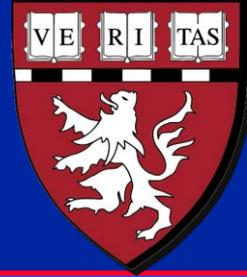




**Massachusetts Institute of Technology
Harvard Medical School
Brigham and Women's Hospital
VA Boston Healthcare System**



2.79J/3.96J/20.441/HST522J

UNIT CELL PROCESSES ASSOCIATED WITH WOUND HEALING

M. Spector, Ph.D.

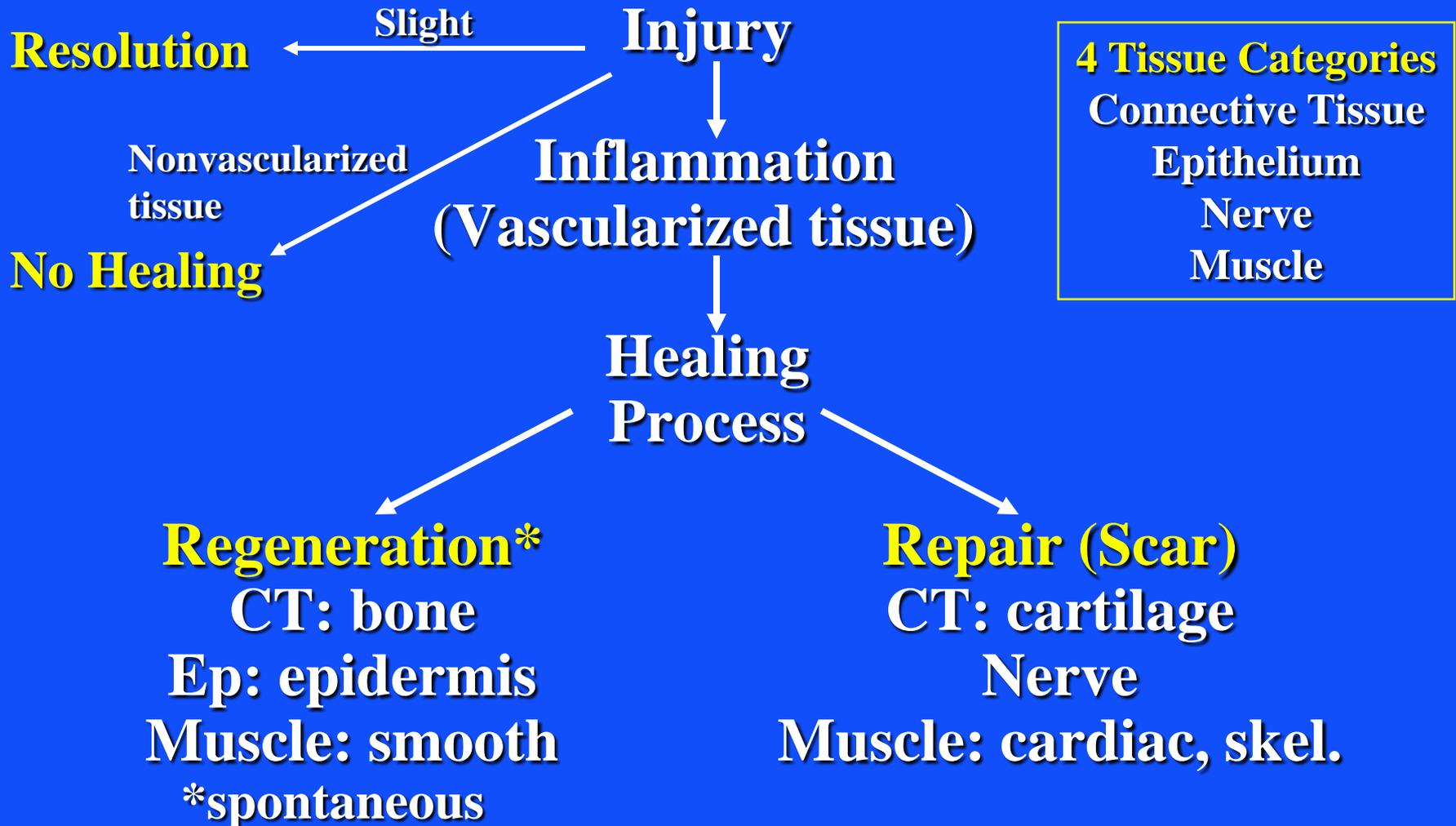
Acute

Chronic

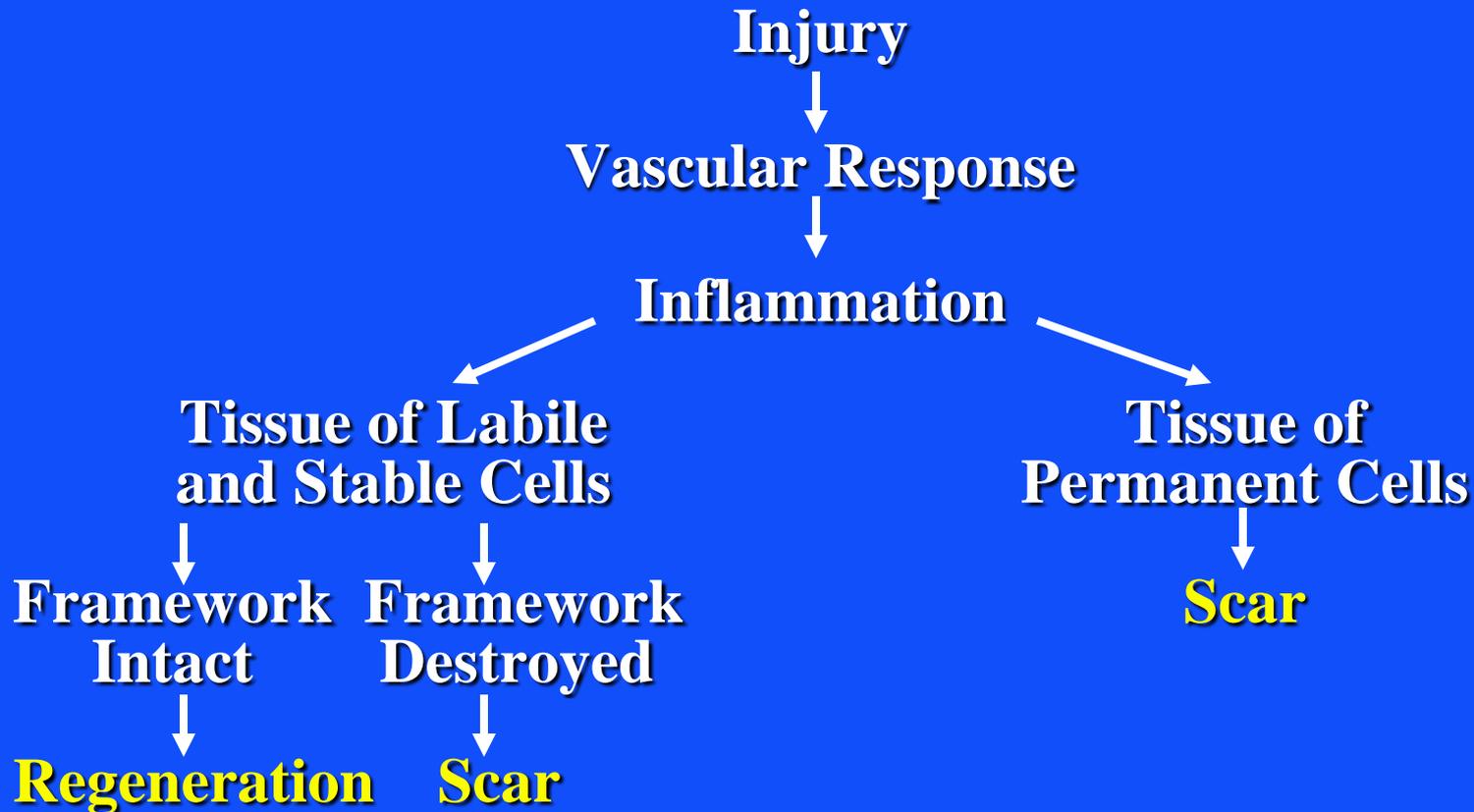
Photos and diagrams of skin wound healing removed due to copyright restrictions.

WOUND HEALING

Roots of the Tissue Response



RESPONSE TO IMPLANTS: WOUND HEALING



Acute Inflammation – Local/Gross Changes

The cardinal signs of acute inflammation are:

Redness

Heat

Swelling

Pain

Loss of function

Granulation Tissue

Photo removed due to copyright restrictions.

UNIT CELL PROCESSES

Regulator



Cell + Matrix

UCP



Product + Regulator

Connective
Tissue
Epithelia
Muscle
Nerve

Integrin

ECM
Adhesion
Protein
Collagen
Biomaterial

Mitosis
Synthesis
Migration
Contraction
Endocytosis
Exocytosis



UNIT CELL PROCESSES

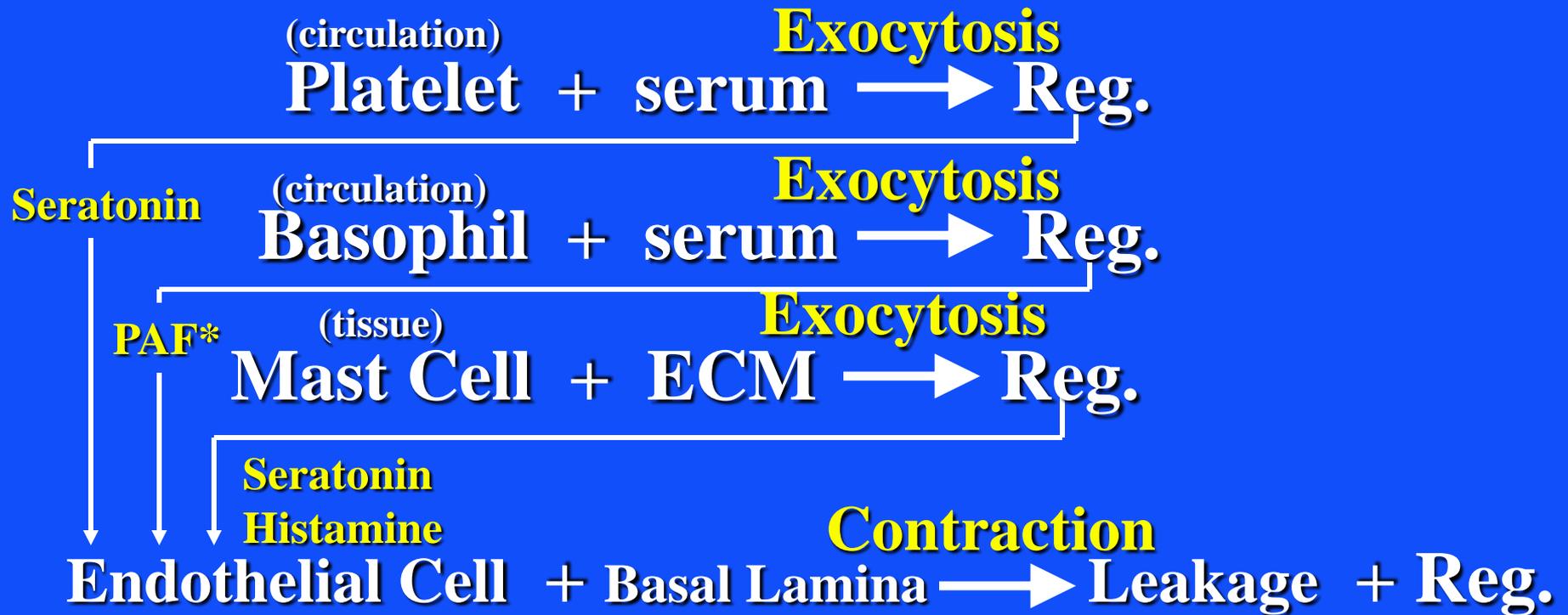
VASCULAR RESPONSE

Diagrams removed due to
copyright restrictions.

Endothelial Cell + Basal Lamina $\xrightarrow{\text{Contraction}}$ Leakage + **Reg.**

UNIT CELL PROCESSES

VASCULAR RESPONSE



* PAF, platelet activating factor

Mast cells can be identified by their darkly staining granules which contain histamine and heparin. They are involved in the inflammatory response and are very common near blood vessels.

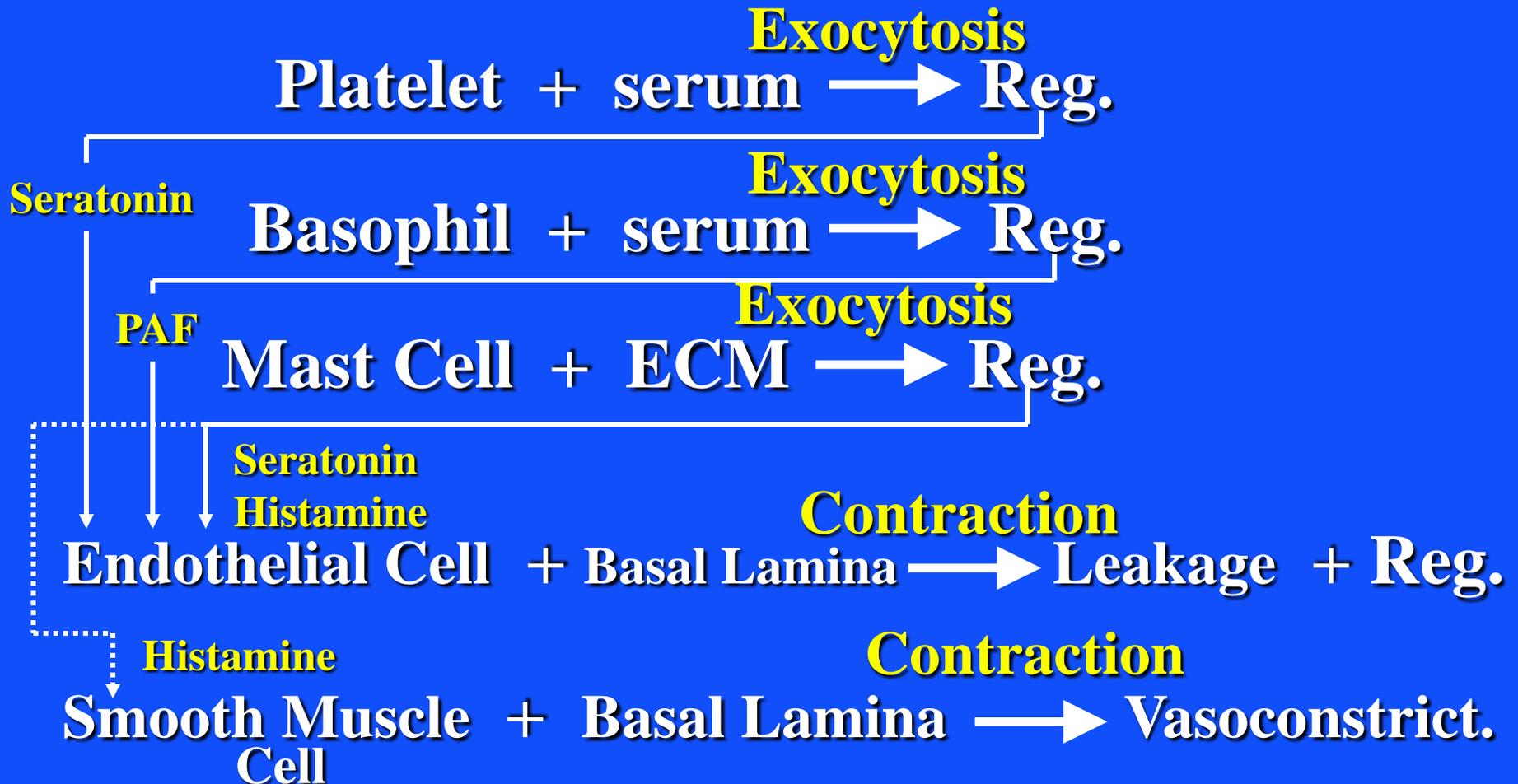
Photo of mast cell removed due to copyright restrictions.

See Figure 10.45 in Berg, J. M. et al. *Biochemistry*. 5th edition. W. H. Freeman, 2002.

<http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=stryer&part=A1378&rendertype=figure&id=A1413>

UNIT CELL PROCESSES

VASCULAR RESPONSE



UNIT CELL PROCESSES

CLOTTING

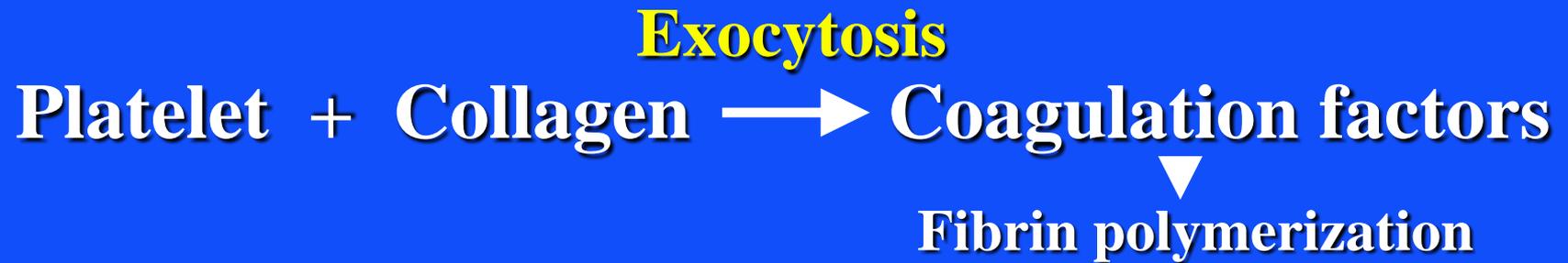


Image removed due to copyright restrictions.

See Fig. 10.2, "The role of platelets in thrombosis."

In Rubin, E., and H. M. Reisner, editors. *Essentials of Rubin's Pathology*. Lippincott Williams & Wilkins, 2008.

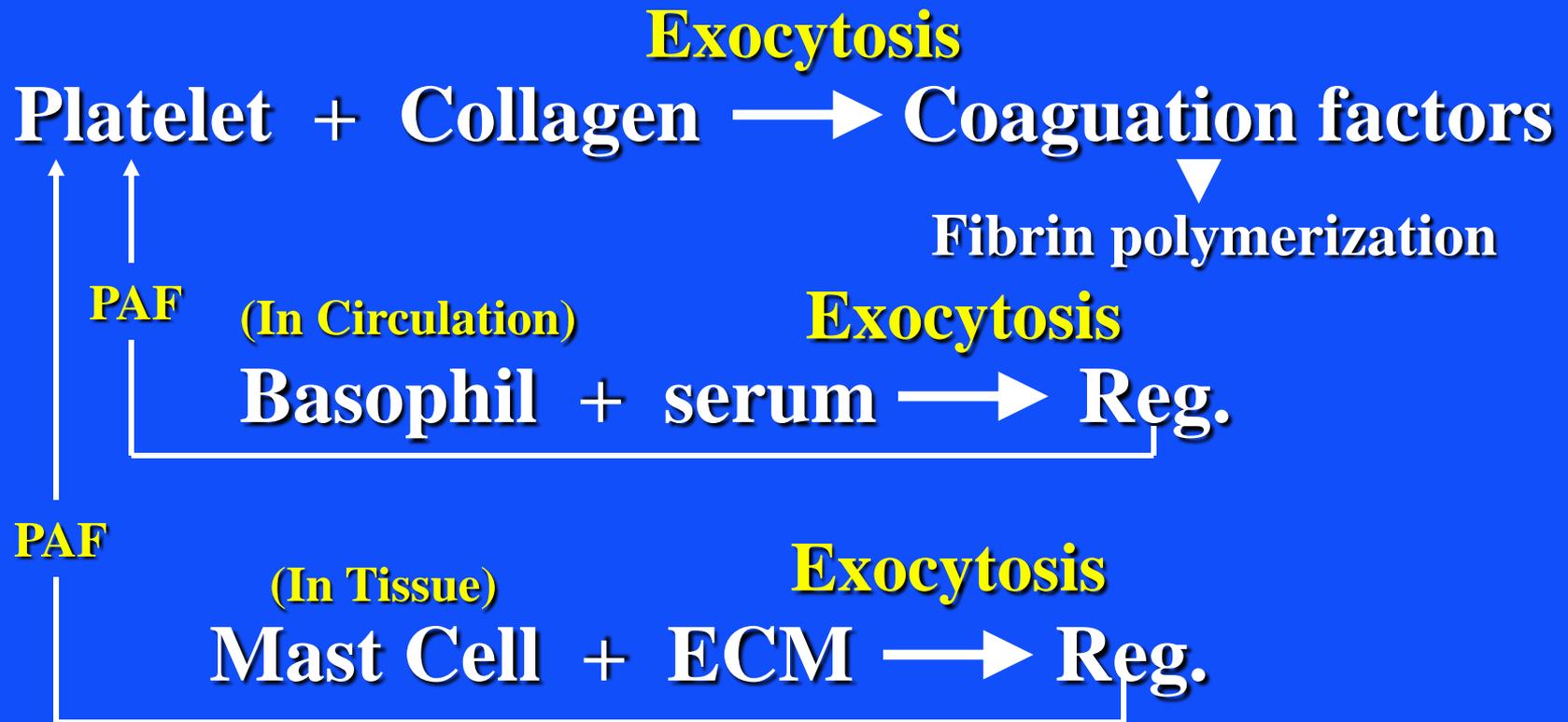
<http://books.google.com/books?id=7HdzBBhtxycC&pg=PA197>

Scanning electron micrograph shows the fine structure of a fibrin clot that has entangled 2 red blood cells. Platelets released from the circulation and exposed to the air use fibrinogen from the blood plasma to spin a mesh of fibrin.

Photo removed due to copyright restrictions.
See <http://www.cellsalive.com/cover7.htm>.

UNIT CELL PROCESSES

CLOTTING



UNIT CELL PROCESSES

PHAGOCYTOSIS

Endocytosis

Macrophage + Part.* → Sol. Part + Reg.

* Cell debris and degraded ECM

Alveolar macrophage phagocytosis of *E. coli* (lung pleural cavity). The macrophage is the large, yellowish cell with projections; the bacterial cells are small, rod-like, blue cells.

Microscope image removed due to copyright restrictions.

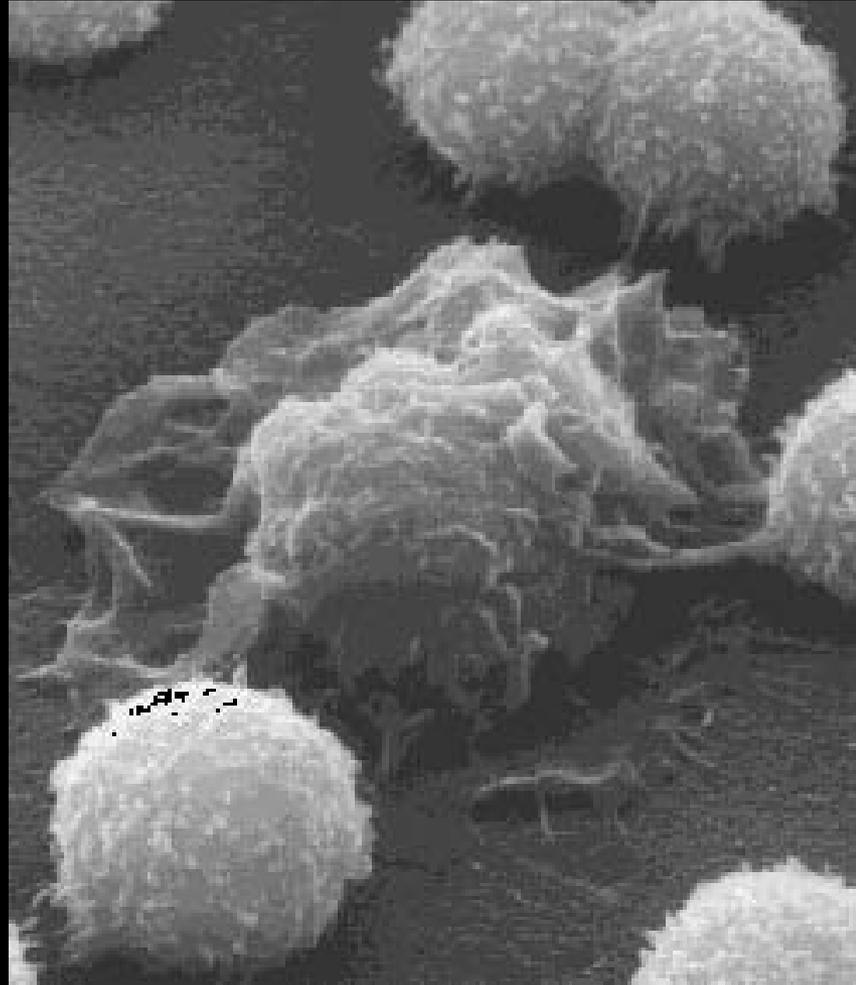
See http://www.visualsunlimited.com/c/visualsunlimited/image/I0000pCnNefPj_tE

(Dennis Kunkel Microscopy)

Scanning electron micrograph shows a human macrophage (gray) approaching a chain of *Streptococcus pyogenes* (yellow). Riding atop the macrophage is a spherical lymphocyte. Macrophages and lymphocytes can be found near an infection, and the interaction between these cells is important in eliminating infection.

Photo removed due to copyright restrictions.
See <http://www.cellsalive.com/cover5.htm>.

This scanning electron micrograph (courtesy of Drs. Jan M. Orenstein and Emma Shelton) shows a single macrophage surrounded by several lymphocytes.



Courtesy of Jan M. Orenstein. Used with permission.

<http://users.rcn.com/jkimball.ma.ultranet/BiologyPages/B/Blood.html>

Macrophage phagocytosing 2 erythrocytes (red blood cells).

Photo removed due to copyright restrictions.

Transmission electron micrograph showing a macrophage

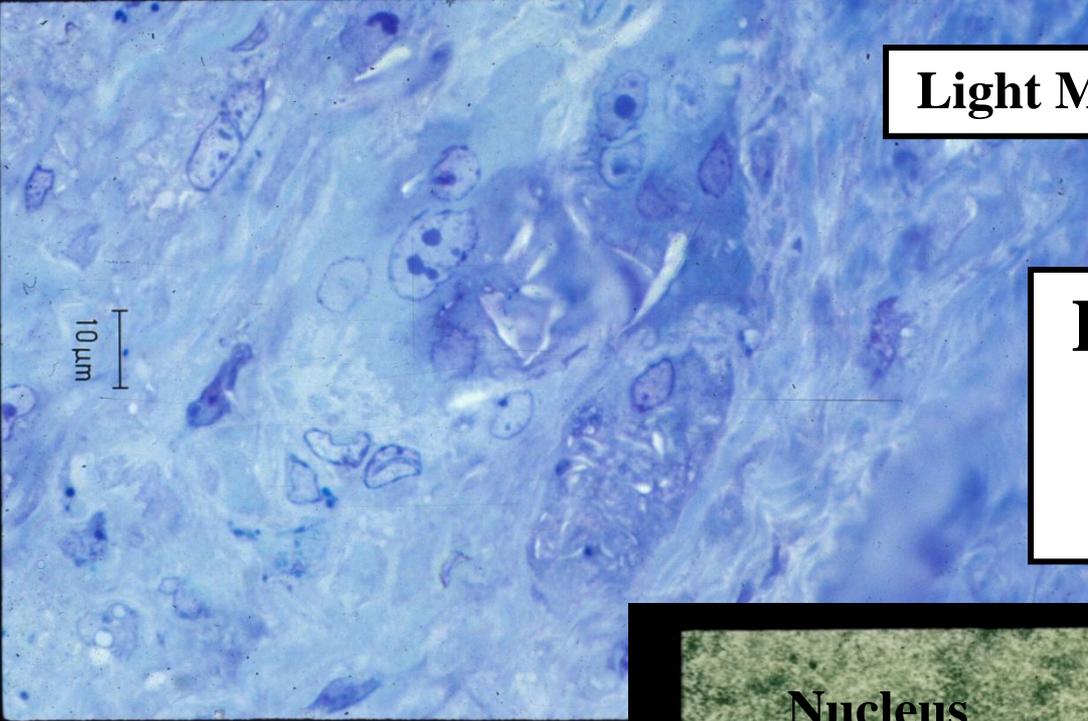
Photo removed due to copyright restrictions.

Macrophage containing engulfed bacteria

The bacteria are colored red for easy identification. The large purple structure at the bottom of the cell is the cell nucleus.

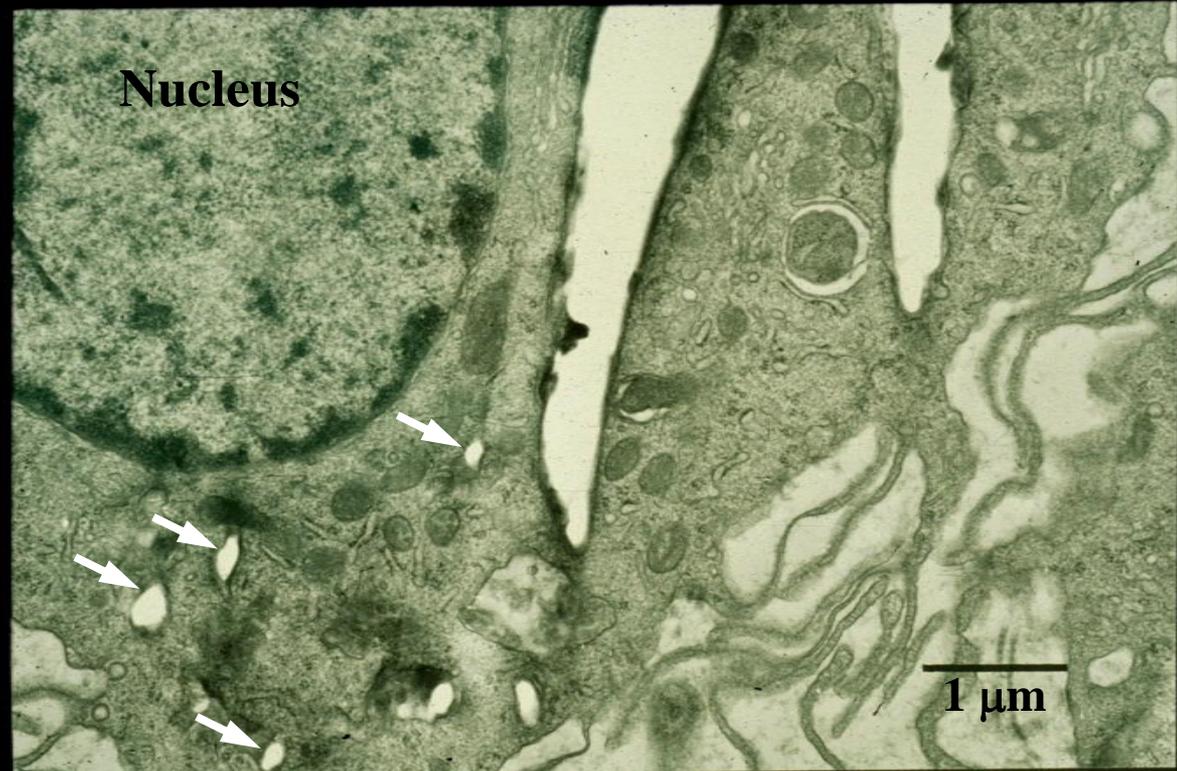
Image removed due to copyright restrictions.

Light Microscopy



Polyethylene Particles in Peri-prosthetic Tissues

**Transmission
Electron
Microscopy, TEM**

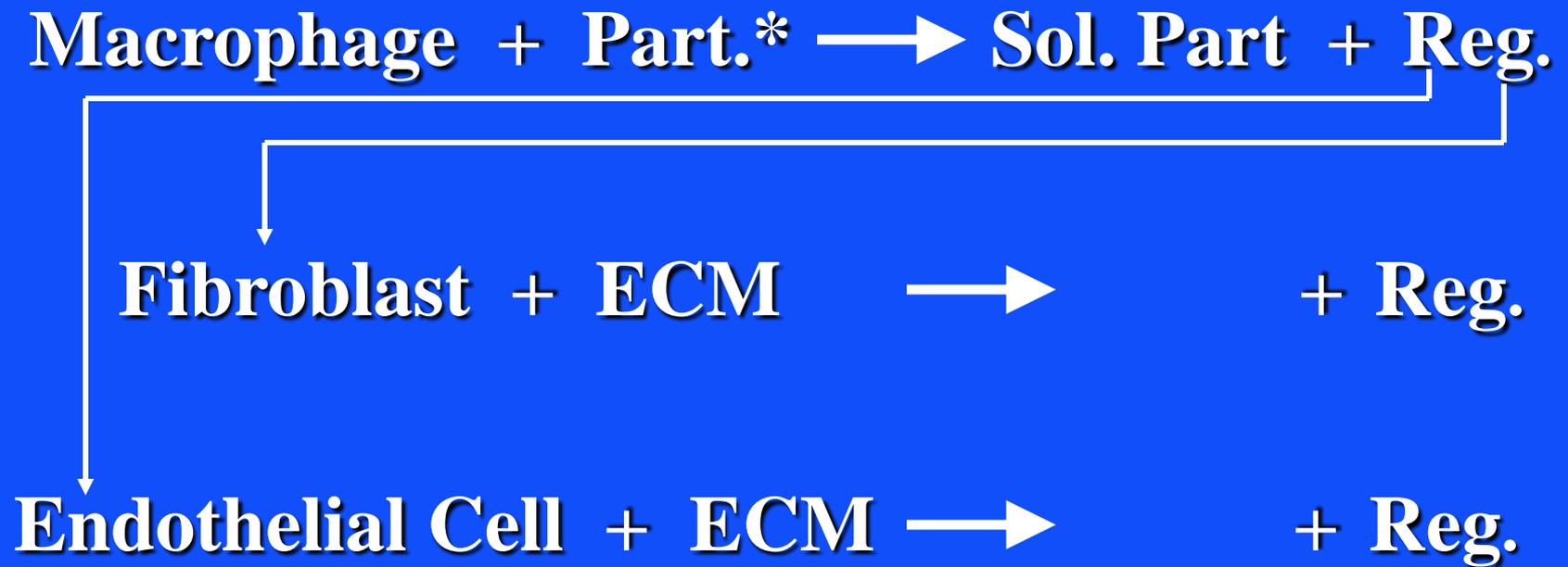


See Benz E, Spector M, *et al.*, *Biomat.* 2001;22:2835

UNIT CELL PROCESSES

PHAGOCYTOSIS

Endocytosis



* Cell debris and degraded ECM

Neovascularization/Angiogenesis/New Blood Vessel Formation

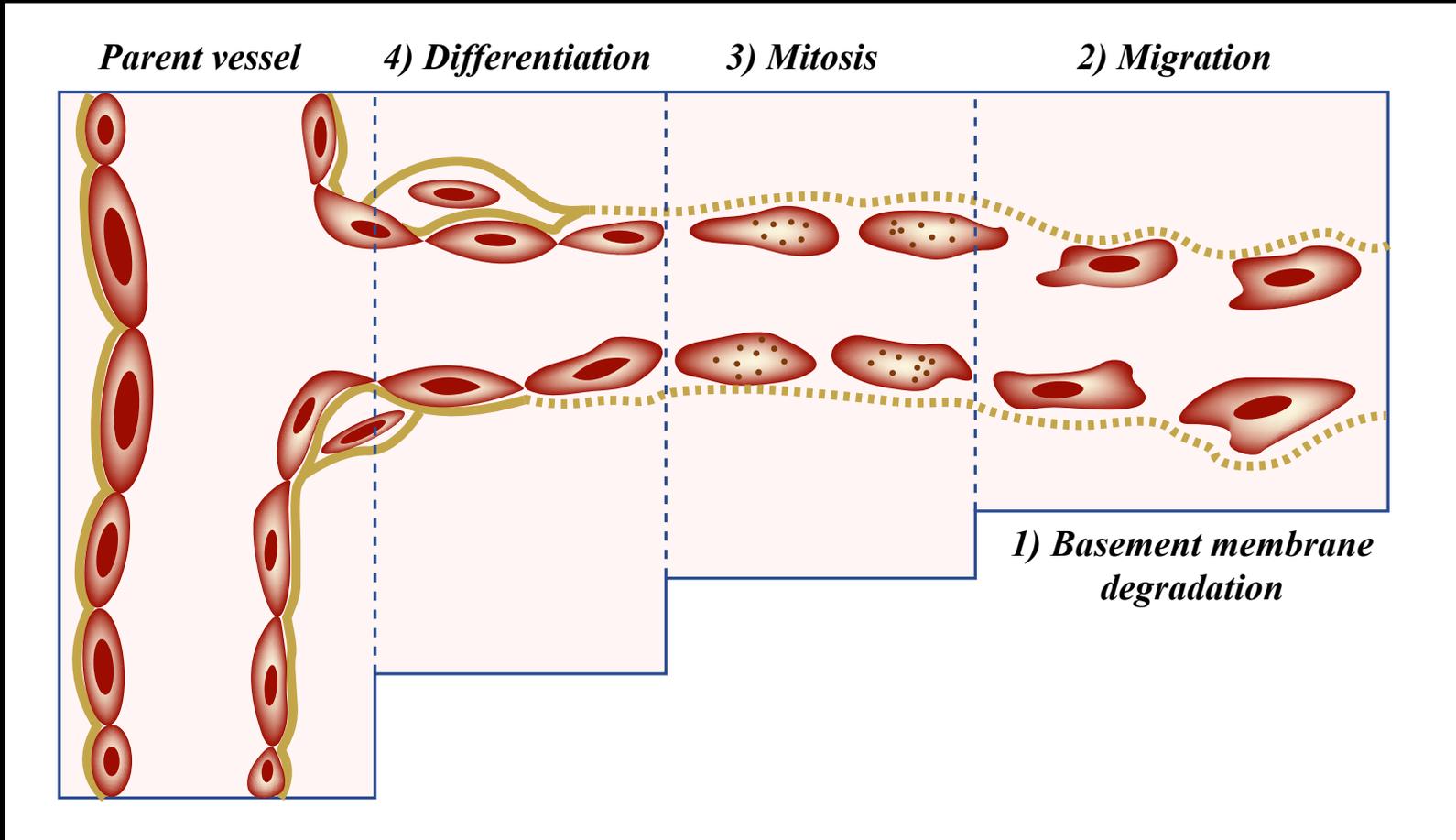


Figure by MIT OpenCourseWare.

UNIT CELL PROCESSES

NEOVASCULARIZATION

Synthesis: enzymes
Endothelial Cell + Basal Lamina \longrightarrow + Reg.

Migration
Endothelial Cell + ECM \longrightarrow + Reg.

Mitosis
Endothelial Cell + ECM \longrightarrow + Reg.

UNIT CELL PROCESSES

NEW COLLAGEN SYNTHESIS

Fibroblast + ECM → + Reg.

Fibroblasts are the most common cell type in connective tissue. They are large, long, branching cells that produce and secrete the collagen fibers and proteoglycans.

Photo removed due to copyright restrictions.

Once the connective tissue has been formed, the immature fibroblast will become a mature and largely inactive fibrocyte. If the tissue becomes damaged however, this fibrocyte can revert to an active fibrocyte.

Photo removed due to copyright restrictions.

UNIT CELL PROCESSES

NEW COLLAGEN SYNTHESIS

Fibroblast + ECM $\xrightarrow{\text{Migration}}$ **+ Reg.**

Fibroblast + ECM $\xrightarrow{\text{Mitosis}}$ **+ Reg.**

Fibroblast + ECM $\xrightarrow{\text{Synthesis}}$ **+ Reg.**

Fibroblast* + ECM $\xrightarrow{\text{Contraction}}$ **+ Reg.**

***Myofibroblast**

UNIT CELL PROCESSES

TGF- β 1



Fibroblast + Collagen $\xrightarrow{\text{Contraction}}$ **Contracture + Reg.**

MIT OpenCourseWare
<http://ocw.mit.edu>

20.441J / 2.79J / 3.96J / HST.522J Biomaterials-Tissue Interactions
Fall 2009

For information about citing these materials or our Terms of Use, visit: <http://ocw.mit.edu/terms>.