factor affecting acquisition of *S. aureus*.

- A significant reduction of bacterial recovery from nurse's hands was effected 6 months following introduction of a 7.5% povidone-iodine wash (Amortegui and Buffenmyer 1978).

In a 6 month, single blinded comparison of two iodophor preparations for handwashing in two well-baby nurseries (cross-over design), a 4mL wash with a 7.5% povidone-iodine (Betadine) demonstrated a reduction in recovery of bacteria from the hand utilizing swab cultures from 78.4% to 22.3% and a 73.2% to 26.5% reduction following use of a second 7.5% iodophor preparation. The authors further reported the reduction of *S. aureus* and Gram negative rods on hands from 11-12% to 1.0-2.0% following handwashing with the test materials.

- Use of a 0.5% iodine/83% ethanol handwash significantly reduced bacterial load on the hands of hospital staff after 4 weeks (Kirita *et al.* 1993)

A 0.5% iodine/83% ethanol hand wash (HAD Hand Wash, Meiji Seika Kaisha, Ltd.) effected mean bacterial reductions of 86.9% to 91.5% respectively initially and after four weeks use in a clinical study. Palm stamp plate recoveries showed that *S. epidermidis*, *S. aureus* and *Bacillus spp.* were eradicated at rates of 75.8 to 100% among 30 hospital staff using the hand wash.

- A significant reduction in total bacteria and Gram negative bacilli on nurses' hands after patient contact was seen with use of a 4% Chlorhexidine gluconate product (Stuart 1986).

A clinical trial in a neurosurgical care unit showed that 4% CHG (Hibiclens, Stuart Pharmaceuticals) significantly reduced total bacteria and Gram negative bacilli on nurses' hands after patient contact (1.4 and 0.9 log₁₀ respectively). In comparison, 0.75% available iodine and bland soap had no significant effect on the same organisms. Trials to measure long term activity again showed that 4% CHG was significantly more effective against Gram negative and *S. aureus* than PVP-I or bland soap and alcohol rinses.

- Disinfection of hemodialysis patients' skin with 4% Chlorhexidine gluconate showed a significant reduction of bacteria at the vascular site four hours after treatment (Goldblum *et al.* 1983).

Disinfection of hemodialysis patients' skin was conducted to compare 4% CHG (Hibiclens) and 7.5% povidone-iodine (Betadine). Samples from 46 patients showed that the use of CHG was associated with a greater number of *S. aureus* nasal carriers (46%, p<0.005) and skin carriers (30%, p<0.05) than PVP-I (35.6 and 23%). However, measurements taken two and four hours after disinfection of the vascular site showed that CHG caused significantly greater reductions of bacteria (p<0.01). In addition, CHG was more effective in eradicating *S. aureus* from patients' skin than PVP-I (54 vs. 8%, p=0.032).

- Routine use of a 1% Triclocarban antibacterial soap significantly reduced the numbers of Gram positive organisms and the prevalence of *S. aureus* (Voss 1975).

In a study of 225 subjects (93 control subjects), the routine use of a 1% Triclocarban antibacterial soap significantly reduced the numbers of Gram positive organisms and the prevalence of *S. aureus* at five out of six skin sites without an increase seen in the growth of Gram negative organisms. The axilla was the only site where the reduction in total aerobic flora was not significant over that of the control group and this may be attributable to the

favorable conditions for growth in that area. The study also suggested a cumulative persistence in the inhibition of *S. aureus* over its 7-month duration.

- Total body washing with 4% CHG reduced counts on the skin of five volunteers heavily colonized with *S. aureus* (Stuart 1986).

Cultures taken from the lip, axilla and groin were reduced by ~ 0.43 to ~ 2.02 \log_{10} after three consecutive five minute washes. In addition, reductions were maintained below baseline for up to 10 days on the skin of two volunteers (baseline $\sim 2.2 \log_{10}$).

- When assayed between patients, significant reductions of total bacteria, staphylococci and streptococci were seen with use of a 0.1% Chlorhexidine gluconate cream by visiting nurses (Gould *et al.* 2000).

A clinical trial involving 17 nurses performing in-home visits demonstrated the residual activity of CHG. Fingerprint samples measured total bacteria, *Staphylococcus* and *Streptococcus* and coliform bacteria on nurses' hands before and after patient contact. A 0.1% CHG cream, applied before patient contact and after handwashing, did not significantly reduce counts immediately after application. However, comparison of counts at the end of one visit to those measured at the start of the next visit (versus untreated controls) showed significant reductions of total bacteria as well as staphylococci and streptococci.

- 60% Isopropanol was significantly more effective in reducing the transfer and in removing aerobic Gram-negative bacilli transferred from carriers' groins to healthcare workers' hands (Eckert *et al.* 1989).

The effect of 60% IPA on transfer of aerobic Gram-negative bacilli (AGNB) from carriers' groins to the hands of healthcare workers was evaluated as well as the removal of AGNB from healthcare workers' hands after contamination. After a 60 second scrub with bland soap the number of AGNB transferred to healthcare workers' hands from carriers with $\approx 3 \log_{10}$ population was reduced by a median of $1.3 \log_{10}$. Sixty second treatment of carrier sites with 60% IPA effected a $3.6 \log_{10}$ median reduction of bacterial transfer ($p < 0.02$). Likewise, using alcohol as a hand rub after transfer of bacteria effected a median reduction of $3.8 \log_{10}$ and reduced counts to 0 in seven of eight trials ($p = 0.004$).

- Use of 60% isopropyl alcohol significantly reduced the transfer of resident aerobic Gram negative bacilli (AGNB) from carrier patients to healthcare workers' hands (Eckert *et al.* 1989a).

A clinical study showed that transfer of resident aerobic Gram negative bacilli (AGNB) to healthcare workers' hands from carrier patients was reduced by about 3.6 log by treating patients' skin with 60% IPA.

- Seventy percent isopropyl alcohol was effective in preventing the transfer of Gram negative bacteria to catheters from healthcare workers' hands contaminated by contact with carrier patients (Ehrenkranz *et al.* 1991).

Bland soap handwash was generally ineffective in preventing hand transfer of Gram negative organisms to catheters following brief contact with a heavily contaminated patient; alcohol rinse was generally effective ($p < 0.001$).

- A Triclocarban bar soap was significantly ($p < 0.05$) more effective in removing *K. pneumoniae* from perineal colonization of male patients with spinal cord injuries (Gilmore *et al.* 1984).

No differences in total aerobic counts were seen among the four test agents in a study of the perineal colonization of male patients with spinal cord injuries. However, a Triclocarban bar soap was significantly ($p < 0.05$) more effective in removing *K. pneumoniae*, a frequent colonizer of these patients, than a 7.5% povidone-iodine scrub or a low pH skin cleanser but not more effective than a 4% Chlorhexidine scrub (Hibiclens).

- Use of 70% ethanol for hand disinfection resulted in a lower incidence of Gram negative bacilli on nurses' hands.

Clinical studies compared the frequency of contamination by *S. aureus* and Gram negative bacilli (GNB) on nurses' hands. Although no detectable difference was noted for *S. aureus* contamination, a lower incidence of GNB was found during the period of 70% ethanol use in the ward when compared to 4% CHG or placebo use (Ayliffe *et al.* 1975).

- Significant reductions in the numbers of Gram negative cultures and kanamycin resistant cultures occurred with use of 7.5% Betadine for routine handwashing by intensive care nursery nurses (Knittle 1975).

Nosocomial infections by Gram negative organisms with kanamycin resistance in an intensive care nursery were investigated: 86.1% of cultures from nurses' hands yielded Gram negative organisms and 48.3% of cultures were positive for kanamycin resistant organisms during a three month period. Switching to gentamicin use in the unit effected a significant reduction of positive cultures. However, replacing 3% hexachlorophene with 7.5% PVP-I (Betadine) as the routine hand wash product reduced the number of Gram negative cultures to 48.7% and the number of kanamycin resistant cultures to 12.8%.

- Institution of an infection control program including use of antimicrobial soap decrease clonal transmission of a multidrug resistant *Acinetobacter* (Raimondi *et al.* 2000).

Following an increase in the incidence of multidrug resistant *Acinetobacter* at a 212 bed medical center, predominantly in a geriatric unit, molecular typing of concurrent and prospective cultures from the environment and noninfected patients revealed that insufficient infection control practices were the cause. Cohorting staff and equipment, isolating affected patients and the use of antimicrobial soap decreased clonal transmission of the organism.

Institutional Settings

- Absenteeism among elementary school teachers and students was significantly reduced when a 62% alcohol gel hand sanitizer was used in classrooms as part of a hand hygiene program (Hammond *et al.* 2000).

Over 6,000 students at 16 schools in Delaware, Ohio, Tennessee and California participated in the study. Teachers and administrative staff were instructed on the use of the 62% ethanol product and students were instructed by teachers to follow their usual handwashing routine in the restroom. In schools using the hand sanitizer students were instructed to use the sanitizer when entering and leaving the classroom and when they sneezed or coughed. Absenteeism due to colds, flu and gastrointestinal disease decreased by 19.8% overall in schools using the 62% alcohol hand sanitizer.

- A significant reduction in respiratory illness in adult day care centers occurred with the introduction of an infection control program including use of an alcohol foam (Falsey *et al.* 1999).

A four-year study of respiratory illness was conducted in three adult day care centers to measure the effect of interventions on infection rates. Staff were educated on the importance of handwashing and given alcohol foam as a supplement to handwashing. They were instructed to use the foam after touching a patient, and after sneezing or coughing in addition to their normal handwashing routine. Infection rates as compared to three years prior to the intervention fell significantly ($p < 0.0001$) from 14.5 to 10.4 per 100 person-months (previous 3 years) to 5.7 per 100 person-months. However, since the number of handwashing episodes was not measured, the authors noted that it was not possible to attribute this decrease solely to use of an antimicrobial hand care product.

- Use of a 60%IPA hand rinse in addition to intervention hygiene instruction significantly reduced the symptoms of enteric disease in family day care homes (Butz *et al.* 1990a).

A 12-month study demonstrated that the use of a 60%IPA hand rinse in addition to intervention hygiene instruction significantly reduced the symptoms of enteric disease in family day care homes, whereas respiratory symptoms were not significantly affected.

- A significant reduction of nosocomial eye and skin/wound infection rates was found with use of a Triclosan hand protectant in addition to handwashing with Chlorhexidine gluconate by staff of a long-term care facility. Methicillin positive cultures were completely eradicated from 80 residents during the period of use of the hand protectant (Hoffmann *et al.* 1999).

A three-month study at a long-term care facility compared nosocomial infection rates as well as colonization of healthcare workers' hands when a Triclosan hand protectant was used as supplement to handwashing with CHG. When compared to the same months in the previous year, when only CHG handwashing was used, nosocomial infection rates were reduced from 9.6 and 15.4% to 5.8 and 7.5% on two floors of the facility. The infection rates were also lower than the rates on those floors for the entire previous year. Reductions of 71% and 60% respectively were effected among nosocomial eye and skin/wound infections. Finger imprint cultures showed average reductions of bacteria on healthcare workers' hands from ~56 colonies/worker to ~43 colonies/worker. Finally, methicillin positive cultures were completely eradicated from 80 residents during use of the supplemental hand protectant.

- Wound healing was significantly better in a group using medicated soap for daily bathing and wound cleansing. Subjects with moderate and severe wounds showed a lower frequency of infection with medicated soap use (Dubow and Winter 1967).

A juvenile detention home housing 40 boys was the site of a study comparing wound infections. Subjects were assigned to groups bathing with either bland soap or soap containing 0.75% hexachlorophene and 0.75% trichlocarban. Cuts, scratches or abrasions were reported and immediately cleaned with the same soap used for bathing. The authors discovered that wound healing was significantly better ($p < 0.001$) in the group using medicated soap. Although no difference in healing among those with mild wounds was detected, subjects with moderate and severe wounds showed a lower frequency of infection when medicated soap was used ($p < 0.01$).

- Use of a topical antimicrobial soap decreased the number of cutaneous bacterial infections over a 6-month period at a military academy (MacKenzie 1970).

A six-month study at the US Naval Academy compared the number of cutaneous bacterial infections among 1201 first year midshipmen. The test group used a bar soap containing 0.75% hexachlorophene and 0.75% triclocarban and the control group used bland soap. Subjects who did not adhere to the protocol (excluding all other antibacterials other than the test soap) were excluded from the study. 3.82% of subjects in the test group developed infections, while 6.84% in the control group were infected ($p < 0.01$). The majority of positive cultures taken from both infected groups yielded coagulase positive staphylococci.

- A reduction in sites infected with corynebacteria was found with use of antibacterial soap over a six-week period by 405 psychiatric in-patients (Somerville *et al.* 1970).

The incidence of *C. minutissimum* and *C. tenuis* skin infections was measured among 405 psychiatric in-patients to determine the effect of an antibacterial soap. Patients and staff were given either a bland bar soap or a bar soap containing a 2% mixture of TCC, Triclosan and cloflucarban and asked to use it during the six-week study. Significant improvements were effected in both groups, but no significant difference was found between treatments, except in comparing the number of sites affected. In this case, the antibacterial soap had a significantly greater effect ($p < 0.05$). The antibacterial soap also reduced scaling more effectively than bland soap ($p < 0.001$).

- Daily use of a topical antimicrobial product was included as part of an antimicrobial regimen which led to the eradication of MRSA (Shahin *et al.* 1999).

Following the identification of an MRSA infection in a child attending a day care center, nasal, throat and perianal sample from children and staff at the center were cultured to identify individuals colonized with the organism. Two children (including the index case) at the center were found to be colonized with MRSA. No staff members were colonized, and one family contact was colonized. Colonized individuals were treated with mupirocin nasal ointment, 0.3% Triclosan daily baths and oral antibiotics if deemed necessary. Within three months, the index case was free of MRSA. The classroom contact and sibling were also cleared of MRSA within one month.

- A significant reduction in bacterial contaminants on hands was seen following use of PCMX and Triclosan wash products (Charbonneau *et al.* 2000).

Contact agar plate sampling and image analysis was used to measure the efficacies of antimicrobial agents in simulated food service situations. Hands were contaminated by handling chicken carcasses. PCMX, Triclosan and alcohol rinses were then used for disinfection. 0.12 to 3.75% PCMX in 48%

IPA significantly reduced bacteria on hands versus baseline counts. Concentrations of at least 0.95% were required to effect 80% or greater reductions. Likewise, 0.1 to 5% Triclosan significantly reduced counts versus baseline. No dramatic increase of efficacy was achieved by Triclosan concentrations above 1%.

Home Settings

- Significant improvement in dermatological effects and significantly fewer organisms were found after use of a 1.5% Triclocarban bar soap by atopic dermatitis patients (Breneman *et al.* 1998).

Patients with atopic dermatitis using a commercial bar soap containing 1.5% triclocarban were compared to those using a non-medicated bar soap to measure dermatological effects and microbial populations on the skin. Patients using the Triclocarban bar soap showed significantly lower scores for primary and secondary dermatological effects. The treatment group had a lower percentage of body areas affected and reported less itching. In addition, the Triclocarban group had significantly lower numbers of total organisms and directionally lower numbers of *S. aureus* than the placebo group.

- Significant improvement in dermatological effects and significantly fewer organisms were found after use of 10% povidone-iodine by atopic dermatitis patients (Akiyama *et al.* 1997).

A case-control study of atopic dermatitis patients demonstrated a 10-100-fold decrease in the density of *S. aureus* and a decrease in erythema and exudation after single, daily treatment with 10% povidone iodine for 14 days.

- Significant improvements in dermatological indicators were seen with the inclusion of a 10% povidone-iodine wash as part of a treatment regimen for 609 patients with atopic dermatitis (Sugimoto *et al.* 1997).

Sugimoto *et al.* conducted studies of atopic dermatitis patients to measure the effect of PVP-I therapy as adjunct to topical antibiotic ointment, and oral antiallergens. (1997) Cultures from the lesions of 609 patients yielded *S. aureus* in 92% of cases. Subsequent tests on 128 patients yielded improvements in 97% of cases, as reported from patient surveys. Patients were instructed to use a 1:1 dilution of 10% PVP-I two to four times daily, for two minutes on facial lesions and 3 minutes on body lesions. In addition, they were instructed to apply antibiotic once daily to lesions and keep lesions moist with bland ointment as well as using oral antiallergens. Patients described decreased itching, skin redness, sleep disturbance, lichenization, bleeding and exudates, most within short periods (several days to 2 weeks). 50% or greater reductions of IgE levels and eosinophilic cell counts were

effected in 54 to 60% of 35 cases tested within three to 15 months of treatment. Three case studies presented revealed even greater reductions of IgE and eosinophilic cell counts from 37 to 88%. In addition, these case studies showed improvement in RAST scores for food allergens with reductions from 71 to 100%.

- A mathematical model developed to predict the risk of acquiring *S. aureus* skin infections and the possible risk reduction afforded by antibacterial soaps showed a considerable reduction in risk of infection from use of antibacterial soap compared to bland soap (Rose and Haas 1999).

A considerable reduction in the risk of infections was shown for antibacterial soap versus bland soap. The example presented predicted that an inoculum of $5 \log_{10}/\text{cm}^2$ after showering presented a risk that could be decreased up to 20-fold by antibacterial soap. Data from studies of *S. aureus* growth kinetics and volunteer trials of dose data was used to construct the model. These data was for infection at one site. No information was available for cases of infection at multiple, independent sites. However, they suggested that probabilities could estimate increased risks when multiple sites were considered.

- Use of topical antimicrobial preparations reduced the recurrence of infective skin lesions (Leigh and Joy 1993).

A study of 26 families with staphylococcal skin infections found that use of Chlorhexidine preparations reduced the recurrence of infective lesions more than combinations of Chlorhexidine treatments combined with topical antibiotic use.

- Use of topical antimicrobial preparations improved inflammation and skin condition when used as an adjunct treatment in acne patients (Brown 1977; Franz *et al.* 1978; Jampani *et al.* 2000; Stoughton and Leyden 1987).

Patients with acne vulgaris symptoms were treated with PVP-I skin cleanser alone or in addition to oral contraceptive, antibiotic, UV light, and topical agents. (Brown 1977) Of the 27 patients completing the study, 19 were judged by a physician to have benefited considerably. Only five showed no change in their condition. Comparison of the groups showed no statistical difference between the adjunct therapies and the PVP-I alone treatment.

Fifty-five patients with mild to moderate acne completed a 12-week study to compare the effects of 0.1% Triclosan and 0.1% Triclosan plus 0.75% propylene phenoxetol creams to a placebo (Franz *et al.* 1978). Both antibacterial creams compared to a placebo caused significantly greater reductions in the number of lesions. The antibacterial formulas effected reductions of 21 to 22% non-inflamed lesions and 43 to 44% inflamed lesions.

In addition, clinical evaluation of the lesions showed that antibacterial treatment reduced the degree to which lesions were inflamed.

In two clinical studies Jampani *et al.* (2000a; 2000b) demonstrated the activity of an antimicrobial hand gel against inflammation causing bacteria. A significant decrease in the number of *P. barbae* lesions was measured clinically and visually among eight patients using the product in a six week study. In addition, significant reductions in the number of acne papules were detected at three days, one week, four weeks and 12 weeks versus baseline measurements among 14 subjects. Digital photographs and visual comparisons to baseline revealed the antimicrobial and anti-inflammatory activity of the product.

The efficacy of 4% CHG (Hibiclens) was compared to 5% benzoyl peroxide and the product vehicle in randomized controlled studies (Stoughton and Leyden 1987). In the first trial, benzoyl peroxide and CHG were both used twice daily for 12 weeks. Both treatments significantly improved the condition of acne patients (BP, $p < 0.001$, CHG, $p < 0.01$) at eight and 12 weeks. The subsequent 12 week study compared CHG to vehicle and showed that CHG again effected significant improvements in patient condition at all times ($p < 0.001$). CHG was also significantly more effective than vehicle at each test period ($p < 0.05$ to 0.001).

- A significant reduction in respiratory illnesses was seen in mothers who used a 2% aqueous iodine hand treatment when exposed to sick children in the home (Hendley and Gwaltney 1988).

Twenty-two families participated in a blinded study to compare the effect of 2% aqueous iodine and placebo in preventing secondary illness in mothers caring for children with respiratory infections. In the four-year study, mothers with one or more children residing in the home were instructed to dip their fingers and thumbs in the antimicrobial solution on waking and before contact with any family member. They were also to reapply the solution every three to four hours or after activities that removed the solution from their hands. Treatment was to begin once respiratory symptoms in the children were noticed and continue until no cold symptoms were observed or for two weeks. Once symptoms were observed, mothers were to contact the nurse, who monitored family members for symptoms and mothers for compliance to the treatment regime. The number of illnesses when compared to numbers of exposure to sick children, 7% was significantly lower among mothers in the treatment group than those in the placebo group (20%, $p = 0.047$).

- A significant reduction in puerperal mastitis was observed among mothers who had a hand disinfectant provided at their bedside (Peters and Flick-Fillies 1991).

A 2 year prospective study of incidence of puerperal mastitis in relation to hand disinfection observed infection rates among 2325 nursing mothers: 2.9% developed mastitis when no hand disinfectant was available at bedside while only 0.65% of those who were provided disinfectant became infected ($p < 0.001$).

- Significant reduction of staphylococci intramammary or teat infections occurred in dairy herds treated with topical antimicrobial preparations including Chlorhexidine gluconate, iodophors, or sodium hypochlorite (Boddie *et al.* 1990; Boddie *et al.* 1997; Hicks *et al.* 1981; Pankey *et al.* 1983; Kovars 1985; Sheldrake and Hoare 1981; Sheldrake and Hoare 1983; National Mastitis Council Research Committee 2000).

Mastitis in dairy cattle has been transmitted by the hands of dairy workers and by shared milking machinery. The use of topical antimicrobial products on the dairy worker's hands as well as on cow teats has led to significant reductions of mastitis and other infections.

The National Mastitis Council published a summary of peer reviewed studies in order to provide data on the efficacy of teat disinfectants. (2000) All articles were published more recently than 1980 and study protocols had to follow those published in the 1991 National Mastitis Council Annual Meeting Proceedings. Significant efficacy ($p < 0.1$ to $p < 0.001$) against several bacterial species was demonstrated under both natural and artificial conditions. Antimicrobial agents tested were effective against *S. uberis*, *C. bovis*, *Staphylococcus* spp., *S. aureus*, *S. agalactiae*, coagulase negative staphylococci, *E. coli*, Gram positive bacilli, *Streptococcus* spp., *S. dysgalactiae*, and Gram negative bacteria. The products tested that were effective against some or all of the aforementioned organisms were: CHG (0.35 to 0.55%); iodine (0.05 to 1%); linear dodecyl benzene sulfonic acid (1.9 to 1.94%); lauricidin plus fatty acids (0.08 to 1%); 0.5% quaternary ammonium chloride; 1.5% alkyl-amino derivatives; sodium chlorite plus fatty acids (0.64%); sodium dichloro-s-triazene-trione (1 to 1.7%); sodium hypochlorite (0.6 to 0.9%); chlorine (2800 to 3000 ppm available); chlorous acid plus chlorine dioxide; 1.67% phosphoric acid plus 2.5% sodium chlorite; and phenol.

- A survey of 427 patients with severe eye infections revealed that 89% used bland soap. In contrast, only 11% used antibacterial soaps (Samalonis 1999).

A subsequent study in the same clinic used double blind cultures of 62 patients with infections to show that 52% of bland soap users had *S. epidermis* and *S. aureus* infections, while only 30% of the antibacterial soap users had infections with the same organisms.

- Use of an alcohol based hand wipe after washing with soap and water significantly reduced the rate of transfer of bacteria from the hands to contact lens (Ly *et al.* 1997).

Upon observation of various hand washing regimes, the authors found that washing with water alone or soap and water increased the number of colony

forming units transferred to contact lenses, but that adding the use of an alcohol based hand wipe after washing with soap and water reduced the rate of transfer significantly.