Considerable interest has been generated in the use of the newer formulations that contain skin sanitizing agents for hand washing in food processing and service establishments. In some areas of the country, the degeming agents have been suggested so often by public health officials that the use of antimicrobial soaps has approached the status of a recommendation. It is the purpose of this paper to briefly review this situation and some of the problems involved in choosing between some of the most common chemical agents that have been suggested for this purpose.

Sanitization of the skin involves a limiting surface that Lane and Blank (22) have described generally as a continuous, relatively smooth layer of dead, flattened, keratinized cells made somewhat irregular by various ridges and furrows, by orifices of sweat glands, and by hair follicles and outgrowths of hair. The cutaneous glands secrete a film over these cells, and this film constitutes the absolute limiting boundary between man and his environment. In this film are included salt, urea, and other substances left behind by evaporation of sweat; sebum, which covers all areas except the palms and soles; and a uniform layer of fat. The cells contain proteins, lipids, and water. The protein is largely keratin, which is insoluble in weak acids, weak alkalies, and salt solutions. If the outer layers of the cells of the epidermis are brought into equilibrium with a solution that has a pH to either side of pH 3.70, the isoelectric point of keratin, swelling of the cells will occur. The skin reacts more strongly to alkalies than to acids. Numerous measurements have shown the pH of the skin to range from 3.5 to 7.0.

Although the relative amounts and kinds of the substances of the skin may vary among individuals and from time to time in each individual (as a result of changes in physiological conditions), the structure and composition of the skin generally provide a good environment for bacterial growth. Foci for the establishment of bacterial flora exist in hair follicles, the sweat and subaceous glands, and the numerous ridges and furrows. Price (29) has classified the bacteria found on the human skin into two groups, the transient and the resident. The transient types are acquired by contact with other persons or objects in the environment. The resident flora comprise organisms that have established themselves and live in dynamic balance as parasites or saprophytes in the skin.

From the standpoint of sanitation in the food establishment, the ideal situation would be sterilization of the skin on the hands of food handlers; however, it is generally agreed that it is impossible to render skin sterile without destroying it. Transient bacteria are readily removed with ordinary soap and water. The resident organisms, however, are more difficult to remove; and scrubbing in hand-washing procedures is a recognition of this fact. In many persons, staphylococci make up a significant part of the resident flora. Because of the pathogenicity of some staphylococci and their ability to produce enterotoxin, major stress has been placed on the destruction, removal, and control of these organisms by hand-washing procedures. Although there is a paucity of reports on the efficacy of germicidal agents for hand washing in food service establishments, much valuable information can be gleaned from the voluminous literature on preoperative or surgical procedures and, to a lesser degree, from studies of the control of bacteria that produce body odor.

Even if surface bacteria are removed, the bacterial population is easily re-established by the emergence of resident organisms from the deeper structures and the addition of transient types acquired by continual contact with objects in the external environment. Price (29) has shown that under normal conditions the skin flora is fully re-established within a week after degeming of the skin. For this reason, the advantages of the deposition of a germicidal residue on the skin after hand washing to exert a continuous antibacterial action on the emerging organisms has been studied. The reliability of data on the efficacy of chemical agents known to be strongly retained on the skin surface is questionable when one moves from the study of operating-room hand-washing procedures (in which most of the rigorous testing has been done), through the simple...
control of body odor, to the hands of the food handler. Optimum control of skin bacteria by antibacterial agents in soaps and hand-washing detergents may depend on continuous use of the antibacterial preparation at work and at home, since washing with ordinary soap might tend to remove residual antibacterial agents quickly. Also, the food handler must usually wash utensils in strong cleansing detergents at least intermittently during the day, which causes swelling of the epidermal layer and disruption of the film of active agent deposited by germicidal soaps. To add to these factors, many of the germicidal agents presently in use are soluble in soap fats and fat solvents, and much of the germicide could be lost from the hands by contact with animal and vegetable oils in foods such as salads, meats, etc. Since optimal reduction of skin bacteria by some antibacterial agents has been reported to be based upon continuous use of the agent for as long as 7 days, these limitations must be considered when such agents are proposed for food-handling operations.

Another factor that has not been adequately considered is the ability of certain transient organisms to change their status and become more or less permanent residents. Price (29) has given the term "colonization" to this mechanism. While many transient types tend to disappear spontaneously from the skin, apparently because the conditions are not suited to their survival or colonization, Price (29) has reported that colon bacilli placed on the hands do not so disappear. He found that prolonged presence of unusual contaminants from wounds, such as Staphylococcus aureus, streptococci, Escherichia coli, Bacillus pyocyaneus (Pseudomonas aeruginosa), resulted in their colonization on the hands as part of the resident flora. Price (29) also noted the appearance and persistence for over a year of a nonpathogenic Trichophyton on the skin of his hands and arms, although this organism had not been encountered previously and was not present in the air of the laboratory. To what extent the colonization mechanism may operate in food handlers exposed to salmonellae in poultry, or to bacteria in abscesses or other pockets of infection in meat carcasses, has not been adequately studied, to the author's knowledge; this perhaps should be considered in the choice of antibacterial hand-washing compounds.

The degree to which mechanical cleansing alone is responsible for removal of skin bacteria is important (29) in the consideration of hand-washing procedures and provides a standard by which the degerming efficiency of antibacterial hand-washing agents can be measured. Price (29) concluded that the amount of friction produced at the skin surface by scrubbing appeared to be the most important variable factor in dislodging the resident flora. More firmly imbedded than the transient bacteria that are only lightly attached to the skin by extraneous grease or oils, the resident organisms cannot be removed by soap and water or simple rinsing without the use of friction. Price (29) showed that rubbing the hands together was more effective than rinsing, but less effective than scrubbing with a soft brush. A soft brush was less efficient than a stiff one. Brushing the skin without soap reduced the resident flora more rapidly than when soap was used, because soap served as a friction-reducing lubricant for brush bristles. Soap, however, increased the efficiency of removal of grease, dirt, and transient bacteria. Price (29) also found brushing with soap in hard water to be more effective than in soft water for removing the basic flora, because hard water precipitated the soap. This finding naturally leads to the possibility that modern detergents, which are not so readily precipitated by hard water, may interfere somewhat with the mechanical cleansing process.

An understanding of these complexities of skin sanitation is needed before an attempt can be made to discuss some of the major types of antibacterial agents that are presently being considered for hand soaps and detergents in food service establishments. Many of the same agents have been proposed for use in lotions or creams. This type of application may be objectionable because of the possibility that the resident bacteria can multiply in the deeper skin layers beneath the preparation (24) and also because of the enhanced possibilities for introduction of the agent into foods.

The Bisphenols

Essentially diphenols, the bisphenols are compounds that contain two hydroxyl (OH) groups, only one of which is neutralized by alkalies in soaps and detergents. The second hydroxyl group on the molecule remains free and is completely active against bacteria. In this characteristic the bisphenols are superior to the older phenolics, in which the single hydroxyl groups are easily inactivated by soaps. Of the many bisphenols that have been synthesized, two are most commonly associated with hand soaps. They are hexachlorophene and bithionol. Both are bacteriostatic agents that act by inhibiting the growth of bacteria rather than by killing the organisms.

Hexachlorophene (also known as G-11, AT-7, Gamophen, Hexosan, Exofine, PhisoheX, Surgicen, and Surofene4 is 2, 2'-Dihydroxy-3, 3', 5, 5', 6, 6'-hexachlorodiphenylmethane or bis-(3, 5, 6-trichloro-2-hydroxyphenyl)methane (26). It is usually

4Mention of commercial products does not infer endorsement by the Public Health Service.
employed in a concentration of 1 to 3% in liquid or solid soaps, lotions, or emulsions (26). Some skin sensitivity reactions have been known to occur in some individuals (26).

Reduction of skin bacteria has been reported to be considerably greater by hexachlorophene soaps than by ordinary soap (14, 24). No significant reduction occurs immediately after application of the agent (14, 24); and, when used as a single scrub, hexachlorophene soaps are not much more effective than ordinary soaps (5, 19, 31). Routine use for 5 to 10 days, however, has been reported (2, 4) to result in a reduction of bacteria as high as 85 to 95% from the original numbers. Only 4% of the food handlers regularly washing with hexachlorophene formulation for a period of over a year harbored coagulase-positive staphylococci, as opposed to a 16% coagulate-positive rate among workers using hexachlorophene-free soap (7). These findings may indicate that some residual antibacterial effect may be present even on individuals who use regular soap away from work. Shemano and Nickerson (32), using hexachlorophene labelled with C-14, found that some of the agent remained on the skin for a considerable time, although some was lost, especially during the first day, by washing with ordinary soap and water. Whether residual agent that remains adsorbed to the skin is as fully active against bacteria as free hexachlorophene is not clear. Some loss of the agent by washing with ordinary soaps between hexachlorophene ablutions is commonly accepted (16).

Following degreasing with hexachlorophene and the attainment of a low bacterial level, the normal count returns about 7 days after the use of the agent is stopped. This delay, however, may not be solely due to a residual adsorbed on the skin, since regeneration times of 1 to 7 days occur after disinfection by other means (29), depending on the thoroughness of treatment.

The activity of hexachlorophene is greatly reduced by organic matter such as body fluids, pus, serum, albumin, milk, etc., and non-ionic detergents and emulsifying agents (31). Although there is no evidence that hexachlorophene-resistant bacteria develop as a result of exposure to the agent (31), Price (28) pointed out that the microbial flora on the hands of different people vary in susceptibility to the agent with some individuals harboring a resistant flora. This finding introduces some uncertainty as to the reliability of hexachlorophene soaps that is probably more serious in the operating room than in food service establishments; nevertheless it must be considered.

In general, the Gram-positive bacteria are most susceptible to hexachlorophene, and Gram-negatives such as E. coli and Salmonella are not greatly affect-
ed (31). Many Gram-negative types are represented among the transient species encountered in food by the food handler. Post and Balzer (27) have reported that hexachlorophene appeared to have some effect on the transient as well as the resident bacterial flora on the hands of four culinary workers. The effect on the Gram-negative organisms was erratic. The authors admitted that the results were inconclusive and in need of further clarification. Furthermore, the small number of workers studied and the diversity of their culinary duties suggest that additional studies should be carried out on a greater number of subjects and more attention given to the type of culinary operation performed and the extent to which workers' contracts with dishwater and food influence the reduction of bacterial flora by hexachlorophene.

Bithionol (also known as XL-7, Actamer, Lorothiodol, and TBP) is termed 2, 2'-thiobis (4, 6-dichlorophenol) or bis (2-hydroxy-3, 5-dichlorophenyl) (26). It is usually employed in concentrations of 1 to 3% in liquid or solid soap formulations for surgical scrub or other skin disinfection. Lower concentrations may be used, one brand containing only 0.4%. Soap containing 1 to 2% bithionol is reported to be at least as active as soap with hexachlorophene. It is also more active against the Gram-positive than the Gram-negative bacteria (1) and is reported to be fungistic (1, 31). After 10 to 12 days of continuous use, the bacterial load on hands is said to be reduced by 89 to 97.4% and levels off with no further reduction (1). It is said to be nonirritating when used in soap.

Bithionol, like hexachlorophene, is claimed to resist removal by soap and water (1). It is said to be strongly absorbed by animal tissues such as skin and hair and works best in the acidic range of pH 5.0 to 6.5 (1). Apparently an active residual is maintained (1) in the presence of alkali in soaps or detergents, but more study is needed on this aspect of both bithionol and hexachlorophene.

The Iodine Compounds

Free Iodine

Elemental iodine is one of the most effective antimicrobial agents known (31). It is essentially bactericidal, dilutions possessing bacteriostatic and bactericidal action being practically identical (18). Under a variety of exaggerated test conditions, iodine in the proper concentrations is uniformly active against a broad spectrum of pathogenic organisms, including the tubercle bacillus, pathogenic fungi, viruses, and even bacterial and fungal spores. Although effective for antiseptic washes and for irrigation purposes over a wide pH range (17), the activity of iodine solutions is markedly enhanced under acid conditions.

Reddish (32) points out that the well-recognized efficacy of iodine is partly due to the margin of safety
under which it has been employed. It is used as a skin antiseptic in hospitals in a concentration of 2%, although a level of 0.02% in solution is germicidal within one minute to a variety of pathogenic organisms, including *S. aureus*. Tinctures of iodine have low surface tensions, and the solvent action of the alcohol dissolves skin oils and facilitates penetration into the epidermal layer, thus destroying both the transient and the resident bacterial flora. Aqueous solutions of iodine have also been used successfully and possess certain advantages as preoperative skin disinfectants, and disinfectants for surgical instruments, clinical thermometers, drinking water, and eating and drinking utensils.

The iodophors are chemical complexes of diatomic iodine and solubilizing agents or carriers, usually synthetic nonionic surfactants. A portion of the iodine becomes firmly bound in the complex and is unrecoverable, but the remainder is "available" and is believed to be responsible for the germicidal activity. The iodophors have been reported to be effective sanitizers, good disinfectants *in vitro*, nonallergenic, relatively nontoxic, and noncorrosive.

The activity of the iodophors is directly related to the amount of titratable iodine present in solution. Titratable iodine content is very pertinent in evaluating commercial iodophors (10). Blatt and Maloney (10) compared three commercial iodophors with aqueous or alcoholic solutions of elemental iodine on the basis of equivalent amounts of titratable iodine and found no significant differences in germicidal effectiveness. These results indicate that germicidal activity is contributed solely by titratable iodine, and any enhancement of germicidal activity is at least partially due to the wetting action of the detergent compound. Blatt and Maloney (10) also found that, once all of the titratable iodine was removed from the compound and after the compound had been allowed to stand, no further iodine could be demonstrated by titration. In the analysis of iodine preparations, it is pertinent that the amount of titratable iodine does not always represent the actual amount of active iodine to be expected under actual conditions of use, because the amount dissociating from the complex at any time is dependent upon the dissociation constant, which is influenced by pH and temperature (12). This amount may be only a fraction of the amount recoverable by titration.

Solutions of elemental iodine, phosphoric acid buffered iodine-I₂, and solutions of certain iodophors with a low pH (even after the addition of test bacteria) are believed to be among the best sanitizing agents (31). Many of the marketed liquid iodophors contain phosphoric acid. A cationic iodophor that possesses an alkaline pH and contains 3.2% elemental iodine has been recommended for disinfection of the skin, for operative procedures, and for disinfection of thermometers and surgical instruments (31). It has been reported (21) to be responsible for a reduction in major postoperative wound infection from 14.8% to 6.5%, although minor infections were not significantly reduced.

Comparisons have been made of the effectiveness of free iodine preparations, iodophors, and hexachlorophene. Goldenberg, *et al.* (19), by culturing washings of the insides of surgeons gloves, found that iodine-detergent surgical scrub was almost three times as effective after 4 minutes of scrubbing (23.5% positive cultures) as a 3% hexachlorophene detergent was after 10 minutes of washing (66.7% positive culture). Recently, King and Price (20), employing the widely used method of Price (29), compared the degemming activity of solutions of several iodophor formulations with simple alcoholic and aqueous solutions that have approximately the same iodine content, and with a scrub with ordinary face soap. Although the iodophors were less effective in reducing bacteria on the skin than were the iodine solutions, they were more effective than ordinary soap. A 2-minute exposure to a tincture of 1% iodine in 70% ethyl alcohol reduced the bacterial flora to less than 20% of the pre-exposure levels (equivalent to 13 minutes of soap and brush scrubbing). The same exposure to the most efficient iodophor reduced the flora to only 54%, equivalent to the efficiency attained in 4 minutes of scrubbing with white soap and brush, or to 35 seconds of exposure to 1% iodine in 70% alcohol. The authors believed that about the only advantage of an iodophor surgical scrub over one incorporating tincture of iodine is that the former is more pleasant and less irritating.

Experimental detergent-iodine cakes containing about 0.7 to 1.0% available iodine have been produced and patented (15), but, to our knowledge, are not yet available commercially (15). The exact details of their composition are not known, and an evaluation should be made when more information is available.

As skin degemming agents for the surgical scrub, the iodophors appear to be generally less efficacious than elemental iodine, but this may be a result of the paucity of information about the amount of titratable and dissociated iodine present in the various compounds under actual conditions of use. The available information does not reveal the presence of true residual activity as occurs with hexachlorophene. The iodophors are attractive to potential users because of the claim that detergency and disinfection can be accomplished simultaneously with the same agent.
THE CHLOROCARBANILIDES

TCC is a 3, 4, 4, trichlorocarbanilide (6). Available information from the manufacturer (6) indicates bacteriostatic activity against staphylococci in dilutions of 1:5 million to 1:10 million, with some fungistic action against skin fungi. TCC is used in soaps in concentrations ranging from 0.5 to 2.0% and is claimed to be unaffected by either nonionic or anionic detergent. Data for Gram-positive bacteria only are included (6). Handwashing tests with TCC were strictly controlled to eliminate the use of other handwashing agents, so no skin retention data are available.

Bacteriostat CH3479 (Irgasan CF-3) is 3-trifluoromethyl 4, 4' dichlorocarbanilide (3). It is used in concentrations of 1% in deodorant soaps or shampoos and in detergents in 0.2 to 0.4% for residual bacteriostatic effect on cotton fabrics. Although ineffective against Gram-negative bacteria, it is claimed by the manufacturer (3) to be more effective than TCC against Gram-positive bacteria.

Although extensive evaluations of TCC and CH3479 are not yet available, these compounds seem to require their exclusive use by the food handler in order to be fully effective.

THE QUATERNARY AMMONIUM COMPOUNDS

The quaternary ammonium germicides ("quats") are another class of synthetic chemical disinfectants which are synthesized to form amines in which the nitrogen in the molecule has a covalence of 5. With the quats, however, the hydrogen atoms are replaced by one or more alkyl groups (CH₃, C₂H₅, etc.), or a phenyl radical, and one or more alkyl groups containing C₈ to C₁₈ carbon chain lengths (31). The quats are characterized further by their ability to depress greatly the surface tension of water. This property places them in a class of chemicals frequently described as wetting or surface active agents, detergents, or dispersing agents. Surface active agents are grouped further between "anionic" detergent (natural soaps and many synthetic soap substrates); "non-ionic" detergents (sudsing agents); and the quats which are "cationic" detergents (substituted ammonia compounds). Only the quats or cationics are discussed in this review.

The antimicrobial properties of quats are attributed to their chemical reactivity and the ease with which they are adsorbed. Likewise, these properties account for their occasional failure. The quats are inactivated by soap, hard waters, lecithin, and other phospholipids, and are adsorbed by charcoal, Bentonite, and agar. They combine readily with proteins and thus are less efficient in the presence of serum, milk, and other food soils (30). By 1954, the quats had been demonstrated to be incompatible with thirty-six chemical agents, among which were iodine, lanolin, pine oil, silicates, polyphosphates, and anionic detergents (23). The number of chemical agents with which the quaternaries are incompatible is about equal to the number of agents with which they are compatible. Thus it is critical that the ingredients of a formulation be compatible with the quaternary used.

The literature is replete with studies on the antimicrobial properties of quats alone and in preparations formulated for a variety of uses. In vitro they appear to be equally effective against many Gram-positive and Gram-negative bacteria, according to one source (31). Other workers found that quaternary ammonium compounds were slightly less effective against the Gram-negative organisms tested (8). Mallman (25) summarized these discrepancies, stating, "By selecting the proper laboratory technic, we can show that the cationics are either poor or unusually good disinfectants."

The most widely used quat is benzalkonium chloride, which is a mixture of alkyl(dimethylbenzyl) ammonium chlorides (26) and marketed under a variety of trade names. It has been widely used in hospitals for disinfection in surgery, and in sanitizing utensils, floors, walls, soiled linen, and in other applications. Since benzalkonium chloride (26) is incompatible with anionic detergents, such as soap, and the mineral content of hard waters interferes with the bactericidal action of the quats (11), it would not be suitable in hand-washing procedures for food handlers whose hands are in constant contact with soaps, detergents, waters of varying degrees of hardness, and food.

DISCUSSION AND CONCLUSIONS

Because of the paucity of studies on food handlers per se, it is difficult to make an absolute judgment of the type of antibacterial agent that ought to be incorporated into hand-washing agents for use by food handlers, or whether one should be used at all. Most of the studies on the efficacy of hand washing compounds have been directed to the evaluation of cosmetic applications or hospital procedures. The standards of efficacy in the former are not sufficiently critical for adoption in the food-service environment, and those for the latter may well be too stringent. At present, the choice of an antibacterial agent for the food handler must be made without full knowledge of the extent to which food pathogens may colonize on the skin of the worker, although allowance for such an eventuality should probably be made.

In the existing literature, the development of an antibacterial residue on the skin, such as occurs with the bithionols, is stressed. In itself, the maintenance
of a continuing low level of bacteria on the hands may not be sufficient evidence for the presence of an active residue with all agents, since Price (29) has demonstrated that full establishment of the normal skin flora after the skin has been thoroughly degermed may require as much as 1 week, regardless of the method used. Nevertheless, the apparent residual antibacterial activity of the bithionols requires consideration of this aspect in the study of hand sanitizing agents.

The aim of hand sanitation is to prevent the transmission of possible pathogenic organisms from the hands through food or from food to food via the hands of the food handler. Since it is obviously not practicable to depend on the continual and exclusive use of antibacterial hand soaps outside of working hours, optimal control of skin bacteria during the hours in which food is being handled is the best that can be achieved. The maintenance of an efficient antibacterial residual on the skin can then probably be subordinated to other considerations. The antibacterial agent should not be chosen on the basis of activity against staphylococci and the Gram-positive bacteria alone. Food handlers may also harbor many Gram-negative bacteria of significance, such as Salmonellae and pathogenic E. coli, as well as Entamoeba histolytica or other pathogens, either as transient flora or possibly as established residents acquired through contact. The control of transient organisms by a more positive method than simple removal by soap and water may be desirable, since transfer from one food to another should be minimized. Also, the consistent use of a broad-spectrum antibacterial agent during the working day would help to prevent possible colonization on the skin of bacteria acquired from foods.

If all of these points are considered together, a good hand-washing agent for food service establishments probably should: (a) kill a wide variety of possible pathogens (inhibition is not sufficient because a single viable one transferred to a food may, under optimal conditions, multiply once the agent is diluted by the food); (b) be present, if possible, in sufficient residual concentration from one ablution to another to effect control during the day; and (c) be non-irritating to skin.

Iodine is the only agent reviewed in this report that appears to satisfy the above criteria in most respects. It is bactericidal and active against a wide variety of both Gram-positive and Gram-negative bacteria and other organisms. Although Blatt and Maloney (10) state that skin flora recovers more rapidly after iodophor treatment than after the application of hexachlorophene treatment, this point requires further study, in view of Price’s findings (29) on regeneration of the bacterial population of the skin. Any iodine preparation selected for study should have a high free-iodine content, whether it be a solid soap or a detergent-iodine complex. It should meet all of the general criteria accepted as necessary for performance of germicidal agents wherever sanitation is important (13). Its penetration into skin and its residual effect during the working day should be determined, as well as the degree to which it is removed by contact with food substances. Emollient additives must be incorporated, and their effect on the germicidal efficiency of the preparation must be definitely established.

The need continues for simple and more reliable and reproducible techniques for measuring changes in the skin flora. Particularly, a method should be devised for the study of frequent changes in levels of skin bacteria that occur during the working day as a result of exposure of the food handler to different foods. Such a method could conceivably shed light on the extent to which hazardous bacteria may be transmitted between ablutions as well as the degree to which a sudden contact with heavily contaminated food staples may overwhelm the capacity of a residual bactericide on the skin to control the spread of these organisms.

From the present consideration of the status and efficacy of the available hand sanitizing agents, one may conclude that frequent and thorough use of ordinary hand soaps, with the aid of a good brush during the working day, is, for practical purposes, about as efficient in controlling skin bacteria as the commonly available germicidal soaps. Practical experience has shown that the frequency of hand-washing by food service personnel may be greatly increased by installing hand washing facilities in the working area, because of the tendency for personnel to correct one another’s lapses in hand sanitation as they occur. This simple expedient tends to greatly enhance the efficacy of the simple soap and brush procedure.

A recent study (9) was reported on the efficiency of bar soaps, without antibacterial additives. The results show that bar soaps do not transfer bacteria among individuals in normal use, nor do they support bacterial growth.

Undoubtedly, some additional benefit will accrue from the use of residual germicidal soaps if they are considered as a supplement to, rather than a replacement for, thorough and frequent scrubbing. While deposition of residual germicide on the skin may be real, it may be nullified by the narrow microbial spectrum affected, possible neutralization by kitchen detergents and food constituents, and the tendency of some germicides to produce sensitivity reactions in some persons.

The use of formulations containing agents with a
broad antibacterial spectrum, such as iodine, presents attractive possibilities which, however, require much further testing in the food service environment.

References


