A SHORTER STERILISING CYCLE FOR SOLUTIONS HEATED IN AN AUTOCLAVE

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The rapid cooling of bottles in an autoclave after steam sterilisation has been investigated. A coarse cold water spray caused breakage by thermal shock, whereas a fine spray prevented this. The time of cooling using this method has been compared with the usual cooling cycle and with that achieved when air was circulated in the chamber. Experimental data for a steriliser containing a charge of 200 × 1 litre bottles is given.

Sterilisation of fluids by heating in an autoclave is normally a lengthy process which may be divided into three phases. The first is the time required to heat the chamber and contents to the sterilising temperature; this is dependent upon the water-equivalent of the steriliser and its contents, the quality of the incoming steam and the condition of the autoclave. Secondly, there is the sterilising period, which is set by the temperature selected for the operation[1,2]. Thirdly, there is the cooling time which is dependent upon the heat capacity of the system and the rate at which heat can be dissipated.

When a steriliser, designed so that heat losses are small, is used with dry saturated steam the heating time is a minimum; the sterilising time at a given temperature may not be shortened, so only the cooling period may be reduced.

Reduction of the cooling period offers the advantages of safety, improvement of product and reduction in costs. For example, when the chamber has reached atmospheric pressure the contents of closed bottles, because of their slow rate of cooling, have an internal pressure above atmospheric pressure, and an explosion may occur or the closure may be blown off.

Hitherto the rate of cooling has been dependent upon the heat transfer of the system to the surrounding air by conduction and radiation: by the means now described the containers are cooled directly. The idea of rapidly cooling large volumes of fluids is not new. An autoclave has been described[3] in which streams of warm water are directed onto the hot containers, but elaborate temperature control of the water is necessary to avoid breaking the bottles. We report a method of reducing the cooling period using cold water without recourse to temperature control systems.

Experimental

The steriliser and recording apparatus have previously been described[4] and in addition an unjacketed autoclave measuring 122 × 114 cm. diameter (48 × 45 in.) was used for confirmatory experiments. Modifications were made so that water under pressure was supplied to spray nozzles within the chambers. Compressed air was also supplied to

ballast the chambers at sterilising pressure as soon as the incoming water condensed the steam. A relief valve set to open at 2 p.s.i. above working pressure was fitted.

Two spray nozzles were positioned opposite each other at either end of the chamber and pointing slightly downwards. They were also off-set in the horizontal plane to produce maximum turbulence (Fig. 1). In the larger steriliser 12 nozzles were positioned at the top of the chamber in three rows of four pointing directly downwards. These nozzles were of the whirling-spray mechanical break-up type.

Deionised or distilled water was necessary to obtain deposit-free surfaces. The rate of flow through the nozzles was measured, and at the working pressure of 100 p.s.i. (7·03 kg./sq. cm.) was 0·5 litres each per minute.

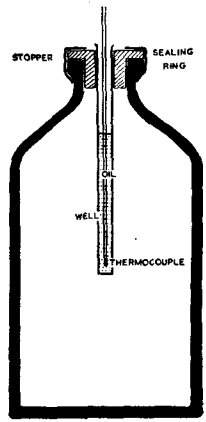

FIG. 1. Arrangement for the insertion of a thermocouple in a transfusion bottle.

To avoid repeated blocking of the nozzles by material flaking from the inner surface of iron or galvanised iron pipes, copper piping was used in the water circuit.

Temperature Measurement

Transfusion bottles. Thermometer wells, filled with high-density oil[5] were produced so that the thermocouple junctions were about the centre of the bottles (Fig. 2).

Ampoules. The neck of a standard 10 ml. ampoule was cut and the cut end flattened to form a lip. A rubber bung, through which the thermocouple wires passed, was inserted into the ampoule neck and wired on. *Vials.* Standard 10 ml. vials were used. Thermocouple wires were passed through a pierced latex plug. *M.R.C. bottles.* The plug was pierced and the thermocouple wires passed through until the junction was below the surface of the liquid. Three such containers were usually used, one at each end of the chamber and the third about the middle. In the larger unjacketed autoclave, in which the charge consisted of three layers of bottles, a bottle was selected near the centre of each layer for temperature measurement.

Measurement of Droplets from Nozzles

A slight variation of an existing method[6] was used. A standard glass microscope slide, 3 in. × 1 in., was evenly coated with magnesium oxide and exposed by a shutter to the spray for a fraction of a second. The droplets caused areas of the oxide film to be disturbed; measurement of the mean diameter of these areas provided a measure of droplet size.

Operating Conditions

Using dry saturated steam at 10 p.s.i. (0·703 kg./sq. cm.) normal practice was followed to the end of the holding period. At this point water was supplied to the spray nozzles at their working pressure, and pressure maintained in the chamber by compressed air. When the liquid in the bottles

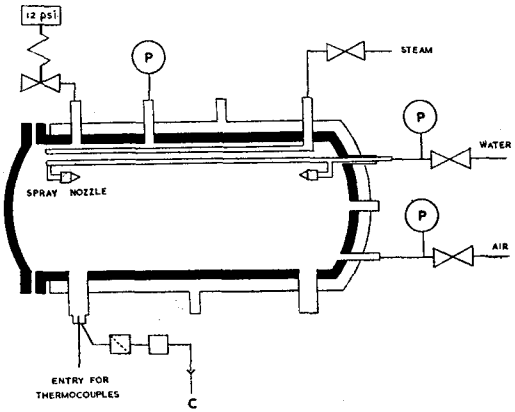

FIG. 2. General arrangement of the steriliser with water spray. Graphical symbols B.S. 1553.

had cooled to its boiling point the supply of air was discontinued and further cooling to 93° (200° F.) achieved by water alone. To prevent waterlogging of the chamber, a steam trap capable of passing the full water flow was fitted.

RESULTS

Experiments with different nozzles indicated that the maximum droplet size became more and more critical as the temperature of the cooling water was reduced: there was no advantage in using a smaller droplet size than that which just fails to crack bottles, as with smaller nozzles the necessary flow of water to the chamber is impeded: at a water temperature of 18° (65° F.) a mean droplet size of 80 μ produced the maximum rate of cooling.

Certain positions of the nozzles caused breakages. Coalescence of small droplets on the upper surface of the chamber caused large drops to fall on to the bottles and produce a thermal shock. With suitably positioned nozzles the major factors associated with the cooling of the

charge were shown to be the water equivalent of the bottles and their contents, and the rate of heat transfer through their walls. Measurements were made with glass and aluminium containers (Fig. 3).

Rates of Cooling

Transfusion solutions. Control experiments showed that with a charge of twenty-four 0·5 litre bottles in the smaller autoclave, 3 hours elapsed before the temperature reached 93° (200° F.) (Fig. 4). In the larger steriliser with a 200 × 1 litre charge, 22 hours were needed to reduce the temperature to 93° (200° F.) (Fig. 5). In other experiments with the smaller autoclave, air was pumped through at the end of the holding period. This process may be described as "air-cooling" and by this means the time to 93° (200° F.) was decreased to 2 hours (Fig. 4).

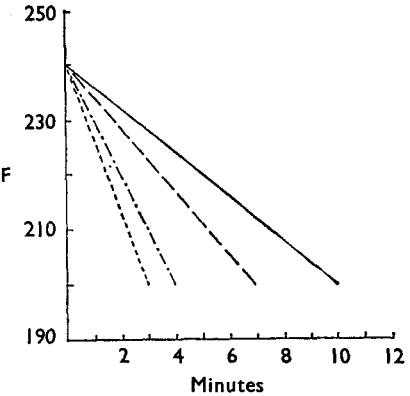

FIG. 3. Water cooling. Comparative rates of cooling of containers.

——— 0·5 l. transfusion, glass
– – – – M.R.C. bottles
– · – · – 0·5 l. transfusion, aluminium
- - - - - - Ampoules and vials

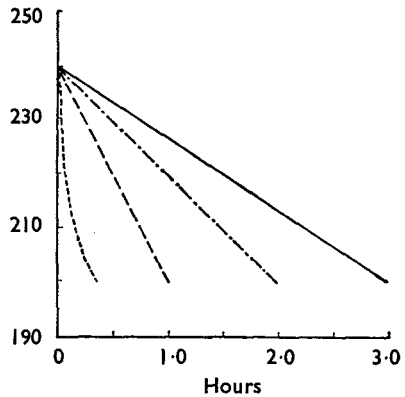

FIG. 4. Natural cooling. Comparison of the rates of cooling of containers under the effect of convection and radiation cooling and without forced circulation.

——— 0·5 l. transfusion free-cooled
– · – · – 0·5 l. transfusion air-cooled
– – – – M.R.C. bottles free-cooling
- - - - - - Ampoules and vials free-cooling

When water cooling was employed with the smaller steriliser, the cooling time was decreased to 10 minutes (Fig. 3) and using the larger steriliser a mere 17 minutes reduced the temperature to 93° (200° F.) (Fig. 5). The glass bottles used have survived more than 50 successive treatments. Aluminium containers of similar size and shape to the bottles needed only 4 minutes to cool to 93° (200° F.) compared with 10 minutes for glass (Fig. 3). This confirms that the thermal conductivity of the walls of the containers is a factor limiting the rate of cooling.

Ampoules. Under unassisted cooling conditions, a charge of 10 ml. ampoules required 20 minutes to reach 93° (200° F.) (Fig. 4). Water cooling reduced this time to 3 minutes (Fig. 3). *Vials.* With 10 ml. vials, the results were similar to those obtained with ampoules (Figs. 3 and 4). *M.R.C. bottles.* A charge of 24 × 0·5 litre bottles each containing

120 ml. of solution was used in the smaller autoclave and an unassisted cooling time of 60 minutes recorded (Fig. 4). Water cooling reduced this time to 7 minutes (Fig. 3).

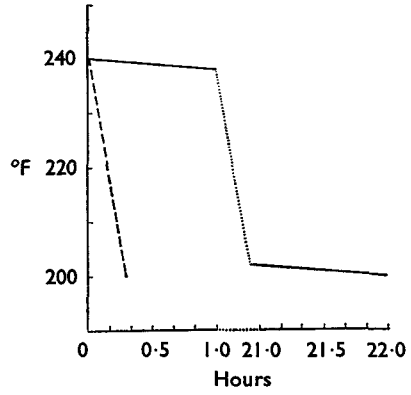

FIG. 5. Cooling curves of 200 one litre bottles of fluid with and without water spray.
——— Free cooling - - - - Water cooling

Effect of Rapid Cooling on Dextrose Injection

One litre bottles containing 5 and 20 per cent Dextrose Injection were processed under normal conditions and also with water cooling. The colour of the solutions was matched against suitable strengths of potassium

TABLE I

EFFECT OF PROCESSES ON DEXTROSE INJECTION

Solution	Treatment	Appearance	Equivalent potassium dichromate
Dextrose injection, 20 per cent ..	Normal	Straw yellow	7 p.p.m.
	Water cooled	Pale yellow	4 p.p.m.
Dextrose injection, 5 per cent ..	Normal	Pale yellow	4 p.p.m.
	Water cooled	Extremely pale yellow	1·5 p.p.m.

dichromate solution as well as being examined visually. Table I shows the results obtained and it is evident that much less discoloration occurs when water cooling is employed.

DISCUSSION

All results show a reduction in the cooling time when the water-cooling method is used. When containers of half or 1 litre transfusion solutions are considered this reduction is large.

It was 22 hours before the temperature of 200 × 1 litre bottles within an unlagged steriliser fell from 115° (240° F.) to 93° (200° F.). The danger of bursting persists until this lower temperature is reached, and presents a hazard if such a batch is removed from the steriliser as soon as the pressure within the chamber has fallen to atmospheric level.

The rate of cooling is limited by the presence of a maximal temperature gradient through the glass walls of the container. If this is exceeded the

glass fractures. The heat capacity of a large cold droplet landing on a hot glass surface is sufficient to bring about the condition of thermal shock. To abstract heat without breaking the bottles it has been found necessary to drench them in a mist of water particles small enough to avoid severe localised cooling and the thermal shock which causes the breakage. Similar experiences have been recorded using standard M.R.C. bottles containing the volume of solution used for blood collection. Vials and ampoules behave in a similar manner but their cooling rate is much higher, because of their greater specific surface and their thinner walls.

Since on a production scale leakage may take place within the steriliser, the closed circuit for the cooling water described previously[3] was discarded. The carbonisation of dextrose solution and the build up of chloride and other salts in the circulating water, which would occur, produces tenacious deposits on the bottle and a risk of corrosion of the steriliser. The optimum droplet size seems to be about 50–100 μ.

REFERENCES

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4. Barson, Peacock, Robins and Wilkinson, *J. Pharm. Pharmacol.*, 1958, 10 *Suppl.*, 47*T*.
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After Mr. Wilkinson presented the paper there was a DISCUSSION. The following points were made.

The positive pressure produced in a large steriliser by steam fell only slowly when the water was introduced due to the "flash" steam production. Only a small amount of air was required to ballast the chamber when the incoming water condensed the steam. The air was fed into the base of the steriliser as a matter of convenience, and had proved the best arrangement, since the air had a greater density than the vapours present and did not interfere with the spray pattern. No shearing of the base of the bottles was caused. The heating and cooling did not exert much strain on the autoclave, and was well within the tolerance of the metal. For insurance purposes a relief valve had to be fitted so that no vacuum was produced. There was no leakage of liquid, either in or out of full or partially filled bottles. In some instances the spray water caused discolouration of aluminium caps if they were in contact with iron.