Introduction to Immunology

Immunity

* Passive Immunity- Immunity that is obtained from a outside source. Example: Antibiotic, Clostrum
* Active Immunity- Immunity that is obtained from the immune system actively defending the body. Example: Vaccines, Immunity after having a disease

The Role of the Immune System

* It protects our bodies from infection, operating via:
  - A first line *nonspecific line* of defence: barriers
  - A second *nonspecific* line of defence: general attack.

Then comes *specific* (i.e. targeted) defence, comprising:

* Primary immune response
  * Launches a response to invading pathogens
* Secondary immune response
  * Remembers past encounters, leading to:
  * Faster response the second time around

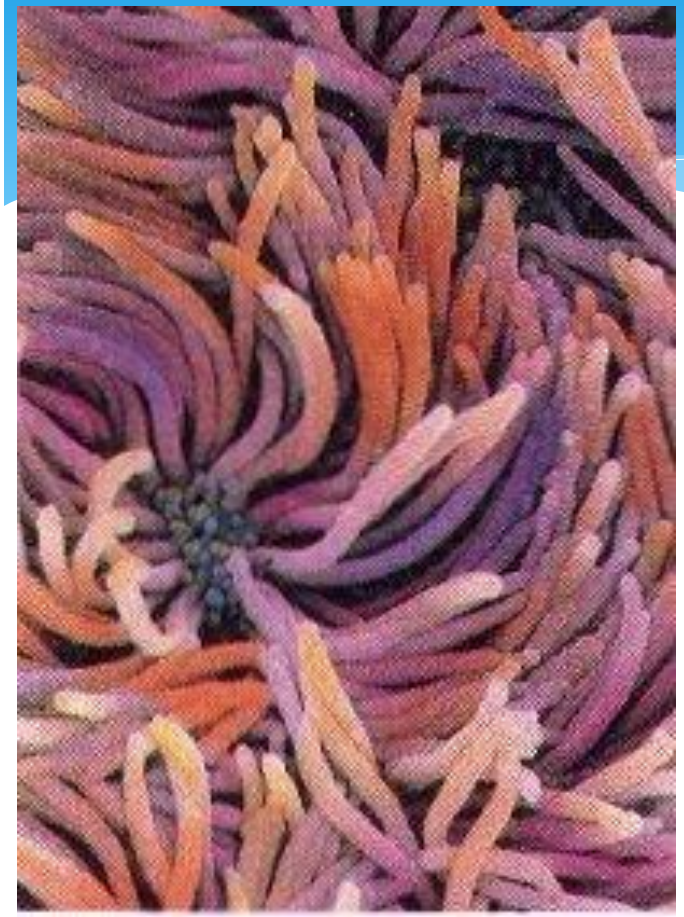
Basics and Terms

* **Pathogen-** is any agent (bacterium, virus, etc) that can cause us trouble
* **Nonspecific Defenses** are the body's first line against disease. They are not directed against a particular pathogen. They guard against al infections, regardless of their cause.
* **Specific defenses** are attempts by the body to defend itself against particular pathogens.
* Since Pathogens must enter the body in order to cause disease, the body's first line of defense is to keep pathogens out. So, what organ is used for this?

Basics continued

* The Body's MOST IMPORTANT Nonspecific Defense is the **SKIN**. UNBROKEN Skin provides a continuous layer that protects almost the whole body. Very Few Pathogens can penetrate the layers of dead cells at the skin's surface.
* Oil and sweat glands at the surface of the skin produce a salty an acidic environment that kills many bacteria and other microorganisms.
* The importance of the Skin as a Barrier against Infections becomes obvious when a small portion of skin is broken or scraped off: Infection almost always follows.
* Infections are a result of the penetration of the broken skin by microorganisms normally present on the unbroken skin.
* Pathogens also enter the body through the Mouth and Nose, but the body has Nonspecific Defenses that protect those openings.

Nonspecific Defenses



* **MUCOUS MEMBRANES** are Tissues that protect the interior surfaces of the body that may be exposed to pathogens.
* They serve as a barrier and secret **MUCUS**, a sticky fluid that traps pathogens.
* **MUCUS, CILIA, and HAIRS** in the Nose and Throat trap Viruses and Bacteria. Pathogens that make it to the Stomach are destroyed by Stomach Acid and Digestive Enzymes.
* Many Secretions of the Body, including mucus, saliva, sweat, and tears, contain **LYSOZYME**, an enzyme that breaks down the cell wall of many bacteria.

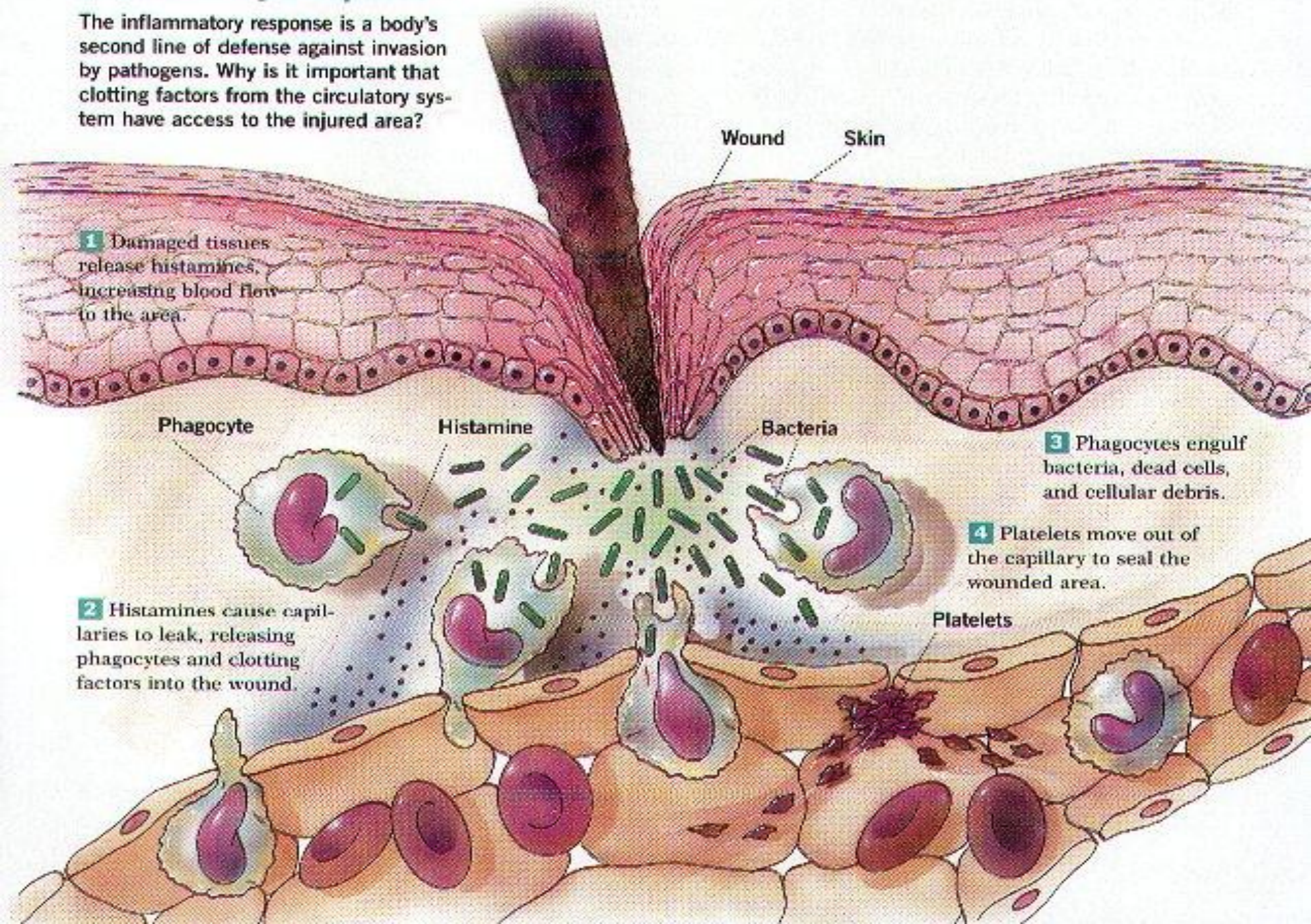
But what happens if something gets past all that ?

The Inflammatory Response

* **This is the SECOND LINE OF DEFENCE**
* When Pathogens get past skin and mucous membranes, and enter the Body, this Second Line of Defence comes into play, triggered by injury to tissues in the body.
* The injured cells release a protein called **HISTAMINE**, which starts the a series of changes called the Inflammatory Response.

Steps of the Inflammatory Response

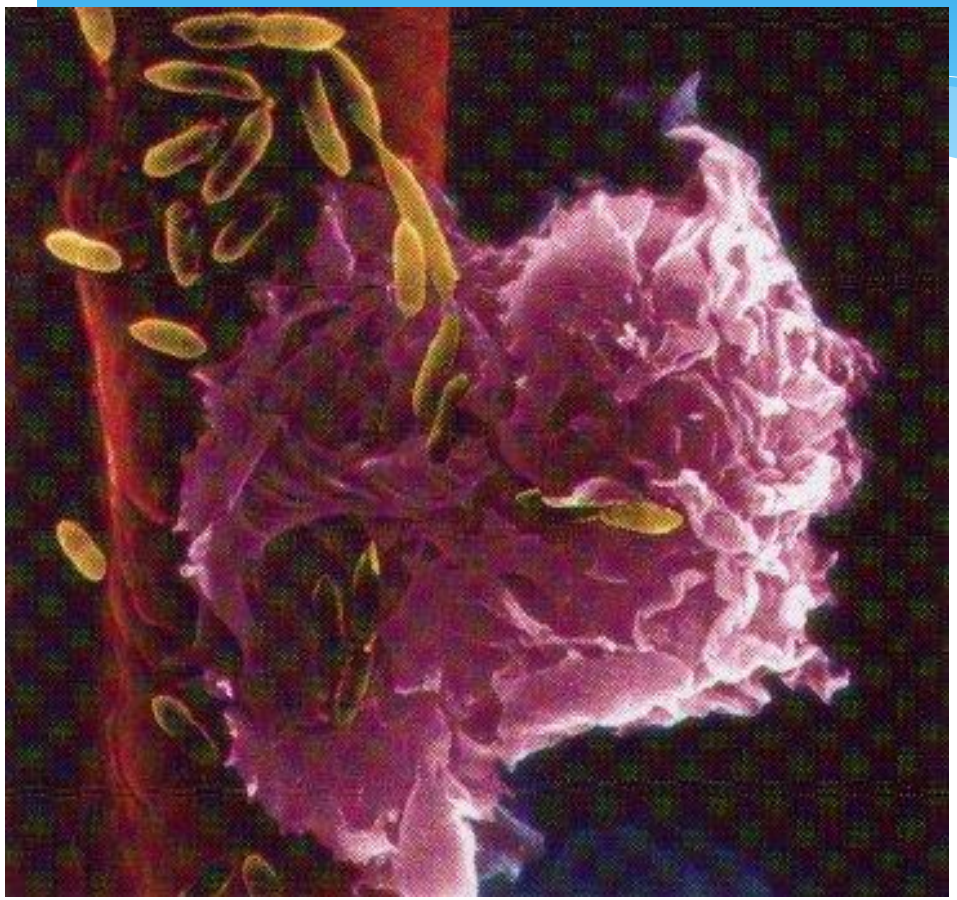
The inflammatory response is a body's second line of defense against invasion by pathogens. Why is it important that clotting factors from the circulatory system have access to the injured area?



Inflammatory Response Continued

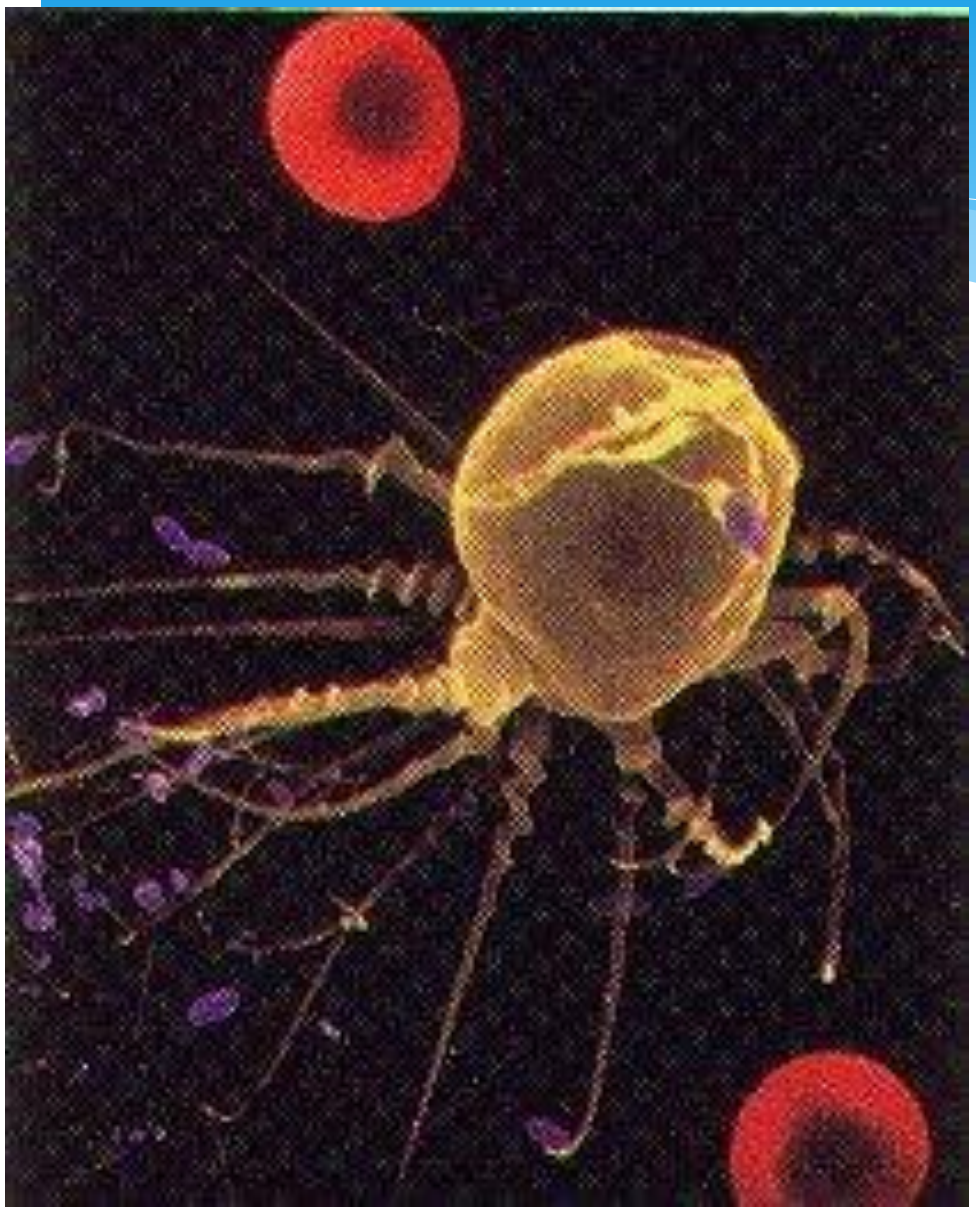
* THE INFLAMMATORY RESPONSE IS A NONSPECIFIC DEFENSE REACTION OF THE BODY TO TISSUE DAMAGE.
* Histamine increases blood flow to the injured area and increases the permeability of the surrounding capillaries, as a result, Fluid and White Blood Cells (WBC) leak from blood vessels into nearby tissue.
* Pathogens are attacked by **PHAGOCYTES**, which are white blood cells that engulf & destroy pathogens

Inflammatory Response Continued



* The most common Phagocyte, 50 to 70 percent of the White Blood Cells in the body, is the **NEUTROPHIL**.
* Neutrophils circulate freely through blood vessels, and they can squeeze between cells in the walls of a capillary to reach the site of infection. They then engulf and destroy any pathogens they encounter

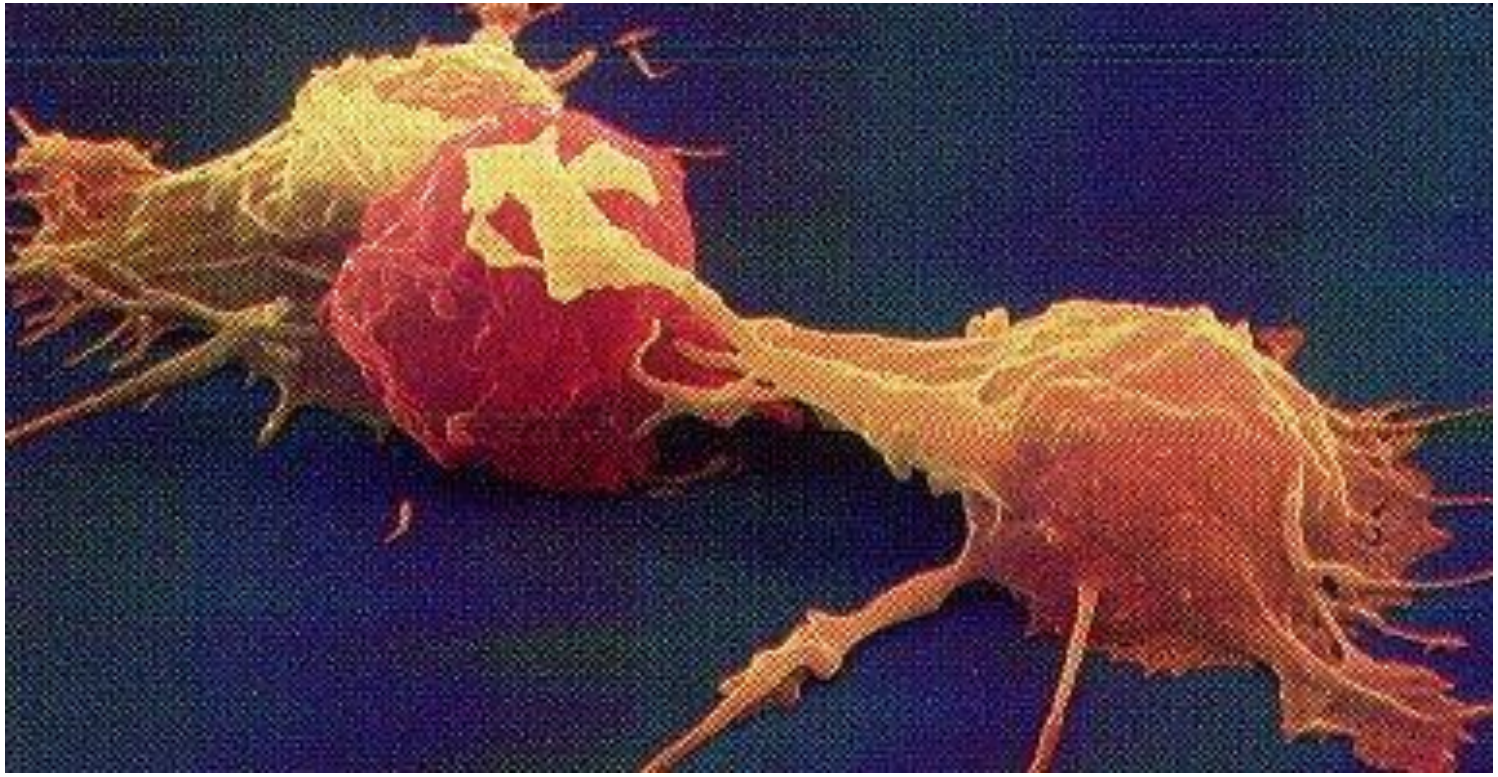
Inflammatory Response Continued



* Another type of Phagocyte (also a White Blood Cell) is the **MACROPHAGE**; they consume and destroy any pathogens they encounter, they also rid the body of worn out cells and cellular debris.
* Some Macrophages are stationed in the tissues of the body, awaiting pathogens, while others move through the tissues and seek out pathogens.

Inflammatory Response Continued

* **NATURAL KILLER CELLS** are large white blood cells that, unlike phagocytes, attack cells that have been infected by pathogens, Not the Pathogen Themselves. They are particularly effective in killing Cancer Cells and Cells Infected with Viruses.
* A Natural Killer Cell punctures the cell membrane of its target cell, allowing water to rush into the cell, causing the cell to burst



But if all that is not enough …

* If a pathogen is able to get past the body's nonspecific defenses, the immune system reacts with a series of specific defenses that attack the disease causing agent.

* This is called the **IMMUNE RESPONSE**

* A substance that triggers the specific defenses of the immune system is known as an **antigen**.

* An **antigen** is a substance that a macrophage (wbc) identifies as not belonging to the body.

The Immune Response

* The Immune Response involves several organs, as well as White Blood Cells in the Blood and Lymph. These include the BONE MARROW, THYMUS, LYMPH NODES, TONSILS, ADENOIDS, AND SPLEEN.
* Each organ of the immune system plays a different role in defending the body against pathogens.
* **Bone Marrow** manufactures the billions of WBC needed by the body every day. Some newly produced WBC remain in the bone marrow to Mature and *Specialize*, while others travel to the **Thymus** to Mature.
* **Lymph Nodes** Filter Pathogens from the Lymph and expose them to White Blood Cells
* The **Spleen**, a fist-sized organ located behind the stomach, Filters Pathogens from the Blood. It is stocked with WBC that respond to the trapped pathogens.

Self/Non-self Distinction

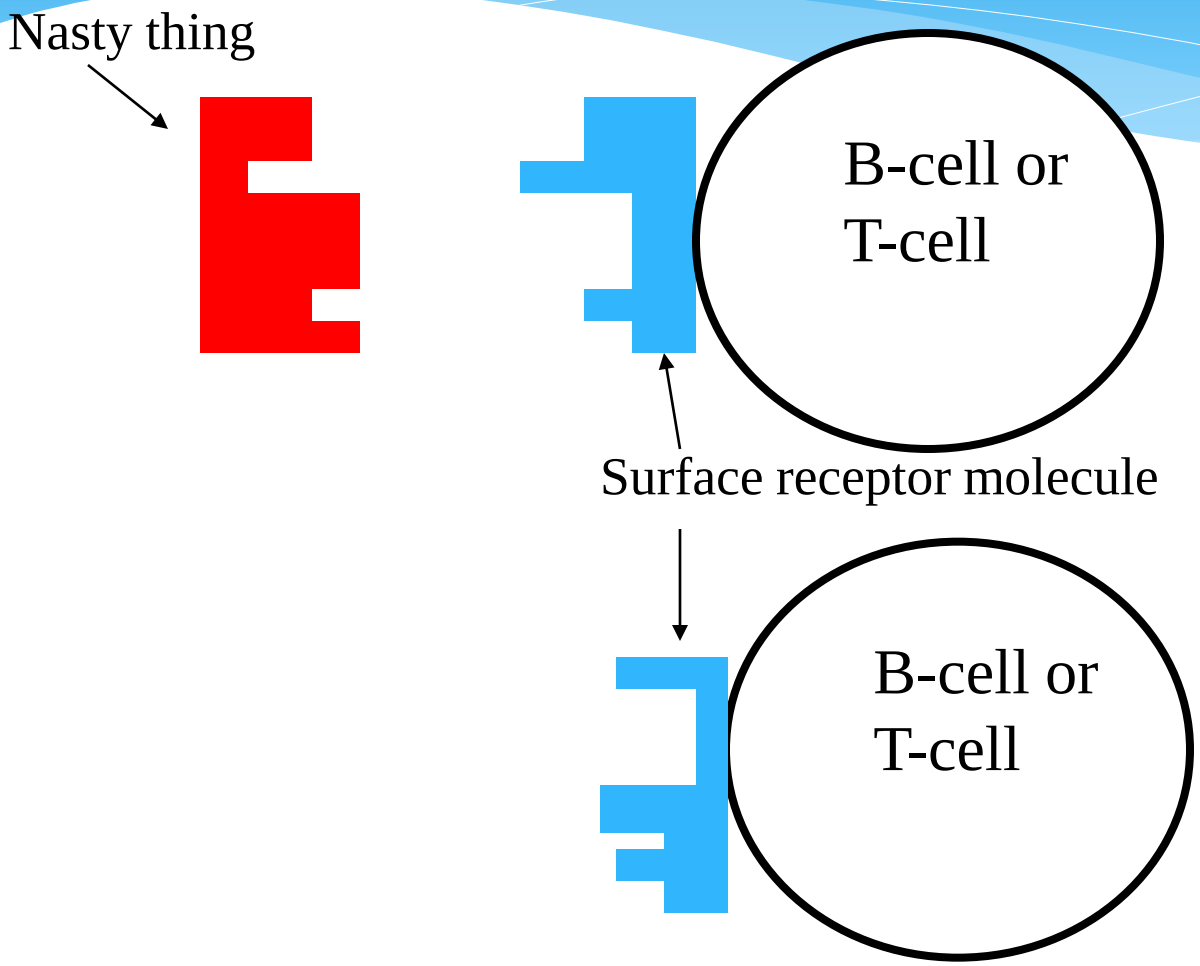
- In order to Respond to Pathogens, but to avoid responding to and destroying cells from its own body, Lymphocytes

- Must be able to recognize a pathogen as a foreign invader and distinguish it from cells of the body.

The Immune Response: The last line of defence

* The general idea is this:
* Something has got through the first lines of defence, and entered the body in force.
* If the body has been invaded by this particular nasty thing before, then special Lymphocytes called **B-Cells** and **T-Cells** are able to recognise these **specific** pathogens, and overwhelm them (thanks to the `immune system memory')
* If this is a new invasion, then the **B-Cells** will **learn how to fight this invader**. (and then

Specific Antigen Recognition



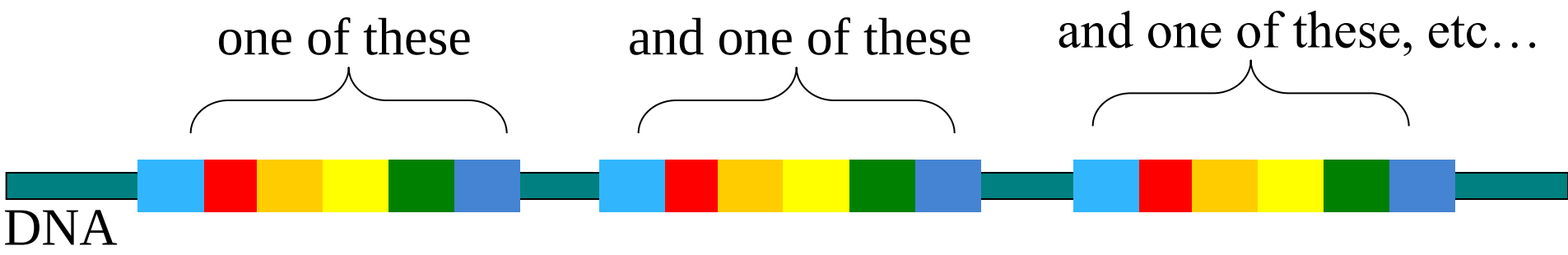
This lymphocyte recognises the red pathogen

This one doesn't

Generating Variety

The receptor molecule is a protein, encoded by a highly variable gene. There is essentially a **combinatorial library of parts** in the genome:

Each B or T cell makes up its receptor by choosing:



The result is that an enormous variety of possible surface receptors could be chosen. This is effectively a method for generating random receptors. Since recognition need not be exact, it is possible in practice for a B or T cell to generate a receptor which matches *any* given antigen.

Generating variety II

In addition, B-Cells (but not so much T cells) also undergo *somatic hypermutation*. Somatic just means in the body, during one's lifetime. Hyper just means `a lot'. In a nutshell:

1. A B-cell recognises an antigen
2. A complex chain of events then leads to this B-cell dividing, creating daughters who produce the same receptor.
3. But these daughter cells may have mutations in their library.
4. Some of the daughters may recognise the antigen even better.
5. Back to 1.

Summary

* A pathogen comes along:
* If it gets through the barriers (skin, etc), nonspecific lymphocytes kill it, as part of the `inflammation' response in reaction to injury.
* If it gets past that (I.e. there's so much of it, it gets into the bloodstream anyway), then the Immune Response comes into play, as follows:
* **If we've seen this one before**, there are antibodies in the blood (secreted by memory cells); these antibodies disable and/or tag the invader. The tagging attracts killer cells to make sure it is destroyed.
* **If we haven't seen this before**, B-cells and T-cells are floating around with a great variety of surface receptors. One of these will at least recognise it a bit. Clonal expansion then happens, and with gene variability and somatic hypermutation we eventually get some B or T cells which are capable of recognising it. The associated antobodies then disable and tag the invaders.

Some Interesting Related Points

- Some ailments are `beyond' the immune system, since they either directly disable it, or work faster than it, or both (or something else).
- **Cancer**: the problem here is uncontrolled growth and multiplication of normal cells. If caused by any specific pathogen (controversial) then it could be that just a tiny amount needs to go unattacked for a short time, and the problem starts.
- **Leukaemia**: a cancer of the bone marrow – it (and its treatment) throw an enormous spanner into the heart of B-cell production.
- **Vaccination**: this is where we deliberately provoke an immune response to small levels of a pathogen (or something similar to it), so that our IS i ready if there is a real infection.
- **AIDS**: some T-cells (called Helper T Cells) are the main players in most of the things we have looked at. E.g. via special messenger molecules, t activate the clonal expansion of B cells! The HIV virus directly attacks
- Helper T-cells, essentially disabling the immune system.