

Journal of Dental Research

<http://jdr.sagepub.com>

Medical Applications of Plastics

Fred Leonard

J DENT RES 1966; 45; 1657

DOI: 10.1177/00220345660450061401

The online version of this article can be found at:

<http://jdr.sagepub.com>

Published by:



<http://www.sagepublications.com>

On behalf of:

International and American Associations for Dental Research

Additional services and information for *Journal of Dental Research* can be found at:

Email Alerts: <http://jdr.sagepub.com/cgi/alerts>

Subscriptions: <http://jdr.sagepub.com/subscriptions>

Reprints: <http://www.sagepub.com/journalsReprints.nav>

Permissions: <http://www.sagepub.com/journalsPermissions.nav>

Citations <http://jdr.sagepub.com/cgi/content/refs/45/6/1657>

Medical Applications of Plastics

FRED LEONARD

*U.S. Army Medical Biomechanical Research Laboratory,
Walter Reed Army Medical Center, Washington, D.C.*

The first section of this report deals with what is generally known to date about synthetic polymers used as surgical repair materials and implants. The second section deals with investigations at Walter Reed Army Medical Center of the homologous series of normal alpha cyanoacrylates, from methyl to octyl, to be used as tissue adhesives and hemostasis-inducing compounds. These compounds effect stoppage of blood by sealing vessels. Some of this latter work has been reported.^{1,2}

Recent advances in surgery have increased the need for providing polymeric materials that can be used in replacing or repairing tissues and organs lost as a result of trauma or disease. The wide range of mechanical properties available in polymers make them attractive candidates for such applications. Although a polymer may possess the desired mechanical properties, however, there is no assurance that it may be used successfully in the body. Biological receptivity is the sine qua non for the long-term utilization of a surgical repair material.

Surgical repair polymers may be of two general types, biostable and biodegradable. Biostable: The interaction between the host and the implant is expected to be minimal, and the implant is expected to maintain its integrity for a lifetime. Biodegradable: The implanted material is expected to degrade at a desirable rate and the products of degradation are expected to be excreted through the normal excretory routes with none of the materials becoming stored in tissues or organs.

The stability or instability of the polymers is dependent on the structure of the polymer and the chemical environment of the organism. An estimation of the reactions of significance in the organism indicates that some of the well-known mechanisms for degradation of polymer molecules are possible in the body, including both oxidative and hydrolytic types.³

Nylon, for example, loses up to 50 per cent of its tensile strength after a year's implantation, presumably due to hydrolytic scission of the amide linkage. Radioactive entities appear in rats' urine from the subcutaneous implantation of C¹⁴-tagged polyethylene after approximately 30 days, possibly as a result of oxidative scission of the polyethylene chain.⁴

Standard methods exist for slowing down the rate of attack on an implanted polymer. These include the preparation of crosslinked, oriented, or highly crystalline polymers as well as polymers with a chain backbone, particularly, that does not contain labile groups. Similar principles relating to the synthesis of stable, highly polymeric materials in environments with which polymer chemists usually deal may be expected to be operative for polymer implants to be used in the body.

Stability studies of some well-known polymers that have been used as implants have been previously reported.^{5, 6}

Suppose now that one can prepare a highly stable polymer. Is there any assurance that the polymer will be biologically receptive? The factors that influence biological receptivity of stable polymers are not known with certainty at present.

The effect of polymers on the tissues may be divided into two general types. There are local effects surrounding the polymer implant and more remote or systemic effects. Among the possible local effects of the polymer on the tissues are acute inflammatory responses accompanied by cell and tissue death or injury, exudate formation, and vascular response, such as redness, as well as more long-term effects such as tumor induction and carcinogenicity.

Among the more remote and systemic polymer effects may be listed antigenicity, hypertension, nephritis, and polymer deposition in various internal organs, resulting in tumors.

The amount of tissue injury and cell necrosis depends on the nature of the irritant. Polymers such as dacron, silicone, and polyethylene are insoluble and "stable" in the body environment and elicit minimal response; in general, they show a typical benign foreign body response. A polymer such as methyl alpha cyanoacrylate elicits an inflammatory response and cell necrosis.

Cell injury or death may lead to the release and degradation of materials normally contained in cells. These substances then may produce effects on local tissue structure and, when absorbed into the blood stream, may affect distant organs.

Tumor formation from polymers is the result of long-term residence in the biological environment and may result from polymers that seem to be quite stable in the body. A considerable amount of literature has been produced in this area of research.

As a result of studies in a particular type of rat, present indications are that all polymers (or other materials), when implanted in film form, elicit malignant tumors; whereas, polymers of the same molecular structure in powder, textile, or porous form do not.

The concept has arisen that nonporous films cast a "metabolic shadow" that interferes with cellular-extracellular exchanges, leading to faulty metabolism. Tumor induction by polymer has been limited to rats, mice, and hamsters, however, and has not been reported yet for dogs or primates.

What are the parameters involved in preparing tissue-compatible materials? What is the relationship between polymer structure and tissue receptivity? What is the effect of the physical and chemical properties of the polymer surfaces and of physical form? What biological end points does one utilize to determine the biological receptivity of a material?

The answers to these questions are not known with certainty at present, and one cannot predict, *a priori*, whether a given polymer will be compatible. Each polymeric material considered for a specific application must be tested empirically, under conditions of intended use in laboratory animals and, if salutary results are obtained, eventually in human beings.

One of the more important research programs on the surgical application of polymers at this center consists of the development of tissue adhesives for use in nonsuture

closure of wounds. The capability of rapidly polymerizing alpha cyanoacrylates to adhere firmly to moist surfaces has evolved considerable medical interest in their potentialities as hemostatic agents and tissue adhesives for closure of wounds in place of, or as adjuncts to, conventional surgical sutures. The requirements for a tissue adhesive are: (1) Ability to polymerize rapidly and to effect a bond between relatively wet surfaces, and (2) biodegradability, so that the adhesive may be applied as a continuous film for the formation of a seal of optimum strength and then slowly disappear from the site of application, not serving as a barrier to healing, and eventually being replaced by the body's own contiguous tissue.

Medical evaluation of methyl alpha cyanoacrylate has revealed that: (1) Adhesive monomer can adhere to tissues of a variety of types and after a time, healing occurs at the bonded site. (2) Both monomer and polymer are histotoxic and elicit acute inflammatory response. (3) The polymer disappears after a time from its initial point of application, indicating that biodegradation was occurring.

Studies were undertaken at this laboratory to determine the nature of the degradation and the products that were produced. The data indicated that in the presence of distilled water alone, *in vitro*, polymethyl alpha cyanoacrylate underwent disastrous chain scission, producing formaldehyde (which was positively identified by derivative formation) and ultimately a cyanoacetate, both of which are toxic substances.

To elucidate structure-tissue reactivity relationships and ultimately develop a less necrotizing adhesive for use in wound closure, the synthesis and medical evaluation for the homologous series of alpha cyanoacrylates were undertaken. It was postulated that the higher homologs would degrade at a slower rate because of their more hydrophobic nature.

The results of the studies to date indicate that, as the homologous series is ascended, the tissue tolerance to monomers and polymers becomes greater. Concomitantly, in accordance with prediction, it has been demonstrated that as the homologous series is ascended, the rate of biodegradation decreases.

The butyl derivative seems to be well tolerated, and it is being actively applied in

animals for wound closure in the oral cavity and in internal organs, particularly in surgically injured livers and intestines. Its application as a burn dressing is under study.

Attempts to induce hemostasis with this series of compounds indicate that it is possible to use them to stop capillary and venous bleeding. The results obtained in arterial bleeding are equivocal.

Summary

Advances in synthetic polymer chemistry have resulted in the production of organic polymers which may have great potential in the repair of damaged tissues or organs. Research in the field of surgical repair polymers is comparatively new and as yet polymer structure tissue compatibility relationships and quantitative biological testing technics have not been clearly delineated. It is not possible now to predict, a priori, whether a polymer will be biologically compatible. Each material must be tested empirically.

At Walter Reed Army Medical Center, an interdisciplinary group is engaged in the

synthesis, characterization, and evaluation of polymers in specific surgical repair applications of important military value, as well as in more basic studies designed to elucidate structure activity relationships and to quantitate evaluation technics. It is hoped that, through this research, knowledge will evolve that will make it possible to tailor surgical repair polymers of long-term utility.

References

1. WOODWARD, S. C., HERRMANN, J. B., CAMERON, J. L., BRANDES, G., PULASKI, E. J., and LEONARD, F. The Histotoxicity of Cyanoacrylate Adhesives in the Rat, *Ann. Surg.*, **162**:113-22, 1965.
2. CAMERON, J. L., WOODWARD, S. C., PULASKI, E. J., SLEEMAN, H. K., BRANDES, G., KULKARNI, R. K., and LEONARD, F. The Degradation of Cyanoacrylate Tissue Adhesive, *Surgery*, **58**:424-30, 1965.
3. KARLSON, P. *Introduction of Modern Biochemistry*. New York, Academic Press, 1963.
4. OPPENHEIMER, B. S., OPPENHEIMER, E. T., DANISHEFSKY, I., STOUT, A. P., and EIRICH, F. R. Further Studies of Polymers as Carcinogenic Agents in Animals, *Cancer Res.*, **15**:333-40, 1955.
5. HARRISON, J. H. Synthetic Materials as Vascular Prostheses, *Amer. J. Surg.*, **95**:3-24, 1958.
6. MOLONEY, G. E. The Effect of Human Tissue on the Tensile Strength of Implanted Nylon Sutures, *Brit. J. Surg.*, **48**:528-30, 1960.