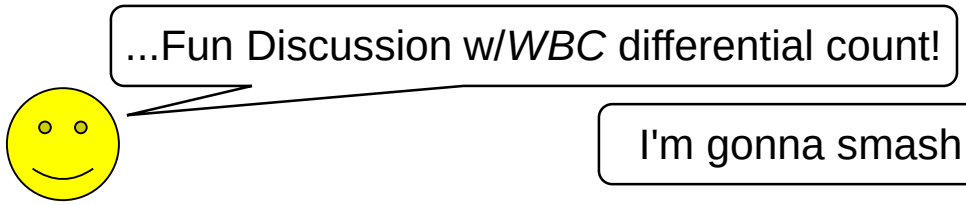
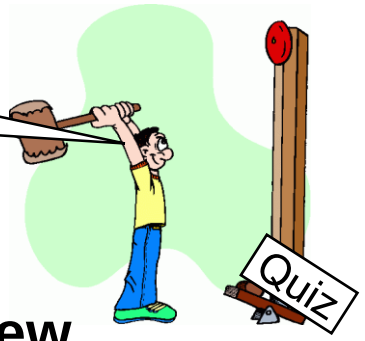
BI 358 Lecture 7





I. ***Announcements*** **Quiz 2 on Digestion & Nutrition! Q? Also, nutrition reports (*.doc/.docx* + *.pdfs*) by e-mail to Stacy or Conor by 5 pm today! Outlines? Lab review.**

II. ***Body Resistance to Infection II*** **G&H ch 32 & 33 + L Sherwood 2012, Stuart Fox, Daniel Chiras, Basiro Davey**

A. ***Med Physiology News*** **Louis Picker @ OHSU on track to cure HIV! Laughter is Medicine, Handwashing *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/

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/superstar_scientist_dr_louis_p.html

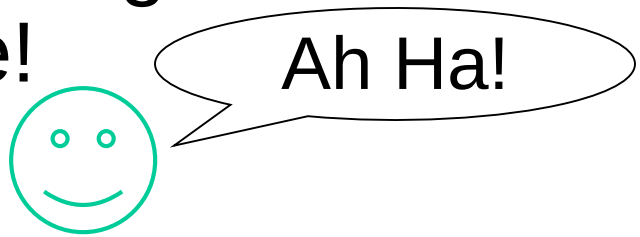
https://www.youtube.com/watch?v=ITwG6O9G81g

Laughter = Medicine!





- Laughter's most profound effects occur on the immune system.
- Laughter ↑γ-interferon, ↑B-cells, ↑T-cells and ↓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!



SEBB Newsletter 1997

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

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

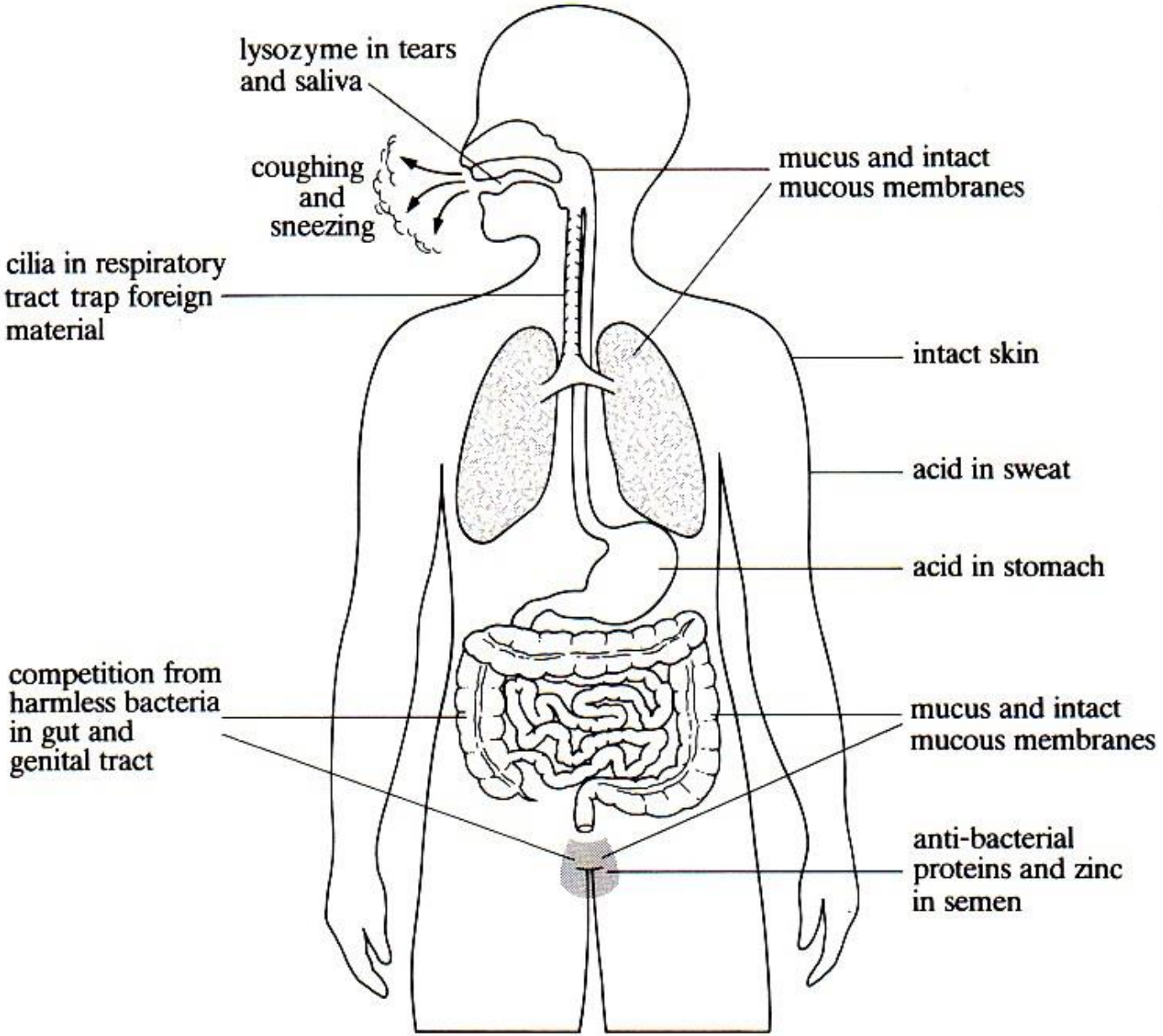
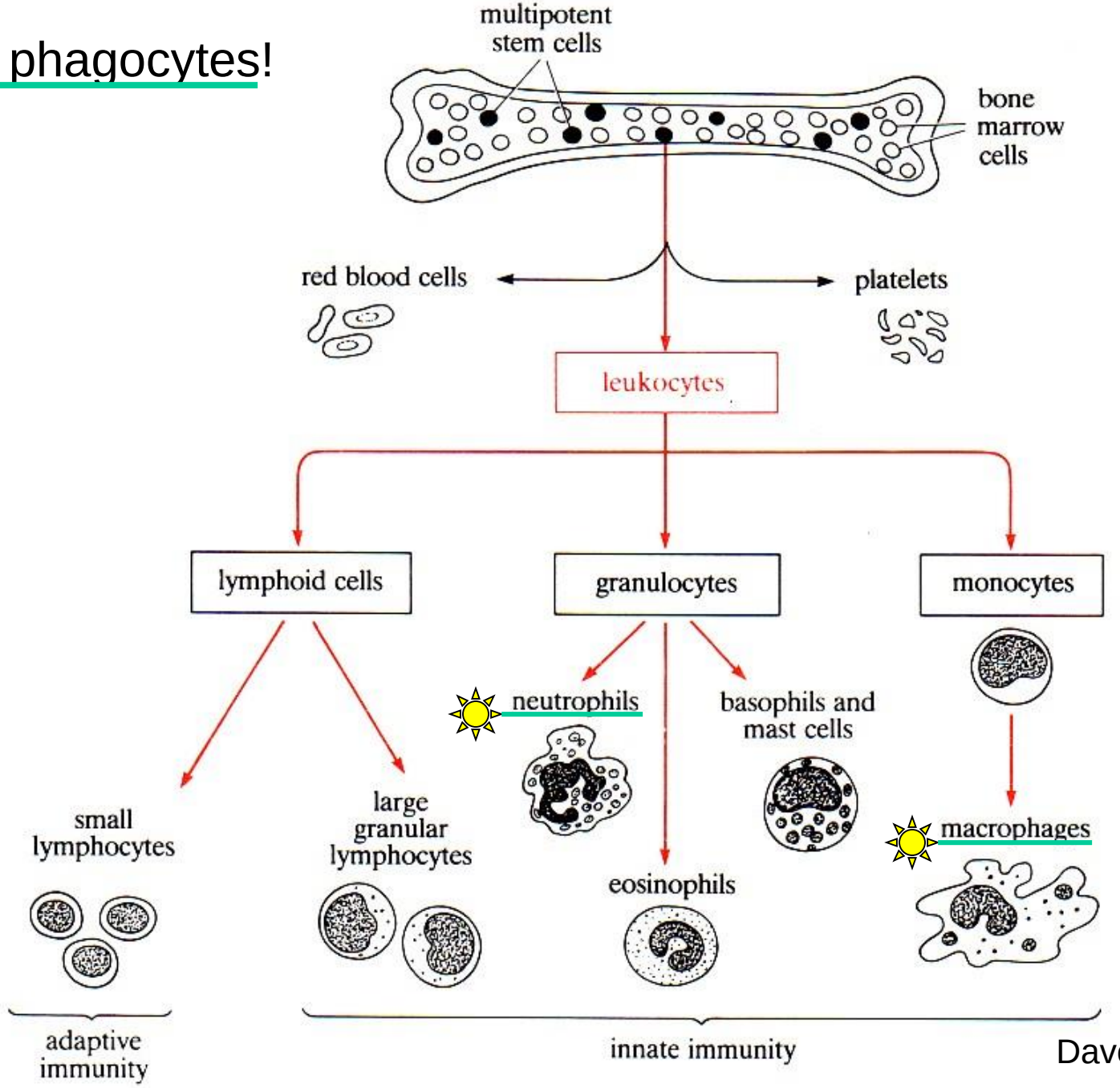


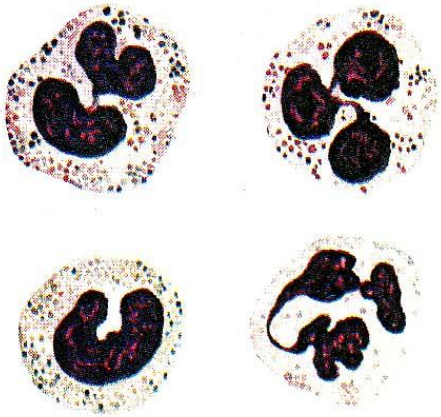
FIGURE 2.1 Summary of the main physical, chemical and mechanical barriers to infection entering the human body.

Davey 1990 p 12

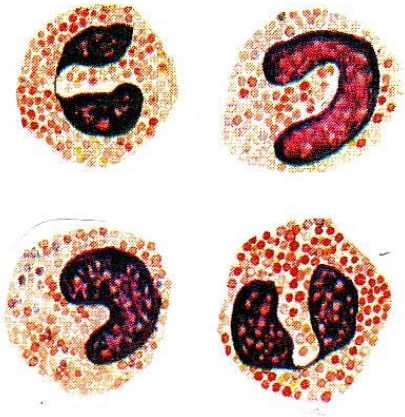
Good phagocytes!



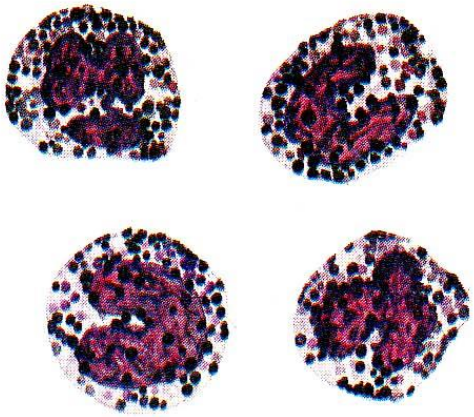
Davey 1990 p 13



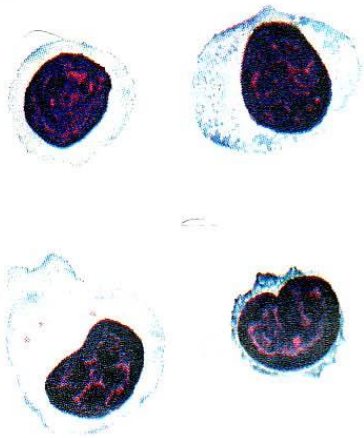
NEUTROPHILS



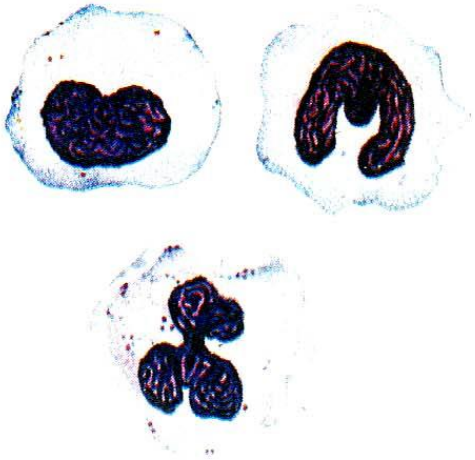
EOSINOPHILS



BASOPHILS

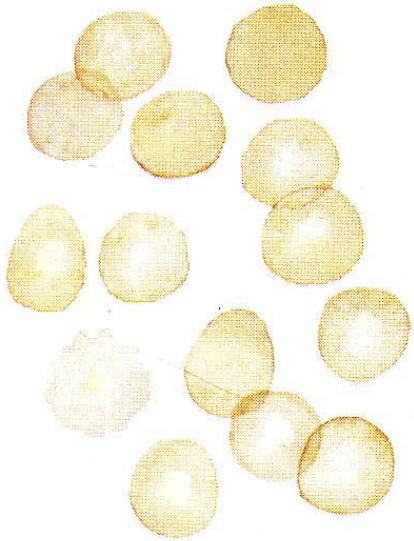


LYMPHOCYTES



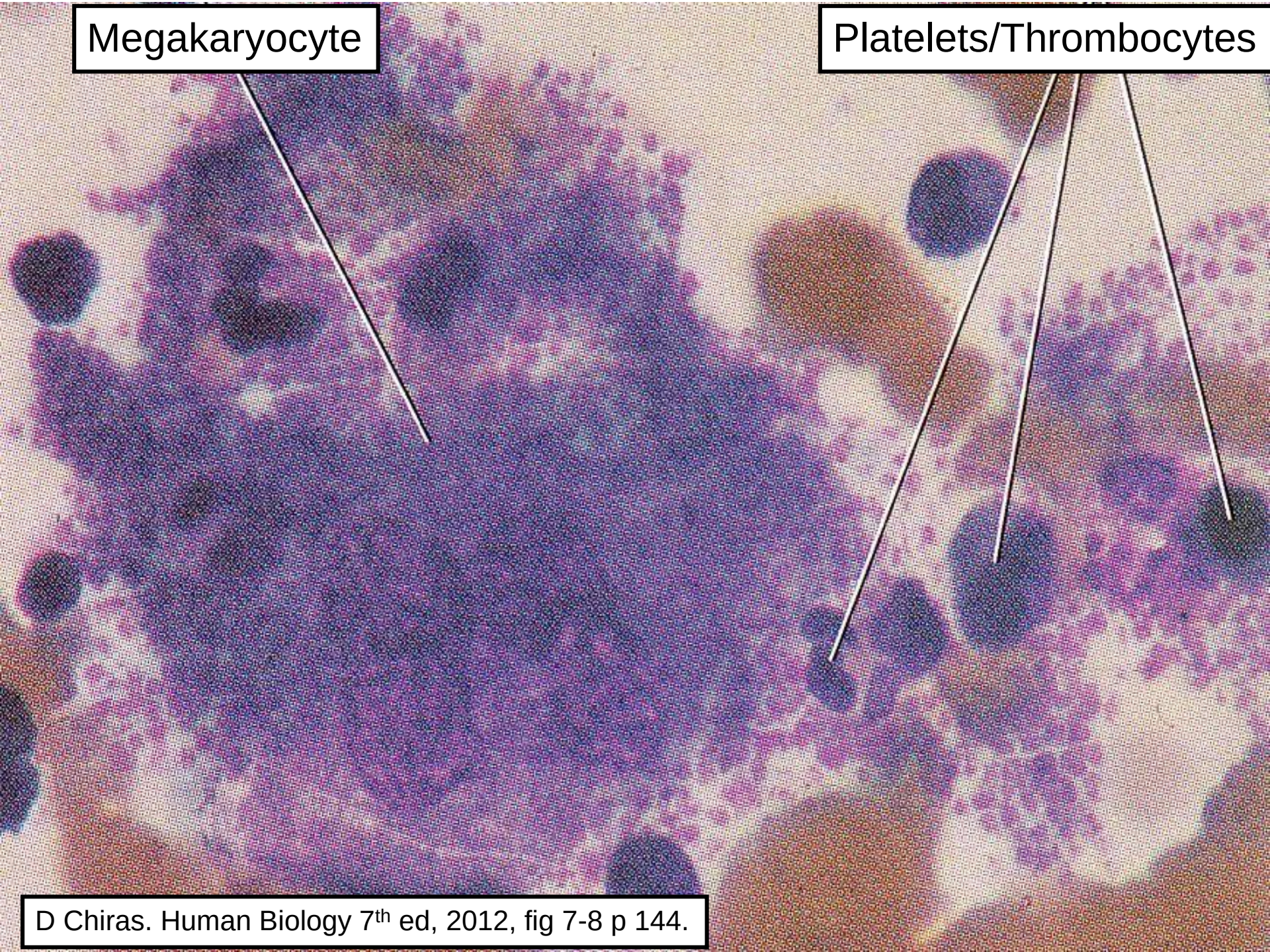
MONOCYTES

PLATELETS

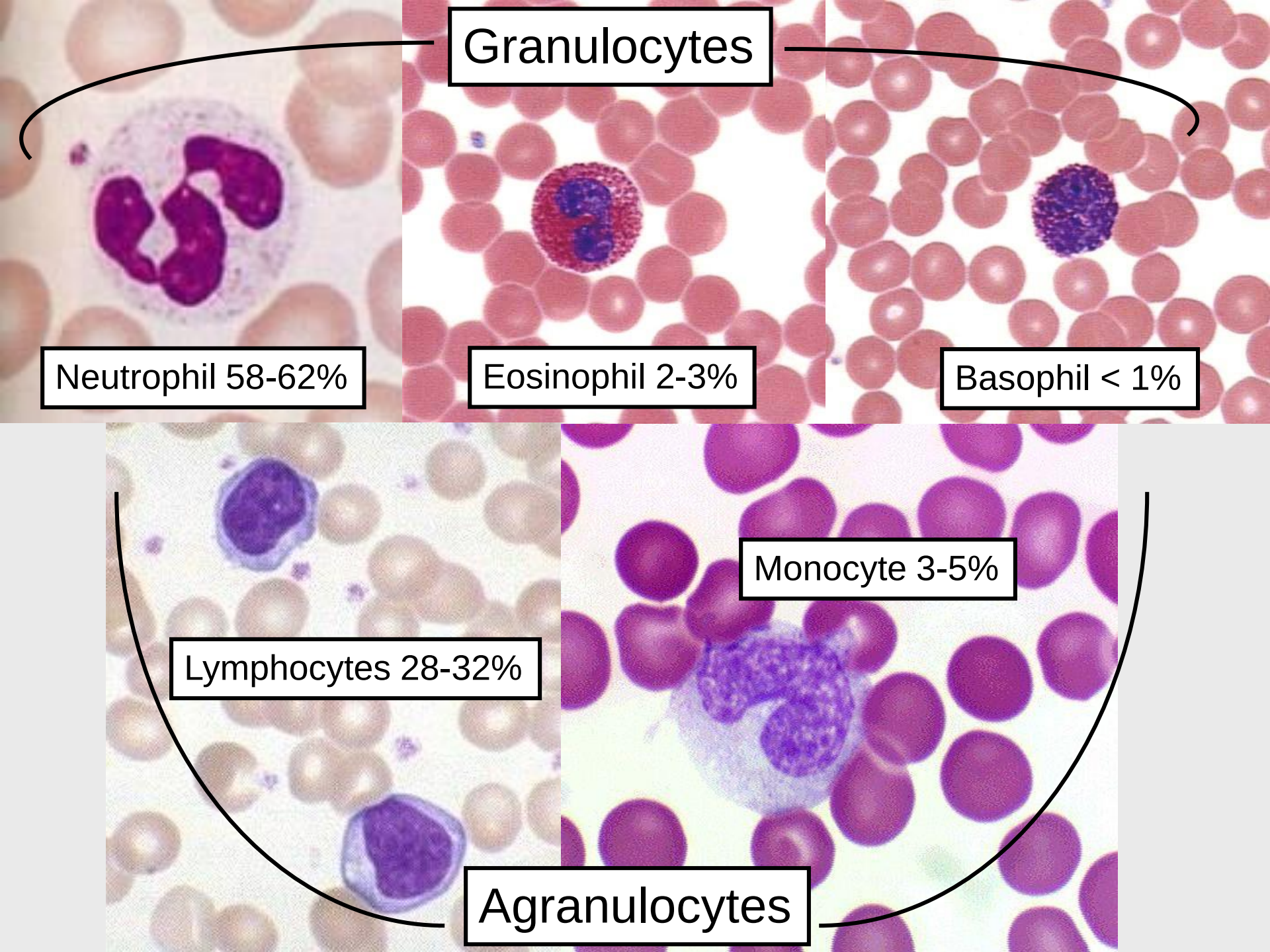


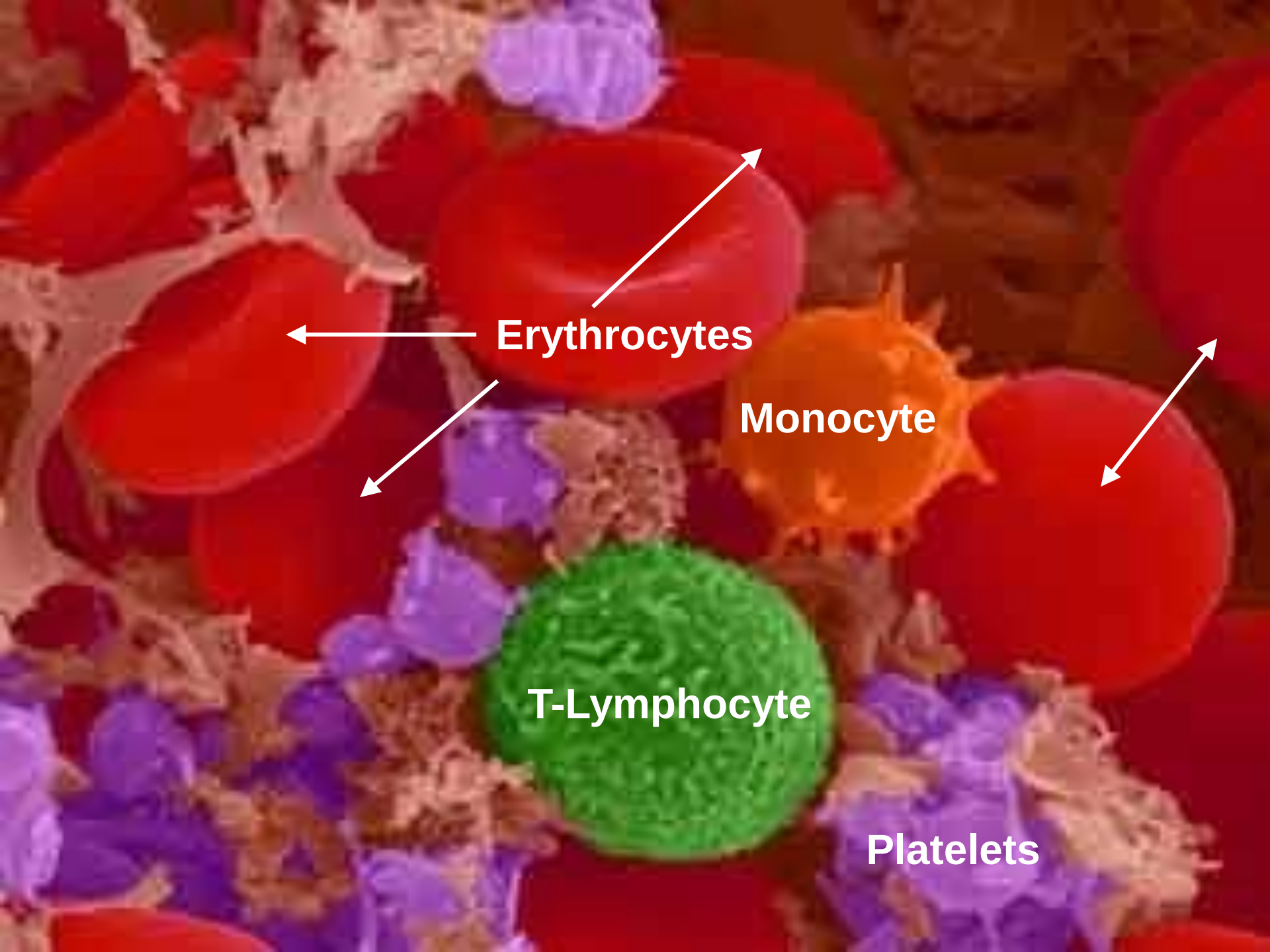
ERYTHROCYTES

SI Fox 1987 p 376



D Chiras. Human Biology 7th ed, 2012, fig 7-8 p 144.


Granulocytes
Neutrophil 58-62%
Eosinophil 2-3%
Basophil < 1%
Lymphocytes 28-32%
Monocyte 3-5%
Agranulocytes


Erythrocytes
Monocyte
T-Lymphocyte
Platelets

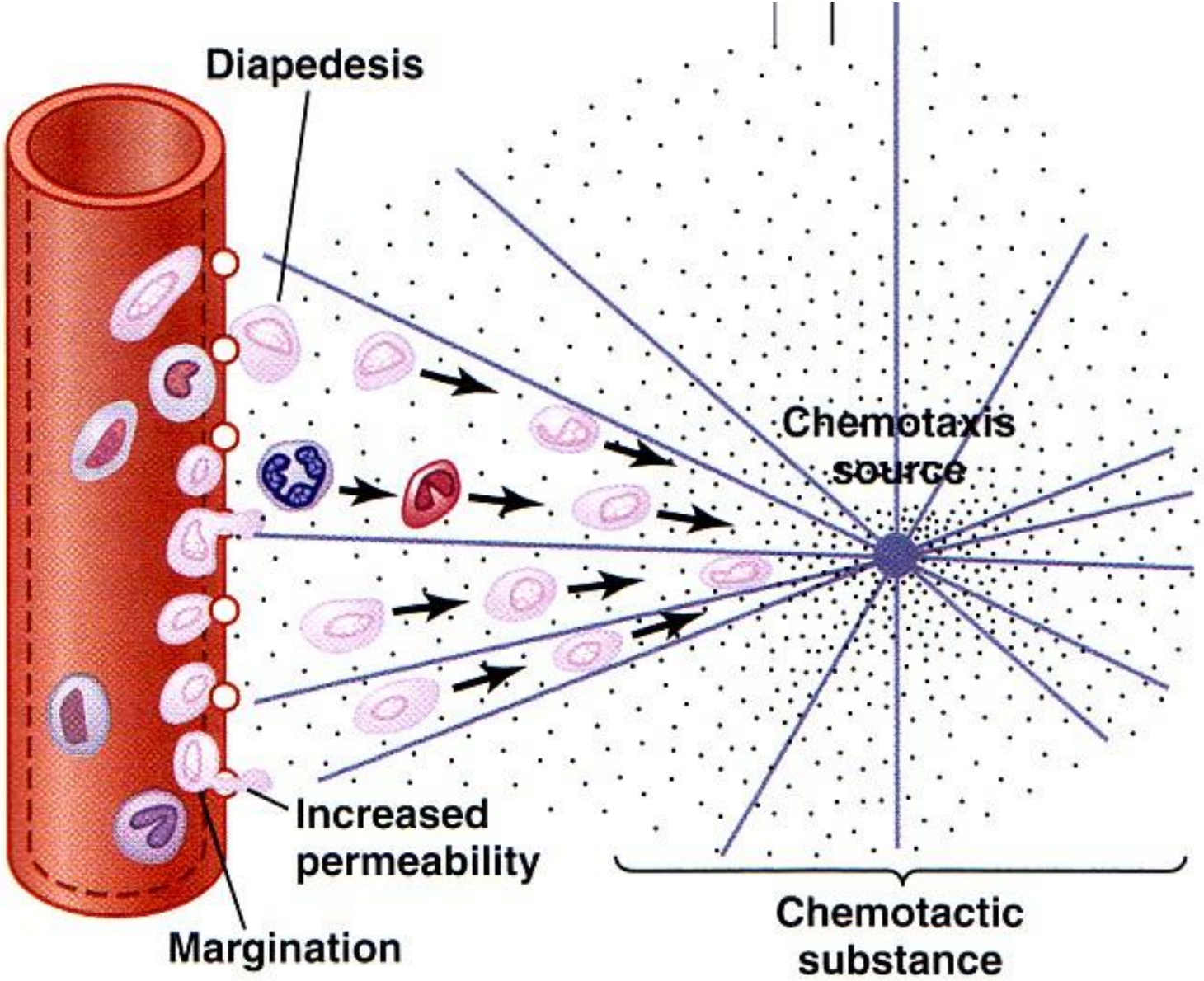
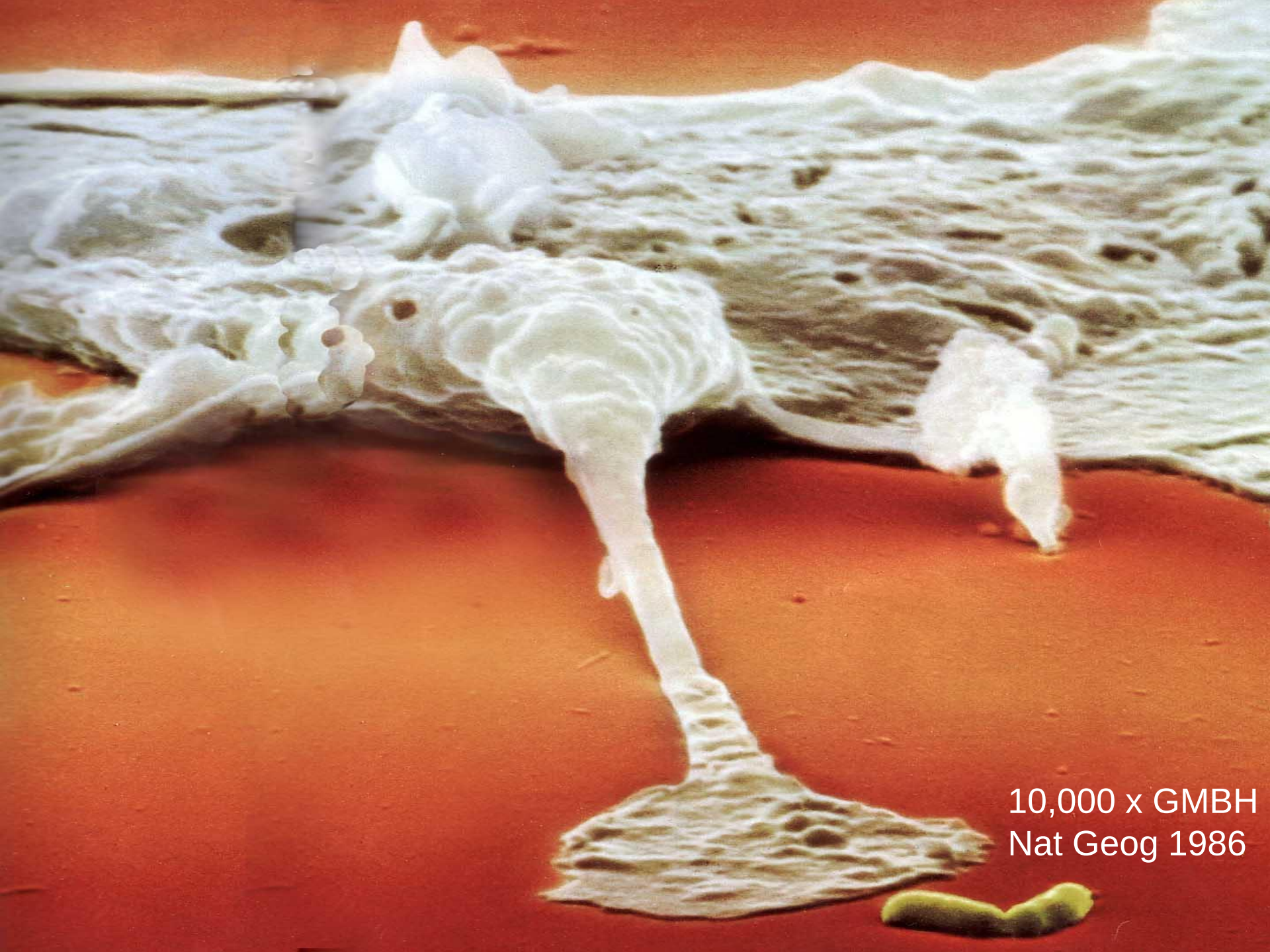
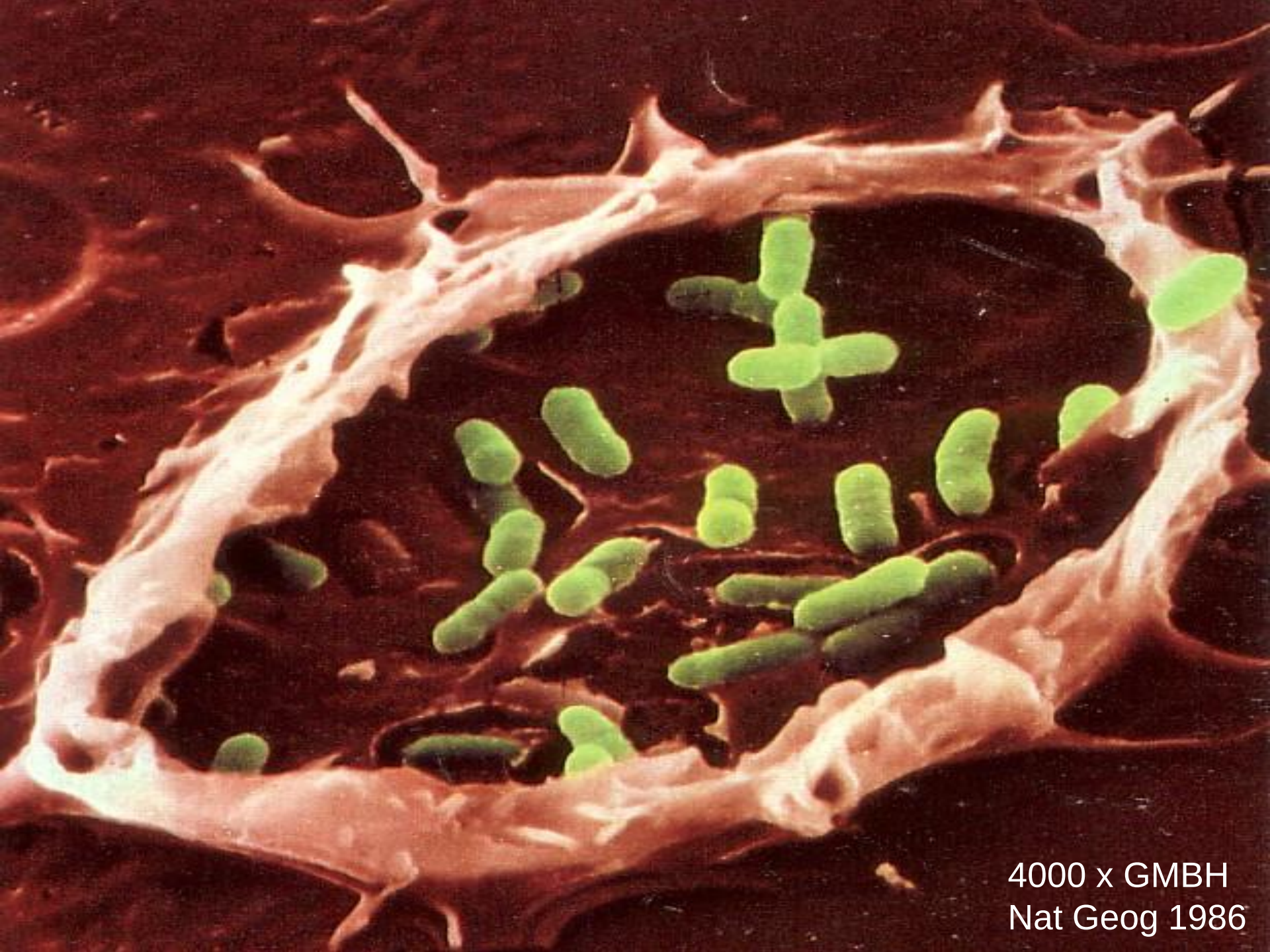
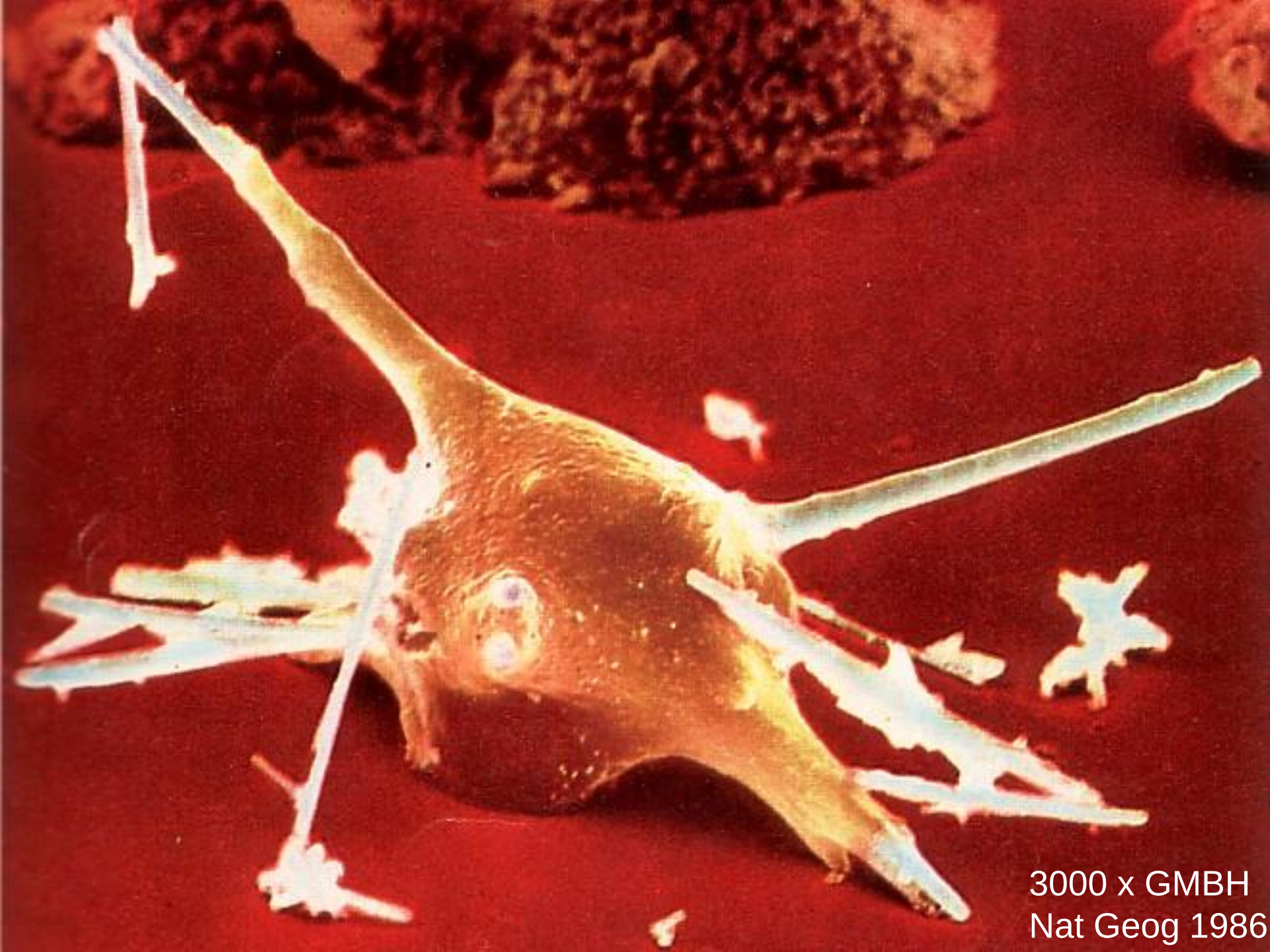


Figure 33-2 Movement of neutrophils by *diapedesis* through capillary pores and by *chemotaxis* toward an area of tissue damage. G&H 2011


10,000 x GMBH
Nat Geog 1986

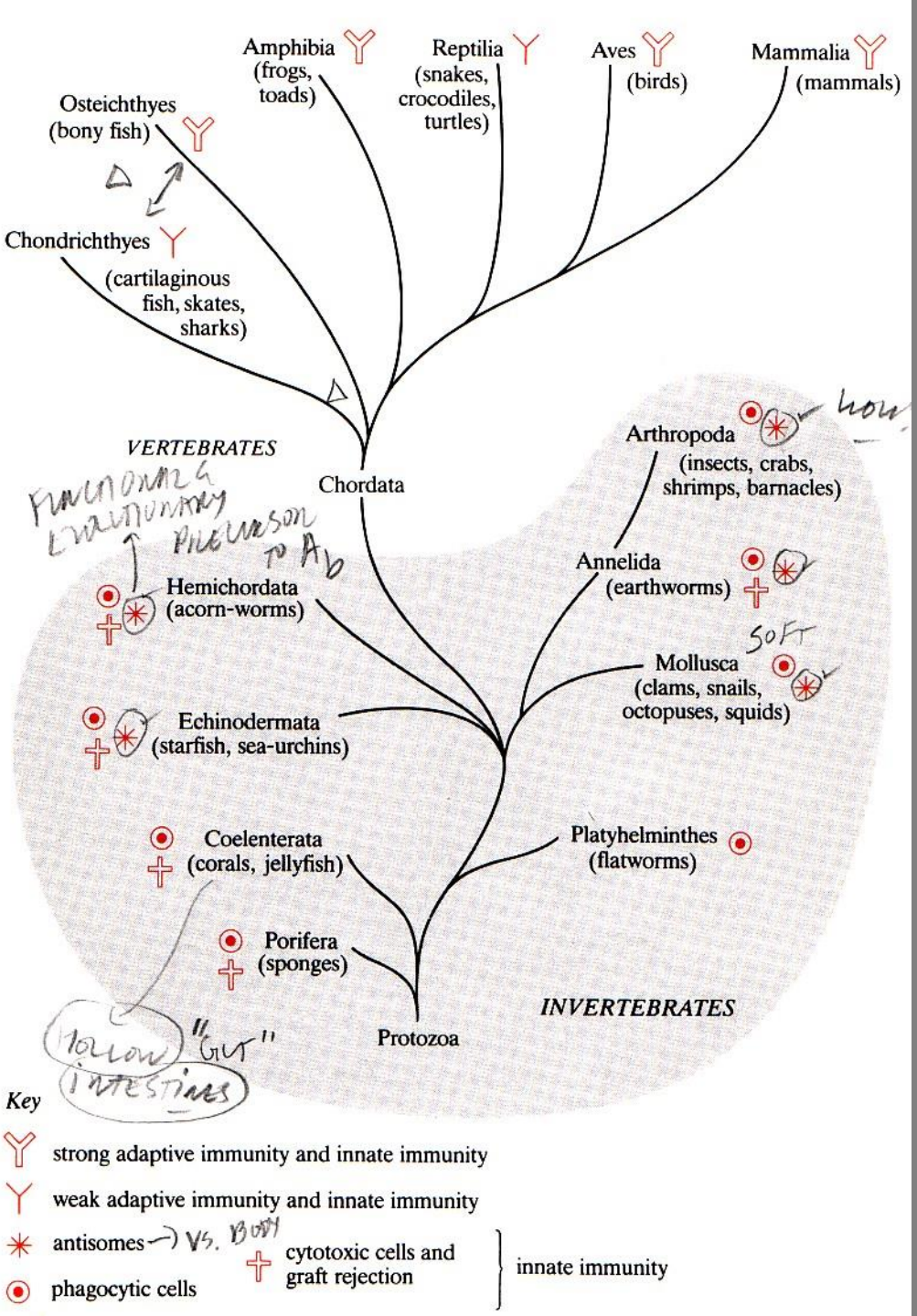

4000 x GMBH
Nat Geog 1986


7000 x GMBH
Nat Geog 1986


3000 x GMBH
Nat Geog 1986

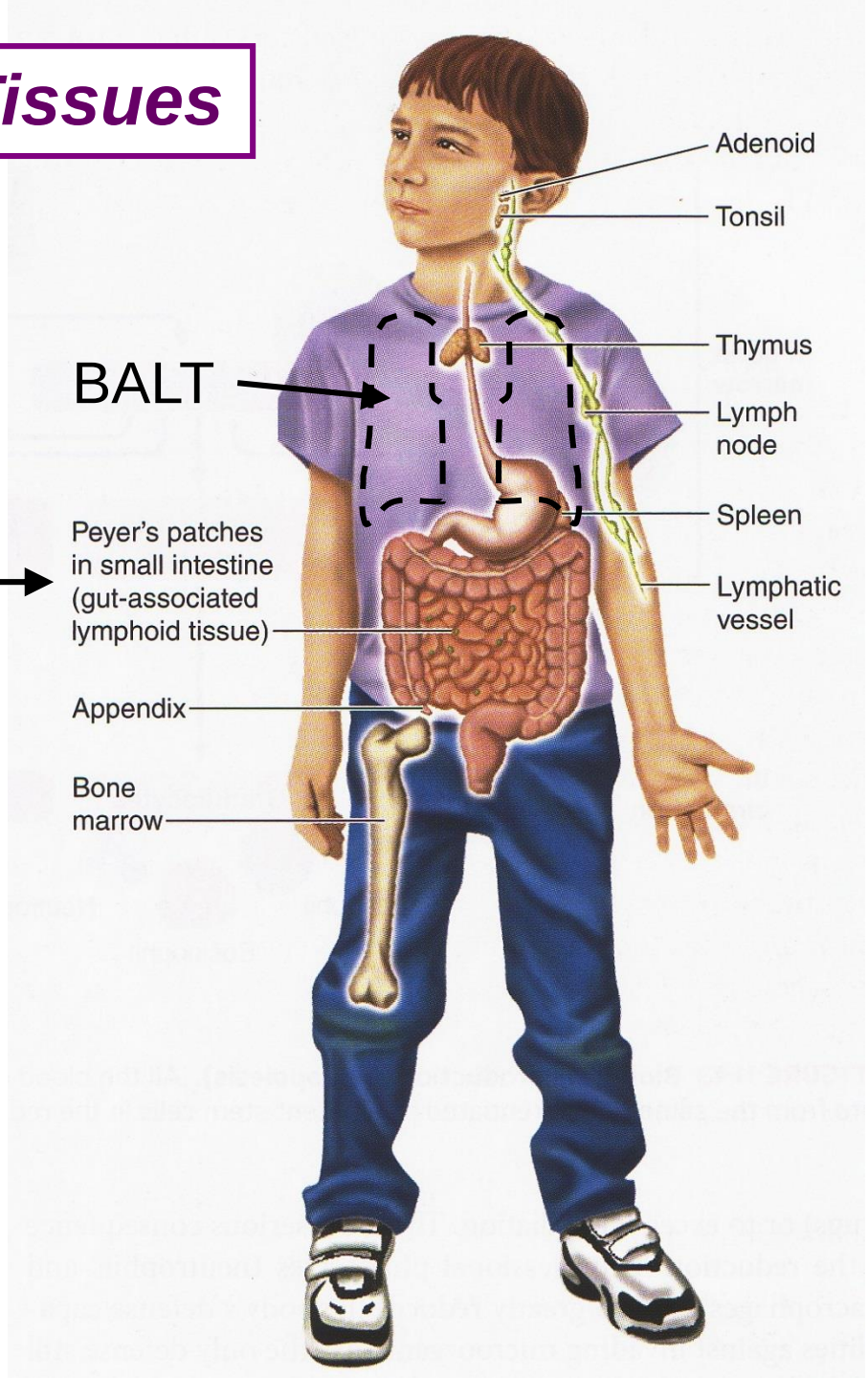
10,000 x GMBH
Nat Geog 1986

7000 x GMBH
Nat Geog 1986



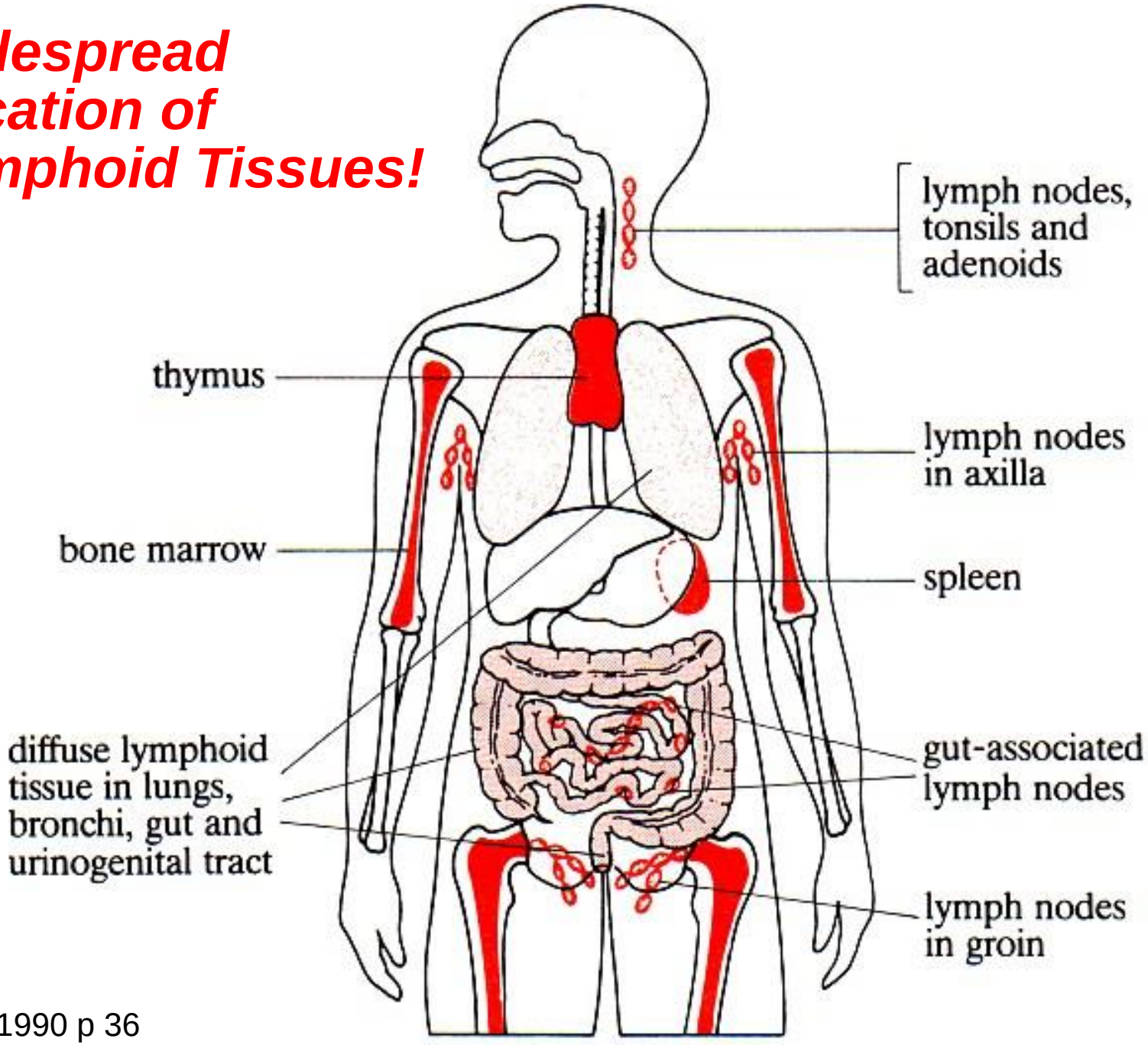
Davey 1990 p 7

Lymphoid Tissues



L Sherwood 2012

Widespread Location of Lymphoid Tissues!

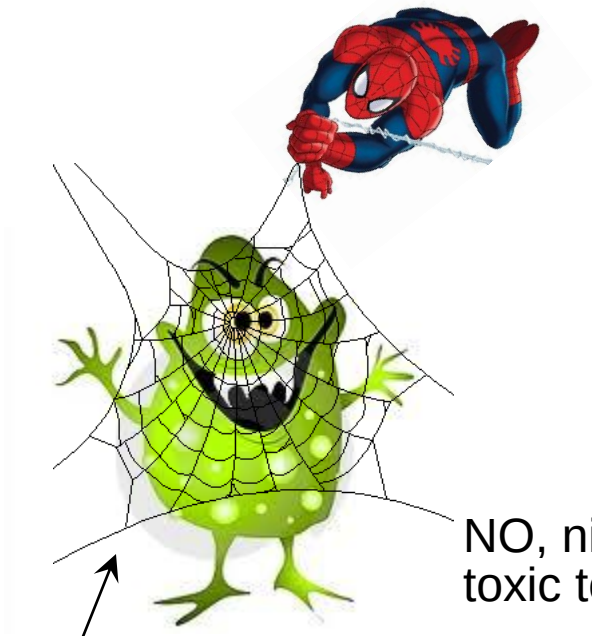


Davey 1990 p 36

Immunity

Innate/Inborn/Nonspecific	Adaptive/Acquired/Specific
1. Immediate, upon exposure to threatening agent	1. Delayed, selective targetting based on prior exposure
2. 1^0 effectors phagocytic specialists: neutrophils & macrophages	2. 1^0 effectors lymphocytes: T- & B-lymphocytes
3. "Eyes" are Toll-like receptors (TLRs) which recognize & bind with generic invader markers	3. "Eyes" are T- and B-cell receptors which bind with specific antigens
4. Inflammation, interferon, natural killer cells, complement (plasma proteins)	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^{2+} requirement

Prostaglandins

↑ Set point
Hypothalamus

NO, nitric oxide
toxic to microbes

EP, endogenous pyrogen

NSAIDs e.g. Aspirin

Should we use?

Lactoferrin
binds Fe^{2+}
↓ Replication

NETs!
Neutrophil
Extracellular
Traps

Kinins
activated

Mast Cells

Neutrophil

Macrophage

Pain receptors
↑ Chemotaxis

Histamine
↑ Vasodilation
↑ Capillary permeability

Anti-histamines

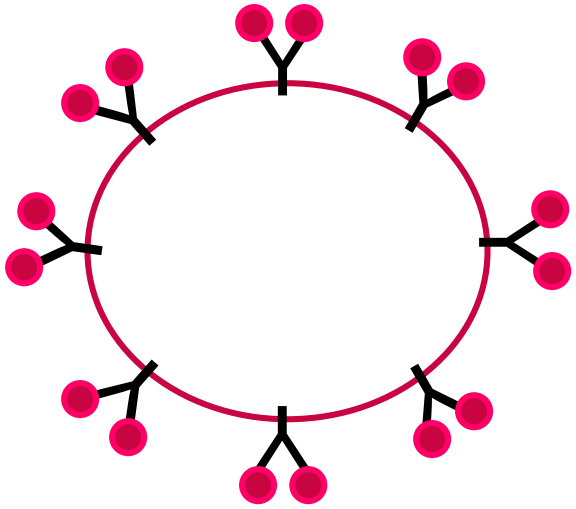

3000 x GMBH
Nat Geog 1986

Allergic Reactions, Mast Cells & Basophils?

Allergen = ●

IgE = Y

up to ½ million per cell!



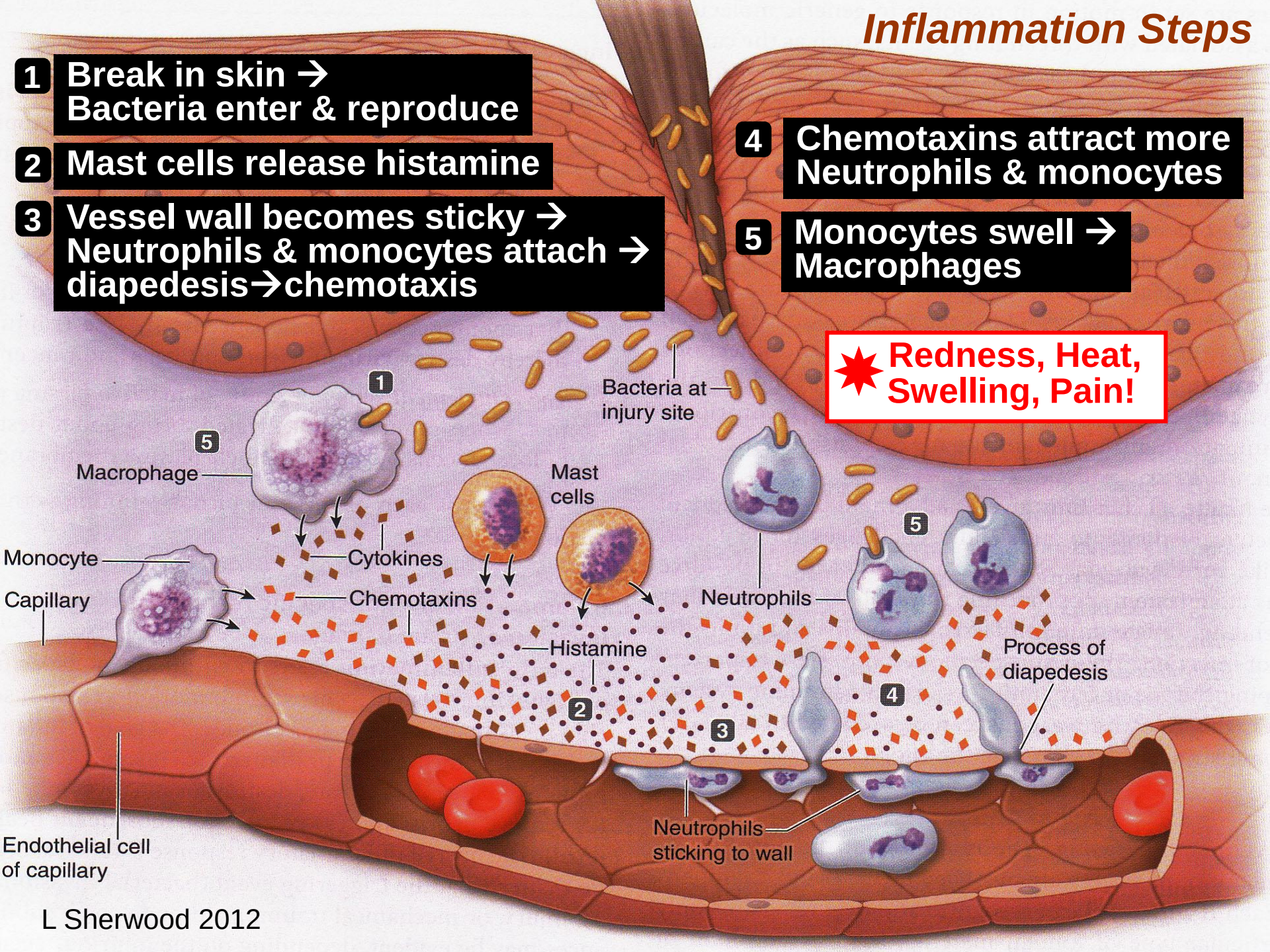
Mucous Membranes/Blood

- 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!



L Sherwood 2012

Glucocorticoids throw blanket over entire inflammatory process!

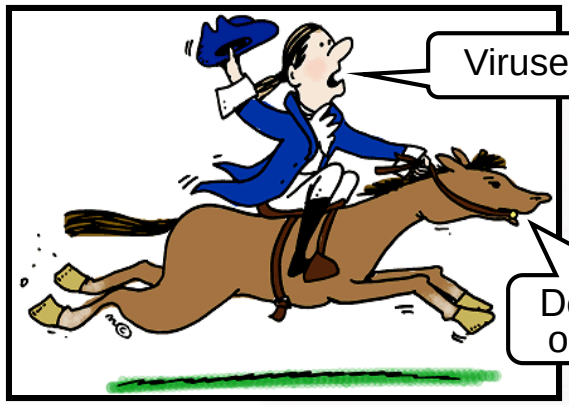
1. Certainly warranted to quiet down immune system during extreme flare ups of arthritis, asthma, poison ivy, rash, but must consider:

2. Destroy lymphocytes in lymphoid tissues.

3. ↓ Antibody/Immunoglobulin (Ig) production.

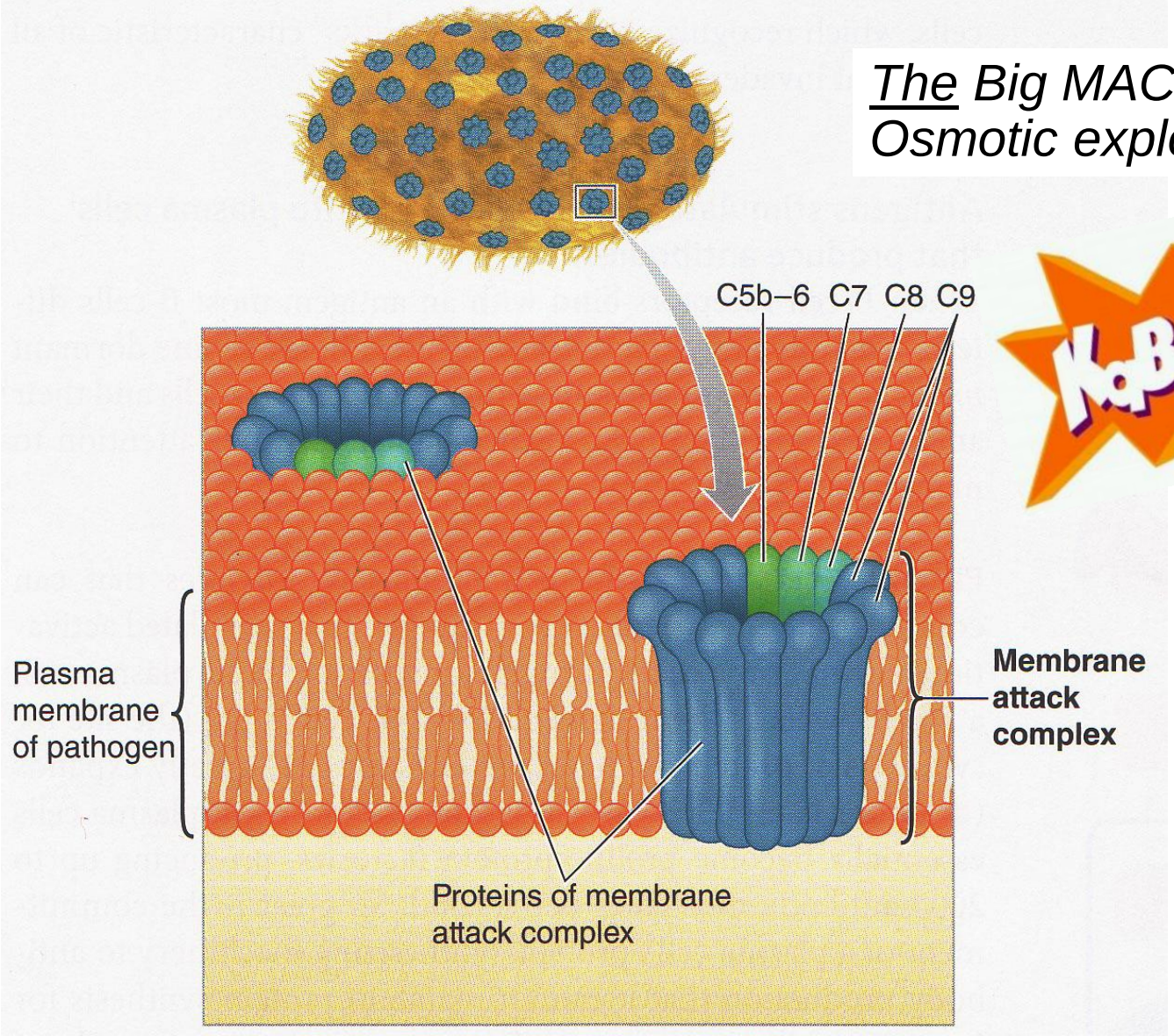
4. Make susceptible to bacterial infections.

Interferon Mechanisms



L Sherwood 2012

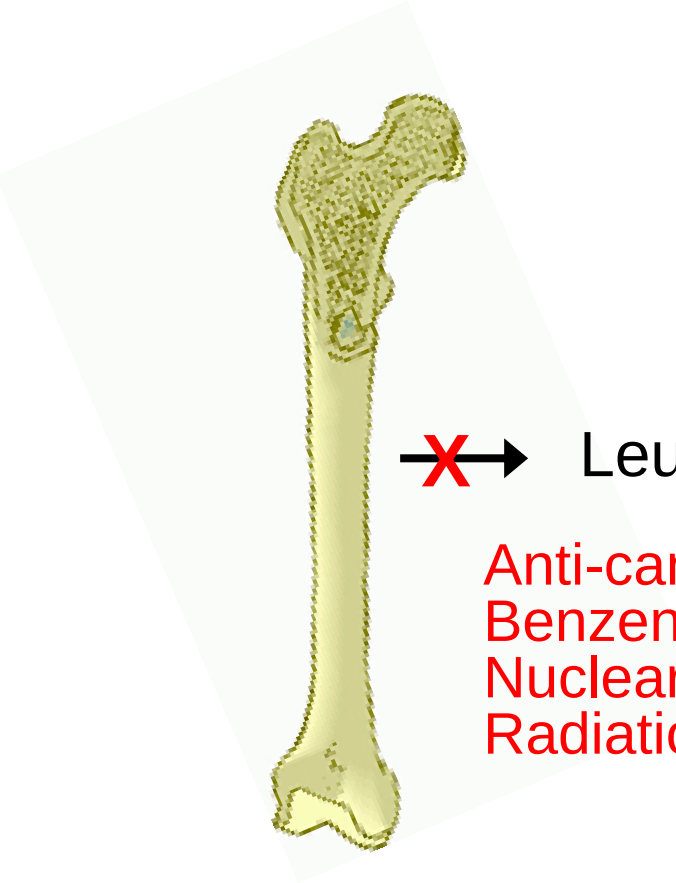
Activated Complement



<u>The</u> Big MAC to ♥!
Osmotic explosion!

L Sherwood 2012

WBC Adverse Effects



✗→ Leukocytes

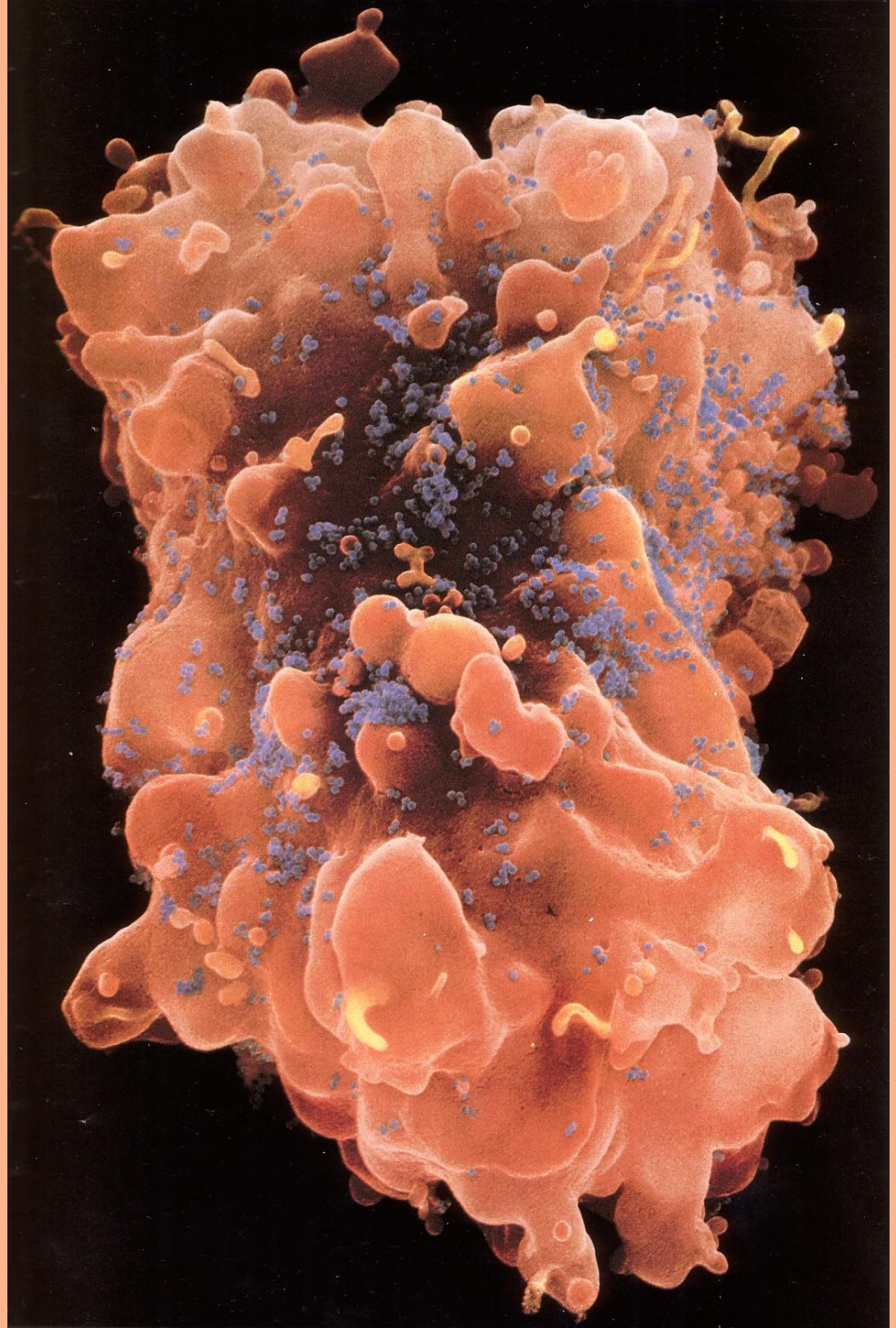
Anti-cancer drugs
Benzene
Nuclear blast
Radiation

↓ Professional phagocytes esp:
Neutrophils
Macrophages

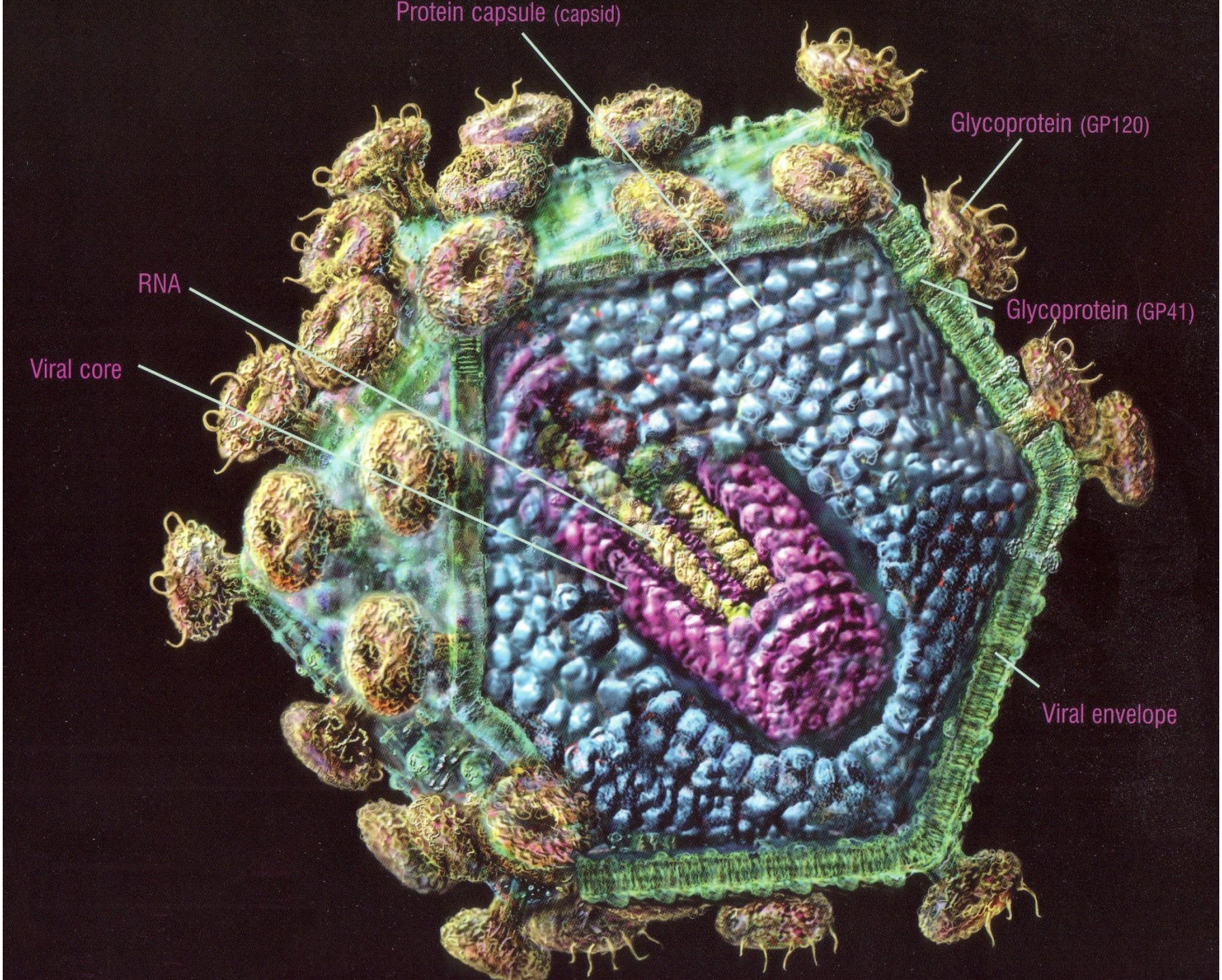
↓ Body defense vs. μ organisms!

Savior Lymphoid tissues or bone marrow transplant?

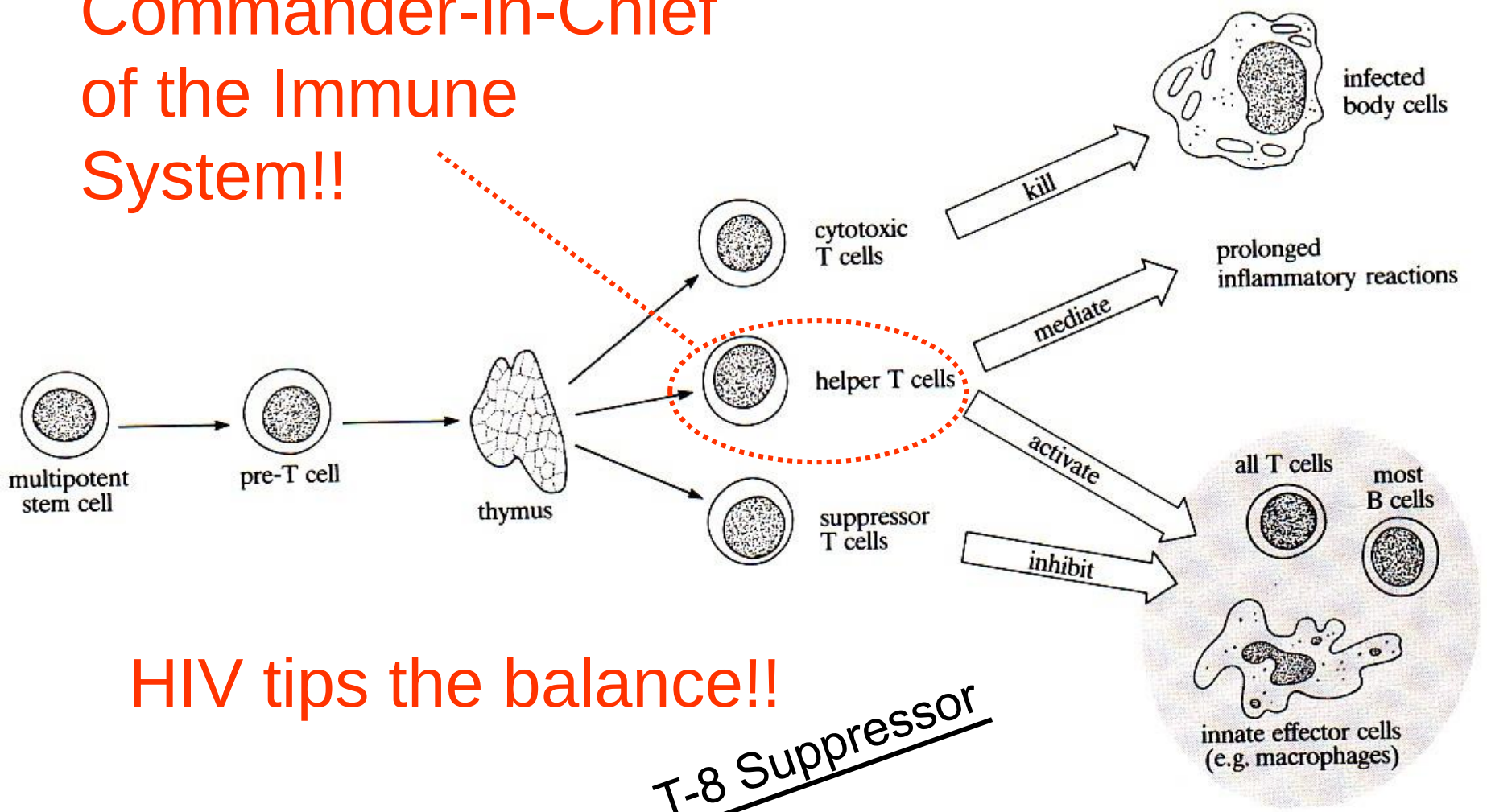
cf: *Leukemia* ≡ uncontrolled WBC proliferation, yet inadequate defense → other cell lines displaced → overwhelming infections & bleeding...



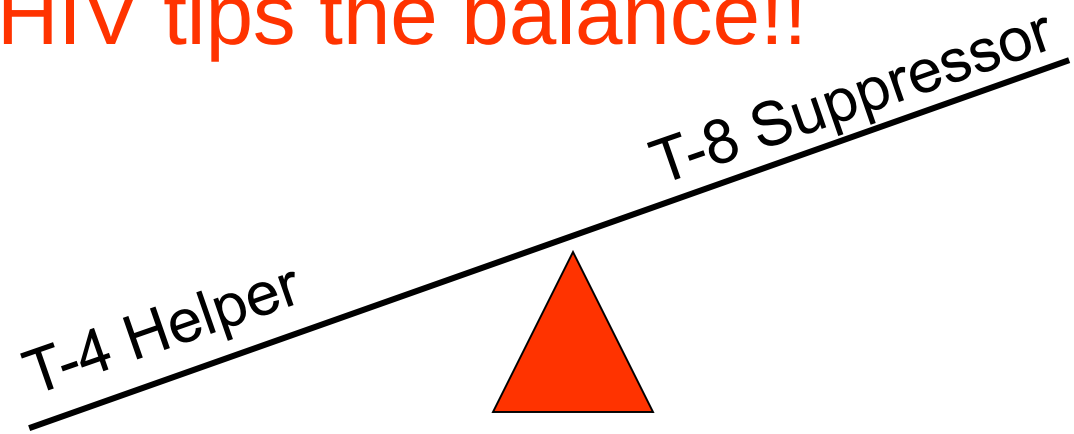
30,000 x GMBH
Nat Geog 1986


Protein capsule (capsid)
Glycoprotein (GP120)
RNA
Glycoprotein (GP41)
Viral core
Viral envelope

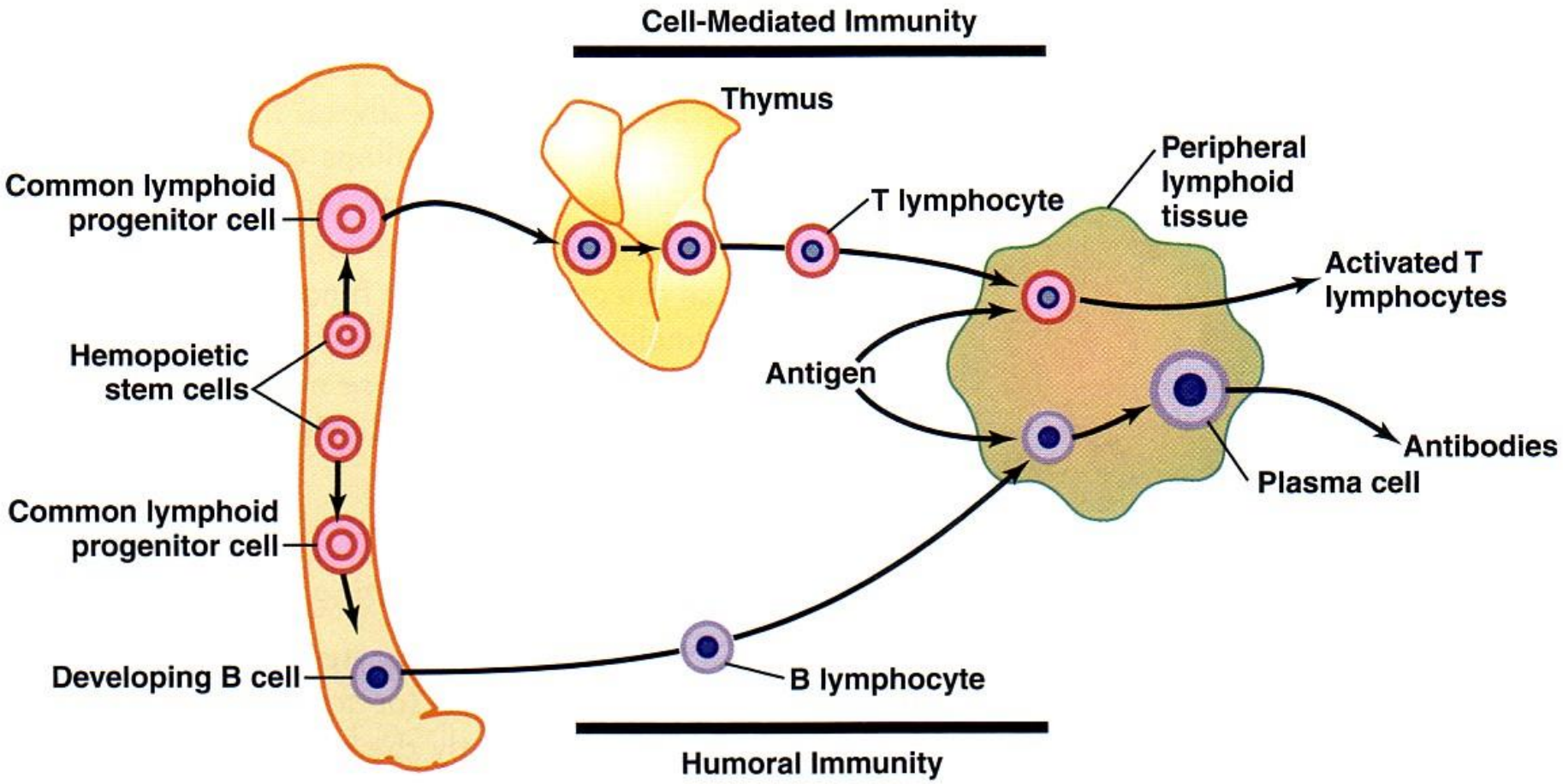
Commander-in-Chief of the Immune System!!



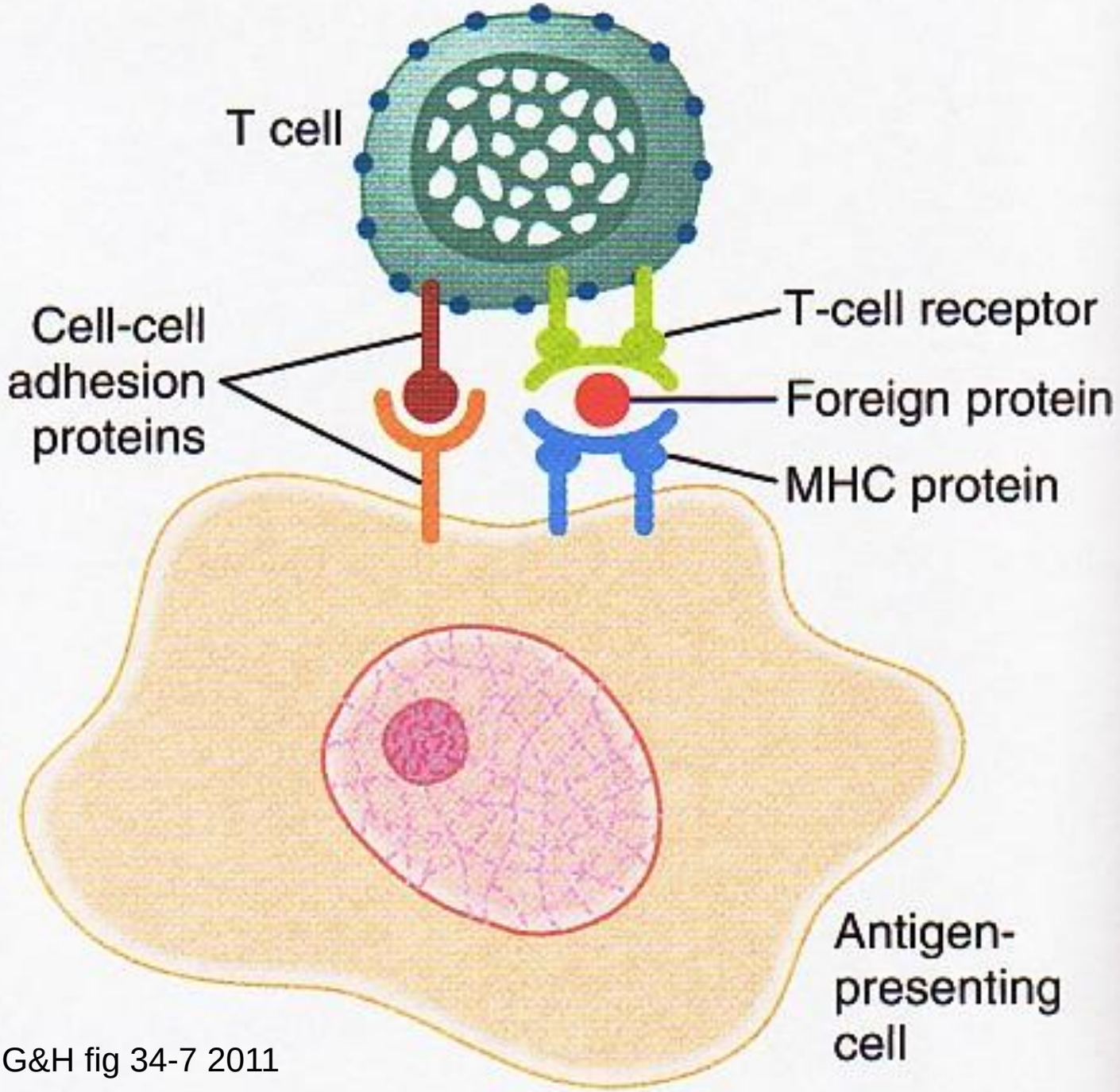
HIV tips the balance!!



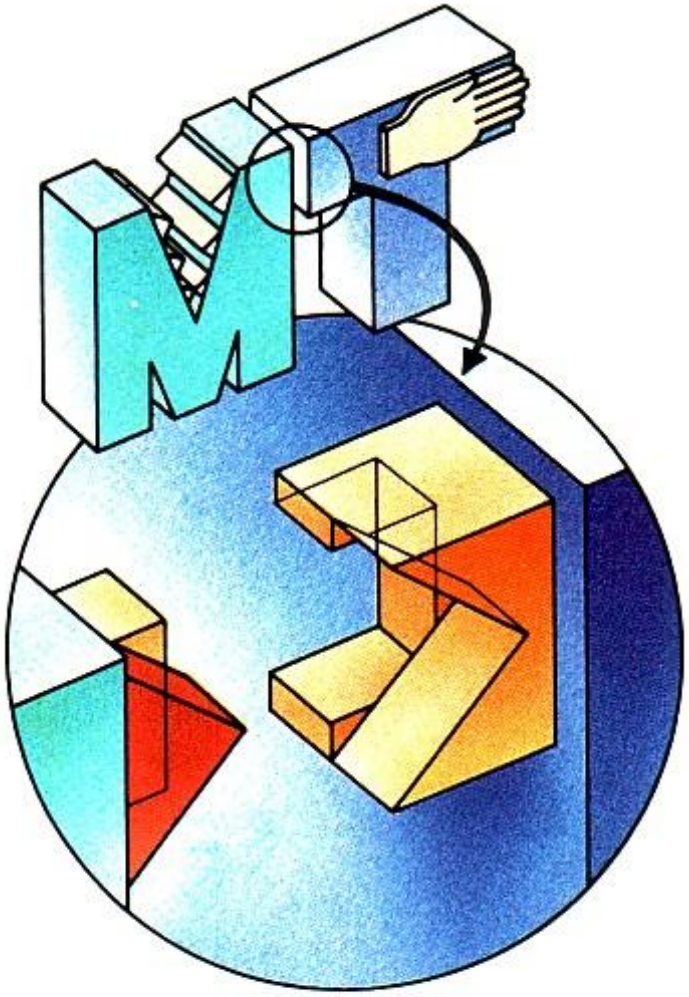
Davey 1990 p 30



G&H fig 34-1 2011



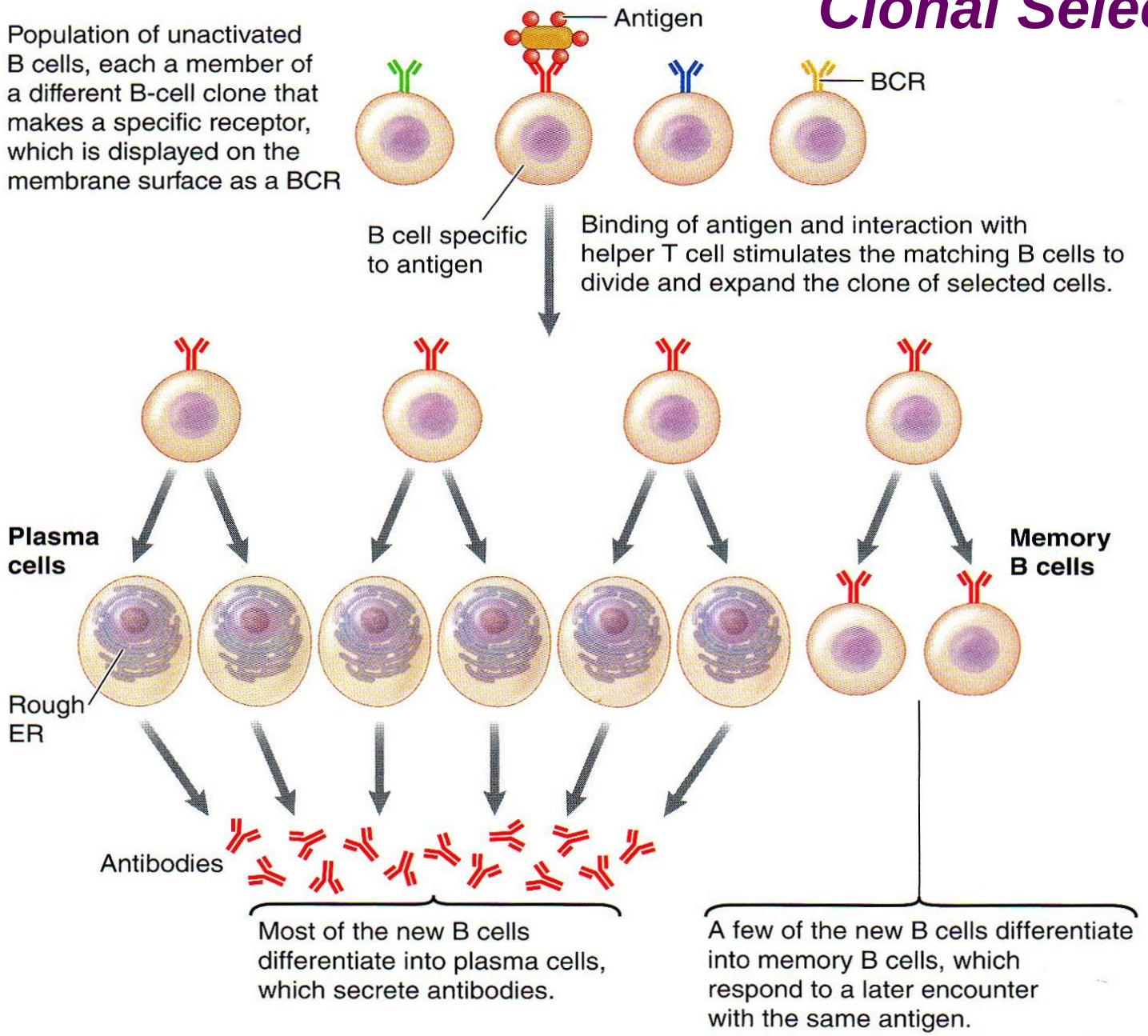
G&H fig 34-7 2011



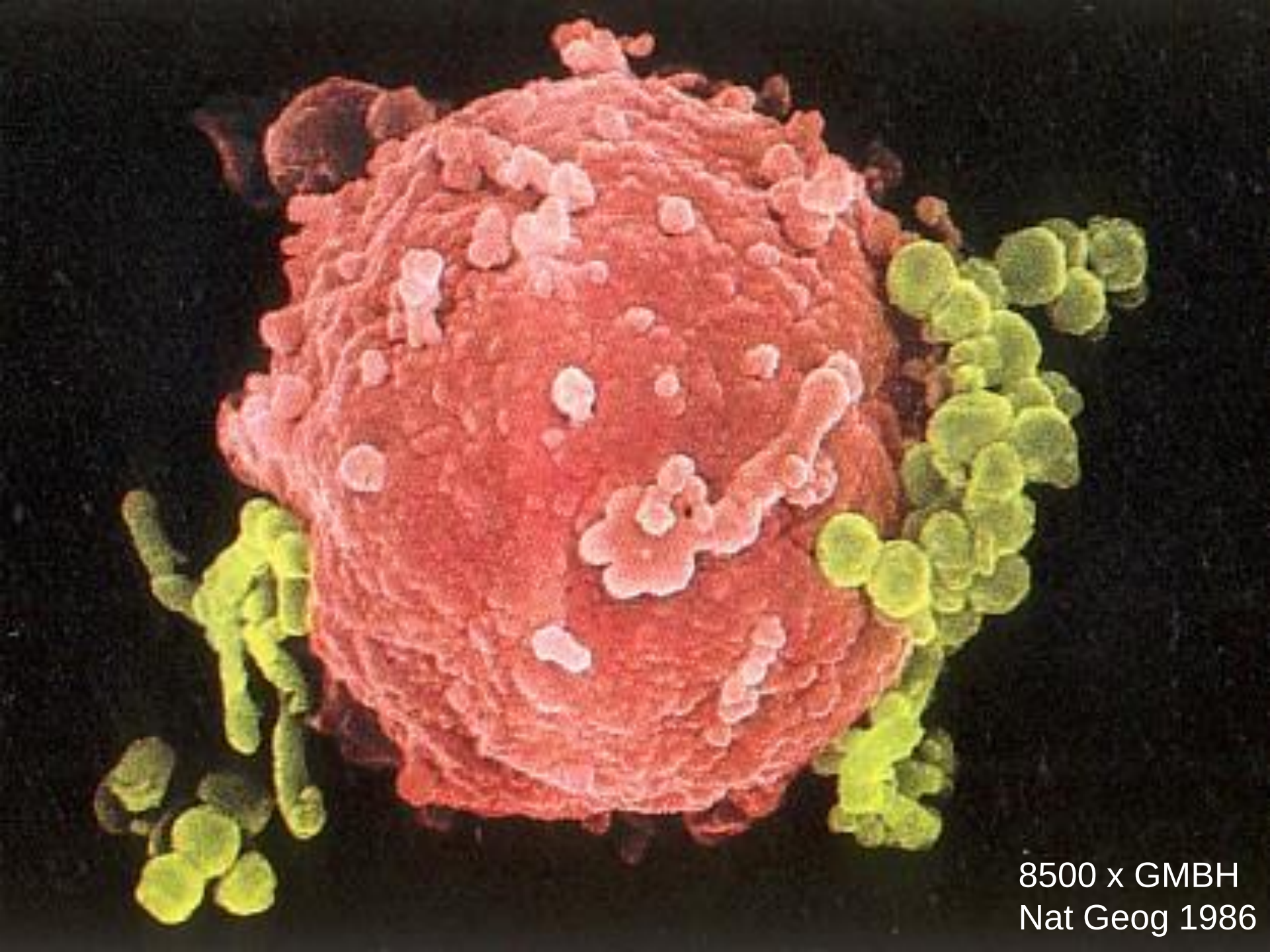
The vital union *that activates a helper T cell takes place only when the T cell recognizes both a "self" marker (rectangle) and a "nonself" antigen (triangle) on a macrophage.*

Nat Geog 1986, p 710

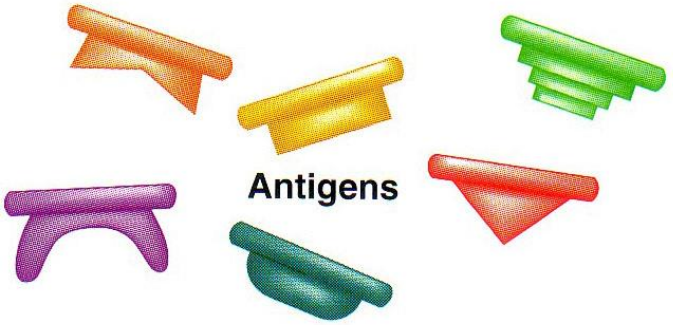
Clonal Selection



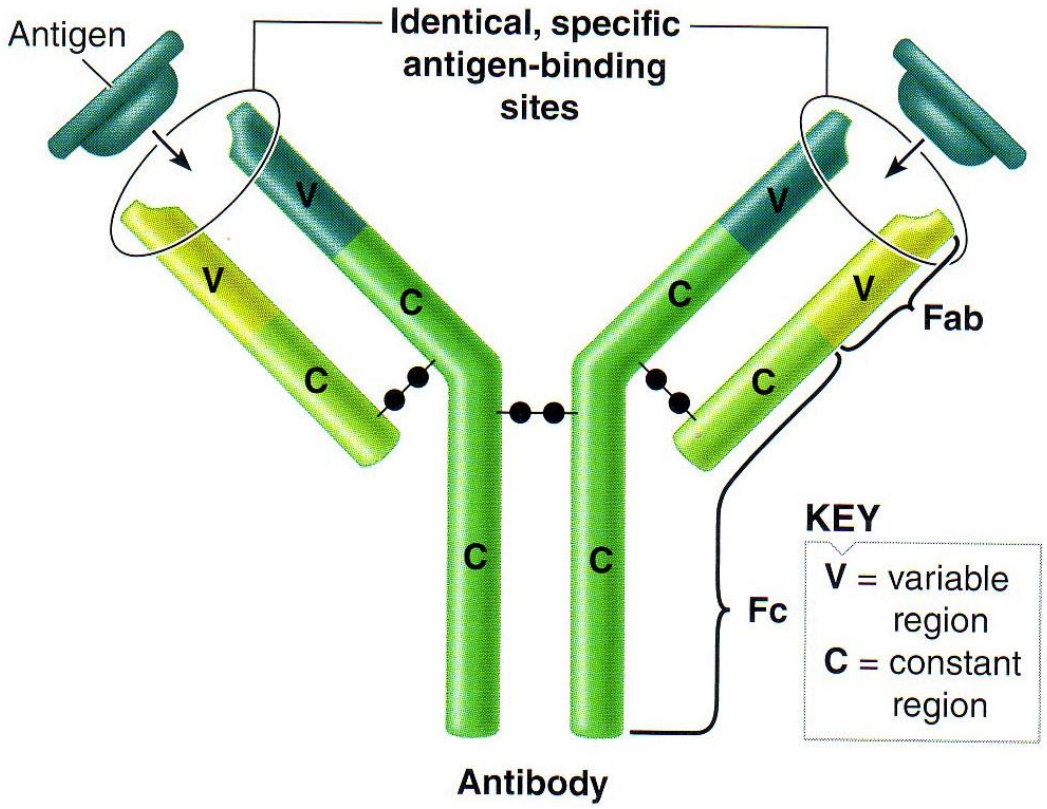
L Sherwood 2012; *cf*: G&H fig 34-2


8500 x GMBH
Nat Geog 1986

Typical IgG Antibody Structure

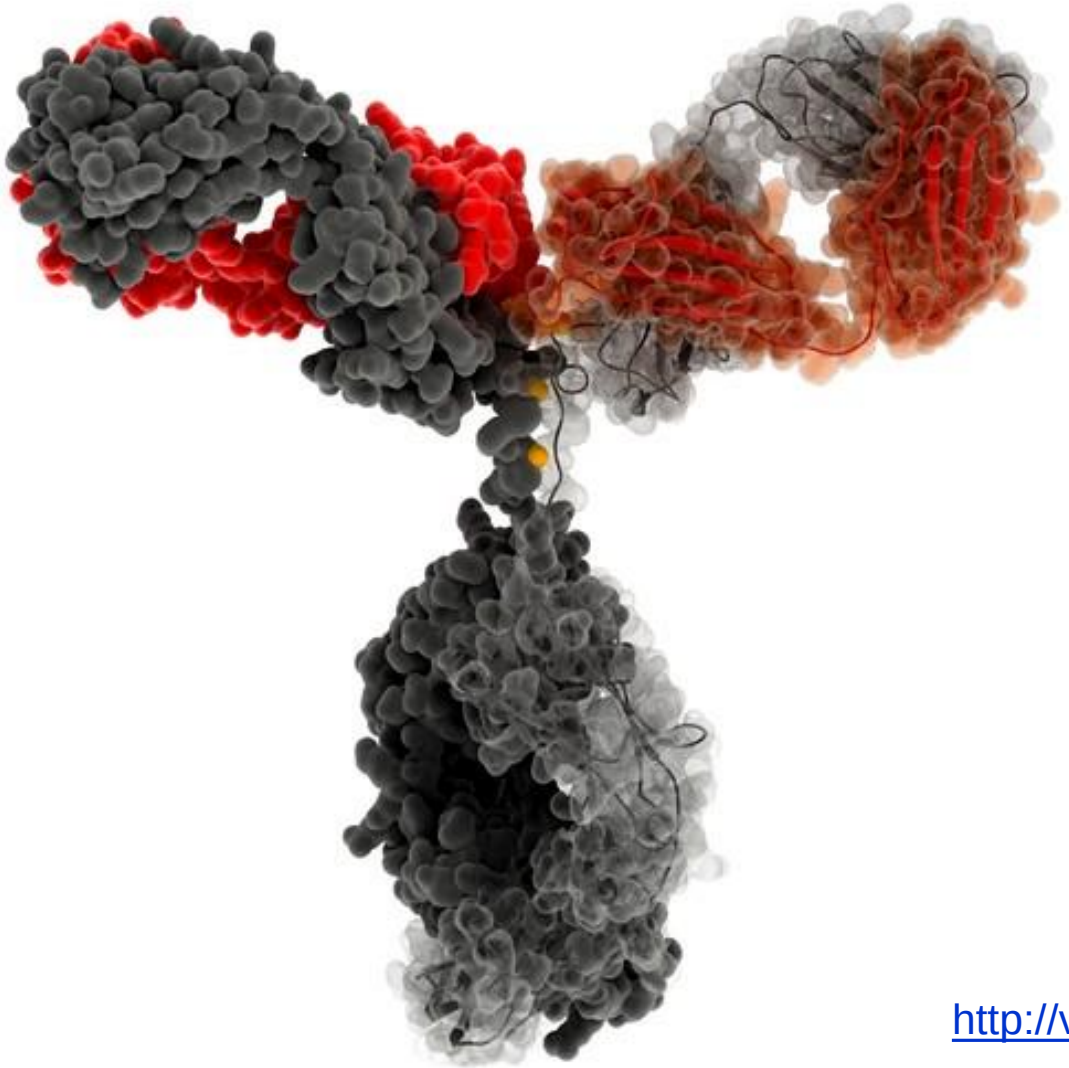


How do antibodies work?



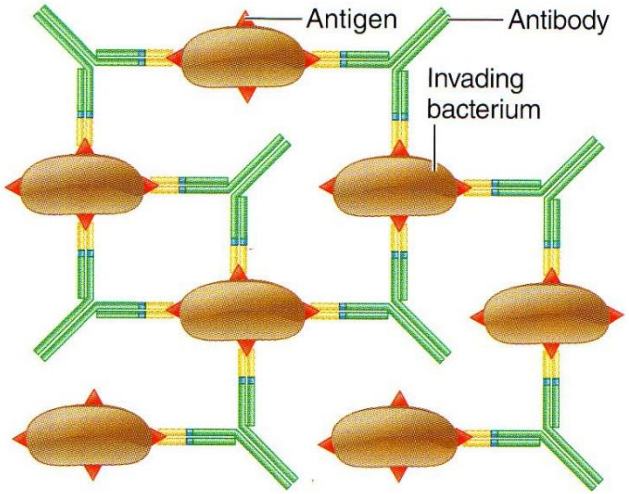
L Sherwood 2012; *cf*: G&H, fig 34-4

Immunoglobulin G

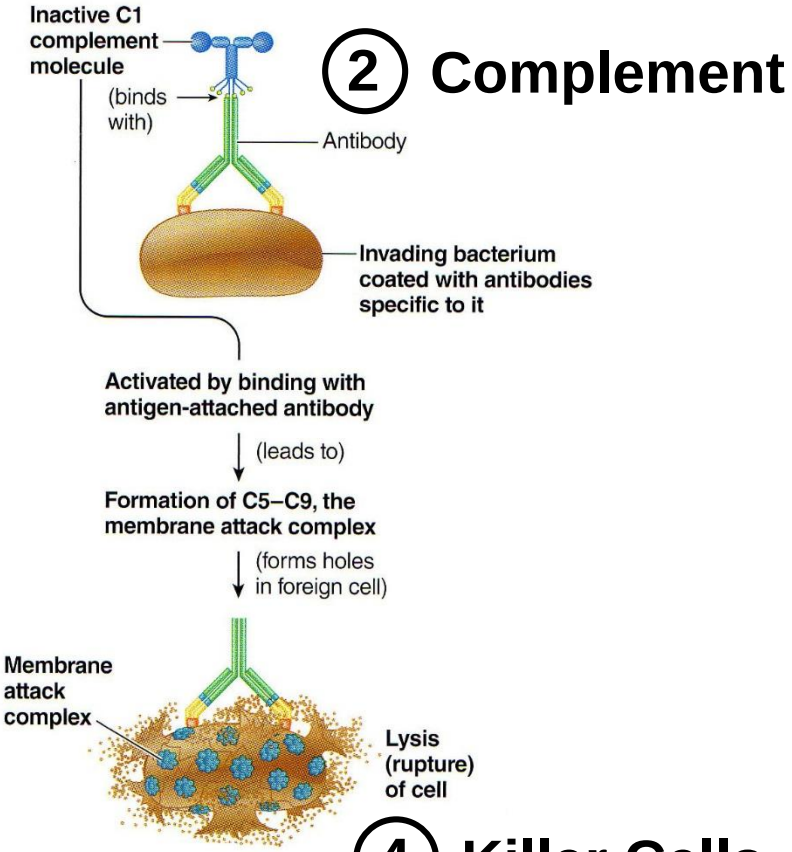


Source:
Visual Science
http://visualscience.ru/en/

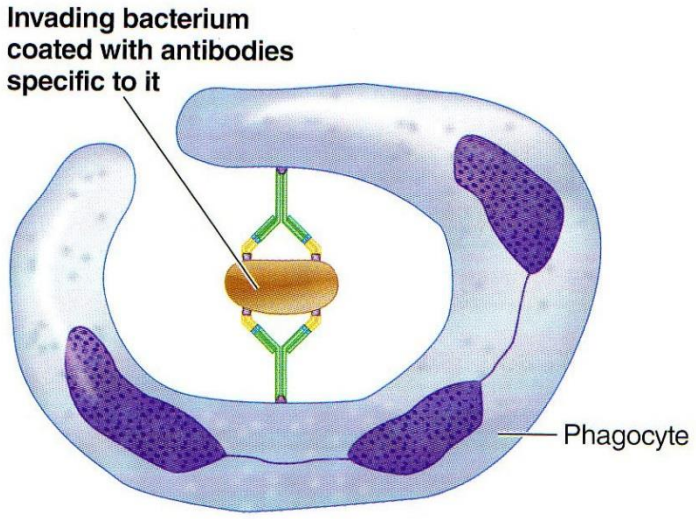
① Agglutination



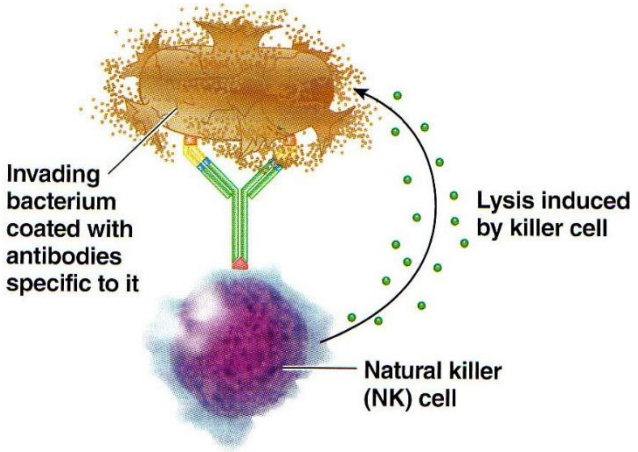
② Complement



③ Opsonization



④ Killer Cells



L Sherwood 2012

TABLE 4.1 Characteristics and functions of the human immunoglobulin classes

G A M D ⇄ E

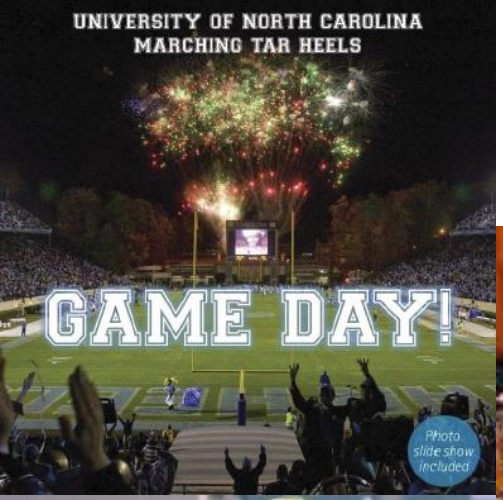
immunoglobulin class	IgG	IgA	IgM	IgD	IgE
heavy-chain type	γ	α	μ	δ	ε
number of constant domains in each heavy chain	3	3	4	3	4
relative molecular mass (M_r) of monomer	150 000	160 000	180 000	185 000	200 000
normally found as polymer?	no	dimer	pentamer	no	no
valency: number of antigen binding sites in 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.

IgE skyrockets in allergies, parasitism, vasculitis, Hodgkin's disease!

Davey 1990 p 49

G A M E D!


UNIVERSITY OF NORTH CAROLINA
MARCHING TAR HEELS
GAME DAY!
Photo slide show included


G A M E D


GAMEDAY

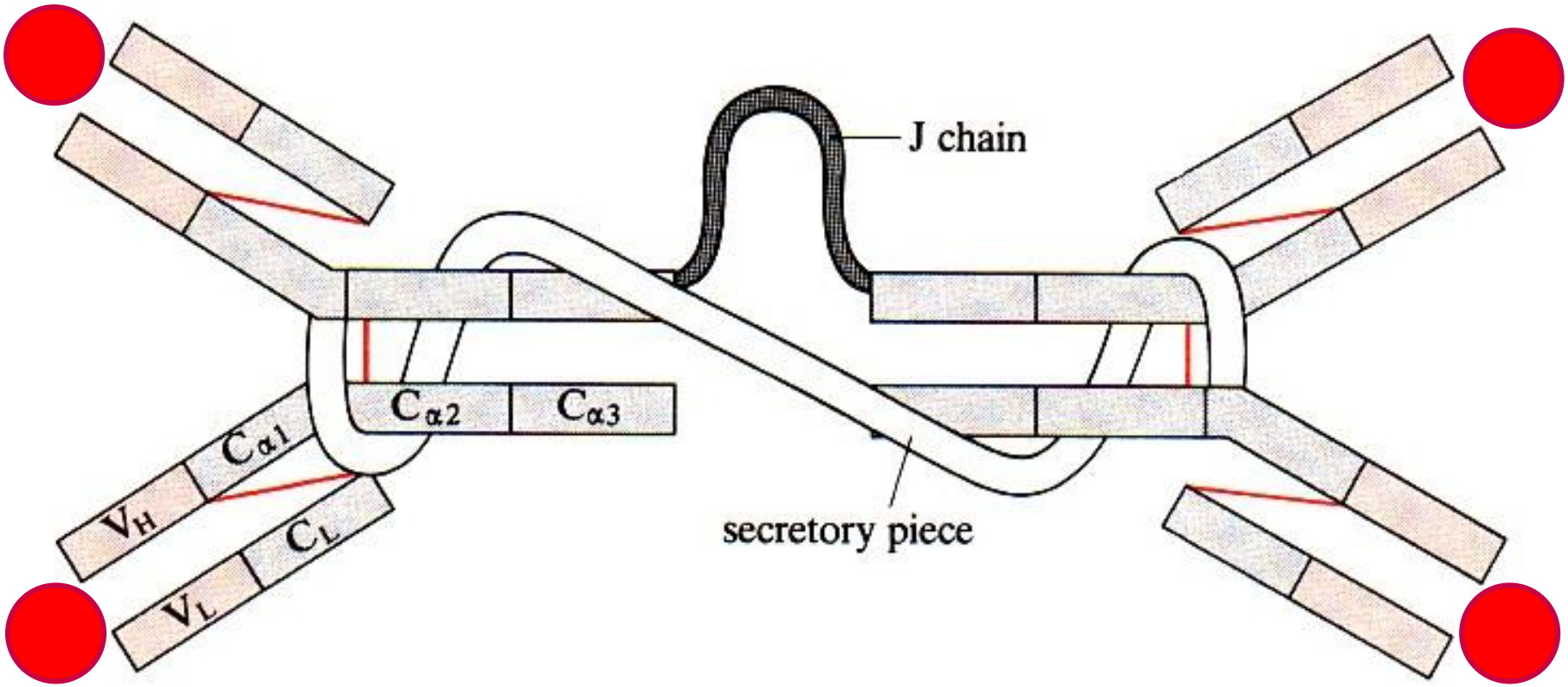

ESPN
COLLEGE GAMEDAY
THE HOME DEPOT


THE HOME DEPOT

IgA = Secretory A_b

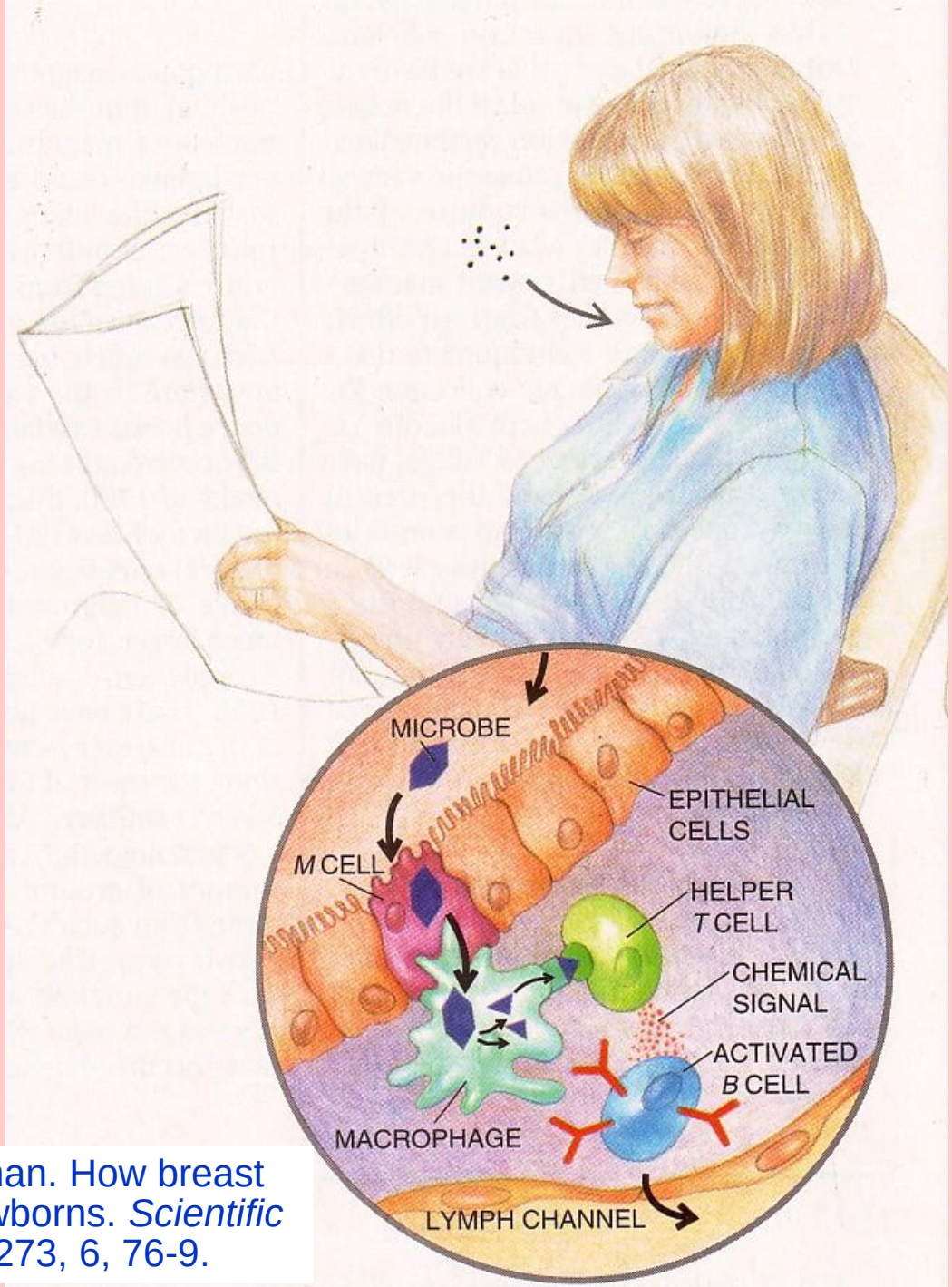
Dimer!!

Antigen/A_g



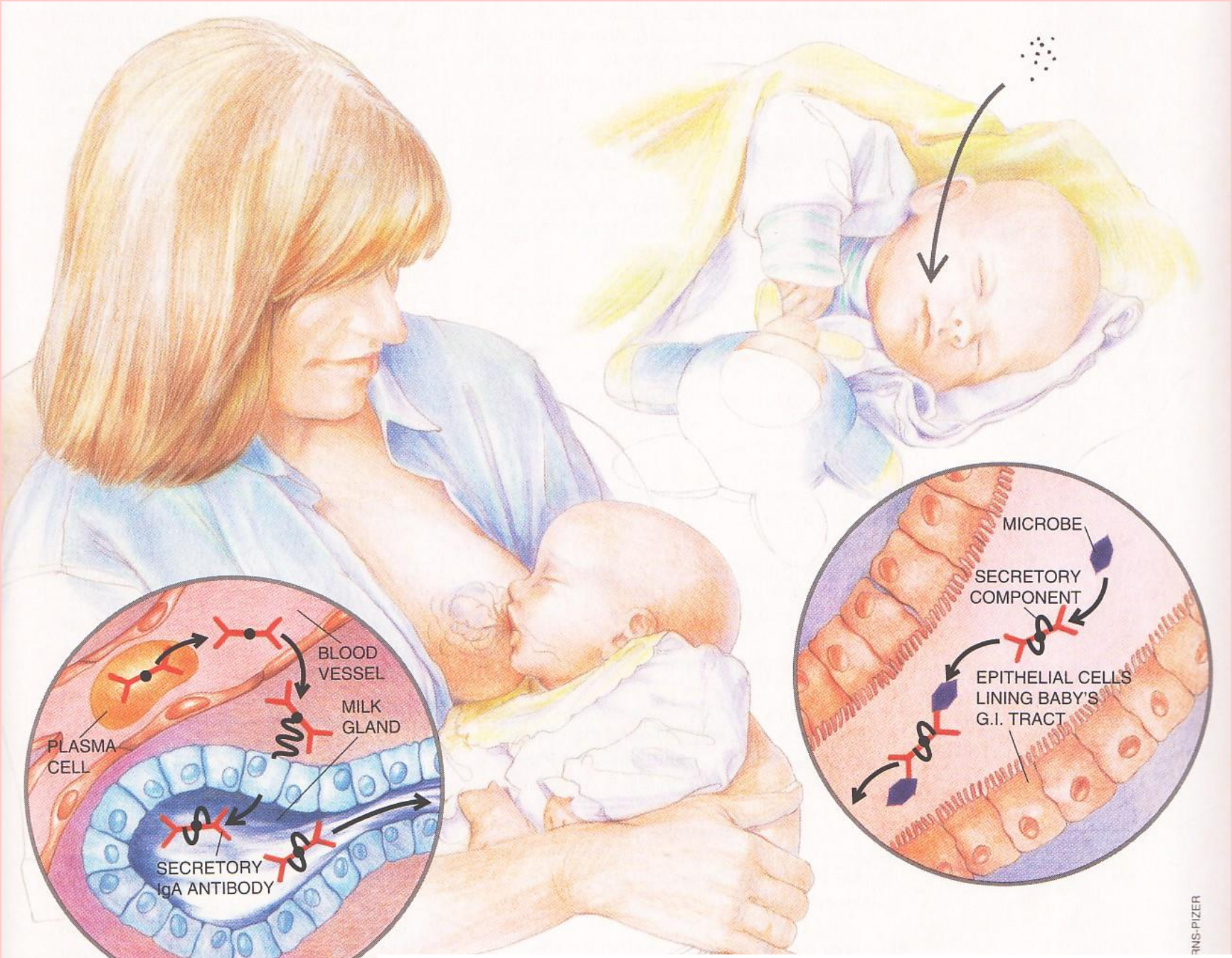
Valence? 4

Davey 1990 p 50



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, injesting 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.

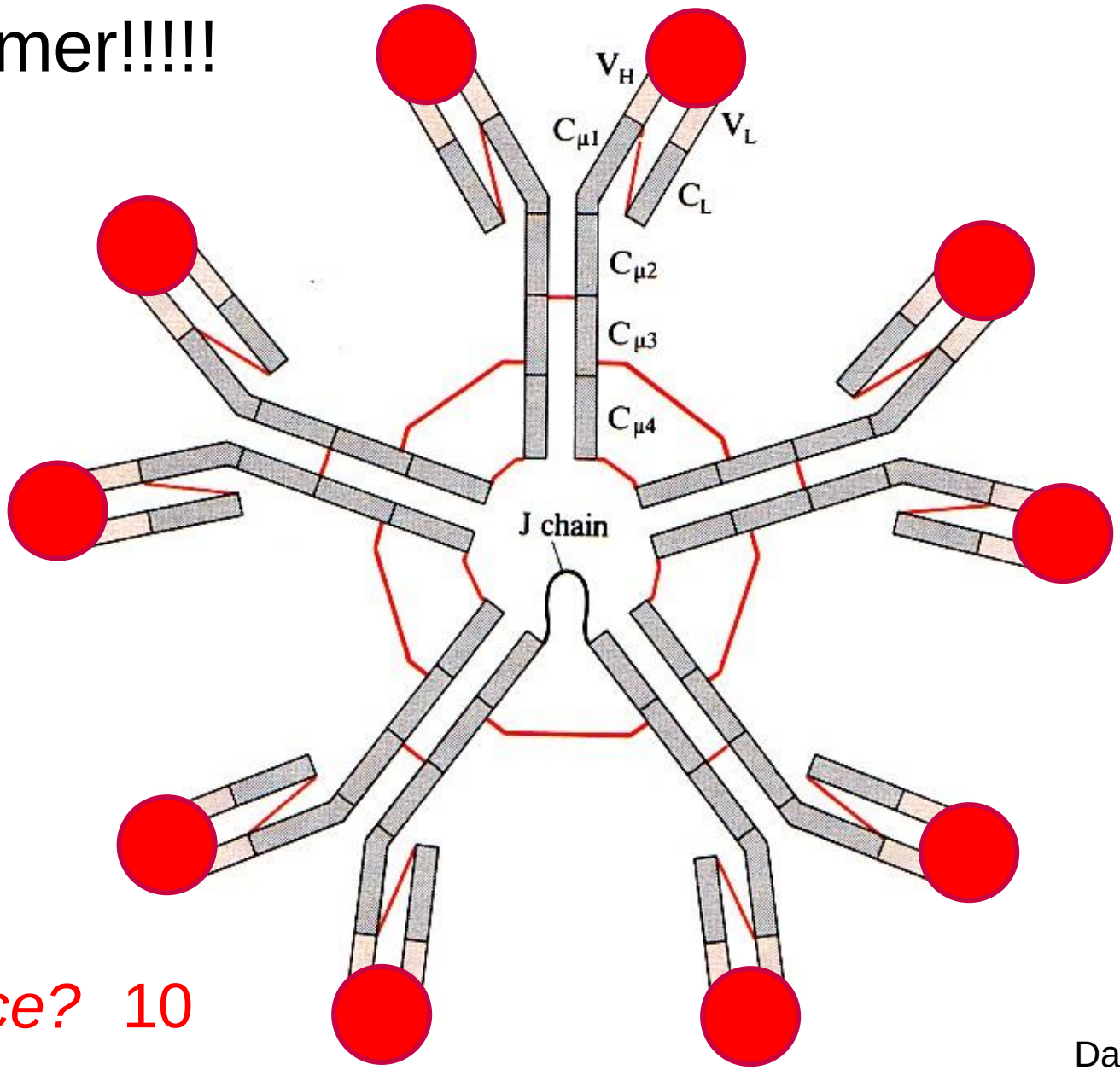
Molecules	
Antibodies of secretory IgA class	Bind to microbes in baby's digestive tract and thereby prevent them from passing through walls of the gut into body's tissues.
B_{12} binding protein	Reduces amount of vitamin B_{12}, which bacteria need in order to grow.
Bifidus factor	Promotes growth of *Lactobacillus bifidus*, 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

Davey 1990 p 51

Immunologic Networks

http://pinterest.com/pin/509470395063175 36/

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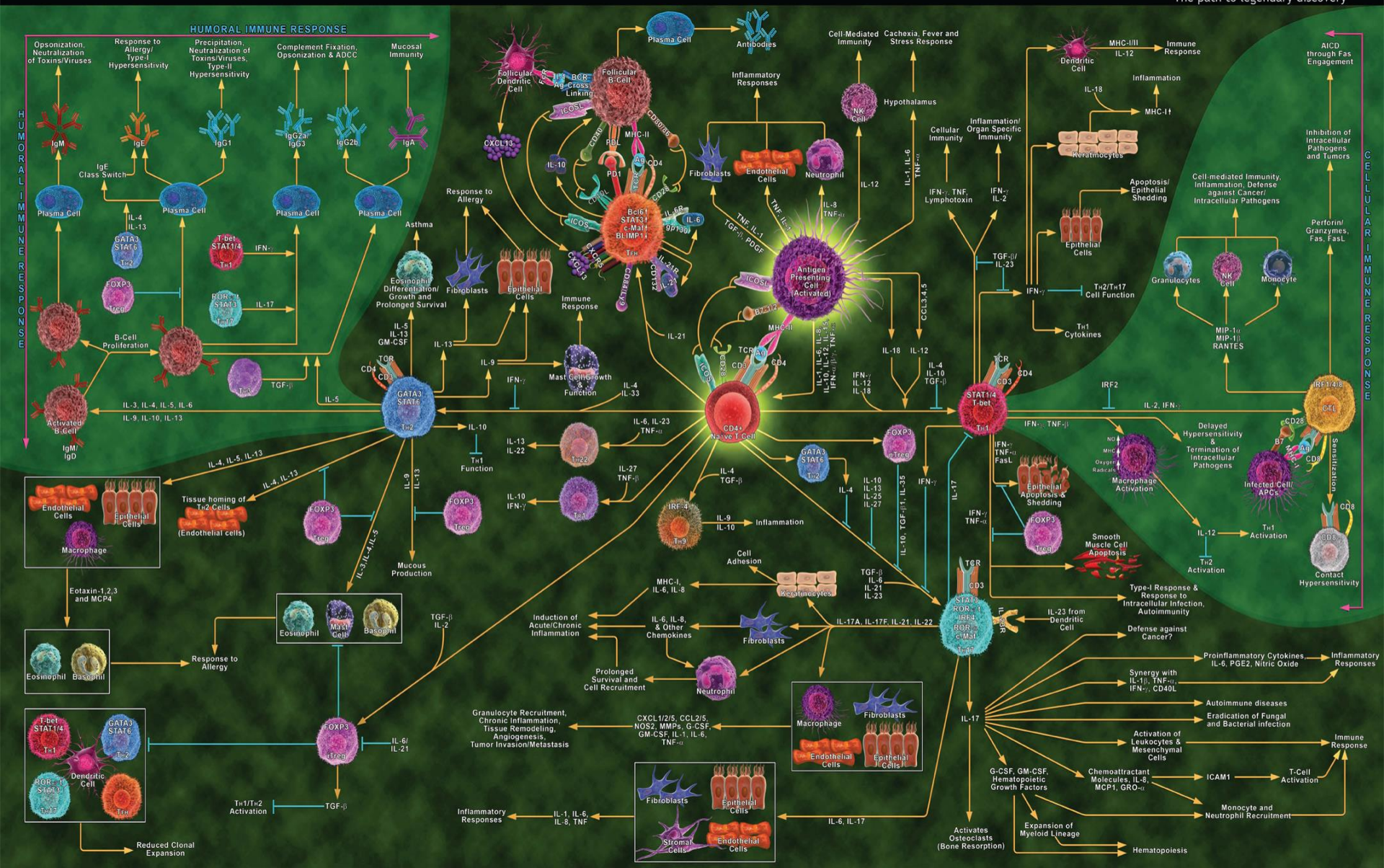

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We would like to thank *Dr. Vijay K. Kuchroo* of Harvard Medical School for his contributions to this poster.

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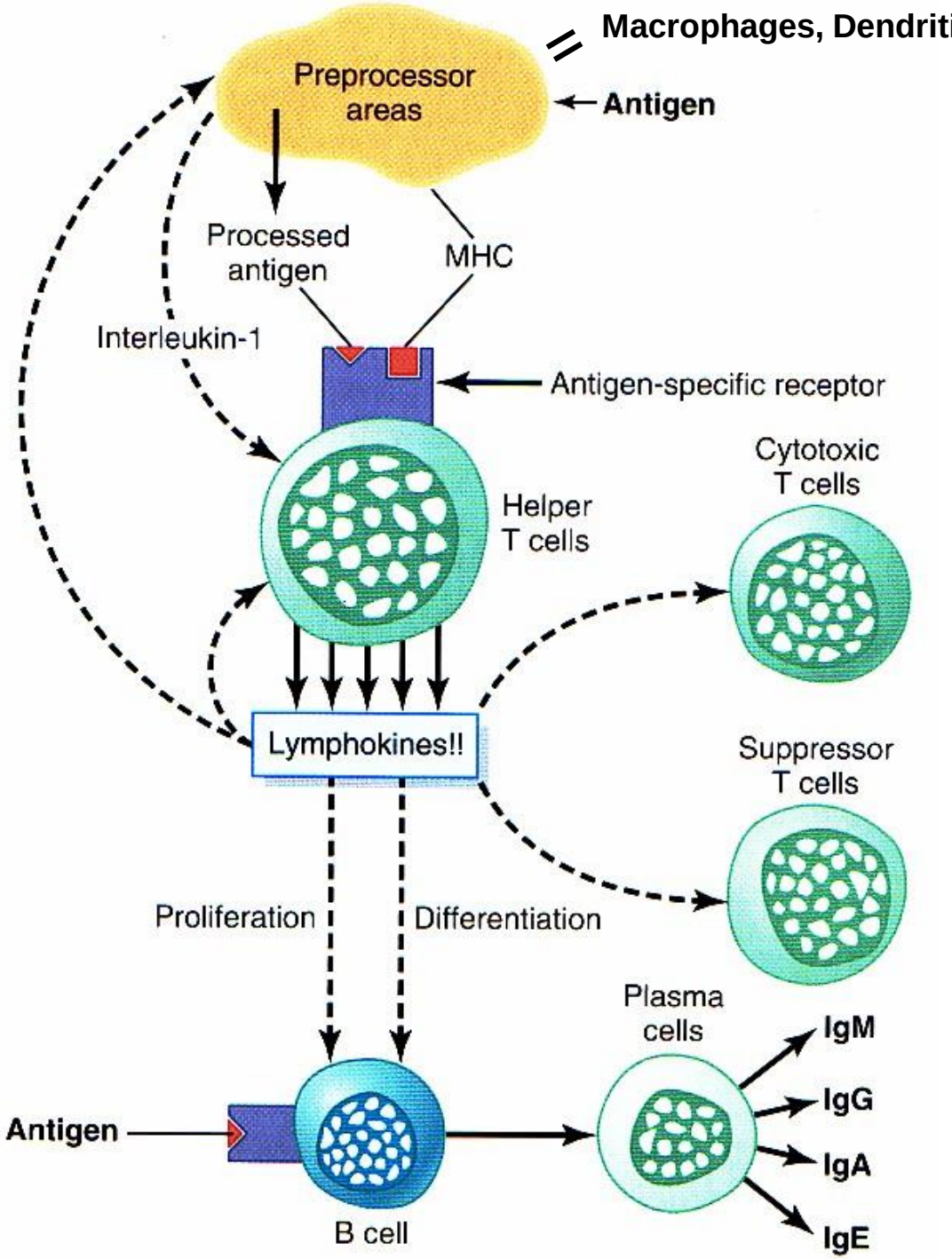
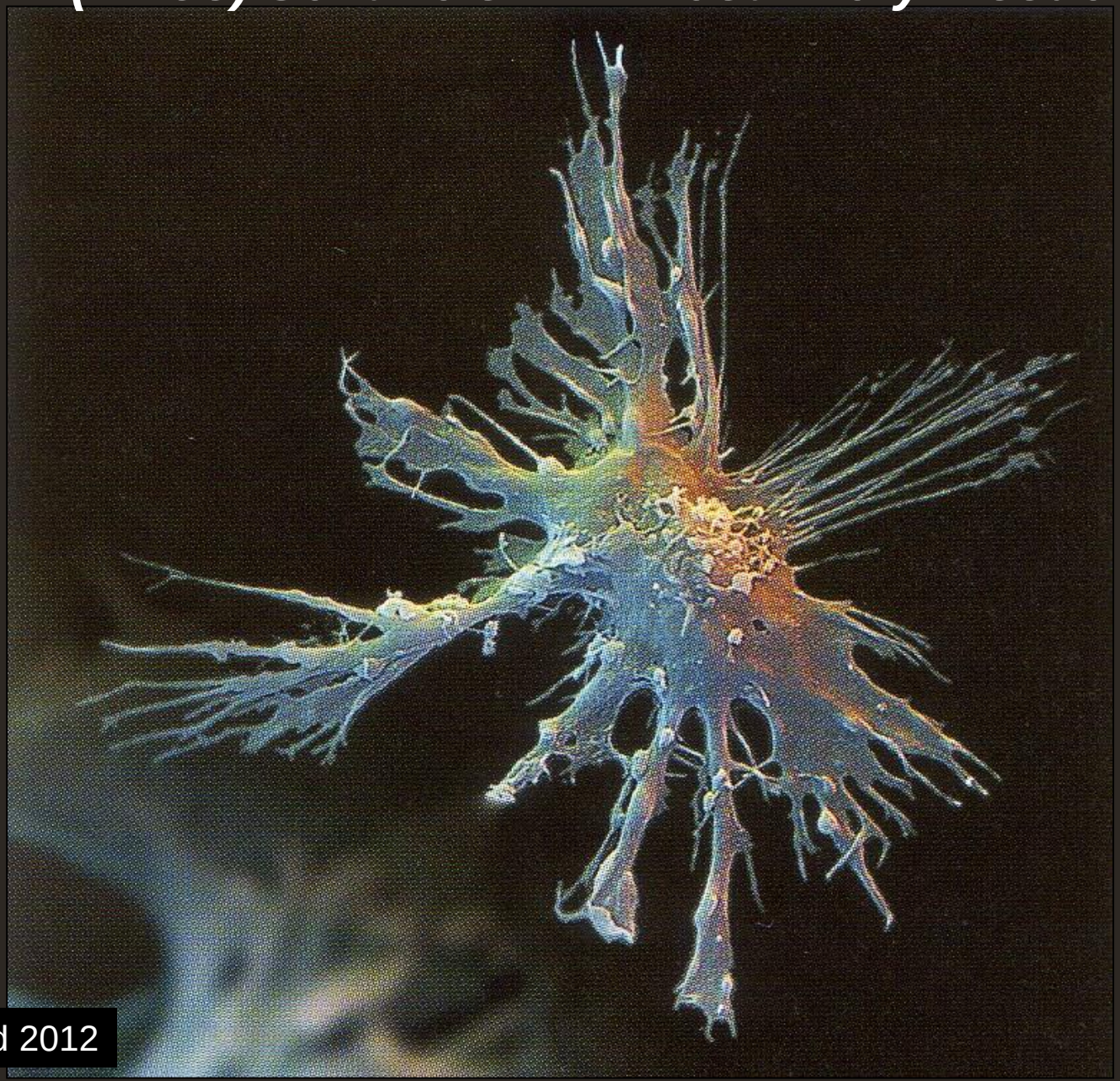


G&H fig 34-8 2011

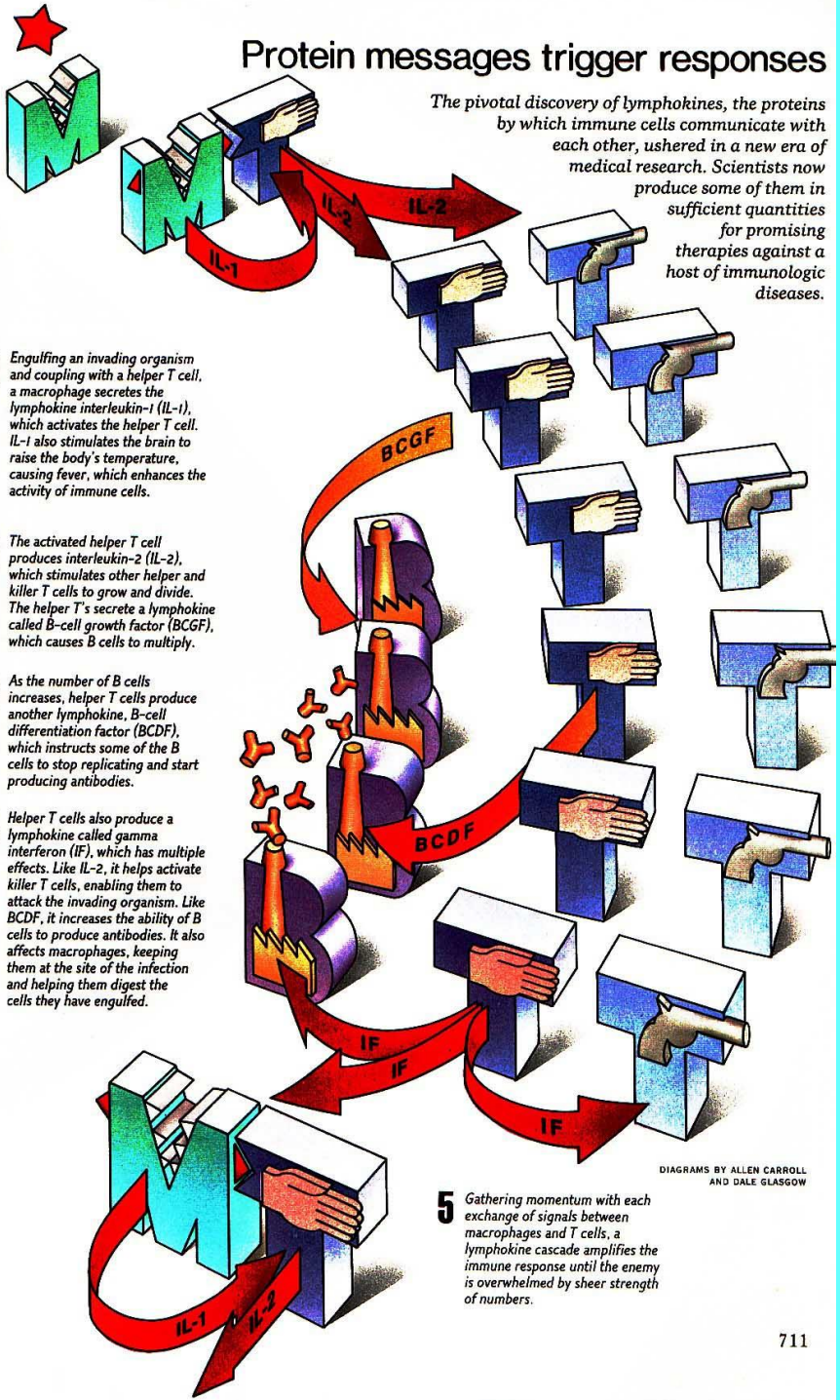
Dendritic Cells: Specialized Antigen-Presenting Cells (APCs) Sentinels in Almost Every Tissue!



L Sherwood 2012

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.*

DIAGRAMS BY ALLEN CARROLL AND DALE GLASGOW

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.*

Nat Geog 1986

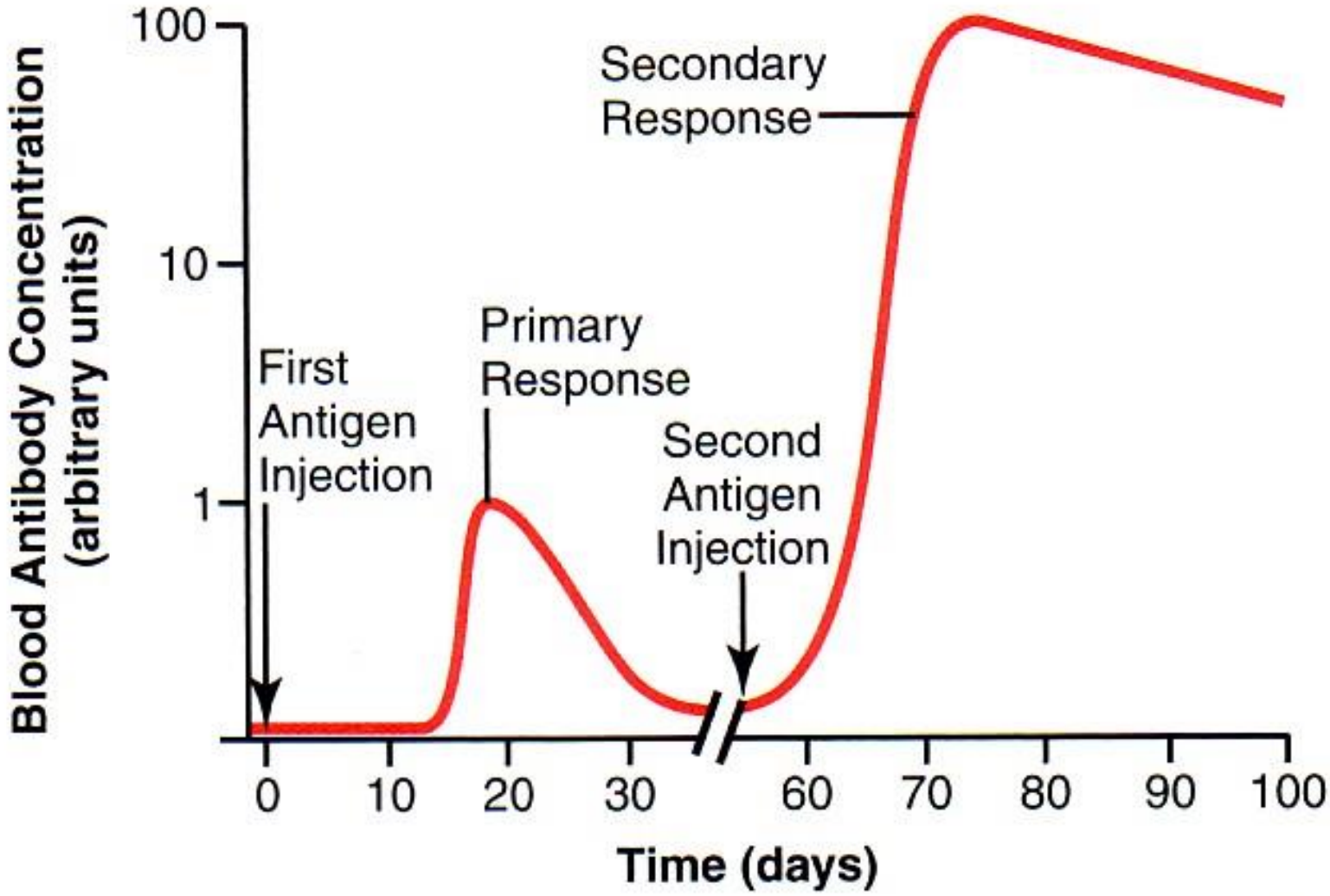


Figure 34-3 Time course of the antibody response in the circulating blood to a primary injection of antigen and to a secondary injection several weeks later.

G&H 2011