

BI 358 Lecture 8

Dr. Kraig is... I g GGGGREAT!!



- I. Announcements** Kraig Jacobson MD, Allergy & Asthma Research Associates, Oak Street Medical, Feb 10, Tues! Last update on outlines and paper drafts. Questions?
- II. Immunology Connections** Ab=Ig structure, Mom's Milk, Immune Regulation + Allergy: *The Wars Within*, Lennart Nilsson
- III. Cardiovascular Physiology** Torstar Books, G&H, Katz, LS, ...
 - A. Cardiovascular system? Figure-8 loop D Chiras (DC), LS
 - B. Fetal development & circulation Torstar..., G&H fig 83- 4
 - C. Layers: peri-, epi-, myo- & endocardium Torstar Books
 - D. ♥ structure & function G&H fig 9-7, LS1...
 - E. Blood flow through ♥ & periphery G&H fig 9-1, LS, DC
 - F. Coronary circulation & the cardiac cycle, composite events G&H fig 21-3, Katz, G&H fig 21-5, 21-6, 21-4; ch 9 fig 9-6
 - G. Autorhythmic cells & ♥'s electrical highway G&H fig 10-1
- III. Lymphatic System** Torstar Books, DC, LS +...

Granulocytes

Neutrophil 58-62%

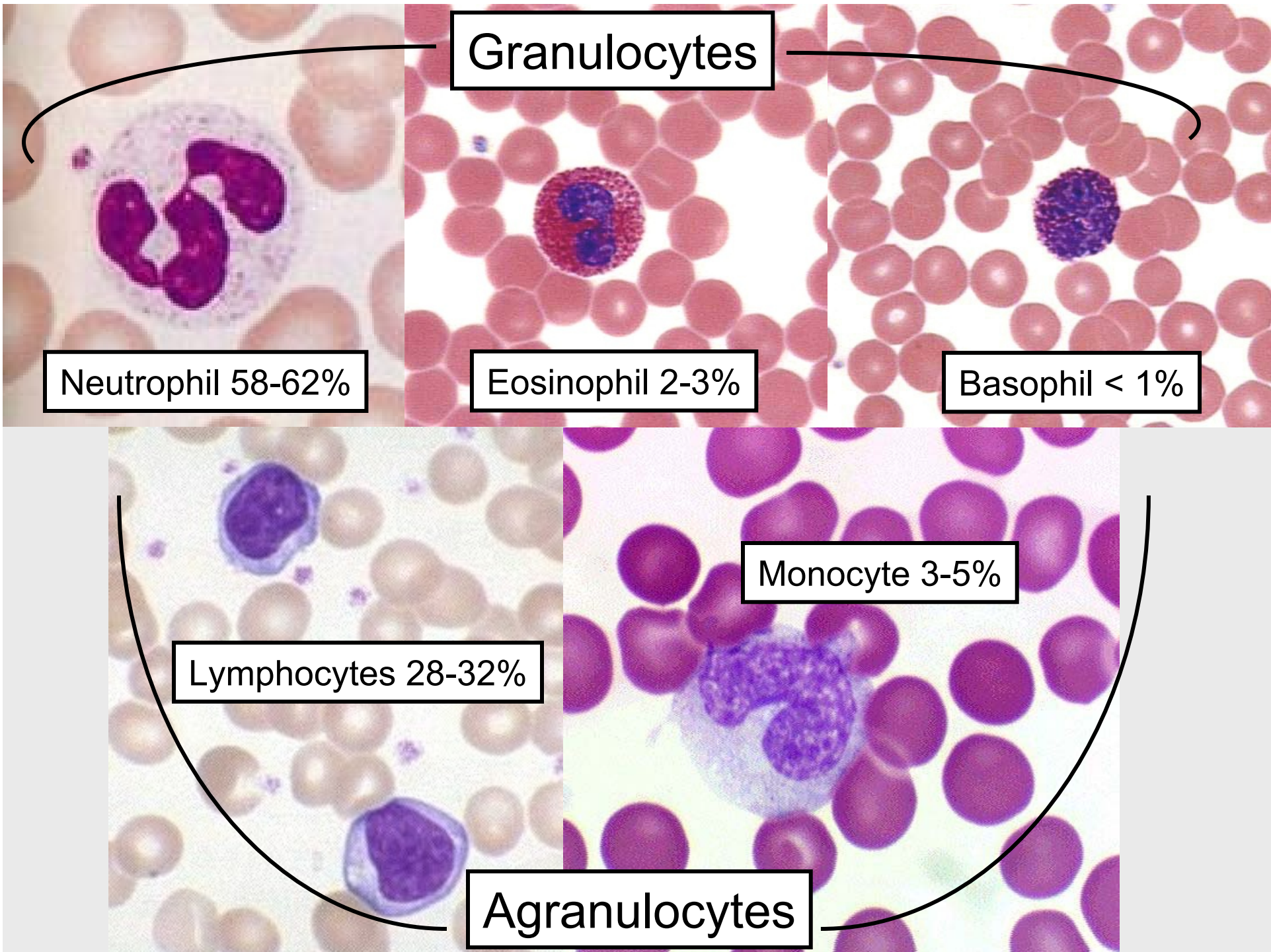
Eosinophil 2-3%

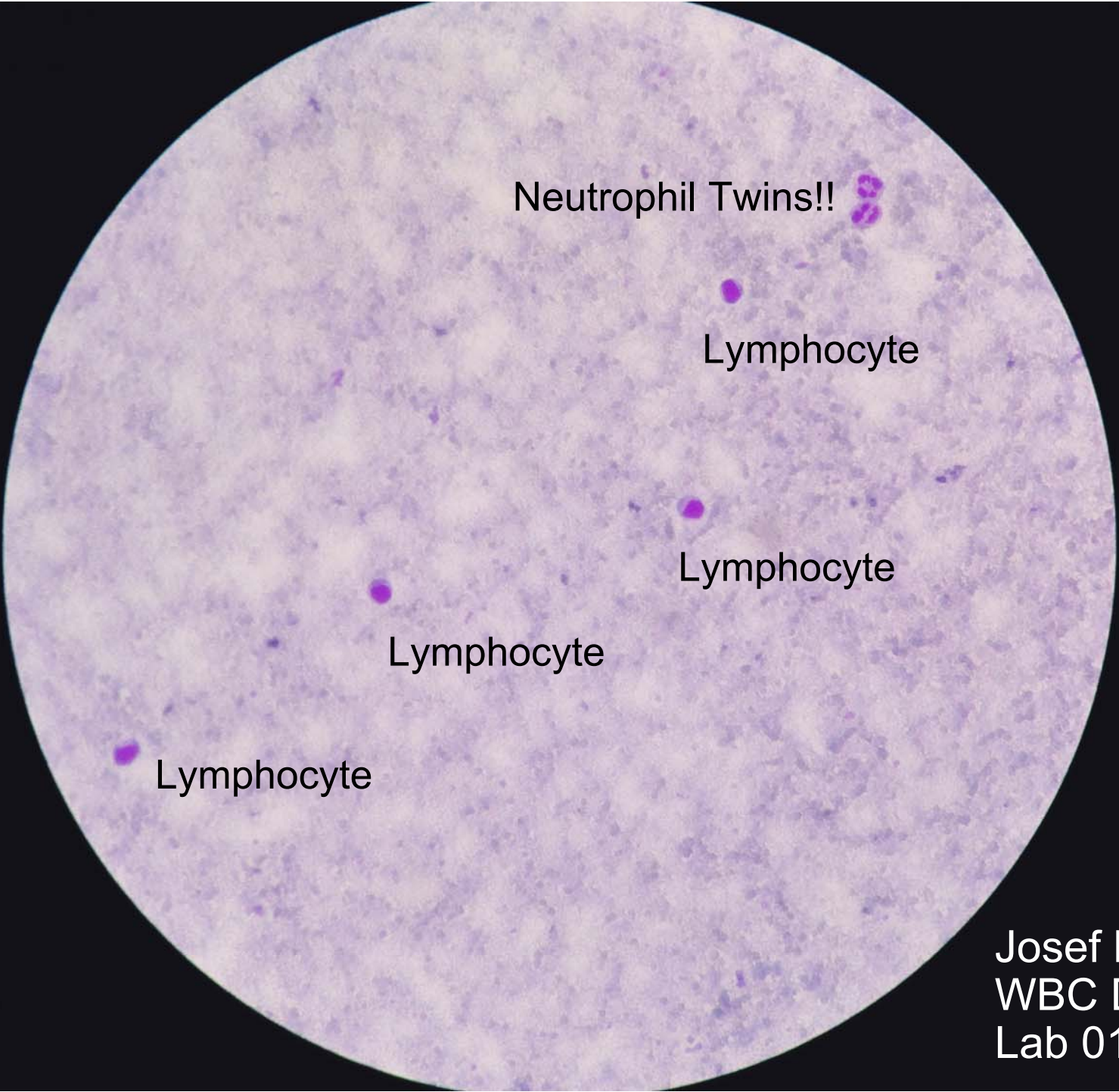
Basophil < 1%

Lymphocytes 28-32%

Monocyte 3-5%

Agranulocytes





Neutrophil Twins!!

A circular field of view from a microscope showing a purple-stained blood smear. The background is filled with numerous small, dark purple-stained cells. Several larger, distinct white blood cells are visible, each with a large, dark purple nucleus and a thin rim of light purple cytoplasm. One pair of these cells is located near the top center, and three other individual cells are scattered in the lower half of the field.

Lymphocyte

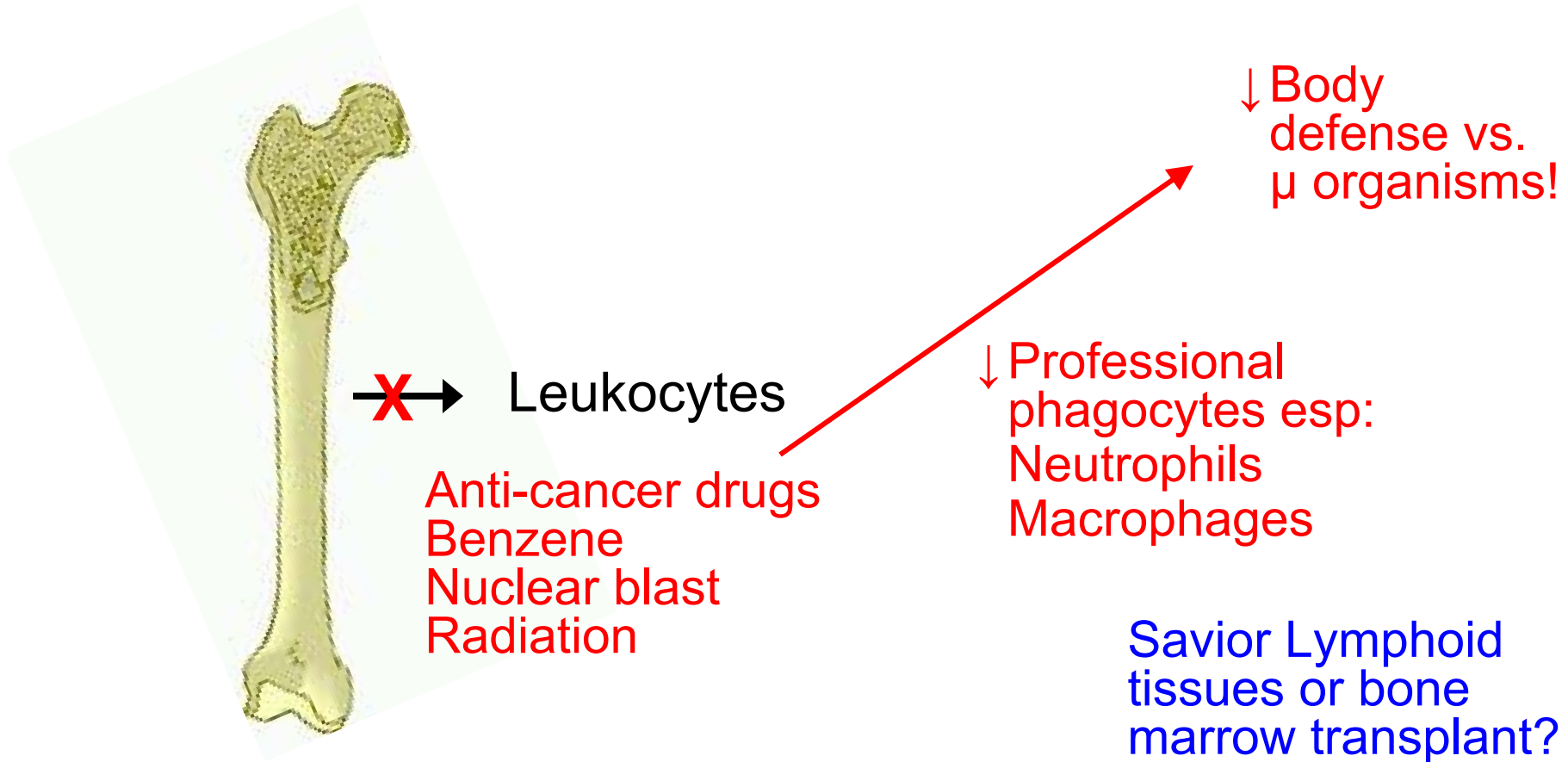
Lymphocyte

Lymphocyte

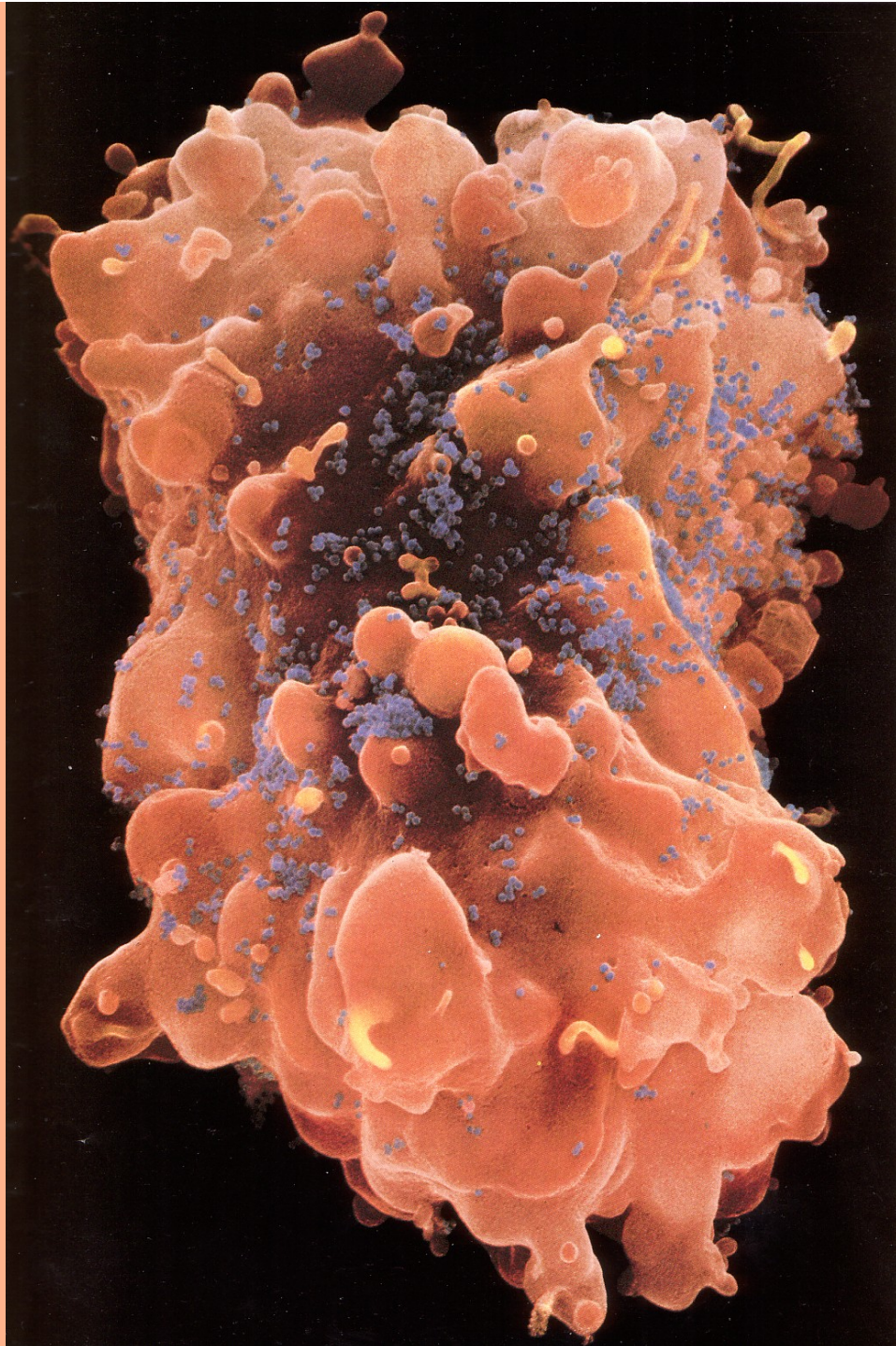
Lymphocyte

Josef Khalifeh
WBC Differential
Lab 012715

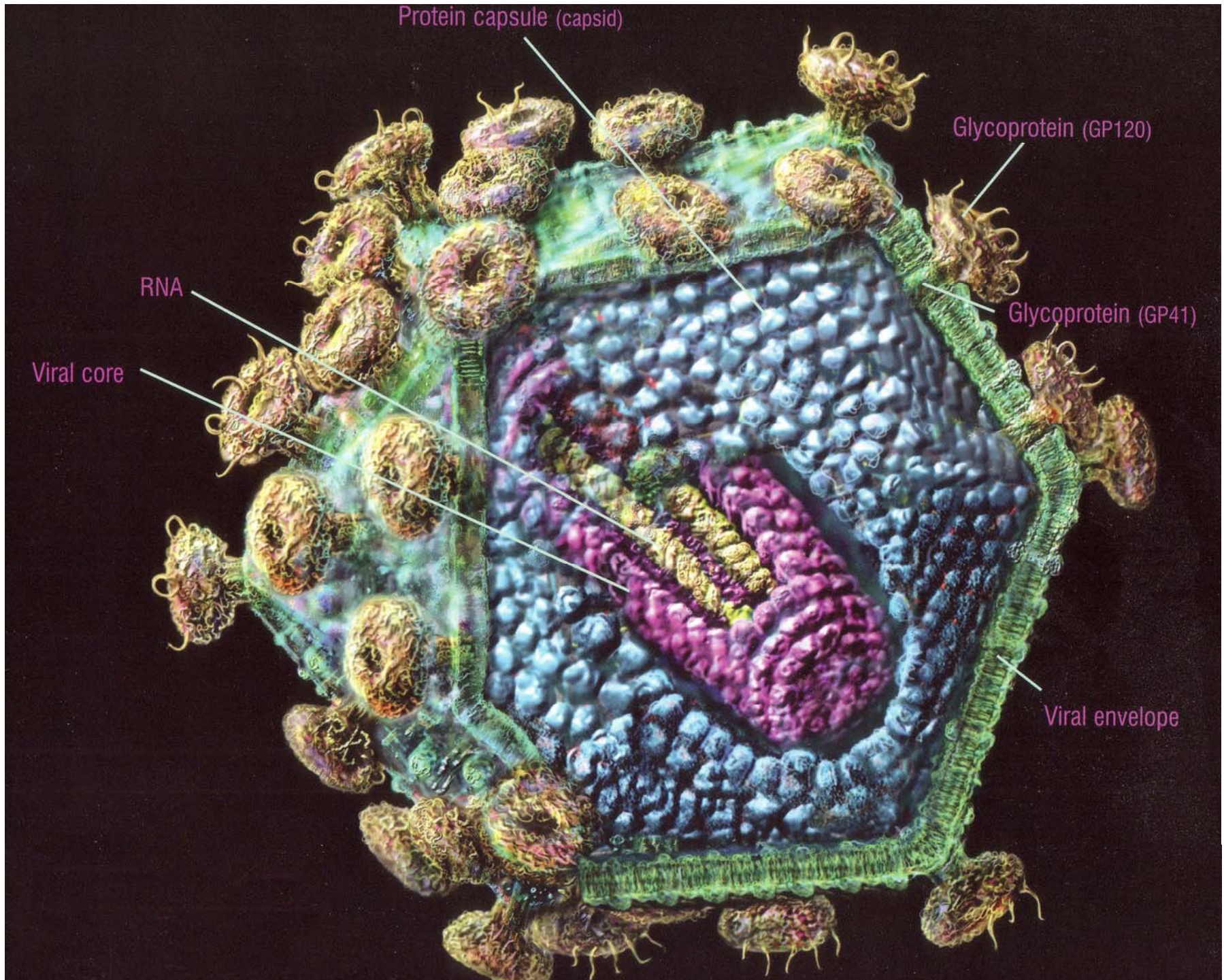
WBC Adverse Effects



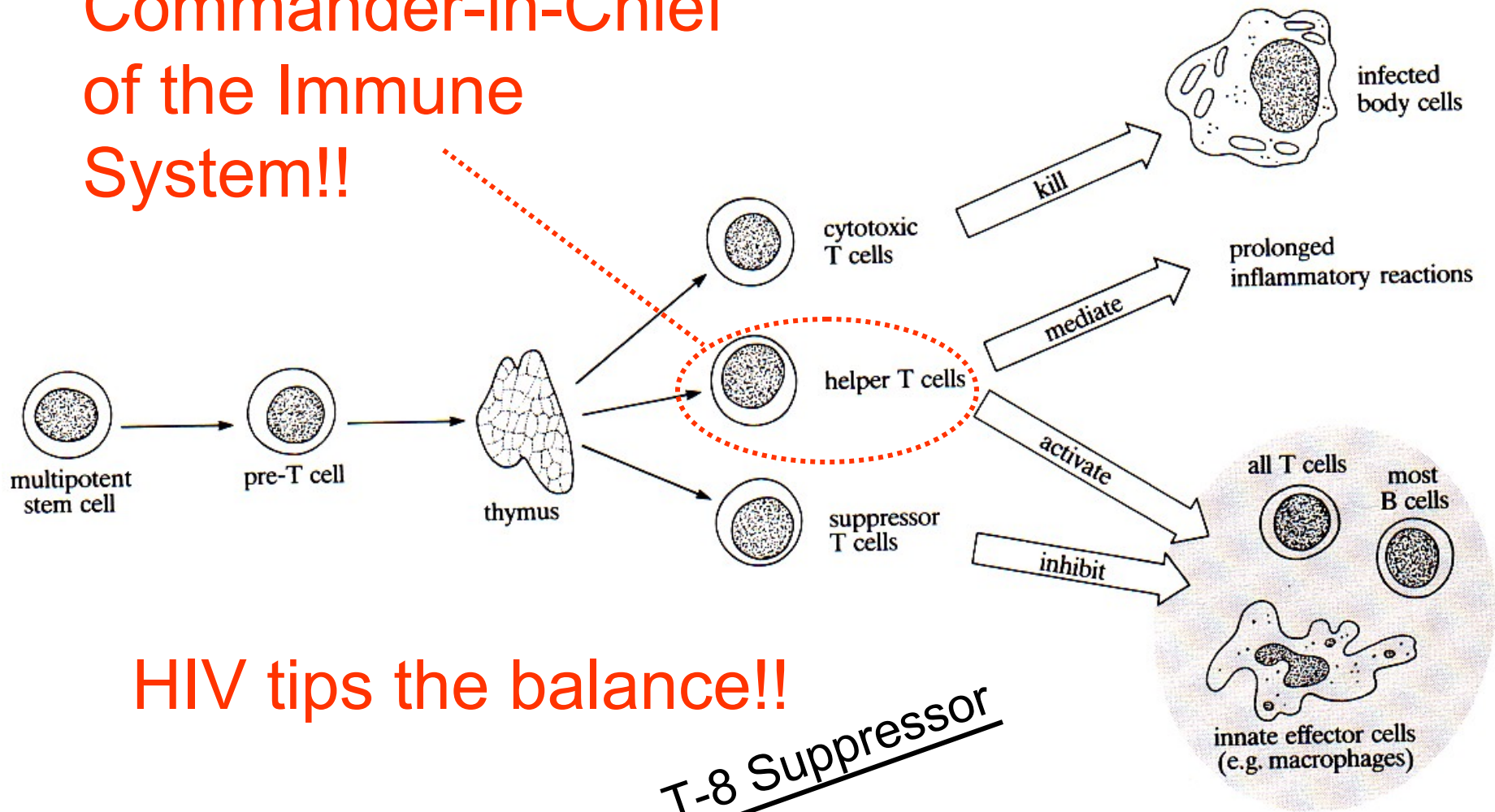
cf: Leukemia \equiv uncontrolled WBC proliferation, yet inadequate defense \rightarrow other cell lines displaced \rightarrow overwhelming infections & bleeding...



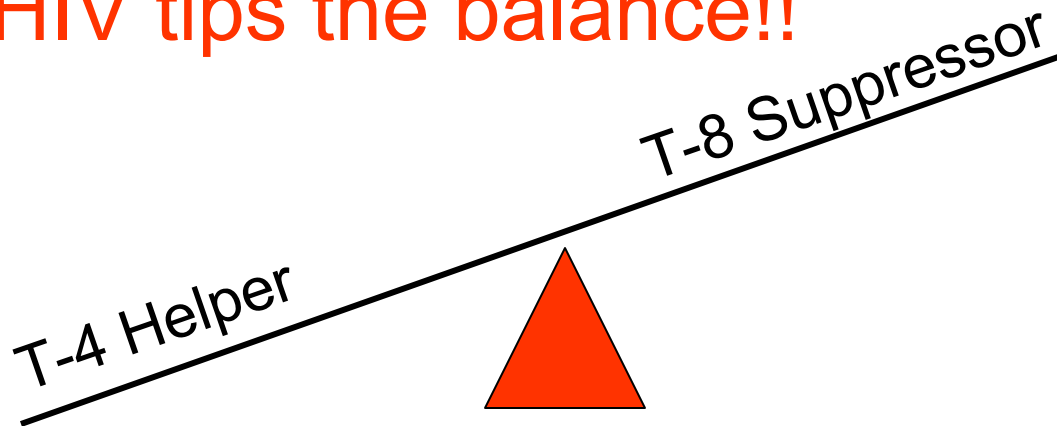
30,000 x GMBH
Nat Geog 1986

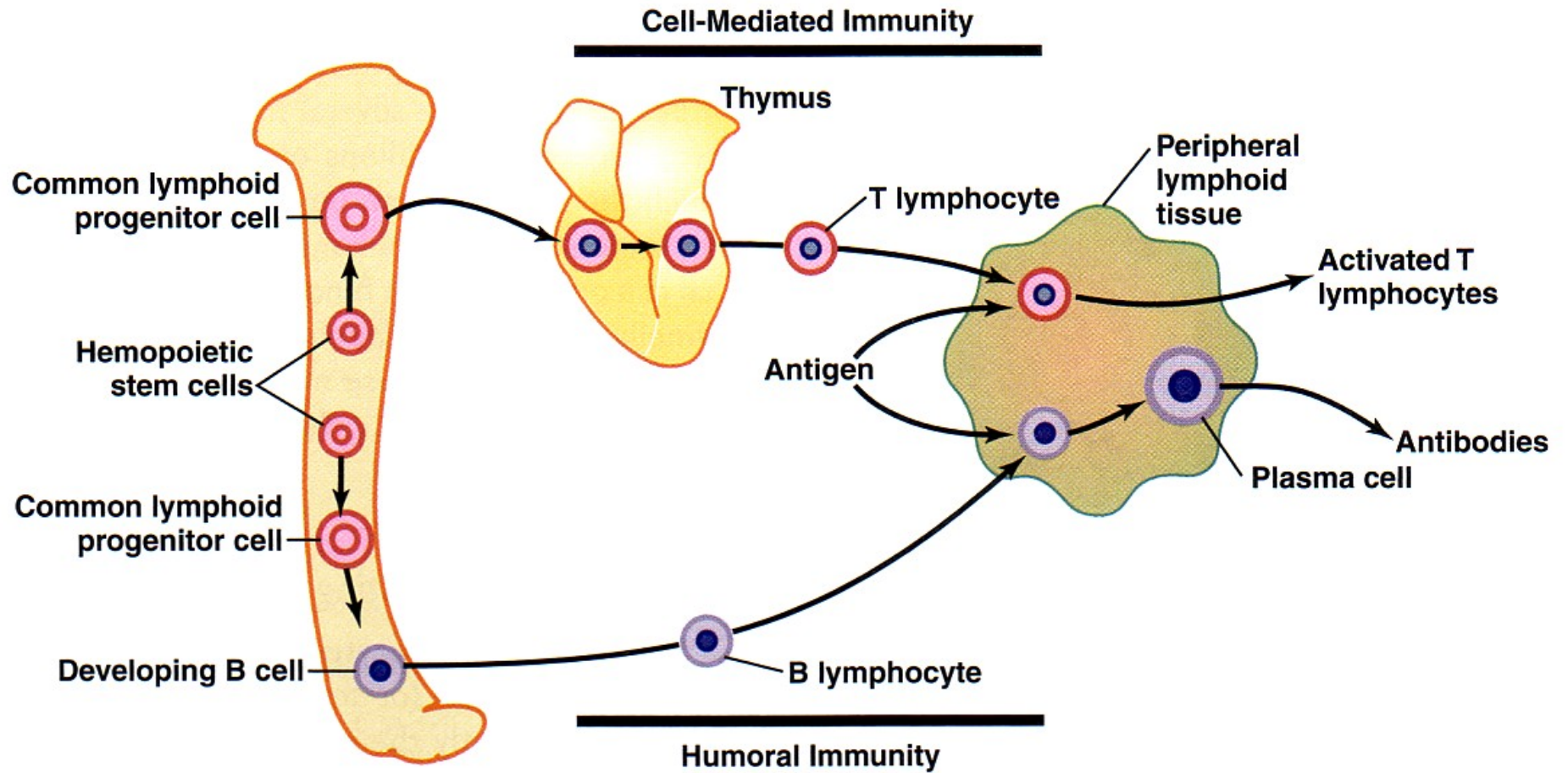


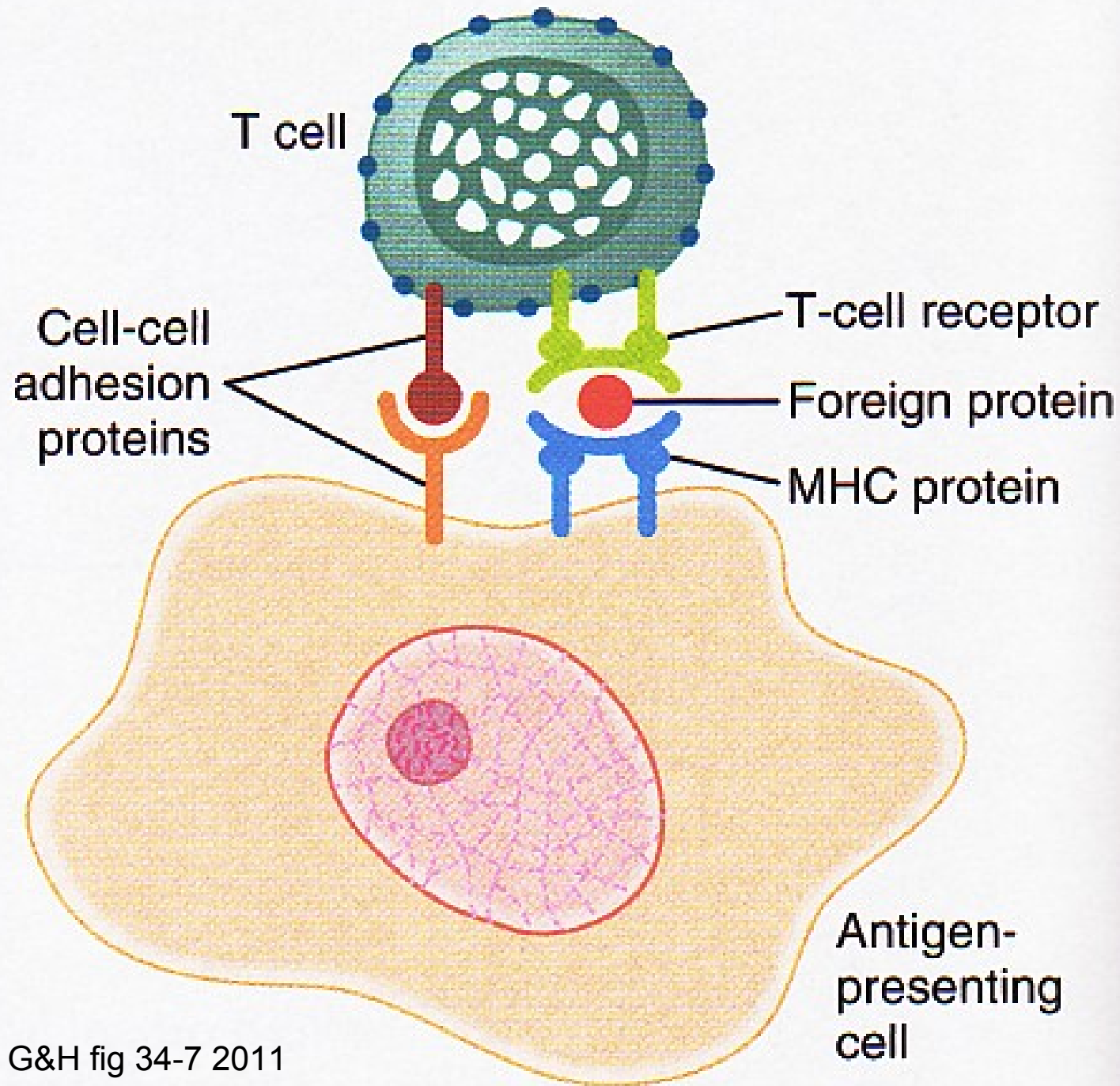
Commander-in-Chief of the Immune System!!



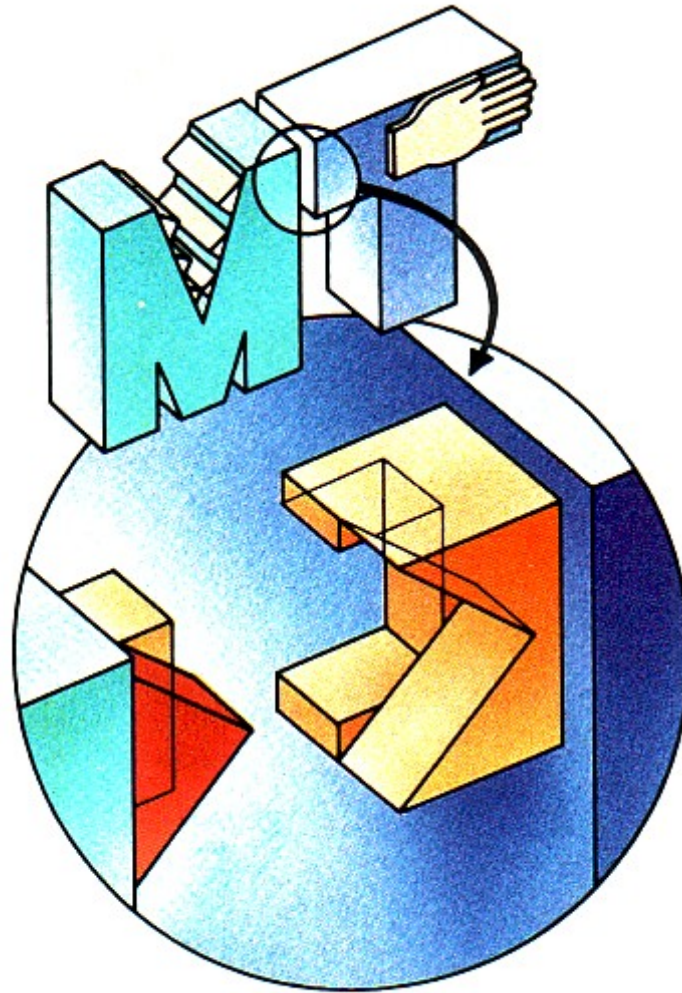
HIV tips the balance!!







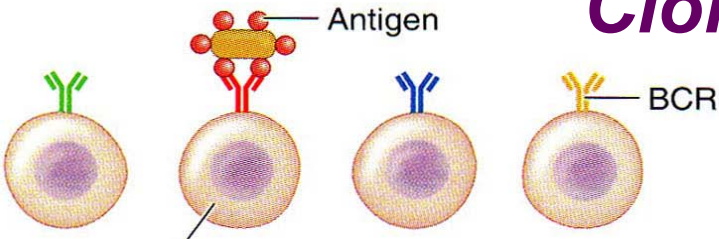
G&H fig 34-7 2011



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.

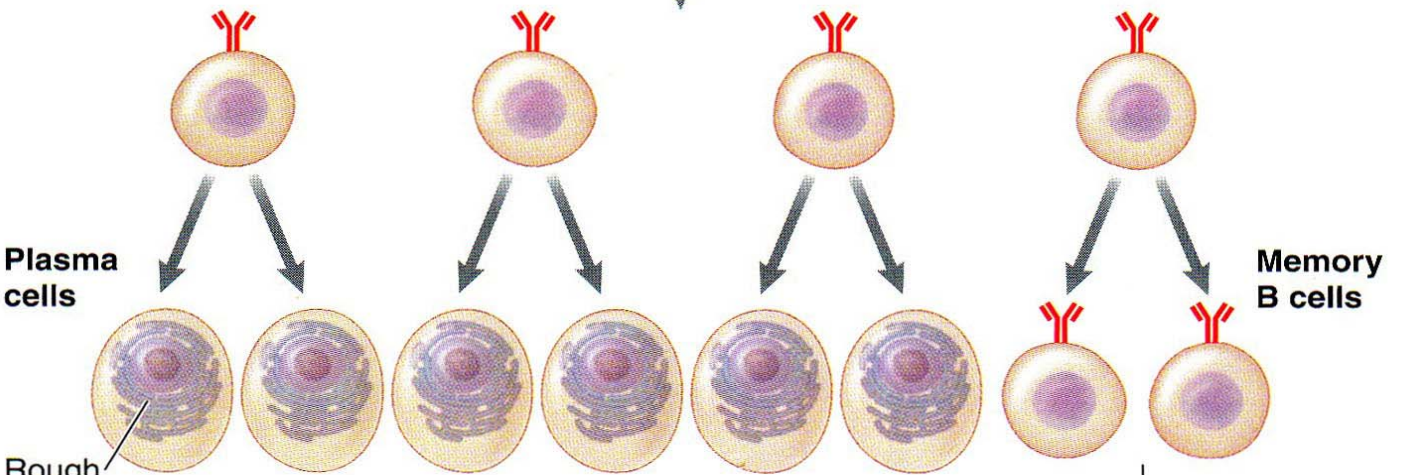
Clonal Selection

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



B cell specific to antigen

Binding of antigen and interaction with helper T cell stimulates the matching B cells to divide and expand the clone of selected cells.



Plasma cells

Memory B cells

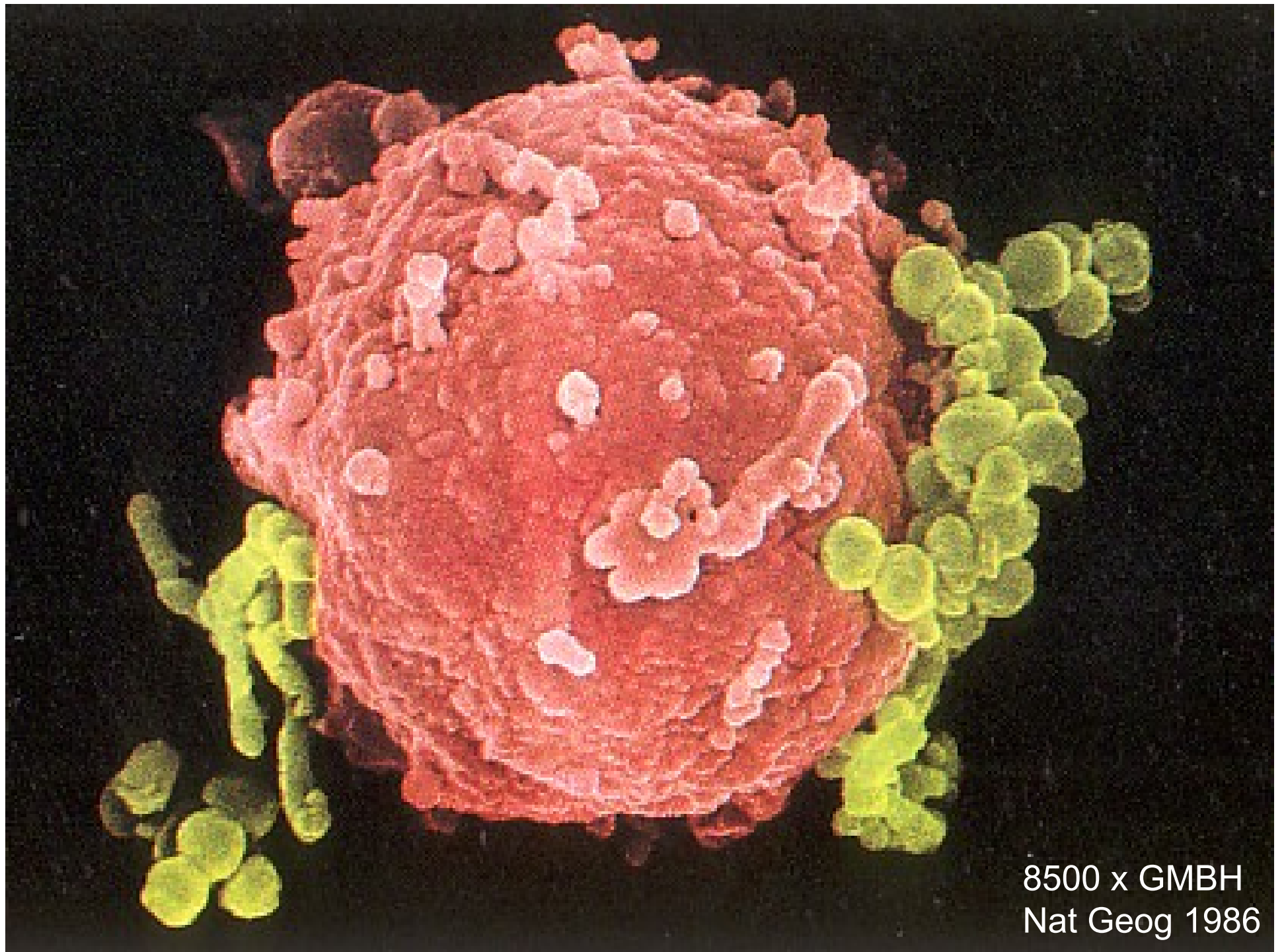
Rough ER

Antibodies

Most of the new B cells differentiate into plasma cells, which secrete antibodies.

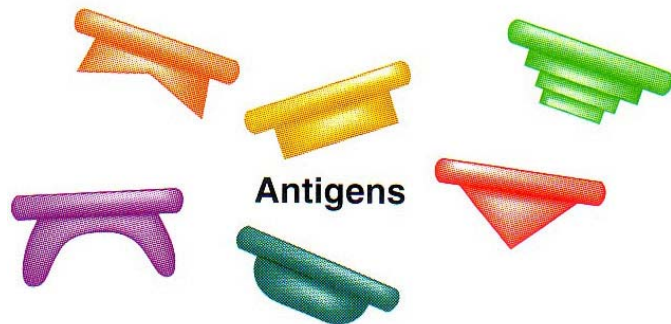
A few of the new B cells differentiate into memory B cells, which respond to a later encounter with the same antigen.

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

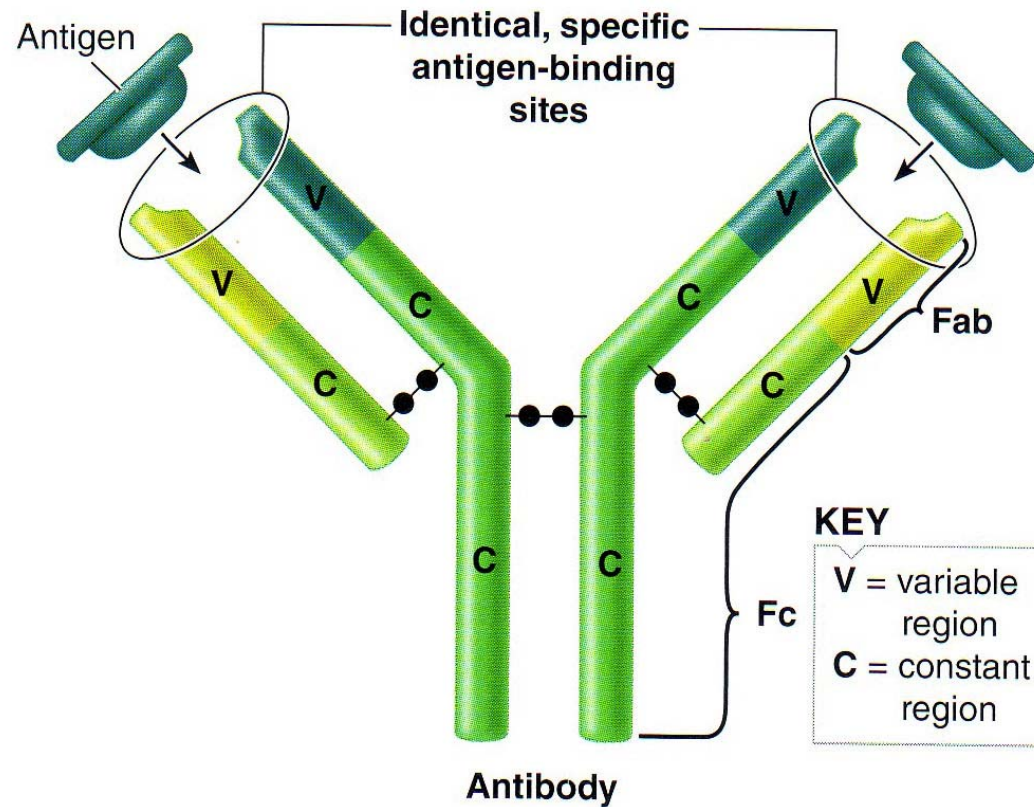


8500 x GMBH
Nat Geog 1986

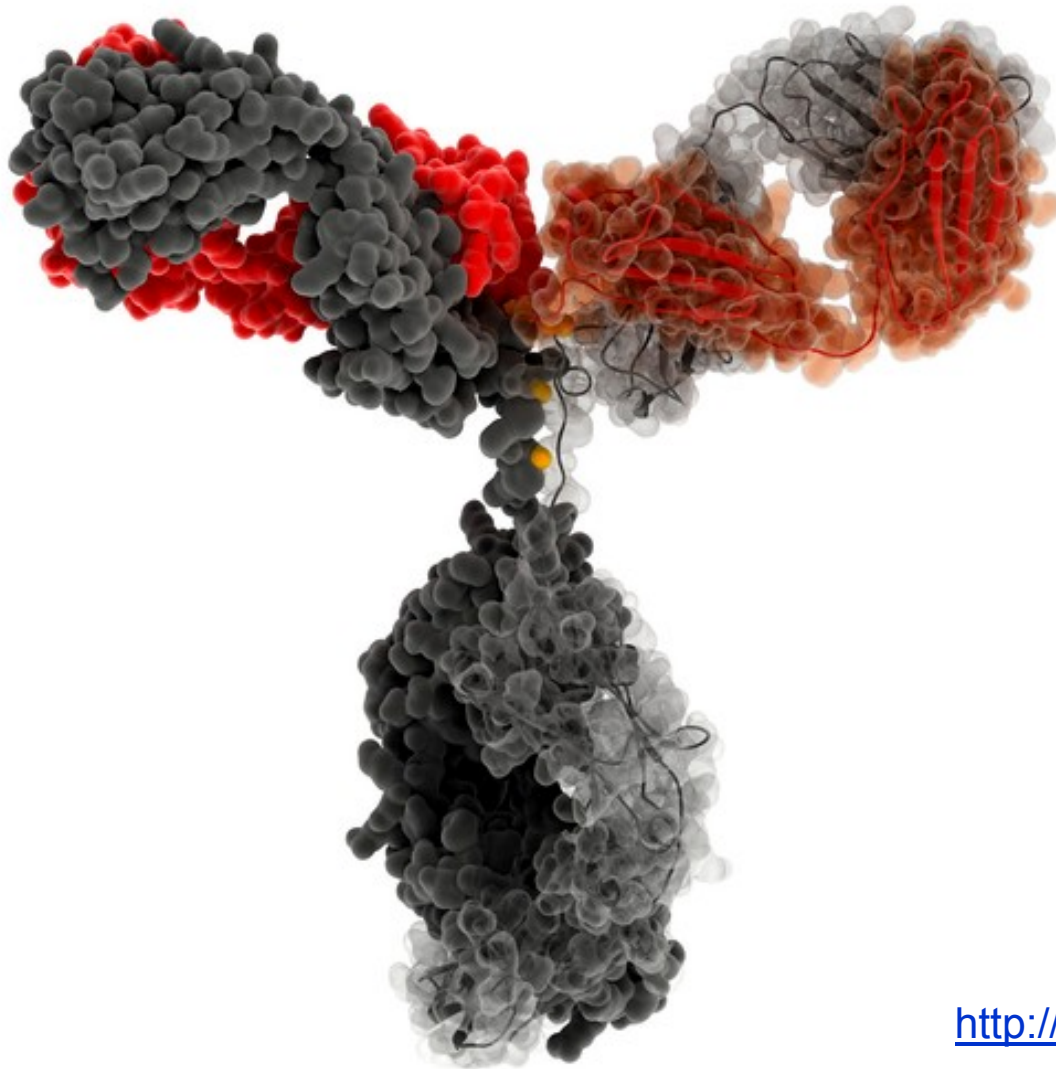
Typical IgG Antibody Structure



How do antibodies work?

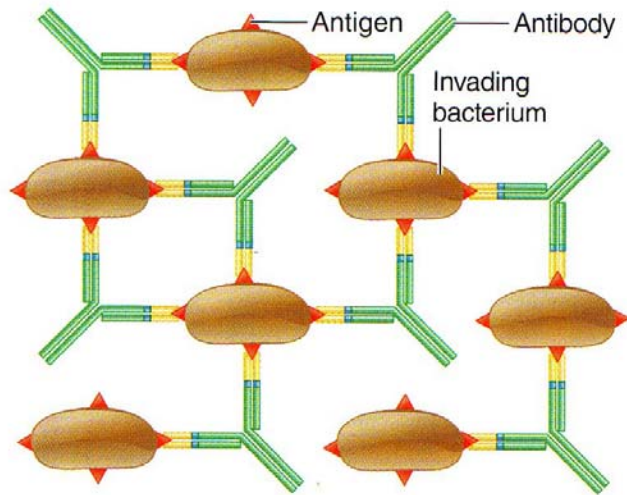


Immunoglobulin G

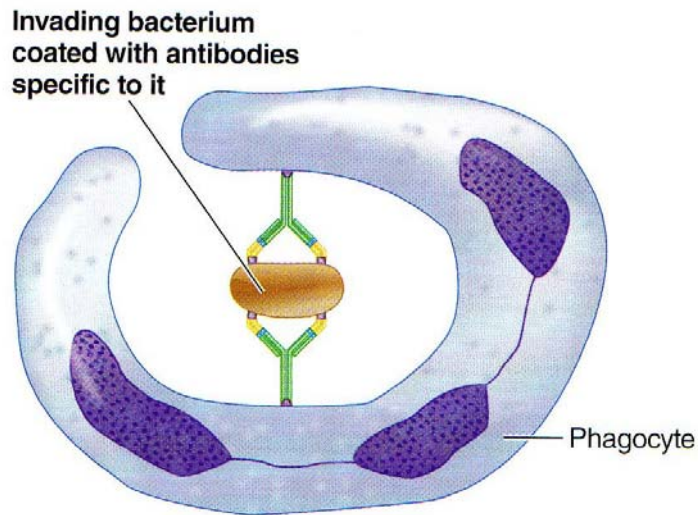


Source:
Visual Science
<http://visualscience.ru/en/>

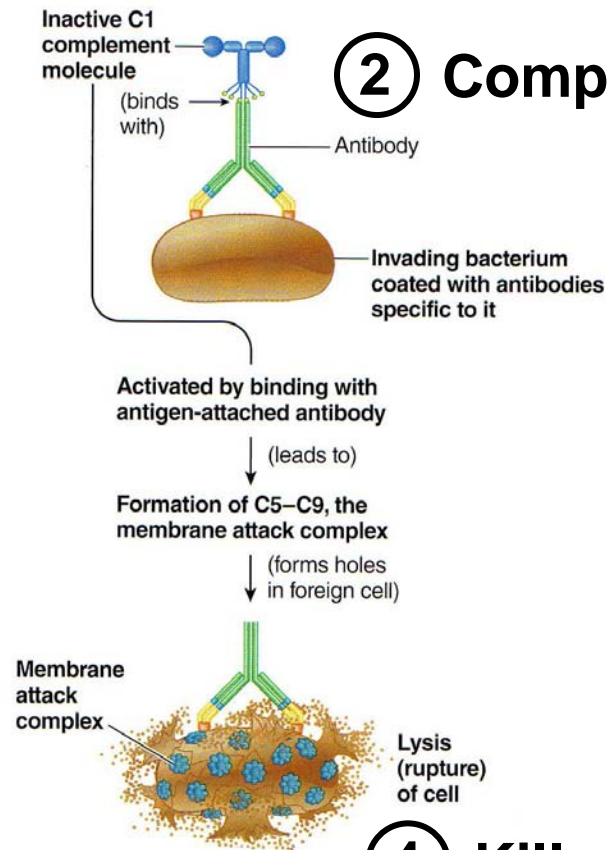
① Agglutination



③ Opsonization



② Complement



④ Killer Cells

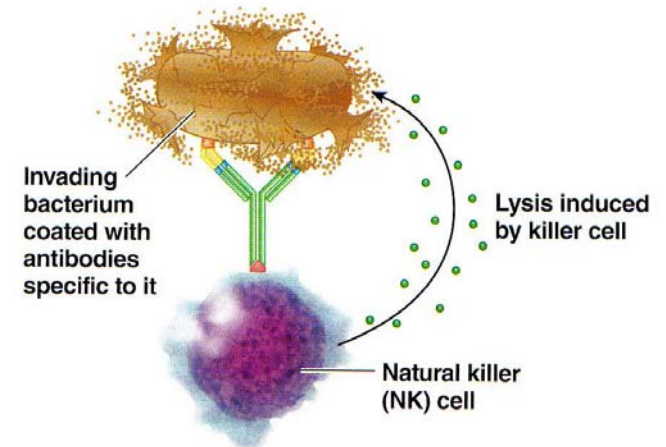
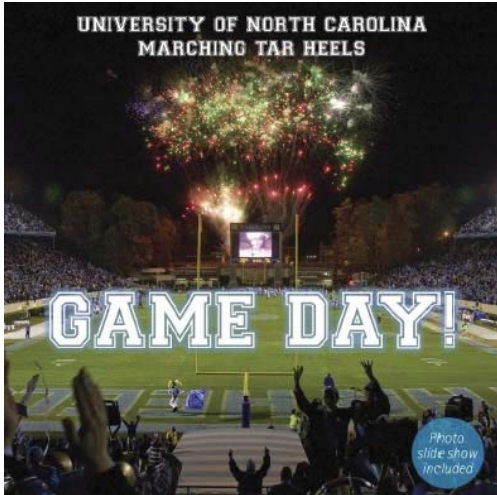


TABLE 4.1 Characteristics and functions of the human immunoglobulin classes

	G	A	M	D	↔ E
immunoglobulin class	IgG	IgA	IgM	IgD	IgE
heavy-chain type	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.

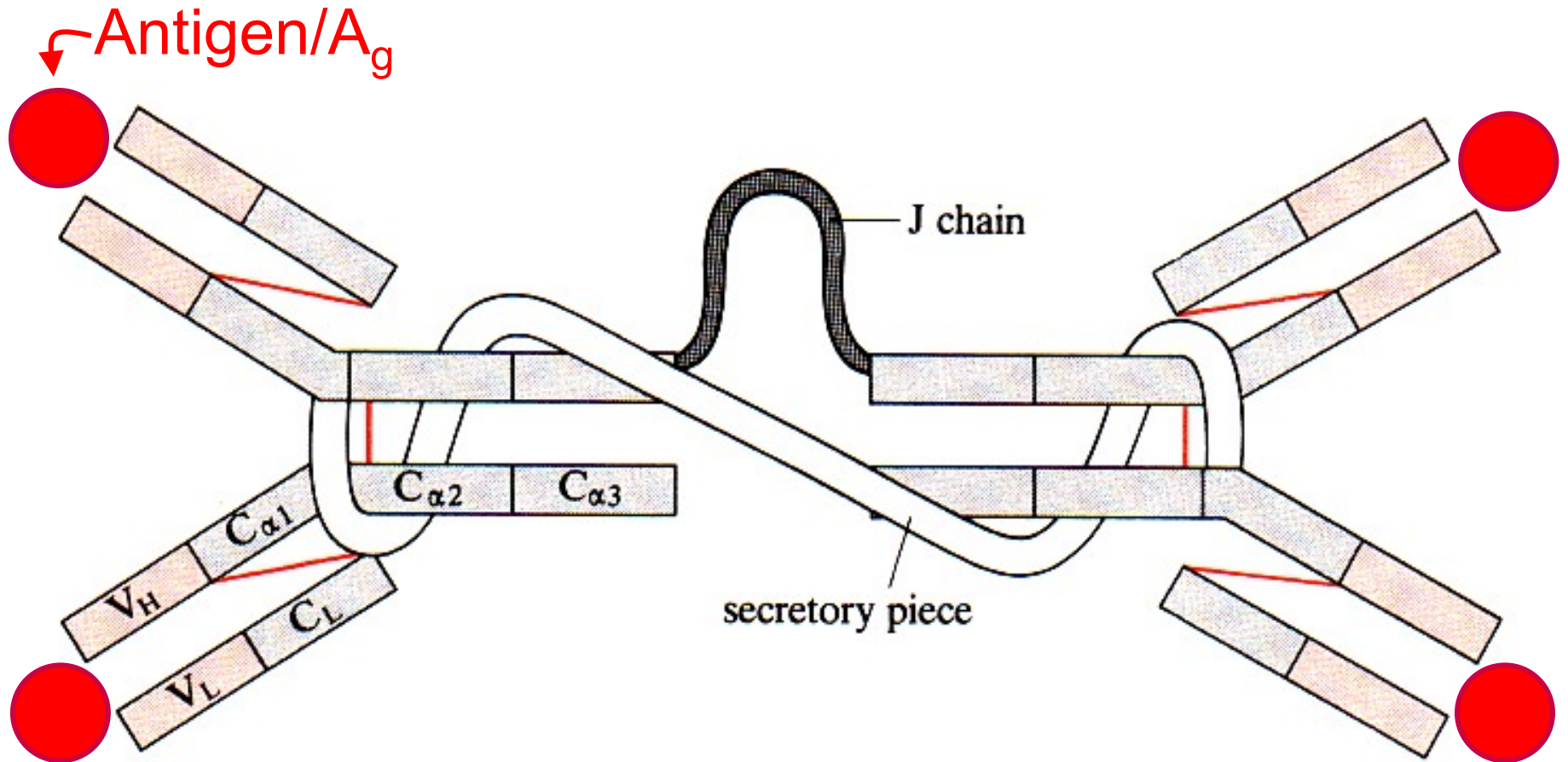


G A M E D!

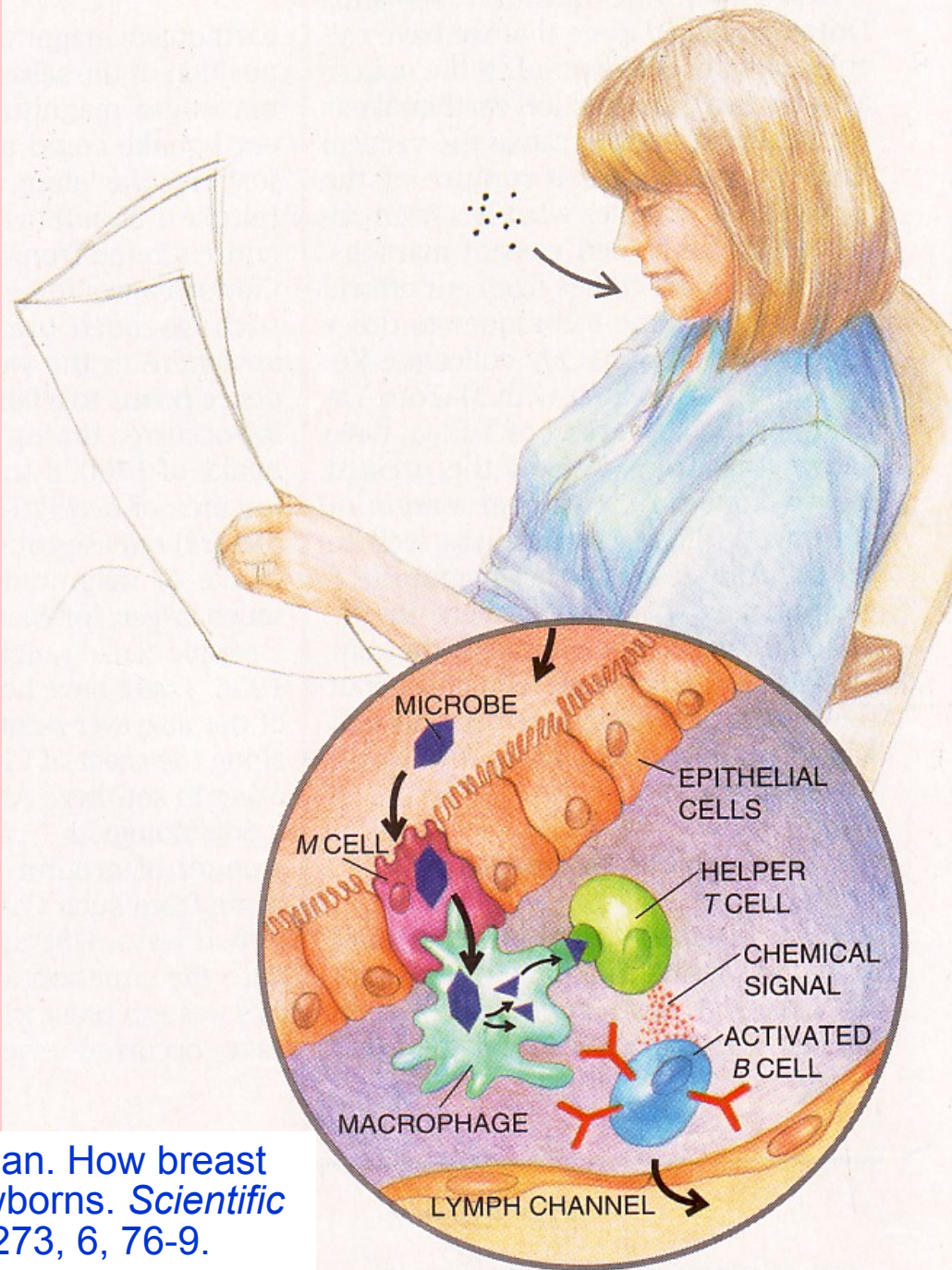


IgA = Secretory A_b

Dimer!!

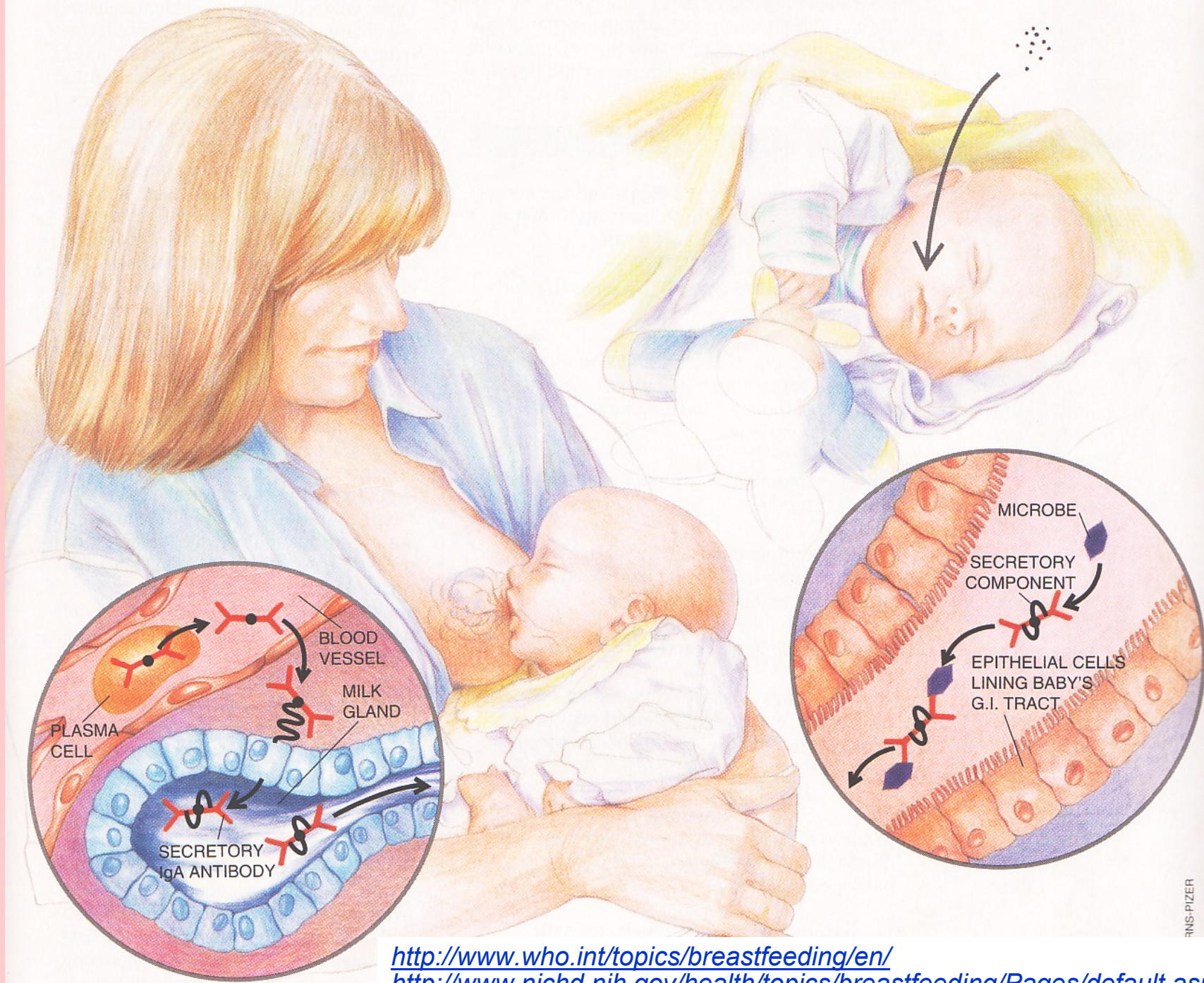


Valence? 4



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
White Blood Cells	
<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.

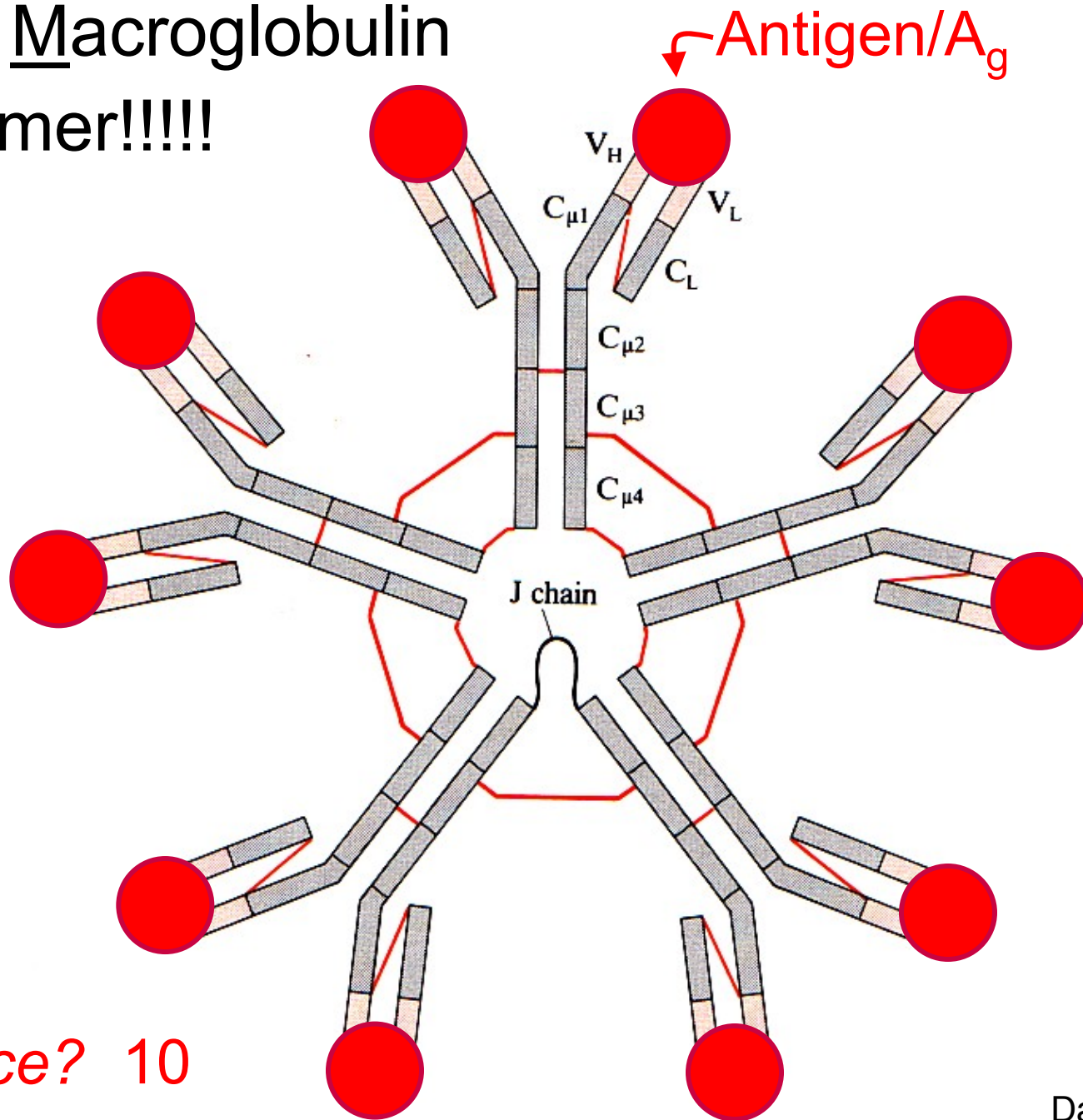
Molecules

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 ₁₂ binding protein	Reduces amount of vitamin B ₁₂ , 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!!!!

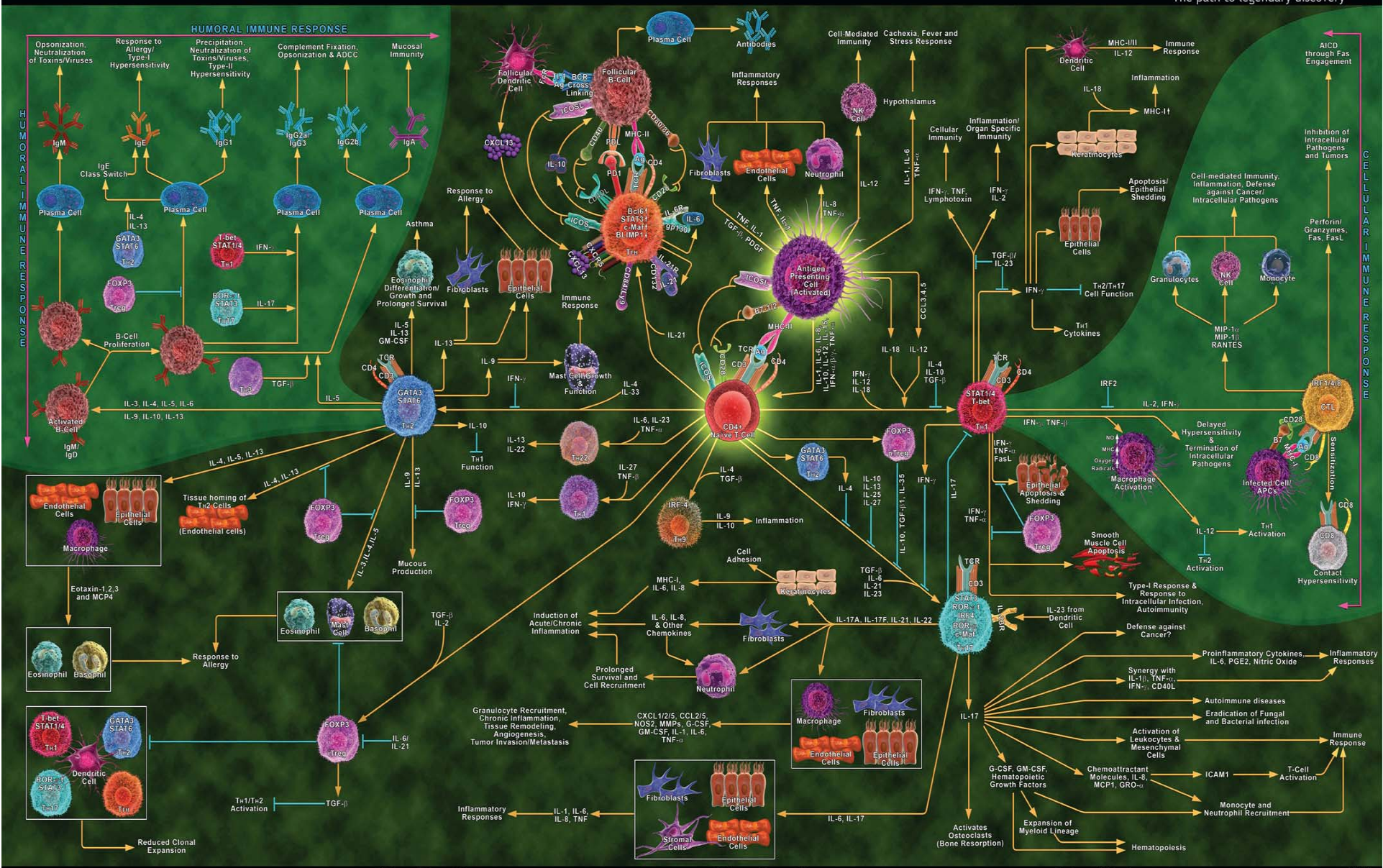


Valence? 10

Immunologic Networks <http://pinterest.com/pin/50947039506317536/>



The path to legendary discovery™



www.biolegend.com

Interactive Poster: biolegend.com/immunologicnetworks

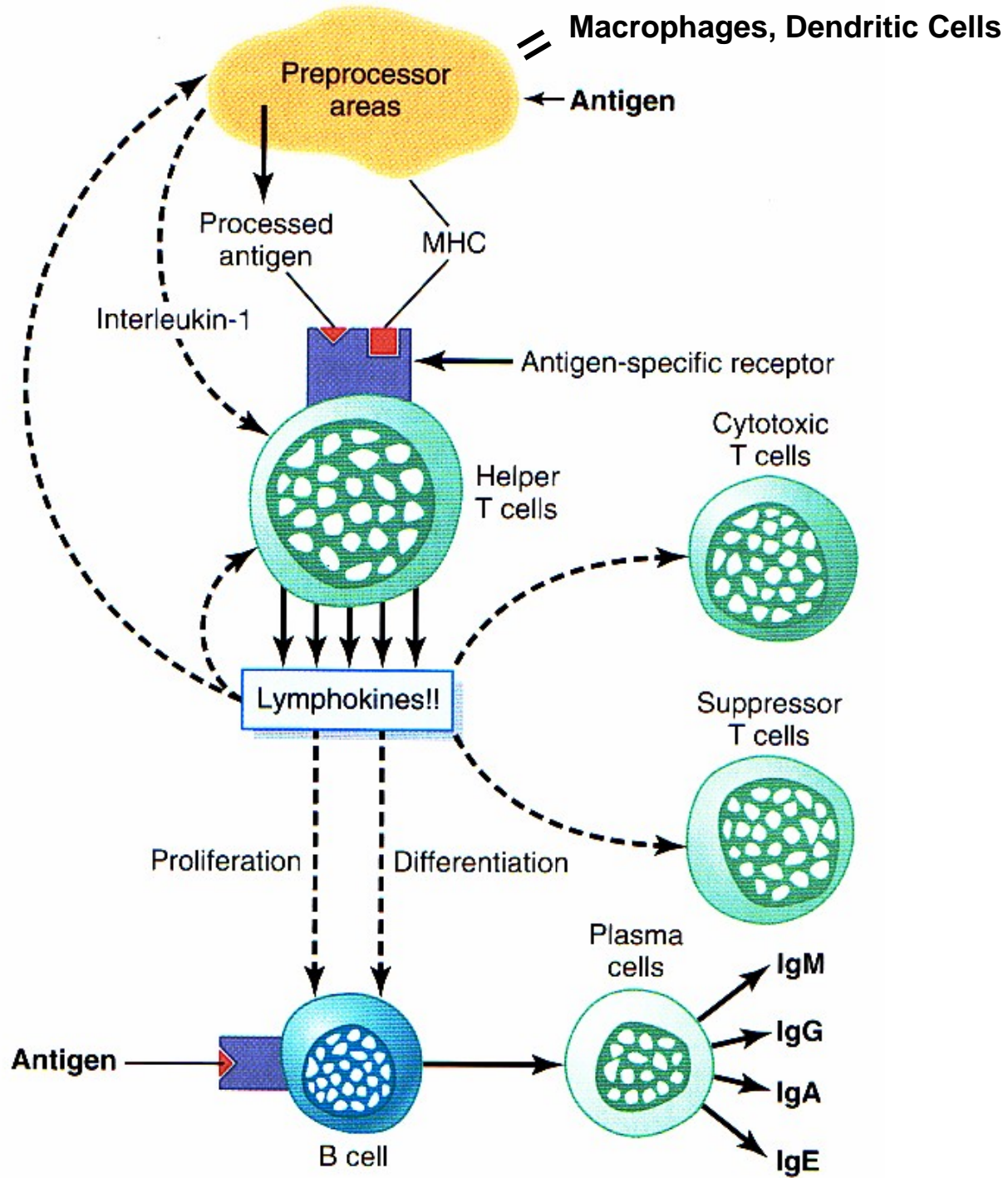
BioLegend Japan KK
 8F, SB bldg., 1-4-6, Nezu, Bunkyo-ku, Tokyo 113-0031, Japan
 Phone: +81-3-3823-9071 Fax: +81-3-3823-9072
 Email: support@biolegend.com Web: www.biolegend.com/jp

BioLegend Europe BV
 Ambachtweg 5, 1422 DS Uithoorn, The Netherlands
 Phone: +31-297-522488 Fax: +31-297-522756
 Email: info@biolegend.com, tech@biolegend.com

BioLegend (Headquarters)
 San Diego, CA 92121, USA
 Toll-Free Phone: 1-877-BioLegend (246-5343)
 Phone: (858) 455-9588 Fax: (877) 455-9587
 Email: customerserv@biolegend.com, techserv@biolegend.com

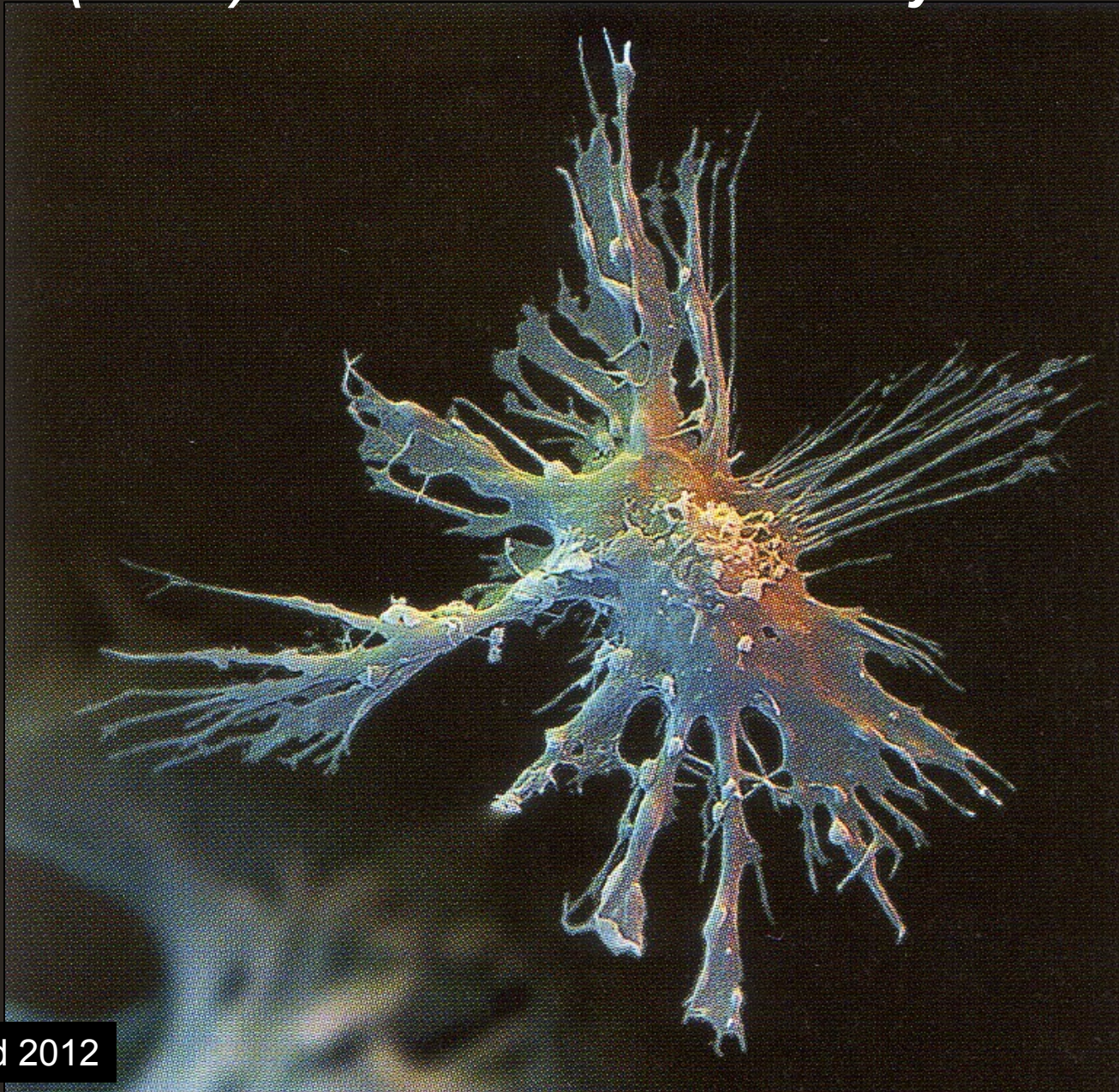
We would like to thank **Dr. Vijay K. Kuchroo** of Harvard Medical School for his contributions to this poster.

Created by ProteinLounge.com in Sep 2011



G&H fig 34-8 2011

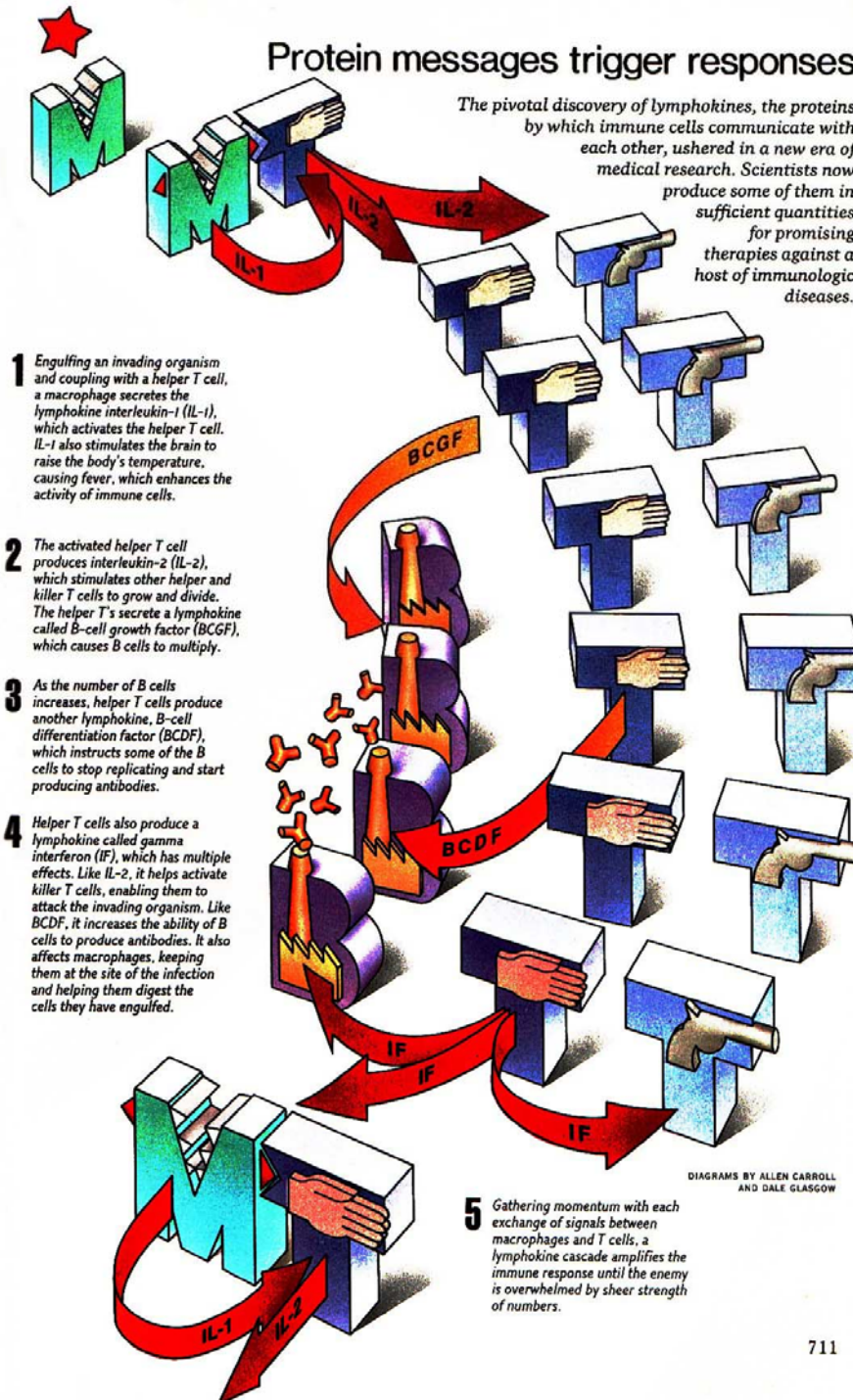
Dendritic Cells: Specialized Antigen-Presenting Cells (APCs) Sentinels in Almost Every Tissue!



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.



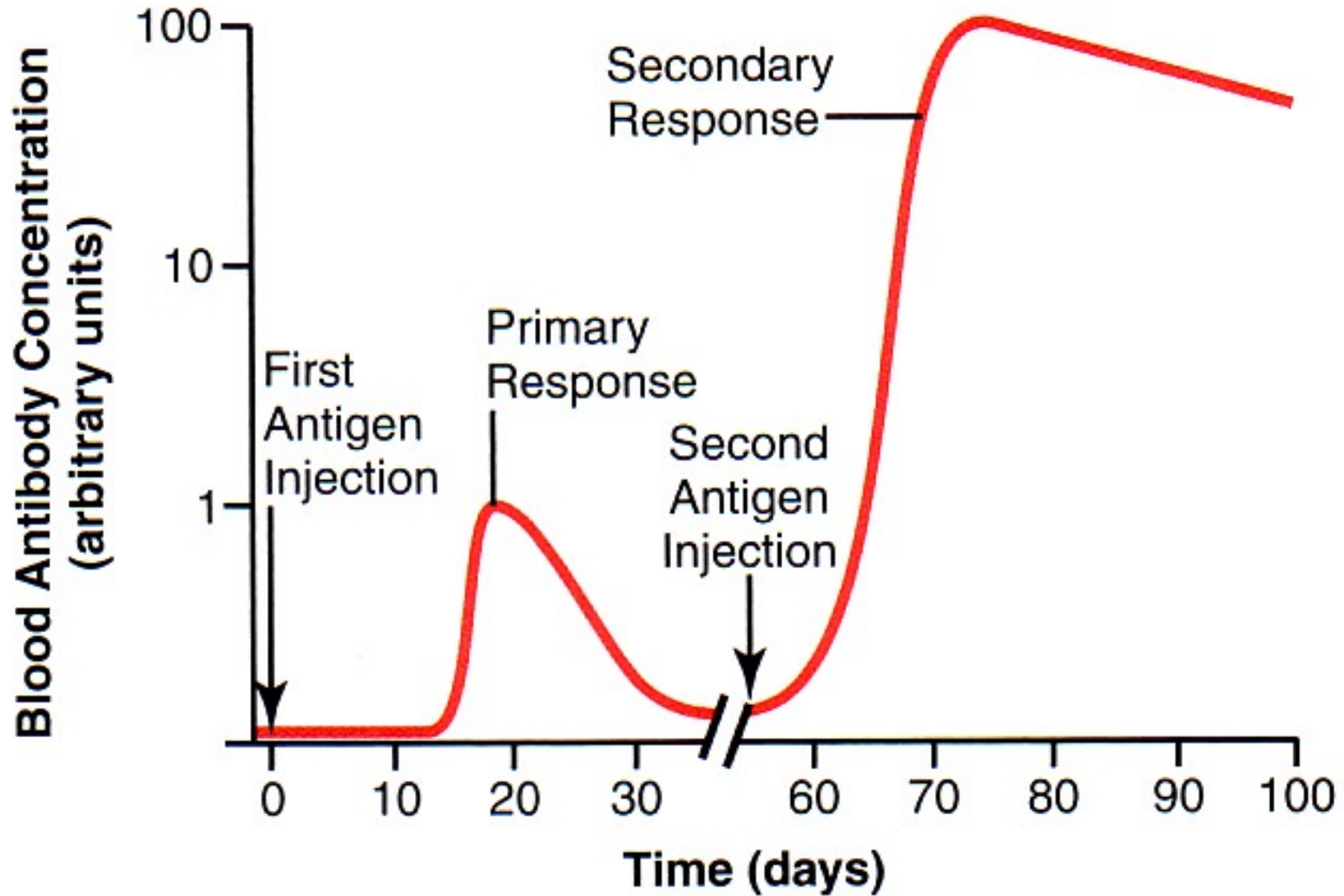


Figure 34-3 Time course of the antibody response in the circulating blood to a primary injection of antigen and to a secondary injection several weeks later.



**Wear Red next Friday (Feb 6th!)
Help raise awareness about
Women & ♥ disease**

<http://www.goredforwomen.org/>

<https://www.goredforwomen.org/about-heart-disease/facts-about-heart-disease-in-women-sub-category/statistics-at-a-glance/>

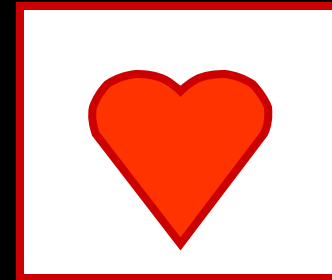
7 Resolutions *to Improve* ♥ *Health in 2014*

- **Quit smoking**
- **Avoid 2nd –hand smoke**
- **Know your numbers**
- **Process out processed foods**
- **Get moving**
- **Get your friends & family on board**
- **Spread awareness**

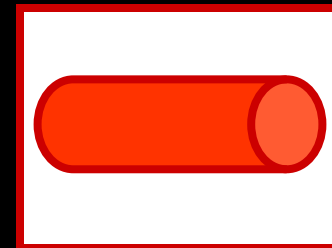


http://www.goredforwomen.org/about-heart-disease/symptoms_of_heart_disease_in_women/just-a-little-heart-attack/

Cardiovascular (CV) = Heart + Vessels + Blood!



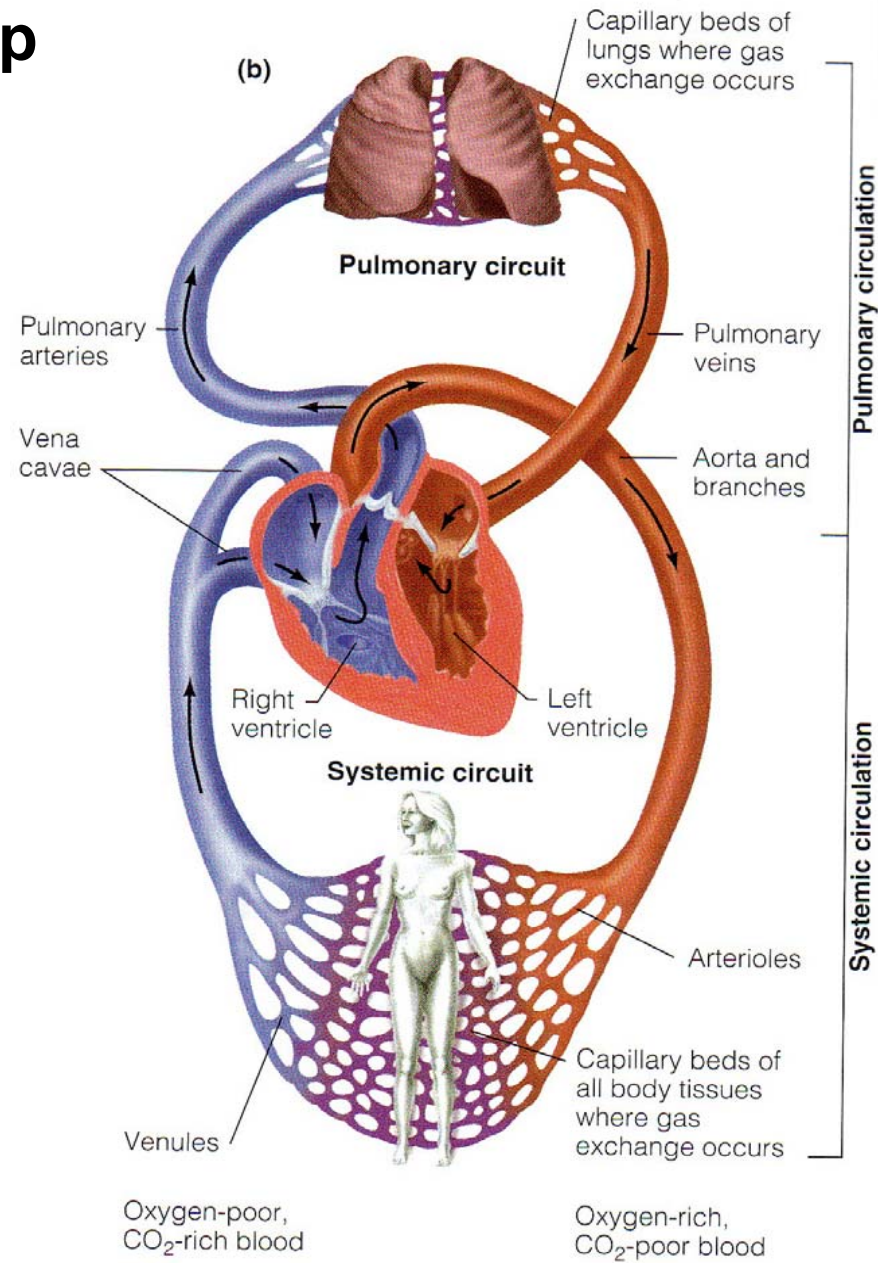
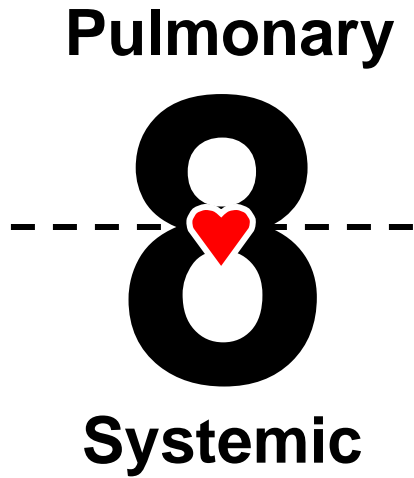
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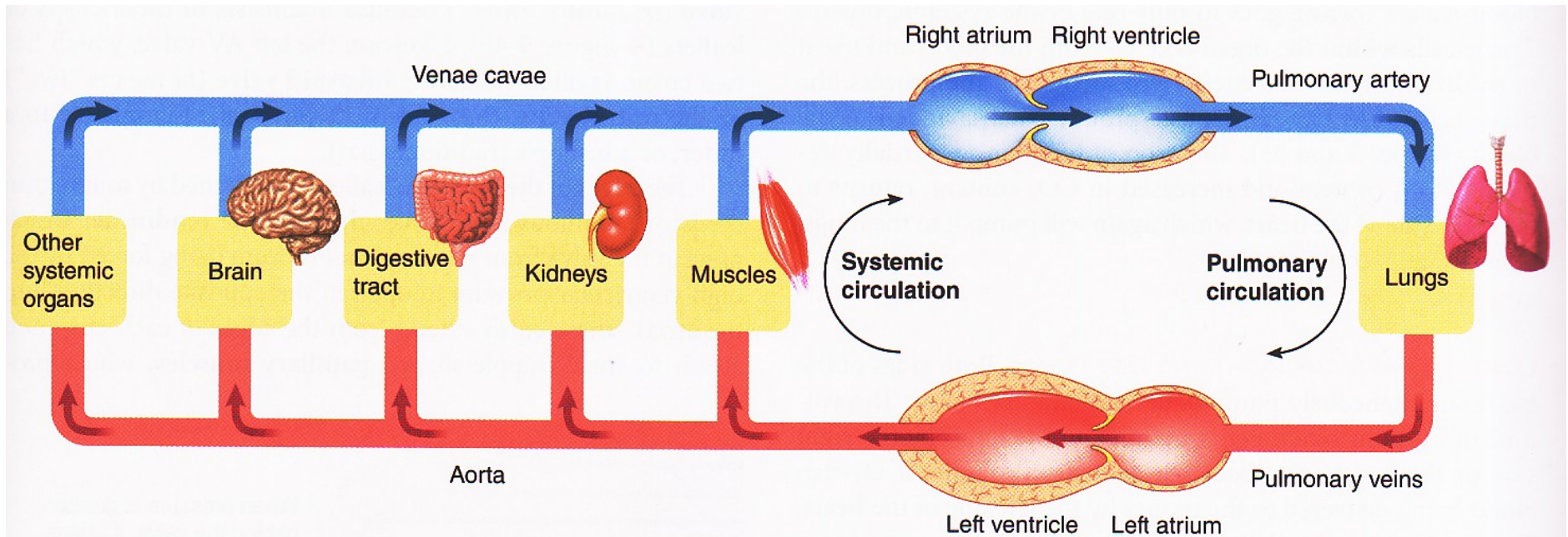
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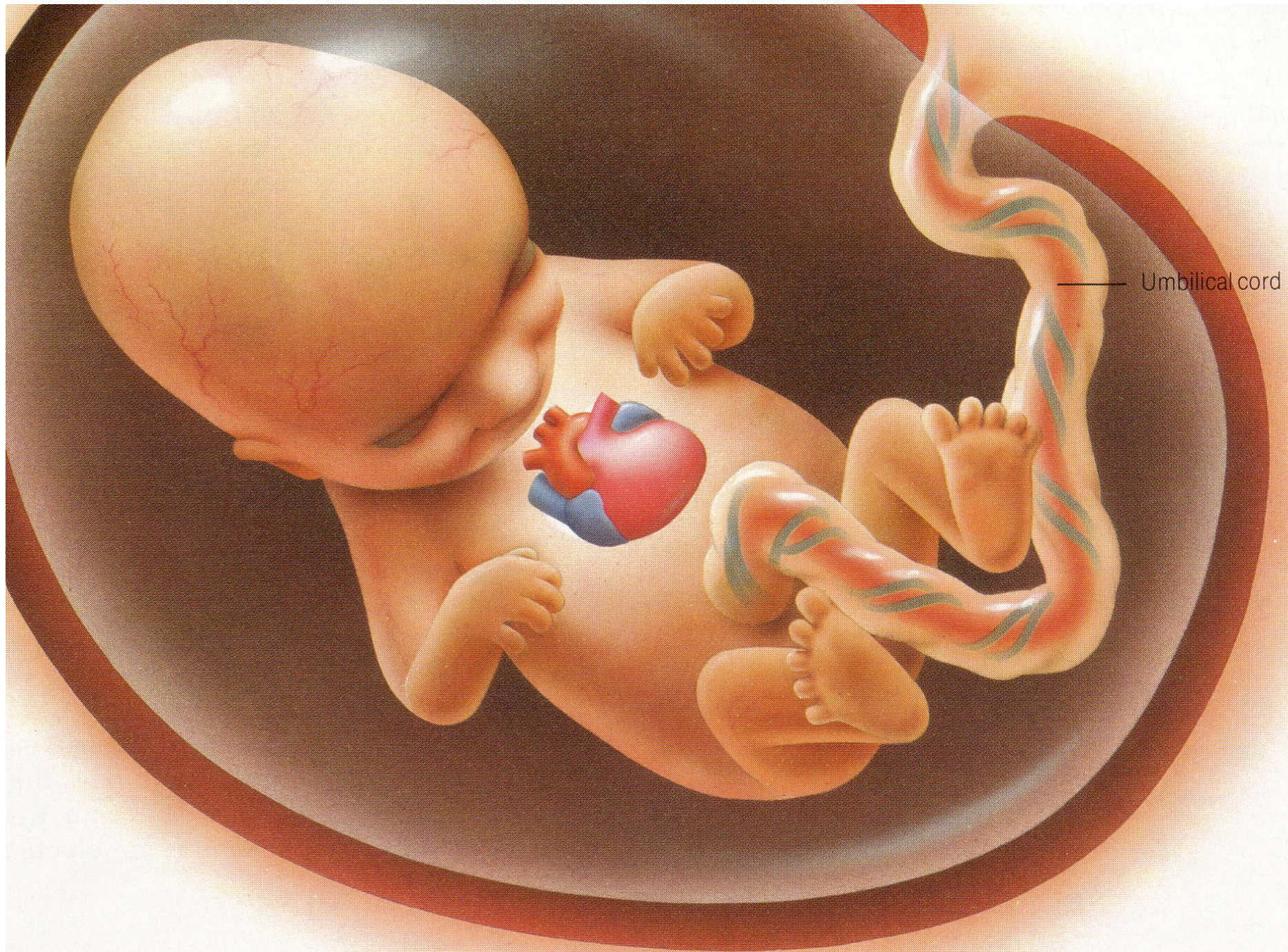


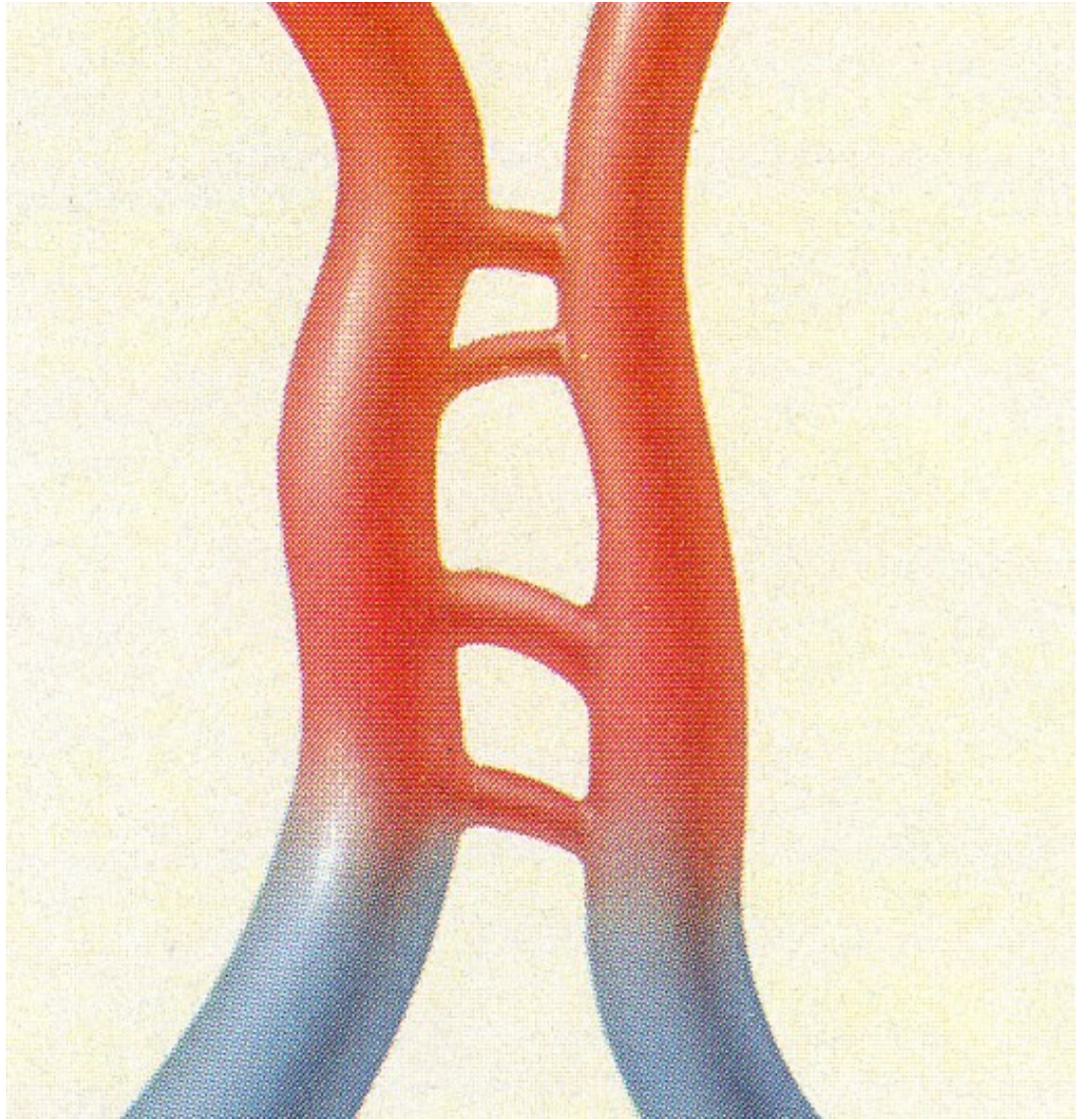
NB: Figure-8 loop

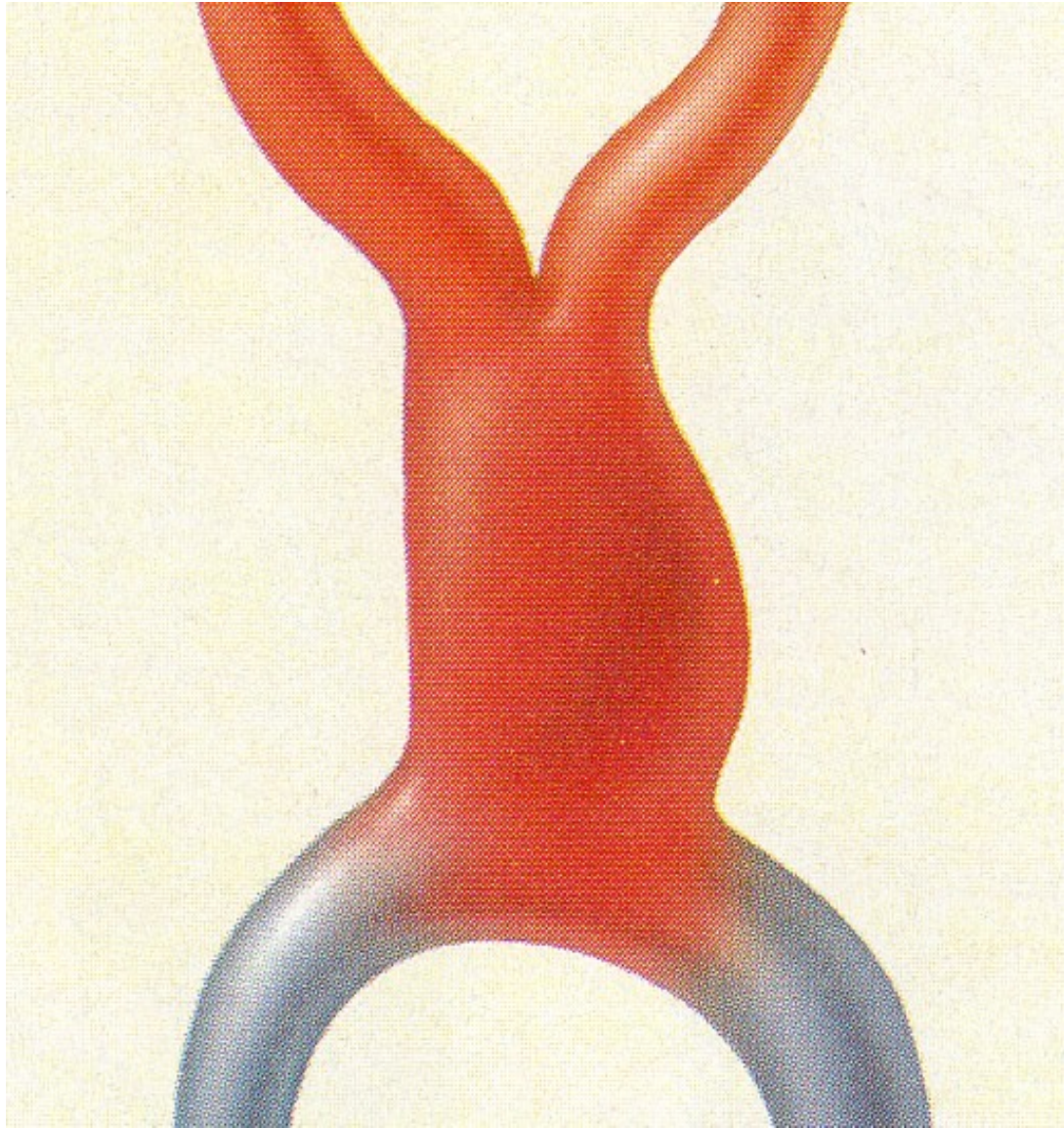


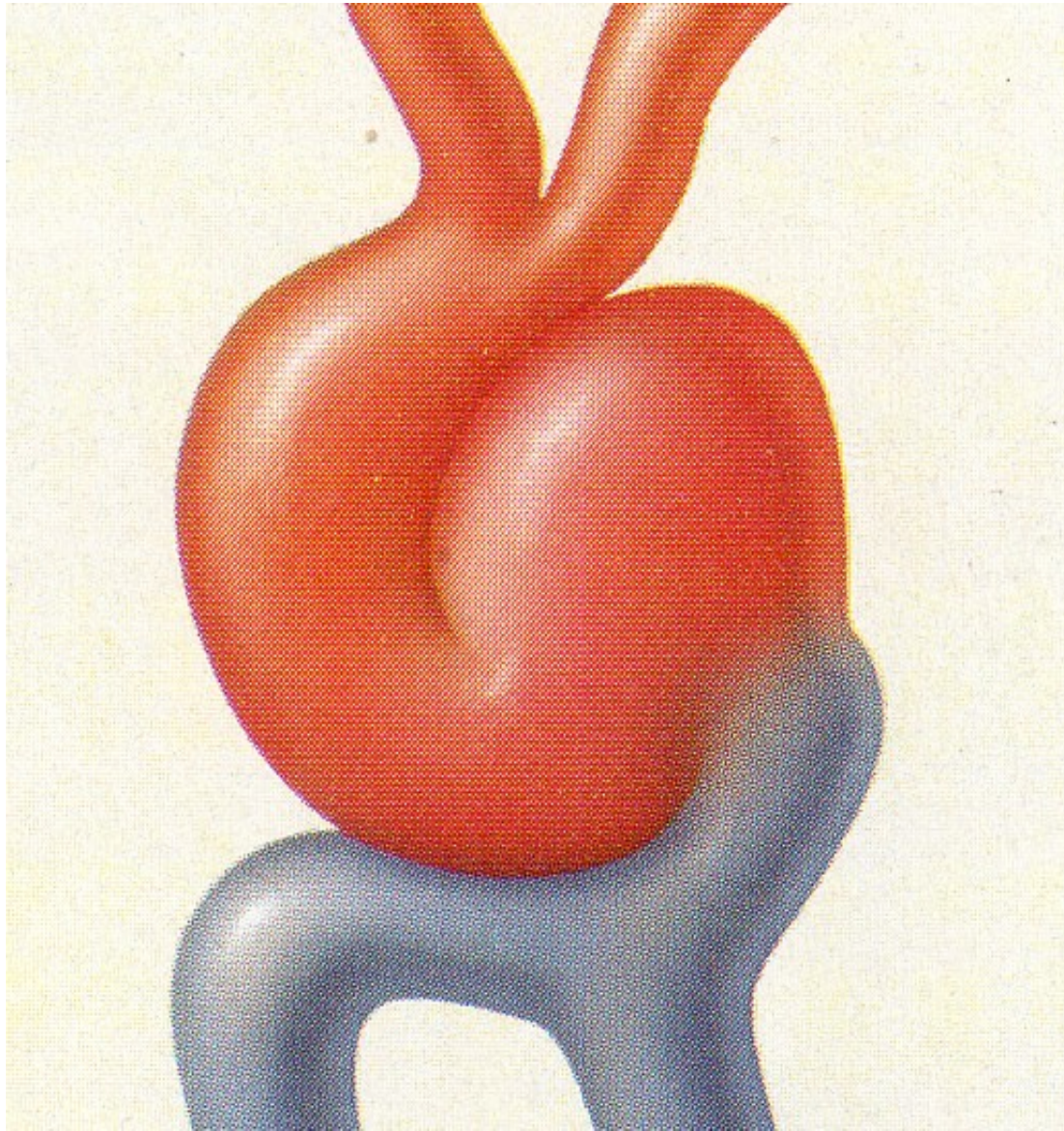
Dual Pump Action & Parallel Circulation



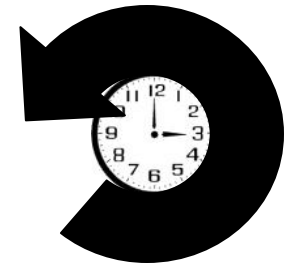


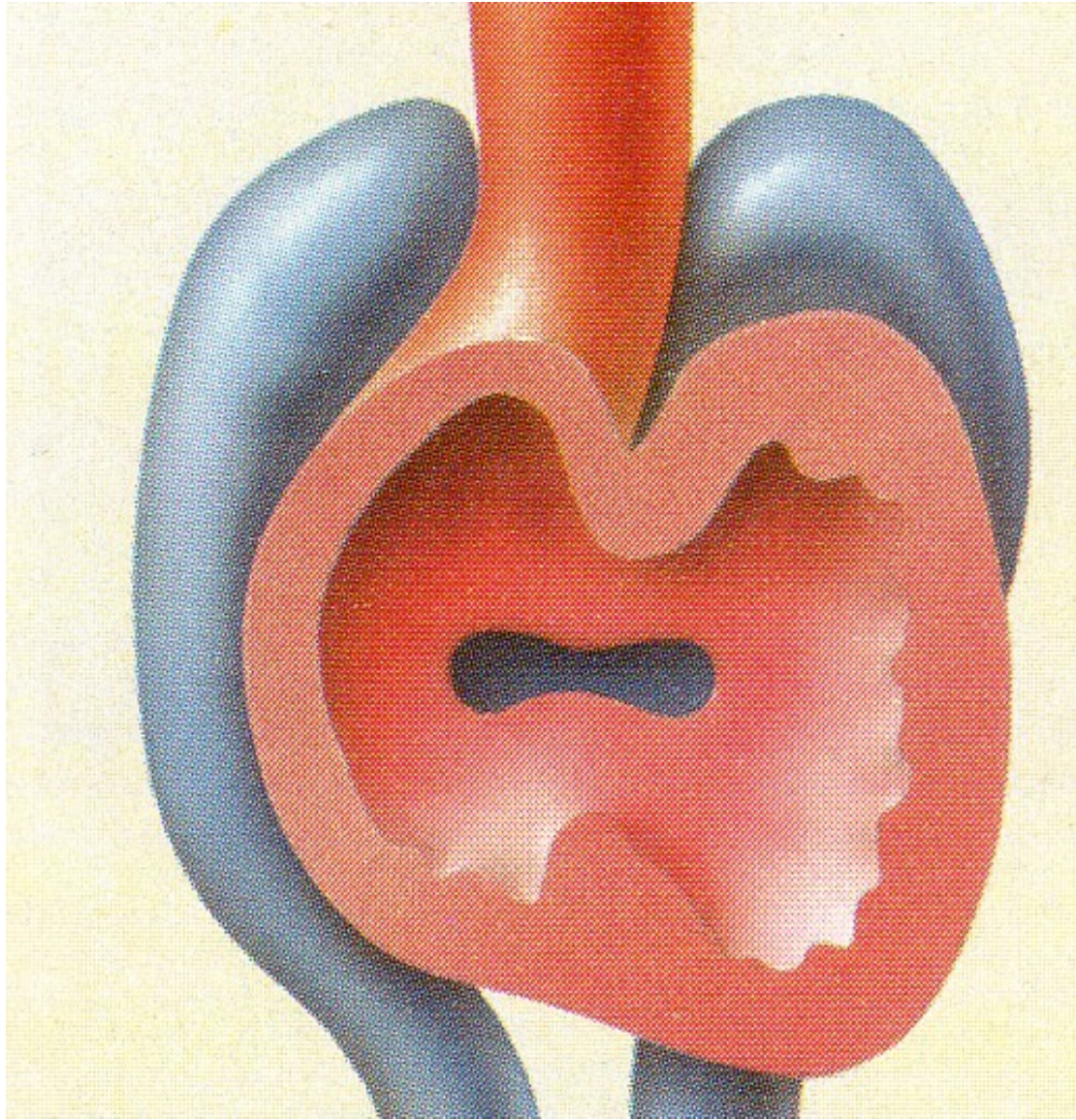


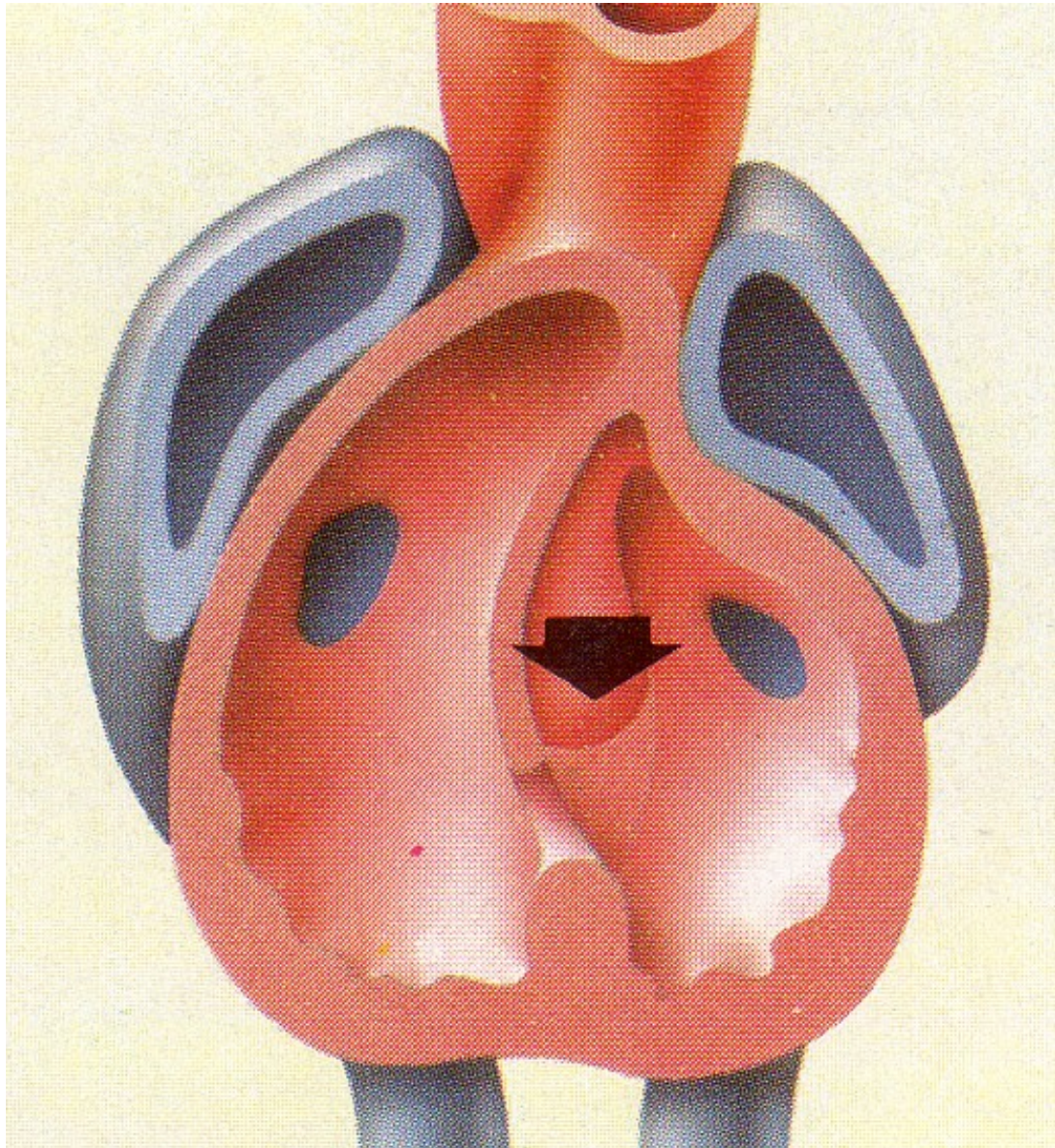




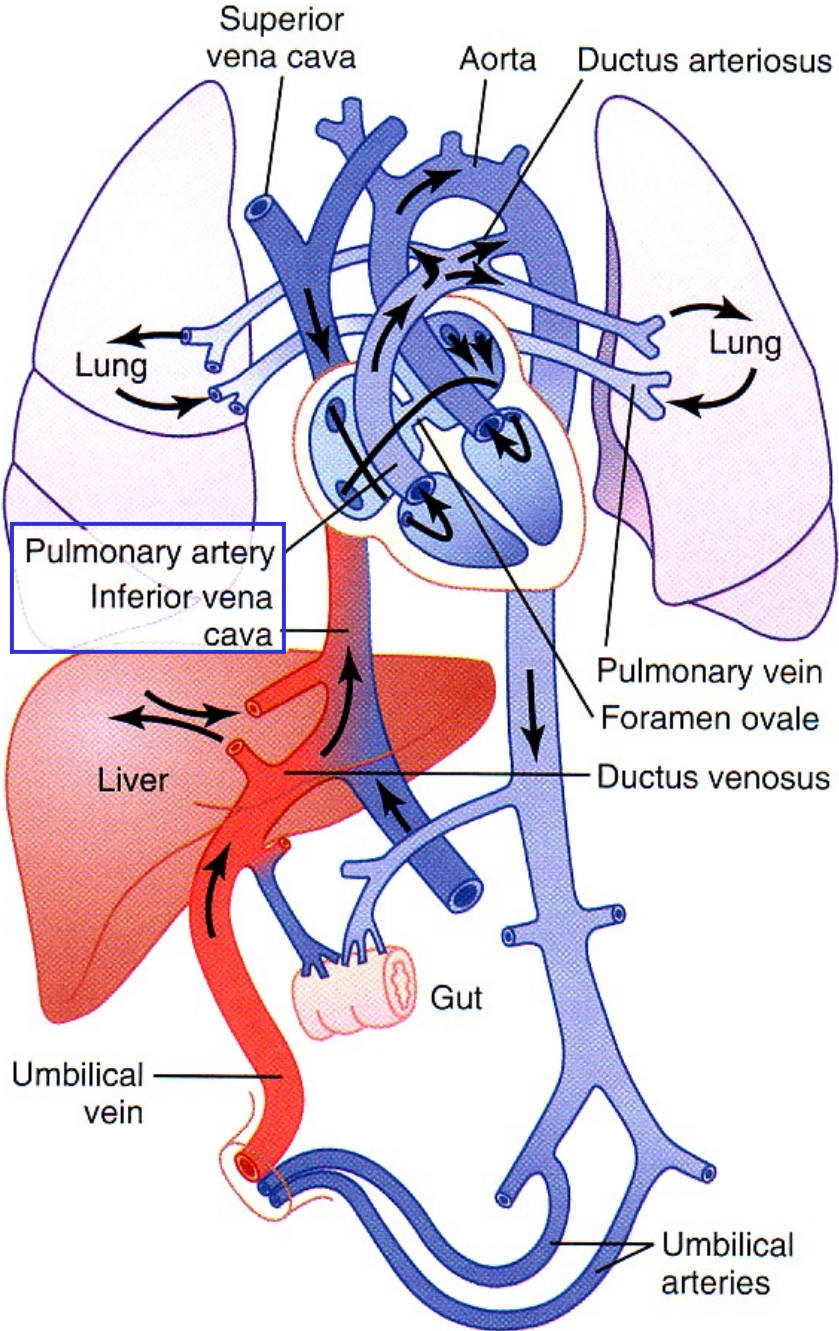
Counter-clockwise



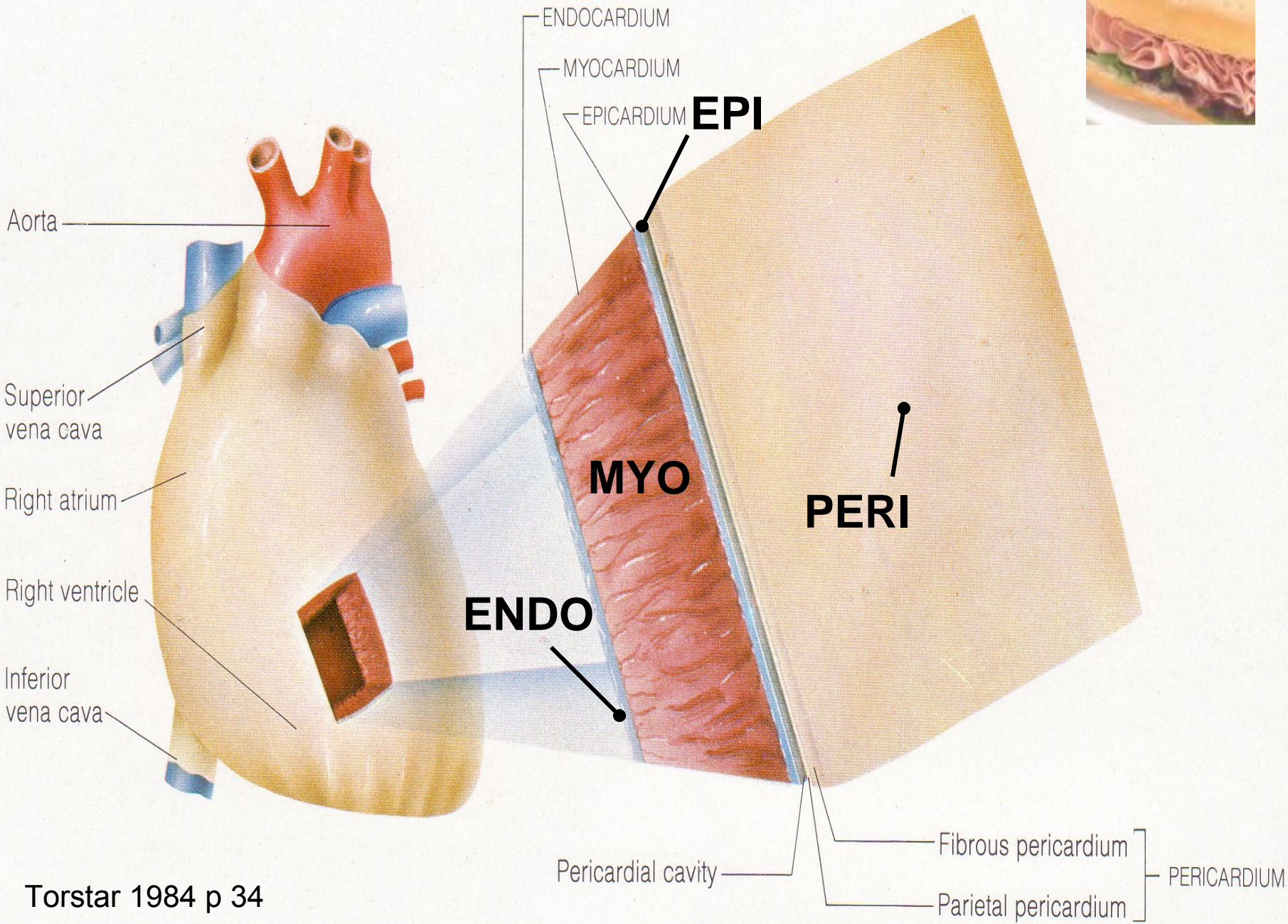





Fetal Circulation
 ≡ *Aqua Animal*
Bypass Lungs
 R → L ♥ Shunt

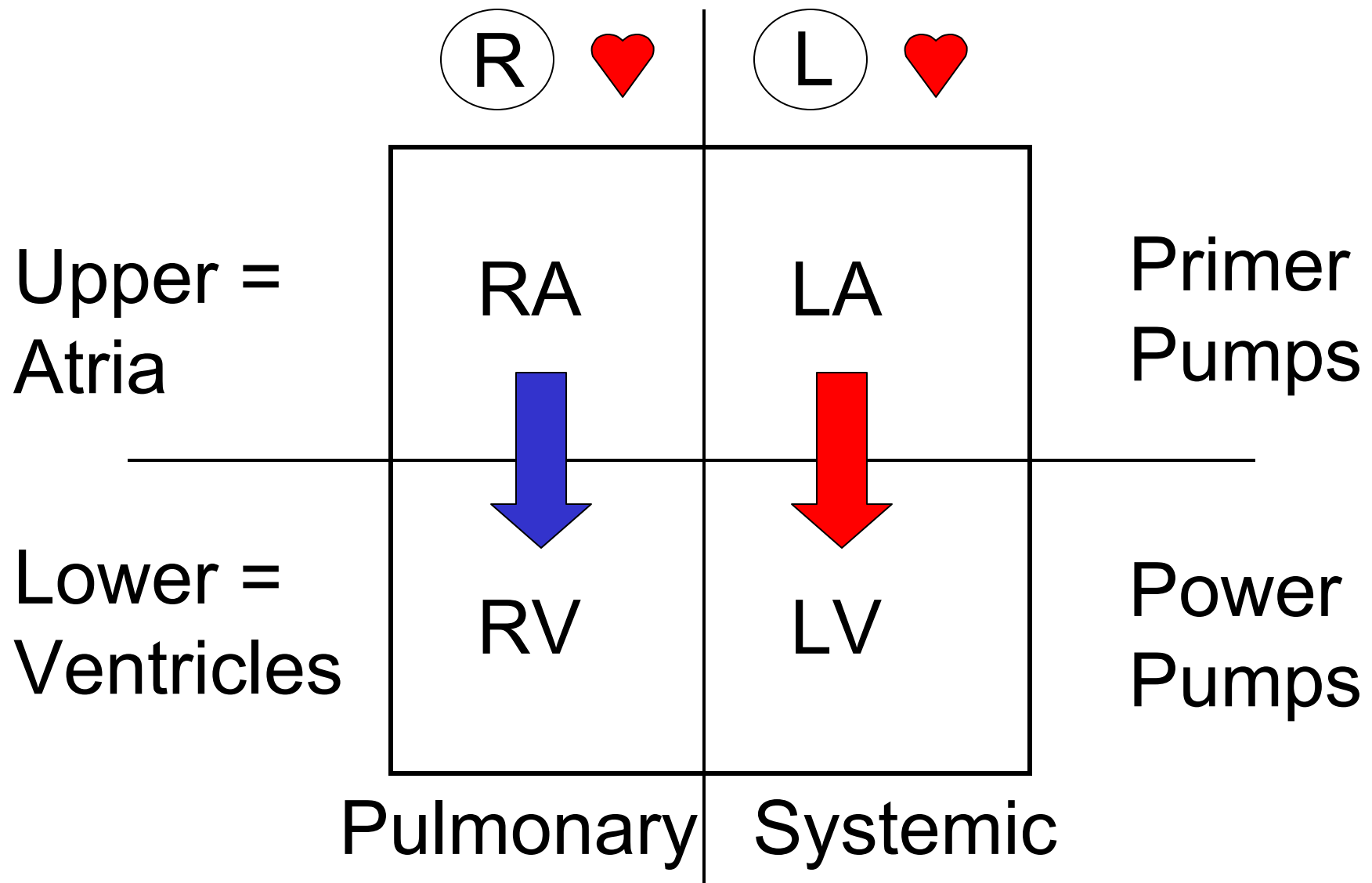


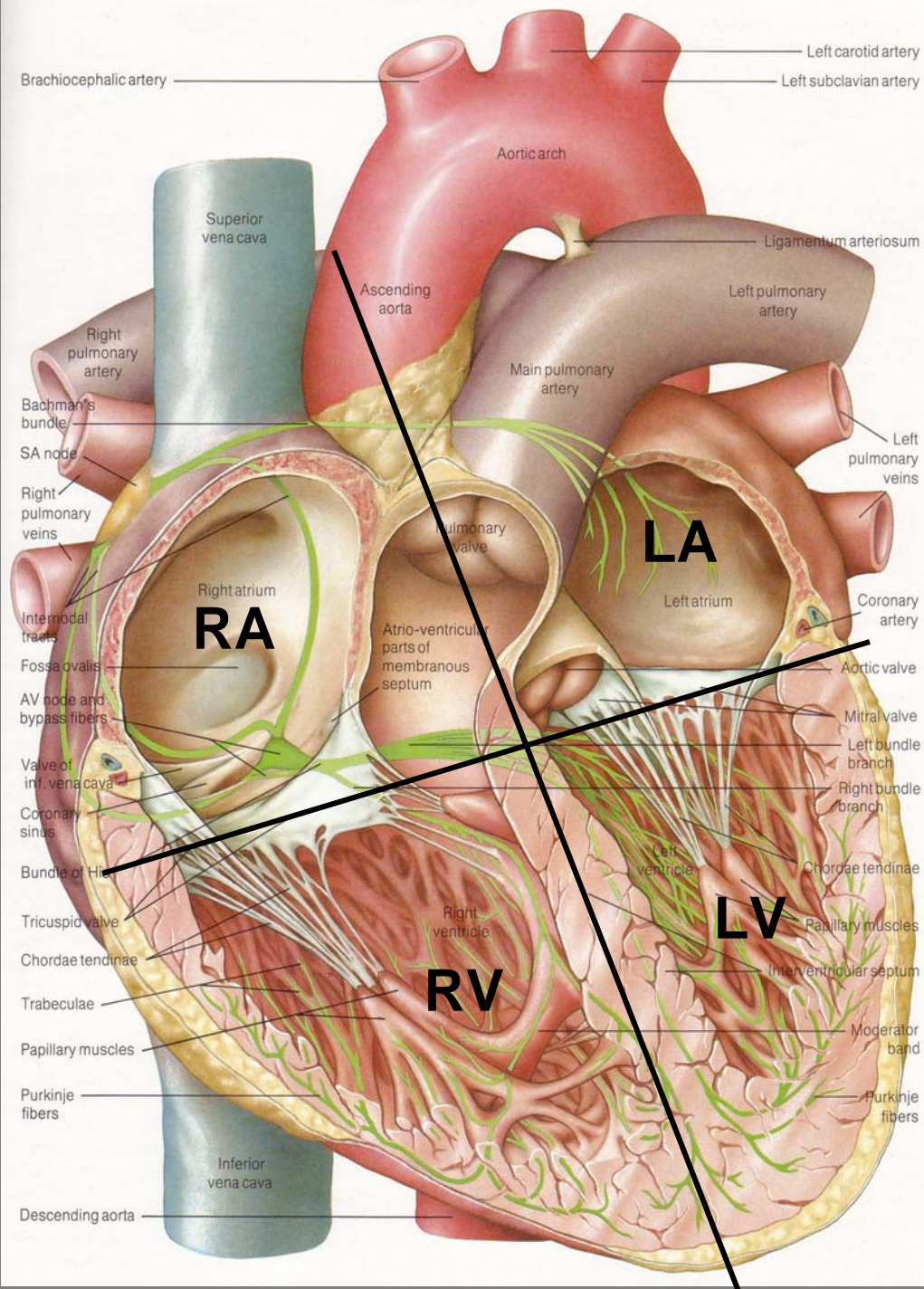
G&H 2011 fig 83-4



Torstar 1984 p 34

Human  = 4-chambered box?
2 separate pumps?





Human ♥ = 4 unique valves?
2 valve sets?

Semilunar = Half-moon shaped

More rigid

1. Pulmonic/Pulmonary
2. Aortic



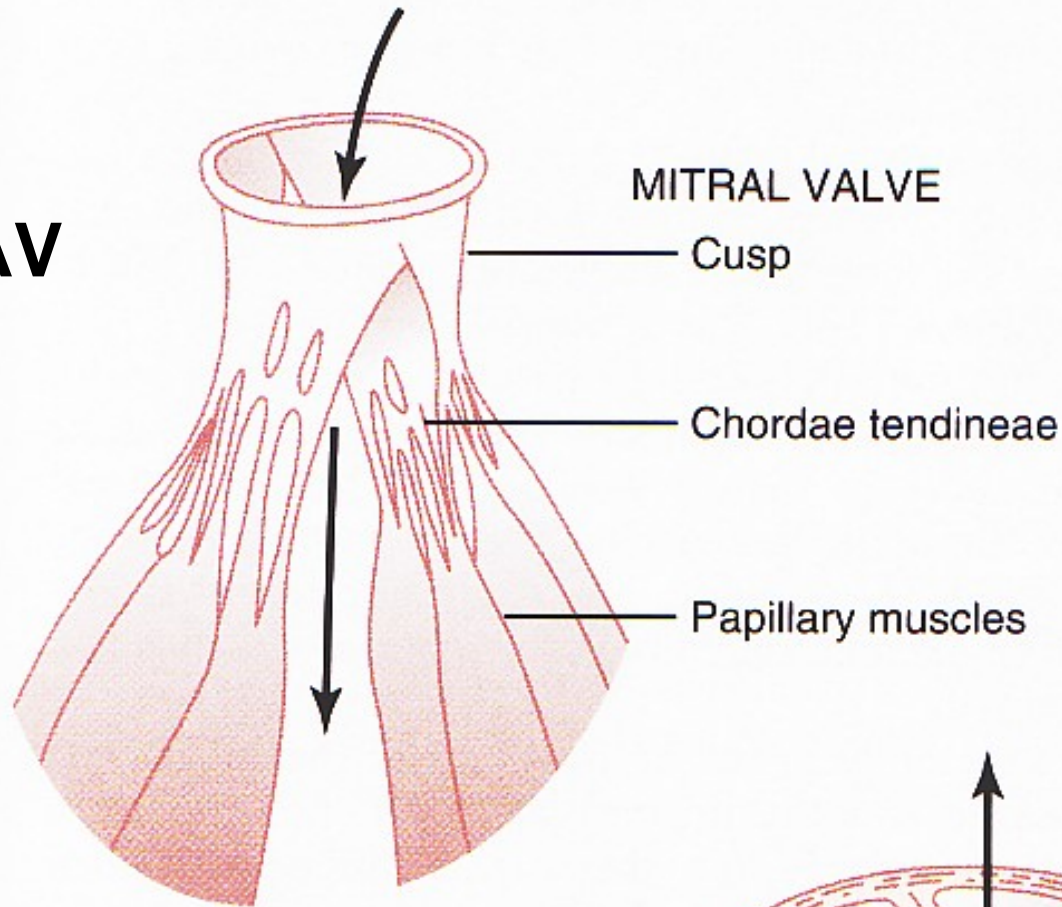
AV = Atrioventricular

More flimsy

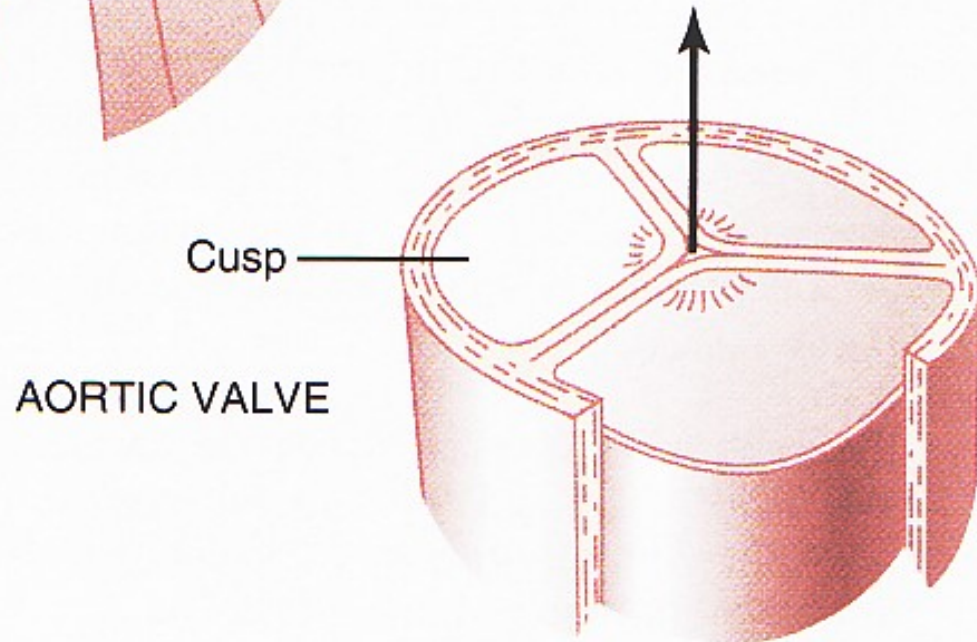
3. (R) AV = Tricuspid
4. (L) AV = Mitral/Bicuspid



(L) AV

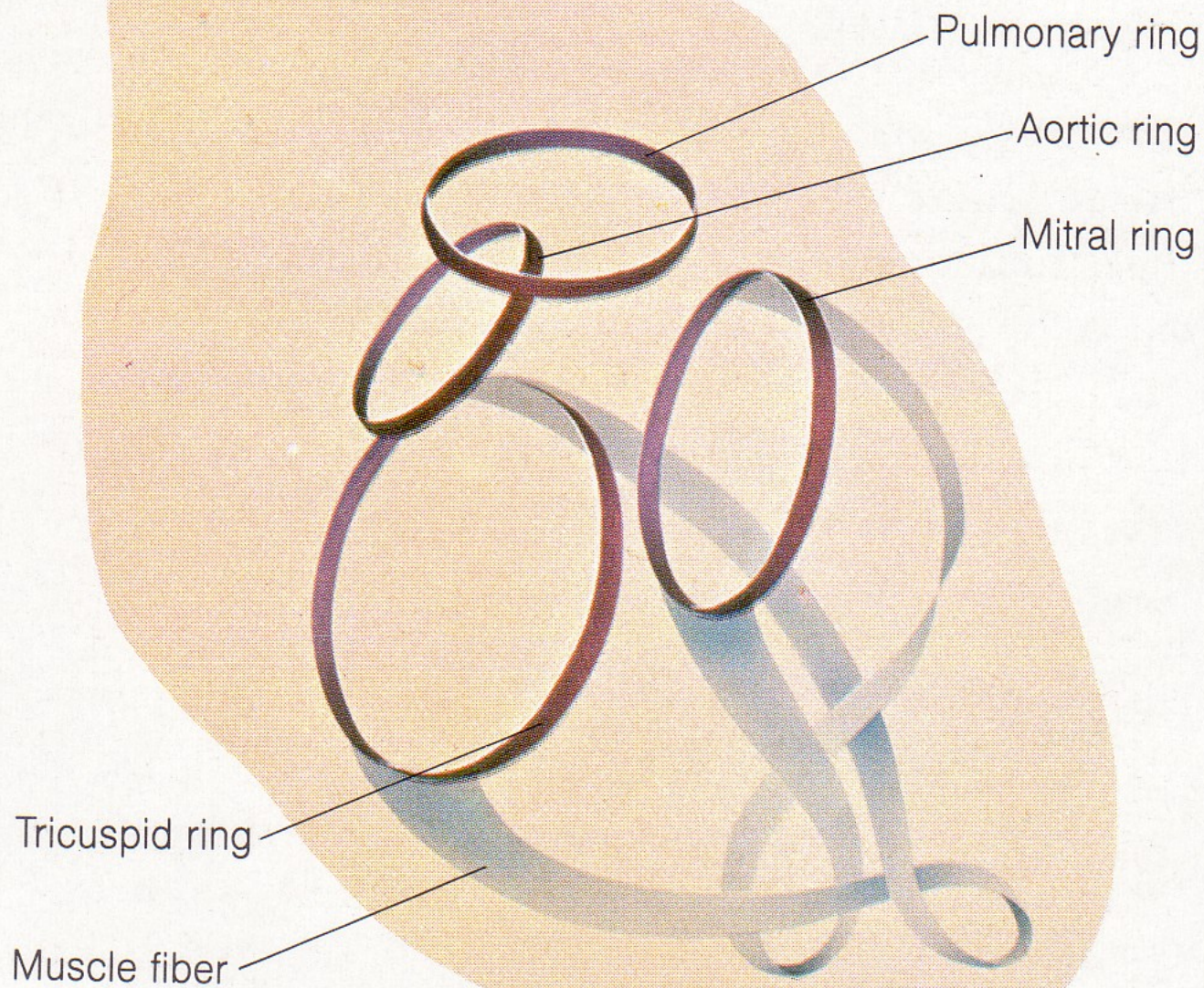


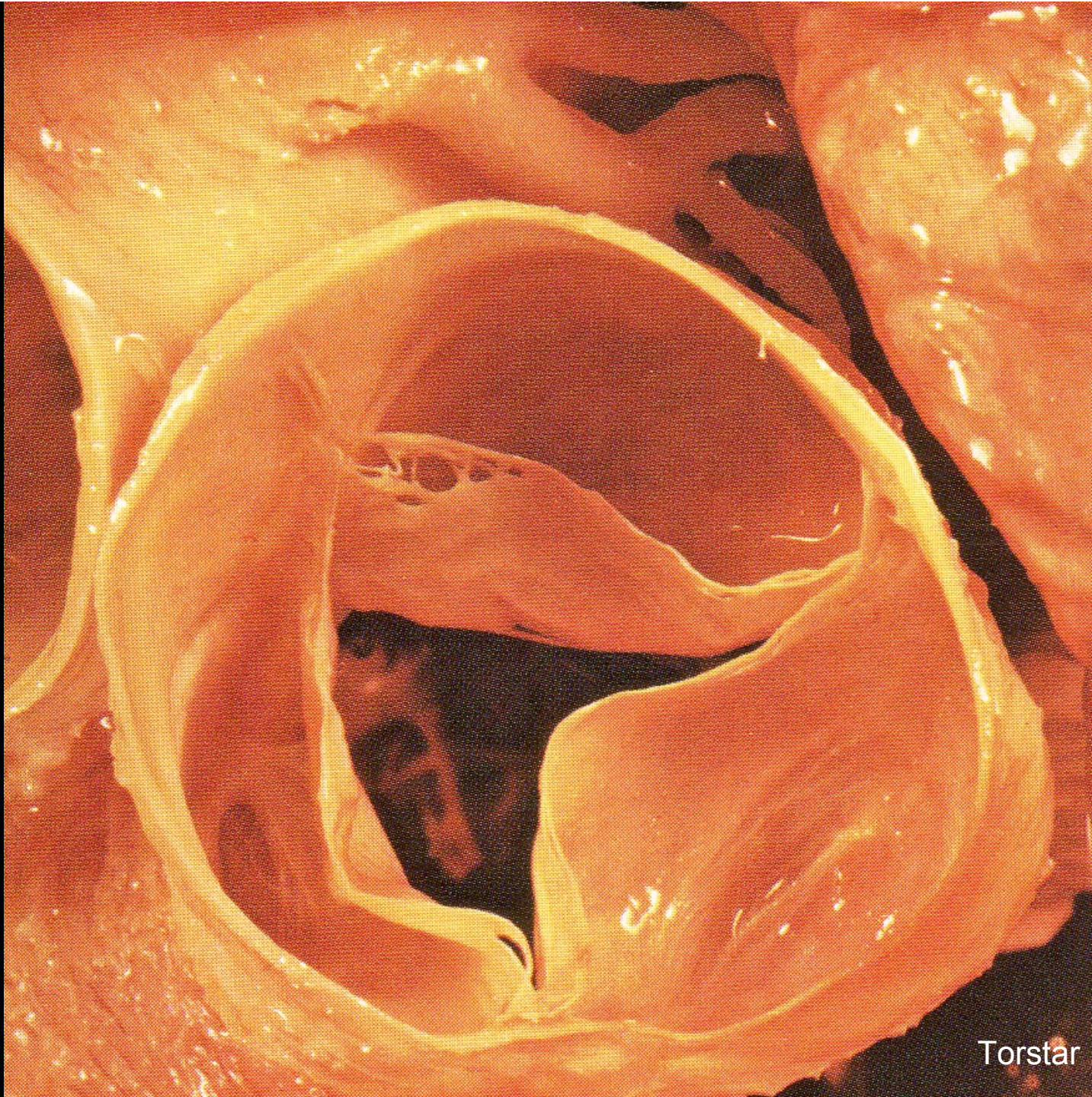
SL

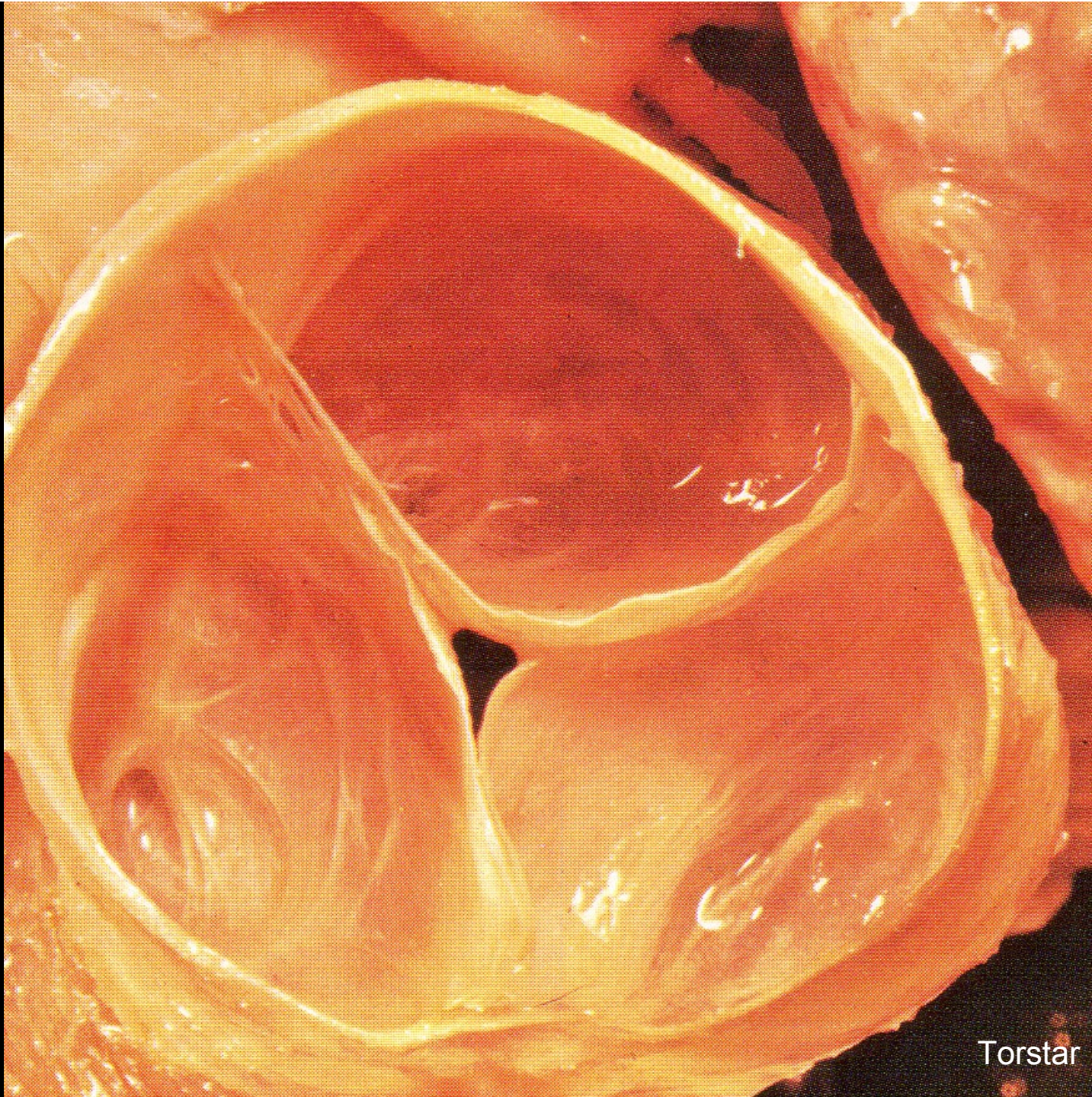


G&H 2006 fig 9-6;
cf: G&H 2011 fig 9-7

Heart Valve Orientation & Scaffolding









What the heck's a *bruit*?
(brwe, brōot) [Fr.] sound \geq
25 subclassifications!

Aneurysmal b. a blowing sound over an aneurysm.

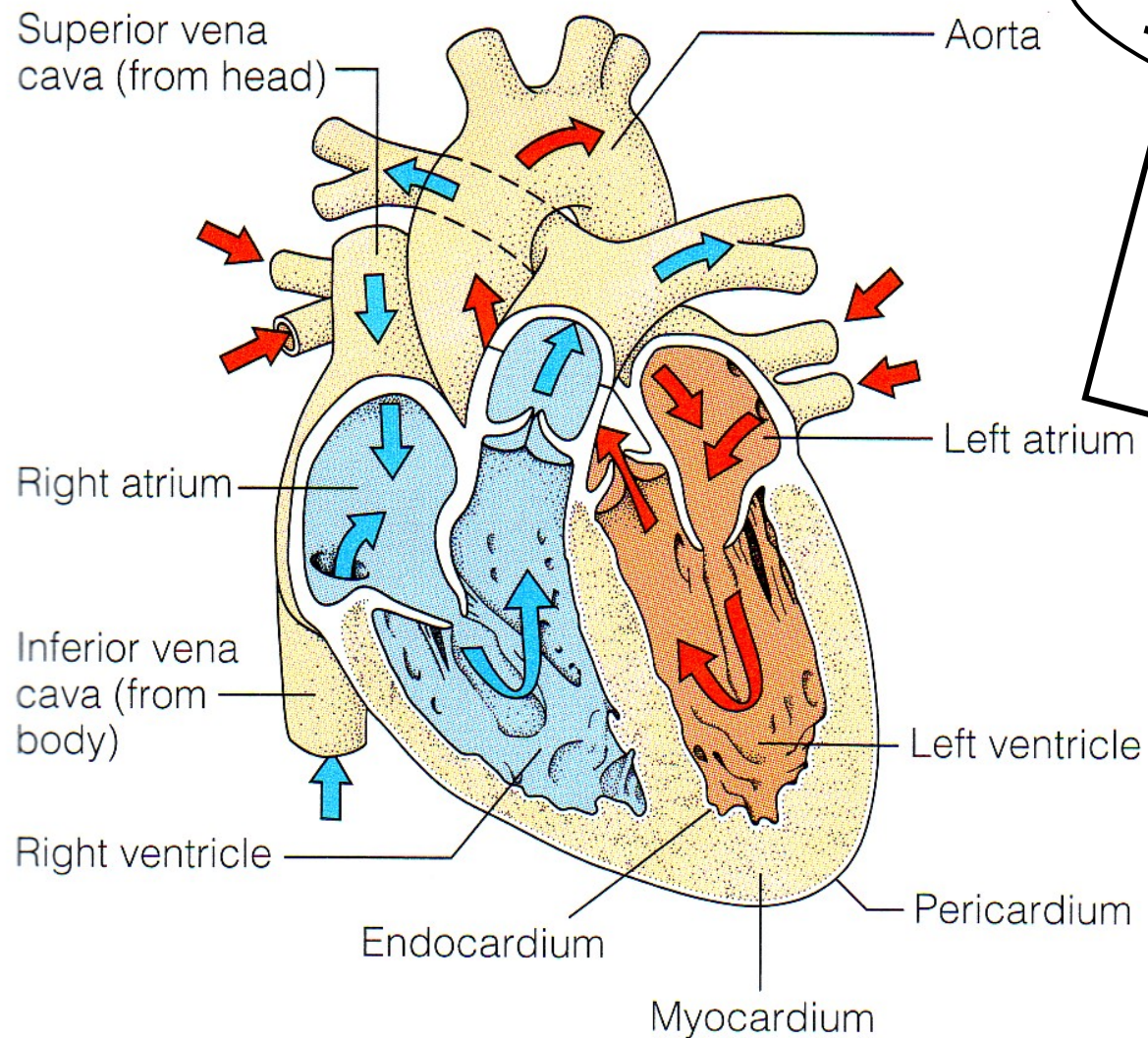
b. de canon [Fr. sound of cannon] abnormally loud 1st heart sound heard in complete heart block.

b. de craquement [Fr. sound of crackling] a crackling pericardial or pleural bruit.

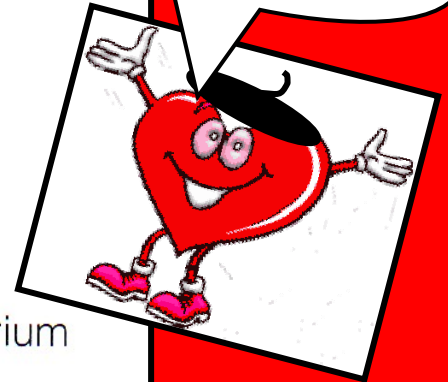
False b. artifact caused by pressure of the stethoscope or derived from circulation of the ear.

b. de lime [Fr. sound of a file] cardiac sound resembling filing.

Veins → Atria → Ventricles → Arteries

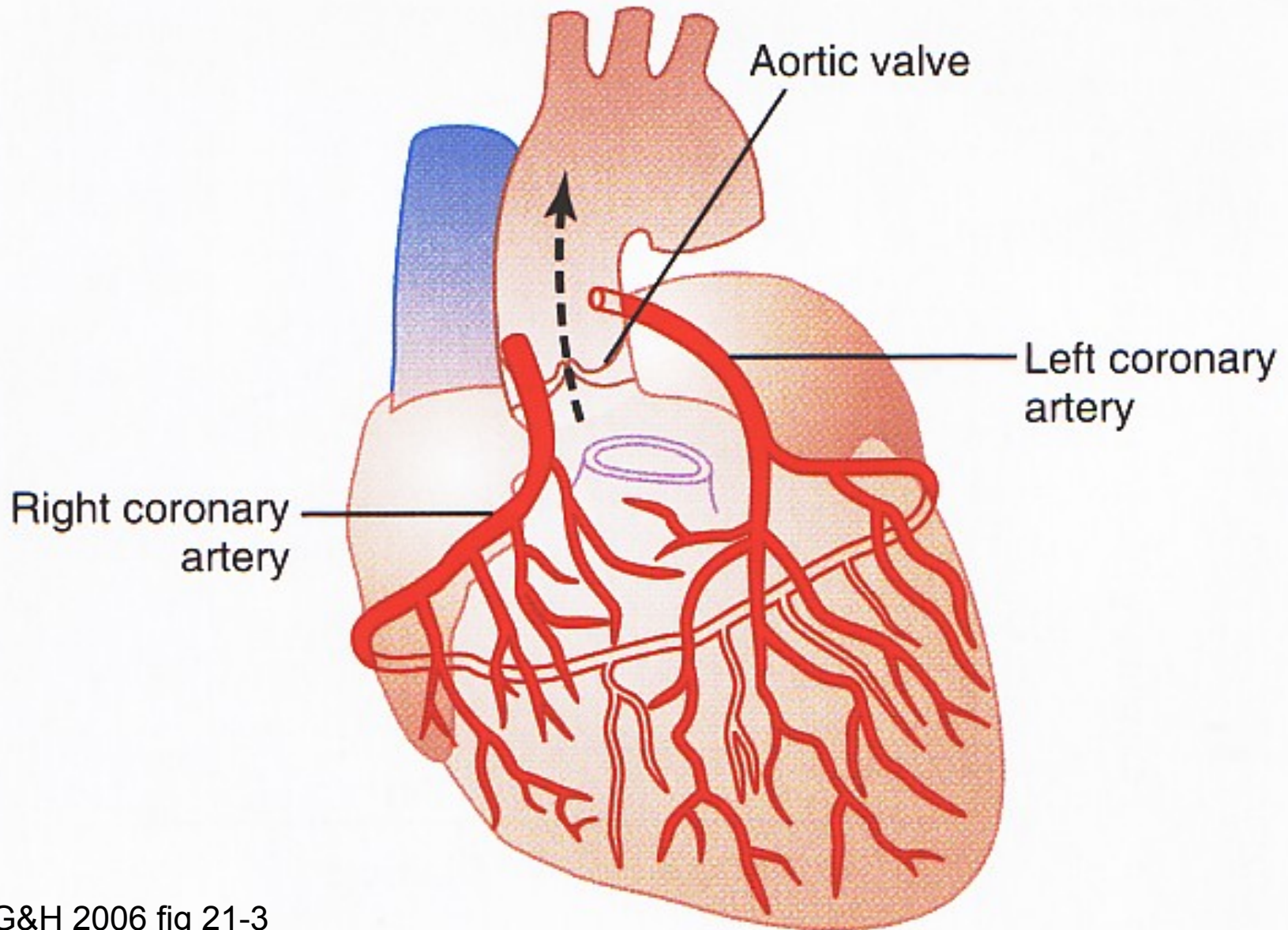


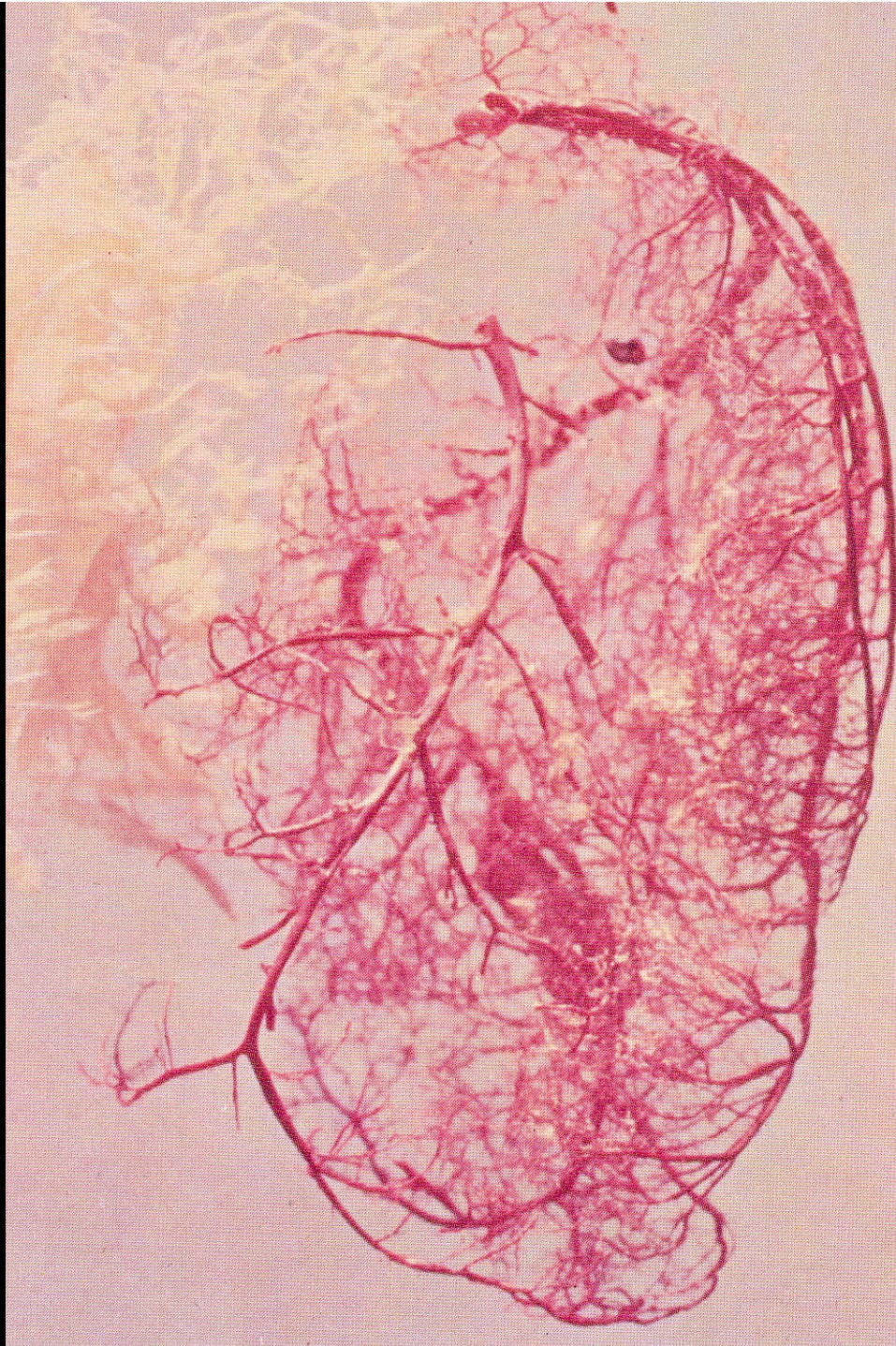
V A V A!



<http://www.nhlbi.nih.gov/health/health-topics/topics/hhw/contraction.html>

Coronary Circulation ≡ Crowns the Heart!





Heart Dominance May Influence Survival

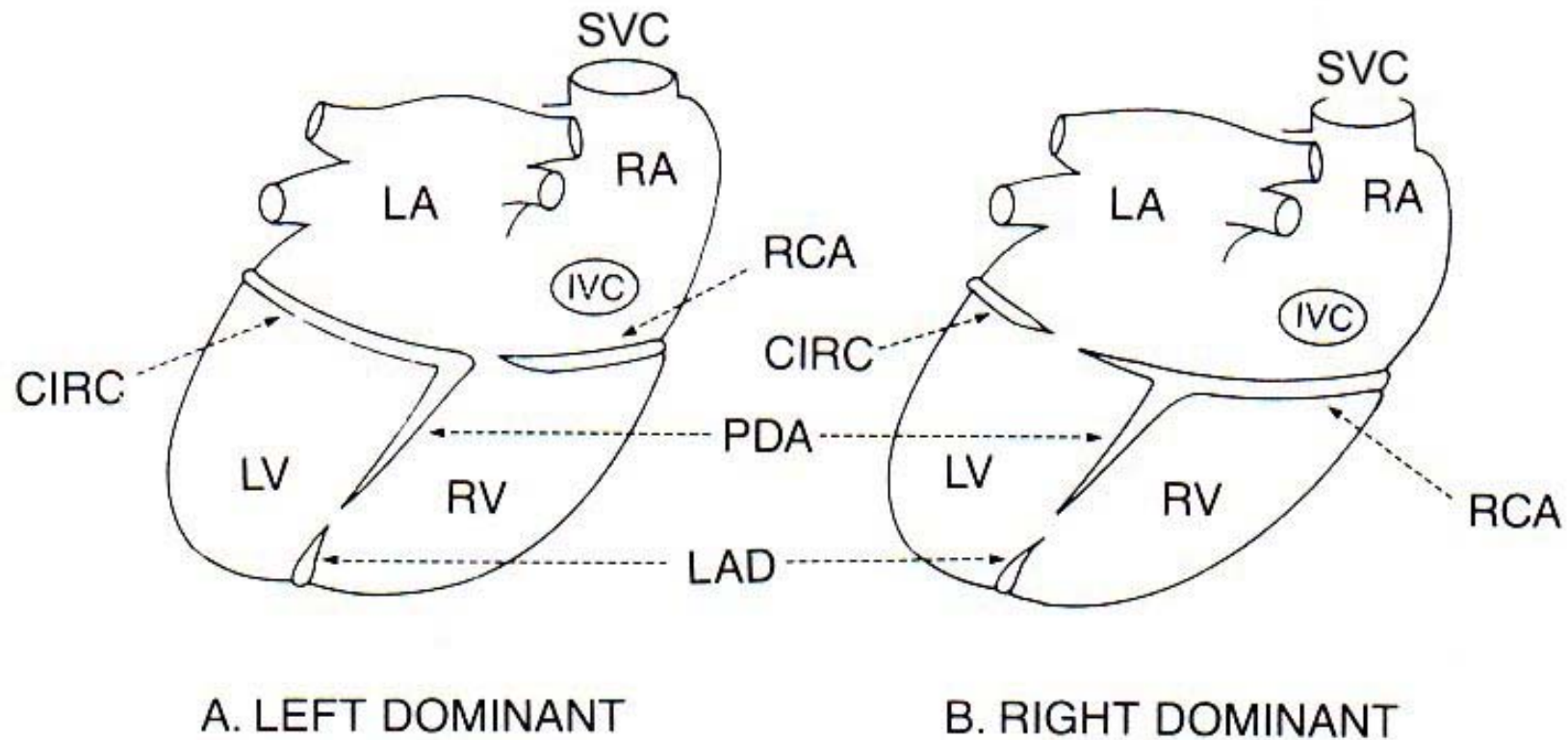
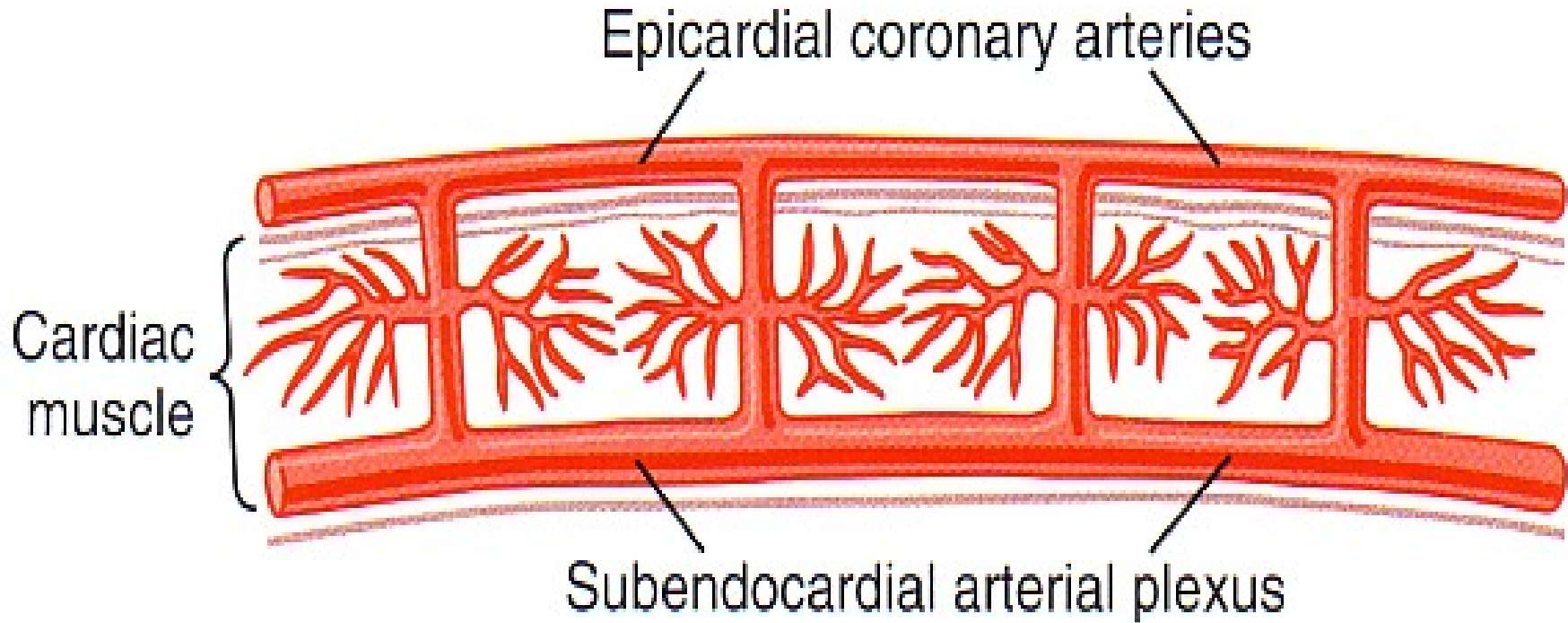
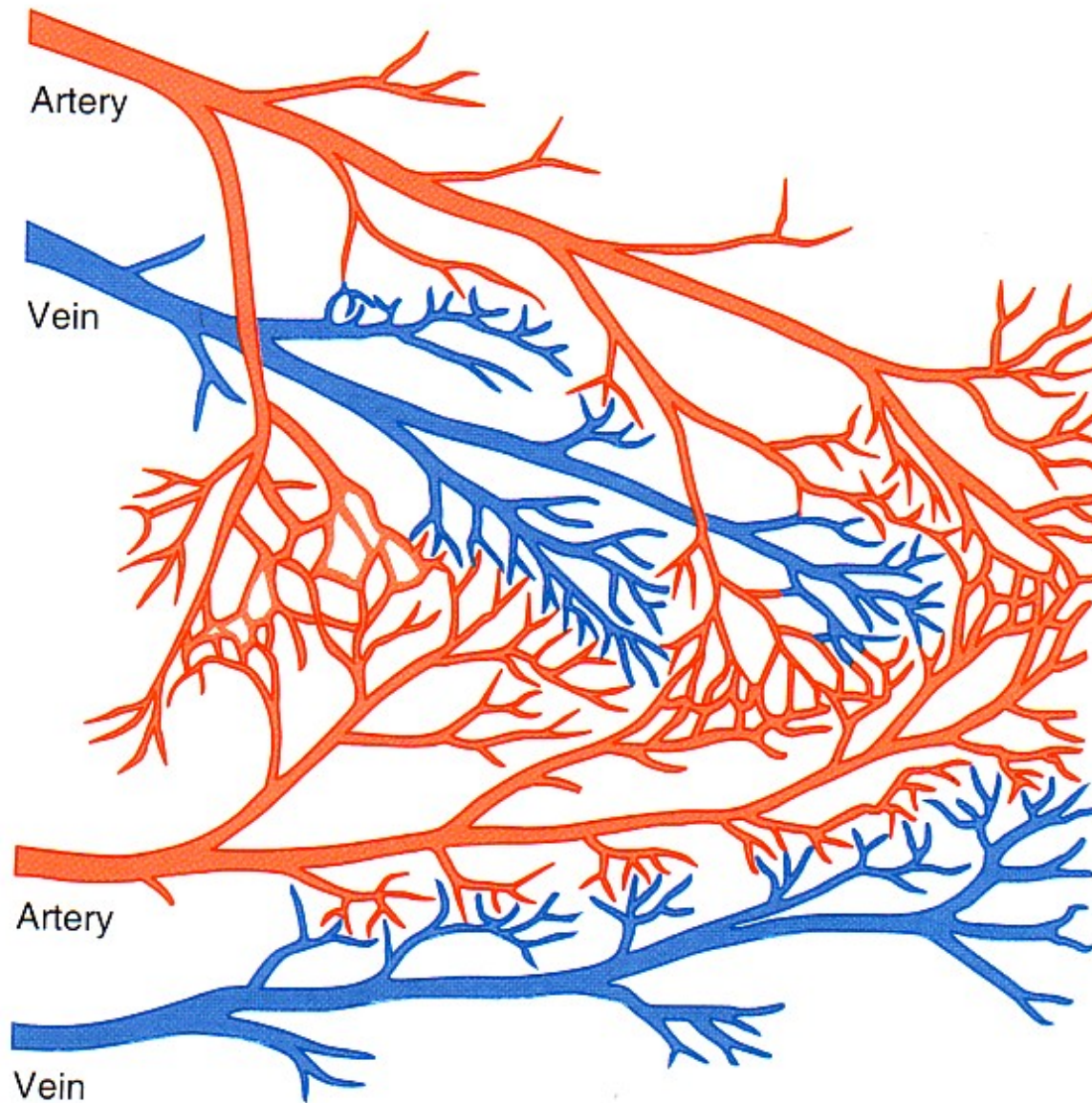


FIG. 1.9. Diagrammatic views of the posterior surfaces of the human heart showing left (A) and right dominant (B) patterns of coronary artery supply. In the left dominant pattern, the posterior descending artery (PDA) is supplied by the circumflex branch of the left coronary artery (CIRC). In the right dominant pattern, the posterior descending artery is supplied by the right coronary artery (RCA). Other abbreviations: LAD, left anterior descending coronary artery; LA, left atrium; RA, right atrium; LV, left ventricle; RV, right ventricle; SVC, superior vena cava; IVC, inferior vena cava.

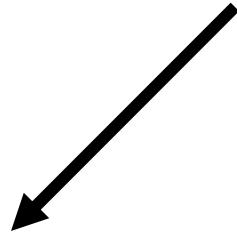
Coronary Arteries Pierce the Heart from Epi to Endo



Anastomoses May Provide Lifesaving Collateral Circulation!!

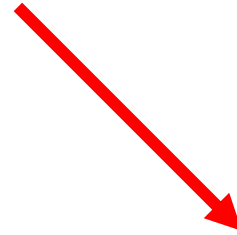


Cardiac Cycle



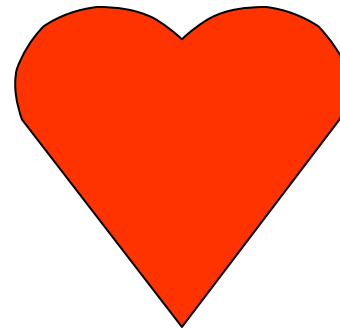
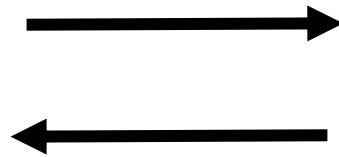
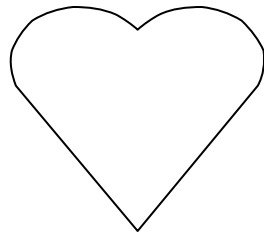
Systole

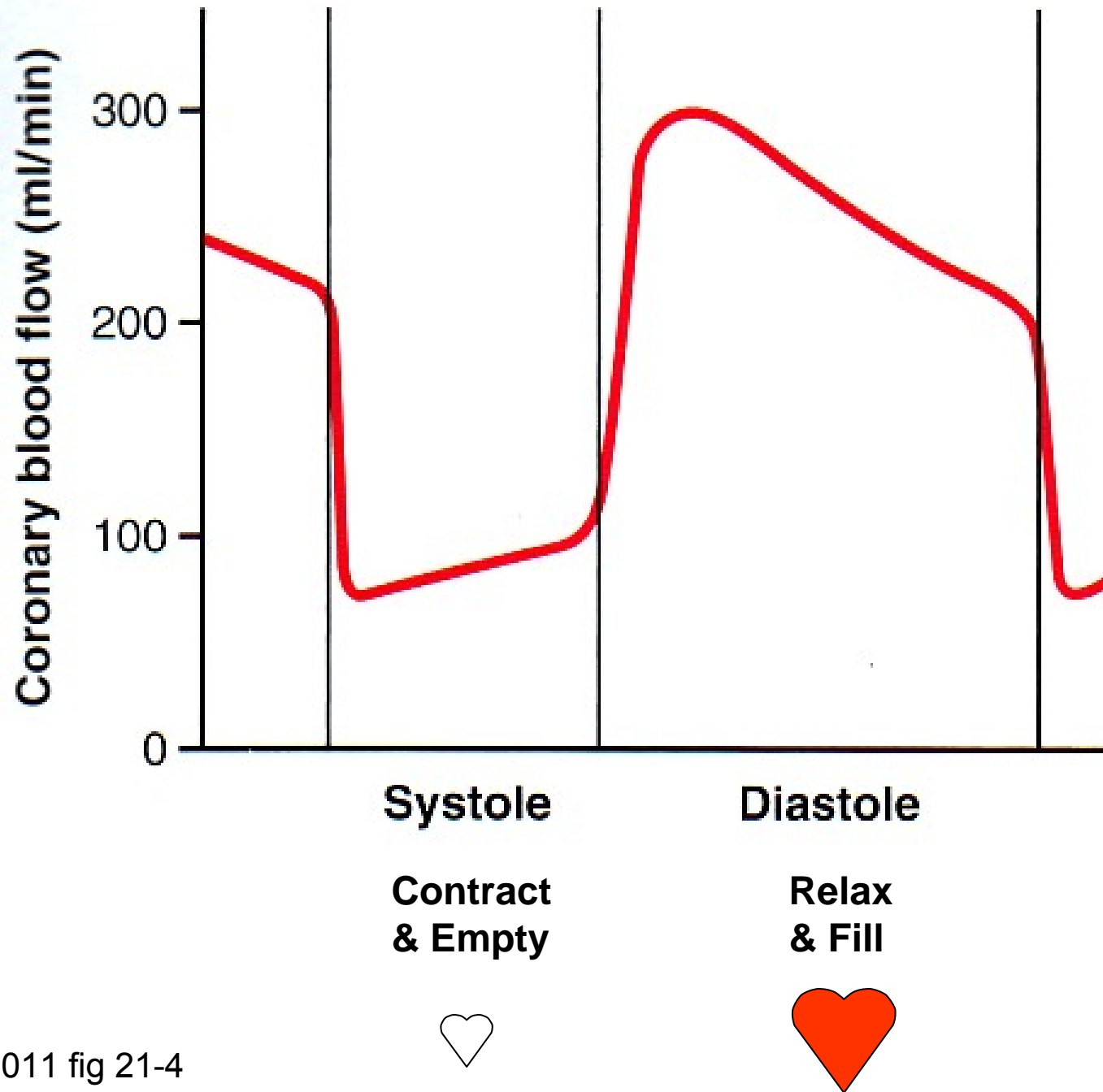
Contract
& Empty



Diastole

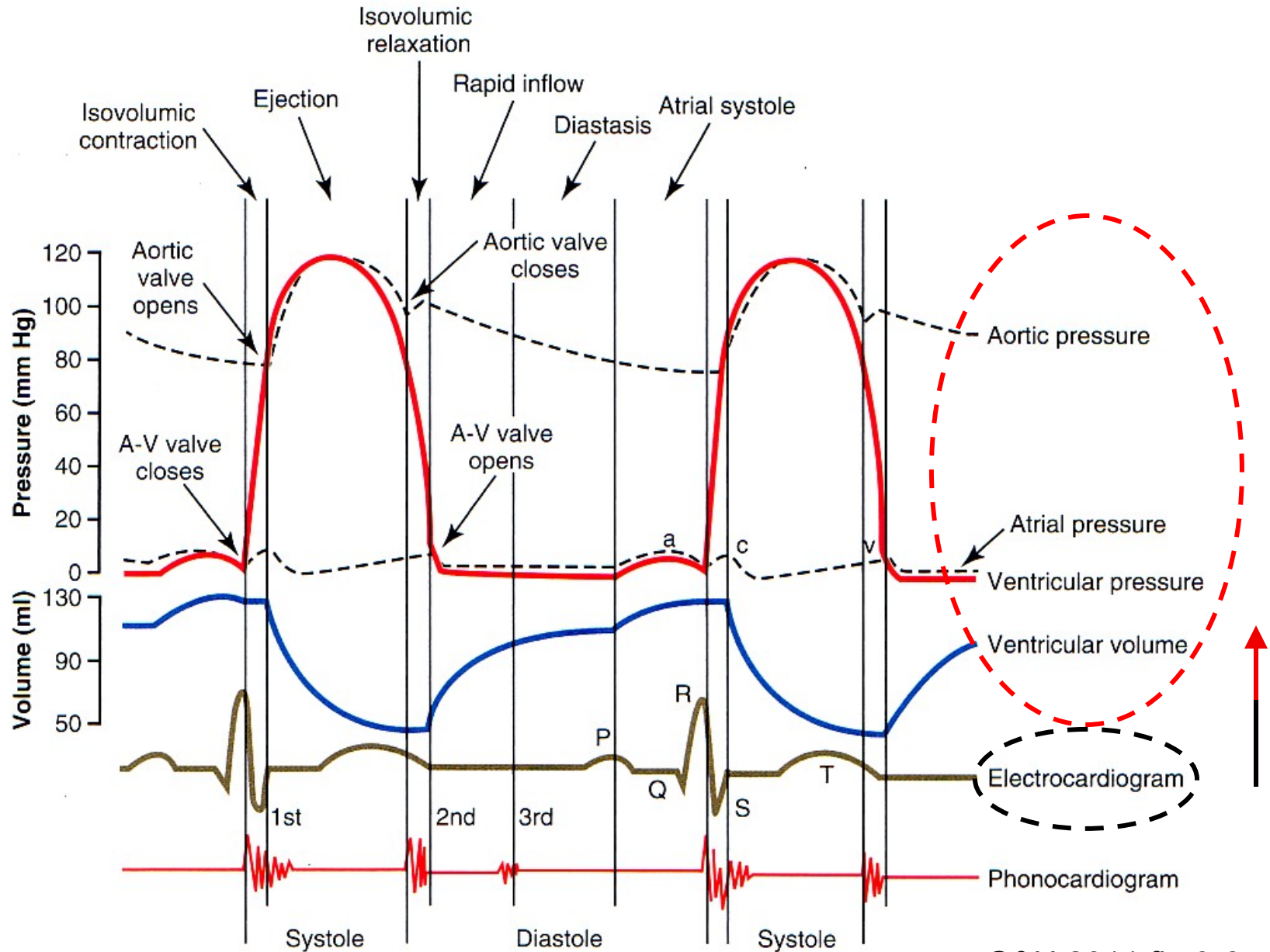
Relax
& Fill



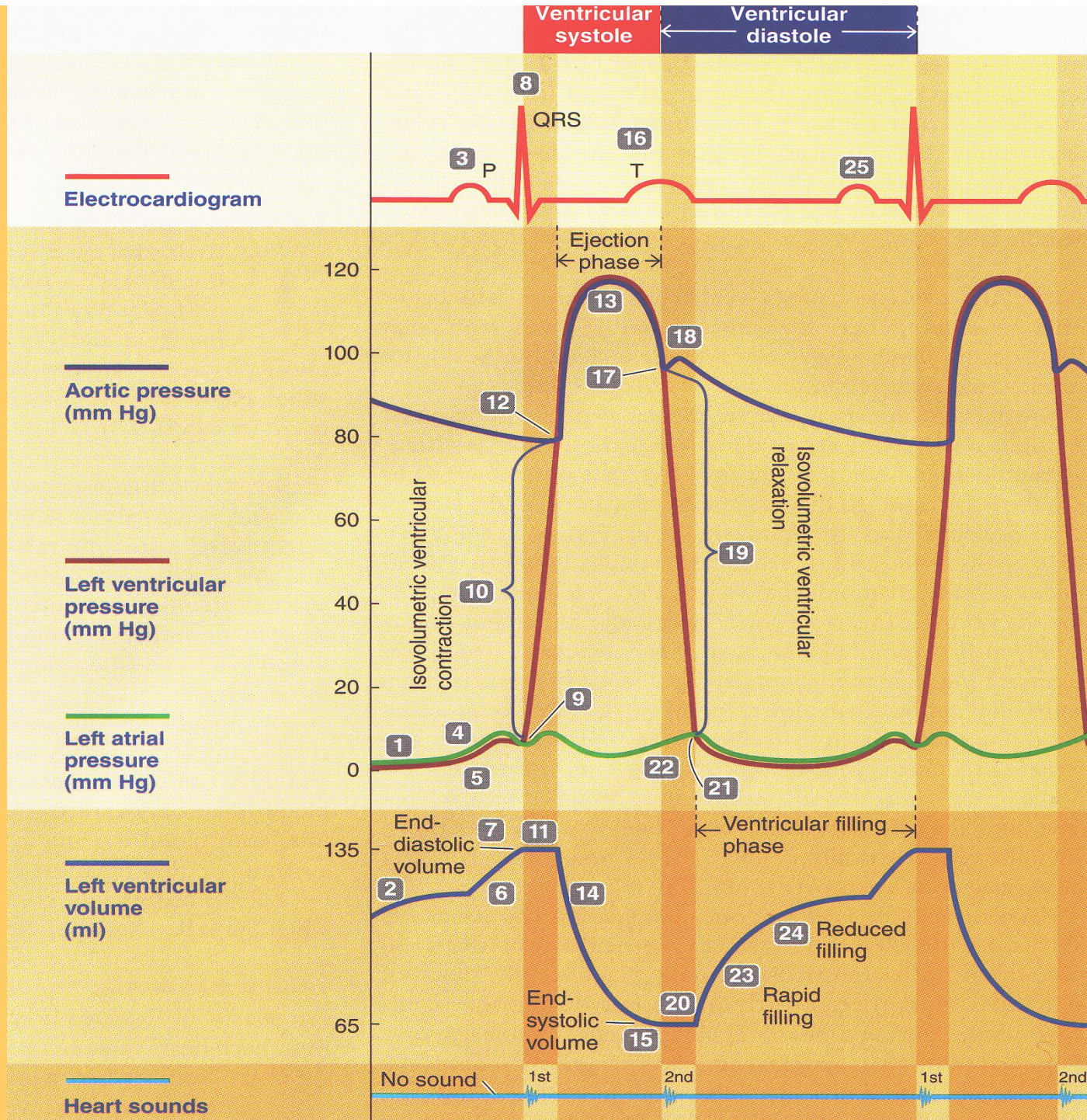


G&H 2011 fig 21-4

Electrical Events Precede *Mechanical Events!*

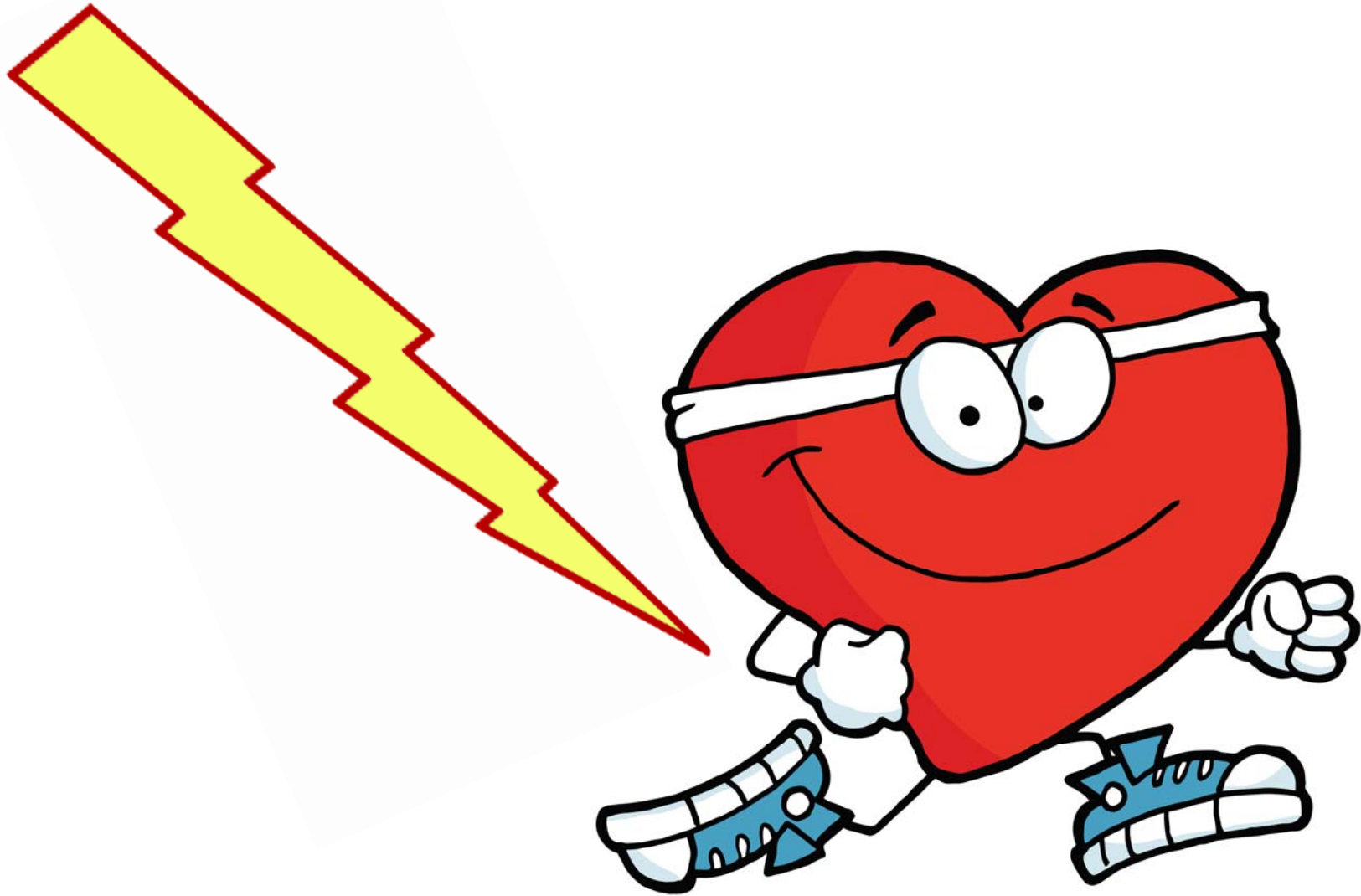


G&H 2011 fig 9-6

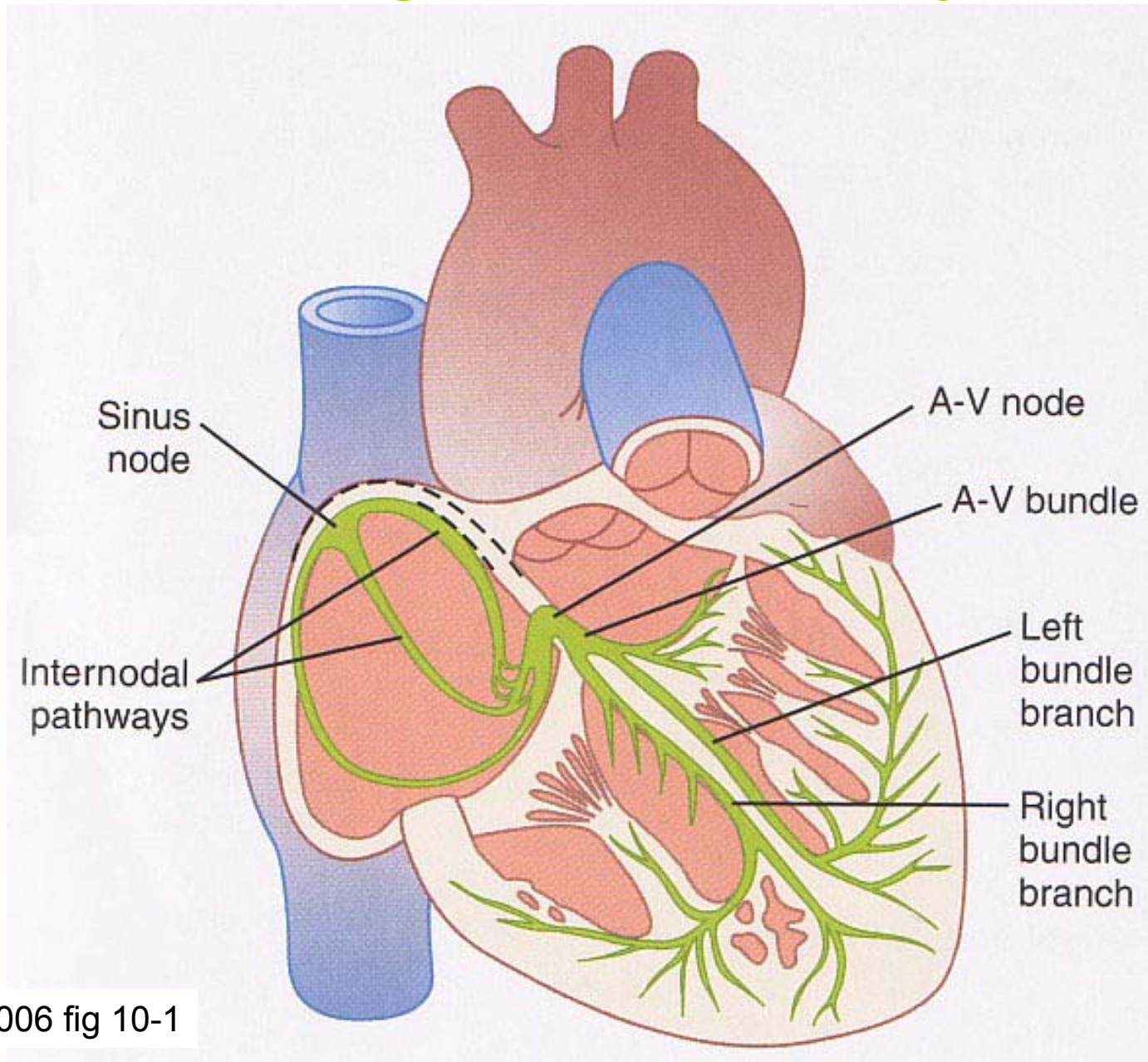


L Sherwood
2012 fig 9-15

(Automatically) Shock the Heart then it Contracts!



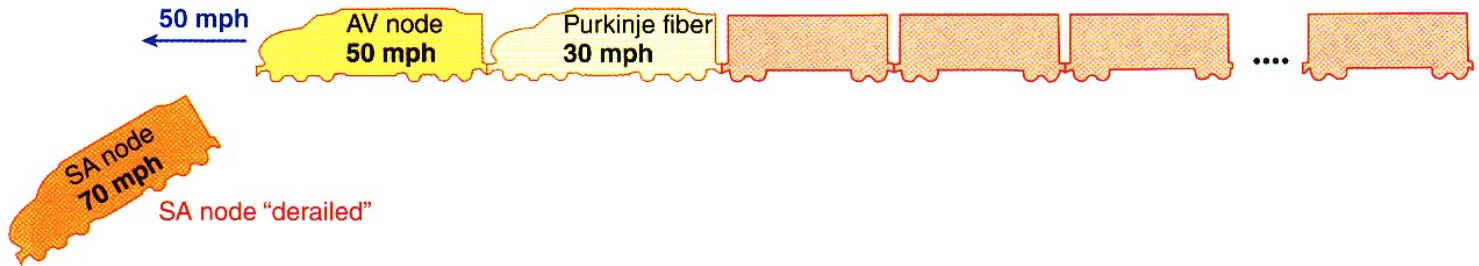
Intrinsic Regulation: Autorhythmic



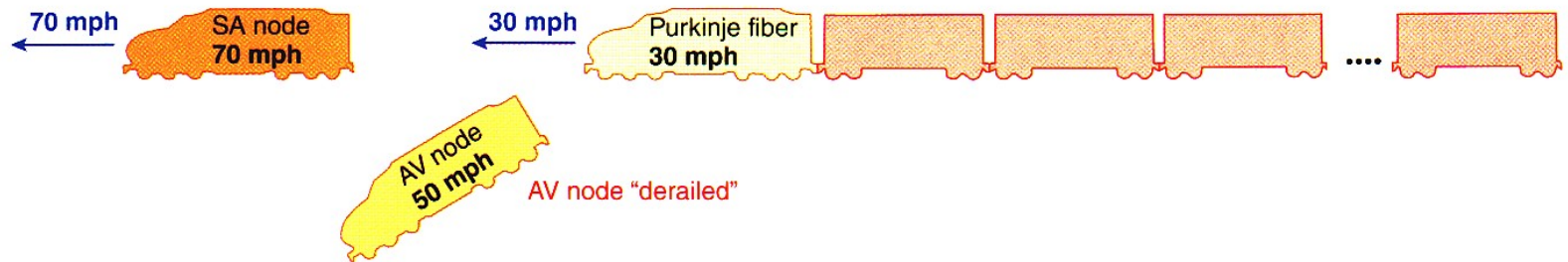
G&H 2006 fig 10-1



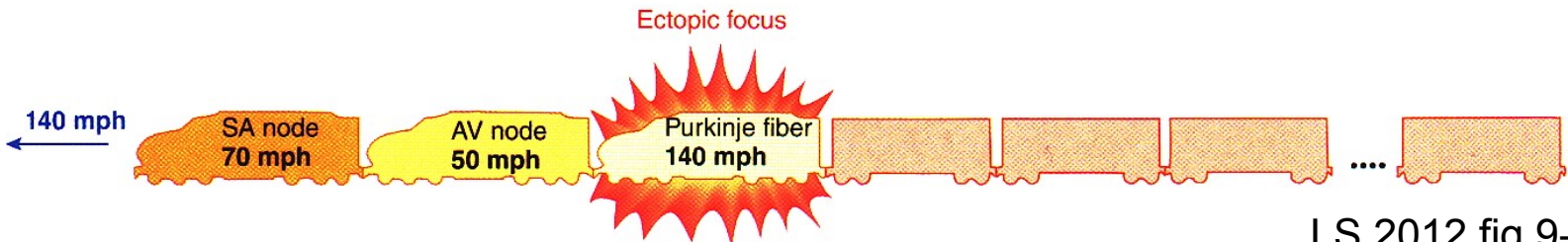
(a) Normal pacemaker activity: Whole train will go **70 mph** (heart rate set by SA node, the fastest autorhythmic tissue).



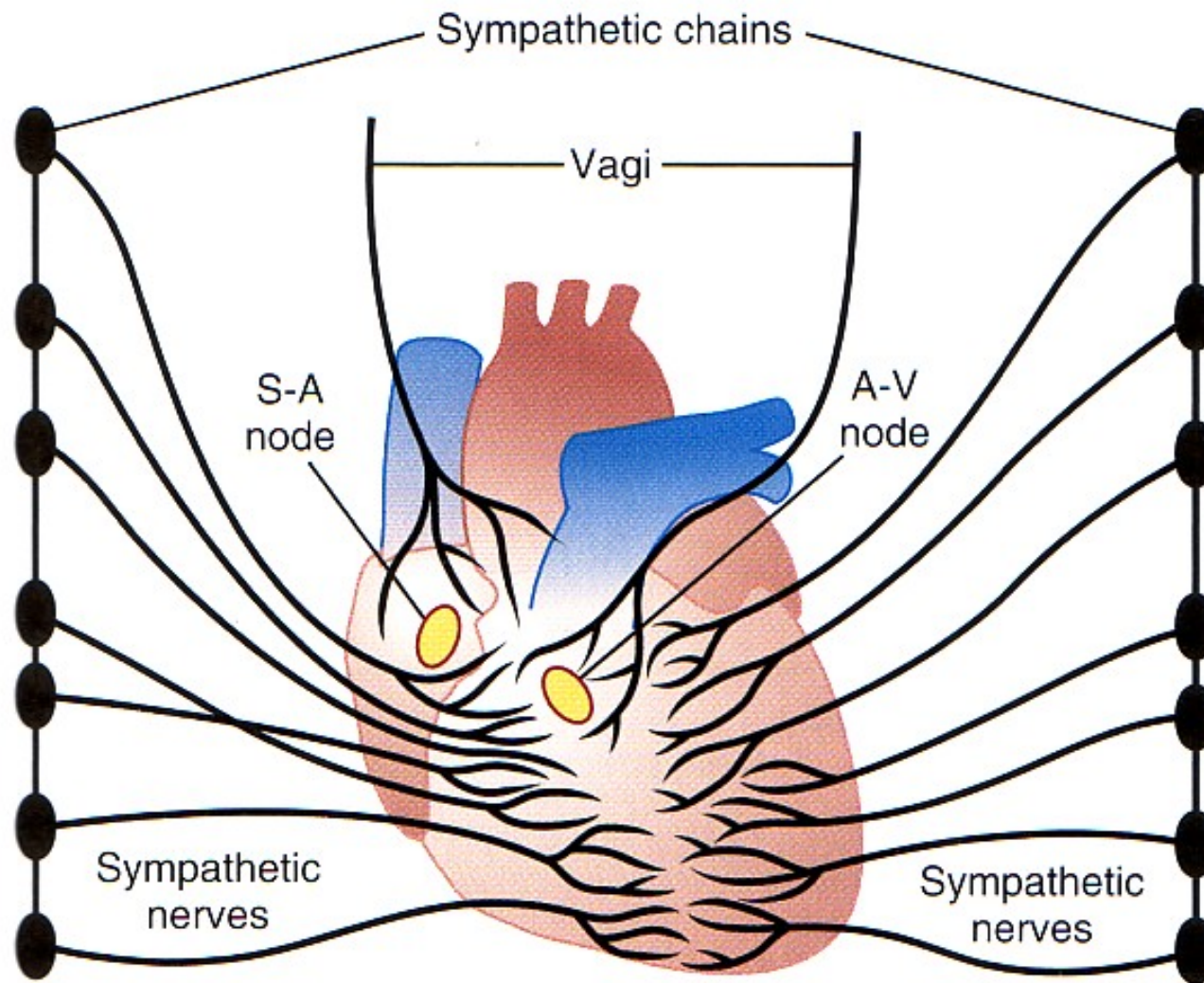
(b) Takeover of pacemaker activity by AV node when the SA node is nonfunctional: Train will go **50 mph** (the next fastest autorhythmic tissue, the AV node, will set the heart rate).



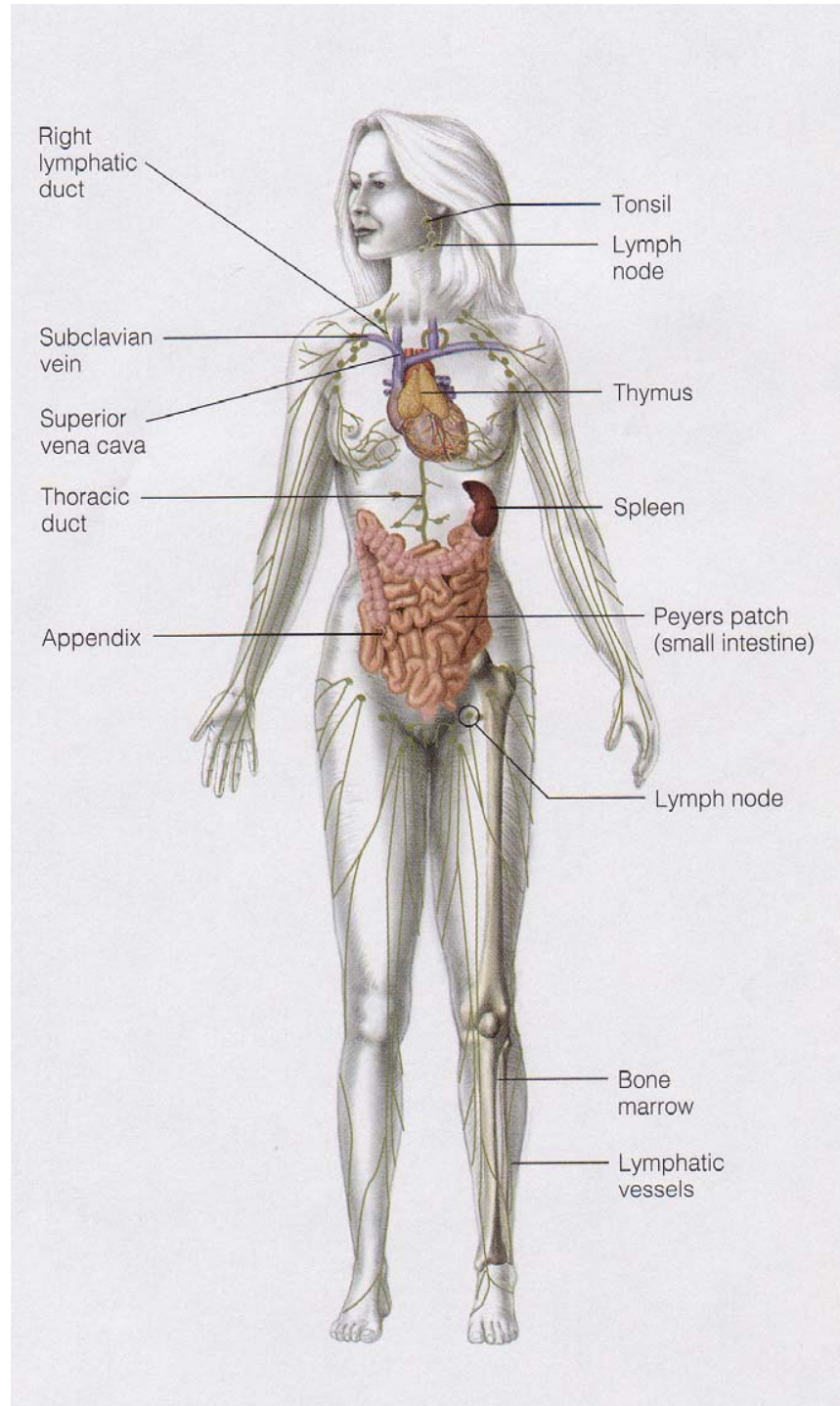
(c) Takeover of ventricular rate by the slower ventricular autorhythmic tissue in complete heart block: First part of train will go **70 mph**; last part will go **30 mph** (atria will be driven by SA node; ventricles will assume own, much slower rhythm).



Extrinsic Regulation: Nervous



**NB: + Extrinsic Hormonal
e.g. Adrenal Epi + NE**

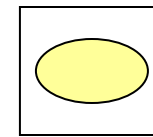


Lymphatic System

1. Lymph Nodes

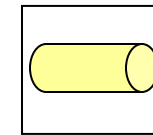
2. Vessels

3. Lymph

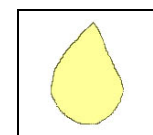


No pump!

+



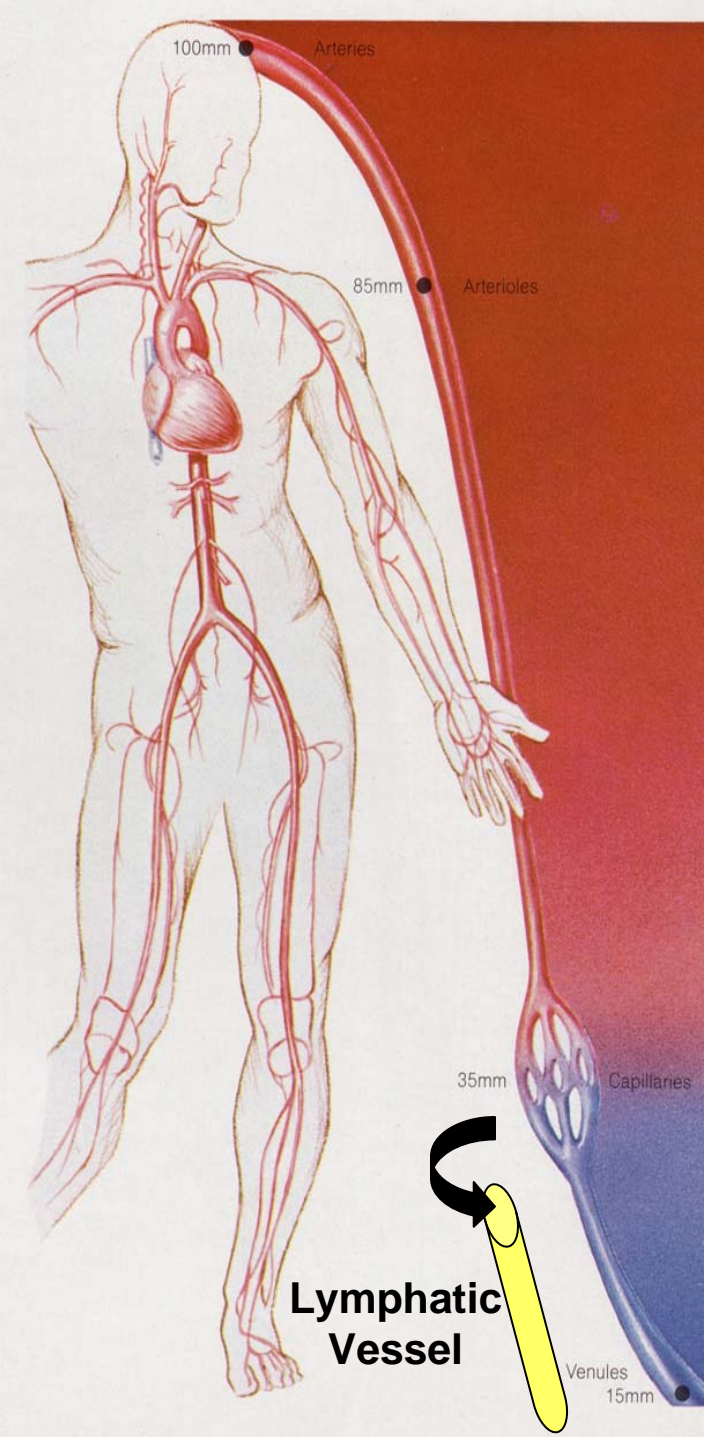
+



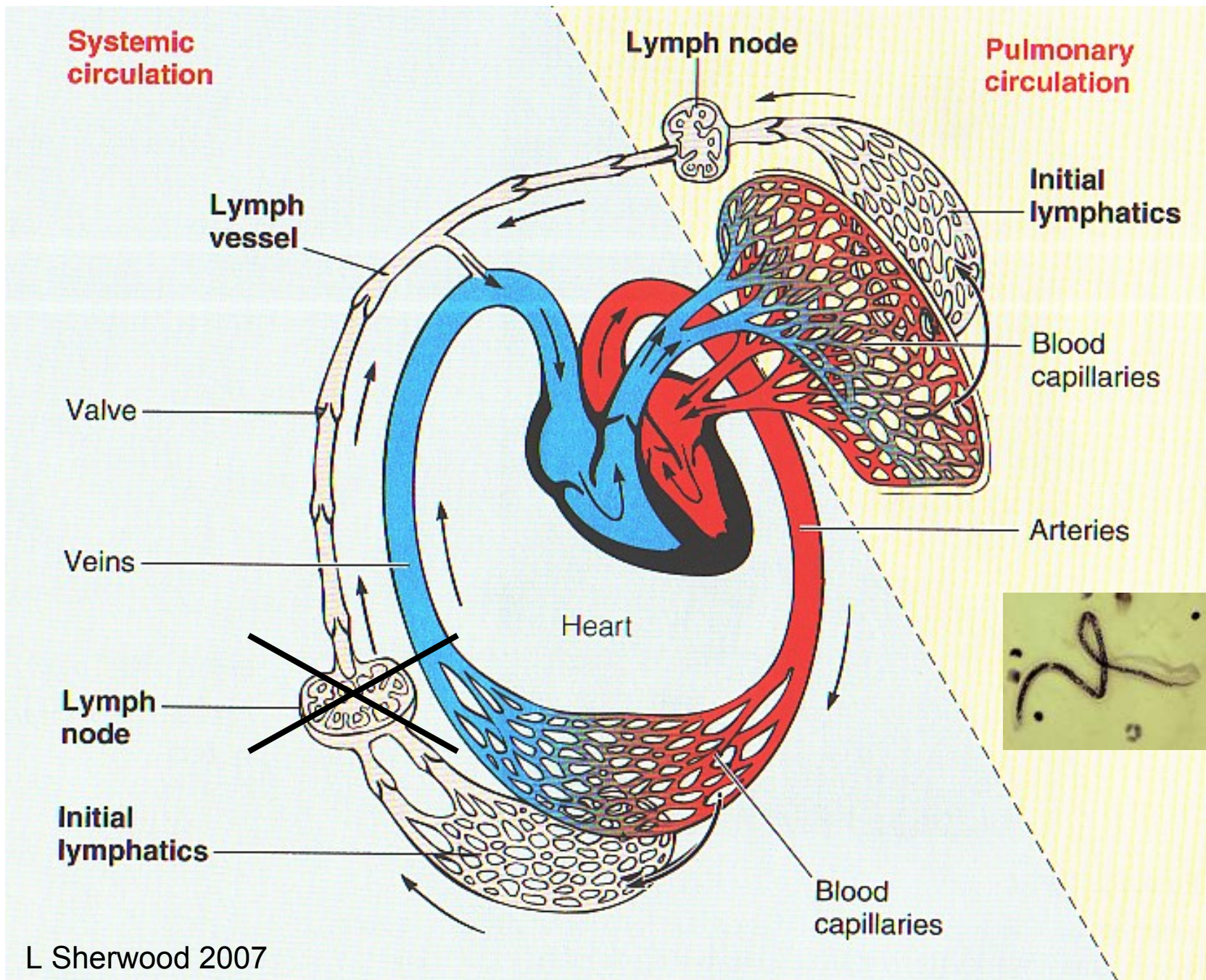
Lymphatic System

**Alternative System of
Circulation
or
Drainage System**

Lymph Vessels || Veins



Torstar Books 1984



L Sherwood 2007

Elephantiasis: Lymphatic Blockage Due to Mosquito-Borne Parasitic Worm



L Sherwood 2007