

WHAT IS ANGIOGENESIS?

Angiogenesis is the formation of new blood vessels from preexisting ones. It is important to differentiate angiogenesis from vasculogenesis, a process that also involves the formation of new blood vessels. Vasculogenesis is the process by which primary blood vessels are formed during the early stages of embryogenesis. In that case, the blood vessels do not emerge from already established ones, as in angiogenesis, but from the differentiation of angioblasts, embryonic cells from mesodermal origin (Vasculogenesis, Risau Flamme). In adults during physiological events and also in the case of specific diseases, angiogenesis is the process by which new blood vessels are formed.

Angiogenesis is a complex process that involves several molecular and cellular mechanisms. (Figure 1).

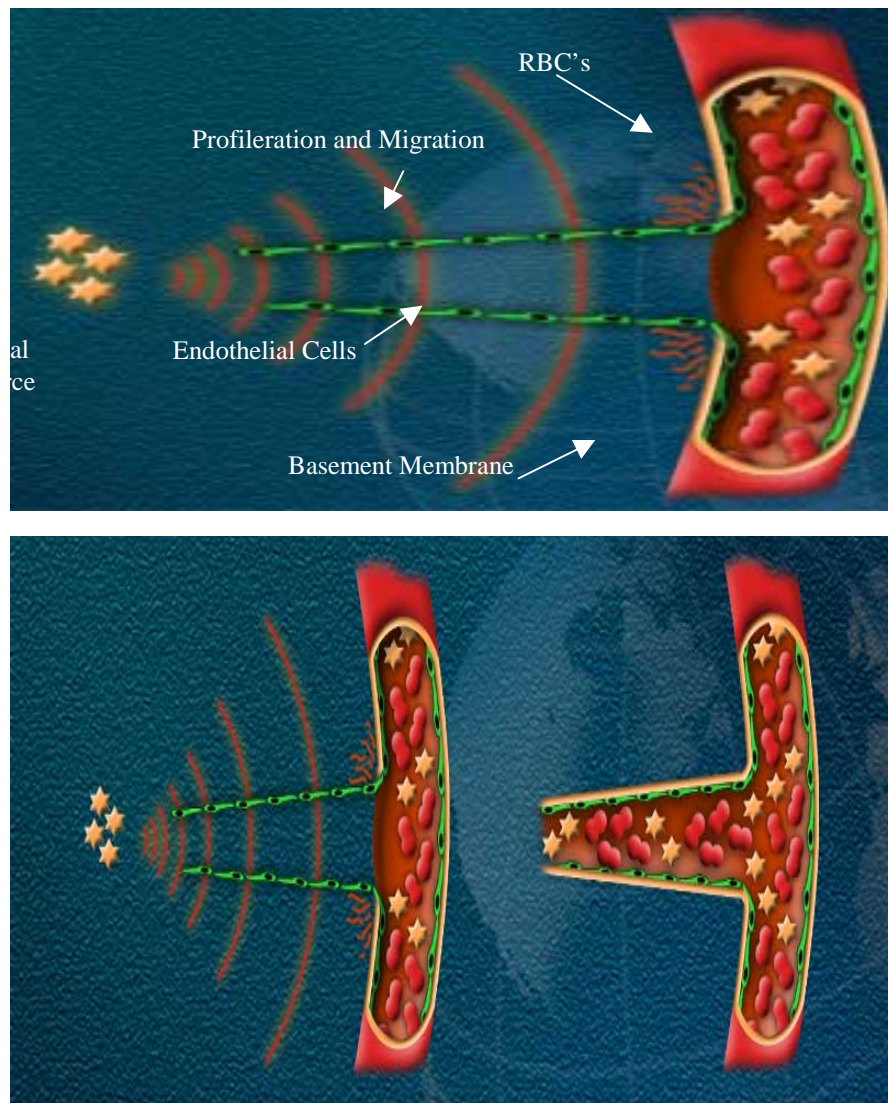


Figure 1. Anatomically speaking, a typical blood vessel is formed of an external envelope called basement membrane and composed mainly of collagen fibers. This envelope is lined on the inside by a monolayer of endothelial cells, the main cellular component of the blood vessel. Red blood cells, immune and inflammatory, “white blood cells” and different soluble nutrients circulate into it. Various triggering events (signal source) can induce the process of angiogenesis. During inflammation or hypoxia, pro-angiogenic factors (growth factors, cytokines) favoring the formation of blood vessels are conveyed to neighboring established blood vessels (step 1). One of the first cellular events observed during the angiogenesis process is the extravasation and migration of inflammatory cells toward the signal source. Through the secretion of additional pro-angiogenic factors, inflammatory cells amplify the signal (step II). Endothelial cells’ response to the pro-angiogenic signal is the secretion of specialized enzymes called matrix metalloproteinases that digest the collagen fibers present in the basement membrane. This creates a breach through which proliferating endothelial cells can migrate in the direction of the signal source (step III). Along their path, endothelial cells produce an extracellular matrix that is assembled into an organized basement membrane, leading to the formation of a functional new blood vessel (step IV). If the signal comes from tumor cells, the angiogenesis process may result in the vascularization of the tumor, thereby promoting tumor growth.

Medical reports published in newspapers and specialized magazines of associate angiogenesis to diseases such as cancer and rheumatoid arthritis. Angiogenesis is not an illness per se nor is it always linked to pathological conditions. In fact, regulated angiogenesis is, first of all, a normal physiological phenomenon. It occurs, for instance, in response to wound healing in adulthood. Angiogenesis is also encountered in patients recovering from heart attacks or strokes. Nonetheless, it is true that angiogenesis can also exacerbate several diseases currently termed as angiogenesis-dependent diseases. Approximately 20 angiogenesis-dependent diseases have been identified so far. The formation of new blood vessels is observed during hemangiomas, hypertrophic scarring, keloids, warts, periodontitis, scleroderma, neovascularization of corneal grafts and neovascular glaucoma. Angiogenesis is also closely linked to the etiology of such diseases as solid tumor cancers, rheumatoid arthritis, psoriasis and a form of degenerative disease affecting retina in the elderly.