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Standard aeration for gas-sterilized plastics

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SUMMARY

In an effort to provide guidelines for standardizing aeration times for plastics sterilized with ethylene oxide, an Aeration Index has been developed. Based on the rate of diffusion of ethylene oxide in selected polymers, the Index provides an indication of the aeration time at ambient temperature (23 °C) for the ethylene oxide concentration in freshly sterilized plastics to drop to 50 parts/10^6.

INTRODUCTION

The increasing use of plastics in the manufacture of items in the field of anaesthesia has brought to light problems related to the sterilization of these thermolabile materials. Traditional methods of sterilization involving the use of wet or dry heat are not acceptable for many polymers which have some degree of heat lability. In these cases the use of the anti-microbial gas, ethylene oxide (shown in Fig. 1), provides a satisfactory means of overcoming the difficulties of sterilizing heat-labile plastic items by conventional methods.

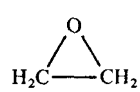

Fig. 1. Ethylene oxide.

One serious disadvantage associated with the use of ethylene oxide gas as a sterilant for plastic articles later brought into contact with body tissues and/or fluids is liberation of the gas which has been absorbed and retained by the polymer during the sterilization process. Toxic effects have been associated with the clinical use of medical plastic devices which have been sterilized with ethylene oxide but from which the residual gas has not been properly eliminated before use. For example, the literature contains numerous cases of tracheal damage from gas-sterilized endotracheal tubes, and instances of burns to the face from anaesthetic face masks (Rendell-Baker & Roberts, 1970*a*; Holley & Gildea, 1971; Lipton *et al.* 1971; Rendell-Baker, 1972). Perhaps the most dramatic case reported was the death of three small children from severe toxic shock following extracorporeal circulation during open-heart surgery; ethylene oxide, dissolved in the polyvinyl chloride tubing of the heart–lung machine, had passed into the circulating blood during perfusion and caused irreversible toxic effects (Stanley, Bertranou, Forest & Langevin, 1971).

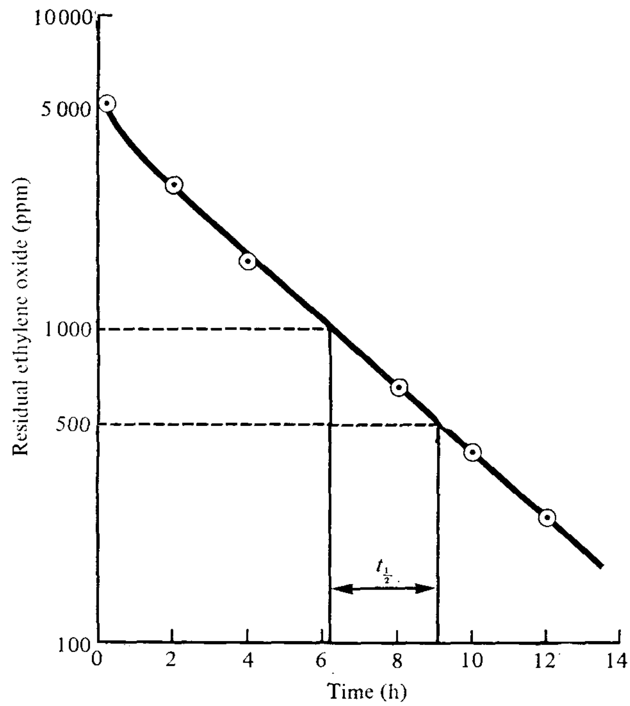

Fig. 2. Semi-log plot of mean concentration of absorbed ethylene oxide in a 1·5 mm thick sheet of red rubber during aeration.

Degassing sterilized articles by aeration is a solution to this problem, but as yet there is no standard aeration for ethylene oxide sterilized polymers. The lack of such a standard may be largely attributed to a paucity of adequately sensitive analytical methods for assaying ethylene oxide residues in polymers and the subsequent interpretation of the effect of polymer structure on the ethylene oxide desorption process.

Studies of elimination of ethylene oxide by aeration have led to a variety of recommendations for aeration times, but the wide variations in the suggested aeration times even for the same polymer indicate continued difficulty in standardizing the procedure (Matsumoto *et al.* 1968; Roberts & Rendell-Baker, 1972; Andersen, 1971, 1973; Sterilization Systems Group, 1970). An Ethylene Oxide Aeration Index is now suggested as a possible solution to this problem.

MATERIALS AND METHODS

Experimental approach

In developing the Aeration Index, the rate of desorption of ethylene oxide from a number of commonly used medical plastics was studied. For this purpose a highly sensitive and accurate assay method based on high vacuum distillation and gas chromatographic analysis was used to detect residual ethylene oxide in thin polymer sheets (Warren, 1971; Whitbourne, Mogenhan & Ernst, 1969; Mogenhan, Whitbourne & Ernst, 1971). Analysis of series of test samples initially containing a uniform concentration of absorbed ethylene oxide was carried out at timed intervals during the aeration period, which was at a room temperature of 23 °C (White, 1975).

Figure 2 shows a typical desorption curve obtained in this manner; the half-life of ethylene oxide was calculated from the slope of the curve, and application of simple diffusion theory yielded a value for the diffusion coefficient of ethylene oxide in each polymer (Crank, 1975):

$$-D = \frac{h^2 \ln (0{\cdot}5)}{\pi^2 t_{\frac{1}{2}}}, \qquad (1)$$

where D = diffusion coefficient (cm²/sec), h = thickness of polymer sheet (cm), $t_{\frac{1}{2}}$ = half-life (sec).

Development of the Aeration Index

Before aeration times could be predicted from a knowledge of the diffusion coefficient, it was necessary to know the ethylene oxide content of each polymer type after a typical sterilization cycle. In consequence, duplicate samples (1·5 mm thick) were wrapped in sterilizing packs (Mediplast) and subjected to a routine sterilization cycle of 1200 mg ethylene oxide/litre for $1\frac{1}{4}$ h at 55 °C in 'The Victoria' Ethylene Oxide Sterilizer (Weymes, 1968). After removal from the sterilizer, the polymer samples were assayed for ethylene oxide.

Whilst the maximum tolerable concentration of residual ethylene oxide is still uncertain, 250 parts/10^6 has been recommended as an interim limit by the Z79 Ethylene Oxide Sub-committee of the American National Standards Institute (Rendell-Baker & Roberts, 1970*b*; Andersen, 1973). Recently the American Food and Drug Administration released official guidelines setting acceptable limits at 250 parts/10^6 for all topical medical devices and 25 parts/10^6 for blood dialysis units, blood oxygenators, heart–lung machines and implants (Food and Drug Administration, 1975). A standard of 50 parts/10^6 for all medical plastics is now suggested in this paper as a realistic and practical proposal.

Accordingly the time for the ethylene oxide content of the sterilized test samples to fall to about 50 parts/10^6 was calculated from a knowledge of the half-life of ethylene oxide in each of the 1·5 mm thick polymer samples. A correlation was observed between the standard aeration times derived in this manner and the diffusion coefficient of ethylene oxide in the polymer. This is shown in Fig. 3.

The relationship is not a simple one. Polymers such as silicone rubber which have a high value of the diffusion coefficient will readily absorb ethylene oxide during sterilization and lose it rapidly on aeration, with the result that aeration times can be very short. Similarly, it is clear that polymers with a low value of the diffusion coefficient, e.g. polyethylene terephthalate, not only lose the gas at an extremely slow rate but also absorb it in a correspondingly slow manner; it is thus unlikely that toxic concentrations of absorbed ethylene oxide will be attained during sterilization. As a result aeration times for such plastics can be short, providing sterilization times have not been prolonged. However, polymers with intermediate values of the diffusion coefficient can absorb and retain significant amounts

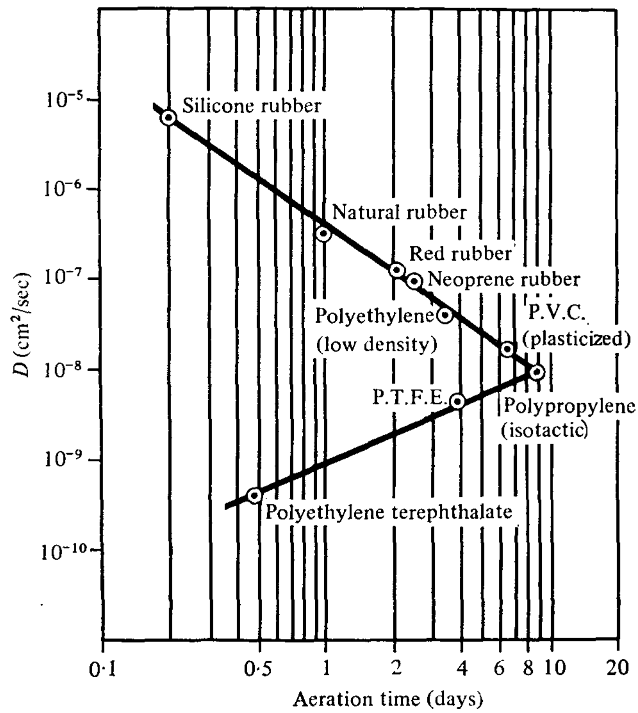

Fig. 3. Plot showing time at 23 °C for the level of residual ethylene oxide in sterilized polymers (1·5 mm thick) to drop to 50 parts/10^6.

of ethylene oxide and aeration of such materials requires due care. Two polymers in particular, plasticized polyvinyl chloride and isotactic polypropylene, require lengthy aeration periods.

As it stands, the Aeration Index applies to the aeration at 23 °C of 1·5 mm thick polymer sheets. Samples of different thicknesses will obviously require different aeration times to drop to 50 parts/10^6 residual ethylene oxide. Figure 4 demonstrates the effect polymer thickness has on the aeration time. Since the rate of clearance of ethylene oxide from a polymer sheet varies inversely as the square of the thickness of the sheet (see equation 1), it would be expected that doubling the thickness would increase the aeration time fourfold for a given polymer. This, however, will only be true for polymers which are saturated with ethylene oxide at the end of the sterilizing period, i.e. polymers such as silicone rubber in which ethylene oxide diffuses very rapidly. For polymers with intermediate values of the diffusion coefficient, saturation with ethylene oxide will not be achieved during sterilization cycles and doubling the thickness effectively halves the residual ethylene oxide concentration; the increase in aeration time is thus not a fourfold one, but of the order of a twofold increase. Polymers with a low value of the diffusion coefficient, e.g. polyethylene terephthalate, will not achieve toxic concentrations of ethylene oxide during sterilization and subsequent aeration times can be short.

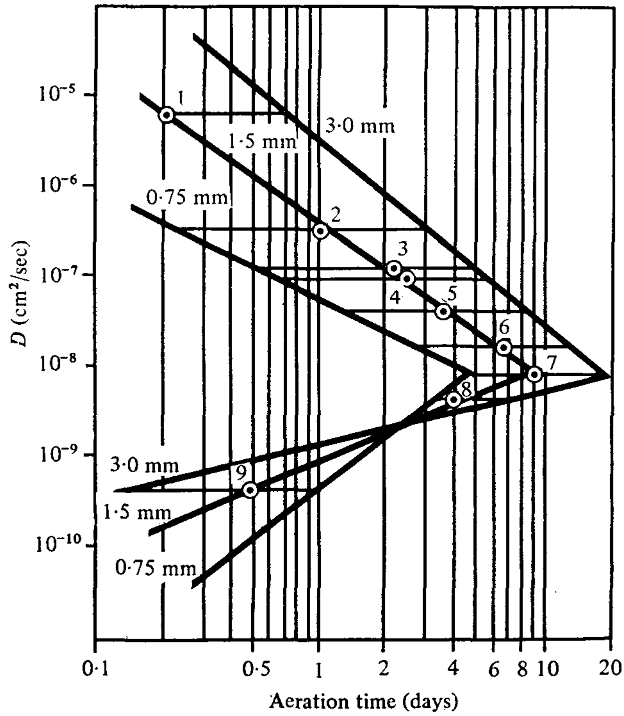

Fig. 4. Effect of polymer thickness on aeration time. Key: 1, Silicone rubber; 2, Natural rubber; 3, Red rubber; 4, Neoprene rubber; 5, Polyethylene (low density); 6, P.V.C. (plasticized); 7, Polypropylene (isotactic); 8, P.T.F.E.; 9, Polyethylene terephthalate.

In the case of thinner samples, a similar argument applies, but in reverse, i.e. the rate of clearance for sheets half as thick (0·75 mm) will be four times as fast, but the concentration of absorbed ethylene oxide will now be correspondingly higher.

Since a thin-walled tube of a wide bore can be regarded as a thin sheet bent round on itself, the Aeration Index can also be used to predict aeration times for tubing of this nature.

RESULTS AND DISCUSSION

Testing the Aeration Index

In order to test the reliability of the Ethylene Oxide Aeration Index, a variety of polymer samples were sterilized with 1200 mg ethylene oxide/litre for $1\frac{1}{4}$ h at 55 °C in 'The Victoria' Ethylene Oxide Sterilizer and subsequently aired at 23 °C. After the predicted aeration time, the samples were assayed for residual ethylene oxide. The findings are shown in Table 1. In every case, the ethylene oxide concentration is in the region of 50 parts/10^6 or less.

It is unlikely that other ethylene oxide sterilizers will operate under the same set of conditions as was used in the development of the Aeration Index. It was therefore necessary to examine the ability of the Index to give a reliable pre-

Table 1. *Residual ethylene oxide in sterilized polymers* after predicted aeration times*

Polymer	Thickness (mm)	Predicted aeration time (days)	Residual ethylene oxide (parts/10^6)
Silicone rubber	1·5	0·2	4
Red rubber	3·0	4	19
EVA copolymer (9% vinyl acetate)	1·5	2·5	9
PVC tubing (6 mm i.d.)	1·5	6·5	30
PVC tubing (4 mm i.d.)	1·0	5	38
Polypropylene	1·5	9	52
Polytetrafluoroethylene	0·5	2	4
Polyethylene terephthalate	0·25	1·5	35

* Sterilization cycle: 1200 mg ethylene oxide/litre for 1¼ h at 55 °C.

Table 2. *Residual ethylene oxide in sterilized polymers after predicted aeration times*

Polymer	Thickness (mm)	Predicted aeration time (days)	Residual ethylene oxide	
			Cycle A* (parts/10^6)	Cycle B† (parts/10^6)
Red rubber	2·5	3	12	23
EVA copolymer (9% vinyl acetate)	1·5	2·5	19	8
PVC tubing (6 mm i.d.)	1·5	6·5	76	67
Polytetrafluoroethylene	0·5	2	25	43

* Sterilization cycle A: 1200 mg ethylene oxide/litre for 6 h at 30 °C.
† Sterilization cycle B: 800 mg ethylene oxide/litre for 6 h at 40 °C.

diction of aeration times for polymers sterilized under different sets of conditions. Table 2 shows concentrations of residual ethylene oxide in polymer samples which have been exposed to different sterilization cycles; these results confirm that the usefulness of the Aeration Index is not restricted to one specific set of sterilizing conditions and that it has wider applications.

It would, of course, be unwise not to realize that this largely theoretical approach has limitations. For instance, articles of unusual design or dimensions might not be easily related to simple shapes such as sheets or tubing. In such situations, two alternatives are open: one is to determine the ethylene oxide content of the individual article by experimentation, the other to let an excessive aeration time elapse before using the sterilized object.

In addition, it should not be forgotten that ideally all ethylene oxide sterilization cycles should be monitored by the inclusion of biological indicators which require to be cultured for several days after removal from the sterilizer. Consequently, it would not be uncommon to have an article which has reached the acceptable limit of residual ethylene oxide after say 2 days but which cannot be issued until the results of the sterility testing are known. A somewhat similar situation arises with the use of heated aerators: operating at around 55 °C, these mechanical aerators can reduce the time required for the elimination of residual ethylene oxide from days to hours (Thomas & Levy, 1970; Roberts & Rendell-Baker, 1972; Stetson, Whitbourne & Eastman, 1976). However, the results of sterility testing should again be awaited before issue of the articles.

Finally, it should not be forgotten that ostensibly the same plastic can vary in formulation from manufacturer to manufacturer. This variation may be reflected in slight differences in the amount of ethylene oxide absorbed by the polymer and in the rate of diffusion of the gas. Consequently, the Aeration Index is not an absolute one, but, as mentioned earlier, is only intended as a fairly reliable guide to the aeration time for a particular plastic type.

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