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Remington: Practice of

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and Editor*

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Table 1—Classes of Antiseptic Agents

Class and agent	Concentration (%)	Uses
Acids		
Acetic acid	0.1-5	Irrigant
Boric acid	2, 17, 5 and 10	Irrigant
Alcohols		
Ethyl alcohol	70, 91 and 100	Antiseptic
Isopropyl alcohol	70	Antiseptic, rubefacient
Aldehydes		
Formaldehyde	37	Disinfectant
Glutaraldehyde	2-3.2	Disinfectant
Biguanide		
Chlorhexidine gluconate	0.12-4	Antiseptic, mouthwash
Carbanilide		
Triclocarban	1.5	Antiseptic soap
Chlorine Compounds		
Sodium hypochlorite	0.1-0.2	Wound irrigant
Oxychlorosene	0.1-0.5	Irrigant
Iodine Compounds		
Iodine	2	Antiseptic
Povidone-Iodine	0.5-10	Antiseptic
Metals		
Organic Mercurial Compounds		
Phenylmercuric acetate	0.02-0.2	Irrigant, antiseptic, preservative
Phenylmercuric nitrate	0.0025-0.004	Irrigant, antiseptic, preservative
Thimerosal	0.1	Irrigant, antiseptic
Silver Compounds		
Mild silver protein	10	Antiseptic
Oxidizing Agents		
Hydrogen peroxide	1.5-3	Wound cleanser, irrigant
Potassium permanganate	0.0025-0.007	Antiseptic, disinfectant
Phenols		
Hexylresorcinol	0.1	Mouthwash, wound cleanser
Hexachlorophene	3	Soap, shampoo
Menthol	0.5	Irrigant, antiseptic
Parachlorometaxyleneol	0.5-2.0	Handwashes, shampoo
Phenol	1	Irrigant, antiseptic
Thymol	0.5-1.0	Irrigant, antiseptic
Triclocarban	0.5-1.5	Antiseptic soap
Triclosan	0.1-2.0	Antiseptic soap
Parabens	0.05-0.25	Preservative
Quaternary Ammonium Compounds		
Benzalkonium choice	0.01-0.5	Mouthwash, irrigant
Cetylpyridinium chloride	0.05-0.5	Mouthwash, irrigant
Benzethonium chloride	0.01-0.3	Mouthwash, irrigant

will exert a greater antimicrobial effect at a given pH than will a mineral acid. This is used to discourage bacterial infections in surgical wounds, to suppress growth by *Pseudomonas aeruginosa* in extensive burns of the skin, as a component of a number of dermatological lotions. It is used to treat external otitis caused by *Pseudomonas*, *Candida* and *Aspergillus* and vaginal infections caused by *Candida*, *Trichomonas* or *Hemophilus vaginalis*. Acetic acid has a long history of lay use as a spermicide. The 0.25% solution is used for bladder irrigation, especially during catheterization. It also is used in mouthwashes/gargles, but the contact time is much too short for the acid to have an effect.

It can cause irritation and inflammation, especially in the vagina.

Dose—Topical, as a 1% surgical dressing, 5% solution in burn therapy, 0.1% dermatological lotion, 1 to 5% solution for otitis and 0.25% for irrigation.

Acrisorcin—see RPS-17, page 1226.

Alcohol—page 1404.

Rubbing Alcohol

Rubbing alcohol, and all preparations coming under the classification of

ments of the US Treasury Department, Bureau of Alcohol, Tobacco and Firearms, using *Formula 23-H* (8 parts by volume of acetone, 1.5 parts by volume of methyl isobutyl ketone and 100 parts by volume of ethyl alcohol). It contains 68.5–71.5% by volume of absolute ethyl alcohol, the remainder consisting of water and the denaturants, with or without color additives, and perfume oils. Rubbing Alcohol contains in each 100 mL not less than 355 mg of sucrose octaacetate or not less than 1.40 mg of denatonium benzoate. The preparation may be colored with one or more color additives, listed by the FDA for use in drugs. A suitable stabilizer also may be added. Rubbing Alcohol complies with the requirements of the Bureau of Alcohol, Tobacco, and Firearms, of the US Treasury Department.

Note—*Rubbing Alcohol must be packaged, labeled, and sold in accordance with the regulations issued by the US Treasury Department, Bureau of Alcohol, Tobacco, and Firearms.*

Description—Transparent, colorless or colored as desired, mobile, volatile liquid; extremely bitter taste; in the absence of added odorous substances, a characteristic odor; flammable; specific gravity of *Formula 23-H* is between 0.8691 and 0.8771 at 15.56°.

Uses—Applied externally as a *cooling, soothing* application for bedridden patients and athletes. It also is used widely for cleansing the surgeon's hands and instruments and for disinfection of the skin prior to penetration of the skin by a hypodermic needle. As an *antiseptic* it is good against vegetative bacteria and fair against fungi and viruses. It is ineffective against spores. It is believed widely that 70% ethanol provides the greatest reduction in bacterial count; however, this is in error. Other concentrations may be more effective, but their rate of kill is slower. In order to reduce the skin bacterial count to 5% of normal, 70% ethanol must be left on the skin for at least 2 min. It is also a feeble *anesthetic* and a mild *counterirritant*. See *Alcohol* (page 1404). *It is not potable.*

Aluminum Acetate Solution—page 871.

Aluminum Subacetate Solution—see RPS-17, page 778.

Aminacrine Hydrochloride—see RPS-18, page 1170.

Bacitracin—page 1305.

Benzalkonium Chloride

Ammonium, alkyl-dimethyl(phenylmethyl)-, chloride; Zephiran Chloride (*Winthrop*); (*Various Mfrs*)

Alkylbenzyl-dimethylammonium chloride [8001-54-5]; a mixture of alkylbenzyl-dimethylammonium chlorides of the general formula $[C_6H_5CH_2N(CH_3)_2R]Cl$, in which *R* represents a mixture of alkyls, including all or some of the group beginning with *n*-C₈H₁₇ and extending through higher homologs, with *n*-C₁₂H₂₅, *n*-C₁₄H₂₉ and *n*-C₁₆H₃₃ comprising the major portion. On the anhydrous basis, the content of *n*-C₁₂H₂₅ homolog is not less than 40%, and the content of the *n*-C₁₄H₂₉ homolog is not less than 20%, of the total alkylbenzyl-dimethylammonium chloride content. The amounts of the *n*-C₁₂H₂₅ and *n*-C₁₄H₂₉ homolog components comprise together not less than 70% of the total alkylbenzyl-dimethylammonium chloride content.

Preparation—By treating a solution of *N*-alkyl-*N*-methylbenzylamine in a suitable organic solvent with methyl chloride, the solvent being so chosen that the quaternary compound precipitates as it is formed.

Description—White or yellowish white, thick gel or gelatinous pieces; aromatic odor and a very bitter taste; solutions are alkaline to litmus and foam strongly when shaken.

Solubility—Very soluble in water and alcohol; 1 g of the anhydrous form dissolves in about 6 mL benzene and in about 100 mL ether.

Incompatibilities—Like other cationic surface-active agents, benzalkonium chloride is incompatible with *soap* and other *anionic agents*. The large organic ions of the two agents are oppositely charged and, in sufficient concentration, can precipitate from solution. *Nitric acid* and *nitrites* cause precipitation.

Uses—A bacteriostatic in low and bactericidal in high concentrations. Gram-positive bacteria are more sensitive than gram-negative bacteria. Indeed, some gram-negative bacteria, especially *Pseudomonas cepacia*, have been known to grow in solutions of this drug and thus to cause epidemics of hospital infections. *Mycobacterium tuberculosis* is also relatively resistant. The antiseptic has a slow action. It requires 7 min for the bacterial count on the skin to be decreased by a mere 50%, while only 36 sec is required by 70% ethanol; to effect a 90% reduction, 25 min is required for this compared to 2 min for the 70% ethanol. Some gram-negative bacteria require hours of exposure to be killed. Tinctures are more rapidly acting and effective.

It is used for application to skin and mucous membranes. It is used widely in OTC ophthalmic solutions and as applications to contact lenses. It also is used for the sterilization of inanimate articles, such as surgical instruments. Its solutions have low surface tension and possess deter-

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Dose—0.01% a skin or t ous solut branes a of the *va demudea* to 1:500 *urethra* to 1:40, *deep w* areas w insolubl and *rut* other ad of meta prevent

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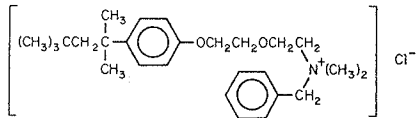
such. It has relatively low systemic toxicity, but poisoning from oral ingestion has been reported. After repetitive use it sometimes may cause dermatitides. Like other cationic surface-active agents, it has certain limitations. It does not destroy bacterial spores, it is ineffective against some viruses, it is inactivated by soap and other anionic surface-active agents and, when applied to the skin, it has a tendency to form a film under which bacteria remain viable. Organic matter from tissue inactivates the drug, so that it has limited efficacy in the disinfection of wounds. It is adsorbed by various organic substances, so that the concentration in a sterilizing solution may drop below the antibacterial level, and the sterilization of surgical gloves, sponges, etc. may be erratic. The drug can cause irritation and damage the epidermis, and it also can cause allergies. In view of the availability of more reliable and more rapidly acting antiseptics, there is little to commend its continued use.

Dose—Topical, 0.02 to 0.5% solution; to the conjunctiva, 0.1 mL of 0.01% aqueous solution. For preoperative disinfection of unbroken skin or treatment of superficial injuries or fungus infections, 1:750 aqueous solution or tincture. For preoperative disinfection of mucous membranes and denuded skin, 1:10,000 to 1:2000; for instillation or irrigation of the vagina, 1:5000 to 1:2000 aqueous solution; for irrigation of widely denuded surfaces, 1:10,000 or 1:5000; for irrigation of the eye, 1:10,000 to 1:5000 aqueous solution; for irrigation of the urinary bladder and urethra, 1:20,000 to 1:5000; for retention lavage of the bladder, 1:20,000 to 1:40,000; for disinfection of deep lacerations, 1:1000; for irrigation of deep wounds, 1:20,000 to 1:3000; for treatment of infected denuded areas with wet dressings, 1:5000; as a detergent solubilizer of water-insoluble drugs, up to 0.5%; for sterile storage of metallic instruments and rubber articles, 1:1000 to 1:750; for sterilization of catheters and other adsorbent articles, 1:500. When the drug is used for sterile storage of metal instruments, sodium nitrite (0.5%) is added to the solution to prevent corrosion of metal.

Dosage Forms—Vaginal Gel: 0.05%; Solution: 0.1 (1 in 1000), 0.133% (1 in 750) and 50%; Tincture: 0.133%; Tincture Spray: 0.133%; Concentrates: 12.8, 17, 17.5 and 50% aqueous, and 17% tincture.

Benzethonium Chloride

Benzenemethanaminium, *N,N*-dimethyl-*N*-[2-[2-[4-(1,1,3,3-tetramethylbutyl)phenoxy]ethoxy]ethyl]-, chloride; (Various Mfrs)



Benzyl dimethyl [2-[2-[*p*-(1,1,3,3-tetramethylbutyl)phenoxy]ethoxy]ethyl] ammonium chloride. [121-54-0] $C_{27}H_{42}ClNO_2$ (448.09).

Preparation—From *p*-diisobutylphenol with dichlorodiethyl ether, dimethylamine and benzyl chloride.

Description—White crystals; mild odor; very bitter taste; melts at about 160°; aqueous solution (1%) slightly alkaline and foams strongly when shaken.

Solubility—1 g in 0.6 mL water, 0.6 mL alcohol, 1 mL chloroform or 6000 mL ether.

Uses—A quaternary ammonium detergent antiseptic and spermicide once used widely. It has the same limitations and erratic behavior that characterize Benzalkonium Chloride (page 1264). Its present uses are as a preservative in ophthalmic preparations, vaginal contraceptive foams and nursing lubricants.

Dose—To the vagina, as a 3.17% solution of the monohydrate; as a preservative, 0.01%.

Dosage Form—Solution: 0.01 and 3.17%.

Benzoic Acid—see RPS-18, page 1235.

Benzyl Alcohol—page 1151.

Bismuth Tribromophenate—see RPS-18, page 1170.

Boric Acid—page 1407.

Butylparaben—see RPS-18, page 1170.

***p*-tert-Butylphenol**—see RPS-18, page 1170.

Carbamide Peroxide

Urea Peroxide; (Various Mfrs)

Urea, compound with hydrogen peroxide (1:1); [124-43-6] $CH_6N_2O_3$ (94.07)

Description—White crystals or crystalline powder; decomposes in air to urea, oxygen and water.

Solubility—1 g in 2.5 mL water; incompatible with alcohol or ether, which cause partial decomposition.

Uses—An oxidant much like hydrogen peroxide. Peroxide ion in sufficient concentration is bactericidal to most bacteria; low concentrations are lethal to anaerobes and microaerophiles. It is used to relieve minor irritation of the gingivae and oral mucosae. The action may be, in part, an antibacterial action against organisms that produce irritating substances, but relief of irritation also may be attributed partly to the high glycerin content of the gel. There may be some efficacy against cankers.

Dose—Topical, to the gums and oral mucosae, as a 11% gel in a water-free gel base, or as a 10% solution in anhydrous glycerol.

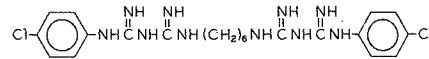
Dosage Forms—Gel: 11%; Solution: 10%.

Cetyl dimethylethylammonium Bromide—see RPS-18, page 1170.

Cetylpyridinium Chloride—see RPS-18, page 1171.

Chlorhexidine Gluconate

D-Gluconic acid, compd with *N,N'*-bis(4-chlorophenyl)-3,12-diimino-2,4,11,13-tetraazatetradecanedimidamide (2:1); Hibiclens, Hibistat (Stuart)



1,1'-Hexamethylenebis[5-(*p*-chlorophenyl)biguanide] di-*D*-gluconate [18472-51-0] $C_{22}H_{30}Cl_2N_{10} \cdot 2C_6H_{12}O_7$ (897.77).

Preparation—Chlorhexidine base may be prepared by refluxing a mixture of hexamethylenebis[dicyandiamide], [NCNHC(NH)-NH-(CH₂)₆]₂, and *p*-chloroaniline hydrochloride in 2-ethoxyethanol at 130°–140° for two hours (Rose and Swain, *CA* 50: 1082h, 1956). The digluconate, diacetate, and dihydrochloride salts may be obtained by neutralizing the base with the respective acids.

Description—Colorless to pale-yellow solution. Usually available in 5 or 20% aqueous solution. pH (5% aqueous solution) 5.5 to 7.0.

Solubility—Very soluble in water; 1 g in 5 mL alcohol or 3 mL acetone.

Uses—Bactericidal to both gram-positive and gram-negative bacteria, although it is not as potent against the latter. It disrupts the plasma membrane of the bacterial cell, and cellular contents are lost.

In a 4% aqueous solution as a surgical scrub, it decreases the cutaneous bacterial population more than either hexachlorophene or povidone-iodine. It is slightly less effective than povidone-iodine if the skin is contaminated with certain gram-negative bacteria. A 1% aqueous solution has erratic antiseptic effects, but a 0.5% solution in 95% ethanol is more effective than a 4% aqueous solution. Chlorhexidine solutions leave a residue on the skin which gives a persistent antibacterial effect lasting 1 or 2 days. Its actions are not affected by blood, pus or soaps.

It is used for the preoperative preparation of both surgeon and patient, for the treatment of superficial skin infections, burns, *acne vulgaris* and the irrigation of wounds and surgical infections. It can be used in the hospital nursery to bathe neonates for prophylaxis against staphylococcal and streptococcal infections. Abroad, it is used as a mouthwash for oral hygiene and oropharyngeal infections, especially aphthous ulcers. It is absorbed onto tooth enamel, where it exerts a persisting action to decrease the growth of dental plaque.

It is absorbed negligibly from the skin and mucous membranes; it has low systemic toxicity. Thus, it would not be expected to cause systemic intoxication from topical application. However, serious injury may occur when it enters open wounds of the eye and deafness may occur if it enters the middle ear through a perforated eardrum. A few cases of sensitization have been reported. Bacterial resistance to the drug has not been reported, but overgrowth (superinfection) by naturally resistant gram-negative bacteria may sometimes occur. Instances of hospital epidemics caused by *Pseudomonas maltophilia* actually growing in its aqueous solutions have been reported. The substance is considerably adsorbed by new glass, and the concentration of weak solutions may thus be lowered; it is not adsorbed by polyethylene.

Dose—Topical, as a 4% cleanser or sponge or 0.5% tincture.

Dosage Forms—Aqueous Emulsion: 4%; Tincture Rinse: 0.5%.

Chlorothymol—see RPS-18, page 1171.

Cloflucarban—see RPS-18, page 1171.

Clorophene—see RPS-18, page 1171.

Cloroxine—see RPS-18, page 1171.