Testing Of Plastics Used For Extra-Corporeal Circulation

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In the manufacture of plastics to be used for extra-coporeal circulation it is necessary to have conclusive proof that the final product will be compatible with blood, tissue and biological fluids. To obtain such proof, the plastic must be tested to show that it is non-toxic, non-hemolytic and non-pyrogenic. Sensitive bio-assay procedures have been developed to detect any toxic effect of the basic plastic resin itself, as well as any of the ingredients which may be added to the basic polymer for purpose of stability of flexibility.

The most popular plastic material used for extra-corporeal circulation is Polyvinyl Chloride (PVC), which will be discussed in this paper, and is obtained by the polymerization of Vinyl Choride and, in its pure form, is an inert, rigid substance, yellowish in color and softens when heated. By further fusion with other substances, generally known as plasticizers, the rigidity of the material can be modified to produce varying degrees of flexibility, dependant upon the quantity of plasticizers added. Stabilizers are then added to help prevent high temperature decomposition. Also, modifiers can be added to obtain clarity, color, radio-opacity or other charateristics required.

All ingredients used for the plasticizers, stabilizers and modifiers are listed in the Federal Register of the Food and Drug Administration. U. S. Department of Health, Welfare and Education and meet the requirements, when tested according to methods recommended in the "Pharmacopoeia of the United States" and "National Formulary".

The test described hereafter was developed by Marcel Nimni, Ph.D. of Bio-Technics Laboratories and was found best suited to detect the degree, if any, of toxicity in PVC Perfusion Tubing after all processess were completed by the manufacturer and was ready for actual perfusion.

Acute Toxicity

A group of ten (10) Swiss mice were injected intravenously via the marginal tail vein using a 27 gauge needle. The solution to be injected was prepared by extracting the plastic material with pyrogen free narmal saline solution (10 gm. per 100 ml. of solution) at 15 psi of pressure for 30 minutees. Observation was made for appearance of any toxic effect.

Tissue & Intermuscular Implantation.

Three (3) Wistar rats and one (1) New Zealand white rabbit were used as test animals. Rats were implanted subcutaneously with the test samples under light anesthesia. After shaving the dorsal area, a transverse incision through the skin was made in the lumbar region. Using the blunt end of forceps, the skin and separated from the underlying connective tissue and the plastic samples were positioned using another forcep in the subcutaneous tissue, not closer than 30 mm. from the wound. The incision was sutured with 11 mm. nickel-silver clips. Samples were removed after periods of 3, 7 and 14 days and tissue studies were conducted for tissue irritation.

Intermuscular implants were made with rabbits anesthetized with sodium (20 mg./Kg.) and ether. Implants were made with a special pellet implanter at the level of the dorsal paravertebral musculature. Samples implanted in the leg muscle were done in duplicate. These sites are checked for irritation on the seventh post-operative day.

Pyrogen Assay

Three (3) rabbits are used for each sample. Tests were conducted in accordance with methods recommended in the U.S.P. XVI and N.F. XI using tested pyrogen free saline. The temperatures of the rabbits are recorded pre-operatively, then each hour for three hours post-operatively.

Hemolytic Effect Of Plastic

The special prepared solution used for acute toxicity tests is also used to determine the hemolytic effect of plastic. A fresh drop of freshly collected rabbit blood is placed in contact with the 10% isotonic extract and signs of hemolysis are recorded.

The same solution is diluted with with distilled water over a range that would initiate hemolysis in orded to test osmotic fragility. The behavior of these samples is then compared to similar dilutions made with normal saline and significant differences are recorded.

Finally, a two part procedure checks storage characteristics and the morphology of blood cells. Heparinized rabbit blood obtained by cardiac puncture was stored in the presence of the plastic under investigation. The degree of heomlysis was recorded at time intervals of 12, 24 and 48 hours.

The cells from heparinized plasma stored in the presence of the plastic material, in a sterile container at 4°C. during 24 hours where observed for morphological alterations. They were compared to a control preparation under the same circumstances. A smear was strained and cell morphology observed.

The conclusions from all of these studies are expressed in measurement of the plastic's compatability with tissue and body fluids and its toxic, hemolytic and pyrogenic characteristics. To the manufacturer, this study and report is his measurement of product quaility; to the extra-corporeal technician, his guarantee of his patient's safety.

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