PHYS30005 Lecture 3

Muscle can be injured in many ways (surgery, tearing, straining, extreme temperature, Chemical injury, etc.)

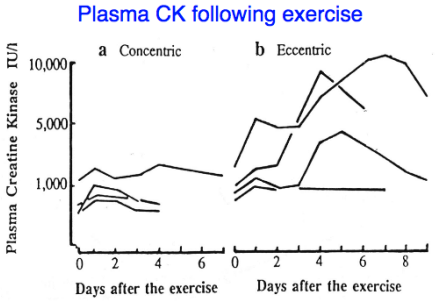
Sequence of muscle injury and repair
-Degeneration
-Inflammation
-Regeneration
-Fibrosis
connective tissue (fibrotic material) will infiltrate where we want muscles to be (undesirable outcome)

Injury ONLY to muscle fibres (immediate and complete restoration with little (if any) fibrosis)
But if extracellular matrix (ECM) compromised…
-more severe injury
-damaged to blood vessels, nerves
-less complete regeneration
-extensive fibrosis
-impaired functional restoration

If we never get full restoration, long-term effect or muscles may get reinjured again

Why muscles get injured by their own actions?
-Heavy load unable to be lifted, and the muscles lengthen.
-Greater forces developed during stretch
-Force is about two folds greater
-Determining the magnitude of the force decrease associated with the stretch-induced injury
→Average force developed during stretch
→Displacement or magnitude of strain

Indirect measures of muscle injury
-Creatine Kinase (CK) release from muscle
-Delayed, highly variable response
-Increase Ca2+ influx
-Decrease in relative maximum force (in absence of fatigue)
-Muscle soreness (in humans)



When we do an exercise, the next time we do the same exercise, it won't hurt as much anymore.
→The muscle has become custom to this type of activity
→This makes a protective effect

If you look under a light microscope of an injured muscle immediately, can't tell the muscles are injured. However, 3 days later, there is a delayed inflammatory response to the muscles

The Force Deficit— The gold standard of injury
•problems quantifying structural damage (light microscopy)
•considerable variability in plasma enzyme levels as indices of injury
•the ↓in max. force, although an indirect measure, provides the most valid measure of the totality of the injury

Concept of Initial Injury
•the initiating event associated with contraction-induced injury is primarily mechanical in nature
•occurs when individual sarcomeres are stretched excessively, damaging some structural component within or between sarcomeres
•the injury may involve any number of fibres within a muscle, and within an individual fibre
•focal injuries
→localized to a few sarcomeres in series or in parallel
•more widespread injuries
→across the entire cross section of the fibre; as observed with electron microscopy

Lengthening damage, at the micro level you can see why it's getting injured

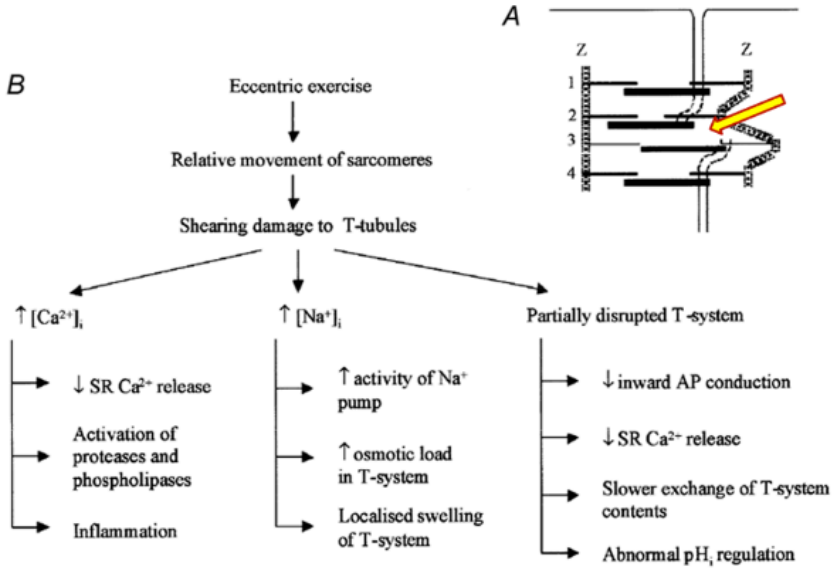
When the sensitive mechanisms in the Z line have been compromised, Ca2+ cannot go down through the muscles

Contraction-mediated damage: initial injury
•mechanical in nature
•immediate structural and functional evidence (force deficit)
•injury may result from a single contraction or the cumulative effects of many lengthening contractions
•tensile stress > tensile strength = structural failure
– disruptions to sarcomeres
– disruption to t-tubules leading to E-C coupling failure
• t-tubules are at the overlap of thick and thin filaments and are assumed to be subject to shearing stress
• where shear stress is greatest - rupture occurs

Witihin a muscle fibre, not all the sacromeres are the same (some ae stronger and some are weaker, thus not all go through trauma)

Sacromere inhomogeneity hypothesis

•a promising hypothesis is that injury is initiated when weak sarcomeres are stretched by stronger sarcomeres that exist in series
→i.e. when a contracting muscle is stretched, the lengthening of individual sarcomeres is not uniform
•due to biological variation, some sarcomeres will be weaker than others
•the weakest sarcomeres are randomly distributed throughout the fibre and are usually those on the descending limb of the tension-length curve
•when stretched, the weak sarcomeres will yield or "pop"
•upon relaxation, some of these sarcomeres will fail to reinterdigitate properly and remain at longer lengths

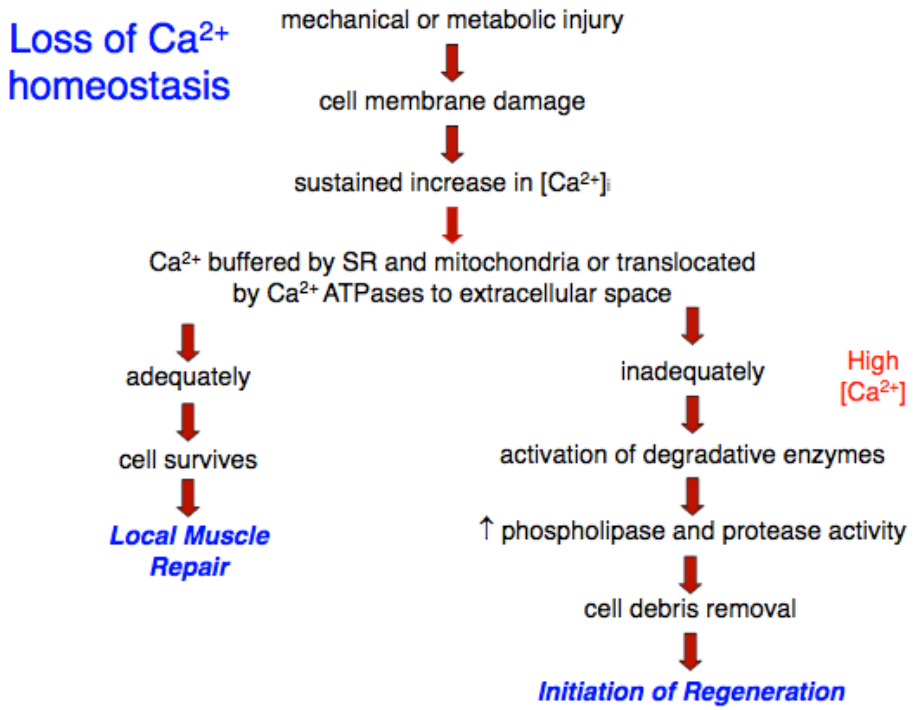


Concept of Secondary Injury

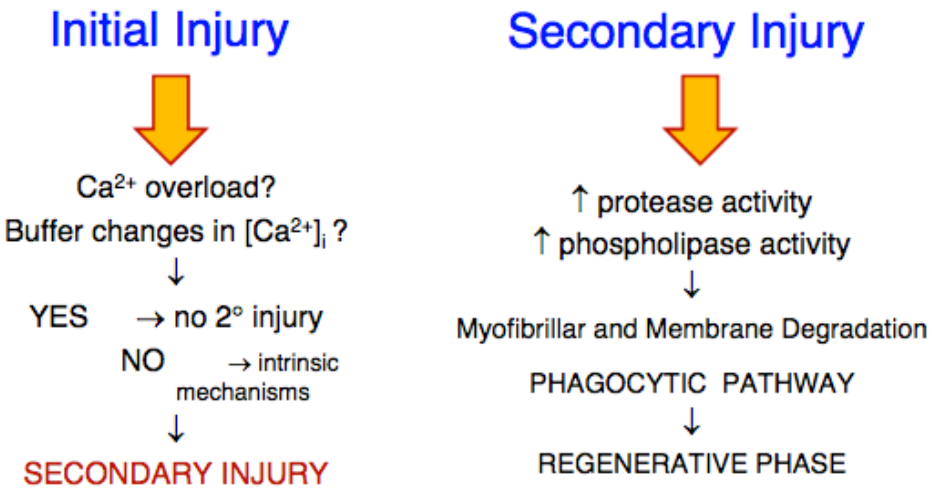
•1-3 days after initial injury - severe morphological damage observed by LM or EM
•enzyme release (CK)
•intensity of muscle pain (delayed onset muscle soreness or 'DOMS')
•quantitative assessment of injury by these methods not possible
•force deficit still provides best assessment of damage and subsequent recovery
•although immediately after an exercise protocol the decrease in force may reflect both fatigue and injury, the deficit remaining following recovery from fatigue in the ability of the muscle to develop force provides the most quantitative and reproducible measure of the totality of a muscle injury

Loss of Ca2+ Homeostasis

If we can't keep Ca2+ down, a chronic level of ca2+ will activate processes that might lead to distruction of the muscle
•an elevation in [Ca2+] at the site of damage
•cellular necrosis is linked with a loss in Ca2+homeostasis
•disruption of the sarcolemma could allow for loss of ion regulation
•SR may become dysfunctional, i.e. unable to resequester Ca2+
•if the fibre is able to handle Ca2+influx effectively and maintain relatively low [Ca2+]I levels, then the injury sequence may never proceed to the next phase



Lengthening muscle actions→Sarcomere inhomogenity→Sarcolemmal disruption



Varying severity of muscle fibre injury

- Minor damage
  - limited intracellular disruption
  - minor damage to cell membrane
  - viability maintained ∴no degeneration
  - intracellular repair, membrane resealing
- Major damage
  - irreparable intracellular disruption
  - compromised cell membrane
  - loss of cell viability and cell degeneration
  - fibre replacement via regeneration

Degeneration and Inflammation
-neutrophils and macrophages recruited to site of injury
-remove necrotic debris
-prepare injury zone for regeneration
-inflammatory response is critical for successful regeneration
-actiavtion of satellite cells (that lie outside the sacrollema, and it sits there doing nothing until it is called (when muscle injures or gets stretched))

- Localised neutrophils
- release degradative enzymes
- destroy debris
- increase vascular permeability
- stimulate monocyte accumulation
- stimulate satellite cells (muscle stem cells)

Myoblasts become the new muscle fibres
So the satellite cells and myoblasts proliferate accompanied by inflammation

Conditioning protocols to confer protection from contraction-induced injury

- repeat bouts of lengthening (eccentric) contractions shown to decrease force deficit
- mechanism? Improved sarcomere homogeneity?
- sufficient recovery between sessions →'training'
- protection lost by "overtraining" or fatigue (lack of sufficient recovery between bouts)

Protection from contraction-induced injury
- "trained" muscle less likely to be injured by a protocol of contractions that previously caused injury
- protection is lost by "overtraining" or fatigue (lack of recovery between bouts)
- mechanism for protective effect?
- possible that trained muscle consists of regenerated fibres that have increased sarcomere homogeneity
- these fibres are less likely to be pulled onto the descending limb of the length-tension relationship when activated and stretched forcibly

regenerated muscle was regenerated to protect the muscle against the same activity again