ON THE STERILITY OF EYE OINTMENTS*

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HARDLY a year passes without a publication on the sterility of eye drops or of methods of ensuring freedom from contaminants. On ophthalmic ointments, however, the literature is sparse.

Fisher, Accousti, and Thompson (1943) found that ointments containing 5 per cent. "sulfanilamide, sulfathiazole, or sulfadiazine" in a water-dispersible base may become contaminated. Lehrfeld and Donnelly (1948) examined 74 tubes of used and unused ophthalmic ointment and found that the contents of the unused tubes were free from contaminants, whereas some used tubes contained organisms; they also found that ointments containing "sulfa" drops or penicillin could become contaminated before the contents of the tubes were exhausted. They commented that it has been the belief that the contents of the tube of ophthalmic ointment were sterile at the beginning and at the end, this being all the more surprising as the tubes of ointment were not marked "sterile". King (1953) found 24 new tubes of ophthalmic ointment to be sterile when examined. Vander Wyk and Granston (1958) tested 83 commercially available ophthalmic ointments, and found only 14.5 per cent. to be sterile; they tried various antibacterial agents in ointment purposely contaminated with *Micrococcus pyogenes* and found 0.5 per cent. benzyl alcohol to be most effective in killing 99.6 per cent. of the organisms present. Benzalkonium chloride at 1:5000 gave 98 per cent. effectivity and 0.5 per cent. Chlorbutanol 89 per cent. effectivity.

Crompton (1963) tested 81 tubes of 27 different proprietary ophthalmic ointments and found 33 per cent. to be contaminated when received from the manufacturer.

Phillpotts (1963), commenting on a *Lancet* annotation of March 23, 1963, stated that "in this country it is very rare for eye lotions, drops, or ointments to be anything but sterile when they leave the dispensary". Ogg (1963) suggested gamma radiation for the sterilization of eye medicaments together with the use of single-dose containers for fluorescein. In the present study a small batch of unused tubes of ointment and a larger batch of used tubes were tested bacteriologically by the following method:

136 tubes of sixteen different kinds of ointments returned after use in wards, clinics, and patients' homes, were tested. Nutrient broth washings were first made from the nozzles and covering caps under aseptic conditions and the nozzles were then passed several times through a Bunsen flame in order to destroy any organisms around the orifice. The ointment remaining in the tube was then expressed into a 100 ml. bottle of Brewer's thioglycollate medium, after discarding the first molten portion.

The bottles of medium were then heated to 45°C. in a water bath for 30 min. in order to melt the ointment and were then placed in a shaking machine for 5 min. to disperse the ointment throughout the medium, after which they were incubated at 37°C. Aerobic and anaerobic cultures were made from any bottles showing obvious growth after 48 hrs' incubation. The samples showing no growth were incubated for a further 48 hrs before being discarded.

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28 tubes of unused ointment issued for ward use were examined by a similar technique with the exception that, after washings had been made from the nozzles and caps, a sample of approximately 3" of ointment was expressed into Brewer's medium.

Results

In the series of 136 tubes of used ointment, 133 (97·8 per cent.) were sterile, and three were contaminated with fungi. From the washings of caps and nozzles, organisms were grown in 31 instances (22·8 per cent.); Gram-positive cocci were present in twenty specimens (14·7 per cent.) (two strains proving to be *Staphylococcus aureus*), fungi in four specimens (2·9 per cent.), and *B. subtilis* in five specimens (3·7 per cent.).

Of the 28 tubes, as issued to the ward before use, the ointment was sterile in all cases, and Gram-positive cocci were grown from the cap and nozzle washings in four instances (14·3 per cent.).

These findings are summarized in the Table:

TABLE
PERCENTAGE CONTAMINATION

Series of Tubes	No. Tested	No. Contaminated	
		Ointment in Tubes	Caps and Nozzles
Used	136	3 (2·2 per cent.)	31 (22·8 per cent.)
Unused	28	0	4 (14·3 per cent.)

Discussion

The tubes tested contained ointments embodying mydriatics, steroids, and antibiotics. The proportion of contamination of caps and nozzles was in the same range whether the ointments contained drugs such as atropine or steroids or antibacterial drugs such as antibiotics or sulphonamides. Among the antibiotics were chloramphenicol, polymyxin, tetracycline, neomycin, penicillin, and others in current use.

The contamination of nozzles seems to occur haphazardly. The number in each group in this series was relatively small and statistical evaluation was not practicable. The largest group was that containing atropine—34 tubes with twelve contaminations. In one brand of chloramphenicol seven of seventeen tubes were contaminated, and in another brand five of eighteen tubes were contaminated.

The British Pharmacopoeia (1963) recommends a base for ophthalmic ointments consisting of ten parts wool-fat, ten parts liquid paraffin, and eighty parts yellow soft paraffin. For sterilization it advises 150°C. dry heat so that the whole is maintained at this temperature for one hour.

Regarding the making up of ophthalmic ointments, the B.P.C. (1959) advises that aseptic precautions should be taken and that the ointment should be put into small sterilized collapsible tubes which are then closed. Theoretically, therefore, the ointments and their containers should be sterile before the tube is opened. In practice, however, 14 per cent. of the caps and nozzles of the unused ointments were

found to be contaminated, and this percentage was much higher for the nozzles and caps of the used ointments. When such contamination occurs in the patient's home, it has little significance, but in hospital the possibility of transferring infection from one patient to another cannot be ignored.

To avoid infection by ointments the following hospital routine is advisable. The tube should never be squeezed direct into the eye, as this makes contamination of the nozzle more likely. The first half inch of ointment should be discarded, and a small amount should then be conveyed to the eye with a sterilized glass rod. Before the cap is replaced the nozzle should be wiped with sterilized lint or gauze.

It is preferable, however, for each patient to have an individual tube. Single doses of ointment in a gelatine capsule give a satisfactory safeguard against infection and their use is advisable in cases in which there is a risk that the corneal epithelium may be damaged and thus serve as a port of entry for infection. This risk is especially high in the outpatients' department after tonometry, removal of corneal foreign bodies, etc., and at all times in the operating theatre. Chloramphenicol is at present available in this form ("Applicaps").

It is advisable to dispense eye ointments in sealed polythene envelopes to preserve the sterility of the tube and its cap and nozzle until the seal is broken.

It is also advisable to use a preservative in the ointment-base, and further tests will show whether benzyl alcohol, which Vander Wyk and Granston (1958) found to be effective, is safe to use in the eye or not. The use of gamma radiation would be an ideal way of ensuring initial sterility, and provided that the container envelopes were impervious to bacteria the ointments would then remain sterile indefinitely.

Summary

Investigations have been carried out regarding the sterility of ophthalmic ointments and containers. Recommendations are made on how to avoid contamination. This has special significance in hospital practice. The use of a preservative is advocated, but it is obvious that the ideal antiseptic should act not only against bacteria but also against fungi and viruses.

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