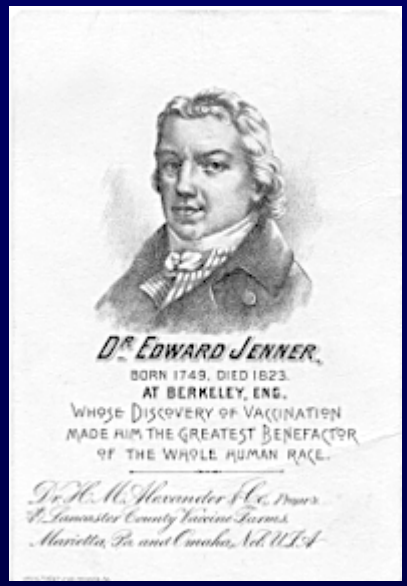
Cells and Tissues of the Immune System

HST.035 Spring 2003

Edward Jenner



http://www.nlm.nih.gov/exhibition/ephemera/pubhealt.html

The origin of immunology is usually attributed to Edward Jenner, who in 1796 discovered that cowpox induced protection against human smallpox. Jenner called his procedure vaccination (after vaccinia, the alternative name for smallpox). Disease prevention through vaccinations have been of the triumphs of modern medicine.

Effectiveness of Vaccinations

Disease	Max. No. (year)	No. in 1999	% Change
Diphtheria	206,939 (1921)	1	~100
Measles	894,134 (1941)	60	~100
Mumps	152,209 (1968)	352	99.8
Polio	21,269 (1952)	0	100
Rubella	57,686 (1969)	238	99.6
Hepatitis B	26,611 (1985)	6,495	75.6

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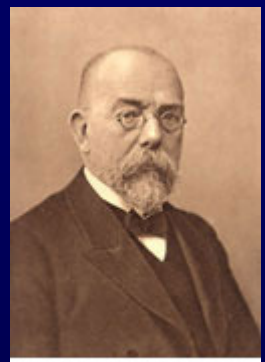
Robert Koch



German microbiologist Robert Koch

http://www2.niaid.nih.gov/newsroom/focuson/tb02/optimism.htm

When Jenner introduced vaccination he knew nothing of the infectious agents that cause disease: it was not until late in the 19th century that Robert Koch proved that infectious diseases are caused by microorganisms, each one responsible for a particular disease, or pathology. We now recognize four broad categories of disease-causing microorganisms, or pathogens: these are viruses, bacteria, pathogenic fungi, and other relatively large and complex eukaryotic organisms collectively termed parasites.

Louis Pasteur

The discoveries of Koch and other great 19th century microbiologists stimulated the extension of Jenner's strategy of vaccination to other diseases. In the 1880s, Louis Pasteur devised a vaccine against cholera in chickens, and developed a rabies vaccine that proved a spectacular success upon its first trial in a boy bitten by a rabid dog. These practical triumphs led to a search for the mechanism of protection and to the development of the science of immunology.

Emil von Behring

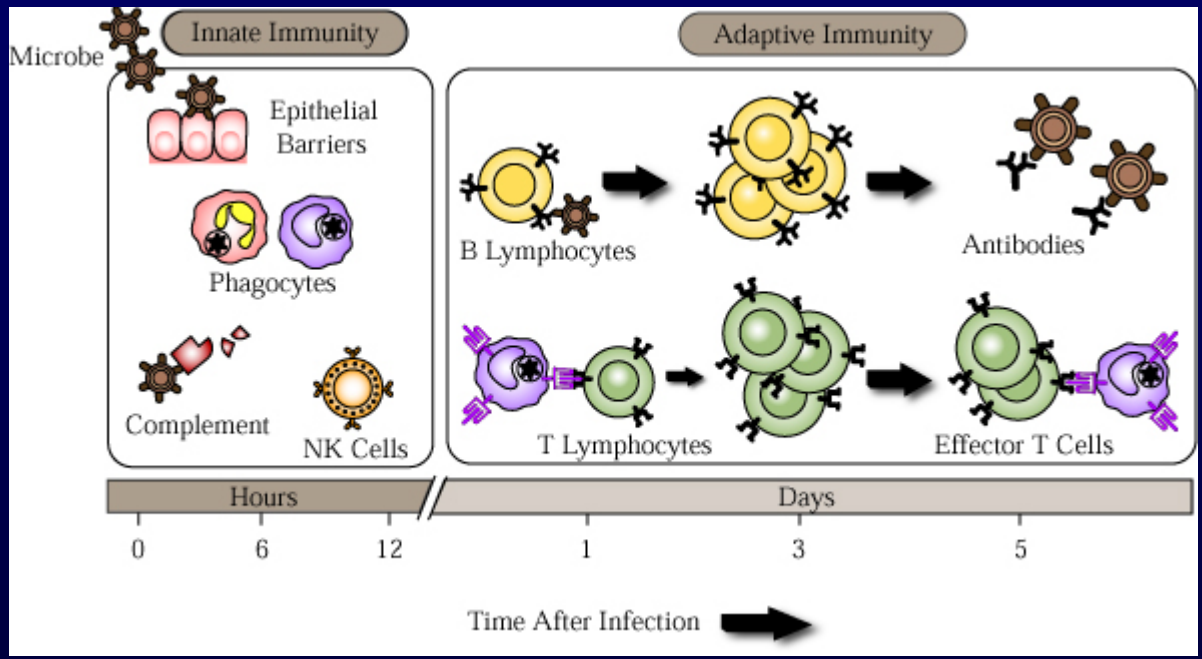
In 1890, Emil von Behring and Shibasaburo Kitasato discovered that the serum of vaccinated individuals contained substances—which they called antibodies—that specifically bound to the relevant pathogen.

Nobel Prizes for Immunological Research

Year	Recipient	Country	Research
1901	Emil von Behring	Germany	Serum antitoxins
1905	Robert Koch	Germany	Cellular immunity to tuberculosis
1908	Elie Metchnikoff Paul Ehrlich	Russia Germany	Role of phagocytosis (Metchnikoff) and antitoxins (Ehrlich) in immunity
1913	Charles Richet	France	Anaphylaxis
1919	Jules Border	Belgium	Complement-mediated bacteriolysis
1930	Karl Landsteiner	United States	Discovery of human blood groups
1951	Max Theiler	South Africa	Development of yellow fever vaccine
1957	Daniel Bovet	Switzerland	Antihistamines
1960	F. Macfarlane Burnet Peter Medawar	Australia Great Britain	Discovery of acquired immunological tolerance
1972	Rodney R. Porter Gerald M. Edelman	Great Britain United States	Chemical structure of antibodies
1977	Rosalyn R. Yalow	United States	Development of radioimmunoassay
1980	George Snell Jean Dausset Baruj Benacerraf	United States France United States	Major histocompatibility complex
1984	Cesar Milstein Georges E. Köhler	Great Britain Germany	Monoclonal antibody
	Niels K. Jerne	Denmark	Immune regulatory theories
1987	Susumu Tonegawa	Japan	Gene rearrangement in antibody production
1991	E. Donnall Thomas Joseph Murray	United States United States	Transplantation immunology
1996	Peter C. Doherty Rolf M. Zinkernagel	Australia Switzerland	Role of major histocompatibility complex in antigen recognition by by T cells

Physiological function of the immune system is to prevent infections and to eradicate infections that have escaped prevention.

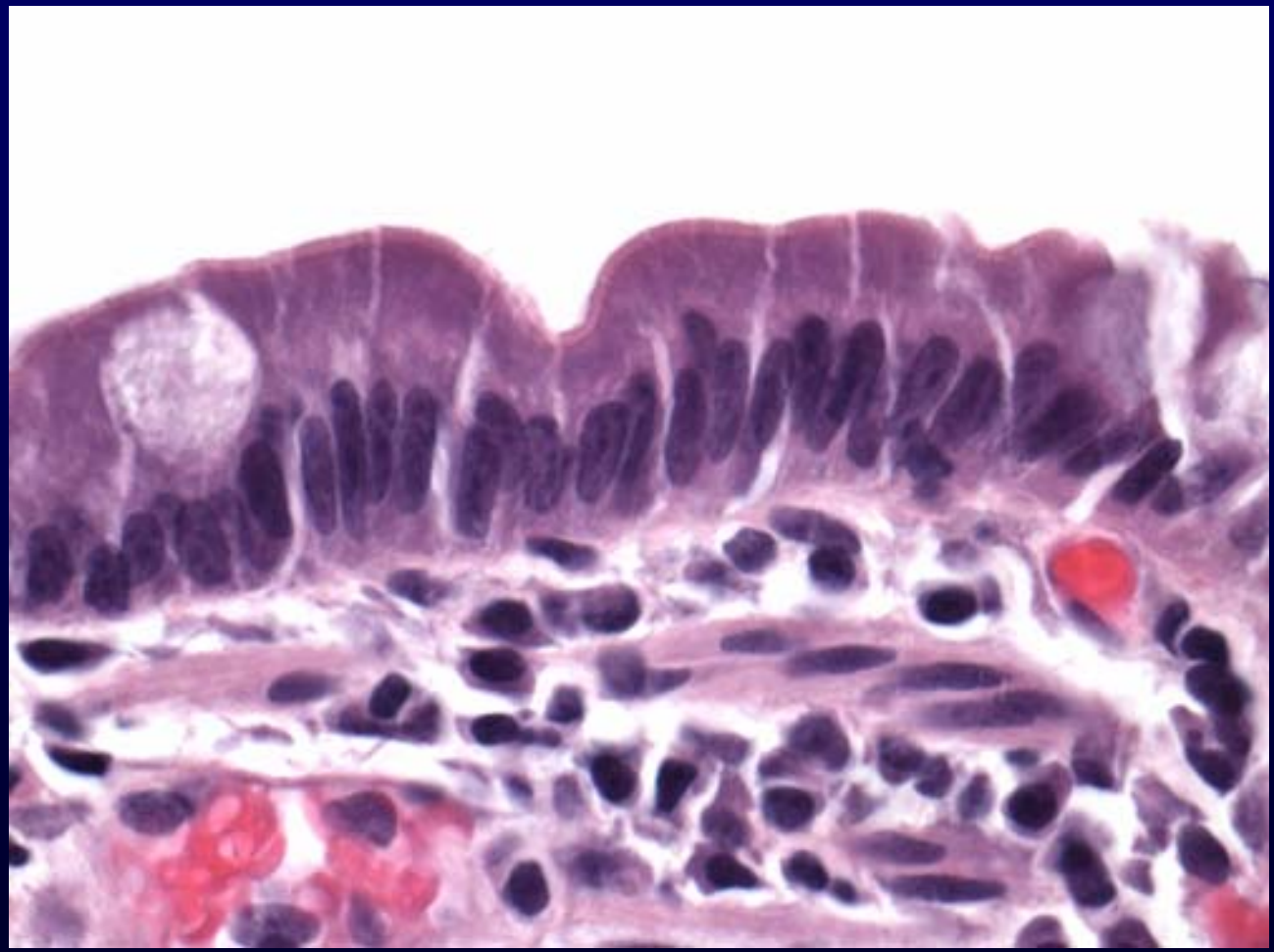
How is it done?



A specific immune response, such as the production of antibodies against a particular pathogen, is known as an adaptive immune response, because it occurs during the lifetime of an individual as an adaptation to infection with that pathogen. In many cases, an adaptive immune response confers lifelong protective immunity to reinfection with the same pathogen. This distinguishes such responses from innate immunity, which is immediately available to combat a wide range of pathogens without requiring prior exposure.

How is it done?

1. Prevent Entry of Microbes



How is it done?

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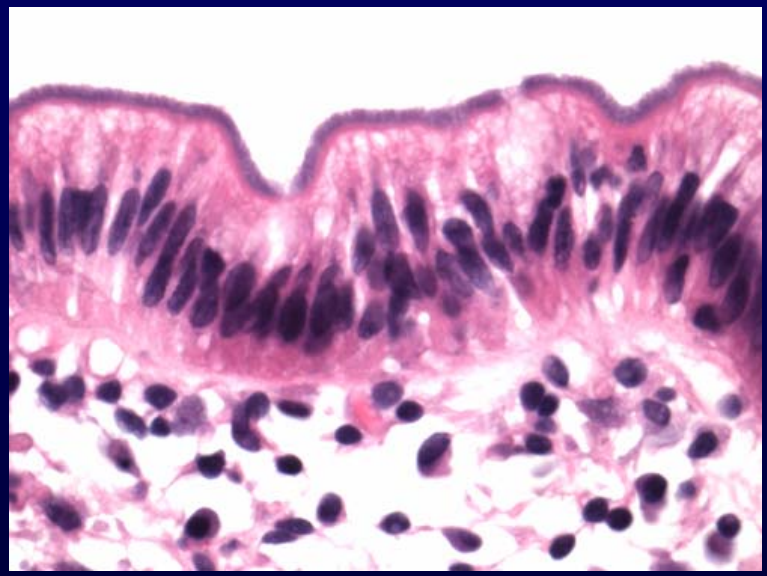
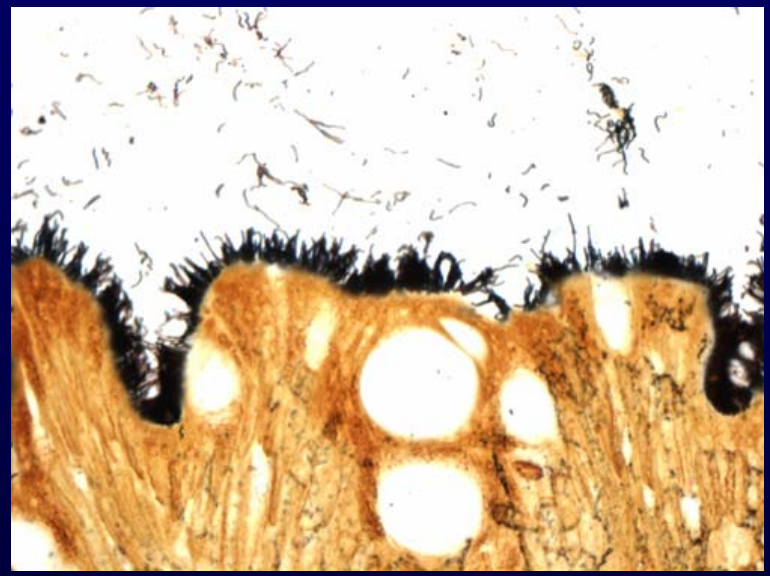




Numerous bacteria are present
on many epithelial surfaces, but
“infections” are rare.

How is it done?

2. Search and Destroy Intruders by Phagocytosis

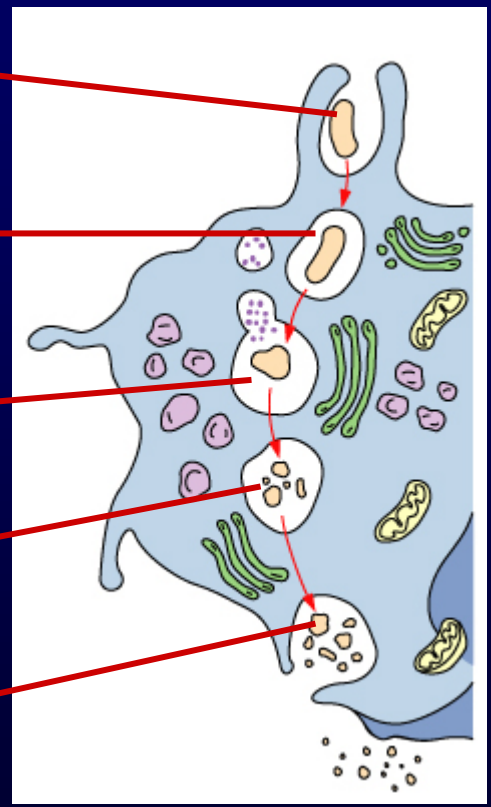
1. Bacterium becomes attached to membrane evaginations called pseudopodia

2. Bacterium is ingested, forming phagosome

3. Phagosome fuses with lysosome

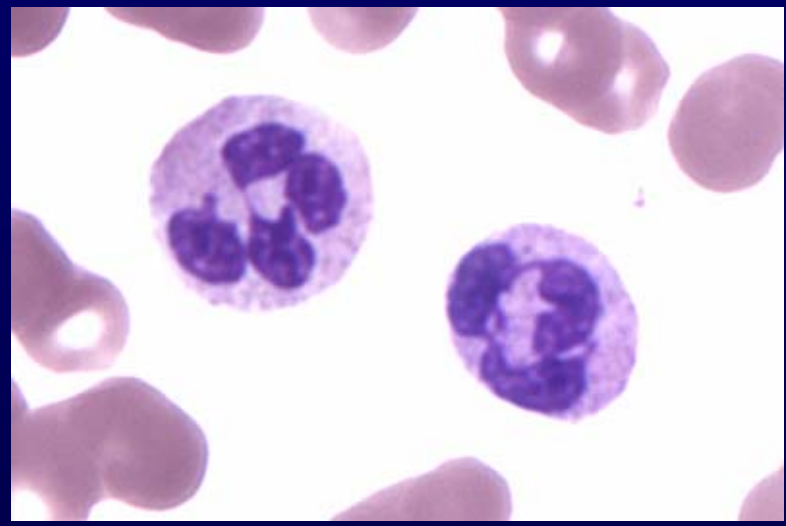
4. Lysosomal enzymes digest captured material

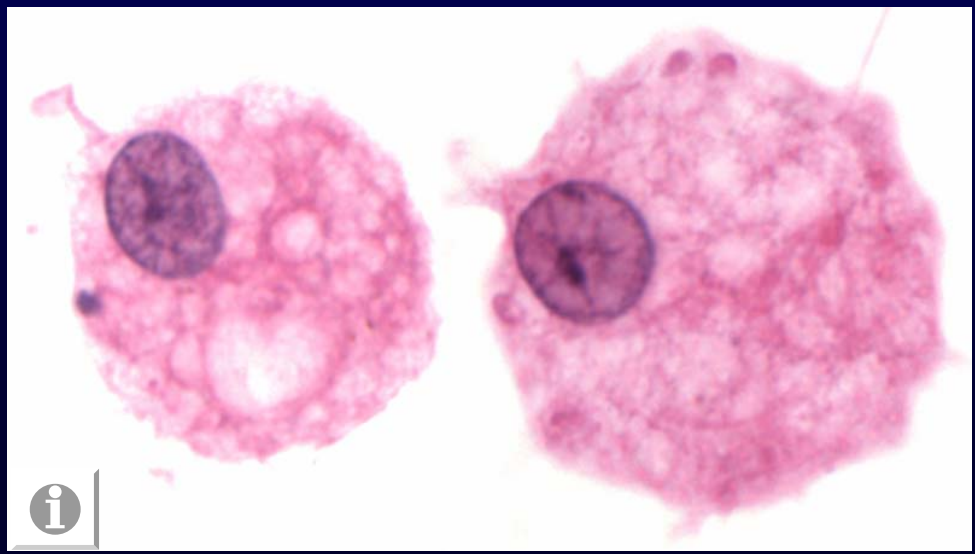
5. Digestion products are released from cell



Professional Phagocytes:
Macrophages and Neutrophils

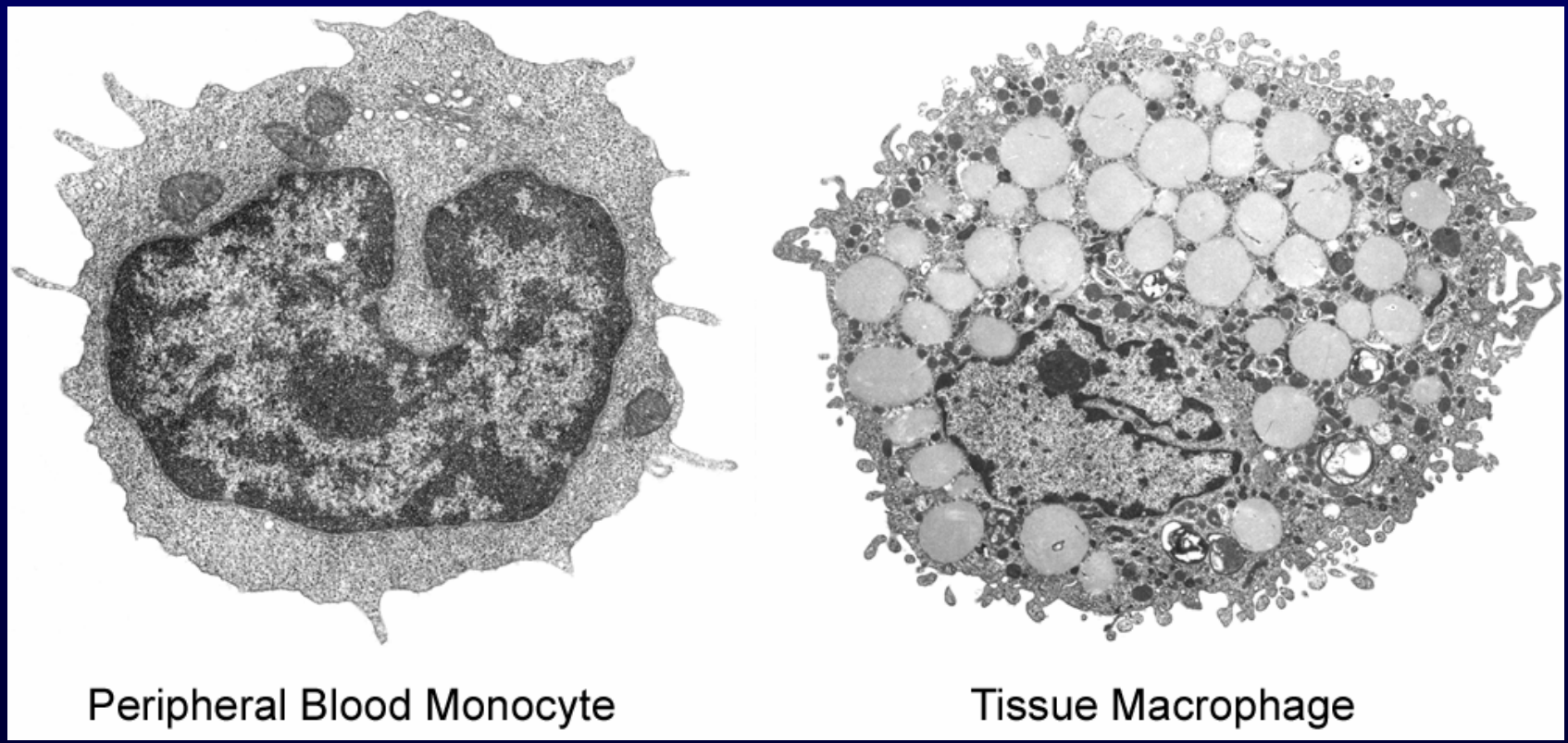
Neutrophils, also know as poly-morphonuclear leukocytes or PMNs, are the most abundant leuckocytes in blood, and the first cell type to respond to most infections.





Monocytes are less abundant than neutrophils in the blood, and differentiate into macrophages in the tissue. Unlike neutrophils which survive only a few hours, macrophages can live for long periods of time in the tissue.

Components of the Mononuclear Phagocytic System



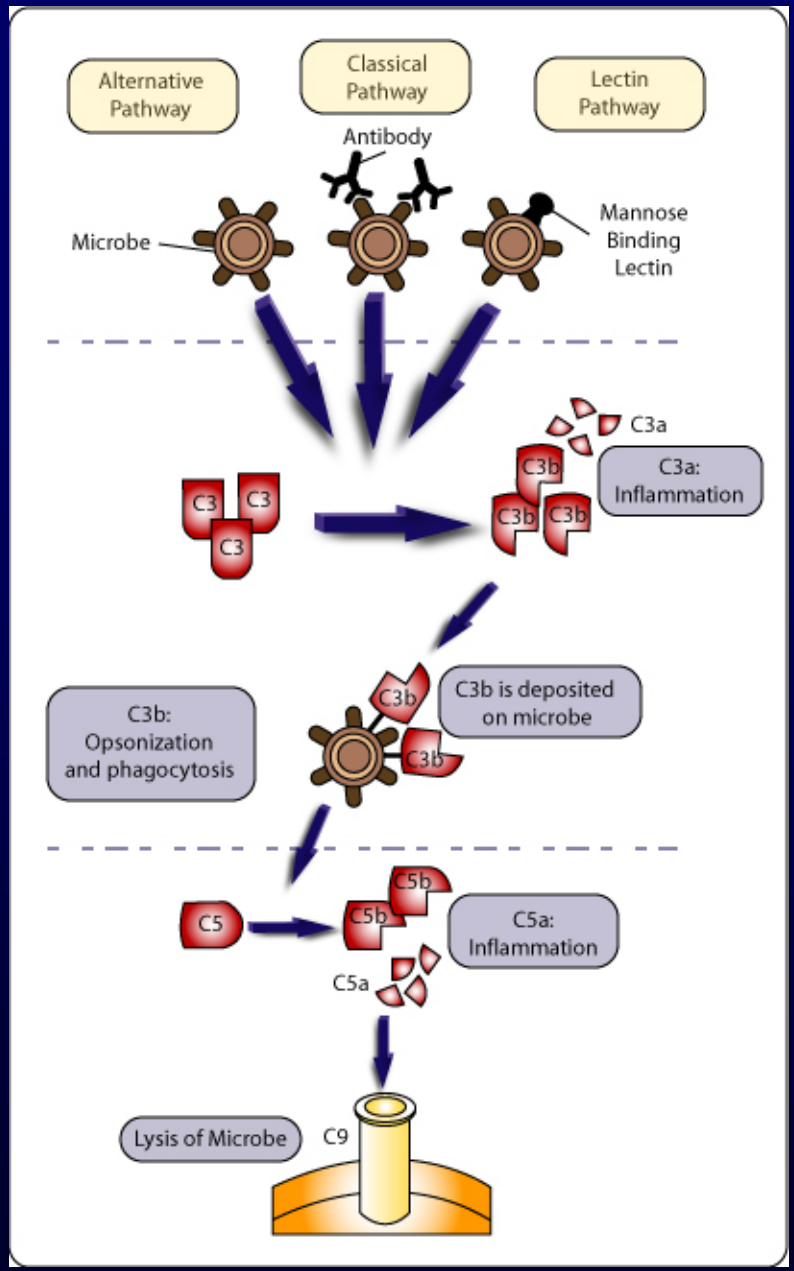
Phagocytosis in Action

How is it done?
3. The Natural Killer (NK) Cells

- Histologically, just a lymphocyte (!) with cytoplasmic granules containing pore-forming proteins such as *perforin*, as well as other proteins that induce target cell apoptosis.
- NK cells respond to intracellular microbes by killing infected cells and by producing the macrophage-activating cytokine, interferon-γ (IFN-γ).
- In turn, macrophages that have encountered a microbe can activated NK cells by the production of interleukin-12 (IL-12).
- NK cells are prevented from destroying host cells by the expression of *"killer inhibitory receptors"* that are specific for the host class I MHC molecules.

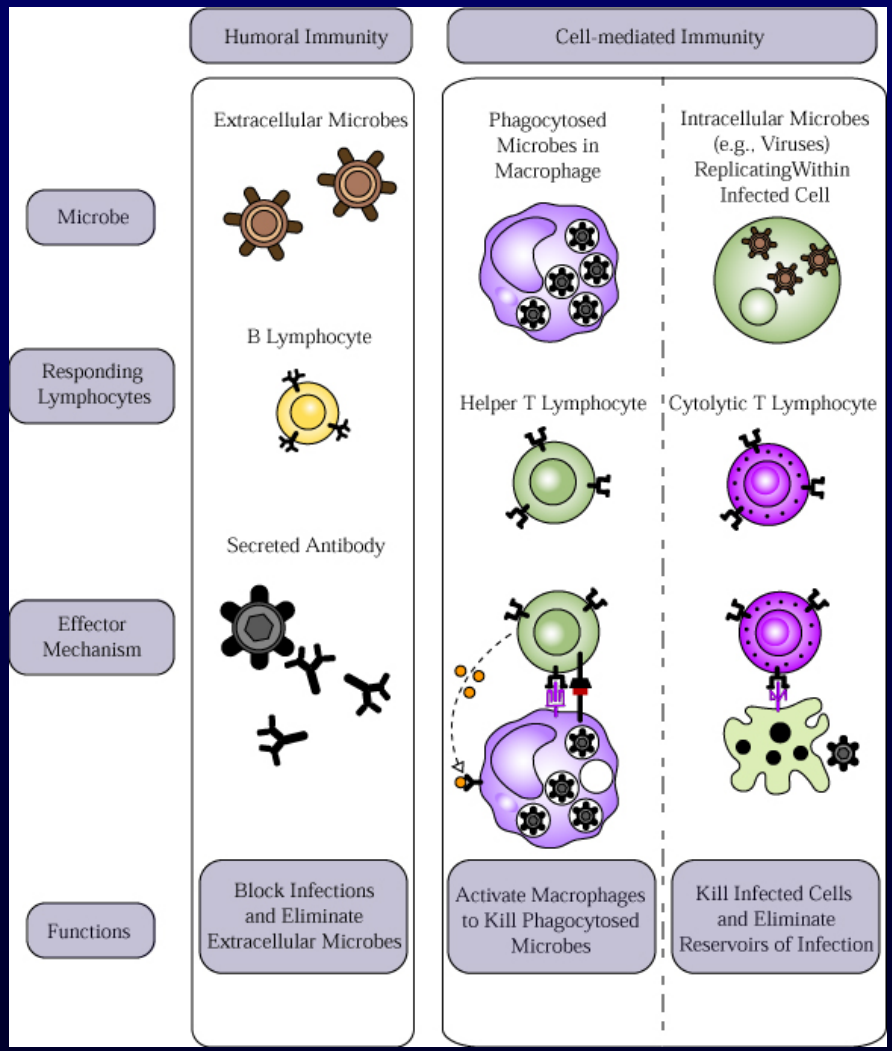
How is it done?
4. The Complement System

- The complement system is a collection of circulating and membrane-associated proteins that lead to an inflammatory and lytic response against microbes.
- In the ***alternative pathway*** the system is triggered directly by the microbes because of the absence of host regulatory proteins on the microbial surface
- In the ***classical pathway*** the system is triggered after antibody bindings to microbes.
- In the ***lectin pathway*** the system is triggered by binding of mannose-binding lectin to terminal mannose residues on the bacterial surface glycoproteins.


Alternative Pathway
Classical Pathway
Lectin Pathway
Antibody
Microbe
Mannose Binding Lectin
C3
C3
C3
C3a
C3b
C3b
C3b
C3a: Inflammation
C3b: Opsonization and phagocytosis
C3b
C3b
C3b is deposited on microbe
C5
C5b
C5b
C5a
C5a: Inflammation
Lysis of Microbe
C9

How is it done?

5. The Adaptive Immune System



Cells of Adaptive Immunity:
1. Antigen-Presenting Cells (APCs)

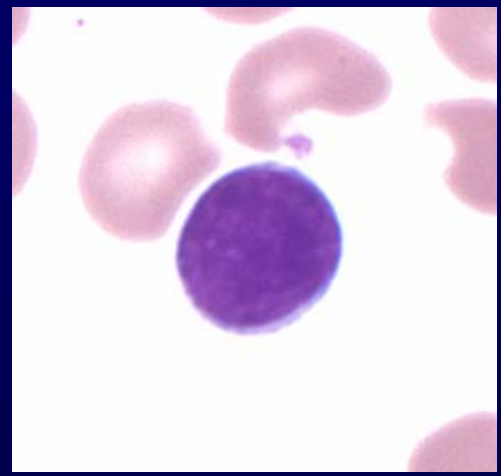
- All potential portal of entry for microbes, as well as most other tissues, contain specialized cells such as ***dendritic cells*** for antigen processing and MHC-II presentation.

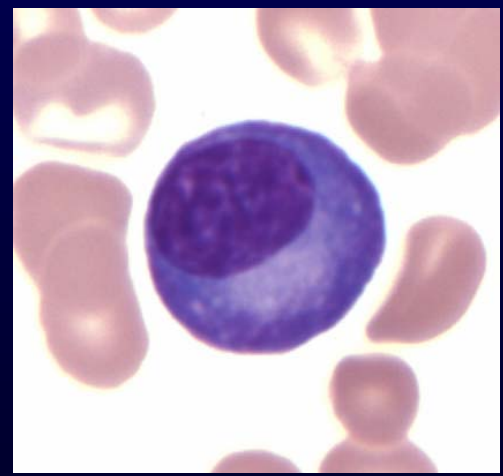
- Dendritic cells have different names according to their location, and are generally characterized by their long branching cytoplasmic processes.

Please see figure 9-13 of Junqueira & Carneiro. *Basic Histology: Text and Atlas*. 10th edition. McGraw Hill. 2003. ISBN: 0071378294.

Cells of Adaptive Immunity:
2. Lymphocytes

- In spite of their diverse and complex functional roles, lymphocytes are simple round cells measuring ~8 to ~15μm in diameter and containing relatively little cytoplasm.
- Mature antibody-producing B-cells or Plasma cells have a characteristic appearance because of their prominent Golgi and RER.
- Otherwise, sub-classification of lymphocytes is difficult to nearly impossible by routine staining, but is easily done by immunohistochemical staining.
- Although isolated lymphocytes are pervasive, organized populations are present in peripheral lymphoid organs: lymph nodes, spleen and the Mucosa-Associated Lymphoid Tissue (MALT).





Peripheral Lymphoid Organs

- The peripheral lymphoid organs are organized to concentrate antigens, antigen-presenting cells, and lymphocytes in a way that optimizes interaction among these cells and the development of adaptive immunity.
- The primary lymphoid organs are:
  - Lymph nodes (numerous and scattered throughout the lymphatic system)
  - Spleen (single abdominal organ)
  - Mucosa-Associated Lymphoid Tissue (diffusely present in the internal and external lining mucosa)

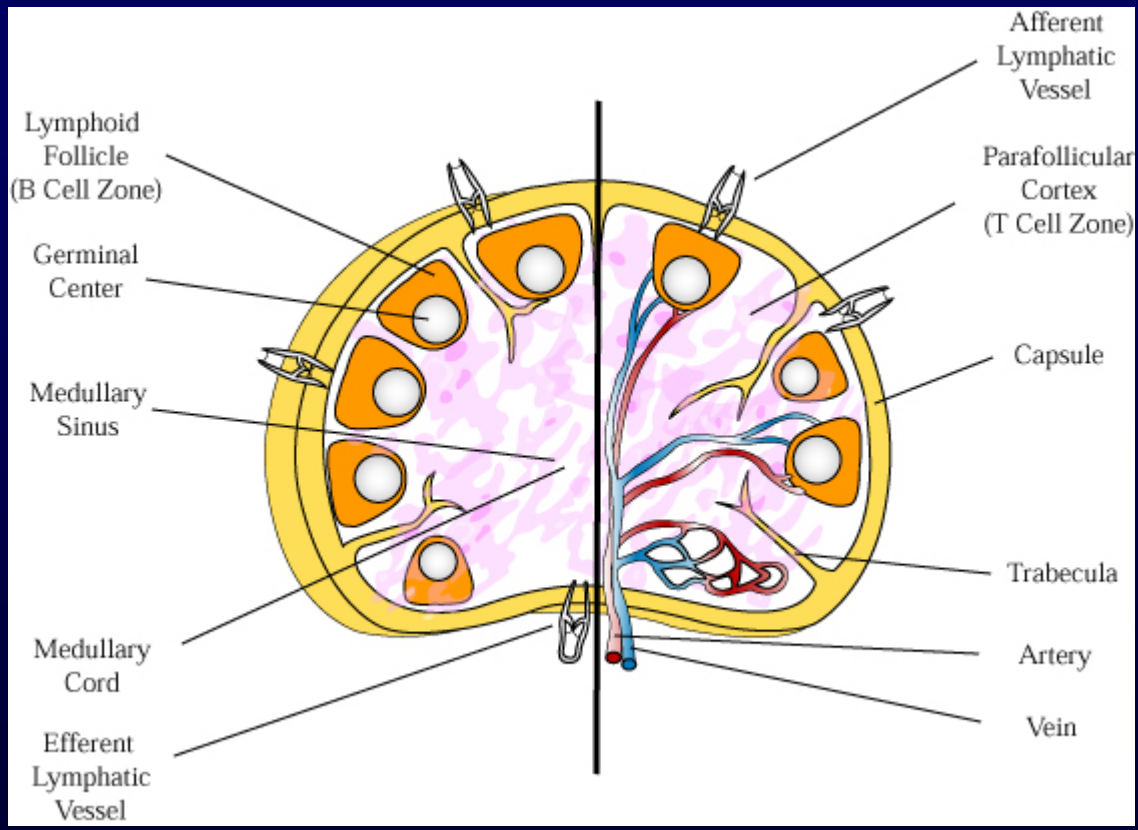
Lymph Nodes

- Encapsulated, small aggregates (typically 0.5-1 cm^3) of lymphoid tissues located along the lymphatic channels.

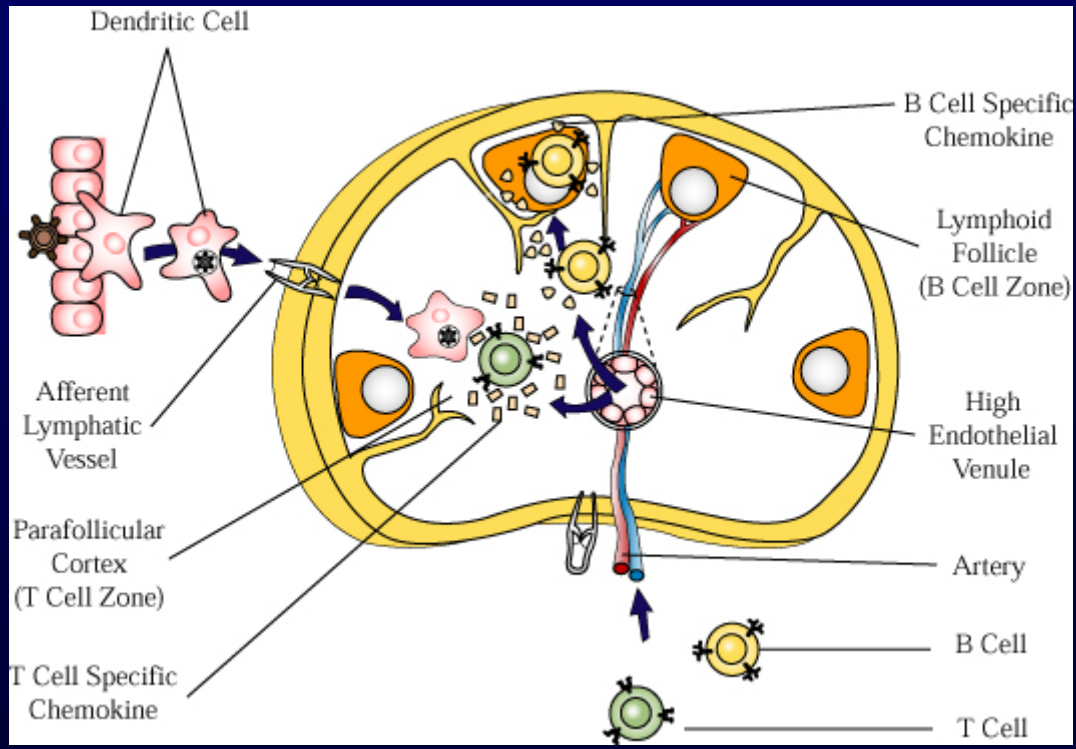
- Lymph nodes screen the entire collection of fluids and fluid-borne particles returning or entering from tissues into the central circulatory system.

(Why do surgeons often take out lymph nodes when they resect cancerous tissues?)

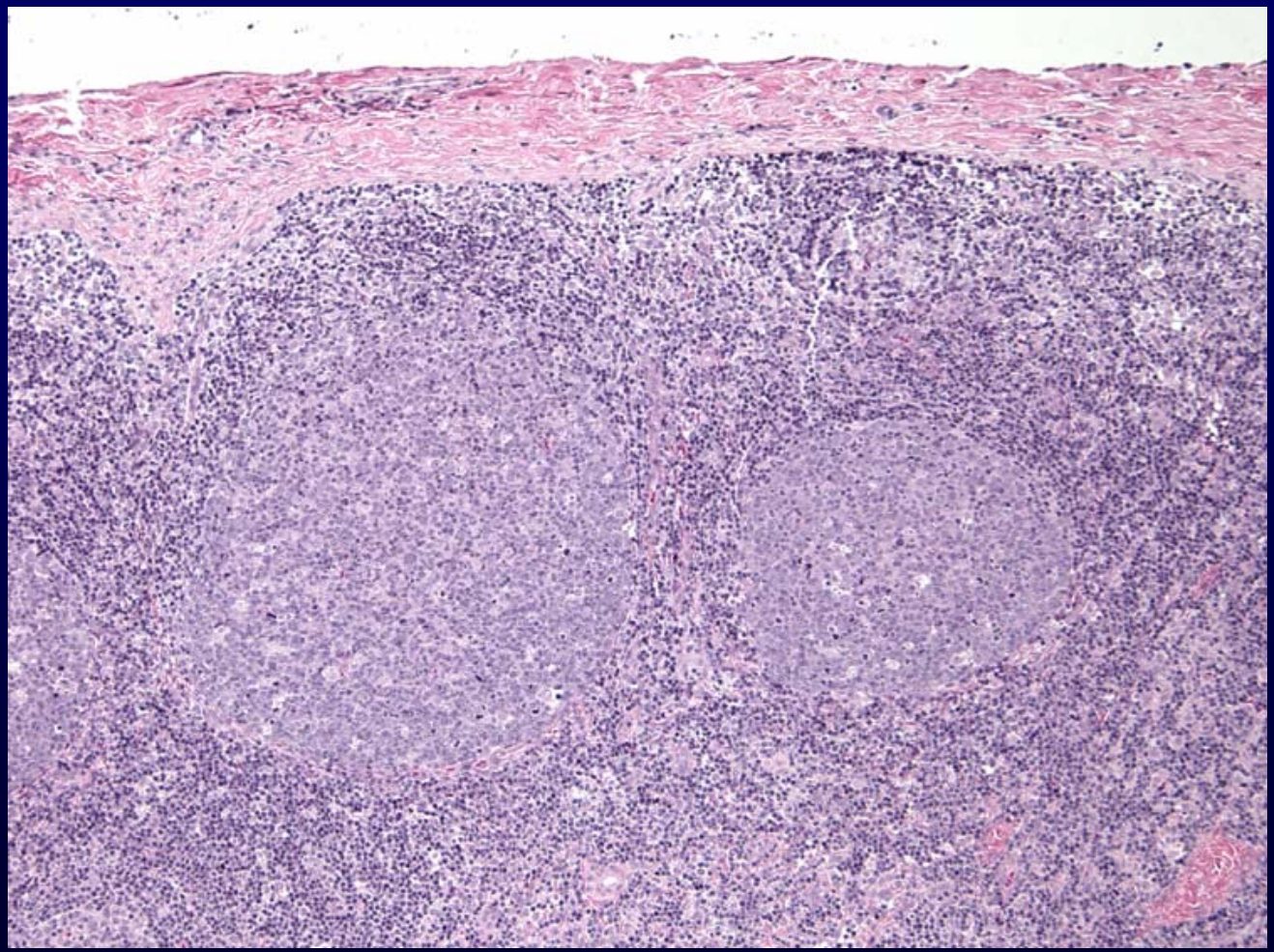
Lymph Nodes


Afferent Lymphatic Vessel
Lymphoid Follicle (B Cell Zone)
Parafollicular Cortex (T Cell Zone)
Germinal Center
Capsule
Medullary Sinus
Trabecula
Medullary Cord
Artery
Vein
Efferent Lymphatic Vessel

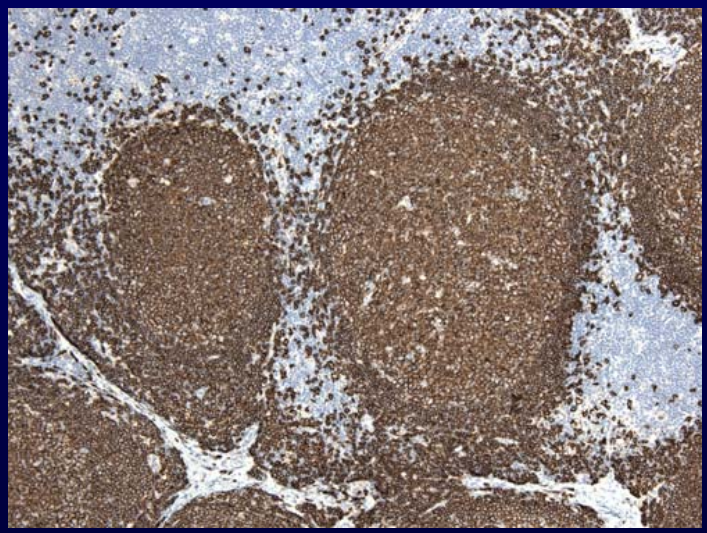
B and T Cell Zones in the Lymph Node



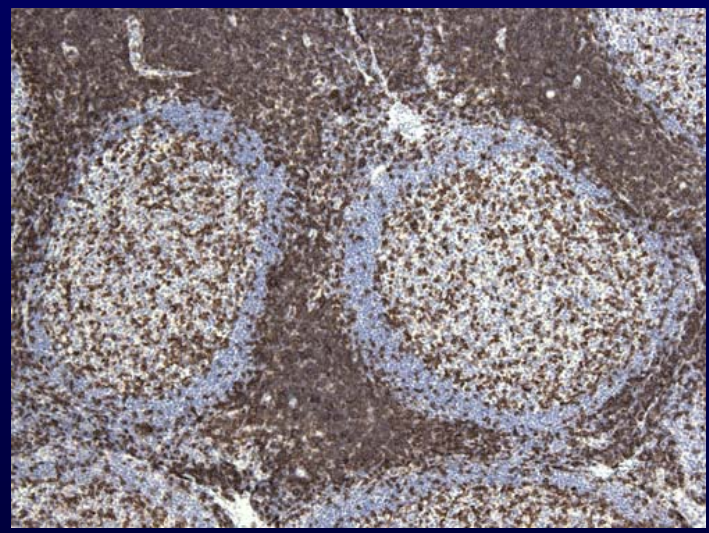
The Lymph Node



The Lymph Node
by Immunohistochemistry



B cells (CD20)



T cells (CD3)

The Spleen

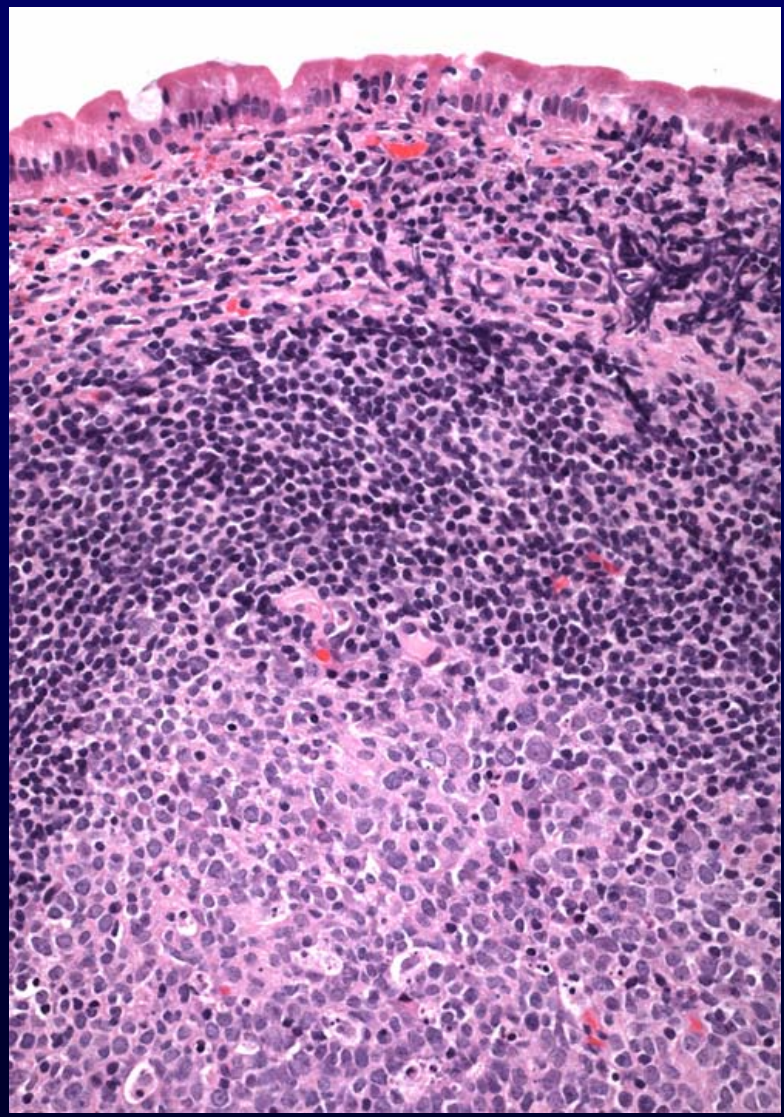
- A large abdominal organ that serves the same function for blood as lymph nodes do for the lymph.

- The spleen also contains abundant macrophages that actively ingest and destroy blood-borne organisms and particles.

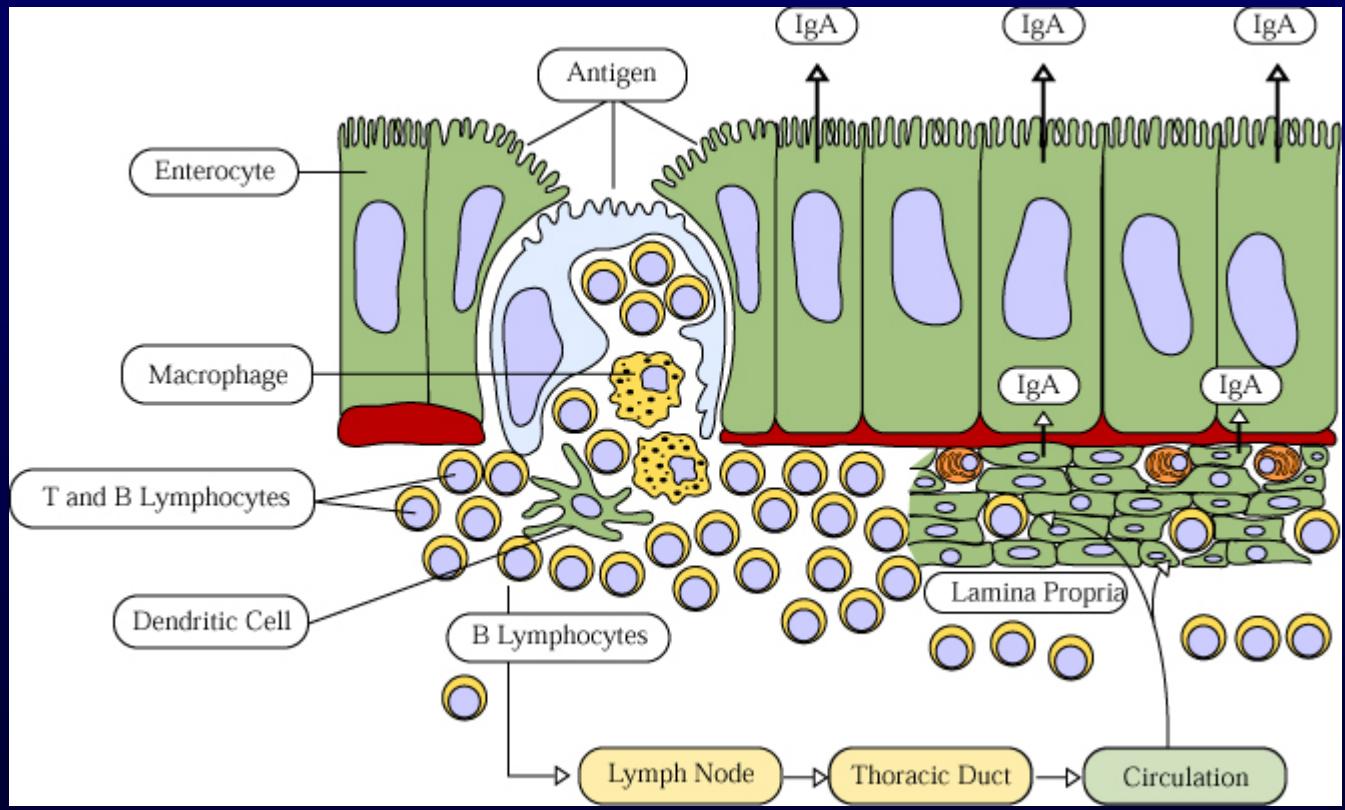
MALT
No so insignificant!

- The intestines contain 70% of immunoglobulin-producing cells in the human body.
- There is 1 intraepithelial lymphocyte (IEL) for every 10-20 lining epithelial cells.
- Pharyngeal tonsils, nasal adenoids and ileal Peyer patches are prominent mucosal lymphoid tissues.

MALT in the Normal Terminal Ileum



M-Cells and PIgR



Supplementary Slides

Review of Lung Structure