Journal of Macromolecular Science, Part A

Persistent Polarization in Polymers and Blood Compatibility

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Persistent Polarization in Polymers and Blood Compatibility*

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SUMMARY

The use of persistent electrical polarization in polymers has been explored as a means of reducing surface thrombogenicity. Parallel efforts have been carried out on the characterization of surface properties related to the electret state in polymers, on the stability of the electret state in desirable prosthetic materials under simulated blood pumping conditions, and on in vitro and in vivo blood compatibility experiments. Preliminary correlations among critical surface tension, electrical polarization, and blood compatibility have been obtained. In vitro blood compatibility has been explored using both a modified Lee-White clotting test and a platelet adsorption experiment. No significant difference in clotting time was found for polarized samples; however, those with a negative charge did adsorb fewer platelets. A series of in vivo studies

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has been carried out using electrified right atrial flags (36) of poly-vinylidene chloride and vena cava rings (22) of FEP Teflon, Hypalon rubber, and Hypalon/2% polysulfonate. Negatively polarized samples showed improved blood compatibility in all cases. About 2/3 of the negatively charged atrial flags showed little or no thrombus and the remainder moderate thrombus whereas 2/3 of the positively charged flags showed severe thrombus. About 3/4 of the negative ring implants showed little or no thrombus. A correlation with anomalous contact angle or low charge was found in 4 of 6 cases of the rings with mod-erate to heavy thrombus.

I. INTRODUCTION

Our group at Thermo Electron and Children's Hospital Medical Center has been working under contract to the National Heart Institute for the last 3 years on the development of blood compatible materials. We have been exploring the use of persistent electrical polarization, often termed the electret effect, to improve the thrombus resistance of polymers.

Since the early work of Abramson [1] on the electrical charge of blood cells, the role of bioelectric factors in maintaining patency through-out the vascular system has been documented in numerous studies. In recent years a series of studies relating surface electrical phenomena and thrombosis has been carried out in the laboratories of P. N. Sawyer and part of this work has been reviewed in a previous paper. Reports from the aforementioned laboratories have shown that the walls of blood vessels are porous and possess negative pore and surface charges [2] which can be modified [3] by both anticoagulants (increased negative charge) and coagulants (decreased negative charge). By extending the same rationale to foreign surfaces, the patency of metal prostheses has been correlated with the position of the metal in the electromotive series and with its spontaneous electrode potential in blood [4].

Similar trends relating charge and blood compatibility among non-metallic surfaces are evident; however, these materials exhibit quite different surface properties, and different mechanisms should be an-ticipated. Charged dielectrics, whether possessing bound ionic groups, adsorbed ionic groups, or internal charge, are static systems which interact with blood by means of double layer forces and chemical binding. Hence, these are rather passive systems compared with the

electrodynamic character of the normal porous endothelium or of reactive electronegative metals.

In spite of fundamental differences between the conducting and non-conducting surfaces, virtually all the surfaces which are "compatible" with blood in vivo are negatively charged. For example, a large number of materials has recently been evaluated for blood compatibility by implantation in the canine vena cava at Johns Hopkins University [5]. The surfaces which remained patent included 1) acrylic latex combined with a sulfonate detergent, 2) polyelectrolyte complexes with excess polyanion, 3) carboxy cellulose, 4) electrets of Teflon and of polysulfonate-cross-linked elastomers, 5) Heparinized surfaces, and 6) fluorinated silicones. All of the aforementioned surfaces have either a negative charge at physiological pH or a negative surface moment. On the other hand, some negative surfaces are not so thrombo-resistant. Glass is a well-known coagulant although it has a large negative zeta potential; carboxylation failed to improve the blood compatibility of silicone rubber [6]. Finally, Hageman factor is activated by a variety of negative surfaces [7] including collagen and sodium stearate (carboxyl groups), ellagic acid, Celite, and kaolin. Hence, in addition to negative charge, other properties such as surface morphology and chemical nature appear to be relevant to the development of better nonthrombogenic surfaces on dielectric metals.

Our work on electrically polarized polymers and elastomers will be described in the following sections. This work involves studies on the electret effect in several materials, including the characterization of surface electrical and physical properties, and on blood compatibility experiments.

II. SURFACE CHARACTERIZATION

A serious impediment to improved correlation between blood compatibility and surface electrical properties of dielectrics is the lack of adequate surface characterization. While no single measurement can provide such characterization, a series of techniques is available for exploring surface electrochemical properties. These include the measurement of charge by electrostatic and electrokinetic techniques, of critical surface tension, of morphology by optical and electron microscopy, and of chemical composition by spectrographic and microchemical analyses. We have carried out measurements of charge and of surface tension to date. We hope to apply some of the other techniques in the future.

A. Techniques for Characterizing the Electret Charge

Electrostatic techniques are usually employed to measure the electret charge; however, since electrets are to be used in blood, the electrokinetic techniques should be considered. We have made both electrostatic and electrokinetic charge measurements on electrets, but the electrostatic have been emphasized. The electrokinetic measurements have shown rather poor reproducibility to date; however, additional experiments are in progress. We believe this measurement may be of primary value as an indicator of surface adsorption and desorption. For example, most uncharged polymers show a negative zeta potential in aqueous media. Haydon [8] has explained this behavior on the basis of a stronger desorption of the cation (usually Na^+) compared to the anion (usually Cl^-) in solution. These negative zeta potentials generally imply rather large (several thousand esu/cm^2) negative charges for nonionic surfaces, but little if any correlation has been found between the charge measured in this manner and blood compatibility [9]. We hope that improved measurements will ultimately permit electrokinetic data to be exploited in this program.

The electret charge usually consists of two superimposed components of opposite polarity which yield a net surface charge. Two types of electrostatic charge measurement can be made on electrets; one gives the net surface charge in air and the second gives the internal polarization (either one or both components). The net surface charge measurement yields rather accurate charge values for hydrophobic materials such as Teflon when the levels of charge are low. Air breakdown limits the measurable charge to about 100 esu/cm^2; more highly charged surfaces may either be partly neutralized by air breakdown or a superimposed double layer may develop. Less hydrophobic surfaces sometimes adsorb water vapor which screens the net charge. The internal polarization measurement involves the release of polarization by heat and the analytic reconstruction of charge densities from the recorded charge release curves. These curves are more informative because of the multilayer characteristic of electret charge; however, curve interpretation is often difficult.

B. Measurement of Heterocharge, Homocharge, and Net Charge

We obtain the internal polarization by reheating an electret film while it is short-circuited through an electrometer and measuring the release of residual charge. A typical charge release curve is shown in Fig. 1 for two electrets of Kel-F. Both samples were heated simultaneously and the discharge currents and temperature recorded as a function of time. The
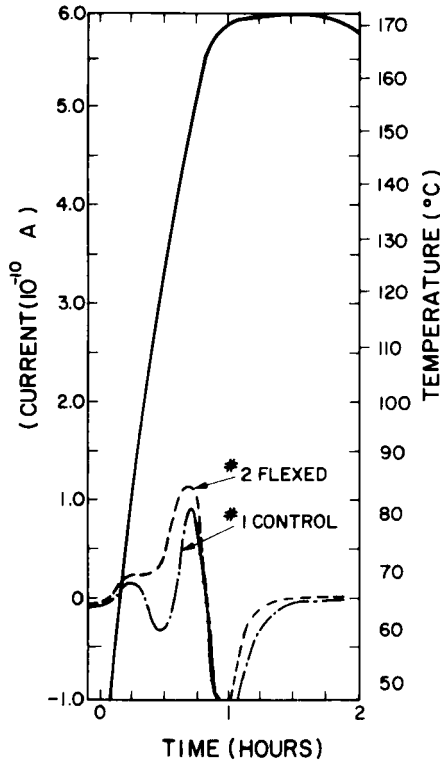
Fig. 1. Thermal discharge curves for internal polarization of Kel-F.

positive peaks were produced by release of heterocharge (a volume polarization produced by conventional dielectric absorption processes) whereas the negative peaks were produced by the release of homocharge (an ionic space charge injected into the surface during polarization by gas breakdown). The time integral of each peak gives the value of each component of charge. One current peak rather than the two shown in Fig. 1 is usually observed; a countercharge may be present in such cases, but it appears to be bound to the electret surface and does not contribute to the

Fig. 2. Net charge measurement by null voltage technique.

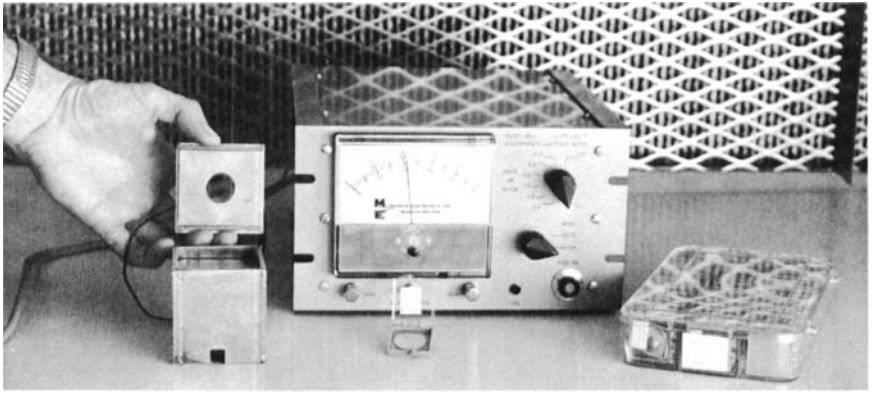measured current. When two peaks overlap as shown in Fig. 1, the curve integrals give lower limits for each component of charge.

The algebraic sum of heterocharge and homocharge is called net charge. Most of the published electret studies have relied on measurement of net charge only. We measured the net surface charge with a noncontacting vibrating probe voltmeter (Monroe Electronic Model 146-2) shown in Fig. 2. This instrument senses the electret surface voltage by means of a vibrating probe, applies a nulling bias to the probe, and reads the null voltage. The surface charge can be calculated readily from the null voltage and electret capacitance. The technique is simple, accurate, and nondestructive.

Typical measurements of net charge, heterocharge, and homocharge for five materials are summarized in Table 1. The materials listed are a polyvinylidene chloride copolymer, Saran I-8 (PVLC); a polychlorotrifluoro ethylene, Kel-F (PCTFE); a polytetrafluoro ethylene-cohexafluoropropylene, Teflon FEP (PFEP); a chlorosulfonated polyethylene, Hypalon 45 (Hypalon); and a polyether urethane, Estane 5714 (Urethane). Metal electrode contacts were used to polarize the electrets unless specified to the contrary.

Certain generalizations can be made for each material with respect to the polarization by referring to Table 1. PVLC showed only a hetero-charge peak on depolarization whereas the measured net charge was small and of the sign of the homocharge. On the basis of these two measurements we calculated that a surface homocharge of charge density slightly greater than the heterocharge must have been present. PFEP and PCTFE have smaller measured values of heterocharge and slightly higher values of net charge than PVLC. For FEP polarized with an ionized gas contact,

Table 1. Characterization of Electret Charge for Thin Polymer Films
(Typical Values of Charge Density in esu/cm^2. 1 μC = 3,000 esu)

Polymer	Net charge		Heterocharge,	Homocharge	
	Measured	Calculated	Measured	Measured	Calculated
PVLC	(-)10		(+)1000-5000		(-)1000-5000[a]
PCTFE	(-)30		(+)20-80		(-)50-110
PFEP	(-)30		(+)10-20		(-)40-50
PFEP (ionized gas)	(-)70	-90	Small	-90[a]	
Hypalon	0-1	(-)500-1000	(-)1000-5000[a]		(+)0-5000
Hypalon (ionized gas)	0-1		Small	-500-1000[a]	
Urethane	0-1		(-)1000-9000		(+)0-9000

[a]Charge values typical of implanted specimens.

in place of the metal electrode, a single homocharge peak was obtained; the charge density obtained for this peak agreed rather well with the measured net charge. Hypalon polarized under similar conditions also gave a large homocharge peak but the measured net charge was always small. Since the surface is slightly hydrophilic, we believe this anomalous behavior resulted from an adsorbed film of water screening the net charge.

C. Internal Charge Distribution

The electret charge has been related to specific ions and dipoles in a few well-defined crystalline materials [10]; however, such correlation has not been made for any polymers. We cannot establish a molecular mechanism on the basis of available data, but a schematic representation of charge can be given. Thus the typical charge distribution obtained for electrets of FEP Teflon polarized with an ionized gas contacting one surface is shown in Fig. 3. The homocharge is in excess, and it results from the injection of electrons and inert gas ions during polarization as shown in Fig. 3. The charge presumably is transferred to fluorocarbon chains and resides near the electret surface. The heterocharge is small and results from ionized impurities and oriented polar chain terminating groups.

We anticipate the elastomers Hypalon and Urethane, as well as polystyrene sulfonate-doped elastomers, to have a charge distribution of the sort shown in Fig. 4. These materials have a number of known ionic groups that should both diffuse and be oriented during polarization. For example, the polystyrene-sulfonate chains drift (depending on temperature and mobility) toward the positive pole during polarization and become oriented by the field whereas counterions drift in the opposite direction. Heat applied during polarization actuates free radical cross-linking agents which provide rigidity to the polarized configuration. This technique differs slightly from the more common polarization procedure in which the reduction in temperature alone freezes-in the configuration. Note that a heterocharge is formed in this case, and that an aqueous solution contacts the surface during polarization. Electrets formed in this manner have performed quite well in vivo, as we will describe shortly.

D. Contact Angle of Electret Surfaces

The surfaces of polymers used in charge studies and in blood compatibility studies are characterized by a contact angle measurement using a drop of water. We find this measurement valuable as a control
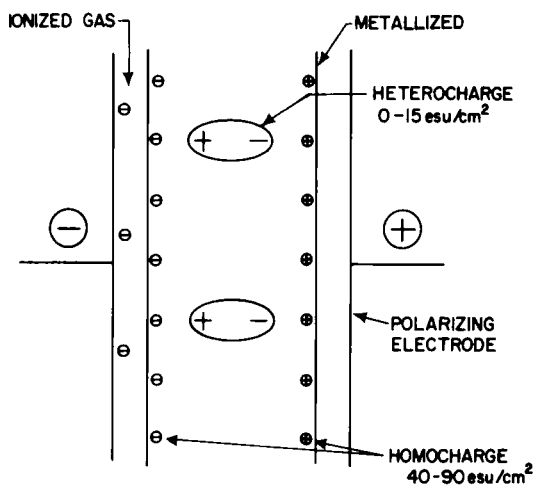
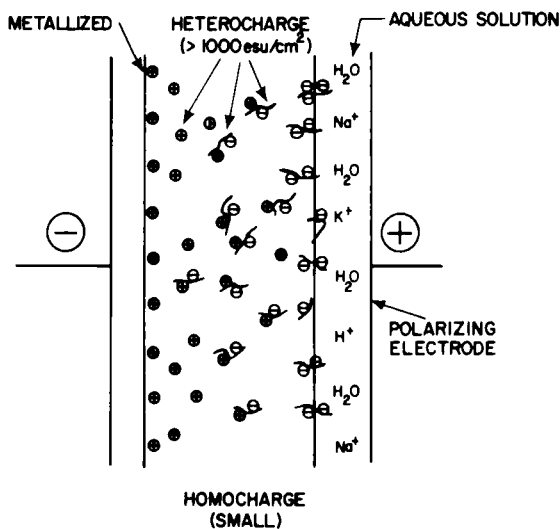Fig. 3. Schematic charge distribution in FEP Teflon electrets.

Fig. 4. Schematic charge distribution in Hypalon and Hypalon-PSS electrets.

for surface uniformity, reproducibility, and freedom from contamination. Some correlations of contact angle change with polarization and with blood compatibility also have been observed. We have made occasional measurements of critical surface tension using a series of homologous organic liquids and have found changes in surface tension similar to changes in the water contact angle. This has added to our confidence in the contact angle measurement.

Typical data on contact angle and change in angle on polarization are shown in Table 2. For PVLC, a decrease of 3 to 6° usually accompanied polarization with metal electrodes, while gas contact caused large and erratic decreases in polarization whether or not the film was being polarized. The large decrease in contact angle presumably resulted from chemical changes such as an increase of surface chloride. Polarized Teflon showed small changes in contact angle whereas Kel-F showed a somewhat greater change. Hypalon showed a considerably greater change when an aqueous contact was used instead of the ionized gas contact. It is rather surprising that the addition of a few per cent polystyrene sulfonate increased the contact angle. For this material, the angle was unchanged on exposure to an ionized gas contact. However, polarization with the aqueous contact caused a very large decrease in contact angle. This large decrease is compatible with the orientation shown in Fig. 4. The contact angle for Estane was decreased by 6° on polarization with an aqueous contact. The addition of sulfonate did produce an additional decrease in contact angle in contrast to the Hypalon-PSS. Electrified Estane-PSS samples showed low contact angles.

E. Charge-Strain Effects

The most critical material application in the artificial heart program is the pump bladder. With this application in mind, we have explored the effects of prolonged flexing on electret charge stability and on transient piezoelectric or charge-strain effects.

To examine the possibility that prolonged flexing and exposure to body fluids might accelerate the rate of charge decay, we flexed a series of electret diaphragms hydraulically using a saline solution. Flexing was carried out for periods of 1 to 15 days at 2 cps and 3 psi to simulate an assist pump. To determine whether this treatment changed the internal polarization, similar samples were stored in a dessicator during the same period and depolarized together with the flexed samples. There was no significant difference in residual charge levels or shape

Table 2. Effect of Electrification on Contact Angle of Polymers

Charge	Contact angle	Polymer	Charge	Contact angle
Ionized Gas Electrode		PVLC I-8	Metal Electrode	
0	25° ± 2°	θ film = 85°	0	84° - 86°
(+)(-)	20° - 60°		(+)(-)	72° - 82°
Ionized Gas Electrode		PFEP	Metal Electrode	
0	107° ± 2°	θ film = 107°	0	107°
(+)(-)	101° - 103°		(-)	105° - 106°
Ionized Gas Electrode		PCTFE	Metal Electrode	
0	94°	θ film = 96°	0	96°
(+)(-)	76° - 90°		(-)	80° - 93°
Ionized Gas Electrode		Hypalon	Aqueous Electrode	
0	89° - 90°	θ film = 89°	0	86° - 91°
(-)	88° - 89°		(-)	82° - 86°
Ionized Gas Electrode		Hypalon-PSS	Aqueous Electrode	
0	93° - 98°	θ film = 93°	0	86° - 96°
(-)	93° - 98°		(-)	67° - 76°
		Estane	Aqueous Electrode	
		θ film = 78°	0	78° av.
			(-)	72° av.
		Estane-PSS	Aqueous Electrode	
		θ film = 65°	0	59° av.
			(-)	50° av.

of depolarization curves for flexed and control samples of PVLC, PFEP, or Hypalon. Electrets of PCTFE which showed double charge peaks were altered by flexing; the heterocharge peak was always reduced in intensity while the homocharge peak was unchanged.

Table 3. Variation of Null Voltage for Electret Films on
Simulated Pump Extension

Material	Dominant polarization	ΔV_{null} at 4.5 psi extension
PVLC	None	± 0.01 v
PVLC	Hetero	–0.1 to +0.5 v
PFEP	None	+3 to +5 v
PFEP	Hetero	25 v
PFEP	Homo	50 v
PCTFE	None	+0.1 to +0.2 v
PCTFE	Hetero	16 v
PCTFE	Homo	50 v
Hypalon	None	±4 v

To explore piezoelectric or charge-strain effects, we have assembled a
measuring device to monitor net surface charge in air while the films are
stressed under extension at 4.5 psi. A summary of results is shown in
Table 3. In general, we believe the changes in surface charge produced
by strain to be negligible for both unpolarized film and electrets. For
unpolarized film, the changes in null voltage under strain varied from about
0.01 V for PVLC to 4 V for Teflon and Hypalon. For electrets, the values
were considerably greater, varying from a fraction of a volt for PVLC to
20-50 V (1 to 3 esu/cm^2) for Teflon and Kel-F. The voltage swings in-
creased with electret null voltage, but at no time did the change exceed
5 to 10% of the total null voltage. In most instances the voltage in-
creased and decreased in proportion to strain. In some cases, however,
a voltage hysteresis was apparent. On the basis of these measurements we
doubt that pump flexing will produce an electropositive surface which
could cause blood damage. However, measurements on other elastomers
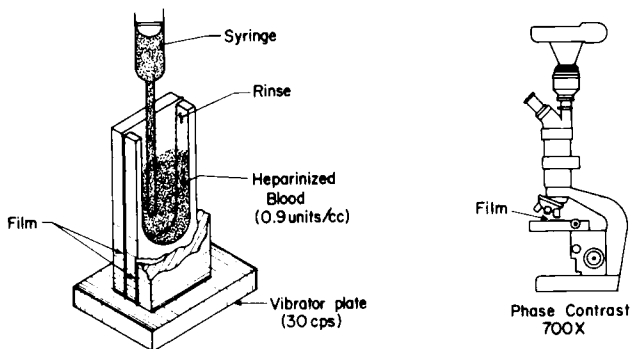and elastomer electrets remain to be made.

Fig. 5. Platelet surface studies.

III. BLOOD COMPATIBILITY EXPERIMENTS

A. In Vitro Experiments

We have carried out in vitro blood compatibility studies during the past 3 years including whole blood clotting time experiments and platelet adsorption experiments. The modified Lee-White technique was used to measure clotting times for whole blood on test surfaces. With this technique we found virtually no difference between electrified and non-electrified materials. Details have been given previously [11]. However, charged surfaces did alter platelet adsorption and these experiments will be described briefly.

The fixture used for platelet adsorption studies is shown in Fig. 5. Two films or coatings to be compared are placed on opposite sides of the cell which is then filled with Ringer's solution. Ringer's was selected for priming and displacing blood after experiments with several other media. The priming solution is displaced with freshly-drawn, heparinized blood (0.9 units heparin/cm^3) in such a manner that blood-air interfaces are avoided. The cell is agitated for 1 min to provide mixing, then the blood is displaced by Ringer's solution. The films are removed and examined for adherent platelets using phase contrast at 700X.

Unpolarized films of Teflon, Kel-F, and cross-linked Hypalon all showed a rather light deposit of platelets of about the same density. Considerably greater platelet adhesion was found for uncross-linked Hypalon. Platelets were generally adsorbed at scratches and imperfections.

We did one series of electrified film studies using Kel-F. For polarized samples of Kel-F film, greater platelet adhesion was found on a positive surface than on an uncharged surface, which in turn had more platelets than a negative surface. Similar results were reported [12] for polarized samples of vinylidene chloride film.

Experiments were also carried out with rings of the type implanted in the vena cava. A modified test cell was designed for ring testing; two rings (test and control) were fitted together in the cell. The same priming and rinsing procedures were followed. Rings were cut in half and stained (Wright's procedure) after exposure to blood. Unpolarized Kel-F rings showed considerably greater adhesion of platelets and cellular elements than Teflon rings. Negatively-polarized Teflon rings with 5 esu/cm^2 homo-charge showed considerably fewer adherent platelets than uncharged rings. Polarized rings with smaller negative charge (1/4 esu/cm^2) had the same platelet deposit as nonpolarized rings. We do not believe the data justifies a quantitative correlation with respect to charge or material; however, in general, the negative surfaces did adsorb fewer platelets.

B. In Vivo Experiments

1. **Right Atrial Tab Implants.** A series of in vivo tab implants was carried out earlier in this program and has been discussed previously [11]. A summary of the results of these experiments is shown in Fig. 6. Implants of 8 X 18 mm were usually located in the canine right atrium and were left in place for 1 to 30 days. Two tabs of polyvinylidene chloride (usually positively and negatively charged) were placed about 2 cm apart. On removal, the tabs were graded for thrombus starting from A for no thrombus and continuing to E for massive thrombus. It will be noted that negative tabs were relatively free of thrombus whereas positive tabs were thrombosed.

2. **Vena Caval Ring Implants.** During the past year, we have fabricated a series of vena caval rings which have been evaluated by Dr. Gott of Johns Hopkins University. The surgical techniques have been described previously [13]. Rings of Teflon were fabricated by machining, and rings of Hypalon and Hypalon-2% polystyrene sulfonate were prepared by coating the elastomer on a metal substrate. All rings were implanted for 2-hr periods. All common, unmodified polymer rings thrombose completely under similar conditions.

The polarizing conditions and in vivo results are shown in Fig. 7 for
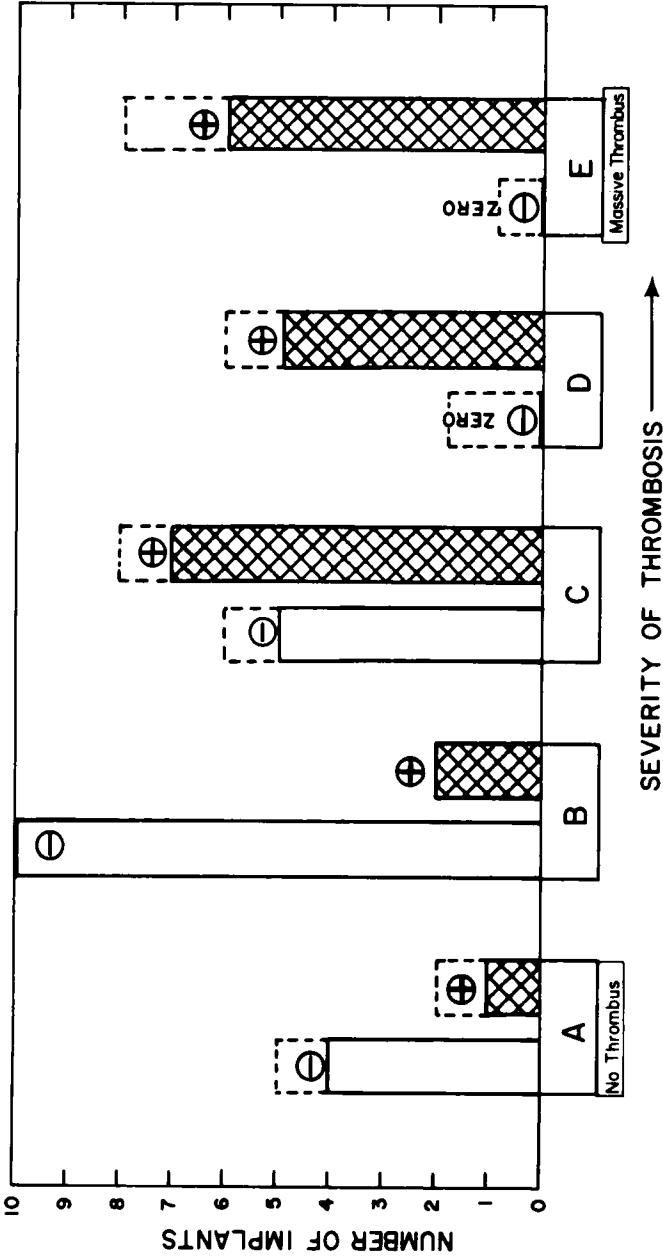
Fig. 6. Summary of in vivo compatibility studies with PVLC electrets.

Lot Number	Material	Date of Implant	Ring Number	Contact During Polarization	Thrombus at 2 hr	Contact Angle			
						θ_o	θ pol	$\Delta\theta$	V null
8	Teflon	3/4/69	1	Ionized Gas		81°	92°	+11	− 400
		3/4/69	2	Ionized Gas		94°	93°	− 1	−1200
		3/5/69	3	Ionized Gas		101°	102°	+ 1	−1200
		3/5/69	4	Ionized Gas		100°	100°	0	−1200

Fig. 7. Summary of acute in vivo blood compatibility test of negatively polarized Teflon vena caval rings. Gas sterilization was used in all cases.

Teflon. All rings were polarized with an ionized gas contact to give a negative homocharge. The -1200 null voltage corresponds to -24 esu/cm^2 net charge. It will be noted that all three of the rings with high negative charge were nearly free of thrombus. Ring No. 1 with the thin covering of thrombus had a considerably lower charge; in addition, the contact angle increased substantially after polarization. Contact angle changes do show a preliminary correlation with blood compatibility. Large increases in contact angle (decreases in surface tension) seem to be undesirable and decreases desirable.

The performance of Hypalon-coated rings is shown in Fig. 8. It will be noted that about two-thirds of the rings were relatively free of thrombus after 2-hr implants. Cross-linking had no obvious effect. Surprisingly, surfaces contacted with water or ionized gas during polarization performed the same. Measurement of net charge has little value for Hypalon since an adsorbed water film screens the surface. It should be noted that rings 5-6 and 3-4 had large increases in contact angle and thrombosed; the other two occluded rings did not show anomalous increases in contact angle.

The performance of polystyrene sulfonate-doped Hypalon rings is shown in Fig. 9. The polyelectrolyte was oriented and cross-linked during polarization to give a negative surface. These rings performed better in general than the plain Hypalon rings since none was occluded completely. We believe the aqueous contact to be preferable for polarization since large decreases in contact angle are produced. One ring did show a thin coating of thrombus, but this ring had a contact angle about 8° higher than the other two which remained free of thrombus.

IV. CONCLUSION

The use of electret techniques to augment the surface electronegativity of polymers and elastomers appears to be effective in improving their blood compatibility. A variety of materials can be treated. Relatively low charge densities are effective in reducing the thrombogenicity of Teflon, presumably by decreasing platelet adhesion. Electrification increases the surface polarity in ionogenic and polar materials as evidenced by increases in critical surface tension. This surface ordering capability should be of increasing value as better guide lines on desirable surface characteristics become available.

Lot Number	Material	Date of Implant	Ring Number	Contact During Polarization	Thrombus at 2 hr		Contact Angle			
							θ_o	θ_{pol}	$\Delta\theta$	V_{null}
3	Hypalon 45	11/18/68	4	Aqueous			82°	89°	+7	-2.0
		11/19/68	5	Aqueous			86°	84°	-2	-1.5
		11/20/68	6	Aqueous			91°	86°	-5	-1.5
		11/21/68	7	Aqueous			90°	82°	-8	-1.0
		11/21/68	8	Aqueous			84°	92°	+8	-2.5
4	Hypalon 45X	11/26/68	10	Aqueous			86°	88°	+2	-2.5
		11/26/68	11	Aqueous			91°	94°	+3	-2.5
		11/27/68	12	Aqueous			92°	95°	+3	-2.0
5	Hypalon 45X		4	Ionized Gas			90°	88°	-2	-2.0
			5	Ionized Gas			89°	89°	0	-2.0
			6	Ionized Gas			77°	99°	+22	-2.0

Fig. 8. Summary of acute in vivo blood compatibility test of negatively polarized Hypalon vena caval rings. Gas sterilization was used in all cases.

Lot Number	Material	Date of Implant	Ring Number	Contact During Polarization	Thrombus at 2 hr		Contact Angle		
							θ_o	θ pol	$\Delta\theta$
6	Hypalon 30X/ 2% PSSA	3/3/69	3	Aqueous			96°	69°	-27
		3/3/69	4	Aqueous			86°	67°	-19
		3/4/69	5	Aqueous			88°	76°	-12
7	Hypalon 30X/ 2% PSSA	3/14/69	2	Ionized Gas			93°	95°	+2
		3/13/69	8	Ionized Gas			95°	92°	-3
		3/14/69	10	Ionized Gas			98°	98°	0
		3/13/69	11	Ionized Gas			97°	98°	+1

Fig. 9. Summary of acute in vivo blood compatibility test of negatively polarized Hypalon-PSS vena caval rings. Gas sterilization was used in all cases.

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