

Lecture 18

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The Role of Inflammation in Tissue Healing

- Cells, lipids, proteins, free radicals, etc. increase vasodilation and vascular permeability
 - o These cells (and other stuff) also interact with each other
- Ex. mast cells can degranulate (releasing granules of histamine) in response to physical injury or substance P or complement proteins or macrophage factors (released by macrophages) -- histamine causes further vasodilation and even more leakiness
- Plenty of stuff (extracellular ligands binding to their receptors on the cell surface) can cause the mast cells to degranulate
 - o Damage, substance P, complement proteins, and macrophages
- Swollen is not inflammation; it's leakiness and water follows
- "functional hyperemia" and "reactive hyperemia" aka the pump
- Metabolism drives blood flow
- Capillaries (capillary beds) is site where oxygen is given to muscle from blood and blood flow
- The pump in summary:
 - o Metabolism determines blood flow
 - o When a muscle fiber contracts, it is a metabolic activity - approximately one second after the initiation of exercise, there is an increase in blood flow in that fiber's direction
 - o The substrates and products of that metabolism include numerous vasoactive molecules; they diffuse into the blood, which provides information about the internal metabolism of that cell
 - o That informs the circulatory system to provide more blood (i.e. more metabolic substrates); the bulk of this delivery is by vasodilation
 - o BUT
 - o Size principle ensures that you recruit your motor units (in an all-or-none fashion) in a specific order; that means some fibers will be active while others will be inactive

- The fibers in a single motor unit are distributed throughout the muscle, not grouped together in neighborly cul-de-sacs
- Those well-scattered muscle cells receive their nutrition by capillaries and capillaries don't have smooth muscle, so they are unable to adjust their volume (diameter adjustments must be made upstream)
- BUT
- Muscle fibers tend to be longer than the capillaries supplying them (thus, multiple suppliers)
- Capillaries receive lots of chemical information from muscle cells
 - RBCs and endothelial cells are probably secreting additional information
- Actual chemicals: hydrogen ion accumulation (pH change), lactate, nitric oxide (by endothelium), adenosine (with or without phosphates), prostaglandins, maybe other eicosanoid explanations (e.g. reducing cytochrome P450 constrictor metabolites), maybe leaked K, possible some bradykinin activity
- What's the point of all this endothelial leakiness?
 - Needed to get chemicals and all these cells and stuff to the area in order to clean before any repair begins to happen
- Pus is a bunch of dead neutrophils accompanied by some living 'phils, a few plasma proteins, and whatever detritus got stuck in that same space
- A few days out from initial injury, when macrophages have their custodial duties under control, they secrete some growth factors, which help initiate the proliferation phase
- Proliferation phase = growth of new tissue (angiogenesis - new blood vessels)
- Fibroblasts are what do your remodeling (cells that synthesize stuff)
 - Progenitor cells: a little bit less freedom than stem cells, but they can still differentiate into the wrong stuff
- MRFs: myogenic regulatory factors
- Myo-D: myoblast determination protein 1
- If you spend your post-injury life toggling between supine and prone postures, healing is limited