

# **Chapter 1A.**

## **Irreversible Healing of Extracellular Matrix.**

# **Outline of three lectures on Irreversible Healing of Extracellular Matrix.**

- A. Irreversible healing of ECMs in different organs.**
- B. Structure and function of naturally occurring ECMs.**
- C. Synthesis of biologically active ECM models.**

# **A. Injury to ECM is Irreversible**

## **Summary:**

- 1. After severe injury, and in contrast to the fetus, the adult heals most organs irreversibly (no regeneration).**
- 2. Most organs are made up of three basic tissues (“tissue triad”): epithelia, basement membrane, and stroma.**
- 3. Epithelia and basement membrane are spontaneously regenerative; the stroma is not.**
- 4. Therefore, the central problem in biomaterials selection for organ replacement by regeneration is synthesis of the stroma.**

**Text: Chaps. 1 and 2 of *Tissue and Organ Regeneration in Adults*, by I.V.Yannas, New York, Springer, 2001 (on reserve in MIT Libraries).**

**Spontaneous regeneration  
of amputated limb in the  
newt (a small amphibian) occurs  
independently of severity of  
injury**

Image removed due to copyright considerations.  
See Figure 1.1 in Yannas, I. V. *Tissue and Organ Regeneration  
in Adults*. New York: Springer-Verlag, 2001.

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See Figure 1.2 in [Yannas].

**The healed liver has the same mass, but a different shape (resected lobes are not regenerated), than the intact organ**

**scarred heart muscle  
(heart attack)**

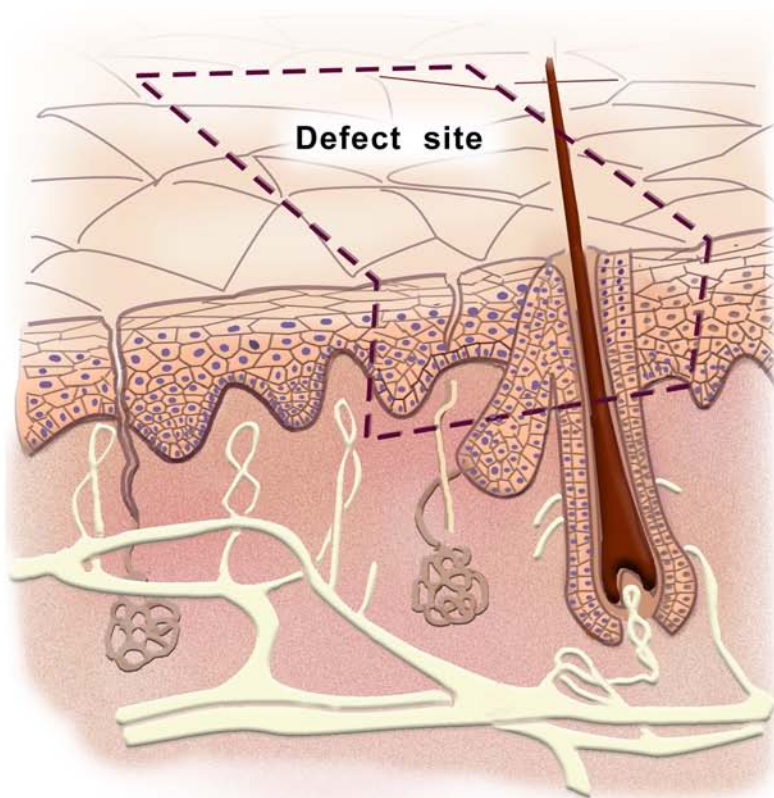
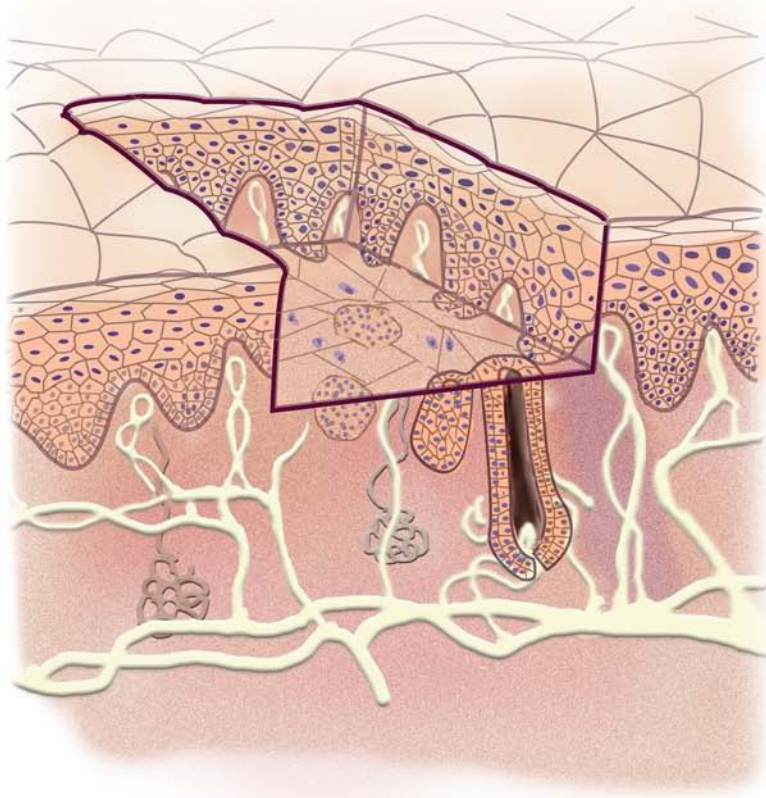
**scarred liver  
(cirrhosis)**

**scarred kidney  
(infection)**

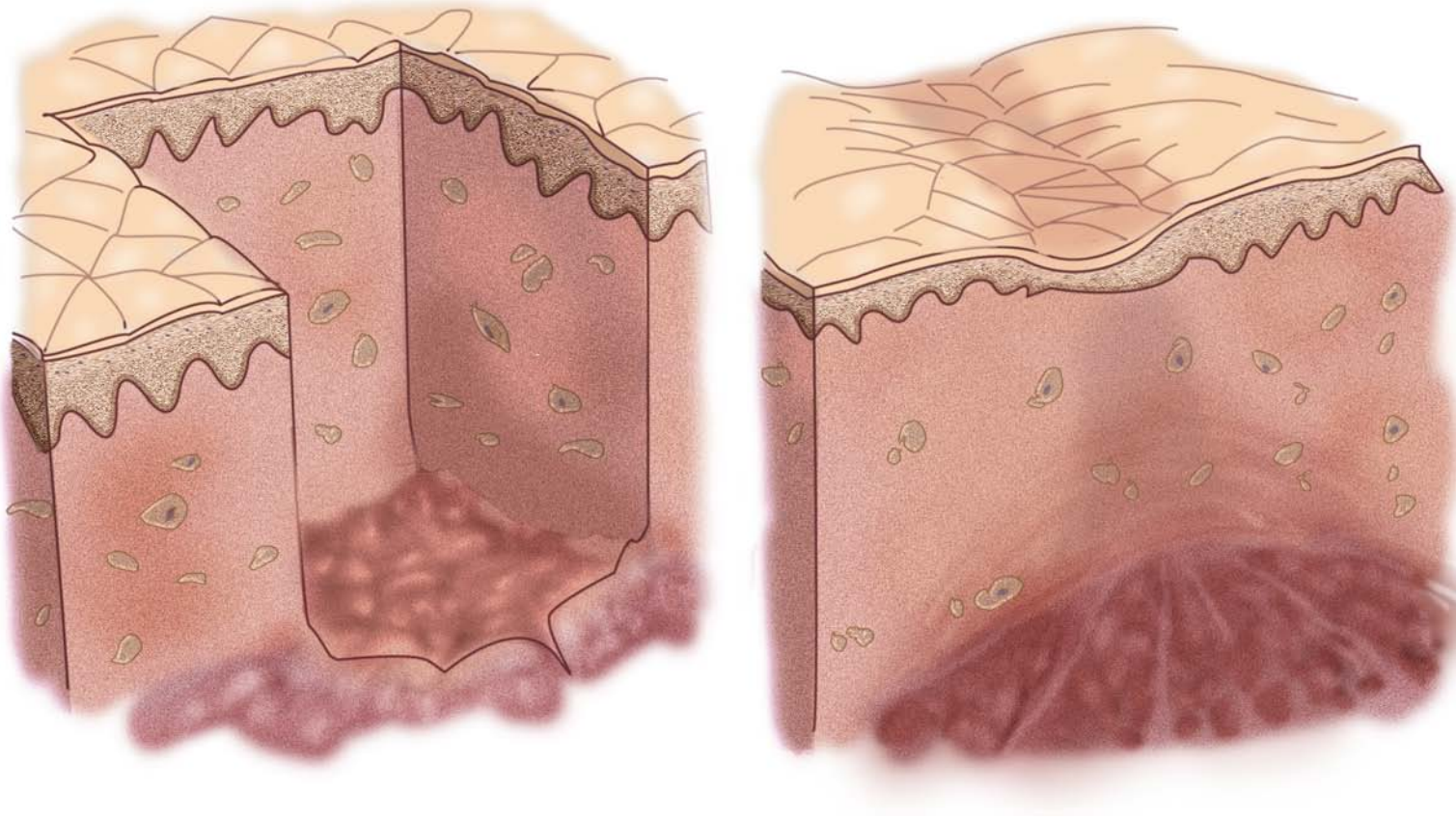
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See Figure 1.3 in [Yannas].

**scarred cornea  
(infection)**

**scarred heart valve  
(rheumatic fever)**



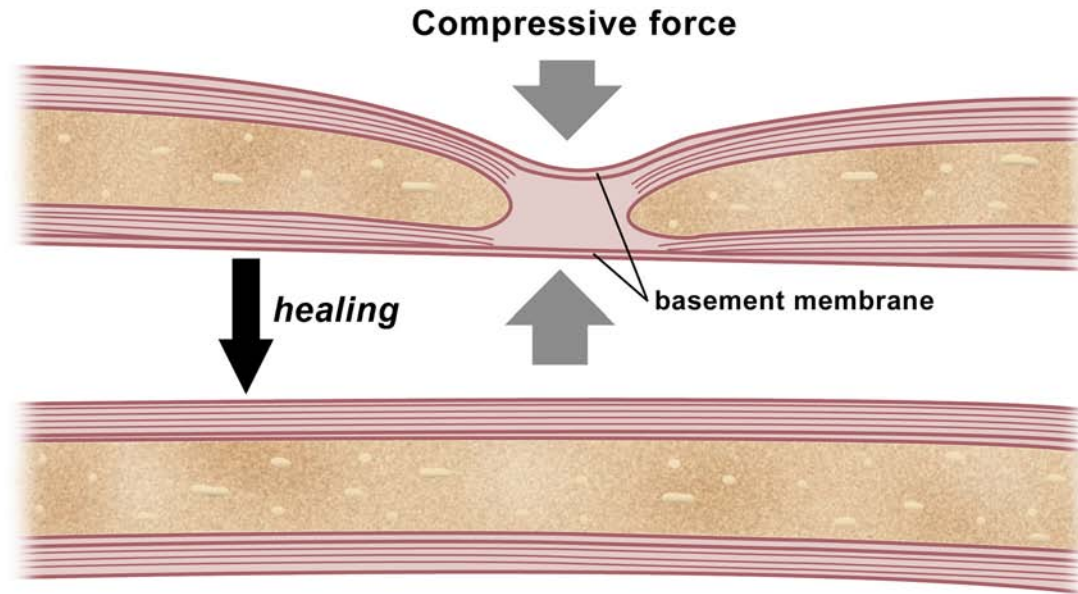
**Spontaneous regeneration of excised epidermis**

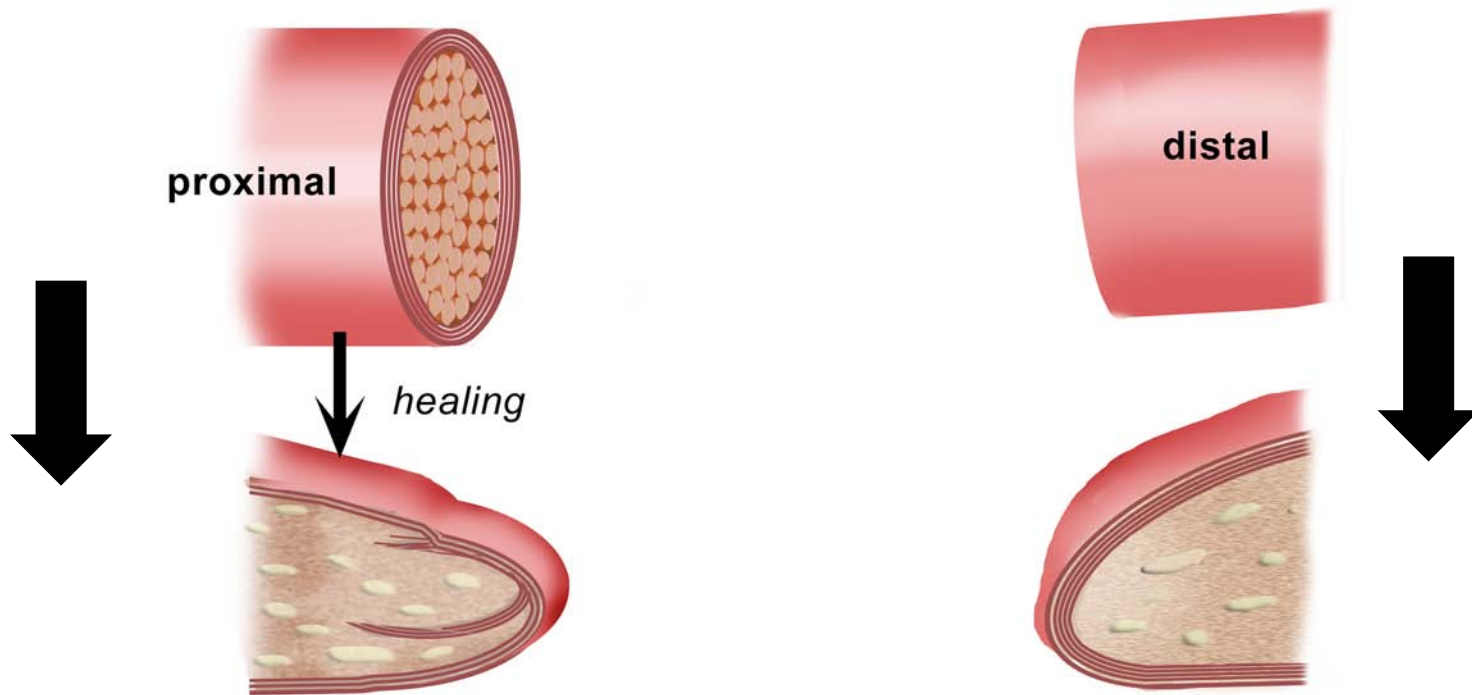


**Spontaneous healing of skin excised to full thickness by contraction and scar formation. The dermis does not regenerate.**



**Mildly crushed  
nerve heals  
spontaneously  
by  
regeneration**





**Transected nerve heals spontaneously by contraction and neuroma (neural scar) formation. No reconnection of stumps.**

Image removed due to copyright considerations.  
See Figure 2.5 in [Yannas].

← **intact nerve with  
myelinated (M)  
axon (A) and  
Schwann cell (S)**

← **spontaneously  
healed nerve  
(following  
transection) is filled  
with collagen fibers  
(scar) but has no  
myelinated axon  
or Schwann cell**

## **injury mode**

**basic blister  
configuration**

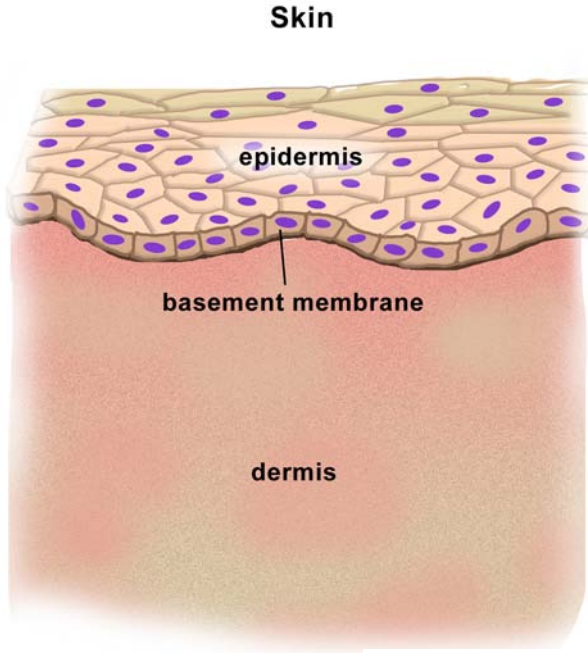
**through epidermis:  
reversible healing**

**between epidermis  
and dermis:  
reversible healing**

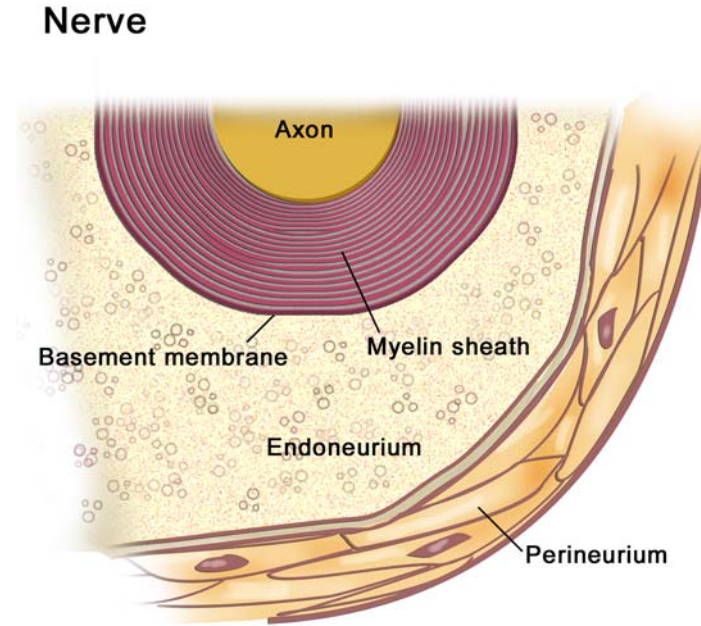
**through dermis:  
irreversible healing**

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See Figure 2.6 in [Yannas].

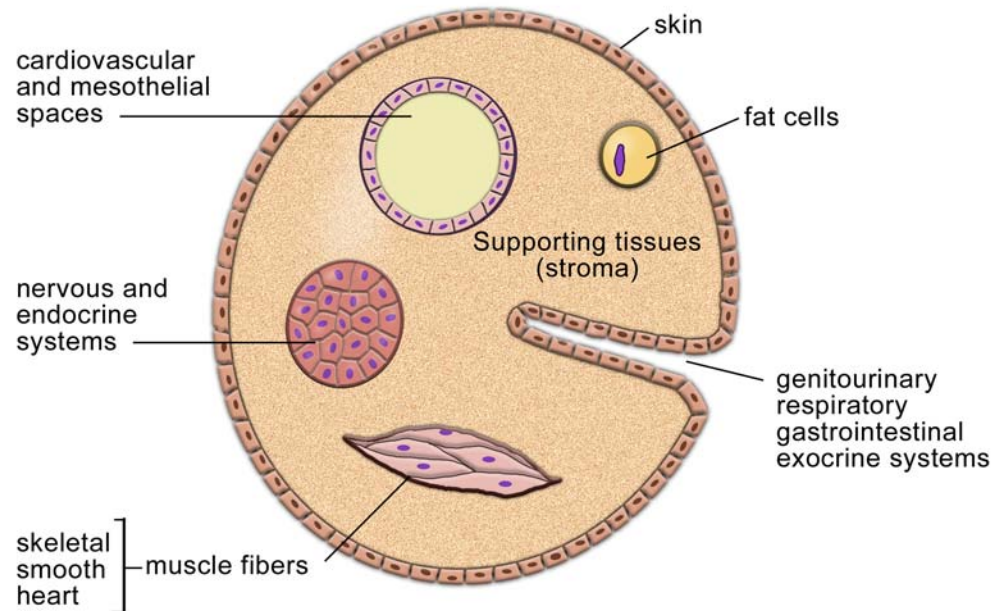
# tissue triad in skin



# tissue triad in nerve



**Cartoon of “organism”  
shows that basement  
membrane  
(thick solid line)  
appears  
In almost all organs**



## SUMMARY SO FAR

	<b>Regenerative tissues. Reversible injury. No contraction.</b>	<b>Nonregenerative tissues. Irreversible injury. Contraction +scar.</b>
<b>SKIN</b>	epidermis	dermis
	BM	
<b>NERVE</b>	myelin	endoneurial stroma
	BM	

# **The Defect Closure Rule**

# Quantitative description of healing processes

- Initial wound area is  $A_0$
- Wound eventually closes up spontaneously. Final area is  $A_f$ .
- Final wound area is distributed among fractions that closed by contraction (%**C**), scar formation (%**S**) or regeneration (%**R**).
- This is the configuration of the final state.
- Wound closure rule:  
**C** + **S** + **R** = 100



<b>Spontaneously healing defect</b>	<b>Configuration of final state</b>
general case	<b>[C, S, R]</b>
ideal fetal healing	<b>[0, 0, 100]</b>
dermis-free skin-- adult rodents	<b>[96, 4, 0]</b>
dermis-free skin-- adult human	<b>[37, 63, 0]</b>
peripheral nerve-- adult rat	<b>[96, 4, 0]</b>
conjunctiva-- adult rabbit	<b>[45, 55, 0]</b>

# Measure C

Images removed due to copyright considerations.  
See Figure 4.1 and 4.2 in [Yannas].

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See Figure 4.7 and Table 4.1 in [Yannas].

**Measure S (qualitative  
assay)**

# Kinetics of change in C

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See Figure 4.3 in [Yannas].