Introduction to the Immune System

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Under Attack from Microbes.

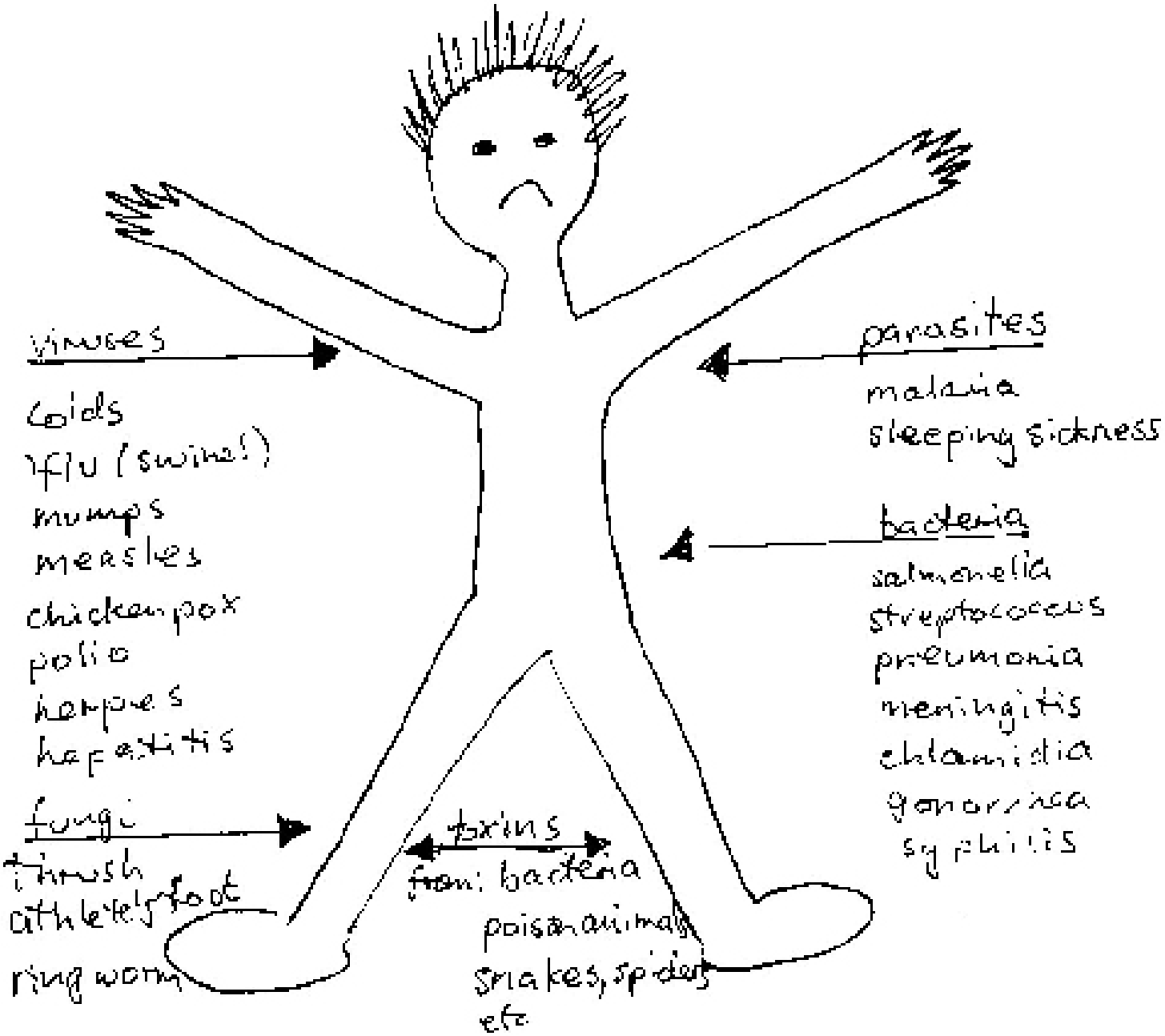
What are microbes and what do they do to us?
Our defence is the Immune System - always on the alert - all out war.

What is the Immune System and where is it?
White blood cells are the immune cells. There are several different kinds - all with a different job to do throughout the body.

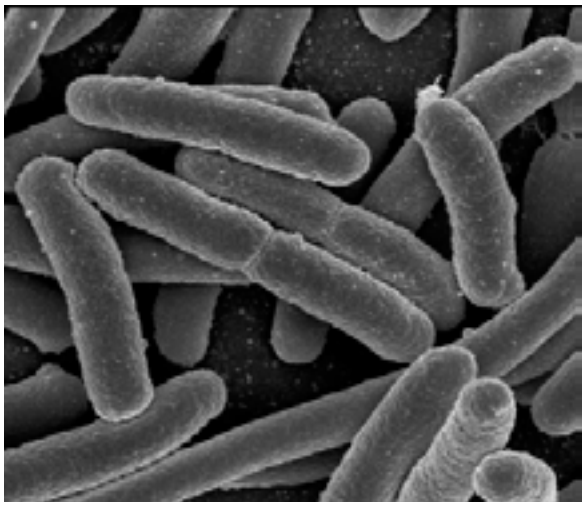
How does the Immune System work?
How do white cells act? - two different kinds:
One lot engulf/surround and eat up. The others kill with antibodies.

Defending ourselves against infection

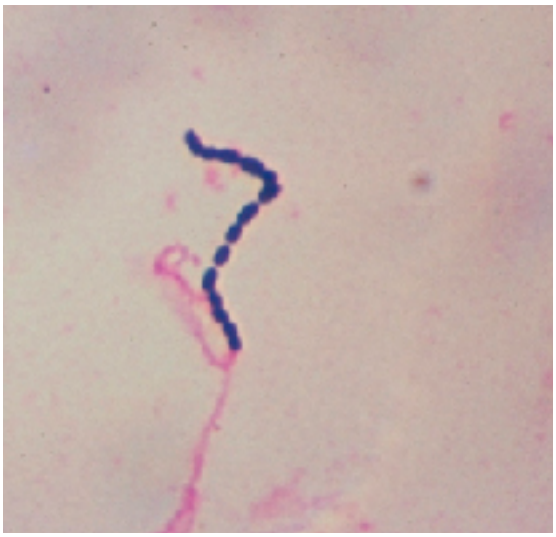
HELP I'M UNDER ATTACK!



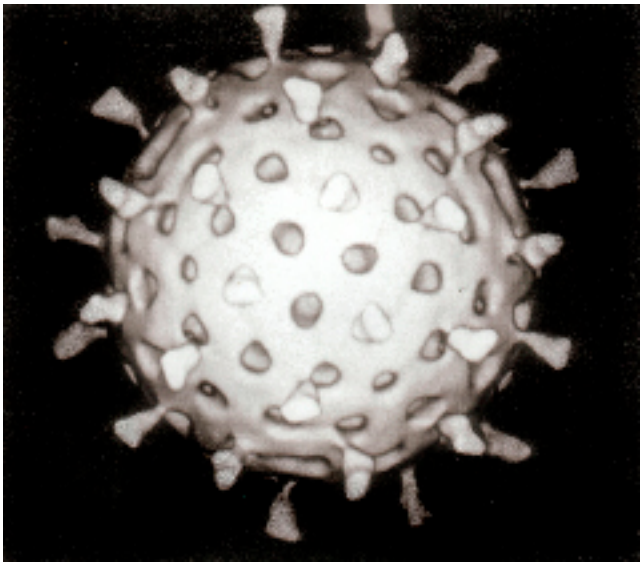
Every day we are under constant attack from millions of all sorts of invisible 'germs' or 'bugs' (bacteria, viruses, parasites and fungi), tiny, single cell organisms; some of which can do us a lot of harm. They get into wounded skin; we breathe them in; we eat them.
Mostly the immune system deals with them without us even knowing. The are killed and eliminated with great efficiency. Sometimes, however, they breach the immune system and we get sick-BUT still our infected wounds heal and we recover from illnesses-that is because the immune system fights on. Still people do sometimes die from infectious illnesses.



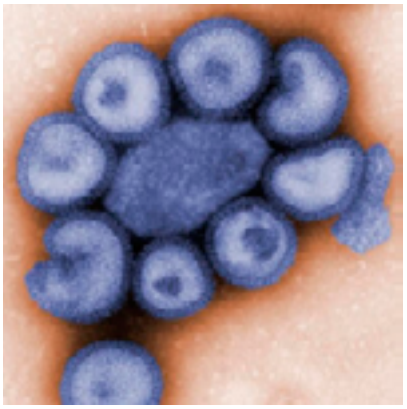
E-Coli – bacterium-causes sickness and diaorrhea



Streptococcus (bacterium) causes sore throat



Rotavirus causes gastroenteritis
The swine flu virus
(This one has antibodies attached to its surface)



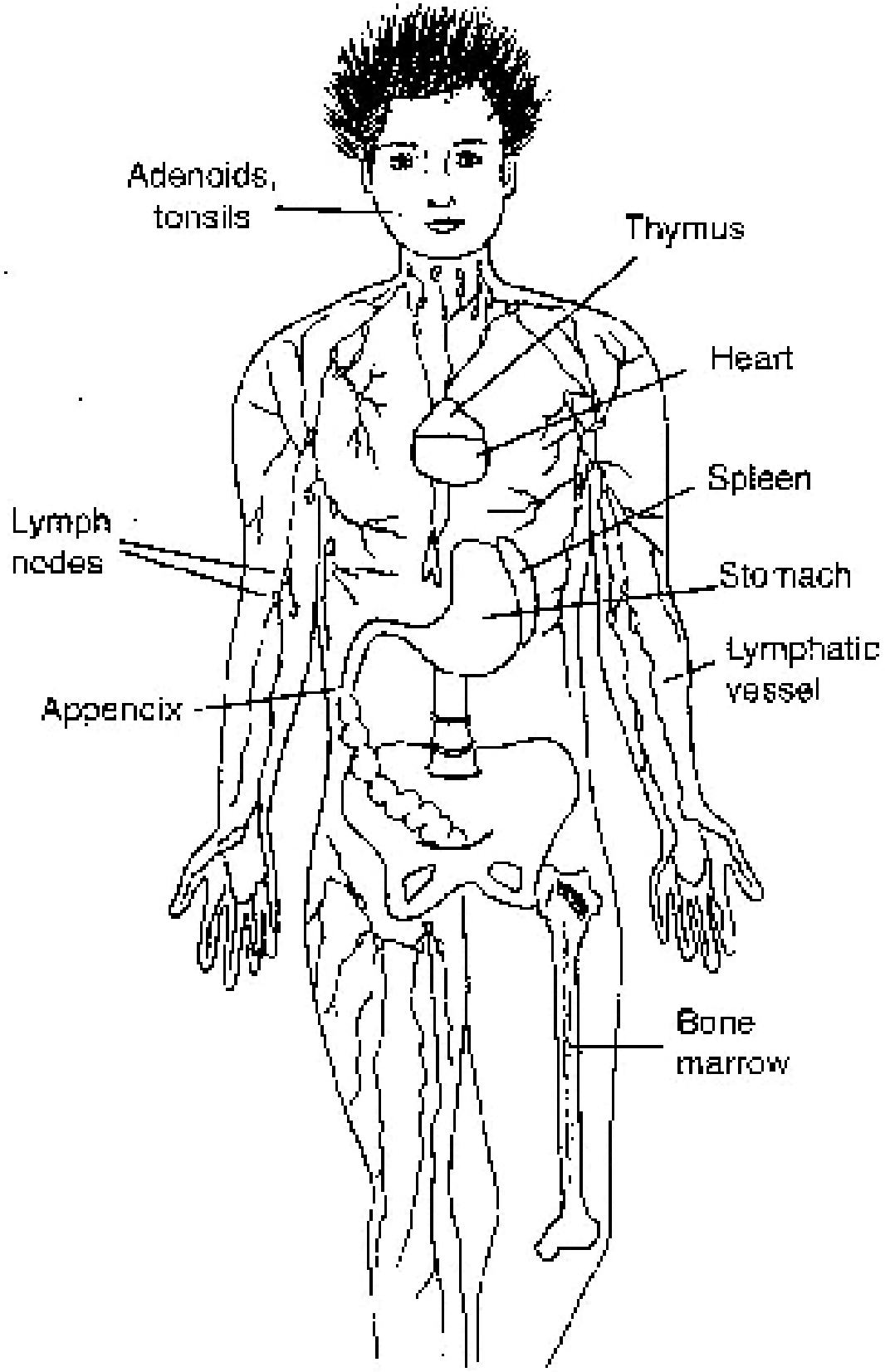
Swine flu virus

Viruses are about one hundredth the size of bacteria: 20 – 400 nm (1nm = 10-9 m)

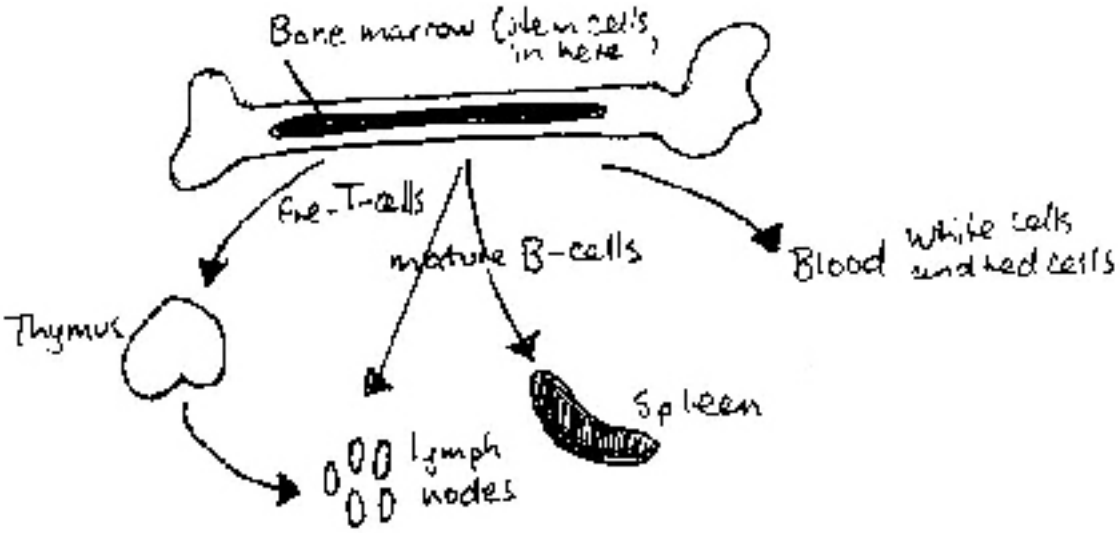
See below for more information to help you imagine the size of these cells and particles

IMMUNE SYSTEM TO THE RESCUE

What is the Immune System and Where is it?
The immune system is very big and is distributed throughout the body.



All cells which work for the Immune System become distributed in all the parts shown. They are transported to the various parts in the blood and move around in the lymphatic system.
However, they all start their lives as simple undifferentiated 'stem' cells, and are all produced in the bone marrow. They then move into the circulation and develop into mature specialized cells in the blood or in parts of the immune system. Some are developed to maturity in the bone marrow.



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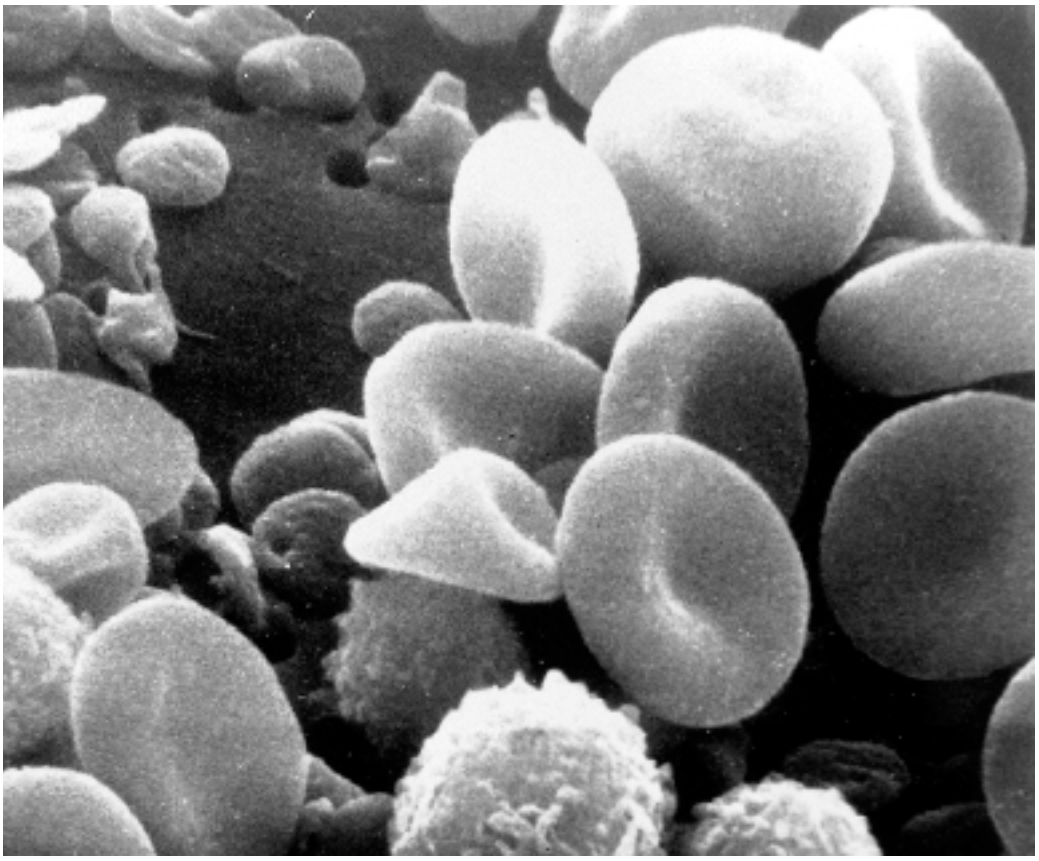
All the immune system cells are white blood cells (sometimes called leucocytes). There are several different leucocytes, all with a different role to play in the fight against infection.

This picture is a scanning electron microscope image of normal circulating human blood. You can see white cells -the round ones with bumpy surfaces, which are immune cells and red cells the doughnut shaped ones. These carry oxygen, but are NOT part of the immune system.



Now here is some information all the different kinds of white blood cells, before we see exactly how they act.

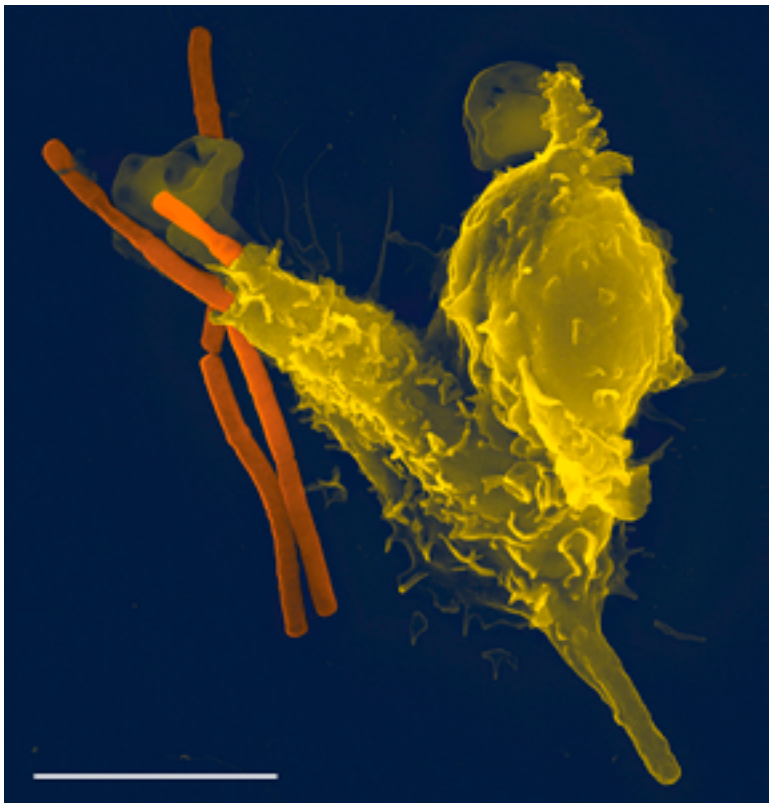
HOW DOES THE IMMUNE SYSTEM WORK?

The specialized cells in all parts of the immune system are the soldiers which fight for us. They are always on the alert, ready move in and attack and kill the invaders wherever and whenever they are needed. They act either by engulfing the microbes and 'eating them up' with special enzymes, or by making special protein molecules called 'antibodies' which recognize the microbes as the enemy. They attach themselves to the microbe and break its cell wall, which kills it.

FIRST LINE OF ATTACK

The first line of attack is carried out by the 'innate' part of the immune system (the part we are born with). It consists of cells which act by engulfing the microbes. They are sometimes collectively called 'phagocytes' because they act by phagocytosis. These cells are always there and always alert and ready to attack any microbe. We say their response is non-specific. The neutrophils are the most abundant of these and are very effective in attacking bacteria and fungi. Neutrophils die when they have killed off a few bugs and form the 'pus' in infected wounds. Macrophages, much larger phagocytes, formed from monocytes, come along and clear up all the debris, so that the wound is eventually healed. Macrophages live much longer than neutrophils. They also help with the next line of attack - i.e. the production of antibodies by B-lymphocytes or B-cells.

Here is a picture of a neutrophil beginning to eat up an anthrax bacterium, which causes a very nasty disease.



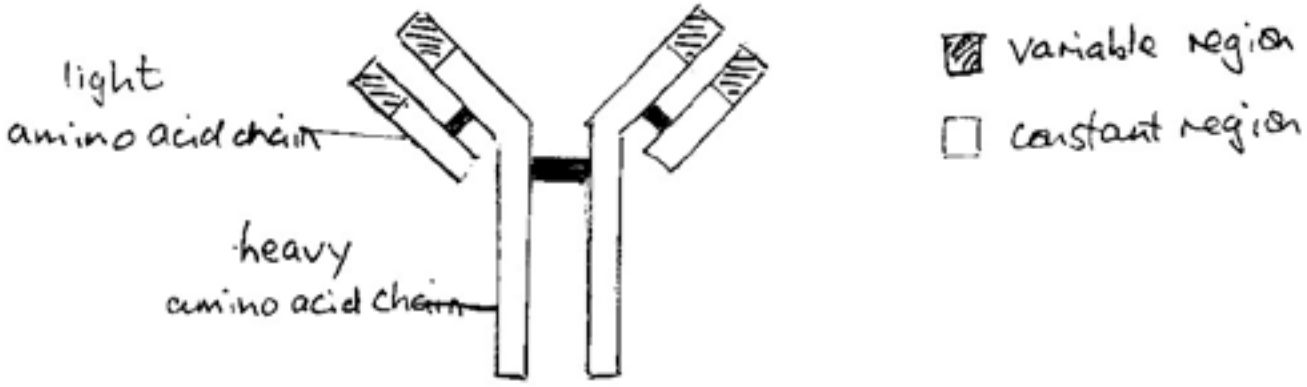
A scanning electron microscope image of a single neutrophil (yellow), engulfing anthrax bacteria (orange). The process is called 'phagocytosis'. The bar represents 5 micrometres (μm). (Published in Wikipedia)

SECOND LINE OF ATTACK

It takes a few days for the second line of attack to begin in earnest. It is carried out by the other kinds of white blood cells called 'lymphocytes'. Its aim is to produce antibodies aimed against the invading microbes to kill them. The antibodies are made by the B-lymphocytes, B-cells for short, with the help of a special kind of lymphocyte called helper T-cells. The B-cells adapt their attack specifically to the particular microbe. This is why the second line of attack is called the 'adaptive' part of the immune system.

Two other kinds of T-cell have a special job that is to kill cells that are infected by viruses. The 'killer T-cell' adapts to kill virus infected cells and the 'natural killer cell' NK-cell is part of the innate immune system and kills viral infected cells without the need to adapt.

This is how an antibody molecule looks

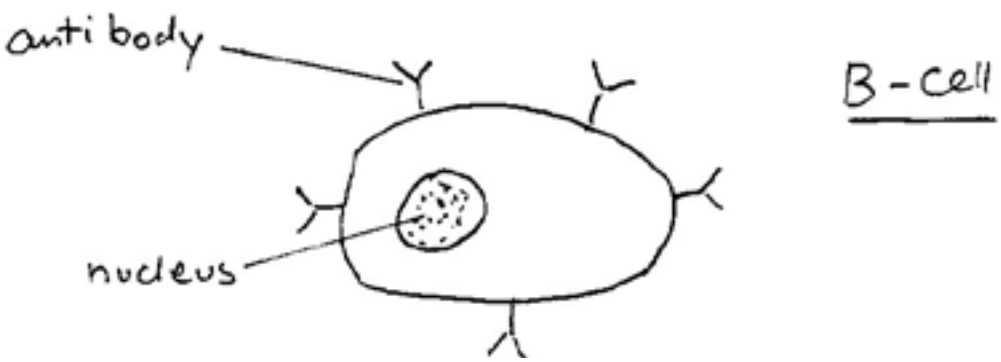


The variable region, which differs from one antibody to the next, allows an antibody to recognize its matching 'antigen' for example, a molecule on the surface of a microbe

The mechanism by which B-cells (with help from the helper T-cells) produce antibodies is extremely complex, but it is well worth thinking about as it a very important part of the immune response to foreign invasion and provides an immunological memory, which means we can only have certain illnesses once. Not only that, but it enables us to be protected by immunization to prevent us having the illnesses at all.

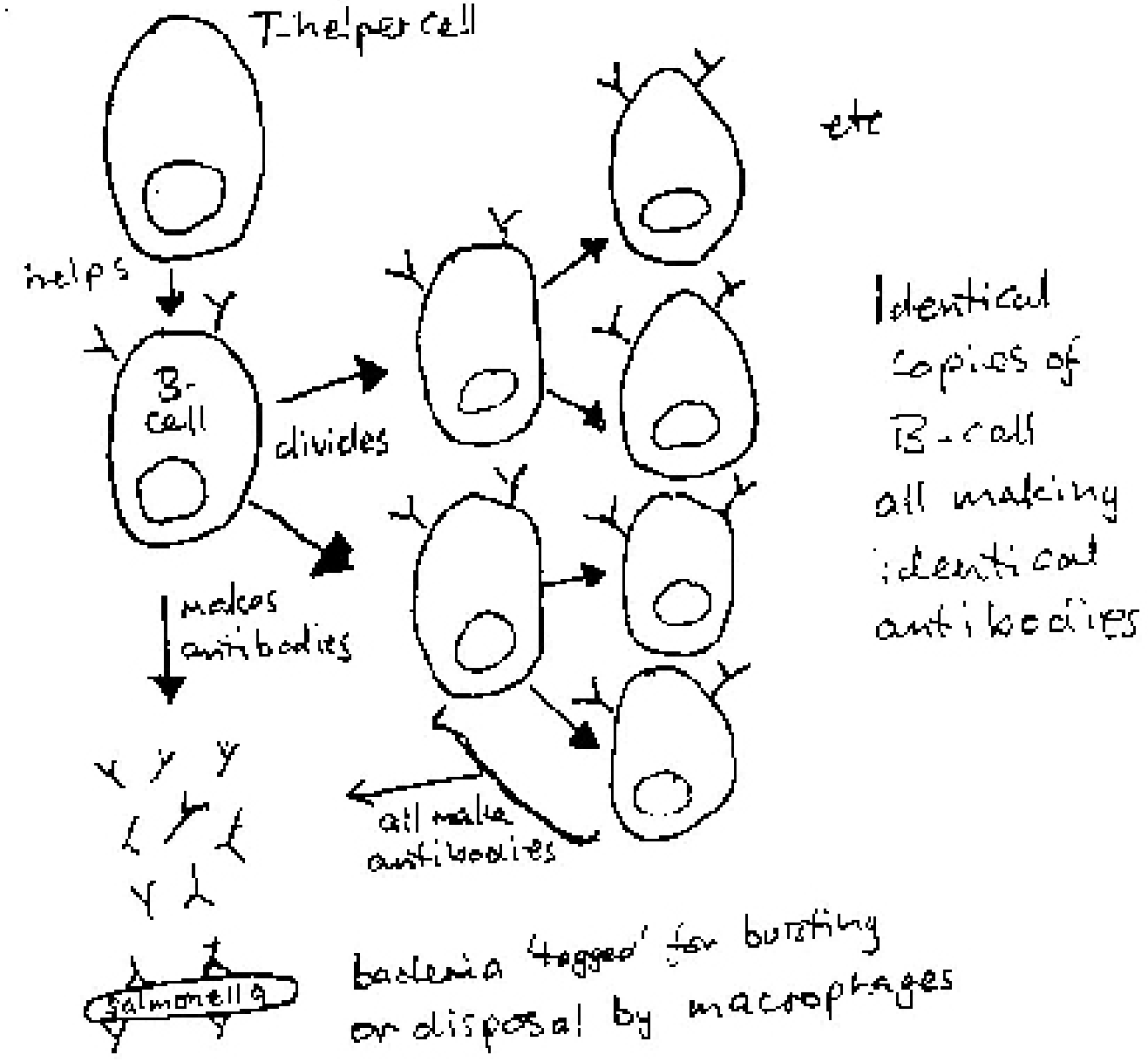
Some lymphocytes from the blood are delivered to the thymus, where they are converted to T-cells (T for Thymus).

Each B-cell is born and raised in the bone marrow. It leaves the bone marrow as a mature cell with a 'random' antibody on its surface. It says 'This antibody I am prepared to produce in bulk should it be needed for defense.' The B-cells head out for the spleen or a lymph node to take up residence.



If a B-cell does NOT encounter a molecule on the surface of a microbe (an antigen), which its antibody recognizes, within about a week, it dies. However, literally billions of B-cells are produced in the bone marrow each day - all with slightly different surface antibodies. Many B-cells are wasted in this way.

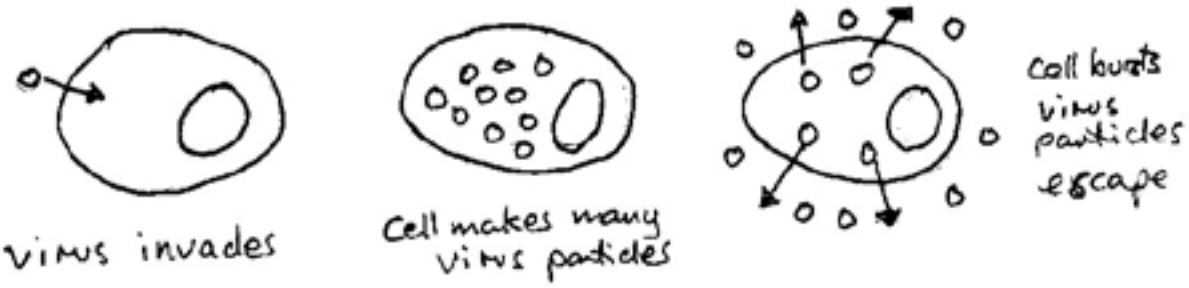
BUT some are very useful because if a B-cell runs into an antigen on the surface of a microbe which its particular antibody recognizes, it becomes activated . With the help of a 'helper'T-cell it will start to divide and produce 'offspring' – two exact copies of itself. These copies divide and so on. In the end many thousand B-cells all with same antibody are produced. All these cells then manufacture many copies of their specific antibody which attach themselves to the microbe antigen. This breaks the microbe cell wall and kills it. With so many B-cells specially adapted to kill a particular invading microbe, illness can be avoided or at least we can recover. The battle is hard, as the microbes reproduces very quickly. That's why so many B-cell and their antibodies are needed.



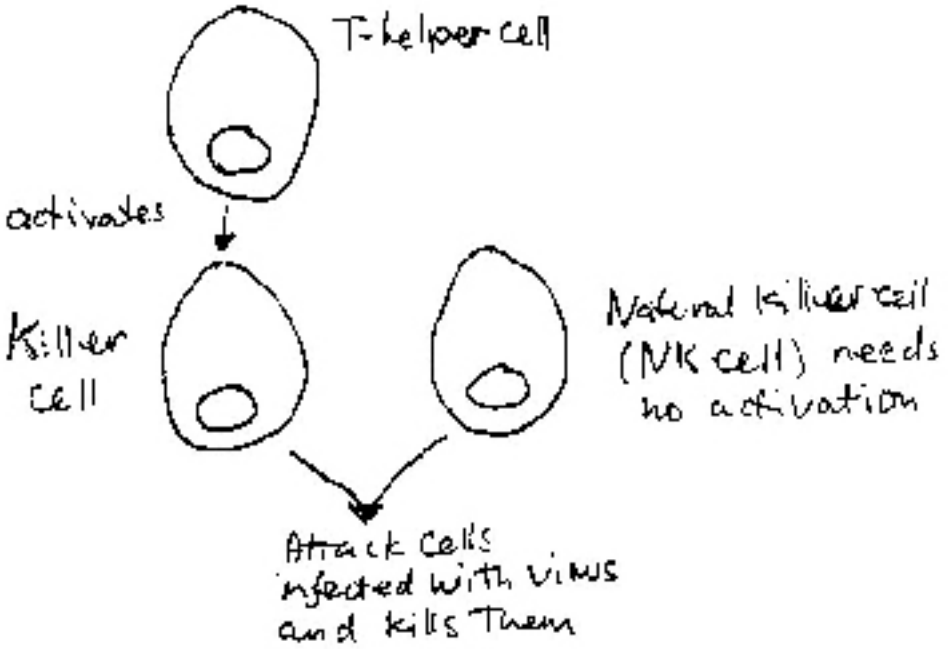
THE SPECIAL CASE OF VIRUSES

Bacteria cells divide in the same way as animal cells, producing two identical daughter cells, which then divide etc (As described for B-cells above.)

But Viruses are unusual as they cannot reproduce in this way. They are unlike other living things as they have no nucleus and no mechanism to reproduce themselves. They are simply very small particles with just DNA, protein and a little lipid. They use the special machinery of the cells they enter to produce many copies of themselves. Eventually the cell bursts and the virus particles are released, ready to invade other cells.



Viruses are attacked by phagocytic cells and antibodies in the same way that bacteria are, but the immune system has extra ways for dealing with them.
(i) The immune cells produce a special chemical called 'interferon' which can stop the virus particles being produced.
(ii) The killer T-cells can detect cells which have been infected by a virus, because they 'look different'. The killer T-cells then become activated and kill the infected cells, so as to stop virus production. Also as soon as the virus particles are released they can be neutralized by antibodies, which prevent them from being reproduced.
(iii) Natural killer T-cells (part of the innate immune system, because they do not need to be activated) spot virally infected cells without having seen one before-and kill them.



IMMUNOLOGICAL MEMORY

The story does not end here. Many of the B-cells live a very long time and can be useful again. If the same microbe dares to attack again, there will be many of them lying in wait ready to replicate (divide) and produce antibodies to it very quickly. This time the microbe doesn't stand a chance, its second attack ends in defeat, before the illness it causes can take over. This is what we call immunological memory. We become 'immune' to the disease after the first attack.

HOW COMPLICATED IS THAT?

As you have seen, the immune system is vast and works in a very complicated manner. The body has had to evolve all these kinds of crafty ways to overcome the constant attack from very many nasty bugs which want to live in and feed off our bodies. The body is a warm cosy place with lots of nutrients-ideal for them to multiply and take us over. They too have developed crafty ways of living off us. Our immune system has to out-wit them for us to survive. It also distinguishes between 'foreign' molecules and its own so that it doesn't start attacking itself – a very vital function!

GERMS AND THE IMMUNE SYSTEM: GETTING A SENSE OF SCALE

To get a grip on just how small the world we are describing really is, we have to use our imaginations...

If you can picture the flat end of a pin, that is about 1mm across. This is a measure we can all relate to. To us this seems small, but when we are talking about germs and the workings of the immune system, we have to think really really small!

- If we placed some bacteria-eating white blood cells ('macrophages') end-to-end across the flat end of a pin we would have room for 50 of them in a line.
- If we did the same for a typical bacterium (called E. coli) we would have room for 500.
- If we did the same again for a typical virus (such as the ones that give us 'flu) we would have room for 10,000 in a line!
- ...and if we did the same yet again for an antibody molecule (an important part of immune defence) we would find room for perhaps 100,000 in a line, that stretched for just 1 millimetre!

Looking at things another way...

If we made our antibody molecule 1cm long (and hence visible)...

...our virus would be 10cm long

...our bacterium would be 200cm (2m) long

...our macrophage would be 20m long!

...and an average-sized human being would be about 1800km (over 1000 miles) tall!!! (This is above twice the length of the island of Great Britain!)

As you can see, we have to really change our perspective to understand how small these things are!

WANT TO KNOW MORE?

This is, of course not the whole story, but hopefully gives you a good idea as to how your body fights infection and infectious diseases. If you find immunology fascinating and want to know more, here are some topics look at:

Vaccination; Allergy; Autoimmune diseases; Immune system in cancer; Immunodeficiency; Organ transplant.

You can find much of the information on the following websites

http://www.howstuffworks.com/immune-system.htm
http://en.wikipedia.org/wiki/Immune_system
http://en.wikipedia.org/wiki/White_blood_cell
http://www.niaid.nih.gov/Publications/immune/the_immune_system.pdf

IDEA FOR ACTIVITY

A battle of Microbes versus Immune cells

Some pupils can be assigned to various bugs (take some bacteria, some viruses) and talk about their size; how and where they get into the human body; how quickly they divide; how many of them in their 'army'; how they use our nutrients to grow and reproduce in our body environment; in the case of viruses how they use the 'machinery' in our cells for protein synthesis to reproduce themselves; how they give us nasty symptoms; how bacteria produce nasty toxic molecules which damage us and make us feel ill.

Versus other pupils who can be assigned various immune cells and talk about how they are produced, what size they are compared to the microbes; what they look like; where they are lying in wait for an attack by microbes; how they move to the site of attack; how they kill the attackers; if they are B-cells how they produce antibodies as part of their counter attack; how they cooperate with other immune cells to enhance their attack (like air support of ground troops); how they hang around in case of further attack by the same bug.