Segmented Polyurethane: A New Elastomer for Biomedical Applications

Abstract. *A segmented polyurethane elastomer, originally developed for elastic thread, is now being used for molded prostheses. Performance of this material when used for components of a heart-assist system warrants a thorough investigation of its effectiveness in a variety of biomedical devices.*

In the course of a research project on artificial heart-assist devices at the National Institutes of Health, we evaluated a variety of elastomeric materials for incorporation in an implantable, roller-type heart pump (*1*). The fact that segmented polyurethane, a polyether polymer (*2*) which until recently had been available only in thread form as Lycra (*3*) spandex, has been successfully used in vivo suggests its use in a wide variety of prosthetic devices such as cannulas, catheters, heart valves, and pacemaker lead-wire insulation.

The usefulness of Lycra spandex is related to the retention of its elastic properties after repeated washing in hot water (*4*). For biomedical use, an evaluation of resistance to hydrolysis seemed necessary, in view of the poor performance in vivo of a polyester urethane used by Mirkovitch *et al.* (*5*). Tests showed that segmented polyurethane (*6*) gained only 5 percent in weight when autoclaved, as compared to 12 percent for the polyester. In addition, its appearance was unchanged, whereas the polyster was blanched and distorted. Ossefort (*7*) demonstrated the susceptibility of polyester urethane to hydrolysis and substantiated the greater stability of polyether-based elastomers. These properties have been shown to be characteristic of urethane foam (*8*).

We determined the short-term effect of blood on segmented polyurethane by immersing it in citrated bovine blood at 37°C for 28 days. No significant degradation of tensile properties was observed, although all samples were uniformly altered in color from white to tan. This discoloration appears to be related to the ability of segmented polyurethane to accept pigments—a feature of commercial value for dyeing fabric.

Prosthetic tubing of practical wall thicknesses cannot be extruded from the polymer by conventional means because of the high concentration of solvent normally present. Extrusion of dry granules results in thermal degradation. We devised the following effective method: (i) the polymer "dough" is applied to a suitable mandrel, (ii) the form is dried to remove the solvent, and (iii) the desired contours are stabilized by a "heat set." This method provides a variety of shapes and sizes to close tolerances with smooth, dense, high-gloss surfaces and does not require expensive molds or special molding equipment.

When segmented polyurethane tubing was used in our roller pumps and implanted in 22 calves, no tubing failures and no changes in tensile properties were observed after continuous operation for as long as 9 days (*9*). Silicone rubber tubing tested under similar circumstances failed in flexure within 2 days and showed 50-percent loss in stress at 100-percent elongation. Several physical properties of segmented polyurethane and of two other elastomers are given in Table 1.

The clotting time in vitro on segmented polyurethane surfaces was compared with that of other materials by a modified Lee-White test on freshly drawn canine and human blood at 37.5°C (Table 2). No standard test for coagulation in vivo is available; however, atrial cannulas and vascular tubing were successfully used as components of a ventricular bypass pump in calves for 1-week periods (Figs. 1 and 2). The components were free of thrombus, and emboli were not observed.

Using the surgical procedures of Gott *et al.* and Whiffen *et al.* (*10*), we placed one ring, fabricated of stainless steel coated with segmented polyurethane, in the inferior vena cava of each of ten dogs. After the usual 2-hour period of exposure to the blood stream—an interval during which most polymer rings not treated with heparin occlude—all ten rings remained patent with only traces of clotting on most.

After Wagner *et al.* (*11*) had placed Lycra sutures in the skin, liver, and bowel, they found little or no reaction to this foreign body or evidence of tumor induction. Our studies, with implantation of patches of the polymer in dogs for a period of 4 weeks, revealed no tumor induction. Although it has been reported that a variety of polymers, including polyurethane and a widely used, implantable silicone rubber, have induced malignant tumors in experimental animals, this has never been shown to occur in man. At present, there are no satisfactory tests to evaluate

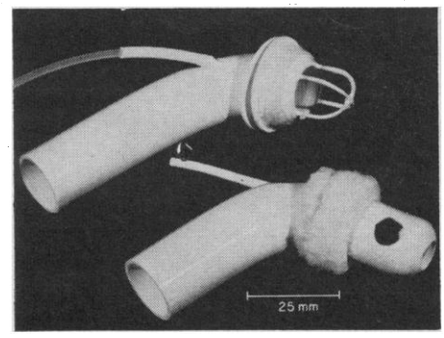

Fig. 1. Possible shapes and smoothness of surfaces of atrial cannulas.

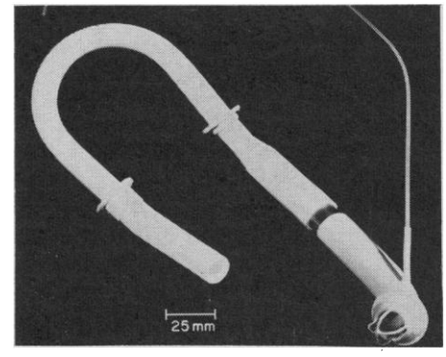

Fig. 2. Complete prosthetic tube for a heart-assist (left ventricular bypass) pump made from segmented polyurethane.

Table 1. Comparison of typical physical properties. The test used for tensile strength, stress, and elongation was ASTM D412-51T; for hardness, it was ASTM D676.

Property	Segmented polyurethane*	Polyester urethane†	Silicone rubber‡
Tensile strength (lb/in.²)	6700	5840	1290
Stress at 100 percent elongation (lb/in.²)	850	700	160
Elongation at break (%)	750	540	560
Hardness (shore A)	75	88	50
Specific gravity	1.1	1.2	1.1

* Polymer T-125, E. I. du Pont de Nemours and Co., Inc. (*9*, *12*). † Estane 5740x1 (virtually cross-linked) data sheet; B. F. Goodrich Co., Cleveland, Ohio. ‡ Silastic 9711, Dow Corning Corp., Midland, Michigan (*9*).

Table 2. Effect of segmented polyurethane and several other surfaces on blood coagulation. Clotting time, given in minutes, represents average value of eight tests each. Silicone rubber is Silastic RTV 382, Dow Corning Corp.

Surface	Clotting time	
	Canine	Human
Glass (pyrex)	10.5	13.1
Siliconized glass	18.4	23.2
Silicone rubber	18.3	27.0
Segmented polyurethane	19.6	27.0

such reactivity. The performance of this new polymer in our study warrants a thorough investigation of its applicability as a prosthetic material in diverse circumstances.

JOHN W. BORETOS
WILLIAM S. PIERCE*
National Institutes of Health, Bethesda, Maryland 20014

References and Notes

1. W. S. Pierce, M. C. Turner, J. W. Boretos, H. D. Metz, S. P. Nolan, A. G. Morrow, *Trans. Amer. Soc. Artif. Intern. Organs* **13**, 299 (1967).
2. Patent to W. Steuber (to Du Pont Co.) for elastic filaments of linear segmented polymers, U.S. patent 2,929,804 (22 March 1960).
3. Trademark, E. I. du Pont de Nemours and Co., Inc.
4. E. Hicks, A. Ultee, J. Drougas, *Science* **147**, 373 (1965).
5. V. Mirkovitch, T. Akutsu, W. Kolff, *Trans. Amer. Soc. Artif. Intern. Organs* **8**, 79 (1962); Estane 5740x1, trademark, B. F. Goodrich Co., Cleveland, Ohio.
6. Polymer T-125, supplied through the courtesy of Textile Fibers Department, E. I. du Pont de Nemours and Co., Inc., Wilmington, Delaware.
7. Z. T. Ossefort and F. B. Testroet, *Rubber Chem. Technol.* **39**, 1308 (1966).
8. S. Steingiser, W. C. Darr, J. H. Saunders, *ibid.* **37**, 38 (1964).
9. Physical testing was done by Dr. R. Stiehler and G. Decker of the National Bureau of Standards, using American Society for Testing and Materials (ASTM) procedures for determining tensile properties.
10. V. L. Gott, D. E. Koepke, R. L. Daggett, W. Zarnstroff, W. P. Young, *Surgery* **50**, 382 (1961); J. Whiffen, R. Dutton, W. P. Young, V. L. Gott, *ibid.* **56**, 404 (1964).
11. M. Wagner, G. Reul, J. Teresi, K. L. Kayser, *Amer. J. Surg.* **3**, 838 (1966).
12. We thank Dr. H. Kobsa and F. Briggs of the Du Pont Textile Fibers Department, Waynesboro, Virginia, for materials and recommendations.

* Present address: Surgical Department, Reading General Hospital, West Reading, Pa.

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Control of Aldosterone Secretion by the Pituitary Gland

Abstract. *In the rat, the pituitary gland is essential for the stimulation of aldosterone secretion by sodium depletion. Hypophysectomy abolishes the response to sodium depletion, whereas whole pituitary gland injections partially restore it. The response cannot be restored by injections of either adrenocorticotropin or growth hormone, nor by adrenocorticotropin plus thyroxin. The pituitary gland must secrete a hormone or possibly several hormones which are necessary for the adrenal gland to respond to sodium depletion.*

Sodium depletion is a potent stimulus of aldosterone secretion. In dog and man, the renin-angiotensin system plays an important role in this response (*1*). The evidence in sheep (*2*) and rats is not so clear (*3–5*).

The role of the pituitary in the regulation of aldosterone secretion has not been fully defined. Injections of adrenocorticotropin (ACTH) into normal dogs or those depleted of sodium (*6*) or into man (*7–9*) markedly stimulate aldosterone secretion initially. In man, with continued ACTH treatment, the secretion rate returns toward control values and even below in rare instances. Dogs (*10*) and rats (*11*) that have been hypophysectomized and humans (*12*) with hypopituitarism show a diminished response of aldosterone secretion to sodium depletion. This has usually been attributed to ACTH deficiency. However, by simultaneous infusion of angiotensin II and ACTH into hypophysectomized, nephrectomized dogs, Mulrow and Ganong (*13*) were not able to stimulate aldosterone secretion to the extent observed in sodium-depleted dogs. Hypophysectomy produced a greater reduction in aldosterone secretion in dogs with secondary hyperaldosteronism than nephrectomy did (*14*). This marked effect was attributed to the absence of ACTH. Nevertheless, this effect of hypophysectomy occurred in conscious, trained dogs with low rates of corticosterone secretion, an indication of low ACTH activity before hypophysectomy.

We studied the role of the pituitary in the response of aldosterone secretion to sodium depletion. Our results indicate that, in the rat, the pituitary is essential for the response and that the pituitary factor is not ACTH.

Male Sprague-Dawley rats (150 to 200 g), either intact or hypophysectomized, were obtained from the Charles River Breeding Laboratory. Upon arrival in the laboratory, the rats were fed for 9 to 14 days either a diet low in sodium or a diet considered to be normal in sodium (*15*). At the end of the experimental period, plasma was collected from the left lumboadrenal vein and was assayed for aldosterone by the double-isotope derivative method (*16*). In most cases, plasma from the lumboadrenal vein was also analyzed for corticosterone by the acid fluorescence method (*17*). The rate of corticosterone secretion and the adrenal gland weight were taken as indexes of ACTH activity. The sodium and potassium concentrations in arterial plasma were also measured.

The results from hypophysectomized rats fed either the normal or low-sodium diets were compared with those from similarly fed intact rats or hypophysectomized rats that had received an intramuscular injection of a whole rat-pituitary gland each day. The pituitary glands, obtained fresh from rats decapitated for other experiments, were frozen until used.

The effect of injections of ACTH on aldosterone secretion was also determined in hypophysectomized rats fed the two diets. In other experiments, the response of sodium-depleted, hypophysectomized rats to treatment with ACTH and thyroxine or to injections of growth hormone was studied. All injections were made each morning of the experimental period, including the day on which the experiment was terminated. The doses of hormones administered were: ACTH, 8 units; thyroxine, 20 μg; and growth hormone, 1 mg.

Acthar gel (*18*) was injected subcutaneously. Thyroxine (*18*), dissolved in distilled water which had been adjusted to *p*H 9.5 with 0.1*N* NAOH, was injected intraperitoneally. The amount of sodium administered with each injection was less than 0.0001 meq. Growth hormone (NIH-GH-B12, 0.97 U.S.P. unit/mg) was also dissolved in distilled water adjusted to *p*H 9.5 as above, but it was injected subcutaneously. Between 2.0 and 3.0 ml of blood from the lumboadrenal vein were collected from each rat. Collection of these samples was begun 0.5 to 5.0 hours after the final injection of the test substance. Those rats receiving the combined therapy of ACTH and thyroxine were given 50 mμ of ACTH intravenously just prior to collection of samples, instead of a final subcutaneous injection of ACTH on the morning of the adrenal vein cannulation.

In hypophysectomized rats, there was no stimulation of aldosterone secretion after sodium depletion (Tables 1 and 2), even though the width of the zona glomerulosa increased. When whole rat pituitary glands were administered to hypophysectomized rats that had been fed a low-sodium diet, there was a marked stimulation of aldosterone secretion. In the sodium-depleted group, this secretion was about nine times that found in the untreated, hypophysectomized rats, but there was only a