

Blood Surfaces in the Extra Corporeal Circuit: A Scanning Electron Microscopic Study

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Research work contained herein supported in part by PHS Grant no. HL 13426, Left Ventricular Bypass for Myocardial Infarction.

ABSTRACT

Despite advances in cardiovascular surgery and the use of new equipment for extracorporeal circulation (ECC), the goal of indefinitely safe ECC is not a reality yet. One of the limiting factors is trauma to the blood as it traverses the extracorporeal circuit. Of the factors that have been implicated as sources of trauma, obstructions or disturbances to flow and surface roughness are the two upon which this study is focused.

The method used was scanning electron microscopy because of the ability to visualize the microtopography of a typical ECC with great depth of field and high magnification. Unused components were examined and included: cannulae, tubing, connectors, bubble oxygenator, and microemboli filter. Only components from the major system (ie., excluding cardiotomy suction) were examined because most of the blood volume is contained within it and repeatedly comes in contact with its surfaces. Samples were examined at 50° tilt from the horizontal at magnifications ranging 100-2500X, with 500X and 1000X considered most useful for visualization of the surfaces on a cellular level.

The results are a series of photomicrographs that show a variety of blood surfaces: some are smooth, and some are rough with ridges, crevices, and surface irregularities often larger than blood cells.

We conclude that rough surfaces do exist within the typical ECC system, and these surfaces are probably responsible, in part, for the trauma blood undergoes during ECC. Long term ECC will require a major improvement in the surface structure of many of the currently used components.

INTRODUCTION

Despite advances in cardiovascular surgery and the use of new equipment for extracorporeal circulation (ECC), the goal of indefinitely safe ECC is not a reality yet.¹ One of the limiting factors is trauma to the blood as it traverses the extracorporeal circuit, for which many factors have been implicated and are listed in Table One. This study is concerned with the last two, namely, obstructions or disturbances to flow and surface roughness.

By use of scanning electron microscopy (SEM) we were able to examine an ECC system and visualize the blood surfaces on a cellular level. SEM is a relatively new tool

in medicine and has only been applied recently in the examination of the blood-foreign surface interface and never systematically of an entire ECC system.

The results are a series of photomicrographs that show a variety of blood surfaces: some are smooth, and some are rough with surface irregularities often larger than blood cells.

In the discussion that follows is a brief review of the literature to define just what constitutes a rough surface and to determine what precautions can be taken to render the ECC system less traumatic.

Imagine now, that you are going on a trip: what the blood near the surfaces is exposed to during ECC is what we shall see in the course of this paper.

MATERIALS AND METHODS

The typical extra-corporeal circuit is really two systems, as suggested by Osborn² and co-workers: a major consisting of blood taken from the vena cavae and returned to the arterial tree and a minor consisting of cardiotomy suction. Although the minor system is most often implicated as the primary source of hemolysis associated with ECC, the present study will focus on the components found in the major system, because most of the blood volume is contained within and repeatedly comes in contact with its surfaces. Secondly, the materials found in the minor system are the same as those in the major. Components of the system include: cannulae, tubing, connectors, oxygenator, and microemboli filter. Further description of these components are listed in Table Two.

All samples examined were taken from unused components, with the exception of the metal connectors which were cleaned in the usual manner following use and steam autoclaved at 270° C. for three minutes. The heat exchanger was not examined in the scanning electron microscope due to its size, but it is assumed that the blood surfaces found in it are similar to those found in the metal connectors which were examined. All blood contact surfaces are highly polished according to the manufacturer.

After cutting with razor blade or hack saw, samples measuring roughly one square centimeter were glued to aluminum stubs, ultrasonically* cleaned in detergent,** and rinsed twice in glass distilled water. Specimens were then blown dry using a Freon-12 "duster" and kept covered, to avoid air-borne contaminants, until placed in a vacuum evaporator for application of a thin (~ 200 Å) gold-palladium coating at 10⁻⁴ torr. Non-conductive specimens must be made conductive for examination in the scanning electron microscope*** and the AuPd coating was also applied to the stainless steel specimens for consistency with the plastic specimens. Stubs with specimens affixed and prepared as above were mounted in the specimen chamber of the microscope and examined.

Magnifications ranged from 10X to 2500X, with 500X and 1000X considered the most useful for visualization to the surfaces on a cellular level. Specimens were viewed with stage tilt 50° from the horizontal, and the photomicrographs are analogous to the view a person standing six feet tall looking at the floor approximately seven feet away would have: what would appear in his general field of vision is what the scanning electron microscope "sees" and records. Changes of magnification change the relative size of the viewer, but the orientation remains the same.

*Bransonic 32, Branson Instr. Co., Stamford, Conn.

**Liqui-Nok, Alconok, Inc., N.Y., N.Y.

***AMR-900, Advanced Metals Research Corp., Bedford, Mass.

Table One

BLOOD TRAUMA IN ECC — FACTORS

1. CARDIOTOMY SUCTION
2. AGE OF BLOOD
3. DEGREE OF OCCLUSION
4. HEMATOCRIT
5. PERICARDIAL FLUID
6. PRESENCE OF LIPIDS
7. TEMPERATURE
8. GAS-BLOOD INTERFACE
9. PRESENCE OF IMPURITIES
10. CHEMICAL NATURE OF WALL
- * 11. OBSTRUCTIONS OR DISTURBANCES TO FLOW
- * 12. SURFACE ROUGHNESS

Table Three

BLOOD TRAUMA IN ECC — KINDS AND MANIFESTATIONS

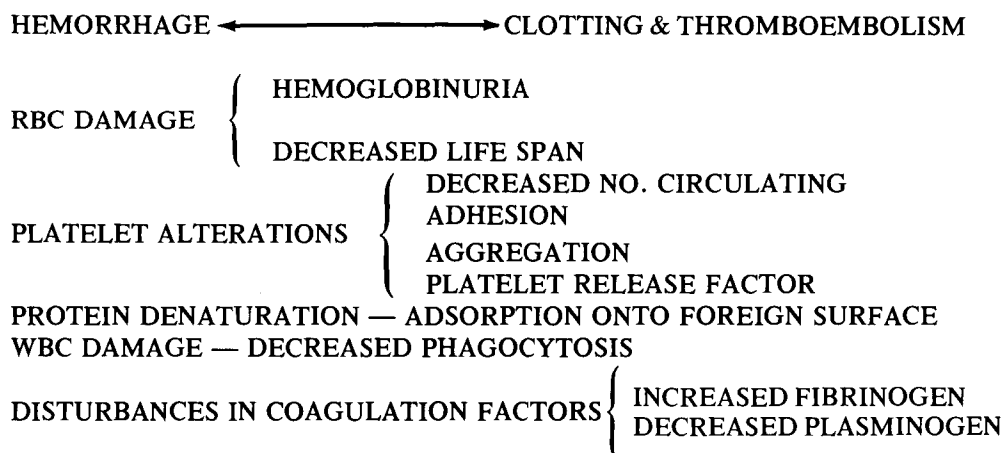


Table Two

COMPONENT	LOCATION	MANUFACTURER	CAT. NO.	DIMENSIONS	MATERIAL
cannula	venous	USCI	1956-S	L 35 cm, 40 F	polyvinyl chloride, wire-reinforced
cannula	arterial	USCI	1858-S (Bardic-1058)	L 15.5 cm, 24 F	polyvinyl chloride
tubing	venous	US Stoneware, Inc.	Tygon S-50-HL	½" ID	polyvinyl chloride
tubing	arterial	US Stoneware, Inc.	Tygon S-50-HL	3/8" ID	polyvinyl chloride
tubing	pump head	Dow-Corning	601-545 Medical Grade Silastic	3/8" ID	silicone rubber
connector	venous cannula/ venous line	Cobe Labora- tories, Inc.	50-518	½" x 3/8" reducer	polycarbonate
connector	arterial line/ arterial can- nula	Sarns, Inc.	6502	3/8" x 3/8"	stainless steel
connectors	heat exchanger: inlet, outlet ports	Sarns, Inc.	6235	3/8"	stainless steel
heat exchanger oxygenator	arterial	Sarns, Inc. Wm. Harvey Research Corp.	6033 H-200	125 cc vol. 0.5-6.5 L/min. blood flow	stainless steel polycarbonate, polyurethane, nylon
microemboli filter	arterial	Pall Corp.	EC 3840	3/8" inlet, out- let ports	polypropylene, dacron polyester

RESULTS

Blood is exposed to many different surfaces during its passage through the typical ECC system, and the photomicrographs that follow represent the culmination of many examinations of all the components in the circuit. Bars, when they appear in the lower right corner are equivalent to $8\ \mu$ (the size of a red blood cell) and are included to gauge the microtopography of a given surface. Arrows, when they appear, indicate direction of flow. In the descriptions accompanying the photomicrographs, "small" and "large" and "rough" and "smooth" are used with reference to blood cell size; that is, small would be below platelet size ($<2\mu$) and large would be greater than white blood cells ($>15\mu$). The circuit will be presented sequentially by the route the blood takes upon leaving the patient's right atrium and entering the venous cannula and ending in the arterial cannula as it reenters normal circulation.

DISCUSSION

Manifestations of blood trauma during ECC can run the gamut from severe hemorrhage on the one hand to clot formation and thrombo-embolism on the other. Perhaps it is because hemoglobinuria is so apparent when it occurs during ECC that hemolysis has been the subject of most studies investigating ECC-induced blood trauma. It is our contention that thrombogenesis and its sequelae is an important manifestation of blood trauma, as well, especially with the increasing use of long term ECC. Just because a patient is heparinized does not mean all of the clotting problems associated with ECC have been solved; subtle, but significant changes in the blood occur post ECC.³ Indeed, a common experience with long term membrane support has been the necessity to change membranes due to thrombus build-up on the membrane surface secondary to decreasing gas transferability, in spite of adequate heparinization.⁴⁻⁶ Table Three outlines the kinds and manifestations of blood trauma.

SEM has been used only recently in the examination of blood surfaces. In 1972, Nachnani,⁷ and co-workers, examined polyethelene and polyurethane vascular catheters and concluded that physical surface defects were an important factor in thrombogenesis. Unfortunately, there was some confusion over the identity of his specimens, and Judkins⁸ rebuttal stated that such a conclusion about surface roughness was premature. In 1973, Lampert and Williams⁹ examined plastic and metal discs for which shear stresses had been calculated pre- and post-exposure to blood in a study investigating surface morphology and its relation to hemolysis. In 1973, Schoen¹⁰ and co-workers, examined intra-aortic balloons pre- and post-implantation, and in 1975, Guidon⁴ and co-workers, examined thrombus formation in a tubular silicone rubber membrane post-prolonged ECC.

However, the first to implicate surface roughness as a cause of hemolysis during ECC were Stewart and Sturridge¹¹ in 1959. They rotated blood in different types of tubing, measured plasma hemoglobins after one hour, and recorded roughness profiles of the tubing by means of a sensitive stylus dragged across the luminal surfaces. One of their conclusions was that the smoother the internal wall, the less hemolysis produced. Others who examined ECC systems and its traumatic effects on blood were Osborn, et al,² in 1962, who concluded that 1) most hemolysis occurs in the minor system (cardiotomy suction) and 2) the type of sucker tip (gently curved vs sharp entry angles) was important in reducing hemolysis. In 1966, Yarborough¹² and co-workers concluded that appurtenances, kinks, constrictions, etc. produced high localized energy loss in blood flow, and lysis at these places was quite severe. The

emerging idea from these studies pointed towards a direct relationship between turbulence and hemolysis.

But it was not until 1966, at the University of Minnesota, with a unique alliance of engineers and doctors, that the first in depth analysis began to study the behavior of blood flow in artificial devices. Their studies utilized freshly drawn, anti-coagulated canine blood or washed and re-suspended red blood cells, and the pertinent observations and conclusions they made over the next five years included:

- 1) hemolysis in tube flow is directly related to a cell-wall interaction¹³⁻¹⁵
- 2) varying the tube length and tube diameter affects hemolysis¹³
- 3) a small fraction of cells in a typical ECC system hit the wall; of those hitting, less than 0.5% hemolyze¹⁵
- 4) the effects of flow induced cell motion has a more marked effect on the other blood elements¹⁴
- 5) pump head occlusion is an important factor due to its promotion of cell-wall contact¹⁶
- 6) Silastic is the best surface for use with a roller pump¹⁷
- 7) in tubular flow, there is a tendency for cells to migrate to the center of the tube¹⁸
- 8) red blood cells can stick to a foreign surface, become elongated, and form roughness elements¹⁸
- 9) the influence of the wall is limited to the zone 15μ nearest the wall¹⁹
- 10) there are two types of hemolysis: immediate, which is lethal, and delayed, which is sublethal^{13, 19, 20}

Their studies make for fascinating reading in learning more about what happens to blood during ECC, but they admitted that the process of a cell approaching a wall was far from well understood.¹⁴

Concurrently, there began appearing in the literature many thrombogenesis studies that represented the tremendous effort that is still underway to overcome the tendency of blood to clot when exposed to foreign surfaces. Despite the fact that the majority of the thrombogenesis studies utilized unheparinized blood in their experiments, their findings cannot be dismissed in gaining an understanding into what happens to blood during ECC. Pertinent observations and conclusions include:

- 1) the blood compatibility of a given anti-thrombogenic surface can be varied by varying the geometrical shape²¹
- 2) the first demonstrable effect when blood is exposed to a foreign surface is a proteinaceous build-up approximately 200 \AA thick within three seconds²²⁻²³
- 3) physical properties such as surface roughness contribute to the effect the surface has on cellular elements and the coagulation mechanism²⁴
- 4) in regions of disturbed flow the formed elements collide with one another which leads to injury of red blood cells, white blood cells, and platelets, which, in turn, leads to enhanced thrombogenesis²⁵
- 5) the micromorphology and submicroscopical architecture determine compatibility²⁶
- 6) roughness encourages cellular deposition²⁷

Like the group at Minnesota, the thrombogenesis researchers acknowledged the magnitude of the problem that still has not been solved. The nature of the blood-polymer interactions are exceedingly complex and far from being understood;^{28 29} the activation of clotting and the adhesion of platelets to a surface is not well understood;³⁰ the molecular level of events is hard to fathom;³¹ there is a lack of a

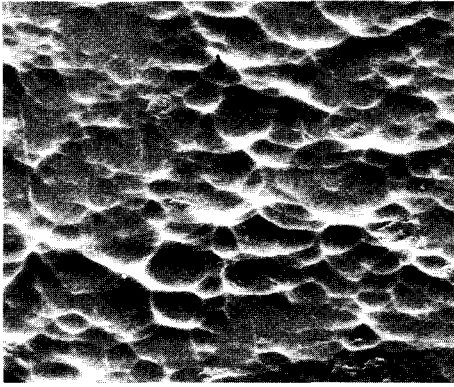


Fig. 1. CANNULA, venous, polyvinyl chloride: uniform surface; gentle indentations and low ridges; generally smooth (500X)

Fig. 2. CONNECTOR, venous cannula/venous line, polycarbonate: non-uniform appearance with rough-edged pits; long scratches parallel to blood flow; jagged edges project from surface (500X)

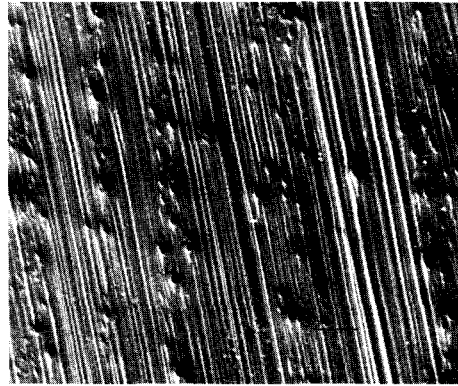
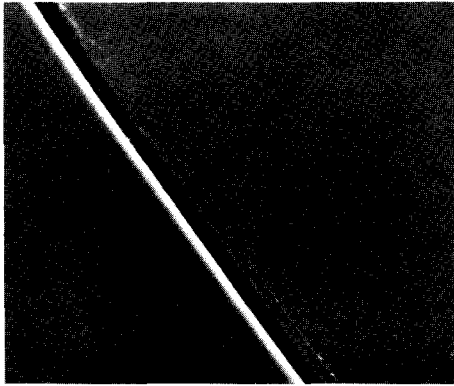


Fig. 3. TUBING, polyvinyl chloride: extremely smooth and uniform; diagonal crevice was left by razor blade to aid focusing on surface; no visible structures on cellular level (500X)

Fig. 4. OXYGENATOR, venous inlet port, polycarbonate: multiple small ridges parallel to blood flow; numerous small pits; fairly uniform surface (1000X)

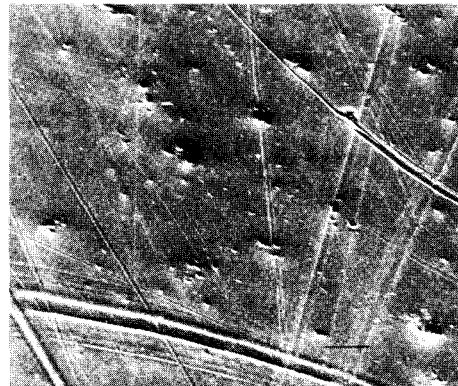
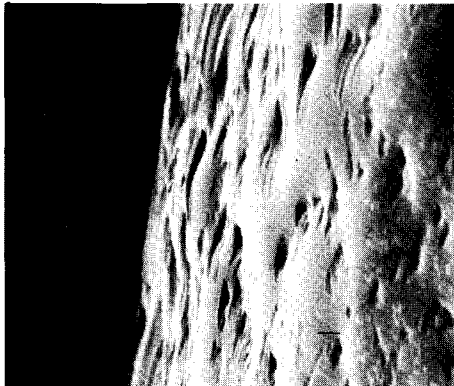


Fig. 5. OXYGENATOR, venous reservoir exit slit, polycarbonate: uniform surface, gently rounded mounds; many small, smooth-edged pits (500X)

Fig. 6. OXYGENATOR, O₂ diffuser, polycarbonate: fairly smooth, uniform surface with occasional small pits and randomly oriented scratches (1000X)

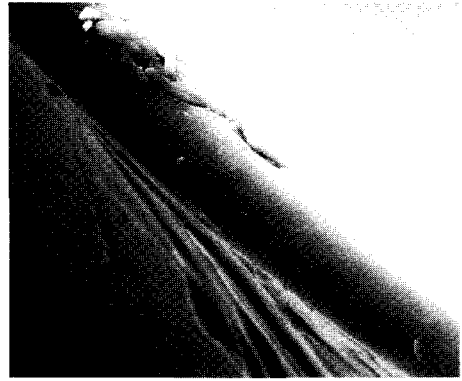
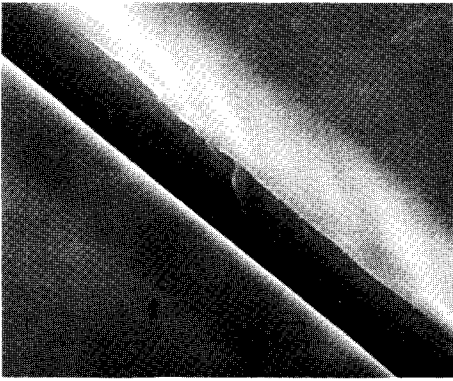


Fig. 7. OXYGENATOR, oxygenating straw, polycarbonate: extremely smooth and uniform; diagonal crevice left by razor blade to aid focusing on surface; no visible structures on cellular level (1000X)

Fig. 8. OXYGENATOR, coarse defoamer, polyurethane: three-sided reticulated foam; fairly uniform in appearance; rounded edges (1000X)

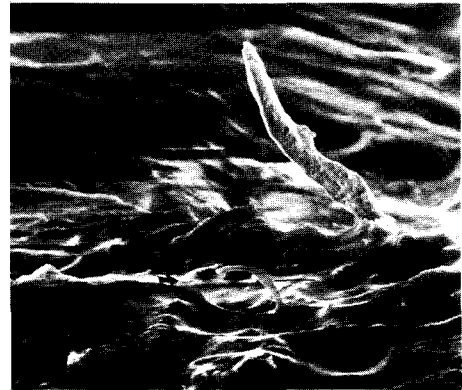
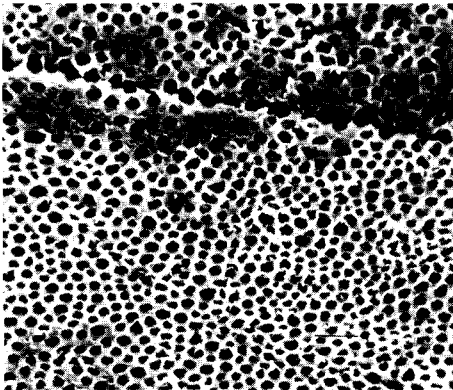


Fig. 9. OXYGENATOR, hydrostatic barrier-cloudy part, polycarbonate: honeycombed surface with multiple small holes and jagged crevices (1000X)

Fig. 10. OXYGENATOR, hydrostatic barrier-inner surface of hole, polycarbonate: very irregular surface with many sharp projections rising 30μ or more perpendicularly to blood flow (1000X)

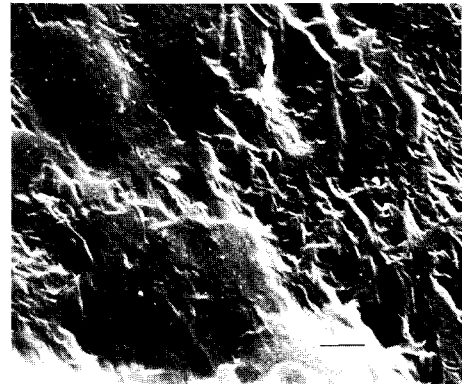
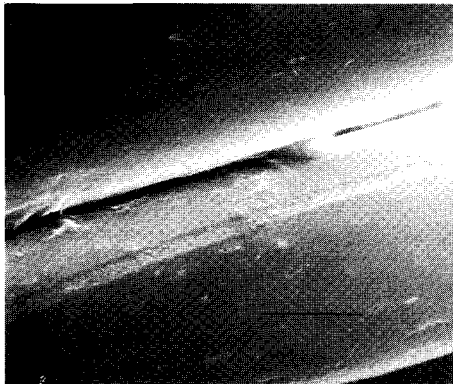


Fig. 11. OXYGENATOR, knitted filter mesh, nylon: uniform, close-lying strands; smooth, with occasional scratches (2500X)

Fig. 12. OXYGENATOR, arterial exit port, polycarbonate: irregular surface; rough-edged, irregularly shaped depressions (1000X)

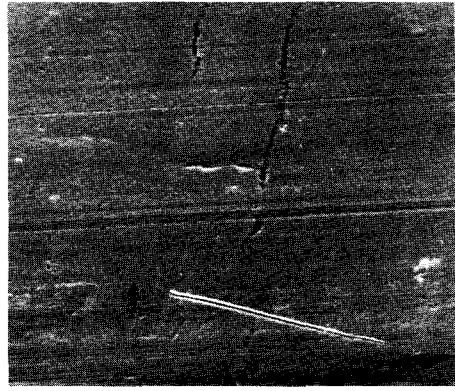
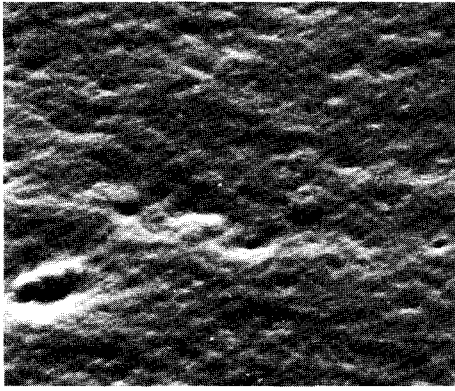


Fig. 13. TUBING, pump head, silicone rubber: fairly smooth, uniform surface; small, flattened blebs; occasional large, smooth-edged depressions(500X)

Fig. 14. CONNECTOR, heat exchanger, stainless steel: fairly smooth, uniform surface; small ridges perpendicular to flow; occasional jagged crevices; occasional scratches (1000X)

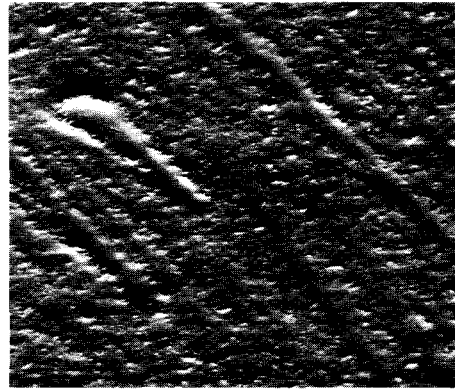


Fig. 15. MICROEMBOLI FILTER, housing, polypropylene: uniform surface; many large ridges perpendicular to blood flow; occasional small, smooth-edged pits; occasional small scratches crossing ridges (1000X)

Fig. 16. MICROEMBOLI FILTER, dispersion plate, polypropylene: fairly smooth, uniform surface with small shallow pits; gently rounded ridges; occasional large flat plateaus (250X)

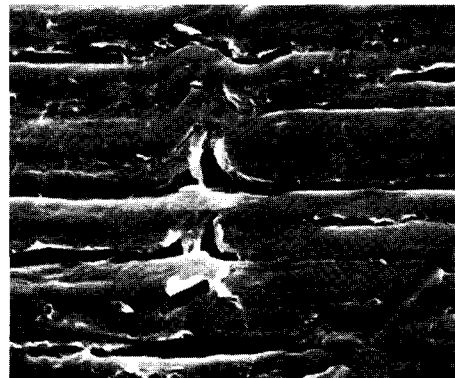
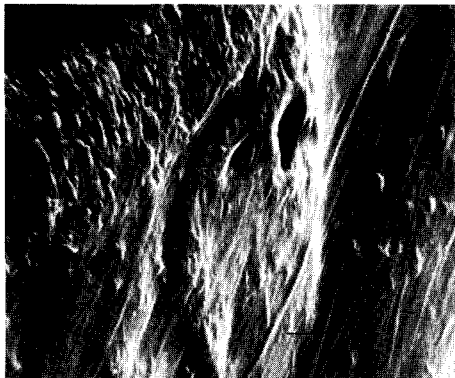


Fig. 17. MICROEMBOLI FILTER, letter detail, polypropylene: irregular surface; long ridges, numerous small blebs; occasional irregularly shaped pits (1000X)

Fig. 18. MICROEMBOLI FILTER, dispersion plate-spoke end, polypropylene: extremely irregular, rough surface with jagged edges, deep crevices, and sharp projections (1000X)

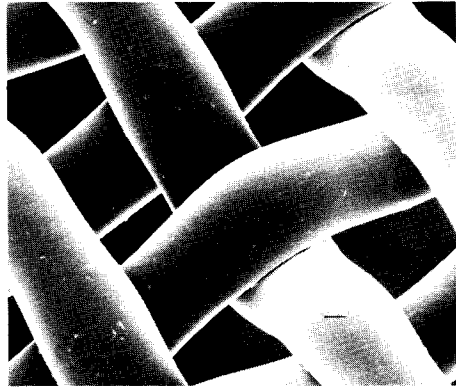
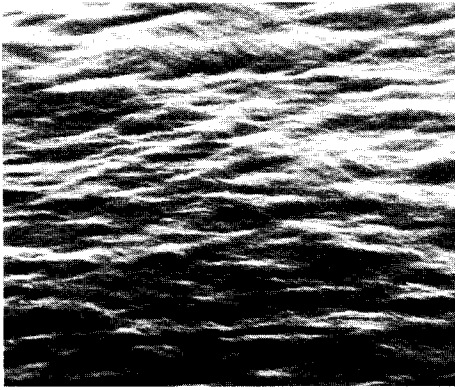


Fig. 19. MICROEMBOLI FILTER element support, polypropylene: uniform surface; gentle undulations; generally, a smooth surface (1000X)

Fig. 20. MICROEMBOLI FILTER, element, dacron polyester: uniform, smooth woven monofilaments; occasional small scratches running lengthwise; approximately 40μ pore size (500X)

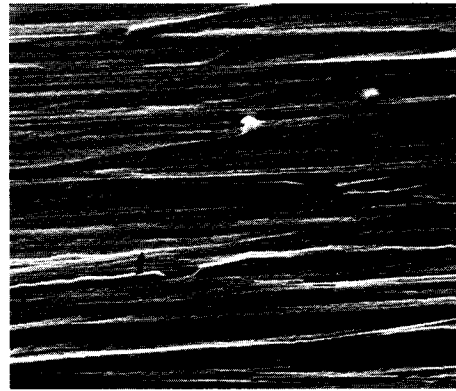
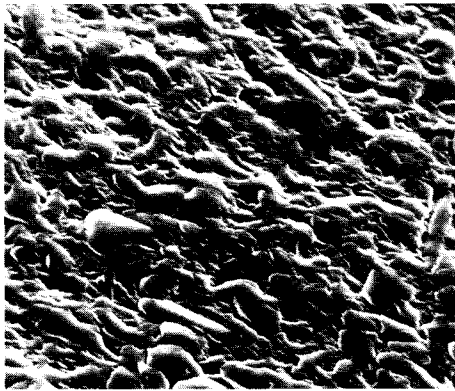


Fig. 21. MICROEMBOLI FILTER, perforated inner support, polypropylene: irregular, rough surface with multiple rounded plaques; jagged crevices in between (500X)

Fig. 22. CANNULA, arterial, polyvinyl chloride: uniform surface with fairly rough ridges perpendicular to blood flow; occasional smooth-edged blebs (500X)



Fig. 23. CANNULA, arterial at tip, polyvinyl chloride: smooth-rough junction; polishing process has removed perpendicular ridges but leaves numerous smooth-edged blebs (100X)

clear understanding of the complex events involved in the interaction of blood with a foreign surface;²⁷ the peculiar properties of vascular endothelium which render it thromboresistant are still not known.²³

What can be gleaned from all of this research in terms of the current SEM study? That is, what has been said specifically in terms of surface roughness that can be useful in interpreting the photomicrographs? The predominant idea of the flow studies is that a distinction is made between laminar and turbulent flow. In laminar flow, there is a cell-free zone near the surface,¹⁹ but in turbulent flow there is cell to cell and cell to wall flux.¹⁸ Structures greater than 10μ promote cell-wall encounters,¹⁸ and the absence of structures less than 1μ is considered smooth.³² In Blackshear's advice to heart valve makers the recommendation was made that surface roughness must be much less than cell size.¹⁸ In the thrombogenesis studies, the predominant idea is that **all surfaces**, except the intact vascular endothelium, are to some extent thrombogenic,³ and specifically, the initiating sites for thrombus formation were observed to be anything greater than 5μ .³³ By these criteria, many of the surfaces we examined may be deemed rough due to the microtopographical features; when considered with the non-laminar flow that exists through much of the circuit, it is not difficult to see why blood is traumatized during ECC.

However, the photomicrographs only hint at the overall phenomena of blood trauma in ECC, and some may even criticize the study as vicarious adventure for looking at unused components. The most active area of research currently investigating the blood-foreign surface interface is directed towards a better understanding of the thin, proteinaceous adsorbate that covers the entire circuit almost immediately upon exposure to blood. These surfaces we have seen are surely altered by such adsorption, but, how and with what significance for blood trauma remains to be discovered. Ironically, in 1968, Garfin,³⁴ and co-workers, observed significant reductions in mechanical hemolysis if the foreign surfaces were coated with one percent albumin, but it was not until 1973 that Lampert and Williams⁸ attempted to correlate surface morphology and mechanical hemolysis. Significantly, the metal and plastic surfaces post-exposure to blood differed morphologically, yet their hemolytic effects were similar, and they concluded that a given material's effect on hemolysis was not directly related to such morphological details as external roughness. Such studies indicate that with the photomicrographs we have, while statements can be made about their relative roughness or smoothness, because they are unused, they are not necessarily the ones presented to the blood during ECC. Such speculation clearly invites post-ECC examination of an identical circuit, and we are beginning such a follow-up study. More study into the precise nature of the protein adsorbate and the mechanism by which it adheres to a foreign surface remains to be done.

In conclusion, what precautions can be taken to render the ECC less traumatic to blood? First of all, much has been said about long term ECC, and the typical circuit we examined would certainly not be the first choice for such a procedure. The circuit we have looked at, despite some rugged-appearing terrain, actually works very well for routine ECC for open-heart surgery, and plasma hemoglobins drawn from patients during the procedure are well within the acceptable range, averaging 0.4-0.6 mg%/minute on by-pass. Removing the bubble oxygenator and even the microemboli filter and substituting a membrane would still leave cannulae, tubing, and connectors. We are dependent upon the manufacturers for components, and improvements in blood surfaces must be made by them. Other conclusions that can be drawn are:

- 1) Rough surfaces do exist in the typical ECC system.
- 2) These surfaces and the attendant disturbances to flow can cause flood trauma.
- 3) The use of one percent albumin in prime can render surfaces less traumatic to blood.
- 4) Minimizing the number of connectors, flow probes, or O₂ probes can reduce turbulence at junctions.
- 5) If blood is used in the prime, preceding it with clear fluids can avoid cellular deposition on the surfaces.
- 6) Long term ECC will require a major improvement in the surface structure of currently used components.

SUMMARY

We have examined unused components from a typical ECC system by SEM and presented photomicrographs that depict blood surfaces on a cellular level. Pertinent observations and conclusions have been drawn from the literature on the subject to define what constitutes a rough blood surface and to determine what precautions can be taken to render the typical ECC system less traumatic to blood.

ACKNOWLEDGEMENTS

The authors would like to thank Mr. Virgil Mumaw, Department of Anatomy, Milton S. Hershey Medical Center for his invaluable assistance with the scanning electron microscope and Drs. Bryce L. Munger, Department of Anatomy and William S. Pierce, Department of Cardiothoracic Surgery, Milton S. Hershey Medical Center for their constructive criticism.

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