



...+ Fun Discussion w/WBC differential count!

## BI 358 Lecture 6

- I. **Announcements** Quiz 2 GI + Nutrition next T! + Nutrition reports (.doc/.docx + .pdfs) by e-mail due < 5 pm to Mae, Abbie, Bella.
- II. **Blood + Immunology** G&H ch 33, 34, 35; Nilsson, Davey, Fox...
  - A. Blood: cell + fragments vs liquid. Plasma vs serum? LS+...
  - B. Red blood cell production, hemoglobin/Hgb, sickle cell Hgb G&H pp 445-51, fig 33-1, 33-2, 33-6 + Fox, LS...
  - C. White blood cell differential, ID & functions, platelets LS, GH
  - D. Immune response, pathogens...Davey fig 2.1, 2.2 pp 12-13
  - E. WBC phagocytosis, lymphoid tissue. *Nat Geographic*, *The Wars Within*, Lennart Nilsson <http://www.lennartnilsson.com/>
  - F. **Medical Physiology News** Handwashing to prevent infection! Laughter as medicine! Centers for Disease Control &...SEBB
  - G. Innate vs adaptive immunity cf: G&H pp 465-70,LS+...  
Innate immunity: inflammation, interferon, complement; HIV
  - H. Antibody (Ab=Ig) structure, subclasses, mechanisms G&H fig 35-4 + LS + Davey fig 2.4 p 19, fig 4.2 p 42, tab 4.1 p 49
  - I. OHSU Researcher Louis Picker HIV/AIDS cure? *Oregon Live*
  - J. Mom's milk overview *Scientific American*
  - K. Immune Regulation + Allergy: G&H fig 35-7, 35-8,...35-3 +

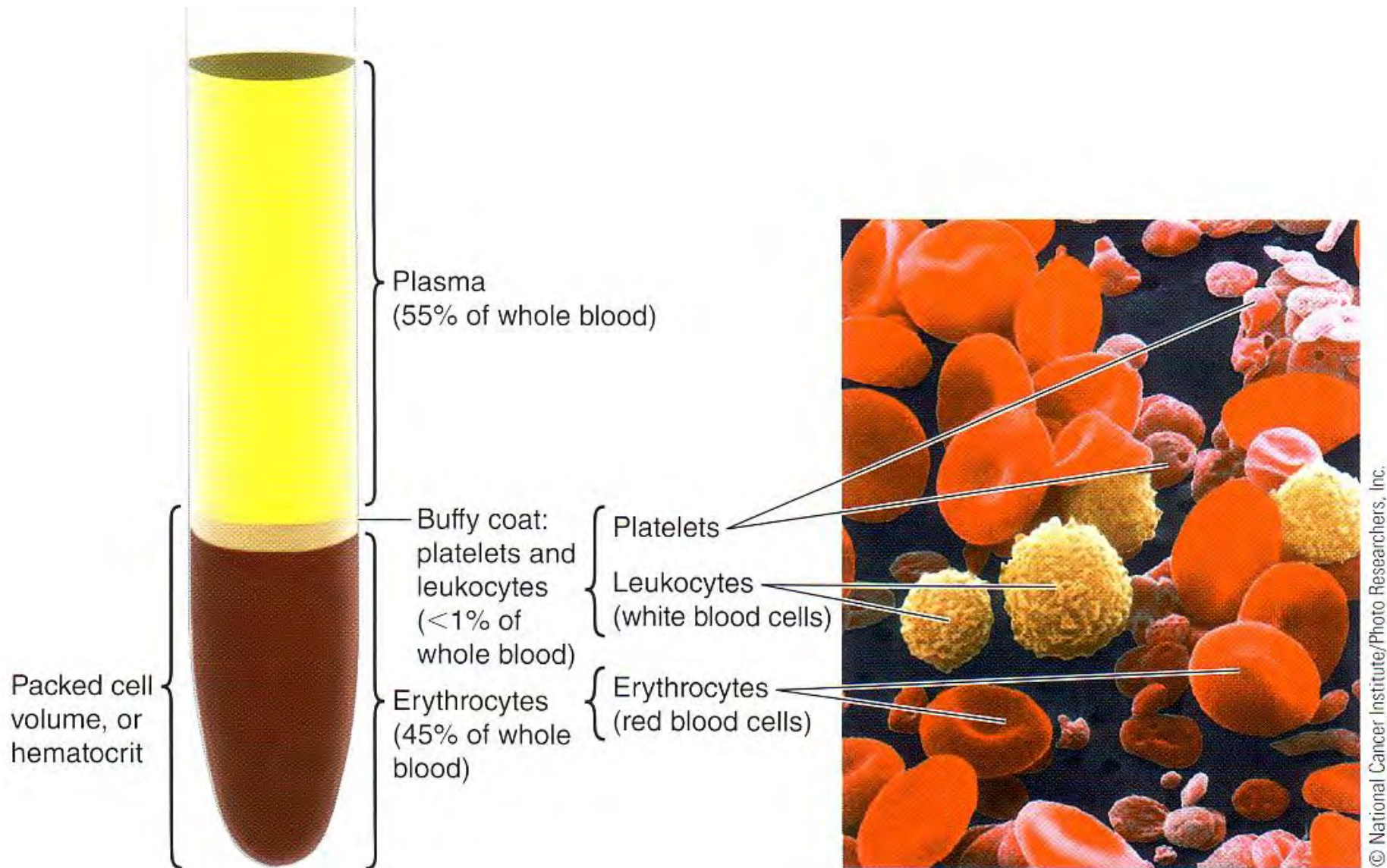


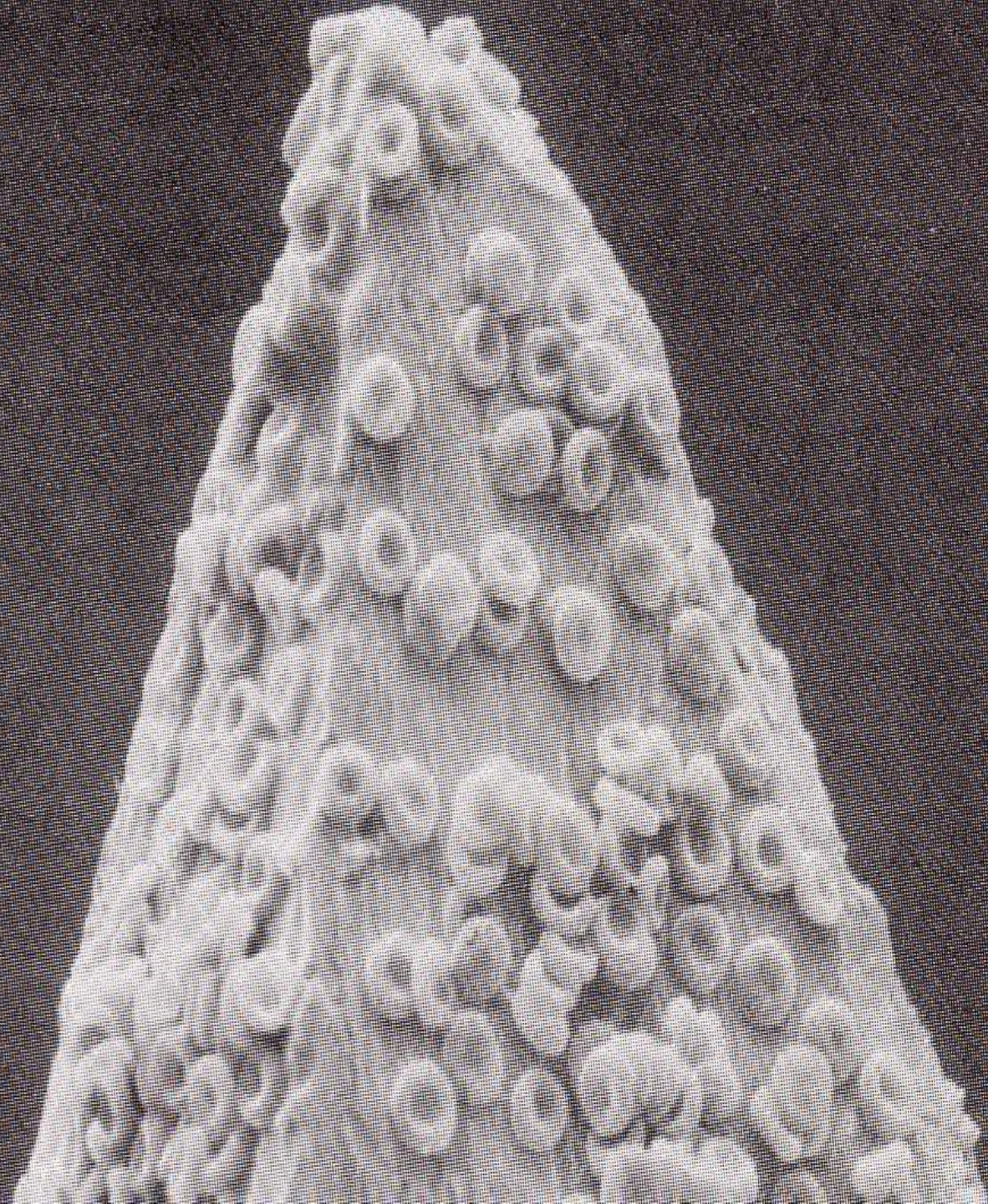
Dr. Kraig Jacobson  
of Oregon Allergy  
Associates is coming  
next Tuesday!

Yes,  
Sherlock!  
Avian &  
human  
immune  
systems  
evolved from  
a common  
reptilian  
ancestor!!

Whoopee! For  
the birds??

# What's in Blood? Plasma & Blood Cells

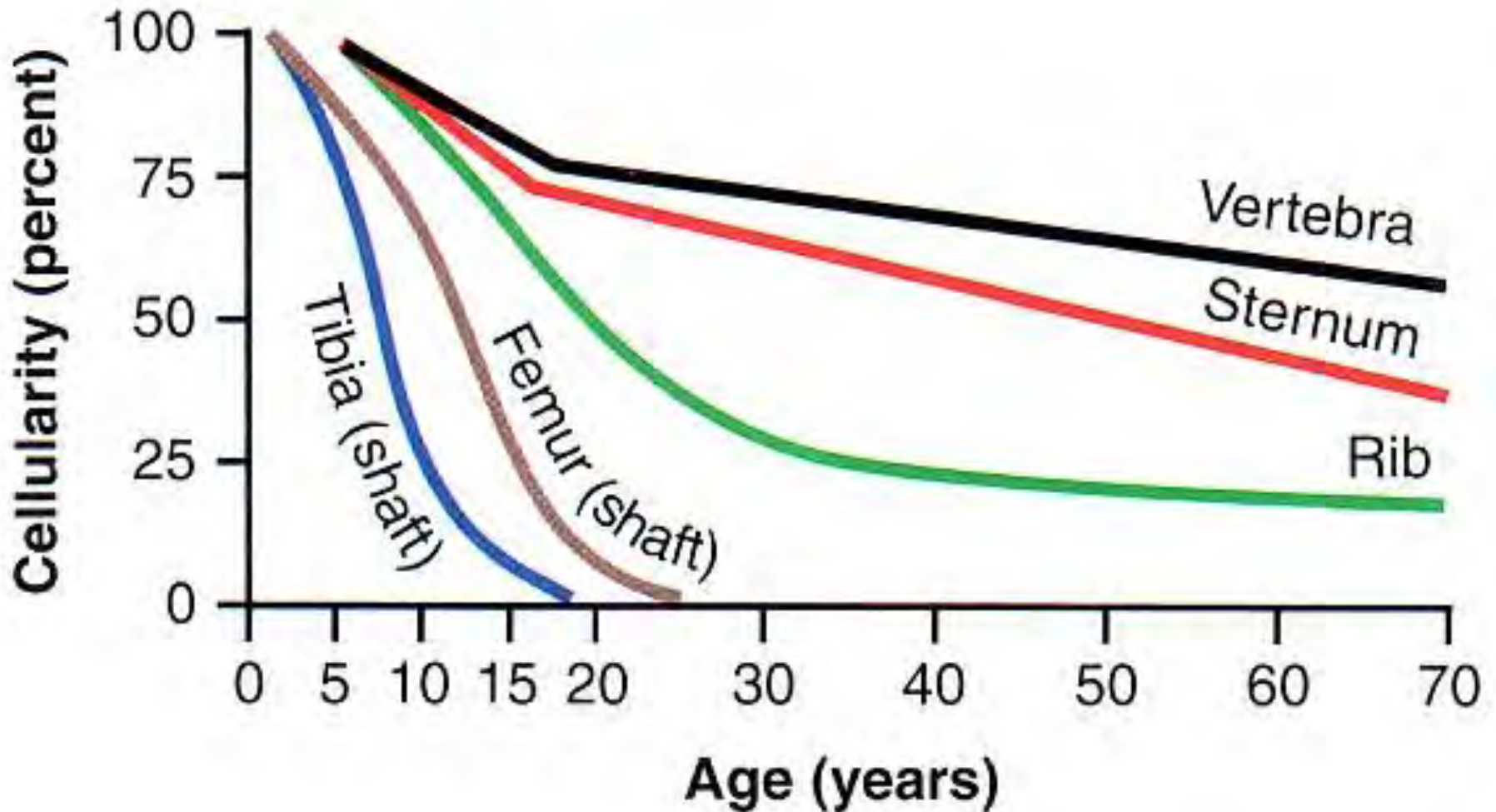




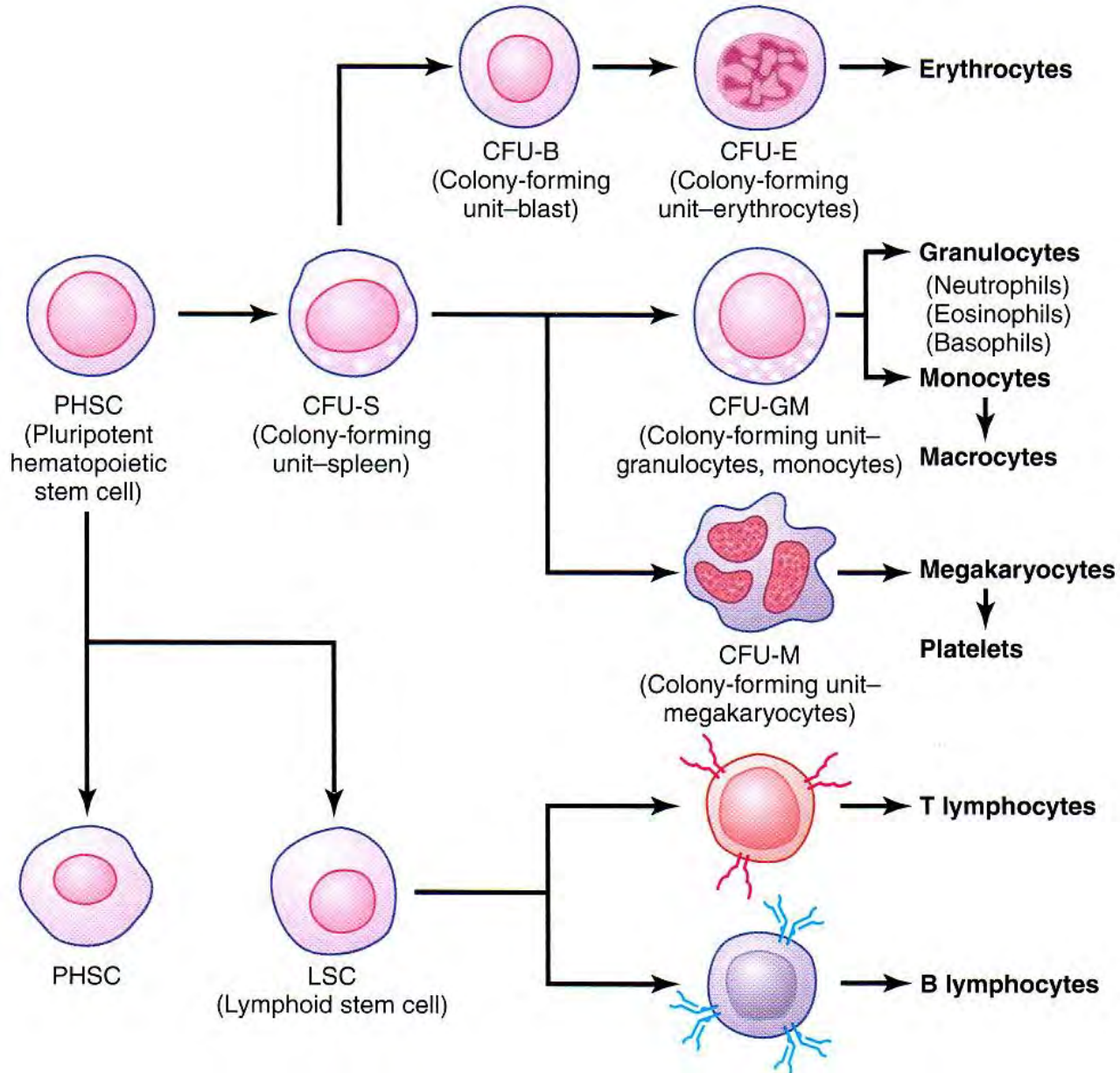


2000 x GMBH,  
Nat Geog 1986  
Jun p 714

# *Dermal bone production of red blood cells*



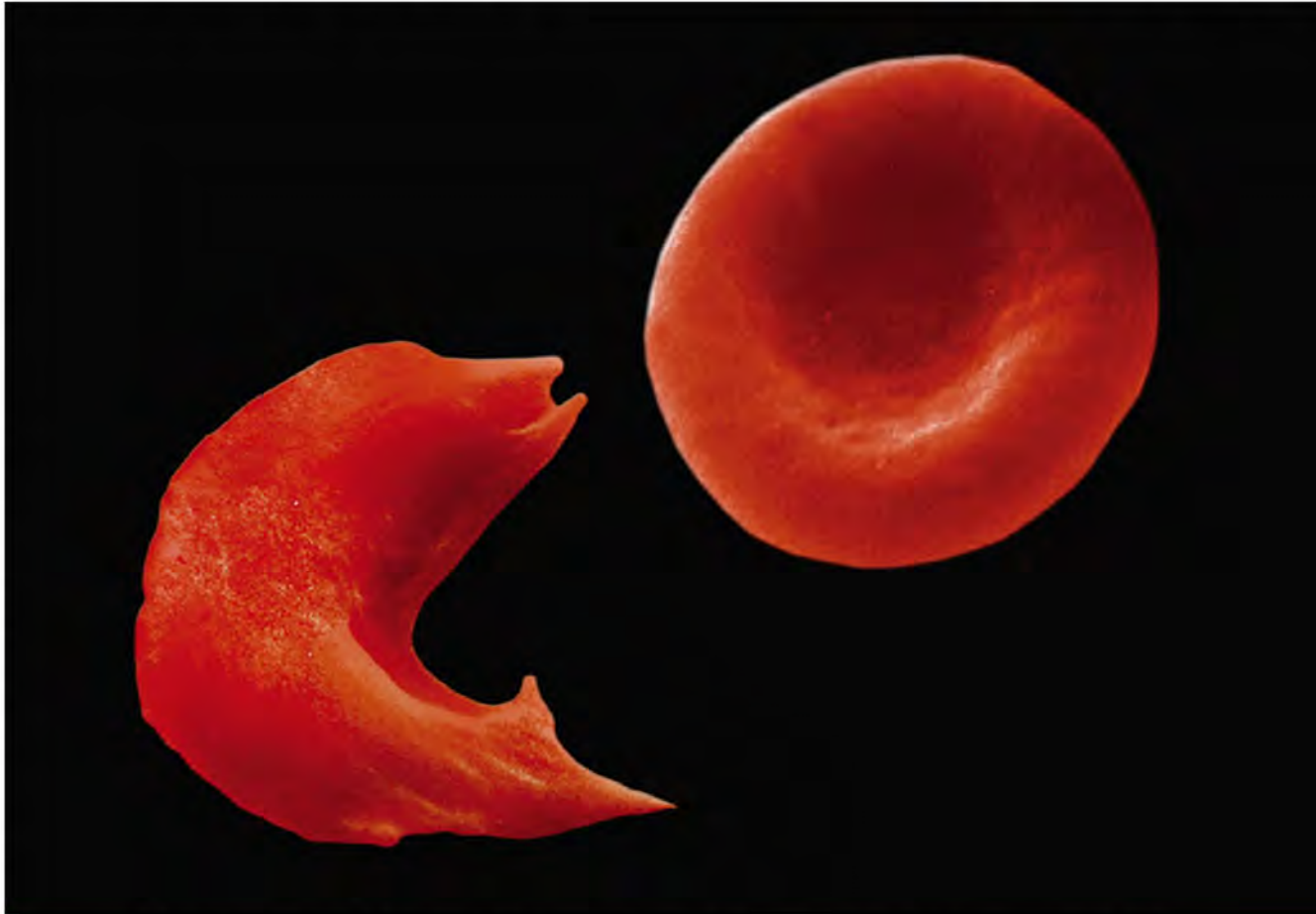
# Pluripotent Hematopoietic Stem Cell Lines



Sickle-shaped blood cells

Normal red blood cells

© Dr. Stanley Flegler/Visuals Unlimited



### What a difference one amino acid can make!

Amino acid sequence of normal hemoglobin:

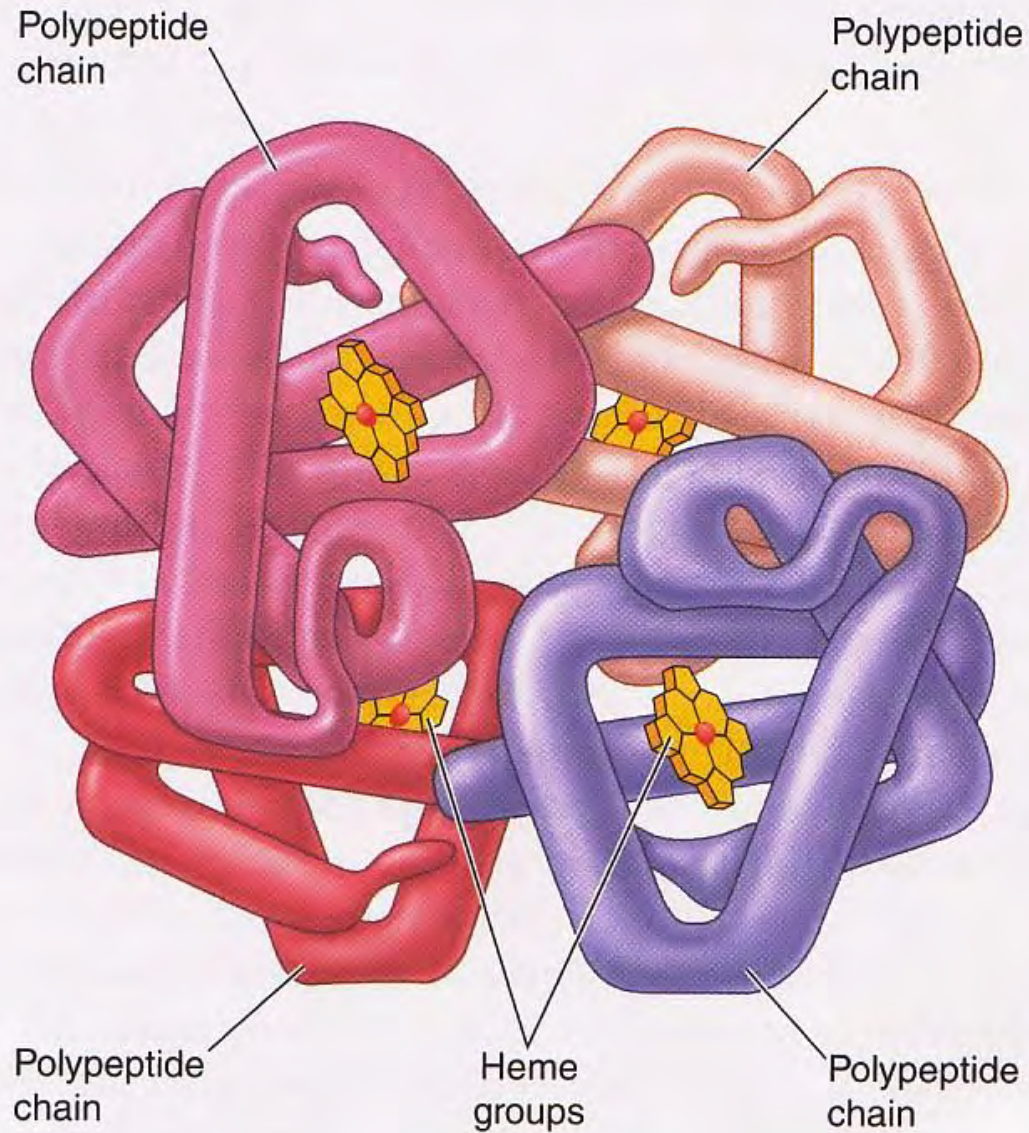
Val — His — Leu — Thr — Pro — Glu — Glu

Amino acid sequence of sickle-cell hemoglobin:

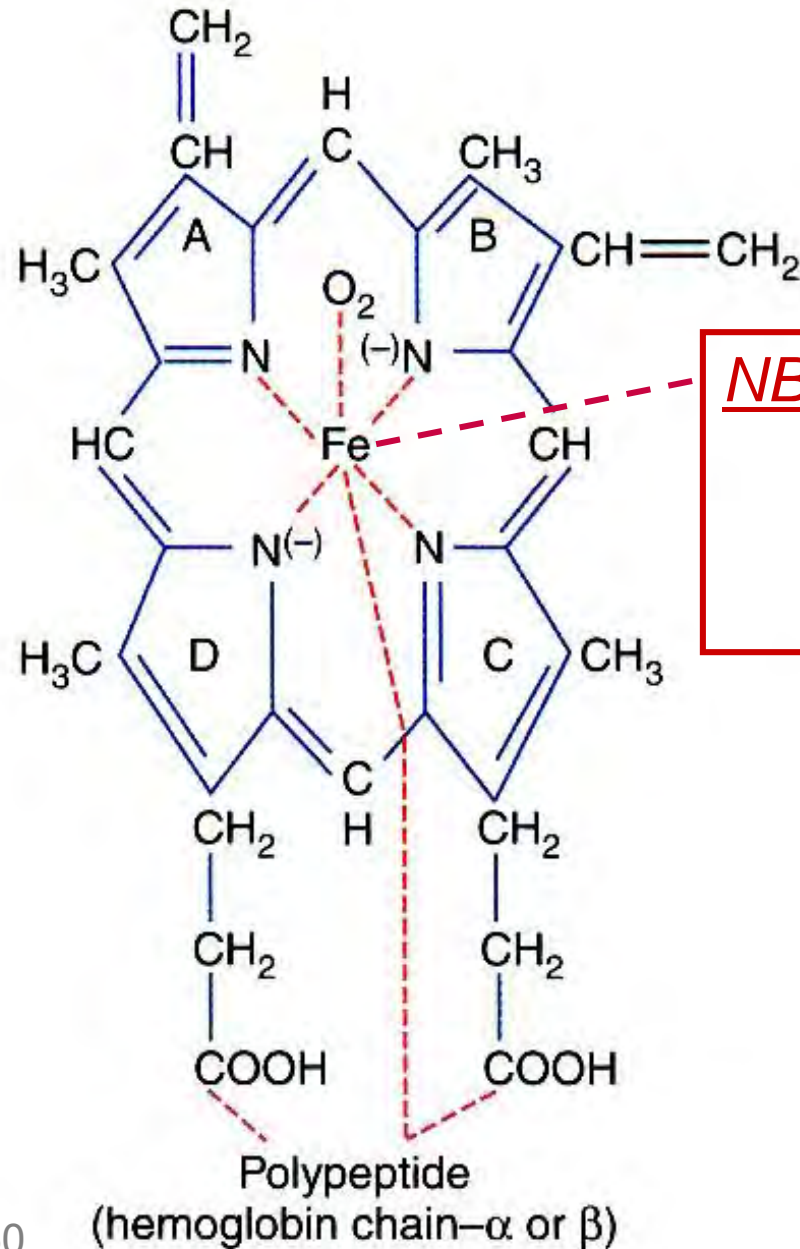
Val — His — Leu — Thr — Pro — Val — Glu

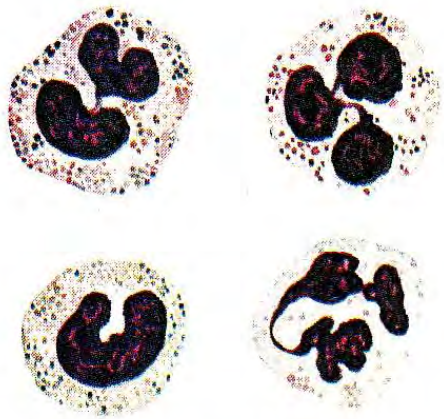


# Hemoglobin Structure

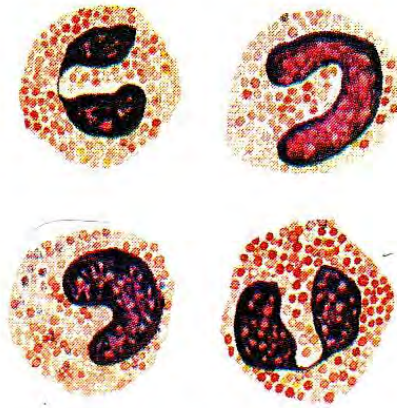


# Heme Structure

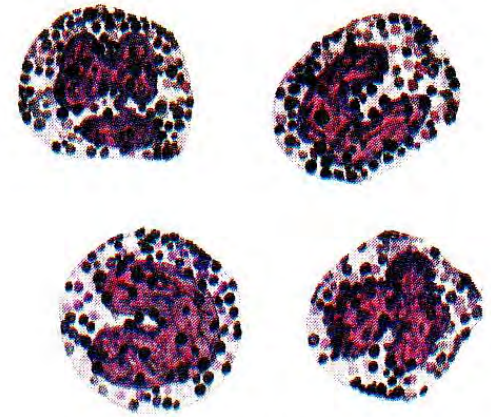




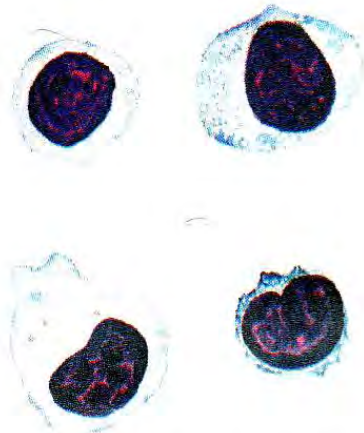
NEUTROPHILS



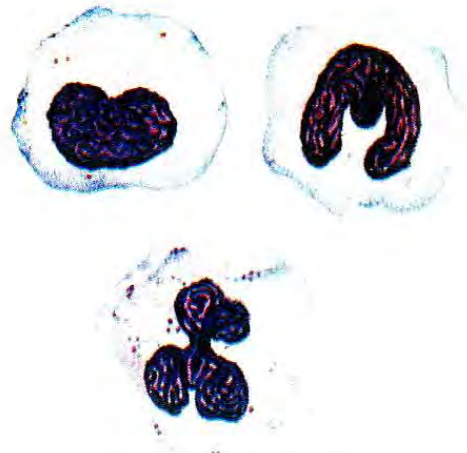
EOSINOPHILS



BASOPHILS



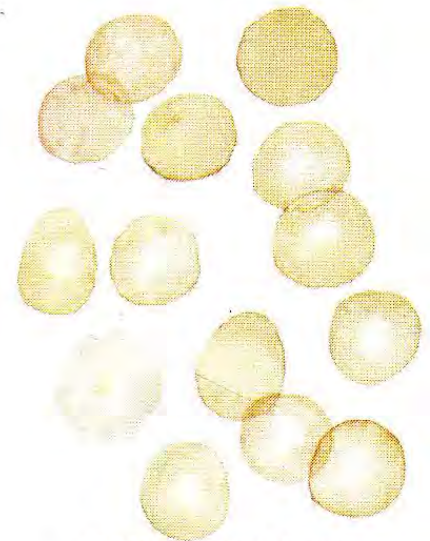
LYMPHOCYTES



MONOCYTES

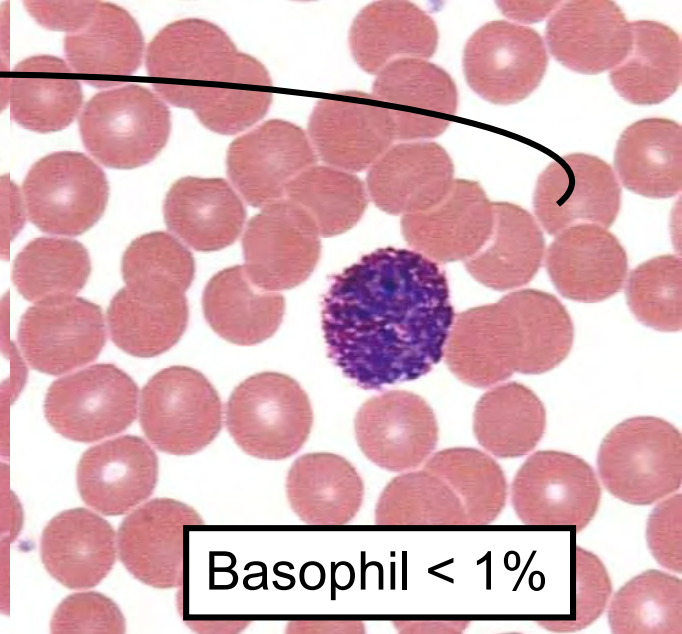
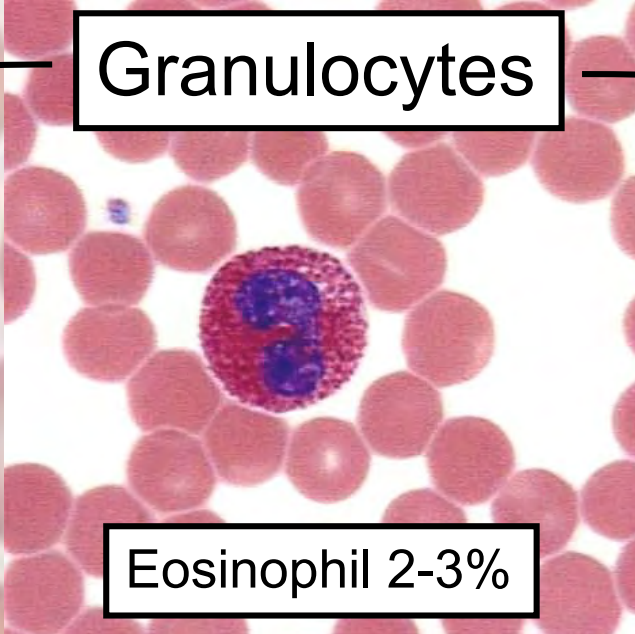
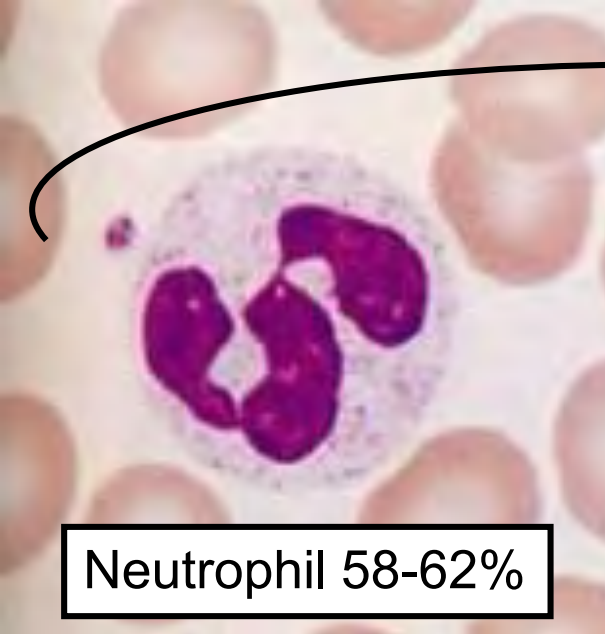


PLATELETS



ERYTHROCYTES

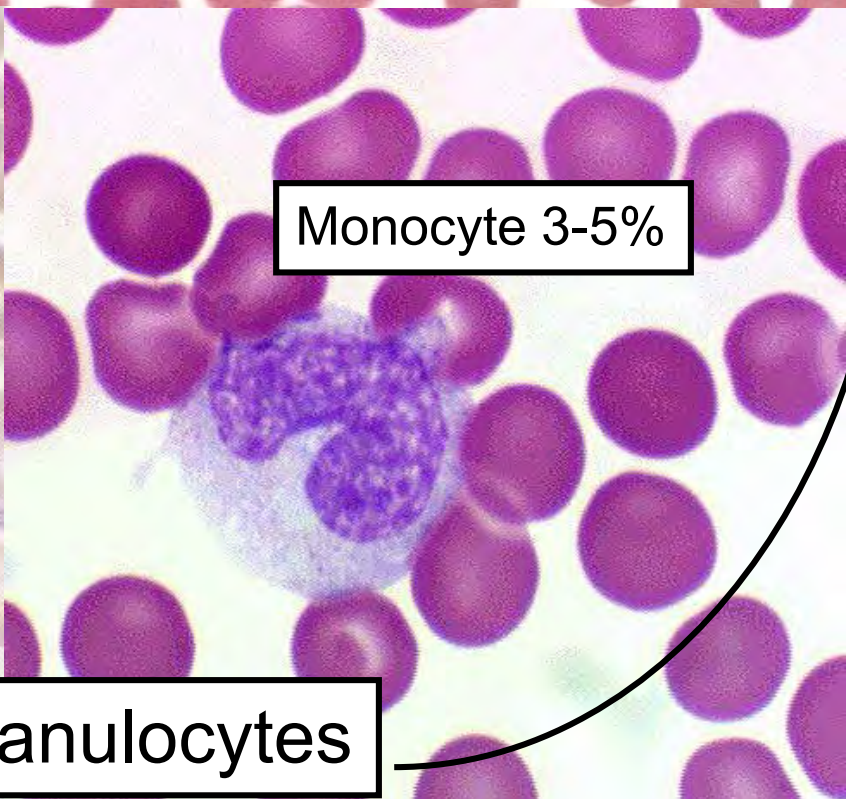
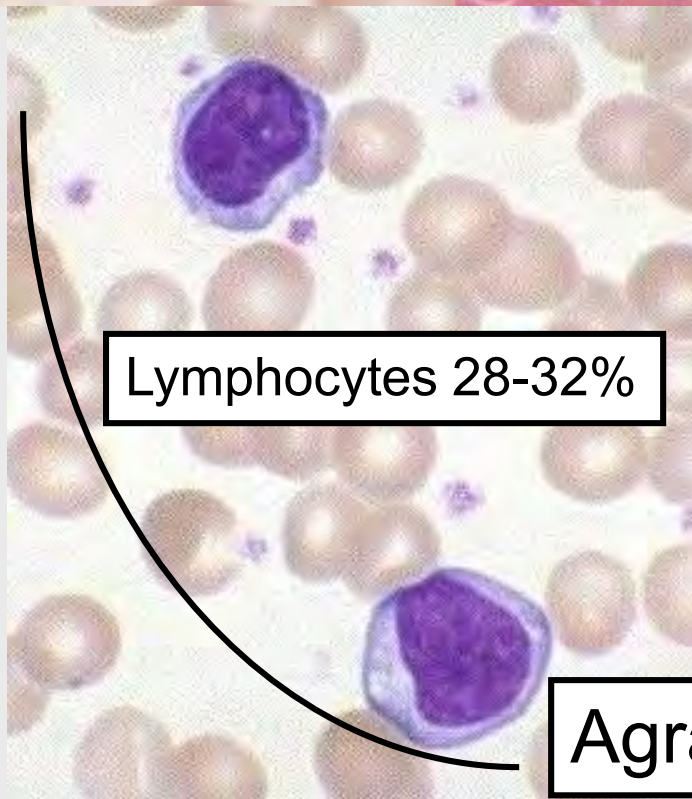
# Granulocytes



Neutrophil 58-62%

Eosinophil 2-3%

Basophil < 1%



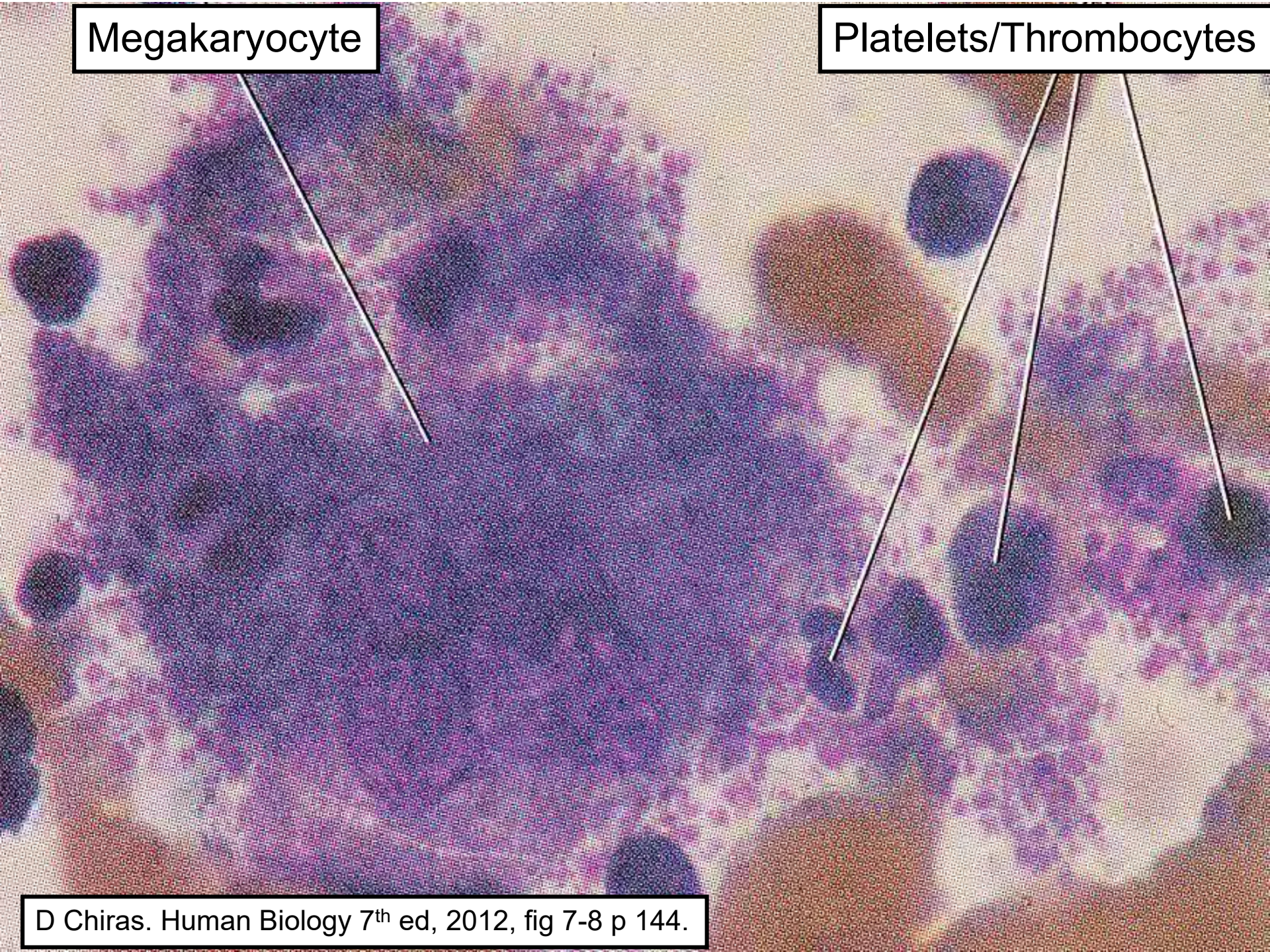
Lymphocytes 28-32%

Monocyte 3-5%

# Agranulocytes

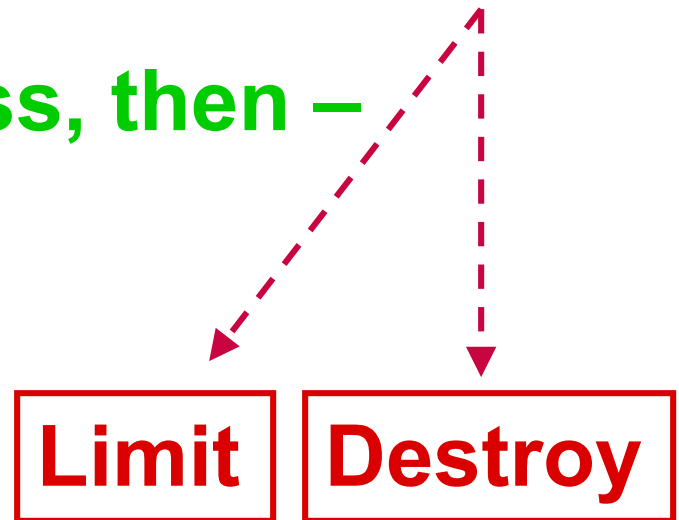
Megakaryocyte

Platelets/Thrombocytes



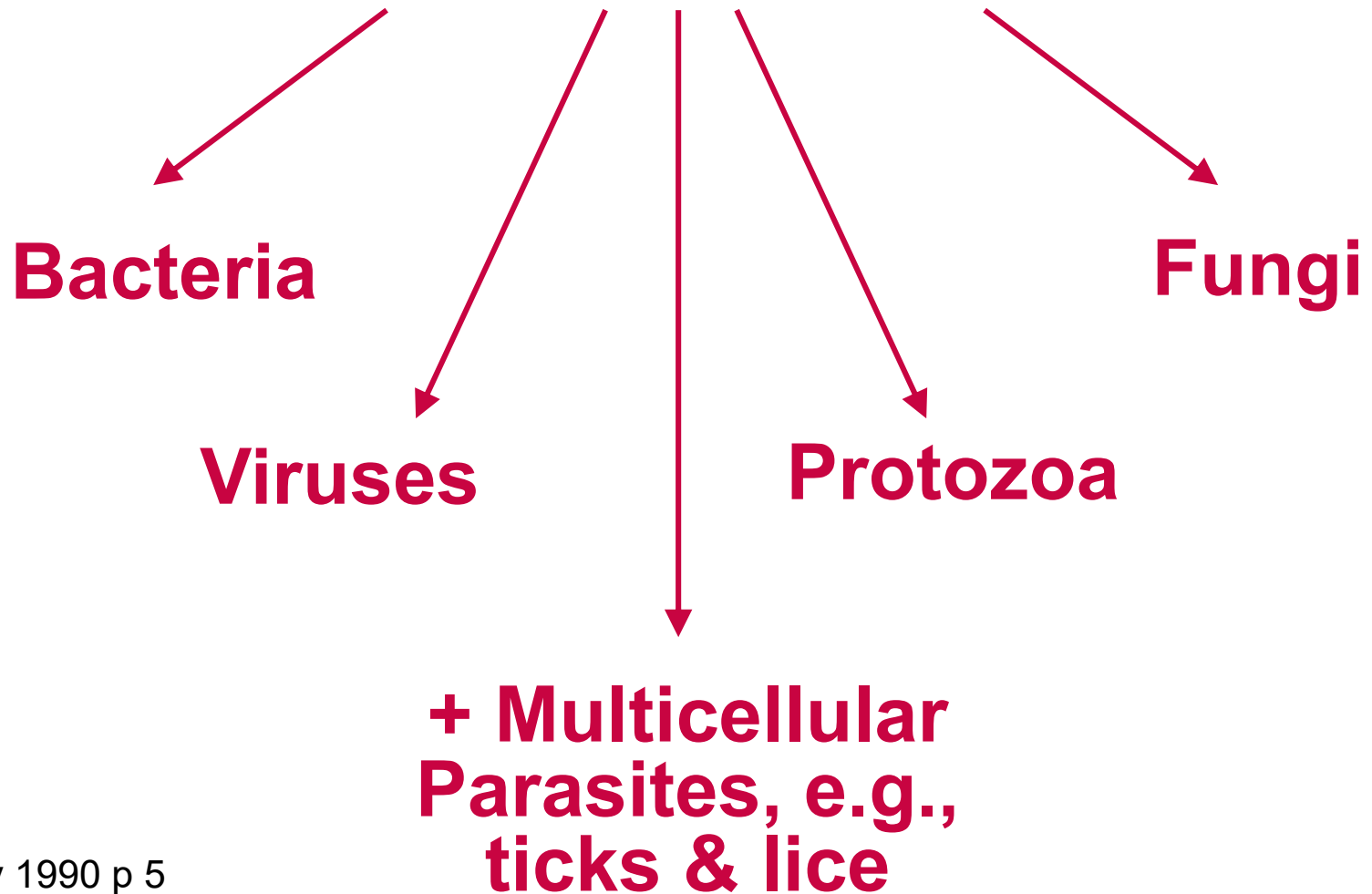
# *Immune Response*

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!**

***World Health Organization 2018 Statistics***

[http://www.who.int/gho/publications/world\\_health\\_statistics/en/](http://www.who.int/gho/publications/world_health_statistics/en/)



# *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!**

# Barriers to Infection

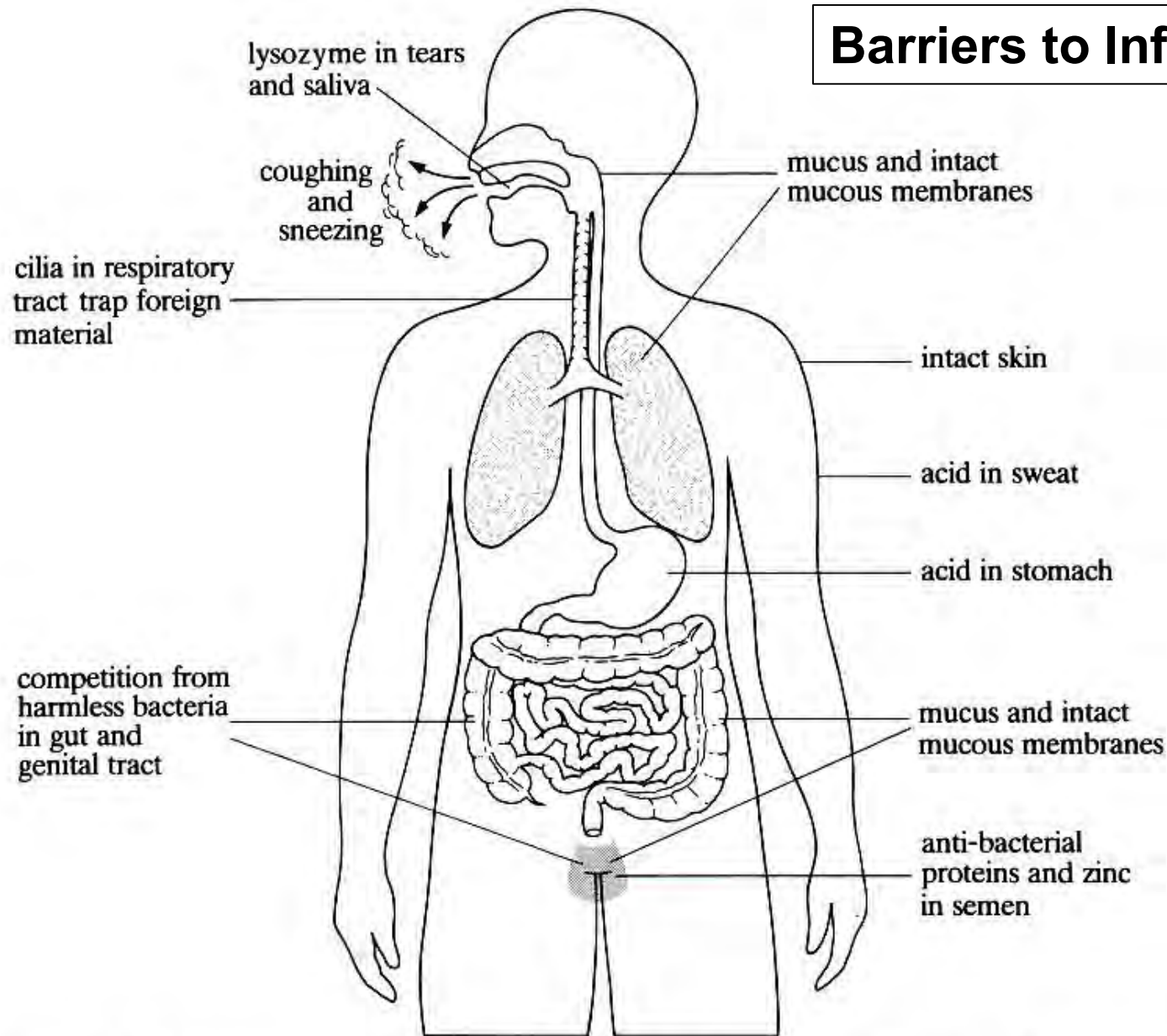
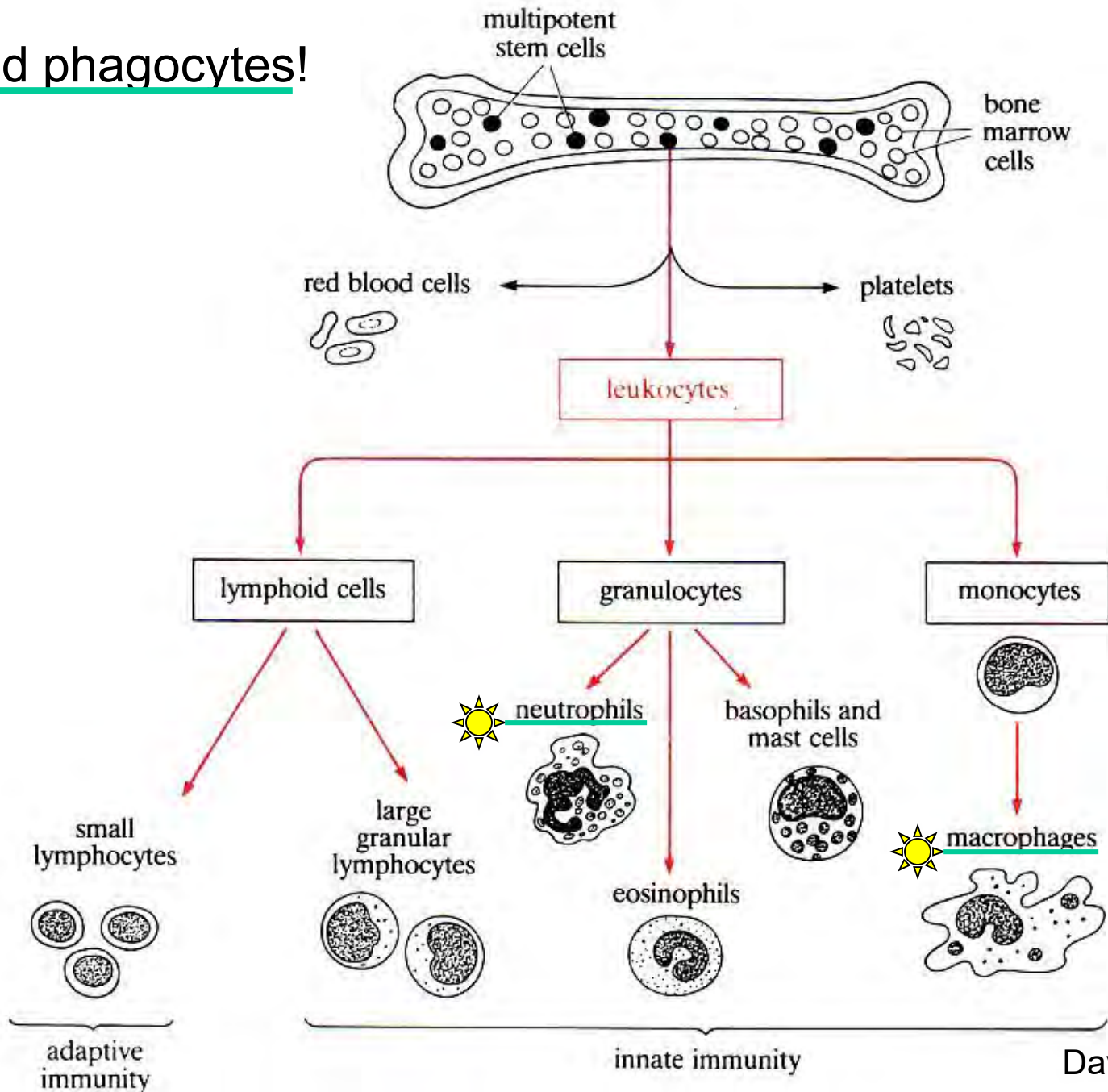
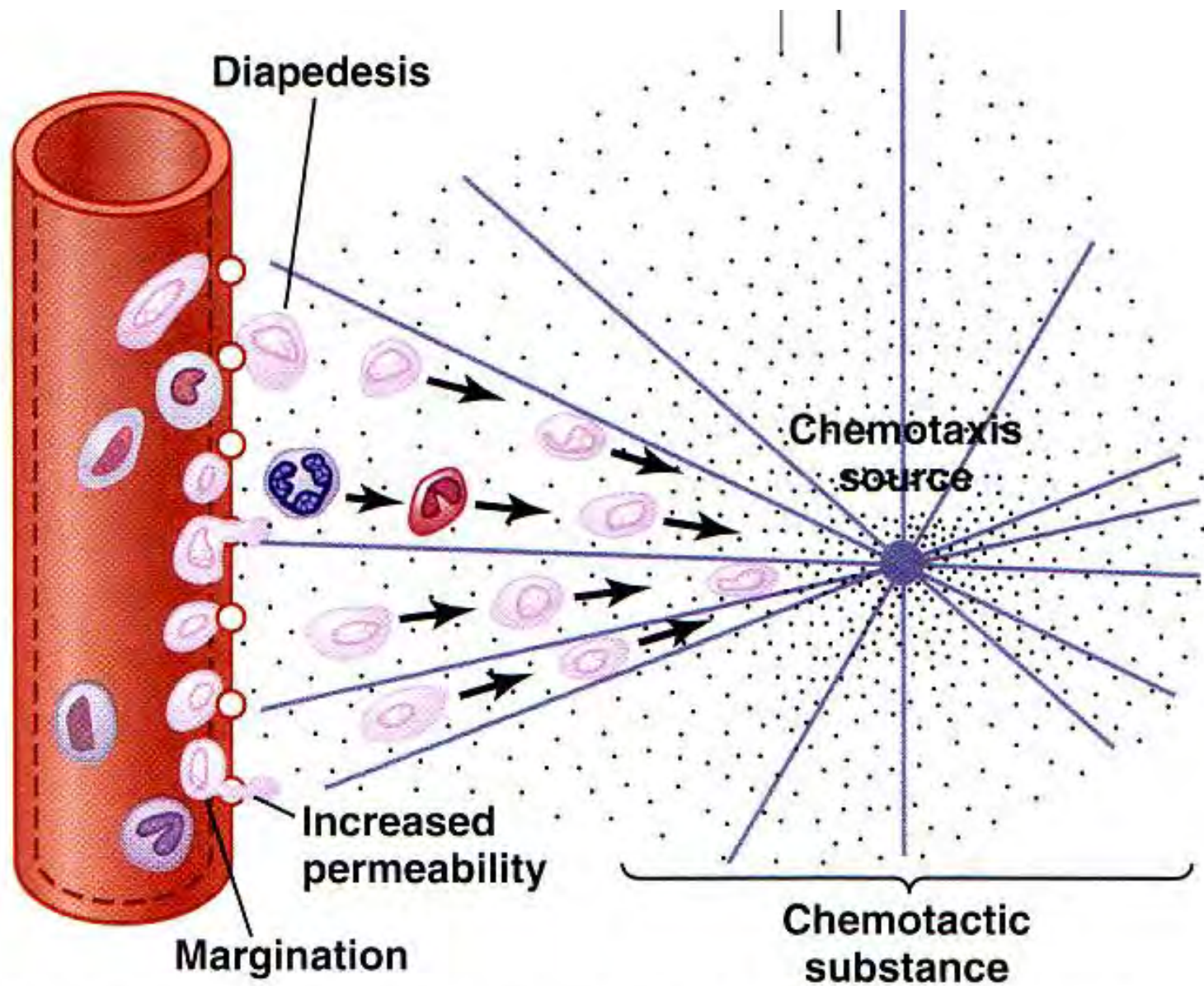


FIGURE 2.1 Summary of the main physical, chemical and mechanical barriers to infection entering the human body.

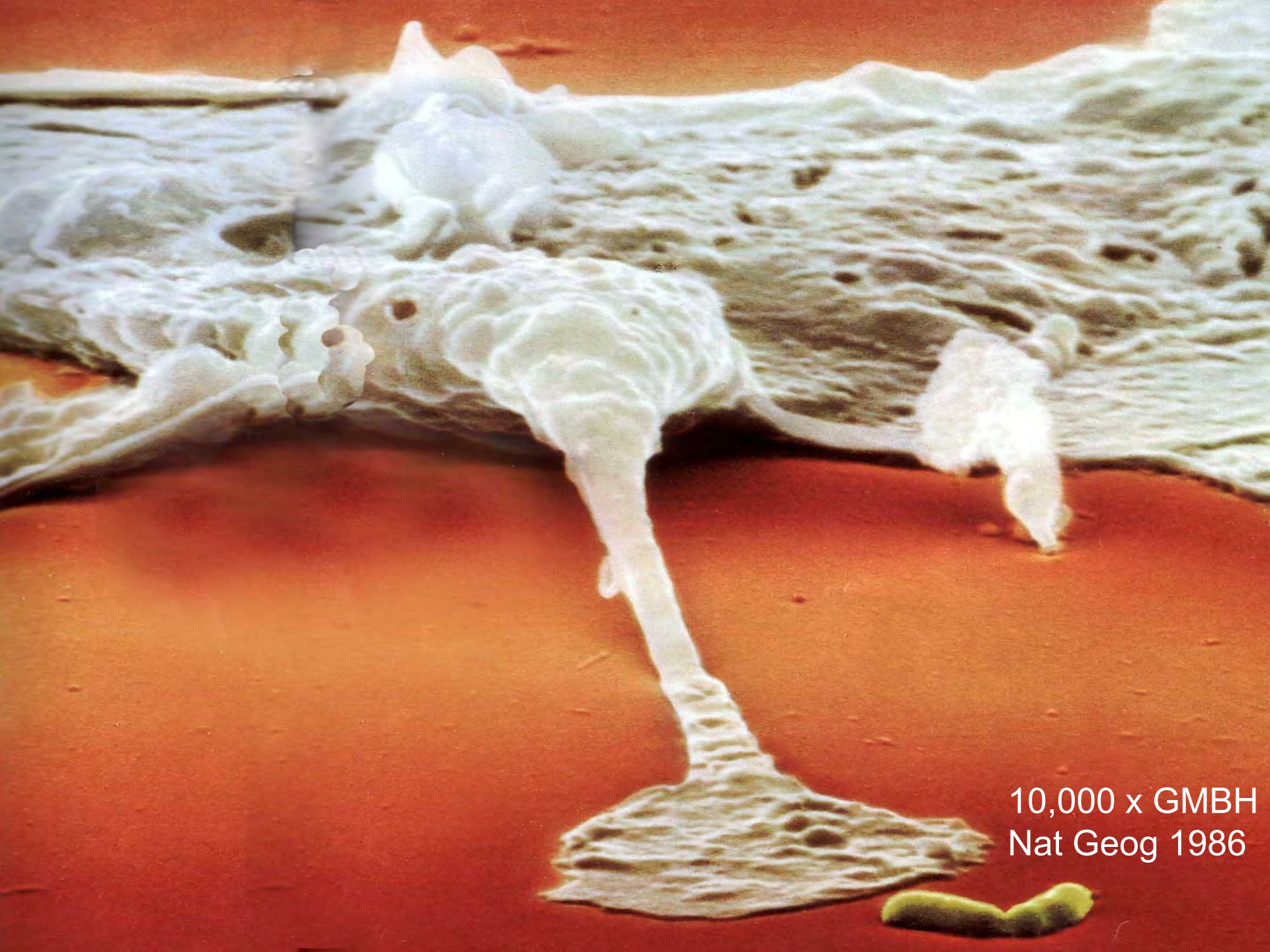
# Good phagocytes!



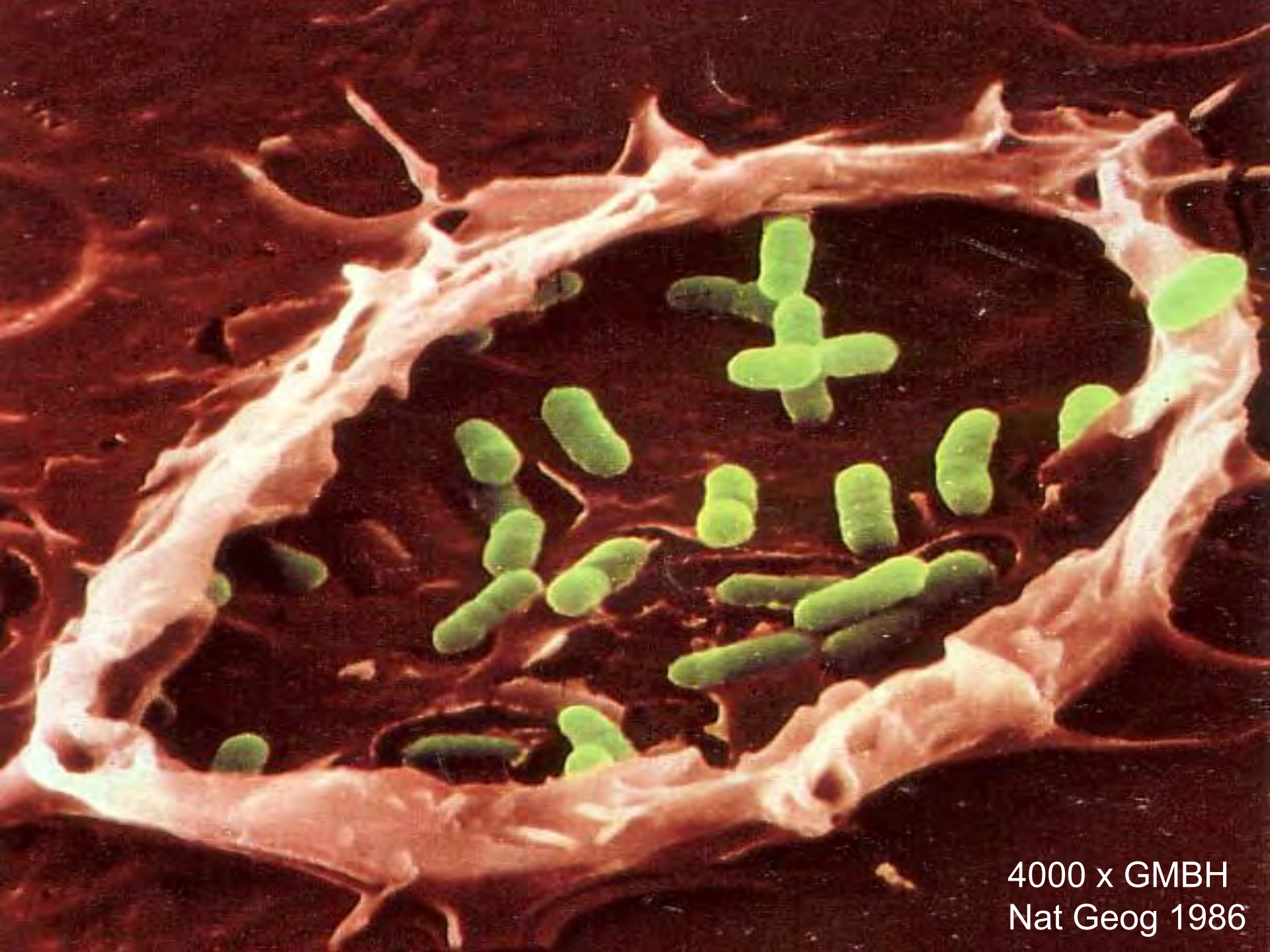


**Figure 33-2** Movement of neutrophils by *diapedesis* through capillary pores and by *chemotaxis* toward an area of tissue damage.

G&H 2011  
 cf. fig 34-2  
 G&H 2016



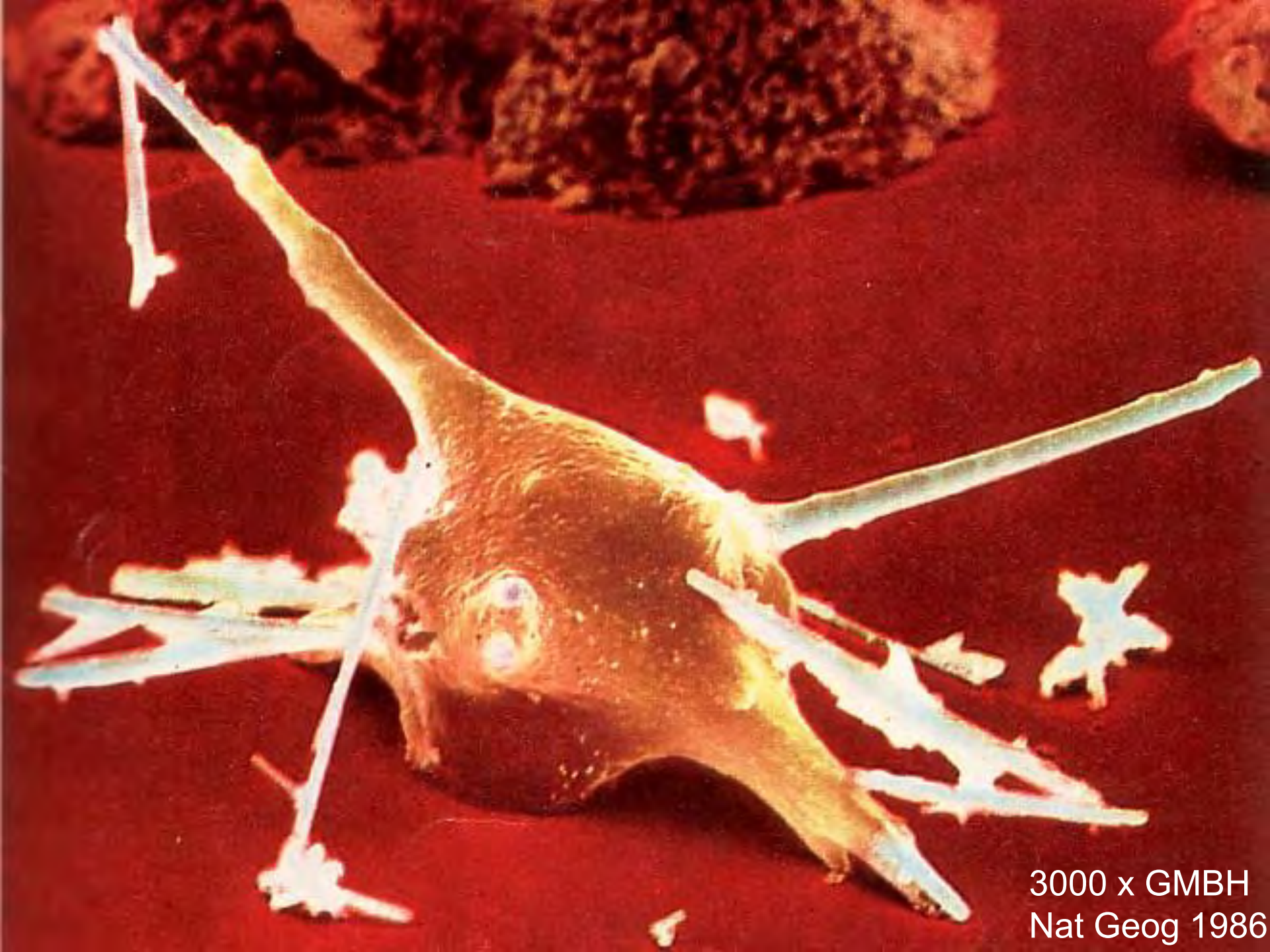
10,000 x GMBH  
Nat Geog 1986



4000 x GMBH  
Nat Geog 1986

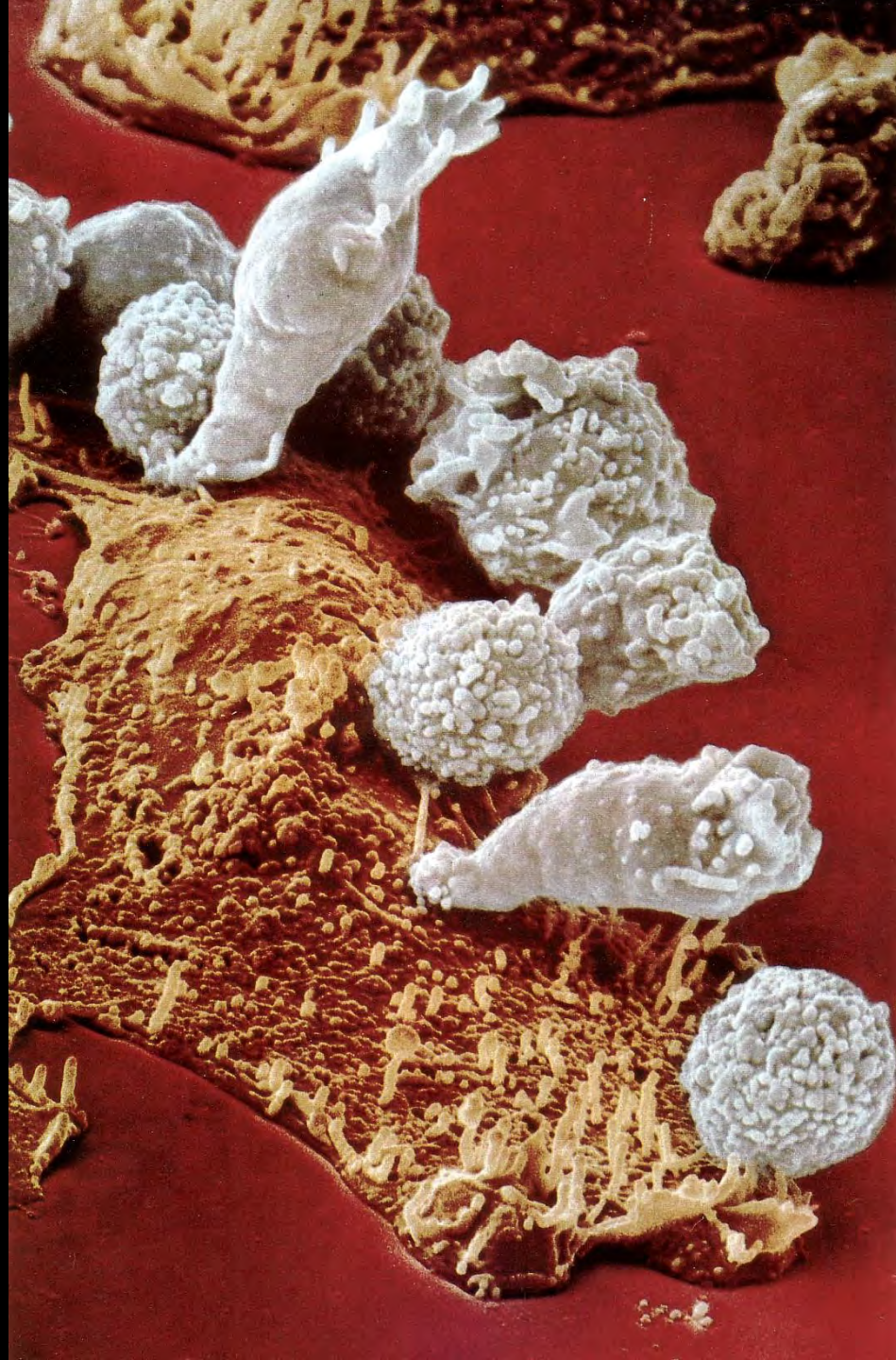


7000 x GMBH  
Nat Geog 1986



3000 x GMBH  
Nat Geog 1986



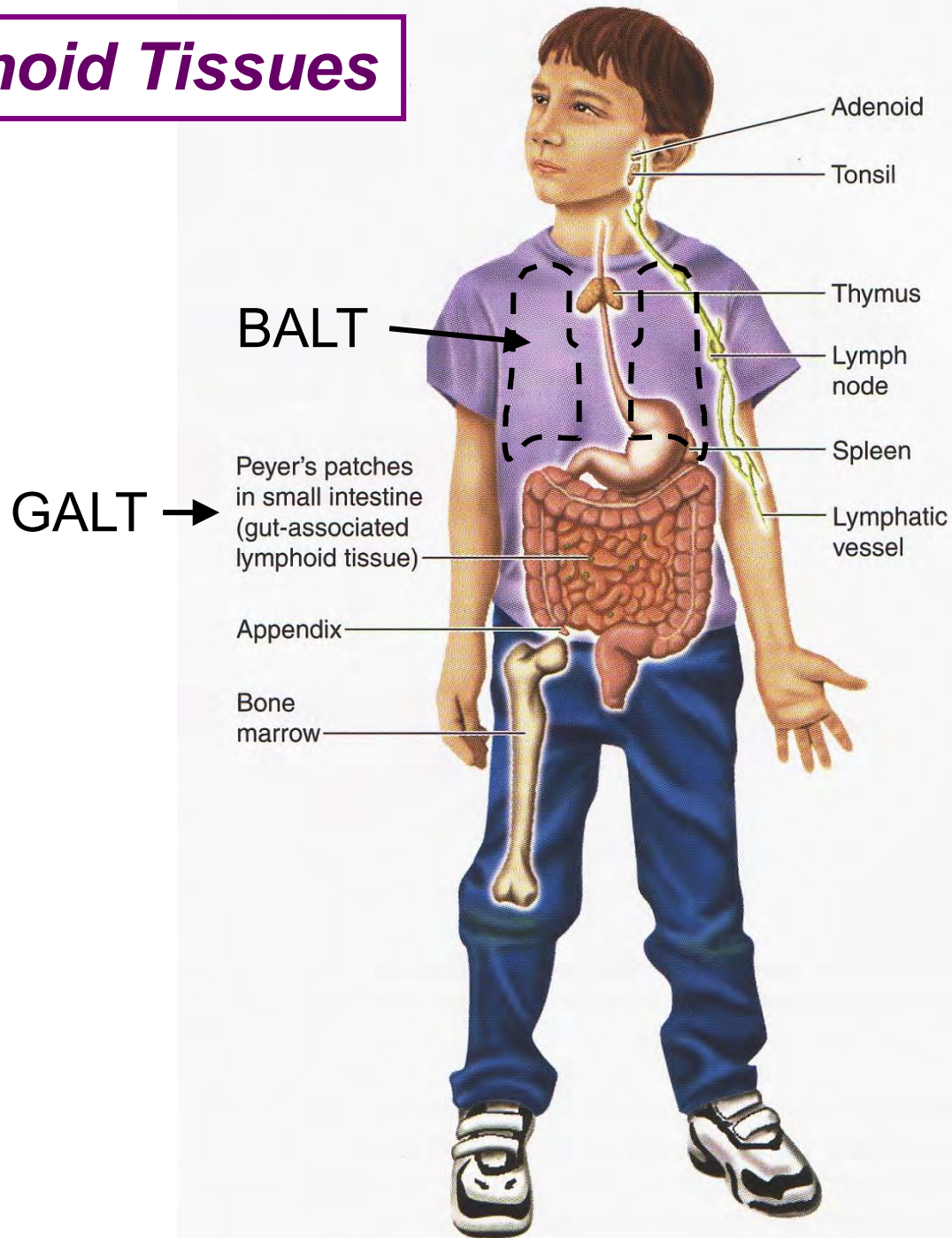


10,000 x GMBH  
Nat Geog 1986

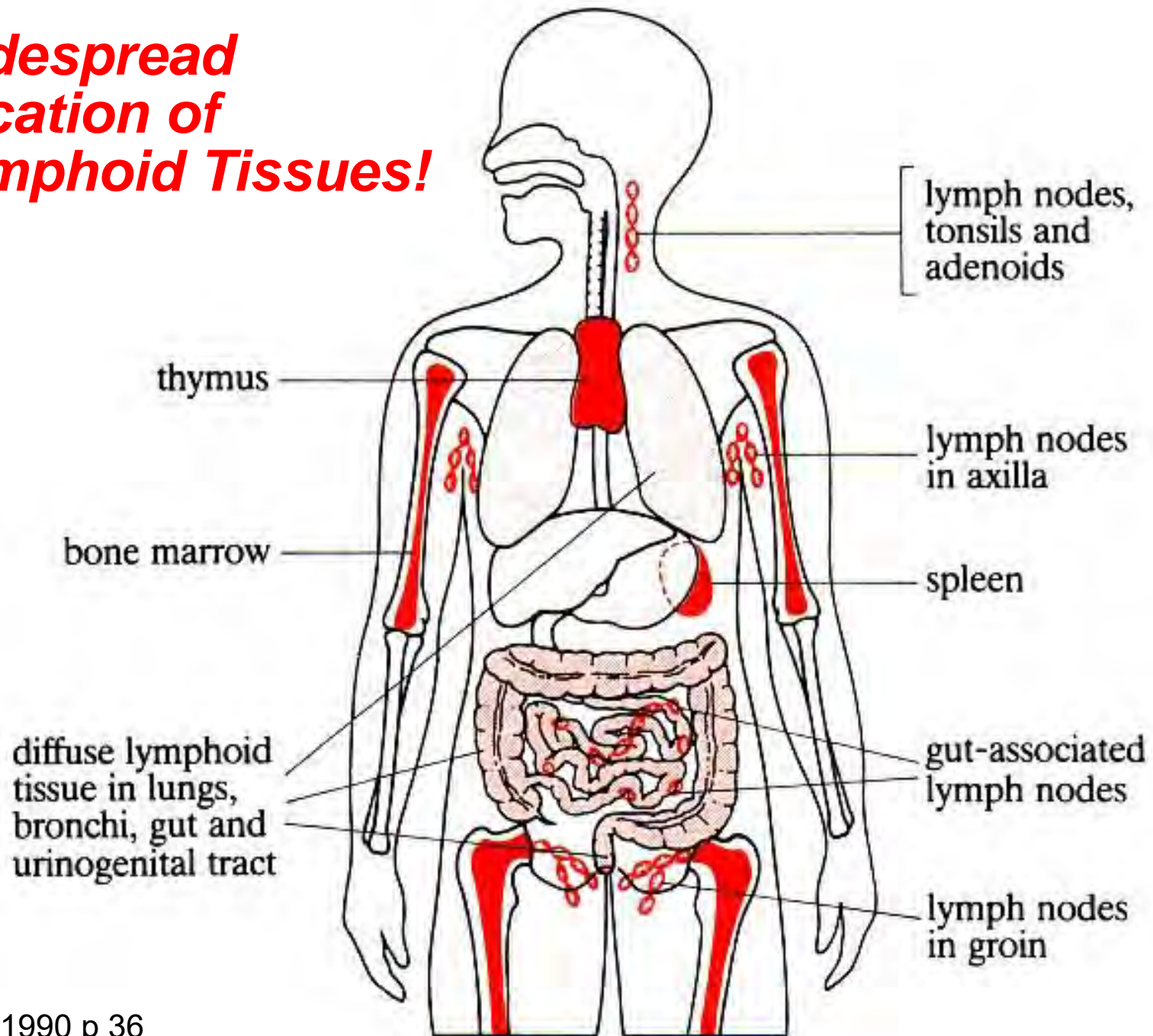


7000 x GMBH  
Nat Geog 1986

# Lymphoid Tissues



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





# Hand-washing

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

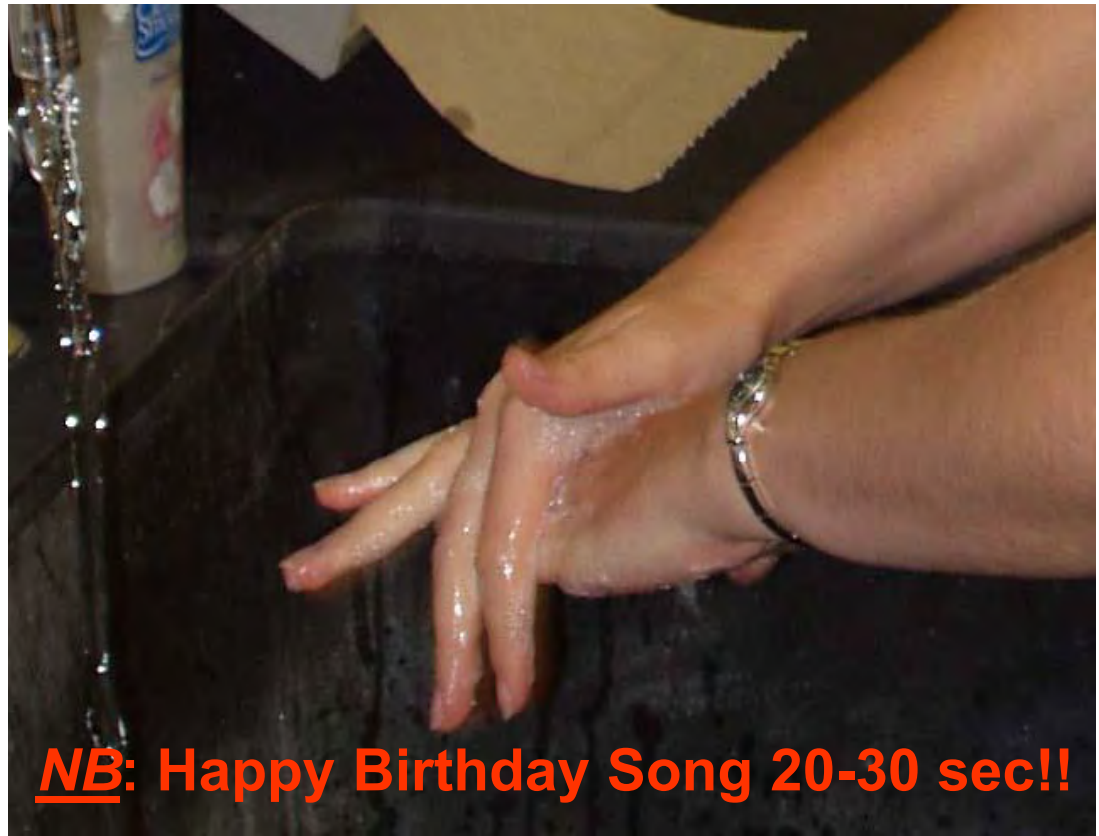
Thoroughly wash with soap and warm running water — rubbing your hands together for at least 10 seconds.

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/>**

# 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!

# Immunity

## Innate/Inborn/Nonspecific

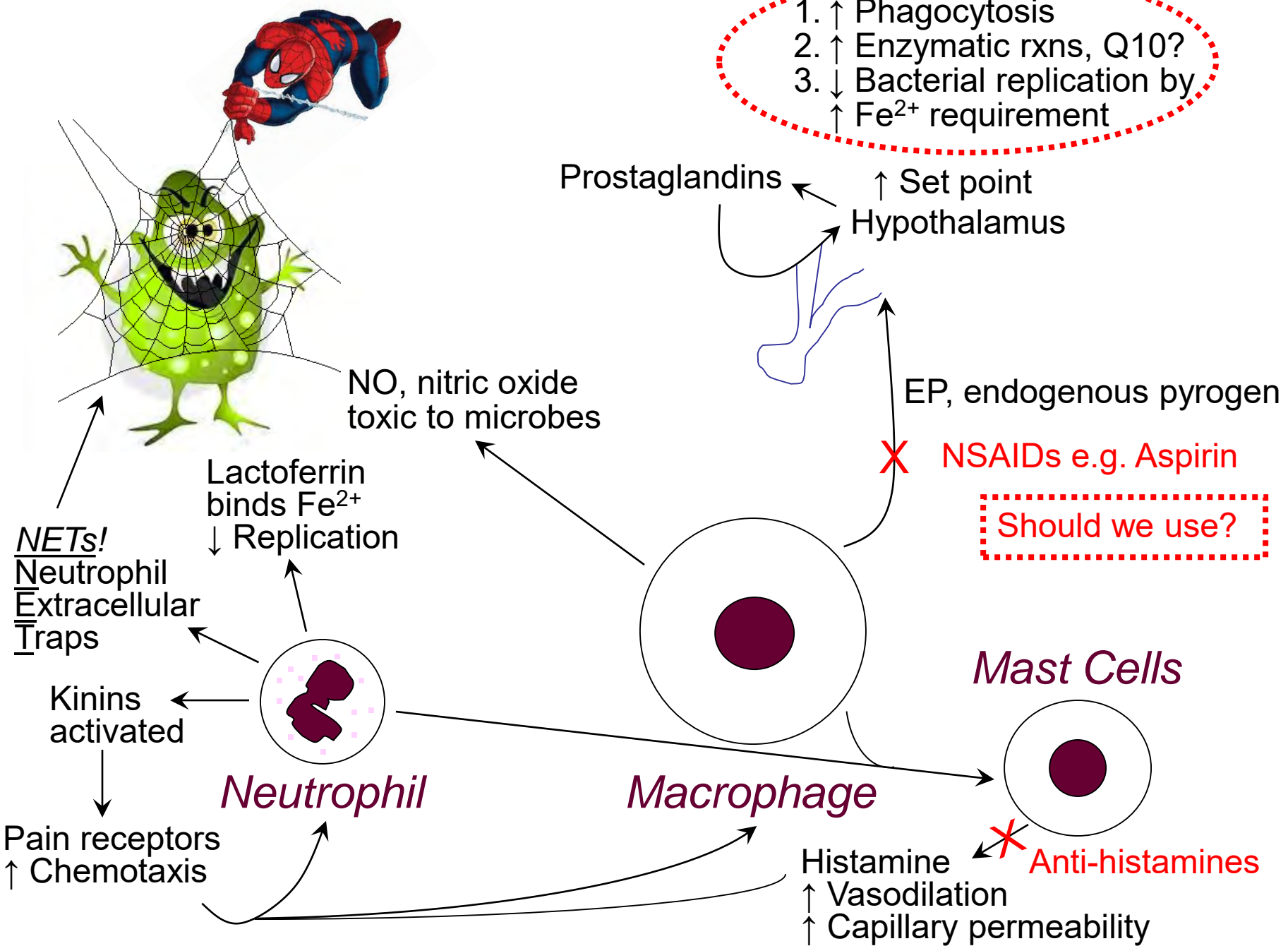
1. Immediate, upon exposure to threatening agent
2. 1<sup>0</sup> effectors phagocytic specialists: neutrophils & macrophages
3. "Eyes" are Toll-like receptors (TLRs) which recognize & bind with generic invader markers
4. Inflammation, interferon, natural killer cells, complement (plasma proteins)

## Adaptive/Acquired/Specific

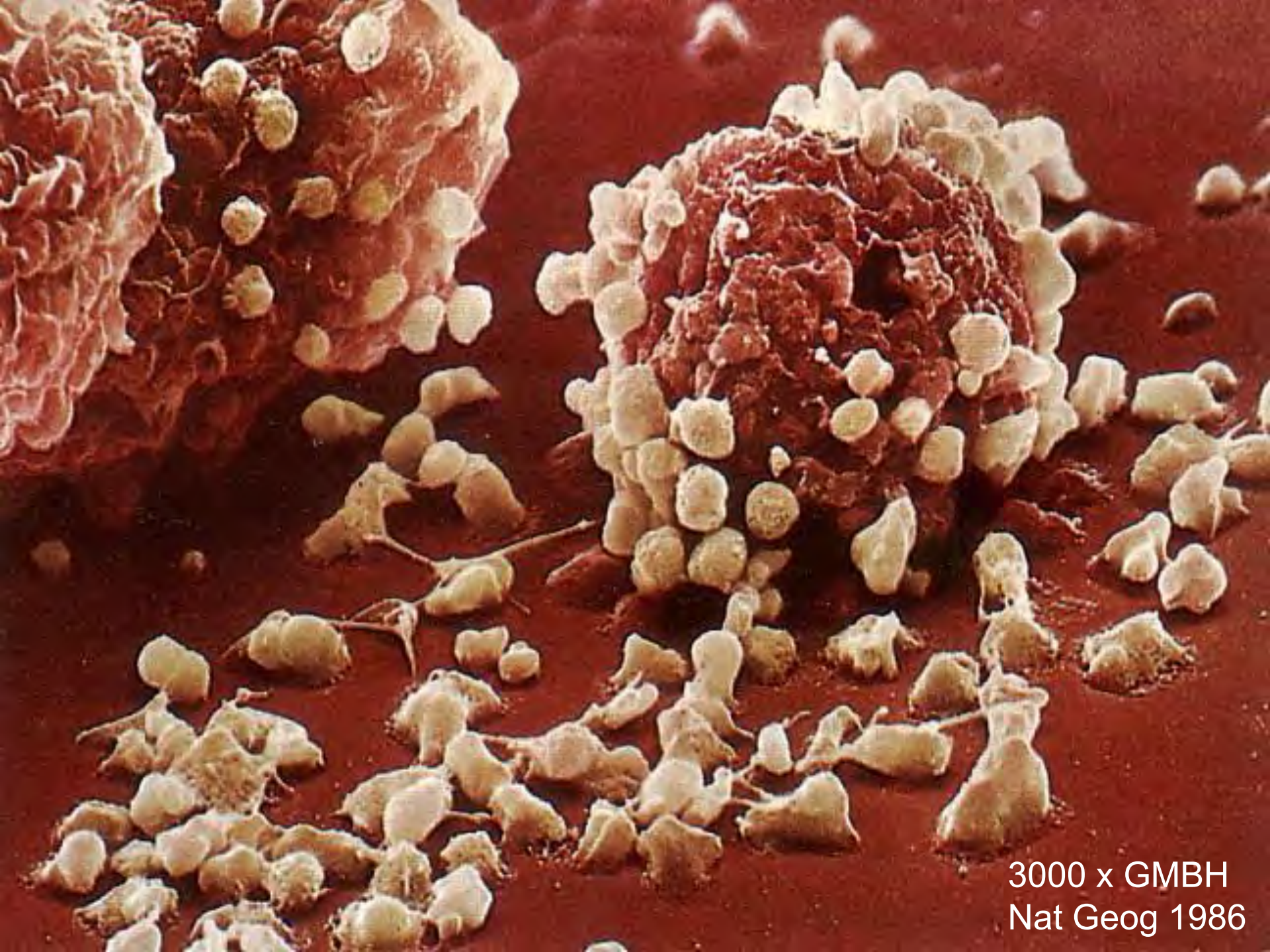
1. Delayed, selective targetting based on prior exposure
2. 1<sup>0</sup> effectors lymphocytes: T- & B-lymphocytes
3. "Eyes" are T- and B-cell receptors which bind with specific antigens
4. Cell-mediated & Humoral (Ab mediated) immunity

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

1. ↑ Phagocytosis
2. ↑ Enzymatic rxns, Q10?
3. ↓ Bacterial replication by ↑ Fe<sup>2+</sup> requirement







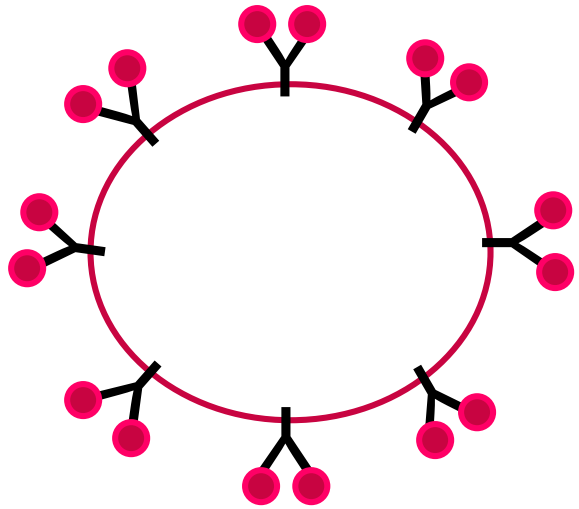
3000 x GMBH  
Nat Geog 1986

# Allergic Reactions, Mast Cells & Basophils?

Allergen = ●

IgE = Y

↑  
up to 1/2  
million  
per cell!



Mucous Membranes/Blood

Bradykinin

Eosinophil & Neutrophil  
Chemotactic Substances

Heparin

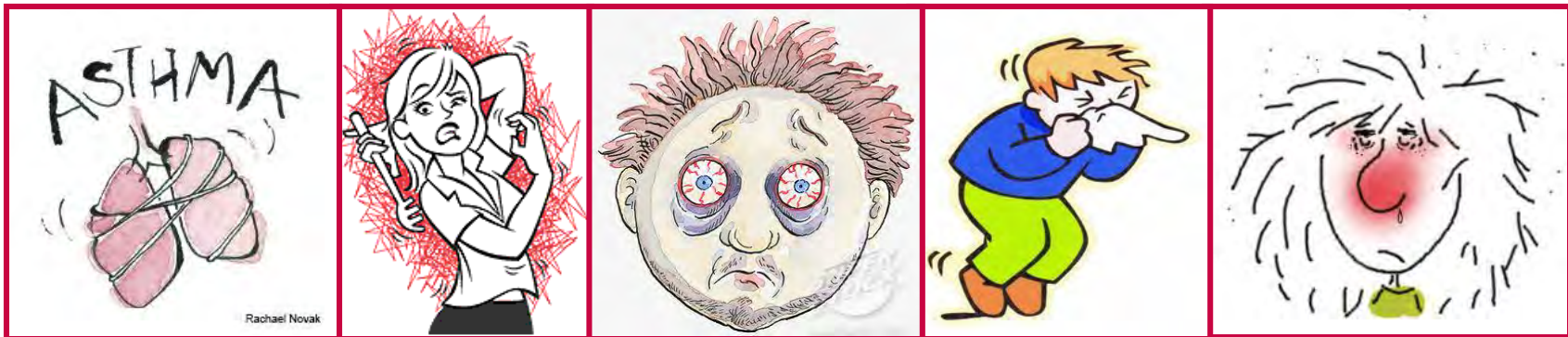
Histamine

Platelet Activating Factors

Protease

Serotonin

Toxic Leukotrienes/SRSA



Rachael Novak

# Inflammation Steps

**1 Break in skin →  
Bacteria enter & reproduce**

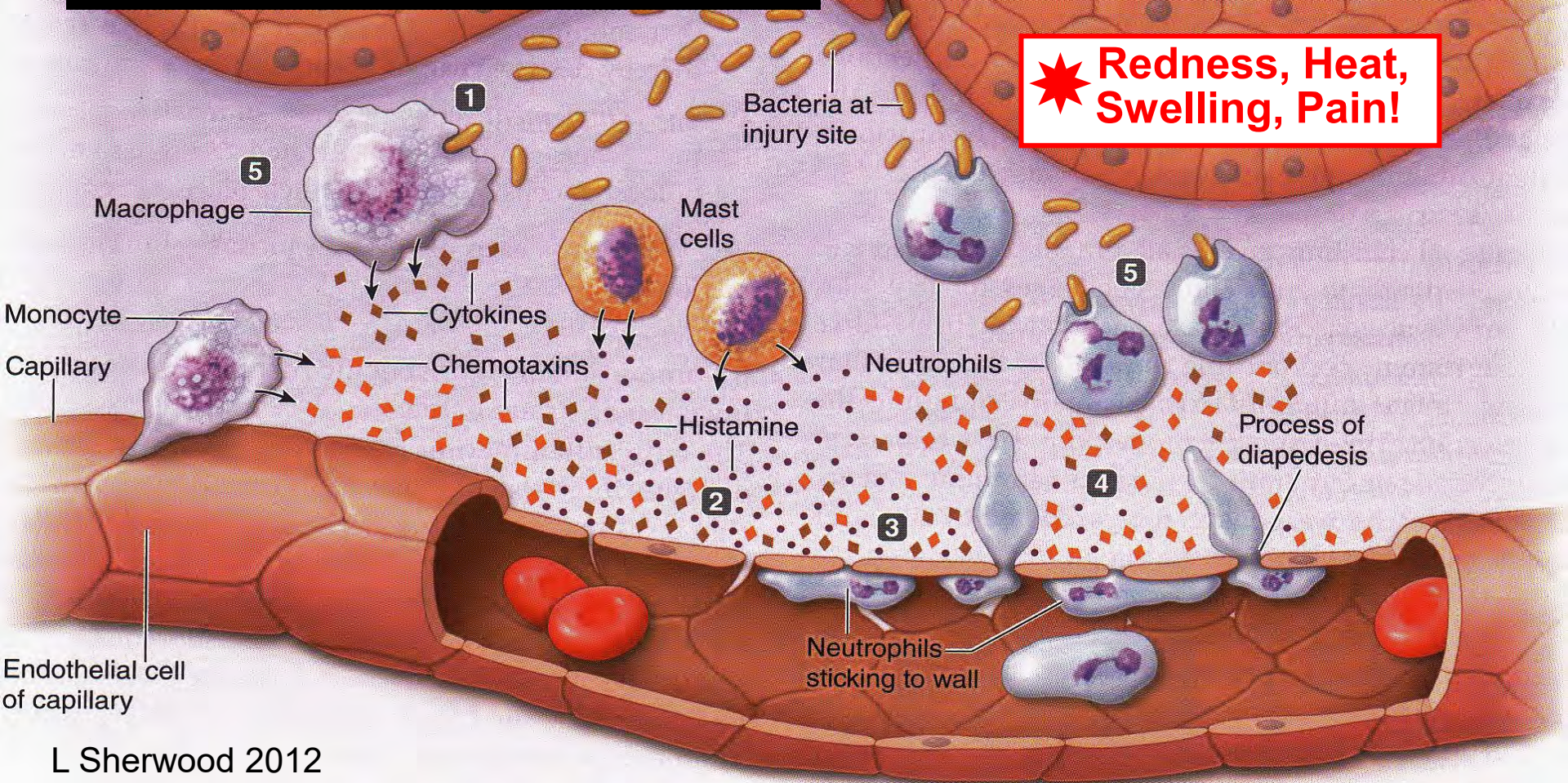
**2 Mast cells release histamine**

**3 Vessel wall becomes sticky →  
Neutrophils & monocytes attach →  
diapedesis → chemotaxis**

**4 Chemotaxins attract more  
Neutrophils & monocytes**

**5 Monocytes swell →  
Macrophages**

**★ Redness, Heat,  
Swelling, Pain!**





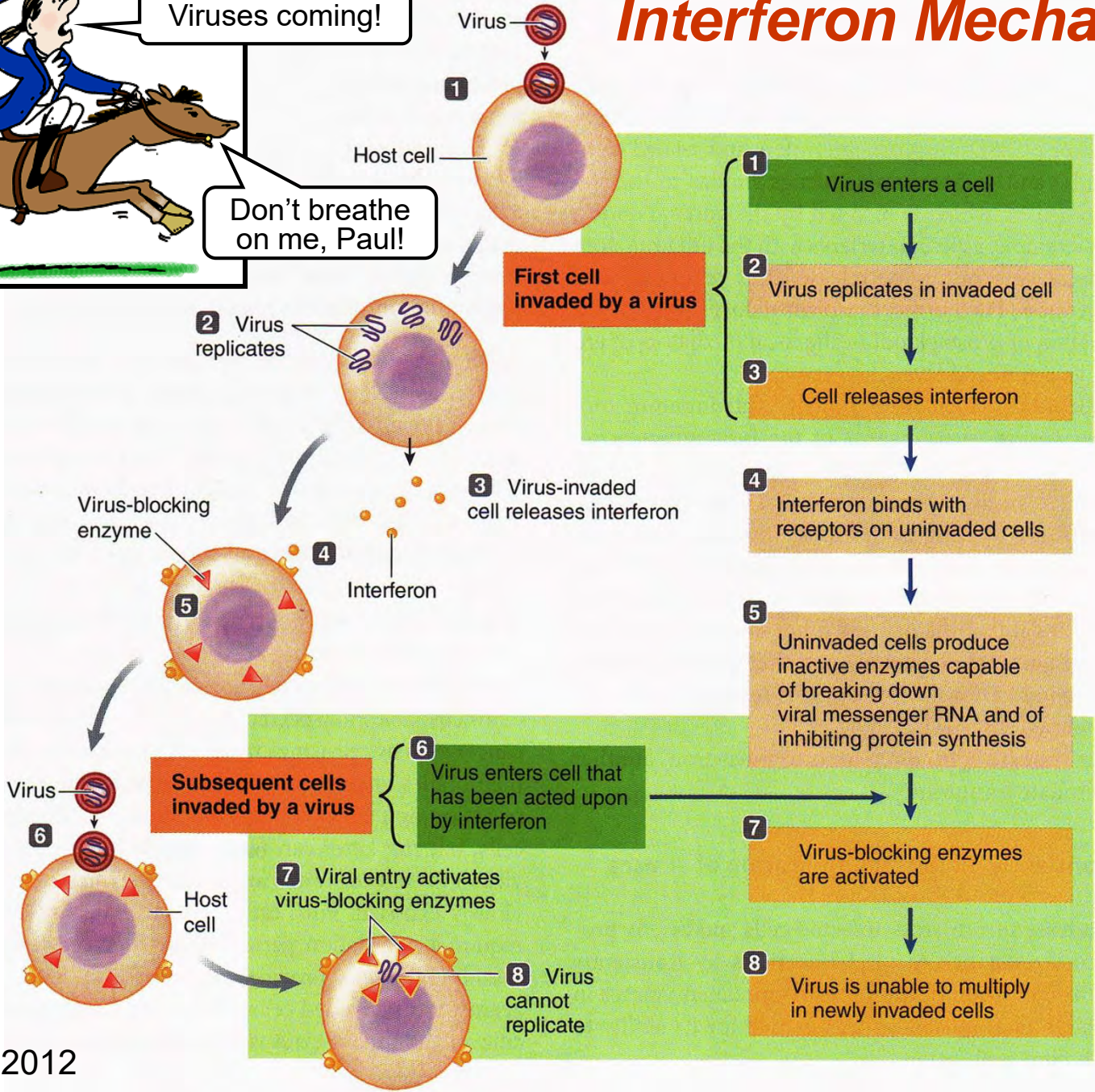
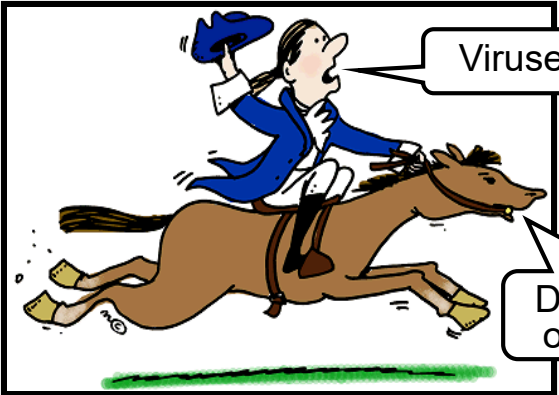
***Glucocorticoids throw blanket over entire inflammatory process!***



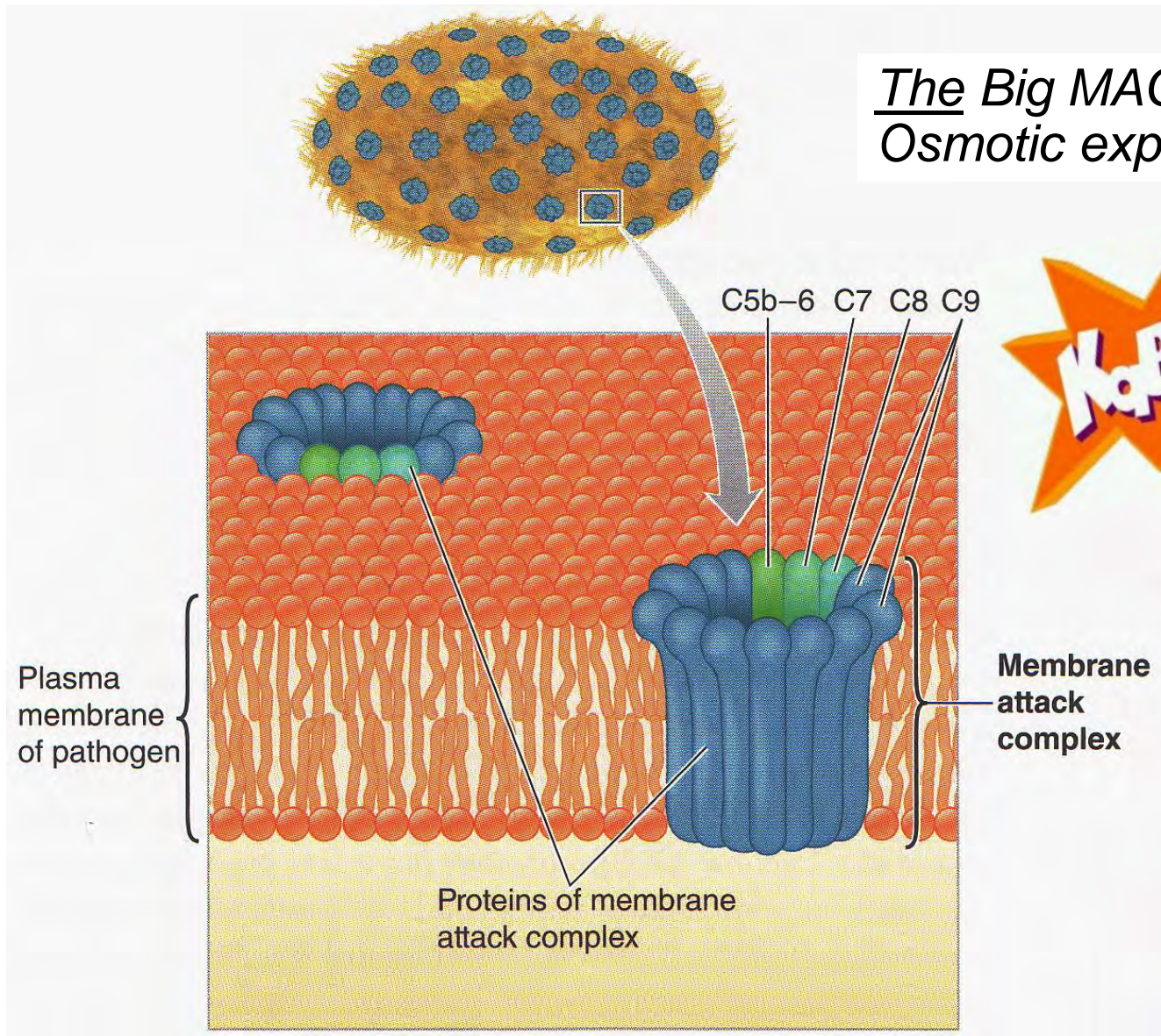
1. Certainly warranted to quiet down immune system during extreme flare ups of arthritis, asthma, poison ivy, rash, but must consider:
2. Destroy lymphocytes in lymphoid tissues.
3. ↓ Antibody/Immunoglobulin (Ig) production.
4. Make susceptible to bacterial infections.



# Interferon Mechanisms



# Activated Complement



*The Big MAC to ❤️!  
Osmotic explosion!*



# WBC Adverse Effects



**X** → Leukocytes

Anti-cancer drugs  
Benzene  
Nuclear blast  
Radiation

↓ Professional  
phagocytes esp:  
Neutrophils  
Macrophages

↓ Body  
defense vs.  
μ organisms!

Savior Lymphoid  
tissues or bone  
marrow transplant?

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



30,000 x GMBH  
Nat Geog 1986



Protein capsule (capsid)

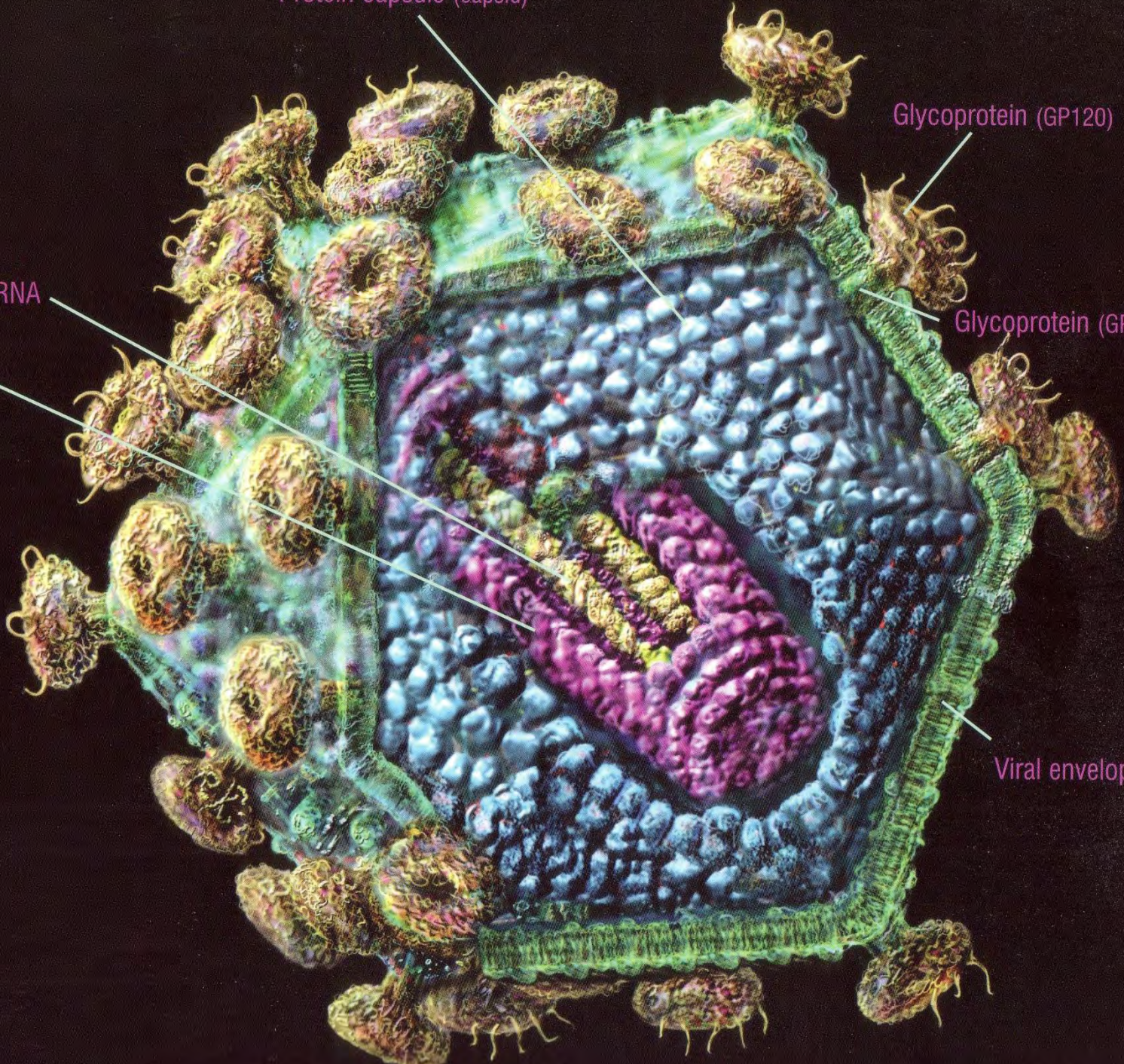
Glycoprotein (GP120)

RNA

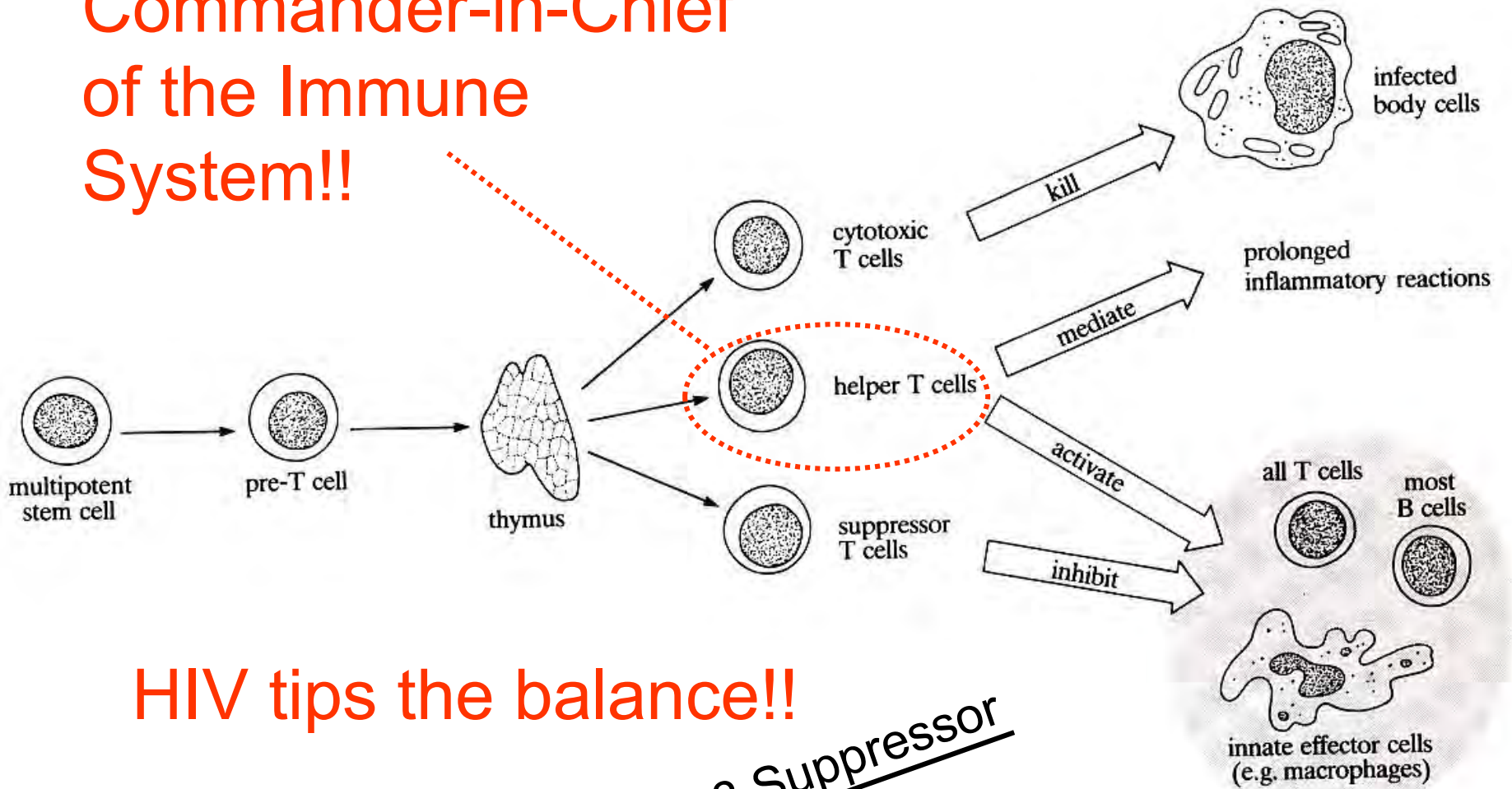
Glycoprotein (GP41)

Viral core

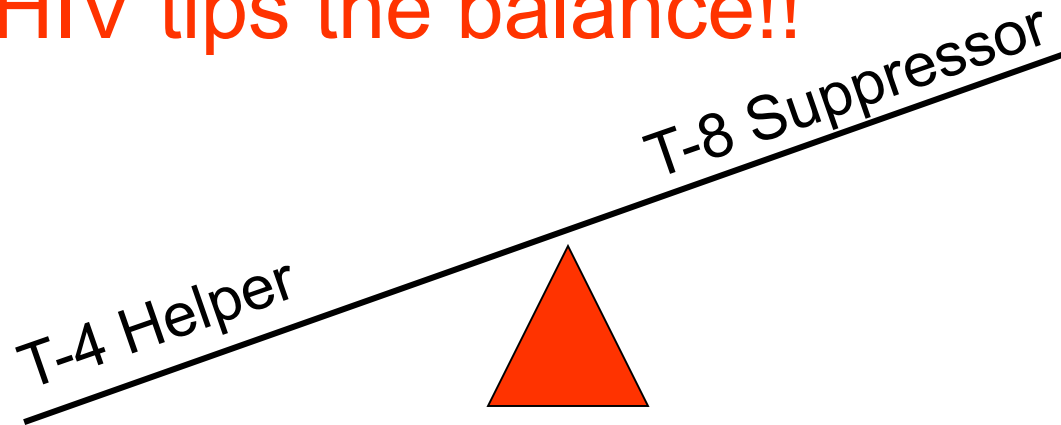
Viral envelope

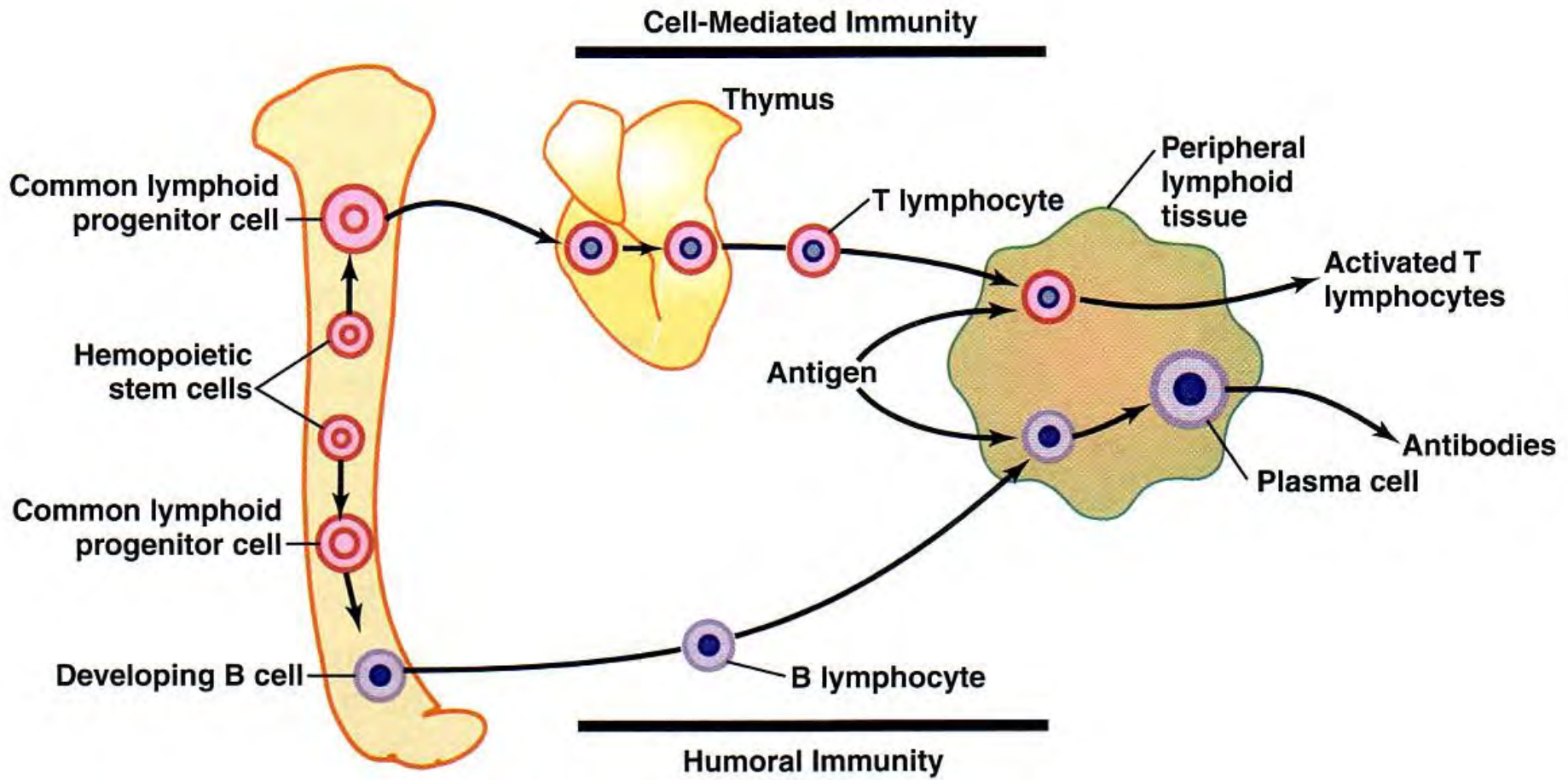


# Commander-in-Chief of the Immune System!!

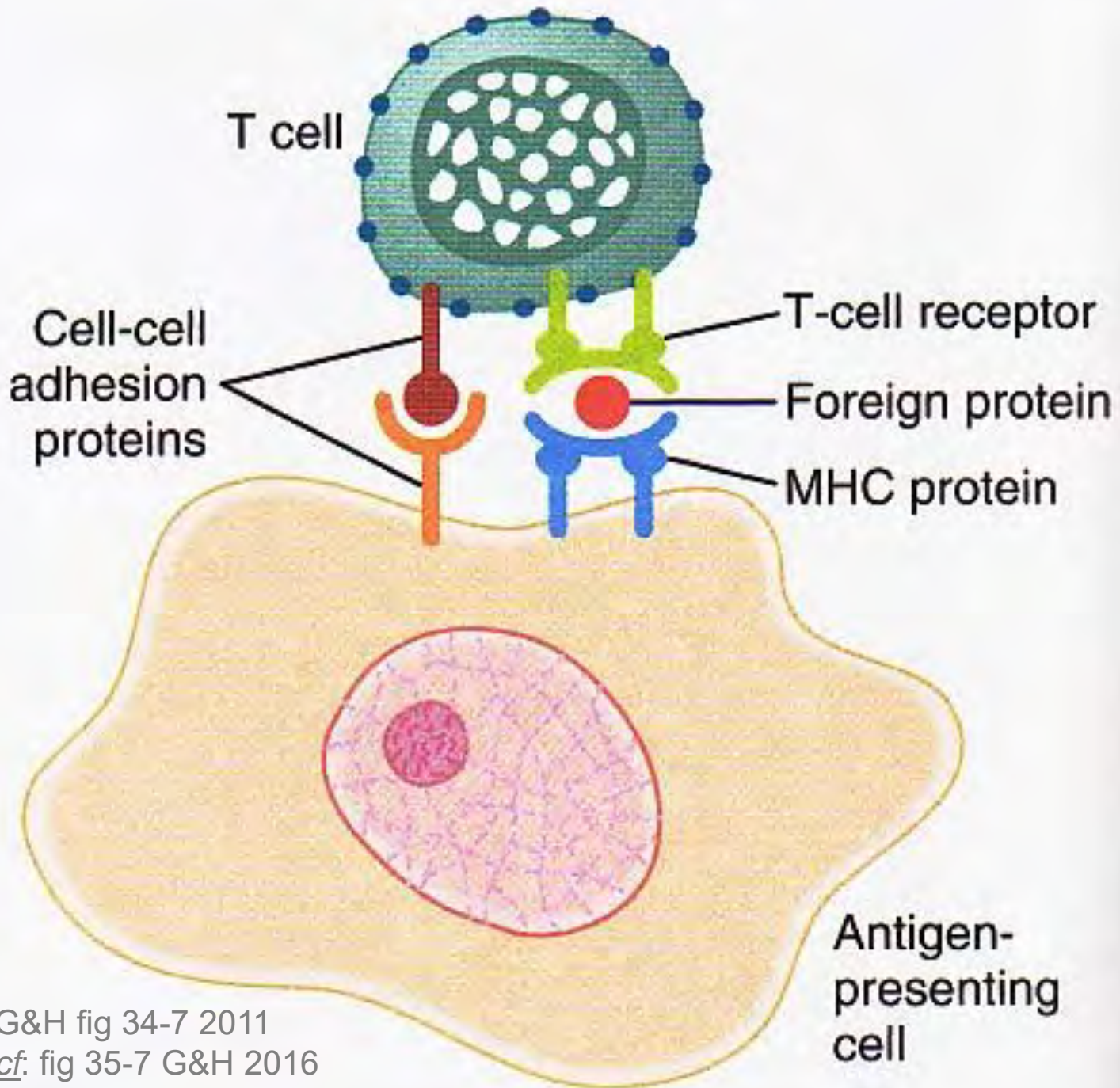


HIV tips the balance!!

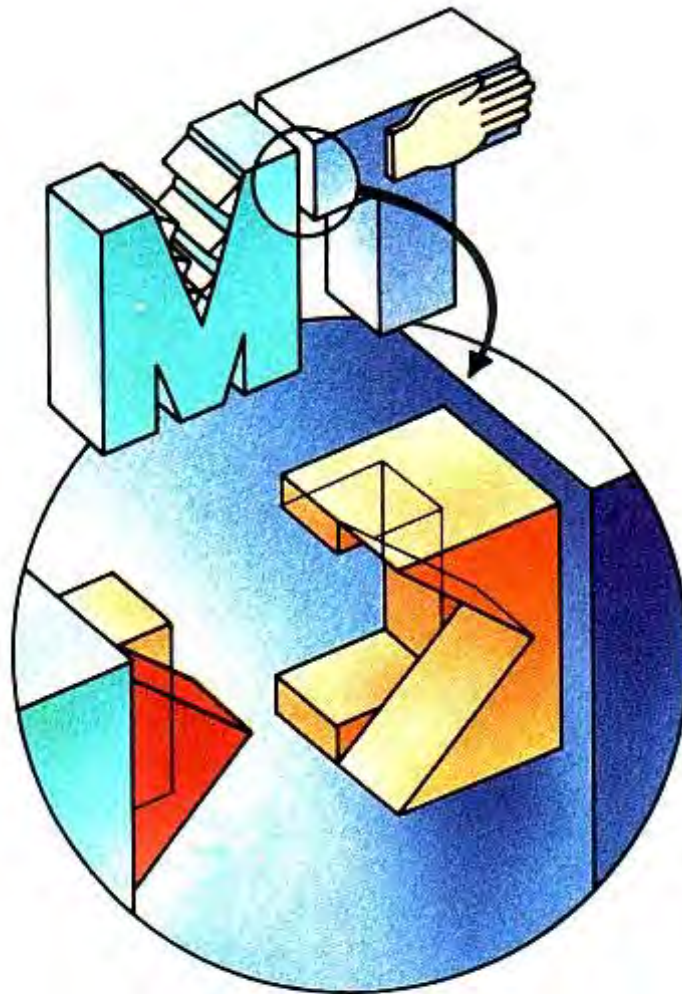




G&H fig 34-1 2011  
 cf: fig 35-1 G&H 2016



G&H fig 34-7 2011  
cf. fig 35-7 G&H 2016

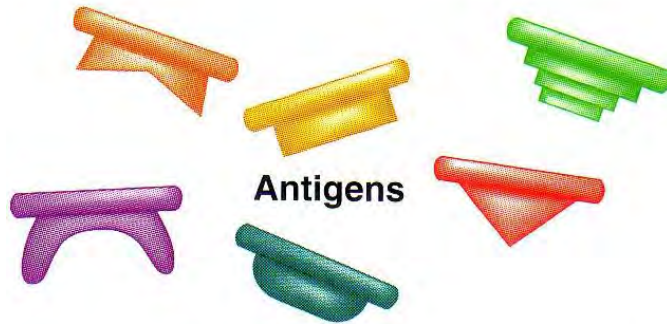


*The vital union that activates a helper T cell takes place only when the T cell recognizes both a “self” marker (rectangle) and a “nonself” antigen (triangle) on a macrophage.*

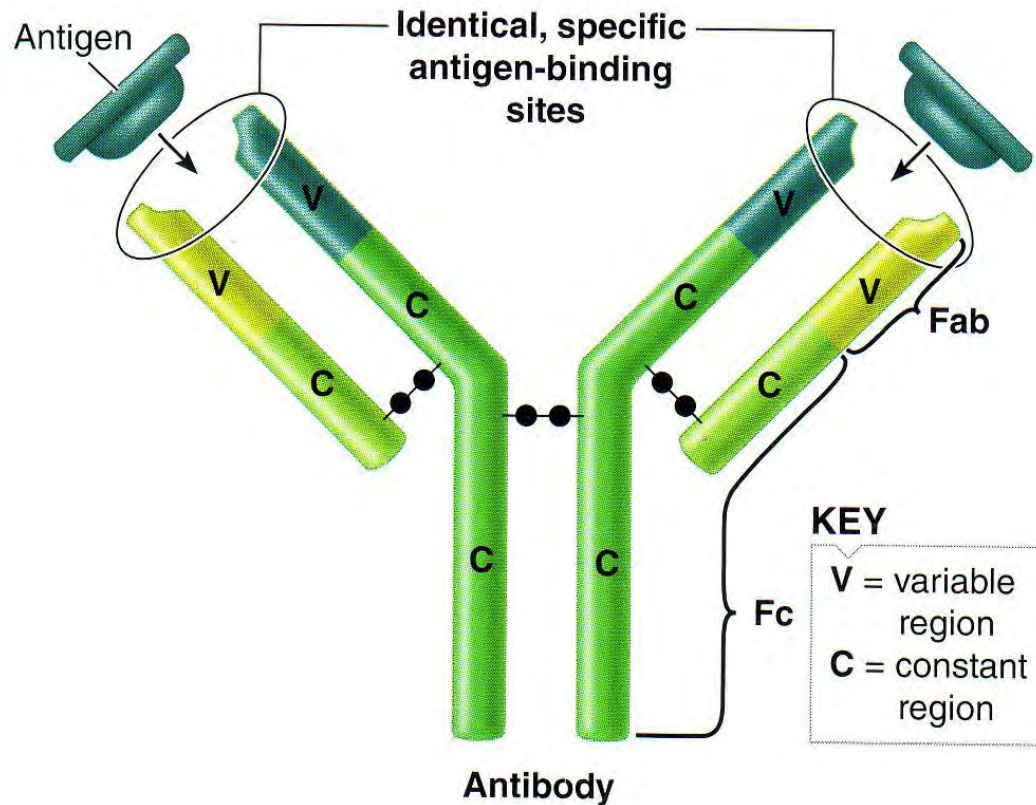


8500 x GMBH  
Nat Geog 1986

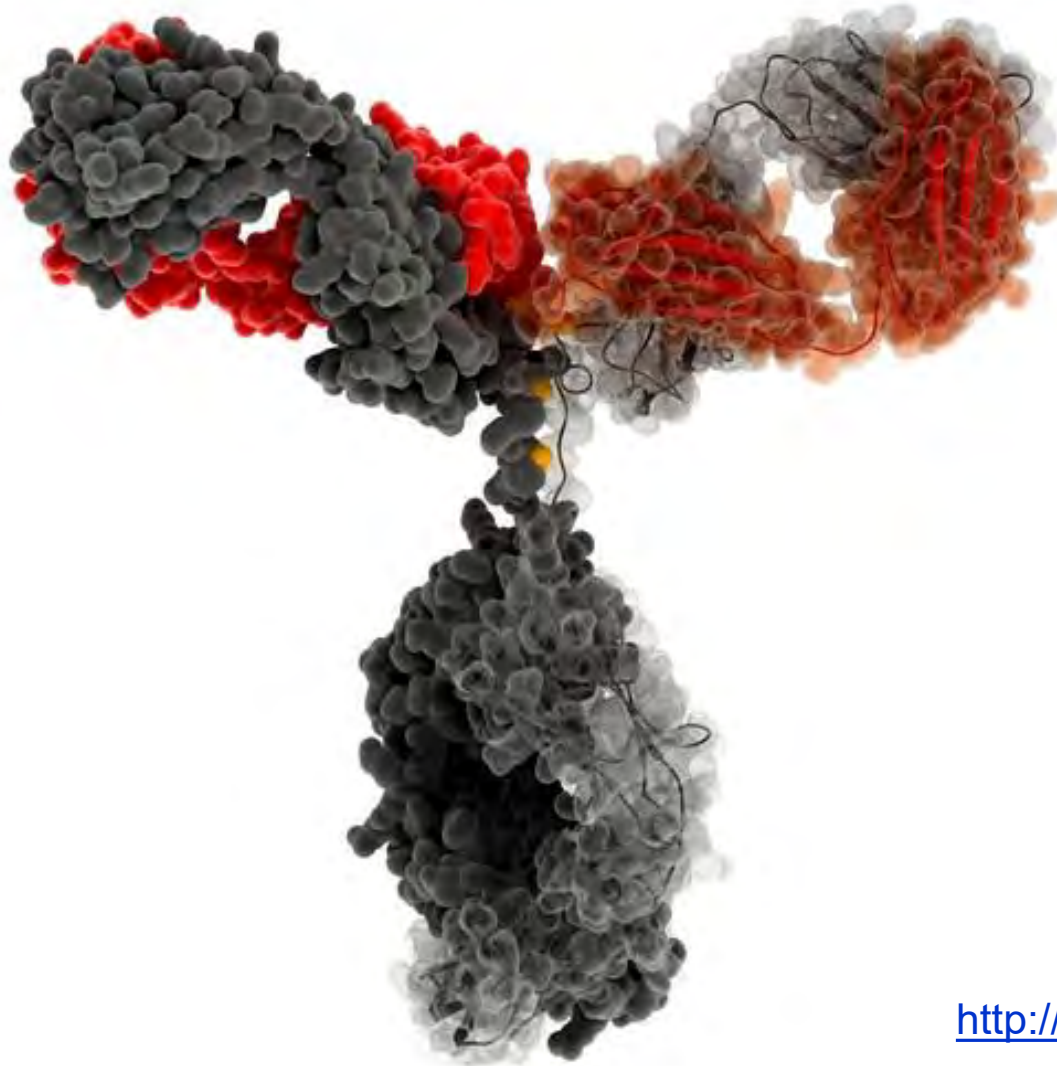
# Typical IgG Antibody Structure



*How do antibodies work?*



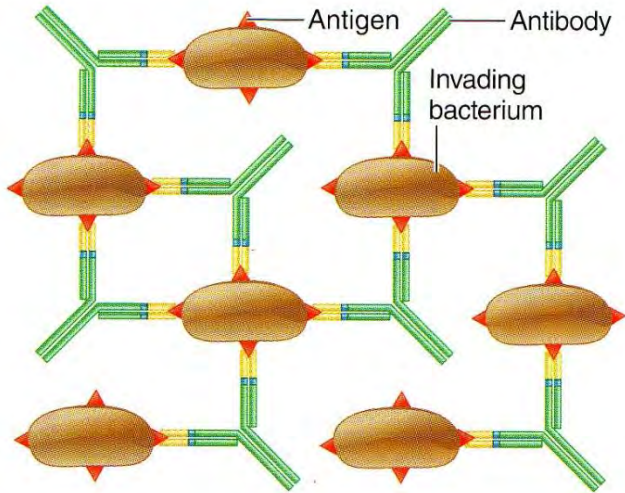
# Immunoglobulin G



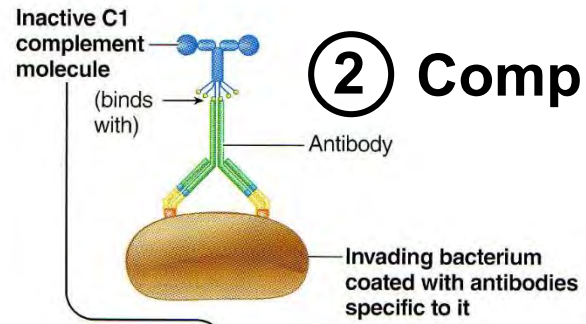
**Source:**  
Visual Science  
<http://visualscience.ru/en/>



# ① Agglutination



# ② Complement

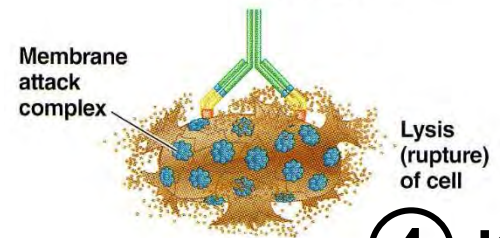


Activated by binding with antigen-attached antibody

(leads to)

Formation of C5-C9, the membrane attack complex

(forms holes in foreign cell)



# ④ Killer Cells

# ③ Opsonization

Invading bacterium coated with antibodies specific to it

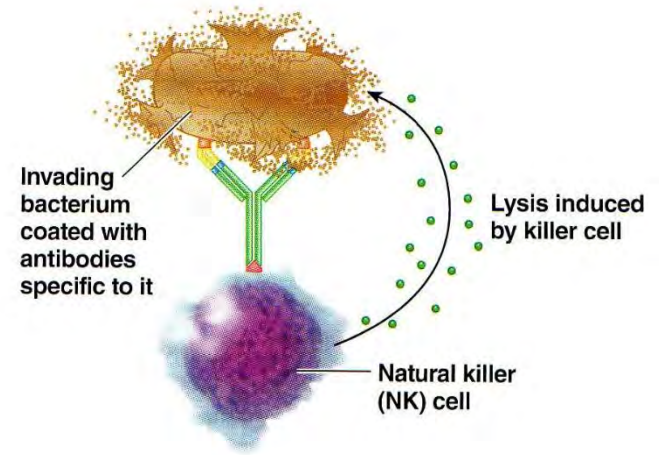
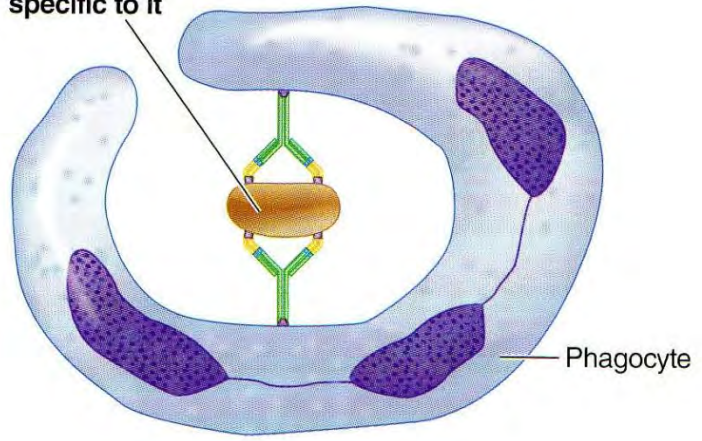


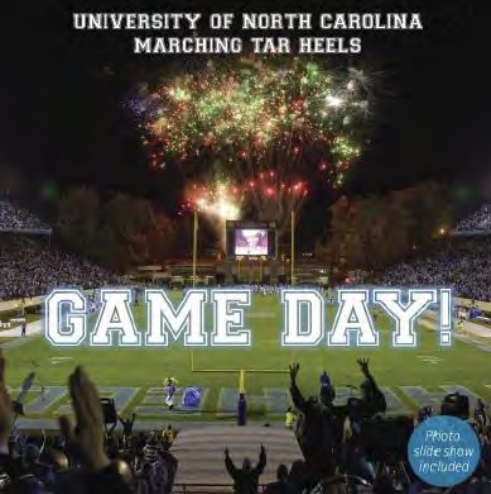
TABLE 4.1 Characteristics and functions of the human immunoglobulin classes

	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.

UNIVERSITY OF NORTH CAROLINA  
MARCHING TAR HEELS

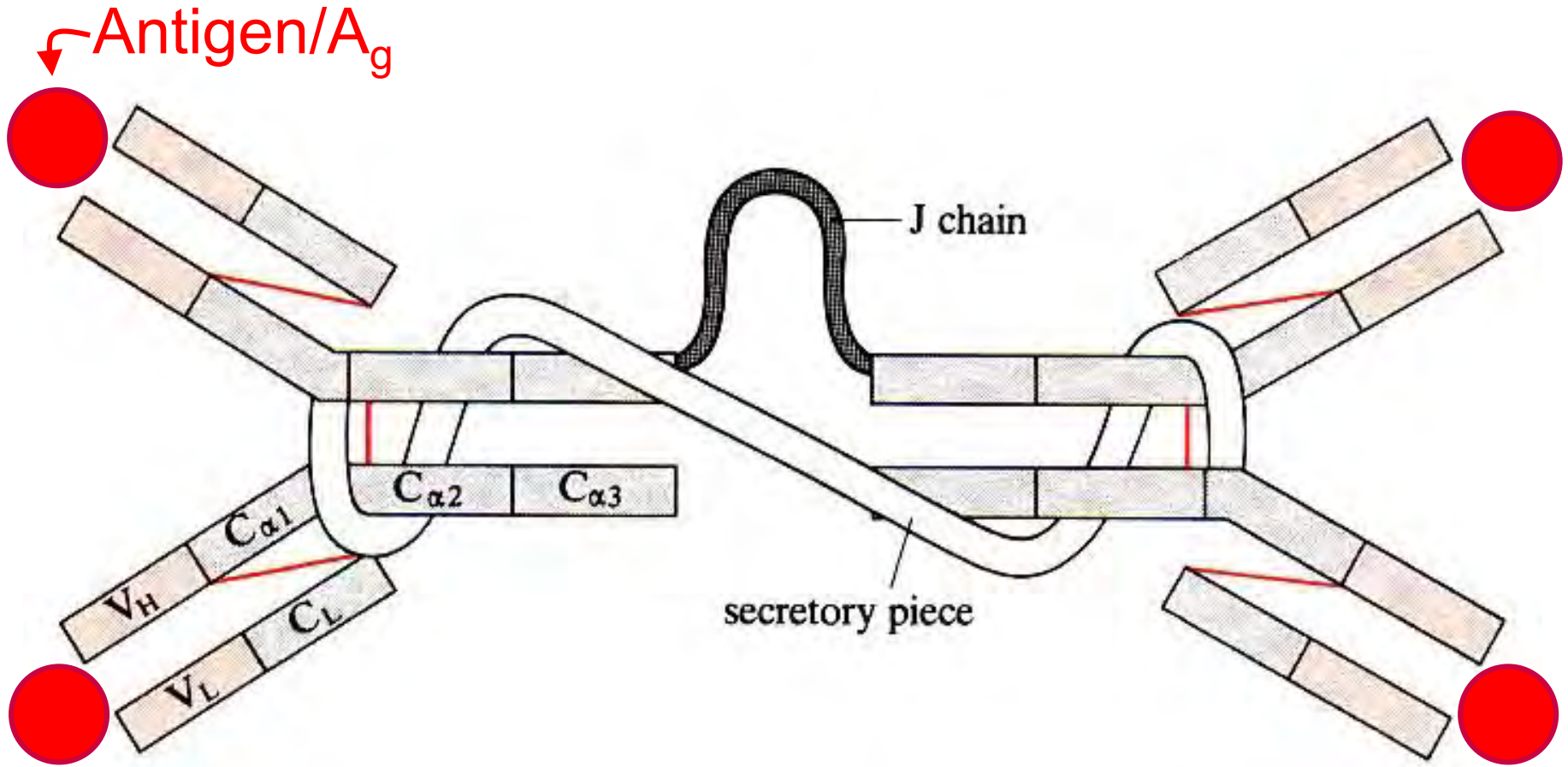


# G A M E D!



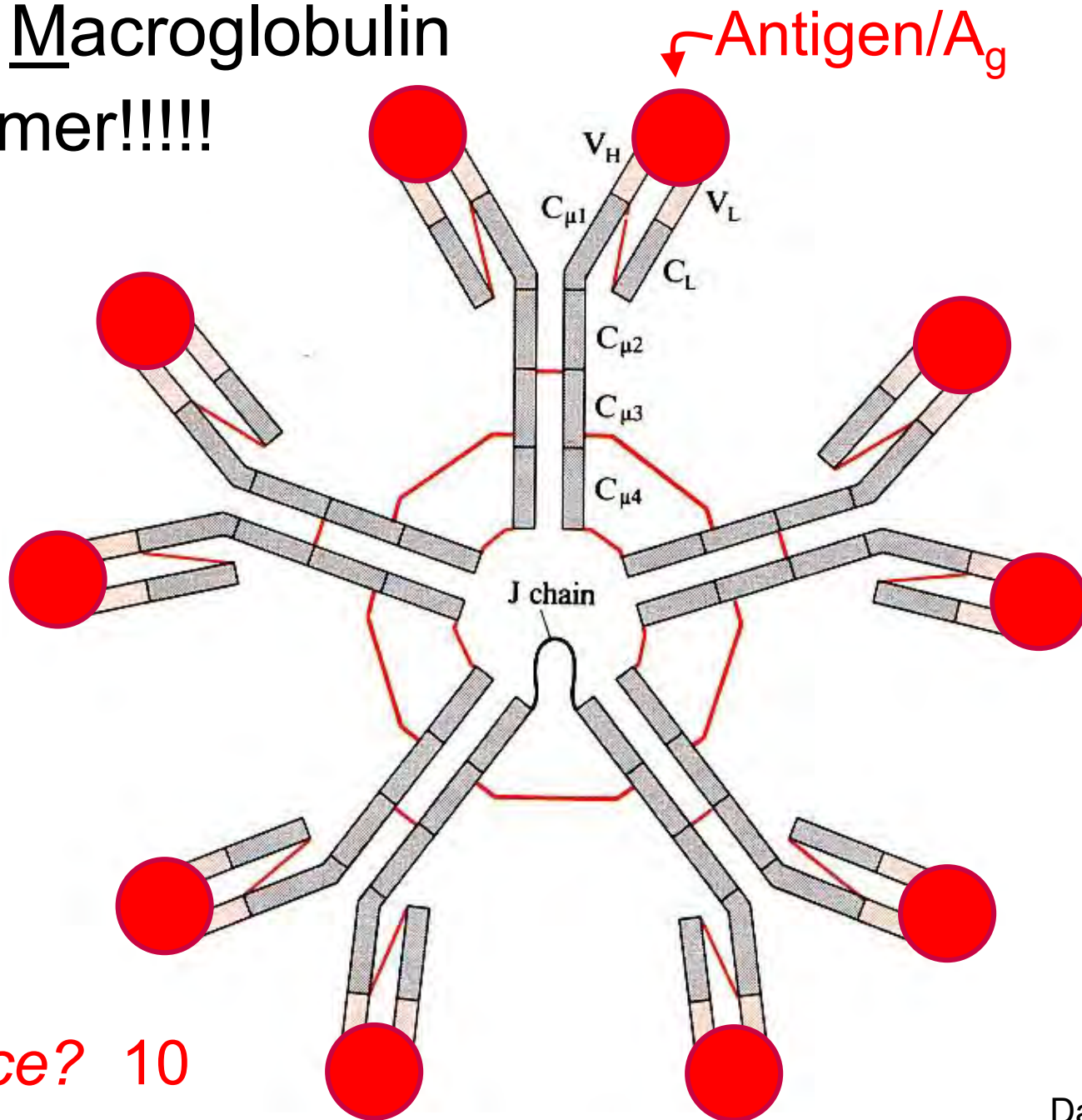
IgA = Secretory A<sub>b</sub>

Dimer!!

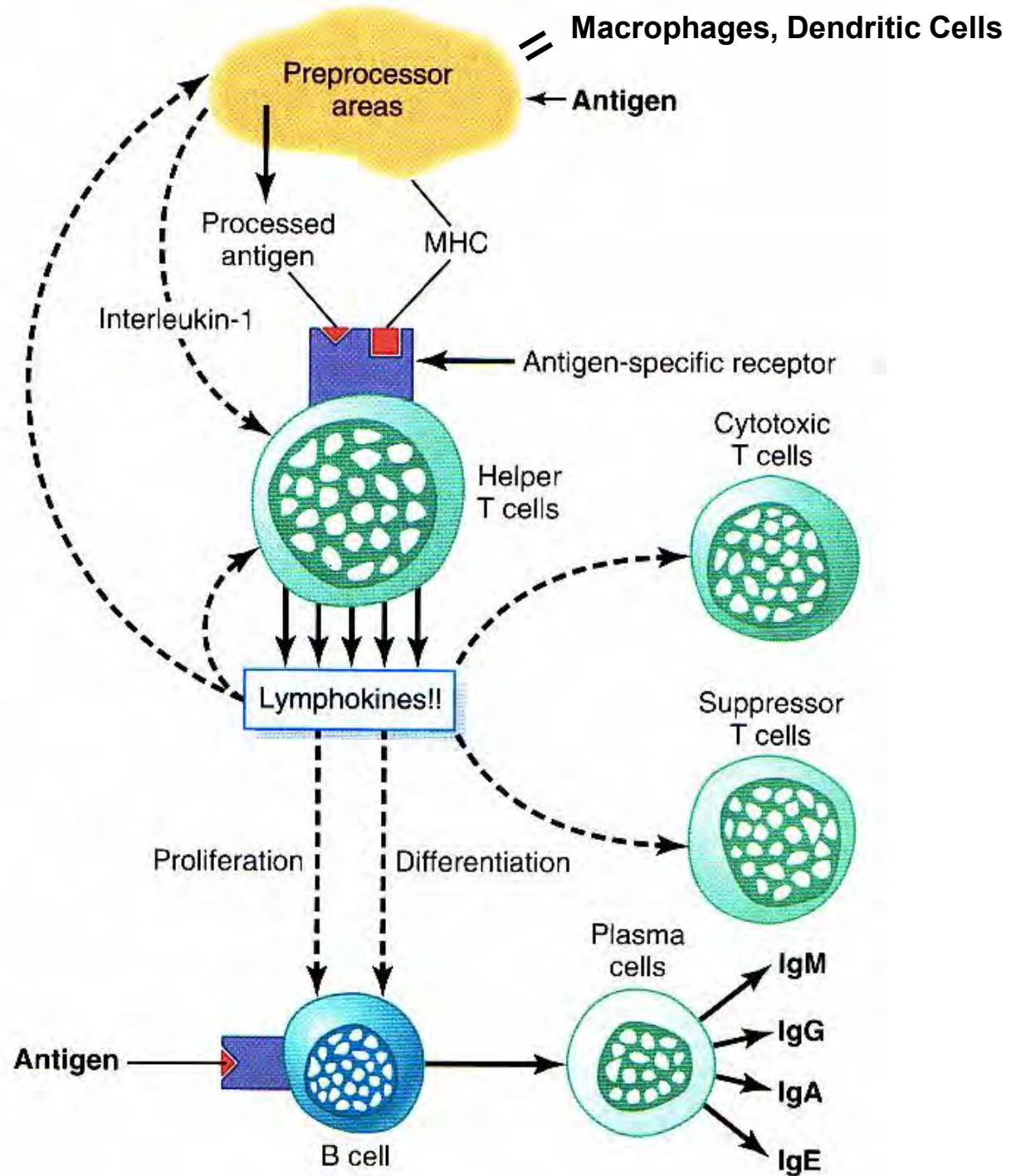


*Valence? 4*

IgM = Macroglobulin  
Pentamer!!!!



*Valence?* 10



G&H 2011 fig 34-8  
 G&H 2016 fig 35-8

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



# *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://educationalgames.nobelprize.org/educational/>





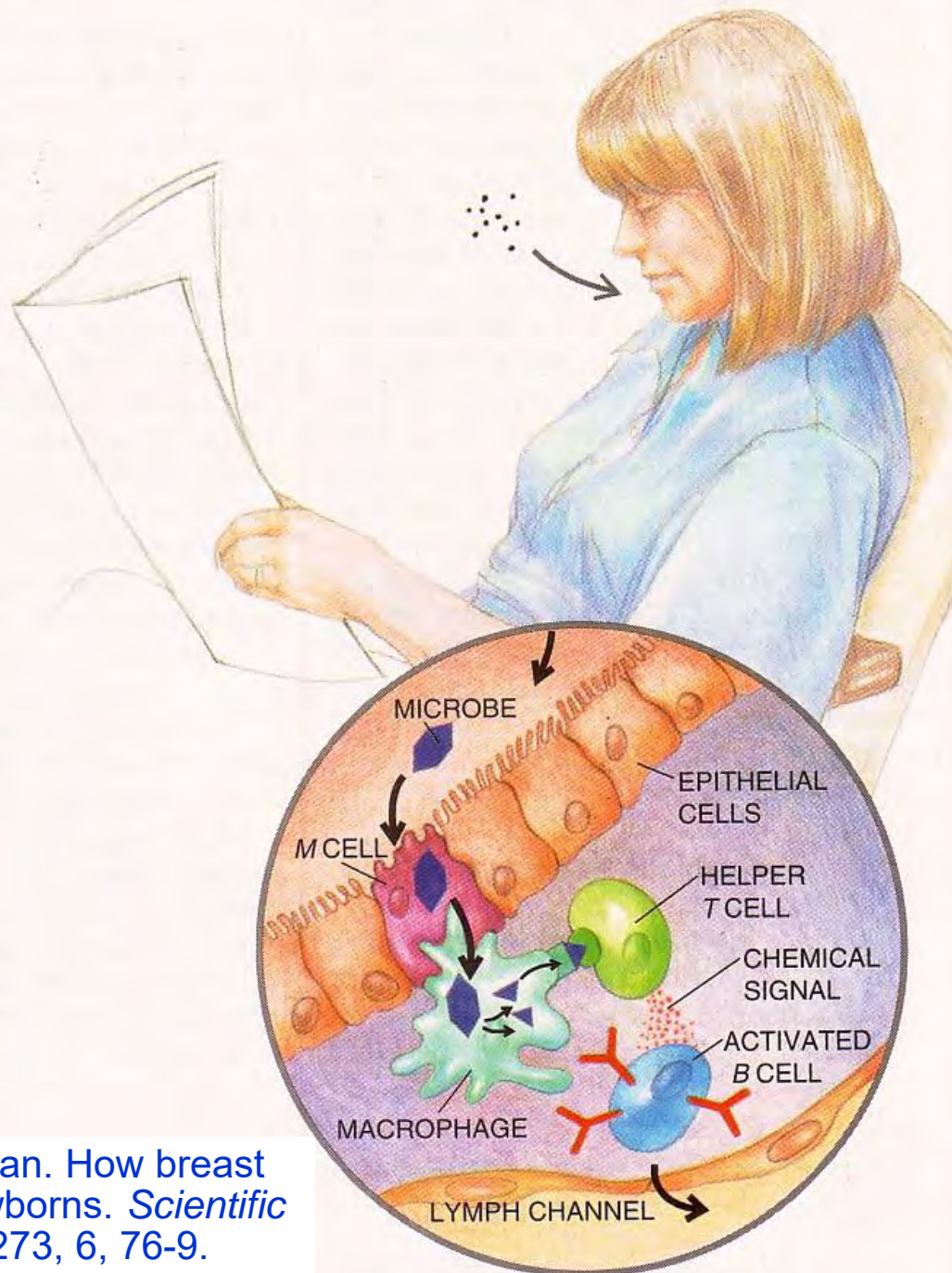
# ***Dr. Louis Picker of OHSU on track to cure HIV!***



[http://www.oregonlive.com/health/index.ssf/2015/11/  
louis\\_pickers\\_hiv\\_vaccine\\_erad.html](http://www.oregonlive.com/health/index.ssf/2015/11/louis_pickers_hiv_vaccine_erad.html)

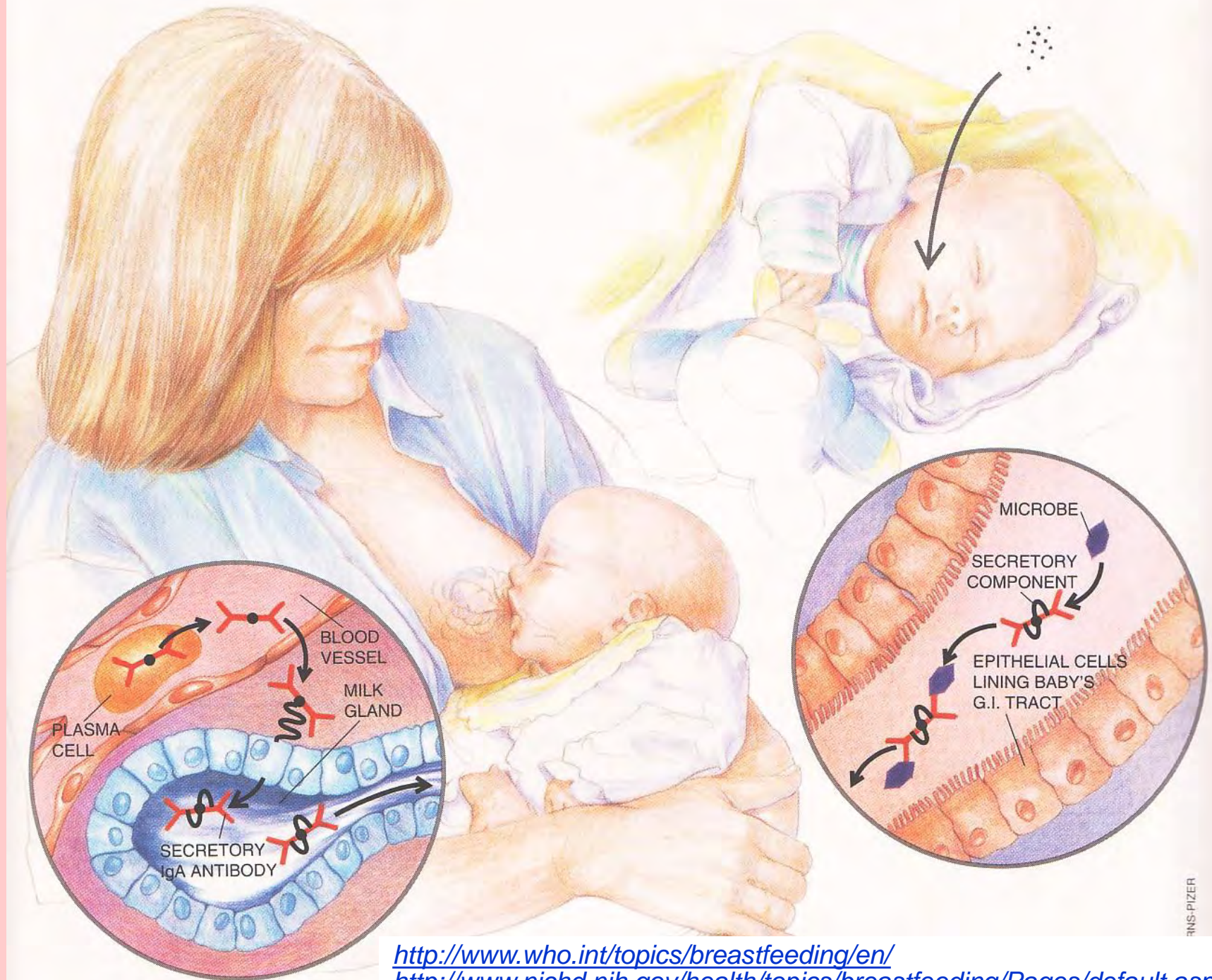
[http://www.oregonlive.com/health/index.ssf/2015/11/  
superstar\\_scientist\\_dr\\_louis\\_p.html](http://www.oregonlive.com/health/index.ssf/2015/11/superstar_scientist_dr_louis_p.html)

<https://www.youtube.com/watch?v=ITwG6O9G81g>



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

Sci Am Dec 1995  
Dana Burns-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

### White Blood Cells

*B* 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.

*T* 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>



# 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.

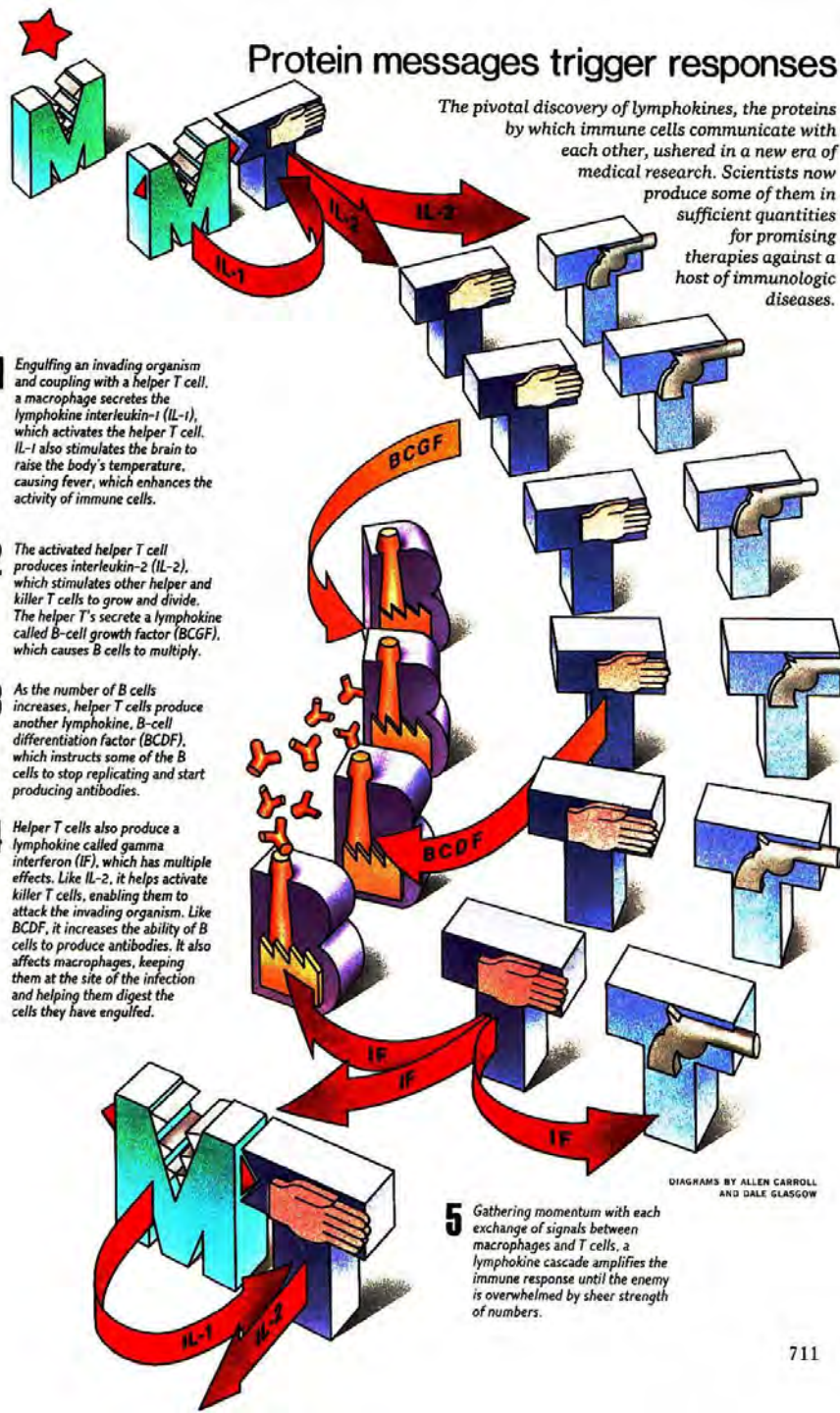
**1** Engulfing an invading organism and coupling with a helper T cell, a macrophage secretes the lymphokine interleukin-1 (IL-1), which activates the helper T cell. IL-1 also stimulates the brain to raise the body's temperature, causing fever, which enhances the activity of immune cells.

**2** The activated helper T cell produces interleukin-2 (IL-2), which stimulates other helper and killer T cells to grow and divide. The helper T's secrete a lymphokine called B-cell growth factor (BCGF), which causes B cells to multiply.

**3** As the number of B cells increases, helper T cells produce another lymphokine, B-cell differentiation factor (BCDF), which instructs some of the B cells to stop replicating and start producing antibodies.

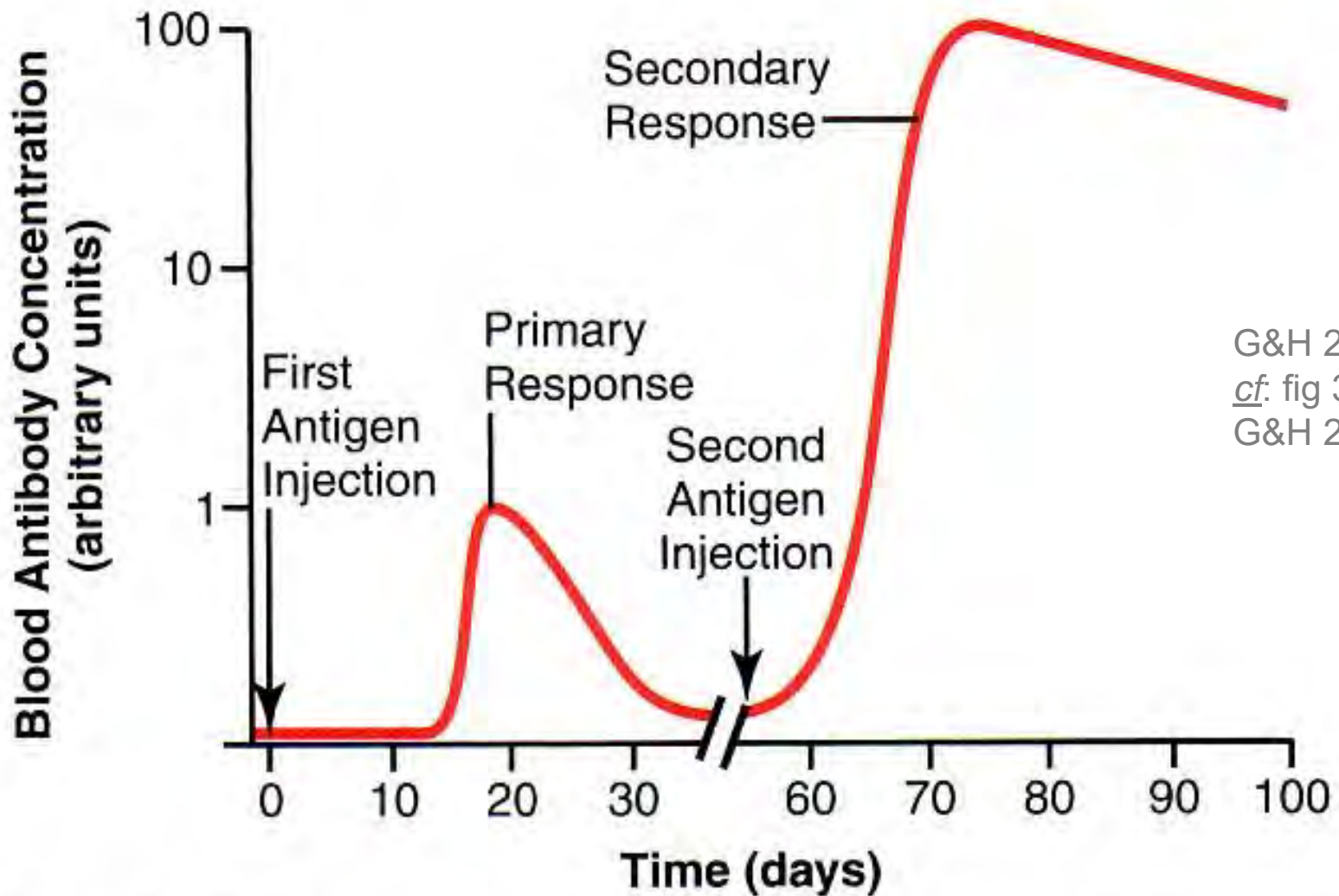
**4** Helper T cells also produce a lymphokine called gamma interferon (IF), which has multiple effects. Like IL-2, it helps activate killer T cells, enabling them to attack the invading organism. Like BCDF, it increases the ability of B cells to produce antibodies. It also affects macrophages, keeping them at the site of the infection and helping them digest the cells they have engulfed.

**5** Gathering momentum with each exchange of signals between macrophages and T cells, a lymphokine cascade amplifies the immune response until the enemy is overwhelmed by sheer strength of numbers.



DIAGRAMS BY ALLEN CARROLL AND DALE GLASGOW





G&H 2011  
*cf.* fig 35-3  
G&H 2016

**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.