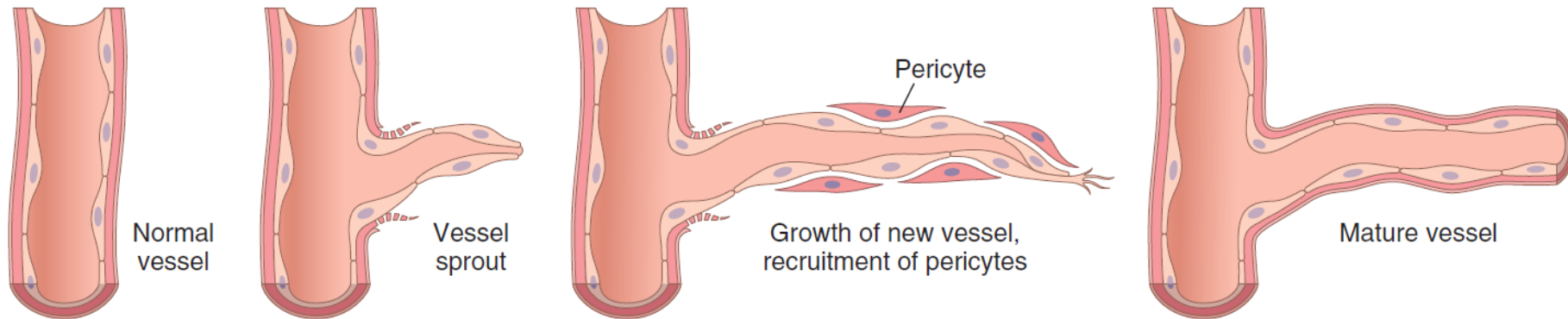


# Angiogenic growth factors



NO → Vasodilation  
VEGF → increased permeability

Separation of pericytes from the abluminal surface

Migration of endothelial cells

Proliferation of endothelial cells just behind the leading front of migrating cells

FGF-2

AngI  
PDGF

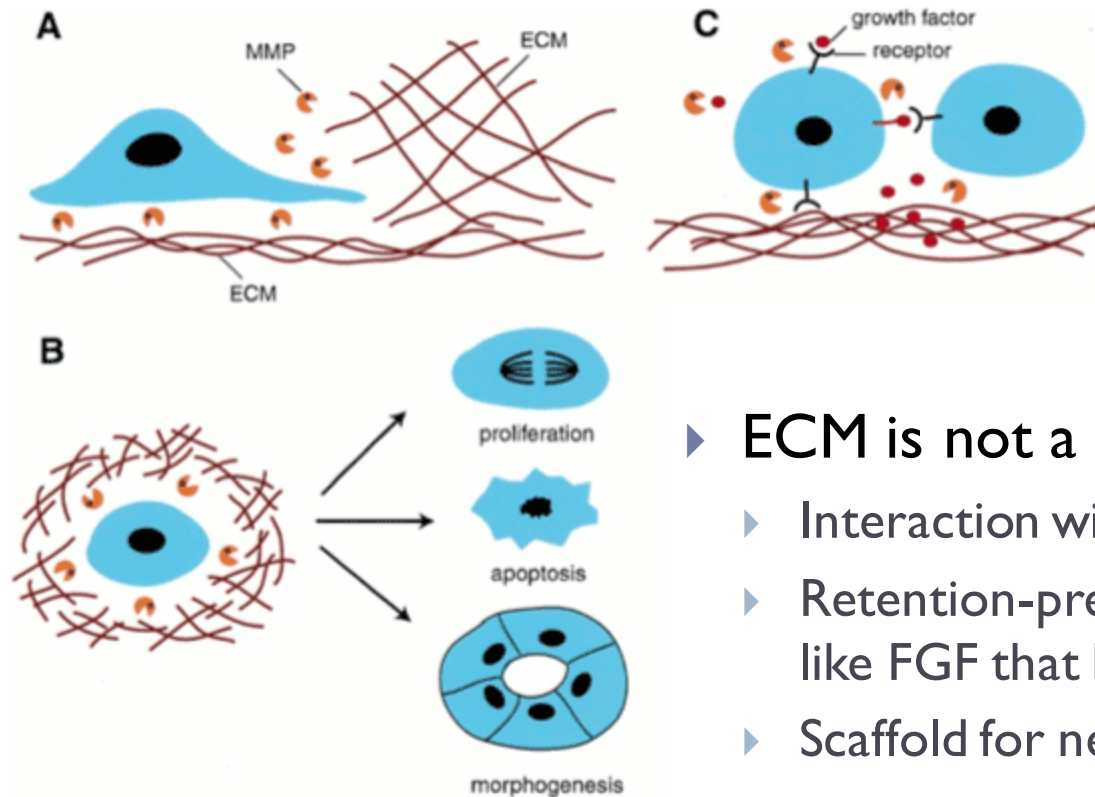
Remodeling into capillary tubes

Recruitment of periendothelial cells

TGF- $\beta$

Suppression of endothelial proliferation & migration  
Deposition of the basement membrane

# Role of the ECM in angiogenesis



## ► ECM is not a passive bystander:

- Interaction with integrins
- Retention-presentation of growth factors like FGF that binds heparan sulfate
- Scaffold for new vessel formation
- Actively remodelled by enzymes like MMPs

## Granulation vs Scar

### A: Granulation tissue

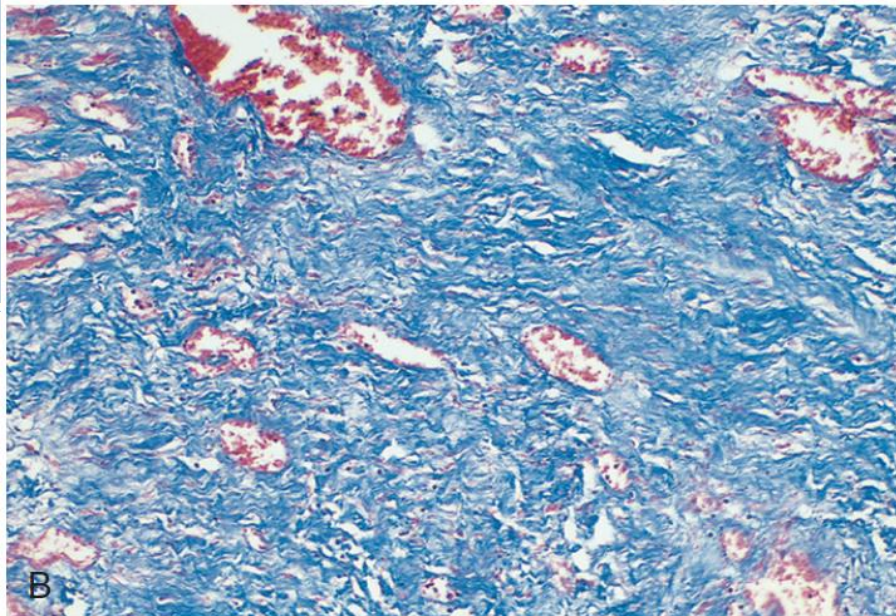
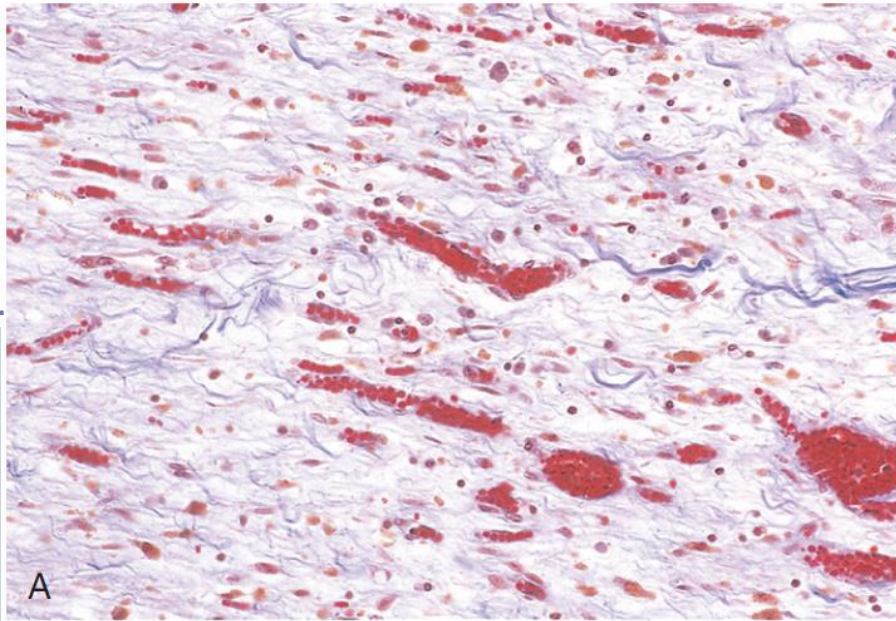
- Angiogenesis
- edema
- loose ECM
- inflammatory cells

### B: Mature scar

- Dense Collagen
- Less blood vessels

Recruitment and activation of fibroblasts by cytokines/growth factors

ECM deposition vs degradation (e.g. MMP)



Less proliferating fibroblasts

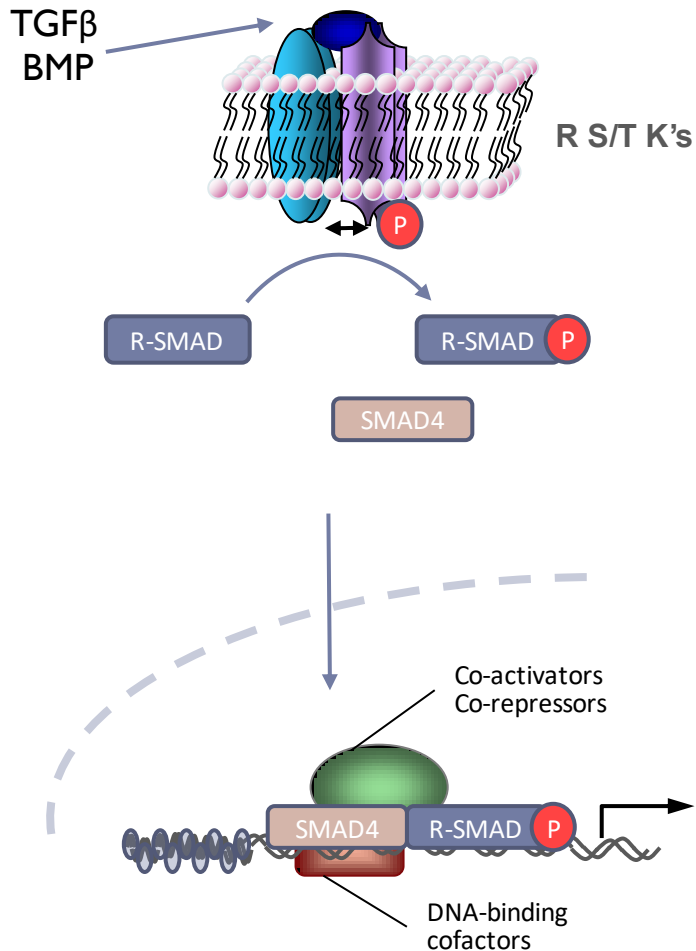
More ECM synthesis

Inactive fibroblasts

Dense Collagen

Vascular regression

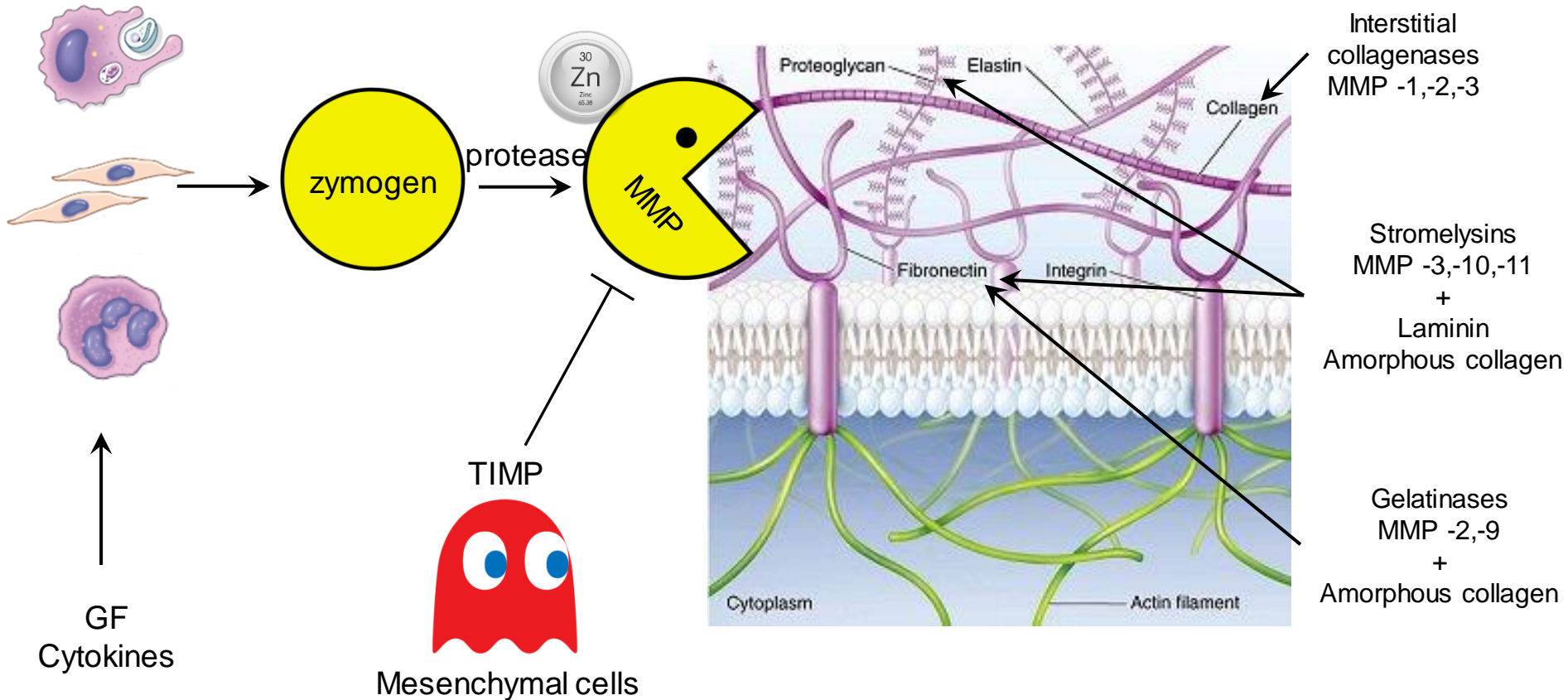
# ECM Deposition/Scar formation growth factors (TGF $\beta$ )



- ▶  $\uparrow$  production of collagen, fibronectin, & proteoglycans
- ▶  $\downarrow$  collagen degradation
  - ▶  $\downarrow$  proteinase activity
  - ▶  $\uparrow$  TIMP activity
- ▶ **Anti-inflammatory**
  - ▶  $\downarrow$  lymphocyte proliferation
  - ▶  $\downarrow$  activity of other leukocytes



# Maturation and reorganization (Remodelling)

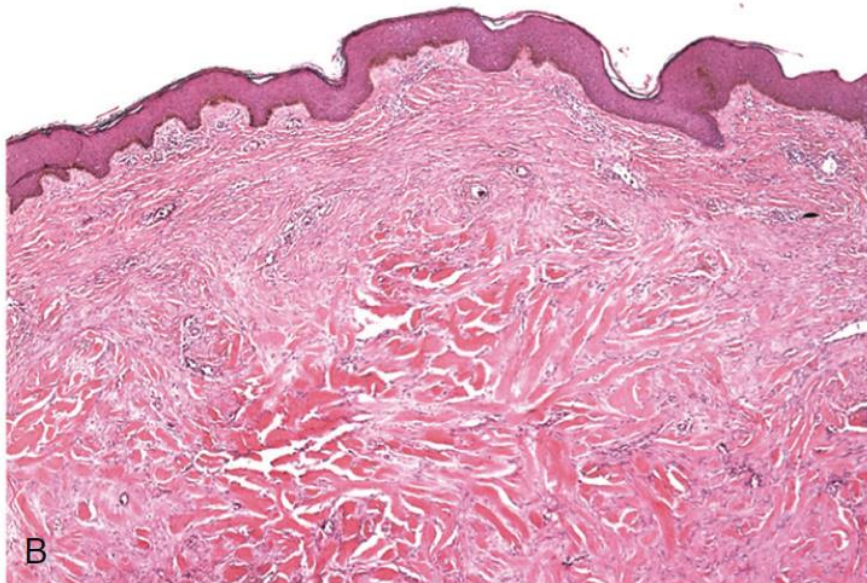


# Factors influencing tissue repair Quiz

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- ▶ Infection
- ▶ Nutrition
- ▶ Glucocorticoids
- ▶ Mechanical
- ▶ Perfusion
- ▶ Foreign bodies
- ▶ Tissue type
- ▶ Injury type
- ▶ Location





## Aberrations of cell growth in repair

Keloid

Proud flesh

## Clinical examples of repair & fibrosis



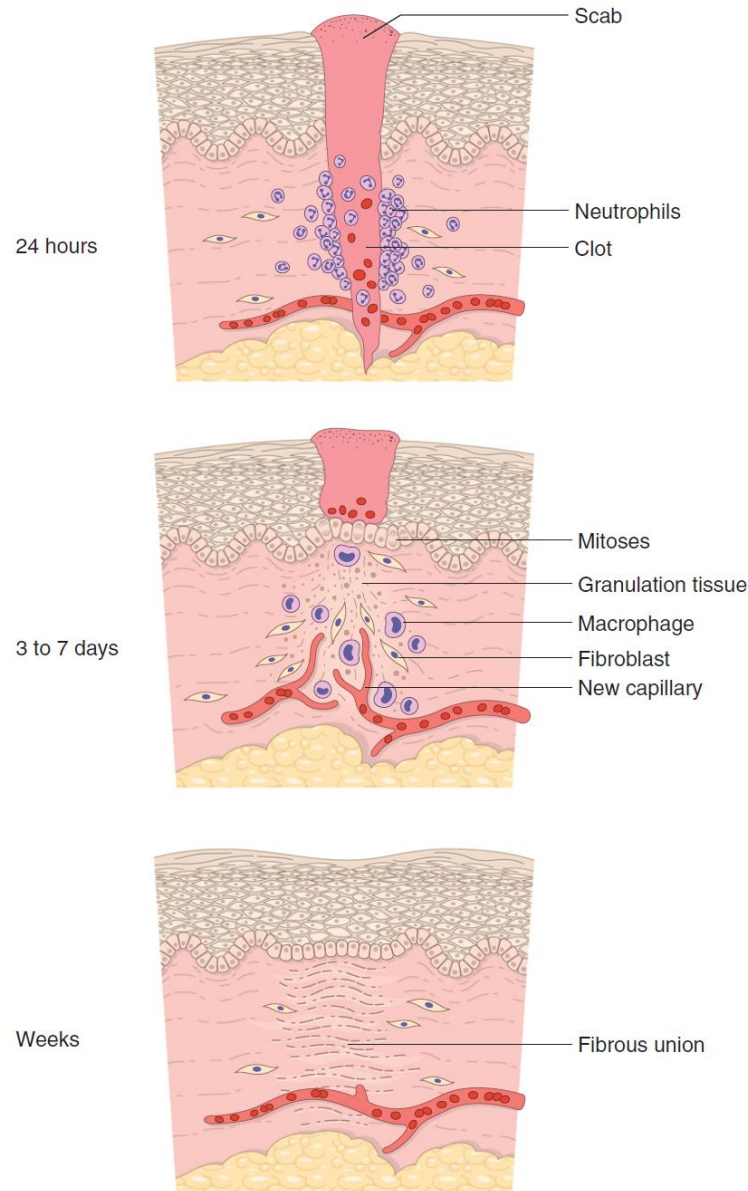
24-48 hours, migration-proliferation of epithelial cells from both edges depositing basement membrane as they progress

Day 3, Collagen fibers at the incision margins are vertically oriented and do not bridge the incision

Day 5, neovascularization reaches its peak & collagen begins to bridge the gap

2<sup>nd</sup> week, blanching Begins (increased collagen & devascularization)

#### HEALING BY FIRST INTENTION



## Healing of Skin Wounds

First intention:

- Focal disruption of the basement membrane
- Little cell death
- Repair by regeneration

Larger clot rich in fibrin & fibronectin

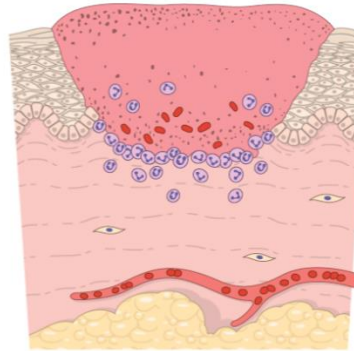
More intense inflammation = inflammation mediated injury

More granulation tissue to cover a wider gap = more scarring

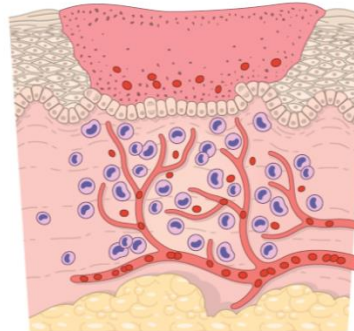
Wound contraction by myofibroblasts

#### HEALING BY SECOND INTENTION

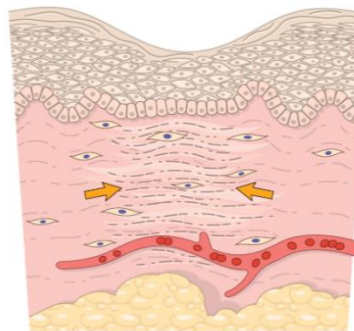
24 hours



3 to 7 days



Weeks



## Healing of Skin Wounds

Second intention:

- Extensive tissue loss
- Intense inflammation
- Combination regeneration & scarring

# Wound strength

