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# Type 1 Diabetes Overview of Immune Response

M1 – Immunology Sequence

Lecture outline

Small groups

Complement self-study

Transplantation self-study

Allergy self-study

Text

Terms and Abbreviations

Summaries--quiz and exam questions

## “Justin Spencer”

Justin was a 16 year old whose type I diabetes was diagnosed at age 10. His symptoms at that time included a 3-month history of increasing fatigue and weight loss of 20 lbs. Despite the weight loss, he had an increased appetite and was consuming large quantities of liquids. His thirst and unusually high liquid intake was accompanied by frequent urination. He has controlled his disease, with mixed success, with injected insulin.

Some of Justin's relatives may have also had type I diabetes. Justin's blood type was B, Rh positive, and his tissue (histocompatibility, HLA) type was A2,24; B7,35; DR3,4.

# Insulin Dependent Diabetes

Epidemiology: Juvenile onset, equally prevalent in boys and girls.  
Often clustered in families.

Symptoms: Frequent urination accompanied by enormous thirst.  
Lethargy.

Laboratory findings: Blood glucose  $>200$  mg/dl; fasting blood glucose  $>120$  mg/dl; insulin low or absent; ketones in urine

Histology: Destruction of beta cells of the pancreas

Well managed for many years by injections of insulin.

Over the long term, many problems (eyes, kidneys, nerve function) slowly emerge.

Origin of a disease state:

Inherited

Chemical toxicity

Trauma

Dietary

Infectious pathogen

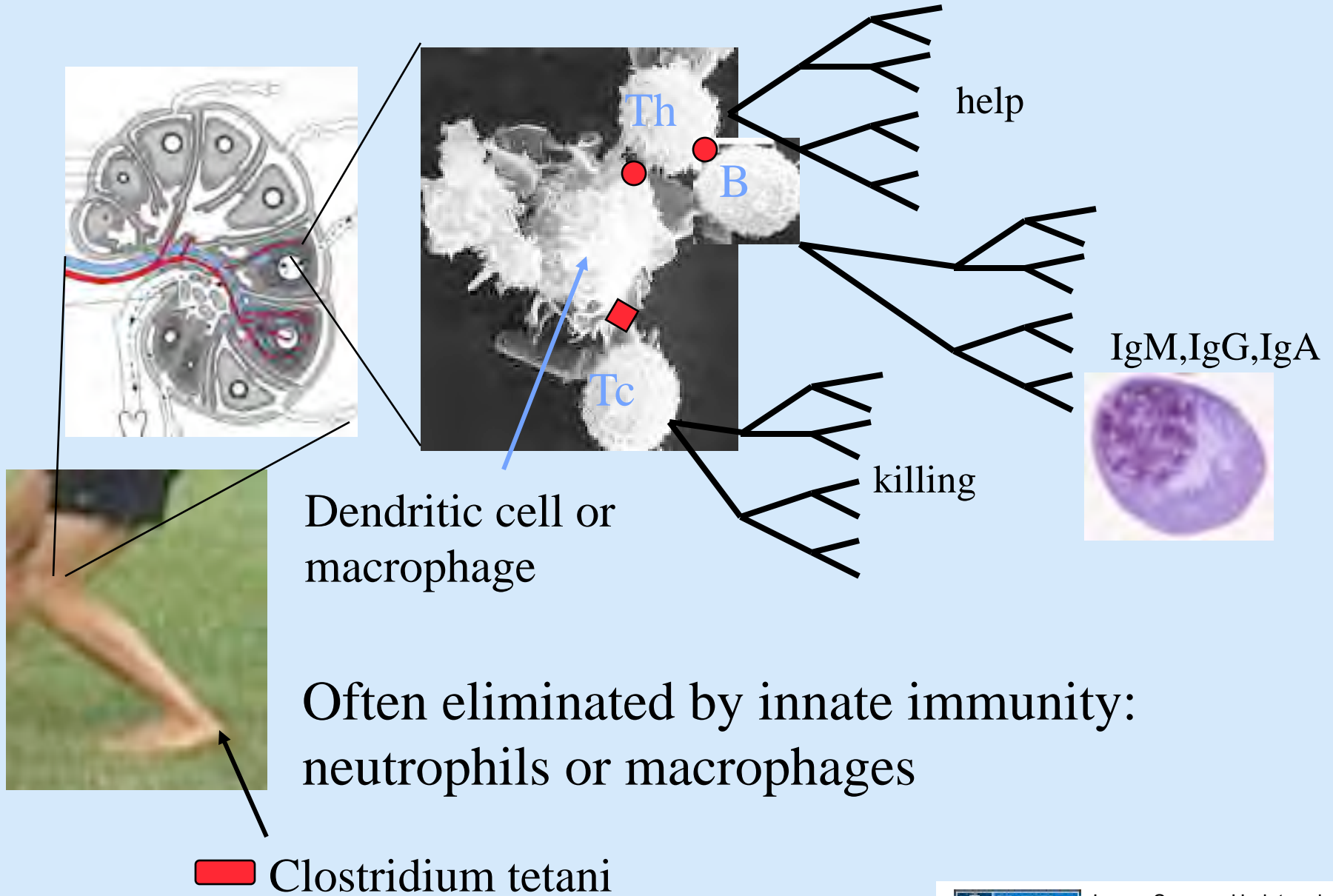
Immune response to self

1. It has been known for some time that juvenile onset, insulin dependent diabetes is an immunologic disease. What is the evidence that this is the case, that the pathology does not have some other origin (an infectious process, chemical toxicity, etc.)?
2. How does an immune response lead to the pathology?



- 1. The general roles of the leukocytes in immune responses.**
- 2. "Antigens" and related terms.**
- 3. Innate and adaptive immunity.**
- 4. The three different phases of an immune response--recognition, activation, effector.**
- 5. The four characteristics that differentiate the immune response from other biological systems--specificity, diversity, memory, tolerance.**

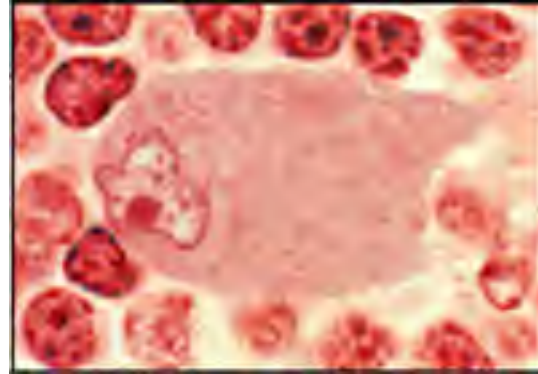
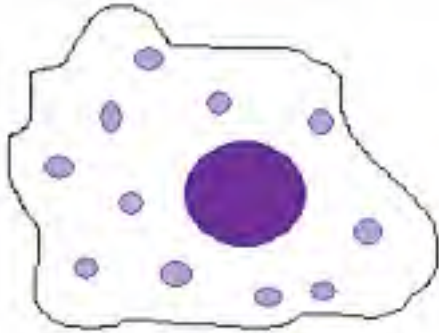
# Simplified overview of an immune response



When a pathogen first enters the body, it travels to the nearest lymph node (or to the spleen) and is taken up there by nonspecific cells. In many cases, these nonspecific cells, or components of the alternative complement pathway, will eliminate the pathogen immediately--innate immunity. Innate immunity is that protection against pathogens which is rapid and does not require specific recognition of the pathogen.

(Tuesday and Wednesday)

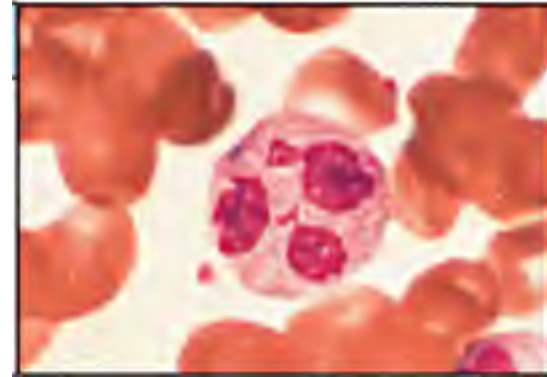
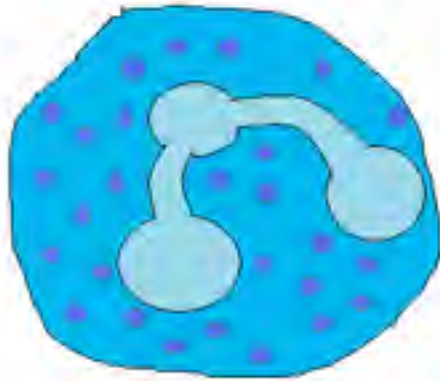
## *Macrophage*



Phagocytosis

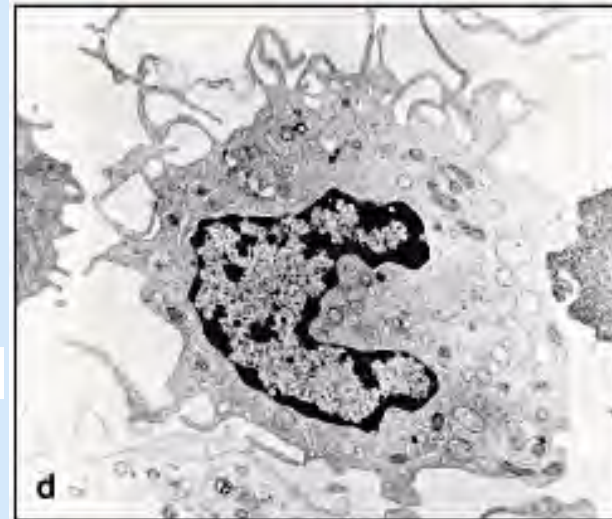
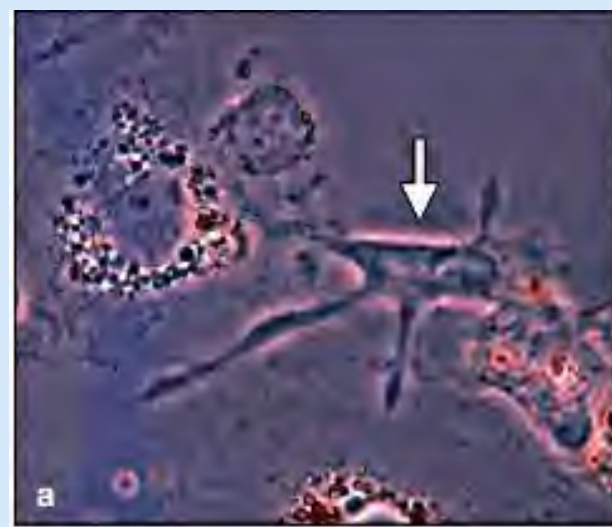
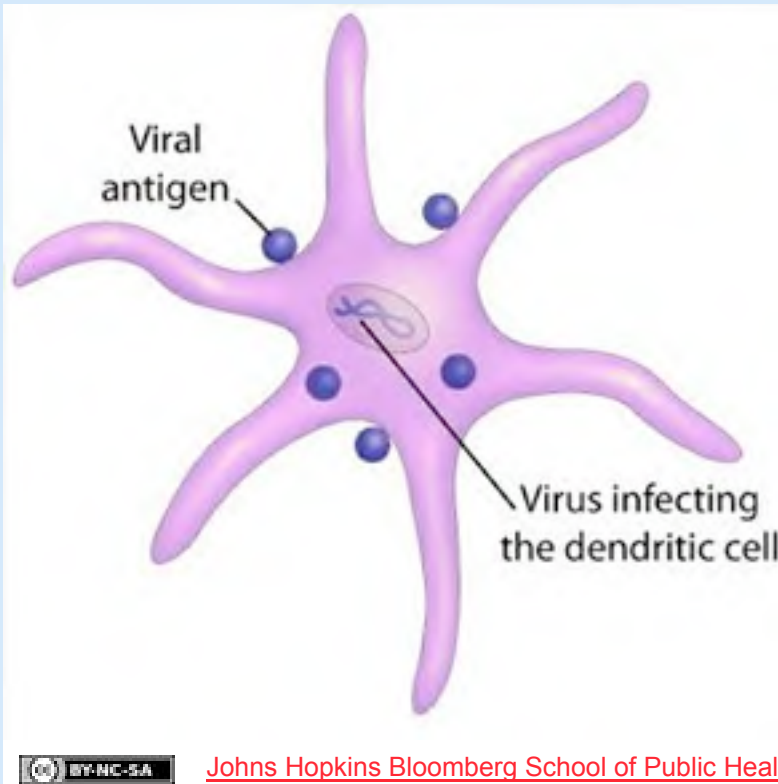
Macrophages are one kind of nonspecific cell a pathogen encounters. These cells treat all “nonself” cells the same, without regard (more or less) to the specific type of pathogen. (More detail tomorrow)

## *Neutrophil*



Phagocytosis and activation  
of bacterial mechanisms

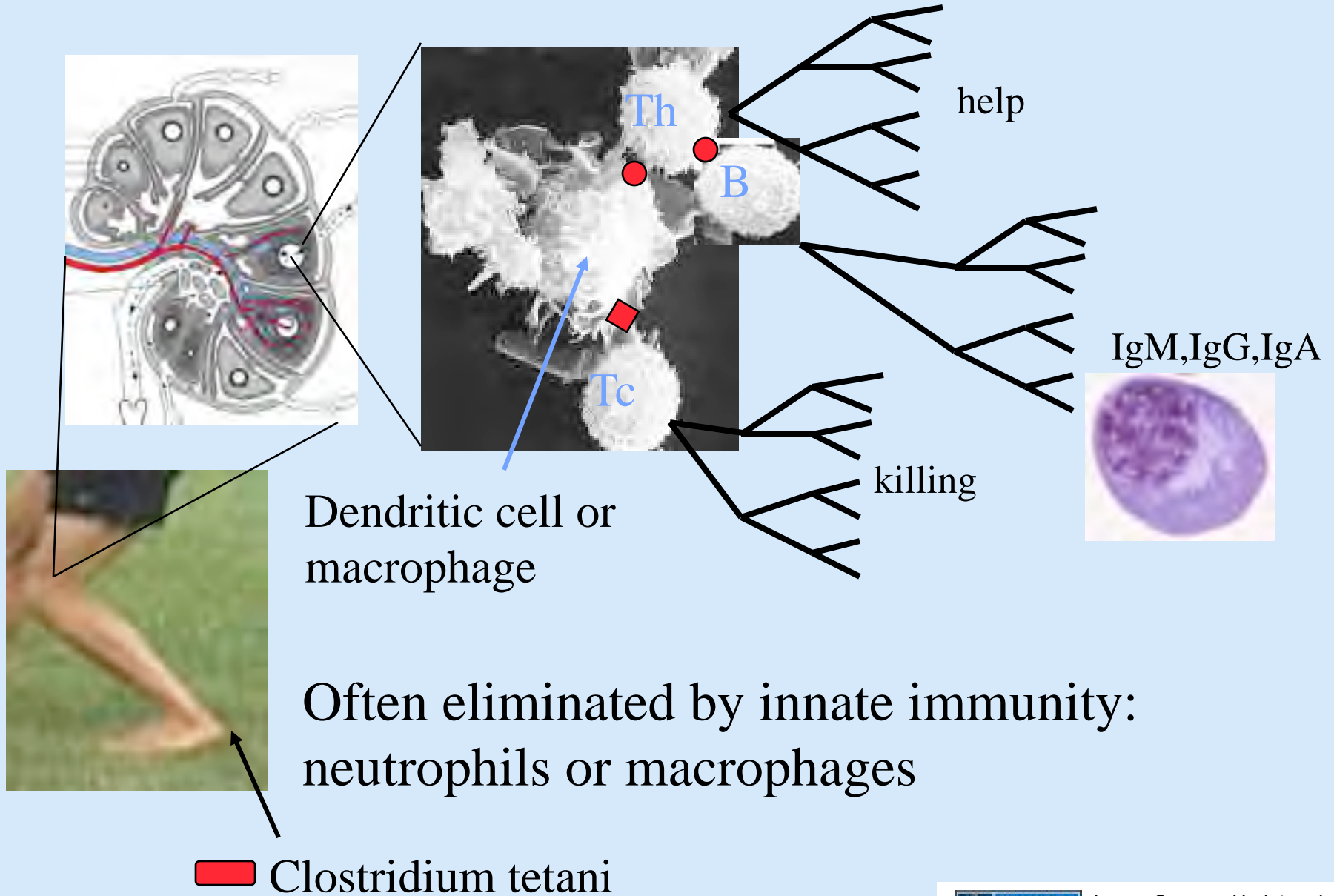
Neutrophils are also called polymorphonuclear leukocytes.



© PD-INEL Janeway. Immunobiology: The Immune System in Health and Disease. Current Biology Ltd./Garland Publishing, Inc. 1997

Dendritic cells are adept at acquiring pathogens and “presenting” them to the immune system.

# Simplified overview of an immune response



Next, lymphocytes with specific antigen receptors recognize the antigen--recognition phase of immune response. Recognition is due to binding of the antigen to the specific receptor on the cell surface.



# Terms Used to Describe Antigens

Antigens--foreign molecules (with a distinctive shape)

Carrier, immunogen--large molecules that are able to elicit an immune response (8 amino acids or larger)

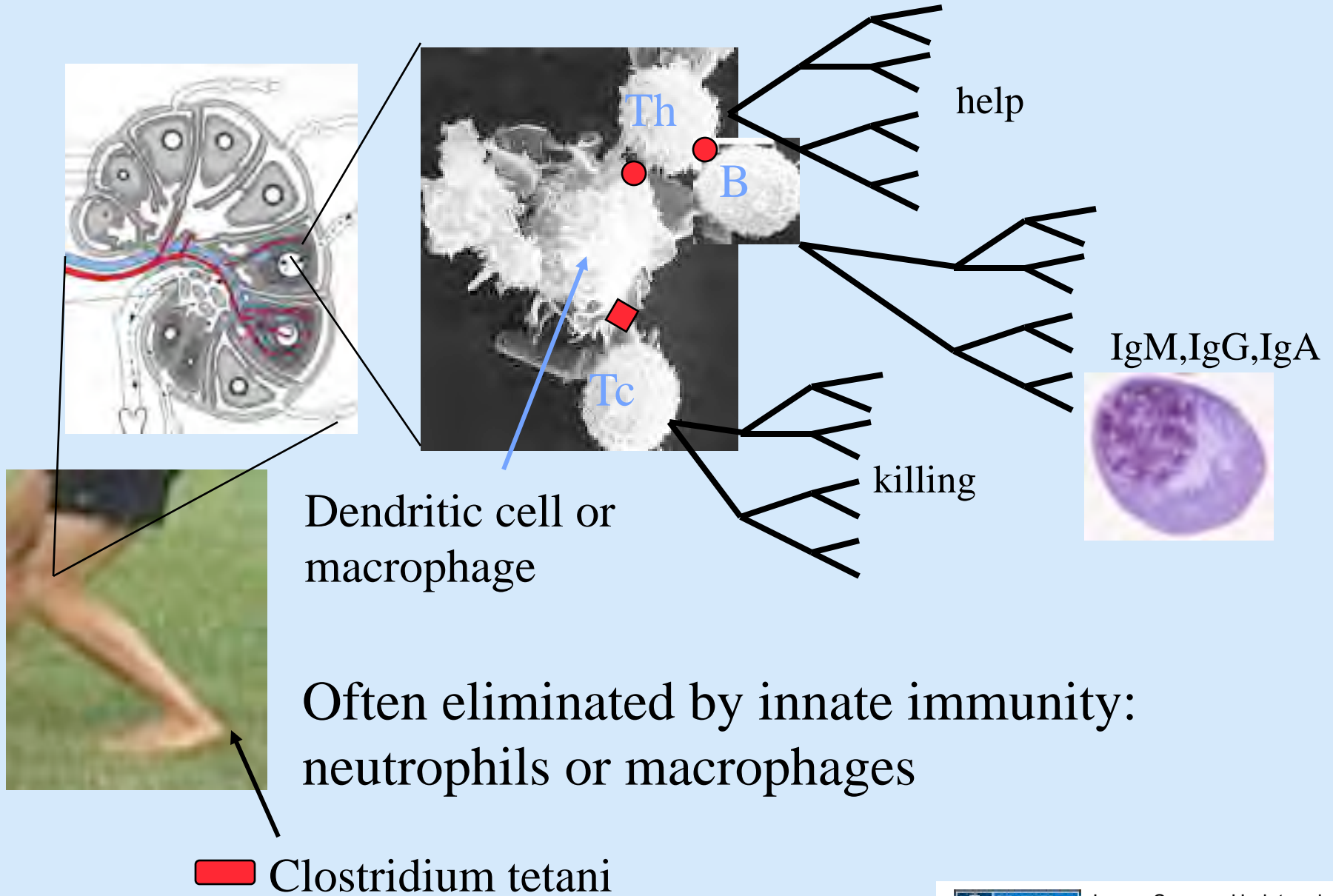
Hapten, determinant, epitope--These are small molecules that cannot elicit an immune response, but can bind to an antibody.

An epitope is that part of an antigen that binds to one antibody.

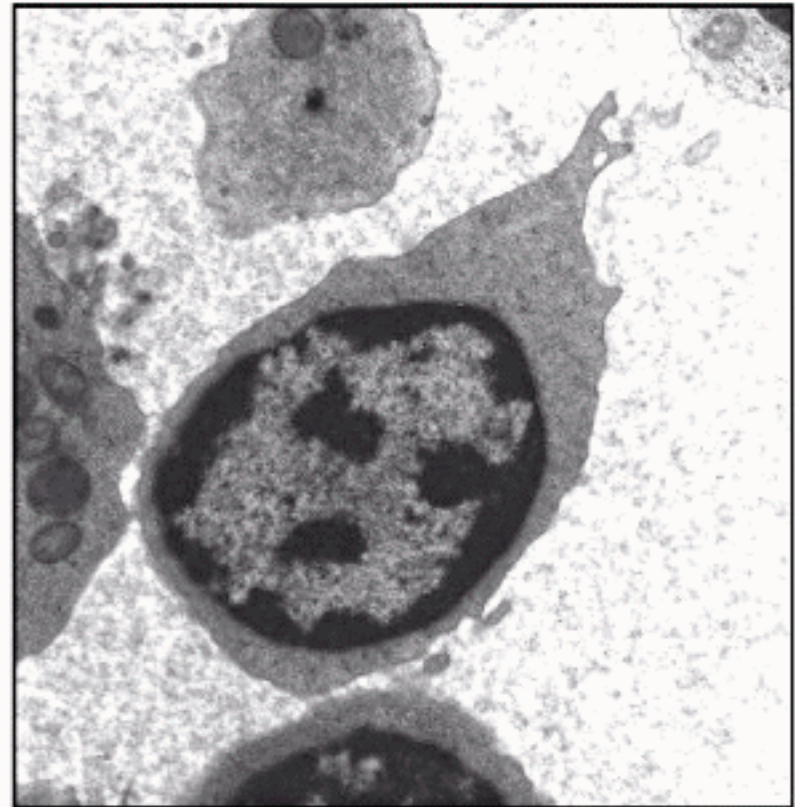
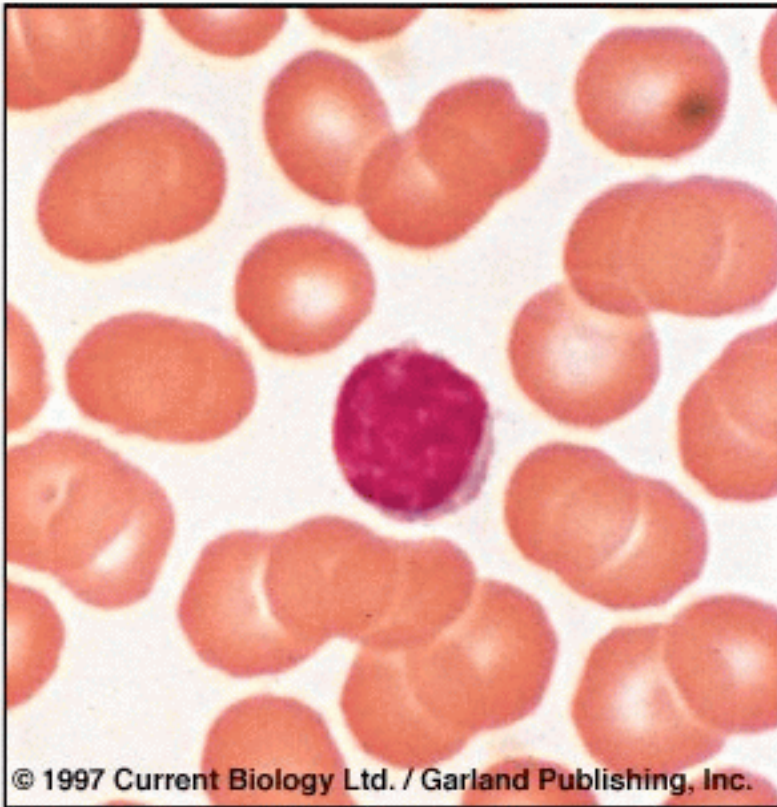
Hapten and Determinant are similar, but not identical, terms.

Antigens (for example, foreign proteins) have many epitopes or haptens or determinants.

# Simplified overview of an immune response



Lymphocytes are small, round white blood cells.



B cells--(in birds) the development of these lymphocytes depends on the Bursa of Frabricius (in the analogous position to human appendix.)

Antibody--protein produced by B cells, or their progeny, that binds antigen. A functional term. There is one antibody for every epitope; a human can express about ten million different antibodies. (lectures 2 and 3)

Immunoglobulin--structural term for antibody

# T cells

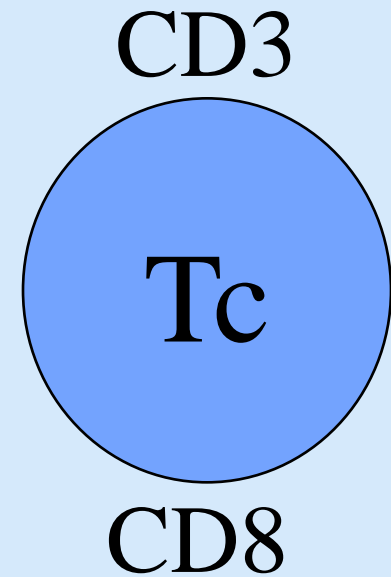
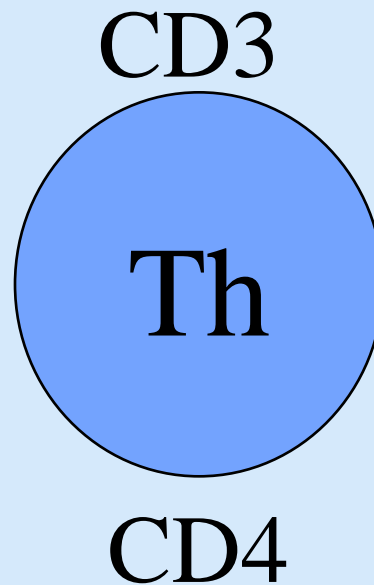
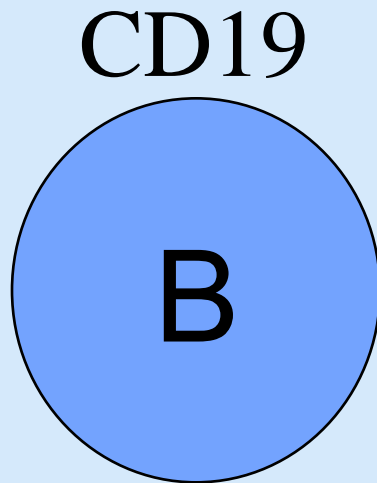
Development depends on the thymus

Have CD3 on their surface

Two types--CD4+ and CD8+

(Dr.Chang's lectures)

In the light microscope, T and B lymphocytes look the same, however they express different cell surface molecules.



Recognition phase: T and B cells recognize the pathogen by binding to receptors on the cell surface.

Activation phase: T and B cells differentiate and divide.

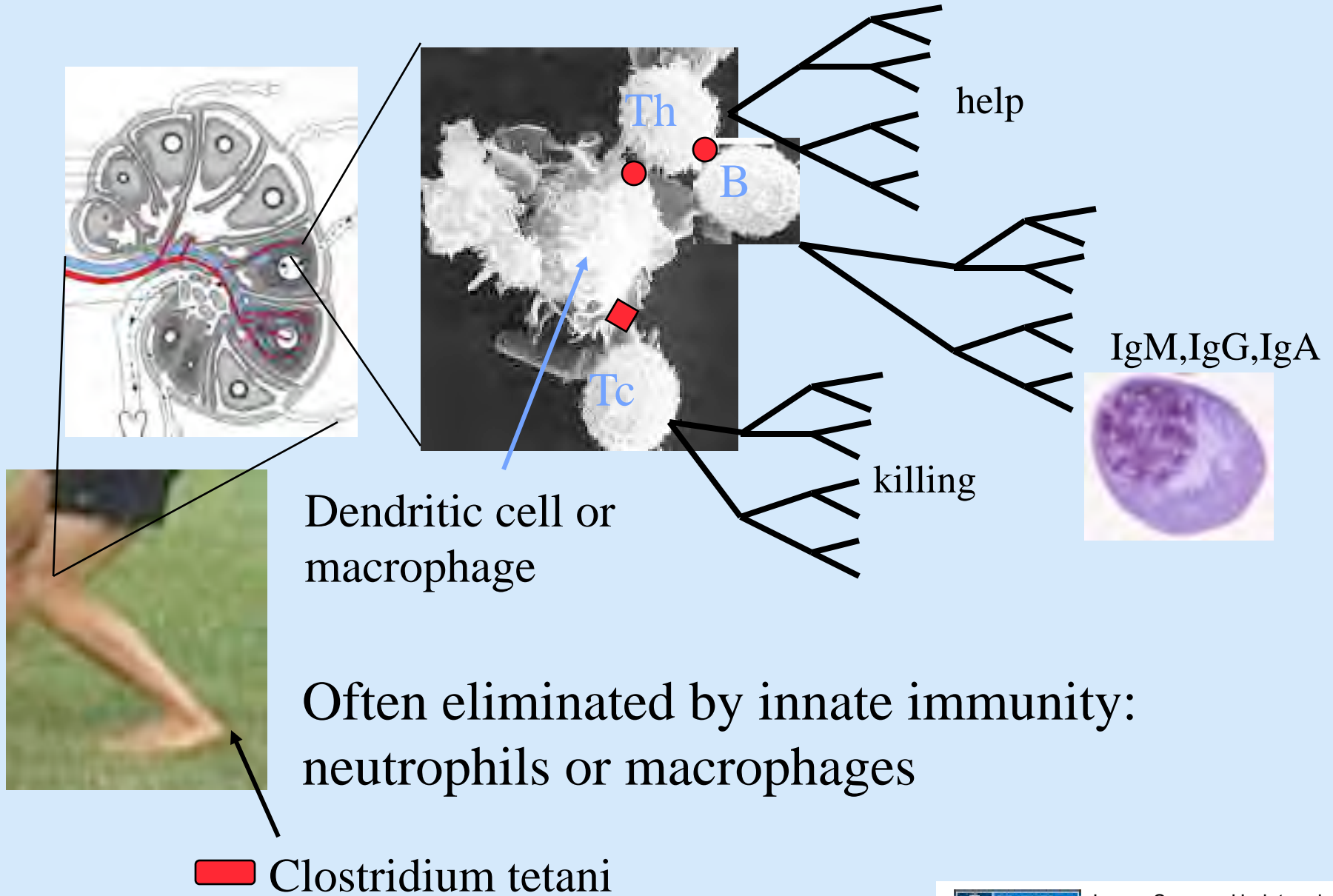
Adaptive immunity is that protection against pathogens that involves specific recognition.



T cells do everything they do by cell to cell contact. Hence, T cell immunity is called cell mediated immunity.

Helper T cells interact with B cells to “help” them make large amounts of antibody. Helper T cells have CD4 on their cell surface.

# Simplified overview of an immune response



Cytotoxic T cells recognize antigens on the surface of cells infected with viruses or intracellular bacteria, and kill those infected cells. These T cells are usually CD8+.

The effector phase of an immune response is when the pathogen are neutralized, or otherwise eliminated.

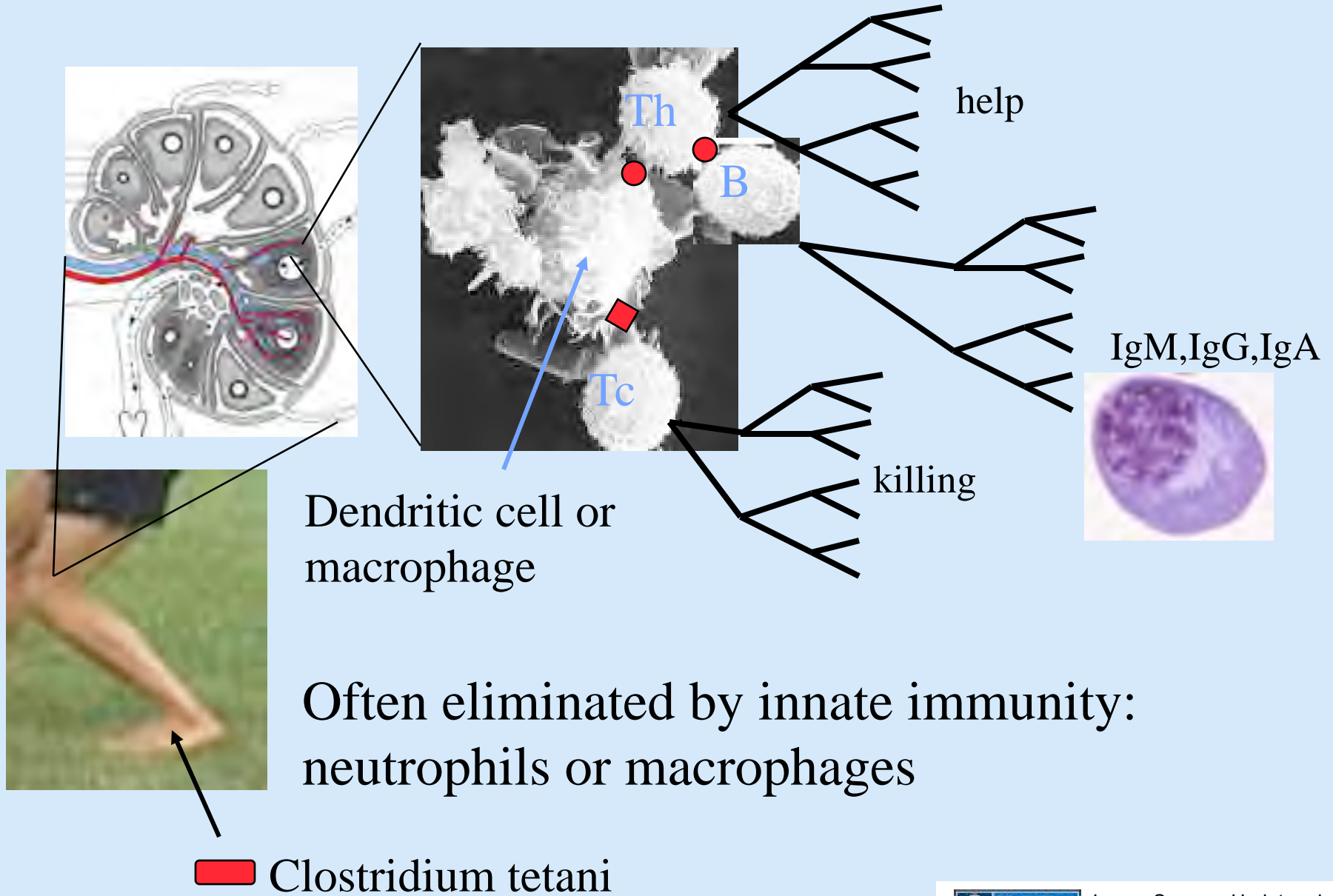
T cell help is an effector phase function.

Helper T cells produce cytokines, proteins secreted by one cell that act on another cell.

Lymphokines are proteins secreted by one white blood cell that act on another cell. If the cell acted upon is another white blood cell, the protein is termed an interleukin (IL).

(Friday)

# Simplified overview of an immune response



Dendritic cell or macrophage

Often eliminated by innate immunity: neutrophils or macrophages

 Clostridium tetani

An effector phase function of B cells is antibody secretion by plasma cells. B cell immunity is called humoral immunity, because it is mediated by a secreted protein, antibody.

## Effector B cell (plasma cell)



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Tuesday and Wednesday

Active immunization results from an immune response mediated by an organism's own immune cells and antibodies. These cells become immune by encountering antigen and going through the recognition, activation, and effector phases of the immune response.

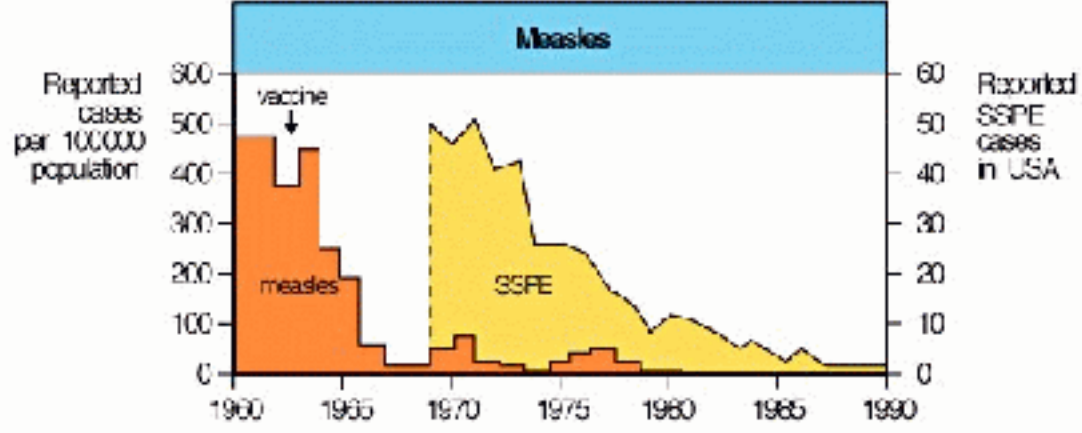
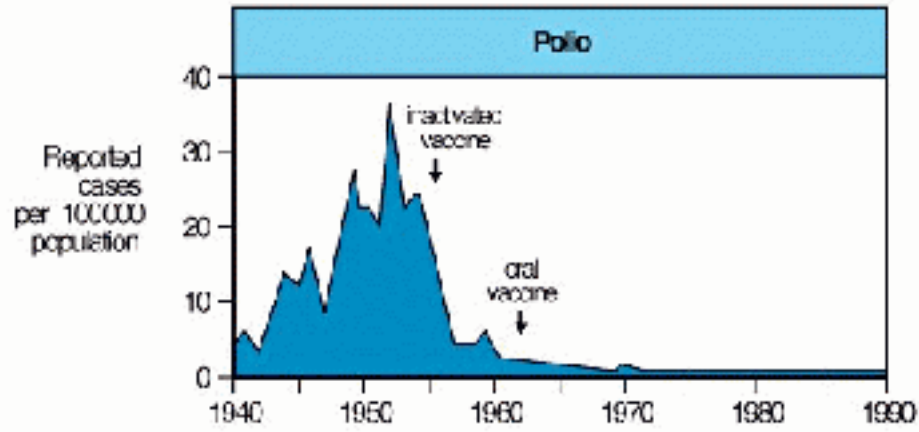
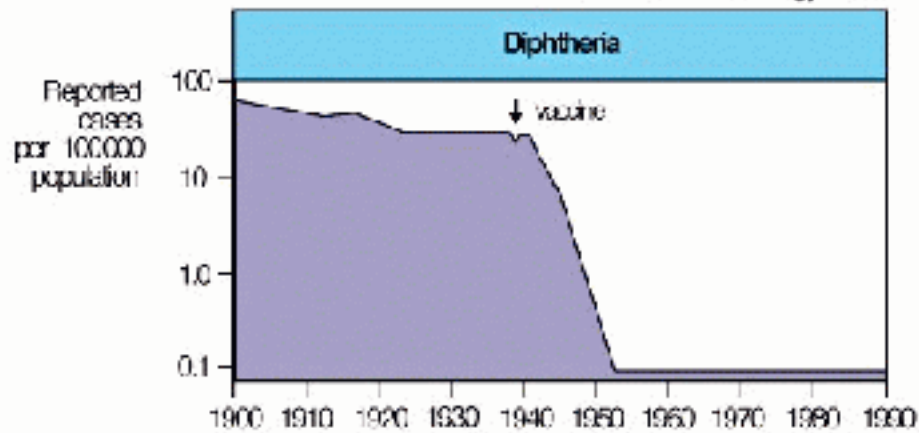
Passive immunization is derived by the administration of immune cells or antibodies from another individual. For example, in treatment of immunodeficiencies.



## Immunological Memory

One of the results of the activation phase of an immune response is the generation of memory T cells and B cells. Upon a subsequent encounter with the pathogen, these lymphocytes make a faster, more vigorous, and qualitatively different immune response.

Memory is the basis of vaccination.



Most of the time, a clinician desires an active immune response:

vaccination

tumor immunity

Sometimes, a clinician prefers the immune response to be inactivated:

transplantation (self study)

allergy (self study)

autoimmune disease (Dr. Fantone and small group)

## Four characteristics of immune responses:

- A. Specificity of recognition by cells and molecules--The cells and molecules in the immune response recognize the particular antigen that they are selected for one million-fold better than (almost) all other antigens.
  
- B. Diversity of recognition--The immune response can recognize ten million or more different antigens.

Monday and Wednesday

C. Memory or secondary responses

D. Tolerance--Depending on how an antigen is encountered, the immune system can become nonresponsive to that antigen. Individuals are (usually) tolerant to self antigens.

## Summary:

1. There are four characteristics that differentiate immune responses from other biological systems: Specificity, diversity, memory, and tolerance.
2. Leukocytes with antigen-specific receptors (T and B lymphocytes) and leukocytes lacking antigen-specific receptors (macrophages, neutrophils, dendritic cells, etc.) mediate immune responses.

3. Innate immunity is rapid, because it does not require specific recognition of pathogens. Adaptive immunity involves the differentiation of antigen-specific T cells and B cells, and is thus fully active at some time after encounter with a pathogen.
  
5. Antigens are foreign molecules. "Carrier and epitope" refer to various subunits of antigens.

5. Antigens on a pathogen are detected as foreign in the recognition phase of an immune response. This recognition of antigen leads to cellular differentiation and division in the activation phase of an immune response.

Following activation, cells and secreted molecules that destroy or neutralize the pathogen are expressed in the effector phase.



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