Foreign-Body Reaction [HW8]

Biocompatibility

All biomaterials introduced in the human body, inevitably, will generate a biological response. The size, shape, and chemical and physical properties of the biomaterial and the physical dimensions and properties of the prosthesis or device are responsible for variations in the intensity and time duration of the inflammatory and wound healing processes.

Biocompatibility is usually defined as "the ability of a material to perform with an appropriate host response in a specific situation." [1]. Generally, intensity and/or time duration of inflammatory reaction can characterize the biocompatibility of a biomaterial, prosthesis, or device.

Foreign-Body Reaction

When biomaterial and medical devices are surgically implanted into the body, a series of molecular and cellular events lead to its encapsulation and isolation from surrounding tissue. This series of events is known as the Foreign Body Reaction (FBR) and can limit the device's overall biocompatibility and function. N.B. these reactions at the tissue/material interface are present during the complete lifetime of the medical device.

The injury to vascularized connective tissue not only initiates the inflammatory responses (innate immunity), it also leads to thrombus formation involving activation of the extrinsic and intrinsic coagulation systems, the complement system, the fibrinolytic system, the kinin-generating system, and platelets. These protein cascades are closely involved in the dynamic phenomenon of protein adsorption and desorption, well-known as the Vroman Effect. From a wound healing perspective, blood protein deposition on a biomaterial surface is called provisional matrix formation. Most common foreign material's surface proteins are albumin, fibrinogen, complement, fibronectin, vitronectin, γ globulin. See Fig. 1 (A).

The edema caused by the surgical procedure of implantation and several chemoattractants, cytokines, growth factors, and other bioactive agents lead to leukocyte migration from the blood and accumulation in the biomaterial site (in addition, mast cell degranulation and release of histamine also was shown to play an integral role in recruiting phagocytes). Together with platelets, leukocytes bind onto the protein-coated surface. Neutrophils have a short lifetime of about 2 days, while macrophages stay in the site for much longer. The faith of many of these cells, namely their adhesion and survival times, is greatly determined by surface-adsorbed proteins and, consequently, by biomaterial surface characteristics. See Fig. 1 (B).

Monocytes' precursors express integrins, with many different types of beta chains, which can bind fibronectin and laminin present in materials' surface. Then, downstream signaling transduction pathways can be activated and affect cytoskeletal rearrangements and formation of adhesion structures. Following adhesion, macrophages will undergo cytoskeleton remodeling in order to spread over the material surface. In the early stages of cell adhesion, macrophages will convert into podosomes, which consist in the previous cells but shows punctate f-actin on plasma membrane extensions. See Fig. 1 (C).

Around day 6/7 after implantation of the medical device, small multinucleated Foreign Body Giant Cells (FBGC) appear on the surface of the biomaterial. These cells can grow to include more than 100 nuclei since they are the result of robust macrophage fusion. Their phagocytic potential far exceeds that of all their component macrophages individually due to their ability to degrade targets extracellularly (very similar to osteoclasts which arise from the same cellular precursor in the bone marrow). Both FBGC and macrophages secrete fibroblast attractants, and the incoming fibroblasts play a key role in creating a dense and organized collagenous matrix around the biomaterial, that has very low vasculature density. See Fig. 1 (D).

This ECM capsule isolates medical devices from the rest of the interstitial tissue and can also often contract it, leading to adverse effects for the medical device function. In fact, resulting from frustrated phagocytosis, macrophages and FBGCs can release mediators of degradation, such as reactive oxygen intermediates (oxygen free radicals), degradative enzymes, and low pH solutions into the zone between the cell membrane and biomaterial surface. To partially prevent this, medical devices and prostheses composed of addition polymers (e.g. polyethylene or polypropylene) usually contain small amounts of antioxidants to inhibit this oxidative process.

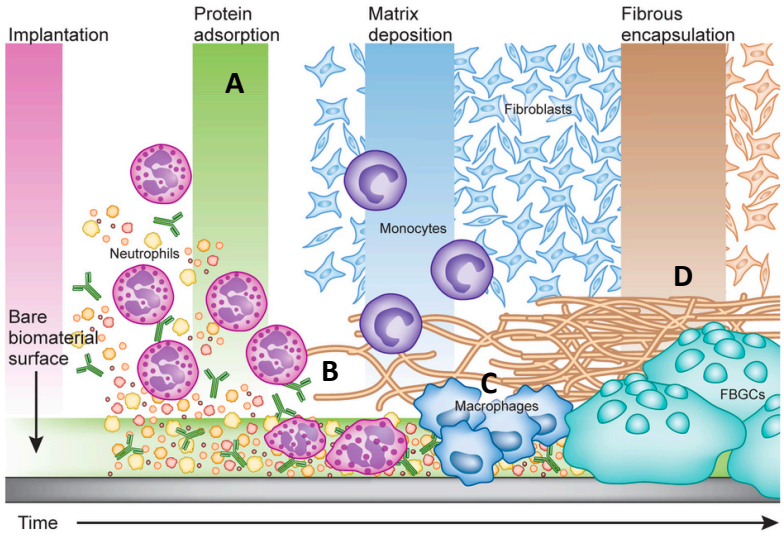

Fig. 1 – Foreign-body reaction over time.

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References

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