

# BLOOD COMPATIBILITY OF MATERIALS

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## INTRODUCTION

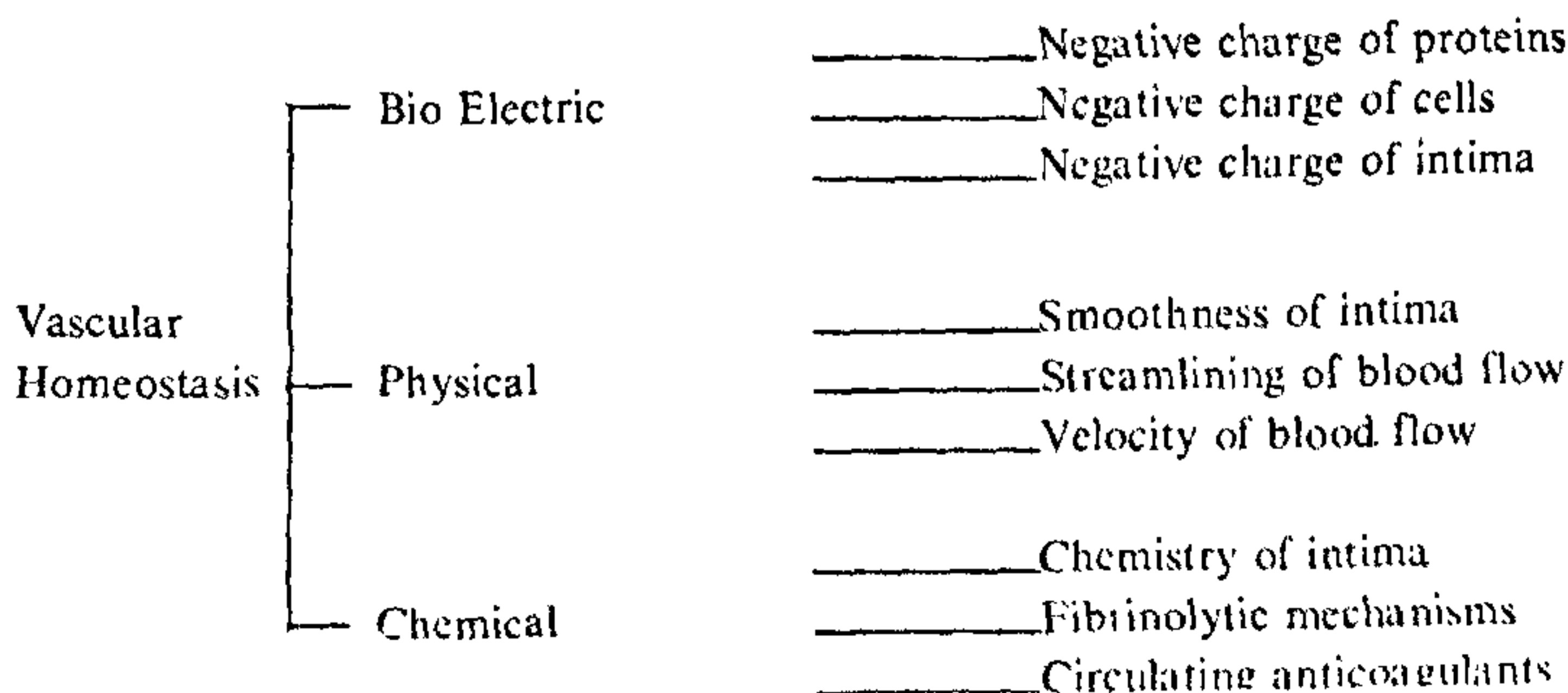
THE problem of oxygen exchange between the atmosphere and living tissues was born with the advent of life on earth. While this problem was relatively simple with unicellular organisms, the evolution of multicellular organisms and animals aggravated the difficulty enormously. The evolutionary answer to the difficulty was the development of circulation which postulated a specialised fluid capable of carrying oxygen, a system of pipes to transport it to diverse tissues and a centrally placed pump to push the fluid to the farthest regions of the body. The need to keep the fluid from solidification was paramount in this system as blockage of the pipes would have imperilled oxygen supply to the tissues and organs. The fluidity of blood in living vessels or vascular homeostasis was therefore the evolutionary answer to this vital need.

Blood clots within minutes of collection in a glass or metal container. Indeed it gels readily on any surface other than its own natural boundary in the blood vessels or the heart. This phenomenon of blood-vessel

wall harmony was noted by John Hunter in the eighteenth century and studied ever since with varying degrees of enthusiasm. Forty years ago, the subject attracted renewed interest as the prospect for replacing blood vessels with plastic tubes appeared on the surgical horizon<sup>1</sup>. What had been an interesting problem for the physiologists until then became a central concern and determinant of cardiovascular surgery overnight.

The diagram below illustrates the elements of vascular homeostasis in so far as it is understood today. Whereas the negative charge of red cells and serum proteins had been known from the early years of the century, the electronegativity of the lining of normal blood vessels was discovered much later<sup>2</sup>. It was Sawyer's original observation and further studies which lent support to the concept that the presence of like charges in the blood elements and vessel wall is responsible for the prevention of intravascular coagulation. Indeed, this concept inspired the development of materials with a negatively charged surface for clinical applications even though it would be a mistake to regard

## VASCULAR HOMEOSTASIS



electronegativity as the sole basis for vascular homeostasis.

In addition to its negative charge, the vascular lining has other important characteristics such as extreme smoothness and non-wettability which correlate directly with thrombo-resistance. Additionally, any minor damage to the lining seems to be repaired in life by the immediate deposition of platelets and fibrin.

The chemical basis of vascular homeostasis is probably no less important than biophysical factors. The presence of anticoagulants such as heparin and heparinoid substances in the lining of blood vessels as well as in blood has been established and may have an important role in preventing clot formation<sup>3</sup>. Similarly the plasminogen plasmin system of serum enzymes may contribute to the prompt lysis of clots which arise from the temporary breakdowns in vascular homeostasis.

The prevention of clotting in vessels also owes a good deal to the constant flow of blood in the body. Stasis promotes clot formation as the experience with leg vein thrombosis in bed-ridden patients has testified over the years. Constant movement of blood is ensured in turn by the skeletal muscle pump peripherally and the right and left ventricular pumps centrally.

#### BLOOD COMPATIBLE SURFACES

From the foregoing discussion, the complex nature of the lining of blood vessels will have become apparent. In a surgical operation to replace blood vessels or heart valves or any bioengineering effort to develop extracorporeal blood circuits, one is therefore obliged to provide a blood compatible surface even though it may not equal the natural lining of blood vessels in physico-chemical properties. In the early years of the twentieth century, efforts to develop blood compatible surfaces were limited to the coating of glass with collodion or paraffin which prolonged the clotting

time and answered the experimental needs in physiology. Subsequently, investigators tended to use new polymeric materials even as they appeared on the market on the chance that they might be inert and blood compatible<sup>4</sup>. This approach of trial and error was surprisingly effective and yielded relatively successful devices such as the first generation of prosthetic heart valves and vascular grafts. Indeed the empirical approach to the development of biomaterials was responsible for major surgical advances in the fifties and sixties even though thoughtful observers had not failed to recognise the limitations of empiricism in this field.

A major advance in blood compatible materials was the serendipitous discovery that a colloidal graphite coated surface could sequentially bond benzalkonium chloride and heparin (GBH) and become antithrombogenic for prolonged periods of time<sup>5,6</sup>. Despite the ionic bonding of heparin which was liable to break and its inapplicability to flexible materials, GBH surface introduced important advances in cardiovascular surgery and paved the way for the development of newer materials<sup>7,8</sup>. An example of newer technology is a heparinised surface which eliminated graphite and utilised a cationic surfactant-tridodecyl methyl ammonium chloride to bond heparin to the basic polymer<sup>9</sup>. Heparinisation of surfaces continues to remain a valid and promising method for making prosthetic surfaces antithrombogenic.

In an alternate approach, the 'foreignness' of polymeric materials was sought to be eliminated by other chemical methods. Lyman, for example, coated them with serum albumin by using glutaraldehyde as a cross linking agent with resultant improvement in blood compatibility<sup>10</sup>. Similarly, preliminary observations by Sharma have suggested that inhibition of clot formation can be achieved by coating plastic surfaces with insulin and trypsin which share the property of low molecular

weight<sup>11</sup>. The burgeoning efforts to enhance the blood compatibility of surfaces include the bonding of anionic radicals such as poly-electrolytes and the application of negatively charged electrets to polymeric materials. They constitute an exciting endeavour in the development of biomaterials today.

Quite distinct from the approach of surface alteration to promote anti-thrombogenicity, a new category of totally inert materials has come into existence in recent years to meet the demand for blood-compatible materials. The prime examples are pyrolytic carbon and a copolymer of polyurethane-polydimethyl siloxane which have found extensive clinical applications. However, the mechanism of their blood compatibility is poorly understood.

Velours, flocked surfaces and fabrics of polyester fall in a different category altogether as their blood compatibility depends on their ability to attract a thin fibrin - platelet layer from blood and simulate the normal lining of blood vessels. These textile materials have undoubtedly contributed to the development of vascular grafts, sewing ring of heart valves, patches for intracardiac repairs and other important applications. Their major drawback is the current difficulty in controlling the deposition and build-up of autologous tissues which might distort the implant or interfere with its function.

#### PROSPECT

Degenerative disease and thrombosis of blood vessels constitute the most important cause of mortality in industrially advanced countries as well as in parts of less advanced countries like India. The mortality figures

indicate only part of the dismal story as the morbidity due to thrombotic disease is even higher. Until a preventive formula emerges from a deeper understanding of degenerative processes and thrombosis, the surgical needs to replace diseased organs will consequently remain if not multiply. Therefore the development of blood compatible materials will necessarily continue to loom large in biomaterials science and biomedical technology in the years ahead. Apart from meeting urgent clinical needs, research on blood compatible materials will also further our understanding of the physico-chemical basis of vascular homeostasis which is a biological phenomenon of vital significance.

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