# 2.79J/3.96J/20.441J/HST522J
# Biomaterials-Tissue Interactions

**ECM does not regenerate spontaneously**
**OR**
**Injury to ECM is Irreversible**

# Reversible and Irreversible injury

# Reversible injury

Figure removed due to copyright restrictions.
See Figure 1.1 in [TORA].

[TORA] = Yannas, I. V. *Tissue and Organ Regeneration in Adults*. New York, NY: Springer-Verlag, 2001. ISBN: 9780387952147. [Preview in Google Books]

**Spontaneous regeneration of amputated limb in the newt occurs independently of severity of injury**

**Goss, 1992**

# Irreversible injury

Photo removed due to copyright restrictions.

**Burn victim suffering from severe contraction and scar formation**

**Tomasek et al., 2000**

# Injury to adult 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).**

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

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See Figure 1.2 in [TORA].

# Pathology resulting from irreversibility of injury in various organs

**scarred heart muscle (heart attack)**

**scarred liver (cirrhosis)**

**scarred kidney (infection)**

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See Figure 1.3 in [TORA].

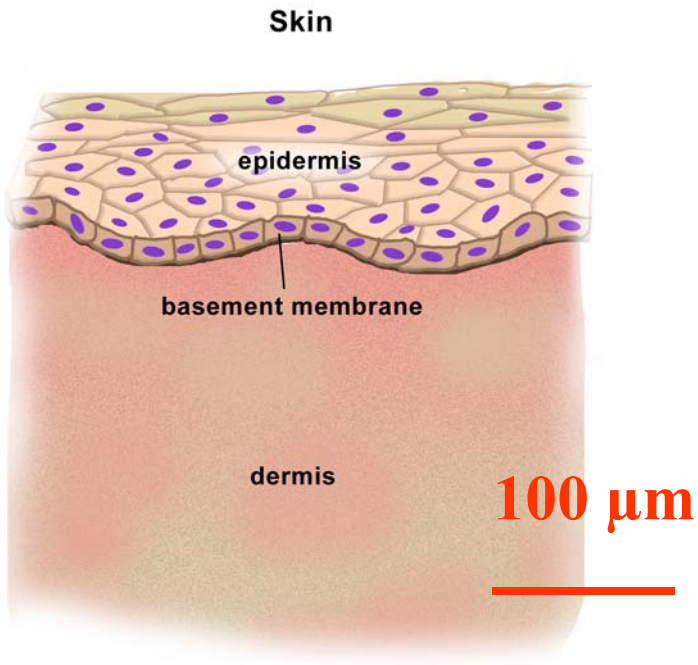
**scarred cornea (infection)**

**scarred heart valve (rheumatic fever)**

# The tissue triad in organs

- **epithelial tissue: 100% cellular, no ECM**
- **basement membrane: 100% ECM , no cells**
- **stroma: cells, ECM, blood vessels**

# Organs are made of tissues which heal differently from each other. The tissue triad in skin and nerves

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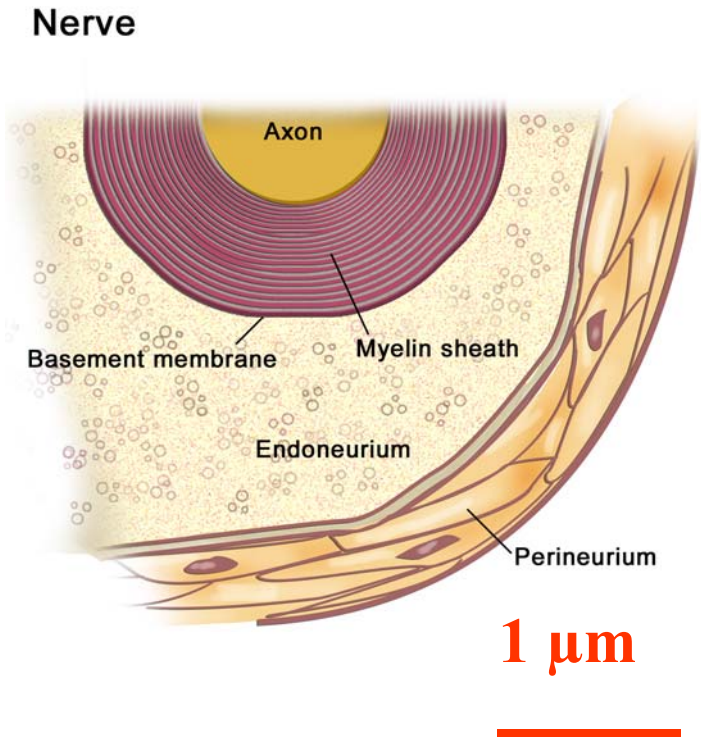


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# Skin. Reversible Injury

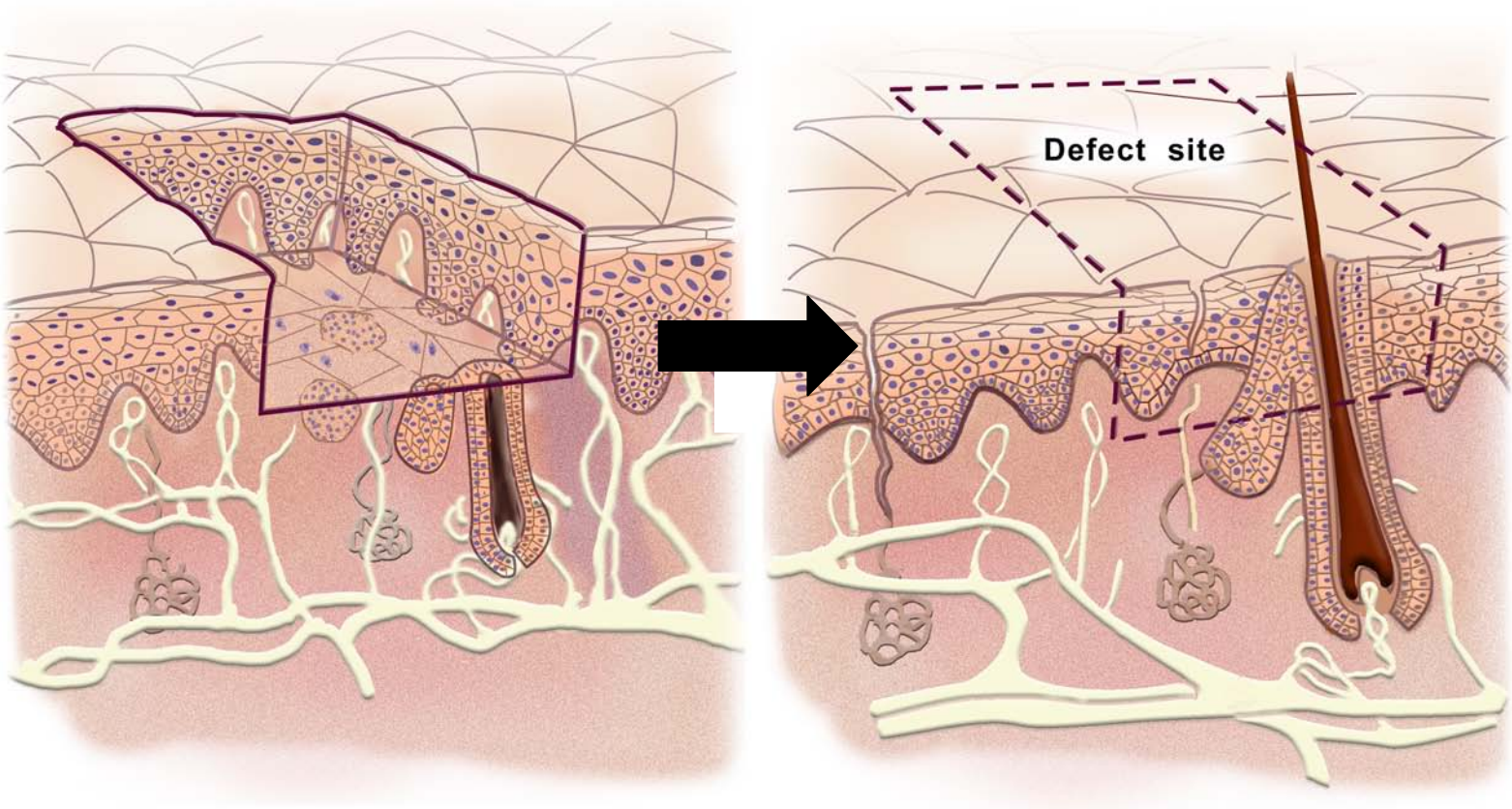



Figure by MIT OpenCourseWare.

Left: a controlled injury (e.g. stripping or blistering) which leaves the dermis intact. Right: the epidermis recovers completely at the defect site. Hair follicles are lined with epidermal tissue and also regenerate.

# Skin. Irreversible Injury

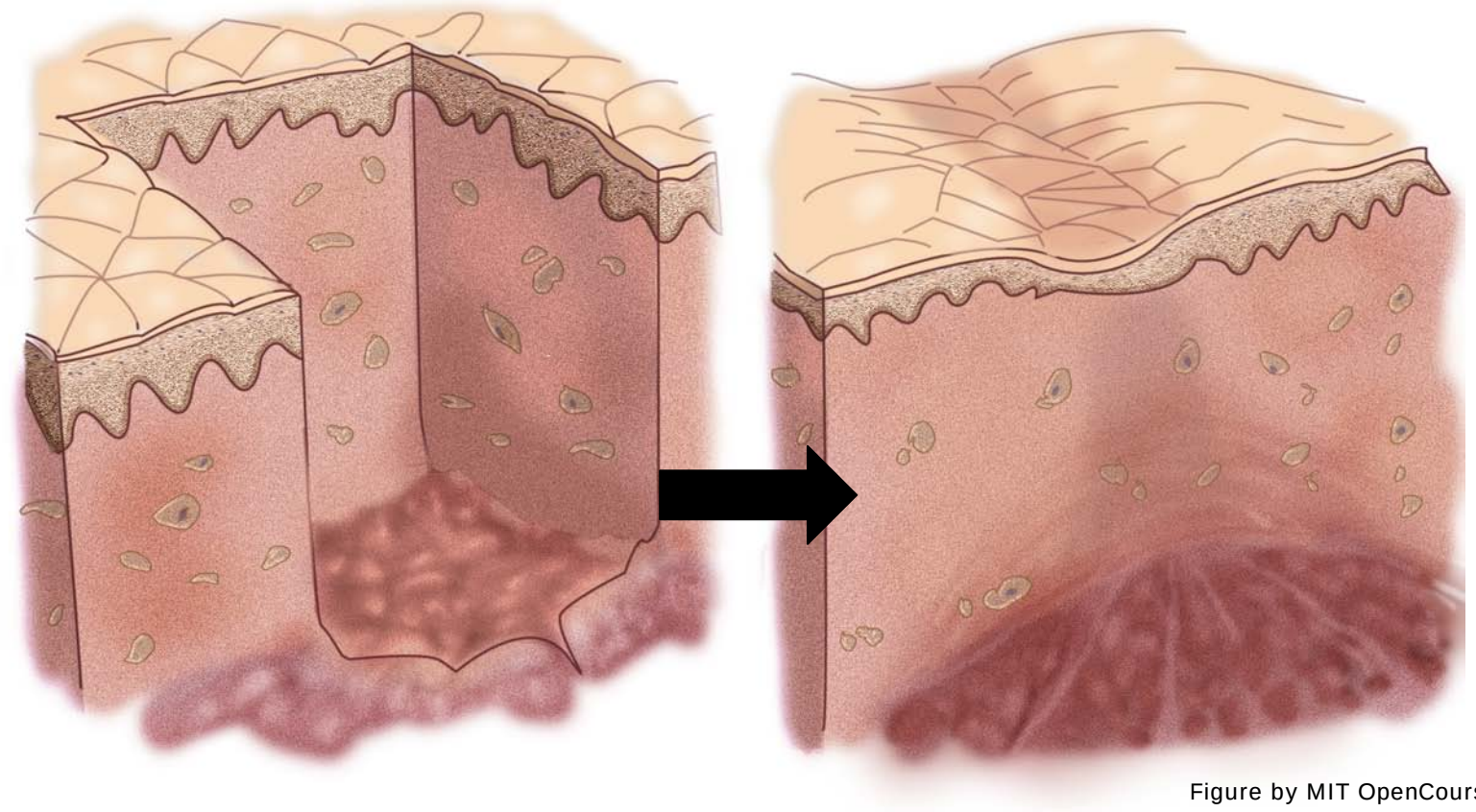


Figure by MIT OpenCourseWare.

Left: Excision of the epidermis and dermis to its full thickness.

Right: Wound edges contract and close, while scar tissue forms simultaneously in place of a physiological dermis. The epidermis that forms over the scar is thinner and lacks undulations (rete ridge).

# Peripheral nerve. Reversible injury

**Mildly crushed nerve heals spontaneously by regeneration**

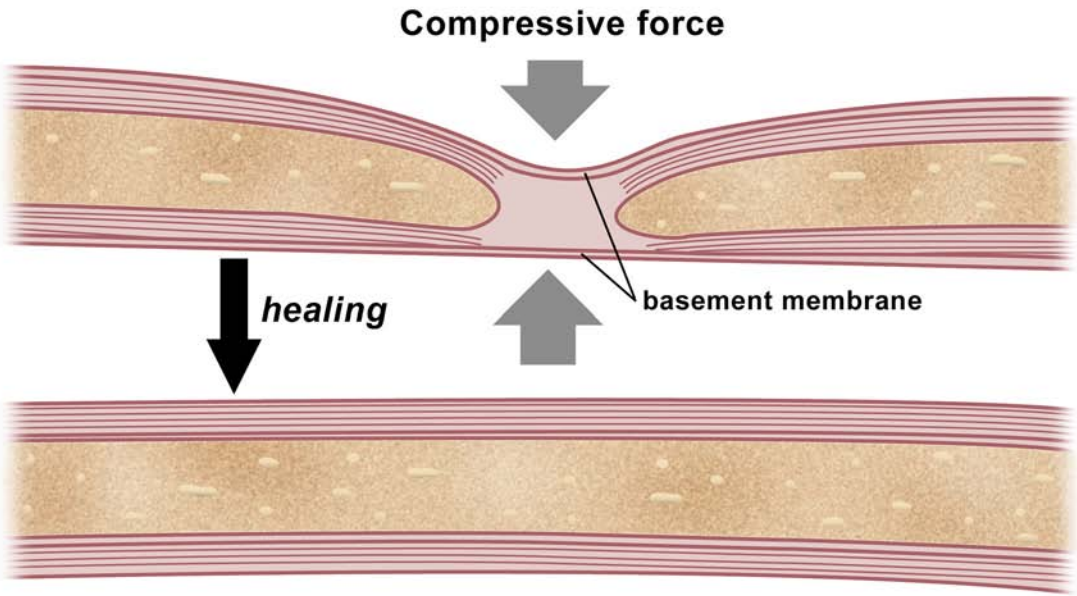



Figure by MIT OpenCourseWare.

Within the nerve fiber, axons and their myelin sheath are regenerative.
Top: Following mild crushing injury, the axoplasm separates and the myelin sheath degenerates at the point of injury. However, the basement membrane stays intact.
Bottom: The nerve fiber regenerates after a few weeks.

# Peripheral nerve. Irreversible injury

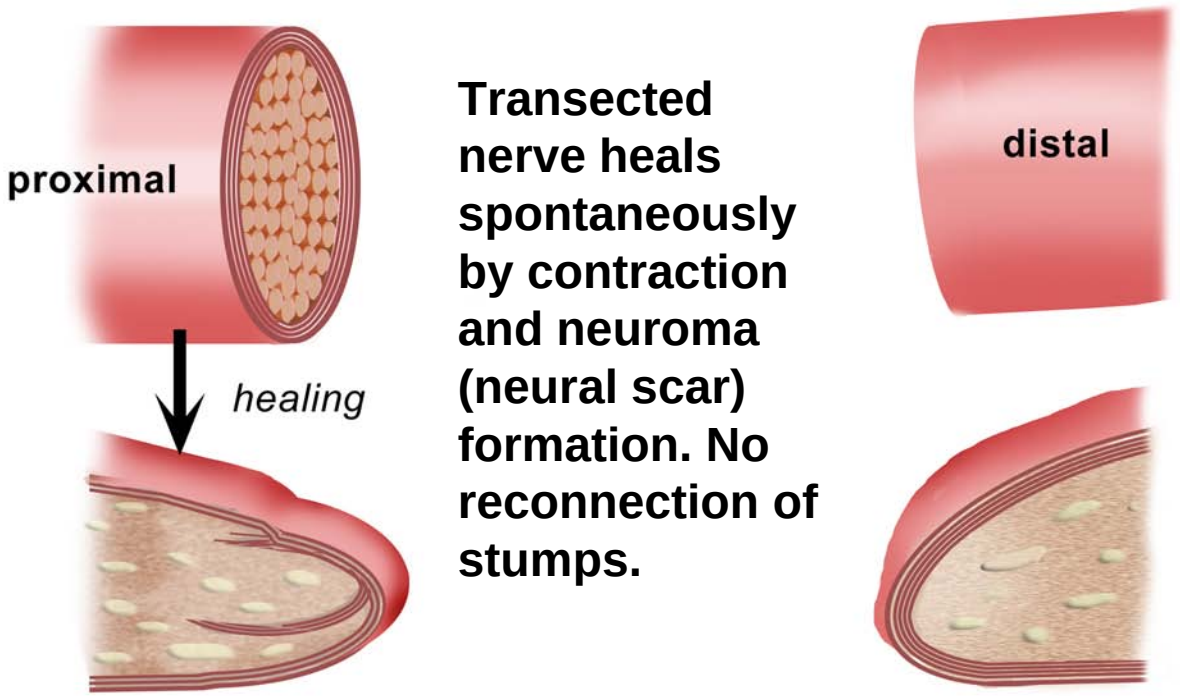



Figure by MIT OpenCourseWare.

Most supporting tissues (stroma) that surround nerve fibers are not regenerative. Thus, while nerve fibers can regenerate following a transection, the other tissues in the nerve trunk cannot regenerate. After transection, the nerve trunk stumps become neuromas -- clumps of scarred tissue that close largely by contraction.

# Peripheral Nerve. Irreversible Injury

Figure removed due to copyright restrictions.
See Figure 2.5 in [TORA].

**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**

**Is the basement membrane regenerative? Yes!**

Figure removed due to copyright restrictions.
See Figure 2.6 in [TORA].

**injury mode**

**basic blister configuration**

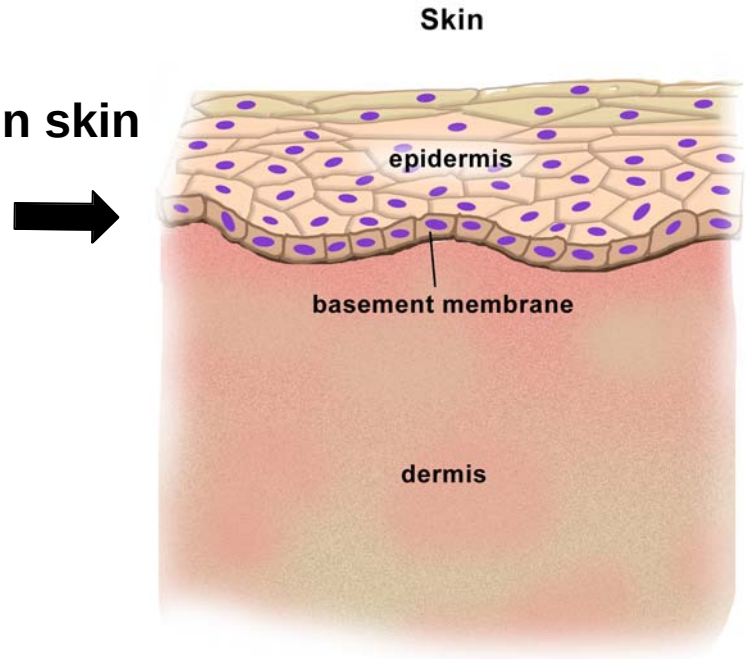
**through epidermis: reversible healing**

**between epidermis and dermis: reversible healing**

**through dermis: irreversible healing**

# Use of tissue triad model with other organs

tissue triad in skin

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Nerve

tissue triad in nerve

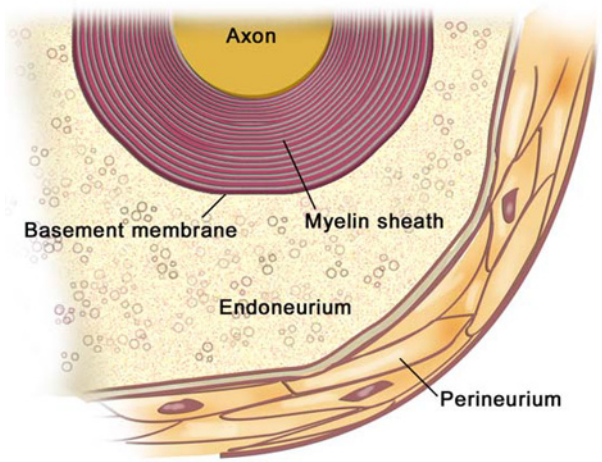


Figure by MIT OpenCourseWare.

**Cartoon of "organism" shows that basement membrane (thick solid line) appears In almost all organsanatomy**

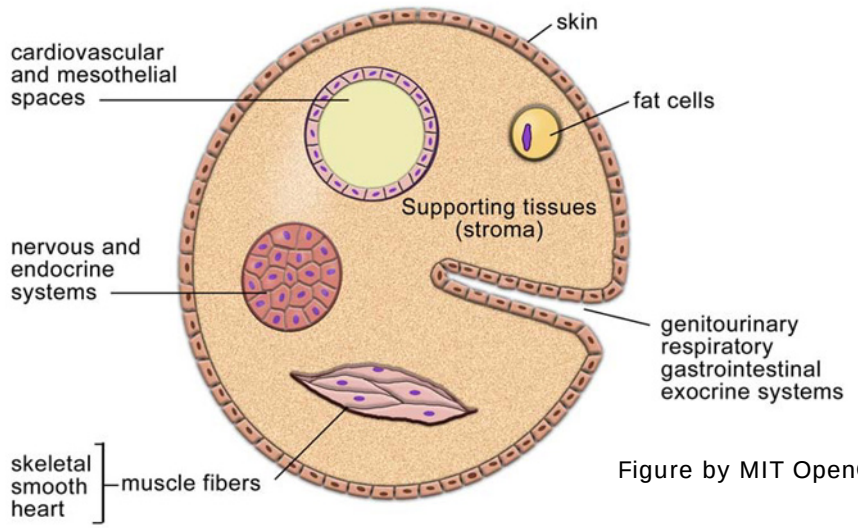


Figure by MIT OpenCourseWare.

# SUMMARY SO FAR

| | Regenerative tissues. Reversible injury. No contraction. | Nonregenerative tissues. Irrever-sible injury. Contraction +scar. |
|---|---|---|
| SKIN | epidermis | dermis |
| | BM | |
| NERVE | myelin | endoneurial stroma |
| | BM | |
| | | |

# Conclusion

**The central problem in organ regeneration is regeneration of the stroma. Once the stroma has been regenerated, epithelial tissues regenerate spontaneously and synthesize the basement membrane as well**

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