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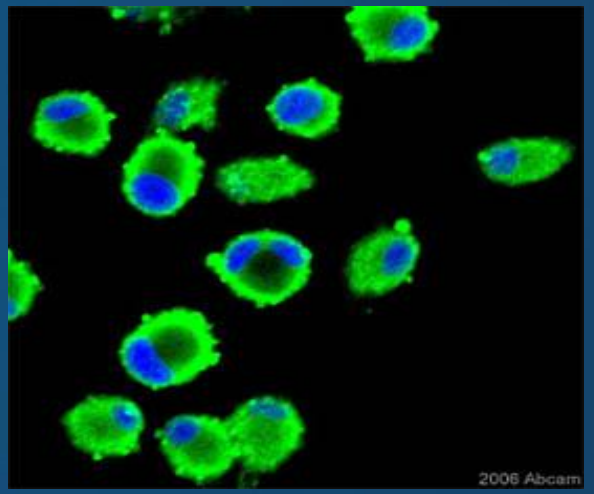


MTF Musculoskeletal Transplant Foundation

ORTHOFIX®

Learning Objectives

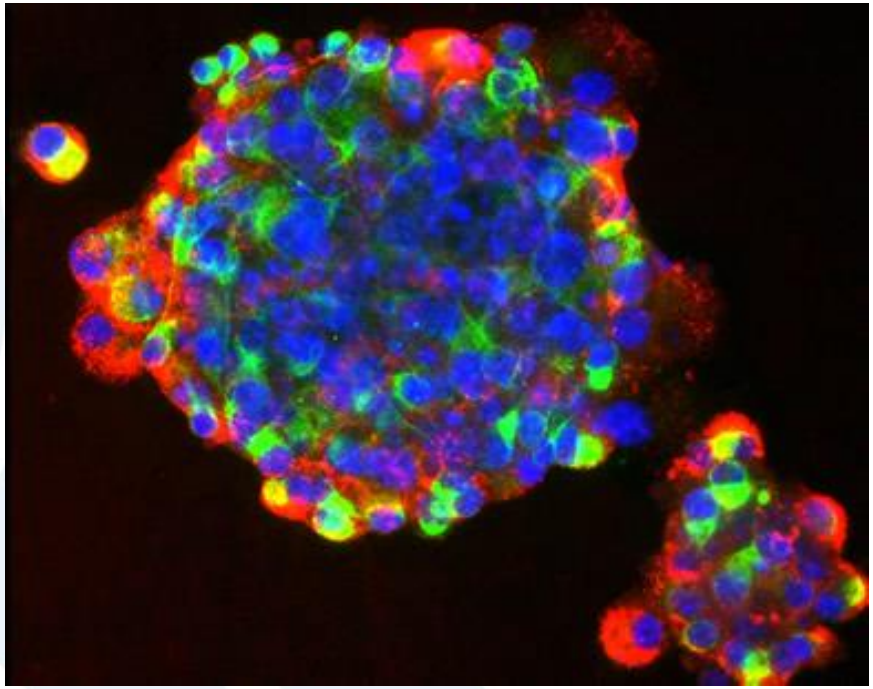
- At the conclusion of this lesson you should be able to:
  - Understand the key terms and definitions regarding stem cells
  - Differentiate between the adult and embryonic stem cells
  - Differentiate between mesenchymal and hematopoietic stem cells lineages
  - Describe the key advantages of mesenchymal stem cells
  - Describe how mesenchymal stem cells (MSC) differentiate into bone cells to create a bone matrix

What Are Stem Cells?

- **Stem cells** have the remarkable potential to develop into many different cell types in the body.

- Serving as a sort of repair system for the body, they can theoretically divide without limit to replenish other cells as long as the person or animal is still alive.

- When a stem cell divides, each new cell has the potential to either remain a stem cell or become another type of cell with a more specialized function, such as a muscle cell, a red blood cell, or a **bone cell**.



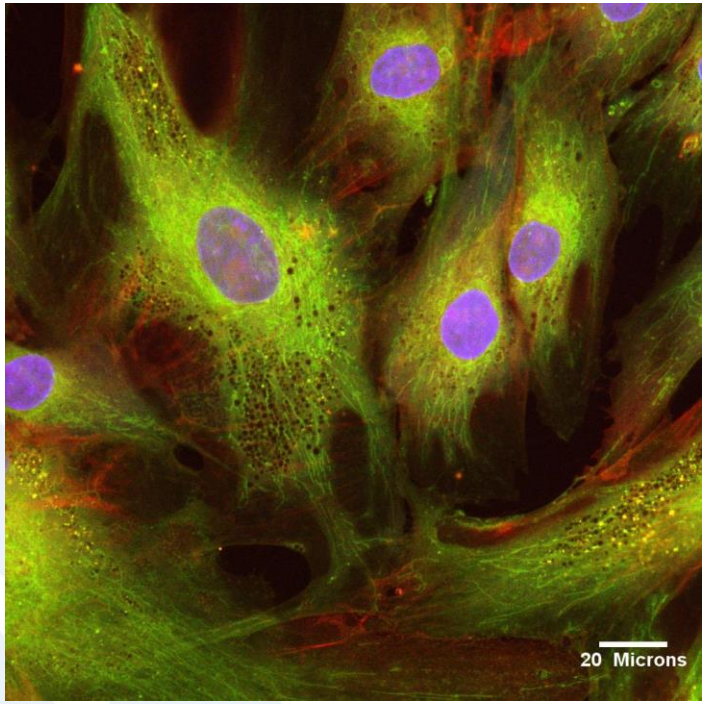
Source: http://stemcells.nih.gov/info/basics/

Stem Cell Potency

- A stem cell's potential is a measure of of the cells ability to differentiate into specialized cells.
- Potency Classifications
  - Totipotent: ability to differentiate into any cell
  - Pluripotent: descendant of totipotent cells, and can form most cells
  - Multipotent: ability to differentiate into specialized cells within a lineage
  - Unipotent : ability to produce only one type of cell

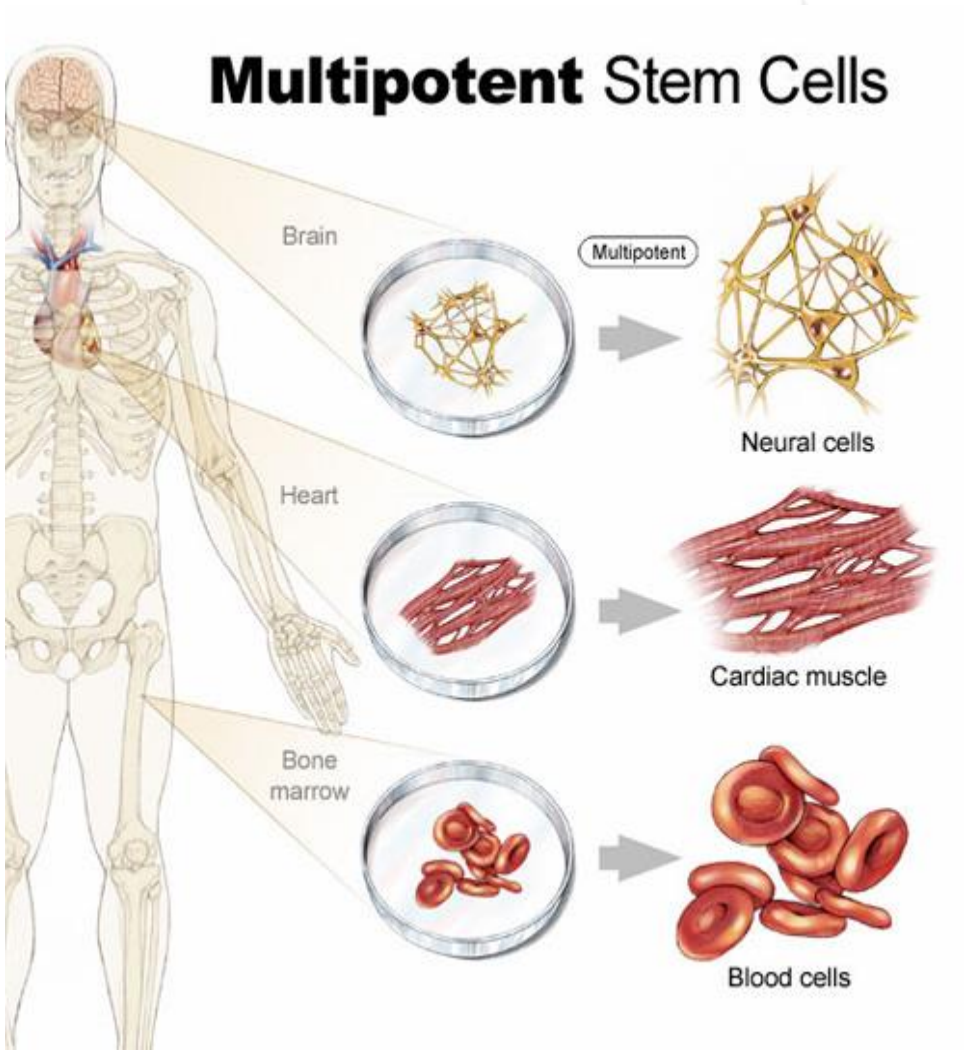
Stem Cell Classifications

- Adult Stem Cells
  - Hematopoetic
    - Multipotent
  - Mesenchymal (Bone Marrow Stromal)
    - Multipotent
- Embryonic Stem Cells
  - Early Embryonic
    - Totipotent
  - Blastocyst Embryonic
    - Pluripotent
  - Fetal Stem Cells
    - Pluripotent
  - Umbilical Stem Cells
    - Multipotent



Source: http://learn.genetics.utah.edu/content/tech/stemcells/sctypes/

Stem Cell Classifications



- Adult Stem Cells
  - Potential: Multipotential
    - Ability to form **SPECIFIC** cells within a lineage
    - Can make multiple copies of themselves over a prolonged period
    - Can give rise to mature cells with specialized functions
  - Primary Role: Maintain or repair tissue
  - Categories:
    - Mesenchymal
      - Bone, cartilage, fat, muscle, nerve cells
    - Hematopoetic
      - Blood Cells

Mesenchymal Stem Cells

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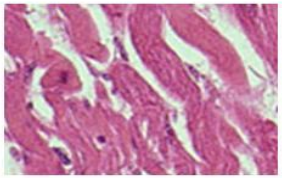
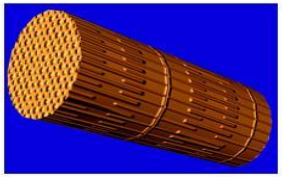
Smooth muscles

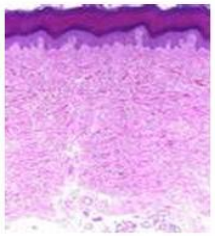


cardiac muscles



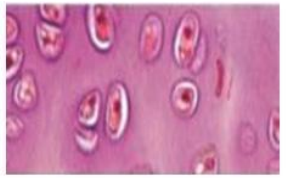
Skeletal muscles

Tendons



Dermal tissues

Neurons



Chondrocytes

Osteocytes

Adipocytes

Teeths

Muscle and Tendon

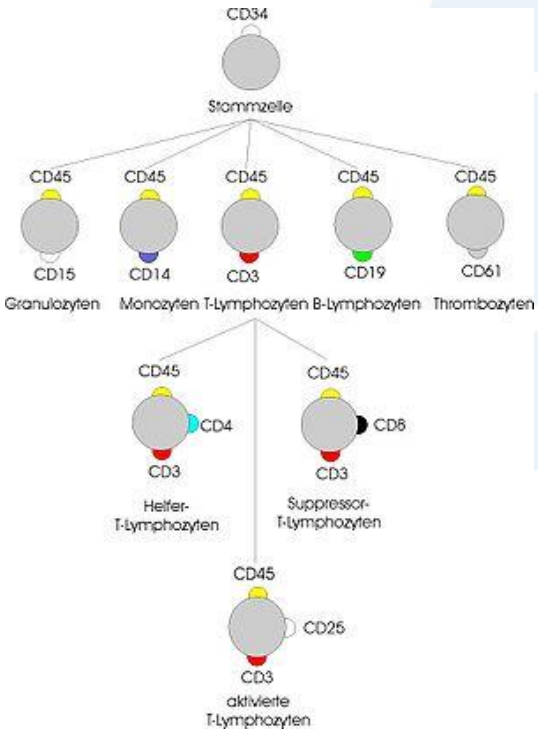
MSC

Bone and cartilage

Retinal Photoreceptor

Others

Stem Cell Identification

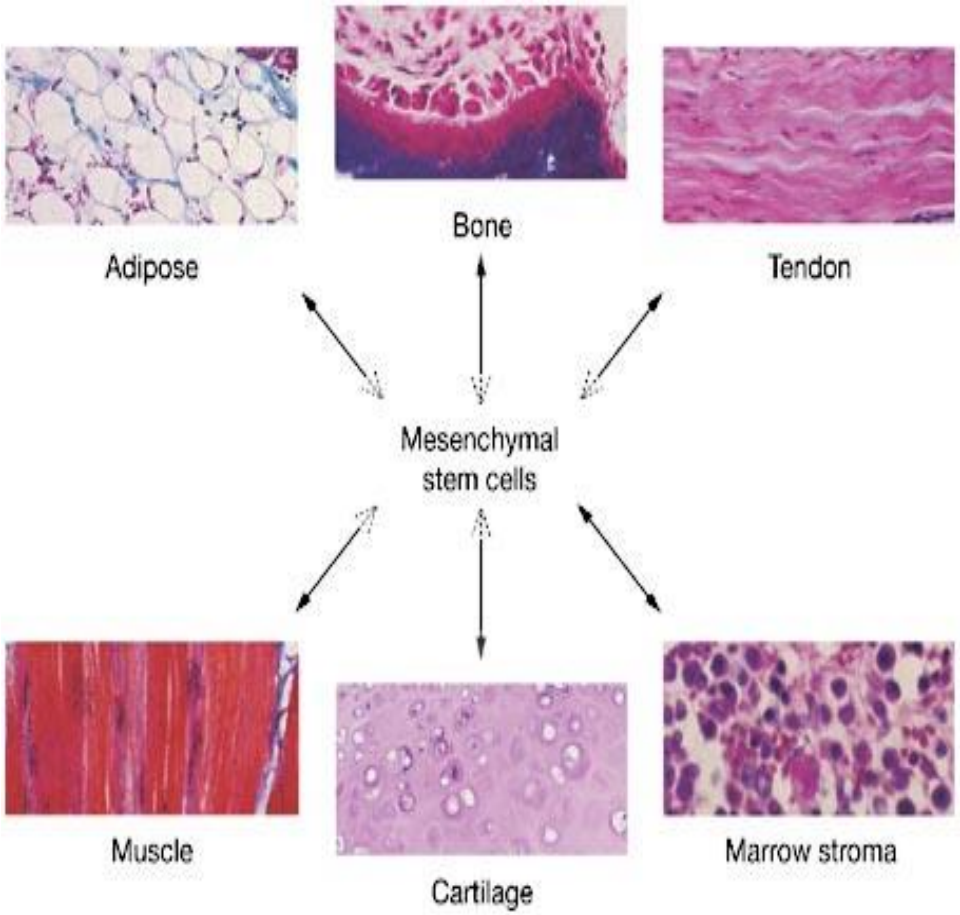


- Cells are identified by their surface markers
- Hematopoetic stem cells are CD 34+,45+, while Mesenchymal Stem Cells (MSCs) are CD 34-,45-
- Mesenchymal stem cells have CD166 markers among many others.

Why is CD34 & 45 relevant?

- **CD34 and CD45** are a cell surface antigen selectively expressed on human hematopoietic progenitor cells
- These antigens can induce an immune response when transplanted into a foreign environment by inducing T-cell activation
- That immune response may result in rejection of the tissue

Therapeutic Advantages of MSCs

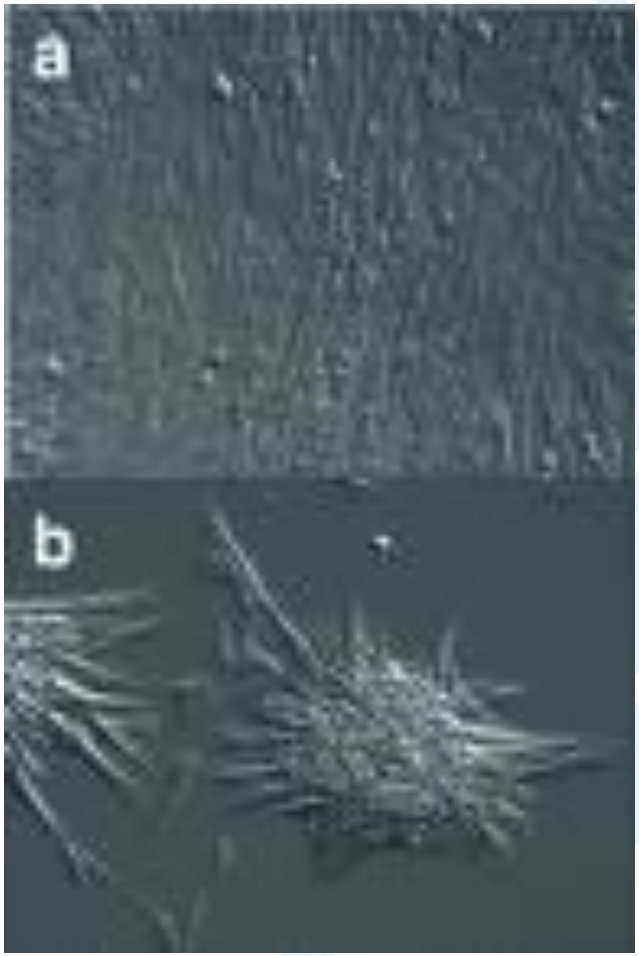


- Hypo-immunogenic
  - Will not illicit an immune response in the recipient
  - Universal donor
- Will differentiate into bone, cartilage, muscle, or fat given the proper signals.

Mixed Lymphocyte Reaction

- A measure of histocompatability
- Lymphocytes from incompatible individuals will stimulate each other to proliferate significantly (immune response)
- Tissue is considered compatible if the test does not generate a MLR

Mesenchymal Stem Cells



- Generate bone, cartilage, fat, and fibrous connective tissue
- CD 34- and CD45-
- CD 166+
- Hypo-immunogenic
  - MSCs do not illicit an immune response
  - Prevent T-cell activation

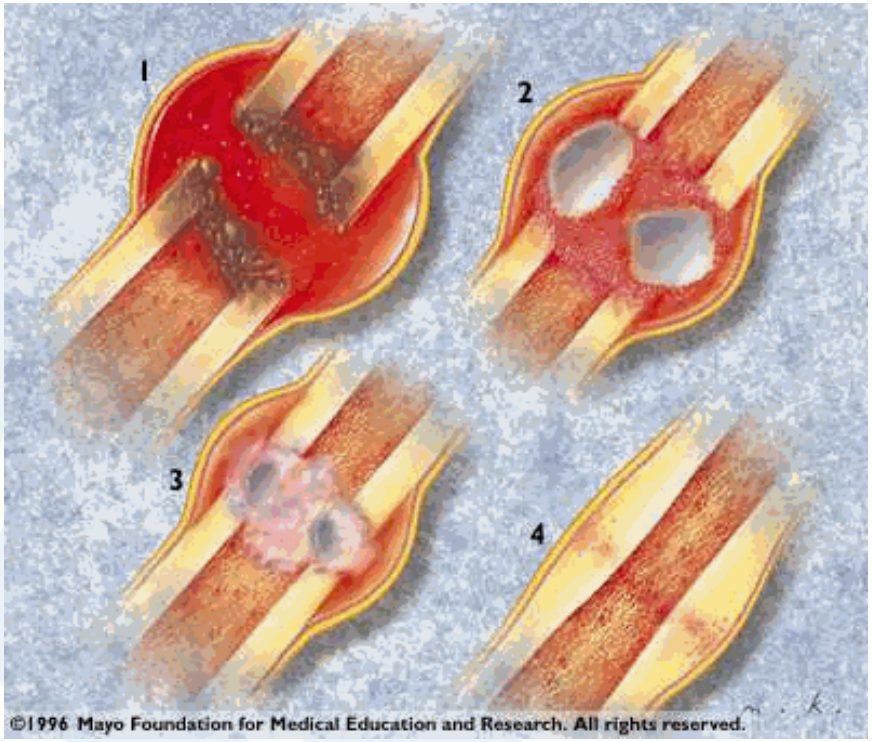
Source: Journal of Inflammation 2005, 2:8

Bone Healing Process

- Three distinct and overlapping phases
  - Early inflammatory phase
  - Repair phase
  - Late remodeling phase

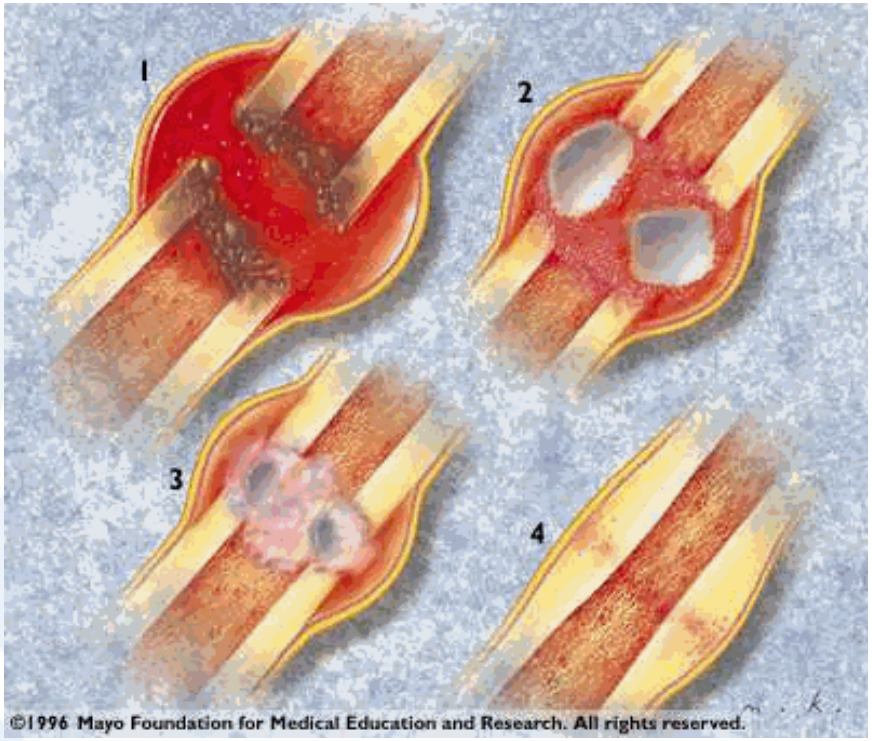
Bone Healing Process

- Inflammatory Stage
  - Hematoma develops at site of osseous injury
  - Prostaglandin mediates infiltration of inflammatory cells (macrophages, lymphocytes, etc.)
    - Granulation tissue forms
    - Angiogenesis
    - **MSC migration**
  - Process may be inhibited by anti-inflammatory medication



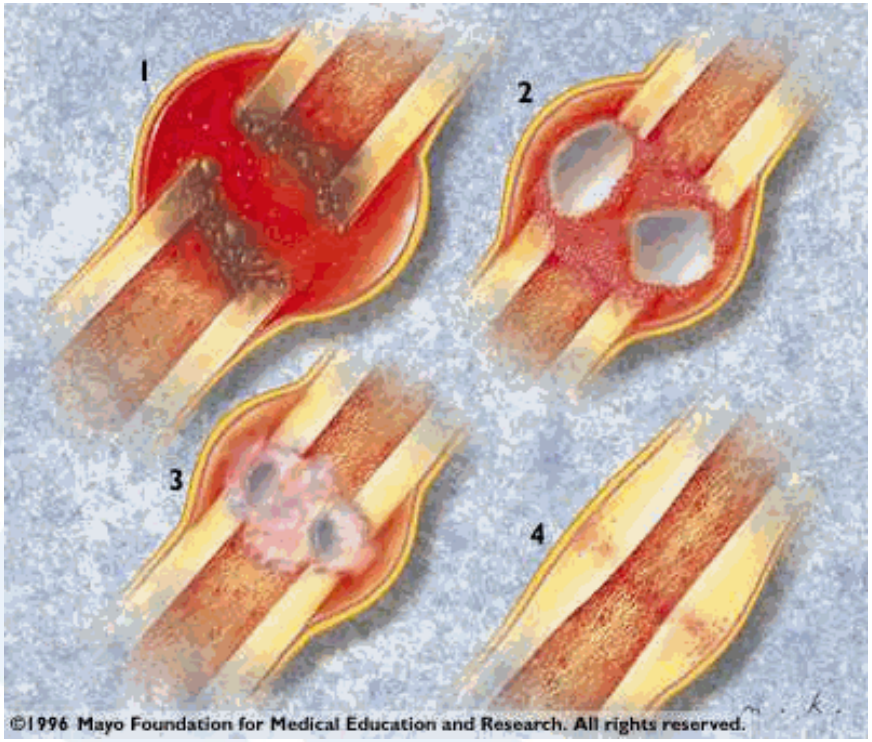
Bone Healing Process

- Repair phase
  - Fibroblasts lay down stroma to support vascular in-growth
  - Collagen matrix developed
  - Osteoid secreted and mineralized creating soft callus which ossifies into woven bone
  - Stabilization essential!
  - Process inhibited by nicotine
  - MSCs differentiate into osteoblasts and become quiescent



Bone Healing Process

- Remodeling Phase
  - Bone reformed to original shape, structure, and strength
  - Strength influenced by axial loading
  - 3-6 months
  - Osteocytes are incorporated into the matrix



Your first question please…