

SAFETY REQUIREMENTS FOR ACRYLIC IMPLANTS*

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REDMOND SMITH (1956) produced further evidence for an irritant, Cetrimide, introduced at the time of operation being the cause of inflammatory reaction when an acrylic lens is inserted into the eye.

Binkhorst and Flu (1956) proposed the use of ultra-violet rays for sterilising intra-ocular prostheses. Their objection to the use of detergents does not take into account the fact that these substances differ greatly in their physico-chemical behaviour with regard to acrylic material, and they offer no method of rendering the lens chemically clean after manufacture. The process of irradiation with ultra-violet light is open to several objections. First, it is not certain that all spores will be destroyed. Also, it is known that ultra-violet light of wavelength 2,537 Å is strongly absorbed by polymethyl methacrylate (Fig. 1).

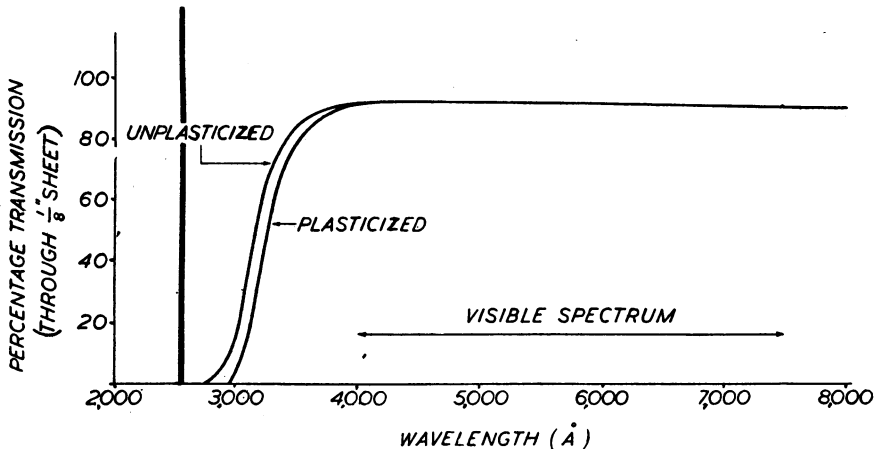


FIG. 1.—Perspex light transmission, visible range. Superposition of emission curve of ultra-violet tube recommended by Binkhorst and Flu (2537 Å) upon the absorption curve of polymethyl methacrylate. (Taken from "Perspex" Acrylic Materials, I.C.I. Plastics Division). The material is virtually opaque to ultra-violet of this wavelength.

This type of ultra-violet radiation is known to degrade acrylic materials with the production of monomer, and the process is accelerated by any rise in temperature. The intense absorption of the radiation by the polymer will cause most of this monomer to be liberated near the surface of the polymer. More evidence is needed to show that a significant amount of the monomer,

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which is highly irritating, is not formed in the surface layers of the lens where it is most easily accessible. It is felt that the apparatus recommended by Binkhorst and Flu does not provide sufficient guarantee against depolymerization by the ultra-violet, especially in view of the overheating which may be brought about by the insulation of the acrylic lens from the air stream by the quartz capsule. For these reasons it is thought that the method described by Binkhorst and Flu may not be sufficiently rigorous.

Materials and Manufacture

Properties of the Material to be Used.—Any material to be permanently inserted into the eye, or indeed elsewhere in the body, should have the following characteristics: it should be insoluble in water, inert to all body fluids, and should never give rise to tissue sensitization; it should have the physical properties required for its proposed use, and it should be able to be shaped to the required form. Some 1,500 patients fitted with contact lenses at the Contact Lens Department, Moorfields Eye Hospital, have worn lenses made from Transpex I regularly for periods up to 5 years, and in no case is there reason to believe that these lenses have provoked an allergic reaction in the eye. Pure polymethyl methacrylate is available under the trade name Transpex I (I.C.I.). It will be referred to either as polymethyl methacrylate or as acrylic. Other commercial materials based upon polymethyl methacrylate are available. Many of them contain fillers and plasticizers or for other reasons do not comply with the rigid standards of purity and full polymerization required for our purpose.

Conditions to be Observed during Manufacture.—The material, as received from the manufacturers, must be washed with warm distilled water to remove traces of gelatine coating adhering to it.

During manufacture no part of the material must be exposed to a temperature exceeding 140° C., above which point depolymerization sets in liberating the highly irritating monomer within the polymerized material from which it will escape into the tissues for a long time. It is almost impossible to detect this change and the only safe procedure is stringent exclusion of the possibility of its occurrence. This means that, during any moulding process, control by an efficient thermostat must be provided, and any machining and grinding must be undertaken under conditions securing effective cooling of the material.

The materials used in any process such as polishing or grinding must not react chemically with the acrylic, or be absorbed by it. Either they must be able to be removed entirely by subsequent treatment or they must be harmless should a trace be introduced into the tissues.

Cleaning and Sterilizing after Production.—When manufacture has been completed we have to clean the surface and sterilize it. The principles underlying this should be to use, as far as possible, chemicals which do not react in any way with the acrylic and which contain only physiologically acceptable ions. The contaminants likely to be found are grease from polishing materials or from handling, aluminium oxide in the form of emery used for grinding, and sintered iron oxide, in the form of rouge, used for polishing.

Physical Chemistry of the Problem

Detergents

(1) The physico-chemical behaviour of detergents towards acrylic is a relatively unexplored subject, but the reaction would be expected to depend upon the general ionic character and molecular structure of the detergents. Cationic detergents are more likely to become absorbed on to the surface than other types, because the surface of polymethyl methacrylate can be acid due to the presence of small amounts of copolymerized methacrylic acid. This would be expected to bind amines fairly strongly, and could be the explanation of the observed strong absorption of Cetrimide. Such cations would nevertheless desorb easily in contact with excess sodium.

(2) Anionic detergents should be free from this possibility of absorption and it would be preferable to use a product such as pure sodium lauryl sulphate.*

(3) Non-ionic detergents might well penetrate fairly easily into the surface layers and they should be avoided.

(4) In critical work, distilled water should be used both to dilute detergents and to wash them away. Tap water forms a detergent scum very easily. Repeated changing of distilled water for washing is preferable.

Hydrochloric Acid

This will diffuse in and out fairly quickly, and it is very doubtful if it would be totally removed by soaking in caustic soda subsequently. If used in high concentration, 30 per cent., a considerable proportion would be un-ionized and this would penetrate easily. While it is broadly true that acrylic is inert to HCl, it is doubtful whether treatment with 30 per cent. HCl might not tend to hydrolyse the material to polymethacrylic acid, especially at the surface. This surface hydrolysis would render the material more liable to adsorb and absorb other materials such as detergents. It has formerly been proposed (Ridley, 1954) to use concentrated hydrochloric acid to remove the sintered iron oxide in the rouge used as a polishing agent. In view of this criticism it is desirable to use an alternative product, such as "Cerirouge" (Thorium Ltd.), as a polishing medium. Cerium oxide is almost entirely inert, and there is no reason to suppose that, in such minute quantity as we are considering, it would have any harmful effect if traces of it were introduced into the eye or other tissues. In the manufacturing process to be described, this difficulty is avoided altogether, since the lenses are produced by pressing between metal dies and no grinding or polishing materials are employed.

* Available as "Empicol" LZ from Marchon Products Ltd.

Caustic Soda

This substance is intensely anionic and will diffuse into acrylic little if at all. It will not harm the material in any way.

A Method of Preparing Acrylic Prostheses

To remove Traces of Grease.—The material will have been cleaned thoroughly by polishing with a clean soft material which has been washed and which contains no impregnated polish. If the lens has been produced by pressing, the material can be protected by latex rubber during the necessary subsequent handling to perfect the edge, and this can be polished with a dry clean bob of linen or swansdown, no grease or polish being used. This technique is recommended.

Notwithstanding that the lens is now mechanically clean, the possibility that a film of grease, trapping dirt and possibly bacteria, is present on the surface must be eliminated, and with suitable precautions it seems desirable to use a detergent for this purpose. Sodium lauryl sulphate 0.1 per cent. at 40° C. for 5 minutes has been shown to remove even the beeswax compound employed in polishing waxes. Its efficacy should be checked for each method of manufacture employed. The lens is now thoroughly washed in distilled water for several minutes to remove surface traces of the detergent.

Sterilization.—Hobbs and Wilson (1942) and Tilley (1946) have shown that caustic soda 10 per cent. at 30° C. for one hour will completely sterilize even the spores of *B. subtilis* (Fig. 2, opposite). If the lenses are mounted in carrying racks made of acrylic and this assembly is fixed within a screw-cap polythene container, the whole assembly can be exposed to 10 per cent. caustic soda without any harmful effect. Metals should be avoided because they are liable to be attacked, and other plastic materials should be avoided because of the risk that they may contain deleterious fillers or plasticizers which may pass into solution during storage. After the assembly has been sterilized, it is removed from the caustic soda bath, emptied, and refilled with caustic soda 0.1 per cent. This concentration is fully protective at room temperature and constitutes a safe storage medium (Fig. 3, opposite). The cap is screwed down tightly and sealed with Sellotape. It is now ready for storage and if necessary for despatch by post.

The possibility that the caustic soda solution might deteriorate during storage, on account of absorption of carbon dioxide from the air through the polythene container or by reason of its fixation by traces of methacrylic acid known to be present in the surface of acrylic materials, was investigated. The screw-cap container was three-quarters filled with 50 ml. nominal 0.1 per cent. caustic soda which on precise analysis proved to be 0.1098 per cent. This was kept in an incubator at 34° C. for 5 weeks. At times it was stood upside down, and from time to time it was shaken thoroughly. This

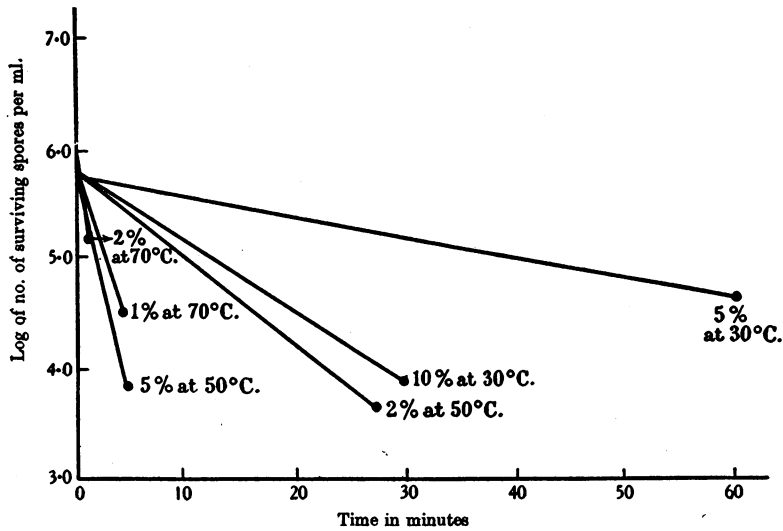


FIG. 2.—Rate of death of spores of *B. subtilis* when submitted to different concentrations of sodium hydroxide at different temperatures (Hobbs and Wilson, 1942).

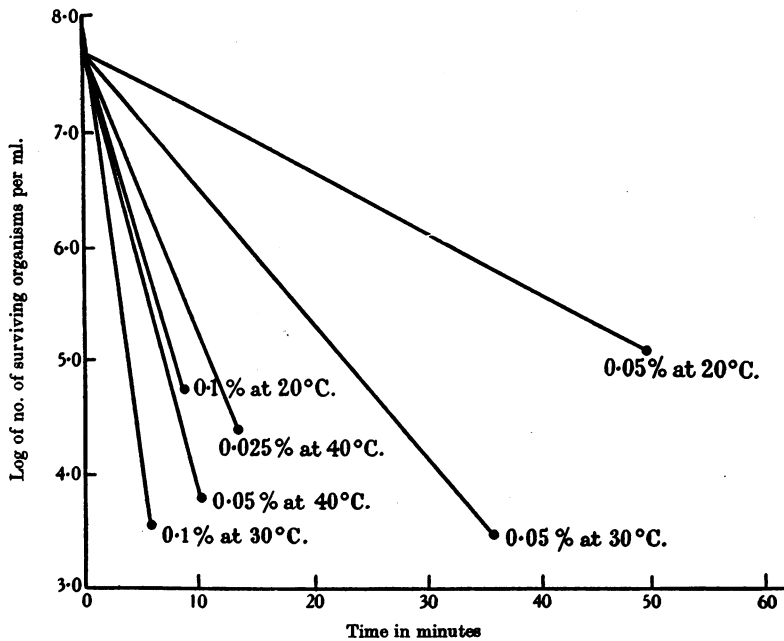


FIG. 3.—Rate of death of *B. coli* when submitted to different concentrations of sodium hydroxide at different temperatures (Hobbs and Wilson, 1942).

rather stringent test showed that the screwed-down lid is completely watertight. At the end of this trial period the concentration of NaOH was found to be 0.1031 per cent. as compared with a wax-lined sealed bottle kept at

room temperature which showed a loss of caustic soda from 0.1098 to 0.1060 per cent. during the same period. The difference between the two samples, 2.9 per cent., is significant. It is possible that a trace of carbon dioxide passes through the polythene wall. It is certain that 0.1 per cent. caustic soda is a safe storage medium for several months at room temperature.

A further control, in which the polythene container was two-thirds filled with disks of methyl methacrylate one mm. thick, giving a total surface area of approximately 700 cm²., was similarly filled with 40 ml. nominal 0.1 per cent. caustic soda and kept for 5 weeks at incubator temperature. This showed a fall from 0.1098 to 0.097 per cent. in 5 days and from 0.097 to 0.060 per cent. in 5 weeks, which indicates a progressive release of acid or fixation of alkali by the methyl methacrylate.

Two observations seem pertinent. The small amounts of acrylic material used in the stand supporting the lenses and in the lenses themselves can have no significant effect upon the concentration of the caustic soda solution. The possibility that methyl methacrylate, in the presence of dilute caustic soda, liberates progressively a minute amount of co-polymerized methacrylic acid is interesting and may well merit further study. The amount is very small. If, however, the equivalent amount of methacrylic acid were liberated from an acrylic implant it might be relevant if it were not eliminated from the eye. All the evidence is against this possibility having significance, since the reactions which have been observed when these lenses have been introduced have been greatest in the early stages. To minimize this possibility the lenses should be stored in 0.1 per cent. caustic soda for 3 months before being re-sterilized and issued for use.

Gloves.—Both in sterilizing and subsequently at operation, it is important to remember that rubber gloves must not be treated with talcum or other dusting powder. In handling caustic soda solutions, rubber gloves, sterilized by boiling in sterile distilled water, should be used wet.

Procedure at Operation

The equipment reaching the surgeon will be a sealed polythene container containing four lenses in a rack (Fig. 4, opposite), a hard glass tube of sodii. bicarb. 0.5 per cent. in distilled water which has been autoclaved after sealing, and a pair of dry, heat-sterilized lens forceps in a sealed glass tube. The container and the glass tubes are placed in spirit to sterilize them externally and are then dried with a sterile towel and placed upon the operating table.

The procedure is as follows:

- (1) Remove the screw-cap and, holding the centre pin with the index finger, pour out the 0.1 per cent. caustic soda.

(2) Open the ampoule and pour the sodii, bicarb. 0.5 per cent. into the container; replace the screw-cap firmly.

(3) Shake thoroughly and leave to stand upside down, so that the lenses and their racks are fully immersed, for 5 minutes.

(4) Remove the screw-cap and pour out the sodii. bicarb. solution.

(5) Lift off the retaining plate. Pick up the lens with the special lens forceps, which have been boiled in distilled water and subsequently sterilized by dry heat, and insert it directly into the eye.

The forceps must not be dipped in any detergent and it is unnecessary to dip them in any fluid whatever. The lens in its tray is sterile and wetted with only a trace of 0.5 per cent. bicarbonate solution. Contamination of either the lens or the forceps during this manoeuvre must be avoided.

Similarly, the special forceps should be kept dry and apart from any possibility of contamination on the table before use.

If rubber gloves are worn by the surgeon or any of his assistants they must not be dusted with talc or any other powder. Cotton gloves or no gloves are preferable. The possibility of introducing talc or other dusting powder into the eye must be excluded absolutely.

Attention may be drawn at this point to the need for the greatest care to be exercised with regard to the anterior chamber wash-out. Relatively large volumes of wash-out are often used in the Harold Ridley operation. The saline should be freshly made up with pyrogen-free distilled water, and should be a Ringer solution such as may be prepared with British Drug Houses tablets No. T.13867.B., one tablet per 540 ml. of water. The solution should be autoclaved. Alternatively, a sterile Ringer solution made up with pyrogen-free distilled water (e.g. Allen and Hanbury Sterivac No. 9: 500 ml.) may be used. The temperature of the irrigating fluid should be 37° C. (98.4° F.), and the irrigation apparatus should be free from foreign particles, detergent, or other contaminants. A Luer Lock glass syringe coated with Silicone grease with a

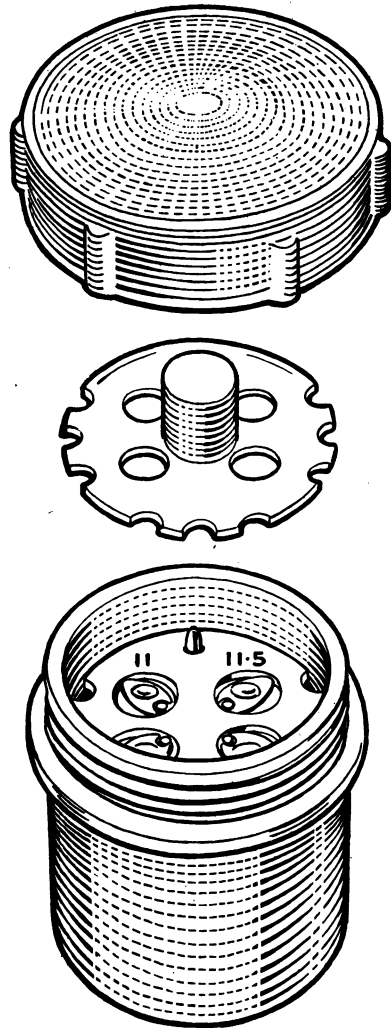


FIG. 4.—Container and method of transporting acrylic intra-ocular lenses (Messrs. Rayner). Strampelli lenses are illustrated. The lower diagram shows the polythene container in which is an acrylic stand carrying four lenses in counter-sunk recesses numbered to identify the four different lenses submitted in each case. Above this is the retaining plate which lies over the lenses localized by a centring pin. The central boss is so designed that, when the retaining plate is in position and the screw-cap illustrated above is screwed down to its flange, all slack in the assembly is taken up and the lenses are localized, but not gripped or in any way distorted.

metal cannula, washed in distilled water and sterilized by dry heat, is preferable to apparatus consisting of rubber and metal tubing which may hold foreign particles or fluids, cannot be fully inspected, and cannot be sterilized by dry heat.

Disposal of Equipment.—When the operation is completed the unused lenses are replaced in their rack, and the empty container is closed and returned to the makers.

Discussion

The procedure laid down is believed to satisfy the requirements defined in the earlier part of this paper:

(1) The material, polymethyl methacrylate, Transpex I (I.C.I.), is inert and is believed to be incapable of evoking a sensitization response in the tissues.

(2) Conditions to be observed during manufacture are laid down.

(3) The process of cleaning described removes any contamination introduced during manufacture without incurring the possibility that harmful material may be carried into the eye.

(4) The sterilizing programme is stringent and the conditions of storage give full protection against infection.

(5) The caustic soda, 0·1 per cent., used for storage is instantly destroyed by 0·5 per cent. sodium bicarbonate introduced in great excess. The resulting ions, sodium and carbonate, are in less than their normal physiological concentration in the tissues, while the bicarbonate in solution is harmless.

(6) We are left with the possibility that during storage some of the caustic soda solution may have been absorbed by the acrylic. The material can absorb up to 0·5 per cent. by weight of water. It is thus possible that, for a Harold Ridley lens weighing about one-tenth of a gramme, one two-millionth part of a gramme of caustic soda might be left in the lens after washing with sodium bicarbonate; for a Strampelli lens the figure would be even less. This minute trace of caustic soda would diffuse out very slowly; the sodium ion is harmless, and the hydroxyl ion will be trapped instantly by the 0·18 per cent. of sodium bicarbonate normally present in the tissue fluids and rendered harmless as carbonate.

It is thought that this rigorous method of manufacture, cleaning, sterilization, and ultimate surgical use may remove many of the disadvantages that have hitherto attached to the use of acrylic implants in ophthalmology.

Summary

(1) The properties necessary in a material to be used as an implant in the eye or other tissues are defined.

(2) Conditions of manufacture necessary to ensure that the prosthesis produced is safe are laid down.

(3) The physico-chemical behaviour of acrylic material is examined and a method of cleaning and sterilizing the prosthesis is described.

(4) A method of storing the prostheses in a special rack immersed in 0.1 per cent. caustic soda in a screw-cap container is described.

(5) The technique of employing this equipment in the operating theatre is detailed.

(6) Emphasis is laid upon the use of dry forceps, not contaminated with any detergent or other antiseptic, to place the prepared lens directly into the eye, and upon the avoidance of any possibility of contamination with talc or other glove powder.

My thanks are due to Lewis B. Holt, D.Sc., Wright Fleming Institute; to the Research Department, Plastics Division, I.C.I., and to the Research Department, Biological Group, Pharmaceuticals Division, I.C.I., for their generous help and advice in the preparation of this paper; to the Photographic Department, Institute of Ophthalmology; and to Messrs. Rayner (London) for the use of Fig. 4, illustrating the equipment they have designed, and for their co-operation in presenting Harold Ridley and Strampelli lenses in conformity with the principles and methods of manufacture and sterilization laid down.

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