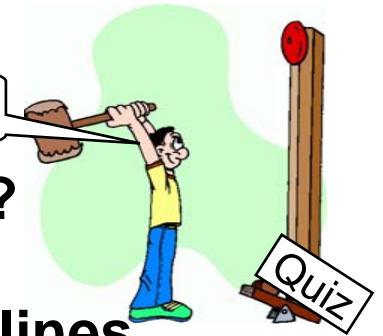


## BI 358 Lecture 7



...Fun Discussion w/WBC differential count!

I'm gonna smash it!



### I. Announcements Quiz 2 on Digestion & Nutrition! Q?

Also, nutrition reports (.doc/.docx + .pdfs) by e-mail to Aleesa or Precious by 5 pm today! Update on outlines.

### II. Body Resistance to Infection II G&H ch 32 & 33 +

L Sherwood 2012, Stuart Fox, Daniel Chiras, Basiro Davey

- A. **MedPhysiology News** Laughter is Medicine, Handwashing  
Former State Employees Benefit Board **SEBB News + CDC**
- B. Connections: WBC differential, demonstration?
- C. Immune response, pathogens, evolution Davey pp 5-12
- D. Recap *cf*: Innate vs. adaptive immunity G&H pp 433-7, LS + ...  
Innate immunity eg inflammation, interferon, complement
- E. Antibody (Ab=Ig) structure, subclasses, mechanisms  
G&H fig 34-4 + LS + Davey fig 2.4 p19, fig 4.2 p42, tab 4.1 p49
- F. Mom's milk *Scientific American*
- G. Immune Regulation + Allergy: G&H fig 34-7, 34-3 + ...  
*National Geographic, The Wars Within, Lennart Nilsson*  
<http://ngm.nationalgeographic.com/ngm/0510/feature1/learn.html>  
<http://pinterest.com/susanknauff/immunology/>

# Laughter = Medicine!



- Laughter's most profound effects occur on the immune system.
- Laughter  $\uparrow$   $\gamma$ -interferon,  $\uparrow$  B-cells,  $\uparrow$  T-cells and  $\downarrow$  stress hormones
- The average child laughs 100s of x/day
- The average adult laughs 12 x/day
- We need to find these lost laughs—and use them to our advantage!



Ah Ha!



## Hand-washing

**The right way to wash your hands:**

Thoroughly wash with soap and warm running water — rubbing your hands together for at least 10 seconds.

Hand-washing is the single most effective thing you can do to reduce the spread of colds and other infectious disease.

It's not necessary to use anti-bacterial soaps when washing up. Regular soap and water do the job just fine.

Also, using germicidal soaps too often may produce antibiotic-resistant bacteria.

*Source: Hospital Infections Program, U.S. Centers for Disease Control and Prevention*



**NB: Happy Birthday Song 20-30 sec!!!**

**<http://www.squidsoap.com/>**

# ***Immunology Websites for Fun Learning!***



[http://highered.mcgraw-hill.com/sites/0072495855/student\\_view0/chapter24/animation\\_the\\_immune\\_response.html](http://highered.mcgraw-hill.com/sites/0072495855/student_view0/chapter24/animation_the_immune_response.html)

<http://www.guardian.co.uk/science/video/2010/nov/01/immune-system-viruses-cells>

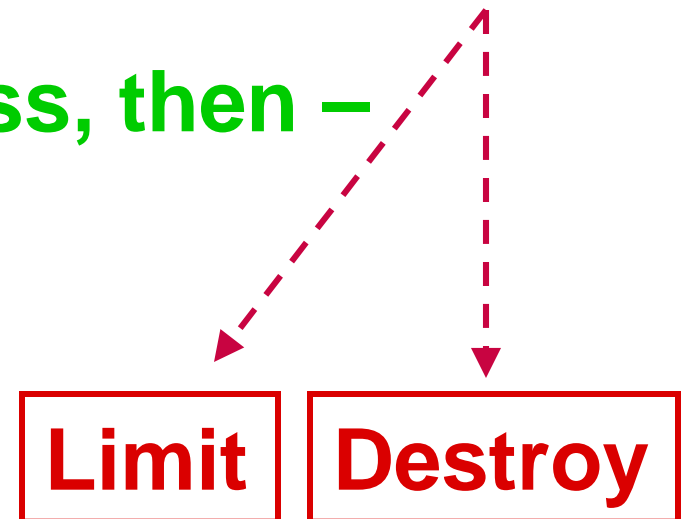


<http://www.nobelprize.org/educational/medicine/immunity/game/index.html>



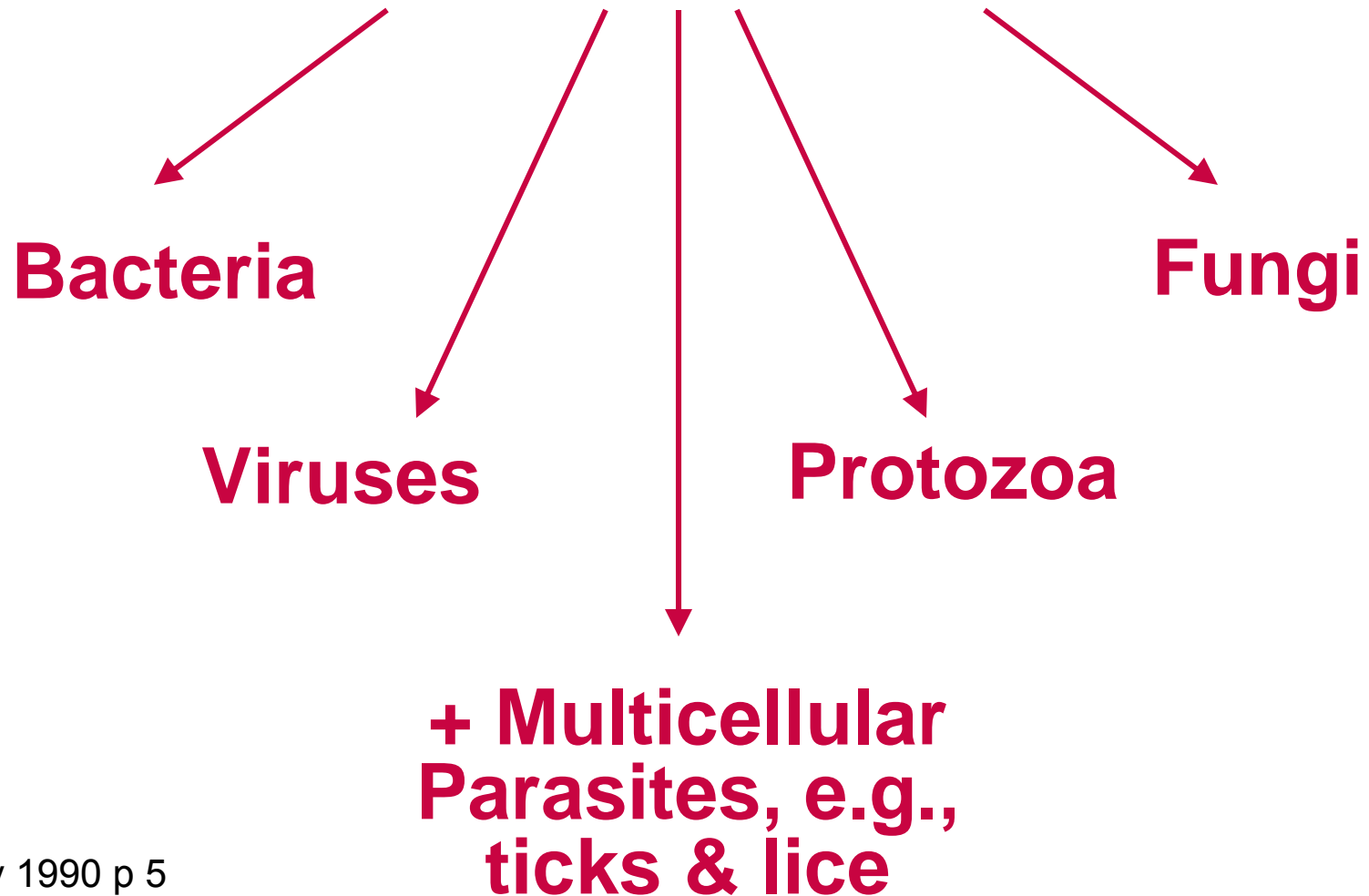
# *Immune Response*

1. Detect invader or ID toxic product.
2. Communicate to network.
3. Recruit coordinated, multi-pronged attack.
4. Amplify & if yes to success, then –
5. Suppress



# *Pathogen?*

## **Microbes that cause disease!**



# ***Pathogens & Parasites Cause:***

- 1. 70-80% of deaths in less developed countries**
- 2. Tens of millions of deaths due to infectious diseases**
- 3. > 20 million childhood deaths per year in Asia, Africa & Latin America due to diarrheal infections alone**
- 4. Yet < 2% deaths in modern, industrialized countries!**

# *Why such striking differences across the world?*

1. **Poor sanitation**
2. **Contaminated water supply**
3. **Contaminated food supply**
4. **Malnutrition**
5. **Existing infections**
6. **Patchy, inadequately-funded vaccinations**
7. **AIDS superimposed on top of 1-6!**



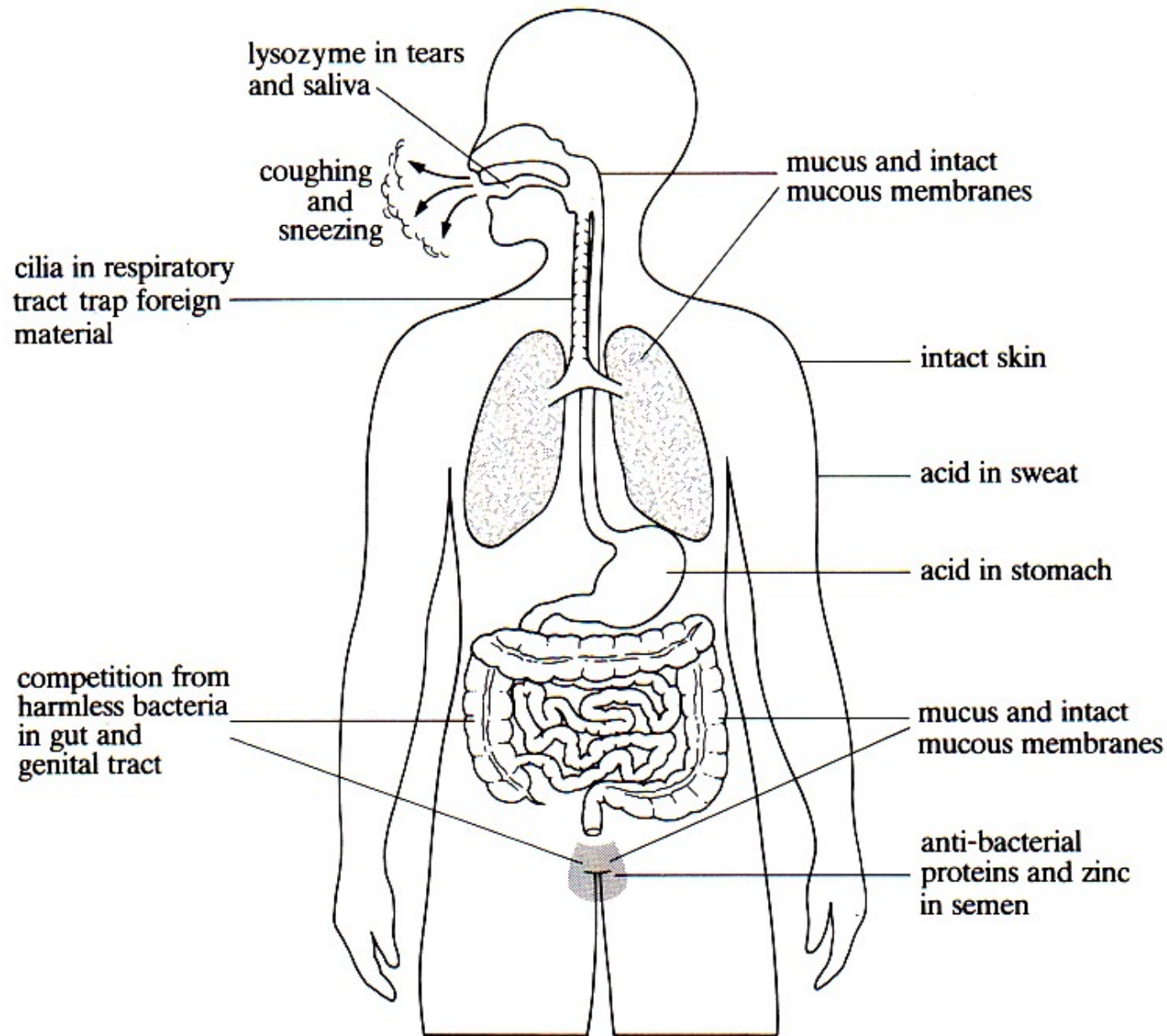
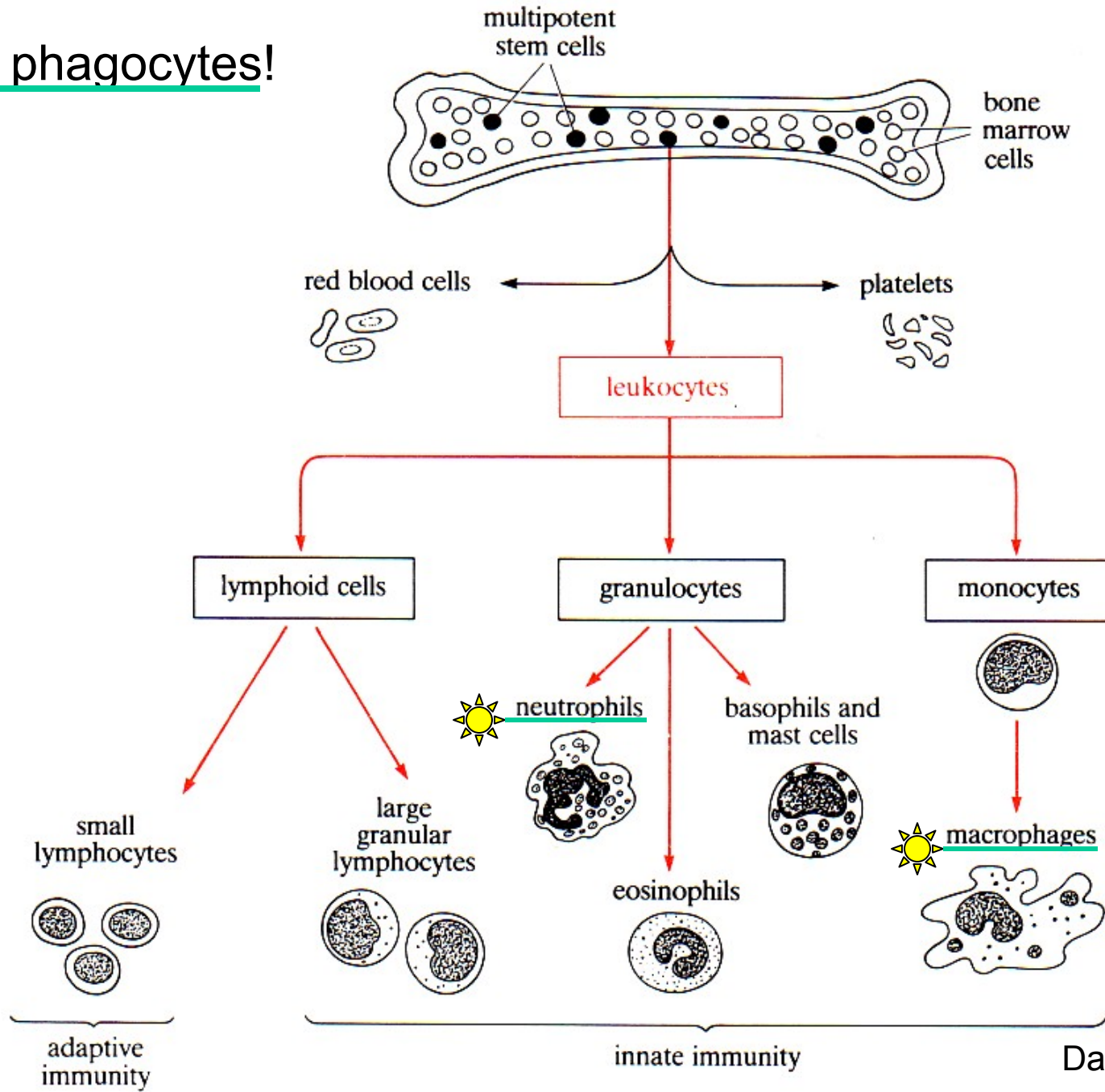


FIGURE 2.1 Summary of the main physical, chemical and mechanical barriers to infection entering the human body.

 Good phagocytes!



Granulocytes

Neutrophil 58-62%

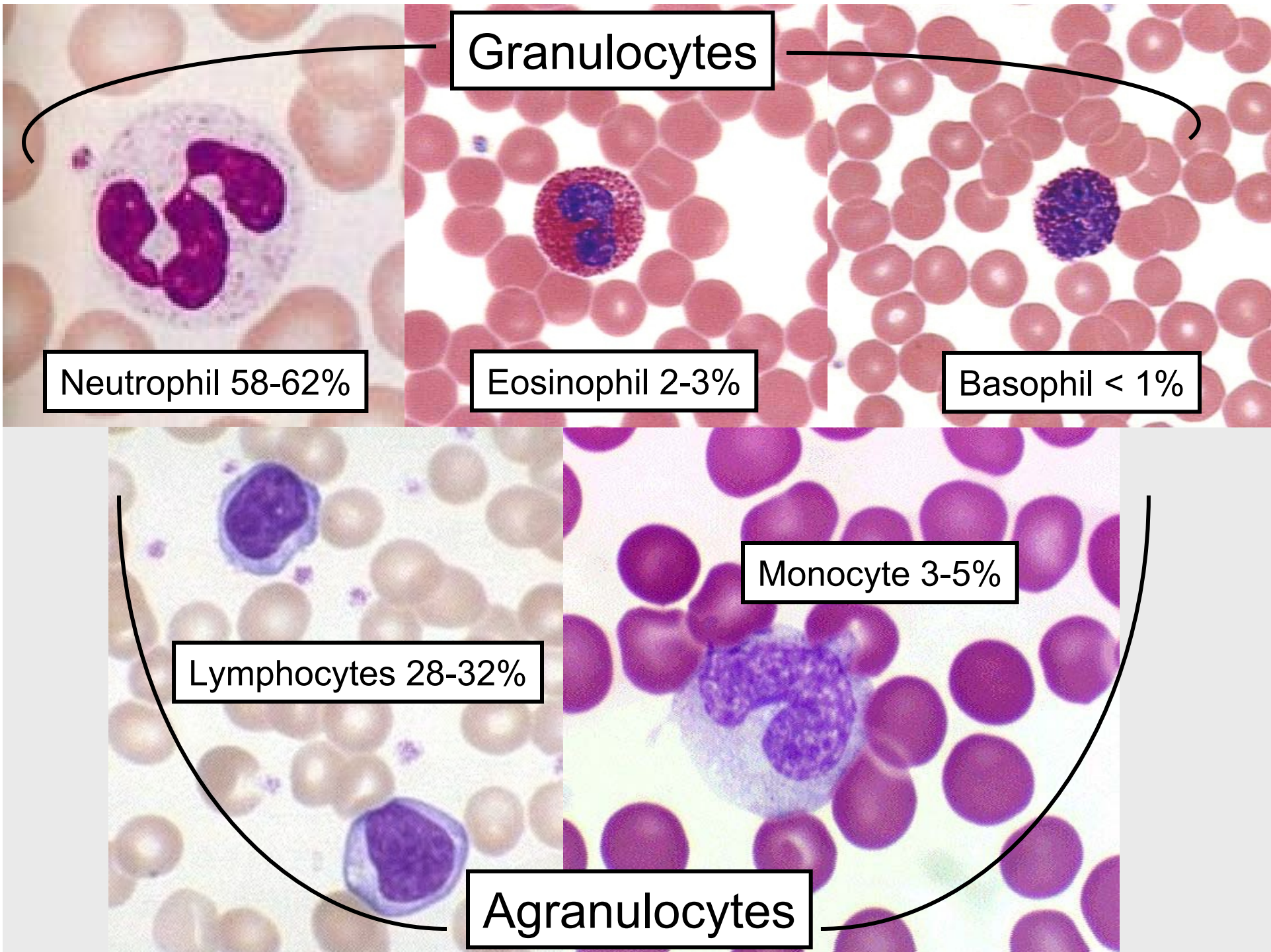
Eosinophil 2-3%

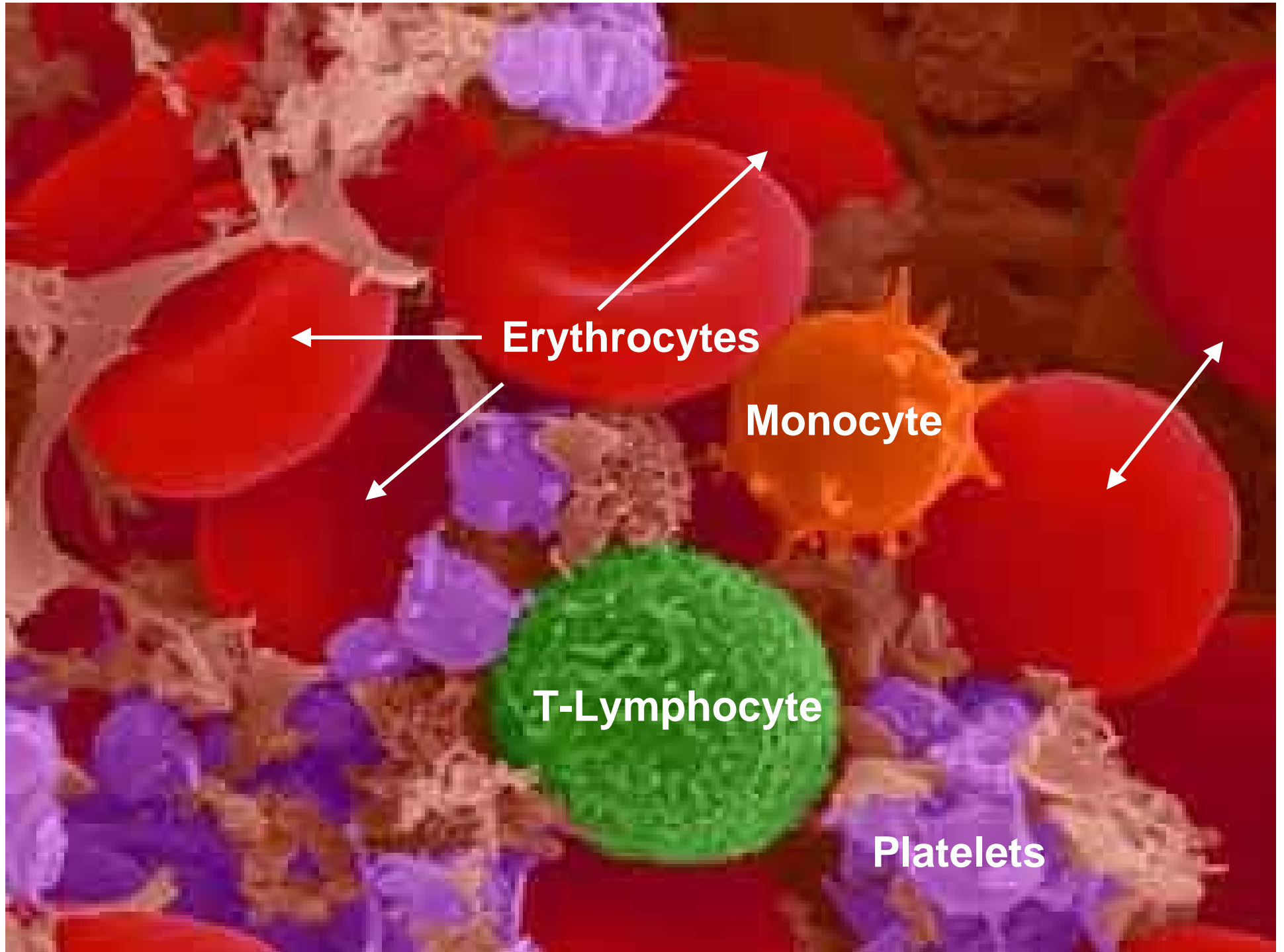
Basophil < 1%

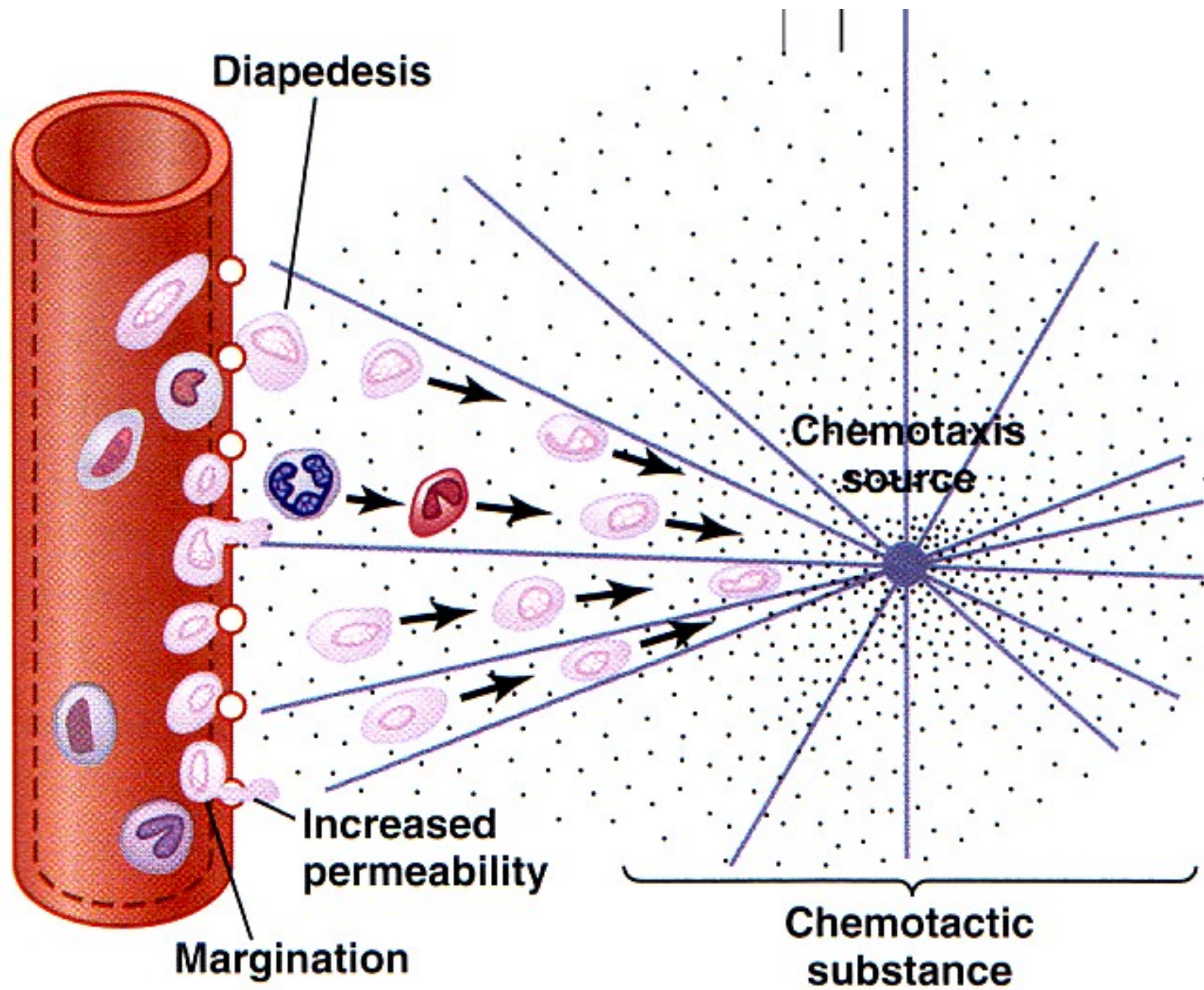
Lymphocytes 28-32%

Monocyte 3-5%

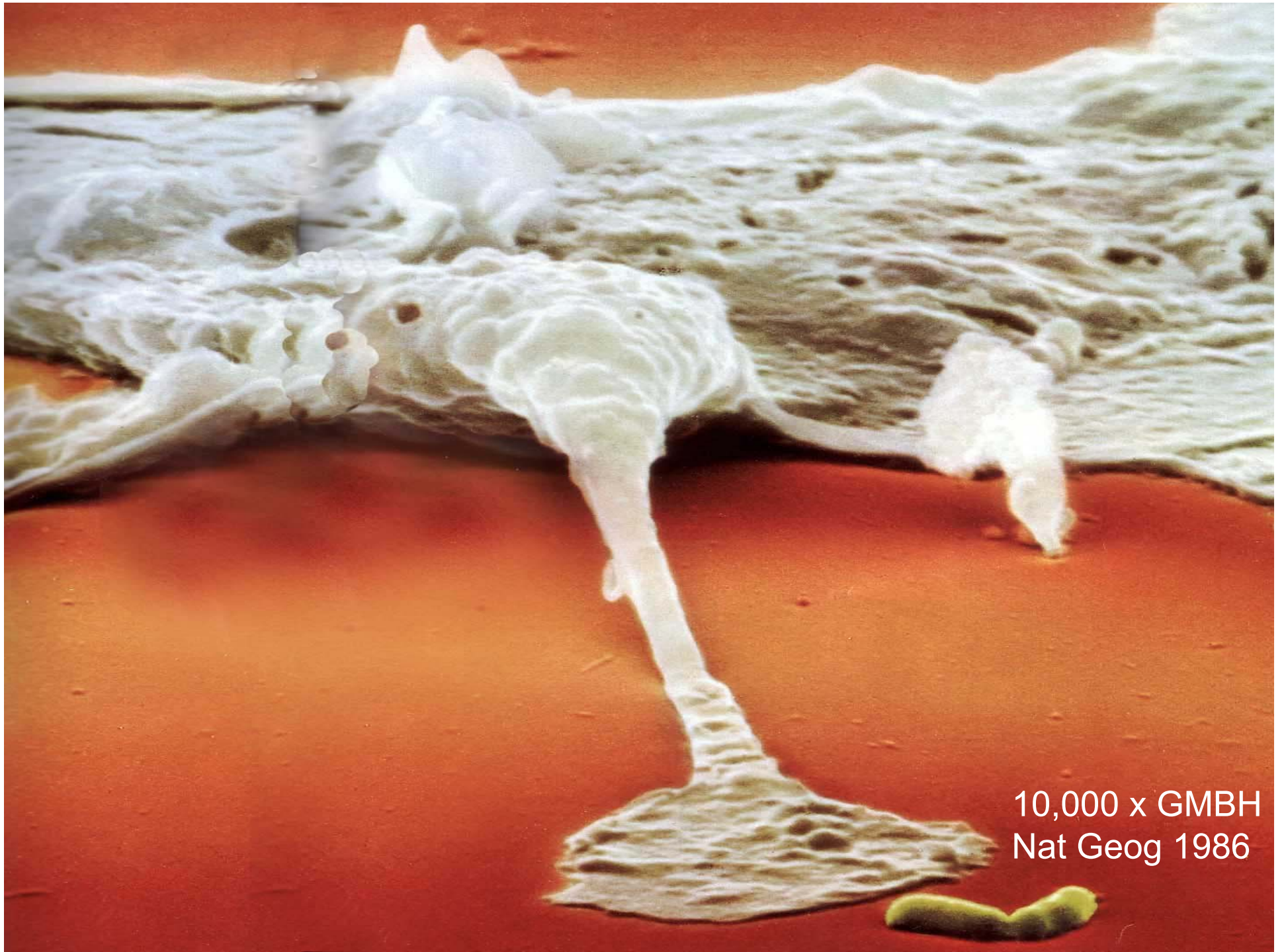
Agranulocytes



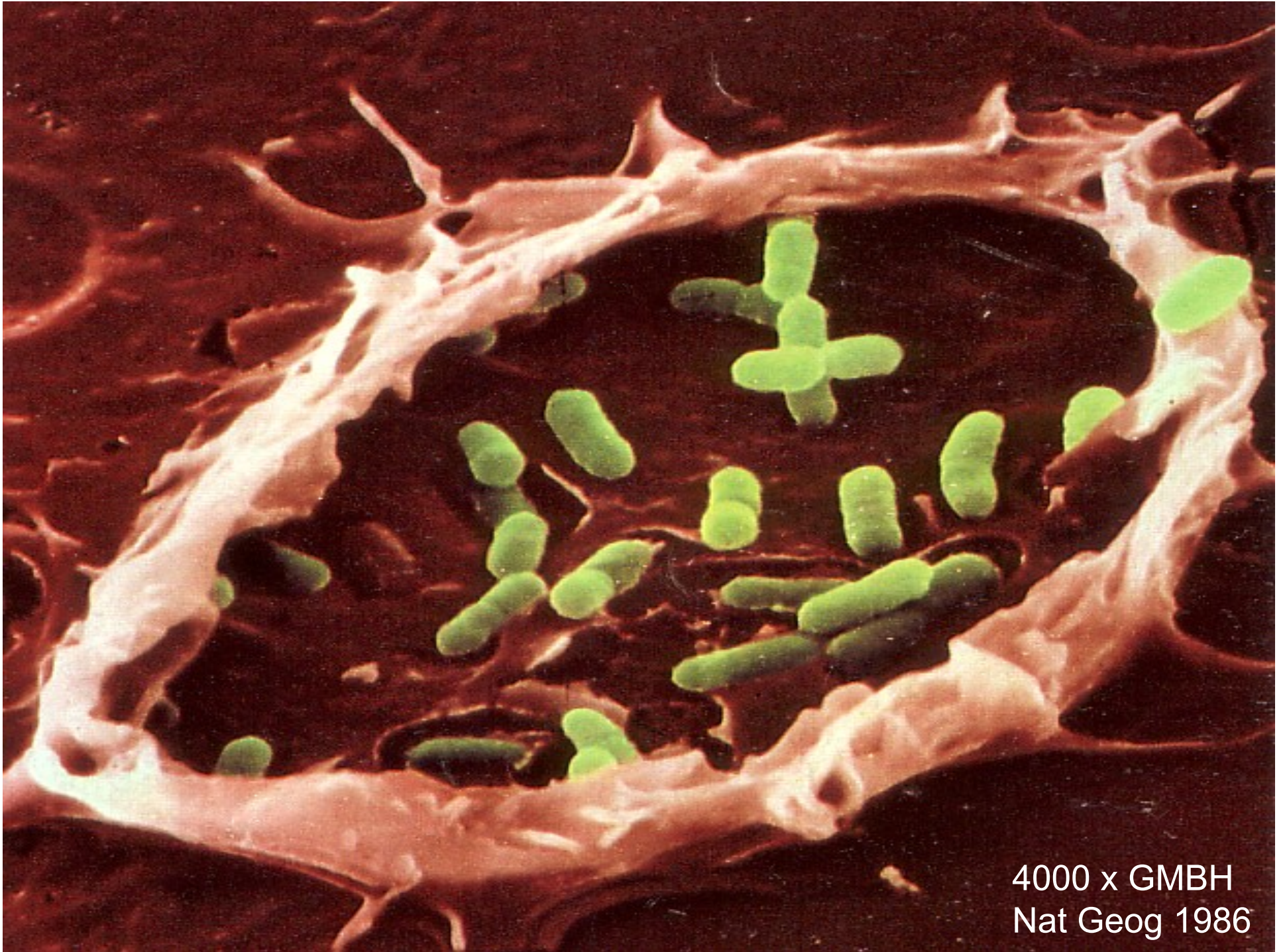




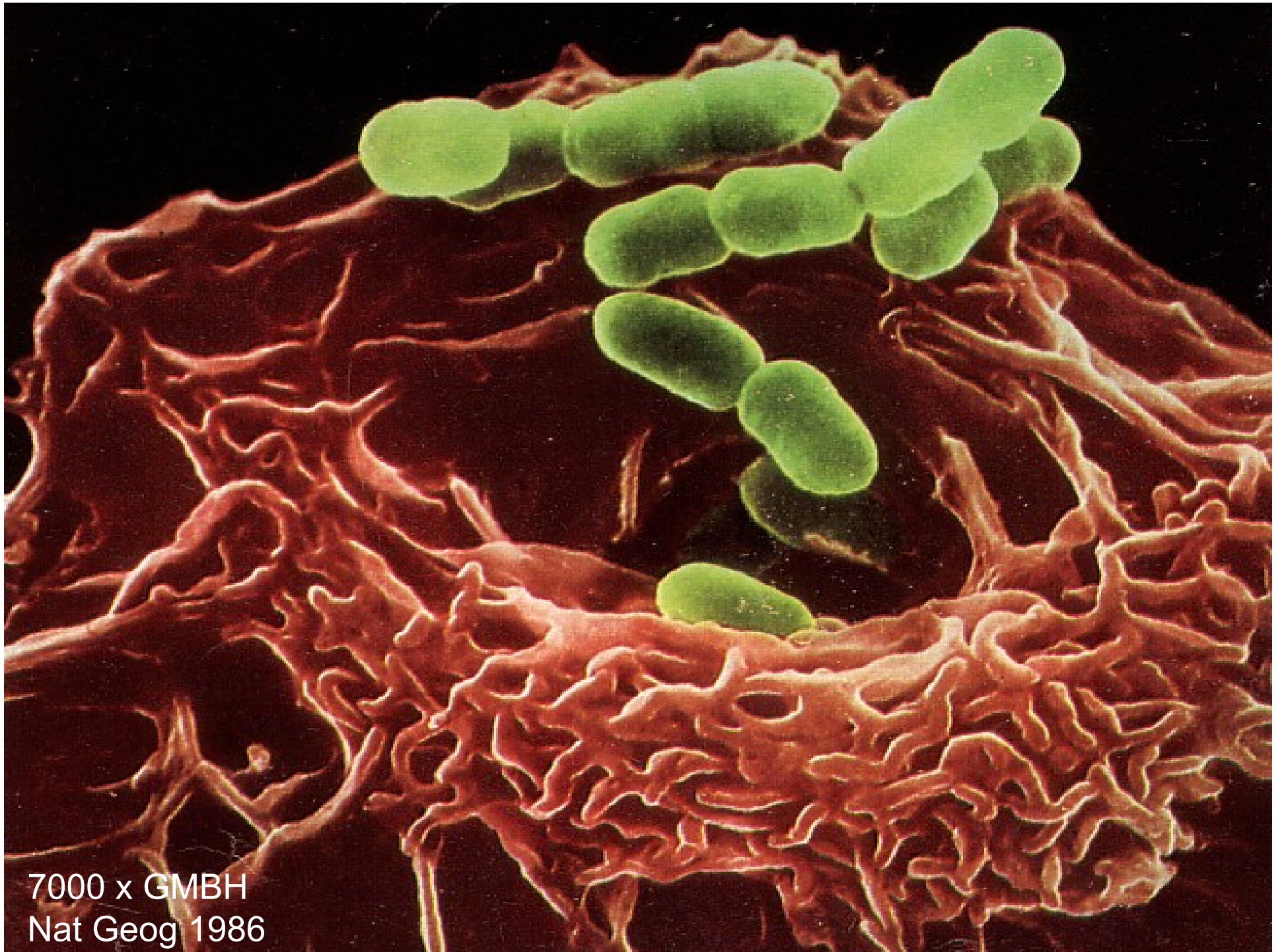
**Figure 33-2** Movement of neutrophils by *diapedesis* through capillary pores and by *chemotaxis* toward an area of tissue damage. G&H 2011



10,000 x GMBH  
Nat Geog 1986

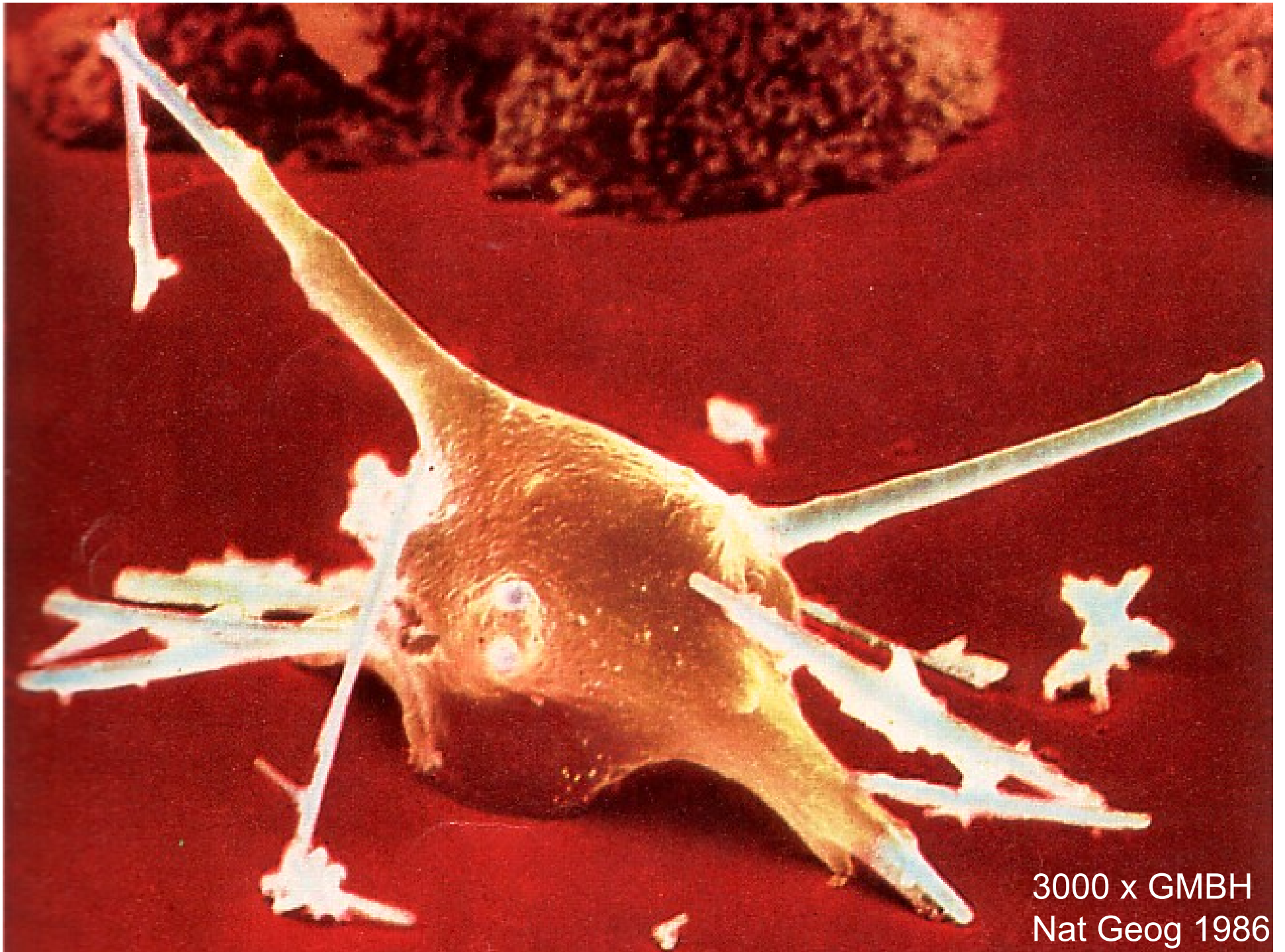


4000 x GMBH  
Nat Geog 1986



7000 x GMBH  
Nat Geog 1986



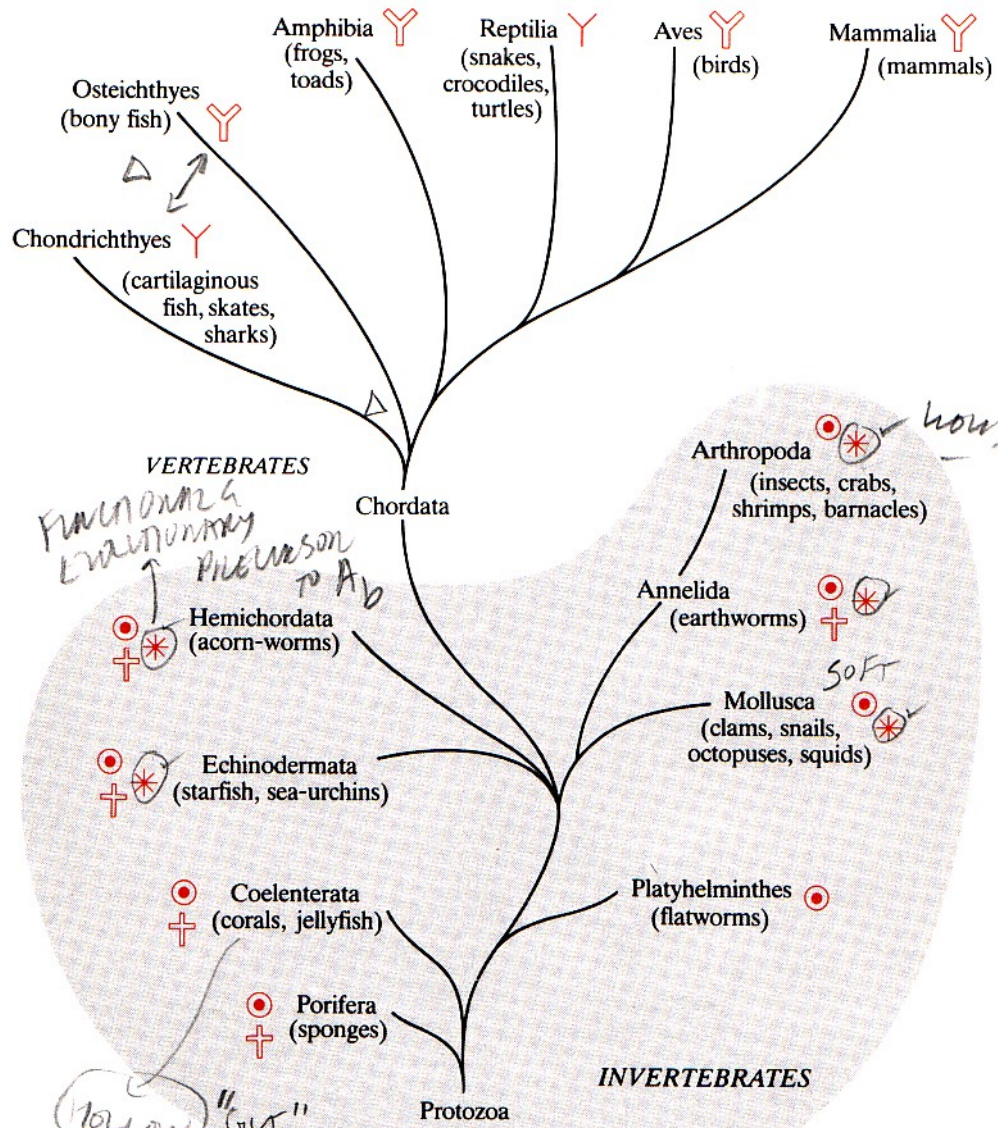




10,000 x GBH  
Nat Geog 1986



7000 x GMBH  
Nat Geog 1986



- Key
- Y strong adaptive immunity and innate immunity
  - Y weak adaptive immunity and innate immunity
  - \* antisomes → vs. B cell
  - ⊕ cytotoxic cells and graft rejection
  - ⊙ phagocytic cells
- } innate immunity

VERTEBRATES

FUNCTIONAL EVOLUTIONARY PROGRESS TO AB

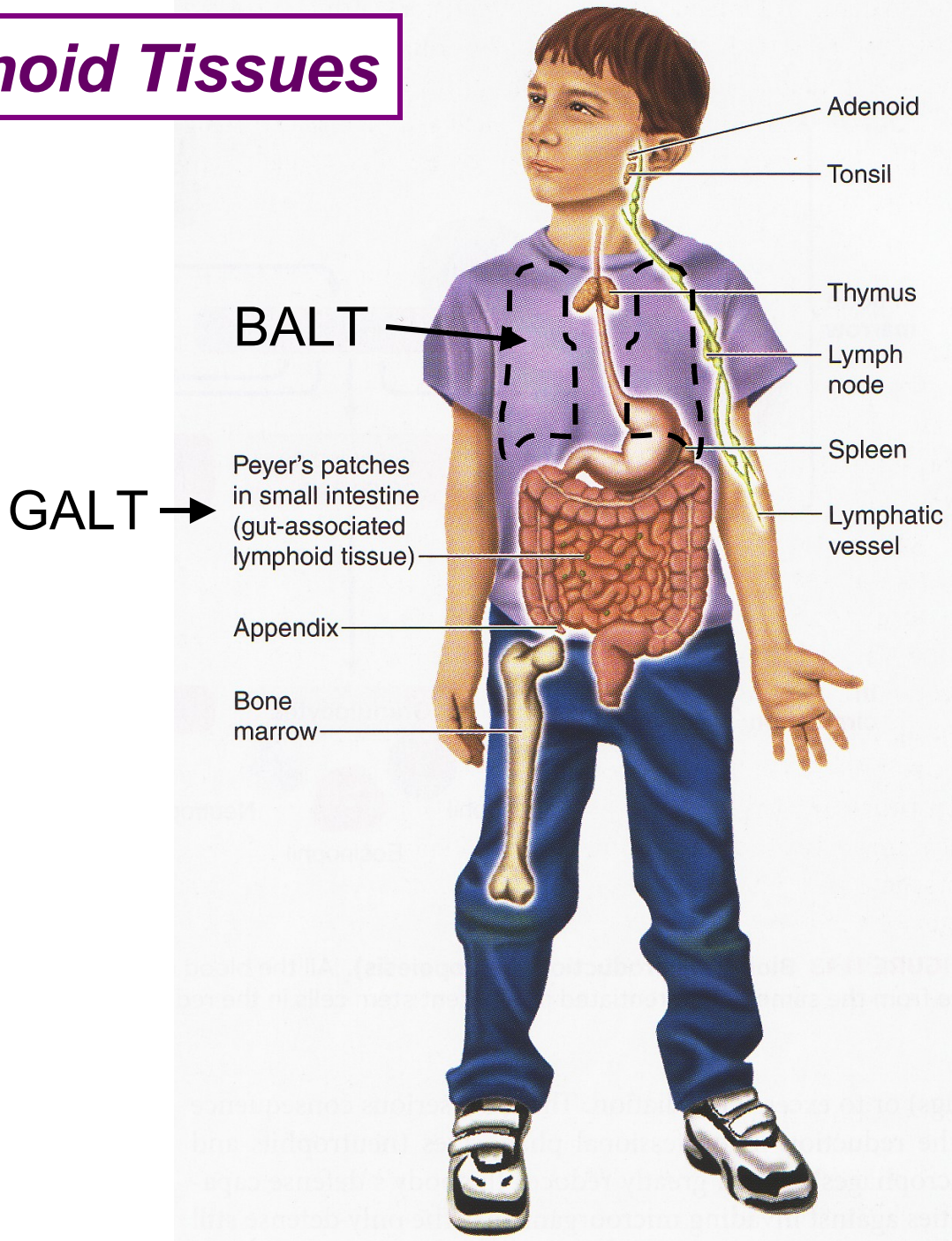
INVERTEBRATES

hollow "GUT" intestines

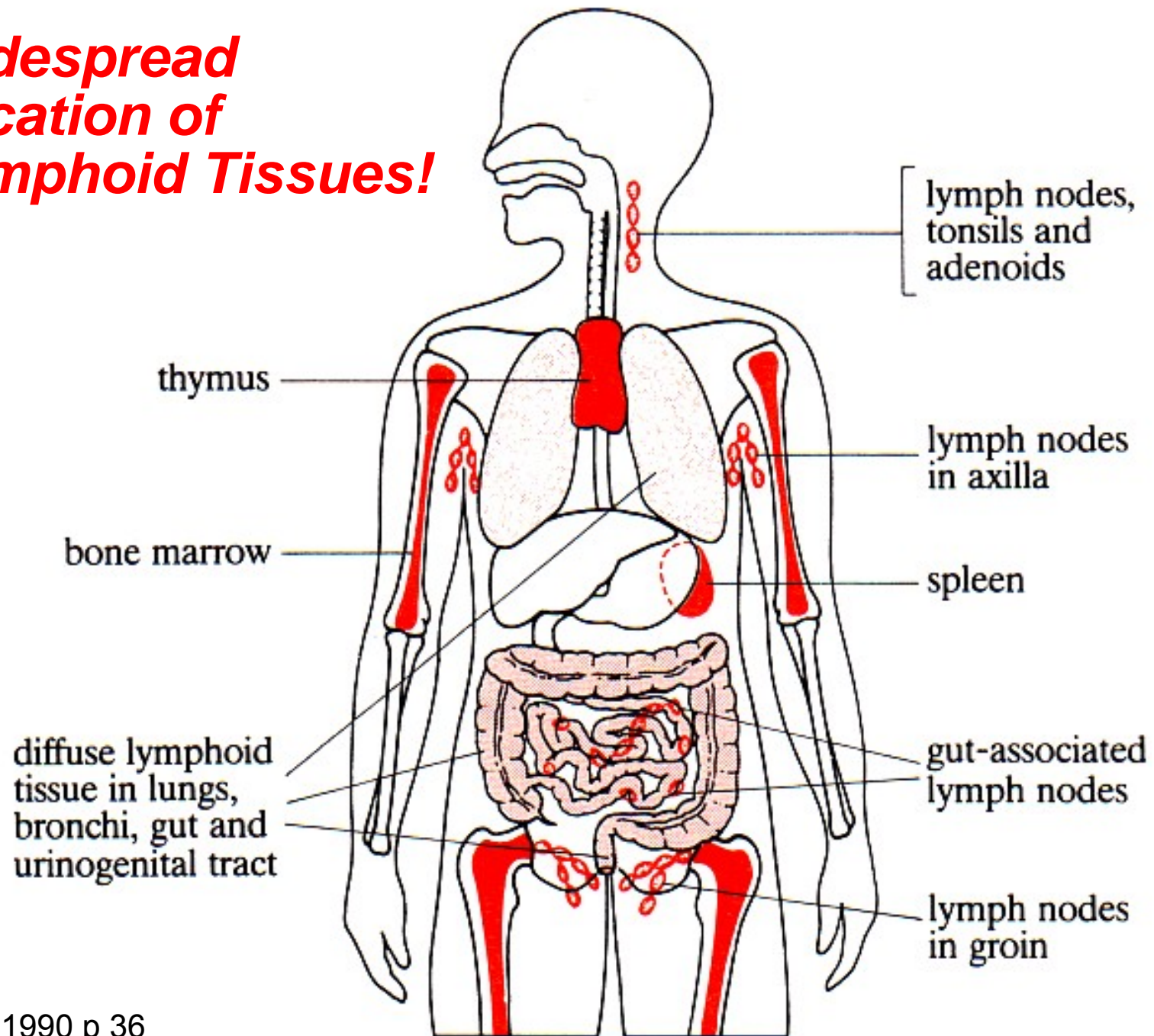
SOFT

how

# Lymphoid Tissues



# ***Widespread Location of Lymphoid Tissues!***



# Immunity

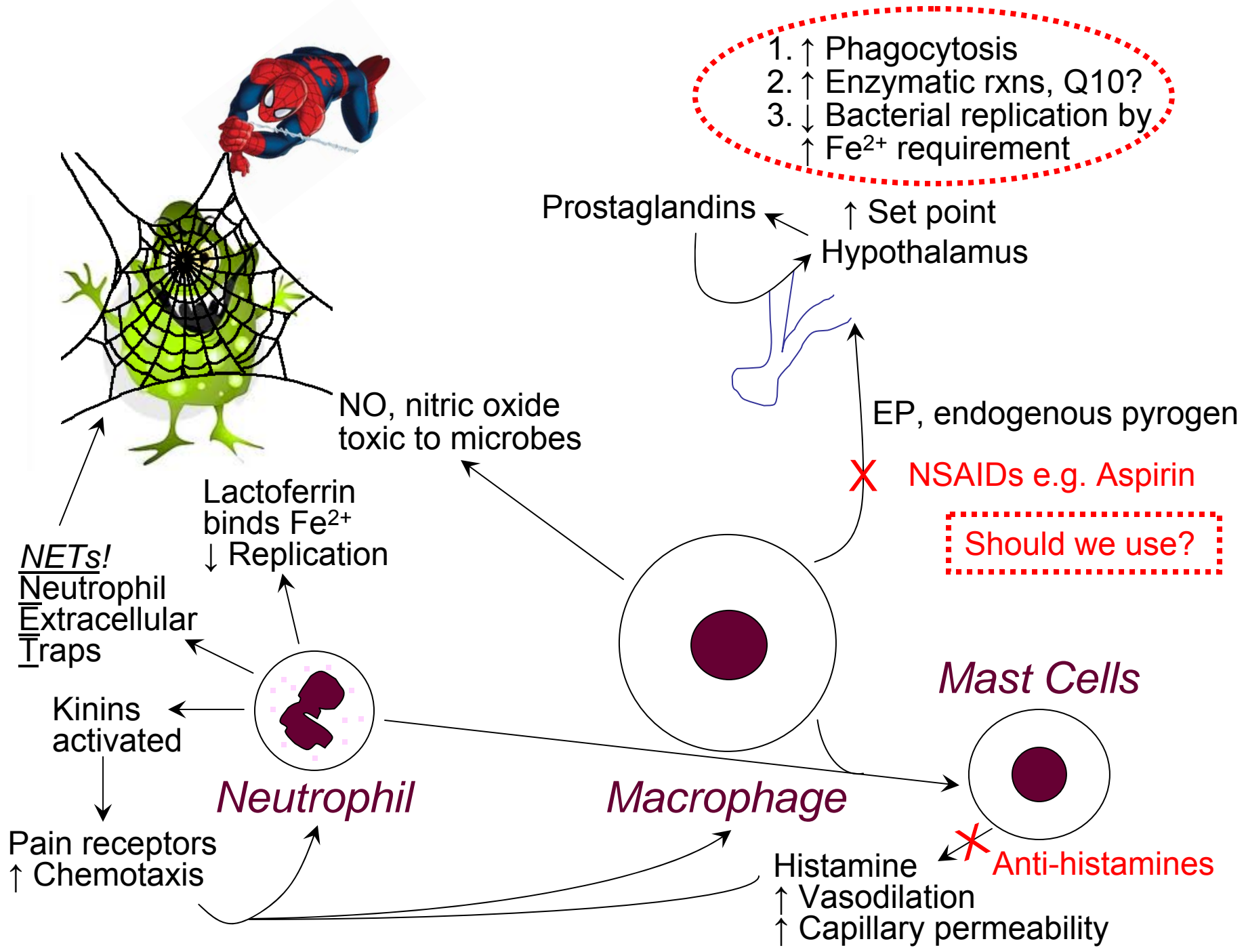
## Innate/Inborn/Nonspecific

1. Immediate, upon exposure to threatening agent
2. 1<sup>0</sup> effectors phagocytic specialists: neutrophils & macrophages
3. "Eyes" are Toll-like receptors (TLRs) which recognize & bind with generic invader markers
4. Inflammation, interferon, natural killer cells, complement (plasma proteins)

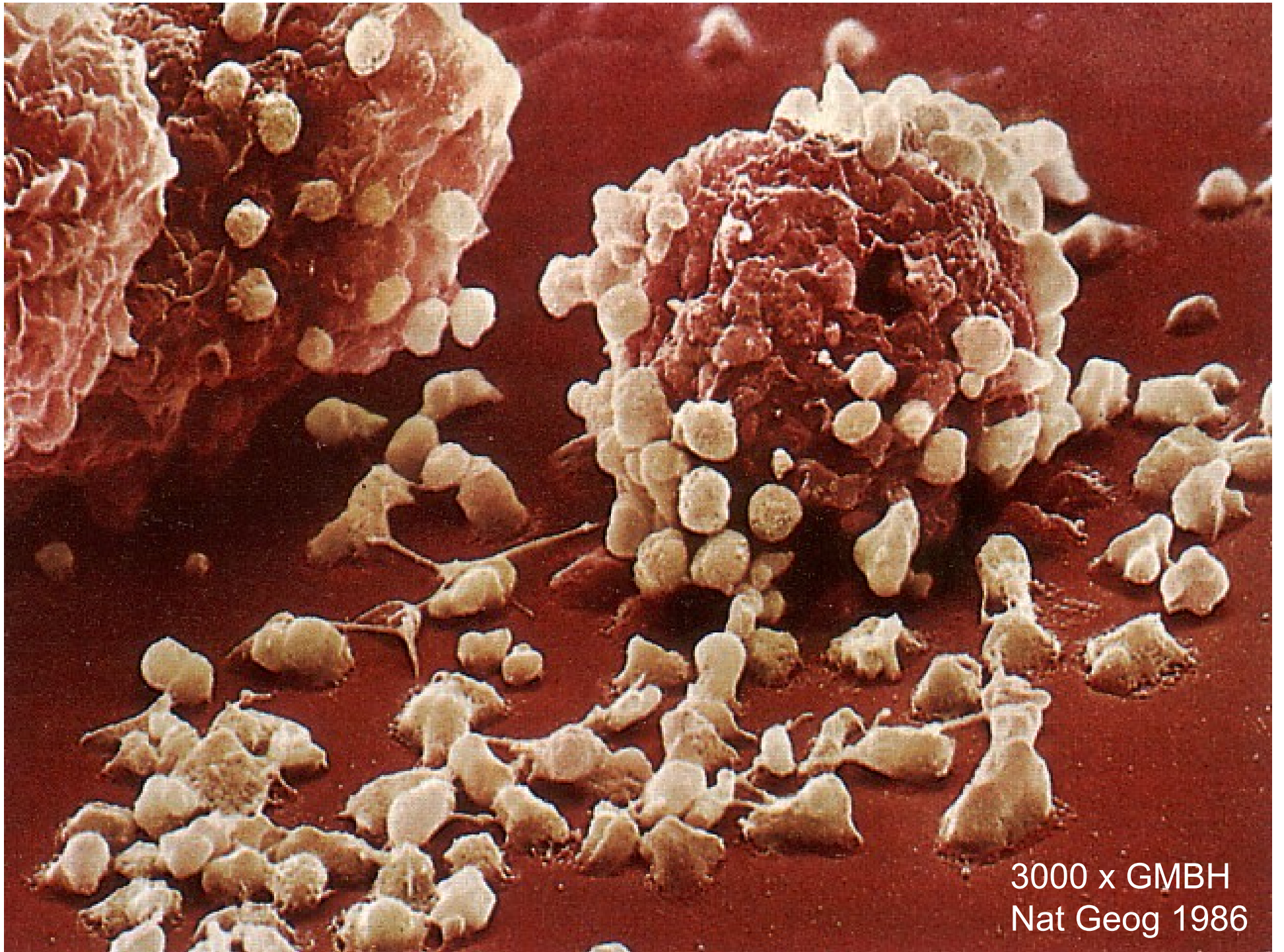
## Adaptive/Acquired/Specific

1. Delayed, selective targetting based on prior exposure
2. 1<sup>0</sup> effectors lymphocytes: T- & B-lymphocytes
3. "Eyes" are T- and B-cell receptors which bind with specific antigens
4. Cell-mediated & Humoral (Ab mediated) immunity

Really, a false separation, as incredible overlap & synergism!



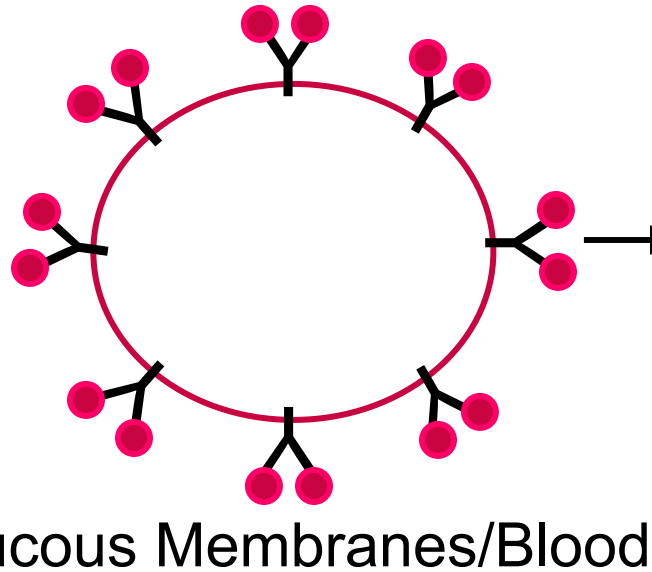




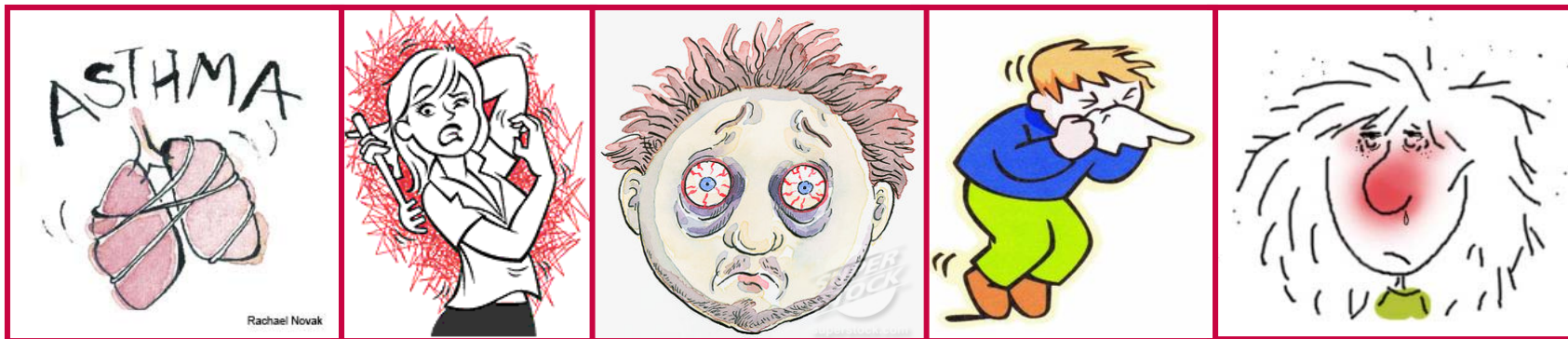
3000 x GMBH  
Nat Geog 1986

# Allergic Reactions, Mast Cells & Basophils?

Allergen = ●  
IgE = Y  
↑  
up to 1/2 million per cell!



- Bradykinin
- Eosinophil & Neutrophil Chemotactic Substances
- Heparin
- Histamine
- Platelet Activating Factors
- Protease
- Serotonin
- Toxic Leukotrienes/SRSA



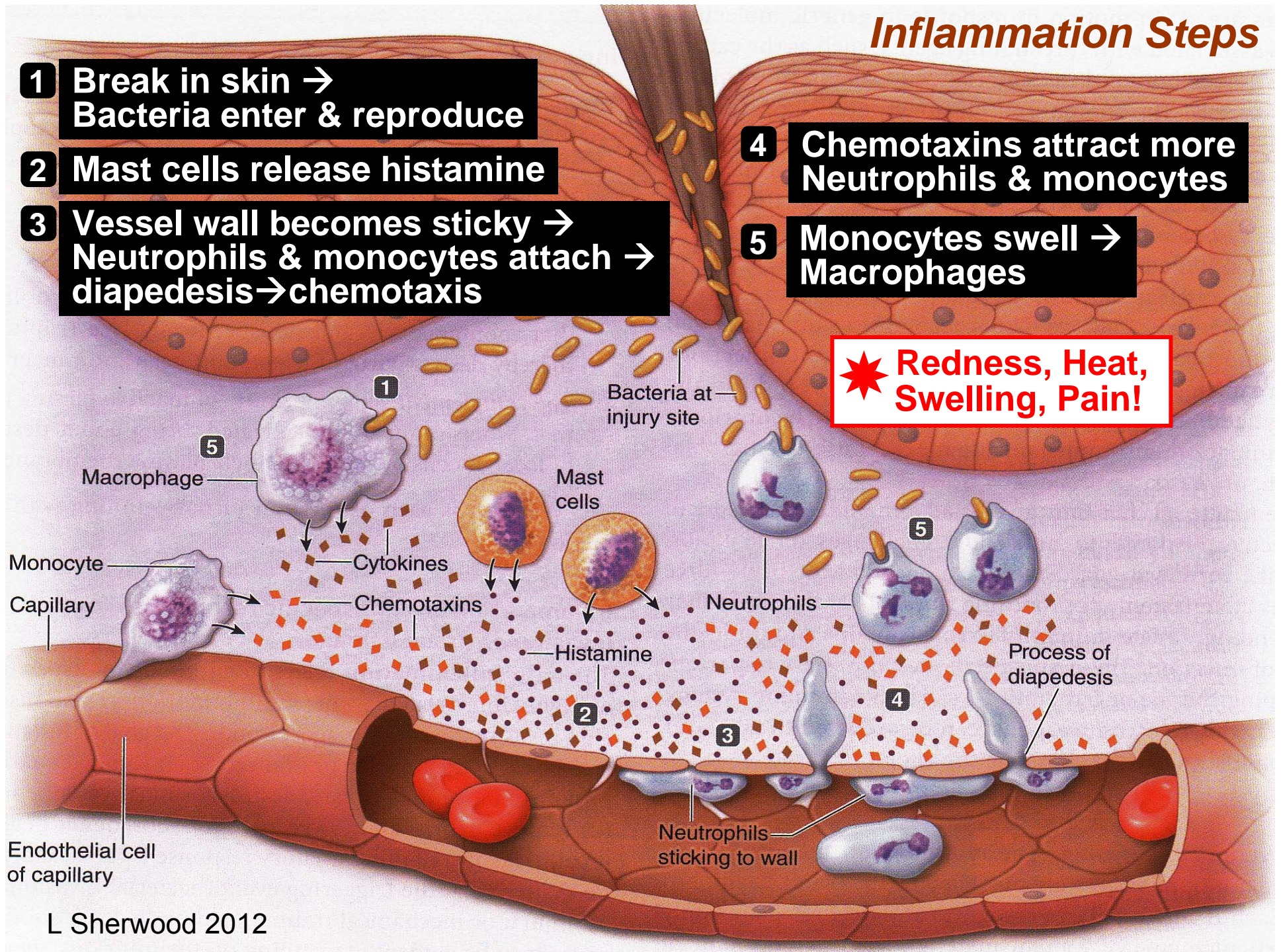
# Inflammation Steps

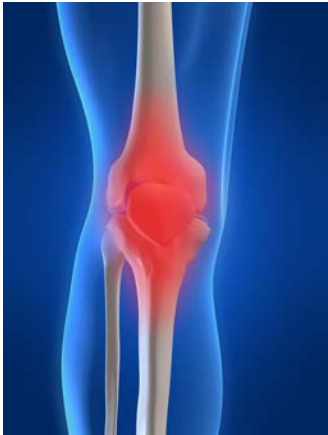
- 1 Break in skin → Bacteria enter & reproduce
- 2 Mast cells release histamine
- 3 Vessel wall becomes sticky → Neutrophils & monocytes attach → diapedesis → chemotaxis

4 Chemotaxins attract more Neutrophils & monocytes

5 Monocytes swell → Macrophages

★ Redness, Heat, Swelling, Pain!





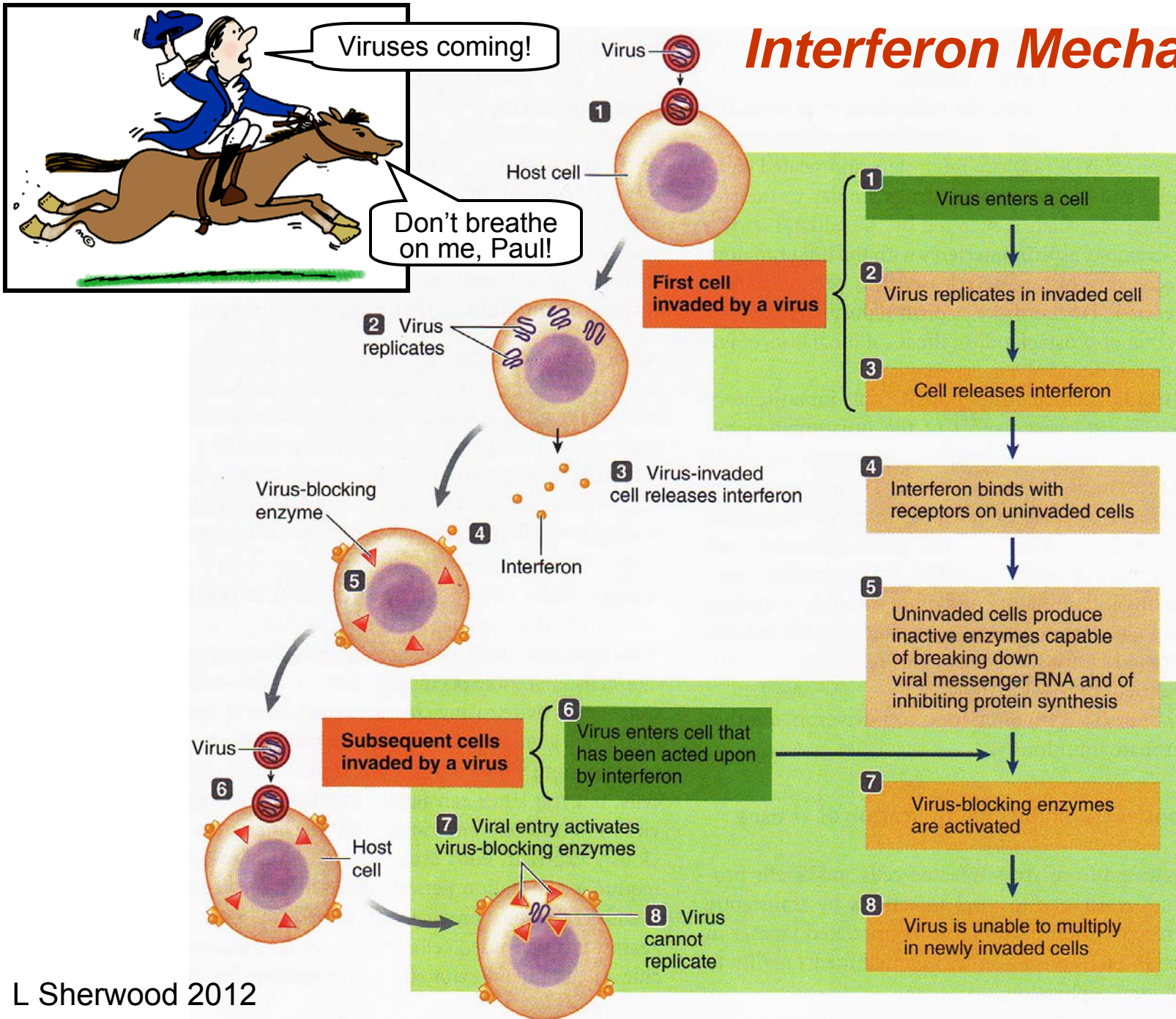
***Glucocorticoids throw blanket over entire inflammatory process!***



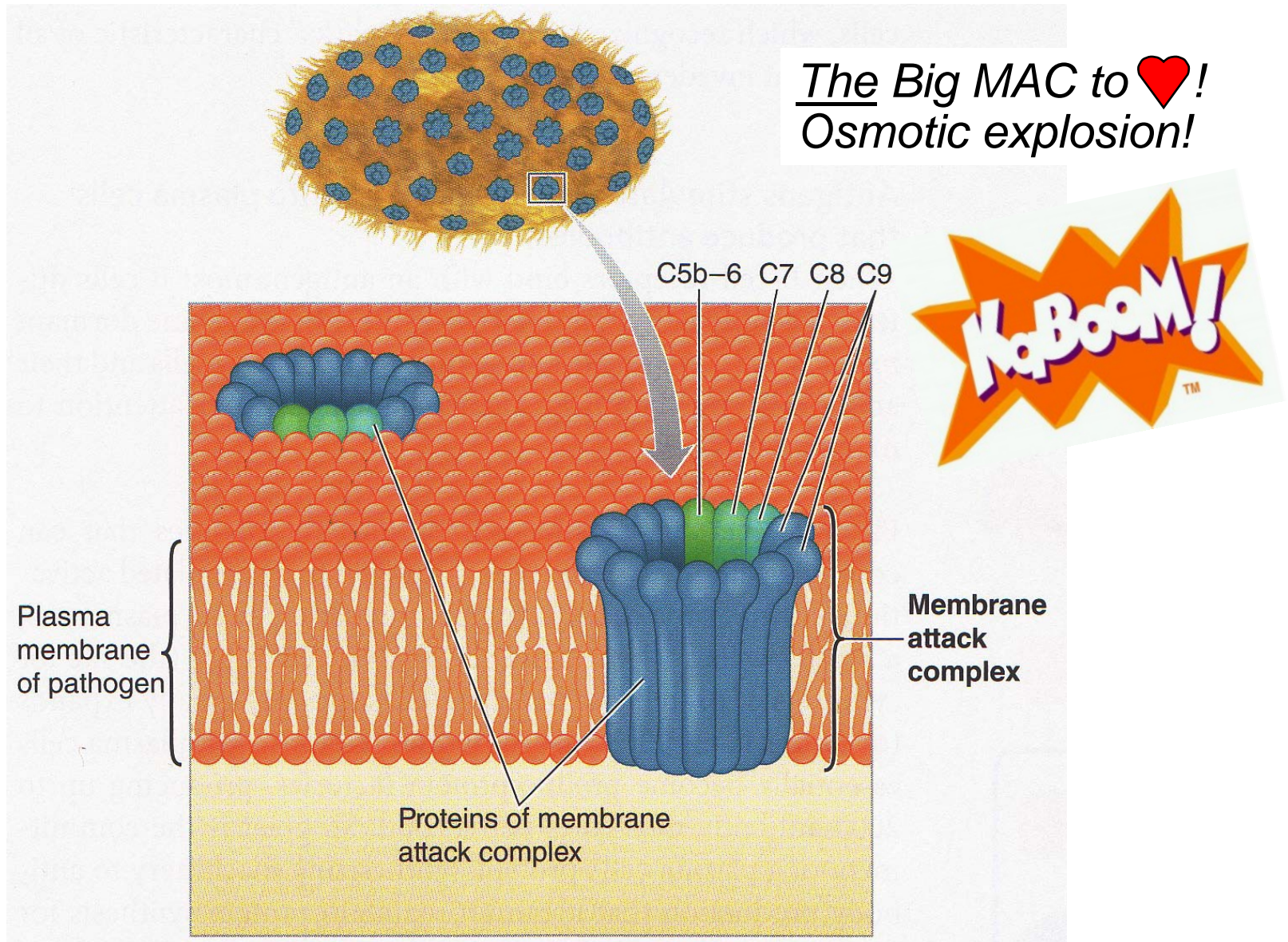
1. Certainly warranted to quiet down immune system during extreme flare ups of arthritis, asthma, poison ivy, rash, but must consider:
2. Destroy lymphocytes in lymphoid tissues.
3. ↓ Antibody/Immunoglobulin (Ig) production.
4. Make susceptible to bacterial infections.



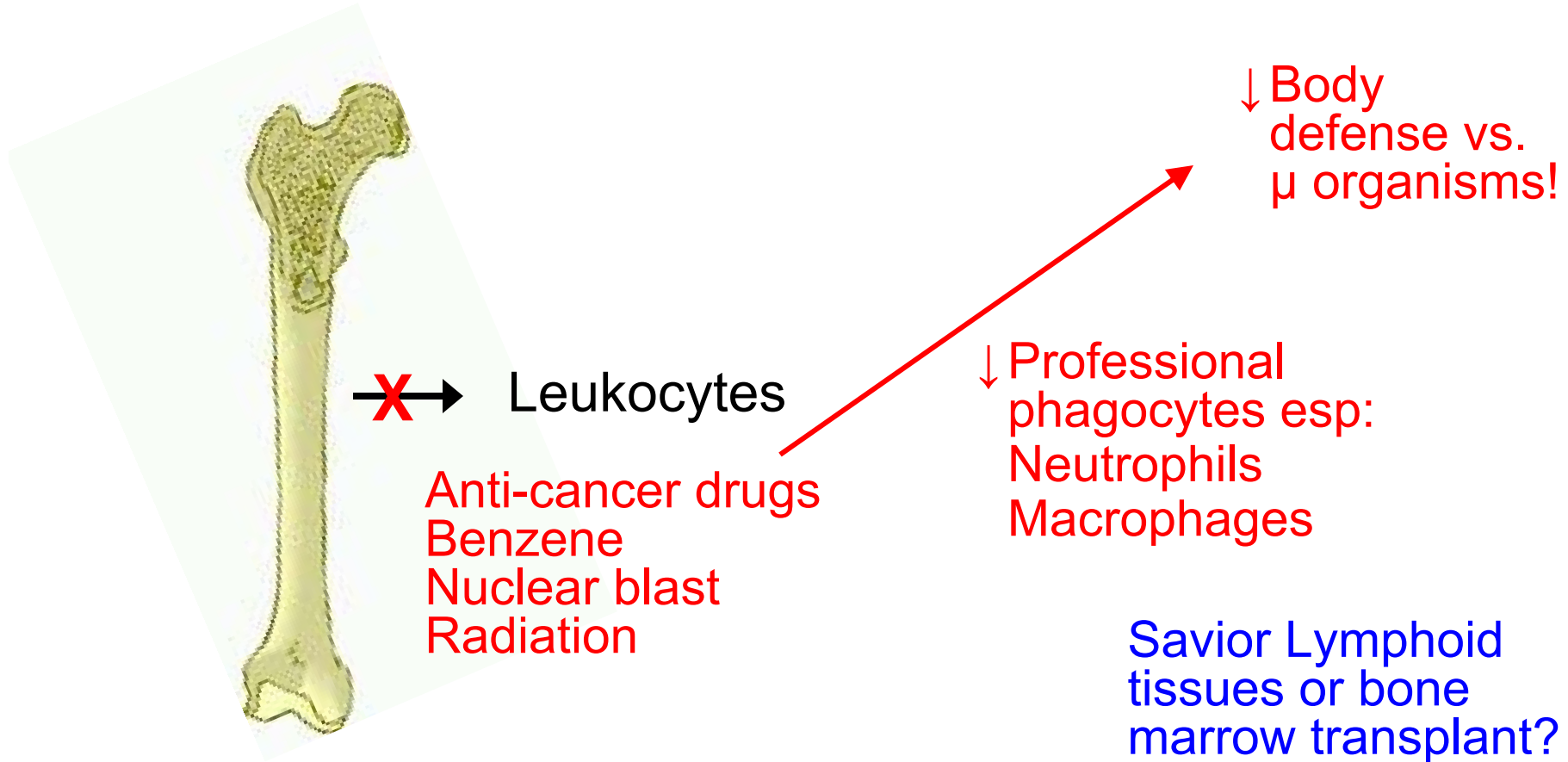
# Interferon Mechanisms



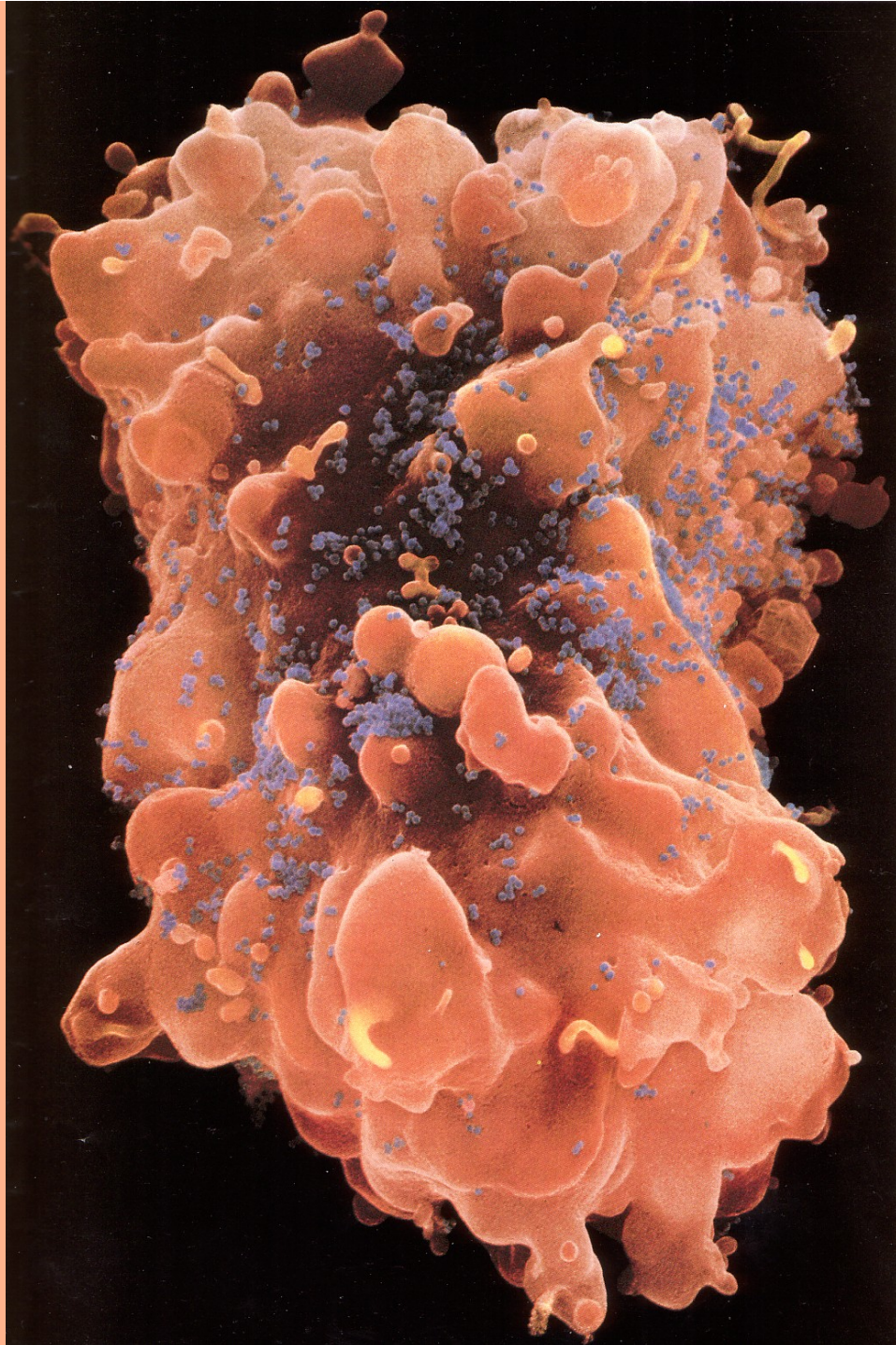
# Activated Complement



# WBC Adverse Effects

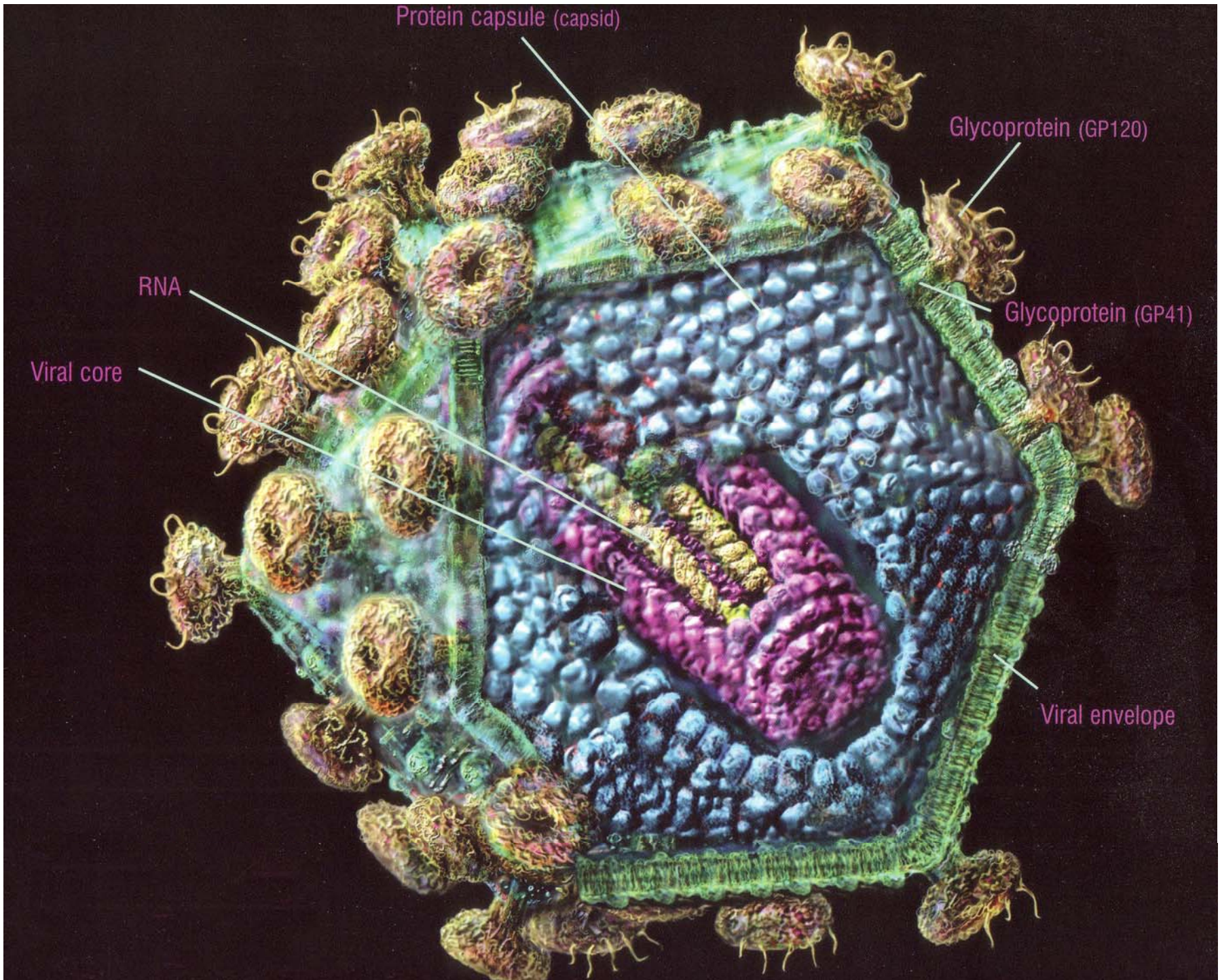


*cf:* Leukemia ≡ uncontrolled WBC proliferation, yet inadequate defense → other cell lines displaced → overwhelming infections & bleeding...

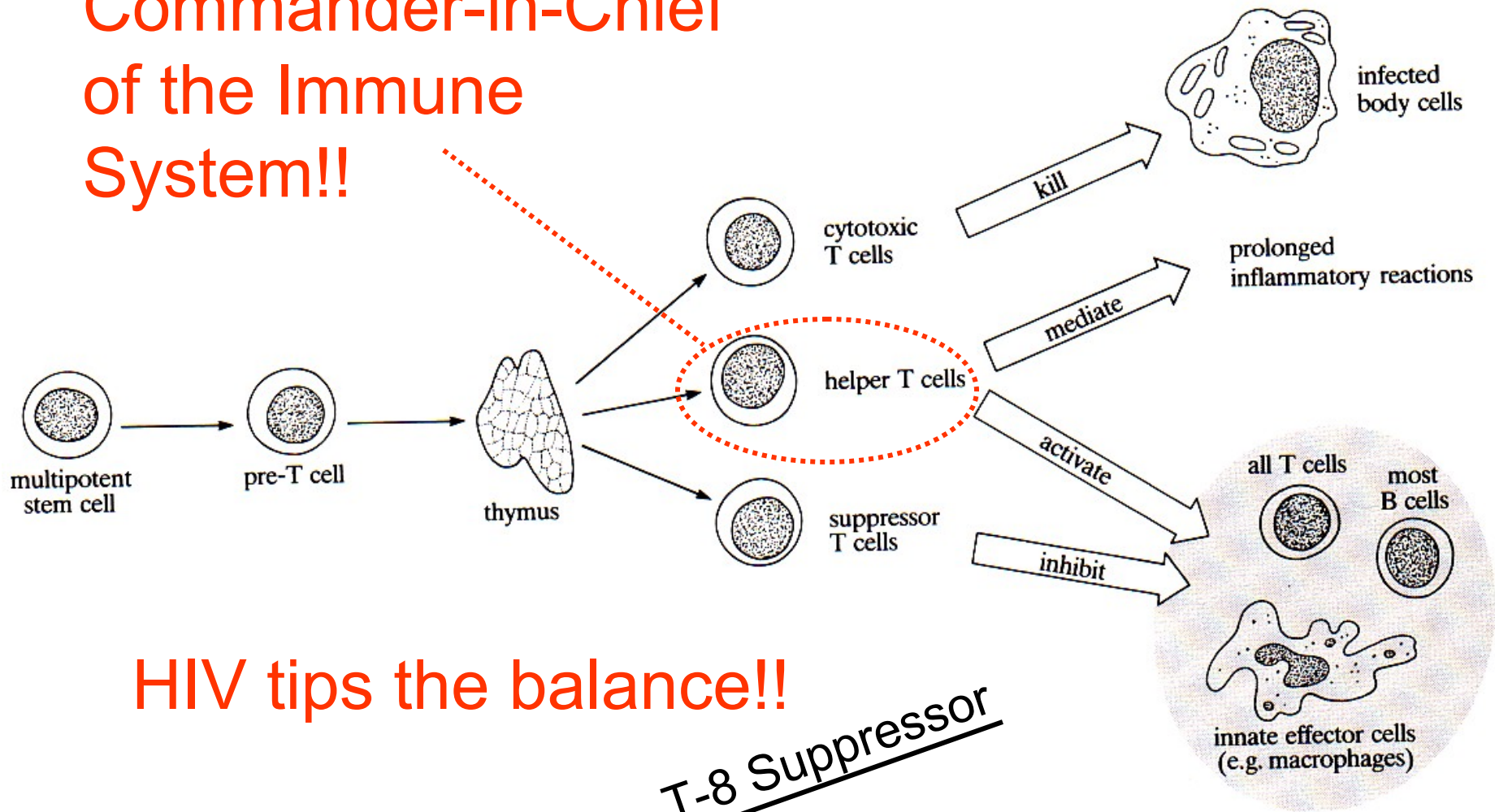


30,000 x GMBH  
Nat Geog 1986

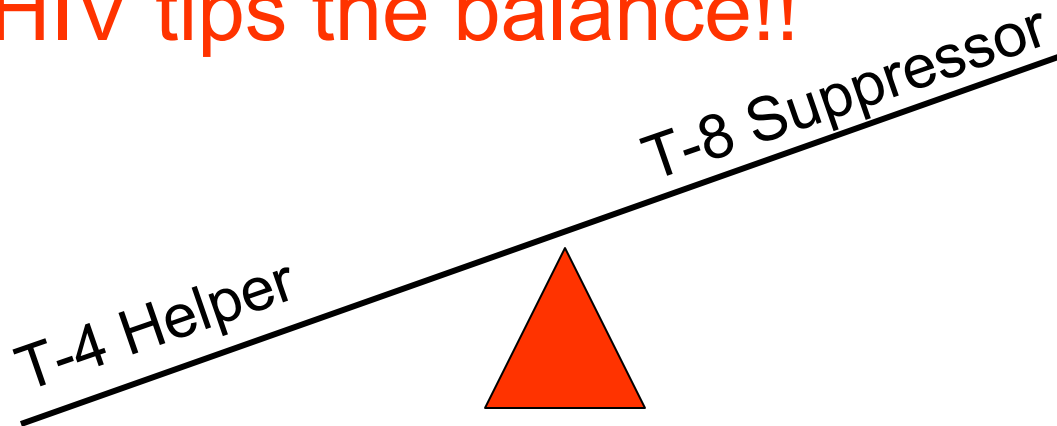


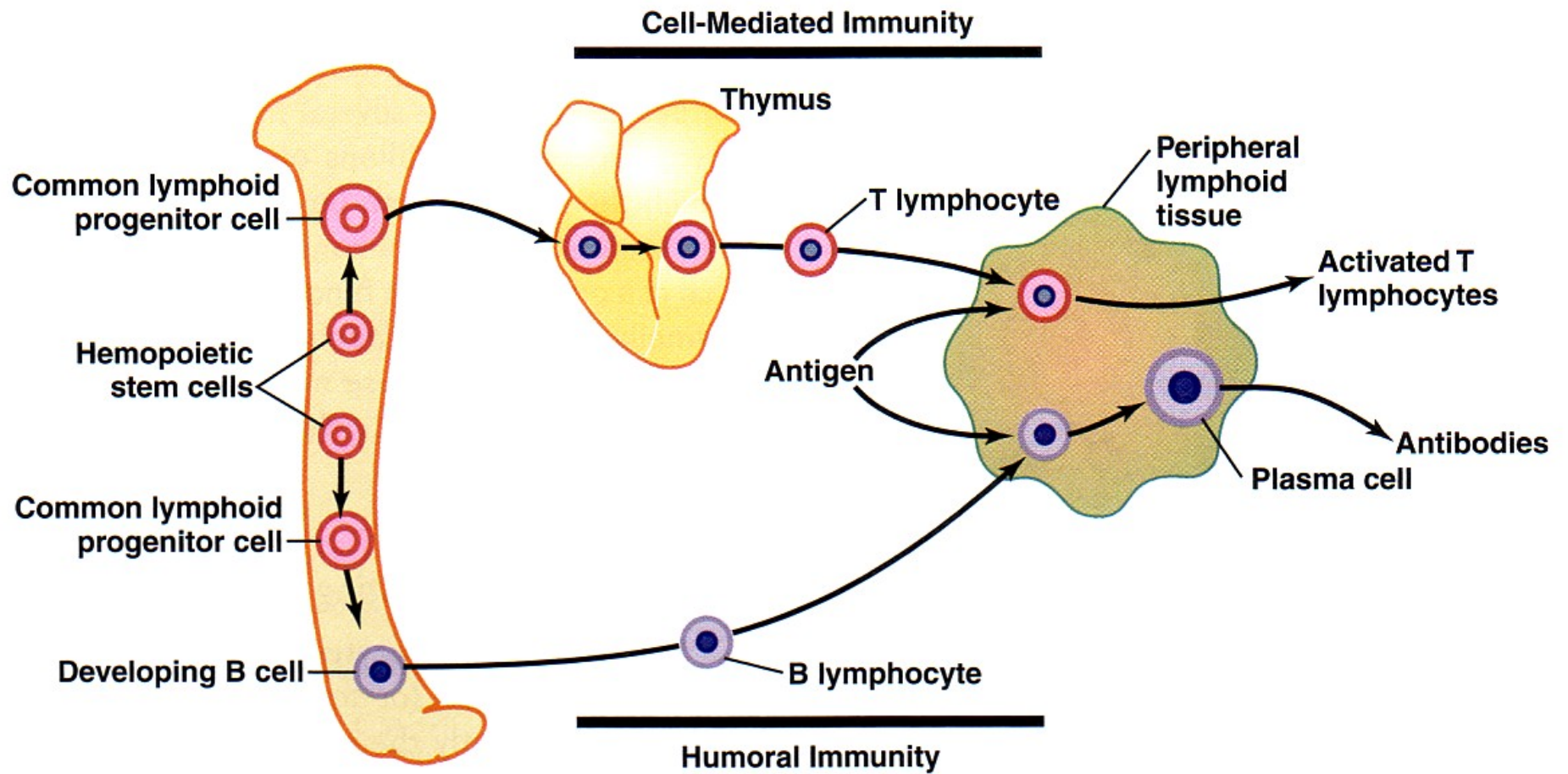


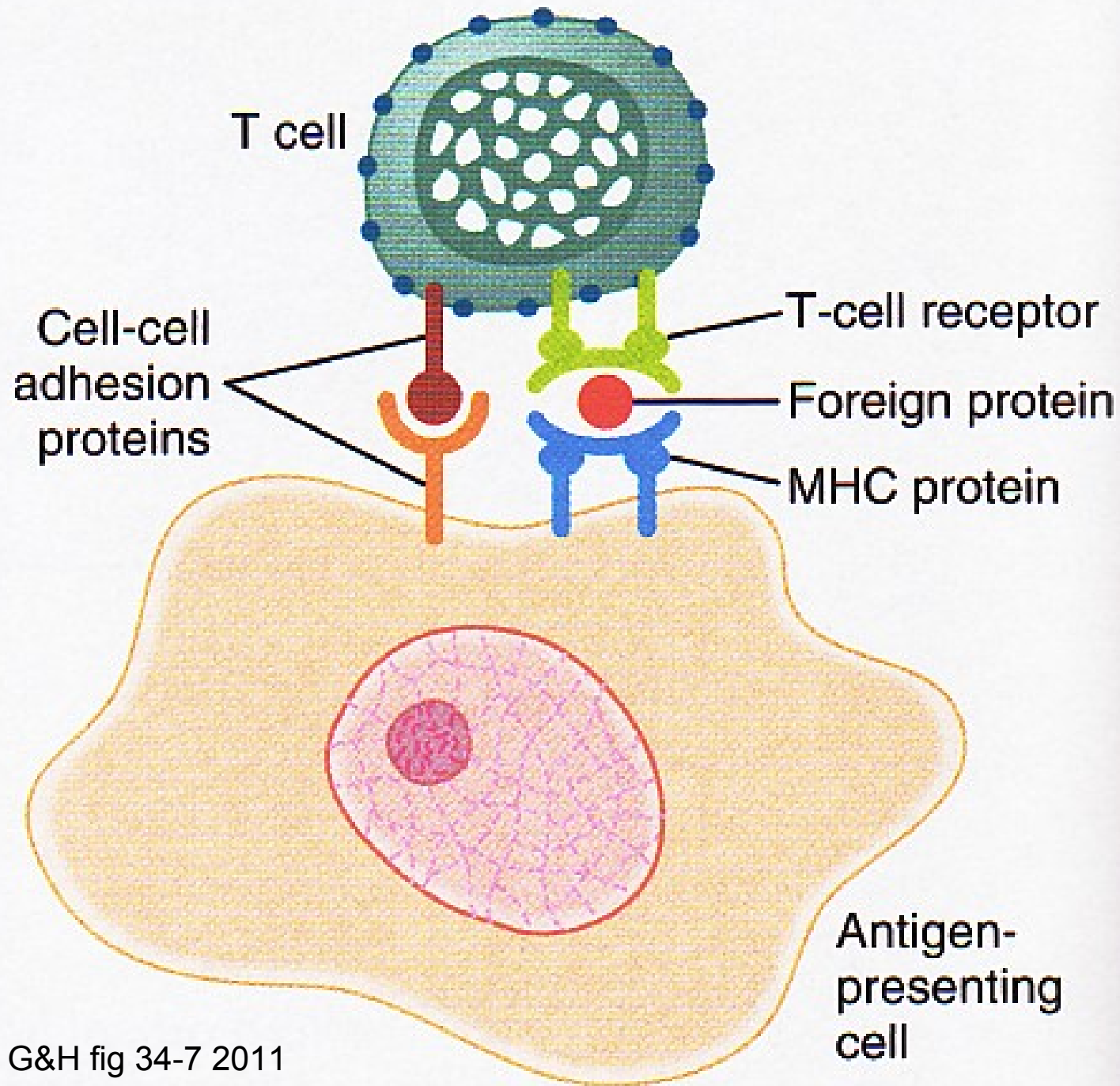
# Commander-in-Chief of the Immune System!!



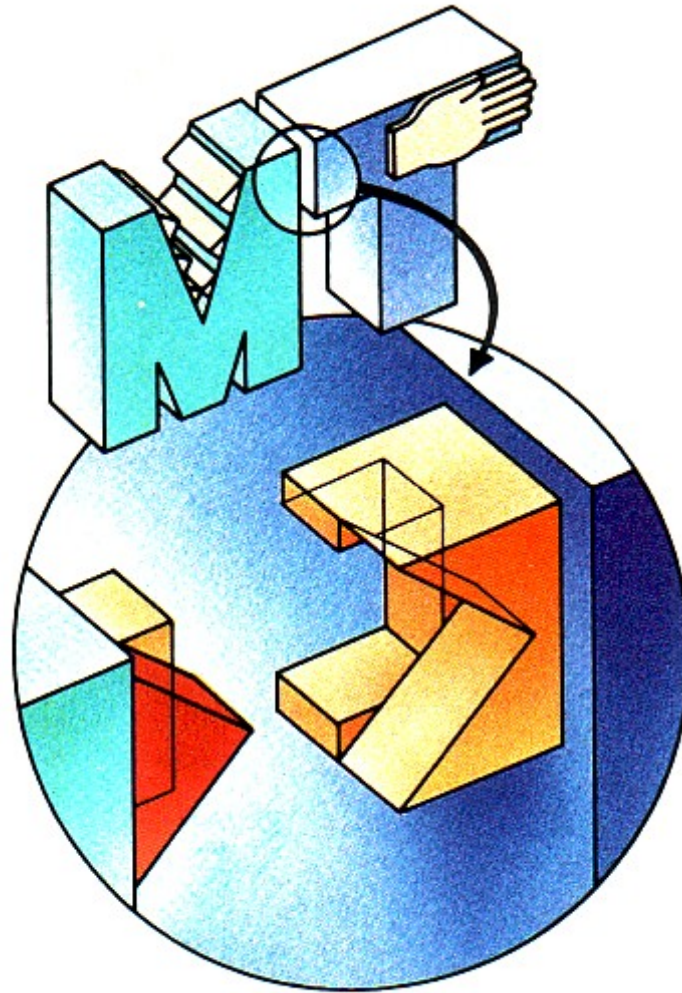
HIV tips the balance!!







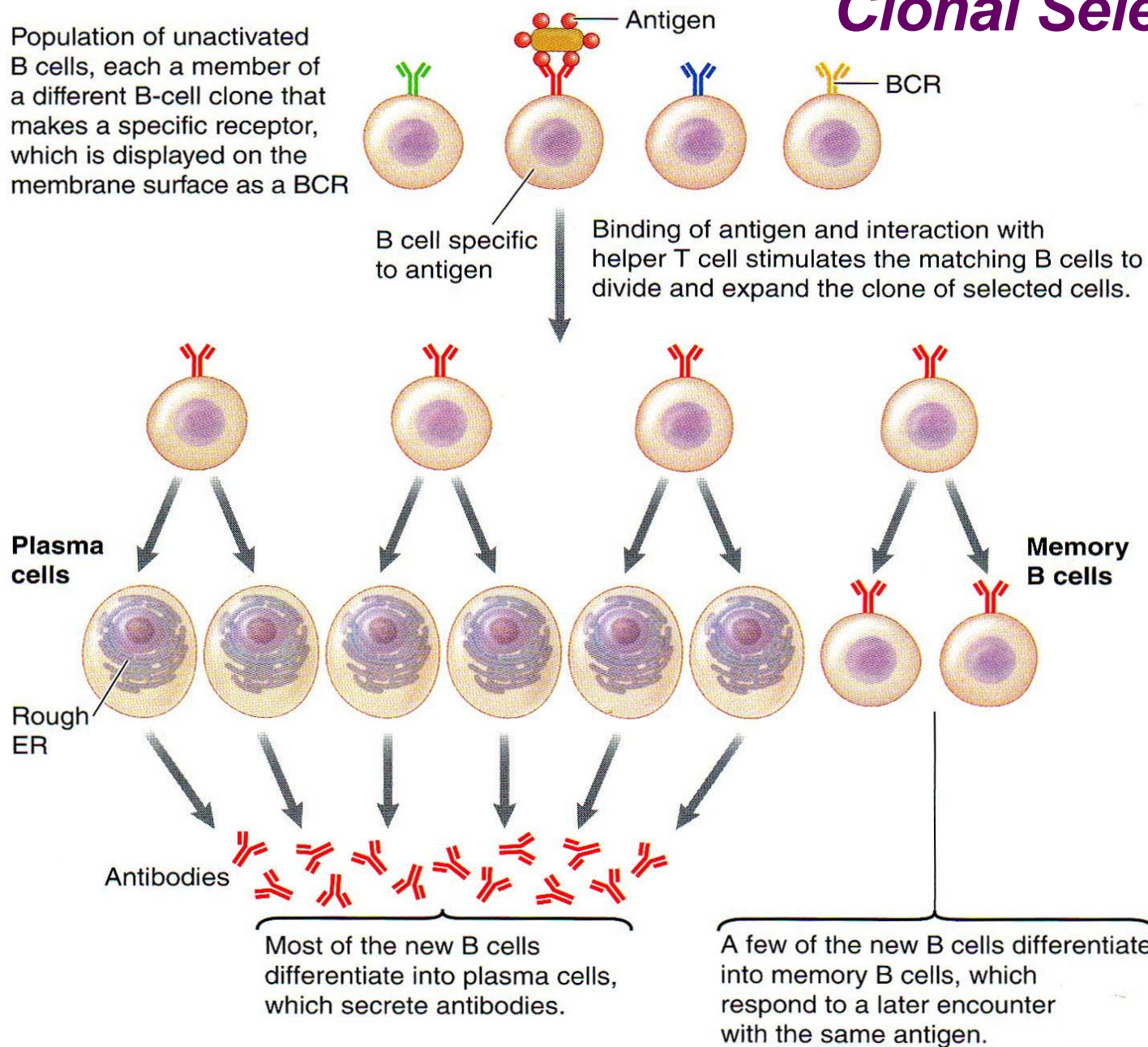
G&H fig 34-7 2011

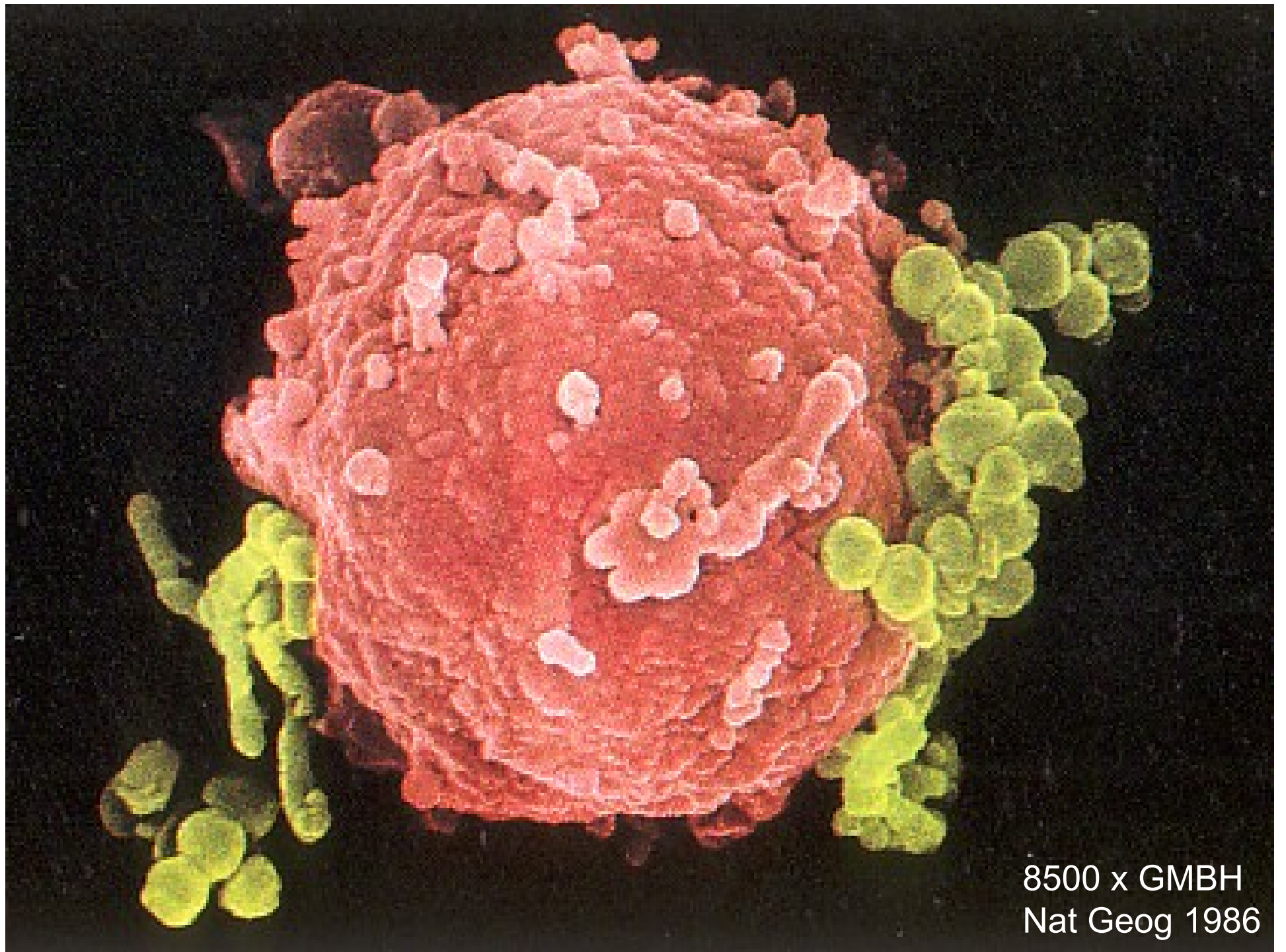


*The vital union that activates a helper T cell takes place only when the T cell recognizes both a "self" marker (rectangle) and a "nonself" antigen (triangle) on a macrophage.*

# Clonal Selection

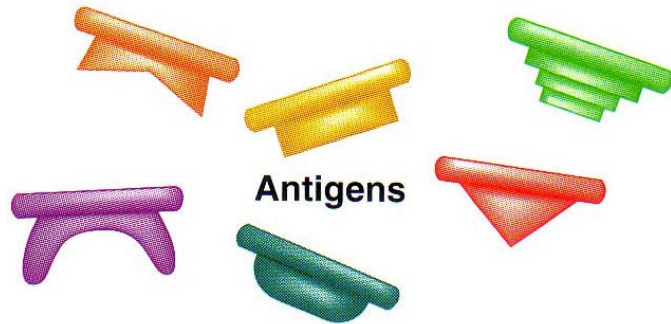
Population of unactivated B cells, each a member of a different B-cell clone that makes a specific receptor, which is displayed on the membrane surface as a BCR



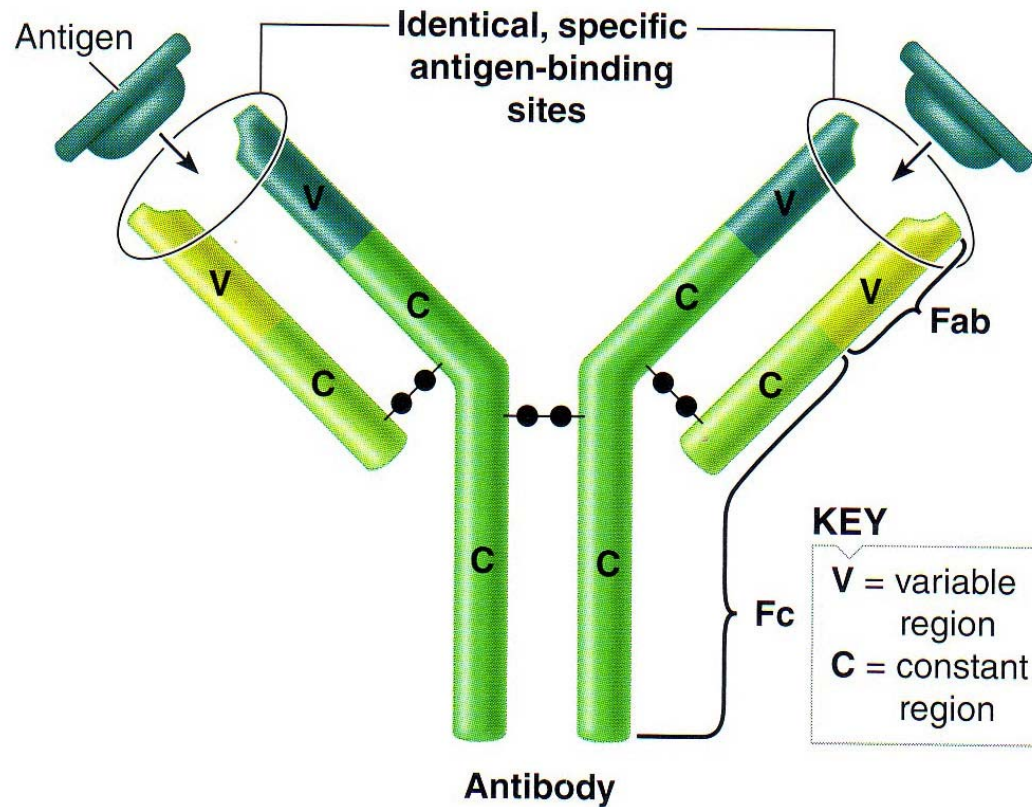


8500 x GMBH  
Nat Geog 1986

# Typical IgG Antibody Structure

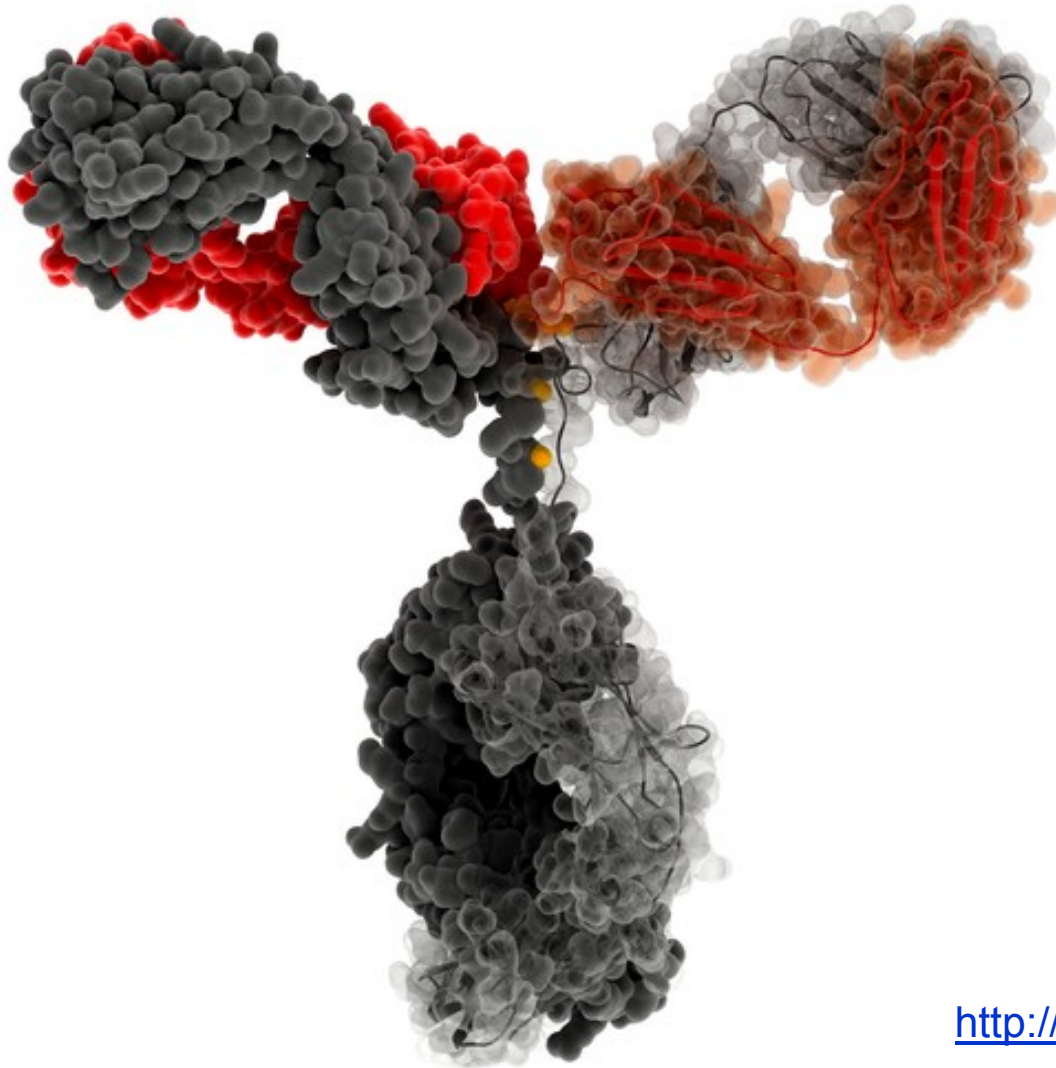


*How do antibodies work?*



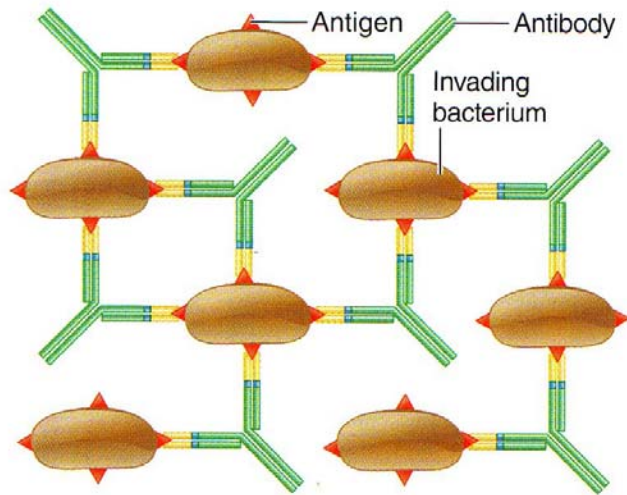


# Immunoglobulin G

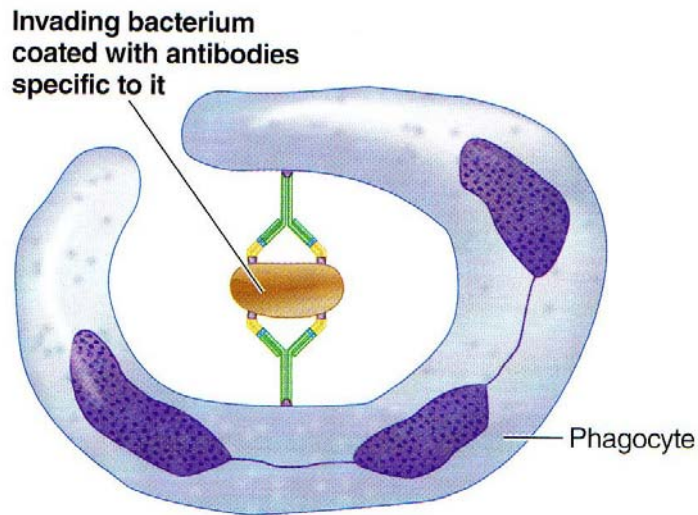


**Source:**  
Visual Science  
<http://visualscience.ru/en/>

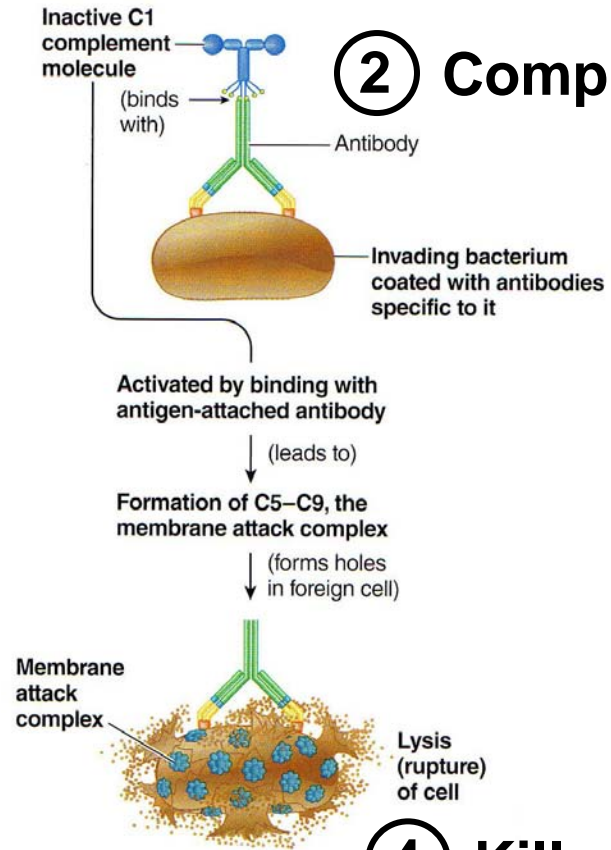
# ① Agglutination



# ③ Opsonization



# ② Complement



# ④ Killer Cells

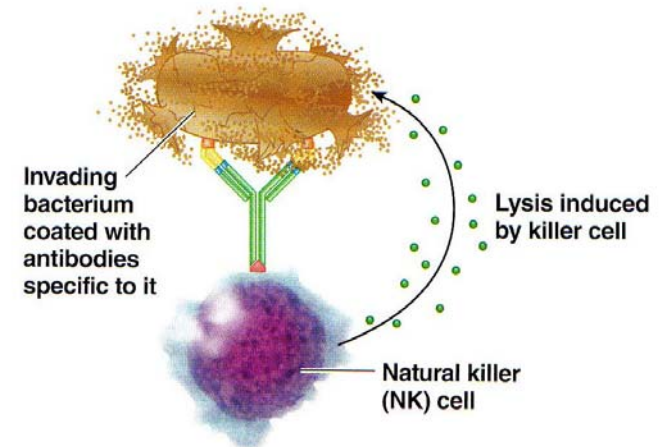
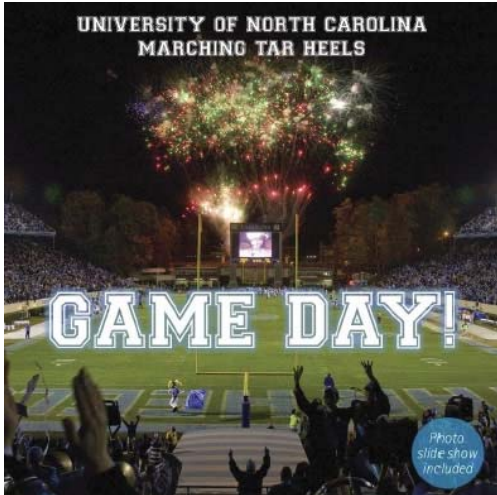


TABLE 4.1 Characteristics and functions of the human immunoglobulin classes

	G	A	M	D	↔ E
immunoglobulin class	IgG	IgA	IgM	IgD	IgE
heavy-chain type	$\gamma$	$\alpha$	$\mu$	$\delta$	$\epsilon$
number of constant domains in each heavy chain	3	3	4	3	4
relative molecular mass ( $M_r$ ) of monomer	150 000	160 000	180 000	185 000	200 000
normally found as polymer?	no	dimer	pentamer	no	no
valency: number of antigen binding sites in normal form (i.e. monomer or polymer)	2	4	10	2	2
percentage of total immunoglobulin in serum	70-80	13-20	6-10	0-1	0.002
serum half-life (days)	23	5.8	5.1	2.8	2.3
ability to trigger complement cascade*	++	—	+++	—	—
can cross placenta from mother to foetus*	+	—	—	—	—
binds to Staphylococcal cell walls*	+	—	—	—	—
binds to macrophage Fc receptors*	+	—	(+)?	—	—
binds to neutrophil Fc receptors*	+	+	(+)?	—	—
binds to mast cell and basophil Fc receptors	—	—	—	—	+++
binds to platelets	+	—	—	—	—



\* For IgG this refers only to some subclasses.

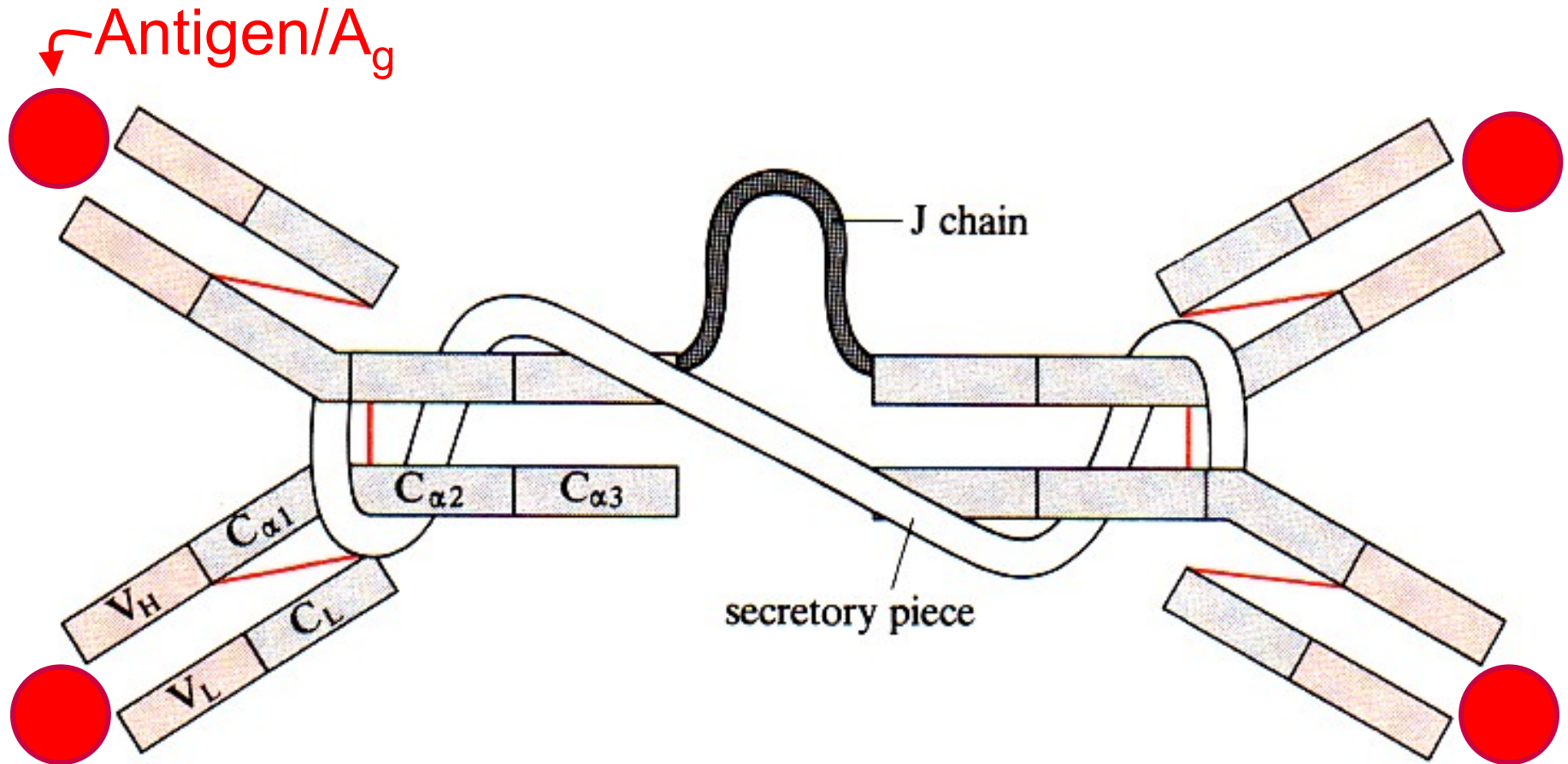


# GAMED!

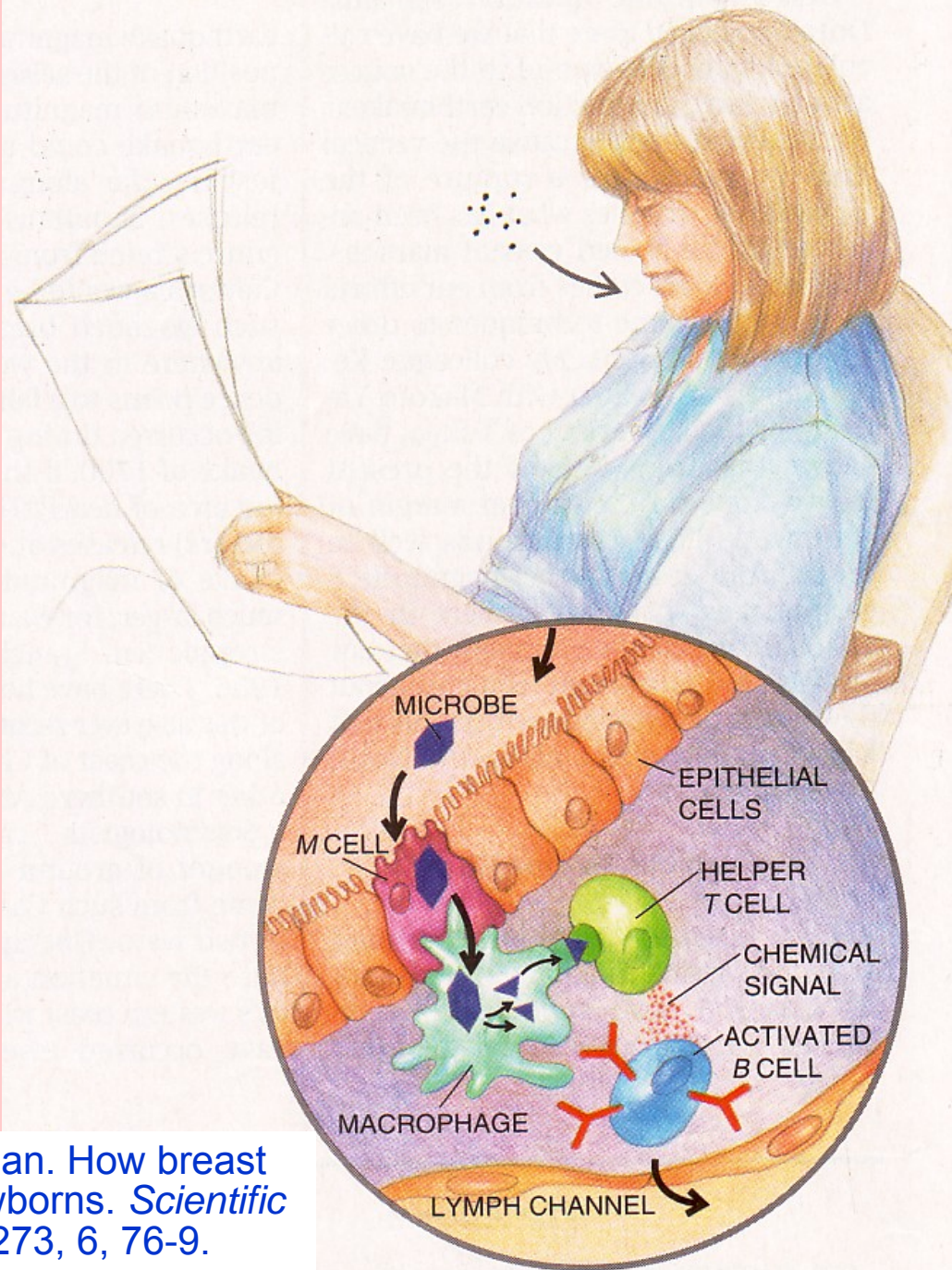


IgA = Secretory A<sub>b</sub>

Dimer!!

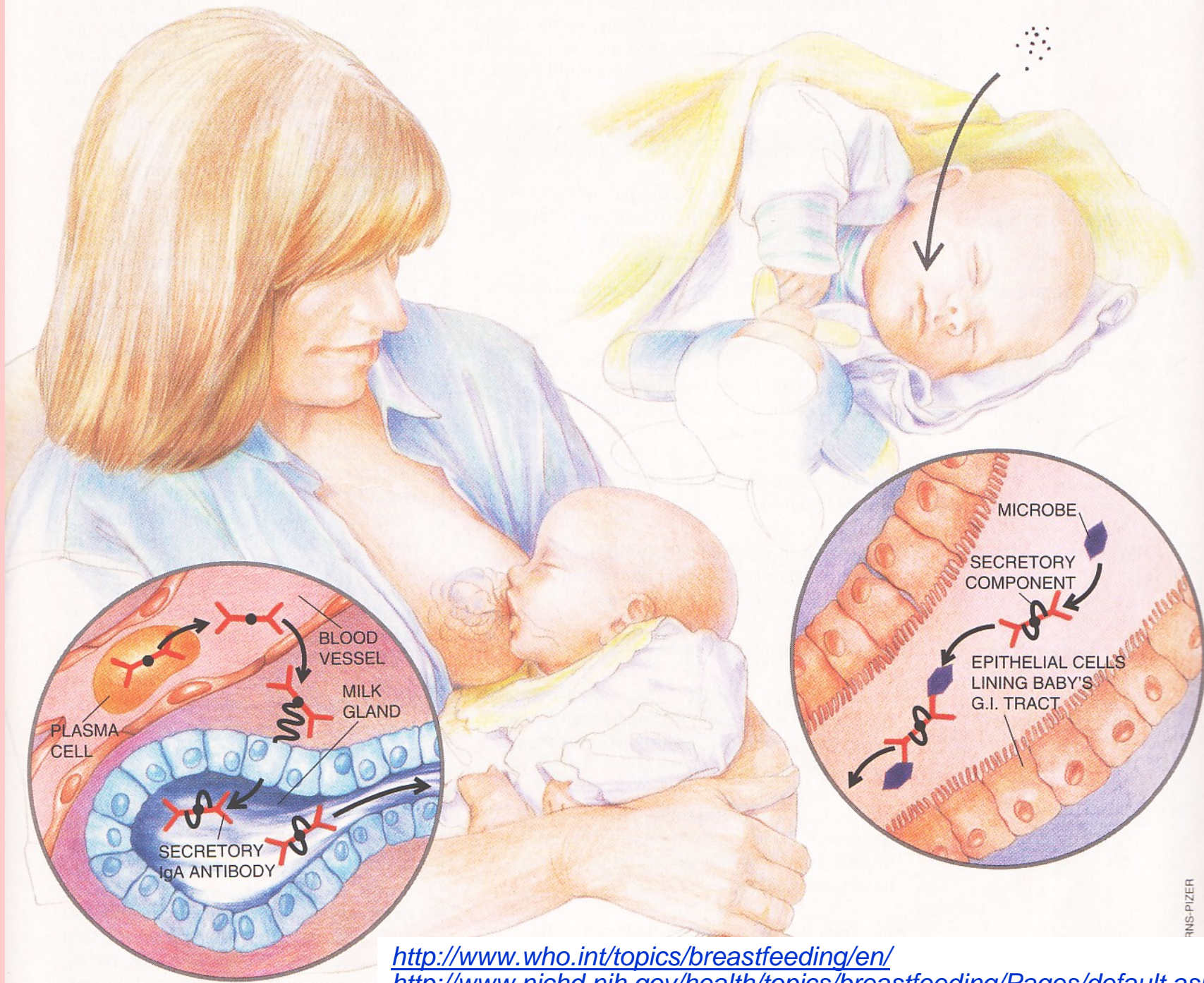


*Valence? 4*



**SOURCE:** J Newman. How breast milk protects newborns. *Scientific American* 1995, 273, 6, 76-9.

Sci Am Dec 1995  
Dana Burns-Pizer



RMS-PIZER

<http://www.who.int/topics/breastfeeding/en/>  
<http://www.nichd.nih.gov/health/topics/breastfeeding/Pages/default.aspx>

# Immune Benefits of Breast Milk at a Glance

Component	Action
<b>White Blood Cells</b>	
<i>B</i> lymphocytes	Give rise to antibodies targeted against specific microbes.
Macrophages	Kill microbes outright in the baby's gut, produce lysozyme and activate other components of the immune system.
Neutrophils	May act as phagocytes, ingesting bacteria in baby's digestive system.
<i>T</i> lymphocytes	Kill infected cells directly or send out chemical messages to mobilize other defenses. They proliferate in the presence of organisms that cause serious illness in infants. They also manufacture compounds that can strengthen a child's own immune response.



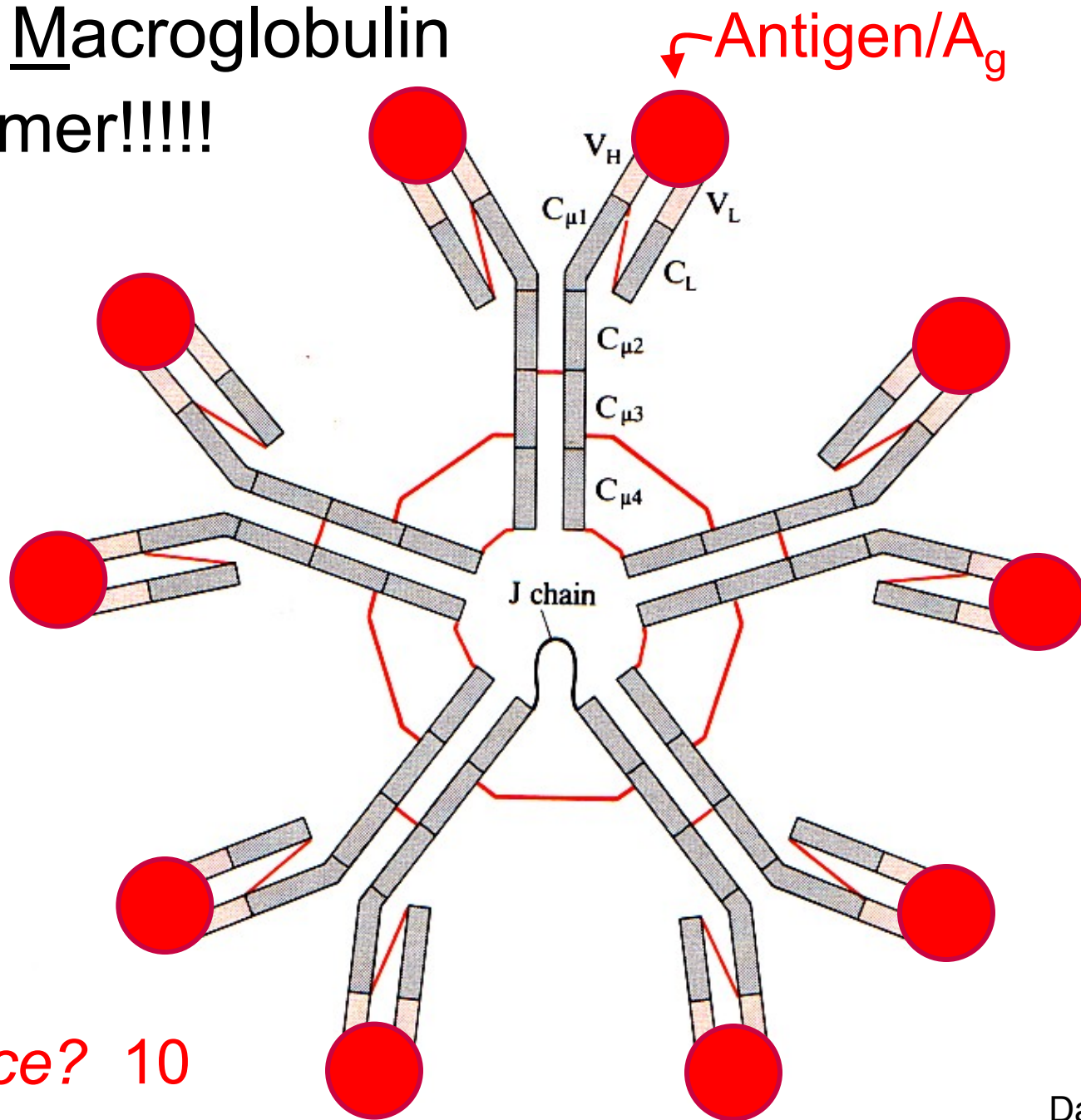
## Molecules

Antibodies of secretory IgA class	Bind to microbes in baby's digestive tract and thereby prevent them from passing through walls of the gut into body's tissues.
B <sub>12</sub> binding protein	Reduces amount of vitamin B <sub>12</sub> , which bacteria need in order to grow.
Bifidus factor	Promotes growth of <i>Lactobacillus bifidus</i> , a harmless bacterium, in baby's gut. Growth of such nonpathogenic bacteria helps to crowd out dangerous varieties.
Fatty acids	Disrupt membranes surrounding certain viruses and destroy them.
Fibronectin	Increases antimicrobial activity of macrophages; helps to repair tissues that have been damaged by immune reactions in baby's gut.
Gamma-interferon	Enhances antimicrobial activity of immune cells.

Hormones and growth factors	Stimulate baby's digestive tract to mature more quickly. Once the initially "leaky" membranes lining the gut mature, infants become less vulnerable to microorganisms.
Lactoferrin	Binds to iron, a mineral many bacteria need to survive. By reducing the available amount of iron, lactoferrin thwarts growth of pathogenic bacteria.
Lysozyme	Kills bacteria by disrupting their cell walls.
Mucins	Adhere to bacteria and viruses, thus keeping such microorganisms from attaching to mucosal surfaces.
Oligosaccharides	Bind to microorganisms and bar them from attaching to mucosal surfaces.

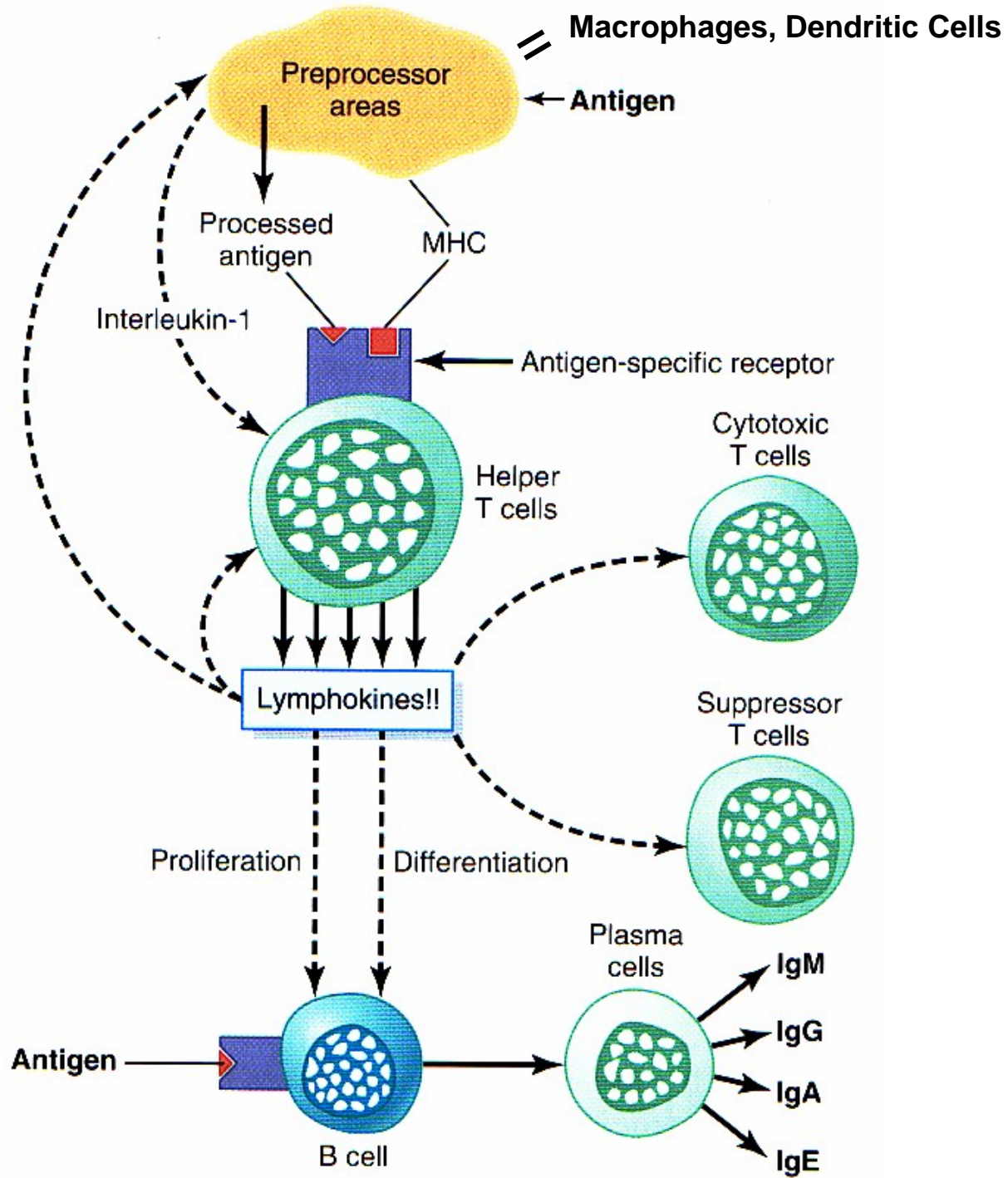
<http://www.scientificamerican.com/article.cfm?id=got-smarts-mothers-milk-m>  
<http://www.mcclatchydc.com/2012/08/28/163784/duke-study-pinpoints-breast-milk.html>

IgM = Macroglobulin  
Pentamer!!!!



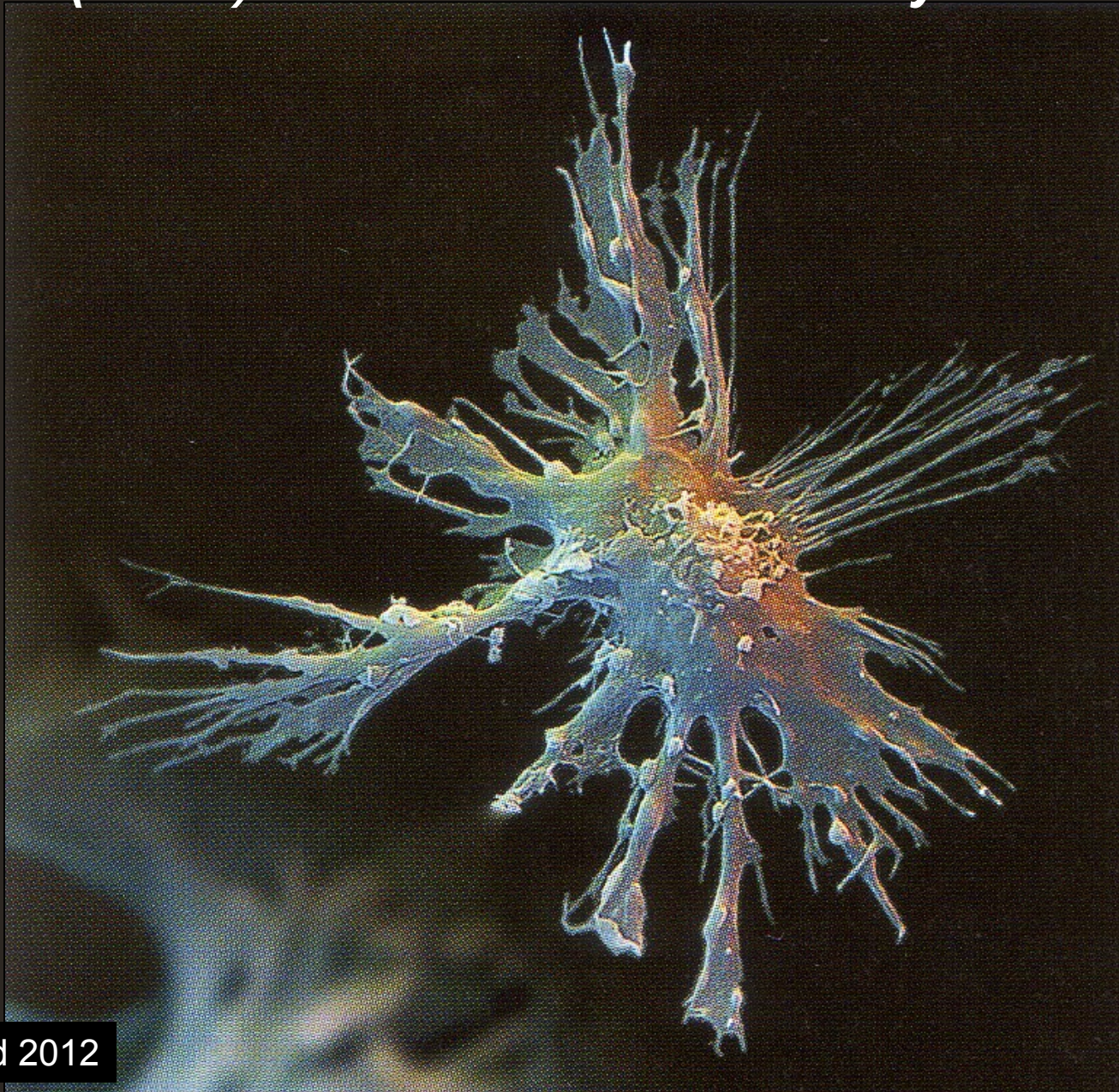
*Valence?* 10





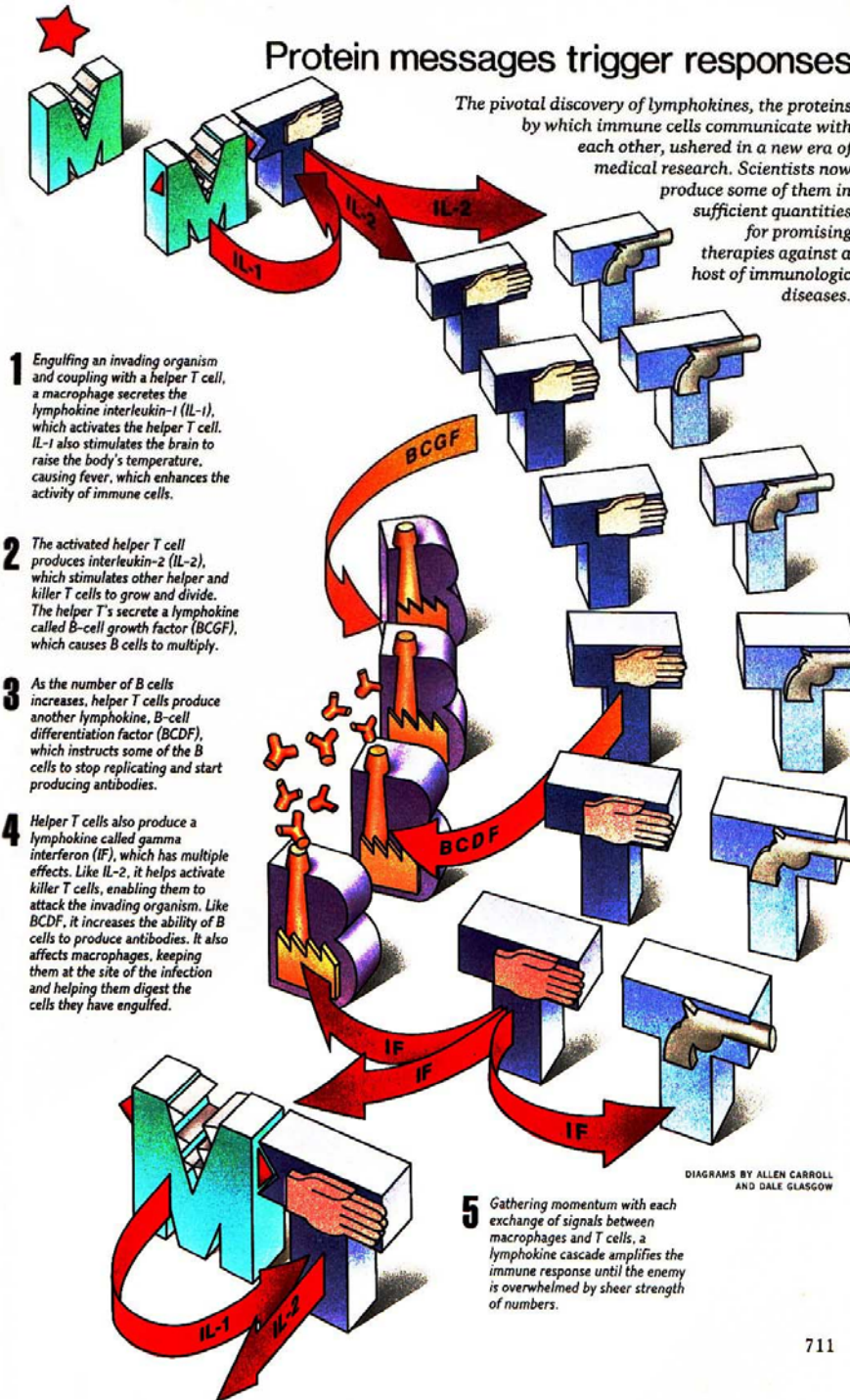
G&H fig 34-8 2011

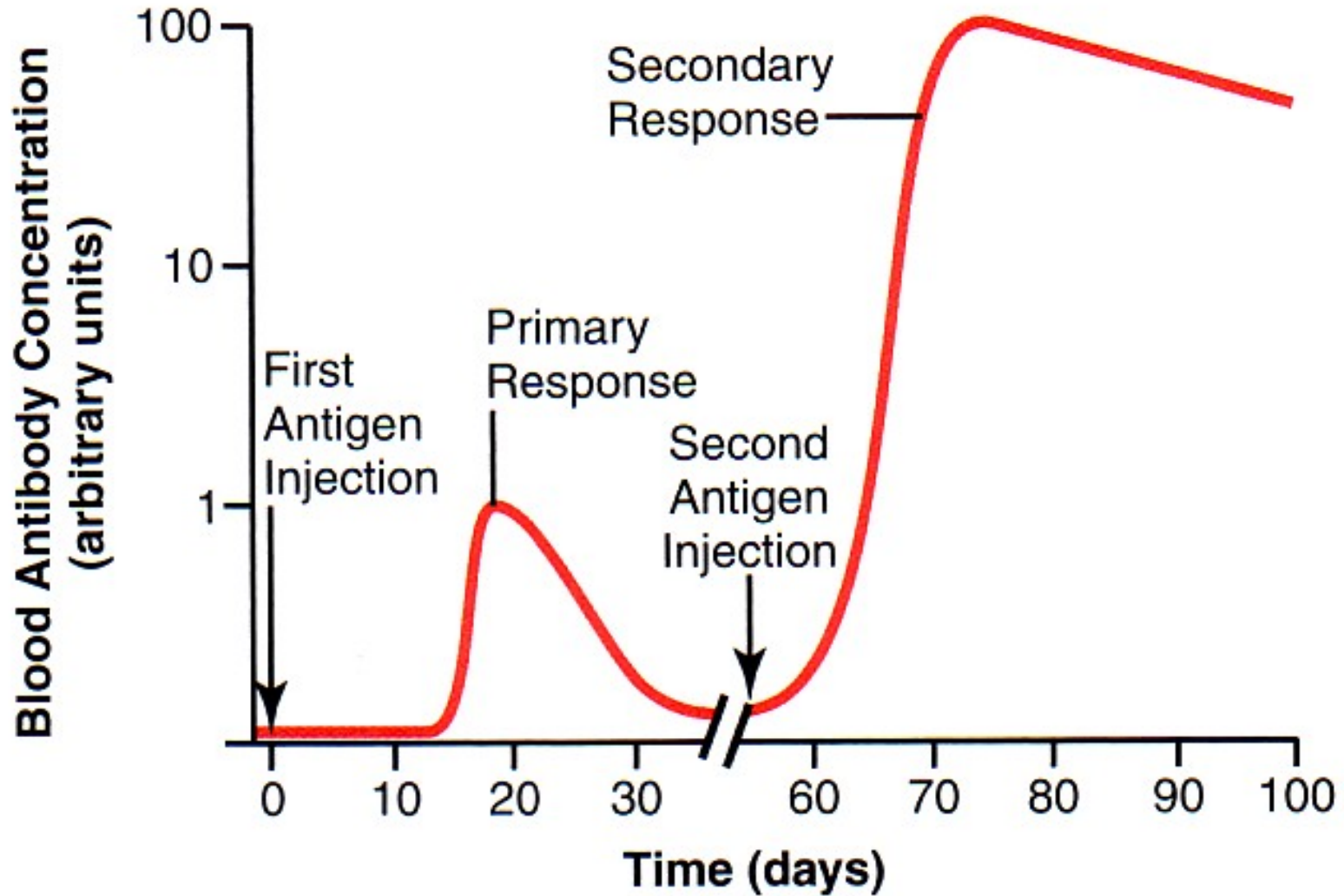
***Dendritic Cells: Specialized Antigen-Presenting Cells  
(APCs) Sentinels in Almost Every Tissue!***



## Protein messages trigger responses

The pivotal discovery of lymphokines, the proteins by which immune cells communicate with each other, ushered in a new era of medical research. Scientists now produce some of them in sufficient quantities for promising therapies against a host of immunologic diseases.





**Figure 34-3** Time course of the antibody response in the circulating blood to a primary injection of antigen and to a secondary injection several weeks later.