minutes), fungicidal (>5 $\log_{10}$ reduction in 20 minutes), bactericidal (>6 $\log_{10}$ reduction in 5 minutes) and virucidal (5 $\log_{10}$ reduction in 5 minutes) [663]. Synergistic sporicidal effects were observed when spores were exposed to a combination of hydrogen peroxide (5.9%–23.6%) and peracetic acid [664]. Other studies demonstrated the antiviral activity of hydrogen peroxide against rhinovirus [665]. The time required for inactivating three serotypes of rhinovirus using a 3% hydrogen peroxide solution was 6–8 minutes; this time increased with decreasing concentrations (18-20 minutes at 1.5%, 50–60 minutes at 0.75%).

Concentrations of hydrogen peroxide from 6% to 25% show promise as chemical sterilants. The product marketed as a sterilant is a premixed, ready-to-use chemical that contains 7.5% hydrogen peroxide and 0.85% phosphoric acid (to maintain a low pH) [69]. The mycobactericidal activity of 7.5% hydrogen peroxide has been corroborated in a study showing the inactivation of >10^5 multidrug-resistant *M. tuberculosis* after a 10-minute exposure [666]. Thirty minutes were required for >99.9% inactivation of poliovirus and HAV [667]. Three percent and 6% hydrogen peroxide were unable to inactivate HAV in 1 minute in a carrier test [58]. When the effectiveness of 7.5% hydrogen peroxide at 10 minutes was compared with 2% alkaline glutaraldehyde at 20 minutes in manual disinfection of endoscopes, no significant difference in germicidal activity was observed [668].). No complaints were received from the nursing or medical staff regarding odor or toxicity. In one study, 6% hydrogen peroxide (unused product was 7.5%) was more effective in the high-level disinfection of flexible endoscopes than was the 2% glutaraldehyde solution [456]. A new, rapid-acting 13.4% hydrogen peroxide formulation (that is not yet FDA-cleared) has demonstrated sporicidal, mycobactericidal, fungicidal, and virucidal efficacy. Manufacturer data demonstrate that this solution sterilizes in 30 minutes and provides high-level disinfection in 5 minutes[669]. This product has not been used long enough to evaluate material compatibility to endoscopes and other semicritical devices, and further assessment by instrument manufacturers is needed.

Under normal conditions, hydrogen peroxide is extremely stable when properly stored (e.g., in dark containers). The decomposition or loss of potency in small containers is less than 2% per year at ambient temperatures [670].

Uses. Commercially available 3% hydrogen peroxide is a stable and effective disinfectant when used on inanimate surfaces. It has been used in concentrations from 3% to 6% for disinfecting soft contact lenses (e.g., 3% for 2–3 hrs) [653, 671, 672], tonometer biprisms [513], ventilators [673], fabrics [397], and endoscopes [456]. Hydrogen peroxide was effective in spot-disinfecting fabrics in patients' rooms [397]. Corneal damage from a hydrogen peroxide-soaked tonometer tip that was not properly rinsed has been reported [674]. Hydrogen peroxide also has been instilled into urinary drainage bags in an attempt to eliminate the bag as a source of bladder bacteriuria and environmental contamination [675]. Although the instillation of hydrogen peroxide into the bag reduced microbial contamination of the bag, this procedure did not reduce the incidence of catheter-associated bacteriuria [675].

A chemical irritation resembling pseudomembranous colitis caused by either 3% hydrogen peroxide or a 2% glutaraldehyde has been reported [621]. An epidemic of pseudomembrane-like enteritis and colitis in seven patients in a gastrointestinal endoscopy unit also has been associated with inadequate rinsing of 3% hydrogen peroxide from the endoscope [676].

As with other chemical sterilants, dilution of the hydrogen peroxide must be monitored by regularly testing the minimum effective concentration (i.e., 7.5%–6.0%). Compatibility testing by Olympus America of the 7.5% hydrogen peroxide found both cosmetic changes (e.g., discoloration of black anodized metal finishes) [69] and functional changes with the tested endoscopes (Olympus, written communication, October 15, 1999).

Iodophors

Overview. Iodine solutions or tinctures long have been used by health professionals primarily as antiseptics on skin or tissue. Iodophors, on the other hand, have been used both as antiseptics and

disinfectants. FDA has not cleared any liquid chemical sterilant or high-level disinfectants with iodophors as the main active ingredient. An iodophor is a combination of iodine and a solubilizing agent or carrier; the resulting complex provides a sustained-release reservoir of iodine and releases small amounts of free iodine in aqueous solution. The best-known and most widely used iodophor is povidone-iodine, a compound of polyvinylpyrrolidone with iodine. This product and other iodophors retain the germicidal efficacy of iodine but unlike iodine generally are nonstaining and relatively free of toxicity and irritancy [677, 678].

Several reports that documented intrinsic microbial contamination of antiseptic formulations of povidone-iodine and poloxamer-iodine [679-681] caused a reappraisal of the chemistry and use of iodophors[682]. "Free" iodine (I_2) contributes to the bactericidal activity of iodophors and dilutions of iodophors demonstrate more rapid bactericidal action than does a full-strength povidone-iodine solution. The reason for the observation that dilution increases bactericidal activity is unclear, but dilution of povidone-iodine might weaken the iodine linkage to the carrier polymer with an accompanying increase of free iodine in solution [680]. Therefore, iodophors must be diluted according to the manufacturers' directions to achieve antimicrobial activity.

Mode of Action. Iodine can penetrate the cell wall of microorganisms quickly, and the lethal effects are believed to result from disruption of protein and nucleic acid structure and synthesis.

Microbicidal Activity. Published reports on the in vitro antimicrobial efficacy of iodophors demonstrate that iodophors are bactericidal, mycobactericidal, and virucidal but can require prolonged contact times to kill certain fungi and bacterial spores [14, 71-73, 290, 683-686]. Three brands of povidone-iodine solution have demonstrated more rapid kill (seconds to minutes) of *S. aureus* and *M. chelonae* at a 1:100 dilution than did the stock solution [683]. The virucidal activity of 75–150 ppm available iodine was demonstrated against seven viruses [72]. Other investigators have questioned the efficacy of iodophors against poliovirus in the presence of organic matter [685]and rotavirus SA-11 in distilled or tapwater [290]. Manufacturers' data demonstrate that commercial iodophors are not sporicidal, but they are tuberculocidal, fungicidal, virucidal, and bactericidal at their recommended use-dilution.

Uses. Besides their use as an antiseptic, iodophors have been used for disinfecting blood culture bottles and medical equipment, such as hydrotherapy tanks, thermometers, and endoscopes. Antiseptic iodophors are not suitable for use as hard-surface disinfectants because of concentration differences. Iodophors formulated as antiseptics contain less free iodine than do those formulated as disinfectants [376]. Iodine or iodine-based antiseptics should not be used on silicone catheters because they can adversely affect the silicone tubing [687].

Ortho-phthalaldehyde (OPA)

Overview. Ortho-phthalaldehyde is a high-level disinfectant that received FDA clearance in October 1999. It contains 0.55% 1,2-benzenedicarboxaldehyde (OPA). OPA solution is a clear, pale-blue liquid with a pH of 7.5. (Tables 4 and 5)

Mode of Action. Preliminary studies on the mode of action of OPA suggest that both OPA and glutaraldehyde interact with amino acids, proteins, and microorganisms. However, OPA is a less potent cross-linking agent. This is compensated for by the lipophilic aromatic nature of OPA that is likely to assist its uptake through the outer layers of mycobacteria and gram-negative bacteria [688-690]. OPA appears to kill spores by blocking the spore germination process [691].

Microbicidal Activity. Studies have demonstrated excellent microbicidal activity in vitro [69, 100, 271, 400, 692-703]. For example, OPA has superior mycobactericidal activity (5-$\log_{10}$ reduction in 5 minutes) to glutaraldehyde. The mean times required to produce a 6-$\log_{10}$ reduction for *M. bovis* using 0.21% OPA was 6 minutes, compared with 32 minutes using 1.5% glutaraldehyde [693]. OPA showed good activity against the mycobacteria tested, including the glutaraldehyde-resistant strains, but 0.5% OPA was not sporicidal with 270 minutes of exposure. Increasing the pH from its unadjusted level (about 6.5) to pH 8 improved the sporicidal activity of OPA [694]. The level of biocidal activity was directly related to the

temperature. A greater than 5-$\log_{10}$ reduction of *B. atrophaeus* spores was observed in 3 hours at 35°C, than in 24 hours at 20°C. Also, with an exposure time ≤5 minutes, biocidal activity decreased with increasing serum concentration. However, efficacy did not differ when the exposure time was ≥10 minutes [697]. In addition, OPA is effective (>5-$\log_{10}$ reduction) against a wide range of microorganisms, including glutaraldehyde-resistant mycobacteria and *B. atrophaeus* spores [694].

The influence of laboratory adaptation of test strains, such as *P. aeruginosa*, to 0.55% OPA has been evaluated. Resistant and multiresistant strains increased substantially in susceptibility to OPA after laboratory adaptation ($\log_{10}$ reduction factors increased by 0.54 and 0.91 for resistant and multiresistant strains, respectively) [704]. Other studies have found naturally occurring cells of *P. aeurginosa* were more resistant to a variety of disinfectants than were subcultured cells [705].

Uses. OPA has several potential advantages over glutaraldehyde. It has excellent stability over a wide pH range (pH 3–9), is not a known irritant to the eyes and nasal passages [706], does not require exposure monitoring, has a barely perceptible odor, and requires no activation. OPA, like glutaraldehyde, has excellent material compatibility. A potential disadvantage of OPA is that it stains proteins gray (including unprotected skin) and thus must be handled with caution [69]. However, skin staining would indicate improper handling that requires additional training and/or personal protective equipment (e.g., gloves, eye and mouth protection, and fluid-resistant gowns). OPA residues remaining on inadequately water-rinsed transesophageal echo probes can stain the patient's mouth [707]. Meticulous cleaning, using the correct OPA exposure time (e.g., 12 minutes) and copious rinsing of the probe with water should eliminate this problem. The results of one study provided a basis for a recommendation that rinsing of instruments disinfected with OPA will require at least 250 mL of water per channel to reduce the chemical residue to a level that will not compromise patient or staff safety (<1 ppm) [708]. Personal protective equipment should be worn when contaminated instruments, equipment, and chemicals are handled [400]. In addition, equipment must be thoroughly rinsed to prevent discoloration of a patient's skin or mucous membrane.

In April 2004, the manufacturer of OPA disseminated information to users about patients who reportedly experienced an anaphylaxis-like reaction after cystoscopy where the scope had been reprocessed using OPA. Of approximately 1 million urologic procedures performed using instruments reprocessed using OPA, 24 cases (17 cases in the United States, six in Japan, one in the United Kingdom) of anaphylaxis-like reactions have been reported after repeated cystoscopy (typically after four to nine treatments). Preventive measures include removal of OPA residues by thorough rinsing and not using OPA for reprocessing urologic instrumentation used to treat patients with a history of bladder cancer (Nevine Erian, personal communication, June 4, 2004; Product Notification, Advanced Sterilization Products, April 23, 2004) [709].

A few OPA clinical studies are available. In a clinical-use study, OPA exposure of 100 endoscopes for 5 minutes resulted in a >5-$\log_{10}$ reduction in bacterial load. Furthermore, OPA was effective over a 14-day use cycle [100]. Manufacturer data show that OPA will last longer in an automatic endoscope reprocessor before reaching its MEC limit (MEC after 82 cycles) than will glutaraldehyde (MEC after 40 cycles) [400]. High-pressure liquid chromatography confirmed that OPA levels are maintained above 0.3% for at least 50 cycles [706, 710]. OPA must be disposed in accordance with local and state regulations. If OPA disposal through the sanitary sewer system is restricted, glycine (25 grams/gallon) can be used to neutralize the OPA and make it safe for disposal.

The high-level disinfectant label claims for OPA solution at 20°C vary worldwide (e.g., 5 minutes in Europe, Asia, and Latin America; 10 minutes in Canada and Australia; and 12 minutes in the United States). These label claims differ worldwide because of differences in the test methodology and requirements for licensure. In an automated endoscope reprocessor with an FDA-cleared capability to maintain solution temperatures at 25°C, the contact time for OPA is 5 minutes.