Chapter 5
Tissue Response in Biomaterials

Biomaterials are now commonly used as implants and other tissue contacting medical devices. Complications of biomaterials and medical devices result largely as a consequence of biomaterial-tissue interactions, which all implants have with the environment into which they are placed. Effects of both the implant on the host tissues and the host on the implant are important in mediating complications and device failure. Most important host reactions to biomaterials and their evaluation are non-specific inflammation and specific immunological reactions, systemic effects, blood-materials interactions, tumor formation, and infection. These interactions arise from alterations of physiological (normal) processes (e.g. immunity, inflammation, blood coagulation) comprising host defense mechanisms that function to protect an organism from deleterious external threats (such as bacteria and other microbiologic organisms, injury, and foreign materials).

- *The inflammatory reaction to biomaterials*

Most biomaterials typically elicit a foreign-body reaction (FBR), a special form of non-specific inflammation. The most prominent cells in the FBR are macrophages, which attempt to phagocytose the material and are variably successful, though complete engulfment and degradation are often difficult. The macrophages, activated in the process of interacting with a biomaterial, may elaborate cytokines which stimulate inflammation or fibrosis. Macrophages are also the first line of defense against pathogens, and the mode of their activation will determine the success or failure of the host response to pathogens.

Biomaterial-tissue interactions:

Biomaterial-tissue interactions can be divided into two parts:

- **Local interactions**:

1. Effect of the material on host tissue:

   Blood-material interactions
   Toxicity
   Modification of healing

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Inflammation
Infection
Tumorigenesis

2. Effect of the environment on the material:
   - Physical-mechanical effects:

     Wear
     Fatigue
     Corrosion
     Stress-corrosion cracking

   - Biological effects:

     Tissue absorption of implants constituents
     Enzymatic degradation
     Calcification

- **Systemic interactions**:

  Embolization
  Hypersensitivity
  Evaluation of implant elements in blood
  Lymphatic particle transport

- *Systemic effects*

Toxicity and hypersensitivity reaction of biomaterials in animals and patients with either stainless steel or cobalt-based orthopaedic total joint replacement components, where elevations of metallic content occur in tissue (at both local and remote sites) and in serum and urine has observed. Cobalt, chromium, and nickel are in this category. At least 10 % of the normal population will be sensitive by skin test to one or more of these metals, at some threshold level.

- *Thromboembolic complications*

Exposure of blood to an artificial surface can induce thrombosis, embolization, and consumption of platelets and plasma coagulation factors, as well as the systemic effects of activated coagulation and complement products, and platelet activation. It is clear that no synthetic or modified biological surface generated by man is as resistant to thrombosis (thromboresistant) as normal unperturbed endothelium (the cellular lining of the circulatory system). Thromboembolic complications are a major cause of mortality with cardiovascular devices. Both fibrin (red) thrombus and platelet (white) thrombus form in association with valves and other cardiovascular devices. Regulatory role of blood platelets in the thrombogenic response to artificial surfaces is important. Platelet adhesion to artificial surfaces strongly resembles that of adhesion to the vascular subendothelium that has been exposed by injury. Nevertheless, the major clinical approach to controlling thrombosis in cardiovascular devices is the use of systemic anticoagulants,

particularly Coumadin® (warfarin), which inhibits thrombin formation but does not inhibit platelet–mediated thrombosis.

- *Tumorigenesis*

The pathogenesis of implant-induced tumors is not well understood; most experimental data indicate that the physical rather than chemical characteristics of the foreign-body primarily determine tumorigenicity. The possibility that implants may be causal to tumor formation is an ever present problem, with contemporary questions related to metal-on-metal hip joints and breast prostheses.

- *Infection*

Infection occurs in as many as 5–10 % of patients with implanted prosthetic devices, and is a major source of mortality. Infections associated with medical devices are often resistant to antibiotics and host defenses, often persisting until the devices are removed. Early implant infections (in first months) are most likely due to intraoperative contamination from airborne sources or non-sterile surgical technique, or to early postoperative complications such as wound infections. In contrast, late infections likely occur by a hematogenous route, and are often initiated by bacteremia induced by therapeutic dental or genitourinary procedures [1].

Reference

1. Lemons JE, Ratner BD, Hoffman AS, Schoen FJ (2013) Biomaterials science. An introduction to materials in medicine, 3rd edn. Elsevier Ltd., Amsterdam