Plasma from Young Donors and Wound Healing

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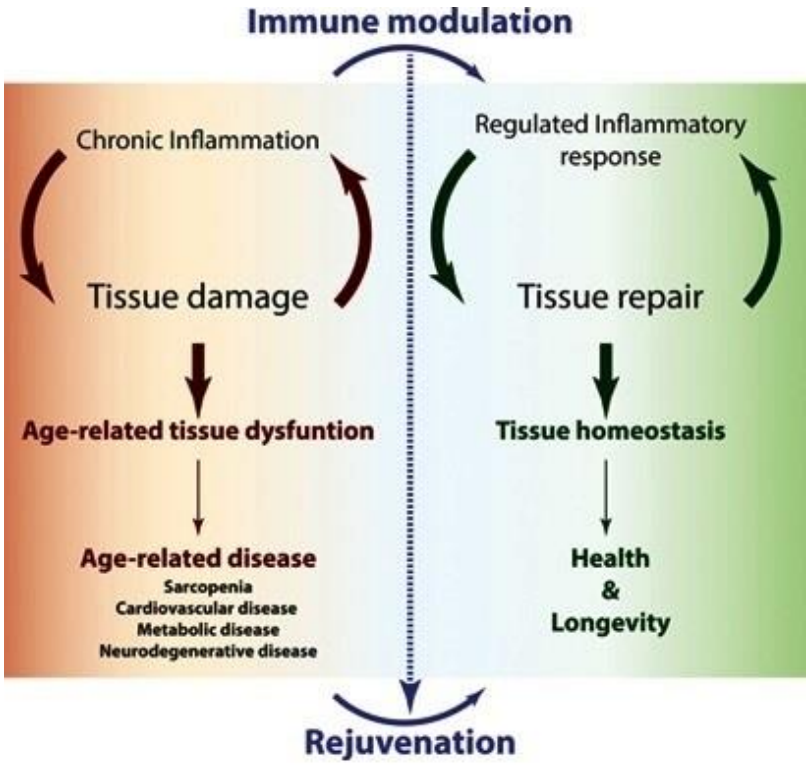
Studies have shown that care for chronic wounds costs approximately $10 billion annually in the United States. It is likely that wound care in adults aged 65 and older accounts for the majority of these costs. Chronic wounds have a profound effect on quality of life (QOL). The effect is like that of kidney or heart failure and QOL decline is particularly precipitous in older adults. The progression to sepsis and death must also be considered because of wound healing dysfunction. As our population continues age this problem will only increase. [1]

In chronic wounds, healing cells proliferate slower and have a "morphology similar to that seen in senescent cells." [2] Fibroblasts from chronic wounds, particularly ulcers of long duration, have significantly poorer responses to healing cytokines and overall growth factors. Under optimal wound healing conditions, early macrophages promote inflammation, but as the healing process continues, a reparative environment emerges. New macrophages clear neutrophils, and heathy tissues grow as inflammation resolves.



Changes arise with aging. Increased levels and prolonged inflammatory processes occur even in healthy individuals. This age-associated inflammation and delay in wound healing may have consequences such as higher rates of infection. Infected wounds in older mice fail to clear the bacteria efficiently and show greater bacterial colonization with increased rates of infection. [3] The chronic inflammation seen with age and chronic conditions increases the number of dysfunctional mitochondria, and older age has been associated with lower levels of antioxidants.

Elderly people are susceptible to this increased damage of oxidative stress due to a decline in the efficiency of their endogenous antioxidant systems. [4]

When inflammation becomes prolonged and persists, it can become damaging and destructive. Several common molecular pathways have been identified that are associated with both aging and low-grade inflammation. "Typical alterations include elevated levels of planktonic and biofilm bacteria, elevated levels of pro-inflammatory cytokines (TNFa, IL-1), elevated levels of proteases (matrix metalloproteinases (MMPs) and neutrophil elastase (NE)), denatured extracellular matrix proteins (collagen, fibronectin) and cellular receptors (TGFb-RII, integrins)." [5] **Monocyte chemoattractant protein-1**(MCP-1) has a key role in the migration and infiltration of inflammatory cells. At the site of inflammation, MCP-1, when at optimal levels, enhances and modulates the expression of other inflammatory factors/cells.

Pressure sore healing was accelerated in mice when exosomes were placed on the wound 1 time a day for 3weeks. This study using human embryonic stem cell-derived exosomes ameliorated endothelial senescence by activating Nrf2 and recover aging-related angiogenic dysfunction, thereby accelerating wound healing in aged mice. [6]

Young Plasma decreases inflammation to aid in wound healing

Healing will become even more robust when the wound is bathed in **all** the factors present in a young milieu. Normal blood plasma contains 1,840,000,000 exosomes per ml and large numbers of antioxidants. [7] Adipose or fat tissue–derived from young (4 month) and old (20 month) mice were cultured in presence of young or old plasma for 3 days. In the young plasma culture, the levels of *p16* and *p21*-inflammatory proteins were significantly reduced, compared to exposure to old serum condition. In addition, *Tnf-α* and *Mcp-1* (inflammatory factors) were significantly diminished in the presence of young serum. These data support that young serum can change the aging stromal vascular fraction (SVF) of adipose tissue that contains healing endothelial progenitors, fibroblasts, lymphocytes, monocyte/macrophages, pericytes, pre-adipocytes and stromal/stem cells, from a senescent and pro-inflammatory phenotype to a young healing environment. [8]

From diabetic ulcers to burns to traumatic burns, creating a decrease in the chronic and pathologic inflammatory process will significantly improve patient care. [9]

References:

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