FOUNDERS AWARD PRESENTATION
The Concept of Metastable Biocompatibility

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Statement of Purpose: This presentation forms part of a sequence of papers that are attempting to analyze the fundamental mechanisms of biocompatibility and the manner in which our understanding of biocompatibility is evolving with changing patterns of biomaterials usage.

The Characteristics of Biocompatibility in Long Term Implantable Medical Devices. A perception has developed over the last decade that the evolution of biomaterials for medical devices has been following a pattern in which so-called bio-inertness has been displaced by new concepts of bioactivity. Indeed, much has been written about the development of second and third generations of biomaterials on the basis of the desirability of intentional interactivity of the material with the host, either to assist in incorporation of the device into the host or to achieve some specific functional activity. The introduction of bioactivity into biomaterials specification has to be predicated on mechanisms whereby specific biomaterials characteristics control specific host responses and that modulation of the former should lead to modification of the latter and the production of better biocompatibility – based performance.

The actual evidence, however, would suggest otherwise. This may be considered from two perspectives, those of clinical experience and of experimental observation. An analysis of the performance of clinical devices over several decades points unequivocally to the conclusion that the best performances are seen with the use of materials that are as inert as possible and that most attempts to induce bioactivity or to intentionally or unintentionally deviate from inertness have led to poorer clinical performance. Over the years, most significant developments in biomaterials specifications have been concerned with the improvement to inertness, or the optimization of functional properties (e.g. mechanical or physical properties) without decreasing inertness.

Thus we can see that the successful long term implantable devices today use a smaller group of acceptable biomaterials than twenty years ago and similar materials have emerged as the preferred options for several and varied applications. The majority of total joint replacement prostheses utilize cobalt – chromium alloys, titanium alloys, UHMW polyethylene and alumina. A minority will have some component with a surface layer of hydroxyapatite. The majority of mechanical heart valves involve the same alloys with a polyester or PTFE based sewing ring and a carbon or carbon coated leaflet or disc. Synthetic vascular grafts use the same polyester and PTFE. Implanted microelectronic devices use titanium for the can and either cobalt - chromium alloys or platinum group alloys for the leads and electrodes, with either silicone elastomer or polyurethane insulation. Intra-ocular lenses and other ophthalmological devices use either PMMA or silicones. Breast implants still just use silicone polymers. Almost every time a material with less than optimal inertness, either chemical or biological, has been introduced, it has produced poorer performance.

From an experimental point of view, there have been very many attempts to correlate material, or material-surface, variables with host response variables. Almost without exception, such correlations have been elusive. Parameters involved with surface chemistry, surface energy, surface topography, hydrophilic / hydrophobic balance, electrical and mechanical properties and many others do not generally correlate with protein, cellular or tissue responses except under a few sets of narrow conditions.

Metastable Biocompatibility The very fact that we know how to control biocompatibility for long term implantable devices by optimising the balance between inertness and mechanical / physical functionality does not mean that we have no biocompatibility failures. Indeed, there are far too many of them. A few are caused by a crass disregard of the basic principles of biocompatibility. Most, however, are associated with the inherent metastability of biocompatibility. The control of the host response through the control of material stability is dependent on the maintenance of a dynamic equilibrium in a series of separate phenomena within both material and host compartments, the disturbance of any one of these equilibrium conditions having the potential to disrupt the progression of the host response. In some cases there may be a threshold value for a reaction parameter that is associated with unacceptable behaviour, but it many cases it may be a subtle single event which triggers a cascade process and the rapid evolution of a clinically disastrous outcome. This is metastable biocompatibility. This Founders Award lecture will explore the evidence for metastability and use examples of both materials – based metastability and host response catalytic processes to explain the generic performance of long term implantable devices.

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